63. *The Resolution of n-Propylpropenylcarbinol. The Refractivity and Optical Rotatory Dispersion of some Substituted Allyl Alcohols.*

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The resolution of *n*-propylpropenylcarbinol (γ -methyl- α -propylallyl alcohol) into its optically active forms, and the properties of some derivatives of the latter, are described.

Comparison of its molecular refractivity and optical rotatory dispersion is made with those of four other optically active substituted allyl alcohols. It is considered probable that these alcohols have the *trans*-configuration. Evidence is adduced that, although the optical rotatory dispersion of the purely alkyl-substituted allyl alcohols is complex, that of the phenyl-substituted allyl alcohols is simple, and it is suggested that a large proportion of the rotatory power of the latter group of compounds is due to induced dissymmetry of the phenyl radical.

SEVERAL investigations, dealing with the chemical and optical properties of optically active substituted allyl alcohols, which have arisen from the peculiar behaviour of $\alpha\gamma$ -dimethylallyl alcohol (I) (Hills, Kenyon, and Phillips, J., 1936, 576) have recently appeared [γ -phenyl- α -methylallyl alcohol (II), Kenyon, Partridge, and Phillips, *ibid.*, p. 85; α -phenyl- γ -methylallyl alcohol (III), *idem*, J., 1937, 207; $\alpha\gamma\gamma$ -trimethylallyl alcohol (IV), Duveen and Kenyon, J., 1936, 1451] and in furtherance of these studies optically active *n*-propylpropenylcarbinol (γ -methyl- α -*n*-propylallyl alcohol) (V) has now been examined.

dl-n-Propylpropenylcarbinol has been described by Reif (*Ber.*, 1906, 39, 1603) and the refractivity of a pure specimen was determined by Auwers and Westermann (*Ber.*, 1921,

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54, 2993). A partial resolution of the alcohol by the fractional crystallisation of the brucine salt of its hydrogen phthalic ester was effected by Levene and Marker (*J. Biol. Chem.*, 1934, **106**, 173), but the maximum rotatory power obtained was only some 8% of that now reported.

A satisfactory resolution by means of the brucine salt could not be effected, although several procedures were tried. Complete resolution was eventually obtained by fractional crystallisation from dry acetone of the strychnine salt of the hydrogen phthalic ester, followed by fractional crystallisation of the *d* + *dl*- and *l* + *dl*-esters obtained by decomposition of the less soluble and the more soluble fractions, respectively, of the strychnine salt. The *d*- and *l*-hydrogen phthalic esters, when hydrolysed with sodium hydroxide, yielded the corresponding optically active alcohols, the rotatory powers of which under different experimental conditions are recorded in Tables I, II, and III. The acetic and benzoic esters and the methyl ether of the *d**-alcohol have been prepared and their rotatory powers are recorded in Tables V—VII.

As experiments are at present in progress on the replacement reactions of this alcohol and its esters whereby a rearrangement to the isomeric α -methyl- γ -*n*-propylallyl alcohol (CHPr^{*}:CH·CHMe·OH) and its esters may occur, it was considered expedient to establish the homogeneity of the optically active alcohol and esters, since rearrangement may occur both during the production of the intermediate *dl*-hydrogen phthalic ester (Kenyon, Partridge, and Phillips, J., 1937, 207) and also during the esterification of the alcohol obtained therefrom by hydrolysis. Accordingly these substances were catalytically reduced; the optically active forms then yielded optically inactive di-*n*-propylcarbinol and its esters respectively, indicating the original substances to be free from structural isomerides.

Optical Rotatory Dispersion of n-Propylpropenylcarbinol and its Derivatives.—The optical rotatory dispersion of *n*-propylpropenylcarbinol in the homogeneous state at 16° (Table I) may be represented, within the limits of experimental error, by the equation

$$\alpha = 1.027/(\lambda^2 - 0.0723); \lambda_0 = 2690 \text{ \AA.}$$

The simplicity can only be apparent, for the rotatory dispersions of solutions of the alcohol show obvious complexity when $1/\alpha$ is plotted against λ^2 and the solution in benzene shows a reversal of sign of rotation (Table II).

TABLE I.

Rotatory Powers of (+)n-Propylpropenylcarbinol at 16° (1, 0.5).

λ .	$\alpha_{\text{obs.}}$	$\alpha_{\text{calc.}}$	$\alpha_{\text{obs.}} - \alpha_{\text{calc.}}$	λ .	$\alpha_{\text{obs.}}$	$\alpha_{\text{calc.}}$	$\alpha_{\text{obs.}} - \alpha_{\text{calc.}}$
6438	+2.98°	+3.00°	-0.02°	5086	+5.48°	+5.51°	-0.03°
5893	3.68	3.73	-0.05	4800	6.40	6.49	-0.09
5780	3.96	3.90	+0.06	4678	6.82	7.00	-0.18
5461	4.58	4.54	+0.04	4358	8.76	8.73	+0.03

TABLE II.

Specific Rotatory Powers of (+)n-Propylpropenylcarbinol in Various Solvents at Room Temperature (1, 2.0).

Solvent.	<i>t</i> .	<i>c</i> .	$[\alpha]_{6438}$.	$[\alpha]_{5893}$.	$[\alpha]_{5461}$.	$[\alpha]_{4358}$.
Benzene	19°	4.830	-1.86°	-0.21°	+0.72°	+2.69°
Chloroform	20	5.245	-7.53	-7.72	-8.30	-13.25
Carbon disulphide	21	5.935	+3.37	+6.24	+8.26	+17.6
Pyridine	22	4.615	+11.5	+15.8	+19.9	+39.4

Furthermore, the magnitude of the rotatory power of the alcohol in the homogeneous state is much reduced with increase of temperature (Table III) and the dispersion ratio $\alpha_{4358}/\alpha_{5461}$ increases from 1.92 at 16° to 2.09 at 65° and to 2.24 at 95°, showing the sensitivity to temperature change (and solvent influence) associated with complex rotatory dispersion.

* In the introductory part of this communication rotatory powers are given for derivatives of the *d*(+)-alcohol, although in some cases the experimental data were determined by using derivatives of opposite configuration.

No evidence of mutarotation was observed and the alcohol retained its original rotatory power after being kept at 34–39° for 15 days.

TABLE III.

Rotatory Power of (+)n-Propylpropenylcarbinol at Different Temperatures (l, 0.5).

<i>t.</i>	α_{5893}	α_{5461}	α_{4358}	<i>t.</i>	α_{5893}	α_{5461}	α_{4358}
16°	+3.68°	+4.58°	+8.76°	65°	+1.88°	+2.35°	+4.90°
26	3.37	4.12	8.05	70	1.69	2.13	4.49
36.5	2.92	3.65	7.23	95	1.01	1.32	2.95
45.5	2.56	3.16	6.35	5 *	4.22	5.13	9.69
54	2.23	2.83	5.66				

* After cooling.

The rotatory powers of (+)n-propylpropenylcarbinyl hydrogen phthalate in various solvents (Table IV) indicate pronounced complex rotatory dispersion when $1/\alpha$ is plotted against λ^2 ; the corresponding benzoic ester in the homogeneous state (Table V) shows a slightly complex rotatory dispersion.

TABLE IV.

Specific Rotatory Powers of (+)n-Propylpropenylcarbinyl Hydrogen Phthalate in Various Solvents at Room Temperature (l, 2.0).

Solvent.	<i>t.</i>	<i>c.</i>	$[\alpha]_{6438}$	$[\alpha]_{5893}$	$[\alpha]_{5780}$	$[\alpha]_{5461}$	$[\alpha]_{4358}$
Alcohol	16°	4.550	+13.3°	+17.05°	—	+22.85°	+46.4°
Benzene	20	4.275	—	+ 6.67	+ 8.31°	+ 9.59	+23.0
Chloroform	19	4.815	—	+ 4.26	+ 5.19	+ 6.33	+17.4
Carbon disulphide	20	4.38	—	-14.7	-15.2	-16.8	-32.0

TABLE V.

Rotatory Power of (+)n-Propylpropenylcarbinyl Benzoate (l, 0.5; t, 20°).

λ	6438	5893	5780	5461	5086	4800	4678	4358
$\alpha_{\text{obs.}}$	+6.47°	+8.50°	+9.19°	+11.16°	+14.00°	+17.39°	+19.05°	+25.76°

The rotatory dispersion of (–)n-propylpropenylcarbinyl acetate in the homogeneous state (Table VI) can, however, be accurately represented by the equation

$$\alpha = -6.14/(\lambda^2 - 0.0452); \lambda_0 = 2120 \text{ A.}$$

It appears, therefore, that under these conditions the rotatory power is predominately due to the induced dissymmetry of the $\text{—C} \begin{smallmatrix} \text{O} \\ \diagup \\ \text{O—} \end{smallmatrix}$ radical, which has an absorption band at 2100 A. (Lowry, "Optical Rotatory Power," 1935, p. 266).

TABLE VI.

Rotatory Powers of (–)n-Propylpropenylcarbinyl Acetate in the Homogeneous State at 21° (l, 0.5).

λ	$\alpha_{\text{obs.}}$	$\alpha_{\text{calc.}}$	$\alpha_{\text{obs.}} - \alpha_{\text{calc.}}$	λ	$\alpha_{\text{obs.}}$	$\alpha_{\text{calc.}}$	$\alpha_{\text{obs.}} - \alpha_{\text{calc.}}$
6438	-16.52°	-16.64°	+0.12°	5086	-28.9°	-28.8°	-0.1°
5893	20.35	20.33	+0.02	4800	33.3	33.2	-0.1
5780	21.25	21.26	+0.01	4678	35.4	35.4	±0.0
5461	24.28	24.30	+0.02	4358	42.4	42.4	±0.0

TABLE VII.

Rotatory Powers of (–)n-Propylpropenylcarbinyl Methyl Ether at 26° (l, 0.25).

λ	$\alpha_{\text{obs.}}$	$\alpha_{\text{calc.}}$	$\alpha_{\text{obs.}} - \alpha_{\text{calc.}}$	λ	$\alpha_{\text{obs.}}$	$\alpha_{\text{calc.}}$	$\alpha_{\text{obs.}} - \alpha_{\text{calc.}}$
6438	- 8.14°	- 8.48°	+0.34°	5086	-13.55°	-13.83°	+0.28°
5893	- 9.89	-10.2	+0.31	4800	-15.36	-15.62	+0.26
5780	-10.98	-10.6	-0.38	4678	-16.10	-16.50	+0.40
5461	-12.00	-11.92	-0.08	4358	-19.67	-19.17	-0.50

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The rotatory dispersion of (—)*n*-propylpropenylcarbinyl methyl ether (Table VII) can be represented by a single-term Drude equation, $\alpha = -3.42/(\lambda^2 - 0.0113)$, but the small value of the dispersion constant, $\lambda_0^2 = 0.0113$, raises a suspicion that two terms of opposite sign may be necessary to express the dispersion over a more extended range of observations.

The Optical Properties of Substituted Allyl Alcohols.—The investigations recorded in the first paragraph have been directed primarily towards the study of the reactions of optically active substituted allyl alcohols, but many optical data have also been recorded and some relationships are indicated below.

TABLE VIII.
Molecular Refractivities.

Compound.	<i>t.</i>	n_D^{20}	d_4^{20}	$[R]_D$ obs.	$[R]_D$ calc.
CHMe:CH·CHMe·OH *	18°	1.4282	0.8382	26.44	26.35
CHMe:CH·CHPr·OH *	14.4	1.4397	0.8422	35.69	35.58
CMe ₂ :CH·CHMe·OH	17	1.4297	0.8461	30.51	30.97
CHMe:CH·CHMe·OAc	26	1.4143	0.8931 (at 25°)	35.83	35.71
CHMe:CH·CHPr·OAc	17	1.4270	0.8815 (at 20°)	45.33	44.95

* Auwers and Westermann (*loc. cit.*). The calculated values are obtained by means of the constants of Eisenlohr (*Z. physikal. Chem.*, 1911, **75**, 605). In the last two examples, the densities are adjusted to the temperature at which the refractive index is determined (−0.0008 unit for +1°).

The agreement with the values calculated from the open-chain formulæ given above appears satisfactory.

In order to account for various reactions and for values in the observed parachors of $\alpha\gamma$ -dimethylallyl alcohol it was tentatively suggested that this substance might contain a large proportion of the isomeric inner ether, $\begin{array}{c} \text{H} \\ \diagup \\ \text{C} \\ \diagdown \\ \text{Me} \end{array} < \begin{array}{c} \text{CH}_2 \\ \diagup \quad \diagdown \\ \text{O} \end{array} > \begin{array}{c} \text{Me} \\ \diagup \\ \text{C} \\ \diagdown \\ \text{H} \end{array}$. A compound of this constitution should have $[R]_D$ 25.21; analogous structures for the other alcohols in Table VIII would have values of $[R]_D$ lower by 1.14 units than those recorded (the value used for a four-membered ring is +0.48, as determined by Östling; *J.*, 1912, **101**, 457). It now appears that the ethylenic link cannot be absent and accordingly a formulation of these compounds is being developed in which the ethylenic character is distributed between the $\alpha\beta$ - and the $\beta\gamma$ -linkage.

Geometrical Configurations.—Alcohols (I), (II), (III), and (V) are considered to be *trans*-isomerides on the following evidence; (I), (III), and (V) are prepared by the interaction of the appropriate Grignard reagent and crotonaldehyde. This aldehyde, obtained by the dehydration of aldol, was found by Kaufler (*Monatsh.*, 1929, **53**, 119) to yield on oxidation principally crotonic acid (*trans*-), together with some *isocrotonic* acid; Blacet, Young, and Roof (*J. Amer. Chem. Soc.*, 1937, **59**, 608), however, have concluded that purified commercial crotonaldehyde consists solely of the *trans*-isomeride, since the ultra-violet absorption spectrum remains unaltered after the crotonaldehyde has been submitted to such treatment as would alter the ratio *cis*- to *trans*- if a certain proportion of the former isomeride were originally present. Alcohol (II) is prepared similarly from cinnamaldehyde, which also should possess the *trans*-configuration, since it is converted by aerial oxidation into cinnamic acid (*trans*-). None of the subsequent operations involved in the resolution of the hydrogen phthalic esters appears likely to cause geometrical inversion and no indications that these carbinols are mixtures of geometrical isomerides have appeared. The *d*- and the *l*-form of γ -phenyl- α -methylallyl alcohol are solids which crystallise readily from various solvents, but an exhaustive research failed to effect any separation.

Rotatory Dispersion.—The range of wave-lengths for which data are available may in some cases be too restricted for the detection of smaller deviations from simplicity of rotatory dispersion, but where the dispersion ratio $\alpha_{4358}/\alpha_{5461}$ remains insensitive to variations of temperature and solvent influence it may be concluded that the rotatory dispersion exhibits real simplicity. Alcohol (I) was demonstrated by Hills, Kenyon, and Phillips (*loc. cit.*) to possess a complex rotatory dispersion and this is shown above to apply also to alcohol (V). Alcohol (IV) in the homogeneous state shows a slight complexity of

rotatory dispersion when $1/\alpha$ is plotted against λ^2 , and the dispersion ratio $\alpha_{4358}/\alpha_{5461}$ is little influenced by changes of temperature, as the following data show :

t	20°	50°	76°
$\alpha_{4358}/\alpha_{5461}$	1.78	1.77	1.75

On the other hand, this dispersion is more susceptible to solvent influence :

Solvent	C_6H_5N	$CHCl_3$	Et_2O
$\alpha_{4358}/\alpha_{5461}$	2.21	1.64	1.90

and in pyridine solution the sign of rotation is reversed.

It thus appears that alcohol (IV) also possesses complex rotatory dispersion.

Unlike the saturated aliphatic secondary alcohols, which uniformly possess simple rotatory dispersions, the alkyl-substituted allyl alcohols hitherto examined all show complexity of rotatory dispersion. The rotatory dispersion of the semi-aromatic alcohol (II) can be represented by a single-term equation (Table IX) :

$$\alpha = 4.425/(\lambda^2 - 0.0876); \lambda_0 = 2960 \text{ \AA.}$$

TABLE IX.

Rotatory Powers of γ -Phenyl- α -methylallyl Alcohol (t, 51°; 1, 0.5).

λ	5780	5461	4358
$\alpha_{obs.}$	17.96°	21.00°	43.23°
$\alpha_{calc.}$	17.97°	21.01°	43.20°
$\alpha_{obs.} - \alpha_{calc.}$	-0.01°	-0.01°	+0.03°

The dispersion ratio is relatively insensitive to changes in temperature :

t	51°	95°
$\alpha_{4358}/\alpha_{5461}$	2.06	2.00

and to the influence of solvents :

Solvent	CS_2	C_6H_6	$COMe_2$	$CHCl_3$
$\alpha_{4358}/\alpha_{5461}$	2.09	1.94	2.06	1.97

The largest deviation from the mean value is found in the benzene solution; the dispersion in this case may be represented, however, by a single-term equation (Table X) :

$$\alpha = 4.97/(\lambda^2 - 0.0742); \lambda_0 = 2730 \text{ \AA.}$$

TABLE X:

Rotatory Powers of γ -Phenyl- α -methylallyl Alcohol in Benzene Solution (c, 4.070; 1, 2).

λ	5893	5780	5461	4358
$\alpha_{obs.}$	+18.2°	+19.4°	+22.2°	+43.0°
$\alpha_{calc.}$	+18.2°	+19.15°	+22.2°	+43.0°
$\alpha_{obs.} - \alpha_{calc.}$	$\pm 0.0^\circ$	+ 0.25°	$\pm 0.0^\circ$	$\pm 0.0^\circ$

The numerical values of the rotatory powers in other solvents are not very different.

The rotatory dispersion of the isomeric alcohol (III) also can be represented by a single-term equation (Table XI) :

$$\alpha = -7.73/(\lambda^2 - 0.0689); \lambda_0 = 2630 \text{ \AA.}$$

TABLE XI.

Rotatory Powers of α -Phenyl- γ -methylallyl Alcohol (t, 20°; 1, 0.5).

λ	5780	5461	4358
$\alpha_{obs.}$	-29.16°	-33.59°	-64.0°
$\alpha_{calc.}$	-29.20°	-33.70°	-63.8°
$\alpha_{obs.} - \alpha_{calc.}$	- 0.04°	- 0.11°	+ 0.2°

and the dispersion ratio is insensitive to changes of temperature :

t	20°	35°	40.5°	62.5°	71°
$\alpha_{4358}/\alpha_{5461}$	1.905	1.883	1.89	1.91	1.92

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No data for its solutions are available, since this alcohol undergoes isomeric change into (II) somewhat readily.

It thus appears that the phenylalkylallyl alcohols exhibit simple rotatory dispersions. The values of λ_0 derived from the equations of Tables IX, X, and XI are respectively 2960, 2730, and 2630 Å., and the tentative suggestion may be made that a large proportion of the rotatory power is due to induced dissymmetry of the phenyl group, since Baly and Tryhorn (J., 1915, 107, 1058) found that a large number of benzene derivatives gave absorption bands in the region 2600—2750 Å., and Kuhn (*Trans. Faraday Soc.*, 1930, 26, 307) attributed a large induced dissymmetry to the benzene nucleus in mandelic acid.

Marked mutarotation was observed in alcohol (I), but alcohols (II), (IV), and (V) do not undergo mutarotation, whence it appears that this property may be associated with the symmetrical substitution in $\alpha\gamma$ -dimethylallyl alcohol. The dispersion ratios at room temperature of the hydrogen phthalic and acetic esters of the various unsaturated alcohols in different solvents are recorded in Table XII.

TABLE XII.

Values of the Dispersion Ratio, $\alpha_{4358}/\alpha_{5461}$, for Derivatives of Alcohols (I)–(V).

Derivative.	Solvent.	(I).	(II).	(III).	(IV).	(V).
Acetate	None	1.79	1.93	3.00	2.00	1.75
Hydrogen phthalate	Et ₂ O	2.01	—	2.10	—	—
" "	C ₆ H ₆	2.11	1.53	—	1.94	2.40
" "	CHCl ₃	2.06	2.41	—	1.86	2.75
" "	CS ₂	1.44	—	—	1.95	1.91
" "	COMe ₂	1.99	1.77	—	—	—
" "	C ₆ H ₅ Br ₂	2.06	—	—	—	—
" "	EtOH	2.01	—	—	1.90	2.03
" "	CCl ₄	2.27	—	—	—	—
" "	NaOH (aq.)	1.98	—	—	—	—

Since the carboxylic esters of saturated aliphatic secondary alcohols exhibit complex rotatory dispersion, those derived from unsaturated alcohols are unlikely to be less complex. The dispersion ratios are in general greater than the value 1.65 associated with saturated aliphatic compounds and approximate to 2.

EXPERIMENTAL.

dl-*n*-Propylpropenylcarbinol (b. p. 63—64.5°/14 mm., n_D^{18} 1.4380) was prepared in 74% yield by the interaction of crotonaldehyde (0.9 mol.) and *n*-propylmagnesium chloride.

dl-*n*-Propylpropenylcarbinyl hydrogen phthalate was prepared by heating the *dl*-alcohol (137 g.) with phthalic anhydride (178 g.) and pyridine (95 g.) at 60—65° for 2 hours. The resultant oil, diluted with acetone, was poured into dilute hydrochloric acid and ice; the acid ester then separated as a solid, m. p. 58—62° (yield, almost theoretical). Purified through its sodium salt and crystallised from carbon disulphide, it formed prisms, m. p. 72.5° (Found, by titration with NaOH: *M*, 260. Calc. for C₁₅H₁₈O₄: *M*, 262).

(+)-*n*-Propylpropenylcarbinyl Hydrogen Phthalate.—Strychnine (625 g.) was dissolved in a solution of the *dl*-hydrogen phthalic ester (491 g.) in dry chloroform; the solvent was removed, and hot dry acetone (1200 c.c.) added. On cooling, the strychnine salt (800 g.) separated. This was thrice recrystallised by solution in the minimum amount of methyl alcohol and addition of acetone. Further recrystallisation did not increase the optical activity of the salt, which was decomposed to yield a dextrorotatory hydrogen phthalic ester having $[\alpha]_{5461} + 19.3^\circ$ in ethyl alcohol. The strychnine salt was readily decomposed by prolonged boiling in acetone solution, and by traces of water in the solvents, and could not be obtained optically pure. After repeated crystallisation from ether–light petroleum (+)-*n*-propylpropenylcarbinyl hydrogen phthalate formed needles, m. p. 74°–75°, and attained the constant rotatory power $[\alpha]_{5461}^{16} + 22.85^\circ$ (*l*, 2.0; *c*, 4.55) in ethyl-alcoholic solution (Found: C, 68.85; H, 6.9. C₁₅H₁₈O₄ requires C, 68.7; H, 6.9%).

Decomposition of the more soluble fractions of the strychnine salt yielded a hydrogen phthalic ester with $[\alpha]_{5461} - 9.5^\circ$ in ethyl-alcoholic solution. By four recrystallisations of its brucine salt from acetone the rotatory power of this hydrogen phthalic ester was raised to a constant value of $[\alpha]_{5461} - 16.0^\circ$ in ethyl-alcoholic solution. Finally, by repeated crystallisation

from ether and light petroleum, optically pure (–)-*n*-propylpropenylcarbinyl hydrogen phthalate was obtained in needles, m. p. 75°, $[\alpha]_{5461}^{20} - 22.5^\circ$ (*l*, 2.0; *c*, 4.610) in ethyl-alcoholic solution, and $[\alpha]_{5461}^{14.5} + 17.2^\circ$ (*l*, 2.0; *c*, 4.60) in carbon disulphide. In view of the failure of both the strychnine and the brucine salts to effect a complete resolution of this hydrogen phthalic ester, its salts with quinidine and cinchonidine were recrystallised from methyl acetate and acetone respectively: these, however, brought about little, if any, separation.

(+)-*n*-Propylpropenylcarbinol.—Steam was passed through a solution of the (+) hydrogen phthalic ester (20 g.) and sodium hydroxide (7 g.) in water (34 c.c.) and from the steam-distillate (+)-*n*-propylpropenylcarbinol, b. p. 63.5°/15 mm., $n_D^{18} 1.4381$, $d_4^{18} 0.839$, was obtained. Its rotatory power is recorded in Table I, and the variations with solvent and temperature in Tables II and III. The carbinol (1.1 g.) was reconverted into its hydrogen phthalic ester, which had $[\alpha]_{5461}^{20} + 21.1^\circ$ (*l*, 2.0; *c*, 4.855), indicating slight racemisation during hydrolysis.

Reduction of (+)-*n*-Propylpropenylcarbinol to Di-*n*-propylcarbinol.—The (+) alcohol ($\alpha_{5461}^{19} + 4.02^\circ$, *l*, 0.5; 2 g.), dissolved in ethyl alcohol (99%; 15 c.c.), was reduced with hydrogen at 2 atms. in the presence of Raney nickel catalyst. The filtered solution was optically inactive to light of λ_{5461} (*l*, 2.0), and yielded optically inactive di-*n*-propylcarbinol, b. p. 66.5°/18 mm., $n_D^{20} 1.4216$, which was converted into its hydrogen phthalic ester, m. p. 60° alone and when mixed with authentic di-*n*-propylcarbinyl hydrogen phthalate.

Absence of Mutarotation in (+)-*n*-Propylpropenylcarbinol.—The (+) alcohol ($\alpha_{5461}^{19} + 4.11^\circ$, $\alpha_{4358}^{19} + 7.70^\circ$, *l*, 0.5) was maintained at 34–39° during 15 days; it was then kept at 20° for 6 hours, and the rotatory power redetermined, $\alpha_{5461}^{20} + 4.10^\circ$, $\alpha_{4358}^{20} + 7.95^\circ$ (*l*, 0.5).

dl-*n*-Propylpropenylcarbinyl acetate, prepared by heating the dl-alcohol (6 g.) with acetic anhydride (8 g.) and pyridine (6 g.), had b. p. 63–64.5°/12 mm., $n_D^{17} 1.4283$ (Found: C, 69.2; H, 10.3. $C_9H_{16}O_2$ requires C, 69.2; H, 10.3%). (–)-*n*-Propylpropenylcarbinyl acetate, prepared similarly from the (+) alcohol ($\alpha_{5461}^{19} + 4.02^\circ$, *l*, 0.5), had b. p. 74°/16 mm., $n_D^{17} 1.4270$, $d_4^{21} 0.8815$, $\alpha_{6438}^{21} - 14.96^\circ$, $\alpha_{5893}^{21} - 18.41^\circ$, $\alpha_{5780}^{21} - 19.23^\circ$, $\alpha_{5461}^{21} - 21.98^\circ$, $\alpha_{5086}^{21} - 26.15^\circ$, $\alpha_{4800}^{21} - 30.18^\circ$, $\alpha_{4678}^{21} - 32.00^\circ$, $\alpha_{4358}^{21} - 38.40^\circ$ (*l*, 0.5).

Reduction of the (–) acetate. The (–) acetate ($\alpha_{5461}^{21} - 21.98^\circ$, *l*, 0.5; 3.6 g.) was reduced in ethereal solution by hydrogen at 2 atms. in the presence of platinum oxide. The filtered solution was inactive to light of λ_{5461} , and yielded optically inactive di-*n*-propylcarbinyl acetate, b. p. 69–70°/17 mm., $n_D^{19} 1.4105$.

dl-*n*-Propylpropenylcarbinyl benzoate, prepared by mixing the dl-alcohol (5.5 g.) with pyridine (5 g.) and adding benzoyl chloride (8.75 g.), had b. p. 146°/12 mm., $n_D^{14} 1.5071$ (Found: C, 76.7; H, 8.4. $C_{14}H_{18}O_2$ requires C, 76.9; H, 8.3%).

(+)-*n*-Propylpropenylcarbinyl benzoate, prepared similarly from the (+) alcohol ($\alpha_{5461}^{18} + 4.45^\circ$, *l*, 0.5), had b. p. 158°/16 mm., $d_4^{18.5} 0.9908$, $n_D^{20} 1.5046$; its rotatory powers are recorded in Table V.

Reduction of the (+) benzoate. The (+) benzoate ($\alpha_{5461}^{20} + 11.16^\circ$, *l*, 0.5; 3.1 g.) was reduced in ethereal solution (20 c.c.) by hydrogen at 2 atms. in the presence of platinum oxide; the filtered solution had $\alpha_{5461}^{18} - 0.12^\circ$ (*l*, 2.0), and from it optically inactive di-*n*-propylcarbinyl benzoate, b. p. 148–150°/11 mm., $n_D^{20} 1.4883$, was obtained.

dl-*n*-Propylpropenylcarbinyl Methyl Ether.—Methyl iodide (8 g.) was added to the potassium-derivative obtained by the interaction of potassium (2 g.) and the dl-alcohol (5.7 g.) in benzene suspension; the crude methyl ether was freed from unreacted alcohol by heating with phthalic anhydride (6.5 g.) and pyridine (3.5 g.) for 2 hours at 65–70°. After redistillation through a short column, dl-*n*-propylpropenylcarbinyl methyl ether had b. p. 135°/760 mm., $n_D^{20.9} 1.4164$, $d_4^{20.5} 0.7902$ (Found: C, 75.0; H, 12.8. $C_8H_{16}O$ requires C, 74.9; H, 12.6%).

(+)-*n*-Propylpropenylcarbinyl methyl ether was similarly prepared from the (–) alcohol ($\alpha_{5461}^{20} - 2.14^\circ$, *l*, 0.5); it had b. p. 135–137°, $n_D^{20.8} 1.4169$, $\alpha_{6438}^{25.5} + 3.73^\circ$, $\alpha_{5893}^{25.5} + 4.53^\circ$, $\alpha_{5780}^{25.5} + 5.03^\circ$, $\alpha_{5461}^{25.5} + 5.50^\circ$, $\alpha_{5086}^{25.5} + 6.21^\circ$, $\alpha_{4800}^{25.5} + 7.04^\circ$, $\alpha_{4678}^{25.5} + 7.38^\circ$, $\alpha_{4358}^{25.5} + 9.01^\circ$ (*l*, 0.2356).

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102. The Molecular Rearrangement of (–)Phenylmethylcarbinyl *dl-p*-Toluenesulphinate.

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A further study has been made of the molecular rearrangement of (–)phenylmethylcarbinyl *dl-p*-toluenesulphinate to *dl-p*-tolyl- α -phenylethylsulphone (Kenyon and Phillips, J., 1930, 1676). Experiments upon *dl*-phenylmethylcarbinyl *p*-toluenesulphinate show that the rearrangement is facilitated in formic acid solution. The rearrangement of the (–)ester in formic acid solution gives the *dl*-sulphone in 75% yield. The hypothesis of Kenyon and Phillips (*loc. cit.*) that the rearrangement occurs *via* ionisation is confirmed with respect to the greater proportion of the sulphone produced, and is elaborated in the light of the results of experiments on the mutarotation of the ester in solvents. In formic acid solution containing sodium formate a mixture of (–) and *dl*-sulphone is produced, but the yield is only 10%, the main product being a mixture of (–) and *dl*-phenylmethylcarbinyl formate. Both these products have the same relative configuration as the original sulphinic ester. Evidence is adduced that the formate arises (i) as a result of formolysis of the sulphinate, giving the (–)formate, (ii) by combination of α -phenylethyl kations with formate anions, giving the *dl*-formate. It is suggested that the (–)sulphone is formed by intramolecular rearrangement; in the presence of an added anion rearrangement *via* ionisation is diverted and only the small proportion of laevorotatory sulphone formed by the intramolecular process is obtained.

It was suggested (Kenyon and Phillips, *Trans. Faraday Soc.*, 1930, 26, 451; Kenyon, Phillips, and Taylor, J., 1931, 384) that reactions which result in Walden inversion take place by way of intermediate complex formation whereby the entering anion becomes associated with the asymmetric carbon atom before detachment of the replaced anion is effected, whilst fission of the optically active molecule into a carbonium kation and an anion before the entering anion becomes associated with it results in racemisation. Subsequently, these suggestions were put forward in more precise forms by Polanyi and co-workers (*Z. physikal. Chem.*, 1932, B, 19, 164; 1933, B, 20, 161) and by Hughes, Ingold, and co-workers (J., 1937, 1252).

The second part of this hypothesis, *i.e.*, preliminary fission of the molecule, has been contested on the ground that it would require more energy than is available under the usual conditions of replacement reactions (Wallis and Moyer, *J. Amer. Chem. Soc.*, 1933, 55, 2598; Olson, *J. Chem. Physics*, 1933, 1, 418; Olson and Halford, *J. Amer. Chem. Soc.*, 1937, 59, 2644; Steigman and Hammett, *ibid.*, p. 2540). Hughes and Ingold (J., 1935, 244) considered that solvation of the molecule may provide the energy required for ionisation, whereas Kenyon and Phillips (J., 1930, 1676) concluded that the spontaneous transformation of (–)phenylmethylcarbinyl *p*-toluenesulphinate (I) into *dl-p*-tolyl- α -phenylethylsulphone (II) provided experimental evidence of ionisation during the course of

the rearrangement. This ionic fission and the racemisation of the liberated kation may be expected to occur more readily in derivatives of α -phenylethane than in those of purely aliphatic secondary alcohols (Hughes, Ingold, and co-workers, *loc. cit.*); it is likely, however, that molecular rearrangement through the intermediate formation of ions is exceptional. For example, Kenyon, Partridge, and Phillips (J., 1937, 207) have provided evidence which suggests that the anionotropic rearrangement of the hydrogen phthalate of α -phenyl- γ -methylallyl alcohol is an intramolecular process. Other investigations (reviewed by Waters, "Physical Aspects of Organic Chemistry," 1935, p. 346 *et seq.*, and by Watson, "Modern Theories of Organic Chemistry," 1937, p. 132 *et seq.*) indicate that intramolecular rearrangement is more common than rearrangement *via* ionisation. If the migrating

radical is optically active and its asymmetric carbon atom retains its octet of electrons during the rearrangement, asymmetry is completely maintained (Jones and Wallis, *J. Amer. Chem. Soc.*, 1926, **48**, 169; Wallis and Nagel, *ibid.*, 1931, **53**, 2787; Wallis and Dripps, *ibid.*, 1933, **55**, 1701); intramolecular migration of an optically active radical containing an asymmetric carbon atom carrying a sextet of electrons results in an optically active product with retention of configuration and partial racemisation (Sprung and Wallis, *ibid.*, p. 3838; Wallis and Bowman, *J. Org. Chem.*, 1936, **1**, 383).

In view of its significance and its unique character, the rearrangement of (—)phenylmethylcarbinyll *dl-p*-toluenesulphinate has been submitted to further study. The rearrangement has also been examined of the homogeneous ester, prepared from (—)phenylmethylcarbinol having $\alpha_{5461} - 11.9^\circ$ (*l*, 0.25); the ester used by Kenyon and Phillips (*loc. cit.*) was prepared from carbinol of $\alpha_{5461} + 5.03^\circ$ (*l*, 0.25). The solid product of the rearrangement, recrystallised once from aqueous ethyl alcohol, gives optically inactive *p*-tolyl- α -phenylethylsulphone in 22% yield.

Table I records the results of experiments using approximately 5 g. of *dl*-sulphinate in 20 c.c. of each of a variety of solvents at laboratory and at elevated temperatures. Col. 2 gives ϵ , the dielectric constant of the solvent at 20°. The yields recorded are percentages of those obtainable if all the sulphinate had been converted into the derivative in question.

The data in Table I show that decomposition occurs at elevated temperatures. The formation of di-*p*-tolyl disulphoxide during the rearrangement has been discussed by Kenyon and Phillips (*loc. cit.*); an alternative mode of formation of the disulphoxide is by the usual decomposition of *p*-toluenesulphinic acid formed, together with styrene, by thermal decomposition of the ester. *p*-Tolyl- α -phenylethylsulphone is stable at 80°, being recovered unchanged after heating at that temperature for 24 hours in the homogeneous state or in nitrobenzene solution. The results of the experiments at room temperature

TABLE I.

Transformation of dl-phenylmethylcarbinyll dl-p-toluenesulphinate in solvents and in the presence of sodium formate and sodium p-toluenesulphinate.

Solvent.	ϵ_{20° .	Reaction at room temp.		Reaction at elevated temp.		
		Duration, days.	Isolated products.*	Temp.	Duration, hours.	Isolated products.
(None)	—	23	Sulphone, 27%; styrene, trace	80°	3	Sulphone, 10% (profound decomp.)
Ethyl ether satd. with HCl†	—	18	Disulphoxide, 22%	—	—	—
Benzene	2.3	21	Sulphone, 9%	80	24	Disulphoxide, 23%
Pyridine	12.4	18	Unchanged sulphinate	—	—	—
Acetone	21.5	—	—	56	24	Unchanged sulphinate
Nitrobenzene	34.1	25	Sulphone, 30%	80	2.5	Sulphone, 9% (profound decomp.)
Acetonitrile	37.5	22	Unchanged sulphinate	80	20	Disulphoxide, 21%
Formic acid	57.0	22	Sulphone, 72; formate, 13%	80	2.5	Sulphone, 54%; formate, trace
Sodium formate‡ in formic acid	—	23	Sulphone, 11; formate, 75; sulphinic acid, 12%	—	—	—
Sodium <i>p</i> -toluenesulphinate§ in formic acid	—	18	Sulphone, 6; formate, 62%	—	—	—

* Sulphone, disulphoxide, formate, and sulphinic acid signify respectively *p*-tolyl- α -phenylethylsulphone, di-*p*-tolyl disulphoxide, phenylmethylcarbinyll formate, and *p*-toluenesulphinic acid.

† The sulphinate was recovered unchanged after 20 days from solution in ethyl ether in the presence of anhydrous potassium carbonate, and from ethereal ammonia and ethereal hydrogen chloride.

‡ 2.5 Mols. per mol. of sulphinate.

§ 1.25 Mols. per mol. of sulphinate

indicate that the rearrangement is favoured in solvents of high dielectric constant, and may be diverted in the presence of added anions; these conclusions are in harmony with the suggestion that the rearrangement occurs *via* ionisation. The comparatively high yield

of sulphone obtained from the rearrangement of the homogeneous sulphinate may be ascribed to the fact that the sulphinate is itself likely to have a high dielectric constant. The difference between the results obtained in nitrobenzene and in acetonitrile solution indicate an unexpected difference in the degree of solvation of the sulphinate in these two solvents, and the facile rearrangement in formic acid solution may be due, not only to the high dielectric constant of this solvent, but also to the ability to solvate both anion and cation, which is peculiar to hydroxylic solvents. If solvation of the kation by formic acid occurs, it must be by electrostatic attraction similar to the hydration of inorganic kations (Day, Hughes, Ingold, and Wilson, J., 1934, 1593), since solvation by co-ordination would result in the formation of phenylmethylcarbinyll formate.

Table II records the products of the rearrangement of the (–)sulphinate, solutions of the same concentrations being used as those described in Table I. The high yield of optically inactive sulphone produced by the rearrangement of the (–)sulphinate in formic acid solution is a convincing confirmation of Kenyon and Phillips's observation that the reaction is accompanied by racemisation.

(–)Phenylmethylcarbinyll formate has the same configuration as the (–)carbinol, because it is converted into this by saponification, a process which does not disturb the bonds of the asymmetric carbon atom (Holmberg, *Ber.*, 1912, 45, 2997; Ingold and Ingold, J., 1932, 756; Polanyi and Szabo, *Trans. Faraday Soc.*, 1934, 30, 508). The (–)formate therefore has the same configuration as the (–)sulphinate, which is formed from the (–)carbinol by a reaction in which the bonds of the asymmetric carbon atom are not disturbed. The formation of a mixture of (–) and dl-phenylmethylcarbinyll formate during the rearrangement of (–)phenylmethylcarbinyll p-toluenesulphinate in the presence of sodium formate cannot be accounted for by any of the hypotheses previously advanced to explain retention of configuration during replacement reactions, *viz.*, occurrence of an even number of consecutive inversion reactions, or the retention by the carbon atom of its electron octet (Kenyon and Phillips, *Trans. Faraday Soc.*, *loc. cit.*), or an intramolecular replacement in which the entering atom and the atom which it replaces are held on the same side of the

TABLE II.

Rearrangement of (–)phenylmethylcarbinyll dl-p-toluenesulphinate in formic acid solution and in the presence of sodium formate and sodium p-toluenesulphinate.

(Optically active products all formed with retention of configuration.)

Solvent.		Formic acid.		H·CO ₂ Na in H·CO ₂ H.		Sodium p-toluenesulphinate in H·CO ₂ H.*
Product.		Sulphone.†	Formate.	Sulphone.†	Formate.‡	Formate.
Crude product	Yield, %	75	trace	13	—	—
	M. p.	127–130°	—	110–115°	—	—
Purified product	Yield, %	60	—	10	75	62
	M. p.	134°	—	127–128°	—	—
	Rotatory power §	nil	—	–65·6°	–9·5°	–0·47°
	% of max. recorded rotatory power	nil	—	63	20	1

* (–) + dl-Sulphinate having 75% of maximum rotatory power was used in this experiment. The solid reaction product contained a high proportion of disulphoxide, which made purification of the sulphone difficult.

† The dl-sulphone has m. p. 134°, and sulphone of $[\alpha]_{5461} +103^\circ$ in chloroform (*l*, 2·0; *c*, 0·6) has m. p. 124–125° (Kenyon and Phillips, *loc. cit.*).

‡ (–)Phenylmethylcarbinyll formate has $\alpha_{5461} -48\cdot90^\circ$ (*l*, 0·236).

§ $[\alpha]_{5461}$ of the sulphone in chloroform (*l*, 2·0; *c*, 2·65); α_{5461} of the formate (*l*, 0·236).

asymmetric carbon atom (Hughes, Ingold, and co-workers, *loc. cit.*). Sulphinic esters of optically active alcohols, however, undergo reactions analogous to the saponification or alcoholysis of carboxylic esters, in which the bonds of the asymmetric carbon atom are not disturbed. For example, (–)phenylmethylcarbinyll p-toluenesulphinate undergoes alcoholysis in ethyl-alcoholic solution (Kenyon and Phillips, J., 1930, *loc. cit.*) with complete retention of configuration. Like sodium acetate in acetic acid solution (Steigman and Hammett, *loc. cit.*), a solution of sodium formate in formic acid is basic, resembling aqueous

sodium hydroxide in that it contains sodium ions, anions in equivalent amount, and the undissociated acid corresponding to these anions. It can therefore react with the sulphinic ester in the same way that aqueous sodium hydroxide reacts with ethyl (+)- α -*p*-toluenesulphinoxypionate (Gerrard, Kenyon, and Phillips, J., 1937, 153) yielding (–)-phenylmethylcarbonyl formate without disturbance of the bonds of the asymmetric carbon atom and therefore uncontaminated by the (+)ester. At the same time the *dl*-formate is produced by the interaction of liberated phenylmethylcarbonyl kations with formate anions. The sum of these two processes is the formation of the mixture of (–) and *dl*-formate with $\alpha_{5461} = 9.52^\circ$ (*l*, 0.236). Since the optically pure ester has $\alpha_{5461} = 48.90^\circ$ (*l*, 0.236), it is concluded that approximately 20% of the formate is optically active and produced by "formolysis," and the remainder is produced from the liberated and immediately racemised carbonium kations. This suggestion is supported by the results of the experiment in formic acid solution in the presence of sodium *p*-toluenesulphinate (Table II). Formate ions are present in this solution, as is shown by the high yield of formate (62%) compared with the low yield of formate in formic acid alone (Tables I and II). The formate produced, however, is almost entirely racemic, because the reaction (formolysis) which results in the formation of optically active formate is repressed by the presence of its products, *p*-toluenesulphinyl ion or *p*-toluenesulphinic acid.

The observations described above support the suggestion that the rearrangement occurs to a preponderating extent *via* ionisation, but the formation of laevorotatory, instead of racemic, *p*-tolyl- α -phenylethylsulphone in 10% yield during the rearrangement of the sulphinate in the presence of sodium formate shows that a small part of the rearrangement can occur by an alternative route. The (–)sulphone has the same relative configuration as (–)-phenylmethylcarbinol, because it can be obtained from the latter by two successive reactions, each of which involves inversion of configuration, *viz.*, conversion of the (–)carbinol into the (+)chloride (Kenyon, Phillips, and Taylor, *loc. cit.*) and conversion of this into the (–)sulphone (Kenyon and Phillips, J., 1930, *loc. cit.*). The (–)sulphone has therefore the same configuration as the (–)sulphinate, which is prepared from the (–)carbinol by esterification with *p*-toluenesulphinyl chloride. Like the (–)formate, described above, the (–)sulphone cannot be derived from the (–)sulphinate by replacement reactions. It is therefore concluded that the mixture of (–) and *dl*-sulphone is formed by intramolecular rearrangement, with retention of configuration and partial racemisation, like the rearrangements described by Sprung and Wallis (*loc. cit.*) and Wallis and Bowman (*loc. cit.*). In this type of rearrangement, an optically active product is obtained because the carbonium kation does not become free; fission of the carbon-oxygen bond and formation of the carbon-sulphur bond occur simultaneously. This process was suggested by Wallis and Moyer (*J. Amer. Chem. Soc.*, 1933, 55, 2598) as the mechanism of the Hofmann rearrangement. If all the (–) + *dl*-sulphone obtained in formic acid-sodium formate solution is produced by intramolecular rearrangement, approximately 15% of the (–)sulphinate undergoes the intramolecular process under these conditions; the racemic fraction of the sulphone obtained may, however, be derived in part from α -phenylethyl kations which fail to react with formate ions.

It is likely that the rearrangement of the sulphinate *via* ionisation is usually accompanied by a minor intramolecular rearrangement. The optically active sulphone is more soluble than the racemic form (Kenyon and Phillips, *loc. cit.*) and, by recrystallisation, a racemic product would therefore be obtained from a sulphone of very low rotatory power. The original explanation of the rearrangement may now be extended as follows:

A = Major reaction, ionic, with racemisation. B = Minor reaction, intramolecular, with retention configuration.

Support for the above scheme is given by observations of the mutarotation of solutions of the (–)sulphinate in formic acid solution, in which the rearrangement takes place most readily, and in acetonitrile solution, in which it does not occur. The results are given in Table III. The rotatory power of the solution in formic acid (*l*, 0.5) falls from $\alpha_{5461}^{17^\circ} - 3.92^\circ$, 20 minutes after dissolution ($\alpha_{5461}^{17^\circ} - 6.7^\circ$ extrapolated to zero time), to $\alpha_{5461}^{17^\circ} - 0.90^\circ$ after 75 minutes, but only a small amount (approximately 10% yield) of phenylmethylcarbinyll formate is formed during this time, the rest of the sulphinate being recovered and having, after isolation from the solution, $[\alpha]_{5461}^{17^\circ} - 61.7^\circ$ in ethyl alcohol (*l*, 2.0; *c*, 1.2); the original sulphinate had $[\alpha]_{5461}^{20^\circ} - 84.3^\circ$ (*l*, 2.0; *c*, 5.13). The mutarotation, which is therefore not due to racemisation or to reaction of the sulphinate, and is too rapid to be reasonably ascribed to variation of the specific rotatory power of the sulphinate as a result of its diminished concentration, must be caused by a reversible modification in the environment of the asymmetric carbon or sulphur atoms of the sulphinate molecule, occurring in solution. It can therefore be ascribed to an incipient disturbance of the molecule, prior to ionisation, corresponding to the stage described as solvation in the above scheme. Solvation in this sense implies, not only the attraction of solvent molecules by the solute, but also enhanced reactivity of the solute and formation of a new structure. Evidence of the second stage of the ionic mechanism, reversible ionisation accompanied by racemisation, is given by the observation that the sulphinate recovered from solution in formic acid after 75 minutes has lost 25% of its rotatory power. The third stage of this mechanism is established by the formation of *dl*-sulphone.

The solution of the (–)+*dl*-sulphinate in acetonitrile, on the other hand, remains unchanged in rotatory power, $\alpha_{5893}^{17^\circ} - 9.46^\circ$ (*l*, 2.0; *c*, 18.6), during 88 hours. The sulphinate recovered from this solution after 23.5 hours has $[\alpha]_{5461}^{17.5^\circ} - 70.3^\circ$ in ethyl alcohol (*l*, 2.0; *c*, 4.88); the original sulphinate had $[\alpha]_{5461}^{20^\circ} - 70.5^\circ$ in ethyl alcohol (*l*, 2.0; *c*, 5.02). These observations are in harmony with the fact that in this solvent the rearrangement does not take place. The subsequent decrease in rotation is due to the general instability of sulphinic esters, resulting in decomposition and racemisation. After 256 hours the rotatory power of the solution falls to $\alpha_{5893}^{17^\circ} - 4.24^\circ$ and the sulphinate recovered from the solution at that time has $[\alpha]_{5461}^{17^\circ} - 43.6^\circ$ in ethyl alcohol (*l*, 2.0; *c*, 4.88).

In ethereal solution in the presence of potassium carbonate the sulphinate shows even greater stability. A solution of the (–)+*dl*-ester in ether, having $\alpha_{5461}^{17^\circ} - 21.52^\circ$ (*l*, 2.0; *c*, 11.4) when freshly prepared, undergoes little change in rotatory power when kept over anhydrous potassium carbonate during 20 days, $\alpha_{5461}^{17^\circ}$ being then -21.26° . The sulphinate is recovered from this solution with undiminished rotatory power. The levorotatory sulphinate undergoes mutarotation in formic acid solution in the presence of sodium formate and sodium *p*-toluenesulphinate, and in nitrobenzene solution (Table IV), but the results cannot be precisely interpreted because certain of the products formed under these conditions are optically active.

TABLE III.

Mutarotation of solutions of levorotatory phenylmethylcarbinyll dl-p-toluenesulphinate in formic acid and in acetonitrile.

In H·CO ₂ H (<i>l</i> , 0.5; <i>c</i> , 23.9).		In CH ₃ ·CN (<i>l</i> , 2; <i>c</i> , 18.6).					
Mins. after dissolution.	$\alpha_{5461}^{18.1^\circ}$	Hours after dissolution.	$\alpha_{5893}^{17^\circ}$	Hours after dissolution.	$\alpha_{5893}^{17^\circ}$	Hours after dissolution.	$\alpha_{5893}^{17^\circ}$
20	–3.92°	0	–9.46°	42.5	–9.45°	160	–7.62°
40	–2.41	1.5	–9.44	88	–9.50	193	–5.91
75	–0.90	11.25	–9.46	112	–9.25	208.5	–5.34
		23.5	–9.44	136.75	–8.57	256	–4.24

EXPERIMENTAL

(–)Phenylmethylcarbinol was prepared by the method of Houssa and Kenyon (J., 1930, 2260), and *dl*- and (–)-phenylmethylcarbinyll *p*-toluenesulphinates by that of Kenyon and Phillips (*loc. cit.*). The (–)sulphinate had $n_D^{17^\circ} 1.5745$; $[\alpha]_{5461}^{20^\circ} - 87.0^\circ$, $[\alpha]_{4358}^{20^\circ} - 150.2^\circ$ (*l*, 2.0; *c*, 4.725) in ethyl alcohol.

Transformation of dl-Phenylmethylcarbinyl dl-p-Toluenesulphinate.—(i) *In the homogeneous state.* (a) At room temperature. The *dl*-ester (15.4 g.) after 26 days at room temperature was converted into a crystalline mass which was washed with light petroleum and ethyl alcohol. The residue (5.7 g.), m. p. 110–115°, was twice recrystallised from aqueous ethyl alcohol; the *p*-tolyl-*dl*- α -phenylethylsulphone (2.7 g.) obtained had m. p. 133–134°, alone or mixed with an authentic specimen. From the concentrated light petroleum and alcoholic wash-liquors, an oil (0.5 c.c.), b. p. 45–60°/16 mm., n_D^{20} 1.518, was isolated, which resinified on addition of a drop of concentrated sulphuric acid and was presumably styrene.

From another specimen of the sulphinate (0.63 g.) the sulphone (0.17 g.) was isolated after 23 days, with m. p. and mixed m. p. 131–133°.

(b) At 80°. The sulphinate (8 g.), when heated on the steam-bath for 3 hours, was converted into a brown crystalline mass from which, by the method described above, 0.8 g. of sulphone, m. p. and mixed m. p. 134°, was obtained.

(ii) *In ethereal solution.* (a) In ethyl ether saturated with hydrogen chloride. A solution of the *dl*-ester (5 g.) in 17 g. of ether saturated with hydrogen chloride, after standing at laboratory temperature for 18 days, was washed with aqueous sodium bicarbonate and with water and dried. The solid residue left after removal of the ether was washed with ethyl alcohol. The solid product (0.6 g.), after recrystallisation from ethyl alcohol, gave di-*p*-tolyl disulphoxide, m. p. and mixed m. p. 78°. From the alcoholic wash-liquor a fraction (2 c.c.), b. p. 76°/22 mm., was obtained, which was presumably α -phenyldiethyl ether (b. p. 67°/14 mm.) formed by interaction of α -phenyl- α -chloroethane with ethyl alcohol.

(b) In ether containing hydrogen chloride (0.7%). A solution of the *dl*-ester (4.4 g.; n_D^{17} 1.5753) in 25 c.c. of ether containing 0.18 g. of hydrogen chloride was washed as above, after standing at room temperature for 21 days. The residue left after removal of the ether consisted of unchanged ester (n_D 1.564).

(c) In ether containing ammonia (0.1%). A solution of the *dl*-ester (5 g.; n_D^{17} 1.5753) in 25 c.c. of ether containing anhydrous ammonia (0.025 g.), after standing at laboratory temperature for 21 days, was washed with water and dried. The sulphinate (n_D^{16} 1.5713) was recovered on removal of the ether.

(d) In ether in the presence of anhydrous potassium carbonate. The *dl*-ester (5 g.; n_D^{16} 1.5756), after standing for 18 days in ether (20 c.c.) with anhydrous potassium carbonate, was recovered unchanged (n_D^{16} 1.5740).

(iii) *In benzene solution.* (a) At room temperature. The sulphinate (5 g.; n_D^{17} 1.5736) was dissolved in benzene (25 c.c.). After 21 days, the benzene was removed and the pasty residue washed with a mixture of light petroleum and ethyl alcohol and recrystallised from aqueous ethyl alcohol. The product (0.45 g., m. p. 132–133°), recrystallised from aqueous ethyl alcohol, gave the *dl*-sulphone, m. p. and mixed m. p. 134°. The light petroleum–ethyl alcohol washings contained 3.8 g. of an oil, which could not be distilled and was presumably sulphinate.

(b) At 80°. The *dl*-ester (6 g.) in benzene (20 c.c.) was heated under reflux for 24 hours, and the benzene then removed by distillation. The solid product was filtered off from the liquid product, and after recrystallisation from alcohol, had m. p. 70–75° (yield 0.75 g.); a second recrystallisation gave di-*p*-tolyl disulphoxide, m. p. (and mixed m. p. with an authentic specimen) 76–77°. From the liquid product (2 c.c.) a few drops were obtained on distillation at 12 mm., bath temp. 150° ($\alpha\alpha'$ -diphenyldiethyl ether has b. p. 154–155°/15 mm.).

(iv) *In pyridine solution.* A solution of the sulphinate (5 g.; n_D^{16} 1.5756) in pyridine (20 g.), after standing at room temperature for 18 days, was diluted with benzene, washed with dilute hydrochloric acid and with water, and dried (calcium chloride). The benzene was removed by distillation (finally at 15 mm.); the residual oil was unchanged sulphinate, n_D^{16} 1.570.

(v) *In acetone solution at 56°.* A solution of the *dl*-sulphinate (9.8 g.; n_D^{16} 1.5761) in acetone (33 g.) was heated under reflux for 24 hours. After removal of the acetone by distillation (finally at 15 mm.), the unchanged ester was recovered, n_D^{16} 1.562.

(vi) *In nitrobenzene solution.* (a) At room temperature. A solution of the *dl*-ester (5 g.) in nitrobenzene (20 g.), after standing at room temperature for 25 days, was heated at 90°/12 mm. until the solvent was removed. The solid residue was washed with alcohol, leaving a crystalline solid (1.85 g., m. p. 121–128°) from which the *dl*-sulphone (1.5 g.; m. p. and mixed m. p. 134°) was obtained by recrystallisation as described above.

(b) At 80°. A solution of the *dl*-sulphinate (5 g.) in nitrobenzene (20 g.) darkened when heated on the steam-bath for 2.5 hours. The nitrobenzene was removed at 130°/65 mm.; from the dark viscous residue the sulphone (0.4 g., m. p. and mixed m. p. 132–134°) was obtained by recrystallisation from aqueous ethyl alcohol.

(vii) *In acetonitrile solution*. (a) At room temperature. A solution of the sulphinate (5 g.; n_D^{17} 1.5736) in acetonitrile (15 g.), after standing at room temperature for 22 days, was diluted with ether-benzene, washed with sodium bicarbonate solution and water, and dried, and the solvents removed by distillation (finally at 15 mm.). The residue of unchanged ester had n_D^{18} 1.568: it remained liquid after standing for 24 hours at -2° , and after inoculation with sulphone and sulfoxide.

(b) At 80° . A solution of the sulphinate (5 g.) in acetonitrile (20 g.) was heated on the steam-bath for 20 hours, and the solvent removed by distillation at 30 mm. The residual oil after two days deposited crystals of di-*p*-tolyl disulphoxide (0.55 g.), m. p. 80° , which after recrystallisation from alcohol had m. p. and mixed m. p. 79° .

(viii) *In formic acid solution*. (a) At room temperature. A solution of the sulphinate (10 g.) in anhydrous formic acid (40 g.), after standing at room temperature for 22 days, was diluted with ether-benzene (1:1) and washed with aqueous sodium bicarbonate (no precipitate was formed on acidifying the wash-liquors). The solvents were removed by distillation; the solid residue (7.2 g., m. p. $129-132^\circ$), recrystallised from aqueous alcohol, gave the sulphone (6.1 g.), m. p. and mixed m. p. 134° . The wash-liquors yielded *dl*-phenylmethylcarbinyll formate, b. p. $94-95^\circ/20$ mm., n_D^{18} 1.5054 (0.7 c.c. approx.).

(b) At 80° . A solution of the sulphinate (7.4 g.) in formic acid (21 g.) was heated on the steam-bath for 2.5 hours, then poured into water and extracted with ether-benzene. The extract was washed with sodium carbonate solution, dried (calcium chloride), and concentrated. The crystalline residue (4.0 g.), recrystallised from aqueous alcohol, gave the sulphone (3.5 g.), m. p. and mixed m. p. 134° . Distillation of a small amount of oil separated from the solid product gave a few drops, b. p. $90^\circ/20$ mm. (phenylmethylcarbinyll formate has b. p. $87^\circ/13$ mm.).

(ix) *In formic acid solution in the presence of sodium formate*. A solution of the sulphinate (15 g., 1 mol.) and anhydrous sodium formate (10 g., 2.5 mols.) in anhydrous formic acid (78 g., 30 mols.), after standing at room temperature for 23 days, was diluted with ether-benzene (1:1), washed with aqueous sodium bicarbonate, dried (sodium sulphate), and the solvents removed. The residue was separated into a crystalline and a liquid fraction. The former (1.6 g., m. p. 133°), recrystallised from aqueous alcohol, gave the sulphone (1.4 g.), m. p. and mixed m. p. $134-135^\circ$; and the latter on distillation gave 6.2 c.c. of material, b. p. $90-91^\circ/16$ mm., n_D^{19} 1.5048, from which on redistillation, *dl*-phenylmethylcarbinyll formate, b. p. $88-88.5^\circ/16$ mm., n_D^{18} 1.5056, d_4^{18} 1.058, was obtained (Found: C, 72.1; H, 6.7. $C_9H_{10}O_2$ requires C, 72.0; H, 6.7%).

Acidification of the sodium bicarbonate wash-liquor precipitated *p*-toluenesulphinic acid (1.1 g.), m. p. $86-87^\circ$ (Found: equiv., by titration with *N*-aqueous sodium hydroxide, 158. Calc. for $C_7H_7SO_2H$: equiv., 156). Recrystallised from hot water, the acid had m. p. $87-88^\circ$, alone or mixed with an authentic specimen.

(x) *In formic acid solution in the presence of sodium p-toluenesulphinate*. A solution of the *dl*-ester (7.0 g., 1 mol.) and sodium *p*-toluenesulphinate (dried at 110° ; 6.0 g., 1.25 mols.) in anhydrous formic acid (36 g.), after standing at laboratory temperature for 18 days, was diluted with ethyl ether, washed with water and with aqueous sodium carbonate, and dried. After removal of the ether and being washed with light petroleum, the solid residue (1.8 g., m. p. $100-105^\circ$) was recrystallised from ether-light petroleum. Two crystal forms which were deposited were separated mechanically and recrystallised separately, giving (a) di-*p*-tolyl disulphoxide, which after two crystallisations from ether-light petroleum had m. p. and mixed m. p. 77° (yield, 0.3 g.); (b) impure *p*-tolyl- α -phenylethylsulphone, which after two recrystallisations from aqueous alcohol had m. p. 130° (yield, 0.35 g.). From the light petroleum wash-liquor above, *dl*-phenylmethylcarbinyll formate was obtained, which after redistillation had b. p. $94.5^\circ/17$ mm., n_D^{21} 1.5075 (yield 2.5 g.). From the sodium carbonate wash-liquor above, *p*-toluenesulphinic acid (1.8 g.) was obtained on acidification (m. p. 87°).

Thermal Stability of p-Tolyl- α -phenylethylsulphone.—The sulphone was not discoloured by heating on the steam-bath for 24 hours and its m. p. ($133-135^\circ$) remained unchanged. The sulphone (0.5 g.) in nitrobenzene (5 c.c.) solution was heated on the steam-bath for 24 hours without discoloration and recovered with unchanged m. p. after removal of the solvent.

Transformation of (—) and (—) + dl-Phenylmethylcarbinyll dl-p-Toluenesulphinates.—(i) *Homogeneous*. The (—)ester (2.05 g.), after standing for 27 days at room temperature, was converted into a solid mass, which was washed with ethyl alcohol and with light petroleum. The residue (0.75 g., m. p. $113-117^\circ$), recrystallised from aqueous alcohol, gave *dl-p*-tolyl- α -phenylethylsulphone (0.45 g.), m. p. $129-131^\circ$, optically inactive in chloroform solution (*l*, 2; *c*, 2.07); recrystallised from aqueous alcohol, the sulphone had m. p. $132-133^\circ$, mixed m. p. with authentic sulphone 134° .

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(ii) *In formic acid solution.* A solution of the (—)ester (4 g.) in anhydrous formic acid (16 g.), after standing at room temperature for 9 days, was diluted with ether–benzene (1 : 1), washed with aqueous sodium bicarbonate, and dried (sodium sulphate), and the solvents removed. The residue was washed with light petroleum. From the crystalline product (3.0 g., m. p. 127–130°), recrystallised from aqueous alcohol, *dl-p*-tolyl- α -phenylethylsulphone (2.4 g.) was obtained, m. p. and mixed m. p. 134°, optically inactive in chloroform solution (*l*, 2.0; *c*, 5.04). From the light petroleum wash-liquor, one drop, b. p. 83°/12 mm. (phenylmethylcarbiny formate), was obtained.

(iii) *In formic acid solution in the presence of sodium formate.* A solution of the (—)sulphin-ate (10.4 g., 1 mol.) and anhydrous sodium formate (6.7 g., 2.5 mols.) in anhydrous formic acid (50 g., 27 mols.), after standing for 19 days at room temperature, was diluted, washed, and concentrated as in (ii) above. From the residual oil, on fractional distillation, a fraction (4.3 c.c.) was obtained with b. p. 88.5°/13 mm., n_D^{18} 1.5066, α_{589}^{17} – 7.92°, α_{5461}^{17} – 9.53° (*l*, 0.236). Redistilled, this fraction was identified as (—) + *dl*-phenylmethylcarbiny formate, b. p. 91°/15 mm.; n_D^{17} 1.5056, α_{589}^{17} – 8.03; α_{5461}^{17} – 9.52 (*l*, 0.236). The solid undistillable residue was washed with aqueous alcohol, and the crystalline product (1.4 g., m. p. 110–115°) was twice recrystallised from aqueous alcohol, yielding (—) + *dl-p*-tolyl- α -phenylethylsulphone, m. p. 127–128°, $[\alpha]_{5461}^{18}$ – 65.6° in chloroform solution (*l*, 2.0; *c*, 2.65). Acidification of the sodium bicarbonate wash-liquor from this preparation precipitated *p*-toluenesulphinic acid (0.7 g.), m. p. and mixed m. p. 86° (Found: equiv., 159).

(iv) *In formic acid solution in the presence of sodium p-toluenesulphinate.* A solution of 7.0 g. (1 mol.) of (—) + *dl*-phenylmethylcarbiny *p*-toluenesulphinate $\{[\alpha]_{5461}^{21}$ – 70.3° in ethyl alcohol (*l*, 1; *c*, 5.1); prepared from (—) + *dl*-carbinol having α_{5461}^{19} – 19.66° (*l*, 0.5)} and 6 g. (1.25 mols.) of sodium *p*-toluenesulphinate (dried to constant weight at 110°) in anhydrous formic acid (36 g., 27 mols.) was kept at room temperature for 18 days. Table IV records the variation in rotatory power of this solution. At the end of 18 days it was diluted with ethyl ether, washed with aqueous sodium carbonate and with water, and dried (calcium chloride). The solid residue left after removal of the solvent was extracted with light petroleum; the crystalline residue {2.2 g., m. p. 79–105°, $[\alpha]_{5461}^{17}$ – 5.4° in chloroform (*l*, 2; *c*, 5.01)}, after three recrystallisations from aqueous ethyl alcohol, had m. p. 100–110°, and was optically inactive in chloroform solution. After two further recrystallisations *dl-p*-tolyl- α -phenylethylsulphone (0.15 g.) was obtained, m. p. and mixed m. p. 135°. From the light petroleum extract, (—) + *dl*-phenylmethylcarbiny formate was obtained, b. p. 90.5–91°/14 mm., n_D^{20} 1.5050, α_{5461}^{21} – 0.47° (*l*, 0.236). Acidification of the sodium carbonate wash-liquor precipitated *p*-toluenesulphinic acid (2.4 g.), m. p. 86°.

(—) *Phenylmethylcarbiny Formate.*—A solution of (—)phenylmethylcarbinol [4 g., α_{5461} – 11.88° (*l*, 0.25)] in mixed formic–acetic anhydride (7 g.), after heating on the steam-bath for 90 minutes, was diluted with ether, and the solution washed with sodium bicarbonate, with water, and dried over sodium sulphate. After removal of the ether, (—)phenylmethylcarbiny formate, b. p. 88.5–89.5°/14 mm., was obtained. After redistillation, it had b. p. 87–87.5°/14 mm., n_D^{18} 1.5048, d_4^{18} 1.057, α_{6438}^{20} – 33.04°, α_{589}^{20} – 40.57°, α_{5780}^{20} – 42.66°, α_{5461}^{20} – 48.90°, α_{4358}^{20} – 88.6° (*l*, 0.236), whence $[\alpha]_{6438}^{20}$ – 132.8°, $[\alpha]_{589}^{20}$ – 163.0°, $[\alpha]_{5780}^{20}$ – 171.6°, $[\alpha]_{5461}^{20}$ – 196.5°, $[\alpha]_{4358}^{20}$ – 356.0°, yield, 4.2 g.

After standing for 11 months in a closed vessel, this formate, which then had $[\alpha]_{5461}^{20}$ – 185.0° (*l*, 0.236), was saponified by heating on the steam-bath with potassium hydroxide (1.25 mols.) in ethyl alcohol for 30 minutes. The solution was extracted with ether, and the extract washed with aqueous potassium carbonate and dried (potassium carbonate), yielding (—)phenylmethylcarbinol, b. p. 95.5–96°/15 mm., n_D^{20} 1.5271, α_{5461}^{20} – 10.90° (*l*, 0.236).

Mutarotation of (—) and (—) + dl-Phenylmethylcarbiny dl-p-Toluenesulphinate in Solution.—

(i) *In formic acid.* The (—) + *dl*-ester of $[\alpha]_{5461}^{20}$ – 84.3° (*l*, 2.0; *c*, 5.13 in ethyl alcohol), n_D^{19} 1.5703, was used. The observations of rotatory power of a solution of this ester (1.5 g.) in formic acid (5.8 g.) are given in Table III. After the last observation had been made, the solution was poured into water and extracted with ether. The extract was dried, and the ether removed. From the residue, phenylmethylcarbiny formate (0.2 c.c.) was obtained, b. p. 86°/12 mm., n_D^{18} 1.5058, leaving (—) + *dl*-phenylmethylcarbiny *p*-toluenesulphinate, n_D^{18} 1.5672, $[\alpha]_{5461}^{17}$ – 61.7° in ethyl alcohol (*l*, 2.0; *c*, 1.20).

(ii) *In acetonitrile.* (—) + *dl*-Ester of $[\alpha]_{5461}^{20}$ – 70.5° in ethyl alcohol (*l*, 2.0; *c*, 5.02), n_D^{20} 1.5740, was used. The observations of rotatory power of a solution of this ester (8.7 g.) in acetonitrile (30.2 g.) are given in Table III. 23.5 Hours after the solution was made, a portion was withdrawn, and the solvent removed by distillation, finally at 0.1 mm. The residual ester

TABLE IV.

Mutarotation of solutions of (-) and (-) + dl-phenylmethylcarbinyl p-toluenesulphinate in nitrobenzene, and in formic acid containing sodium formate and sodium p-toluenesulphinate.

[$l = 2.0$ except where otherwise indicated. t = Time (hours) after dissolution.]

(-)Ester in nitrobenzene.				(-)Ester (3.09 g.) in H·CO ₂ H (16.4 g.) with H·CO ₂ Na (2.0 g.).		(-)Ester (1.96 g.) in H·CO ₂ H (15.2 g.) and H·CO ₂ Na (1.83 g.).		(-) + dl-Ester (7.0 g.) in H·CO ₂ H (36 g.) and sodium p- toluenesulphinate (6.0 g.).	
Solution kept at 31°.									
(c, 4.80.)		(c, 17.3.)							
t .	$\alpha_{5893}^{17^\circ}$	t .	$\alpha_{5893}^{17^\circ} *$	t .	$\alpha_{5461}^{17^\circ}$	t .	$\alpha_{5461}^{19^\circ}$	t .	$\alpha_{5461}^{18^\circ}$
0.5	-4.90°	1	-2.20°	0.5	-16.79°	0.1	-12.16°	45	-8.70°
20	-4.59	18	-2.33	2.5	-16.57	2.0	-11.84	69	-7.44
43	-0.63	66	-2.34	3.75	-16.46	19.5	-10.76	95	-6.31
47	-0.46	74	-2.31			67.5	-9.45	118	-5.60
66.5	-0.18	90	-2.27			75	-9.26	165	-4.46
71.5	-0.15	120	-2.20			92	-8.93	218	-3.79
		140	-2.15			122	-8.46	310	-2.82
		165	-1.93			143	-8.19	381	-2.47
		186	-1.65			167	-7.90	434	-2.21
		234	-1.31			188	-7.58		
		288	-0.82			236	-7.32		
						289	-7.00		

* $l = 0.25$.

had $n_D^{17.5^\circ} 1.5752$, and $[\alpha]_{5461}^{18^\circ} - 70.3^\circ$ in ethyl alcohol (l , 2.0; c , 4.88). The ester recovered in the same way after 256 hours had $n_D^{17.5^\circ} 1.5740$, $[\alpha]_{5461}^{18^\circ} - 43.6^\circ$ in ethyl alcohol (l , 2.0; c , 4.88); it remained liquid when kept for 24 hours at -2° .

(iii) *In nitrobenzene.* The observations are given in Table IV. Darkening of the solution prevented observation after 288 hours. The specific rotatory power of the ester in nitrobenzene solution does not vary with concentration sufficiently to affect these results: $[\alpha]_{5893}^{17^\circ} - 51.1^\circ$ (l , 2.0; c , 4.80), $[\alpha]_{5893}^{17^\circ} - 50.5^\circ$ (l , 2.0; c , 1.02).

(iv) *In formic acid solution containing sodium formate.* The changes in rotatory power of a solution of the (-)ester in formic acid in presence of 2.5 and of 3.6 molar proportions of sodium formate are given respectively in the third and fourth sections of Table IV. The first solution after 3.75 hours was poured into water and extracted with ether, the extract washed with aqueous sodium bicarbonate, dried, (sodium sulphate), and the ether removed. The residual sulphinate gave no distillate at $130^\circ/13$ mm. It had $n_D^{19^\circ} 1.5703$, and $[\alpha]_{5461}^{20^\circ} - 84.3^\circ$ in ethyl alcohol (l , 2.0; c , 5.130).

(v) *In formic acid containing sodium p-toluenesulphinate.* Table IV gives the change in rotatory power of the solution, the preparation of which is described above.

(vi) *In ether containing potassium carbonate.* The (-) + dl-ester {1.76 g., $[\alpha]_{5461}^{20^\circ} - 70.5^\circ$ in ethyl alcohol (l , 2.0; c , 5.02); $n_D^{20.5^\circ} 1.5740$ } in solution in ether (9.8 g.) with potassium carbonate (0.7 g.) was observed polarimetrically (l , 2.0). The original rotation, $\alpha_{5461}^{17^\circ} - 21.52^\circ$, was maintained, the value after 20 days being $\alpha_{5461}^{18^\circ} - 21.26^\circ$. Ether was then removed from the filtered solution, finally at 0.1 mm., yielding (-) + dl-ester having $n_D^{19^\circ} 1.5753$, $[\alpha]_{5461}^{19^\circ} - 70.8^\circ$ in ethyl alcohol (l , 2.0; c , 4.775).

The formic acid used in these experiments was prepared from the 98–100% acid by repeated solidification and partial liquefaction, the fluid being rejected.

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122. The Condensation of *p*-Toluenesulphinic Acid and its Esters with Acetone.

By C. L. ARCUS and J. KENYON.

p-Toluenesulphinic acid and its esters condense with acetone to produce *p*-tolyl- β -(β -methylpentan- δ -onyl)sulphone (I) and evidence supporting this formulation of the condensation product is given. Further evidence is adduced that the condensation proceeds, not by an exchange of carbonium kations, but probably by a rearrangement of diacetonyl *p*-toluenesulphinate which results from alcoholysis of the sulphinic esters by the diacetonyl alcohol present in the equilibrium mixture.

DURING an investigation of the molecular rearrangement of phenylmethylcarbinyll *p*-toluenesulphinate (Arcus, Balfe, and Kenyon, this vol., p. 485) the condensation of this ester, and also of β -octyl *p*-toluenesulphinate, with acetone was observed; it was known from a previous unpublished investigation in this laboratory that ethyl *p*-toluenesulphinate and *p*-toluenesulphinic acid condense with acetone. These observations have been correlated and are now presented.

From a solution of *p*-toluenesulphinic acid in acetone there separates, after heating, a compound, m. p. 94°, which has been identified as *p*-tolyl- β -(β -methylpentan- δ -onyl)sulphone (I) on the following evidence. It contains no free hydroxyl group, since it does not undergo acetylation, but contains a carbonyl group, since it furnishes a *semicarbazone*, from which the original ketone is regenerated by hydrolysis. It is a sulphone and not a sulphinic ester, since it is not oxidised by perhydrol, a reagent which converts sulphinates into sulphonates. It may be oxidised with acid permanganate solution, but the only product isolable is *p*-sulphobenzoic acid.

Decomposition with aqueous alkali yields *p*-toluenesulphinic acid and mesityl oxide, the latter indicating the nature of the aliphatic portion of the molecule.

Finally this compound may be synthesised by the slow condensation of *p*-toluenesulphinyl chloride with diacetone alcohol:

The sulphinic esters do not condense with acetone nearly so readily as the free acid, since di-*p*-tolyl disulphoxide is the only isolable product after ethyl *p*-toluenesulphinate has been heated in acetone solution. On prolonged keeping at room temperature of solutions in acetone of ethyl, β -octyl, and phenylmethylcarbinyll *p*-toluenesulphinates, however, condensation to *p*-tolyl- β -(β -methylpentan- δ -onyl)sulphone occurs. The alcohols displaced in the last two cases have been isolated.

In view of the last result, and also of the non-formation either of olefinic compounds or of ethyl-, β -octyl-, and α -phenylethyl-sulphones, dissociation of the sulphinic esters to give carbonium kations is improbable, *e.g.*,

also

In the presence of a constant equilibrium proportion of diacetone alcohol, alcoholysis of the sulphinic esters will occur, without rupture of the O-R bond; such alcoholyses have been observed for (—) phenylmethylcarbinyll *p*-toluenesulphinate (Kenyon and Phillips, J., 1930, 1676) and for ethyl *p*-toluenesulphinate by *l*- β -octyl alcohol (Phillips, J., 1925, 127, 2552). The *p*-toluenesulphinic ester of diacetone alcohol first produced can then undergo rearrangement into *p*-tolyl- β -(β -methylpentan- δ -onyl)sulphone, as it appears to do during the synthesis of this substance from diacetone alcohol and *p*-toluenesulphinyl chloride.

EXPERIMENTAL.

The Interaction of Ethyl p-Toluenesulphinate and Acetone.—(a) *At the ordinary temperature.* A solution of ethyl *p*-toluenesulphinate (17 g.) in acetone (75 c.c.) was kept in a closed vessel for 5 years. On evaporation of the solution, crystalline leaflets (23.3 g.), m. p. 72–75°, separated, which after recrystallisation from ether had m. p. 94° (Found: C, 61.6; H, 7.3; S, 13.3. $C_{13}H_{18}O_3S$ requires C, 61.4; H, 7.1; S, 12.6%).

(b) *At higher temperatures.* A solution of ethyl *p*-toluenesulphinate (3 g.) in acetone (15 c.c.) was heated under reflux for an hour and then kept at the ordinary temperature for several days. The crystals (0.8 g.) which separated consisted entirely of di-*p*-tolyl disulphoxide, m. p. 76°.

The Interaction of dl-Phenylmethylcarbiny l p-Toluenesulphinate and Acetone.—A solution of *dl*-phenylmethylcarbiny l *p*-toluenesulphinate (7.5 g.) in acetone (25 g.) was kept at the ordinary temperature for 7 months. On evaporation, crystals separated, which had m. p. 87–90° (2.6 g.) after washing with light petroleum, m. p. 94° after recrystallisation from benzene (Found: S, 12.2%), and furnished the semicarbazone, m. p. 173° (decomp.), by the method described below. The light-petroleum wash-liquor yielded phenylmethylcarbinol (1 g.), b. p. 70°/20 mm., n_D^{20} 1.5243.

The Interaction of dl-β-Octyl p-Toluenesulphinate and Acetone.—A solution of *dl*-β-octyl *p*-toluenesulphinate (5 g.) in acetone (30 c.c.) was kept for 6 months. The crystalline residue obtained on evaporation was washed with ethyl alcohol and recrystallised, yielding colourless plates (2.0 g.), m. p. 94° alone and when mixed with the product of the condensation of *dl*-phenylmethylcarbiny l *p*-toluenesulphinate with acetone. The substance furnished the semicarbazone, m. p. 172° (decomp.). From the alcoholic wash-liquor, *dl*-β-octyl alcohol (1 g.), b. p. 81°/20 mm., n_D^{20} 1.4285, was obtained.

The Interaction of p-Toluenesulphinic Acid and Acetone.—A solution of *p*-toluenesulphinic acid (7 g.) in dry acetone (30 c.c.) was gently heated for 1 hour and then allowed to evaporate at the ordinary temperature; crystals separated which, after washing with sodium carbonate solution and recrystallisation from ether, had m. p. 94° (4.8 g.).

p-Tolyl-β-(β-methylpentan-δ-onyl)sulphone.—The compound, m. p. 94°, which separated during the above reactions is assigned the structure of *p*-tolyl-β-(β-methylpentan-δ-onyl)sulphone and undergoes the following reactions.

It is slightly soluble in boiling water, from which, on cooling, it crystallises in leaflets. It separates unchanged from a warm solution in acetic anhydride, and is unaffected by perhydrol in acetone solution. It is oxidised by potassium permanganate in warm acetic acid solution, but the only product which could be isolated was *p*-sulphobenzoic acid, m. p. 257–259° (decomp.).

The compound (3 g.) was added to sodium carbonate (1 g.) in aqueous solution and the distillate obtained on passing a current of steam was warmed with semicarbazide hydrochloride (2 g.) and sodium carbonate (1 g.); on cooling, crystals (0.75 g.), m. p. 156°, of mesityl oxide semicarbazone separated. From the residual liquor of the steam distillation, on acidification, *p*-toluenesulphinic acid (1.7 g.), m. p. 86°, was obtained.

The compound (5 g.), when heated in aqueous alcoholic solution with semicarbazide hydrochloride (5 g.) and sodium acetate (4.2 g.), furnished leaflets (5.0 g.), which on recrystallisation from hot alcohol yielded the semicarbazone of *p*-tolyl-β-(β-methylpentan-δ-onyl)sulphone, m. p. 173° (decomp.) (Found: C, 53.4; H, 6.8; S, 9.9. $C_{14}H_{21}O_3N_3S$ requires C, 54.0; H, 6.8; S, 10.3%).

This semicarbazone is unaffected by hot aqueous alcoholic solutions of either oxalic acid or sodium hydroxide, but is rapidly hydrolysed on dissolution in cold concentrated hydrochloric acid, from which crystals, m. p. 94° alone or mixed with the original compound, separate after a few seconds.

Preparation of p-Tolyl-β-(β-methylpentan-δ-onyl)sulphone from Diacetone Alcohol and p-Toluenesulphiny l Chloride.—*p*-Toluenesulphiny l chloride (9.0 g.) was added in portions to an ice-cold mixture of diacetone alcohol (5.8 g.) and pyridine (4.5 g.), and the whole kept at the ordinary temperature for 5 weeks. The solid product was then triturated with dilute hydrochloric acid and recrystallised from ether, forming leaflets (5.0 g.), m. p. 94° alone or when mixed with the compound obtained by the interaction of acetone and ethyl *p*-toluenesulphinate.

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127. Reduction of the Carbonyl Group in Unsaturated Ketones, and the Interconversion of Geometrical Isomerides during such Reduction.

By C. L. ARCUS and J. KENYON.

The unsaturated ketone *n*-butylideneacetone is reduced by aluminium isopropoxide to α -methyl- γ -*n*-propylallyl alcohol without simultaneous etherification or reduction of the double bond. Since both the *cis*- and the *trans*-form of the ketone yield identical products, this reagent appears to facilitate interconversion of geometrical isomerides.

DURING an experimental study of the reactions of *n*-propylpropenylcarbinol (Arcus and Kenyon, this vol., p. 312), the preparation of dl- α -methyl- γ -*n*-propylallyl alcohol (I) became

desirable. It has now been prepared by the reduction of *n*-butylideneacetone (II), the *cis*- and *trans*-forms of which were described by Eccott and Linstead (J., 1930, 905). The *cis*-form was prepared by condensing *n*-butaldehyde with acetone and allowing the (exothermic) reaction to proceed unchecked. The slow addition of *n*-butaldehyde to a cooled mixture of acetone and alkali yields the ketol $\text{CHPr}^a(\text{OH})\cdot\text{CH}_2\cdot\text{COMe}$, which, on dehydration with anhydrous oxalic acid gives the *trans*-form of (II). These isomerides have different physical constants and yield different semicarbazones.

Reduction was effected with a solution of aluminium isopropoxide in isopropyl alcohol by the Ponndorf-Meerwein method (Meerwein and Schmidt, *Annalen*, 1925, 444, 221;

Ponndorf, *Z. angew. Chem.*, 1926, 39, 138): Lund (*Ber.*, 1937, 70, 1520) has shown that, by this method, unsaturated ketones yield mainly the isopropyl ethers of the unsaturated alcohols initially produced. In the present instance the reaction was stopped as soon as the evolution of acetone had markedly diminished, and although some polymerisation was observed, neither the isopropyl ether nor the saturated alcohol was encountered.

From the product of reduction of the *cis*- and of the *trans*-isomeride of the ketone it was possible in each case to isolate—by means of the hydrogen phthalic ester—only one, and the same, alcohol. Since Eccott and Linstead (*loc. cit.*) found the isomeric ketones strongly resistant to configurative change and to yield high-boiling products with alkaline catalysts, it appears very probable that interconversion of geometrical isomerides occurs at the stage when the alcohols exist as aluminium alkoxides.

The identity of α -methyl- γ -*n*-propylallyl alcohol was demonstrated by catalytic reduction to methyl-*n*-amylcarbinol.

EXPERIMENTAL.

Reduction of cis-n-Butylideneacetone.—The crude ketone, b. p. 71–77°/16 mm., prepared by the method of Eccott and Linstead (*loc. cit.*), was dried by addition of an equal volume of dry benzene and removal of the latter by distillation through a column; the remaining ketone had b. p. 80°/27 mm. By the special procedure of Eccott and Linstead it furnished a semicarbazone having, after three recrystallisations from aqueous alcohol, m. p. 155°.

This material (132 g.) was added to a solution of aluminium isopropoxide in isopropyl alcohol (3N, 620 c.c.; prepared by the procedure of Lund, *loc. cit.*), and the mixture heated on a steam-bath in a flask fitted with a return condenser through which water at 65–70° was circulated; acetone distilled over, but the isopropyl alcohol was returned. After 4 hours the excess of isopropyl alcohol was removed under diminished pressure, and the residue decomposed with ice and dilute sulphuric acid. From an ethereal extract, washed, and dried with potassium carbonate, the crude alcohol, b. p. 69°/17 mm., was obtained. This (39 g.) was heated with a suspension of phthalic anhydride (51 g.) in pyridine (27 g.) at 60–70° for 2 hours, and the cooled product extracted with dilute aqueous ammonia. Extraction of the acidified ammoniacal solution with ether yielded a crystalline product (73 g.), which after two crystallisations from light petroleum gave dl- α -methyl- γ -*n*-propylallyl hydrogen phthalate in needles, m. p. 67° (Found, by titration with NaOH: *M*, 262. $\text{C}_{15}\text{H}_{18}\text{O}_4$ requires *M*, 262).

dl-α-Methyl-γ-n-propylallyl alcohol. Steam was passed through a solution of the hydrogen phthalic ester (16 g.) and sodium hydroxide (5.4 g.) in water (27 c.c.); extraction of the distillate yielded the *alcohol*, b. p. 66–67°/16 mm., n_D^{18} 1.4391, d_4^{17} 0.834 (Found: C, 73.8; H, 12.4. $C_7H_{14}O$ requires C, 73.6; H, 12.4%). Its *p-nitrobenzoate*, formed by adding *p*-nitrobenzoyl chloride (1.6 g.) to a solution of the alcohol (1.0 g.) in pyridine (0.7 g.) and after an interval heating the mixture at 60° for an hour, separated from light petroleum in plates, m. p. 29.5° (Found: C, 64.6; H, 6.6. $C_{14}H_{17}O_4N$ requires C, 63.8; H, 6.5%). Its *p-xenylurethane*, prepared by heating a mixture of the alcohol (1.2 g.) with *p*-xenylcarbimide (2.0 g.) on the steam-bath for an hour, separated from ether-light petroleum in needles, m. p. 87° (Found: C, 77.4; H, 7.35. $C_{20}H_{23}O_2N$ requires C, 77.7; H, 7.5%).

Reduction of trans-n-Butylideneacetone.—The ketol (heptan-δ-ol-β-one), prepared according to Eccott and Linstead (*loc. cit.*), b. p. 99°/15 mm., was dehydrated with anhydrous oxalic acid, and the resulting *trans-n*-butylideneacetone, b. p. 61–63°/12 mm., dried by the method described above. It furnished, by the procedure indicated above, a semicarbazone having, after three recrystallisations, m. p. 126°, not increased by further recrystallisation. This material (160 g.), reduced in the same manner as the *cis*-isomeride, yielded the crude alcohol, b. p. 64°/14 mm. This was converted into its hydrogen phthalic ester (100 g.) which, after recrystallisation from light petroleum, formed needles, m. p. 67° alone or when mixed with the hydrogen phthalate of the alcohol obtained by the reduction of the corresponding *cis*-ketone.

Reduction of dl-α-Methyl-γ-n-propylallyl Alcohol to dl-Methyl-n-amylcarbinol.—The alcohol (3.3 g.) in ether (24 c.c.) was reduced with hydrogen at 2 atm., in the presence of the platinum catalyst of Adams, Voorhees, and Shriner ("Organic Syntheses," 8, 92). The solution yielded *dl*-methyl-*n*-amylcarbinol, b. p. 64–65°/13 mm., n_D^{17} 1.4226; the hydrogen phthalate had m. p. 57.5° (Pickard and Kenyon, J., 1911, 99, 45, recorded b. p. 73.5°/20 mm., n_D^{20} 1.4209; *dl*-hydrogen phthalic ester, m. p. 57–58°).

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**360. The Mechanism of Replacement Reactions in Allyl Compounds :
Reactions of (+)-n-Propylpropenylcarbinol and its Derivatives.**

By C. L. ARCUS and J. KENYON.

From a study of the replacement reactions of the hydrogen phthalic ester and of the chloride of (+)-n-propylpropenylcarbinol, it is concluded that the reactions

proceed *via* dissociation into the ion $\text{CHMe}\cdot\overset{\oplus}{\text{CH}}\cdot\text{CHPr}$, leading to racemisation and isomerisation. Two general mechanisms of substitution reactions in allyl compounds are formulated from a consideration of results now, and previously, reported, and their stereochemical consequences considered.

An explanation of the behaviour on saponification of the hydrogen phthalic esters of substituted allyl alcohols, which is normal in alkaline, abnormal in neutral solutions, is suggested.

SEVERAL investigations on the isomerisation occurring during replacement reactions of substituted allyl alcohols have been described (Prévost, *Compt. rend.*, 1927, 185, 1283 ;

Meisenheimer and Beutter, *Annalen*, 1934, 508, 58; Burton, J., 1928, 1650; Young and Lane, *J. Amer. Chem. Soc.*, 1938, 60, 847). The study of such reactions by the use of optically active substituted allyl alcohols was initiated by Hills, Kenyon, and Phillips (on $\alpha\gamma$ -dimethylallyl alcohol; J., 1936, 576) and was extended to those of derivatives of (–)- α -phenyl- γ -methylallyl alcohol by Kenyon, Partridge, and Phillips (J., 1937, 207).

The pronounced loss of optical purity is a striking feature of these reactions. Hills, Kenyon, and Phillips observed the following replacements (in course of publication) :

		Optical purity, %.
$\begin{array}{c} \text{(+)-CHMe}\cdot\text{CH}\cdot\text{CHMe} \\ \\ \text{CO}_2\text{H}\cdot\text{C}_6\text{H}_4\cdot\text{CO}\cdot\text{O} \end{array}$	$\xrightarrow{\text{H}\cdot\text{CO}_2\text{H}}$	$\text{CHMe}\cdot\text{CH}\cdot\text{CHMe}\cdot\text{O}\cdot\text{CHO} \dots\dots\dots 0\cdot7$
	$\xrightarrow{\text{AcOH}}$	$\text{CHMe}\cdot\text{CH}\cdot\text{CHMe}\cdot\text{OAc} \dots\dots\dots 0\cdot8$
	$\xrightarrow{\text{MeOH}}$	$\text{CHMe}\cdot\text{CH}\cdot\text{CHMe}\cdot\text{OMe} \dots\dots\dots 6\cdot0$
	$\xrightarrow{\text{O}}$	$\text{CHMe}\cdot\text{CH}\cdot\text{CHMe}\cdot\text{OBu}^a \dots\dots\dots 8\cdot0$
		1912

and Kenyon, Partridge, and Phillips (*loc. cit.*) the following:

The difficulty in interpreting the mechanism of replacement reactions of $\alpha\gamma$ -dimethylallyl derivatives is enhanced by the fact that, owing to the symmetrical character of the molecule, α and γ entrances yield the same chemical product, and the question as to whether entrance into the γ -position results in the formation of an optically active derivative cannot be settled.

The replacement reactions of derivatives of the less symmetrical (+)-*n*-propylpropenylcarbinol have now been examined; the resolution of this alcohol and the optical rotatory powers of its derivatives have already been reported (Arcus and Kenyon, this vol., p. 312). The production of an optically active derivative by entrance of the substituent group into the γ -position may be detected in this case by catalytic reduction of the reaction product, whereupon that optical activity due to a *n*-propylpropenylcarbinyl derivative is removed (owing to the production of a symmetrical di-*n*-propylcarbinyl derivative) whilst any optical activity due to a derivative of α -methyl- γ -*n*-propylallyl alcohol will persist as the optical activity of a methyl-*n*-amylcarbinyl derivative.

In view of the possibility of encountering the derivatives of α -methyl- γ -*n*-propylallyl alcohol, a knowledge of this compound was desirable, and its preparation and properties have been described (Arcus and Kenyon, this vol., p. 698). It was not found possible efficiently to separate mixtures of the isomeric alcohols, *n*-propylpropenylcarbinol and α -methyl- γ -*n*-propylallyl alcohol, which were the products of replacement reactions of certain derivatives of the former compound. Mixtures of the *p*-xenylurethanes, the *p*-nitrobenzoates, and the hydrogen phthalic esters underwent but little separation on recrystallisation; the hydrogen phthalic esters of the corresponding reduced alcohols, di-*n*-propylcarbinol and methyl-*n*-amylcarbinol, also are not readily separable. Estimation, by physical means, of the composition of a mixture of the unsaturated alcohols is also not possible owing to the similarity of the constants of these isomerides.

	B. p.	$n_D^{18^\circ}$	$d_4^{18^\circ}$
<i>n</i> -Propylpropenylcarbinol	64°/15 mm.	1.4381	0.839
α -Methyl- γ - <i>n</i> -propylallyl alcohol	66°/16 mm.	1.4391	0.833

These considerations led to the adoption of the following procedure for the investigation of the product of a given reaction of (+)-*n*-propylpropenylcarbinyl hydrogen phthalate or of (–)- Δ^8 -8-chloroheptene. The product, which is referred to as a heptenyl derivative, was isolated as a constant-boiling fraction having physical constants in agreement with those of the corresponding pure *n*-propylpropenylcarbinyl derivative; after its rotatory power had been determined, the product was reduced with hydrogen at 2 atm. in the presence of either nickel or platinum catalyst, and the rotatory power of the reduced product was determined.

The results of replacement reactions of (+)-*n*-propylpropenylcarbinyl hydrogen phthalate with acetic, formic, and benzoic acids are given in Table I.

The optical result of these reactions is seen to be complete, or almost complete, racemisation. Moreover, when the acetate was reduced, the product was optically inactive. In no case therefore is an optically active derivative of α -methyl- γ -*n*-propylallyl alcohol formed, and hence no asymmetry is transferred to the C' atom. [Had such an optically active derivative been formed, the methyl-*n*-amylcarbinyl derivative obtained on re-

duction would certainly possess a sufficiently high rotatory power for detection; for the alcohol has $[\alpha]_{5893} + 10.32^\circ$ (homogeneous) (Pickard and Kenyon, J., 1911, **99**, 45; 1914, **105**, 830), and the acetate has $[\alpha]_{5893} + 5.02^\circ$ in ethyl alcohol.]

Hence, such optical activity as is shown by a product of the replacement reaction is due to a derivative of *n*-propylpropenylcarbinol. Comparison of the rotatory power of the acetate derived from the replacement reaction in Table I with the acetate prepared by the action of acetic anhydride on (+)-*n*-propylpropenylcarbinol shows that the former has been produced with inversion of configuration and has 0.2% of the maximum recorded

TABLE I.

Replacement Reactions of (+)-*n*-Propylpropenylcarbinyl Hydrogen Phthalate.

(+)-Hydrogen phthalate: $[\alpha]_{5461}$ in EtOH.	Optical purity, %.	Reaction mixture.	Temp.	Product, and optical properties.
+15.8°	69	H.P.,* 5 g. CH ₃ ·CO ₂ H, 20 g.	32°	Acetate, $\alpha_{5461} + 0.05^\circ$ (<i>l</i> , 0.5) = 0.2% of maximum; hence, inversion = 0.3%
+9.77	43	H.P., 11 g. H·CO ₂ H, 4 g.	80	<i>dl</i> -Formate
+7.8	34	H.P., 20 g. Ph·CO ₂ H, 27 g.	125	<i>dl</i> -Benzoate

* H.P. = Hydrogen phthalate.

rotatory power. This reaction proceeded slowly (the time for one-half total change in rotation being 317 hours) and was followed polarimetrically (Table III). The benzoate obtained in the last experiment in Table I was saponified with alcoholic potash, and the resultant heptenol converted into the *p*-xeny lurethane, which was found to be a mixture.

(-)- Δ^8 - δ -Chloroheptene was prepared by adding (+)-*n*-propylpropenylcarbinol mixed with pyridine to cooled phosphorus trichloride; since the last reagent, in the presence of pyridine, is believed to react invariably with inversion (Frankland, J., 1913, **103**, 713; Hughes, Ingold *et al.*, J., 1937, 1252), the chloride obtained will possess a configuration opposite to that of the carbinol.

The results of replacement reactions with water, methyl alcohol, and the acetate ion are given in Table II. Reduction of the first two products afforded optically inactive substances (λ_{5461}).

The optical results of the replacement reactions of the chloro-compound are similar to those of the hydrogen phthalic ester. (1) There is much, or complete, racemisation.

TABLE II.

Replacement Reactions of (-)- Δ^8 - δ -Chloroheptene.

Rotation of original alcohol.	Optical purity, %.	Rotation of chloride.	Reaction mixture.	Temp.	Product, and optical properties.
$\alpha_{5461}^{20^\circ} + 4.10^\circ$ (<i>l</i> , 0.5)	95	$\alpha_{5461}^{22^\circ} - 1.68^\circ$ (<i>l</i> , 0.5)	Chloride, 4.2 g. Na ₂ CO ₃ , 2.3 g. H ₂ O, 45 g.	65°	Carbinol, $\alpha_{5461}^{23^\circ} + 0.04^\circ$ (<i>l</i> , 0.24) = 2% opt. pure; hence inversion = 2%
$\alpha_{5461}^{16.5^\circ} - 5.44^\circ$ (<i>l</i> , 2.0)	30	$\alpha_{5461}^{16^\circ} + 0.59^\circ$ (<i>l</i> , 0.5)	Chloride, 6.3 g. K ₂ CO ₃ , 6.3 g. MeOH, 12.6 g.	80	Methyl ether, $\alpha_{5461}^{12^\circ} + 0.09^\circ$ (<i>l</i> , 0.5) = 0.38% opt. pure; hence inversion = 1.3%
$\alpha_{5461}^{16.5^\circ} - 5.44^\circ$ (<i>l</i> , 2.0)	30	$\alpha_{5461}^{21^\circ} + 0.48^\circ$ (<i>l</i> , 0.5)	Chloride, 6.1 g. NaOAc, 5.5 g. HOAc, 14.4 g.	65	<i>dl</i> -Acetate

(2) In no case is the reduced product optically active, whence no optically active derivative of α -methyl- γ -*n*-propylallyl alcohol is produced and no asymmetry is transferred to the C γ atom. (3) Again, the whole of the optical activity is due to derivatives of *n*-propylpropenylcarbinol. The fact that the chloride is produced from the alcohol with inversion of configuration, together with a comparison of the sign and magnitude of the rotatory powers of the alcohol and the methyl ether produced in the first two reactions in Table II with those of the (+)alcohol and the methyl ether prepared from the (+)alcohol (by a method which

does not disturb the bonds of the asymmetric carbon atom), leads to the following conclusions. In the first reaction the carbinol is produced from the chloride with inversion of configuration and has 2% of the maximum rotatory power; in the second reaction the chloride undergoes alcoholysis to the methyl ether with inversion of configuration, and the ether has 1.3% of its maximum rotatory power.

An undetermined part of this great loss of optical activity occurs during the conversion of the alcohol into the chloride. The rotatory power of the latter is, however, of the same order as that of the alcohol from which it is derived, whereas the products of replacement reactions of the chloride possess rotatory powers of an order lower than that of the chloride. It is therefore likely that the bulk of the racemisation occurs during the reactions of the chloride, and not during its preparation.

The first experiment in Table II was repeated with the *dl*-chloride, a portion of the resultant heptenol being converted into the hydrogen phthalate, and a second portion reduced to the saturated alcohol, which was converted into its hydrogen phthalic ester. Both these hydrogen phthalates were mixtures. Under the conditions employed for the third reaction in Table II, it was found that the chloride does not react to an appreciable extent with the solvent, acetic acid.

From a study of the molecular rearrangement of (–)-phenylmethylcarbinyl *dl*-p-toluenesulphinate (Arcus, Balfe, and Kenyon, this vol., p. 485), it was concluded that a free carbonium kation ($\text{CHMePh}^{\oplus}$) was liberated during this rearrangement, and that this kation possesses an effectively planar configuration; the dissociation into this kation is facilitated by a medium of high dielectric constant, and by solvation, in particular by hydroxylic solvents. The latter condition was present in all the above experiments, the solvents being water, methyl alcohol, and carboxylic acids. In view of the racemisation and isomerisation occurring during the replacement reactions of the hydrogen phthalic ester and the chloride of (+)-*n*-propylpropenylcarbinol, it may therefore be postulated

that the carbonium kation $\text{CHMe}\cdot\text{CH}\cdot\text{CHPr}^{\oplus}$, which is effectively planar, is an intermediate in these reactions. Such an ion will lead to the formation of racemic products, and afford the possibility of entry by the substituent group at either the C^{α} or the C^{γ} atom, yielding a mixture of heptenyl derivatives.

Similar carbonium kations have been postulated by Prévost (*loc. cit.*) as intermediates in a number of reactions of compounds $\text{CHR}\cdot\text{CH}\cdot\text{CH}_2\text{X}$ and $\text{CHRX}\cdot\text{CH}\cdot\text{CH}_2$ during which isomerisation leading to a mixed product occurs. Young and Lane (*loc. cit.*) conclude from a study of the reaction of hydrogen bromide under defined conditions with crotyl alcohol, $\text{CHMe}\cdot\text{CH}\cdot\text{CH}_2\cdot\text{OH}$, and methylvinylcarbinol, $\text{CHMe}(\text{OH})\cdot\text{CH}\cdot\text{CH}_2$, that the major part of the reaction of each alcohol occurs *via* the common resonating ion

$\text{CHMe}\cdot\text{CH}\cdot\text{CH}_2^{\oplus}$, yielding mixtures of the bromides $\text{CHMe}\cdot\text{CH}\cdot\text{CH}_2\text{Br}$ and $\text{CHMeBr}\cdot\text{CH}\cdot\text{CH}_2$. The difference (up to 12%) in composition of the mixtures of bromides from the two alcohols is attributed to subsidiary bimolecular substitutions whereby each alcohol yields the corresponding bromide.

The reactions recorded in Tables I and II are accompanied by up to 2% inversion of configuration at the C^{α} atom. This may arise from a subsidiary mechanism of substitution in which the substituent group becomes attached to the asymmetric carbon atom before the dissociation of the displaced group, leading to a Walden inversion (Kenyon and Phillips, *Trans. Faraday Soc.*, 1930, 26, 451). Alternatively, during the above dissociation into a carbonium kation, the receding anion may shield that side of the carbon atom to which it was attached from the attacking molecules or ions, causing a small preponderance of the inverted configuration (Hughes, Ingold, *et al.*, J., 1937, 1252). It may be noted that the stereochemical consequences assigned by those authors to the two mechanisms of substitution denoted $\text{S}_{\text{N}}1$ and $\text{S}_{\text{N}}2$ do not, in such cases, furnish unequivocal information about the mechanism of a reaction from its stereochemical result; a replacement reaction accompanied by extensive racemisation may occur either by $\text{S}_{\text{N}}1$ or by a preponderating $\text{S}_{\text{N}}1$ mechanism with subsidiary $\text{S}_{\text{N}}2$.

A replacement reaction in an allyl compound has been studied kinetically by Meisenheimer and Beutter (*loc. cit.*). For the reaction of cinnamyl chloride with potassium acetate they found that (a) in acetic anhydride solution the reaction is approximately of the second order with regard to $[\text{CHPh}\cdot\text{CH}\cdot\text{CH}_2\text{Cl}]$ and $[\text{KOAc}]$, and cinnamyl acetate only is produced; (b) in acetic acid solution the reaction is intermediate between first and second order and the product is a mixture of cinnamyl acetate and phenylvinylcarbinyl acetate. A mechanism involving a termolecular reaction (one molecule being that of activated solvent) was proposed. The facts receive an alternative explanation if the reaction is regarded as proceeding by two courses. The first, involving slow preliminary ionisation followed by combination with acetate ion:

will be kinetically of the first order, and the kation $\overline{\text{CHPh}\cdot\text{CH}\cdot\text{CH}_2}^{\oplus}$ will permit the formation of a mixed product of cinnamyl and phenylvinylcarbinyl acetates.

The second course requires attack by the acetate ion on a molecule of cinnamyl chloride, is bimolecular, and should yield cinnamyl acetate only:

(These mechanisms are essentially those developed generally by Hughes and Ingold, J., 1935, 244, and designated $\text{S}_{\text{N}}1$ and $\text{S}_{\text{N}}2$.)

In the non-hydroxylic medium, acetic anhydride, the solvation necessary for ionisation does not appear to occur, and the reaction follows the second course. In acetic acid the first mechanism becomes effective, the kinetics approach towards the first order, and a mixture of acetates is produced.

It thus appears that the replacement reactions of substituted allyl compounds may be represented generally by a combination of two such mechanisms:

the first (unimolecular) leading to an equilibrium mixture of allyl isomers, and stereochemically, to much racemisation; the second (bimolecular) resulting in one product and a high degree of inversion of configuration about the C^{α} atom. The relative importance of these two mechanisms will be determined by the nature of the medium and reagent and the groups R_1 and R_2 .

The liberation of the anion $\text{X}^{\ominus}$ in the above reactions is facilitated by the tautomeric (+ T) effect of the allyl group. Further, in those compounds in which R_1 is an alkyl group (*e.g.*, α - γ -dimethylallyl alcohol, α -phenyl- γ -methylallyl alcohol, and n -propylpropenylcar-

binol), the latter contributes a favourable inductive effect: $\text{Me} \rightarrow \text{CH}=\text{CH}\text{—}\overline{\text{CHR}_2\text{—X}}$.

Compounds in which R_2 is the phenyl group are less stable than the isomers in which this group occupies the position R_1 , the former passing into the latter (Burton, *loc. cit.*; Kenyon, Partridge, and Phillips, *loc. cit.*). The last authors, from a study of the facile rearrangement of α -phenyl- γ -methylallyl derivatives into those of γ -phenyl- α -methylallyl alcohol, concluded that the migrating anions are not kinetically free, since there is a high retention of asymmetry; also, the rearrangement is not markedly promoted by increasing dielectric constant of the medium, and the change was found to proceed at ordin-

ary temperatures in the solid state in a single crystal of the hydrogen phthalic ester. The great ease with which this rearrangement proceeds appears to be due to the addition of the tautomeric (+ *T*) effect of the phenyl group to the electromeric effects already mentioned: $\text{Me} \rightarrow \text{CH}=\text{CH}-\text{CH}-\text{Ph}$. The α -phenylallyl esters (in which a γ -alkyl

group is absent) also rearrange into their cinnamyl isomers (Burton, *loc. cit.*), but less readily than do the corresponding α -phenyl- γ -methylallyl compounds (Duveen, *Compt. rend.*, 1938, 206, 1185).

Since an alkyl radical cannot supply the tautomeric (+ *T*) effect of the phenyl nucleus, rearrangements similar to the above should proceed much less readily amongst the purely aliphatic allyl compounds. This accords with the following observations: on heating *dl*- α -phenyl- γ -methylallyl hydrogen phthalate (with an equal weight of pyridine), and the *dl*-*p*-nitrobenzoate (alone), on the steam-bath for 1 and 2½ hours, respectively, these esters were very largely converted into the *dl*- γ -phenyl- α -methylallyl isomerides (Kenyon, Partridge, and Phillips, *loc. cit.*). After similar treatment, the hydrogen phthalic esters and *p*-nitrobenzoates of the isomeric *n*-propylpropenylcarbinol and α -methyl- γ -*n*-propylallyl alcohol were recovered unchanged.

Change Undergone by (+)-n-Propylpropenylcarbinyl dl-p-Toluenesulphinate.—On adding *p*-toluenesulphinyl chloride to a cooled solution of (–)-*n*-propylpropenylcarbinol in pyridine, the (+)-*p*-toluenesulphinic ester is obtained by a method which does not involve rupture of a bond of the asymmetric carbon atom. On standing, the homogeneous ester undergoes a spontaneous change into a non-saponifiable substance with accompanying racemisation. This substance is presumed to be a sulphone, but repeated attempts failed to isolate a pure material. Specimens of the *dl*- and of the (+)-esters were maintained at 32°, the fall in saponification value was followed by periodic determinations with alcoholic potassium hydroxide, and the rotation of the (+)-ester was also observed. The apparent ester content and the rotatory power fall concurrently after a period of induction.

Racemisation occurring during Saponification of the Hydrogen Phthalic Esters of Substituted Allyl Alcohols.—It was found by Hills, Kenyon, and Phillips (*loc. cit.*) that, by saponification of optically pure (+)- $\alpha\gamma$ -dimethylallyl hydrogen phthalate with 5*N*-sodium hydroxide, the optically pure alcohol was obtained; but that saponification in aqueous sodium acetate and carbonate gave the racemic alcohol. Further, when saponified with aqueous sodium carbonate, (+)- γ -phenyl- α -methylallyl hydrogen phthalate yielded the *dl*-alcohol, but saponification with 5*N*-sodium hydroxide, or with 2·5*N*-aqueous-alcoholic sodium hydroxide gave the (+)alcohol in a state approaching optical purity; less concentrated solutions of sodium hydroxide caused increasing racemisation (Kenyon, Partridge, and Phillips, J., 1936, 85). (+)-*n*-Propylpropenylcarbinyl hydrogen phthalate on saponification with 5*N*-sodium hydroxide gave the (+)alcohol, which was reconverted into its hydrogen phthalic ester having 93% of its original rotatory power. On saponification in aqueous sodium acetate, the (+)hydrogen phthalic ester gave an optically inactive heptenol; its *p*-xeny lurethane proved to be a mixture.

At some stage during the saponification with sodium acetate it appears likely that the carbonium kation $\overline{\text{CHR}_1\cdot\text{CH}\cdot\text{CHR}_2}$ has been liberated, leading to racemisation and permitting isomerisation; it appears also that this ion was not liberated during saponification with sodium hydroxide. That the ion might arise by dissociation of the liberated alcohol is intrinsically unlikely, and Kenyon, Partridge, and Phillips (*loc. cit.*, 1937) have observed that the easily isomerised α -phenyl- γ -methylallyl alcohol is stable in the presence of strong and weak alkali. An explanation is suggested according to which the hydrogen phthalic ester is regarded as an *o*-substituted benzoic ester which follows different courses of saponification according as the *o*-substituent is the carboxyl ion or the undissociated carboxyl group.

In strongly alkaline solution the hydrogen phthalic ester will exist as the ion, and the carboxylic anion will increase the electron availability at the position ortho to it, leading

to inductive effects opposing the release of R as a carbonium kation : saponification in this case will proceed in the normal manner, in which the O—R bond is not broken (Ingold and Ingold, J., 1932, 756; Polanyi and Szabo, *Trans. Faraday Soc.*, 1934, 30, 508).

When the saponification is conducted in solution with sodium acetate or carbonate, the hydrogen phthalic ester will be present partly as the sodium salt and partly as the undissociated ester-acid. In the latter, the substituent ortho to the esterified carboxyl group is now an undissociated carboxyl group, which attracts electrons, causing a deficiency at the position ortho to it, and thereby promoting the separation of R as the kation $R^{\oplus}$. Since R is an allyl radical, it can readily undergo electron displacements permitting dissociation :

By the reaction of this carbonium kation with water or with hydroxyl ion, a racemised equilibrium mixture of the isomeric allyl alcohols results.

A comparison of the ease of separation of the carbonium kation from (a) the ionised and (b) the un-ionised hydrogen phthalic ester may be made; if R is a hydrogen atom, then the ease of separation is in proportion to (a) the second and (b) the first dissociation constant of phthalic acid. These constants are 3.1×10^{-6} and 1.26×10^{-3} , respectively, whence it appears that the un-ionised hydrogen phthalic ester will liberate the carbonium kation some 500 times more readily than will the ionised hydrogen phthalic ester.

EXPERIMENTAL.

The *dl*- and (+)-*n*-propylpropenylcarbinols were prepared by methods previously described (Arcus and Kenyon, *loc. cit.*).

dl-*n*-Propylpropenylcarbinyl *p*-nitrobenzoate, prepared by adding *p*-nitrobenzoyl chloride (6.2 g.) to a mixture of the *dl*-alcohol (3.8 g.) and pyridine (2.7 g.) and heating them at 80° for 1 hour, separated from aqueous alcohol in plates, m. p. 40—41° (Found : C, 63.6; H, 6.4. $C_{14}H_{17}O_4N$ requires C, 63.8; H, 6.5%).

The *p*-xenylurethane of *dl*-*n*-propylpropenylcarbinol, prepared by heating the *dl*-alcohol (1.2 g.) with *p*-xenylcarbimide (2.0 g.) at 80° for 1 hour and extracting the mixture with hot light petroleum, separated from this solvent in needles, m. p. 103.5° (Found : C, 77.3; H, 7.5. $C_{20}H_{23}O_2N$ requires C, 77.7; H, 7.5%).

dl-*n*-Propylpropenylcarbinyl formate, prepared by heating the *dl*-alcohol (4 g.) with formic-acetic anhydride (6 g.) for one hour at 80°, had b. p. 53—54°/11 mm., n_D^{14} 1.4285, d_4^{20} 0.873 (Found : C, 68.4; H, 10.2. $C_8H_{14}O_2$ requires C, 67.6; H, 10.0%).

dl-*n*-Propylpropenylcarbinyl *p*-toluenesulphinyl chloride was prepared by the slow addition of *p*-toluenesulphinyl chloride (19.2 g., prepared according to Phillips, J., 1925, 127, 2552) to an ice-cooled mixture of the *dl*-alcohol (12.4 g.) and pyridine (9.7 g.); an equal volume of dry ether was then added. Subsequently, more ether was added, and the extract washed with dilute hydrochloric acid, then with sodium carbonate, and dried (calcium chloride). On removal of the ether, a yellow oil remained; it decomposed without distilling when heated to 150° at < 0.1 mm. Traces of unreacted carbinol were therefore removed by heating to 90° at < 0.1 mm.; the product then had n_D^{20} 1.5273 (Found : S, 13.0. $C_{14}H_{20}O_2S$ requires S, 12.7%).

(+)-*n*-Propylpropenylcarbinyl *p*-toluenesulphinate was similarly prepared from the (—)-alcohol having α_{5461}^{17} — 5.44°, (*l*, 2.0); it had n_D^{17} 1.5271, α_{5893}^{17} + 1.85°, α_{5780}^{17} + 2.07°, α_{5461}^{17} + 2.27° (*l*, 0.5).

dl- Δ^2 -8-Chloroheptene was prepared by the slow addition of a mixture of *dl*-*n*-propylpropenylcarbinol (11.4 g.) and pyridine (1.6 g.) to phosphorus trichloride (5.2 g.) at 0°; after standing at room temperature for 1.5 hours, the upper layer was decanted and redistilled; it had b. p. 49°/21 mm., n_D^{21} 1.4430, d_4^{18} 0.879 (Found : Cl, 26.4. $C_7H_{13}Cl$ requires Cl, 26.7%).

(—)- Δ^2 -8-Chloroheptene, similarly prepared from the (+)-alcohol having α_{5461}^{20} + 4.10° (*l*, 0.5), had b. p. 44°/14 mm., n_D^{21} 1.4430, α_{6438}^{22} — 1.21°, α_{5893}^{22} — 1.48°, α_{5461}^{22} — 1.68°, α_{4358}^{22} — 3.20° (*l*, 0.5).

It was desired to reduce catalytically the last compound in order to ascertain its degree of optical purity, but the C—Cl bond is rapidly attacked. To dry ether containing the reduced platinum catalyst of Adams, Voorhees, and Shriner ("Organic Syntheses," 8, 92), *dl*- Δ^8 -chloroheptene (6.7 g.) was added, and hydrogen supplied at 2 atm. The initial rapid absorption ceased, but recommenced on addition of sodium carbonate, whence it appears that the reaction is inhibited by the production of hydrogen chloride. After the theoretical quantity of hydrogen required for saturation had been absorbed, the solution yielded a mixture of chloroheptene and chloroheptane, b. p. 101°/183 mm., n_D^{19} 1.4363, $d_4^{12.5}$ 0.883 (Found: C, 63.4; H, 10.3. Calc. for $C_7H_{13}Cl$: C, 63.4; H, 9.9. Calc. for $C_7H_{15}Cl$: C, 62.4; H, 11.25%).

Saponification of (+)-*n*-Propylpropenylcarbinyl Hydrogen Phthalate.—(i) In 5*N*-sodium hydroxide. This has been described by Arcus and Kenyon (*loc. cit.*). (ii) In aqueous sodium acetate. A current of steam was passed through a solution of the (+)hydrogen phthalic ester ($[\alpha]_{5461}^{18} + 20.0^\circ$ in ethyl alcohol; 13 g.) and sodium acetate (9 g.) in water (50 c.c.). The distillate was saturated with potassium carbonate, and extracted with ether. The latter yielded a heptenol (4 g.), b. p. 63°/15 mm., n_D^{18} 1.4379, optically inactive to light of λ 5461. It furnished a *p*-xenylurethane which was a mixture, m. p. 70–80°, from which, after 6 crystallisations from methylene chloride–light petroleum, the *p*-xenylurethane of *dl*-*n*-propylpropenylcarbinol, m. p. 102–104°, alone or mixed with an authentic specimen, was obtained.

Stability of the Hydrogen Phthalates and *p*-Nitrobenzoates of *n*-Propylpropenylcarbinol and α -Methyl- γ -*n*-propylallyl Alcohol.—*dl*-*n*-Propylpropenylcarbinyl hydrogen phthalate (3 g.) and pyridine (3 g.) were heated together at 80° for 80 minutes. Ether was added, and the solution washed with dilute hydrochloric acid and dried (calcium chloride). On evaporation and addition of light petroleum, the hydrogen phthalic ester separated as needles, m. p. 72.5°, alone or mixed with the original material. Similar treatment of *dl*- α -methyl- γ -*n*-propylallyl hydrogen phthalate gave the pure ester, m. p. 67.5°, alone or when mixed with the original material.

0.2 G. of each of the isomeric *p*-nitrobenzoates was maintained at 80° for 1 hour; the melts were allowed to supercool, and each was inoculated with a trace of its isomeride. After solidification, the *n*-propylpropenylcarbinyl ester had m. p. 41°, and the α -methyl- γ -*n*-propylallyl ester m. p. 29°, *i.e.*, each was unaltered.

Change undergone by (+)-*n*-Propylpropenylcarbinyl *p*-Toluenesulphinate.—The *dl*-ester, n_D^{18} 1.5271, was kept in a thermostat at 32°; portions were removed at intervals, and the saponification value determined by means of alcoholic potassium hydroxide.

<i>t</i>	0 *	7.5 hrs.	24 hrs.	72 hrs.	97 hrs.	120 hrs.	33 days
Apparent ester content, % ...	83	81	70	24	25	24	25

* This observation relates to the ester as prepared.

A similar experiment was performed with the (+)sulphinate, placed in a 0.5-dm. tube in the thermostat, and periodically removed, allowed to cool, and the rotation measured.

<i>t</i> (hrs.)	0	2.2	19.7	45
α_{5461}^{20}	+2.25°	+2.27°	+2.43°	–0.04°
Ester content, %, by saponification	84	—	—	21

Repeated attempts to isolate a pure product of this change were unsuccessful.

Replacement Reactions of (+)-*n*-Propylpropenylcarbinyl Hydrogen Phthalate.—(i) With formic acid. A mixture of the (+)hydrogen phthalate ($[\alpha]_{5461} + 9.77^\circ$ in ethyl alcohol; 11 g.) and anhydrous formic acid (4 g.) was heated on the steam-bath for 1 hour. From the ethereal extract, after washing with sodium carbonate and drying (calcium chloride), heptenyl formate (2.5 g.) was obtained, b. p. 54°/12 mm., n_D^{17} 1.4266, optically inactive to light of λ_{5461} (*l*, 0.25). The sodium carbonate solution afforded phthalic acid (4.9 g.), m. p. 200–205° (decomp.).

(ii) With acetic acid. A solution of the (+)hydrogen phthalate ($[\alpha]_{5461}^{18} + 15.8^\circ$ in ethyl alcohol; 5.0 g.) in acetic acid (m. p. 17°, 20 g.) was kept at 32°, periodically removed, cooled, and the rotatory power determined. The results are given in Table III (temp., approx. 18°; *l*, 2.0).

TABLE III.

<i>t</i> , hrs.	0	17	46	65	90	112	160	184	233	258
α_{5461}	+2.06°	+1.91°	+1.83°	+1.74°	+1.55°	+1.28°	+1.10°	+0.95°	+0.66°	+0.51°
<i>t</i> , hrs.	376	449	497	544	597	664	736	833	1001	1169
α_{5461}	–0.16°	–0.50°	–0.75°	–0.93°	–1.09°	–1.24°	–1.38°	–1.56°	–1.70°	–1.69°

Ether was added, and the extract filtered from the remaining phthalic acid, which crystallised from hot water, m. p. 200–204° (decomp.) (0.5 g.). The ethereal extract, washed with sodium

carbonate, and dried (calcium chloride), yielded heptenyl acetate, b. p. 73°/17 mm., n_D^{21} 1.4264, $\alpha_{5461}^{20} + 0.05^\circ$, $\alpha_{5893}^{20} + 0.03^\circ$ (l , 0.5); it (0.5 g.) was reduced in ethyl-alcoholic solution (7 c.c.) by hydrogen at 2 atm. in the presence of Raney nickel catalyst. The filtered solution, which showed no unsaturation, was inactive to light of λ_{5461} .

(iii) *With benzoic acid.* A mixture of *n*-propylpropenylcarbinyl hydrogen phthalate ($[\alpha]_{5461} + 7.8^\circ$ in ethyl alcohol; 20 g.) and benzoic acid (27 g.) was kept at 120–130° for one hour. The cooled mixture was triturated with ether. The filtered ethereal extract, washed with sodium carbonate, and dried (sodium sulphate), yielded *dl*-heptenyl benzoate (2.3 g.), b. p. 149°/13 mm., n_D^{15} 1.5048, optically inactive to light of λ_{5461} (l , 0.25). This material was saponified with alcoholic potassium hydroxide on the steam-bath for one hour; the ethereal extract, washed with water and dried, gave a heptenol, b. p. 61°/13 mm. (0.7 g.). This latter with *p*-xenylcarbimide yielded a mixture from which after six crystallisations the *p*-xenylurethane of *n*-propylpropenylcarbinol, m. p. 100° alone and mixed with an authentic specimen, was obtained.

Replacement Reactions of (–)- Δ^{β} - δ -Chloroheptene.—(i) *By hydroxyl.* (–)- Δ^{β} - δ -Chloroheptene [$\alpha_{5461}^{22} - 1.68^\circ$ (l , 0.5), prepared from (+)-*n*-propylpropenylcarbinol having $\alpha_{5461}^{20} + 4.10^\circ$ (l , 0.5); 4.2 g.] was kept at 65° for 4 hours, with shaking, in a solution of sodium carbonate (2.3 g.) in water (45 g.). The suspension was saturated with potassium carbonate and extracted with ether, which yielded a (+)heptenol (1.2 g.), b. p. 63°/16 mm., n_D^{22} 1.4372, $\alpha_{5461}^{23} + 0.04^\circ$ (l , 0.236). On reduction of this material in ethereal solution (10 c.c.) with hydrogen at 2 atm. in the presence of platinum catalyst, the theoretical volume was rapidly absorbed, yielding a heptanol, b. p. 62°/15 mm., n_D^{19} 1.4207, optically inactive to light of λ_{5461} (l , 0.236).

dl- Δ^{β} - δ -Chloroheptene was hydrolysed by this method, giving a heptenol, b. p. 68°/17 mm., n_D^{20} 1.4388, which was converted into its hydrogen phthalic ester, a mixture which was not separated after repeated crystallisation from carbon disulphide and light petroleum. Reduction of the heptenol gave a heptanol, b. p. 64°/16 mm., n_D^{16} 1.4212, which was converted into its hydrogen phthalic ester, a mixture not separable by recrystallisation from ether–light petroleum.

(ii) *By methoxyl.* (+)- Δ^{β} - δ -Chloroheptene [$\alpha_{5461}^{16} + 0.59^\circ$ (l , 0.5), prepared from (–)-*n*-propylpropenylcarbinol having $\alpha_{5461}^{17} - 5.44^\circ$ (l , 2.0); 6.3 g.], dissolved in anhydrous methyl alcohol (13 g.), was heated with potassium carbonate (6.3 g.) on the steam-bath for one hour. The ethereal extract, washed with water and dried (calcium chloride), yielded (+)methyl heptenyl ether (3.5 g.), b. p. 133–135°/760 mm., n_D^{19} 1.4221, $\alpha_{5461}^{19} + 0.09^\circ$ (l , 0.5). This was reduced in ethereal solution (35 c.c.) with hydrogen at 2 atm. in the presence of platinum catalyst; the theoretical volume was absorbed in 2 hours, producing *dl*-methyl heptyl ether, b. p. 136°/760 mm., n_D^{18} 1.4056, optically inactive to light of λ_{5461} (l , 0.25).

(iii) *By acetate ion.* *dl*- Δ^{β} - δ -Chloroheptene (9.4 g.) did not react when heated in acetic acid (m. p. 17°, 22 g.) solution at 65° for 40 minutes, and was recovered having b. p. 46°/19 mm., n_D^{17} 1.4452.

(+)- Δ^{β} - δ -Chloroheptene [$\alpha_{5461}^{21} + 0.48^\circ$ (l , 0.5), prepared from (–)-*n*-propylpropenylcarbinol having $\alpha_{5461}^{17} - 5.44^\circ$ (l , 2.0); 6.1 g.] and anhydrous sodium acetate (5.5 g.), dissolved in acetic acid (14.4 g.), were heated at 65° for one hour. The ethereal extract, washed with sodium carbonate and dried (calcium chloride), yielded *dl*-heptenyl acetate, b. p. 68°/16 mm., n_D^{19} 1.4270, optically inactive to light of λ_{5461} (l , 0.5).

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194. The Mechanism of the Hofmann Reaction. Retention of Optical Activity during the Reaction with (+)Hydratropamide.

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The Hofmann rearrangement of (+)hydratropamide into (–)-α-phenylethylamine has been examined. This reaction provides a favourable case for observing whether any dissociation of the amide molecule occurs during the Hofmann rearrangement, since the electron-releasing properties of the α-phenylethyl radical should favour this dissociation with subsequent racemisation of the liberated radical, while the comparatively high rotatory power of (–)-α-phenylethylamine would facilitate the detection of racemisation.

It is found that optical activity is almost completely retained during the rearrangement of (+)hydratropamide, in confirmation of the conclusions of previous workers that the Hofmann rearrangement is substantially an intramolecular reaction. A formulation of the rearrangement is suggested.

It appears to be established that the Hofmann reaction of amides proceeds by the following stages :

the molecular rearrangement, in which the group R becomes detached from the carbon and attached to the nitrogen atom, being confined to the third stage of the process.

The following evidence indicates the rearrangement to be intramolecular rather than one which involves dissociation of the molecule into free ions or radicals. Whitmore and Homeyer (*J. Amer. Chem. Soc.*, 1932, **54**, 3435) have observed that *tert.*-butylacetamide yields neopentylamine quantitatively: $\text{CMe}_3\cdot\text{CH}_2\cdot\text{CO}\cdot\text{NH}_2 \longrightarrow \text{CMe}_3\cdot\text{CH}_2\cdot\text{NH}_2$, whereas those reactions in which the temporary existence of the cation $\text{CMe}_3\cdot\text{CH}_2^+$ may occur lead to *tert.*-amyl derivatives, *e.g.*, $\text{CMe}_3\cdot\text{CH}_2\text{I} + \text{NaOAc} \longrightarrow \text{CMe}_2\text{Et}\cdot\text{OAc} + \text{NaI}$.

On performing the Hofmann reaction with (+)benzylmethylacetamide, Wallis and Nagel (*ibid.*, 1931, **53**, 2787) obtained α-benzylethylamine in apparent optical purity; further, Wallis and Moyer (*ibid.*, 1933, **55**, 2598) submitted an optically active compound of the diphenyl type to the Hofmann reaction, again obtaining an apparently optically pure amine :

Dissociation of the diphenyl radical from the amido-group at any stage of the reaction would have permitted free rotation and resulted in a racemic product. It may be pointed out that in neither of the last two cases was a direct evaluation of the optical purity of the resultant amine made by comparison of its rotatory power with that of the active amine prepared by resolution of the *dl*-compound.

(+)-Hydratropamide, $\text{CHMePh}\cdot\text{CO}\cdot\text{NH}_2$, has now been prepared and submitted to the Hofmann reaction; this particular amide was selected for the following reasons. The resultant α-phenylethylamine has been resolved by numerous workers (references given in "Organic Syntheses," Vol. XVII, 80); moreover, the radical $\text{CHMePh}\cdot$ would be expected to exhibit a stronger tendency towards electron release than the radicals $\text{CH}_2\text{Ph}\cdot\text{CHMe}\cdot$ and $\text{C}_{10}\text{H}_7\cdot\text{C}_6\text{H}_2(\text{NO}_2)_2$, so that if rearrangement by dissociation of the

amide molecule, with consequent racemisation, can occur, it would be more evident in the case of the rearrangement of hydratropamide than in the cases which have previously been reported. From a study of the rearrangement of (–)phenylmethylcarbinyl *p*-toluenesulphinate into *dl*- α -phenylethyl-*p*-tolylsulphone (Arcus, Balfe, and Kenyon, J., 1938, 485) it was concluded that the reaction

involves the liberation of the cation CHMePh^+ ; dissociation into this cation, which is planar, is favoured by the use of hydroxylic solvents of high dielectric constant. It was therefore considered that, should dissociation occur during the Hofmann reaction, hydratropamide would provide a favourable example for its detection. Finally, as the rotatory powers of both hydratropic acid and α -phenylethylamine are of considerable magnitude, any racemisation which occurs during the reaction can be estimated with some degree of accuracy.

dl-Hydratropic acid was prepared as described in the experimental section, and by fractional crystallisation of its strychnine salt as described by Raper (J., 1923, 123, 2557) optically pure (+)hydratropic acid was obtained. A method is described for the preparation of (–)hydratropic acid also.

(+)Hydratropamide, prepared through the acid chloride, was treated with a solution of bromine in sodium hydroxide and (–)- α -phenylethylamine obtained. The optical rotatory power of the latter was determined (after extraction and distillation, processes which are unlikely to effect any change in the optical purity of the product) and compared with the value $\alpha_{\text{D}}^{15.5} - 22.92^\circ$ (*l*, 0.5), the highest in the literature, obtained by Ingold and Wilson (J., 1933, 1503) who resolved the *dl*-base with *d*-bromocamphorsulphonic acid. Four separate experiments were carried out with the following results:

Observed Rotatory Powers of Hydratropic Acid and of α -Phenylethylamine obtained from it (l, 0.5).

	Hydratropic acid.	Optical purity, %.	α -Phenylethylamine.	Optical purity, %.	Retention of optical activity, %.
(i)	$\alpha_{\text{D}}^{16} \text{ }_{5461} + 62.18^\circ$	100	$\alpha_{\text{D}}^{15} \text{ }_{5461} - 21.81^\circ$	95.1	95.1
(ii)	$\alpha_{\text{D}}^{16.8} \text{ }_{5461} + 62.07^\circ$	100	$\alpha_{\text{D}}^{16} \text{ }_{5461} - 21.92^\circ$	95.6	95.6
(iii)	$\alpha_{\text{D}}^{19} \text{ }_{5461} + 55.22^\circ$	90.0	$\alpha_{\text{D}}^{17} \text{ }_{5461} - 19.65^\circ$	85.8	95.3
(iv)	$\alpha_{\text{D}}^{18} \text{ }_{5461} - 15.85^\circ$	25.8	$\alpha_{\text{D}}^{17} \text{ }_{5461} + 5.75^\circ$	25.1	97.2
					Mean 95.8

It is seen that asymmetry is almost completely retained during the rearrangement. The mechanism of rearrangement during the Hofmann reaction has been represented in two ways. Stieglitz and also Wallis (review on molecular rearrangements by Wallis, "Organic Chemistry," Gilman, Vol. I, 1938, 720) postulate the formation of a univalent nitrogen compound:

The rearrangement has also been formulated as analogous to the Beckmann rearrangement (Franklin, *Chem. Reviews*, 1934, 14, 219; Sidgwick, "Organic Chemistry of Nitrogen," 1937, p. 146):

There appears to be no evidence that the bromine atom is at any time attached to the carbonyl carbon atom; however, this representation indicates that if the movements of R– and Br– are simultaneous, it is unnecessary to postulate the existence of a univalent nitrogen atom.

It was shown by Hantzsch (*Ber.*, 1902, 35, 226, 3579) that the bromo-amide forms a

salt by interaction with the alkali, the anion of which was formulated as in (I). If it is assumed that the initial salt-forming reaction is

then (I) and (II) should undergo resonance, and the anion and its rearrangement may be represented by

expulsion of the bromine anion and movement of the group R- being simultaneous.

A tendency to electron release by R (+ I effect) will promote the liberation of Br[⊖] and increase the ease of rearrangement:

This is in accordance with the observation of Hauser and Renfrow (*J. Amer. Chem. Soc.*, 1937, 59, 121) that the rates of decomposition (by sodium hydroxide at 30°) of a number of *p*- and *m*-substituted *N*-bromobenzamides increase as the dissociation constants of the corresponding benzoic acids decrease.

A secondary effect may be observed when R is a semiaromatic group; attachment of aromatic nuclei should weaken the R-C bond [analogously to the formation of free radicals by dissociation of C(Ar)₃-X] and thereby promote rearrangement. This has been observed by Jones and Hurd (*ibid.*, 1921, 43, 2422) in the closely related hydroxamic acid rearrangement,

where the ease of rearrangement increases as R- is successively -CH₂Ph, -CHPh₂, and -CPh₃.

Since very little racemisation was observed in the above reaction with (+)hydratropamide, it appears certain that the group R- does not migrate as an ion or free radical [it is also very improbable that the anion (III) would further dissociate into a carbonium cation], but that the electronic changes during the movement of R- are such that electronic sharing between R- and the structure C≡N- is continuous.

It may be noted that the Hofmann reaction should be a reliable procedure in the determination of the relative configurations of compounds of the type Cabc·CO₂H and Cabc·NH₂, as has been suggested by Braun and Friehmelt (*Ber.*, 1933, 66, 684).

EXPERIMENTAL.

dl-Hydratropic acid was prepared, in larger amounts, by oxidation (by far the most conveniently, with potassium permanganate and magnesium sulphate in aqueous acetone solution) of hydratropaldehyde obtained by a modification of methods due to Tiffeneau (*Ann. Chim. Phys.*, 1907, 10, 176), Klages (*Ber.*, 1905, 38, 1969), and Cohen, Woodman, and Marshall (*J.*, 1915, 107, 898) based on the reactions:

(+)*Hydratropic Acid*.—A solution of strychnine (90 g.) and *dl*-hydratropic acid (40 g.) in warm 75% aqueous alcohol (400 c.c.), after standing overnight in the ice-chest, deposited 60 g. of strychnine salt in the form of glassy rhombs; concentration of the filtrate yielded a second crop (25 g.). After five recrystallisations, optical purity was reached, and the strychnine salt yielded *d*-hydratropic acid (8.5 g.), b. p. 143°/12 mm., which sets to a mass of transparent, flat rhombs, m. p. 29°: in view of its considerable alteration of rotatory power with change of temperature, the following values were determined (*l*, 0.5).

<i>t.</i>	α_{5893}	α_{5780}	α_{5461}	α_{4358}	<i>t.</i>	α_{5780}	α_{5461}	α_{4358}
13.6°	—	+55.04°	+63.08°	+112.5°	23°	+53.03°	+60.73°	+109°
16.0	+51.81°	—	62.16	111.2	25	52.30	59.80	108
16.2	—	54.30	62.30	111.7	30	51.30	58.62	105.7
17.75	—	—	61.85	—				
19.4	—	53.55	61.30	110				

Specific rotatory powers of the acid in solution are given below.

Collected Specific Rotatory Powers.

Solute.	Solvent.	<i>c.</i>	<i>l.</i>	$[\alpha]_{5893}$	$[\alpha]_{5461}$	$[\alpha]_{4358}$
<i>d</i> -Hydratropic acid *	CHCl ₃	3.060	2	+ 74.8°	+ 90.9°	+162°
"	C ₆ H ₆	3.4825	2	92.5	110.3	197
" (Na salt)	H ₂ O	3.247	2	5.8	6.3	9.2
<i>d</i> -Hydratropamide	CHCl ₃	2.733	2	58.3	71.5	130
<i>d</i> - α -Phenylethylacetamide	EtOH	2.340	2	-165	-195	-370

* *d*-Configuration is assigned arbitrarily to (+)hydratropic acid for the purpose of description.

(-)*Hydratropic Acid*.—From the first mother-liquor from the strychnine salt there was recovered hydratropic acid (12 g.) with $\alpha_{5893}^{19^\circ}$ -32.28° (*l*, 0.5), which, on being kept in the ice-chest for several days, deposited a crop of crystals; the liquid acid drained from the crystals had $\alpha_{5893}^{19^\circ}$ -26.6° (*l*, 0.5). The crystals were melted, allowed to recrystallise, and again drained from the liquid acid. When the process was repeated a third time there was obtained (-)hydratropic acid (4 g.) in hard, glassy, flat rhombs, m. p. 29°, and (supercooled) $\alpha_{5461}^{17^\circ}$ -61.68° (*l*, 0.5).

In view of the readiness with which this separation takes place the—presumed—optically pure (+)hydratropic acid described above was melted, inoculated, and when crystallisation was about two-thirds complete, the liquid portion was drained away. The rotatory power of the re-melted acid was identical with that of the original acid, thus increasing very considerably the probability that optical purity had been reached by the fractional crystallisation of strychnine hydratropate.

This is the more desirable because Levene and Marker (*J. Biol. Chem.*, 1933, 100, 692), who fractionally crystallised its quinine salt, give $[\alpha]_{5893}^{25^\circ}$ -74.1° as the maximum value of *l*-hydratropic acid in the homogeneous condition, whereas Ott and Krämer (*Ber.*, 1935, 68, 1657) state, without recording any experimental details, that optically pure *d*-hydratropic acid has $[\alpha]_{5893}^{20^\circ}$ +89.7°. Also, during the present investigation it was found that laevorotatory hydratropic acid with $\alpha_{5893}^{19^\circ}$ -27.1° (*l*, 0.5) gives a beautifully crystalline cinchonidine salt which was recrystallised successively from acetone, methyl acetate (twice), and aqueous alcohol without the rotatory power of the liberated hydratropic acid being increased beyond $\alpha_{5893}^{19^\circ}$ -36° (*l*, 0.5). On the other hand, Raper (*loc. cit.*), whose method we have used, gives for the *d*-acid $[\alpha]_{5893}$ +76.2° in chloroform solution, but records no value for the homogeneous acid, owing to the small amount available.

Even in this most favourable case we found it advantageous to allow the crystallisation to proceed undisturbed and to decant the mother-liquor; when the containing vessel is scratched, a considerable amount of strychnine salt of low optical activity is brought out of solution.

An attempt was made to obtain *l*-hydratropic acid by the recrystallisation from ether of *l* + *dl*-hydratropamide (from hydratropic acid of $\alpha_{5893}^{19^\circ}$ -25.5°, *l* 0.5), but after three crystallisations the resulting amide had only $[\alpha]_{5461}$ -43.9° in chloroform solution.

A crystal of *d*-hydratropic acid was at room temperature placed in contact with a similar crystal of *l*-hydratropic acid: they slowly melted and the resulting *dl*-acid remained liquid after being kept at -5° for several days.

(+)*Hydratropamide* was prepared by warming a mixture of (+)hydratropic acid (7.5 g.) and phosphorus trichloride (2.8 g.) at 60–70° for an hour and pouring the upper mobile layer of hydratropyl chloride dropwise into ammonia (25 c.c.; *d* 0.880) at -18°. The precipitated crystalline hydratropamide was removed by filtration, washed with cold water, and air-dried; it (7.2 g.) had m. p. 96–97° and rotatory powers given above. It separated from warm water, in which it was but sparingly soluble, in slender, long needles, or from chloroform–light petroleum in lustrous leaflets, m. p. 103–104° (Found: N, 8.9. C₉H₁₁ON requires N, 9.4%).

(-) α -*Phenylethylamine*.—The (+)hydratropamide (6.8 g., uncrystallised so as to avoid any possible separation of optical isomerides) was gradually added to a cooled solution of sodium hydroxide (8 g.) and bromine (8.3 g.) in water (50 c.c.). The resulting cloudy solution was gently heated on the steam-bath for 20 minutes until separation of the amine appeared to be

complete. Extraction with ether yielded (–)- α -phenylethylamine (3.5 c.c.), b. p. 73°/14 mm., $\alpha_{589}^{18^\circ}$ – 18.20°, $\alpha_{546}^{18^\circ}$ – 21.81°, $\alpha_{435}^{18^\circ}$ – 37.3° (*l*, 0.5), $d_4^{17.5^\circ}$ 0.9762, $d_4^{25^\circ}$ 0.9702, $d_4^{31^\circ}$ 0.9650.

(–)- α -Phenylethylacetamide, prepared by the action of acetic anhydride on the (–)amine, separated from aqueous acetic acid in leaflets, m. p. 103–104°, and had the rotatory powers given above. Götze (*Ber.*, 1938, 71, 2289), who prepared the acetyl derivative of (–)- α -phenylethylamine with $[\alpha]_{589}^{33^\circ}$ – 33°, gives m. p. 101–102° and $[\alpha]_{589}^{170^\circ}$ in ethyl-alcoholic solution.

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356. *The Mechanism of the Hydrolysis of $\alpha\gamma$ -Dimethylallyl Chloride.*

By C. L. ARCUS and J. W. SMITH.

The hydrolysis of $\alpha\gamma$ -dimethylallyl chloride in aqueous acetone has been followed by a conductometric method, and shown to follow a unimolecular law, in accord with the mechanism deduced from stereochemical observations. The apparent incompleteness of the reaction in the conductivity cell employed is attributed to adsorption of the $\alpha\gamma$ -dimethylallyl chloride on the platinum-blackened electrodes.

In a recent study of replacement reactions in allyl compounds (Arcus and Kenyon, J., 1938, 1912) it was found that the hydrolysis of (—)- Δ^{β} - δ -chloroheptene (γ -methyl- α -*n*-propylallyl chloride) is accompanied by great loss of optical purity and that a mixture of isomeric heptenols results. From these observations it was considered that the reaction proceeds by a unimolecular mechanism, in which the rate is controlled by the slow primary dissociation into a solvated carbonium kation:

The hydrolysis of (—)- $\alpha\gamma$ -dimethylallyl chloride has a similar stereochemical result (Hills, Kenyon, and Phillips, J., 1936, 576) and a similar mechanism should apply.

The rate of hydrolysis of *dl*- $\alpha\gamma$ -dimethylallyl chloride in aqueous acetone (75% by vol.) at 0° has now been studied. This compound was selected in preference to Δ^{β} - δ -chloroheptene because its symmetrical substitution precludes the formation of an isomeride during its preparation from the corresponding alcohol. The velocity of the reaction proved too great to permit determination of the liberated hydrogen chloride by withdrawal of portions of the solution and titration with alkali or silver solutions. Accordingly, the conductivity of the solution during the process of hydrolysis was determined at suitable intervals, and the corresponding concentrations of hydrogen chloride were deduced by reference to the conductivities of known solutions of hydrogen chloride in the same solvent. (A similar method has been applied to the alcoholyses of substituted triphenylmethyl chlorides by Nixon and Branch, *J. Amer. Chem. Soc.*, 1936, 58, 492.)

Experiment 1.

Wt. of $\alpha\gamma$ -dimethylallyl chloride, 0.350 g.

<i>t</i> (mins.).	[HCl].	$k \times 10^4$ (calc. from <i>t</i> = 0).	$k \times 10^4$ (calc. from <i>t</i> = 33 mins.).
5	0.0006	58.5	—
10	0.0012	59	—
15	0.00175	58.5	—
22	0.0025	58	—
33	0.00365	58	—
42	0.00452	58	57.5
53	0.00553	58	57.5
94	0.0088	58	58
108	0.00973	58	58
132	0.01115	58	57.5
155	0.01235	57.5	57.5
216	0.01482	57	57
262	0.01618	57	56.5
298	0.0170	56.5	56
325	0.0175	56	55.5
1 day	0.0209		

Final concn. of HCl by titration = 0.02105 =
93% of theoretical.

Experiment 2.

Wt. of $\alpha\gamma$ -dimethylallyl chloride, 0.341 g.

<i>t</i> (mins.).	[HCl].	$k \times 10^4$ (calc. from <i>t</i> = 0).	$k \times 10^4$ (calc. from <i>t</i> = 32 mins.).
4	0.00048	60	—
9	0.00108	61	—
15	0.00173	59.5	—
20	0.00226	59	—
32	0.00348	59	—
42	0.0044	58	56.5
52	0.0053	58	57.5
77	0.00733	58	58
116	0.00995	58	58
141	0.0113	57.5	57.5
174	0.01282	57.5	57
197	0.0137	57	57
253	0.01545	56.5	56.5
302	0.01655	56	55.5
328	0.0170	55.5	55
3 days	0.02028		

Final concn. of HCl by titration = 0.0205 =
93% of theoretical.

The hydrolysis of our sample of $\alpha\gamma$ -dimethylallyl chloride by the above solvent in glass vessels yielded 98% of the theoretical amount of hydrogen chloride, and the reverse

reaction between $\alpha\gamma$ -dimethylallyl alcohol and hydrogen chloride could not be detected at the concentrations used. It was found, on the other hand, that the hydrolysis in the conductivity cell proceeded to the extent of only 93%. This difference is ascribed to adsorption of $\alpha\gamma$ -dimethylallyl chloride on the platinum-black coated electrodes. The final concentration of hydrogen chloride was employed for the calculation of the first-order velocity constants given in the table. Concentrations of hydrogen chloride are given as the normality at 0°.

It is evident that the reaction is substantially of the first order, in agreement with the unimolecular mechanism deduced from the stereochemical result.

EXPERIMENTAL.

dl- $\alpha\gamma$ -Dimethylallyl chloride was prepared by slow addition of a mixture of *dl*- $\alpha\gamma$ -dimethylallyl alcohol (25 g.) and pyridine (5 g.) to phosphorus trichloride (15 g.) cooled in ice-acetone. After standing at room temperature for 1.5 hours, the upper layer was decanted and redistilled. It had b. p. 68°/270 mm. [Found, by saponification with alcoholic potassium hydroxide: *M*, (i) 106.2, (ii) 106.2. Calc.: *M*, 104.6].

Acetone was purified *via* its sodium iodide compound (Shipsey and Werner, J., 1913, 103, 1255), dried with calcium chloride, and redistilled. The solvent used was prepared by adding distilled water (1 vol.) to acetone (3 vols.) at 22°; it had no measurable conductivity; 75 c.c. of acetone and 25 c.c. of water, both at 22°, yielded 97.3 c.c. of solvent at 22° and 94.5 c.c. at 0°.

The conductivities of the solutions were measured with the apparatus described by Righellato and Davies (*Trans. Faraday Soc.*, 1933, 29, 429), in which the bridge reading is directly proportional to conductivity. (This method permitted determination of minima to ± 1 unit, corresponding to $\pm 0.00002N\text{-HCl}$.) The conductivity cell comprised a wide-mouthed glass bottle of about 250 c.c. capacity into which dipped a pair of parallel platinum disc electrodes mounted on a rigid glass framework passing through the stopper of the bottle. The electrodes, about 4 sq. cm. in area and 1 cm. apart, were coated with platinum black. A further tube passing through the stopper of the bottle, normally kept closed, served for the introduction and removal of solution.

The solvent (150 c.c.) and conductivity cell were cooled to 0° in a well-stirred bath of ice and water. About 100 c.c. of the solvent were decanted into the cell, and *dl*- $\alpha\gamma$ -dimethylallyl chloride was added rapidly from a weighing bottle fitted with a teat-pipette; the remainder of the solvent was added with agitation of the cell. Thereafter the conductivity of the solution was measured at suitable intervals, the apparatus being maintained at 0° throughout. Finally, the cell and its contents were kept overnight at room temperature, cooled to 0°, and the conductivity redetermined. Portions of the solution were then titrated with sodium hydroxide.

0.1158, 0.1178, and 0.0995 G. of *dl*- $\alpha\gamma$ -dimethylallyl chloride were added to 50 c.c. portions of the solvent, the hydrolyses were allowed to proceed at room temperature for 1, 3, and 3 days, respectively, in closed flasks, and the hydrogen chloride liberated was titrated with sodium hydroxide; the concentrations found were 97.4, 98.2, and 97.4% of the theoretical.

To test for the occurrence of a back-reaction, the conductivity at 0° of a solution of hydrogen chloride in the same solvent (0.0198*N* at 0°) was measured; *dl*- $\alpha\gamma$ -dimethylallyl alcohol (0.488 g.) was then added to 159 c.c. of the solution. The conductivity at 0° remained unaltered during 3 days.

For purposes of calibration, 150 c.c. of a solution of hydrogen chloride in the same solvent (0.0203*N* at 0°), measured at 0°, were placed in the cell, and the conductivity at 0° determined. Then 50 c.c. were withdrawn and replaced by 50 c.c. of solvent, measured at 0°, and the conductivity redetermined. This was repeated twice. The measurements were duplicated, the maximum difference between corresponding readings from the two experiments being 0.5%, and the bridge-readings plotted against concentrations of hydrogen chloride at 0°.

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II. THE PHOTOCHEMICAL DECOMPOSITION OF L-ASCORBIC ACID. II

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(Received 28 November 1939)

In a recent investigation [Kellie & Zilva, 1938] it was shown that in the presence of air, *L*-ascorbic acid in aqueous solution, when exposed to ultraviolet light, was oxidized without the aid of sensitizers to dehydroascorbic acid. Furthermore, it was found that even in the absence of atmospheric oxygen the exposure to this light brought about a destruction of the vitamin. In the anaerobic experiments in which small quantities of ascorbic acid were used the amount of dehydroascorbic acid present after the exposure at pH 7 was so small as to throw doubt on its formation. At pH 3 on the other hand although the quantity of ascorbic acid which was decomposed by the ultraviolet light was less than at pH 7, the reduction of the residual solution with H₂S produced an appreciable rise in the indophenol-reducing capacity of the solution. That this actinic decomposition of *L*-ascorbic acid under anaerobic conditions was not due to oxidation brought about by the last traces of O₂ which could not be removed by repeated exhaustion and refilling with N₂ was shown by the fact that the quantities of ascorbic acid which disappeared after prolonged exposure required considerably larger amounts of O₂ for their oxidation than those which could possibly be present in solution even without previously removing from it the dissolved air.

This observation on the anaerobic photolysis of *L*-ascorbic acid required further elucidation and experiments for this purpose are described below. In the original investigation ascorbic acid was determined by titration with 2:6-dichlorophenolindophenol and any rise in the indophenol-reducing capacity after reduction with H₂S was assumed to be dehydroascorbic acid. The determination of pure *L*-ascorbic acid in aqueous solution by titration with indophenol is beyond criticism and great reliance can also be placed on the interpretation that the rise in the indophenol-reducing capacity in the *L*-ascorbic acid solutions exposed to the light in the presence of air after treatment with H₂S is due to the reduction of the reversibly oxidized form of the compound produced by the oxidation of some of the ascorbic acid. In the case of the anaerobic experiments, however, it was considered desirable to obtain additional evidence for the assumption that the increase in the reducing capacity of the exposed solutions after treatment with H₂S was really due to the formation of *L*-ascorbic acid. A method for the determination of ascorbic acid based on the production of furfuraldehyde was therefore employed in the present investigation. The results obtained with this method were similar to those observed when indophenol was used, thus supporting the view that even under anaerobic conditions oxidation of ascorbic acid with the formation of dehydroascorbic acid takes place during the exposure of the reduced compound to ultraviolet light.

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Determination of l-ascorbic acid as furfuraldehyde

The procedure adopted by us was based on the observation of Herbert *et al.* [1933] that by heating *l*-ascorbic acid with boiling 12% HCl it readily gave furfuraldehyde which could be determined as the phloroglucide yielding 87% of the theoretical value. As the application of the customary formula for the correction of the solubility of the phloroglucide yielded fictitious results with the quantities of ascorbic acid with which we worked we had recourse to the following empirical method which was found to be sufficiently accurate for our purpose. To a solution calculated to contain about 30 mg. of ascorbic acid were added half the volume of conc. HCl and sufficient 12% HCl to bring the volume up to 100 ml. This solution was then distilled over a free flame at first slowly and then at a rate yielding 30 ml. of distillate per 10 min. until 360 ml. of distillate were collected. The volume in the distilling flask was kept constant by periodical additions of 50 ml. 12% HCl. A quantity of phloroglucinol (about $2\frac{1}{2}$ times the weight of the expected furfuraldehyde) dissolved in 12% HCl was added to the filtered distillate with stirring. The solution was made up to 400 ml. and allowed to remain at room temperature overnight to allow the black precipitate to separate completely. The precipitate was then collected by filtration in a sintered-glass crucible, washed with 150 ml. of water without being allowed to become dry, dried at 100° for 4 hr. and weighed after cooling in a desiccator. The equivalent quantity of *l*-ascorbic acid was ascertained from a graph (Fig. 1)

Fig. 1.

which was constructed by plotting the weights of the phloroglucide against the weights of *l*-ascorbic acid from which they were obtained. We have ascertained that solutions of dehydroascorbic acid distilled under the above conditions yielded a small quantity of phloroglucide which corresponded approximately to 10% of its equivalent of ascorbic acid. As will be seen later the quantities of dehydroascorbic acid involved in our experiments were of an order that could

not seriously vitiate the assessment of the *l*-ascorbic acid in the exposed solutions before they were reduced with H_2S . Roe [1936] claims that dehydroascorbic acid does not yield any furfuraldehyde at all when boiled with HCl .

*The formation of dehydroascorbic acid from l-ascorbic acid
by irradiation under anaerobic conditions*

As the rise in the indophenol-reducing capacity of irradiated *l*-ascorbic acid solutions after treatment with H_2S was more marked in acid than neutral solution these experiments were carried out at pH 3.6. 50 mg. of *l*-ascorbic acid were dissolved in 100 ml. of sodium acetate-acetic acid buffer solution prepared with quartz-distilled water which was boiled and cooled immediately before use, and the solution was irradiated in a quartz tube of 125 ml. capacity. Before irradiation the tube was evacuated 3 times and filled with pure N_2 3 times and the solutions were therefore finally irradiated in N_2 at atmospheric pressure. The quartz tube was exposed for 4 hr. to a Hewittic Y 2 mercury lamp at a distance of 9 in. with constant turning. The temperature of the solution gradually rose to 46° during this time. After cooling 1 ml. 1% NaCN was added to the irradiated solution and 40 ml. were removed for furfuraldehyde determination. At the same time 5 ml. were titrated with indophenol. A further 45 ml. were then placed in a wash bulb through which H_2S was passed for 5 min. and, after sealing the vessel, were allowed to remain overnight. After thoroughly displacing the H_2S by a current of pure N_2 the following day, the furfuraldehyde content was determined in 40 ml. and another 5 ml. were again titrated with indophenol.

Table 1. *Oxidation of l-ascorbic acid during anaerobic irradiation
(initial concentration of l-ascorbic acid, 50 mg. per 100 ml.)*

Exp.	Indophenol-reducing capacity (mg. <i>l</i> -ascorbic acid per 100 ml.)				Determination as furfuraldehyde (mg. <i>l</i> -ascorbic acid per 100 ml.)			
	After irradia- tion	After reduction	Differ- ence	Destroyed during irradiation	After irradia- tion	After reduction	Differ- ence	Destroyed during irradiation
1	30.4	36.3	5.9	19.6	29.8	32.6	2.8	20.2
2	32.4	37.6	5.2	17.6	31.2	36.9	5.7	18.8
3	32.25	36.8	4.55	17.75	32.0	33.9	1.9	18.0
4	30.8	34.4	3.6	19.2	30.8	33.8	3.0	19.2
5	30.3	35.5	5.2	19.7	31.0	33.5	2.5	19.0
6	31.2	36.7	5.5	18.8	30.6	35.5	4.9	19.4

Table 2. *mg. of l-ascorbic acid per 100 ml. determined by indophenol titration*

Initial concentration	Time of exposure hr.	After irradiation	After reduction	Difference	Destruction per hr.
50	4.0	33.2	39.8	6.6	4.2
50	6.5	24.0	30.5	6.5	4.0
50	6.5	22.8	29.2	6.4	4.2
50	8.0	18.0	27.4	9.4	4.0
100	4.0	84.1	88.2	4.1	4.0
100	6.5	74.0	84.0	10.0	4.0

It will be seen from Table 1 that although both methods yielded consonant results for the total quantity of *l*-ascorbic acid destroyed during irradiation, this was not the case when the *l*-ascorbic acid in the exposed solution was determined

by these methods after reduction with H_2S . The results obtained by the furfur-aldehyde method show nevertheless that considerable quantities of dehydro-ascorbic acid were formed during irradiation. This point will receive comment later. It may be mentioned here that the disappearance of the ascorbic acid was due to the action of the light and not to the rise in temperature of the exposed solution since there was no significant loss in similar solutions kept at 47° for 4 hr. in the dark.

The probable dependence of the disappearance of ascorbic acid on the intensity of the irradiation

In Table 2 are given figures for the disappearance of *l*-ascorbic acid in solution in two concentrations exposed during different periods of time. These experiments were carried out successively so that the actinic output was in all probability of the same intensity in each case. The fact which emerges from these results is that the quantity of *l*-ascorbic acid which disappeared per hour was the same in every experiment; the destruction was therefore proportional to the time of exposure. These results also indicate that the output of actinic energy by the lamp which we used was too low for the disappearance of *l*-ascorbic acid to be affected by variation in the concentrations employed. It would thus appear, as one would expect, that the chemical change is dependent on the intensity of the irradiation.

The protection of l-ascorbic acid by glutathione during anaerobic irradiation

Experiments were then carried out with the purpose of ascertaining whether the formation of dehydroascorbic acid takes place in solutions in which glutathione is present. A protective action of glutathione could be explained

Table 3. *Protection of l-ascorbic acid by glutathione during anaerobic irradiation*

Solution	Time of irradiation hr.	mg. <i>l</i> -ascorbic acid per 100 ml.		
		Initial content	After irradiation	After reduction
With glutathione	0.5	47.5	47.8	46.5
Without glutathione	0.5	44.0	39.3	41.0
With glutathione	2.0	49.0	45.3	44.3
Without glutathione	2.0	45.0	35.0	34.8
With glutathione	4.5	48.8	40.1	38.8
Without glutathione	4.5	45.6	24.2	23.9
Control solution containing no ascorbic acid	4.5	0.5	2.5	1.0
With glutathione	Kept in dark in incubator at 47° for 4.5 hr.	52.5	53.0	52.3
Without glutathione		48.5	45.3	43.5

Table 4. *Screening of l-ascorbic acid during anaerobic irradiation*

Composition of screening solution	mg. <i>l</i> -ascorbic acid per 100 ml.		
	Initial content	After irradiation	After reduction
Water only	48.0	17.0	16.0
0.100 g. glutathione in 50 ml. recently boiled and cooled quartz distilled water	46.5	40.8	39.0
0.34 g. KH_2PO_4 , 2.0 ml. <i>N</i> NaOH in 50 ml. of solution, pH 7.4	47.3	17.0	17.5
0.34 g. KH_2PO_4 , 2.3 ml. <i>N</i> NaOH, 0.100 g. glutathione, in 50 ml. of solution, pH 7.4	47.3	42.5	41.5

either by its reduction of the formed dehydroascorbic acid or by its absorption of rays responsible for the photochemical oxidation of the *L*-ascorbic acid. Two experiments were performed with this end in view. In both experiments the solutions were exposed at the physiological pH of 7.4.

In the first experiment 50 mg. of *L*-ascorbic acid, 0.68 g. KH_2PO_4 and 4.23 ml. of *N*/1 NaOH were made up to 100 ml. with quartz-distilled water (recently boiled and cooled). To 50 ml. of this solution 0.1 g. of crystalline glutathione and 0.33 ml. of *N*/1 NaOH were added. Both solutions were then at pH 7.4 and were placed in quartz flasks which were evacuated, filled with nitrogen and irradiated as before. Aliquot portions of solutions were titrated with indophenol at pH 3 before and immediately after each exposure. The exposed solutions were also reduced with H_2S and titrated again. It will be seen from Table 3 that in the presence and in the absence of glutathione there was a progressive disappearance of *L*-ascorbic acid during the exposure but, whilst in presence of glutathione after $4\frac{1}{2}$ hr. irradiation the loss was of the order of 20%, in its absence the destruction amounted to about 45%. This observation leaves no doubt that the glutathione had a protective action on the actinic decomposition of the *L*-ascorbic acid. It may be noted that no dehydroascorbic acid could be demonstrated in these solutions since there was no increase in the indophenol titre after reduction with H_2S .

In order to show that the protective action of the glutathione was mostly, if not entirely, due to its absorptive capacity for the active radiation, the following experiment was devised. 10 ml. of a solution of *L*-ascorbic acid, prepared as in the preceding experiment and also buffered at pH 7.4, were placed in a small quartz tube (approximate capacity 15 ml.). This tube was evacuated and filled with N_2 as before and placed concentrically within a larger quartz tube as shown in Fig. 2. The *L*-ascorbic acid was then exposed for $4\frac{1}{2}$ hr. when the screening solution consisted of water, buffer or solutions containing 0.2% of glutathione. It is seen from Table 4 that the glutathione had in this case a protective action of the same order as in the preceding experiment. Also in this experiment, owing to the high pH, no dehydroascorbic acid was found.

DISCUSSION OF RESULTS

The results show conclusively that about two-thirds of the increase in the indophenol titration values after reduction of the exposed solutions of *L*-ascorbic acid could be traced to the formation of dehydroascorbic acid. The remaining third may have been due either (a) to the formation of some unknown substance during irradiation which, like dehydroascorbic acid, on reduction with H_2S yielded an indophenol-reducing substance, or (b) to some chemical change incurred during the reduction of the solution which interfered with the furfuraldehyde determination. Whatever be the explanation of the lack of agreement

Fig. 2. A, layer of liquid paraffin employed to prevent oxidation when glutathione was present in the screening solution; B, atmosphere of nitrogen; C, screening solution; D, *L*-ascorbic acid solution.

in the ascorbic acid contents of the irradiated and reduced solutions as determined by the two methods, it is noteworthy that dehydroascorbic acid was formed beyond doubt during the exposure to ultraviolet light in quantities requiring more O_2 than the traces which could possibly have been present in the *l*-ascorbic acid solutions after repeated exhaustion and refilling of the tube with N_2 .

Since Tian [1911] claimed that traces of O_2 together with H_2O_2 are formed when water is exposed to ultraviolet light of 190 $m\mu$, attempts were made by us to detect the formation of O_2 and of H_2O_2 during irradiation of buffer solutions under our experimental conditions, in order to ascertain whether the oxidation was due to this agency. Utilizing the $Ti(SO_4)_2$ test for H_2O_2 and the $Mn(OH)_2$ test for O_2 we could not detect the presence of either. That O_2 and H_2O_2 formed from water during the irradiation could not be responsible for the production of dehydroascorbic acid was also shown by the fact that the reversible oxidation of *l*-ascorbic acid took place even when it was screened during exposure by water which according to Tian's claims should have filtered out the short wave ultraviolet light capable of decomposing water. One is, therefore, forced to the conclusion that the ultraviolet light decomposed some of the ascorbic acid in solution with the formation of an oxidizing substance or substances which in their turn dehydrogenated some of the undecomposed *l*-ascorbic acid. The additional observation that in the presence of glutathione *l*-ascorbic acid in solution is protected from this process of dehydrogenation suggests that such oxidation is not likely to take place *in vivo* even if ultraviolet light were to penetrate superficial tissues containing vitamin C. Furthermore, any dehydroascorbic acid formed would simultaneously be reduced by the glutathione present.

SUMMARY

The observation made by Kellie & Zilva that dehydroascorbic acid is formed by exposing *l*-ascorbic acid anaerobically in buffer solution to ultraviolet light has been confirmed by using the furfuraldehyde method for the determination of ascorbic acid. The evidence shows that the extent of the reaction is dependent on the intensity of the ultraviolet radiation.

It is assumed that some ascorbic acid is decomposed during the exposure with the formation of a substance or substances capable of dehydrogenating some of the undecomposed *l*-ascorbic acid.

Glutathione, whether present in solution with the *l*-ascorbic acid or acting as a screen in a buffer solution, exercises a protective action against dehydrogenation.

It is improbable that any ultraviolet light penetrating superficial tissues containing *l*-ascorbic acid would bring about the oxidation of the vitamin *in vivo*.

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The Structure of Arachidonic and Linoleic Acids

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(Received 3 September 1942)

Early in 1940 Shinowara & Brown described the results of the ozonolysis of methyl arachidonate and of its oxidation by KMnO_4 in acetone solution. As a result of their experiments they formulated arachidonic acid as $\Delta^{6,10,14,18}$ -eicosatetrenoic acid (I):

They emphasized that this structure was not fully confirmed and must be regarded only as a tentative suggestion. Before the appearance of this paper, Dolby, Nunn & Smedley-MacLean had for some time been engaged in elucidating the structure of this acid, using the method of alkaline permanganate oxidation and as their results were entirely at variance with those obtained by Shinowara & Brown, they published a preliminary account [1940] indicating that arachidonic acid was $\Delta^{5,8,11,14}$ -eicosatetrenoic acid (II):

The evidence for this structure was that glutaric and succinic acids were the only dibasic acids isolated; the amount of glutaric acid obtained was very small but it gave no depression in melting-point when mixed with the pure acid. From the other end of the molecule a fraction of volatile fatty acids was obtained which behaved like a mixture of valeric and caproic acids. The melting-point of the *p*-bromophenacyl caproate separated by fractional crystallization was not raised to that of the pure compound, and it was considered desirable at some future time to confirm this result. The authors felt justified, however, in proposing the formula (II) for arachidonic acid.

From the biological point of view, the structure of arachidonic acid is of considerable importance. According to the results of Smedley-MacLean & Hume [1941] the rat synthesizes elupanodonic acid (docosapentenoic acid) only if linseed oil acids are supplied, and it is considered probable that these acids are also the precursors of arachidonic acid in the body. If the formula of Dolby *et al.* were correct, the 11 terminal carbon atoms of arachidonic and linoleic acids would be identically linked and the biological synthesis would involve the addition of 2 carbon atoms at the carboxyl end of the molecule and the introduction of double bonds at the 5, 6 and 8, 9 positions of the C_{20} chain or in the 3, 4 and 6, 7

positions of the C_{18} chain. On the other hand, the tentative formula suggested by Shinowara & Brown bore no resemblance to that of linoleic acid and did not contain the structure

characteristic of the linseed acids. A comparison of the ozonolysis products of methyl arachidonate and ethyl linoleate was therefore undertaken by the present authors, together with an acetone-permanganate oxidation of the former, and the investigation had been almost completed when a communication from Mowry, Brode & Brown [1942] appeared in which the formula (I) tentatively suggested by Shinowara & Brown was withdrawn and that proposed by Dolby *et al.* (II) entirely confirmed. The later work of the American authors had been carried out on a large scale, using 197 g. of arachidonate in place of 11 g. employed in our experiments, enabling them to isolate relatively large quantities of purified oxidation products.

An eicosatetrenoic acid has been isolated by Toyama & Tsuchiya [1935] from fish oil which gave on oxidation only acids containing 4 carbon atoms. They therefore considered it to be $\Delta^{4,8,12,16}$ -eicosatetrenoic acid which contains 4 of the groupings

and in which the characteristic linseed acid structure is absent. This acid has been designated arachidonic acid, but it seems certain that it is not identical with the arachidonic acid prepared from ox suprarenal fat, and it is unfortunate that the same name should be employed. We suggest that the name arachidonic acid be reserved for that originally isolated by Hartley [1909] from pig's liver, to which the constitution $\Delta^{5,8,11,14}$ -eicosatetrenoic acid is assigned, and that the name should not be used to describe the acid obtained from fish oil.

A survey of the literature showed that apparently the only work on the ozonolysis of linoleic acid was by Takahashi [1921] whose results cannot be reconciled with the commonly accepted formula. This provided an additional reason for completing the present work. Takahashi ozonized the acid prepared from soya-bean and rice-bean oils; among the products he identified normal butyric acid and the corresponding aldehyde, glutaric acid and its di-aldehyde, azelaic acid and its half aldehyde. He therefore represented the double bonds as occurring

in the 9:10 and 14:15 positions (III) instead of in the 9:10 and 12:13 positions (IV) as has been generally accepted:

Takahashi stated that the tetrabromo- and tetrahydroxy-stearic acids obtained from his linoleic acid were identical with those prepared from the linoleic acid of poppyseed oil. Haworth [1929] prepared linoleic acid from both soya bean and poppyseed oils, and obtained products by oxidation with acetone-permanganate, and with alkaline permanganate, which were in agreement with formula (IV). Birosel [1937] found the linoleic acid prepared from soya bean oil identical with that from cottonseed oil; both gave the normal tetrabromo- and tetrahydroxy-stearic acids. Ethyl linoleate has now been prepared from linoleic acid tetrabromide (M.P. 114–115°), obtained from maize oil, and on ozonolysis it gave products in agreement with formula (IV) ($\Delta^{9,12}$ -octadecadienoic acid). We therefore do not confirm the results of Takahashi.

Erdmann, Bedford & Raspe [1909] have ozonized linolenic acid (V) and its esters:

They adopted the view of Harries that the ozonide decomposes giving an atom of nascent oxygen for each ozonide group, and that this oxygen may react with H_2O forming H_2O_2 or may oxidize the aldehydes to acids; under these conditions the lower aliphatic aldehydes are those most easily oxidized. Further oxygen is available because linolenic acid and its ethyl ester, when ozonized in chloroform solution, yield the ozonide peroxide; the increase in weight noted indicates this to be the case also for ethyl linoleate. The ozonide of methyl arachidonate was decomposed without removal of solvent but it is likely that it also is an ozonide-peroxide. Erdmann *et al.* [1909] found that the grouping

yielded an ozonide which, with water, gave formylacetic acid, the latter decomposed at 60° to acetaldehyde and CO_2 :

In our experiments, on decomposing the ozonides, acetaldehyde was trapped in 2:4-dinitrophenylhydrazine solution and CO_2 in NaOH solution.

Methyl arachidonate was prepared from arachidonic acid octabromide obtained from ox supranal fat kindly supplied to us by Messrs Allen and Hanburys Ltd. It had the characteristics recorded in the experimental portion. The observed molecular refractivity was 100.4 units, the calculated value being 99.05. It is considered from this result that in pure methyl arachidonate the double bonds are not conjugated, and that the slight exaltation shown is to be ascribed to the incidence of rearrangement of double bonds into conjugated positions in a fraction of the ester during distillation; this is regarded by Farmer & van den Heuvel [1938] as unavoidable except in molecular stills. The exaltation may be due in part to anomalous dispersion, since the refractive index for λ_{5461} was found to be lower than that for λ_{5893} . The products isolated were identified by the melting-point and by the mixed melting-point with an authentic specimen, the dibasic acids directly, the monobasic acids after conversion into *p*-bromophenacyl esters, and the aldehydes after conversion into 2:4-dinitrophenylhydrazones. The amounts of the products were estimated as far as possible, and where the yields are considerable, though none are nearly quantitative, they are recorded in Table 1; in all three experiments the only volatile acids found were caproic and acetic, and on the assumption that only these were present the quantities given in Table 1 were calculated from the weights and equivalent weights of the various sodium salts.

Table 1. Ozonolysis of methyl arachidonate

	Methyl arachidonate	CO ₂	Acetaldehyde 2:4-dinitrophenyl- hydrazone	Na caproate	Na acetate
Wt. (g.)	5.74	0.966	1.976	0.686	2.046
Moles ($\times 10^{-3}$)	18.0	22.0	8.8	5.0	25.0
Ratio	1.0	1.2	0.5	0.3	1.4

Glutaric acid was identified and the presence of caproic aldehyde indicated. The figure given for sodium acetate must be regarded as approximate.

Oxidation of methyl arachidonate by acetone- KMnO_4

	Methyl arachidonate 5.0 g. less 1.0 g. recovered	CO ₂	Acetic acid	Caproic acid
Wt. (g.)	4.0	2.38	0.86	0.82
Moles ($\times 10^{-3}$)	12.6	54.1	14.3	7.1
Ratio	1.0	4.3	1.1	0.6

Oxalic acid was identified and succinic acid and caproic acid were indicated. A hydrocarbon identified as $n\text{-C}_{27}\text{H}_{56}$, and polymerized material (0.63 g.) were also isolated.

Ozonolysis of ethyl linoleate

	Ethyl linoleate	CO ₂	Na caproate	Azelaic acid
Wt. (g.)	3.37	0.259	0.848	0.753
Moles ($\times 10^{-3}$)	10.9	5.9	6.1	4.0
Ratio	1.0	0.5	0.6	0.4

Acetaldehyde 2:4-dinitrophenylhydrazone was identified.

The caproic acid found in the ozonolysis of methyl arachidonate indicates that the molecule contains the fragment

The non-volatile fraction was easily oxidized by permanganate giving a product containing an ester group and a carboxyl group, and saponification of this material gave glutaric acid as the only product detected. This sequence of reactions is consistent with the conversion of (impure) glutaric half-aldehyde methyl ester into methyl hydrogen glutarate and then to glutaric acid indicating the terminal portion of the molecule to be

The remaining 9 carbon atoms yielded 1.9 moles of acetyl radical (as acid and aldehyde) which certainly indicated 3 rather than 2 moles. The yield of CO_2 is low, but comparison with the ethyl linoleate experiment points to the presence of 3 moles of CO_2 . Having regard to the results of Erdmann *et al.* [1909] three

groups are present and must be adjacent. From these results it is concluded that arachidonic acid has the formula (II).

Farmer & van den Heuvel [1938] oxidized with acetone-permanganate a methyl docosahexenoate containing several

groups and found that the ethylenic carbons were oxidized to carboxyl so that these groups gave (presumably via malonic acid) acetic acid. Haworth [1929] oxidized linoleic acid with this reagent, and found a similar rupture of the ethylenic groups, but here the malonic acid, traces of which were detected, gave oxalic acid. We have oxidized methyl arachidonate under conditions resembling those of Farmer & van den Heuvel [1938]. The reaction did not proceed smoothly; 20 % of unoxidized ester was recovered after 37 hr., a considerable amount of polymerized material was formed, and a small quantity of a hydrocarbon, identified by melting-point and analysis as $n\text{-C}_{27}\text{H}_{56}$, was isolated. The last must have been formed under the somewhat strenuous and prolonged reaction conditions; it was not encountered during ozonolysis. It is considered that the methyl arachidonate was slowly oxidized at the double bonds, giving caproic acid, malonic acid (which mainly decarboxylated to give acetic acid but which was also oxidized to oxalic acid) and glutaric acid, which was further oxidized to succinic acid. (The reaction mixture becomes strongly alkaline and apparently hydrolyses the ester group.)

Ozonolysis of the ethyl linoleate yielded caproic acid, indicating the grouping

The sequence azelaic half-aldehyde ethyl ester, ethyl hydrogen azelate, azelaic acid could be followed fairly precisely giving the terminal part of the molecule as

The acetaldehyde and CO_2 indicate the remaining 3 carbon atoms to have been

The commonly accepted formula (IV) for linoleic acid is therefore confirmed.

EXPERIMENTAL

Melting-points and boiling-points are corrected.

Ozonolysis of methyl arachidonate. Methyl arachidonate was prepared by reduction of arachidonic acid octabromide (60 g.) with zinc (60 g.) in methyl alcohol (600 ml.) containing HCl and subsequent esterification according to Ault & Brown [1934]. It (6.25 g.) had b.p. $177\text{--}178^\circ/0.35\text{ mm.}$, i.v. $n_D^{20} = 1.4811$ (calculated for $\text{C}_{19}\text{H}_{31}\text{COOCH}_3$, 319) and $n_D^{24} = 1.4828$, $n_D^{461} = 1.4811$, $\delta_D^{20} = 0.905$, whence R_D obs. = 100.4; R_D calc. 99.0 [Eisenlohr, 1911] or 99.05 [Swietoslawski, 1920].

The ester (5.86 g.) was dissolved in chloroform (40 ml.), cooled in ice and ozonized by passing a current of 8 % ozone through the solution; portions of the solution were withdrawn for test with Br in CCl_4 , until (after 22 hr.) no unsaturation remained. Water (45 ml.) was added to the ozonide solution, which was cloudy and smelt aldehydic. The whole was slowly heated to 98° in a distilling flask connected by ground joints to a condenser and a receiver, and thence to a wash bottle containing 600 ml. of saturated solution of 2:4-dinitrophenylhydrazine in 2N HCl, and a long wash tube containing N NaOH (175 ml.) in a column 26 cm. high; CO_2 -free air was aspirated through the apparatus. The hydrazine solution was then removed and replaced by fresh reagent and steam passed, aspiration being continued. In this way CO_2 , acetaldehyde, non-volatile, and volatile fractions were separated.

The ice-cooled NaOH solution was titrated with N H_2SO_4 using phenolphthalein and then methyl orange, and 0.966 g. CO_2 were found. A slight excess of H_2SO_4 was added and 87 % of the solution was distilled off; the distillate contained volatile acid equivalent to only 2 % of the found CO_2 .

The 2:4-dinitrophenylhydrazine solution yielded crude acetaldehyde 2:4-dinitrophenylhydrazone (1.875 g. m.p. of the two ppts. $142\text{--}144^\circ$ and $149\text{--}159.5^\circ$) from which fractional crystallization gave the pure compound m.p. 169° mixed m.p. $168.5\text{--}169^\circ$ with authentic acetaldehyde 2:4-dinitrophenylhydrazone (m.p. 169°).

The solution of non-volatile compounds was filtered from a small quantity of oily polymer, an equal volume of saturated brine added, and the

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solution repeatedly extracted with ether, and dried with Na_2SO_4 , yielding 1.53 g. of material. This was suspended in hot Na_2CO_3 solution and treated with 193 ml. KMnO_4 ($N/10$) to oxidize aldehyde to carboxyl, on the assumption that 80 % would be glutaric half-aldehyde methyl ester. The solution was acidified (H_2SO_4), extracted repeatedly with ether, and the extract washed, dried (Na_2SO_4) and evaporated. The residue was first titrated with, and then quantitatively saponified with, alcoholic potash. (Found: COOMe , 14; COOH , 42 %. Calc. for $\text{HOOC}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{COOMe}$: COOMe , 40; COOH , 31 %.) The saponified solution, after dilution with water and evaporation of the alcohol, was acidified (H_2SO_4), saturated with salt, and extracted with ether, first by shaking and then for 8 hr. in a continuous extractor. The former extract gave a brown solid which, after crystallization from chloroform-light petroleum, was dissolved in hot water, filtered and evaporated; it then had m.p. 61–65.5° but could not be identified. The second extract gave a white solid which was similarly treated, then repeatedly recrystallized from benzene, and which yielded a small quantity of glutaric acid, m.p. 92.5–93.5° and mixed m.p. 95.5° with authentic glutaric acid (m.p. 97.5–98°).

To the distillate, consisting of chloroform and aqueous layers, more chloroform was added and the whole titrated with N NaOH , with shaking, in a separating funnel. The chloroform solution was separated, dried (Na_2SO_4) and the solvent removed, the latter was mechanically shaken with an excess of a solution of 2:4-dinitrophenylhydrazine in 2*N* HCl , when it gave a derivative, which after repeated crystallization, had m.p. 152–152.5° (0.101 g.) and was probably impure acetaldehyde 2:4-dinitrophenylhydrazone. The neutral residue, after removal of chloroform, was distilled, giving a small distillate, b.p. 70–130°; this furnished a 2:4-dinitrophenylhydrazone which after recrystallization had m.p. 100–101.5°. The mixed m.p. with authentic caproic aldehyde 2:4-dinitrophenylhydrazone (m.p. 109°) was 103–104°.

The aqueous solution after evaporation and drying to constant weight in a vacuum desiccator, gave 2.732 g. of sodium salt having equivalent 91.3 (from the amount of N NaOH used). (The same procedure for estimating the equivalent of sodium salts was employed a number of times below.) This was dissolved in water (110 ml.), acidified (H_2SO_4) and distilled; the first 26 ml. and the next 75 ml. of distillate were collected. The last was neutralized and yielded a sodium salt (1.378 g., equiv. 83.7), giving a *p*-bromophenacyl derivative which melted for the most part at 81–85° (*p*-bromophenacyl acetate has m.p. 87–87.5°), but which contained a higher melting impurity. We made a number of attempts but were unable to separate the latter. A portion of the

sodium salt was refluxed with dilute H_2SO_4 and the solution distilled; the distillate on neutralization gave a sodium salt having equiv. 83.2 (sodium acetate has equiv. 82), but again we were unable to prepare a pure *p*-bromophenacyl ester.

The first fraction of distillate contained a layer of oily acid which was pipetted off, and the solution again distilled; 6.3 ml. of this distillate were taken, combined with the oily acid and neutralized giving 0.403 g. of a sodium salt, equiv. 127. It was converted into its *p*-bromophenacyl derivative which, after three recrystallizations, had m.p. 70.5–71.5° and mixed m.p. 71–71.5° with authentic *p*-bromophenacyl caproate of m.p. 71.5–72°.

Oxidation of methyl arachidonate by acetone-KMnO₄. Methyl arachidonate (5.0 g.) was dissolved in dry acetone (300 ml.) and heated under reflux in an apparatus in which the returning acetone percolated through KMnO_4 . In the course of 37 hr. 36.6 g. of the last were used without the appearance of a pink coloration; since only 31.4 g. would be necessary to convert each ethylenic link into two carboxyl groups, the oxidation was stopped. The solution was filtered from the manganese mud and the latter washed with acetone. The acetone was evaporated and the residue taken up in light petroleum and washed with NaOH solution and with water (added to bulk aqueous extract below). After drying (Na_2SO_4) and removal of solvent, unchanged ester (1.0 g.) remained.

The manganese mud was dried and leached out with 500 ml. boiling water. The latter after filtration, evaporation and desiccation yielded 11.9 g. of salts (A). The desiccated manganese mud now weighed 19.6 g. The CO_2 content of these two fractions (which contained volatile organic acids) was determined as follows. An aqueous solution of the material was heated to boiling under reflux in a current of CO_2 -free air, the top of the condenser being connected to a wash bottle containing $N/10$ $\text{Ba}(\text{OH})_2$. Dilute H_2SO_4 was run into the solution and the liberated CO_2 swept through. The baryta solution was filtered and titrated against $N/10$ HCl . The difference from a blank gave the CO_2 trapped, and a correction for imperfections in this method was applied from control experiments with known quantities of carbonate. The extracted, dry, manganese mud and the salts (A) contained 48.9 and 119.4 mg. $\text{CO}_2/\text{g.}$ respectively.

The salts (A) (3.7 g.) were dissolved in water, acidified (H_2SO_4) and steam distilled.

Successive fractions of distillate	10	10	10	150	180
(ml.)					
Na salt: wt. (mg.)	123	74	55	321	87
equiv.	103.5	98	97	90	172

A repetition with 7.65 g. of salts (A) yielded three fractions of sodium salts: 0.685 g., equiv. 93; 0.211 g.,

equiv. 86; 0.265 g., equiv. 115. The first of these fractions was dissolved in a minimum of water, acidified (H_2SO_4), extracted repeatedly with ether, and the extract dried (Na_2SO_4) and evaporated. The residue was fractionated by distillation through a series of three bulbs which were successively heated in an air-bath. The fraction (20 mg.) taken at air-bath temperature, $195\text{--}225^\circ$, was converted via the acid chloride to the anilide which had m.p. $79.5\text{--}81.0^\circ$, mixed m.p. $80\text{--}81.5^\circ$ with caproic anilide (m.p. 96°), and mixed m.p. $55\text{--}56.5^\circ$ with *n*-valeric anilide (m.p. $61.5\text{--}62^\circ$). The fraction was thus probably caproic acid. The mid-fraction of sodium salts (0.308 g.) yielded a *p*-bromophenacyl derivative (0.721 g.) of m.p. 70° ; five recrystallizations gave *p*-bromophenacyl acetate, m.p. $83\text{--}83.5^\circ$ and mixed m.p. 86° with the authentic compound (m.p. $87\text{--}87.5^\circ$).

There remained in the steam distillation flask a tar and an aqueous solution; the former (insoluble in benzene and in ether) was dissolved in acetone, dried (Na_2SO_4), and after removal of solvent weighed 0.404 g. The aqueous solution was extracted with ether in a continuous extractor for 22 hr. and with fresh solvent for a further 6 hr. On removal of the ether the residue was dissolved in hot acetone (in which nearly all of it dissolved), filtered, and cooled, when crystals, 49 mg., m.p. 55° , were deposited. After two recrystallizations from benzene-acetone, it had m.p. $57\text{--}58^\circ$. (Found: C, 84.6; H, 15.0 %. $n\text{-C}_{27}\text{H}_{56}$ has m.p. $58.5\text{--}59.5^\circ$, C, 85.2; H, 14.9 %.) Addition of two volumes of light petroleum to the acetone filtrate yielded an oil which crystallized. The product after draining and washing with ether had m.p. $99\text{--}100^\circ$ and was dissolved in water, filtered, evaporated and desiccated over H_2SO_4 . The residue (45.5 mg.) had m.p. $160\text{--}161.5^\circ$ (decomp.); a portion was converted into the ammonium salt which yielded pyrrole on ignition with zinc dust, indicating succinic acid. A further portion was titrated with NaOH, giving equiv. 51.3, and the solution was acidified (acetic acid), treated with CaCl_2 solution, and the precipitate titrated in acid against KMnO_4 at 60° , whence 33.2 mg. (anhydrous) oxalic acid were obtained.

The acetone-light petroleum solution on evaporation yielded a residue (C_6H_6), which after washing had m.p. $99\text{--}100^\circ$. It was dissolved in water, filtered and evaporated and yielded hydrated oxalic acid (41 mg., equiv. 63.2).

Ozonolysis of ethyl linoleate. Corn (maize) oil acids (177 g.; i.v. Hübl=114) were brominated (40 ml. bromine) in light petroleum solution. The solid product was recrystallized from hot benzene yielding tetrabromostearic acid m.p. $114\text{--}115^\circ$. It (44 g.) was reduced with zinc dust according to Brown & Fraenkel [1938]. The linoleic acid was esterified with EtOH-HCl and gave ethyl linoleate

(12.8 g.), b.p. $173.5^\circ/0.5\text{ mm.}$; i.v. Hübl=161 (calc. 164.8); this (3.5 g.) was ozonized as before, saturation being reached after 9 hr. The chloroform was removed as far as possible in a water pump vacuum at 40° , yielding a colourless oil (4.90 g. Theory, assuming a *bis*-ozonide-peroxide, 4.75 g.).

Cold water (35 ml.) was added to the ozonide and decomposition was allowed to proceed in apparatus similar to that used for methyl arachidonate except that five small wash bottles were employed, the first containing a saturated solution of 2:4-dinitrophenylhydrazine in 2*N* HCl, the second the same reagent in alcoholic H_2SO_4 and the last three *N* NaOH (75 ml. each). The water-bath was raised to boiling point over a period of 1 hr. and a slow current of CO_2 -free air continued overnight. The contents of the 2:4-dinitrophenylhydrazine wash bottles were then replaced by fresh reagent in 2*N* HCl solution, and steam passed in place of the air current, aspiration through the wash train being continued. Finally the distillate and the solution of non-volatile material in the flask were both saturated with salt and extracted with ether and the latter dried (Na_2SO_4).

The NaOH solution was cooled and titrated with *N* HCl, using phenolphthalein and methyl orange successively and 0.259 g. CO_2 was found.

Of the 2:4-dinitrophenylhydrazine solutions, the alcoholic one gave no appreciable yield, whilst the first and second aqueous ones gave respectively two products (0.151 and 0.035 g.), m.p. $107\text{--}109^\circ$ and 87° , which on recrystallization had m.p. $145.5\text{--}147.5^\circ$ and $137\text{--}143^\circ$. These were combined and after four recrystallizations had m.p. 160° and mixed m.p. $168\text{--}169^\circ$ with authentic acetaldehyde 2:4-dinitrophenylhydrazone (m.p. $168.5\text{--}169^\circ$).

Evaporation of the ethereal solution of non-volatile products gave a semi-solid mass which was washed with ether-light petroleum yielding crude azelaic acid (0.122 g.), m.p. $100.5\text{--}102.5^\circ$. The residue from evaporation of the washings was suspended in hot Na_2CO_3 solution and titrated with KMnO_4 until the reaction slowed down (required 63.9 ml. of KMnO_4 , 0.06*N*). The solution was acidified (H_2SO_4), extracted with ether, the extract washed, dried (Na_2SO_4), and evaporated, giving a semi-solid (1.286 g.). This was dissolved in alcohol and titrated with alcoholic potash and then saponified with excess of this reagent. (Found: carboxyl equiv. 213 and ester equiv. 216; $\text{HOOC}(\text{CH}_2)_7\text{COOEt}$ has mol. wt. 205). The solution was acidified (HCl), cooled and filtered, yielding crude azelaic acid (0.641), m.p. $102.5\text{--}103^\circ$. The azelaic acid was recrystallized once from hot water, when it had m.p. $107.5\text{--}108^\circ$ alone, or mixed with authentic azelaic acid (m.p. $106.5\text{--}108^\circ$).

The ethereal solution of the distillate was titrated, with shaking, in a separating funnel with *N* NaOH. No pure product was isolated from the neutral ether; a carbonyl group was present since reaction occurred with 2:4-dinitrophenylhydrazine but no identifiable hydrazone was isolated; a semicarbazone could not be formed.

The aqueous solution gave a sodium salt (0.875 g.), equiv. 135. This was dissolved in water (55 ml.), acidified (H_2SO_4) and distilled. The first 20 ml. and the next 29 ml. of distillate gave Na salts, 0.380 g., equiv. 136, and 0.317 g., equiv. 132, respectively. The former was converted into its *p*-bromophenacyl derivative which had m.p. 71.5–72° and mixed m.p. 71–72° with authentic *p*-bromophenacyl caproate (m.p. 71.5–72°).

SUMMARY

1. The results of ozonolysis and of acetone- $KMnO_4$ oxidation of methyl arachidonate are in agreement with the constitution (II) $\Delta^{5,8,11,14}$ -eicosatetraenoic acid, for arachidonic acid, which was proposed by Dolby *et al.* [1940].

2. Contrary to the results of Takahashi [1921] ozonolysis of ethyl linoleate yields products in accordance with the generally accepted structure for linoleic acid, $\Delta^{9,12}$ -octadecadienoic acid (IV).

We desire to express our gratitude to Prof. D. Keilin for hospitality at the Molteno Institute and to Dr F. G. Mann for permission to use the ozonolysis apparatus in the University Chemical Laboratory, Cambridge.

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60. *The Mechanism of the Reaction of (–)Phenylalkylcarbinols with Hydrogen Bromide.*

By C. L. ARCUS.

Levene and Rothen (*J. Biol. Chem.*, 1939, **127**, 237), having determined the rotations of the bromides produced by the action of hydrogen bromide on (–)phenyl-methyl-, -ethyl-, and -*n*-propyl-carbinols at temperatures from -80° to $+20^{\circ}$, expressed the view that the three mechanisms of substitution known as S_N1 , S_N2 , and S_N1 do not suffice to explain these curves. An explanation is now put forward in which the participation of each mechanism in the total reaction is represented by a distribution curve about a maximum at a certain temperature, and it is found that the algebraic sum of the optical results of the three mechanisms reproduces the experimental curves.

The "domain" of each mechanism, represented by the area between its distribution curve and the temperature axis, has been calculated for the three reactions.

LEVENE and ROTHEN (*loc. cit.*) have determined the sign and magnitude of the rotation of the α -phenyl-ethyl-, -*n*-propyl, and -*n*-butyl bromides produced by the action of hydrogen bromide, in the absence of solvent, on (–)phenyl-methyl-, -ethyl-, and -*n*-propyl-carbinols, at temperatures from -80° to $+20^{\circ}$. The percentage optical purity of these bromides varies with temperature of reaction according to Fig. 1 for α -phenylethyl-bromide (the propyl analogue gives a very similar curve) and to Fig. 2 for the *n*-butyl compound. Values for the first two compounds approach large negative limits at -80° ; with increasing temperature they fall to zero, and then rise to a positive maximum, from which they slowly fall. The (–) α -phenyl-*n*-butyl bromide produced

at -80° appears to have reached a limiting negative optical purity; with increasing temperature a curve is followed similar in shape to those of the other two, but which is always negative.

The method employed was the same throughout. Dry hydrogen bromide was introduced very slowly into an evacuated flask containing the carbinol and maintained at the required temperature. The reaction was allowed to proceed substantially to completion. The excess hydrogen bromide was pumped off, and the bromide isolated and distilled. Hence, for a single carbinol the only variable is the reaction temperature, and for different carbinols reacting at the same temperature the only variable is the structure of the carbinol.

Three mechanisms of substitution applicable to these reactions have been described. A bimolecular mechanism leading to complete inversion has been proposed by Kenyon and Phillips (*Trans. Faraday Soc.*, 1930, 26, 451) and investigated kinetically by Hughes, Ingold, and Masterman (J., 1937, 1196). For the reaction of an alcohol with hydrogen bromide this mechanism (S_N2) is

A unimolecular mechanism was proposed by Hughes and Ingold (J., 1935, 244), in which the molecule undergoing substitution slowly ionises and the carbonium cation reacts with the entering group (S_N1):

The carbonium cation is flat, but it is shielded from attack by the withdrawing group, whence the inverted configuration preponderates. Hughes, Ingold, and Scott (J., 1937, 1201) found the hydrolysis of α -phenylethyl chloride in water and aqueous acetone to be unimolecular and to result in 2–17.5% excess of the inverted configuration.

A third mechanism (S_Ni) for the replacement of hydroxyl by halogen has been described (Cowdrey, Hughes, Ingold, Masterman, and Scott, J., 1937, 1252; Hughes, Ingold, and Whitfield, *Nature*, 1941, 147, 206); an addition compound is formed, and if sufficient electron release is available to the carbon atom undergoing substitution, a rearrangement leading to retention of configuration occurs.

The addition compound is probably formed by hydrogen bonding. The valency angle of the hydrogen bond is 180° , but bending to 120° is known in the *o*-nitrophenols, and bending to a quasi-cyclic structure by electrostatic attraction between the bromine and the carbon atoms may occur as a preliminary to reaction.

From the literature, Hughes, Ingold, and Scott (*loc. cit.*) concluded that when phenylmethylcarbinol and α -phenylethyl bromide have the same sign of rotation they are of the same configuration; Levene and Rothen (*loc. cit.*) further concluded from an analysis of the rotatory dispersions of these compounds that phenyl-methyl-, -ethyl-, and -*n*-propyl-carbinols with the same sign of rotation have the same configuration, and similarly for the three bromides. Hence, for all three reactions retention of sign means retention of configuration.

At low temperatures, the retention of configuration in all three reactions, together with the formation of a white crystalline addition compound in the reaction with the ethyl carbinol, indicates that S_Ni predominates at such temperatures. This is superseded, with rising temperature, by replacement with inversion until -30° , -27.5° , and -17.5° , respectively, are reached for the three reactions, whereupon movement in the direction of retention occurs. Since this movement results in larger rotatory powers for α -phenyl-*n*-butyl bromide, Levene and Rothen concluded that the change is due, not to the commencement of racemisation, but to the coming into play of a second mechanism leading to retention and that "consequently the mechanisms (above) do not suffice . . . since, of the three only one proceeds with retention, whereas the present observations point to two mechanisms connected with retention."

It is now shown that, on certain assumptions, these three mechanisms suffice to explain the form of the rotation-temperature curves.

Mechanism S_N2 is considered to result in complete inversion; for S_N1 , 10% inversion is estimated as an approximate value in the light of the results of Hughes, Ingold, and Scott (*loc. cit.*). The intramolecular mechanism S_Ni is considered to give complete retention. This is supported, for the phenylalkylcarbinols, by the almost complete retention observed during the (intramolecular) Hofmann and Curtius rearrangements

in which the radical CHMePh $\cdot$ migrates (Arcus and Kenyon, J., 1939, 916; Kenyon and Young, J., 1941, 263). Then, considering the reaction of one carbinol with hydrogen bromide at one temperature, the phenylalkyl bromide is assumed to result from a combination of the three mechanisms, there being no experimental evidence for the existence of further mechanisms, applicable to the reaction conditions, of substitution of OH by Br. Since each mechanism has a characteristic optical result, it should be possible to determine, from the optical purity of the bromide, the percentage of the total reaction due to each mechanism. The bromide isolated was the product of the completed reaction, and hence these percentages refer to the reaction as a whole. The com-

position of the reaction medium changes as the reaction proceeds and the relative importance of the mechanisms may vary with time during the reaction; this aspect, however, is not discussed, and no assumptions are made about it. The percentages deduced are averages over the whole reaction period and their variations with changes in temperature and structure are described.

FIG. 1.

FIG. 2.

Finally, the assumption was made that the plot against temperature of the participation of any mechanism in the total reaction would, in general, be a distribution curve diminishing in a sigmoid curve on either side of a maximum at a certain temperature. (If one mechanism were to gain total control of the reaction above or below a certain temperature, then its maximum would be extended as a straight line over the range of total control.) Such a distribution curve represents the variation with temperature of the probability (the average probability over the whole reaction period) that a molecule of carbinol, when several mechanisms of reaction are possible to it, will react by one given mechanism.

The rotations of optically pure bromides were taken from the graphs of Levene and Rothen, small extrapolations being necessary for the methyl and the ethyl carbinol. The experimental rotations were then converted from $[M]_{5780}$ to percentage optical purity, and smooth curves were drawn through the resulting values; then, if b , c , and d are the percentages of the total reaction proceeding by mechanisms S_N1 , S_N2 , and S_N1 , respectively, and α is the percentage optical purity of the product, at a given temperature,

$$b + c + d = 100 \text{ and } \alpha = -(b - c - 0.1d)$$

A third relation is supplied by the assumption that the curves b , c , and d are distribution curves which are always positive and have only one point of inflection between successive stationary points. It was then found by successive trial that if these conditions were to be satisfied the range of permissible variation is small. Representative values of b , c , and d have been calculated for 16 values of α for each bromide, and these values for α -phenyl-ethyl and α -phenyl- n -butyl bromide are plotted in Figs. 1 and 2, respectively.

Thus the three mechanisms S_N1 , S_N2 , and S_N1 , leading respectively to retention, inversion, and to much racemisation with some inversion (estimated at 10%), when their participations in the total reaction vary according to the distribution curves b , c , and d , yield bromides whose optical purity varies with temperature according to the experimental curves.

S_N1 approaches or attains a maximum at -80° , indicating that formation of the addition complex is favoured at low temperatures. S_N1 tends towards a maximum at

above $+20^\circ$, showing ionic fission of $R\cdot OH_2^+$ to be predominant at higher temperatures. S_N2 is at a maximum at intermediate temperatures, approximately -25° to -30° , which are presumably low enough

to check ionisation and high enough to diminish the addition of hydrogen bromide which yields the complex of S_{Ni} .

In view of the assumptions made, the distribution curves are not numerically exact, but the following relationships may be noted. The "domain" of each mechanism between the temperatures considered, -80° to $+20^{\circ}$, can be represented by the area between its distribution curve and the axis of temperature; these areas, expressed as % of the total area, are:

	Carbinol: CHMePh·OH.	CHEtPh·OH.	CHPr ⁿ Ph·OH.
S_{Ni}	41.3	43.2	62.4
S_{N2}	23.6	22.1	17.6
S_{N1}	35.2	34.6	20.0

With increasing electron release by the methyl, ethyl, and *n*-propyl groups, the domain of S_{N2} diminishes, that of S_{Ni} is markedly increased, and that of S_{N1} decreases. The last two mechanisms are both known to be promoted by electron release by groups attached to the carbon atom undergoing substitution (Hughes, Ingold, *et al.*, *loc. cit.*), and it is inferred that when, as here, conditions permit these two mechanisms to compete, S_{Ni} is promoted more strongly by electron release than is S_{N1} . This can be seen in the region 0° to $+20^{\circ}$ in Figs. 1 and 2; here S_{N2} is of relatively little importance and, with increasing electron release, S_{Ni} competes successfully with S_{N1} . This situation is entirely compatible with the known effect of electron release in promoting S_{N1} over S_{N2} when these two mechanisms compete in the absence of S_{Ni} .

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11.

D. Sc. 1955
CORRESPONDENCE

THE TERNARY BOND

SIR,—In the course of a study of the changes in bonding which occur during rearrangement and substitution, it has been found that a number of reactions are best represented as proceeding

through intermediates which contain a "ternary bond" $\text{A} \overset{\text{X}}{\underset{\text{B}}{\triangle}}$.

In such a bond three atoms are bonded by one electron-pair (two of the atoms are throughout also linked by a normal single or double bond). Bonding of this type has been proposed and discussed by Dewar¹ and by Walsh.^{2, 3} The ternary bond is a structure permitting the formal preservation of octets, called into being in electron-deficient situations and tending to be replaced by more normal bonding when conditions permit.

The reactions involving the ternary bond are all particular cases of the following two general formulations (in which the nature or absence of the groups p, q, r, s and of electrical charges is not particularized):

The formation of the ternary bond with the release of Y and its disappearance with the addition of Z are both of the nature of substitutions with inversion, the new bond forming at the side of B or A opposite to the old bond.

Stereochemically the results of I and II are as follows. If X is an optically active carbon atom then I (a) and II (a) provide mechanisms whereby X moves from A to B with retention of its configuration. If B is an asymmetric carbon atom (X now, in general, a symmetrical group or atom) then I (b) provides a mechanism for substitution at B with retention of configuration; also, if B is an asymmetric carbon atom, I (a) permits the migration of X from A to B with retention of optical activity but inversion of configuration at B. Finally, if A is an asymmetric carbon atom, I (a) permits X to migrate to B with retention of optical activity but inversion of configuration at A.

These formulations have been applied to a number of rearrangements and substitutions and it is hoped to present a more complete account elsewhere.

I wish to thank Dr. J. Kenyon, F.R.S., and Dr. J. W. Smith for helpful discussions.

I am, Sir, etc.,

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June 11, 1947

¹ Dewar, M. J. S., J. C. S., 1946, 406.

² Walsh, A. D., Nature, 1947, 159, 165 and 712.

³ Walsh, A. D., J. C. S., 1947, 89.

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320. The Reaction of Bromine with Silver (+)- α -Phenylpropionate. An Electrophilic Bimolecular Substitution.

By C. L. ARCUS, A. CAMPBELL, and J. KENYON.

The reaction of bromine in carbon tetrachloride solution with silver (+)- α -phenylpropionate yields (+)- α -phenylethyl bromide with inversion of configuration. It is considered that the positive-halogen compound, $\text{CHPhMe}\cdot\text{CO}\cdot\text{OBr}$, is first formed and that reaction subsequently proceeds according to equation (i) (below), with the similar reactions (ii) and (iii) as possible subsidiary reactions. All are bimolecular substitutions with inversion of configuration effected by the electrophilic reagent, positive bromine. The partial racemisation which occurs during this reaction is attributed to the experimentally-observed racemisation of (+)- α -phenylethyl bromide in solution in carbon tetrachloride by bromine in the presence of silver bromide.

Hell-Volhard bromination of (+)- α -phenylpropionic acid yields ($\pm$)- α -bromo- α -phenylpropionic acid.

INTERACTION of one equivalent of the silver salt of an aliphatic or substituted aliphatic carboxylic acid with two equivalents of bromine yields the alkyl bromide containing one carbon atom less than the original acid; numerous examples from the literature are cited by Kleinberg (*Chem. Reviews*, 1947, **40**, 386). The mechanism which has been generally accepted for this reaction (Birckenbach, Goubeau, and Berninger, *Ber.*, 1932, **65**, 1339; Bockemüller and Hoffmann, *Annalen*, 1935, **519**, 165; Kleinberg, *loc. cit.*) is that an intermediate positive-halogen compound $\text{R}\cdot\text{CO}\cdot\text{OBr}$, the acyl hypobromite, is formed:

This undergoes decarboxylation to give the alkyl bromide, RBr .

Bockemüller and Hoffman (*loc. cit.*) obtained the following evidence for the existence of the acyl hypobromites. Silver butyrate was shaken with bromine in carbon tetrachloride solution, and the product filtered. The yellowish-green filtrate, which was free from silver, liberated iodine from acidified potassium iodide solution, whereby its oxidising power was determined. The total bromine content was one-half of that of a solution of bromine of equal oxidising power,

as compared with

Further, the butyryl hypobromite so prepared combined with *cyclohexene* to give 2-bromo-*cyclohexyl* butyrate:

The use of a silver-free filtrate (as distinct from a suspension of the silver salt in bromine-carbon tetrachloride) precluded the possibility that the 2-bromo-*cyclohexyl* butyrate might be formed as follows:

Birckenbach *et al.* (*loc. cit.*) had earlier effected the reaction of silver acetate and iodine in ether at -80° and by adding *cyclohexene* to the filtrate had obtained 2-iodo-*cyclohexyl* acetate.

Determinations of oxidising power and of bromine content, and addition to *cyclohexene*, gave analogous results with a solution of benzoyl hypobromite, which was similarly prepared.

These findings demonstrate the existence in solution of compounds of the structure $\text{R}\cdot\text{CO}\cdot\text{OBr}$

and indicate the bromine to be a "positive" halogen such as exists in hypobromous acid and the *N*-bromoamides and in contrast with the bromine of alkyl and acyl bromides.

In order to elucidate further the mechanism of the substitution of carboxyl by bromine, silver α -phenylpropionate, prepared from the acid having $\alpha_{D}^{15} + 42.3^\circ$ (*l*, 0.5) (optical purity, 81.7%), was treated in boiling carbon tetrachloride suspension with two equivalents of bromine; it gave, in good yield, α -phenylethyl bromide, $\alpha_{D}^{16} + 46.2^\circ$ (*l*, 1.0) [optical purity, 35.2%, by comparison with the highest recorded rotatory power of this compound, $\alpha_{D}^{18} + 131.4^\circ$ (*l*, 1.0); Gerrard, *J.*, 1946, 741].

The retention of asymmetry during this substitution is thus 43.1%, and the following data permit comparison of the configurations of the acid and the bromide. (+)- α -Phenylpropionic acid has been converted, with retention of configuration, into (–)- α -phenylethylamine by the Hofmann, and other, rearrangements (Arcus and Kenyon, *J.*, 1939, 916; Kenyon and Young, *J.*, 1941, 263; Campbell and Kenyon, *J.*, 1946, 25). With nitrous acid the (–)-amine has been found (Campbell, unpublished results) to yield (+)- α -phenylethyl alcohol with 14.8% retention of asymmetry; it is concluded that during this reaction the diazonium ion $\text{CHMePh}\cdot\text{N}_2^+$ dissociated into nitrogen and the ion $^+\text{CHPhMe}$, and that the latter reacts with water to form the alcohol with a preponderance of the inverted configuration, due to shielding of the original point of attachment by the released nitrogen molecule. Finally, (+)- α -phenylethyl alcohol and (+)- α -phenylethyl bromide have the same configuration (Hughes, Ingold, and Scott, *J.*, 1937, 1201). Thus (+)- α -phenylpropionic acid and (+)- α -phenylethyl bromide have opposite configurations, and the silver salt–bromine reaction proceeds with inversion of configuration.

The following mechanism for the reaction is put forward. α -Phenylpropionyl hypobromite, $\text{CHPhMe}\cdot\text{CO}\cdot\text{OBr}$, is first formed, and two molecules of this compound react according to equation (i) to yield α -phenylethyl bromide, carbon dioxide, and two ions which combine to regenerate one molecule of α -phenylpropionyl hypobromite:

followed by

followed by

It is possible that molecular bromine may react by a similar mechanism (ii) to yield α -phenylethyl bromide, carbon dioxide, and ions which combine to regenerate bromine. Finally, a small concentration of bromine cations may be either set up by reactions (i) and (ii) or may exist in equilibrium with $\text{CHPhMe}\cdot\text{CO}\cdot\text{OBr}$ or with Br_2 , and reaction may then proceed by (iii) in which α -phenylethyl bromide and carbon dioxide are formed and bromine cation is regenerated. All the reactions (i), (ii), and (iii) yield α -phenylethyl bromide with inversion of configuration and in each of them the attacking reagent is positive bromine, *i.e.*, bromine which tends to separate or which has separated with a sextet of electrons.

The configuration of the α -phenylethyl bromide resulting from these reactions would be completely inverted; the bromide obtained experimentally was inverted, but also partly racemised. The possibility that there may be a subsidiary mechanism of reaction in which a planar α -phenylethyl fragment is formed at one stage or which proceeds with retention of configuration is not excluded, but it appears most probable that the racemisation is due to the action of bromine and silver bromide on the fully inverted (+)- α -phenylethyl bromide during the period elapsing between its formation and the completion of the experiment. Experimental results leading to this explanation are described below.

It is concluded that the silver α -phenylpropionate–bromine reaction is mainly or entirely a bimolecular substitution with inversion of configuration effected by the electrophilic reagent, positive bromine. It appears to be the first established example of this class of replacement reaction.

The following experiments were carried out in order to elucidate the cause of the partial racemisation which occurred during the silver salt reaction. (+)- α -Phenylethyl bromide was dissolved in carbon tetrachloride and heated under reflux for 1 hour with silver bromide and

bromine (0.7 equivalent); the recovered α -phenylethyl bromide was 99.8% racemised. During this experiment some hydrogen bromide was evolved, indicating the occurrence of bromination. From a similar experiment, in which silver bromide but no bromine was used, there was obtained, after heating for 3 hours, α -phenylethyl bromide which was racemised only to the extent of 0.6%. A similar experiment in which bromine (2.0 equivalents) but no silver bromide was used gave, after 3 and 19 hours, respectively, 38.4 and 99.0% racemisation. Thus racemisation is rapid when bromine and silver bromide are present together, slower with bromine alone, and slight with silver bromide alone.

The mechanism of racemisation of α -phenylethyl bromide by bromine, with catalysis by silver bromide, is uncertain. It may be due to bimolecular halogen exchange, which has been shown (Hughes, Juliusberger, Scott, Topley, and Weiss, *J.*, 1936, 1173) to be the mechanism of the racemisation of α -phenylethyl bromide by lithium bromide in solution in acetone. Alternatively, it may be due to a free radical reaction, $RBr + Br_2 \longrightarrow R^{\cdot} + Br_2 + Br^{\cdot}$, followed by $R^{\cdot} + Br^{\cdot} \longrightarrow RBr$.

Further work bearing on the mechanism of this racemisation is in progress.

A Hell-Volhard bromination of (+)- α -phenylpropionic acid has been carried out by converting the acid into the acid bromide and heating the latter with bromine; the resultant bromo-acid bromide with water gave optically inactive α -bromo- α -phenylpropionic acid. The isolation of the acid involved a crystallisation, so that the optically active acid, had it been present in small proportion, might have been removed; further, the reaction conditions might have caused racemisation of the optically active acid after its formation. With these reservations, the formation of optically-inactive α -bromo- α -phenylpropionic acid is consistent with bromination *via* the (symmetrical) enolic form of α -phenylpropionyl bromide, a mechanism of reaction which has been discussed by Watson ("Modern Theories of Organic Chemistry," 2nd edition, Oxford, 1941, p. 166).

EXPERIMENTAL.

($\pm$)- α -Phenylpropionic acid was prepared by the method of Campbell and Kenyon (*loc. cit.*) and resolved according to Arcus and Kenyon (*loc. cit.*).

Silver-salt-Bromine Reaction.— α -Phenylpropionic acid having $\alpha_{D}^{15} +42.3^{\circ}$ (*l*, 0.5) (11.2 g.) was dissolved in one equivalent of N-NaOH (75 ml.), and to this solution was added silver nitrate solution until no further precipitate resulted. The grey precipitate was filtered off, washed, and dried *in vacuo* (yield, 18.0 g.). This silver salt was suspended with stirring in boiling, dry carbon tetrachloride (100 ml.), to which was added dry bromine (11.1 g., 2.0 equivs.). The solution was heated under reflux until all the colour had disappeared and then for a further hour. It was filtered from silver bromide, washed with sodium hydrogen carbonate solution and then with water, and dried (Na_2SO_4). Fractionation gave (+)- α -phenylethyl bromide, b. p. 98–99°/20 mm. (7.1 g.), having $\alpha_{D}^{16} +46.2^{\circ}$ (*l*, 1.0).

Racemisation of (+)- α -Phenylethyl Bromide.—A specimen of α -phenylethyl bromide, kindly supplied by Dr. W. Gerrard, had b. p. 80.5–83.5°/8 mm. and $\alpha_{D}^{18} +96.6^{\circ}$ (*l*, 1.0). This (3.3 g.) was dissolved in dry carbon tetrachloride (48 ml.), the solution having $\alpha_{D}^{18} +8.89^{\circ}$ (*l*, 2.0). Silver bromide (7.4 g.) and bromine (0.95 g., 0.7 equiv.) were added, and the mixture was boiled under reflux for 1 hour; acid fumes were evolved. The solution was washed with, successively, water, sodium thiosulphate solution, and water, and dried (Na_2SO_4); it had $\alpha_{D}^{15} +0.03^{\circ}$ (*l*, 2.0). Fractionation gave α -phenylethyl bromide (1.1 g.), b. p. 86°/7 mm., $\alpha_{D}^{15} +0.21^{\circ}$ (*l*, 1.0), and a fraction, b. p. 126°/8 mm., which solidified. The solid was dissolved in carbon tetrachloride, and light petroleum added; crystals (0.3 g.), m. p. 73–74°, separated, unchanged by further crystallisation from light petroleum. α -Phenylethyl bromide having $\alpha_{D}^{18} +104.7^{\circ}$ (*l*, 1.0) was prepared by the method of Gerrard (*loc. cit.*). It (7 g.) was dissolved in dry carbon tetrachloride (40 ml.) and heated under reflux with powdered silver bromide (5 g.) for three hours. Fractionation gave α -phenylethyl bromide (5.4 g.), b. p. 96°/18 mm., $\alpha_{D}^{18} +104.1^{\circ}$. α -Phenylethyl bromide (6.5 g.) having $\alpha_{D}^{18} +104.2^{\circ}$ (*l*, 1.0) was dissolved in carbon tetrachloride (37 ml.), bromine (5.7 g., 2.0 equivs.) was added, and the solution boiled under reflux for three hours. A portion (13 ml.) was then removed, washed with aqueous sodium thiosulphate, dried (Na_2SO_4), and fractionated; it yielded α -phenylethyl bromide (2.0 g.), b. p. 96–97°/18 mm., $\alpha_{D}^{17} +32.1^{\circ}$ (*l*, 0.5). The remaining solution was boiled under reflux for a further sixteen hours, giving, after purification as before, α -phenylethyl bromide (3.1 g.), b. p. 96–97°/20 mm., $\alpha_{D}^{18} +0.5^{\circ}$ (*l*, 0.5).

Hell-Volhard Bromination of (+)- α -Phenylpropionic Acid.— α -Phenylpropionic acid having $\alpha_{D}^{15} +42.3^{\circ}$ (*l*, 0.5) (7.5 g.) was warmed to 60° for $\frac{1}{2}$ hour with phosphorus tribromide (13.5 g.). The upper mobile layer was decanted and heated with bromine (8 g.) under reflux in an oil-bath at 140–150° for four hours. The resultant liquid was poured into water and then set aside overnight. An oil was produced which dissolved completely in sodium hydroxide solution. This solution was acidified and extracted with ether, and the extract was dried (Na_2SO_4) and distilled, to yield a fraction, b. p. 175–180°/25 mm. (5 g.), which partly solidified. Crystallisation from carbon disulphide by addition of light petroleum gave optically inactive α -bromo- α -phenylpropionic acid (4 g.), m. p. 91–93° (Fittig and Kast, *Annalen*, 1880, 206, 28, record m. p. 93°).

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578. *The Polymerisation of Methacrylamide and the Alkaline Hydrolysis of the Polymer.*

By C. L. ARCUS.

The preparation of methacrylamide and its polymerisation in toluene and in ethyl acetate, catalysed by benzoyl peroxide, are described. The polymer is soluble in water and hygroscopic.

Rates of alkaline hydrolysis of acetamide, methacrylamide, and polymethacrylamide at 97° have been determined. The first two amides are rapidly and completely hydrolysed; the hydrolysis of polymethacrylamide proceeds fairly rapidly until 70% of the original nitrogen content has been evolved as ammonia and then becomes very slow. An explanation of the incomplete hydrolysis is put forward in which the steric and polar effects of hydrogen bonding between the remaining amide groups and adjacent-carboxyl ions inhibit further reaction with hydroxyl ions.

GROUPS attached to a large (polymeric) molecule are modified in reactivity by steric and polar factors characteristic of the molecule. The present work is part of an attempt to elucidate the effects of these factors. It is desirable to select for investigation reactions which can be carried out with reagent and polymer in homogeneous solution. Polymethacrylamide, which is soluble in water, has been prepared, and its alkaline hydrolysis studied.

Bruylants and Castille (*Bull. Sci. Acad. roy. Belg.*, 1927, 13, 779) prepared a somewhat impure specimen of methacrylamide and found that on boiling its solution in benzene an amorphous polymer was formed. The preparation of the monomer from acetone cyanohydrin is described in U.S.P. 2,140,469, and the preparation of aqueous solutions of the interpolymers of methacrylamide with methacrylic and maleic acids, with potassium persulphate as catalyst, is described in B.P. 475,671. No satisfactory description of the preparation of polymethacrylamide has been found.

Methacrylamide, $\text{CH}_2=\text{CMe}\cdot\text{CO}\cdot\text{NH}_2$, was prepared by shaking methyl methacrylate with excess of ammonia at room temperature for 7 days. Polymerisation, catalysed by benzoyl peroxide, was effected in solution in toluene. It was found that the following conditions are necessary in order to obtain a satisfactory yield of polymethacrylamide: (a) a concentrated solution of monomer, obtained by using toluene at its b. p., 111°, which lies at the m. p. of methacrylamide, 110—111° (it is necessary to avoid so great a concentration that when partial polymerisation has occurred an almost solid mass is formed); (b) addition of the benzoyl peroxide (2.4% of the weight of the monomer) in small quantities over a period and not as a single addition; (c) maintenance of an atmosphere of nitrogen. The total reaction time was 3.5 hours.

Experiments, otherwise identical, having 4 : 1, 3 : 1, and 2.5 : 1 (ml. : g.) ratios of toluene to methacrylamide gave respectively 75, 78, and 89% yields of polymethacrylamide. The intrinsic viscosities of 1% aqueous solutions of these polymers, viz., $[\eta]_c = (1/c) \ln \eta_{\text{soln.}}/\eta_{\text{H}_2\text{O}}$, where c = g. of polymer in 100 ml. of solution, were respectively 0.55, 0.61, and 0.12.

The most concentrated polymerisation solution gave the highest yield of polymer but with a marked reduction in average molecular weight. Polymerisation was also carried out in solution in ethyl acetate, in which the maximum attainable concentration is lower than in toluene and the maximum temperature is limited by the b. p. (77°); reaction for 20 hours with 5.0% of benzoyl peroxide gave a 45% yield of polymethacrylamide having $[\eta]_c$ 0.09.

Polymethacrylamide was obtained as a fine, white hygroscopic powder; the dry polymer when kept at 80% relative humidity for 24 hours absorbed 24% of its weight of water.

The monomer contained the theoretical quantity of nitrogen, 16.5%. Two specimens of polymethacrylamide (A and B, see Experimental) contained respectively 14.8 and 14.9% of nitrogen. The lowering of the nitrogen content below that for $[\text{CH}_2\cdot\text{CMe}(\text{CO}\cdot\text{NH}_2)]_n$ is caused by the presence of phenyl and benzoate end-groups from the benzoyl peroxide, and to some hydrolysis and imide formation occurring during the removal of solvent from the polymer, which was effected by alternate heating and maintenance in a vacuum. Similar but more extensive imide formation was observed by Staudinger and Urech (*Helv. Chim. Acta*, 1929, 12, 1107) during the polymerisation of acrylamide.

The percentage weights (*i.e.*, g. of unit in 100 g. of polymer) of amide units (I) (N, 16.5%), imide units (II) (N, 9.1%), acid units (III), and end groups (Ph and Ph·CO₂) in the polymer (preparation B) have been estimated in the following way. The content of end groups is

considered (from data described below) to be 2.3%. The acid-unit content was found, by titration of the polymer, to be 4.6%. The percentage weights, x and y , of amide and imide units can be found from the equations

$$14.9 = (16.5x + 9.1y)/100 \text{ and } x + y + 2.3 + 4.6 = 100 \text{ whence } x = 87.2 \text{ and } y = 5.9\%.$$

Part of this specimen was subjected to hydrolysis in 3.7*N*-sodium hydroxide for 2 hours, and on acidification the hydrolysed polymer (75% of the original weight) was precipitated. It contained N, 4.9%; the incompleteness of hydrolysis is discussed below. In order to permit

FIG. 1.

calculation, the assumption has been made that during hydrolysis all the imide rings are opened, yielding amide and carboxyl groups (of which the former may further hydrolyse to carboxyl). With this assumption, the nitrogen content, 4.9%, is equivalent to 29.9% of amide units. The content of acid units was found by titration to be 67.8%. The content of phenyl and benzoate end groups, is, by difference, 2.3%. This value has been applied, above, to the original polymer.

When attempts were made to estimate the amide content of polymethacrylamide by alkaline hydrolysis and titration of the ammonia evolved, it was found that the reaction does not go to completion. Further, as already described, the polymer isolated from the alkaline hydrolysis of polymethacrylamide had a nitrogen content 33% of that of the original polymer.

The rates of hydrolysis of acetamide, methacrylamide, and polymethacrylamide (preparation B) in 1.8*N*-sodium hydroxide at 97° have been determined (see Fig. 1). The progress of reaction was followed by periodical estimation of the evolved ammonia as described on p. . . . Acetamide and methacrylamide were rapidly and completely hydrolysed; hydrolysis of polymethacrylamide proceeded until 70% of the total nitrogen content had been evolved and then became very slow. The percentage of available nitrogen evolved has been calculated for acetamide and methacrylamide from the theoretical nitrogen contents, and for polymethacrylamide from the experimental value, 14.9%.

The following second-order constants (in moles⁻¹ ml. min.⁻¹) have been calculated from the data of Fig. 1.

Amide.	Period, mins.	<i>k</i> .	Amide.	Period, mins.	<i>k</i> .
Acetamide	14—36	76	Polymethacrylamide	12—23	21
Methacrylamide	16—56	57	„	23—47	12
			„	47—114	1.6

$$k = 2.303v[(\log(b - x) - \log(a - x) - (\log b - \log a)]/t(b - a).$$

where *a*, *b*, and *x* are moles, respectively, of amide, sodium hydroxide, and ammonia evolved. *v* is the volume (in ml.), and *t* the time (in mins.).

When 70% of the nitrogen content of polymethacrylamide had been evolved, there remained N, 4.5%, equivalent to 27.2% of amide units. Of the groups present in the original polymer, the imide units, 5.9%, yielded on hydrolysis 3.3% of acid units and 3.3% of amide units; the latter together with the 87.2% of amide units originally present total 90.5%, of which 27.2% remained unhydrolysed, whence 63.3% were hydrolysed, yielding 64.1% of acid units. There were 4.6% acid units in the original polymer, and the hydrolysed polymer therefore contained 3.3 + 64.1 + 4.6 = 72.0% of acid units. (These percentage weights relate to the weight of the original polymethacrylamide.) The ratio of amide groups to carboxyl groups at this point was 27.2/85.1 : 72.0/86.1 or 1 : 2.6.

The cessation of hydrolysis is attributed to the effects of hydrogen bonding of the amide groups by carboxyl ions. One amide group can undergo bonding with one or with two carboxyl ions, and the latter may be adjacent to the amide group (IV) or attached to another part of the chain or to a different molecule (V). Through the formation of structures of types (IV) and (V) hydrogen bonding causes the polymer molecules to take up more compact

arrangements and the approach of hydroxyl ions is hindered. The effectiveness of the steric hindrance is increased by the methyl groups attached to the carbon atoms which are α - to the amide and carboxyl groups.

Further, a polar effect arises from the hydrogen bonding. The N-H electron-pair is partly released towards the nitrogen atom and a fractional negative charge is relayed to the amide carbon atom. The approach of the hydroxyl ion in the first stage of hydrolysis

is rendered more difficult by this polar effect. The experimental results described above indicate that when the ratio of carboxyl ions to amide groups attains the value 2.6 : 1 the combined steric and polar retardation effects reduce the rate of hydrolysis nearly to zero.

It is possible that the polymer, when this state has been reached, has a structure in which each amide group is bordered by two carboxyl ions which form hydrogen bonds only with the given amide group; *i.e.*, structures of type (VI) are present but not those of type (VII).

The minimum carboxyl : amide ratio necessary to fulfil these conditions is 2 : 1, and for this the arrangement of groups shown in (VI) is required. The random hydrolysis of amide groups in polymethacrylamide is unlikely to lead to the optimum distribution (VI) of carboxyl ions;

at the cessation of hydrolysis when the conditions of hydrogen bonding described above are present, the carboxyl : amide ratio exceeds 2 : 1 and the structure of the polymer is of type (VIII).

EXPERIMENTAL.

Methylene chloride was washed with potassium carbonate solution, dried (K_2CO_3), distilled, and the fraction of b. p. 41—41.5° collected. Ethyl acetate was washed twice with sodium carbonate solution, twice with water, dried ($CaCl_2$), distilled, and the fraction of b. p. 76.5—77.5° collected. Toluene was washed thrice with dilute hydrochloric acid, thrice with 3*N*-sodium hydroxide, dried (K_2CO_3), distilled, and the fraction of b. p. 110.5—112° collected. Methyl methacrylate was washed thrice with *N*-sodium hydroxide, thrice with water, dried ($CaCl_2$), distilled, and the fraction of b. p. 100—101.5° collected.

Benzoyl peroxide was dried ($CaCl_2$) in a vacuum; the peroxide content, determined by reaction with sodium iodide in acetic anhydride solution and titration of the liberated iodine with sodium thiosulphate (Nozaki, *Ind. Eng. Chem. Anal.*, 1946, **18**, 583), was (i) 97.8, (ii) 98.3%.

Methacrylamide Monomer.—Methyl methacrylate (76 g.) was shaken mechanically with ammonia (390 ml., *d* 0.885) daily for 7 days in a stoppered bottle. A homogeneous solution was formed which was evaporated in 3 portions at 19 mm. in a water-bath at 78°. The product was dried ($CaCl_2$) to constant weight (65 g.) in a vacuum. A white mass resulted which was broken into small pieces and heated under reflux with methylene chloride (580 ml.), and the solution filtered (warm-water funnel); the residue was similarly extracted with 60 ml. of methylene chloride. Monomeric methacrylamide crystallised from the filtrates on cooling in ice, and two further crops were obtained from the mother-liquor; total yield 48 g. (75%), m. p. range 95—109°. Repeated crystallisation from methylene chloride gave thin plates, m. p. 110—111° (Bruylants and Castille, *loc. cit.*, record m. p. 102—106°) [Found: N, (i) 16.4, (ii) 16.6. Calc. for C_5H_7ON : N, 16.5%].

At the b. p. of the solution, 1.0 g. of methacrylamide was dissolved by 11.4 g. of methylene chloride.

In the above preparation, the ratio of methyl methacrylate (in g.) to ammonia (in ml.) was 1 : 5; similar preparations with ratio 1 : 3 (7 days' reaction) gave (i) 70, (ii) 63% yield, and with ratio 1 : 2 (29 days' reaction) 28% yield.

Polymethacrylamide.—Specimens of polymethacrylamide were characterised by determining the intrinsic viscosity, $[\eta]$, of a 1% solution of the polymer in water, a No. 1 B.S.S. Ostwald viscometer being used at 25°.

(A) Methacrylamide (15.0 g.) was dissolved in toluene (61 ml.) in a flask, fitted with a reflux condenser and a mechanical stirrer, immersed in an oil-bath kept (thermo-regulator) at $120^\circ \pm 1.5^\circ$. A current of nitrogen was passed through the solution. A solution of benzoyl peroxide in toluene was added from a burette fitted to the apparatus; 9 ml. of solution containing 0.36 g. of peroxide were added in 11 portions during 3 hours. After a further $\frac{1}{2}$ hour the reaction mixture was filtered, and the polymer thrice washed by heating it under reflux with 30 ml. of methylene chloride and filtering it off. It was dried to constant weight by repeatedly heating it at 100° and allowing it to cool in a vacuum in the presence of calcium chloride and paraffin wax. The polymethacrylamide so prepared was a fine, white powder, 11.3 g. (75%), $[\eta]$, (i) 0.54 (*c*, 0.872), (ii) 0.55 (*c*, 0.874) [Found: N, (i) 15.0, (ii) 14.6%].

(B) Methacrylamide (15.0 g.), dissolved in toluene (45 ml.), was polymerised under the conditions recorded for (A) with catalysis by 0.36 g. of benzoyl peroxide dissolved in 13 ml. of toluene and added in 10 portions during 3 hours; reaction was continued for a further $\frac{1}{2}$ hour. The polymer was washed and freed from solvent as above (11.8 g., 78%); it had $[\eta]$, (i) 0.60 (*c*, 0.764), (ii) 0.61 (*c*, 0.899) [Found: N, (i) 14.8, (ii) 15.0%]. This polymer was dissolved in cold water and titrated with sodium hydroxide, with phenolphthalein as indicator; 1.000 g. required (i) 0.53, (ii) 0.55 ml. of 1.00*N*-sodium hydroxide for neutralisation.

(C) Methacrylamide (15.0 g.), dissolved in toluene (38 ml.), was polymerised under the conditions recorded for (A) with catalysis by 0.38 g. of peroxide dissolved in 7 ml. of toluene and added in 6 portions during 3 hours; reaction was continued for a further $\frac{1}{2}$ hour. The polymethacrylamide was washed and freed from solvent as for (A) (13.3 g., 89%); it had $[\eta]$, (i) 0.12 (*c*, 0.919), (ii) 0.12 (*c*, 0.919).

(D) Methacrylamide (10.2 g.), dissolved in ethyl acetate (40 ml.), was polymerised under the conditions recorded for (A) but with the flask immersed in a water-bath at 85°. Polymerisation was catalysed by 0.51 g. of peroxide added in 4 portions during 20 hours. The polymer was washed (20-ml. portions of methylene chloride) and freed from solvent as for (A); 4.6 g. (45%) were obtained, $[\eta]$, 0.09 (*c*, 0.950).

Polymethacrylamide has a strong tendency to retain solvents and is hygroscopic. Specimens for analyses and viscosity determinations were further heated at 110° for 1 hour at 12 mm. in the presence of phosphoric oxide; during this treatment a small quantity of monomer separated as a crystalline sublimate, m. p. 110—111°.

Polymethacrylamide (preparation B), dried (P_2O_5) as above, was kept in a "humidor" over saturated aqueous ammonium chloride solution (80% relative humidity) at 13—20° and increased in weight as follows:

Time	4 hrs.	24 hrs.	54 hrs.	8 days	16 days	83 days
Increase, %	12	24	27	29	26	25

The polymer was dissolved in cold water and titrated with sodium hydroxide (phenolphthalein); 1.000 g. (dry) required (i) 0.47, (ii) 0.43 ml. of 1.00*N*-sodium hydroxide, indicating that there had been no hydrolysis under these humid conditions.

To a solution of polymethacrylamide (preparation C, 1.00 g.) in 10.0 ml. of water were added with stirring, at 32°, 5.0 ml. of methyl alcohol. Polymer was precipitated; it was filtered off, dried ($CaCl_2$) in a vacuum, and weighed 0.58 g. A similar experiment but with 10.0 ml. of methyl alcohol yielded 0.79 g. of polymer. These results indicate a method of fractionation.

Method for Rates of Hydrolysis.—The amide (approximately 0.01 mole) was weighed into the tube A (Fig. 2); the weights taken were:

Expt.	Amide.	Weight, g.	Expt.	Amide.	Weight, g.
i	Acetamide	0.5815	iv	Methacrylamide	0.8503
ii	"	0.6100	v	Polymethacrylamide (B)	0.7764
iii	Methacrylamide	0.8671	vi	"	0.7753

5 ml. of water and 25 ml. of 2.30N-sodium hydroxide were then added from pipettes. Approximately 75 g. of N/5-sulphuric acid were weighed into the trap *B*. The tube *A* was connected to the rest of the apparatus, and the rod *C* adjusted to touch the surface of the liquid in *A*; *A* was then immersed in an oil-bath fitted with a stirrer and thermo-regulator and kept at $107^{\circ} \pm 1^{\circ}$. Throughout the experiment a slow stream of nitrogen was passed through the apparatus. At intervals, measured from the time of immersion in the oil-bath, 5 ml. of acid (5.02 g.) were removed by pipette from *B* and titrated with N/4-sodium hydroxide, with methyl-red as indicator. At the end of the experiment, *B* and its contents were weighed as a check on evaporation from or distillation into *B*, and the net weight change was found to be very small. The temperature of the solution in *A* rose to 95° during the first 8 minutes after immersion of *A* in the oil-bath and remained thereafter at $97^{\circ} \pm 2^{\circ}$. The temperature difference between the oil-bath and the solution in *A* was due to the reflux of water between *A* and the anti-splash bulb. After 3 hours, the level of the solution in *A* had fallen slightly owing to evaporation, and sufficient water was added through *D* to restore contact between the surface of the solution and *C*.

FIG. 2.

The various acid contents were calculated in ml. of 1.000N-sulphuric acid; then we have: (millimoles of ammonia evolved at time *t*) = (initial acid content of *B*) - (sum of acid contents of portions withdrawn, for titration, up to *t*) - (acid content of *B* at *t*).

The results obtained for acetamide, methacrylamide monomer, and polymethacrylamide (preparation B) are plotted in Fig. 1.

Polymer recovered from Hydrolysis.—Polymethacrylamide (3.6 g.; preparation B) was dissolved in 24 ml. of water, and a solution of 6.8 g. sodium hydroxide in 22 ml. of water was added. A coagulum was formed which soon dissolved; the solution (3.7N. in NaOH) was heated on a steam-bath for 2 hours. The clear solution was added, with washes, to 40 ml. of 5N-hydrochloric acid, and the whole heated on a steam-bath, cooled in ice, and filtered. The precipitate was thrice washed by suspending it in water, heating on a steam-bath, cooling in ice, and filtering off, and then dried (CaCl_2) in a vacuum. It weighed 2.7 g. [Found: N, (i) 4.8, (ii) 5.05%]. This polymer was dissolved in sodium hydroxide, and the solution neutralised to phenolphthalein with sulphuric acid, and it was found that 1.000 g. of polymer neutralised (i) 7.90, (ii) 7.86 ml. of 1.000N-sodium hydroxide.

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90. *Experiments relating to the Resolution of Tertiary Alcohols: the Resolution and Deamination of α -Naphthylphenyl-*p*-tolylmethylamine, and the Curtius, Hofmann, and Schmidt Reactions with 2-Methyl-2-phenylhexanoic Acid.**

By C. L. ARCUS, J. KENYON, and S. LEVIN.

α -Naphthylphenyl-*p*-tolylmethylamine has been resolved *via* the (+)- and (−)-camphorsulphonates. The (+)-amine hydrochloride with sodium nitrite yielded (±)- α -naphthylphenyl-*p*-tolylcarbinol. (±)-2-Methyl-2-phenylhexanoic acid * (I) gave, *via* the chloride and azide, (±)-2-amino-2-phenylhexane (II); the (+)-acid gave the (−)-amine. The amide of (I) with sodium hypochlorite gave (II) in low yield. Sodium azide in sulphuric acid-chloroform decomposed (I), yielding aniline (55%); the mechanism of this reaction is discussed. The preparation of some ω -alkylacetophenones is described.

NUMEROUS secondary alcohols have been resolved through the alkaloidal salts of their hydrogen phthalates (or succinates), but the many similar attempts with tertiary alcohols have failed, with the exception of isobutylethylmethylcarbinol (Doering and Zeiss, *J. Amer. Chem. Soc.*, 1948, **70**, 3966; 1950, **72**, 147). It was considered desirable to ascertain if amines of the type $\text{CRR}'\text{R}''\text{NH}_2$, where R, R', R'' are alkyl or aryl groups, could be obtained in optically active forms. No report of the resolution of such an amine or of its preparation by the degradation of an optically active acid $\text{CRR}'\text{R}''\text{CO}_2\text{H}$ has been found, although the following optically active amines have been prepared by the Hofmann reaction with amides the α -carbon atoms of which are tertiary and form part of an alicyclic ring: (+)-aminodihydrocampholytic acid (Noyes and Phillips, *Amer. Chem. J.*, 1900, **24**, 290), (+)-fenchelylamine hydrochloride (Wallach, *Annalen*, 1909, **369**, 81), (+)-aminolauronic acid (Weir, *J.*, 1911, **99**, 1270), (−)-aminoisodihydrocampholytic acid (Noyes and Nickell, *J. Amer. Chem. Soc.*, 1914, **36**, 118). Amines of similar type which were presumably optically active but for which no rotation data are given have been prepared as follows: camphelylamine, by the Hofmann reaction with the corresponding amide (Errera, *Gazzetta*, 1892, **22** (i), 205); and, by the Schmidt reaction with the corresponding acid, camphelylamine, fenchelylamine, dimethylcamphelylamine (von Braun, *Annalen*, 1931, **490**, 125; von Braun and Kurtz, *Ber.*, 1934, **67**, 225).

α -Naphthylphenyl-*p*-tolylmethylamine, prepared by the action of ammonia on the corresponding methyl chloride, has now been resolved by fractional crystallisation of the (+)- and the (−)-camphorsulphonate, the enantiomeric amines having $[\alpha]_{589}^{17} \pm 1.3^\circ$ in carbon disulphide. Reaction of the (+)-amine hydrochloride (optical purity, 51%) with sodium nitrite gave optically inactive α -naphthylphenyl-*p*-tolylcarbinol. It is inferred that the intermediate carbonium cation is of sufficiently long life to yield equal amounts of (+)- and (−)-carbinol by reaction with a hydroxyl ion or water and that shielding by the released nitrogen molecule is here unimportant.

Since Hofmann, Curtius, and Schmidt reactions with (+)- α -phenylpropionic acid gave (−)-1-phenylethylamine with a high degree of retention of asymmetry and of configuration (Arcus and Kenyon, *J.*, 1939, 916; Kenyon and Young, *J.*, 1941, 263; Campbell and Kenyon, *J.*, 1946, 25) it was decided to carry out these reactions with optically active 2-methyl-2-phenylhexanoic acid * (I). The chloride of the (±)-acid with sodium azide in aqueous acetone and in toluene gave (±)-2-amino-2-phenylhexane (II) in 27 and 25% yield respectively. Repetition of the reaction in aqueous acetone with the chloride of the (+)-acid (optical purity, 29%) gave (II) having $\alpha_{589}^{16} - 0.66^\circ$ (homogeneous; *l.*, 0.5) which yielded a benzoyl derivative having $[\alpha]_{589}^{18} + 3.5^\circ$ (in benzene).

* Geneva numbering, $\text{CO}_2\text{H} = 1$.

From the reaction of the ($\pm$)-amide of (I) with sodium hypochlorite, the ($\pm$)-amine (II) was isolated as the benzoyl derivative in 10% yield; the reaction was not repeated with optically active material.

Aniline (55% yield) was the sole basic product isolated from the reaction of the ($\pm$)-acid (I) with sodium azide in chloroform-sulphuric acid. Addition of bromine to the neutral products of reaction, and distillation, yielded a fraction the boiling point and bromine content of which indicated it to be dibromohexane(s). The most probable course of reaction appears to be the following:

It is intended to investigate in greater detail the mechanism of this reaction; it may be noted that (a) 1-methyl-1-phenyl-*n*-amyl isocyanate is not abnormally unstable in the absence of sulphuric acid, because the Curtius reaction yielded the expected amine (II); (b) the Schmidt reaction with triethylacetic acid gave a mixture of lower amines, lower ketones, and triethylacetamide (Schuerch and Huntress, *J. Amer. Chem. Soc.*, 1949, **71**, 2238); (c) in contrast to the disintegration occurring with these two acids, trimethylacetic acid, 1-methylcyclohexanecarboxylic acid (Schuerch and Huntress, *ibid.*, p. 2233), the terpene acids investigated by von Braun (*loc. cit.*), and podocarpic acid (Briggs, De Ath, and Ellis, *J.*, 1942, 62) yield as the principal product of the Schmidt reaction the expected amine having the amino-group attached to a tertiary carbon atom.

The preparation of ($\pm$)- α -benzylpropiophenone, ($\pm$)-2-benzyl-2-methylhexanoylbenzene* and ($\pm$)-2-ethyl-2-methylhexanoylbenzene is described.

EXPERIMENTAL.

*α -Naphthylphenyl-*p*-tolylmethylamine.*— α -Naphthylphenyl-*p*-tolylcarbinol and its chloride were prepared by a modification of the method of Schlenk and Meyer (*Ber.*, 1919, **52**, 17), who record m. p. 109–110° and 142–144° for the carbinol and chloride respectively.

To a solution of α -naphthylmagnesium bromide, prepared from α -bromonaphthalene (45.5 g.) and magnesium (5.4 g.), in ether (135 ml.), heated under reflux, was added gradually, with stirring, a solution of phenyl-*p*-tolyl ketone (43.5 g.) in ether (200 ml.). After 4 hours the mixture was cooled and decomposed with ice-ammonium chloride, yielding ($\pm$)- α -naphthylphenyl-*p*-tolylcarbinol, m. p. 109°. This material was dissolved in ether and a current of hydrogen chloride passed in for several hours. A little acetyl chloride was added to remove the water formed during the reaction. The solvent was distilled and the residue on crystallisation from light petroleum (b. p. 40–60°) yielded α -naphthylphenyl-*p*-tolylmethyl chloride, m. p. 142° (25 g., 33% yield from the ketone).

Dry ammonia was passed through a solution of the chloride (25 g.) in benzene (550 ml.), until no more ammonium chloride separated. After filtration, and evaporation of the solvent, addition of light petroleum (b. p. 40–60°) to the residue gave a light brown powder, which on recrystallisation from alcohol gave ($\pm$)- α -naphthylphenyl-*p*-tolylmethylamine, small white needles, m. p. 127–128° (Found; C, 89.1; H, 6.5; N, 4.2. $\text{C}_{24}\text{H}_{21}\text{N}$ requires C, 89.1; H, 6.6; N, 4.3%).

Resolution. To a solution of ($\pm$)- α -naphthylphenyl-*p*-tolylmethylamine (21.0 g.) in alcohol (300 ml.) was gradually added a solution of (+)-camphorsulphonic acid (15.1 g.) in water (80 ml.); a salt (15.8 g.) gradually separated. Four recrystallisations from aqueous alcohol yielded a camphorsulphonate (8.2 g.), the amine from which had attained a constant rotation. This salt (4 g.) was agitated with 0.1N-sodium carbonate (300 ml.) and ether. The ethereal layer was repeatedly washed with aqueous sodium carbonate, then dried (CaSO_4), and the solvent evaporated. The residue was recrystallised from alcohol and gave α -naphthylphenyl-*p*-tolylmethylamine (2.2 g.), m. p. 128°, $[\alpha]_{\text{D}}^{17} -1.3^\circ$ (c, 3.7 in carbon disulphide). A similar resolution with (–)-camphorsulphonic acid yielded α -naphthylphenyl-*p*-tolylmethylamine having $[\alpha]_{\text{D}}^{17} +1.3^\circ$ (c, 4.7 in carbon disulphide).

On passing dry hydrogen chloride through a solution of ($\pm$)- α -naphthylphenyl-*p*-tolylmethylamine in dry ether, the hydrochloride separated as a white precipitate, m. p. 150–155° (decomp.). The amine was recovered nearly quantitatively on treating the hydrochloride with aqueous sodium carbonate. A specimen of the amine having $[\alpha]_{\text{D}}^{17} +1.0^\circ$ (c, 5.5 in carbon disulphide) yielded a hydrochloride having $[\alpha]_{\text{D}}^{17} +1.5^\circ$ (c, 6.7 in water), $+1.3^\circ$ (c, 6.1 in 0.1N-hydrochloric acid).

Deamination. To a solution of ($\pm$)- α -naphthylphenyl-*p*-tolylmethylaniline hydrochloride (4.2 g.) in water (75 ml.) was added a solution of sodium nitrite (2.4 g.) in water (25 ml.). A white crystalline mass separated; water (50 ml.) was added and the whole boiled. Benzene was then added and the mixture stirred with heating under reflux for 24 hours. The benzene layer was washed repeatedly with 3*N*-hydrochloric acid and with warm water, dried (CaSO_4), and treated with charcoal and with alumina. After removal of the benzene under reduced pressure, the residue (2.9 g.) was allowed to crystallise slowly from ligroin, ($\pm$)- α -naphthylphenyl-*p*-tolylcarbinol (1.2 g., 31%), m. p. 109° alone or mixed with authentic material, being obtained (Found: C, 88.3; H, 6.2. Calc. for $\text{C}_{24}\text{H}_{20}\text{O}$: C, 88.7; H, 6.4%). Repetition with α -naphthylphenyl-*p*-tolylmethylaniline hydrochloride having $[\alpha]_{589}^{20} +1.0^\circ$ (in water) gave optically inactive carbinol.

Curtius, Hofmann, and Schmidt Reactions with 2-Methyl-2-phenylhexanoic Acid.—To a solution of α -phenylpropionitrile (79 g.; b. p. 114°/16 mm.; prepared according to Campbell and Kenyon, *loc. cit.*) and *n*-butyl bromide (85 g.) in dry benzene (100 ml.) was added a suspension of sodamide (24.5 g.) in benzene. After an initial brisk reaction the whole was heated, with stirring, on a steam-bath for several hours. Water was then added and the benzene layer repeatedly washed with water and dried (CaSO_4). After distillation of the benzene, the residue was distilled and gave 1-methyl-1-phenylamyl cyanide, b. p. 147°/16 mm. (80 g., 71%) (Found: C, 83.2; H, 9.2; N, 7.6. $\text{C}_{13}\text{H}_{17}\text{N}$ requires C, 83.3; H, 9.2; N, 7.5%).

The nitrile (17 g.) was heated under reflux for 10 days in a solution of potassium hydroxide (16 g.) in alcohol (90 ml.) and water (25 ml.). The alcohol was then distilled off, water added, and the whole acidified and extracted with benzene. Evaporation of the benzene extract yielded a mixture of the acid, the amide, and some unchanged nitrile. Fractionation of the mixture gave the acid still containing some amide. This material was dissolved in excess of alkali and repeatedly extracted with chloroform; acidification of the alkaline solution gave 2-methyl-2-phenylhexanoic acid, b. p. 173°/16 mm. (Found: equiv., 208.0. Calc. for $\text{C}_{12}\text{H}_{17}\text{CO}_2\text{H}$: equiv., 206.3).

Resolution of the acid was carried out according to Conant and Carlson (*J. Amer. Chem. Soc.*, 1932, **54**, 4055), by recrystallising the quinine salt from aqueous alcohol until the acid obtained on decomposing a portion of the salt had attained a constant rotation. The fully-active acid had the rotatory powers recorded in the table.

λ :	4358	4678	4800	5086	5461	5893	6438	
<i>2-Methyl-2-phenylhexanoic acid.</i>								
Solvent.	<i>c.</i>	Temp.	<i>a</i> (<i>l</i> , 0.5):					
None	—	15°						
Et_2O	6.41	15°	$[\alpha]$:	+23.3°	+19.4°	+19.3°	+16.4°	+13.8°
CS_2	1.00	17°	$[\alpha]$:					+26.0°
								+11.6°
								+9.4°
								+21.4°
<i>2-Amino-2-phenylhexane.</i>								
None	—	16°	<i>a</i> (<i>l</i> , 0.5):					
Et_2O	1.00	17°	$[\alpha]$:	−1.70°	−1.32°	−1.25°	−1.03°	−0.83°
CS_2	1.00	17°	$[\alpha]$:					−1.3°
0.5 <i>N</i> -HCl	1.00	16°	$[\alpha]$:					−1.2°
								−2.3°
								+0.3°

2-Methyl-2-phenylhexanoyl chloride (11.1 g.), b. p. 123°/18 mm. (Found: equiv., 114. Calc. for $\text{C}_{12}\text{H}_{17}\text{COCl}$: equiv., 112.3), was prepared by the action of thionyl chloride (50 ml.) on the acid (11.5 g.). To an ice-cooled solution of the acid chloride (15.4 g.) in acetone (150 ml.) was added, with stirring, a solution of sodium azide (5 g.) in water (20 ml.). After $\frac{1}{2}$ hour sufficient water was added to give a homogeneous solution and stirring was continued for 1 hour. Water (200 ml.) was added and the oil which separated was extracted with ether and dried (CaSO_4); after filtration, toluene was added, the ether distilled off, and the remaining solution refluxed for several hours. Concentrated hydrochloric acid (150 ml.) was added and the whole heated with stirring on a steam-bath for 6 hours. After extraction with benzene, the aqueous layer was evaporated to small volume, and excess of sodium hydroxide solution was added. An oil separated which was extracted with ether; evaporation of the latter and distillation of the residue yielded 2-amino-2-phenylhexane (2.7 g.), b. p. 127°/18 mm., which by Schotten-Baumann benzoylation gave 2-benzamido-2-phenylhexane (3.4 g.) which separated from benzene-ligroin in small silky needles, m. p. 146—147° (Found: C, 80.9; H, 8.5; N, 4.9. $\text{C}_{19}\text{H}_{23}\text{ON}$ requires C, 81.0; H, 8.2; N, 4.9%). Evaporation of the toluene layer (above) and addition of ether gave a material which separated from benzene-light petroleum (b. p. 40—60°) as small crystals (0.6 g.) of 2-amino-2-phenylhexane hydrochloride, m. p. 144—147°, soluble in water (Found: Cl, 16.5. $\text{C}_{12}\text{H}_{17}\text{NCl}$ requires Cl, 16.1%). It yielded a benzoyl derivative having m. p. 146—147° alone or mixed with the above benzoyl derivative. By this procedure 2-methyl-2-phenylhexanoic acid (9.7 g.) having $[\alpha]_{589}^{18} +6.3^\circ$ (*c.* 1.00 in carbon disulphide) gave (−)-2-amino-2-phenylhexane (1.6 g.) having the rotatory powers recorded in the table, which yielded a benzoyl derivative having $[\alpha]_{589}^{18} +3.5^\circ$ (*c.* 1.00 in benzene).

To a solution of 2-methyl-2-phenylhexanoyl chloride (8.8 g.) in dry toluene (40 ml.) was added sodium azide which had been activated with hydrazine hydrate according to Nelles (*Ber.*, 1932, **65**, 1345). The mixture was heated under reflux with stirring for 8 hours, cooled, and filtered, the solvent removed by distillation, and the residue heated for several hours on the steam-bath with concentrated hydrochloric acid. The aqueous layer was made alkaline with sodium hydroxide solution and extracted with ether; after drying (CaSO_4) and removal of the ether, the residue gave on distillation 2-amino-2-phenylhexane, b. p. 127°/18 mm., which was converted into the benzoyl derivative (1.7 g.), m. p. 146—147°.

2-Methyl-2-phenylhexanoyl chloride (12 g.) was gradually added to aqueous ammonia (200 ml.; d 0.88), and the whole evaporated on a steam-bath. The oil so obtained was extracted with benzene and dried (NaOH), the solvent removed, and the 2-methyl-2-phenylhexanoamide distilled; it had b. p. $187^{\circ}/15$ mm. (Found: C, 75.6; H, 8.8; N, 6.5. $C_{13}H_{19}ON$ requires C, 76.0; H, 9.3; N, 6.8%). The amide (2.0 g.) was shaken with sodium hypochlorite solution (60 ml.; prepared from 2.2 g. of chlorine and 6 g. of sodium hydroxide) at 40° until it dissolved. The solution was then heated to 80° ; a yellow oil separated which was extracted with benzene, concentrated hydrochloric acid was added to the extract, the benzene was evaporated, and the residue heated for several hours. After extraction with ether, the aqueous solution was evaporated to small volume; Schotten-Baumann benzoylation then gave 2-benzamido-2-phenylhexane, m. p. $146-147^{\circ}$ (0.3 g.).

To a solution of 2-methyl-2-phenylhexanoic acid (5.5 g.) in chloroform (45 ml.) was added concentrated sulphuric acid (13 ml.); sodium azide (2.1 g.) was added, with vigorous stirring, at such a rate that the temperature was kept at $40-45^{\circ}$. Stirring was continued for 1 hour with heating on the steam-bath, and the reaction mixture poured into water. The aqueous layer was repeatedly extracted with small quantities of chloroform and then made alkaline with aqueous sodium hydroxide. An oil was liberated which was extracted with benzene, the extract dried (K_2CO_3), and the benzene distilled off. The residue on distillation yielded aniline (1.2 g.), b. p. $80^{\circ}/18$ mm. (Found: C, 77.4; H, 7.7; N, 14.7. Calc. for C_6H_7N : C, 77.4; H, 7.5; N, 15.1%), identified by conversion into toluene-*p*-sulphonanilide, m. p. 103° , and acetanilide, m. p. 113° .

The chloroform extract was subjected to alkaline extraction [whereby unchanged acid (0.6 g.) was recovered] and dried (K_2CO_3), and bromine added gradually until a brown colour just persisted. The chloroform solution was washed with aqueous sodium thiosulphate and the solvent evaporated off; the residue on distillation gave dibromohexane, b. p. $95^{\circ}/15$ mm. (Found: Br, 64.3. Calc. for $C_6H_{12}Br_2$: Br, 65.4%). Repetitions of the Schmidt reaction with the reactants in the same proportions at temperatures between 37° and 54° gave aniline in similar yields.

To a solution of propiophenone (170 g.) in dry benzene (650 ml.) was slowly added a suspension of sodamide (51 g.) in benzene; the whole was heated under reflux with stirring for several hours until no further ammonia was evolved. Benzyl chloride (160 g.) was then added with continued stirring and heating. Water was added to the cooled reaction mixture, the benzene layer washed with water and dried (Na_2SO_4), and the solvent evaporated off. The residue on distillation yielded ($\pm$)-*a*-benzyl-propiophenone (159 g.), b. p. $181^{\circ}/10$ mm. (Found: C, 85.7; H, 7.4. $C_{16}H_{16}O$ requires C, 85.7; H, 7.2%).

Reaction, under similar conditions, of ($\pm$)-*a*-benzylpropiophenone (155 g.) with sodamide (27 g.) and *n*-butyl bromide (95 g.) gave ($\pm$)-2-benzyl-2-methylhexanoylbenzene (58 g.), b. p. $192-196^{\circ}/13$ mm. (Found: C, 85.2; H, 8.1. $C_{26}H_{24}O$ requires C, 85.6; H, 8.6%).

Under similar conditions propiophenone (53 g.) in benzene (650 ml.), sodamide (53 g.), and *n*-butyl bromide (186 g.) in benzene (100 ml.) yielded ($\pm$)-2-methylhexanoylbenzene (148 g.), b. p. $123^{\circ}/23$ mm. This material (148 g.) in benzene (650 ml.) was treated similarly with sodamide (38 g.) and ethyl iodide (122 g.), the latter being run beneath the surface of the reaction mixture; there was obtained ($\pm$)-2-ethyl-2-methylhexanoylbenzene (100 g.), b. p. $140^{\circ}/13$ mm. (Found: C, 82.2; H, 10.0. $C_{18}H_{22}O$ requires C, 82.5; H, 10.2%).

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357. *Heterogeneous Catalysis of the Racemisation of (+)-1-Phenylethyl Bromide.*

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(+)-1-Phenylethyl bromide in solution in carbon tetrachloride saturated with hydrogen bromide at 73° undergoes racemisation only at a solid surface; the mechanism of racemisation is discussed. Under the conditions employed, the order of effectiveness in catalysis of racemisation is: silver bromide > charcoal > powdered glass $\gg$ potassium bromide. The presence of styrene dibromide in the solution accelerates racemisation.

(+)-1-Phenylethyl bromide with bromine in carbon tetrachloride becomes racemised, but some substitution to form hydrogen bromide and (optically inactive) styrene dibromide occurs, and it is uncertain whether bromine-exchange between 1-phenylethyl bromide and elementary bromine takes place; when silver bromide is present racemisation is rapid.

It was observed (Arcus, Campbell, and Kenyon, *J.*, 1949, 1510) that 1-phenylethyl bromide in solution in carbon tetrachloride racemised rapidly when heated under reflux in the presence of silver bromide and bromine. Hydrogen bromide was evolved during the heating and a small quantity of a compound, shown below to be styrene dibromide, was isolated. Racemisation was much less rapid with bromine alone, and slight with silver bromide alone. The formation of styrene dibromide on heating 1-phenylethyl bromide with bromine was observed by Schramm (*Ber.*, 1885, 18, 354). In the present investigation, the rates of racemisation of 1-phenylethyl bromide in solution in carbon tetrachloride containing hydrogen bromide or bromine in the presence of various solids, have been measured.

The rate of racemisation of 1-phenylethyl bromide in solution in anhydrous acetone in the presence of dissolved lithium bromide was found to be twice the rate of halogen-exchange as determined by the use of lithium bromide containing radioactive bromine (Hughes, Juliusberger, Scott, Topley, and Weiss, *J.*, 1936, 1173), whence the racemisation is due to bimolecular halogen-exchange:

occurring in homogeneous solution. 1-Phenylethyl chloride has been observed to undergo homogeneous unimolecular racemisation in solution in sulphur dioxide (Bergmann, Polanyi, and Szabo, *Z. physikal. Chem.*, 1933, B, 20, 161):

racemisation being due to dissociation to give the planar carbonium ion. Racemisation of 1-phenylethyl chloride occurs by an allied mechanism in the presence of heavy-metal chlorides in solution in organic solvents (Böhme and Bodendorf, *Annalen*, 1935, 516, 1; Böhme, *Ber.*, 1938, 71, 2372); a complex is formed which ionises:

This mechanism receives support from the facts that an increase in the dielectric constant of the solvent generally increased the rate of racemisation, and that addition of hydrogen chloride or lithium chloride diminished the rate of racemisation by competing with the organic halide for complex-formation with the heavy-metal chloride. Both unimolecular and bimolecular homogeneous racemisations in the presence of constant concentrations of added reagents give rise to a first-order fall in optical rotation, and, as indicated above, other data are necessary to distinguish these two mechanisms.

1-Phenylethyl bromide underwent 10% racemisation in 5 hours when kept at 73° in solution in carbon tetrachloride saturated with hydrogen bromide (Fig. 2, A). A saturated solution of hydrogen bromide in carbon tetrachloride had no measurable conductivity, and hence hydrogen bromide does not dissociate in this solvent. It is inferred that the racemisation in A did not

arise by any mechanism (*e.g.*, bimolecular substitution similar to that with lithium bromide in acetone) which requires appreciable concentrations of ions in homogeneous solution; the rate of racemisation in the presence of hydrogen bromide increased on increasing the surface by the addition of powdered glass (Fig. 1, *B*) and it is concluded that the racemisation in *A* occurred at the glass surface of the flask. A 38-fold increase in surface resulted in a 130-fold increase in the initial velocity of racemisation (Table I). The fractured glass surfaces thus appear more efficient than the fused surface of the flask; a similar effect for the exchange of bromine between hydrogen bromide and ethyl bromide at 180–260° was observed by Peri and Daniels (*J. Amer. Chem. Soc.*, 1950, **72**, 424).

Racemisation was most rapid with hydrogen bromide in the presence of silver bromide; the initial rate was 320 times that for *A*, and the solution was optically inactive after 30 minutes (Fig. 1, *C*). Senter (*J.*, 1910, **97**, 346) observed that the silver bromide formed has a marked

FIG. 1.

FIG. 2.

catalytic effect on the hydrolysis of α -bromopropionic and α -bromo-*n*-butyric acids in aqueous silver nitrate; a similar effect was noticed by Baker (*J.*, 1934, 987) for the alcoholysis of benzyl bromide by ethyl-alcoholic silver nitrate. Kappanna (*Proc. Indian Acad. Sci.*, 1935, **2**, A, 512) concluded that in the reaction of sodium α -bromopropionate with aqueous silver nitrate, reaction occurs almost entirely between α -bromopropionate ions and silver ions adsorbed on the surface of the silver bromide. Cowdrey, Hughes, Ingold, and Masterman (*J.*, 1937, 1236, 1243) concluded from the stereochemical and kinetic evidence that the following reactions, *viz.*, (i) hydrolysis and alcoholysis of 2-*n*-octyl bromide in aqueous alcohol containing suspended silver oxide or dissolved silver nitrate or acetate, (ii) hydrolysis of 1-phenylethyl chloride in aqueous acetone with suspended silver oxide, (iii) methoxylation of methyl α -bromopropionate with methyl-alcoholic silver nitrate, and (iv) the hydrolysis of the acid and its sodium salt with a suspension of silver oxide in water or aqueous acetone, proceed wholly or partly by reaction between the halogen-containing organic molecule (or the anion in the cases of the acid and its salt) adsorbed on to the silver halide surface, and that of the silver oxide when present, and the

hydroxylic solvent or a hydroxyl or alkoxyl ion. The carbon-halogen bond of the adsorbed halide is stretched and weakened, an adsorbed silver ion detaches the halogen, and the resulting carbonium cation reacts with an adsorbed solvent molecule or appropriate reagent ion. (+)-1-Phenylethyl chloride in benzene solution yielded with silver nitrite a largely racemised 1-phenylethyl nitrite (Eastman and Ross, *J. Amer. Chem. Soc.*, 1946, **68**, 2398) in accord with reaction *via* dissociation of the organic halide on the silver nitrite-silver chloride surface.

It is considered that the silver bromide in the present experiments functioned similarly. The alkyl-bromine bond of an adsorbed 1-phenylethyl bromide molecule is weakened by the interaction of silver ions with the bromine. The adsorbed hydrogen bromide functions as reagent, either by supplying bromide ions (i) or directly (ii). Further, the functions of the silver ions may be in part taken over by adsorbed protons, as in (iii) and (iv):

The reactions (i)–(iv) lead to racemisation by bimolecular substitution. Some part of the racemisation may proceed by ionisation of the 1-phenylethyl bromide assisted by weakening of the carbon-bromine bond through silver ions (v) or protons (vi), the planar carbonium cation combining to yield the (±)-bromide (vii) and (viii).

Unlike the other catalytic solids investigated, which in the absence of hydrogen bromide effected no racemisation, some specimens of silver bromide had appreciable racemising effect: (a) a specimen of silver bromide which had been kept for 3 months caused no racemisation in 2 hours at 73°; (b) a recently-prepared specimen caused 39% racemisation in 2 hours; (c) another recently-prepared specimen caused 22% racemisation in the first hour and thereafter the rotation of the solution remained constant. These results show a similarity to those of Langer (*J. Chem. Physics*, 1943, **11**, 11) who, using sodium bromide containing radioactive bromine, found that there is exchange of bromide ions between silver bromide and aqueous sodium bromide at a rate which decreases with the age of the silver bromide, and finally ceases. Racemisation in the presence of silver bromide alone must proceed by (i) or by (v) followed by (vii), the bromide ion here being that normally present in the silver bromide lattice only.

The much greater rate of racemisation with hydrogen bromide-silver bromide than with silver bromide alone points to attack by adsorbed hydrogen bromide (ii) or bromide ions derived therefrom (i), *i.e.*, to racemisation through inversion mechanisms. Nevertheless, the possibility that some part of the effect of the hydrogen bromide lies in providing adsorbed protons which assist the ionisation of 1-phenylethyl bromide (vi), as well as promoting inversion by mechanisms (iii) and (iv), is not excluded.

The system hydrogen bromide-potassium bromide is much less effective in racemisation than hydrogen bromide-silver bromide, probably owing to the lesser capacity for adsorption of the potassium bromide surface (Fig. 2, D).

In the presence of hydrogen bromide-charcoal, the initial rate of racemisation of 1-phenylethyl bromide was slightly less than half that in the presence of hydrogen bromide-silver bromide (Fig. 1, E).

Since glass, potassium bromide, and charcoal do not themselves effect racemisation, it is

concluded that racemisation when hydrogen bromide is present is due to the operation on the solid surfaces of inversion mechanisms (iii) and (iv) together, possibly, with the ionisation mechanism (vi) followed by (vii) and (viii).

When hydrogen bromide was passed through a solution of 1-phenylethyl bromide in carbon tetrachloride containing styrene dibromide (Fig. 2, *F*), the rate of racemisation was 7 times that for *A*. The mechanism whereby the rate is increased is not known.

The racemisation of any compound by any mechanism in which enantiomeric molecules of the compound suffer reaction at the same rate would be expected to occasion a first-order fall in rotation, provided that conditions are kept constant. In the present work (which was designed to give comparative rates only), racemisation in *B* and *E* was of first-order [for *B* (i), *B* (ii), and *E*, k is 0.045, 0.043, and 0.068 min.⁻¹, respectively]; *A* and *C* were respectively too slow and too fast to permit an estimation of the order; and racemisation in *D* and *F* was zero order (for *D* and *F*, k is 0.0026 and 0.00095 mole l.⁻¹ min.⁻¹, respectively). It is possible that during the last two experiments there occurred the formation of an active surface or complex at a rate comparable with the rate of racemisation, yielding an apparently zero-order racemisation.

The course of racemisation in the presence of bromine and bromine-silver bromide is now considered in the light of the above results. Solutions of 1-phenylethyl bromide in carbon tetrachloride containing bromine (1.0 equiv.) after 4 hours at 73° lost 40% of the initial rotatory power (Fig. 2, *G*) and very little bromine remained. Hydrogen bromide was evolved and, in addition to (±)-1-phenylethyl bromide, styrene dibromide was isolated at the end of the experiment. Similar solutions in the presence of silver bromide lost 94% of the initial rotatory power in one hour and became optically inactive after 3 hours (Fig. 2, *H*); hydrogen bromide and styrene dibromide were again formed.

TABLE I.

Expt.	Racemisation of 1-phenylethyl bromide in the presence of:	Racemisation in first 10 mins., %.	Relative extent of racemisation in first 10 mins.
<i>A</i>	HBr	0.3	1
<i>B</i>	HBr + powdered glass	38	130
<i>C</i>	HBr + AgBr	97	320
<i>D</i>	HBr + KBr	5.7	19
<i>E</i>	HBr + charcoal	43	140
<i>F</i>	HBr + styrene dibromide	2.2	7
<i>G</i>	Bromine	10	33
<i>H</i>	Bromine + AgBr	66	220

Thus in the experiments involving bromine, the system hydrogen bromide-styrene dibromide was present, but the racemisation effected by this system, the components of which were present in much smaller concentrations than for *F*, could not have been more than a fraction of the racemisation observed in *G* and *H*. The styrene dibromide isolated from these experiments was optically inactive so that, in proportion as this compound was formed, optically active material was diminished. It has not been found possible to deduce from the data whether or not these two sources of loss of rotatory power account for the whole of the loss occurring in the absence of silver bromide. Assessment is made difficult by the racemisation of 1-phenylethyl bromide which occurs when this compound is separated from styrene dibromide by distillation; 39% racemisation occurred during the distillation of a prepared mixture at 88°/19 mm. Gerrard (*J.*, 1945, 852) found certain specimens of 1-phenylethyl bromide to undergo extensive racemisation on redistillation. It is thus uncertain whether 1-phenylethyl bromide undergoes exchange of bromine ions or atoms with elementary bromine, except that the rate of exchange under the conditions employed cannot be rapid.

In the bromine-silver bromide experiments there was present, in addition to the two sources of loss of rotatory power described above, the system hydrogen bromide-silver bromide which has been shown to be very effective in racemisation; the possible catalytic effect of silver bromide on bromine-exchange between 1-phenylethyl bromide and elementary bromine could not be detected in the presence of these other sources of loss of optical activity. An equation of kinetic order 1.8 empirically satisfies the fall in rotatory power [k for *H* (i) is 0.28 mole^{-0.8} l.^{0.8} min.⁻¹] but, since the concentrations of bromine and hydrogen bromide alter with time, the value 1.8 has no simple significance.

EXPERIMENTAL.

(±)-1-Phenylethyl alcohol was resolved by Downer and Kenyon's method (*J.*, 1939, 1156). The optically active bromide was prepared by an unpublished method due to Dr. W. Gerrard: phosphorus oxybromide (17.2 g., 0.66 mol., prepared according to Gerrard, Nechvatal, and Wyvill, *Chem. and Ind.*,

1947, 29, 437) in carbon disulphide (20 ml.) was added dropwise to a solution of (–)-1-phenylethyl alcohol ($\alpha_D^{17} -44.35^\circ$, l 1.0; 11 g.) and pyridine (14.4 g., 2 mols.) in carbon disulphide (40 ml.) at -10° . After 2 hours the reaction mixture was filtered, and the filtrate washed with dilute sulphuric acid, aqueous sodium carbonate, and water, and dried (K_2CO_3). After removal of the carbon disulphide under reduced pressure the residue was distilled and gave (+)-1-phenylethyl bromide (7.0 g., 42%), b. p. $86-87^\circ/11$ mm., $n_D^{21} 1.5605$, $\alpha_D^{22} +130.96^\circ$ (l 1.0).

(±)-1-Phenylethyl bromide was prepared from the (±)-alcohol and hydrobromic acid (d 1.49) by the method of Norriss, Watt, and Thomas (*J. Amer. Chem. Soc.*, 1916, 38, 1078); it was twice redistilled and had b. p. $84-84.5^\circ/10$ mm., and the variation of n_D with temperature was determined:

t	17°	18°	19°	20°	21°	22°	23°	24°	25°
n_D	1.5634	1.5629	1.5625	1.5619	1.5614	1.5609	1.5604	1.5599	1.5595

Carbon tetrachloride was kept over calcium chloride, distilled from fresh reagent, and the process repeated with phosphoric oxide; it was kept over the latter and distilled immediately before use.

Silver bromide was prepared by adding a slight excess of aqueous potassium bromide (10%) to aqueous silver nitrate (10%); it was washed by thrice boiling with water and filtering, dried at 100° , powdered, and again dried at 100° . Potassium bromide was dried by heating at $150^\circ/20$ mm. for 2 hours. Absorbent charcoal (B.D.H.; coarse grains) was dried by heating at $150^\circ/1$ mm. for 2 hours. Silica (B.D.H.) was powdered and dried by heating at $150^\circ/2$ mm. for 2 hours.

Pyrex glass tubing was washed with concentrated nitric acid and water, dried at 150° , powdered, and sieved mechanically; the portion which passed through a 1/100-inch mesh but not a 1/150-inch mesh was collected, boiled with aqua regia and then 4 times with water, and dried at 130° for 4 hours. The surface area of the glass powder was determined by Kendrick's method (*J. Amer. Chem. Soc.*, 1940, 62, 2838) and that of Barrett, Birnie, and Cohen (*ibid.*, p. 2841) which depends on the fact that the average of the areas of projection of a unit plane in all random positions is $\frac{1}{2}$ unit, whence the average area of projection of a solid is $\frac{1}{2}$ of its surface area, since half the planes constituting the surface mask the other half. Small quantities of glass powder were placed on a microscope slide (*a*) by sprinkling, (*b*) by lowering the slide on to a small heap, whereupon, when the slide was withdrawn, a layer of powder adhered. Three slides were prepared by each method and photographed at linear magnification 75, and the areas of the images of the particles on the photographic plate measured with a planimeter. The number of particles per g. (N) was determined by weighing small quantities of powder on a microbalance and counting them on a ruled slide under a low-power microscope: found, (i) 1.039×10^6 , (ii) 1.036×10^6 . Then, where A = average area of a particle image, the surface area per g. of powder = $4AN/75^2 = 710 \text{ cm.}^2/\text{g.}$

Bromine was kept with phosphoric oxide for 3 days and then distilled from fresh reagent.

Hydrogen bromide was prepared by passing hydrogen saturated with bromine through a heated tube and then through a column packed with copper turnings (to remove any unreacted bromine) (*Org. Synth.*, Coll. Vol. II, p. 338). At the beginning and end of each experiment the rate of passage of hydrogen bromide was determined by passing the gas into water (50 ml.) for 5.0 minutes and titrating the solution with 0.1N-sodium hydroxide. The absence of bromine in the hydrogen bromide was confirmed by testing a similarly prepared solution with potassium iodide and starch.

TABLE II.

Expt.	1-Phenylethyl bromide, g.	CCl_4 to, ml.	Additional reagents.
A	2.00	20	HBr, 2.3 g./hr.
B (i)	1.00	10	" 2.2 " ; glass, 1.00 g.
B (ii)	1.00	10	" 2.1 " ; glass, 1.00 g.
C (i)	1.00	10	" 2.3 " ; AgBr,* 2.00 g.
C (ii)	2.00	20	" 2.2 " ; AgBr, 4.00 g.
D	1.50	15	" 2.1 " ; KBr, 1.50 g.
E	1.70	17	" 2.2 " ; charcoal, 0.57 g.
F	1.00	10	" 2.5 " ; styrene dibromide, 0.50 g.
G (i)	3.85	40	Bromine,† 1 equiv.
G (ii)	2.00	20	" 1 " ; AgBr, 4.00 g.
H (i)	2.00	20	" 1 " ; AgBr, 6.00 g.
H (ii)	3.00	30	" 1 " ; AgBr, 6.00 g.

* Freshly prepared.

† Added as a standard solution in CCl_4 .

Procedure.—The solution of 1-phenylethyl bromide in carbon tetrachloride and the additional reagents were placed in a 50-ml. Pyrex flask fitted (ground-glass joint) with a condenser through which, in those experiments in which hydrogen bromide was used, passed an inlet tube reaching nearly to the bottom of the flask, and to which was fitted an exit tube bearing a calcium chloride tube. The flask was immersed in a thermostat kept at $73.4^\circ \pm 0.1^\circ$ and, in experiments in which a solid was present, the flask was shaken by attaching it to a motor-driven crank. Portions (1–2 ml.) of solution were withdrawn initially and at intervals, and the rotatory power determined; in the experiments with bromine, the withdrawn portion was washed with aqueous sodium sulphite (15%) and dried (Na_2SO_4) for 10 minutes before determination of the rotatory power. The reagents used are given in Table II.

In the experiments A and F, in which racemisation occurred slowly, correction was made for the concentration of the solution by evaporation of the solvent in the course of the experiment. The flask and the contents were weighed initially, before withdrawing each specimen for the determination of

rotation, and after returning the specimen to the flask. Then, where α_0, w_0 are the initial rotation and weight of the solution and α_t, w_t are the rotation after time t and the weight immediately before withdrawing the specimen for determination of this rotation, we have $\alpha_{\text{unracemised}, t} = \alpha_0 w_0 / w_t$, where $\alpha_{\text{unracemised}, t}$ is the rotation the solution would have exhibited had evaporation only, without racemisation, occurred. The percentage of initial rotatory power after time $t = 100\alpha_t w_t / \alpha_0 w_0$. Further, where w'_t is the weight of solution after replacing the specimen used for rotation, and $\alpha_{t'}, w_{t'}$ are the rotation after t' and the weight immediately before the determination of rotation, we have $\alpha_{\text{unracemised}, t'} = \alpha_0 w_0 w'_t / w_t w_{t'}$, and the percentage of initial rotatory power after time $t' = 100\alpha_{t'} w_{t'} w'_t / \alpha_0 w_0 w_t$. In this way corrections were applied for both the concentration of the solution due to evaporation and the small manipulative losses ($w_t - w'_t$, etc.).

In a number of experiments the solution remaining at the end was washed with aqueous sodium carbonate, if hydrogen bromide was present, or with aqueous sodium sulphite, if bromine was present, and with water, and dried (Na_2SO_4). Carbon tetrachloride was removed under reduced pressure, and the residue distilled, yielding 1-phenylethyl bromide having the following characteristics:

Expt.	A.	B (i).	C (ii).	D.	E.	G (i).	G (ii).	H (ii).
n_D^{20}	1.5619	1.5623	1.5628	1.5622	1.5611	1.5654	1.5589	1.5648
t	20°	19°	18°	20°	22°	18°	25°	18°
% of original rotatory power	84	Nil	Nil	Nil	Nil	51	25	Nil

From G (i) was obtained a fraction, b. p. 125–132°/10 mm., which solidified; after repeated recrystallisation from ethyl alcohol it yielded styrene dibromide, m. p. 72–73°, optically inactive in ethyl alcohol. The residue from G (ii), after distillation of the 1-phenylethyl bromide, was optically inactive in solution in ethyl alcohol and similarly yielded styrene dibromide, m. p. 72.5–73.5° alone and mixed with a specimen of m. p. 73–73.5° prepared according to Glaser (*Annalen*, 1870, **154**, 154). The residue from H (ii) also yielded styrene dibromide, m. p. 72°. A larger quantity of the bromination product was prepared, in order to confirm its identity, as follows: bromine (4.9 g., 4.2 equivs.) was added dropwise to ($\pm$)-1-phenylethyl bromide (2.7 g.) containing a little iodine: hydrogen bromide was evolved. The mixture was heated for 3 hours on a steam-bath and kept overnight. The solid product was washed with 3N-sodium hydroxide and with water and dried; it (3 g.) was distilled, and the fraction, b. p. 148–151°/22 mm., was thrice recrystallised from light petroleum, giving needles, m. p. 70–72°, undepressed by the materials from G (i) and H (ii). Oxidation of this bromo-compound (5 g.) with potassium permanganate (10 g.) and sodium carbonate (2.5 g.) in water (240 ml.) gave benzoic acid (1 g.) which, twice recrystallised from water, had m. p. 120–121° alone and mixed with an authentic specimen.

Control Experiments.—A solution of (–)-1-phenylethyl bromide (1.00 g.; $\alpha_D^{25} -56.95^\circ$, l 0.5) in carbon tetrachloride (to 10 ml.) had $\alpha_D^{25} -4.05^\circ$ (l 0.5); silver bromide (2.00 g., freshly prepared) was added, and the whole heated with shaking at 73.4°. After 1 hour the solution had $\alpha_D^{25} -3.13^\circ$, and after 3 further hours $\alpha_D^{25} -3.11^\circ$ (l 0.5), 76.8% of the initial value, and on evaporation gave (–)-1-phenylethyl bromide having $\alpha_D^{25} -44.18^\circ$ (l 0.5), 77.6% of the original value. A similar experiment employing another specimen of freshly-prepared silver bromide, in which heating was continued for 2 hours, gave 1-phenylethyl bromide having 60.6% of the initial rotatory power. From an experiment similar to the last but employing 3-months aged silver bromide (0.65 g.), (–)-1-phenylethyl bromide (0.8 g.), and carbon tetrachloride (to 8 ml.), the (–)-1-phenylethyl bromide was recovered having 99.9% of the original rotatory power.

Solutions of (+)-1-phenylethyl bromide (2.00 g.) in carbon tetrachloride (to 20 ml.) suffered no racemisation on heating at 73.4° for 2 hours alone and with (a) powdered glass (2.00 g.), (b) potassium bromide (2.00 g.), or (c) styrene dibromide (1.00 g.); on addition of charcoal (0.67 g.) to such a solution the rotatory power fell to 77.0% of the initial rotatory power, but this was due to adsorption since the (+)-1-phenylethyl bromide recovered on evaporation was unchanged in rotatory power. On addition of silica to a similar solution of (–)-1-phenylethyl bromide, the silica swelled and became dark red. The rotation of the solution fell rapidly and became zero after 2 hours. Neither the solution, on evaporation, nor the silica, on heating to 200°/24 mm., yielded any 1-phenylethyl bromide.

Carbon tetrachloride was placed in a 3-necked flask fitted with an inlet tube passing below the surface of the liquid, an exit tube, and a conductivity cell of the dipping type. The resistance of the carbon tetrachloride, measured with a Mullard bridge, was approximately 1.1×10^7 ohms at 25°; this value remained unchanged when (a) the flask was kept at 73.4°, (b) the carbon tetrachloride was saturated at 73.4° with hydrogen bromide by passing the latter at 2.8 g./hour for 30 minutes, (c) hydrogen bromide was passed continuously at 73.4°, or (d) the carbon tetrachloride was saturated with hydrogen bromide at 25°.

Hydrogen bromide was passed at 4.8 g./hour for 30 minutes into carbon tetrachloride (50 ml.) at 73.4°; 20 ml. of the saturated solution were added to water (50 ml.) and titrated with standard sodium hydroxide. The determination was twice repeated with fresh solvent, and similar determinations were made at 25°. Solubility of hydrogen bromide in carbon tetrachloride: at 25°, 0.87, 0.85, 0.90 g./100 ml. of solution; at 73.4°, 0.106, 0.109, 0.108 g./100 ml. of solution.

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THE SCHMIDT REACTION WITH ARYLCARBINOLS

By C. L. Arcus and R. J. Mesley

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Evidence has accumulated that the Schmidt reaction, in which acids, ketones, and olefines react with hydrazoic acid in the presence of strong acids, proceeds *via* carbon cations.¹ Many of the reactions of di- and triarylcbinols indicate that carbon cations are readily formed from these compounds, and it appeared that they might undergo a Schmidt reaction.

Four arylcbinols have been reacted, in solution in chloroform, with sodium azide and sulphuric acid and, after dilution with water, the following products were obtained :

Carbinol	Products from Schmidt reaction
benzhydrol	aniline, benzaldehyde
<i>p</i> -methylbenzhydrol	<i>p</i> -toluidine, benzaldehyde
fluorenol,	phenanthridine,
triphenylcbinol	triphenylmethyl azide

(The formation of benzylideneaniline by the reaction of a solution of benzhydrol in benzene containing hydrazoic acid with thionyl chloride has been described,² and triphenylmethyl azide has been prepared by the reaction of triphenylmethyl perchlorate in chloroform with sodium azide.³)

The course of reaction is considered to be :

With triphenylcbinol the stable azide (i) is the product, from fluorenol the Schiff's base (ii, here phenanthridine) is obtained, and the benzhydrols yield the aldehyde (iii) and the amine (iv).

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The Hofmann Reaction with Polymethacrylamide

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As part of a program of study of the reactivity of groups attached to large molecules, the reaction of polymethacrylamide in aqueous solution with hypobromite and hypochlorite has been investigated.

Jones, Zomlefer, and Hawkins,¹ in the course of attempts to prepare polyvinylamine by various methods, reacted polyacrylamide with hypobromite; products having nitrogen contents 9.7, 11.3, 12.1, and 15.0% were isolated, the values being much lower than those for polyacrylamide (19.7%) or polyvinylamine (32.5%), indicating removal of nitrogen by hydrolysis of the amide, or otherwise. One product is formulated as a polymeric amino acid:

but no determination of the primary amino or carboxyl content is recorded.

The main product of the Hofmann reaction with polymethacrylamide is a polymer containing a small quantity of amine units (I), considerable carboxyl units (II), probably alkylacylurea units (III), and also unreacted amide units (IV). The polymer is soluble in dilute alkali, insoluble in

water and dilute acids, but soluble in strongly acid media, precipitating on dilution.

In the course of attempts to obtain a larger conversion to amine, a number of modifications in procedure, recorded in the Experimental Part, were employed, but the polymers obtained were in all cases essentially similar (Table I). Two polymers had an amine unit content of 5.5 and 1.2%, which is in accord with the lack of basic properties; in other experiments the quantity of amine present in the acidic filtrates after precipitation of the polymer was determined, and varied from 2.4 to 4.0% (% = g. amine units formed from 100 g. polymethacrylamide). A considerable proportion of the amide groups underwent alkaline hydrolysis, the acidic equivalents of the polymers ranging from 428 to 206. A clue to the fate of further amide groups is given by the percentage of nitrogen not released as ammonia by subjecting the polymer to hydrolysis with concentrated alkali. It has been found² that the hydrolysis of polymethacrylamide proceeds

fairly rapidly until there remain 27% of the amide units (= 4.5% nitrogen), and then becomes very slow; an explanation based on the hydrogen bonding of amide groups by carboxyl ions has been put forward. For three polymers from the Hofmann reaction higher values, 6.3, 7.6, and 8.7% for "resistant" nitrogen were found, and it appears probable that this is due to the formation of difficultly hydrolyzable alkylacylurea groups.

It is established that the Hofmann reaction may yield an alkylacylurea as the principal product³; it is formed by the reaction of an isocyanate with a halogeno-amide in the presence of alkali:⁴

By reacting succinamide with hypobromite, Weidel and Roithner⁵ obtained dihydroureacil (V), which proved very resistant to both alkaline and acid hydrolysis, in 55–60% yield; alkylacylurea formation is therefore indicated to be the main reaction when amide groups are held in proximity in the molecule. The analogous Hofmann reaction with polymethacrylamide would yield 7-membered cyclic alkylacylurea units:

Some support for the conclusion that alkylacylurea units are present in the polymer is given by the following observations relating to the monomer. Benzoylation of the filtrate from one polymer-hypochlorite reaction gave a small quantity of *N*- α -methylvinyl-*N*-benzoyl-*N'*-methacrylurea (VI). Polymethacrylamide contains, after washing thoroughly, a small quantity of monomer, which sublimates if the polymer is heated in a vacuum,² and (VI) is considered to be formed from this monomer by reactions (1) to (3),

followed by benzoylation at the alkylated nitrogen of the urea. That (VI) was formed in this manner was confirmed by subjecting the monomer to reaction conditions similar to those for the polymer, when (VI) was obtained in 13% yield, and acetone, the "normal" product of the Hofmann reaction with methacrylamide, was isolated as the 2,4-dinitrophenylhydrazones in 11% yield.

EXPERIMENTAL

Methacrylamide monomer was prepared and polymerized by methods previously described.² Intrinsic viscosities, $[\eta]_c = (1/c) \ln(\eta_{\text{soln}}/\eta_{\text{soln}})$, were determined with 1% aqueous solutions of the polymers at 25°C.

TABLE I. THE HOFMANN REACTION WITH POLYMETHACRYLAMIDE

Ex- peri- ment No.	A		B		C		Time <i>t</i>		Polymer			
	Polymeth- acrylamide [η] ^c	H ₂ O, ml.	Halogen g. equivs. ^a	Alkali g. equivs. ^a	H ₂ O, ml.	NaOH g. equivs. ^a	H ₂ O, ml.	hr. min.	Amine units, % ^b alent ^c	Amide units, % ^d	Total amide units, N, % as NH ₂	N % not Filtrate amide units % ^e
(1)	—	3.9	25	Br 8.0 2.2	KOH 11.2 4.3	50	—	1 45	2.5	5.5	275	—
(2)	0.09	10.1	80	Cl 9.2 2.2	NaOH 10.4 2.2	105	75	2 0	6.6	1.2	206	—
(3)	"	4.5	140	" 1.3 0.7	" 2.2 1.1	20	16	2 0	4.0	—	—	4.0
(4)	"	4.1	100	" 1.2 0.7	" 2.1 1.1	20	—	1 0	3.4	—	—	2.9
(5)	"	10.1	105	" 9.2 2.2	" 16.0 3.4	140	—	1 15	9.0	—	265	7.5 8.8 7.6 3.8
(6)	0.11	8.5	85	" 8.5 2.4	" 9.6 2.4	95	90	— 45	3.6	—	325	7.6 10.0 8.7
(7)	"	8.5	85	" 6.4 1.8	" 11.2 2.8	90	—	— 20	3.9	—	390	29.1 11.1 6.3
(8)	0.54	8.5	110	" 11.8 3.3	" 13.4 3.4	190	370	2 15	4.6	—	388	— 12.2 — 3.9
(9)	0.14	8.5	110	" 11.8 3.3	" 13.3 3.3	170	370	2 15	4.8	—	428	— 12.3 — 2.4

^a Relative to the polymethacrylamide, taking the theoretical equivalent weight, 85, for the latter.^b % = g. amine units contained in 100 g. polymer, determined by the Van Slyke method.^c By dissolving in alkali and neutralizing to phenolphthalein. Since dihydroureacil is a weak acid, alkylacetylurea units probably contribute to the total acidity of the polymer, so that the equivalent cannot with certainty be converted to content of carboxylic acid units.^d Equivalent to the ammonia evolved on boiling with 4.5 N NaOH for 2 hours and steam distilling.^e % = g. amine units formed from 100 g. polymethacrylamide. The filtrates were evaporated to dryness and the residues dissolved in water, made alkaline with sodium hydroxide and acidified with acetic acid (to ensure absence of free hydrochloric acid) and subjected to Van Slyke determinations.

Procedure for Hofmann Reaction. Polymethacrylamide in solution *A* (Table I) was allowed to react (under the conditions detailed in the next paragraph) with the halogen and the alkaline solution *B*. The whole was then heated with solution *C* on a steambath for time *t*. After cooling the solution was acidified to Congo red with hydrochloric acid; the polymer then precipitated and, after reheating, was filtered off. It was washed by thrice suspending in water and filtering, and dried over calcium chloride in a vacuum.

In experiment (1) the bromine was added, with stirring and cooling in ice, to solution *A*, followed by solution *B*. It was found, in further experiments, that the rate of reaction of solutions of hypobromite with polymethacrylamide is very slow (one reaction solution still contained hypobromite after 11 months at room temperature) and accordingly the more reactive hypochlorite was used. The hypochlorite was prepared from solution *B* and the stated weight of chlorine and, in (2), (6), (7), (8), and (9), was added with stirring and cooling to solution *A*. In (3), with the intention that a relatively small proportion of amide groups might be converted to amine with a minimum of opportunity for interaction to form alkylacylurea, the hypochlorite was added to the hot solution *A*. In (4) the solution *A* was heated under reflux with 30 ml. methanol and the hypochlorite was then added; in (5), solution *A* was added to a cooled mixture of the hypochlorite with 50 ml. methanol. These procedures were intended to give a urethan, hydrolysis of which would yield an amine; the polymers obtained closely resembled those from reactions in the absence of methanol. In (6), solution *C* was heated on a steambath in a flask fitted with a stirrer and a reflux condenser and solution *A*, after the addition of the hypochlorite, was added during 2 hours; heating was continued for 45 minutes. To one-half the filtrate from the polymer was added 19 g. sodium hydroxide and, after cooling, the solution was shaken with 3.0 ml. benzoyl chloride. A solid (1.2 g.) separated which was heated with water, the solution filtered from a dark residue and cooled, when crystals separated. The *N*- α -methylvinyl-*N*-benzoyl-*N'*-methacrylurea after repeated recrystallization from ethanol had a melting point of 127.5–128.5°C. (Found: C, 66.3; H, 5.9; N, 10.2. $C_{15}H_{16}N_2O_3$ requires C, 66.2; H, 5.9; N, 10.3%.) In two experiments, (8) and (9), directed to the preparation of polymers containing a maximum of alkylacylurea groups, the polymethacrylamide-hypochlorite solutions were allowed to stand 4 and 3 days, respectively, during which time the hypochlorite contents fell to 2% and 5% of the initial values, before adding the solutions *C*.

Properties of the Polymer. The specimens of polymer from the Hofmann reaction were pale buff powders. Polymer (8) contained: C, 59.0; H, 7.9; N, 12.2; Cl, 2.6%. Polymer (9) contained: C, 59.3; H, 7.8; N, 12.3; Cl, 2.4%. These polymers, derived from polymethacrylamide having $[\eta]_c$ 0.54 and 0.14, respectively, both had $[\eta]_c$ 0.11 in 0.25 *N* NaOH. Polymethacrylamide having $[\eta]_c$ 0.61 was heated with 3.7 *N* NaOH for 2 hours and gave a polymer the equivalent and nitrogen content

of which indicated it to contain 67.8% acid units and 29.9% amide units; this hydrolyzed polymer had $[\eta]_c$ 0.70 in 0.25 *N* NaOH. The fall in $[\eta]_c$ during reaction with hypochlorite and alkali is therefore not due to hydrolysis of amide to carboxyl, and is attributed to the occurrence of degradation.

Portions (0.20 g.) of polymer (6) dissolved, on heating on a steambath, in concentrated hydrochloric and nitric acids, 90% phosphoric acid, and 65% sulfuric acid (4 ml. of each). Each solution was poured with stirring into 25 ml. water, when polymer separated as a flocculent precipitate which was filtered off, and washed and dried as above. The solutions yielded, respectively, 0.18, 0.18, 0.19, and 0.18 g. polymer.

Specimens of polymer remained insoluble in dilute acid and low in amine content after heating in a sealed tube with concentrated hydrochloric acid at 135°C. for 23 hours, and with 3 *N* NaOH at 100°C. for 25 hours.

Hofmann Reaction with Monomer. To an ice-cooled suspension of 8.5 g. methacrylamide in 17 ml. water was added a solution of sodium hypochlorite (110 ml., 7.1 g. Cl_2 , 8.0 g. NaOH); after 1 hour the solution was added in the course of 25 minutes to a solution of 20 g. sodium hydroxide in 90 ml. water which was heated under reflux with mechanical stirring; after a further 20 minutes the solution was cooled in ice. Benzoyl chloride (18 ml.) was added with shaking in 4 portions, with filtration after each addition. The crude product (2.8 g.) was thrice boiled with 6 ml. water and from the filtered extracts there separated *N*- α -methylvinyl-*N*-benzoyl-*N'*-methacrylurea, 1.8 g., m.p. 126–127°C., which after recrystallization from ethanol had m.p. 127.5–128°C. alone and mixed with the specimen from (6). The filtrate from benzylation was distilled; 60 ml. of the distillate (115 ml.) was allowed to react with an excess of a solution of 2,4-dinitrophenylhydrazine in 2 *N* HCl and yielded 1.3 g. of hydrazone, m.p. 121–122°C., which after twice recrystallizing from ethanol had m.p. 125.5–126°C. alone and mixed with an authentic specimen of acetone 2,4-dinitrophenylhydrazone having m.p. 126°C.

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Synopsis

The reaction of polymethacrylamide, $[-\text{CH}_2\text{C}(\text{CH}_3)(\text{CONH}_2)-]_n$, in aqueous solution with hypobromite and hypochlorite has been investigated. Different reaction procedures yielded polymers which were similar, and which contained a small number of primary amino groups, considerable carboxyl and unreacted amide groups and, probably, alkylacylurea groups formed by interaction between adjacent isocyanate and halogenoamide groups. Analytical data supporting these conclusions are presented. The polymer from the Hofmann reaction is soluble in dilute alkali and also in strongly acid media,

precipitating on dilution. Methacrylamide monomer reacts with hypochlorite to give *N*- α -methylvinyl-*N'*-methacrylurea and acetone.

Résumé

La réaction de la polyméthacrylamide $[-CH_2C(CH_3)(CONH_2)-]_n$ en solution aqueuse avec l'hypobromite et l'hypochlorite de sodium a été étudiée. Les différentes méthodes fournissent des polymères semblables; ils contiennent un nombre peu élevé de groupes aminés primaires, un nombre considérable de groupes acides et groupes amides primitifs, de même que vraisemblablement des groupes alcoylacryluriques; ceux-ci sont dus à l'interaction de groupes isocyanique et halogéno-amide voisins. Des résultats analytiques confirmant ces conclusions sont présentés. Le polymère issu de la réaction de Hoffmann est soluble dans les alcalis dilués, de même que dans les milieux acides forts; il en précipite par dilution ultérieure. La méthacrylamide monomérique réagit avec l'hypochlorite pour donner la *N*- α -methylvinyl-*N'*-méthacrylurée en même temps que de l'acétone.

Zusammenfassung

Die Reaktion von Polymethacrylamid, $[-CH_2C(CH_3)(CONH_2)-]_n$, in wässriger Lösung mit Hypobromit und Hypochlorit wurde untersucht. Verschiedene Reaktionsprozesse ergaben ähnliche Polymere. Diese enthielten eine kleine Anzahl primärer Aminogruppen, eine erhebliche Menge Karboxyl- und nicht reagiert habende Amidgruppen und wahrscheinlich Alkylacrylharnstoffgruppen, die durch Interaktion zwischen benachbarten Isocyanat- und Halogenamidgruppen gebildet wurden. Es werden analytische Daten gegeben, die diese Schlüsse bestätigen. Das nach der Hofmann'schen Reaktion gebildete Polymer ist in verdünntem Alkali löslich, wie auch in stark saurem Milieu, und fällt bei Verdünnung aus. Methacrylamid-Monomer reagiert mit Hypochlorit unter Bildung von *N*- α -Methylvinyl-*N'*-methacrylharnstoff und Aceton.

Received September 21, 1951

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By ALTON E. BAILEY, *Votator Division, The Girdler Corporation, Louisville, Kentucky.* 1950. 6 x 9. 371 pages, 150 illus., 66 tables. \$7.50

This volume collects from rather widely scattered sources all available material on the subject. It also correlates and interprets the experimental data in such a manner as to reveal the interrelationships between different phenomena associated with phase transformation, as well as the systematic variations that occur in specific properties of fats with similar variation in their molecular structure. The text has been written primarily for the practical oil and fat chemist or technologist, although portions are of interest to physical chemists at large.

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277. The Addition of Acyl Hypobromites to Styrene.

By D. C. ABBOTT and C. L. ARCUS.

Acyl hypobromites, prepared by the reaction of bromine with silver (+)- and (−)-2-ethylhexanoates, add to styrene to form (+)- and (−)-2-bromo-1-phenylethyl 2-ethylhexanoates,* hydrolysis of which yields optically inactive phenylglycol; it is concluded that racemisation does not occur during hydrolysis and, therefore, that the two configurations at the new asymmetric centre are formed in equal quantities.

Acetyl hypobromite by addition to styrene forms 2-bromo-1-phenylethyl acetate.

By the addition of bromine to (+)-4-phenylbut-3-en-2-ol, Kenyon and Partridge (*J.*, 1936, 1313) obtained a mixture of unequal quantities of the dibromo-alcohols (I) and (II). Only two of the four possible isomers were formed and they are here represented as the products of *trans*-addition to the *trans*-alcohol. Oxidation of the mixed dibromo-alcohols gave an optically-active mixture of the enantiomeric ketones (III) and (IV). These reactions, in

which two new centres of asymmetry are formed with one configuration preponderating and the original centre is subsequently rendered symmetrical, constitute a (partial) asymmetric synthesis.

The asymmetric synthesis just described was effected by the addition of a symmetrical reagent to an optically active compound containing a double bond, and it was decided to attempt an asymmetric synthesis in the reverse way, by adding an optically active reagent to a symmetrical olefin. Several examples of the addition of acyl hypobromites (formed by the reaction of two equivalents of bromine with the silver salt of the acid) to *cyclohexene* have been recorded (Bockemüller and Hoffmann, *Annalen*, 1935, 519, 165; Uschakow and Tschistow, *Ber.*, 1935, 68, 824)—they give the 2-bromocyclohexyl esters—and the acyl hypobromite derived from an optically active acid appeared to be a possible reagent for an asymmetric synthesis. Styrene used was because only one new asymmetric centre is formed and, after removal of the acyl group, diastereoisomerism cannot occur.

Silver (+)-2-ethylhexanoate* and bromine were allowed to react in carbon tetrachloride at -15° ; the colour disappeared after 10 minutes; reaction of styrene with the solution then gave (+)-2-bromo-1-phenylethyl 2-ethylhexanoate. Alkaline hydrolysis of this ester yielded (±)-phenylglycol. Silver (−)-2-ethylhexanoate similarly gave the (−)-ester and then (±)-phenylglycol.

The most probable course for the hydrolysis is considered, from the results of Winstein and Buckles for the reaction of 2-acetoxy-3-bromobutanes with silver acetate (*J. Amer. Chem. Soc.*, 1942, 64, 2780), to be:

* Geneva numbering, $\text{CO}_2\text{H} = 1$.

the last stage occurring by normal alkaline hydrolysis with acyl-oxygen fission. The bonding of the new asymmetric centre remains unchanged on this mechanism. It is possible, in the second stage of reaction, for the hydroxyl ion to attach itself to this centre, yielding 2-hydroxy-2-phenylethyl 2-ethylhexanoate; this would result in inversion but not in racemisation.

It is concluded that racemisation did not occur during the hydrolysis of the bromo-ester to phenylglycol and, therefore, that addition occurred symmetrically yielding the intermediates (VII) and (VIII) in equal quantities. The result implies that there is no appreci-

able difference in the rates of formation of the diastereoisomeric critical complexes (V) and (VI).

Acetyl hypobromite, prepared from silver acetate and bromine, gave with styrene an ester, the physical constants of which agreed closely with those of the 2-bromo-1-phenylethyl acetate prepared by Marvel and Moon (*J. Amer. Chem. Soc.*, 1940, **62**, 40) by the acetylation of styrene bromohydrin, and it is inferred that the 2-ethylhexanoates above are also 2-bromo-1-phenylethyl esters.

The (+)- and (-)-2-ethylhexanoic acid recovered from the hydrolyses were respectively 36 and 40% racemised. Racemisation is probably due to the removal of a proton from C_(a) during hydrolysis:

Kenyon and Young (*J.*, 1940, 216) found that (-)-ethyl 2-ethylhexanoate, when heated with one equivalent of sodium ethoxide in alcohol for 20 minutes at 80°, was completely racemised.

EXPERIMENTAL

Carbon tetrachloride was kept over calcium chloride and distilled, then dried with, and distilled from, phosphoric oxide; it was kept over the latter.

Bromine was twice shaken with an equal volume of concentrated sulphuric acid and distilled from phosphoric oxide.

Styrene was kept over sodium sulphate and was distilled, a little quinol having been added, immediately before use.

2-Ethylhexanoic acid was prepared and resolved by the method of Kenyon and Platt (*J.*, 1939, 633).

(+)-2-Ethylhexanoic acid (19.8 g.) was added to warm N-sodium hydroxide (130 ml.) and

the solution titrated with further aqueous sodium hydroxide until just alkaline to phenolphthalein. This solution was added dropwise with stirring to a warm solution of silver nitrate (23.4 g.) in water (100 ml.); the precipitated silver (+)-2-ethylhexanoate was washed with water, acetone, and ether. It was dried (CaCl_2) in a vacuum, finely ground, and dried again (P_2O_5) in a vacuum; the yield was 34.2 g. (99%). Silver (–)-2-ethylhexanoate and silver acetate were prepared similarly.

Addition Reactions.—A suspension of the silver salt (15.2 g.) of (+)-2-ethylhexanoic acid (b. p. 118–121°/15 mm., $\alpha_{\text{D}}^{22} +15.07^\circ$, l 2.0; 93% optically pure) in carbon tetrachloride (150 ml.) was cooled, in ice-salt at between –20° and –10°, and vigorously stirred while a solution of bromine (9.5 g.) in carbon tetrachloride (25 ml.) was added. After 10 minutes all colour of bromine had disappeared, and styrene (6.3 g.) in carbon tetrachloride (25 ml.) was added; stirring and cooling were continued for 30 minutes. The reaction mixture was allowed to attain room temperature and filtered through sintered-glass. The filtrate was twice washed with aqueous sodium hydrogen carbonate (25 ml., 20%) and dried (Na_2SO_4). The carbon tetrachloride was distilled and unchanged styrene removed at 100°/15 mm. The residue on distillation yielded two fractions: (i), b. p. 110–120°/1 mm., which solidified and, after recrystallisation from aqueous alcohol, gave styrene dibromide (0.9 g.), plates, m. p. 73° alone and when mixed with an authentic specimen of m. p. 73°; and (ii), (+)-2-bromo-1-phenylethyl 2-ethylhexanoate (12.0 g., 60%), b. p. 152–156°/1.5 mm., $n_{\text{D}}^{25} 1.5081$, $\alpha_{\text{D}}^{18} +0.88^\circ$ (l 0.5) (Found: C, 58.9; H, 7.0; Br, 24.7. $\text{C}_{16}\text{H}_{23}\text{O}_2\text{Br}$ requires C, 58.7; H, 7.1; Br, 24.4%).

A similar experiment with the silver salt (14.8 g.) of (–)-2-ethylhexanoic acid (b. p. 122–125°/17 mm.; $\alpha_{\text{D}}^{18} -2.95^\circ$, l 0.5; 75% optically pure) gave styrene dibromide (1.9 g.), m. p. 69–71°, m. p. 73° after recrystallisation, and (–)-2-bromo-1-phenylethyl 2-ethylhexanoate (6.6 g., 35%), b. p. 150–154°/1 mm., $n_{\text{D}}^{25} 1.5080$, $\alpha_{\text{D}}^{17} -0.61^\circ$ (l 0.5) (Found: C, 58.8; H, 7.3; Br, 24.8%).

A similar experiment with silver acetate (33.4 g.) yielded 2-bromo-1-phenylethyl acetate (29.1 g., 60%) having b. p. 100–104°/0.6 mm., $n_{\text{D}}^{25} 1.5391$ and, after redistillation, b. p. 98–100°/0.3 mm., $n_{\text{D}}^{25} 1.5389$ (Found: C, 49.2; H, 4.6; Br, 33.3. Calc. for $\text{C}_{10}\text{H}_{11}\text{O}_2\text{Br}$: C, 49.4; H, 4.6; Br, 32.8%). Marvel and Moon (*loc. cit.*) record b. p. 105–107°/3 mm., $n_{\text{D}}^{20} 1.5380$.

Hydrolyses.—2-Bromo-1-phenylethyl acetate (1.8 g.) was heated under reflux for 3 hours with *N*-sodium hydroxide (20 ml.). The cooled solution was saturated with potassium carbonate and extracted with ether. The extract was dried (Na_2SO_4) and ligroin (b. p. 100–120°) added, whereupon there separated phenylglycol (0.6 g., 60%), m. p. 64–65° (Found: C, 69.4; H, 7.4. Calc. for $\text{C}_8\text{H}_{10}\text{O}_2$: C, 69.5; H, 7.3%); its dibenzoate had m. p. 93–94°. Milas and Sussman (*J. Amer. Chem. Soc.*, 1937, 59, 2346) record m. p. 65–66° and m. p. 92–93° for phenylglycol and the dibenzoate.

(+)-2-Bromo-1-phenylethyl 2-ethylhexanoate (3.3 g.) was similarly hydrolysed for 10 hours with 3*N*-sodium hydroxide (40 ml.). The ethereal extract (dried with K_2CO_3) was optically inactive (c 5, l 2.0) and yielded phenylglycol (0.9 g., 65%), m. p. 63–65° and, after recrystallisation from ether–ligroin, m. p. 64.5–65.5°. The aqueous solution was acidified with hydrochloric acid and extracted with ether. The extract was dried (Na_2SO_4) and distilled, and yielded (+)-2-ethylhexanoic acid (1.2 g., 80%), b. p. 223–225°, $\alpha_{\text{D}}^{15} +2.40^\circ$ (l 0.5), whence the acid had undergone 36% racemisation.

From a similar hydrolysis of (–)-2-bromo-1-phenylethyl 2-ethylhexanoate (3.3 g.) there was obtained an ethereal extract having $\alpha_{\text{D}}^{14} -0.02^\circ$ (c 5.9, l 2.0) which gave phenylglycol (1.0 g., 74%), m. p. 60–62°, m. p. 64–65° and optically inactive in ether (c 3.7, l 2.0) after recrystallisation. From the aqueous solution there was recovered (–)-2-ethylhexanoic acid (1.25 g., 83%), b. p. 223°, $\alpha_{\text{D}}^{15} -1.80^\circ$ (l 0.5), whence the acid had undergone 40% racemisation.

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**504. The Addition of Bromine to (+)-1-Phenylallyl Alcohol
and the Oxidation of the (+)-Dibromo-alcohol.**

By C. L. ARCUS and H. E. STRAUSS.

1-Phenylallyl alcohol, to which free bromine does not add satisfactorily, yields 2:3-dibromo-1-phenylpropanol on reaction with pyridine hydrobromide perbromide. (+)-1-Phenylallyl alcohol forms the (+)-dibromo-alcohol; the latter on oxidation with chromic anhydride-acetic acid yields ($\pm$)- $\alpha\beta$ -dibromopropiophenone. Similar reactions with (-)-1:3-dimethylallyl alcohol and (+)-1-methyl-3-phenylallyl alcohol are known to give optically active dibromo-ketones. It is concluded that $\alpha\beta$ -dibromopropiophenone, which has an asymmetric centre only at C_(α), becomes racemised through the occurrence of enolisation during oxidation; the dibromo-ketones derived from the 1:3-disubstituted allyl alcohols are not racemised because they have at C_(β) an additional asymmetric centre, which is not subject to racemisation by enolisation.

KENYON and PARTRIDGE (J., 1936, 1313) found that addition of bromine to (-)-1:3-dimethylallyl alcohol (I) yielded a (+)-2:3-dibromo-4-pentanol (II) which on oxidation with chromic anhydride in glacial acetic acid gave a (+)-2:3-dibromo-4-pentanone (III). These reactions constitute a partial asymmetric synthesis: the original centre of asymmetry has been rendered symmetrical by oxidation and the optical activity of the ketone is due to new centres of asymmetry having been formed with the possible configurations present in unequal amounts. Similar reactions with (+)-1-methyl-3-phenylallyl alcohol (IV) yielded (-)-3:4-dibromo-4-phenylbutan-2-ol (V) and (-)-3:4-dibromo-4-phenylbutan-2-one (VI). Four diastereoisomeric dibromo-alcohols may theoretically be formed from one optical isomer of (I) or (III), *e.g.*, from the *d*-allyl alcohol, the *dd'd''*, *dl'l''*, *dd'l''*, *dl'd''*-dibromo-alcohols; however, by fractionally crystallising a specimen of (V) prepared from fully active (IV), Kenyon and Partridge isolated only two diastereoisomeric forms. These diastereoisomers, which were obtained in unequal amounts, on oxidation separately gave enantiomeric (+)- and (-)-dibromo-ketones (VI).

It was decided to attempt an asymmetric synthesis with 1-phenylallyl alcohol (VII), an apparently simpler case because the dibromo-ketone (IX) has only one asymmetric centre.

From the reaction of bromine with 1-phenylallyl alcohol Klages and Klenk (*Ber.*, 1906, 39, 2553) and Moureu and Gallagher (*Bull. Soc. chim.*, 1921, 29, 1010) isolated only 1:2:3-tribromo-1-phenylpropane. We have repeated the reaction in dry chloroform, carbon tetrachloride, and carbon disulphide; absorption of bromine virtually ceased when 60—70% of that required to form the dibromo-alcohol had been added, and 1:2:3-tribromo-1-phenylpropane crystallised and was isolated in 5—10% yield; none of the dibromo-alcohol (VIII) was isolated. In order to minimise the concentration of free bromine, the reagent pyridine hydrobromide perbromide (Djerassi and Scholtz, *J. Amer. Chem. Soc.*, 1948, 70, 417) was then used; from its reaction with 1-phenylallyl alcohol in glacial acetic acid 2:3-dibromo-1-phenylpropanol (VIII) and 1:2:3-tribromo-1-phenylpropane were isolated in 47% and 6% yield respectively. Repetition of this reaction with (+)-1-phenylallyl alcohol yielded (+)-2:3-dibromo-1-phenylpropanol and optically inactive 1:2:3-tribromo-1-phenylpropane; oxidation of this (+)-dibromo-alcohol with chromic anhydride in glacial acetic acid gave optically inactive $\alpha\beta$ -dibromopropiophenone (IX) in 25% yield.

By analogy with the syntheses reported by Kenyon and Partridge an optically active ketone was to be expected. The substantial differences between (IX) and the two ketones (III) and (VI) are: (a) the presence in (III) and (VI) of a second asymmetric centre, not adjacent to the carbonyl group, and (b) the fact that the double bond in the enol of (IX) is conjugated with a phenyl group, tending to stabilise the enol. Ingold and Wilson (*J.*, 1934, 773) found (+)-2-*o*-carboxybenzylindan-1-one (X) to be stable in glacial acetic acid solution, but to become half-racemised in 4 minutes at 20° when hydrogen bromide is present in 0.002M-concentration. (+)-*sec*.-Butyl phenyl ketone in acetic acid containing nitric acid (1.19N) becomes half-racemised in 23 minutes at 36.75° (Bartlett and Stauffer, *J. Amer. Chem. Soc.*, 1935, 57, 2580). The reaction mechanisms discussed by these authors require as an intermediate either the enol

—C=C—OH or its mesomeric anion $\text{—}\overset{\text{O}^-}{\text{C}}=\text{C—}$ $\leftrightarrow$ $\text{—}\overset{\text{O}}{\text{C}}=\text{C—}$, both of which imply a planar configuration for the α -carbon atom. Since oxidation of (VIII) to (IX) was by chromic anhydride in glacial acetic acid, the medium was probably sufficiently acid to catalyse the racemisation of the ketone.

Retention of asymmetry during the similar oxidation of (II) to (III) and (V) to (VI) is considered to be due to the immunity of the β -carbon atom to racemisation by enolisation. Two enols $\text{CHBr}\cdot\text{CBr}\cdot\text{C}(\text{OH})\cdot\text{CH}_3$ and $\text{CHBr}\cdot\text{CHBr}\cdot\text{C}(\text{OH})\cdot\text{CH}_2$ are possible; in the latter the asymmetric centres are not involved; when the former resumes the keto-form the configuration of the asymmetric centre at the β -carbon atom appears to permit one configuration of the >CHBr group to be formed much more readily than the other, yielding as product a single diastereoisomer of the dibromo-ketone.

EXPERIMENTAL

Ligroin refers to petroleum of b. p. 100—120°.

1-Phenylallyl alcohol was prepared and resolved by Duveen and Kenyon's method (*J.*, 1939, 1697). Seven recrystallisations of the quinidine salt of 1-phenylallyl hydrogen phthalate from methyl acetate were necessary to yield the optically pure quinidine salt of the (+)-hydrogen phthalate. The (+)-1-phenylallyl hydrogen phthalate obtained from this salt had m. p. 57.5—60°, $[\alpha]_{\text{D}}^{25} + 51.0^\circ$, $[\alpha]_{\text{D}}^{22} + 61.8^\circ$ in carbon disulphide (*l*, 2.0; *c*, 5.03) (Found: equiv., 284. Calc. for $\text{C}_{17}\text{H}_{14}\text{O}_4$: equiv., 282). These rotatory powers are 20% higher than those recorded by Duveen and Kenyon for their hydrogen phthalate, which was an oil. The methyl acetate mother-liquors from the resolution yielded the quinidine salt of the (−)-hydrogen phthalate; it was recrystallised from acetone and gave on decomposition (−)-1-phenylallyl hydrogen phthalate, m. p. 58—60°, $[\alpha]_{\text{D}}^{20} - 50.8^\circ$, $[\alpha]_{\text{D}}^{20} - 61.7^\circ$ (*l*, 2.0; *c*, 5.01 in carbon disulphide). The (+)-1-phenylallyl alcohol obtained from this ester by saponification had b. p. 79—82°/3 mm., $n_{\text{D}}^{25} 1.5372$, $d_4^{16} 1.027$, $\alpha_{\text{D}}^{17} + 5.10^\circ$, $\alpha_{\text{D}}^{17} + 6.59^\circ$ (*l*, 0.5), the rotatory powers being only 1% greater than those recorded by Duveen and Kenyon. Saponification of the (+)-hydrogen phthalate yielded (−)-1-phenylallyl alcohol having $\alpha_{\text{D}}^{17} - 5.12^\circ$, $\alpha_{\text{D}}^{17} - 6.61^\circ$ (*l*, 0.5).

(±)-1-Phenylallyl alcohol was conveniently purified by conversion into the hydrogen phthalate, and recrystallisation and hydrolysis of the latter; the alcohol so prepared had b. p. 75—78°/1 mm., $n_{\text{D}}^{25} 1.5373$.

Bromine-addition and Oxidation.—(a) With (±)-1-phenylallyl alcohol. Bromine (1.2 g.) in chloroform (16 ml.) was added dropwise to (±)-1-phenylallyl alcohol (1.0 g.); the solvent and excess of bromine were removed by drawing dry air through the flask. The residual oil partly crystallised; the solid was filtered off and recrystallised from ethyl alcohol, needles (0.2 g.), m. p. 121—122°, being obtained which, after repeated recrystallisation, yielded 1 : 2 : 3-tribromo-1-phenylpropane, m. p. 124—125° (Found: C, 30.7; H, 2.2; Br, 67.0. Calc. for $\text{C}_9\text{H}_5\text{Br}_3$: C, 30.3; H, 2.5; Br, 67.2%). Grimaux (*Bull. Soc. chim.*, 1873, 20, 121) records m. p. 124°. Carbon tetrachloride and carbon disulphide were also used as solvents; the solution of bromine was added from a burette and absorption almost ceased when 0.60—0.70 mol. of bromine had been added. 1 : 2 : 3-Tribromo-1-phenylpropane was isolated in yields of 5—10%.

Pyridine hydrobromide perbromide, red needles, m. p. 135—138° (decomp.), was prepared according to Djerassi and Scholtz (*loc. cit.*) (these authors record m. p. 134°) except that one

additional equivalent of hydrobromic acid was employed. When one equivalent only of hydrobromic acid was used the product, after three recrystallisations, had m. p. 120—125°.

(±)-1-Phenylallyl alcohol (3.0 g.) was allowed to react with pyridine hydrobromide perbromide (7.2 g.) by the method described below for the (+)-alcohol; after the separation of 1 : 2 : 3-tribromo-1-phenylpropane (0.44 g.), m. p. 124—125°, the product was twice distilled and yielded (±)-2 : 3-dibromo-1-phenylpropanol (3.1 g.), an almost colourless viscous oil, b. p. 145.5—147.5°/3 mm. (Found: C, 36.8; H, 3.4; Br, 54.9. $C_9H_{10}OBr_2$ requires C, 37.3; H, 3.6; Br, 54.5%). Crystals slowly appeared in the liquid; they were filtered off and, after being washed with ligroin-acetic acid and recrystallised from hot ligroin, had m. p. 124—125° alone or mixed with authentic 1 : 2 : 3-tribromo-1-phenylpropane.

(±)-2 : 3-Dibromo-1-phenylpropanol (0.2 g.) and phenyl isocyanate (0.09 g.) were heated on a steam-bath for 3 hours. Benzene, and then ligroin, were added to the product; the solution was filtered and set aside overnight; the urethane then separated. After recrystallisation from ether-light petroleum (b. p. 40—60°), (±)-2 : 3-dibromo-1-phenylpropyl phenylcarbamate (0.08 g.) was obtained as colourless rectangular crystals, m. p. 148—149° (Found: C, 46.6; H, 3.8; N, 3.5; Br, 38.8. $C_{16}H_{15}O_2NBr_2$ requires C, 46.5; H, 3.6; N, 3.4; Br, 38.7%). An exactly similar preparation with 4-diphenyl isocyanate gave (±)-2 : 3-dibromo-1-phenylpropyl 4-diphenylcarbamate, m. p. 115—117° (Found: C, 54.6; H, 4.0; N, 2.6. $C_{22}H_{19}O_2NBr_2$ requires C, 54.0; H, 3.9; N, 2.9%).

Oxidation of (±)-2 : 3-dibromo-1-phenylpropanol (4.5 g.) by the method described below for the (+)-alcohol yielded αβ-dibromopropiophenone (1 g.), long colourless rhombs, m. p. 51—53° (Found: C, 37.5; H, 2.7; Br, 54.4. Calc. for $C_9H_8OBr_2$: C, 37.0; H, 2.7; Br, 54.8%). Beaufour (*Bull. Soc. chim.*, 1913, 13, 356) records m. p. 56°.

(b) *With (+)-1-phenylallyl alcohol.* (+)-1-Phenylallyl alcohol (14.1 g.; $\alpha_{D}^{20} + 4.13^\circ$, l , 0.5) was dissolved in glacial acetic acid (140 ml.). To the mechanically stirred solution, pyridine hydrobromide perbromide (33.8 g.) was added in portions; the reaction mixture was kept at 12—15°, some crystals of acetic acid being present throughout. After 45 minutes the solution was poured into water (1 l.), and the whole extracted four times with ether. The combined ethereal extracts were repeatedly washed with dilute hydrochloric acid, with aqueous sodium hydrogen carbonate and with water, and dried ($MgSO_4$). The ether was distilled and the oil which remained was dissolved in hot cyclohexane. On cooling, needles separated which were filtered off and, after thrice recrystallising from hot ethyl alcohol, gave 1 : 2 : 3-tribromo-1-phenylpropane (1.3 g.), m. p. 125—127°, optically inactive in chloroform. Evaporation of the cyclohexane filtrate at 20 mm. yielded (+)-2 : 3-dibromo-1-phenylpropanol having $[\alpha]_{D}^{17} + 10.6^\circ$ (l , 2.0; c , 5.00 in chloroform). This specimen of the dibromo-alcohol (undistilled, 25.7 g.) was dissolved in glacial acetic acid (260 ml.). To the solution, at 60°, chromic anhydride (9 g.) was added in portions during 1 hour. The solution was poured into water (1.5 l.) and thrice extracted with ether; the combined ethereal extracts were repeatedly washed with aqueous sodium hydrogen carbonate, and with water, and dried (Na_2SO_4). The oil remaining after evaporation of the ether was seeded with a crystal of αβ-dibromopropiophenone and kept for 2 days, whereupon it crystallised. After being collected and washed with a small quantity of ligroin, the solid (13.2 g.) was recrystallised from light petroleum (b. p. 40—60°) and yielded αβ-dibromopropiophenone (4.5 g.), m. p. 51—53°, optically inactive in chloroform and in carbon disulphide. A further quantity (1.8 g.) of (±)-αβ-dibromopropiophenone, and also (±)-1 : 2 : 3-tribromo-1-phenylpropane (0.3 g.), were isolated from the filtrates. On evaporation of the latter, a lachrymatory oil (5.7 g.) remained; it had $[\alpha]_{D}^{21} - 28.7^\circ$ (c , 4.81 in chloroform) and on distillation gave a fraction, b. p. 108—114°/0.3 mm., from which (±)-αβ-dibromopropiophenone was isolated.

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612. *The Conversion of Silver (+)-2-Ethylhexanoate into
(+)-3-Bromoheptane.*

D. Sc.

By D. C. ABBOTT and C. L. ARCUS.

1955

The reaction of bromine with silver (+)-2-ethylhexanoate, from which previous investigators have obtained ($\pm$)-3-bromoheptane, has been found to yield (+)-3-bromoheptane when the silver bromide formed (a catalyst for bromine exchange) is removed at an early stage.

Attempts to repeat the conversion of silver α -phenylpropionate into 1-phenylethyl bromide (Arcus, Campbell, and Kenyon, *J.*, 1949, 1510) have not given satisfactory yields of the bromide; 1-phenylethyl α -phenylpropionate has been isolated from the products of reaction.

THE conversion of the silver salt of a carboxylic acid to an alkyl bromide by reaction with two equivalents of bromine in carbon tetrachloride has been carried out with the silver salts

of several optically active acids. The formation of (+)-1-phenylethyl bromide by the reaction of bromine with silver (+)- α -phenylpropionate has been described (Arcus, Campbell, and Kenyon, *J.*, 1949, 1510). Bell and Smyth (*ibid.*, p. 2372) allowed bromine to react, with cooling, with silver (+)- and (–)-2-ethylhexanoate and, after 15 minutes' heating, obtained ($\pm$)-3-bromoheptane from each reaction. [Arnold and Morgan (*J. Amer. Chem. Soc.*, 1948, **70**, 4248) had earlier obtained ($\pm$)-3-bromoheptane by heating (+)- and (–)-2-ethylhexanoic acids first with silver acetate and then for 7 hours with bromine; Doering and Farber (*ibid.*, 1949, **71**, 1514) have pointed out that heating for this time with silver bromide may have racemised the 3-bromoheptane.] From silver (+)- α -benzylbutyrate Bell and Smyth obtained (–)-2-bromo-1-phenylbutane having $[\alpha]_{5461} -2.85^\circ$ (in alcohol), but a similar experiment with silver (–)- α -benzylbutyrate gave ($\pm$)-2-bromo-1-phenylbutane.

It has been found (Arcus and Boyd, *J.*, 1951, 1580) that racemisation of (+)-1-phenylethyl bromide in solution in carbon tetrachloride is catalysed by silver bromide. Freshly prepared silver bromide effects some racemisation and the rate is greatly increased when hydrogen bromide is present. Racemisation is ascribed to bromine exchange at the surface of the silver bromide. Since bromine yields hydrogen bromide by substitution in 1-phenylethyl bromide, it was not possible to ascertain whether bromine exchange with elementary bromine takes place.

It appeared that it would be advantageous to remove the silver bromide as early as practicable and, if possible, before stage (2) commences; accordingly, silver (+)-2-ethylhexanoate was allowed to react with bromine in carbon tetrachloride, the silver bromide was removed by filtration, and the filtrate heated for completion of stage (2). Three experiments, in which the bromine was added at approximately 15° , 5° , and -15° , yielded (+)-3-bromoheptane having $\alpha_{5893} +0.13^\circ$, $+0.15^\circ$, and $+0.39^\circ$ [l 1.0; calculated for the fully-active (+)-acid] respectively.

The retention of optical activity indicates that the 3-heptyl group cannot have an extended life as a free radical or as an ion; further information cannot be deduced because the configurational relation between (+)-2-ethylhexanoic acid and (+)-3-bromoheptane is not known.

It was intended to apply this method to the reaction with silver α -phenylpropionate but attempts, nine in all, by the original method and modifications of it failed to yield appreciable quantities of 1-phenylethyl bromide; the only identified product was 1-phenylethyl α -phenylpropionate. The ester $\text{R}\cdot\text{CO}_2\text{R}$, which is probably formed according to the equation

has been reported as a product from a number of silver salt-bromine reactions (from silver butyrate, Bockemüller and Hoffmann, *Annalen*, 1935, **519**, 185; silver laurate, Lüttringhaus and Schade, *Ber.*, 1941, **74**, 1565; silver benzoate, phenylacetate, and *o*-nitrobenzoate, Oldham, *J.*, 1950, 105).

EXPERIMENTAL

2-Ethylhexanoic acid was prepared and resolved by the method of Kenyon and Platt (*J.*, 1939, 633); the (+)-acid of maximum rotation had b. p. 117–119°/15 mm., d_4^{17} 0.908, n_D^{25} 1.4231, $[\alpha]_{589}^{17} + 8.89^\circ$ (homogeneous), 99% optically pure by comparison with Kenyon and Platt's value.

Silver (+)- and (–)-2-ethylhexanoates were prepared, and carbon tetrachloride and bromine were dried, by methods previously described (Abbott and Arcus, *J.*, 1952, 1516).

A suspension of the silver salt (10.0 g.) of (+)-2-ethylhexanoic acid ($\alpha_{589}^{25} + 15.07^\circ$, l 2.0, 93% optically pure) in carbon tetrachloride (100 ml.) was cooled, in ice and salt at between -10° and -15° , and a solution of bromine (6.2 g.) in carbon tetrachloride (25 ml.) was added during 15 minutes with vigorous stirring. After a further 15 minutes' stirring, the reaction mixture was filtered by suction through a sintered-glass filter in a closed apparatus. The filtrate was heated under reflux for 30 minutes, cooled, washed with aqueous sodium metabisulphite (20%; 20 ml.), with aqueous sodium carbonate (20%, 25 ml.), and with water, and dried (Na_2SO_4). The solvent was evaporated and the product distilled: (+)-3-bromoheptane (2.5 g.), b. p. 64–70°/26 mm., n_D^{25} 1.4481, $\alpha_{589}^{21} + 0.19^\circ$ (l 0.5), was obtained which after redistillation had b. p. 65–67°/25 mm., n_D^{25} 1.4482, $\alpha_{589}^{21} + 0.18^\circ$ (l 0.5) (Found: C, 47.1; H, 8.8; Br, 44.6. Calc. for $\text{C}_7\text{H}_{15}\text{Br}$: C, 46.9; H, 8.4; Br, 44.6%).

The silver salt (8.0 g.) of (–)-2-ethylhexanoic acid ($\alpha_{589}^{27} - 3.40^\circ$, l 0.5, 82% optically pure) was allowed to react similarly for 55 minutes at $0-10^\circ$; the filtrate was not heated. (–)-3-Bromoheptane (2.7 g.), b. p. 66–68°/26 mm., $\alpha_{589}^{20} - 0.07^\circ$ (l 0.5), was obtained which after redistillation at the same b. p. had n_D^{25} 1.4481, $\alpha_{589}^{20} - 0.06^\circ$ (l 0.5) (Found: Br, 44.5%).

The silver salt (19.2 g.) of (+)-2-ethylhexanoic acid ($\alpha_{589}^{20} + 3.74^\circ$, l 0.5, 92% optically pure) was allowed to react similarly for 2½ hours at $10-15^\circ$; the filtrate was heated under reflux for 1 hour. (+)-3-Bromoheptane (4.6 g.), b. p. 65–68°/24 mm., $\alpha_{589}^{25} + 0.27^\circ$ (l 2.0), was obtained which after redistillation had b. p. 63–65°/22 mm., n_D^{25} 1.4482, $\alpha_{589}^{23} + 0.06^\circ$ (l 0.5) (Found: Br, 44.6%).

To (±)- α -phenylpropionic acid (30 g.) was added *N*-sodium hydroxide (175 ml.); the solution was titrated with further aqueous sodium hydroxide until just alkaline to phenolphthalein. The solution was warmed to 50° and to it was added, dropwise with stirring, a warm solution of silver nitrate (34 g.) in water (200 ml.); the precipitated silver (±)- α -phenylpropionate was washed with water, acetone, and ether and dried (P_2O_5) in a vacuum. It (50 g.) was finely ground and re-dried.

To a well-stirred suspension of silver (±)- α -phenylpropionate (10.5 g.) in carbon tetrachloride (80 ml.), boiling under reflux on a steam-bath, a solution of bromine (6.4 g.) in carbon tetrachloride (20 ml.) was added during 15 minutes. The reaction mixture was heated until the bromine colour had disappeared (1½ hours) and then for a further hour; it was allowed to cool, then filtered through a sintered-glass filter, and the filtrate treated as described above. On distillation an oil (4.0 g.) was obtained which boiled over the range $90-210^\circ/17$ mm. This product, combined with that from a similar experiment, was distilled; fractions of b. p. $90-182^\circ/20$ mm. and b. p. $182-194^\circ/20$ mm. were collected, both of which deposited crystals on cooling. These were filtered off and recrystallised from aqueous alcohol, bromine-free rhombs, m. p. 73° , of 1-phenylethyl α -phenylpropionate being obtained (Found: C, 79.8; H, 6.9. $\text{C}_{17}\text{H}_{18}\text{O}_2$ requires C, 80.3; H, 7.1%). This ester (1.1 g.) was heated with potassium hydroxide (0.5 g.) in diethylene glycol (3 ml.) and yielded an alcohol, the phenylurethane of which had m. p. $88-89^\circ$ alone and when mixed with an authentic specimen (m. p. 89°) of the phenylurethane of 1-phenylethyl alcohol. The acid obtained from this hydrolysis was converted into its silver salt, which was ignited [Found: Ag, (i) 42.6, (ii) 42.4. Calc. for $\text{C}_9\text{H}_9\text{O}_2\text{Ag}$: Ag, 42.0%]. Various procedures—addition of undiluted bromine to the hot silver salt suspension, similar addition at room temperature, addition of bromine in carbon tetrachloride at -15° , addition of the silver salt suspension to the bromine solution at 55° —followed by heating under reflux gave little product having b. p. approximating to that of 1-phenylethyl bromide ($84^\circ/10$ mm.); widely-boiling fractions were obtained from which only 1-phenylethyl α -phenylpropionate was isolated.

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553. Addition and Substitution with the Bromine Cation in Aqueous Solution.

By D. C. ABBOTT and C. L. ARCUS.

REACTION between bromine and an olefin in the presence of a nucleophilic reagent HA or A⁻, leading to the formation of the compound >CBr-CA<, proceeds as in (1):

The bromine anion competes with the added nucleophilic reagent and in so far as the competition is successful the dibromide is formed (2).

It has been found (Derbyshire and Waters, *J.*, 1950, 573) that, when a silver salt is added to a solution of bromine in water or acetic acid containing sulphuric acid, bromine anion is removed as insoluble silver bromide and the reactions

are allowed to proceed, yielding a substantial concentration of bromine cations. The bromine cation is probably hydrated, and the hydrate (as annexed) is identical with hypobromous acid plus a proton.

$\left[\begin{array}{c} \text{H} \\ \diagup \quad \diagdown \\ \text{O}-\text{Br} \\ \diagdown \quad \diagup \\ \text{H} \end{array} \right]^+$ This method (in addition to providing bromine cations) should, by the removal of bromine anions, increase the probability of reaction of an added nucleophilic reagent with the intermediate complex cation. The results recorded below for the interaction of bromine with styrene in aqueous acetic acid-sulphuric acid show that formation of 2-bromo-1-phenylethyl acetate is increased, and that of styrene dibromide decreased, by the presence of silver ion.

Attack of the bromine cation (prepared by the interaction of bromine, aqueous sulphuric acid, and silver nitrate) on α -phenylpropionic acid gave α -*p*-bromophenylpropionic acid; the bromine atom of this was not readily hydrolysed and oxidation yielded *p*-bromobenzoic acid. Some of the *o*-isomer may also have been formed; no substitution appeared to have occurred in the aliphatic part of the original acid.

Experimental.—Additions. (a) To a briskly-stirred suspension of silver acetate (17.0 g.) and styrene (10.4 g.; freshly distilled; b. p. 144—145°) in 6*N*-sulphuric acid (150 ml.) containing glacial acetic acid (50 ml.) a solution of bromine (16.0 g.) in glacial acetic acid (75 ml.) was added during 1½ hours. After a further ½ hour's stirring, the precipitated silver bromide (18.7 g., 100%) was separated by filtration through sintered glass, and the filtrate extracted with ether. The extract was washed with aqueous sodium carbonate and dried (MgSO₄) and the ether removed. The product (13.1 g.) yielded fractions: (i) b. p. 84—86°/0.7 mm., n_D^{25} 1.5689 (2.7 g.); (ii) b. p. 91—95°/0.7 mm., n_D^{25} 1.5595 (5.4 g.) (Found: C, 48.3; H, 4.5; Br, 37.6. Calc. for a 83:17 mixture of C₁₀H₁₁O₂Br and C₈H₈Br₂: C, 47.2; H, 4.3; Br, 37.5%); and (iii), b. p. 96—104°/0.7 mm., n_D^{25} 1.5560 (2.0 g.).

Fraction (ii) (1.8 g.) was heated under reflux with 3*N*-sodium hydroxide (10 ml.) for 6 hours. The solution was saturated with potassium carbonate and extracted with ether. The extract was dried (Na₂SO₄) and ligroin (b. p. 100—120°) added; needles, m. p. 62—64°, of phenyl-ethylene glycol separated (0.9 g., 90%), which after recrystallisation from ether-ligroin had m. p. 64—65° alone and mixed with an authentic specimen of m. p. 64.5—65.5°. Similar hydrolysis of styrene dibromide (12.3 g.) with *N*-sodium hydroxide (135 ml.) for 6 hours yielded the glycol (1.3 g., 20%), m. p. 64—65°.

(b) From an experiment similar to (a), but without silver acetate, there was obtained a product (19.0 g.) which deposited styrene dibromide (6.0 g.), m. p. 68—70° (after recrystallisation from aqueous alcohol, m. p. 72—73° alone or mixed with an authentic specimen of m. p. 72—73°).

The liquid product gave fractions : (i) b. p. 91—95°/1 mm. (5.9 g.), which on cooling deposited styrene dibromide (2 g.), m. p. 72—73°, and (ii) b. p. 96—97°/1 mm., n_D^{25} 1.5664 (3.3 g.).

(c) From an experiment similar to (a), but without silver acetate and with sodium bromide (20.6 g., 2 mols.) dissolved in the aqueous sulphuric acid, there was obtained styrene dibromide (11.9 g.), m. p. 68—71° (m. p. 72—73° after recrystallisation).

(d) To a mixture of styrene, acetic acid, and aqueous sulphuric acid, as in (a), bromine (16.0 g.) and glacial acetic acid (75 ml.) were added separately and simultaneously, with vigorous stirring. There was obtained styrene dibromide (16.1 g.), m. p. 71—73° (m. p. 72—73° after recrystallisation).

The yields of styrene dibromide isolated from (a), (b), (c), and (d) were respectively nil, 30, 45, and 61%.

Substitution. A solution of silver nitrate (8.5 g.) in water (50 ml.) was added dropwise during 1 hour to a well-stirred mixture of α -phenylpropionic acid (7.5 g.), bromine (8.0 g.), and 3N-sulphuric acid (150 ml.). Stirring was continued for 1 hour, the silver bromide was filtered off, and the filtrate and silver bromide were extracted with ether. The extract was dried (Na_2SO_4), the ether distilled off, and the viscous oil so obtained dissolved in aqueous sodium carbonate. This solution was extracted with ether, then acidified, and again extracted. The latter extract was dried (MgSO_4) and the ether evaporated; the product on distillation yielded α -bromophenylpropionic acid (principally the *p*-isomer), b. p. 138—141°/1 mm., n_D^{25} 1.5594 (4.8 g.) (Found : C, 47.7; H, 4.1; equiv., 227.2. Calc. for $\text{C}_9\text{H}_9\text{O}_2\text{Br}$: C, 47.2; H, 4.0%; equiv., 229.0). The acid gave no bromide ion when heated for 15 minutes with alcoholic N-potassium hydroxide. The acid (2.95 g.) was heated under reflux for 1½ hours with potassium permanganate (10.0 g.) and sodium carbonate (5.0 g.) in water (150 ml.); concentrated hydrochloric acid (25 ml.) was added and sulphur dioxide passed in. The acid which separated was extracted with ether. The extract was dried (Na_2SO_4) and evaporated; the product (2.1 g., 80%) was thrice recrystallised from aqueous alcohol and yielded *p*-bromobenzoic acid, leaflets, m. p. 250—252° alone or mixed with an authentic specimen of m. p. 251—253°.

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35. *The Interaction of Triphenylmethanol, Fluoren-9-ol, and Diphenylmethanol with Hydrazoic Acid in the Presence of Sulphuric Acid.*

By C. L. ARCUS and R. J. MESLEY.

By reaction with hydrazoic acid in the presence of sulphuric acid, triphenylmethanol yields azidotriphenylmethane, fluoren-9-ol yields phenanthridine and 9-azidofluorene, and diphenylmethanol yields aniline, benzaldehyde, and azidodiphenylmethane. 9-Azidofluorene has been prepared from 9-chlorofluorene; its acid-catalysed decomposition yields phenanthridine, and spontaneous decomposition (on storage or heating) yields 9-iminofluorene.

A mechanism, based on carbonium-ion formation, is proposed for the reaction of di- and tri-arylmethanols with hydrazoic and sulphuric acids.

IN order to account for the observed products from the reaction of ketones, carboxylic acids, and olefins with hydrazoic acid in the presence of a strong acid, mechanisms have been proposed in which carbonium ions of the following forms are essential intermediates: for ketones the polarised molecule (I) (Briggs and Lyttleton, *J.*, 1943, 421) and the proton-adduct (II) (Sanford, Blair, Arroya, and Sherk, *J. Amer. Chem. Soc.*, 1945, **67**, 1941; Newman and Gildenhorn, *ibid.*, 1948, **70**, 317; Smith, *ibid.*, p. 320), for carboxylic acids

the proton-adduct (III) (Newman and Gildenhorn, *loc. cit.*; Schuerch and Huntress, *ibid.*, 1949, **71**, 2233; Arcus, Kenyon, and Levin, *J.*, 1951, 407) and its dehydro-form (IV) (Newman and Gildenhorn, *loc. cit.*), and for 1:1-diarylethylenes the proton-adduct (V) (McEwen, Gilliland, and Sparr, *J. Amer. Chem. Soc.*, 1950, **72**, 3212).

Numerous alkylations effected with di- and tri-arylmethanols have been recorded, and reaction probably proceeds *via* the carbonium ion:

Further, di- and tri-arylmethanols form coloured solutions in sulphuric acid, a property attributed to the formation of carbonium ions (Balfe, Kenyon, and Searle, *J.*, 1950, 3309; Gold and Tye, *J.*, 1952, 2172, where earlier references are given), and cryoscopic measurements with such solutions yield van't Hoff *i* factors of approximately 4 (Newman and Deno, *J. Amer. Chem. Soc.*, 1951, **73**, 3644; Gold, Hawes, and Tye, *J.*, 1952, 2167, where earlier references are given), a value attributed (Newman, *J. Amer. Chem. Soc.*, 1941, **63**, 2431) to ionisation according to equation (1). In view of the evidence for the formation of carbonium ions from di- and tri-arylmethanols, it seemed probable that these alcohols would, in the presence of sulphuric acid, react with hydrazoic acid. The reaction with triphenylmethanol, fluoren-9-ol, and diphenylmethanol has been investigated; a preliminary note has appeared (*Chem. and Ind.*, 1951, 701).

The reaction with triphenylmethanol yielded azidotriphenylmethane; it is considered that the carbonium ion, formed as in (1), reacts with hydrazoic acid to give the proton-adduct of the azide (2), which releases a proton to yield the free azide (3).

Azidotriphenylmethane has been prepared by the action of nitrous acid on triphenylmethylhydrazine (Wieland, *Ber.*, 1909, **42**, 3026) and by the interaction of triphenylmethyl perchlorate with sodium azide (Lifschitz and Girbes, *Ber.*, 1928, **61**, 1488). Wieland found azidotriphenylmethane to be remarkably stable: it decomposed at about 180° when heated (Senior, *J. Amer. Chem. Soc.*, 1916, **38**, 2718, decomposed the azide at 225° and isolated benzophenone and aniline after hydrolysing the product) and, when the azide was added to sulphuric acid, a temperature of about 200° was required to effect appreciable decomposition. The azide is stable under the conditions of the present reaction, from which it was the main product.

The reaction with fluoren-9-ol yielded phenanthridine. In this instance the proton-azide adduct, formed as in (2), is considered to rearrange with loss of nitrogen to give the proton-adduct of an imine (4); loss of a proton yields the base (5), which is here a stable heterocycle, and reaction terminates at this stage. From one experiment, which gave a relatively low yield of phenanthridine, 9-azidofluorene was isolated, and this compound has also been prepared from 9-chlorofluorene and sodium azide. Reaction of 9-azidofluorene with sulphuric acid at 25° gave phenanthridine in good yield. On long storage or on heating, 9-azidofluorene decomposed to give 9-iminofluorene; this reaction, which is being further investigated, may proceed by a free-radical mechanism. It is concluded that the entity which undergoes rearrangement during the hydrazoic-sulphuric acid reaction is the proton-adduct of the azide and not the free azide.

The Schmidt reaction with (+)- α -phenylpropionic acid proceeds with a high retention of asymmetry and, probably, of configuration (Campbell and Kenyon, *J.*, 1946, 25), indicating the mechanism to be an intramolecular exchange of bonding at one face of the migrating carbon atom. From this result, together with the fact that the phenanthridine arises by a ring-expansion, the act of rearrangement, above, is considered to be intramolecular:

Electronic sharing between the migrating carbon atom of the ring A and the CH-NH fragment is continuous, and the four electrons initially present as the A-CH bond and the nitrogen lone-pair appear finally as the A-NH bond and the π -electrons of the NH=CH bond.

The reaction with diphenylmethanol yielded benzaldehyde and aniline. The products are considered to arise from hydrolysis (6) of the imine formed by reactions (1)–(5); this course for the reaction is in accord with the observation of Schmidt and Klavehn (D.R.-P. 583,565) that benzylideneaniline is produced by the reaction of thionyl chloride with a solution of diphenylmethanol in benzene containing hydrazoic acid. Azidodiphenylmethane has been isolated from the neutral, non-aldehydic fraction of the reaction products. Attempts to prepare the azide in larger quantity by interaction of diphenylmethyl chloride and sodium azide gave specimens which had suffered considerable loss of nitrogen. Reaction of the azide so prepared, and of the fraction containing the azide, with sulphuric acid at 25° yielded, in each case, aniline and benzaldehyde.

Equations (1)–(6) are proposed for the course of the reaction with di- and tri-aryl-methanols; the stabilities of the compounds from the successive stages control the proportions in which these compounds appear in the final product from individual alcohols.

Improved preparations of the hydrazones of benzophenone and fluorenone are recorded.

EXPERIMENTAL

96% Sulphuric acid was used except where otherwise stated.

The Hydrazoic Acid-Sulphuric Acid Reaction.—(a) *With triphenylmethanol.* To a suspension of sodium azide (4.2 g.) in chloroform (13 ml.), cooled in ice, sulphuric acid (9 ml.) was slowly added with stirring. The ice was replaced by a water-bath maintained at 25°, and a solution

of triphenylmethanol (10 g.) in chloroform (40 ml.) added during 1 hour. Stirring was continued for $\frac{1}{2}$ hour, ice (75 g.) was then added, and the mixture was kept overnight and filtered. The aqueous layer was extracted with ether. The combined ether and chloroform solutions were washed with water and dried (Na_2SO_4), and the solvents evaporated; addition of a little alcohol caused the separation of a solid (7.7 g.), which, recrystallised from alcohol, yielded azidotriphenylmethane, white needles (6.5 g.), m. p. 64° (Found: C, 80.0; H, 5.5; N, 14.5. Calc. for $\text{C}_{19}\text{H}_{15}\text{N}_3$: C, 80.0; H, 5.3; N, 14.7%). Wieland, and Lifschitz and Girbes, *loc. cit.*, record m. p. 64° and 65° . The filtrate from the above product yielded a small quantity of a 2:4-dinitrophenylhydrazone having m. p. $236\text{--}237^\circ$ alone and when mixed with benzophenone 2:4-dinitrophenylhydrazone. The acid aqueous solution (above) was made alkaline with sodium hydroxide solution and extracted with ether; the extract yielded azidotriphenylmethane (0.2 g.).

(b) *With fluoren-9-ol.* To hydrazoic acid-sulphuric acid solution (from sodium azide, 2.7 g.; chloroform, 12 ml.; and sulphuric acid, 6.1 ml.), at 25° , a suspension of fluoren-9-ol (4.3 g.; m. p. $154\text{--}155^\circ$; Bachmann, *J. Amer. Chem. Soc.*, 1933, **55**, 772) in chloroform (23 ml.) was added in small portions during 20 minutes; stirring was continued for 1 hour, and crushed ice (100 g.) was then added. The mixture was warmed to 50° , stirred for 40 minutes, kept overnight, and filtered. The chloroform layer was shaken mechanically for 30 minutes with *n*-sulphuric acid (50 ml.) and washed with water. The aqueous part of the reaction mixture was shaken with chloroform (15 ml.). The two acidic aqueous solutions were combined and made alkaline with sodium hydroxide solution, warmed (to coagulate the precipitate), cooled and filtered. The phenanthridine so obtained crystallised from light petroleum (b. p. $60\text{--}80^\circ$) as rectangular plates, m. p. $106\text{--}107^\circ$ [*mercurichloride*, buff needles, m. p. $195\text{--}198^\circ$ (Found: Hg, 40.5; Cl, 21.3. $\text{C}_{13}\text{H}_9\text{N}, \text{HgCl}_2$ requires Hg, 40.4; Cl, 21.4%) (Pictet and Ankersmit, *Annalen*, 1891, **266**, 147, and Sielisch and Sandke, *Ber.*, 1933, **66**, 433, record m. p. 197° and $195\text{--}207^\circ$, but no analysis); picrate, m. p. 245° (Found: C, 56.3; H, 3.0; N, 13.6. Calc. for $\text{C}_{19}\text{H}_{13}\text{O}_6\text{N}_4$: C, 55.9; H, 3.0; N, 13.7%) (Pictet and Ankersmit, *loc. cit.*, give m. p. $\leq 220^\circ$)]. Evaporation of the combined chloroform solutions, above, yielded a non-basic oil. The yields from repetitions of hydrazoic acid-sulphuric acid reactions, despite efforts to maintain identical conditions, varied considerably. There was obtained: phenanthridine (i) 2.55 g., (ii) 1.94 g., (iii) 2.98 g.; non-basic material (i) 1.00 g., (ii) 1.64 g., (iii) 0.84 g. The non-basic material (ii) deposited crystals which on recrystallisation from aqueous alcohol yielded 9-azidofluorene (Found: C, 75.3; H, 4.4; N, 20.4. $\text{C}_{13}\text{H}_9\text{N}_3$ requires C, 75.3; H, 4.4; N, 20.3%), m. p. 41° and m. p. 43° when mixed with a specimen of m. p. $44\text{--}45^\circ$ prepared as below.

Concentrated hydrochloric acid (200 ml.) containing fluoren-9-ol (22 g.) was boiled for 5 minutes. The solid product, recrystallised from light petroleum (b. p. $60\text{--}80^\circ$), yielded 9-chlorofluorene (20.5 g., 85%), needles, m. p. $90\text{--}91^\circ$. A solution of 9-chlorofluorene (20 g.) in methanol (60 ml.) was heated under reflux with sodium azide (10 g.) for 4 hours, then poured into water, and extracted with ether; the extract was washed with aqueous sodium hydroxide, and with water, dried (Na_2SO_4), and evaporated, giving a solid which yielded 9-azidofluorene (16 g., 77%), needles, m. p. $44\text{--}45^\circ$ (from aqueous alcohol), readily soluble in chloroform, hot alcohol, or hot benzene, sparingly soluble in ether, light petroleum (b. p. $40\text{--}60^\circ$), or carbon disulphide. After 2 months 9-azidofluorene had become yellow and recrystallisation from ligroin (b. p. $100\text{--}120^\circ$) gave 9-iminofluorene, pale yellow needles, m. p. 124° (Found: C, 87.0; H, 5.1; N, 7.0. Calc. for $\text{C}_{13}\text{H}_9\text{N}$: C, 87.1; H, 5.1; N, 7.8%). Pinck and Hilbert (*J. Amer. Chem. Soc.*, 1934, **56**, 490) record m. p. 124° . The imine (1.0 g.) was heated under reflux for 30 minutes with sulphuric acid (30%; 40 ml.) and yielded fluorenone (0.87 g.), m. p. 83° alone or mixed with an authentic specimen. 9-Azidofluorene was gently heated above its m. p., vigorous decomposition occurring with formation of a solid which on recrystallisation from ligroin yielded the imine.

To 9-azidofluorenyl azide (4.9 g.) in chloroform (35 ml.), at 25° , sulphuric acid (6.1 ml.) was added dropwise, with stirring which was continued for a total of 30 minutes. Crushed ice (100 g.) was added and the mixture treated as described under (b), yielding phenanthridine (i) 3.5 g., (ii) 3.1 g., m. p. 106° alone or mixed with an authentic specimen (*mercurichloride*, m. p. $195\text{--}197^\circ$, mixed m. p. $195\text{--}198^\circ$). Evaporation of the final chloroform solution yielded an amorphous solid, (i) 1.0 g., (ii) 0.9 g., containing sulphur but not nitrogen, m. p. $>300^\circ$.

(c) *With diphenylmethanol.* A solution of diphenylmethanol (10 g.) in chloroform (20 ml.) was allowed to react with a hydrazoic acid-sulphuric acid (from sodium azide, 5.5 g.; chloroform 17 ml.; and sulphuric acid, 9.2 ml.), with subsequent addition of ice (100 g.) and warming, as described for fluoren-9-ol. Next morning the mixture was filtered from sulphur-

containing material. The chloroform layer was shaken mechanically for 30 minutes with N-sulphuric acid (40 ml.). The acidic extract was combined with the aqueous part of the reaction mixture and extracted with ether. The aqueous layer was then made alkaline with sodium hydroxide solution and thrice extracted with ether, the extracts were washed with water, dried (Na_2SO_4), and evaporated, yielding aniline, b. p. 183° , n_D^{25} 1.5800 (benzoyl derivative, m. p. and mixed m. p. 161°). The chloroform and ether solutions were combined and evaporated, and the residue was shaken mechanically for 1 hour with a solution prepared as follows: sufficient water was added to sodium carbonate decahydrate (25 g.) to cover the crystals, and sulphur dioxide was passed until the solution was saturated. Chloroform (20 ml.) was added to the mixture, which was then filtered and separated. The solid bisulphite compound together with the aqueous solution was warmed with sulphuric acid (40%; 45 ml.) until the evolution of sulphur dioxide ceased; after cooling, the mixture was twice extracted with ether and the extract dried (Na_2SO_4). Evaporation of the ether yielded benzaldehyde, b. p. 178° (2:4-dinitrophenylhydrazone, m. p. and mixed m. p. 236°). In a control experiment 83% of the benzaldehyde originally present was isolated by this method. The chloroform extract of the bisulphite reaction mixture gave on evaporation a neutral liquid. There were obtained: aniline (i) 1.07 g., (ii) 2.05 g.; benzaldehyde (i) 0.48 g., (ii) 0.65 g.; neutral product (i) 8.4 g., (ii) 7.0 g. The neutral products were combined; distillation of a portion (2.5 g.) yielded *acidodiphenylmethane* (1.7 g.), b. p. $135^\circ/4$ mm., n_D^{25} 1.5883 (Found: C, 74.7; H, 5.3; N, 20.3. $\text{C}_{13}\text{H}_{11}\text{N}_3$ requires C, 74.6; H, 5.3; N, 20.1%). Another portion (5.0 g.) was dissolved in chloroform (12 ml.) and allowed to react with sulphuric acid (4 ml.) as described for 9-azido-fluorene; crushed ice (100 g.) was added and the product kept overnight. It was separated as described above and yielded aniline (0.93 g.), benzaldehyde (0.90 g.), and neutral product (0.83 g.).

Two experiments were carried out as described under (c) except that 90% sulphuric acid (12.2 ml.) was used and diphenylmethanol (9.2 g.) in chloroform (20 ml.) was added during 1 hour and stirring continued for $\frac{1}{2}$ hour; there were obtained: aniline (i) 1.6 g., (ii) 2.18 g.; benzaldehyde (i) 0.68 g., (ii) 1.15 g.; neutral product (i) 6.6 g., (ii) 4.3 g.

A solution of diphenylmethyl chloride (30 g.) in ethyl alcohol (99%; 45 ml.) (methanol and aqueous acetone were less satisfactory) was heated under reflux for 4 hours with sodium azide (15 g.). There was obtained impure azidodiphenylmethane (24 g.), b. p. $116\text{--}118^\circ/1$ mm., n_D^{25} 1.5702 (Found: C, 80.6; H, 6.9; N, 9.1%; Cl, 0), which by interaction with sulphuric acid, as described for the neutral product from (c), yielded aniline, benzaldehyde, and a neutral liquid product.

Benzophenone (19 g.), hydrazine hydrate (100%; 7 g.), and butyl alcohol (20 ml.) were heated under reflux for 3 hours. On cooling, a solid separated which on recrystallisation from alcohol (99%) yielded benzophenone hydrazone (11 g., 55%), rods, m. p. 99° . Fluorenone (8 g.), hydrazine hydrate (100%; 3.2 g.), and methanol (3 ml.) were heated under reflux on a water-bath for 5 minutes; the solid product, recrystallised from methanol, yielded fluorenone hydrazone (7.5 g., 89%), yellow needles, m. p. $148\text{--}149^\circ$. These preparations appear more satisfactory than, respectively, that of Curtius and Rauterberg (*J. pr. Chem.*, 1891, **44**, 194; *Org. Synth.*, 1944, **24**, 53) which employs ethyl alcohol in an autoclave for benzophenone hydrazone, and that of Wieland and Roseu (*Annalen*, 1911, **381**, 231) which uses ethyl alcohol for fluorenone hydrazone and, as we have confirmed, yields fluorenone azine as a major product.

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398. *The Hofmann Reaction with α - and β -Hydroxy-amides :
Reactions of the Intermediate isoCyanates.*

By C. L. ARCUS and D. B. GREENWOOD.

A mechanism for the (Weerman) degradation of an α -hydroxy-amide $R\cdot CH(OH)\cdot CO\cdot NH_2$ is proposed in which the aldehyde $R\cdot CHO$ is formed by the elimination of cyanate ion from the intermediate anion $^-\text{O}\cdot CHR\cdot NCO$.

Methyl *N*-1-methoxyethylcarbamate has been prepared; its acidic hydrolysis yields acetaldehyde, carbon dioxide, and ammonia, but not methylamine.

Salicylamide with hypochlorite in strongly alkaline solution yields 4 : 5-benzoxazol-2-one (Graebe and Rostovzeff, *Ber.*, 1902, **35**, 2747), but in less basic solutions 5- and 3-chloro-2-hydroxybenzamides are formed; the mechanism of the reaction is discussed.

β -Hydroxy- β -phenylpropionamide with bromine and methanolic sodium methoxide yields 5-phenyloxazolid-2-one.

THE main characteristics of the Hofmann reaction with different types of hydroxy-amide are already known, but the mechanisms of a number of reactions within this field have not been fully elucidated; several such reactions have now been investigated.

It has been established (Ault, Haworth, and Hirst, *J.*, 1934, 1722; Haworth, Peat, and Whetstone, *J.*, 1938, 1975) that the reaction of aqueous hypochlorite and alkali with an α -hydroxy-amide yields the aldehyde together with the cyanate ion (1), and that a similar reaction with an α -methoxy-amide yields the aldehyde and ammonia, but no cyanate (2). Ault *et al.* consider that in (2) the hydrolysis of the *isocyanate* proceeds *via*

the carbamate (I; $R' = Na$), a conclusion supported by the observation that benzaldehyde and ammonia are formed quantitatively by alkaline hydrolysis of methyl *N*- α -methoxybenzylcarbamate (I; $R = Ph$, $R' = Me$). These authors suggest that in (1) "the formation of a co-ordinated intermediate product (II), in place of a carbamic acid, is responsible for the marked difference in the character of the end products." It is now

suggested that (1) proceeds by an elimination mechanism: the electron-attracting *isocyanate* group renders the hydroxyl-hydrogen atom weakly acidic, and the anion (III) is formed either by direct ionisation or by the attack of a hydroxyl ion, electronic movements as shown then yielding the aldehyde and cyanate ion:

Methylation of the hydroxyl group renders this process impossible, in accordance with the experimental finding.

Haworth *et al.* (*loc. cit.*), following earlier work by Irvine and Pryde (*J.*, 1924, **125**, 1045) and Humphreys, Pryde, and Waters (*J.*, 1931, 1298), isolated the cyclic urethanes (IV; $m = n = 2$; and $m = 1$, $n = 3$) from the reaction of aqueous hypochlorite with

2:3:5:6- and 2:3:4:6-tetramethylgluconamide; these compounds respectively contain a 6- and a 7-membered ring formed by intramolecular reaction between a hydroxyl and an isocyanate group. The reaction with 3:5:6-trimethylgluconamide, which bears hydroxyl groups at C₍₂₎ and C₍₄₎, yielded 2:4:5-trimethylarabinose and cyanate; no cyclic urethane could be isolated. It is inferred from this result that elimination *via* (III) is more rapid than urethane formation.

Methyl *N*-1-methoxyethylcarbamate (I; R = R' = Me) has been prepared by the reaction of α -methoxypropionamide with bromine and methanolic sodium methoxide. Acidic hydrolysis of this carbamate yielded acetaldehyde, and nearly the theoretical quantities of carbon dioxide and ammonia; methylamine was absent. The following course for the hydrolysis appears to be the most probable. The amido-link is first hydrolysed:

Since methylamine is not a product of the reaction the ion (V) does not react as in (VI), and further hydrolysis occurs:

Graebe and Rostovzeff (*Ber.*, 1902, 35, 2747), by the action of sodium hypochlorite (2 mols.) and sodium hydroxide (4.5 mols.) on salicylamide, obtained 4:5-benzoxazol-2-one (VII); this preparation has been repeated. Further, it has been found that the inter-action of equimolar quantities of hypochlorite and salicylamide yields 5- and 3-chloro-2-hydroxybenzamides; no (VII) was isolated. Reaction in the presence of two mols. of alkali gave a similar result. It is concluded that the anion of the *N*-chloroamide (VIII), the essential precursor to the Hofmann rearrangement, is formed only when the hydroxyl-ion concentration is high, electron-release from the existing phenoxide ion opposing the removal of a second proton. The Hofmann reaction is therefore inhibited in solutions which are not strongly alkaline, and substitution (by hypochlorous acid, hypochlorite ion, or chloramine) then occurs in the nucleus.

Reaction of β -hydroxy- β -phenylpropionamide with bromine and methanolic sodium methoxide yielded the 5-membered cyclic urethane, 5-phenyloxazolid-2-one (IX), a result analogous to the formation of (VII) and of the 6- and 7-membered cyclic urethanes (IV; $m = n = 2$) and (IV; $m = 1, n = 3$).

EXPERIMENTAL

Amides were prepared by the reaction of esters with ammonia under the conditions described in the first preparation.

Ethyl α -methoxypropionate (51 g.; Nieman, Benson, and Read, *J. Org. Chem.*, 1943, 8, 397) and ammonia (d 0.88; 300 ml.) were shaken mechanically in a stoppered bottle; when the mixture had become homogeneous it was kept for 10 days and then evaporated under reduced pressure. The distilled product, b. p. 111°/18 mm., was recrystallised from benzene-cyclohexane and yielded α -methoxypropionamide (42 g.), m. p. 81° (Found, by hydrolysis with aqueous-alcoholic 0.5*N*-potassium hydroxide: equiv., 101. Calc. for C₄H₉O₂N: equiv., 103). Gauthier (*Ann. Chim.*, 1909, 16, 315) records m. p. 81°.

Ethyl salicylate (70 g.), with ammonia (400 ml.) and ethanol (60 g.) for 6 days, yielded salicylamide (54 g., from benzene-acetone), m. p. 137°.

Ethyl β -hydroxy- β -phenylpropionate (10.5 g.; Hauser and Breslow, *Org. Synth.*, 1941, 21, 51), with ammonia (150 ml.) for 2 days, yielded β -hydroxy- β -phenylpropionamide (8.9 g., from chloroform-ethanol), m. p. 122—123°. Posner (*Ber.*, 1905, 38, 1129) records m. p. 122—123°.

Methyl N-1-Methoxyethylcarbamate.—Sodium (4.7 g.) was allowed to react with dry methanol (100 ml.) and to the solution, cooled in ice, was added α -methoxypropionamide (10.3 g.) in methanol (30 ml.); bromine (16.3 g.) was added dropwise with stirring, the mixture being kept below 2°. It was then heated under reflux for 15 min., cooled, and made neutral to phenolphthalein with glacial acetic acid, and the methanol distilled off through a short column; the residue was extracted with ether. The extract was washed with saturated brine, dried (Na_2SO_4), and evaporated. The product on distillation yielded *methyl N-1-methoxyethylcarbamate* (7.3 g.), b. p. 77°/16 mm., n_D^{25} 1.4241 (Found: C, 45.4; H, 8.2; N, 10.2. $\text{C}_5\text{H}_{11}\text{O}_3\text{N}$ requires C, 45.1; H, 8.3; N, 10.5%).

Hydrolyses. Methyl *N-1-methoxyethylcarbamate* (1.5 g.) was weighed into a flask which was then connected to two traps, the first cooled in ice, the second with solid carbon dioxide. The second trap was connected to a calcium chloride-filled U-tube which had been saturated with carbon dioxide and purged with hydrogen, a weighed U-tube the first two-thirds of which were filled with soda-lime and the last third with calcium chloride, and finally to a soda-lime guard tube. 4N-Sulphuric acid (40 ml.) was run into the flask which was then heated with steam. Carbon dioxide-free hydrogen was passed through the apparatus during the hydrolysis, which was allowed to proceed for 4 hr., by which time the weight of the central tube (after it had been purged with carbon dioxide-free air) had become constant. In a control experiment with sodium hydrogen carbonate, 98% of the theoretical quantity of carbon dioxide was collected. An aliquot of the hydrolysis solution (which gave no carbylamine with chloroform and alkali) was used for a Kjeldahl determination of ammonia. The following tests were applied to the ammonium chloride obtained on evaporation: (a) it was insoluble in hot absolute alcohol; (b) the filtrate from extraction with 96% alcohol gave no colour with 2:4-dinitrochlorobenzene, or when warmed to 75° with tetrachloroquinone. Methylamine was therefore absent. From the contents of the traps there was prepared a semicarbazone having m. p. 160° alone and when mixed with authentic acetaldehyde semicarbazone of m. p. 161—162°, and a dimedone derivative having m. p. 139° alone and when mixed with authentic acetaldehyde-dimedone compound having m. p. 139°. There were obtained carbon dioxide (i) 105, (ii) 100%, and ammonia (i) 94, (ii) 96% of the theoretical quantities.

The hydrolysis of methyl *N-1-methoxyethylcarbamate* (2.66 g.) with 1.5N-sodium hydroxide (200 ml.) for 1½ hr. at 50° and finally at 95° (the absorption tubes were omitted) yielded a tar (0.46 g.) and, in the colder trap, a solid which decomposed at 70° to ammonia and acetaldehyde; these products were presumed to be, respectively, acetaldehyde resin and acetaldehyde-ammonia. A portion of the hydrolysis solution was treated with pyridine, sufficient acetic acid to render the mixture acid, chloroform, and 1% aqueous copper sulphate: the chloroform layer developed no blue colour, whence cyanate was absent.

Salicylamide-Hypochlorite Reactions.—(a) Salicylamide (3.0 g.) yielded, by Graebe and Rostovzeff's method (*loc. cit.*), a product, the benzene solution of which was heated with charcoal at 65° for 1 hr.; on cooling there separated 4:5-benzoxazol-2-one (1.0 g.), colourless crystals, m. p. 140—141° (these authors record m. p. 138—139°). Admixture with salicylamide depressed the m. p. by 40°.

(b) A solution of salicylamide (16.4 g.) in water (50 ml.) was cooled to 0°, 0.92M-sodium hypochlorite (130 ml.) was added with stirring during ¾ hr., and the mixture was heated on a steam-bath for ¾ hr. Next day the solution was saturated with carbon dioxide, which precipitated amides (13.9 g.); acidification with hydrochloric acid yielded a precipitate (2.0 g.) which after recrystallisation from water had m. p. 157° alone and when mixed with salicylic acid. The amides were fractionally crystallised from aqueous dioxan and yielded 5-chloro-2-hydroxybenzamide (3.5 g.), m. p. 227—228° (Found: C, 49.2; H, 3.5; N, 8.0; Cl, 20.4. Calc. for $\text{C}_7\text{H}_6\text{O}_2\text{NCl}$: C, 49.0; H, 3.5; N, 8.2; Cl, 20.7%) (Biltz and Stepf, *Ber.*, 1904, 37, 4024, record m. p. 226—227°), and 3-chloro-2-hydroxybenzamide (7.5 g.), m. p. 183—184° (Found: C, 49.0; H, 3.7; N, 7.9; Cl, 20.1%) (Hirwe, Rana, and Gavankar, *Proc. Indian Acad. Sci.*, 1938, 8, A, 208, record m. p. 174—175°).

(c) Salicylamide (2.0 g.), 0.87M-sodium hypochlorite (18 ml.), and 0.88N-sodium hydroxide (34 ml.) were allowed to react as in (b). The solution was then progressively acidified with hydrochloric acid, and material which separated was removed, as follows: to pH 8.5, a precipitate which after recrystallisation from benzene-dioxan had m. p. 225—227° alone and m. p. 226—227° when mixed with 5-chloro-2-hydroxybenzamide from (b); to pH 6.8, material

m. p. 170—194°; to pH 2, an oil of b. p. approx. 240°, which solidified and appeared to be chlorophenol(s).

5-Phenyloxazolid-2-one.—Bromine (4.2 g.) was allowed to react with β -hydroxy- β -phenylpropionamide (4.1 g.) and methanolic sodium methoxide (from 1.2 g. of sodium and 150 ml. of methanol) by the procedure used for the preparation of methyl *N*-1-methoxyethylcarbamate; the mixture was heated under reflux for $\frac{3}{4}$ hr. and then made neutral to phenolphthalein with glacial acetic acid, and the greater part of the methanol was distilled off. Ether was added to the residue, the precipitated sodium bromide was filtered off, and the solvents were distilled; the product, after warming in aqueous solution with charcoal and recrystallisation from water, yielded *5-phenyloxazolid-2-one* (2.0 g.), m. p. 89—90° (Found: C, 65.8; H, 5.5; N, 8.7. $C_9H_9O_2N$ requires C, 66.2; H, 5.6; N, 8.6%). Schroeter (D.R.-P. 220,852) who prepared this compound by heating β -hydroxy- β -phenylpropionyl azide, records m. p. 87—88.5°, but no analysis. *5-Phenyloxazolid-2-one* (0.28 g.) was heated on a steam-bath for $1\frac{1}{2}$ hr. with 4*N*-sodium hydroxide (3 ml.); drops of oil separated. To the cold mixture, benzoyl chloride (0.25 g.) was added with shaking. The product was next day filtered off and after recrystallisation from aqueous alcohol yielded 2-benzamido-1-phenylethanol (0.26 g.), m. p. 147.5—148.5°. Rosenmund (*Ber.*, 1913, 46, 1046) and Wolfheim (*Ber.*, 1914, 47, 1440) record m. p. 147° and 148—149.5° respectively.

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THE SYNTHESIS OF PHENANTHRIDINES BY THE INTERACTION OF FLUORENE DERIVATIVES WITH HYDRAZOIC AND SULPHURIC ACIDS

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It has been found¹ that the interaction of fluorene with hydrazoic acid in the presence of sulphuric acid yields phenanthridine. This reaction has now been extended to the synthesis of substituted phenanthridines (Table I). The reaction is carried out by adding the carbinol or olefin, alone or in chloroform solution, to a solution of hydrazoic acid in chloroform and concentrated sulphuric acid, with vigorous stirring at 25°.

From a fluorene derivative substituted in one of the positions 1, 2, 3, 4, there can (potentially) arise a pair of phenanthridines, substituted in positions 1 and 8, 2 and 7, 3 and 6, 4 and 5, respectively. One of the pair of isomeric phenanthridines usually predominates and it is tentatively concluded that the ring having the greater electron-release is that which migrates during rearrangement.

The first stage in the reaction is probably the formation of a carbon cation from the fluorene¹; this cation can also be formed by the addition of a proton to the appropriate olefin, and it has been found that 9-benzylidenefluorene yields 9-benzylphenanthridine, which is also given by 9-benzylfluorene-9-ol.

The nitrophenanthridine m.p. 180°, obtained from the reaction with 2-nitrofluorene-9-ol, is identified as the 7-isomer, in agree-

Table I

The Formation of Phenanthridines from Fluorenes

Fluorene	M.p. (corr.)	C, H, N, %	Phenanthridine	M.p. (corr.)	C, H, N, %
2-Nitrofluorene-9-ol	129°		7-Nitrophenanthridine	180° Found : C ₁₃ H ₈ O ₂ N ₂ :	70.1 3.6 12.9 69.65 3.6 12.5
2-Aminofluorene-9-ol	197°		7-Aminophenanthridine	203° Found : C ₁₃ H ₁₀ N ₂ :	80.2 4.95 14.5 80.35 5.25 14.45
2-Methoxyfluorene-9-ol	160° Found : C ₁₄ H ₁₂ O ₂ :	79.35 5.95 79.25 5.7	2(7)-Methoxyphenanthridine 7(2)-Methoxyphenanthridine	90° Found : 58° Found : C ₁₄ H ₁₁ ON :	80.6 5.35 6.6 80.8 5.2 6.6 80.4 5.3 6.7
3-Nitrofluorene-9-ol	157° Found : C ₁₃ H ₈ O ₂ N :	68.45 4.15 6.2 68.7 4.0 6.15	6-Nitrophenanthridine	193° Found :	69.75 3.65 12.4
9-Methylfluorene-9-ol	175°		9-Methylphenanthridine	85° Found : C ₁₄ H ₁₁ N :	86.9 5.9 7.2 87.0 5.75 7.25
9-Benzylfluorene-9-ol	141°		9-Benzylphenanthridine	112° Found : C ₂₀ H ₁₅ N :	88.7 5.6 5.15 89.2 5.6 5.2
9-Benzylidenefluorene	76°		9-Benzylphenanthridine	112°	

Reaction is considered to proceed by the rearrangement of the proton-adduct of an azide :

ment with Ritchie²; this compound has been converted into 7-nitrophenanthridone, 9-chloro-7-nitro-phenanthridine, and 7-aminophenanthridine and its ethoxycarbonyl derivative, these compounds agreeing in m.p. with those described in the literature.^{3,4} The substance m.p. 159—161°, reported by Caldwell and Walls⁴ as 7-nitrophenanthridine, appears to have been a 1 : 1 complex of 2- and 7-nitrophenanthridines, which we have prepared from the components.

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743. The Mechanism of the Schmidt Reaction with *o*-Benzoylbenzoic Acid.

By C. L. ARCUS and M. M. COOMBS.

The interaction of *o*-benzoylbenzoic acid with hydrazoic and sulphuric acids yields 6-oxo-2-phenyl-4:5-benz-1:3-oxazine (II); *N*-benzoylanthranilic acid (Badger, Howard, and Simons, *J.*, 1952, 2849) arises from a subsequent hydrolysis. A mechanism for the reaction is proposed in which the oxazine is formed by ring-expansion from the cyclic cation (I).

2-*p*-Toluoylebenzoic acid, by a similar reaction, yields 6-oxo-2-*p*-tolyl-4:5-benz-1:3-oxazine.

BADGER, HOWARD, and SIMONS (*J.*, 1952, 2849) have allowed *o*-benzoylbenzoic acid in solution in trichloroacetic acid, and also in chloroform, to react with hydrazoic acid in the presence of sulphuric acid: the reaction mixtures were finally poured into water. From the reaction in trichloroacetic acid there was obtained *N*-benzoylanthranilic acid (91%); reaction in chloroform gave this acid and 6-oxo-2-phenyl-4:5-benz-1:3-oxazine (II) in 31% and 67% yield respectively. These authors envisage the reaction as that of a substituted benzophenone, and have adopted (and slightly modified) a mechanism which Smith and his co-workers (*J. Amer. Chem. Soc.*, 1948, **70**, 320; 1950, **72**, 2503, 3718) have proposed for ketones:

We have repeated the reaction using the trichloroacetic acid method of Badger *et al.*, and obtained *N*-benzoylanthranilic acid (78%); by a modified procedure using chloroform as solvent the oxazine was obtained in 80% yield. The following facts relating to the reaction have been ascertained:

The oxazine, when its solution in trichloroacetic-sulphuric acid is diluted with water, becomes largely hydrolysed to *N*-benzoylanthranilic acid. If the acid solution is diluted with chloroform and the mixture shaken with cold water, the oxazine can be recovered nearly quantitatively and, when the acidic solution from the Schmidt reaction in trichloroacetic acid is similarly treated, the oxazine (91%) is obtained. The oxazine is thus the actual product of the interaction of *o*-benzoylbenzoic acid with hydrazoic-sulphuric acid in both trichloroacetic acid and chloroform.

N-Benzoylanthranilic acid, in either chloroform or trichloroacetic acid, undergoes ring closure when treated with sulphuric acid, as in the Schmidt reaction procedure; the oxazine can be isolated in good yield from the former solvent, and also from the latter provided that chloroform is added as a diluent.

Newman, Kuivila, and Garrett (*ibid.*, 1945, **67**, 704) have found that *o*-benzoylbenzoic acid in solution in sulphuric acid has a van't Hoff *i* factor of 3.8, in agreement with ionisation according to equation (2), which requires *i* = 4. Further evidence for the cyclic

structure of the cation is provided by the observation (Newman, *ibid.*, 1942, 64, 2324) that considerable methyl *pseudo-o*-benzoylbenzoate is formed (reaction 3) when a solution of *o*-benzoylbenzoic acid in sulphuric acid is poured into methanol.

It is now suggested that 6-oxo-2-phenyl-4:5-benz-1:3-oxazine arises from the interaction of the cation (I) with hydrazoic acid, followed by a ring-expansion (4), closely analogous to that occurring during the formation of phenanthridine by the reaction of hydrazoic-sulphuric acid with fluoren-9-ol (Arcus and Mesley, *J.*, 1953, 178). The four electrons initially present as the A-CPh bond and the nitrogen lone-pair appear finally as the A-NH bond and the π -electrons of the NH=CPh bond.

It has been found (above) that *N*-benzoylanthranilic acid is converted into the oxazine under the conditions of the Schmidt reaction in either chloroform or trichloroacetic acid, whence the possibility cannot be excluded that reaction proceeds by mechanism (1), followed by ring closure of the acid. However, in view of the evidence of Newman *et al.* for the cyclic structure of the cation, it is concluded that mechanism (3) (which results directly in the oxazine) is the more probable.

The migratory aptitudes shown by different groups during the Schmidt reaction of ketones have been studied by Badger and Smith and their co-workers (*loc. cit.*) and by Westland and McEwen (*J. Amer. Chem. Soc.*, 1952, 74, 6141); mechanism (4) implies that the migratory aptitude of the *o*-carboxyphenyl group cannot properly be compared with the aptitudes of groups which do not interact with the carbonyl group.

2-*p*-Toluoylbenzoic acid (in solution in chloroform) reacted with hydrazoic-sulphuric acid to yield 6-oxo-2-*p*-tolyl-4:5-benz-1:3-oxazine.

EXPERIMENTAL

The Schmidt Reaction.—*o*-Benzoylbenzoic acid. Badger, Howard, and Simons (*loc. cit.*) refer to their procedure with trichloroacetic acid as method *B*, and to that with chloroform as method *A*; these designations have been retained.

o-Benzoylbenzoic acid (4.52 g.) yielded, by method *B*, *N*-benzoylanthranilic acid (3.75 g., 78%), m. p. 176–178°. This reaction was repeated, but the acidic solution was poured into chloroform (200 ml.). The chloroform solution was washed with water and with aqueous sodium hydrogen carbonate, dried (Na₂SO₄), and evaporated. 6-Oxo-2-phenyl-4:5-benz-1:3-oxazine (4.05 g., 91%), m. p. 120°, was obtained; after recrystallisation from ethanol, it (2.8 g.) had m. p. 123°.

o-Benzoylbenzoic acid (4.52 g.), subjected to the Schmidt reaction by the method (*A'*) described below for 2-*p*-toluoylbenzoic acid, yielded 6-oxo-2-phenyl-4:5-benz-1:3-oxazine (3.55 g., 80%), m. p. 122.5° (Found: C, 75.5; H, 4.4; N, 6.3. Calc. for C₁₄H₉O₂N: C, 75.3; H, 4.1; N, 6.3%).

Hydrolysis and Ring Closure.—(a) 6-Oxo-2-phenyl-4:5-benz-1:3-oxazine (3.05 g.) gave, by method *B* (sodium azide omitted), *N*-benzoylanthranilic acid (3.05 g., 93%), m. p. 177°.

(b) *N*-Benzoylanthranilic acid (2.25 g.) yielded, by method *A'* (sodium azide omitted), 6-oxo-2-phenyl-4 : 5-benz-1 : 3-oxazine (1.85 g., 89%), m. p. 123°.

(c) The oxazine (0.30 g.) was heated with trichloroacetic acid (2.0 g.) and sulphuric acid (0.8 ml.) for 1 min. to 50° and the solution was poured into water. The precipitate was filtered off, washed, and dried; it yielded *N*-benzoylanthranilic acid (0.26 g., 80%), m. p. 177°. A similar experiment, but with heating for 4 hr. at 50°, gave *N*-benzoylanthranilic acid (0.20 g., 62%), m. p. 178°. The oxazine was recovered unchanged after it had been kept overnight in a refrigerator together with the diluted mixed acids, a process which forms part of procedure *B*.

(d) A solution of the oxazine, prepared and heated as in (c), was poured into chloroform (25 ml.). From the chloroform solution, treated as described for the Schmidt reaction, the oxazine (0.25 g., 83%) was recovered. From a similar experiment, but with heating for 4 hr. at 50°, the oxazine (0.28 g., 93%), m. p. 121°, was recovered.

(e) *N*-Benzoylanthranilic acid (0.50 g.), trichloroacetic acid (4.0 g.), and sulphuric acid (0.75 ml.) were heated to 50°; the solution was treated as in (d). 6-Oxo-2-phenyl-4 : 5-benz-1 : 3-oxazine (0.38 g., 82%), m. p. 121°, was obtained.

2-p-Toluoylbenzoic Acid.—Sulphuric acid (98%; 15 ml.) was added dropwise to a stirred mixture of sodium azide (2.6 g.) and chloroform (15 ml.) at 0°. A solution of 2-*p*-toluoylbenzoic acid (4.8 g.) in chloroform (15 ml.) was added at 30° during 1 hr.; stirring was continued for 2 hr. at this temperature and the mixture was then poured into cold water (250 ml.). The chloroform layer was separated, washed with aqueous sodium carbonate and with water, dried (Na₂SO₄), and evaporated; the product, on recrystallisation from ethanol, yielded 6-oxo-2-*p*-tolyl-4 : 5-benz-1 : 3-oxazine (4.15 g., 88%), m. p. 155° (Found: C, 76.1; H, 4.7; N, 6.1. Calc. for C₁₅H₁₁O₂N: C, 76.0; H, 4.7; N, 5.9%). Zentmeyer and Wagner (*J. Org. Chem.*, 1949, 14, 967), who prepared this compound by heating *N*-toluoylanthranilic acid with acetic anhydride, record m. p. 154.5°.

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