42. *The Stereochemistry of 2 : 2'-Disubstituted Diphenyls. Part III. The Optical Resolution of* o-(2-Dimethylaminophenyl)phenyltrimethyl-ammonium Iodide.
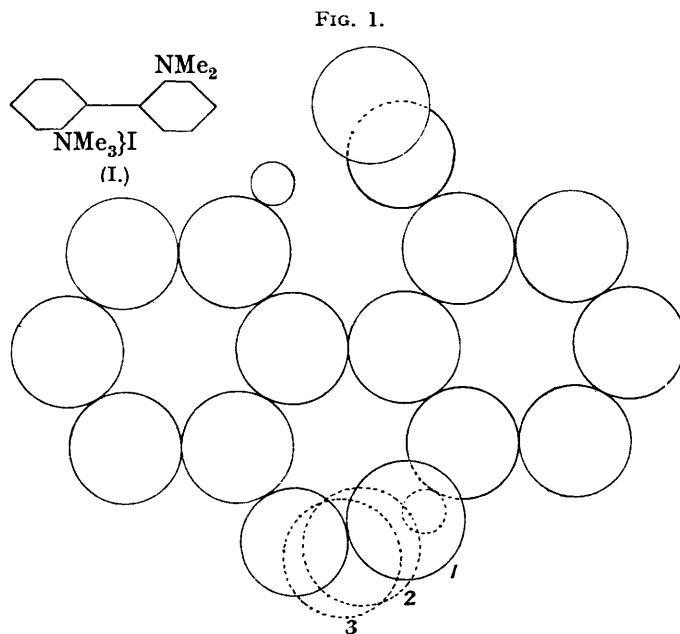
By Florence R. Shaw and E. E. Turner.

The molecular dissymmetry of phenyl benzidine-2 : 2'-disulphonate and of diphenyl-2 : 2'-disulphonic acid has been ascribed to the " dynamic " effect of the ·SO_3Ph and ·SO_3H groups, respectively (J., 1932, 2021, 2394). We have now prepared o-(2-*dimethyl-aminophenyl*)*phenyltrimethylammonium iodide* (I; Fig. 1), a diphenyl derivative containing in position 2 a group which should have a dynamic effect, and in position 2' one which should readily pass the opposed nucleus. The nitrogen atom is the smallest atom capable of carrying three other atoms in tetrahedral disposition, and the methyl group is the smallest group which can be attached to it in these circumstances. Yet Fig. 1 shows that, if the radius of the nitrogen atom is 0·70 Å., and that of a (methyl) carbon atom is

0·77 Å., collision must occur between the right-hand nucleus and the methyl groups in the (rotating) NMe_3 system. Circles 1, 2, and 3 represent the maximum, mean, and minimum effects of the carbon atoms in these methyl groups. The hydrogen atoms in the latter are not shown, but a model indicates that they materially increase the effect produced by the carbon atoms carrying them. The two nuclear hydrogen atoms shown are given radii of 0·29 Å., *i.e.*, the smallest value which has been assigned to hydrogen (see below). In the upper half of the diagram the dimethylamino-group is shown in the position producing least volume effect.

The collision area is considerably larger with ·NMe_3}X than with ·SO_3R, and therefore it seemed probable that, owing to the powerful dynamic effect of the one group, the quaternary iodide would exhibit molecular dissymmetry.

The iodide was obtained by the direct union of methyl iodide and 2 : 2'-bisdimethylaminodiphenyl (a substance which exhibits marked triboluminescence), and was con-

FIG. 1.

NMe₂

NMe₃}I

(I.)

verted into the *d*-camphor-10-sulphonate. When this was crystallised from a mixture of alcohol, benzene, and light petroleum, it underwent sharp resolution. Nearly half of the salt present was sparingly soluble, and the rest was very soluble. Recrystallisation of the sparingly soluble salt from alcohol–light petroleum gave d-o-(2-*dimethylaminophenyl*)-*phenyltrimethylammonium* d-*camphor-10-sulphonate*, having $[\alpha]_{5791}^{20°} + 60·6°$ in alcohol. The *l*-quaternary *d*-camphorsulphonate was obtained in an impure form, $[\alpha]_{5791}^{20°} - 32·0°$, from the mother-liquors. When treated with potassium iodide, it gave an impure *l*-quaternary iodide having $[\alpha]_{5791}^{20°} - 44·8°$, whereas the pure *d*-quaternary *d*-camphor-

sulphonate gave the *d*-quaternary *iodide*, with $[\alpha]_{5791}^{20°} + 50·5°$ in water. Similar resolution of the *dl*-quaternary *l*-camphorsulphonate gave the less soluble *l*-quaternary l-*camphorsulphonate* with $[\alpha]_{5791}^{20°} - 60·6°$ in alcohol. This in turn gave the *l*-quaternary *iodide*, having $[\alpha]_{5791}^{20°} - 50·6°$ in water. The quaternary iodides show simple dispersion, the camphorsulphonates anomalous, as would be expected :

	$[\alpha]_{5461}^{20°}/[\alpha]_{5791}^{20°}.$	$[\alpha]_{4358}^{20°}/[\alpha]_{5461}^{20°}.$	$[\alpha]_{4358}^{20°}/[\alpha]_{5791}^{20°}.$
Camphorsulphonates in EtOH	1·155	1·850	2·137
d-Camphorsulphonate in H_2O	1·138	1·833	2·085
Iodides in H_2O	1·132	1·554	1·760
Calc.	1·124	1·570	1·765

Cold aqueous solutions of the *d*- and the *l*-iodide retain their optical activity indefinitely. At 99·5°, racemisation is by no means rapid, the period of half-racemisation being 125 minutes (annexed table and Fig. 2, curves A and B) :

d-Iodide (curve A).						*l*-Iodide (curve B).
Time, min.	*a*.	*k*.	Time, min.	*a*.	*k*.	Mean $k = 0·0024$.
0	+0·49°	—	192	0·17°	0·0024₀	
38	0·40	0·0023₂	244	0·12	0·0025₀	Limits, 0·0023₁
78	0·32	0·0024₇	340	0·07	0·0024₉	and 0·0024₉.
125	0·25	0·0023₄		Mean *k* 0·0024		

Since the iodides and the camphorsulphonates must be completely ionised in dilute aqueous solution, it was interesting to compare the rates of racemisation of the quaternary ions present in the two types of salt. The d-quaternary d-camphorsulphonate underwent half-racemisation (allowing for the constant rotation due to the camphorsulphonate ion) in 116 minutes, *i.e.*, in a slightly, but definitely, shorter time than the d-iodide. The results are given in curve C, which shows the observed angles, and in curve D, which shows the same angles less the constant contribution (0·34°) of the camphorsulphonate ion (temperature, 99·5°; concentration, about three times that of the iodides; aqueous solution).

Mean k found, 0·0026. Limits, 0·0025 and 0·0027.

It was important to determine the effect of introducing a second positive charge into the molecule of the d-iodide, and this was done as follows : An aqueous solution contain-

Fig. 2.
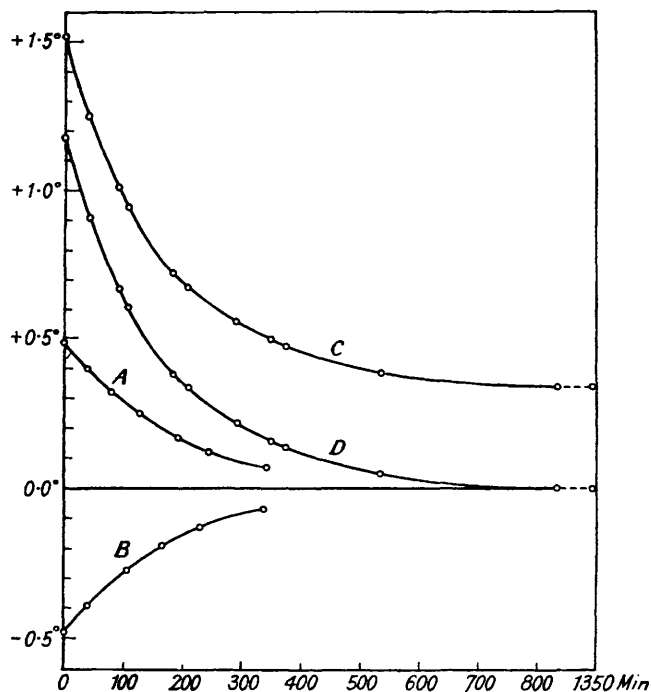
ing 0·1036 g. of the d-iodide and 1 c.c. of N-hydrochloric acid in 20 c.c. gave $\alpha_{5791}^{20°} + 0·17°$ ($l = 2$), whence $[\alpha]_{5791}^{20°} + 16·4°$. The $\alpha_{5791}^{20°}$ for the d-iodide would have been $+ 0·52°$ in absence of acid. Addition of a drop of concentrated hydrochloric acid did not affect the observed angle, which reverted to 0·51° on neutralisation of the solution, showing that the effect in presence of the acid was due to conversion of ·NMe$_2$ into ·NMe$_2$H$^+$, and not to racemisation.

As a formal subsidiary investigation, the salts of 2 : 2′-bisdimethylaminodiphenyl with d-camphorsulphonic and d-camphoric acid were studied. No evidence of resolution or activation was obtained.

The results now recorded, of which a brief preliminary note was published in *Nature* (1932, **130**, 315), suggest that a suitably 2 : 3′-disubstituted diphenyl should be capable of resolution. This and other matters are under investigation.

In order to define our position, we wish to state what we have hitherto regarded as implied, namely, that, though deductions of the kind made in the present paper and in Parts I and II (*locc. cit.*) indicate that certain compounds *should* exhibit optical activity,

it must not be inferred, in the present state of knowledge, that other compounds in which (according to the superficial significance of the numerical data used) a smaller effect of the same type is shown are *not* capable of exhibiting enantiomorphism. In the first general survey of the possible causes of molecular dissymmetry in the diphenyl series, Turner and Le Fèvre (*Chem. and Ind.*, 1926, 831) drew attention to the three properties of an atom or group which should be considered in any discussion of effects produced in the 2-, 2'-, 6-, and 6'-positions in diphenyl, *viz.*, (*a*) volume, (*b*) electrical properties, and (*c*) mass. At that time, the electrical properties were regarded as important because it was then on record, for example, that 4 : 6 : 4' : 6'-tetranitrodiphenic acid *was easily racemised*. Now that this acid is known to possess high optical stability, the justification for our " internuclear " effect disappears, but this does not affect the importance of the three effects enumerated above. Effect (*c*) can never be fundamental, but should probably be taken into account, for example, when rotation of a 2-substituent group is involved (dynamic effect), for the masses of two colliding components of one and the same molecule must be instrumental to some degree in determining the result of the collision. The two other effects (*a*) and (*b*) cannot be sharply separated one from the other. The electrical (polar) effect of an atom *A* attached to one nucleus must vary according to the polar characteristics of atoms, not directly combined with *A*, but attached to the second nucleus in such positions that they approach near to *A* in space. The electrical properties will, in general, give atoms effective radii considerably greater than those deduced from, *e.g.*, X-ray analysis; in fact, the latter may be taken as minimum radii. In illustration of this point it may be noted that Kleiderer and Adams (*J. Amer. Chem. Soc.*, 1931, **53**, 1575) resolved 2 : 2'-difluoro-6 : 6'-diamino-3 : 5 : 3' : 5'-tetramethyldiphenyl, but calculation shows that a nitrogen atom of radius 0·70 Å. can pass another similar atom or a fluorine atom (0·64 Å.). The effective radius of a nitrogen atom is therefore in this instance greater than 0·70 Å., and/or that of a fluorine atom is greater than 0·64 Å. Only experimental work can show how far this result is due to simple volume effects and how far to polar ones. At the moment, both effects must be regarded as included in any reference to the effective radius of any atoms concerned. Nevertheless, some basis for calculating collision effects is necessary.

The results obtained in this series show that, although we actually have to deal with molecules in solution, it is justifiable, in planning further experimental work, to make use of molecular dimensions deduced from measurements of solids. Apart from this, X-ray analysis of crystalline hexamethylbenzene (Lonsdale, *Proc. Roy. Soc.*, 1929, **123**, 494) gives data not seriously different from those obtained by the electron-diffraction method using benzene and *cyclo*hexane as *vapours* (Wierl, *Ann. Physik*, 1931, **8**, 541) (radii in Å.) :

	Aromatic C.	Aliphatic C.
X-Ray analysis	1·45	1·54
Electron-diffraction	1·39	1·51

Real difficulty, however, attaches to any consideration of the hydrogen atom, since the above two methods afford no guide, and the effective volume (*i.e.*, volume + polar effect) must be abnormal owing to the unscreened positive nucleus. The difference of opinion about the " radius " of a combined hydrogen atom is shown by the fact that Meisenheimer and Höring (*Ber.*, 1927, **60**, 1425) disregarded the volume effect of the hydrogen atoms in 2 : 2'-diamino-6 : 6'-dimethyldiphenyl on the assumption that they were embedded in the valency electron spheres of the carbon and nitrogen atoms carrying them, and Vegard and Sollesnes (*Phil. Mag.*, 1927, **4**, 985), from measurements on tetramethylammonium iodide by the Debye–Scherrer method, concluded that the hydrogen atoms had radii of 0·85 Å. By examining a number of limiting cases we hope to provide some answer to this problem. At the moment, it may be concluded that the *effective* radius of a hydrogen atom attached to an aromatic nucleus is less than 0·7—0·8 Å., for calculation shows that, if it were as large as this, diphenic acid itself should exhibit optical activity.

EXPERIMENTAL.

2 : 2'-*Dinitrodiphenyl.*—The following method gives uniformly good results, provided that suitable " copper-bronze " is used. 120 G. of *o*-chloronitrobenzene were briskly boiled in a wide hard-glass tube (bath initially at 260—265°) while copper-bronze (80 g.) was stirred in during 20 min. After another 10 min., *o*-dichlorobenzene (equal in vol. to the reaction mixture) was added, the whole well stirred, the liquid filtered hot, the solid residue washed with $C_6H_4Cl_2$, and the total filtrate treated with light petroleum (b. p. 40—80°) until it was faintly cloudy. Filtration of the resulting cold suspension gave 48—50 g. (occasionally as much as 57 g.) of almost pure, though dark-coloured, 2 : 2'-dinitrodiphenyl. Low yields are obtained if the condensation is not carried out vigorously, or if heating is prolonged after the main reaction has subsided.

2 : 2'-*Diaminodiphenyl.*—The dinitrodiphenyl was readily reduced by Fe filings, H_2O, and a little HCl aq. or AcOH (cf. Le Fèvre, J., 1929, 733). The base was isolated by pouring the hot Fe paste into cold acetone, distilling the ketone from the filtered liquid, and extracting the residue with dil. HCl; yield, 65% after pptn. by NH_3 aq. and one crystn. from EtOH.

2 : 2'-*Bisdimethylaminodiphenyl.*—This base was examined crystallographically by Mieleitner (*Z. Kryst. Min.*, 1915, **55**, 51), but its prepn. has not hitherto been described. A mixture of diaminodiphenyl (30 g.) and H_2O (30 c.c.) was shaken for 10 min. with three lots (32, 32, and 42 c.c.) of Me_2SO_4, being made alkaline with 10% NaOH aq. between the additions. The final mixture, containing the tetramethyl base as a solid cake, was heated at 100° for 15 min., cooled, made alkaline, and filtered. The base, cryst. from EtOH containing a little NH_3 aq., was almost pure (28—30 g.) : its solution (1 mol.) in dil. HCl was poured into KI (1·2 mols.) in much boiling H_2O; on cooling, 2 : 2'-bisdimethylaminodiphenyl hydriodide, m. p. 256—257°, separated in colourless prisms, almost insol. in cold H_2O (Found : I, 34·3. $C_{16}H_{21}N_2I$ requires I, 34·5%). The base, liberated from a solution of this salt in much boiling H_2O by excess of NH_3 aq. and cryst. from abs. EtOH and then from light petroleum (b. p. 40—60°), formed plates, m. p. 72—73° (corr.) (Found : C, 80·0; H, 8·5; N, 11·7. Calc. : C, 79·9; H, 8·4; N, 11·7%). Blue-violet flashes are emitted when a hard lump is splintered with a knife or shaken in a tube, or when the solid is rubbed with a glass rod. The effect is, if anything, more pronounced at liquid-air temperature.

The *chloroplatinate* formed minute golden rhombic prisms (Found in salt dried in vac. over SiO_2 gel : Pt, 28·3. $C_{16}H_{20}N_2,H_2PtCl_6,2H_2O$ requires Pt, 28·4%).

dl-o-(2-*Dimethylaminophenyl*)*phenyltrimethylammonium Iodide.*—The tetramethyl base was heated with MeI (2 parts) in a sealed tube at 100° for 2 hr., the product freed from MeI by evapn. and dissolved in boiling H_2O, any acidity removed by NH_3 aq., and the liquid rapidly filtered at about 50° or extracted with warm toluene. The cold aq. solution deposited the quaternary *iodide* as long stout prisms; slow spontaneous evapn. produced well-defined rhombic crystals. After crystn. from H_2O, the iodide had m. p. 190—192° (corr.), with brisk evolution of MeI (Found : C, 53·6; H, 6·05; I, 33·2. $C_{17}H_{23}N_2I$ requires C, 53·4; H, 6·1; I, 33·2%). The m. p. of this methiodide and those of the active iodides depend on the rate of heating. The figures recorded were obtained with a bath initially at 180°.

Resolution Experiments.—(a) d-*Camphorsulphonates.*—dl-Dimethylaminophenylphenyltrimethylammonium iodide (15·28 g.) and the equiv. silver *d*-camphor-10-sulphonate were boiled under reflux in 200 c.c. abs. EtOH and 50 c.c. H_2O for 30 min. The filtered solution was evaporated, the residue freed from H_2O by repeated evapn. with small quantities of C_6H_6–EtOH and dissolved in a boiling mixture of 250 c.c. C_6H_6 and 12 c.c. abs. EtOH, and the filtered solution treated with 100 c.c. light petroleum (b. p. 60—80°). Hair-like needles began to separate after a few min., and after 30 min. in the ice-chest separation had ceased. Filtration gave 7·05 g. of almost pure *d*-quaternary *d*-camphorsulphonate (*A*), having $[\alpha]_{5791}^{20°} + 59\cdot4°$ in 99·4% EtOH ($\alpha_{5791}^{20°} + 1\cdot88°$; *c*, 1·5820; *l*, 2). Addition of 100 c.c. light petroleum to the mother-liquor caused separation, within 30 min., of a further 2·15 g. of similar material (*B*), having $[\alpha]_{5791}^{20°} + 59\cdot9°$. The combined wt. of *A* and *B*, 9·2 g., is 95% of the possible *dd*-salt, assuming no complications. Salt *A* was dissolved in 35 c.c. hot abs. EtOH, the solution filtered, and then treated with 140 c.c. light petroleum (b. p. 60—80°) and 70 c.c. light petroleum (b. p. 40—60°). The camphorsulphonate (4·0 g.) separated in needles, m. p. 189—190° (corr.), having $[\alpha]_{5791}^{20°} + 60\cdot6°$, $[\alpha]_{5461}^{20°} + 70\cdot0°$, and $[\alpha]_{4358}^{20°} + 129\cdot7°$ ($\alpha + 2\cdot05°$, $+ 2\cdot37°$, and $+ 4\cdot39°$; *c*, 1·6925; *l*, 2). It was crystallised from EtOH–light petroleum, and the 3·5 g. of optically pure d-o-(2-*dimethylaminophenyl*)*phenyltrimethylammonium* d-*camphor-10-sulphonate* obtained had m. p. 189—190° (corr.), $[\alpha]_{5791}^{20°} + 60\cdot6°$, $[\alpha]_{5461}^{20°} + 70\cdot0°$, and $[\alpha]_{4358}^{20°} + 129\cdot3°$ ($\alpha + 1\cdot87°$,

+ 2·155°, and + 3·98°; *c*, 1·5395; *l*, 2). Further crystn. had no effect on m. p. or sp. rotation (Found : C, 66·6; H, 7·7. $C_{27}H_{38}O_4N_2S$ requires C, 66·6; H, 7·9%). In aq. solution the pure *dd*-salt had $[\alpha]_{5791}^{20°}$ + 52·3°, $[\alpha]_{5461}^{20°}$ + 59·5°, and $[\alpha]_{4358}^{20°}$ + 109·1° (α + 1·52°, + 1·73°, and + 3·17°; *c*, 1·4535; *l*, 2).

The mother-liquor of salt *B* was evaporated to dryness, and a solution of the residue in a little H_2O filtered and then added to a conc. aq. solution of 20 g. of KI. The white cryst. quaternary iodide pptd. was dried at 100° (4·5 g., equiv. to 5·7 g. of quaternary camphorsulphonate) and had $[\alpha]_{5791}^{20°}$ − 18·9° in H_2O. It was treated with silver *l*-camphor-10-sulphonate in boiling aq. EtOH as above, and the crude quaternary *l*-camphorsulphonate was crystallised from abs. EtOH–light petroleum (b. p. 40—80°). The salt obtained (1·5 g.) had $[\alpha]_{5791}^{20°}$ − 56·7°. Recrystn. from the same solvent gave 1·05 g. with $[\alpha]_{5791}^{20°}$ − 59·4°. Treatment of an aq. solution of this salt with aq. KI gave an almost pure *l*-iodide having $[\alpha]_{5791}^{20°}$ − 49·4° in H_2O.

In another resolution expt., a mother-liquor, corresponding to that from which *B* separated, was dried over anhyd. Na_2SO_4, and then treated with light petroleum (b. p. 40—80°) until it became cloudy. After some hr., woolly masses of needles separated, having $[\alpha]_{5791}^{20°}$ − 32·0° in EtOH. This impure *ld*-salt, when treated with KI, gave a quaternary iodide which, after being rapidly cryst. from H_2O, had $[\alpha]_{5791}^{20°}$ − 44·8°.

(b) l-*Camphorsulphonates.*—The *dl*-iodide (11·46 g.) and the equiv. silver *l*-camphor-10-sulphonate were caused to react as in (a). The mixed camphorsulphonates were crystallised by means of 185 c.c. C_6H_6, 9 c.c. abs. EtOH, and 150 c.c. light petroleum (b. p. 60—80°). The crude *ll*-salt separated in 30 min. (6·05 g.), and had $[\alpha]_{5791}^{20°}$ − 54·1°. Crystn. from abs. EtOH–light petroleum gave 4·5 g., m. p. 189—190° (corr.), $[\alpha]_{5791}^{20°}$ − 60·2° (α − 1·815°; *c*, 1·5705; *l*, 2). Recrystn. of this salt had no effect on the m. p. and gave 3·0 g. of pure l-o-(2-*dimethylaminophenyl*)*phenyltrimethylammonium* l-*camphor*-10-*sulphonate*, with $[\alpha]_{5791}^{20°}$ − 60·6°, $[\alpha]_{5461}^{20°}$ − 69·9° and $[\alpha]_{4358}^{20°}$ − 129·9° (α − 1·83°, − 2·11°, and − 3·92°; *c*, 1·5080; *l*, 2) (Found : C, 66·7; H, 7·6%). In another expt., the crude *ll*-salt first obtained was crystallised twice from abs. EtOH–light petroleum, and then had $[\alpha]_{5791}^{20°}$ − 60·5°, $[\alpha]_{5461}^{20°}$ − 70·3°, and $[\alpha]_{4358}^{20°}$ − 129·3°.

A solution (EtOH) containing 0·1458 g. of each of the salts, *dd*- and *ll*-, in 20 c.c. had $\alpha_{5791}^{20°}$ 0·00°.

d-o-(2-*Dimethylaminophenyl*)*phenyltrimethylammonium iodide* was obtained by mixing warm conc. aq. solutions of the pure *dd*-camphorsulphonate and KI. The salt separated suddenly in spherical aggregates of needles. After being dried in vac. over conc. H_2SO_4, it melted at 190—192° (corr.) with evolution of MeI, and had $[\alpha]_{5791}^{20°}$ + 50·5°, $[\alpha]_{5461}^{20°}$ + 57·0°, and $[\alpha]_{4358}^{20°}$ + 88·9°, in H_2O (α + 0·97°, + 1·095°, and + 1·71°; *c*, 0·4804; *l*, 4) (Found : C, 53·2; H, 6·0; I, 33·2%).

l-o-(2-*Dimethylaminophenyl*)*phenyltrimethylammonium iodide*, obtained similarly, had m. p. 190—192° (corr.) (evolution of MeI), and $[\alpha]_{5791}^{20°}$ − 50·6°, $[\alpha]_{5461}^{20°}$ − 57·4°, and $[\alpha]_{4358}^{20°}$ − 88·9° (α − 0·96°, − 1·09°, and − 1·69°; *c*, 0·4744; *l*, 4) (Found : C, 53·3; H, 6·1; I, 33·1%).

Racemisation Velocities.—These were determined by heating the solutions in sealed glass tubes at 99·5°, and observing the rotation at intervals after sudden chilling to 20°.