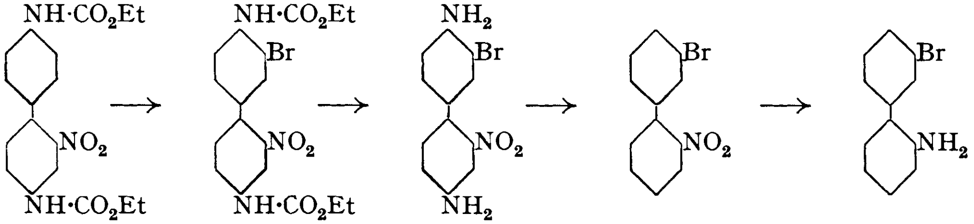
377. *The Optical Activity of a Diphenyl Derivative, the Dissymmetry of which is caused by the Space Effect of only one Group.*

By (Miss) Mary S. Lesslie and Eustace E. Turner.

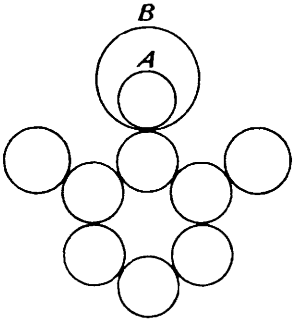
In a recent communication (Shaw and Turner, this vol., p. 135) it was pointed out that a suitably 2 : 3′-disubstituted diphenyl should show molecular dissymmetry. The condition which must be satisfied is that the 2-substituent either must, if an atom, have a radius equal to or greater than that (1·33 Å.) of iodine (Type I), or, if a group attached to the 2-position through an atom smaller than that of iodine, must exhibit a " dynamic " effect (Type II). At that time we had already attempted the resolution of 2-iododiphenyl-3′-carboxylic acid (Type I). This acid was very difficult to obtain, and the resolution of its alkaloidal salts could not be effected. We have now examined two compounds of Type II, the 2-substituent being $\cdot\overset{+}{\text{N}}\text{Me}_3\}\overset{-}{\text{X}}$ in the one and $\cdot\overset{+}{\text{As}}\text{Me}_3\}\overset{-}{\text{X}}$ in the other (radius of As atom, 1·2 Å.). Both compounds contain bromine in the 3′-position, and were prepared from 3-bromo-2′-aminodiphenyl, the latter being obtained according to the scheme :



The de-amination of large quantities of 3-bromo-2′-nitrobenzidine by the usual method (diazotisation in concentrated sulphuric acid, etc.) proved tedious, but was conveniently effected by a new process: the dry bisdiazoborofluoride of the bromonitrobenzidine is very readily prepared, and undergoes rapid, smooth conversion into the bromonitrodiphenyl when it is added to a boiling solution of concentrated sulphuric acid in absolute alcohol. No difficulty was experienced in converting 3-*bromo*-2′-*aminodiphenyl* into 3-*bromo*-2′-*dimethylaminodiphenyl*, but the tertiary base showed little tendency to combine with methyl iodide. Polar solvents, such as acetonitrile, did not appreciably aid the combination, nor did methyl sulphate or methyl *p*-toluenesulphonate exhibit reactivities very different from that of methyl iodide. Prolonged action of the latter at 175° gave 3′-*bromodiphenylyl*-2-*trimethylammonium iodide* in small, but practicable, yield. This result is of interest, as it demonstrates the considerable steric effects about the nitrogen atom in this particular compound. The non-reactivity of the tertiary base is in contrast with the ready reactivity of *p*-bromodimethylaniline; at the same time, it is not entirely due to steric effects, since 2 : 2′-bisdimethylaminodiphenyl combines readily with methyl iodide (Shaw and Turner, *loc. cit.*).

The tertiary ammonium iodide was converted into the corresponding *d*-camphorsulphonate and *d*-α-bromocamphor-π-sulphonate, but both of these substances were deliquescent glasses, resolution of which proved impossible.

Tertiary arsines containing the $AsMe_2$ group usually combine readily with methyl iodide, and, because the arsenic atom is so large, the combination should be little affected by such steric factors as would depress the reactivity of the small nitrogen atom. The annexed figure shows that, whereas the nitrogen atom (*A*) is sheltered by the two *o*-methyl groups in *N*-dimethylmesidine, the arsenic atom (*B*) in 2 : 4 : 6-*trimethylphenyldimethylarsine* is relatively easy of access. (No H atoms are shown in the diagram, nor the methyl groups attached to N or As.) It is known (Hofmann, *Ber.*, 1872, **5**, 718) that dimethylmesidine does not combine with methyl iodide even at 150°, but in confirmation of our expectations we now find that 2 : 4 : 6-*trimethylphenyldimethylarsine* combines with methyl iodide, and even with ethyl iodide, at room temperature.



Similarly, 3′-*bromodiphenylyl*-2-*trimethylarsonium iodide* was obtained without any difficulty from methyl iodide and the tertiary arsine, which was prepared from 3-bromo-2′-aminodiphenyl according to the scheme: $\cdot NH_2 \longrightarrow \cdot AsO(OH)_2 \longrightarrow \cdot AsCl_2 \longrightarrow \cdot AsMe_2$. In the first stage, the pure diazoborofluoride was used instead of the customary aqueous diazo-solution. This has the advantage of avoiding all such impurities as phenols and nitrous acid. In contrast with the analogous nitrogen derivative, the arsonium iodide was highly crystalline, as were the d-*camphor*-10-*sulphonate* and the *d*-α-*bromocamphor*-π-*sulphonate*.

When the arsonium camphorsulphonate was crystallised, definite indications of resolution were obtained (see p. 1591). Decomposition of a crop having $[\alpha]_{5791}^{20^\circ} + 19{\cdot}2^\circ$ gave an arsonium iodide, which had $\alpha_{5791}^{20^\circ} + 0{\cdot}09^\circ$ and $\alpha_{5461}^{20^\circ} + 0{\cdot}12^\circ$ ($l = 2$; $c = 1{\cdot}711$) in 50% aqueous acetone but became inactive after being heated in the solution at 100° for 2 hours: the activity, therefore, was not due to the presence of camphorsulphonate.

Sharp separation of the arsonium camphorsulphonate could not be effected, and the arsonium bromocamphorsulphonate was therefore examined: the polarimetric behaviour of this substance on crystallisation is described on p. 1592. The *dl-d*-salt was never obtained during fractional crystallisation, but was always produced when any of the actual crops was caused to racemise in aqueous solution at 100°. The racemisation of the salts rules out the possibility that the differences in rotation of the crops were due to changes within the bromocamphorsulphonic ion (King, J., 1919, **115**, 976; Kipping and Tattersall, J., 1903, **83**, 918). The silver bromocamphorsulphonate used was made from pure bromocamphor; the intermediate ammonium *d*-α-bromocamphor-π-sulphonate was crystallised eight times from water, and had $[\alpha]_{5791}^{20^\circ} + 90{\cdot}2^\circ$ in water (Pope and Read, J., 1910, **117**, 2199, give $+ 90{\cdot}02^\circ$).

The melting points of the crops having $[\alpha]_{5791}^{20^\circ} + 46{\cdot}8^\circ \pm 0{\cdot}2^\circ$ were sharp, whilst those of intermediate crops had a range of several degrees. This indicates that the crops of highest rotation were specimens of *d*-arsonium *d*-bromocamphorsulphonate.

Treatment of a specimen of this *d*-*d*-salt having $[\alpha]_{5791}^{20^\circ}$ + 47·0° with potassium iodide gave an arsonium iodide having $[\alpha]_{5791}^{20^\circ}$ + 1·5° in absolute alcohol, gradually becoming inactive at room temperature. Decomposition of another specimen of bromocamphorsulphonate having $[\alpha]_{5791}^{20^\circ}$ + 46·6° gave an iodide with $[\alpha]_{5791}^{20^\circ}$ + 1·0° and $[\alpha]_{5461}^{20^\circ}$ + 1·2°, completely racemising in alcoholic solution over-night.

The small value of the specific rotation of the iodide corresponds with the small difference in rotation between the *dl*-arsonium and the purest specimen of the *d*-arsonium bromocamphorsulphonate, and is of the same order as that ($[\alpha]_D$ + 1·8°) observed for 2 : 4 : 6 : 2′ : 4′ : 6′-hexachlorodiphenyl-3 : 3′-dicarboxylic acid by White and Adams (*J. Amer. Chem. Soc.*, 1932, **54**, 2107).

EXPERIMENTAL.

2-*Nitrobenzidine*.—The following method, improving that of Täuber (*Ber.*, 1894, **27**, 2628) gave uniformly good results if pure benzidine was used. The latter (92 g.) was dissolved in 860 c.c. of 100% sulphuric acid at 10—15°. Finely ground potassium nitrate (50·5 g.) was added with careful stirring within ½ hour, the temperature being kept at 15—20°. After a further ½—1 hour, the solution was poured into 1500 c.c. of water, and the resulting solution into 6 l. of steam-heated boiling water. The clear solution was cooled rapidly. Separation of 2-nitrobenzidine sulphate began at about 35° and was complete at 20°. The sulphate was filtered off; 30-g. portions of the moist salt were ground to a stiff paste with water, and excess of concentrated aqueous ammonia added, with grinding. The base was freed from sulphate by dissolving it in alcohol containing a little ammonia, and pouring the solution into a large volume of water. The yield of pure base was 107 g. (93·5%).

2-*Nitro*-NN′-*dicarbethoxybenzidine*.—A boiling solution of 100 g. of 2-nitrobenzidine and 132 g. of diethylaniline in 1 l. of alcohol was gradually treated with 114 g. of ethyl chloroformate. Boiling was continued for 10 minutes after the vigorous reaction was complete. The solution was then diluted with water : the diurethane, which crystallised in theoretical yield, had m. p. 190—192° (corr.) after recrystallisation from ethyl alcohol. Le Fèvre and Turner (J., 1928, 252) gave 187—188°.

3-*Bromo*-2′-*nitro*-NN′-*dicarbethoxybenzidine*.—Bromine (23·3 c.c.) (1 mol. excess), dissolved in 1 vol. of glacial acetic acid, was added to a hot (100°) solution of 80 g. of the diurethane and 37 g. of anhydrous sodium acetate in 1090 c.c. of glacial acetic acid. The mixture was boiled for 10 minutes, and poured into a large bulk of water; the *bromo-diurethane*, which crystallised, had m. p. 145—147° after recrystallisation from alcohol (87 g.; 90% yield) (Found : Br, 18·0. $C_{18}H_{18}O_6N_3Br$ requires Br, 17·7%).

3-*Bromo*-2′-*nitrobenzidine*.—Water (250 c.c.) was cautiously added to a solution of 100 g. of the diurethane in 500 g. of concentrated sulphuric acid. The temperature rose to 150°, and was maintained for 10—15 minutes; the hydrolysis was then complete. The solution was poured into water, and concentrated aqueous ammonia added. The base separated as brick-red needles, and crystallised from alcohol in deep golden-red needles, m. p. 155—156° (corr.) (yield. 80%) (Found : Br, 26·3. $C_{12}H_{10}O_2N_3Br$ requires Br, 25·9%).

Deamination of 3-*Bromo*-2′-*nitrobenzidine*.—(*a*) The base (21 g.) was heated with a mixture of 150 g. of concentrated sulphuric acid and 75 c.c. of water. The cool paste obtained was treated with ice and solid sodium nitrite (20 g.) at − 5°; 75 c.c. of 20% oleum were added, the temperature being kept below 30°. The product was gradually added to 1 l. of boiling ethyl alcohol, and the solution boiled under reflux for 2 hours. The solution was diluted with a large excess of water, and extracted with ether. The extract was washed with alkali and with water and dried over calcium chloride, and the solvent removed. The residue was distilled under reduced pressure (b. p. 210°/15 mm.). Yield, 10 g. (52%).

(*b*) The base (60 g.) was heated with 120 c.c. of concentrated hydrochloric acid for an hour on the water-bath, *i.e.*, until it was completely converted into the hydrochloride. The paste was cooled, ice added, and a solution of 27 g. of sodium nitrite in 60 c.c. of water stirred in (10 minutes, addition under surface), ice being added as required. The diazo-solution was filtered, and hydroborofluoric acid added. The diazoborofluoride was filtered off and dried in a vacuum over sulphuric acid (yield, 96 g.). It was added gradually to a boiling mixture of 10 parts of absolute ethyl alcohol and 2 parts of concentrated sulphuric acid, and the solution then boiled for 10 minutes, treated with excess of brine, and worked up as in (*a*). Yield of pure product, 42 g. (78%).

3-*Bromo*-2′-*nitrodiphenyl* crystallises from absolute alcohol in pale yellow prisms, m. p. 53—54° (corr.) (Found : Br, 28·8. $C_{12}H_8O_2NBr$ requires Br, 28·8%). Its constitution rests on that of the bromonitro-diurethane, which can hardly be in doubt (2-bromo-2′-nitrodiphenyl has m. p. 66—67°; Mascarelli and Gatta, *Atti R. Accad. Lincei*, 1931, **13**, 887).

3-*Bromo*-2′-*aminodiphenyl*.—Bromonitrodiphenyl (60 g.) was dissolved in 60 c.c. of hot glacial acetic acid and treated with a solution of stannous chloride (240 g.) in concentrated hydrochloric acid. When the reaction was over, the solution was poured into an aqueous solution of sodium hydroxide (390 g.), and the whole extracted with ether. The solvent was removed, and the residue distilled under reduced pressure. Yield of pure base, 51 g. 3-*Bromo*-2′-*aminodiphenyl*, b. p. 195°/11 mm., crystallises from aqueous ethyl alcohol in elongated hexagonal plates, m. p. 69—70° (corr.) (Found : Br, 32·6. $C_{12}H_{10}NBr$ requires Br, 32·2%). Reduction of the bromonitrodiphenyl in aqueous alcohol with iron and a trace of acid was less satisfactory than the method described.

3-*Bromo*-2′-*dimethylaminodiphenyl*.—3-Bromo-2′-aminodiphenyl (25 g.) was methylated with 150 c.c. of methyl sulphate and aqueous alkali. The product had b. p. 176—178°/9 mm., or 187—188°/12 mm., and crystallised from alcohol in long prismatic needles or in hexagonal plates, m. p. 47—48° (Found : Br, 29·4. $C_{14}H_{14}NBr$ requires Br, 29·0%). The *chloroplatinate* formed irregular crystals (Found : Pt, 20·2. $C_{28}H_{28}N_2Cl_6Br_2Pt$ requires Pt, 20·3%).

3′-*Bromodiphenylyl*-2-*trimethylammonium Iodide*.—A solution of 5 g. of the pure tertiary base in 10 c.c. of freshly purified methyl iodide was heated in a sealed tube at 175° for 8 hours, and allowed to cool over-night. The viscous product, when rubbed with anhydrous ether, became a powder, which was dissolved in absolute alcohol, and precipitated with anhydrous ether. The deliquescent *methiodide* obtained could not be further purified, and decomposed on heating (Found : I, 29·6. $C_{15}H_{17}NBrI$ requires I, 30·4%).

3′-*Bromodiphenylyl*-2-*arsonic Acid*.—The bromoaminodiphenyl (43 g.) was heated with 110 c.c. of concentrated hydrochloric acid, the product cooled, and a concentrated aqueous solution of sodium nitrite (15 g.) stirred in, ice being added as required. The filtered diazo-solution was treated with hydroborofluoric acid, and the precipitated diazoborofluoride filtered off and washed. It was made into a paste with water, and added at room temperature to a solution of 35 g. of arsenious oxide and 100 g. of anhydrous sodium carbonate in 600 c.c. of water, the mixture being well stirred. Copper sulphate solution was added occasionally. The reaction was vigorous. Ether was added towards the end and the mixture was heated at 50° for 5 minutes. Aqueous ammonia was then added till the green precipitate redissolved, the solution was cooled, and a lump of brownish tar squeezed and removed. Concentrated hydrochloric acid was added to the filtered solution, and the *arsonic acid* was precipitated. The yield was variable, and never exceeded 13 g. The arsonic acid crystallises from aqueous alcohol in needles, m. p. 189—190° (corr.) (Found : Br, 22·8. $C_{12}H_{10}O_3BrAs$ requires Br, 22·4%).

3′-*Bromodiphenylyl*-2-*trimethylarsonium Iodide*.—The arsonic acid (12·6 g.) was reduced in the usual manner with sulphur dioxide, hydrochloric acid, and iodine, and the dichloroarsine taken up in benzene. The benzene solution was dried with calcium chloride, freed from hydrogen chloride by aeration, and added to methylmagnesium iodide made from 56 g. of methyl iodide and 20 g. of magnesium (with decantation). When the vigorous reaction was over, the mixture was decomposed with water and hydrochloric acid, the ether–benzene layer washed with water and dried over calcium chloride, and the solvent removed. The residual oil was heated under reflux for 1 hour with a little absolute alcohol and excess of methyl iodide. The solution was cooled, and dry ether added; 15 g. of *methiodide* were then precipitated (89% yield, calc. on arsonic acid used). It crystallised from ethyl alcohol–ether in prisms, m. p. 183—184° (corr.) (Found : I, 26·5. $C_{15}H_{17}BrIAs$ requires I, 26·5%).

3′-*Bromodiphenylyl*-2-*trimethylarsonium* d-*Camphor*-10-*sulphonate*.—The arsonium iodide (13·5 g.) was treated in boiling ethyl-alcoholic solution with silver *d*-camphor-10-sulphonate (9·6 g.); after removal of the silver iodide, and evaporation of the solvent, 16·1 g. of the *arsonium camphorsulphonate* were obtained. It crystallised from acetone–light petroleum (b. p. 40—60°) in thin hexagonal plates. Successive crops had $[\alpha]_{5791}^{20^\circ}$ + 19·2° to + 21·8° in ethyl alcohol. Repeated crystallisation of these from acetone–light petroleum gave crops the specific rotation of which was + 19·2°, varying by very small amounts to a maximum of + 21·8° [Found for a specimen having $[\alpha]_{5791}^{20^\circ}$ + 19·6° and m. p. 219—220° (corr.) : C, 51·7; H, 5·7. $C_{25}H_{32}O_4BrSAs$ requires C, 51·4; H, 5·5%].

3′-*Bromodiphenylyl*-2-*trimethylarsonium* d-α-*Bromocamphor*-π-*sulphonate*.—Interaction of

7·2 g. of the arsonium iodide with 6·3 g. of silver bromocamphorsulphonate in boiling absolute ethyl-alcoholic solution, followed by filtration and evaporation, gave 9·3 g. of arsonium bromocamphorsulphonate. This was dissolved in benzene, containing a very little alcohol to aid solution, and light petroleum (b. p. 60—80°) was added. Rosettes of fine needles (7 g.) separated, and these, on recrystallisation, gave 4 g., and on one further crystallisation gave two crops, one (2·8 g.) having $[\alpha]_{5791}^{20^\circ}$ + 47·0° in water ($l = 2$; $c = 2{\cdot}081$; $\alpha = +\ 1{\cdot}955^\circ$) and a second (0·5 g.) having $[\alpha]_{5791}^{20^\circ}$ + 44·4° ($l = 2$; $c = 2{\cdot}038$; $\alpha = +\ 1{\cdot}81^\circ$). Further recrystallisation did not raise the specific rotation of the crop having $[\alpha]_{5791}^{20^\circ}$ + 47·0°. When the rotation solution was heated at 100° for 1 hour and for 2½ hours, the rotation fell to + 42·5° (difference in observed angle, 0·185°) and + 41·9° respectively. Similarly the + 44·4° crop underwent racemisation to + 41·3° (difference in observed angle, 0·12°).

The resolution was repeated with 6 g. of initial material and similar results were obtained.

In another series of experiments, the solvent was changed. 3 G. of arsonium bromocamphorsulphonate were crystallised from acetone, and 0·4 g. obtained having $[\alpha]_{5791}^{20^\circ}$ + 45·5°. Addition of benzene gave 0·8 g. having $[\alpha]_{5791}^{20^\circ}$ + 45·3°, and, from the mother-liquor, on addition of light petroleum (b. p. 60—80°), were obtained 1·3 g., which, after recrystallisation from acetone-benzene, had $[\alpha]_{5791}^{20^\circ}$ + 46·6°. The resolution was twice repeated on larger amounts of material, acetone, benzene, and light petroleum being used in this manner. A better separation was effected than with the alcohol mixture. The highest rotation obtained was $[\alpha]_{5791}^{20^\circ}$ + 46·6°, and the lowest + 43·0°. These, and all intermediate crops, underwent racemisation in aqueous solution at 100° to give $[\alpha]_{5791}^{20^\circ}$ + 41·5° ± 0·4°, which is therefore the specific rotation of the *dl*-arsonium *d*-bromocamphorsulphonate. In view of the small differences in rotation between the various crops, all polarimetric readings were made independently by each of us, and, as a further check, constancy of the dispersion ratio $[\alpha]_{5461}^{20^\circ}/[\alpha]_{5791}^{20^\circ}$ was demanded. The pure partial racemate was never actually isolated as a crop, nor was there any sign of the *l*-*d*-salt.

d-*3′-Bromodiphenylyl-2-trimethylarsonium* d-*α-bromocamphor-π-sulphonate* crystallises in rosettes of needles, m. p. 184—185°, and has $[\alpha]_{5791}^{20^\circ}$ + 46·8° ± 0·2° in water, and $[\alpha]_{5461}^{20^\circ}$ + 54·4° ± 0·2°. It is readily soluble in water, ethyl alcohol, and hot acetone and sparingly soluble in benzene and light petroleum (Found : C, 45·3; H, 4·9. $C_{25}H_{31}O_4Br_2SAs$ requires C, 45·3; H, 4·7%). An intermediate crop having $[\alpha]_{5791}^{20^\circ}$ + 43·0° had m. p. 180—183° (Found : C, 45·2; H, 5·0%).

2 : 4 : *6-Trimethylphenyldimethylarsine.*—A filtered Grignard reagent prepared from 20 g. of bromomesitylene and 5 g. of magnesium was treated with an ethereal solution of 23 g. of dimethyliodoarsine in an atmosphere of hydrogen. Vigorous interaction occurred, and when it was over, the mixture was decomposed with water and dilute hydrochloric acid, the ethereal layer separated, washed three times with dilute hydrochloric acid, then with water, then twice with 25% sodium hydroxide solution, and finally with water, and dried over potassium carbonate, and the solvent removed. The residue, distilled under reduced pressure, gave 9 g. of colourless, highly refractive liquid, b. p. 138—139°/20 mm. The arsine could not be freed from traces of bromomesitylene (Found : As, 30·9. $C_{11}H_{17}As$ requires As, 33·5%).

The arsine combined with cold methyl iodide in a few minutes, and also, though more slowly, with ethyl iodide. At 100° the reaction with ethyl iodide was rapid.

The *methiodide*, colourless leaflets from alcohol, or alcohol–ether, has m. p. 219—220° (corr.) (Found : I, 34·9. $C_{12}H_{20}IAs$ requires I, 34·7%). The *ethiodide*, colourless leaflets from alcohol-ether, has m. p. 174—175° (corr.) (Found : I, 33·5. $C_{13}H_{22}IAs$ requires I, 33·4%).

We thank the Royal Society, the Chemical Society, and the Dixon Fund Committee of the University of London for grants.

BEDFORD COLLEGE, UNIVERSITY OF LONDON. [*Received, November 7th,* 1933.]