282. *The Stereochemistry of 2 : 2′-Disubstituted Diphenyls. Part I. The Optical Resolution of Phenyl Benzidine-2 : 2′-disulphonate.*

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AN accurate model of the diphenyl molecule made with the atomic radii 0·725 Å for carbon (Lonsdale, *Proc. Roy. Soc.*, 1929, **123**, 494) and 0·37 Å for hydrogen (Birge and Jeppesen, *Nature*, 1930, **125**, 463) shows (Fig. 1) that, if an atom or group X of radius 1·18 Å is present in both the 2- and the 2′-position, the model can be arranged so that the two benzene nuclei are co-planar as well as co-axial. At the same time, the atom or group X in position 2 (2′) is in actual contact with the hydrogen atom in position 6′ (6); therefore, although this configuration is possible in a *model*, it could not be reproduced in a molecule, since it would imply the close contact of actual combination between the groups X and the two hydrogen atoms touching them. The di-X-substituted diphenyl therefore should have a non-planar configuration and exhibit molecular dissymmetry. Moreover, even if the radius of X were less than 1·2 Å, *e.g.*, 1·1 Å, a planar configuration would probably be prevented, for it is unlikely that X could come within 0·1 Å of the hydrogen atom.

Diphenyl derivatives containing in the 2 : 2′-positions either bromine (atomic radius, 1·13 Å; Mecke, "Bandspektra, Handb. Phys.," 1929) or iodine atoms (atomic radius, 1·33 Å; Mecke, *Z. Physik*, 1927, **42**, 390; *Physikal. Z.*, 1927, **28**, 479) should therefore be capable of exhibiting optical activity, or at any rate asymmetric induction, and the same may be true of a diphenyl derivative having these positions occupied by atoms of sulphur, the atomic radius (r_S) of which appears to be between 0·88 Å (Mischke, *Z. Physik*, 1931, **67**, 106) and 1·17 Å (Goldschmidt, *Geochem. Vert.*, 1927, **8**, 21; *Ber.*, 1927, **60**, 1263). The distance between the centres of the oxygen and sulphur atoms in potassium sulphate has been given (Goldschmidt, *loc. cit.*) as 1·64 Å, and the atomic radii of singly and of doubly bound oxygen are respectively 0·70 and 0·60 Å (*Ann. Reports*, 1931, 385): since the S—O link in potassium sulphate is semi-polar, the first figure should be taken, which gives $r_s = 1·64 - 0·70 = 0·94$ Å.

FIG. 1.

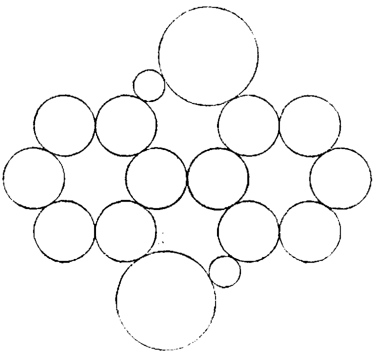
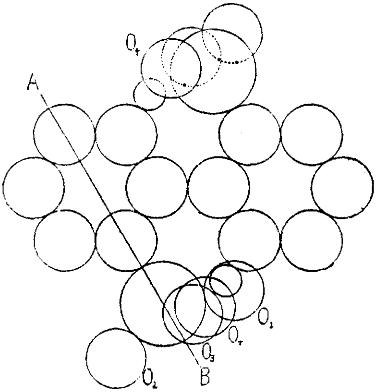


FIG. 2.



In view of these facts, and for other reasons cited below, we prepared *phenyl benzidine*-2 : 2′-*disulphonate*,

$$SO_3Ph{\cdot}C_6H_3(NH_2){\cdot}C_6H_3(NH_2){\cdot}SO_3Ph,$$

and attempted its optical resolution. From an absolute ethyl-alcoholic solution of the base (1 mol.) and *d*-camphorsulphonic acid (2 mols.), either a dl-*base* d-*acid* salt, $[\alpha]_{5791}$ + 24·3°, or a l-*base* d-*acid* salt, $[\alpha]_{5791}$ + 15·2°, separated first, and from an absolute methyl-alcoholic solution either the *dl*-base *d*-acid salt or the d-*base* d-*acid* salt, $[\alpha]_{5791}$ + 38·1°, crystallised first. By inoculation of the ethyl-alcoholic solution with *l*-base *d*-acid salt, the separation of partial racemate could be prevented, but straightforward re-crystallisation of the impure *l*-base *d*-acid salt was accompanied by complete racemisation. Moreover, the *d*-base *d*-acid salt could not be obtained from the ethyl-alcoholic mother-liquors, nor the *l*-base *d*-acid salt from the methyl-alcoholic. Corresponding salts were obtained by means of *l*-camphorsulphonic acid.

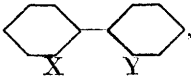
Although these results suggested salts of a very easily racemised base, the specific rotation, $[\alpha]_{5791}$ − 24·6°, of an acetone solution of the *l*-base remained unchanged during 3 days. Addition of a little pyridine to the acetone solution caused no racemisation during 24 hours, although the base was rendered inactive when its pyridine solution was kept for 10 minutes at 100°. We were unable to study the racemisation of the base and its hydrochloride, since these were insoluble even in hot alcohol, in which the camphorsulphonates had been shown to racemise.

Phenyl benzidinedisulphonate differs in two important respects from all other diphenyl compounds which have been resolved: (1) It has only two substituents in the 2 : 2′ : 6 : 6′-positions. 1 : 1′-Dinaphthyl-8 : 8′-dicarboxylic acid was resolved by Stanley (*J. Amer. Chem. Soc.*, 1931, **53**, 3104) and Meisenheimer and Beisswenger (*Ber.*, 1932, **65**, 32), but there is one marked difference between derivatives of 1 : 1′-dinaphthyl and those of diphenyl, *viz.*, groups attached to the 8- and 8′-positions in the dinaphthyl have a rigidity of spatial orientation which cannot be reproduced in the diphenyl series proper, and therefore each series must be treated separately. (2) The atom (sulphur) attached to the 2 : 2′-positions is itself attached to *three* other atoms, whereas compounds previously resolved have contained, in those positions, atoms to which not more than *two* other atoms have been directly attached (NO_2, CO_2H, etc.). Consideration of Fig. 2 shows that, whilst if the sulphur atom carried only two oxygen atoms these could swing away from the opposed 2′-hydrogen atom, this cannot happen nearly so readily when there are three oxygen atoms attached to the sulphur. In constructing the diagram, a mean value of 1·0 Å has been taken for r_S, and 0·70 Å for r_O.

Fig. 2 (bottom half) shows that, if the centres of (1) the carbon atoms in the left-hand benzene nucleus, (2) the sulphur atom attached to it, and (3) one oxygen atom (O_1) are in a plane, then (assuming a tetrahedral disposition of the sulphur valencies), neither the 6′-carbon atom nor the hydrogen attached to it can be in that plane. When the sulphur atom is rotated about the axis AB until an oxygen atom (O_2) is in the above plane, but on the side away from the 6′-carbon atom, the two other oxygen atoms (O_3) are in the positions where they can produce least effect as regards the 6′-hydrogen atom, and it is clear that in a purely mechanical model this hydrogen atom could pass both the sulphur and the oxygen atoms. On the average, however, one oxygen atom will be in the mean position represented by O_4, since the sulphur atom is capable of rotation about the axis AB. In this average position, the oxygen atom will cause dissymmetry of the whole molecule, and this effect is made more powerful owing to the fact that a similar situation is present on the other side of the diphenyl nucleus (SO_2·OPh group attached to carbon atom 2′; O_4 in the mean position, and the other two oxygens in the correct positions relative to O_4 shown in the top half of the diagram), for it is unlikely that the rotations of the two sulphur atoms would synchronise.

Experiments are in progress to determine to what extent this "dynamic" effect of atoms attached to atoms (particularly ones with radii considerably less than 1·0 Å) substituted in the 2- and 2′-positions can function.

We have also been investigating the resolution of various 2 : 2′-disulphonic acids of diphenyl, and until our experiments are carried further only general conclusions can be drawn as to the possible effect of the phenyl (ester) groups present in our optically active base. They cannot be the prime cause of dissymmetry, and would appear merely to render one oxygen atom in each sulphophenoxyl group a slightly more efficient obstacle.

While these investigations were in progress, Stanley and Adams's failure to resolve diphenyl- and benzidine-2 : 2′-disulphonic acid, which they thought might exhibit molecular dissymmetry, was published (*J. Amer. Chem. Soc.*, 1930, **52**, 4471). Their method (*ibid.*, p. 1200) of calculating the probable obstacle effect of groups in the 2-, 2′-, 6-, and 6′-positions, *e.g.*, in the compound 

, is, essentially, to regard X and Y as taking effect along the straight line (2·90 Å in length) joining the centres of the 2- and 2′-carbon atoms. Thus, for X = Y = CH_3, Stanley and Adams add together values for the links C_2—CH_3 and C_2'—CH_3, and obtain the figure 3·46 Å. The difference, 3·46—2·9, *viz.*, 0·56 Å, is called the "interference." This method appears to have little theoretical justification, and could be used for prediction purposes only when summation of the C_2—X and C_2'—Y links gives a figure either considerably larger or considerably smaller than 2·9 Å.

EXPERIMENTAL.

Phenyl 2-*chloro*-5-*nitrobenzenesulphonate* was obtained by heating 2-chloro-5-nitrobenzenesulphonyl chloride (50 g.), PhOH (30 g.), and anhyd. Na_2CO_3 (20 g.) at 100° until reaction ceased. H_2O was added, and the solid washed with alkali. It (53 g.) formed needles, m. p. 92—93°, from light petroleum (b. p. 60—80°)–C_6H_6 (Found: Cl, 11·3. $C_{12}H_8O_5NClS$ requires Cl, 11·3%), and was reduced by $SnCl_2$ in AcOH–HCl aq. to the 5-*amino*-ester, small needles, m. p. 75—76°, from EtOH aq. (Found : S, 11·3. $C_{12}H_{10}O_3NClS$ requires S, 11·3%).

2-Iodo-5-nitrobenzenesulphonic Acid.—A cold conc. solution containing 50 g. of *p*-nitroaniline-2-sulphonic acid, 25 g. of anhyd. Na_2CO_3, and 20 g. of $NaNO_2$ was added to dil. H_2SO_4 and ice and then poured into KI (60 g.) in dil. H_2SO_4. The Na salt of the iodosulphonic acid (75 g.) did not react with finely divided Cu in boiling H_2O (compare Barber and Smiles, J., 1928, 1145).

2-Iodo-5-nitrobenzenesulphonyl chloride (47 g.), obtained from the sodium salt (50 g.) and PCl_5 (1·75 mols.), formed colourless plates, m. p. 122—123°, from AcOH aq. (Found : Cl + I, 46·9. $C_6H_3O_4NClIS$ requires Cl + I, 46·7%).

Phenyl 2-iodo-5-nitrobenzenesulphonate (24 g.), obtained from the chloride (20 g.), PhOH (10 g.), and anhyd. Na_2CO_3 (6 g.) at 100°, crystallised from EtOH in long rectangular needles, m. p. 128—129° (Found : I, 31·35. $C_{12}H_8O_5NIS$ requires I, 31·3%).

Phenyl 4 : 4′-Dinitrodiphenyl-2 : 2′-disulphonate.—(a) Phenyl 2-chloro-5-nitrobenzenesulphonate was heated with an eq. wt. of copper-bronze at 275°, the product extracted with hot *o*-$C_6H_4Cl_2$, and the solvent removed. The residue of *disulphonate* crystallised from EtOH aq. in needles, m. p. 149—150°, but the yield was poor and variable (Found : S, 11·2. $C_{24}H_{16}O_{10}N_2S_2$ requires S, 11·5%). (b) Phenyl 2-iodo-5-nitrobenzenesulphonate (240 g.) and copper-bronze (240 g.) were heated at 205°. The disulphonate (112 g.) crystallised from the *o*-$C_6H_4Cl_2$ extract on cooling.

dl-*Phenyl Benzidine-2 : 2′-disulphonate.*—The above disulphonate (11 g.) in AcOH (38 c.c.) was boiled for 2 hrs. with $SnCl_2$ (42 g.) in conc. HCl (38 c.c.), cooled, and rendered strongly alkaline. The solid was repptd. from excess of hot dil. HCl by alkali and crystallised from light petroleum (b. p. 60—80°)–Me_2CO or AcOEt; small square plates, m. p. 226—227° (Found : S, 12·6. $C_{24}H_{20}O_6N_2S_2$ requires S, 12·9%). Yield, 80 g. from 120 g. of dinitro-compound.

Optical Resolution of dl-*Phenyl Benzidine-2 : 2′-disulphonate.*—A solution of the base (10 g.) and *d*-camphorsulphonic acid (9·4 g.) in hot abs. EtOH (900 c.c.) deposited, on cooling, 9 g. of salt in long rectangular needles, $[\alpha]_{5791}$ + 21·5° in EtOH ($l = 4$; $c = 0·2502$; $\alpha_{5791} = +0·215°$). The mother-liquor on concn. gave 1·9 g. of salt in fine needles, $[\alpha]_{5791}$ + 14·9°, and then 1·8 g., $[\alpha]_{5791}$ + 15·2° : these two crops were combined.

The mother-liquor, allowed to evaporate spontaneously or concentrated by distillation, gave salts having $[\alpha]_{5791}$ + 22·6°. No trace of *d*-base *d*-acid salt was obtained.

The salts having $[\alpha]_{5791}$ + 21·5° and + 22·6° both gave inactive base when decomposed with cold dil. NH_3 aq. The mixture of salts having $[\alpha]_{5791}$ + 14·9° and + 15·2° decomposed to give a base having $[\alpha]_{5791}$ − 21·4° in Me_2CO.

On crystallising the partial racemate from EtOH, the rotation increased to $[\alpha]_{5791}$ + 24·3° (in EtOH).

The salt having $[\alpha]_{5791}$ + 15·2°, when crystallised from EtOH, gave a salt with $[\alpha]_{5791}$ + 23·4°, showing that the salt had racemised in hot EtOH.

In another resolution with *d*-camphorsulphonic acid (20 g. of base and 18·8 g. of Reychler's acid), the solution was seeded with the salt having $[\alpha]_{5791}$ + 14·9°. The crop which separated had $[\alpha]_{5791}$ + 15·2° and again gave a *l*-base.

During a number of experiments there were obtained crops with $[\alpha]_{5791}$ intermediate between + 15° and + 20°. These on being decomposed gave *l*-base of lower rotation than did the salt having $[\alpha]_{5791}$ about + 15°.

A mixture of 1 mol. of *dl*-base with 2 mols. of *d*-camphorsulphonic acid had $[\alpha]_{5791}$ + 24·8° in EtOH. A mixture of 1 mol. of base with 1 mol. of acid was very sparingly soluble in EtOH, and its rotation could not be taken. This clearly shows that none of the above crops could have been of the type 1 base, 1 acid; a typical analysis of one of these crops is recorded: 0·5702 g. of salt, titrated with *N*/10-KOH, required 11·8 c.c. $C_{44}H_{52}O_{14}N_2S_4$ requires 11·9 c.c.

The racemic base (10 g.) and *l*-camphorsulphonic acid (9·4 g.) were dissolved in 1 l. of hot EtOH. On cooling, 10·9 g. of salt were obtained having $[\alpha]_{5791}$ − 21·4° in EtOH ($l = 4$; $c = 0{\cdot}2464$; $\alpha_{5791} = -0{\cdot}21°$). The conc. mother-liquor gave 3·3 g. of salt, $[\alpha]_{5791}$ − 16·3°. This salt when decomposed gave a *d*-base having $[\alpha]_{5791}$ + 26·3° in Me_2CO. As before, the partial racemate crystallised in long rectangular needles, and the diastereoisomeric salt in fine needles. On gradual or rapid removal of the rest of the mother-liquor, only racemic salt was obtained. No trace of the *l*-base *l*-acid salt was obtained.

The racemic base (5 g.) and *d*-camphorsulphonic acid (4·7 g.) were dissolved in 500 c.c. of hot MeOH. On cooling, 3·3 g. of salt separated, having $[\alpha]_{5791}$ + 38·1° in EtOH ($l = 4$; $c = 0{\cdot}2492$; $\alpha_{5791} = +0{\cdot}38°$). This salt when decomposed with NH_3 aq. gave a base with $[\alpha]_{5791}$ + 9·9° in Me_2CO. The salt having $[\alpha]_{5791}$ + 38·1°, after being boiled in MeOH, had $[\alpha]_{5791}$ + 20·4° in EtOH.

d-*Phenyl benzidine*-2 : 2′-*disulphonate* crystallised from Me_2CO–light petroleum (b. p. 60—80°) in leaflets, m. p. 222—223°, and had $[\alpha]_{5791}$ + 28·0° in Me_2CO ($l = 4$; $c = 0{\cdot}1338$; $\alpha_{5791} = +0{\cdot}15°$) (Found: S, 12·9%).

l-*Phenyl benzidine*-2 : 2′-*disulphonate* was similarly obtained, m. p. 222—223°, $[\alpha]_{5791}$ − 24·6° in Me_2CO ($l = 4$; $c = 0{\cdot}1524$; $\alpha_{5791} = -0{\cdot}15°$).

Preliminary experiments carried out over a year ago showed that the racemic base condensed with *d*-oxymethylenecamphor to give a compound which crystallised from mixtures of $CHCl_3$ or C_6H_6 and light petroleum in fractions having different specific rotations. They demonstrated that the base was capable of optical activity, but it was found impossible to remove the camphor group by the ordinary methods.

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