186. *Molecular Dissymmetry due to symmetrically placed Hydrogen and Deuterium. Part I. The Resolution of α-Pentadeuterophenylbenzylamine.*

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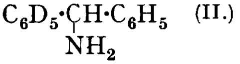
The preparation of organic compounds containing deuterium has rendered possible an examination of the very intriguing possibility of optical activity due to dissymmetry arising from the difference between hydrogen and deuterium. We have been engaged on the question for nearly a year, and in view of the failure of Gärtner and Erlenmeyer (*Helv. Chim. Acta*, 1936, **19**, 331) to obtain evidence of dissymmetry in one case, we think it advisable to place on record work proving that resolution of such compounds is possible.

According to the theory of Boys (*Proc. Roy. Soc.*, 1934, *A*, **144**, 655), such activity might be expected to be small, and our results might be taken to confirm this. No calculation of the extent of the activity from the theoretical views of Werner, Kuhn, and Born has yet been made on account of the lack of certain physical data. The actual preparation of a suitable compound of the type CXYHD is no easy matter and after considering various possibilities we decided to examine α-pentadeuterophenylbenzylamine (II). The main reason for this choice was the hope that a compound containing phenyl and pentadeuterophenyl would give a greater activity than one in which the dissymmetry was due to single atoms of hydrogen and deuterium.

Pentadeuterobenzophenone (I) was prepared from hexadeuterobenzene (J., 1935, 851) and benzoyl chloride by the Friedel–Crafts reaction. Although this reaction may be criticised on account of the reported interchanges, (i) $C_6H_6 + 6DCl \xrightleftharpoons{Al_2Cl_6} C_6D_6 + 6HCl$ (Klit and Langseth, *Nature*, 1935, 956) and (ii) $C_6D_6 + Cl{\cdot}CO{\cdot}NH_2 \xrightarrow{Al_2Cl_6} C_6D_3H_2{\cdot}CO{\cdot}NH_2$ (Erlenmeyer, *loc. cit.*, p. 337), the experimental conditions were arranged to expedite the removal of the evolved deuterium chloride and the analytical data prove that the deuterium content was unaltered. The exchange of deuterium and hydrogen in balanced amounts between the two benzene nuclei is much less likely to occur; nevertheless this problem is being investigated by the examination of the Beckmann transformation of pentadeuterobenzophenoneoxime. This compound was reduced in alkaline solution to the amine (II) and the base was resolved by fractional crystallisation of its d- and l-*hydrogen tartrates*, the specific rotations of which reached constant values of ± 13·2° after some ten recrystallisations from ethyl alcohol and light petroleum mixtures. The oxalates of the *d*- and *l*-bases obtained from these salts only displayed the low activity of $\alpha \pm 0{\cdot}02°$, corresponding to $[\alpha]_D - 2{\cdot}5°$ for the *oxalate* obtained from the d-*tartrate* and $+ 2{\cdot}2°$ for the enantiomorphous form. In this connection it should be noted that in the case of α-phenylethylamine the less soluble tartrates formed are the *d*-base *l*-tartrate and the *l*-base *d*-tartrate. In view of the fact that salts of α-phenylethylamine show much lower activities than the base itself, we determined the rotation of the free base (II) in alcohol with the aid of a micropolarimeter tube and found $\alpha - 0{\cdot}136°$ and $+ 0{\cdot}041°$ for 4·77% and 1·64% solutions. This gives $[\alpha]_D^{16°} - 5{\cdot}7°$ and $+ 5{\cdot}0°$ respectively.

(I.) $C_6D_5{\cdot}CO{\cdot}C_6H_5$


$C_6D_5{\cdot}\underset{NH_2}{CH}{\cdot}C_6H_5$ (II.)

Further work in this field is in progress. As the necessary lens system to get the best results from the use of the micropolarimeter tube cannot be obtained for a considerable time, we now lay claim to have proved the resolvability of the base (II), rather than to have obtained its actual specific rotation to a high degree of accuracy.

Experimental.

Pentadeuterobenzophenone (I).—Hexadeuterobenzene (0·6 g.) was placed in a small flask (3 c.c.) fitted with a short ground-in condenser tube cooled at the bottom by a water condenser and at the top by a jacket containing solid carbon dioxide. Carbon disulphide (1 c.c.) and finely powdered aluminium chloride (0·75 g.) were added, and the whole cooled in solid carbon dioxide.

Benzoyl chloride (0·8 g.) was added, the condenser attached, and the mixture refluxed for 12 hours, a trap containing caustic potash being attached directly to the condenser tube to remove the evolved deuterium chloride. The product was decomposed by boiling with water (5 c.c.) and hydrochloric acid (1 c.c.) and extracted with ether; the extract was washed with dilute caustic soda solution and water and dried over sodium sulphate. After removal of the ether, pentadeuterobenzophenone (0·95 g.) distilled at 160°/15 mm.

Pentadeuterobenzophenoneoxime.—Pentadeuterobenzophenone (0·95 g.) in alcohol (9 c.c.) was refluxed for 2 hours on the water-bath with hydroxylamine hydrochloride (1·1 g.) in water (2·7 c.c.) and caustic potash (1·8 g.) in water (2·7 c.c.). After pouring into water (12 c.c.) and acidification with dilute sulphuric acid, the *oxime* (0·95 g.) was filtered off and recrystallised from alcohol; m. p. 140°, undepressed by benzophenoneoxime (Found : C, 77·0; water, 48·4. $C_{13}H_6D_5ON$ requires C, 77·2; water, 51·4%).

α-Pentadeuterophenylbenzylamine (II).—Pentadeuterobenzophenoneoxime (0·95 g.) was reduced in dilute alkaline solution by heating for 6 hours on the water-bath with 4% sodium amalgam (150 g.), dilute acetic acid being added occasionally to diminish the concentration of alkali. The base was extracted with ether (five extractions), and the ethereal solution dried over sodium sulphate. After removal of the ether the free base (0·89 g.) was obtained as a yellow oil, which rapidly absorbed carbon dioxide.

Resolution.—l-*α-Pentadeuterophenylbenzylamine* d-*hydrogen tartrate.* Pentadeuterophenylbenzylamine (0·89 g.) was converted into the d-*hydrogen tartrate* by addition of an aqueous solution of *d*-tartaric acid (0·7 g.) and evaporation to dryness. This acid tartrate (1·2 g.), recrystallised from alcohol–light petroleum, formed fine needles, m. p. 181° (Found : C, 60·3; water, 52·0. $C_{13}H_8D_5N,C_4H_6O_6$ requires C, 60·3; water, 52·1%. $C_{13}H_{13}N,C_4H_6O_6$ requires C, 61·3; water, 51·4%). On further recrystallisation the specific rotation increased regularly from + 10·8° to a limiting value of + 13·2° for l-*α-pentadeuterophenylbenzylamine* d-*hydrogen tartrate,* m. p. 181° (Found : C, 60·4; water, 55·2%).

d-*α-Pentadeuterophenylbenzylamine* l-*hydrogen tartrate.* From the collected mother-liquors, the corresponding salt with *l*-tartaric acid was prepared. The l-*hydrogen tartrate* (0·65 g.), m. p. 181°, was recrystallised from alcohol–petroleum until the constant value of $[\alpha]_D$ — 13·2° was obtained (Found : C, 60·5; water, 53·9%).

No. of recrystns.	3	4	7	8	9	10
Substance, g.	0·92	0·85	0·44	0·348	0·270	0·265
$[\alpha]_D$	+10·8°	+11·3°	+12·6°	+13·0°	+13·3°	+13·2°

No. of recrystns.	3	5	9	11	13
Substance, g.	0·29	0·25	0·21	0·14	0·088
$[\alpha]_D$	−10·4°	−10·5°	−11·3°	−13·4°	−13·1°

l-*α-Pentadeuterophenylbenzylamine Oxalate.*—*l*-Pentadeuterophenylbenzylamine *d*-hydrogen tartrate (0·27 g.) was shaken with caustic soda solution, an ethereal extract of the base washed with alkali and water and dried over sodium sulphate, and the ether removed through a fractionating column, leaving the base (0·16 g.); this was treated with an aqueous solution of oxalic acid (0·06 g. of the dihydrate), giving the normal *oxalate* (0·16 g.) which, recrystallised from water, formed needles, m. p. 204°; mixed with benzhydrylamine oxalate, m.p. 205° (Found : C, 72·1; water, 54·7. $2C_{13}H_8D_5N,C_2H_2O_4$ requires C, 72·1; water, 56·2%). Approximately 0·4% alcoholic solutions of this oxalate gave α — 0·023°, — 0·017°, and — 0·024°, corresponding to $[\alpha]_D^{17°}$ — 2·6°, — 2·4°, and — 2·5° respectively. The mean deviation from the mean for a series of sixty observed readings was 0·006°.

d-*α-Pentadeuterophenylbenzylamine Oxalate.*—The corresponding oxalate from the *d*-pentadeuterophenylbenzylamine *l*-hydrogen tartrate ($[\alpha]_D$ — 13·3°) gave values of + 0·013° and + 0·015°, corresponding to $[\alpha]_D^{16°}$ + 1·9° and + 2·2°. The mean deviation from the mean was 0·005°.

l-*α-Pentadeuterophenylbenzylamine.*—*l*-Pentadeuterophenylbenzylamine oxalate ($[\alpha]_D$ — 2·5°) was converted into the free base. About 10 mg. of this amine and about 0·25 c.c. of alcohol were weighed accurately into a small weighing-bottle by means of a microbalance. The density of the solution was determined with a micropyknometer (J., 1935, 1220), and hence the concentration of the base calculated. A micropolarimeter tube, 5 cm. in length, was filled with the solution and values for α of — 0·14° observed, giving $[\alpha]_D^{16°}$ — 5·7° for the free base in a 4·77% solution in alcohol. The mean deviation from the mean of the readings was 0·010°.

d-*α-Pentadeuterophenylbenzylamine.*—*d*-Pentadeuterophenylbenzylamine oxalate (7 mg., $[\alpha]_D$ + 2·2°) was converted into the free base (5·5 mg.). A 1·64% solution of this amine in alcohol gave observed rotations of 0·041°, giving a value for $[\alpha]_D^{16°} = +5·0°$. The mean deviation from the mean over a series of twenty readings was 0·009°.

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