

104. Molecular Dissymmetry due to Restricted Rotation in the Benzene Series: An Optically Active Ethylenic Derivative.

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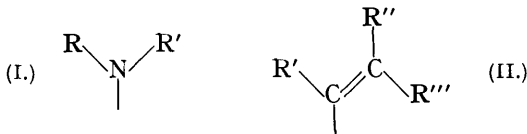
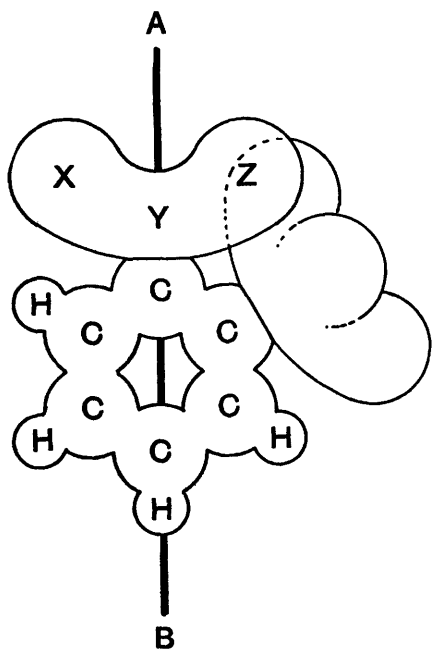
o-(β -Dimethyl- α -isopropylvinyl)phenyltrimethylammonium iodide (VI) has been synthesised and resolved through the corresponding *d*-bromocamphorsulphonate. The *d*- and *l*-iodides were obtained with molecular rotations $[M]_{5461} + 55^\circ$ and -58° . The molecular dissymmetry of the compound is referred to the restrictive effect of the NMe_3 group on the rotation of the adjacent $\text{CPr}^{\beta}:\text{CMe}_2$ group about the single bond linking it to the benzene nucleus. The optical activity is stable at 100° .

The analogous compound (VII) in which a β -hydrogen atom of the vinyl group is unsubstituted could not be resolved.

MOLECULAR dissymmetry arising from the restriction of rotation about a single bond (first observed in the diphenyl series by Christie and Kenner, J., 1922, 121, 614) was shown by one of us and K. A. C. Elliott (J., 1928, 1292) to occur in *peri*-substitution derivatives of naphthalene, and later, with R. M. Kelham (J., 1937, 274), in certain *o*-substituted derivatives of benzene.

The derivatives of naphthalene and benzene in which this effect was demonstrated contained a grouping XYZ (figure) which could rotate about the axis AB when the adjacent positions (*o*- or *peri*-) were occupied by hydrogen atoms, but was confined between more or less narrow limits of rotation when a large substituent, such as $-\text{SO}_3^-$ or $-\text{NMe}_3^+$, was introduced into one of these positions.

The types of structure available for the rotating complex are limited by the necessity for (or, at any rate, the desirability of) planar configuration, and those most obviously suitable are the substituted amino-group (I) and the substituted vinyl

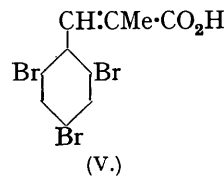
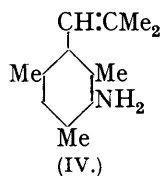
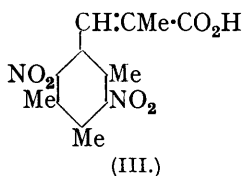


group (II) (the former being effectively planar on account of the easy transition between its two non-planar forms).

In the experiments of Mills and Elliott and of Mills and Kelham (*loc. cit.*) a substituted amino-group was employed. In the present communication it is shown that a substituted

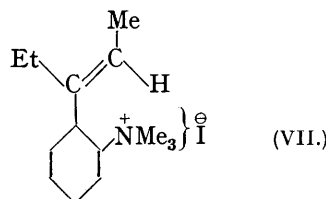
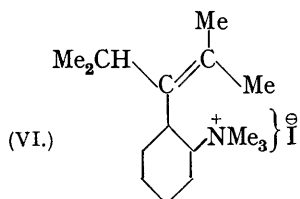
vinyl group likewise suffers restriction of rotation when attached to a benzene nucleus with a suitable *o*-substituent.

Compounds containing a substituted vinyl group have been investigated from this point of view by Maxwell and Roger Adams (*J. Amer. Chem. Soc.*, 1930, 52, 2959), who examined the compounds (III), (IV), and (V), but found them non-resolvable into optical



antimers—presumably on account of the presence of an α -hydrogen atom in the $\beta\beta$ -disubstituted vinyl groups (CH:CRR') employed. With a hydrogen atom in this position the vinyl-benzene link can probably be distorted so as to allow the 'CRR' complex to pass over the *o*-substituents.

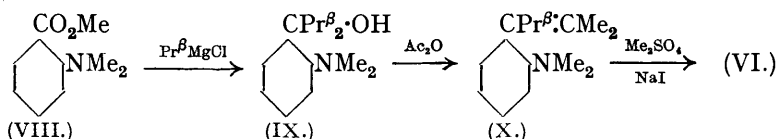
The compound (VI), in which we have been able to demonstrate the effect of restricted rotation, contained the $\beta\beta$ -dimethyl- α -isopropylvinyl group as the rotating complex, and the kationic $-NMe_3^+$ group as the obstructing *o*-substituent.



It was resolved into stable, optically active components by means of *d*-bromocamphorsulphonic acid, the *d*- and *l*-iodides obtained showing the molecular rotations $[M]_{5461} + 55^\circ$ and $- 58^\circ$. The optical stability of these salts was very considerable, and their aqueous solutions retained their optical activity practically undiminished after 8 hours' boiling. This resistance to racemisation, which contrasts markedly with the optical lability of the compounds containing a substituted amino-group as the rotating complex, is in accordance with the large overlap of the groups indicated by the atomic dimensions concerned.

The melting point-composition curve of the *d*- and *l*-iodides approximates to a horizontal straight line, indicating that the enantiomorphous salts form mixed crystals. The atomic groups $(CH_3)_2CH\cdot$ and $(CH_3)_2C\cdot$: thus seem to be somewhat readily interchangeable in the crystal lattice.

We also examined the compound (VII), which differs from (VI) in containing the methylethylvinyl group in place of the dimethylisopropylvinyl group, but found it non-resolvable—presumably on account of the insufficient overlap of the substituent groups.



The compound (VI) was obtained from methyl *o*-dimethylaminobenzoate (VIII). Treatment of this ester with isopropylmagnesium chloride gave the tertiary alcohol (IX), which on dehydration with acetic anhydride yielded the vinyl derivative (X). The latter, heated with methyl sulphate, gave a quaternary ammonium salt from which the iodide (VI) was finally obtained.

EXPERIMENTAL.

Methyl o-Dimethylaminobenzoate (VIII) (compare Willstätter and Kahn, *Ber.*, 1904, 37, 408).—Methyl sulphate (630 g.) was added in six portions, with cooling as necessary, to fused methyl anthranilate (750 g.), and the mixture heated for 1 hour on a water-bath. The resulting

viscous mass was dissolved in water, sodium hydroxide solution added to give an alkaline reaction, and the product extracted with ether. After removal of the ether, the foregoing treatment with methyl sulphate (1 equiv.), followed by addition of alkali and ether extraction, was repeated on the product. The crude ester thus obtained was boiled with excess of acetic anhydride; the mixture was poured into water and acidified with hydrochloric acid and the acetyl derivatives of the unchanged and the monomethylated ester were removed by filtration. Methyl *o*-dimethylaminobenzoate was then liberated with alkali and extracted with ether. It had b. p. 137—142°/17 mm. Yield, 540 g.

o-Dimethylaminophenyl-diisopropylcarbinol (IX).—A mixture of methyl *o*-dimethylaminobenzoate (80 g.) and ether (100 c.c.) was dropped into an ice-cooled, stirred ethereal solution of isopropylmagnesium chloride prepared from isopropyl chloride (78.5 g.) and magnesium (24 g.). The whole was heated for 30 minutes on the water-bath and left overnight; ice and dilute sulphuric acid were then added. The solution was neutralised with excess of sodium bicarbonate solution, and the ethereal layer dried over sodium sulphate. On evaporation of the ether the *carbinol* crystallised in large hexagonal prisms sufficiently pure for the following stage (yield, 65% of the theoretical). Recrystallised from dilute alcohol, the *carbinol* had m. p. 66° (Found : C, 76.7; H, 10.8; N, 6.2. $C_{15}H_{25}ON$ requires C, 76.6; H, 10.7; N, 6.0%).

o-Dimethylamino- $\beta\beta$ -dimethyl- α -isopropylstyrene (X).—The *carbinol* (IX) was boiled with excess of acetic anhydride for 12—14 hours. The acetic acid and unchanged anhydride were removed by distillation and the residual oil was fractionated under reduced pressure. The fraction, b. p. 127—132°/15 mm., was the unsaturated base (X); the higher fractions contained unchanged *carbinol*. With aqueous perchloric acid (X) gave a crystalline *perchlorate*, which could be crystallised from benzene—light petroleum (Found : C, 56.6; H, 8.1; N, 4.4; Cl, 11.0. $C_{15}H_{23}N, HClO_4$ requires C, 56.7; H, 7.6; N, 4.4; Cl, 11.2%).

o-($\beta\beta$ -Dimethyl- α -isopropylvinyl)phenyltrimethylammonium Iodide (VI).—The base (X) was heated with methyl sulphate (10% excess) at 130° for 1 hour. The gummy product was dissolved in water, the solution made alkaline to phenolphthalein with sodium hydroxide, and unchanged tertiary base removed by ether extraction. The yellow crystalline quaternary *picrate* was then precipitated by adding aqueous picric acid solution. It can be recrystallised from dilute alcohol (Found : C, 57.2; H, 6.3; N, 12.3. $C_{22}H_{28}O_7N_4$ requires C, 57.4; H, 6.1; N, 12.2%).

The precipitated *picrate* was added to excess of saturated sodium iodide solution, and the mixture extracted with chloroform. On evaporation of the chloroform the *iodide* was left; after recrystallisation from acetone and absolute ether, it was obtained as colourless needles, m. p. 160° (Found : C, 53.4; H, 7.4; N, 3.9; I, 35.2. $C_{16}H_{26}NI$ requires C, 53.5; H, 7.2; N, 3.9; I, 35.4%).

Optical Resolution of the Quaternary Iodide (VI).—The inactive *iodide* was converted into the *d*-bromocamphorsulphonate by treatment in aqueous solution with an equivalent quantity of silver bromocamphorsulphonate. The residue from the evaporated filtrate was recrystallised from anhydrous acetone—ether. Resolution of the bromocamphorsulphonate was effected by crystallisation from benzene. The first crop was an evident mixture of two crystalline forms—long needles and short prisms, the latter being the less soluble. By extracting the mixture with a little hot benzene and recrystallising the undissolved residue from benzene, repeating these operations three times, and then again recrystallising the product from benzene, a salt was obtained which had in aqueous solution ($c = 1.187$, $l = 2$, $\alpha_{5461} = 1.26^\circ$) a molecular rotation $[M]_{5461} + 288^\circ$. Since the molecular rotation of the *d*-bromocamphorsulphonate anion is 346° (Pope and Read, J., 1910, **97**, 2200), this value indicated that the salt contained the cation derived from the *l*-base with a molecular rotation of about -58° .

The *l*-*iodide* was obtained from this bromocamphorsulphonate by saturating the aqueous solution with sodium iodide and recrystallising the precipitate from anhydrous chloroform—ether (Found : C, 53.8; H, 7.6; N, 3.8; I, 35.5%), m. p. and mixed m. p. with the inactive *iodide* 160°. The molecular rotation of the *l*-*iodide* in aqueous solution ($c = 1.185$, $l = 2$, $\alpha_{5461} = -0.38^\circ$) was $[M]_{5461} - 58^\circ$.

To get the bromocamphorsulphonate of the *d*-base, the benzene extracts and mother-liquors obtained in isolating that of the *l*-base were united, and the dissolved material caused to crystallise by the addition of light petroleum (b. p. 60—80°). The crop deposited was extracted with insufficient benzene for complete solution, and the extract left to crystallise after addition of a little petrol. After this process had been repeated thrice, a crop of fine needles was obtained containing a few large prisms of the less soluble isomer, which were removed by hand-picking. The needles were then recrystallised twice more from benzene, yielding a product with the molecular rotation $[M]_{5461} + 394^\circ$, which was used for preparing the *d*-*iodide* by the same

method as had been used for the *l*-antimer (Found : C, 53.7; H, 7.5; N, 3.9; I, 35.5%), m. p. and mixed m. p. with the inactive iodide 160°. The molecular rotation $[M]_{5461}$ found for the *d*-iodide in aqueous solution ($c = 1.005$, $l = 2$, $\alpha_{5461} = 0.305^\circ$) was $+ 55^\circ$.

Aqueous solutions of the *d*- and of the *l*-iodide were found to have retained at least 97% of their activity after keeping at 100° for 8 hours.

o-Dimethylaminophenyldiethylcarbinol.—Methyl *o*-dimethylaminobenzoate (80 g.), dissolved in ether (100 c.c.), was added to an ethereal solution of ethylmagnesium bromide prepared from ethyl bromide (109 g.) and magnesium (24 g.). The carbinol was isolated in the same way as the diisopropyl homologue as an oil which could not be obtained crystalline. Aqueous perchloric acid gave a *perchlorate*, crystallising from water in long needles (Found : C, 50.6; H, 7.0; N, 4.4; Cl, 11.4. $C_{13}H_{21}ON, HClO_4$ requires C, 50.7; H, 7.2; N, 4.5; Cl, 11.4%).

o-Dimethylamino- β -methyl- α -ethylstyrene.—The carbinol was dehydrated by boiling with acetic anhydride, and the unsaturated base, b. p. 117—122°/18 mm., isolated in the same way as the $\beta\beta$ -dimethyl homologue (X). Aqueous picric acid gave a *picrate*, which was recrystallised from dilute alcohol (Found : C, 54.6; H, 5.5; N, 13.7. $C_{13}H_{19}N, C_6H_3O_7N_3$ requires C, 54.5; H, 5.2; N, 13.4%).

o-(β -Methyl- α -ethylvinyl)phenyltrimethylammonium Iodide.—The tertiary base was converted into the quaternary *picrate* and thence into the *iodide*, m. p. 157°, in precisely the same manner as the dimethyl homologue (X) (Found for the picrate : C, 55.3; H, 5.6; N, 13.0. $C_{20}H_{24}O_7N_4$ requires C, 55.5; H, 5.6; N, 12.9%. Found for the iodide : C, 50.9; H, 6.8; N, 4.4; I, 38.5. $C_{14}H_{22}NI$ requires C, 50.7; H, 6.6; N, 4.2; I, 38.4%).

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