2. *A Determination of Molecular Symmetry in the αβ-Diethyldibenzyl Series.*

By C. H. Carlisle and Dorothy Crowfoot.

X-Ray crystallographic measurements on a number of compounds belonging to the diethylstilbene and diethyldibenzyl series have been carried out. These have proved that the higher-melting isomers in the diethyldibenzyl series which are derived from solid diethyldibenzyl are *meso*-compounds, whereas the lower-melting isomers from liquid diethyldibenzyl are racemic.

During the preparation of diethyldibenzyl derivatives related to diethylstilboestrol, two isomeric sets of compounds are encountered which should theoretically belong severally to the *meso*- and the racemic stereoisomeric series (Dodds, Goldberg, Lawson, and Robinson, *Proc. Roy. Soc.*, 1939, *B*, **127**, 140; Kerschbaum, Kleedorfer, Prillinger, Wessely, and Zajic, *Naturwiss.*, 1939, **27**, 131). The distinction between the two series is of interest in view of the very different biological activity of the different isomers; and this distinction can be made through comparatively simple *X*-ray crystallographic measurements on certain of the compounds concerned.

The use of *X*-ray measurements in this connection depends on the fact that the individual molecules of a *meso*-compound must themselves possess symmetry, whereas those in a racemic compound or mixture are asymmetric. Detailed *X*-ray analysis necessarily reveals the molecular symmetry in the course of the complete structure determination; but this is a long process and it is often possible (cf. Astbury and Yardley, *Phil. Trans.*, 1924, *A*, **224**, 221; Bernal, *Ann. Reports*, 1933, **30**, 411) to make use of the first and rapid stages of *X*-ray measurement to deduce this property. In certain crystal structures where the molecules possess symmetry, this symmetry contributes to that of the crystal as a whole, and consequently the number of molecules in the unit cell is smaller than the number of asymmetric units required by the crystallographic space-group present. Here, simple measurement of the crystal unit cell size, density, and space-group suffices to determine the molecular symmetry. The principal limitations to the general application of these measurements are two-fold. First, often the molecular symmetry (particularly where this is high) does not appear in the crystal symmetry; and secondly, crystals occasionally show higher symmetry than that actually contributed by the molecules owing to statistical disorder in the crystal structure. In the present problem it is possible to surmount these difficulties by examining a sufficient number of different types of compounds belonging to the two series. Several of these prove favourable for the symmetry determination, and since these include a variety of chemical derivatives, the probability that statistical disorder is present and might affect the conclusions reached is extremely small.

The following table records the *X*-ray measurements carried out on the two series of diethyldibenzyl derivatives and also includes for comparison data on diethylstilboestrol and several related compounds. In the diethylstilbene series there is a double bond at the centre of the molecule, and doubtless the general arrangement of the groups around this bond is *trans*- in the compounds examined, *i.e.*, the molecules in all cases have a centre of symmetry. However, this point is clearly established by the present measurements only in the case of diethylstilboestrol dipropionate. In the other compounds the situation may be similar to that in stilbene itself, where detailed analysis has demonstrated molecular symmetry not apparent from the preliminary measurements (Robertson, *Proc. Roy. Soc.*, 1936, *A*, **154**, 187; 1937, *A*, **162**, 568). Dihydroxydiphenylhexadiene, which is different in type but may be included here, is proved by the measurements to have a centre of symmetry, as would be expected.

Seven compounds have been examined in the diethyldibenzyl series. Diethyldibenzyl itself has only been studied in the one isomeric form, the other being liquid. Of the remaining six compounds, three are derived from the solid dibenzyl (a), and three from the liquid dibenzyl (b). The *X*-ray measurements prove that solid diethyldibenzyl and

Compound.	M. p.	Space-group.	No. of asymmetric units required in unit cell.	No. of molecules in unit cell.	*a*, A.	*b*, A.	*c*, A.	*β*.	*d*.
β-Diethylstilbene	70—71°	$P2_1/c$	4	4	7·66	20·18	9·33	93°	1·071
αβ-Diethylstilboestrol + C_6H_6	171	$P2_1/a$	4	4	10·93	12·78	13·75	90	1·189
4 : 4′-Dimethoxy-*αβ*-diethylstilbene	123—124	$P2_1/n$	4	4	7·79	24·24	10·62	122	1·154
αβ-Diethylstilboestrol dipropionate	104	*Pbca*	8	4	9·74	8·15	27·5	—	1·142
4 : 4′-Dihydroxy-*γδ*-diphenyl-$\Delta^{\beta\beta}$-hexadiene	227—228	*Pcab*	8	4	18·9	5·41	14·4	—	1·184
αβ-Diethyldibenzyl (*a*)	89—90	$P2_1/a$	4	2	7·38	19·27	5·75	117	1·089
4 : 4′-Dihydroxy-*αβ*-diethyldibenzyl (*a*)	184	$P2/a$ approx. to Pc/a	4	4	13·93	5·96	24·39	89° 20′	(1·063)
4 : 4′-Dihydroxy-*αβ*-diethyldibenzyl (*b*)	128	$P2_1/n$	4	4	7·76	18·13	11·33	92	1·143
4 : 4′-Diamino-*αβ*-diethyldibenzyl (*a*)	140	$P2_1/a$	4	2	5·50	15·21	9·35	98	1·135
* 4 : 4′-Diamino-*αβ*-diethyldibenzyl (*b*)	97—98	*Cc*	4	4	10·15	19·89	7·67	89	1·136
4 : 4′-Dicarbomethoxy-*αβ*-diethyldibenzyl (*a*)	145—146	$P\bar{1}$	2	1	7·97	8·39	8·30	*α*≃102 *β*≃ 98 *γ*≃113	1·194
4 : 4′-Dicarbomethoxy-*αβ*-diethyldibenzyl (*b*)	95	$P2_1/a$	4	4	15·06	7·76	17·7	108	1·175

* This was the only compound of those in this table in which the test for polarity was positive.

the diamino-compound derived from it have molecules containing a centre of symmetry, since both crystallise with two molecules in the unit cell and space-groups requiring four asymmetric units. These therefore belong to the *meso*-series. The ester (a) is in a similar category except that the space-group determination, since it depends on a negative test, *viz.*, the absence of a pyroelectric effect, is not so rigid. The crystallography of the dihydroxy-derivative (a) does not provide conclusive evidence of molecular symmetry, though even here certain confirmation that this is the *meso*-form is given by the pseudosymmetry of the crystal. The remaining three compounds, derived from liquid diethyldibenzyl, all show crystal structures in which the asymmetric unit may well be the molecule itself. The positive pyroelectric effect shown by diaminodiethyldibenzyl (b) is perhaps some positive evidence that the molecules in this crystal have no centre of symmetry, and consequently that the crystal is racemic.

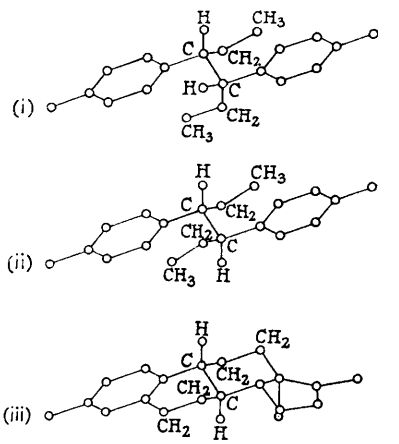


Diagram to illustrate the relation of the stereochemical form of the isomers of 4 : 4′-dihydroxy-αβ-diethyldibenzyl to that probably present in oestrone. Possible atomic arrangement in :

(i) d- *or* l-4 : 4′-*Dihydroxy-αβ-diethyldibenzyl* (*series b*).
(ii) meso-4 : 4′-*Dihydroxy-αβ-diethyldibenzyl* (*series a*).
(iii) *Oestrone.*

There are similarities, though not very close, between the crystallography of certain members of both isomeric series and that of oestrone or other compounds of the natural sex-hormone and sterol series. These similarities probably express little more than the fact that the configurations of the molecules of both diethyldibenzyl series are of an extended form, perhaps that illustrated in the figure, or the variety found in dibenzyl itself (Robertson, *Proc. Roy. Soc.*, **1935**, *A*, **150**, 348). This being so, it is an interesting fact that the stereochemical arrangement of the atoms in the *meso*-series of diethyl derivatives (a) above, which is biologically the most active series, is very closely related to the stereochemical form deduced for the natural sex hormones. The fact that the *meso*-compounds have a centre of symmetry in the crystals proves that the disposition of the atoms about the central carbon–carbon bond is of the *trans*-type considered

characteristic of the junction between rings B and C of the sterol sex-hormone series (see figure).

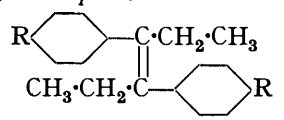
Experimental.

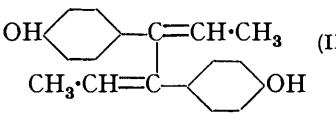
X-Ray Technique.—*X*-Ray single-crystal photographs of each compound, about three crystallographic axes, were taken on the Stubbins rotation camera. In two cases, those of diethyldibenzyl and diaminodiethyldibenzyl (b), Weissenberg photographs were taken about the symmetry axes, to confirm the presence of glide elements in the respective space-groups. The cell dimensions recorded are probably correct to $\pm 1\%$.

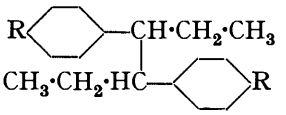
Density.—In all cases the density was determined by the flotation method in sodium chloride solution. The probable limits of error are $\pm 0{\cdot}5\%$.

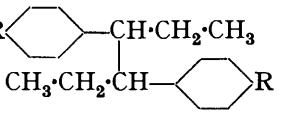
Test for Polarity.—The crystals, in turn, were placed on a well-cleaned copper plate and immersed in liquid air. A positive effect is observed if the crystals stick to the plate (Martin, *Min. Mag.*, **1931**, **22**, 519).

Morphology and Optics.

(I.) 

(II.) 

(III*a*.) 

(III*b*.) 

$\alpha\beta$-Diethylstilbene (I; R = H)	Monoclinic plates, {010} dominating, bounded by {100}, {001}, and {101}. γ parallel to b, α 12° from the a axis in the acute angle. Positive. $2E \simeq 60°$.
$\alpha\beta$-Diethylstilboestrol (I; R = OH) + C_6H_6	Monoclinic prisms, elongated along [100], bounded by {010} and {001}. α parallel to b; β and γ approximately parallel to a and c respectively. Positive.
4 : 4′-Dimethoxy-$\alpha\beta$-diethylstilbene (I; R = OMe)	Monoclinic plates with {010} dominating, bounded by {100} and {001}. γ parallel to b, β 20° from the a axis in the obtuse angle. Positive. $2E \simeq 27°$.
$\alpha\beta$-Diethylstilboestrol dipropionate (I; R = Et·CO·O)	Rhombic plates, {001} dominating, bounded by {110}. α, β, and γ parallel to a, b, and c respectively. Positive. $2E \simeq 52°$.
4 : 4′-Dihydroxy-$\gamma\delta$-diphenyl-$\Delta^{\beta\delta}$-hexadiene (II)	Rhombic laths elongated along [010], bounded by {100}, {001}, and {101}. α, β, and γ parallel to b, a, and c respectively. Negative. $2V \simeq 20°$.
$\alpha\beta$-Diethyldibenzyl (a) (III*a*; R = H)	Monoclinic plates, {010} dominating, bounded by {100} and {001}. γ parallel to b; α lies 10° from the a axis in the acute angle. Negative. $2V \simeq 30°$.
4 : 4′-Dihydroxy-$\alpha\beta$-diethyldibenzyl (a) (III*a*; R = OH) [+ $x H_2O$ or C_2H_5OH ?]	Monoclinic laths elongated along [010], bounded by {001} and {100}. Twins on {001}. β parallel to b, α and γ approximately parallel to a and c respectively. Positive. $2V \simeq 60°$.
4 : 4′-Dihydroxy-$\alpha\beta$-diethyldibenzyl (b) (III*b*; R = OH)	Monoclinic prisms, elongated along [100], bounded by {011} and {101}. β parallel to b, γ lies 22° from the c axis. Positive. $2V \simeq 54°$.
4 : 4′-Diamino-$\alpha\beta$-diethyldibenzyl (a) (III*a*; R = NH_2)	Monoclinic plates with {001} dominating, bounded by {010}, {110}, {011}. α parallel to b, γ lies 12° from the c axis in the acute angle. Positive. $2E \simeq 34°$.
4 : 4′-Diamino-$\alpha\beta$-diethyldibenzyl (b) (III*b*; R = NH_2)	Monoclinic plates with {001} dominating. β parallel to b, α about 17° from the a axis. Negative. $2V \simeq 60°$.
4 : 4′-Dicarbomethoxy-$\alpha\beta$-diethyldibenzyl (a) (III*a*; R = CO_2Me)	Anorthic plates with {001} dominating, bounded by {100} {010}, and {$\bar{1}$10}. Optic axial plane 25° from ⊥ to {001}. "Fast" extinction in (001) 10° to a axis in the acute angle. Negative. $2V \simeq 60°$.
4 : 4′-Dicarbomethoxy-$\alpha\beta$-diethyldibenzyl (b) (III*b*; R = CO_2Me)	Monoclinic laths elongated along [010], with faces {001}, {201}, and {010}. β parallel to b; γ lies 9° from the c axis in the acute angle. Negative. $2E \simeq 52°$.

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