

tracted with ether, the ether layer washed several times with water, then the solvent dried and removed by distillation. The residue was taken up in hot ethanol and cooled to deposit 1.85 g. (38.2%) of brownish prisms, m.p. 125–130°. A portion of this material was decolorized with Norit and recrystallized twice from ethanol to give white prisms, m.p. 130–131.5°. This material was used for the n.m.r. spectrum.

*Anal.* Calcd. for  $C_{13}H_{17}Cl_2Br$ : C, 34.23; H, 1.55. Found: C, 34.34; H, 1.60.

The structure of the products, inferred from the method of synthesis, was confirmed by the n.m.r. spectrum. Each of the substituted phenyl compounds gave the characteristic four-line AB multiplet expected for *para*-substitution on the aromatic nucleus.

[CONTRIBUTION FROM THE MELLON INSTITUTE, PITTSBURGH, PENNSYLVANIA]

## Nuclear Magnetic Resonance Spectra of Substituted Ethanes. II. *meso*- and *dl*-2,5-Diphenylhexanediol-2,5

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The high-resolution proton magnetic resonance spectra of the title compounds have been obtained and analyzed in terms of chemical shifts and coupling constants. Expressions for the coupling constants in terms of rotamer populations and characteristic *gauche* and *trans* coupling constants are given, and it is shown that the forms of these expressions confer some unique advantages upon compounds of this type, as subjects for the study of rotational isomerism about the central bond.  $\Delta H$  for the *meso* compound is estimated at 1.1 kcal., that for the *dl*-compound as 1.4 kcal., with the *s-trans* arrangement of the bulky groups preferred over the *gauche* arrangement.

### Introduction

Several studies<sup>1-6</sup> have been made of the proton n.m.r. spectra of 1,2-disubstituted ethanes, both for the purpose of finding appropriate values for H,H-coupling constants between pairs of protons in the *trans* and *gauche* relations to each other, and with the idea of measuring relative populations of rotamers assuming reasonable values for these constants. In the typical case of a disubstituted ethane,  $XCH_2CH_2Y$ , the conformers are those shown in Fig. 1. The populations of the three forms are related:  $p_2 = p_3 = (1 - p_1)/2$ .

Since at most temperatures interconversion between the three rotamers is rapid, n.m.r. constants which are weighted averages of those in the three forms are observed. With the usual assumption<sup>1</sup> that in a given compound *gauche* and *trans* oriented protons are coupled by characteristic amounts,  $J_g$  and  $J_t$ , one may write

$$J_{AB} = J_{A'B'} = \frac{1 + p_1}{2} J_g + \frac{1 - p_1}{2} J_t \quad (1)$$

and

$$J_{AB'} = J_{A'B} = (1 - p_1)J_g + p_1J_t \quad (2)$$

whence

$$2J_{AB} + J_{AB'} = 2J_g + J_t \quad (3)$$

$$p_1 = (J_{AB'} - J_g)/(J_t - J_g) = (J_t + J_g - 2J_{AB})/(J_t - J_g) \quad (4)$$

Two difficulties frequently occur in the analysis of the data. First, if the values of  $J_{AB}$  and  $J_{AB'}$  are nearly the same, the spectrum may display deceptive simplicity,<sup>1,4,7</sup> and only the sum of the two constants is exactly determinable under these circumstances. Second, even if exact values for this pair of constants

can be obtained, the question of which value belongs to which constant remains. The assignment cannot be made from the spectrum.<sup>8</sup> Equation 3 may be of help in discarding unreasonable values (since studies on the size of this sum have been made on ethyl derivatives and in other cases).<sup>1,9</sup> If, for example, the pair of numbers (+6 c.p.s., +8 c.p.s.) were obtained for the two constants, then the two interpretations  $J_g = +4$ ,  $J_t = +12$ ,  $p_1 = 0.5$ , and  $J_g = 4$ ,  $J_t = 14$ ,  $p_1 = 0.2$  would appear about equally attractive. Nor would lowering the temperature to increase the proportion of more stable rotamers be of any help: the same qualitative behavior would be observed whichever assignment were correct.

When a methylene group is adjacent to one carbon bearing three unlike substituents, the two protons of the methylene group are magnetically nonequivalent, and may display different chemical shifts.<sup>10</sup> This suggests that 1,2-disubstituted ethanes, where the substituents are such asymmetric groups, might be suitable for studies aimed at determining the populations of rotamers about the central C-C single bond. Such compounds can exist in *meso*- and *dl*-forms. The rotamers are as shown in Fig. 2.

For the *meso* compound, where the *gauche* forms are of equal energy and population, one may write, with the same assumptions as for  $XCH_2CH_2Y$  compounds

$$J_{AA'} = J_{BB'} = (1 - p_1)J_g + p_1J_t \quad (5)$$

$$J_{AB} = J_{A'B'} = J_{gem} \quad (6)$$

$$J_{AB'} = J_{A'B} = \frac{1 + p_1}{2} J_g + \frac{1 - p_1}{2} J_t \quad (7)$$

$$J_{AA'} + 2J_{AB'} = 2J_g + J_t \quad (8)$$

$$p_1 = (J_{AA'} - J_g)/(J_t - J_g) = (J_t + J_g - 2J_{AB'})/(J_t - J_g) \quad (9)$$

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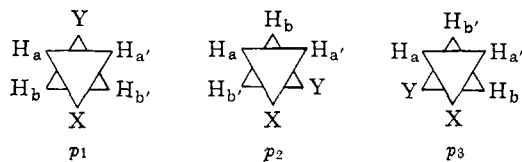


Figure 1.

In this case, there is little likelihood of confusing  $J_{AB}$  and  $J_{AB'}$ , since  $J_{gem}$  is of opposite sign<sup>11</sup> to  $J_{vic}$  and is of predictable magnitude.<sup>12</sup> Furthermore,  $J_{AB}$  is expected to be reasonably temperature independent, while  $J_{AB'}$  may be variable with temperature (provided  $p_1 \neq p_2$ ).

For the *dl*-compound,  $p_2$  may not equal  $p_3$ ; this might be detectable from an inequality of  $J_{AA'}$  and  $J_{BB'}$ , but such an inequality might be concealed by a deceptively simple spectrum! Whether or not  $p_2 = p_3$ , with the usual assumptions

$$J_{AA'} = p_1 J_g + p_2 J_g + p_3 J_t \quad (10)$$

$$J_{BB'} = p_1 J_g + p_2 J_t + p_3 J_g \quad (11)$$

$$J_{AB'} = p_1 J_t + p_2 J_g + p_3 J_g \quad (12)$$

$$= p_1 J_t + (1 - p_1) J_g$$

whence

$$J_{AA'} + J_{BB'} + J_{AB'} = 2J_g + J_t \quad (13)$$

and

$$p_1 = (J_{AB'} - J_g)/(J_t - J_g) = (J_t + J_g - J_{AA'} - J_{BB'})/(J_t - J_g) \quad (14)$$

$J_{AB}$  and  $J_{A'B'}$  are again identical with  $J_{gem}$  and should be easily distinguishable from  $J_{AB'}$  by virtue of magnitude, temperature independence, and near equality with  $J_{AB}$  in the *meso* compound. In the *meso*- and *dl*-compounds it would also be expected that the sums corresponding to  $2J_g + J_t$  should agree closely, since the effects of electronegative substituents, strain, etc., should be nearly identical in the two isomeric compounds.<sup>13</sup>

Measurements have been made at two temperatures on the *meso*- and *dl*-forms of 2,5-diphenylhexanediol-2,5. The results conform closely to expectation. The dimethyl ethers of these two compounds were also prepared and examined, but proved unsuitable because of accidental equality of the chemical shifts.

### Experimental

**2,5-Diphenylhexanediol-2,5.**—A mixture of the *meso*- and *dl*-forms was prepared by the method of Freeman<sup>14a</sup> and separated into its components by crystallization from tetrahydrofuran, methanol, and methylene chloride. The *dl*-form melted at 158.2–159.0° (lit.<sup>14b</sup> 158.5), the *meso*-form at 143.4–144.4° (lit.<sup>14b</sup> 136°).

**N.m.r. spectra** were obtained on saturated solutions of the compounds in pyridine; a Varian A-60 n.m.r. spectrometer, equipped with variable temperature probe, was used. The calibration of the spectrometer is checked daily using *o*-dichlorobenzene.

The  $A_2B_2$  spectra were first analyzed crudely by the procedure of Pople, Schneider, and Bernstein,<sup>8</sup> then the parameters were refined using the iterative computer program,<sup>15</sup> LAOCOON II.

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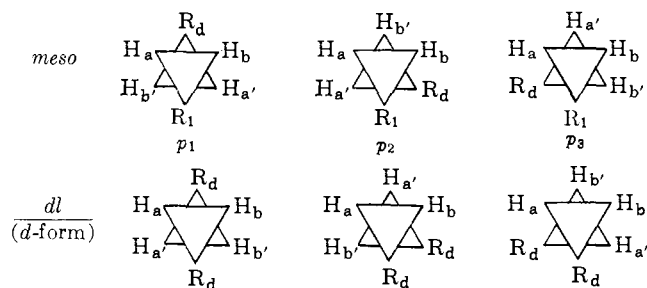


Figure 2.

$J_{AA'}$  and  $J_{BB'}$  were assumed identical. The spectra were fitted within experimental error: for the *meso*-form, the r.m.s. error in line fitting was 0.08 c.p.s.; for the *dl*-form, 0.04 c.p.s.

### Results

The results of the analyses are given in Table I. Also included in the table are the standard deviations for the parameters in each case, as given by the program LAOCOON II. The error quoted is, approximately, the change in that parameter which would double the error in fitting the observed spectrum. In actual fact, the program gives, not the errors of the individual parameters, but of the linearly independent combinations of these which correspond to the major axes of the ellipsoid of error. Thus, any "sneaky" errors will be detected. In the present cases there were none. Twenty to twenty-four transitions were assigned and matched in each spectrum. The spectra obtained at higher temperatures were more clearly resolved, as the lines were narrower; the trend in errors shown in Table I reflects this behavior.

The parameters fit the various tests well. The appropriate sums equal to  $2J_g + J_t$  for the four cases are: 21.48 c.p.s. (*meso*, 35°), 21.32 (*meso*, 91°), 21.35 (*dl*, 35°), and 21.41 (*dl*, 91°). Abraham and Pachler<sup>1</sup> have reported equivalent sums for the protons in the central methylenes of levulinic ester (20.4 c.p.s.), levulinic acid (20.4 c.p.s.), and 4-cyano-2,2-dimethylbutyraldehyde (21.8 c.p.s.).  $J_{AB}$  for both compounds is of appropriate sign and magnitude for a geminal coupling constant with no neighboring unsaturation or unshared electron pairs.<sup>12</sup>

In order to interpret the results in terms of rotamer population, it is necessary to assume some values for  $J_g$  and  $J_t$ . We will assume  $J_g = 4.10$  and  $J_t = 13.20$ . These values are calculated using a least-squares correlation<sup>15</sup> of 64 selected carefully measured coupling constants on compounds of known geometry or rotamer distribution and take into account the effect of electronegative substituents. This pair of values also satisfies the sum rules (eq. 8 and 13) well.

Substituting in eq. 9 and 14, one obtains for the low energy *trans* form

$$p_1 = 0.85 \text{ (meso, 35°)}$$

$$p_1 = 0.81 \text{ (meso, 91°)}$$

$$p_1 = 0.78 \text{ (dl, 35°)}$$

$$p_1 = 0.71 \text{ (dl, 91°)}$$

$\Delta H$  is probably effectively constant over this temperature range;  $\Delta H$  between the two forms in the *meso*-compound is reckoned to be 1.1 kcal., favoring the *s-trans* isomer; for the *dl*-compound it is 1.4 kcal., also favoring the *s-trans* isomer. The difference in the two

TABLE I  
N.M.R. PARAMETERS FOR *meso*- AND *dl*-2,5-DIPHENYLHEXANEDIOL-2,5 AT 35 AND 91°

	<i>meso</i>		<i>dl</i>	
	35°	91°	35°	91°
$\delta\nu$	17.85 ± 0.18	12.74 ± 0.10	13.27 ± 0.13	8.19 ± 0.11
$J_{AA'} = J_{BB'}$	11.86 ± .31	11.40 ± .22	5.07 ± .21	5.40 ± .25
$J_{AB'} = J_{A'B}$	4.81 ± .23	4.96 ± .15	11.21 ± .19	10.61 ± .14
$J_{AB} = J_{A'B'}$	-13.36 ± .22	-13.71 ± .18	-13.62 ± .14	-13.81 ± .13

values should not be taken seriously. Entropy changes are of the order of 1 e.u. or less.

In both cases the chemical shift between the A and B protons diminishes markedly with increased temperature, reflecting a more nearly equal distribution of rotamers about the single bonds joining the methylene groups with the asymmetrically substituted carbon

atoms. There appears as yet to be no way of interpreting this phenomenon quantitatively.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, WAYNE STATE UNIVERSITY, DETROIT, MICH.]

## Mass Spectrometry in Carbohydrate Chemistry. Ethylene Dithioacetal Peracetates

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The mass spectra of the ethylene dithioacetal peracetyl derivatives of D-glucose, D-arabinose, 2-deoxy-D-glucose, and 6-deoxy-L-galactose, and of the ethylene dithioacetal pentaacetyl-*d*<sub>15</sub> derivative of D-glucose, are discussed. The ethylene dithioacetal portion of the molecule can be recognized by the intense peak at *m/e* = 105 resulting from C-1-C-2 cleavage of the monosaccharide with charge retention on C-1. The characteristics of the mass spectra can be related to the position of deoxy groups in the carbohydrates; the molecular weight can be determined from a fragment peak at *M* - 59 (*M* - OCOCH<sub>3</sub>).

### Introduction

Dithioacetal derivatives of carbohydrates are often used for characterization and identification and as intermediates in the preparation of other sugar derivatives. Dithioacetal derivatives and their peracetates are easily prepared and are stable compounds. In the form of a dithioacetal peracetate, a carbohydrate exists in an acyclic structure.

Dithioacetal and dithioacetal derivatives of carbonyl functions are reported to be desirable derivatives for mass spectrometric purposes.<sup>1,2</sup> Introduction of an ethylene dithioacetal function into a steroid quenches the characteristic fragmentation behavior of the keto function; peaks characteristic of the ethylene dithioacetal portion of the molecule predominate.<sup>1</sup> Since sulfur can better accommodate charge than oxygen, the dithioacetals exhibit more prominent molecular ion peaks than their oxygen analogs.

Diethyl dithioacetal peracetyl derivatives of carbohydrates have been studied mass spectrometrically.<sup>2</sup> These derivatives, which are usually crystalline, are volatile enough and thermally stable enough for introduction into a conventional inlet system. In contrast to the acetyl,<sup>3,4</sup> O-methyl,<sup>5</sup> and O-isopropylidene<sup>6</sup> derivatives of carbohydrates, the diethyl dithioacetal peracetates exhibit a molecular ion peak from which the molecular weight can be directly determined. From their mass spectra, the peracetates of aldohexose, keto-

hexose, aldopentose, 2-deoxyhexose, and 6-deoxyhexose diethyl dithioacetals can be differentiated from each other. Stereochemical differences are of little influence on the fragmentation.

As an extension of the study of dithioacetal peracetyl derivatives of carbohydrates upon electron impact, the mass spectra of ethylene dithioacetal peracetates of D-glucose (I), D-arabinose (II), 6-deoxy-L-galactose (III), and 2-deoxy-D-glucose (IV) are presented and discussed here. The mass spectrum of D-glucose ethylene dithioacetal pentaacetate-*d*<sub>15</sub> (I, Ac = COCD<sub>3</sub>) is not shown, but the *m/e* positions of the peaks corresponding to those in the undeuterated analog, Fig. 1, are given in the discussion in parentheses, e.g., *m/e* = 43(46). Metastable peaks in the mass spectra given in Fig. 1-4 are listed in Table I.

TABLE I  
METASTABLE PEAKS IN FIG. 1-4

Figure	Fragmentation	Calculated	Found
1	105 → 61	35.4	35.5
	(105 → 61)	35.4	35.6) <sup>a</sup>
	189 → 147	114.3	114.6
	(192 → 148)	114.1	114.5) <sup>a</sup>
2	105 → 61	35.4	35.5
	189 → 147	114.3	114.6
	246 → 186	140.6	141.0
3	105 → 61	35.4	35.6
	189 → 147	114.3	114.5
4	228 → 186	151.7	152.1

<sup>a</sup> The position of the peak in the mass spectrum of Ia (I, Ac = COCD<sub>3</sub>) is given in parentheses.

**The Molecular Weight. Fragmentation Series 1 and 2.**—In contrast to the mass spectra of the diethyl dithioacetal peracetates,<sup>2</sup> the mass spectra of the ethylene dithioacetal peracetates show no molecular

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