

Conformational Preferences in Diastereomers. V. Hydrogen-Bonding Systems

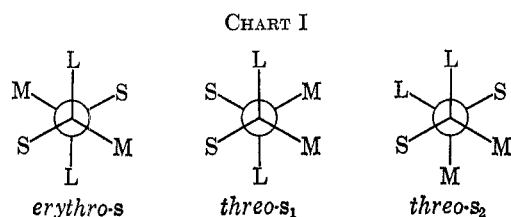
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Received April 15, 1968

In several alkyl-substituted phenylethanediols and in two propanediols, the increase in size of the alkyl substituent results in generally increasing coupling constants in the *erythro* isomers. In the *threo* isomers, diminishing coupling constants are observed. Diastereomers with *t*-butyl substituents are again anomalous. The *erythro* isomers generally have lower coupling constants than the *threo* isomer in carbon tetrachloride. In hydrogen-bonding solvents such as dimethyl sulfoxide or pyridine, the coupling constants are much larger for the *erythro* isomers and smaller for the *threo* isomers than those in carbon tetrachloride. The effect of dilution was also to increase coupling constants for the *erythro* isomers and to diminish coupling constants for the *threo* isomers. These effects are in contrast with the observations in a rigid system, 3-methyl-1,2-cyclohexanediol. In the open-chain system, infrared data showed that the solvent effects were associated with reduction of intermolecular hydrogen bonding. In one set of isomers at very low concentration, time-averaging runs disclosed coupling constants rather similar to those determined at high concentrations. The results are interpreted in terms of changes from polymeric and dimeric to monomeric diols.

Previous work in nonhydrogen-bonding systems¹⁻⁸ has shown that the *erythro-s* isomer of an *erythro-s*-*threo-s* pair of diastereomers usually has the larger vicinal coupling constant, J (the suffix *s* indicates that the definition of *erythro* is based on the size of groups).⁹ Thus, as Chart I shows, the preferred *trans* arrangement



of the large group, *L*, and *trans* medium groups, *M*, imposes a *trans* relationship on the small groups (hydrogen), resulting in a large vicinal coupling constant.^{10,11} The *threo-s* isomers are usually conformationally mixed to a greater extent than the *erythro-s* isomers.¹² In some types of *threo-s* diastereomers⁷ a trend toward lower J values has been observed upon increasing the size of the groups involved, suggesting the growing importance of conformer *threo-s*₁, in which the large groups are again *trans*. In other types of *threo* diastereomers quite large J values are observed.^{3,5,6} Thus *threo-s*₂ is quite highly populated even though the large groups are *gauche*. The conformer *threo-s*₂ exhibits two sets of *gauche* interactions between sizable groups,

whereas *threo-s*₁ shows three such interactions.¹² The former behavior is often, though not exclusively, associated with the presence of alkyl groups. The latter type frequently occurs with "soft" substituents such as aryl or carboxyl. However, the reason for the difference in behavior is not completely understood as yet.

The above behavior is not to be expected in systems in which substantial attractive interactions exist between two or more groups.^{5,13-19} The present study is concerned with such an attractive interaction, intramolecular hydrogen bonding. *A priori*, three types of behavior might be anticipated depending on the strength of the hydrogen bond.

(A) In weak or nonhydrogen-bonding systems, the conformation is determined primarily by nonbonded interactions between the larger groups (as in Chart I). Little effect of concentration or of solvent is expected, although some groups such as hydroxyl may prefer a more open conformation to facilitate hydrogen bonding with solvent.²⁰

(B) In moderately strong hydrogen-bonding systems, the hydrogen bond may override the nonbonded interactions between the large groups, resulting in quite a different conformation than those shown in Chart I. However, the effect of solvent should be large, since some types of solvents may break up the intramolecular hydrogen bond, resulting in conformations similar to those in Chart I.

(C) In strong intramolecular hydrogen-bonding systems, the conformation is dominated by the hydrogen bond. However, little effect of concentration or of

- (1) F. Anet, *J. Amer. Chem. Soc.*, **84**, 747 (1962).
- (2) A. Bothner-By and C. Naar-Colin, *ibid.*, **84**, 743 (1962).
- (3) J. Ralston and K. Yates, *ibid.*, **91**, 1469 (1969).
- (4) R. C. Fahey, *ibid.*, **88**, 4681 (1966); M. Dewar and R. C. Fahey, *ibid.*, **85**, 3645 (1963).
- (5) M. E. Munk, M. Meilahn, and P. Franklin, *J. Org. Chem.*, **33**, 3480 (1968).
- (6) M. C. Cabaleiro and M. D. Johnson, *J. Chem. Soc., B*, 565 (1967).
- (7) C. A. Kingsbury and W. B. Thornton, *J. Org. Chem.*, **31**, 1000 (1966).
- (8) See also (a) M. Buza and E. I. Snyder, *J. Amer. Chem. Soc.*, **88**, 1161 (1966); (b) R. J. Jablonski and E. I. Snyder, *ibid.*, **90**, 2316 (1968); (c) R. A. Newmark and C. H. Sederholm, *J. Chem. Phys.*, **43**, 602 (1965); (d) S. Brownstein, *Can. J. Chem.*, **39**, 1677 (1961).
- (9) H. E. Zimmerman and W. Chang, *J. Amer. Chem. Soc.*, **81**, 3634 (1959).
- (10) (a) M. Karplus, *ibid.*, **85**, 2870 (1963); (b) A. Bothner-By, *Advan. Magnetic Resonance*, **1**, 195 (1965).
- (11) E. Garbisch, Jr. and M. Griffith, *J. Amer. Chem. Soc.*, **90**, 6543 (1968).
- (12) See J. L. Mateos and D. J. Cram, *ibid.*, **81**, 2756 (1959); D. Y. Curtin, *Record Chem. Progr.*, **15**, 111 (1954); H. Felkin, *Bull. Soc. Chim. Fr.*, 1050 (1956); M. S. Newman, *J. Chem. Educ.*, **32**, 344 (1955).

(13) J. B. Hyne, *Can. J. Chem.*, **39**, 2536 (1961), and related papers. This work emphasizes the fact that dihedral angles may be other than 60°. While we recognize the fact that the molecules in question have varying dihedral angles, as well as bond angles and bond lengths to some extent, to achieve the most comfortable arrangement, we will, as before, picture dihedral angles as 60° for convenience.

(14) M. Stiles, R. Winkler, Y. Chang, and L. Traynor, *J. Amer. Chem. Soc.*, **86**, 3337 (1964).

(15) L. Erickson, *ibid.*, **87**, 1867 (1965).

(16) J. W. Huffman and R. P. Elliott, *J. Org. Chem.*, **30**, 365 (1965).

(17) C. G. Overberger and T. Kurtz, *ibid.*, **31**, 288 (1966).

(18) J. Cancelli, J. Basselier, and J. Jacques, *Bull. Soc. Chim. Fr.*, 1906 (1963).

(19) See also W. Chilton and R. C. Krahn, *J. Amer. Chem. Soc.*, **90**, 1318 (1968).

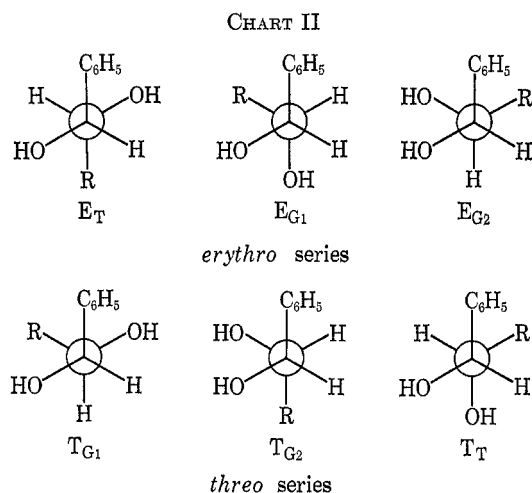
(20) L. M. Jackman and N. S. Bowman [*ibid.*, **88**, 5565 (1966)] have also considered the effect of intermolecular hydrogen bonding on conformation.

solvent is anticipated, since a hydrogen bond of high stability would not be easily disturbed.^{14,21}

The compounds of this study are the vicinal diols **1** and **2**, which are believed to be examples of case B above.



The coupling-constant data are listed in Table I. These data will be discussed with reference to the conformers shown in Chart II.



The data in Table I show that the *erythro* diastereomers generally have lower J values than the *threo* isomers, somewhat similar to other studies of hydrogen-bonding systems.^{5,14,16,18} The *erythro t*-butyl compound **6** (and also probably *threo-6* and **-9**) is out of line in comparison with other *erythro* isomers. This fairly common phenomenon^{8,22} is thought to be due to a different mode of relieving nonbonded interactions than internal rotation.²³ Bond-angle deformations involving the methyl groups of the *t*-butyl function or of the *t*-butyl group itself are thought to be important. For **3-5**, increasing the size of the R group in the *erythro* isomers generally results in increasing J values, indicative of the growing importance of conformer E_T ($J_{AB} = 10-13$ Hz).^{10,11} A similar change for the *threo* isomers involved decreasing J values, showing the importance of T_{G1} and/or T_{G2} ($J_{AB} \cong 3$ Hz), most likely the latter conformer, since the largest groups may again be *trans*.

In order that maximum and minimum coupling constants may be roughly approximated, a rigid system was investigated. Three of the four isomers of 3-methyl-1,2-cyclohexanediol were obtained and the nmr data for the suggested structures are given in Chart III.²⁴

(21) (a) O. L. Chapman and R. W. King, *J. Amer. Chem. Soc.*, **86**, 1256 (1964); (b) O. L. Chapman, R. W. King, and W. Welstead, Jr., *ibid.*, **86**, 4968 (1964); (c) I. Kolthoff, M. Chantooni, Jr., and S. Bhowmik, *ibid.*, **90**, 23 (1968); (d) N. Bauld and Y. Rim, *J. Org. Chem.*, **33**, 1303 (1968).

(22) D. C. Best and C. A. Kingsbury, *ibid.*, **33**, 3252 (1968).

(23) D. C. Best, G. Underwood and C. Kingsbury, *Chem. Commun., Part D*, 627 (1969).

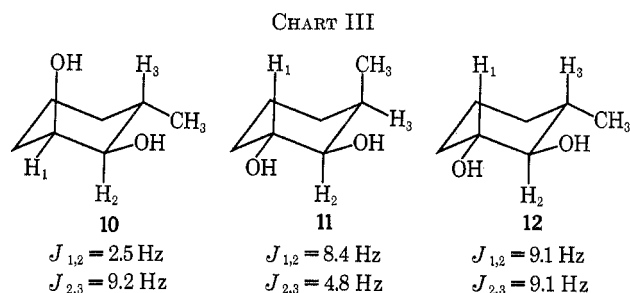
(24) The comparison of a cyclohexane system such as **10** or **12**, included at the behest of the referee, to an open-chain system such as **8** is not necessarily valid. The variation of dihedral angles to achieve the most "comfortable" arrangement differs. The infrared $\Delta\nu$ of the *cis*-diol **10** (45 cm^{-1})

TABLE I
NMR COUPLING CONSTANTS^a IN SYSTEMS 1 AND 2

Compd	R	Isomer	$-J_{AB}$ (CCl ₄), ^b Hz				J_{AB} ^{c,d} (DMSO)
			10% ^e	5%	2.5%	1.3%	
3	CH ₃	<i>erythro</i> ^f	Insol	3.8	4.0	4.0	5.3
		<i>threo</i>	7.8	7.7	7.6	7.5	6.4
4	C ₂ H ₅	<i>erythro</i>	3.8	3.9	4.2	4.4	5.7
		<i>threo</i>	7.6	7.3	7.1	6.9	6.1
5	<i>i</i> -C ₃ H ₇	<i>erythro</i> ^f	Insol	5.6	5.7	5.8 ^g	7.5
		<i>threo</i>	7.1	6.8	6.5	6.4	6.2
6	<i>t</i> -C ₄ H ₉	<i>erythro</i>		5.2 ^h	5.5	5.8	6.7
		<i>threo</i>	2.6 ^h		2.6	2.6 ^g	2.6
7	CH ₂ C ₆ H ₅ ⁱ	<i>threo</i>		6.5	6.2	6.0 ^g	4.7

^a Data was taken from expanded spectra on a Varian A-60D instrument vs. tetramethylsilane as internal standard. A trace of trifluoroacetic acid was added to promote rapid exchange. ^b These coupling-constant data have duplicated the spectrum at selected concentrations using computer simulation techniques. ^c Concentration 10%. ^d For system 2, the solutions were composed of 75% CCl₄ and 25% DMSO to avoid trouble from spinning side bands. ^e 10% sample by weight per unit solvent volume. ^f Slightly heated for solubility reasons. ^g Approximate value; an expanded spectrum was not possible. ^h Approximate concentration. ⁱ The *erythro* value is ca. 4.2 Hz, as observed from a solution of mixed diastereomers.

For the *cis*-diol **10** and the *trans*-diol **12**, the major couplings were verified by spin decoupling and the spectra were simulated by computer techniques using the approximate chemical shifts for H₃ derived from spin-decoupling data. The data in Chart III accurately



duplicated the splitting pattern for H₂, but difficulty was encountered with the H₁ pattern, probably owing to the extensive coupling (real and virtual) with several other ring protons. The *cis* isomer **10** shows a vicinal

is larger than that of the *trans*-diol **12** (35 cm^{-1}): R. W. Wright and R. Marchessault, *Can. J. Chem.*, **46**, 2567 (1968). Further, *cis*-diols are reported to form acetones, unlike *trans*-diols: J. Boeseken and J. van Giffen, *Rec. Trav. Chim. Pays-Bas*, **39**, 183 (1920). The dihedral angle between the *cis* axial-equatorial hydroxyl groups is thought to have become compressed,¹¹ and the dihedral angle between *trans* equatorial-equatorial hydroxyls has become widened, possibly to relieve across ring nonbonded interactions. Quite the opposite trend in the $\Delta\nu$ factors is observed for *erythro-8* (comparable with **10**) and *threo-8* (see the ensuing discussion). Any similarity in J values may be coincidental. See also H. Feltkamp and N. C. Franklin, *Tetrahedron*, **21**, 1541 (1965).

coupling constant^{24,25} reasonably close to that observed for the most closely analogous open-chain compound, *erythro*-8. On the other hand, 12 shows a somewhat larger $J_{1,2}$ value than that observed for *threo*-8 (or any of the other *threo* compounds), indicating that the open-chain compounds are more conformationally mixed owing to competition between T_T and T_G conformers. Compound 11 is also not conformationally pure. Although the infrared $\Delta\nu$ factors for 11 and 12 are similar (ca. 35 cm^{-1}), the apparent intensity of the intramolecularly bonded hydroxyl absorption for 11 is only ca. 60% that of 12. The infrared data, coupled with rather low $J_{1,2}$ and rather high $J_{2,3}$ values, show that the conformer of 11 with equatorial methyl and diaxial hydroxyl groups is substantially populated. However, the dominant conformation of 11 (Chart III) prefers equatorial hydroxyl functions at the expense of placing the methyl group axial.

Unlike the open-chain compounds, 10 and 12 were insensitive to the solvent change from deuteriochloroform to pyridine. Compounds 10 and 12 were also insensitive to a twofold dilution in carbon tetrachloride.

The effect of concentration on the coupling constants of the open-chain materials is given in Table I. For the *erythro* isomers, the effect of dilution is generally a trend toward higher J values. For the *threo* isomers the trend is the opposite. Although the changes were rather small in some cases, repetition always gave similar results. The effect of adding a second hydrogen-bonding material, such as ephedrine, to a constant concentration of *erythro*-3 or -9 was diminishing J values. Upon adding ephedrine to *threo*-5, increasing J values were observed.

The effect of moving from carbon tetrachloride to the intensely hydrogen-bonding solvent dimethyl sulfoxide (DMSO) is also shown in Table I. In the latter solvent, intermolecular hydrogen bonding between diols and much of the intramolecular hydrogen bonding, if any, is thought to be eliminated.²¹ In DMSO, the *erythro* isomers usually show larger J values than in carbon tetrachloride. Again the *threo* isomers usually show smaller J values for the same solvent change. For 3, a more complete study of the effect of solvent²⁶ is given in Table II. Moving from nonpolar solvents to pro-

contrast, a model nonhydrogen-bonding compound having the same carbon skeleton, 1,2-dibromo-1-phenylpropane,³ showed little or no change in J_{AB} (10.2 Hz) for the *erythro* isomer and a slight increase from the original J_{AB} (5.4 Hz) for the *threo* isomer for the same solvent variation.²

Infrared data were obtained for systems 1 and 2 for the same range of concentrations in carbon tetrachloride utilized for the nmr studies. Qualitatively, the results are similar to the studies of Kuhn and others.²⁷⁻³⁴ For the *threo* isomers, three absorptions were noted (7, however, was anomalous): (A) sharp peak at ca. 3620 cm^{-1} , very likely the free hydroxyl absorption; (B) somewhat broader peak of similar apparent intensity at 3560-3585 cm^{-1} , probably the intramolecularly bound hydroxyl; (C) a broad absorption at ca. 3400 cm^{-1} , probably the polymeric hydroxyl absorption. In the 10% solutions the polymeric absorption was strongly dominant. Dilution eliminated much of the polymeric absorption, but at 1.3% (the minimum concentration at which most nmr spectra could be run) it was still a sizable peak. It is noteworthy that the size of the polymeric absorption peak was less for 5 and 6 than for 3 and 4, probably the effect of steric hindrance to external association.

For the *erythro* isomers 1, an infrared peak was observed at ca. 3630 cm^{-1} upon which a shoulder was evident, in addition to the concentration-dependent peak at ca. 3400 cm^{-1} . The shoulder was very likely due to the intramolecular hydrogen-bonded hydroxyl.³⁰ For system 2, however, separated free and intramolecularly bonded hydroxyl peaks were evident (e.g., $\Delta\nu$ is 45 cm^{-1} for *erythro*-9 compared with 60 cm^{-1} for *threo*-9). The effect of dilution for all *erythro* isomers was generally similar to the *threo* isomers described above. In all cases, the intramolecular hydrogen bond is less stable for the *erythro* than for the *threo* isomers (as judged from the lower $\Delta\nu$).^{5,13,14} As others have pointed out,^{5,13,29,31} distortion of the dihedral angles to relieve the R-phenyl interaction increases the hydroxyl-hydroxyl distance in the *erythro* isomers, thus weakening the hydrogen bond.

It is difficult to assess what role, if any, hydroxyl-phenyl hydrogen bonding plays. The $\Delta\nu$ factor ascribed to hydroxyl- π interaction²⁹ is roughly similar to the $\Delta\nu$ observed for hydroxyl-hydroxyl bonding; therefore, the above infrared results could as easily be the effect of the former type of interaction. However, the nmr data are difficult to explain in any rational manner in terms of conformations dominated by hydroxyl- π bonding. In competition between bonding to a nonbonded pair on oxygen as opposed to the delocalized electrons of a π system, the former would seem more probable (bond energy ca. 4 kcal, in the ideal case) than the latter (interaction energy ca. 1 kcal). Never-

TABLE II

VICINAL COUPLING CONSTANTS AS A FUNCTION OF SOLVENT^a FOR 3

	CCl_4	CDCl_3	CH_3OH	CH_3COCH_3	Pyridine ^b	CH_3SOCH_3
<i>erythro</i>	3.8 ^c	4.1	5.1	4.7	5.0	5.4
<i>threo</i>	7.8	7.4	7.0	7.0	6.9	6.4

^a Concentration 10% except as indicated. ^b Concentration 5% in pyridine. ^c Concentration 5%.

gressively more strongly hydrogen-bonding solvents involves an increase in J_{AB} for *erythro*-3 and a decrease for the *threo* isomer. The coupling constants observed in chloroform solution are substantially different from those in carbon tetrachloride, consistent with the weak hydrogen-bonding properties of the former. In

(25) These J values are reasonably close to those given for similar cyclohexane systems: R. A. B. Bannard, *Can. J. Chem.*, **44**, 775 (1966); F. A. L. Anet, *ibid.*, **41**, 2331 (1963).

(26) See however, E. I. Snyder, *J. Amer. Chem. Soc.*, **85**, 2624 (1963); K. Deb and R. J. Abraham, *J. Mol. Spectrosc.*, **23**, 393 (1967); also ref 2 concerning solvent effects.

(27) L. P. Kuhn, *J. Amer. Chem. Soc.*, **74**, 2492 (1952); **76**, 4323 (1954); **80**, 5950 (1958).

(28) A. Cole and P. R. Jeffries, *J. Chem. Soc.*, 4391 (1956).

(29) J. Sicher and J. Farkas, *Collect. Czech. Chem. Commun.*, **20**, 1391 (1955); J. Sicher, M. Cherest, Y. Gault, and H. Felkin, *ibid.*, **28**, 72 (1963).

(30) W. Mosher and N. Heindel, *J. Org. Chem.*, **28**, 2154 (1963).

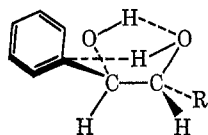
(31) N. Mori, S. Omura and Y. Tsuzuki, *Bull. Chem. Soc. Jap.*, **38**, 2199 (1965); **38**, 1630 (1965).

(32) H. Buc, *Ann. Chim.*, **8**, 409 (1963); 431 (1963).

(33) H. Agahigian, J. Moraveck, and H. Gauthier, *Can. J. Chem.*, **41**, 194 (1963).

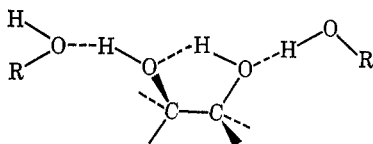
(34) See, however, R. Piccolini and S. Winstein, *Tetrahedron Lett.*, No. 13, 4 (1959).

theless, the hydroxyl- π interaction may be of some importance in the *erythro* isomers in which the hydroxyl-hydroxyl bond is weakened by other factors. A further complication is possible simultaneous hydroxyl-hydroxyl and hydroxyl-phenyl bonds, as illustrated below.³⁵

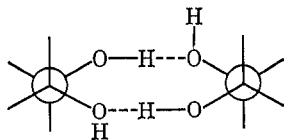


In any case, the effect of dilution on the nmr J values (Table I) is related to diminishing amounts of intermolecular association, as determined from the infrared spectra. However, in one case it was possible to determine the nmr spectra of a pair of isomers under conditions in which intermolecular association was small. Under time-averaging conditions³⁶ (concentration 0.1% in carbon tetrachloride), *erythro*-5 exhibited a J value of 5.8 Hz and *threo*-5 a value of 6.4 Hz, rather similar to the data in Table I taken at higher concentrations.

Concerning the nmr data, a group of related questions remain to be answered. First, why are the conformations populated by the isomers 5 similar under conditions favoring intermolecular association compared with intramolecular association? Second, of the changes which do occur on dilution or solvent change, why are increasing J values observed for the *erythro* isomers, and decreasing J values for the *threo* isomers? To partially rationalize these questions, it should be pointed out that the polymeric hydroxyl groups at high concentrations may in fact involve many intramolecularly bonded and therefore *gauche* hydroxyl groups.



A second possibility, which helps to account for the *erythro* as well as the *threo* data, consists of dimeric molecules. Dimers have been implicated in the association pattern of simple alcohols. The difunctional molecules of this study should exhibit the same phenomenon to a greater extent.³⁷ Thus the dimer and the intramolecularly hydrogen bonded monomer would both



require conformations T_T and T_{G_2} for the *threo* isomers and E_{G_1} and/or E_{G_2} for the *erythro* isomers.^{38,39}

(35) D. Horton, J. Hughes, and J. Thomson, *J. Org. Chem.*, **33**, 728 (1968).

(36) The 100-MHz accumulation runs, as well as the 100-MHz spectra of 10-12, were ably determined by R. W. King, Iowa State University.

(37) (a) E. D. Becker, *J. Chem. Phys.*, **31**, 269 (1959); (b) J. C. Davis, Jr., K. S. Pitzer, and C. Rao, *J. Phys. Chem.*, **64**, 1744 (1960); (c) G. Dana, J. Chucho, and M.-R. Monot [*Bull. Soc. Chim. Fr.*, 3308 (1967)], in an elegant study, postulated dimeric association of certain related glycols.

(38) H. Matsuura and T. Miyazawa [*Bull. Chem. Soc. Jap.*, **40**, 85 (1967)] have presented other lines of evidence for *gauche* hydroxyls (in the liquid state) of ethanediol.

Concerning the effect of dilution,^{37c} it is suggested that the *threo* conformer T_T is relatively more important in the dimeric and polymeric forms owing to minimum steric hindrance to external association.²⁷ Going to the intramolecularly bonded monomer, T_{G_2} becomes somewhat more important, since in this conformer the largest groups may again be *trans*. The increase in J values for the *erythro* isomers is more difficult to explain. Possibly the nonhydrogen-bonded conformer E_T becomes somewhat more important on dilution, since the intramolecular bond in E_{G_1} and/or E_{G_2} is none too stable.

The much larger effect of moving to highly polar solvents such as DMSO is superficially similar to the effects of dilution. For the *threo* isomers, hydroxyl-hydroxyl hydrogen bonding is largely replaced by bonding to DMSO. There is no particular necessity for conformer T_T in DMSO, and the other conformers become increasingly populated, resulting in a lower coupling constant. For the *erythro* isomers E_T is formed at the expense of E_{G_1} and/or E_{G_2} and a larger J value results.

Experimental Section

Compounds *erythro*- and *threo*-3 were prepared by acid-catalyzed opening of the epoxide. The substrate, 1-phenyl-2,3-epoxypropane (10.7 g, 0.08 mol), in 20 ml of ether was stirred overnight with 0.5 ml of perchloric acid in 100 ml of water. The ether layer was separated, and the aqueous layer was extracted with 50 ml of ether. The combined ether layers were extracted with dilute sodium bicarbonate solution and dried over magnesium sulfate. Evaporation of the solvent left an oil that could not be crystallized. The oil was chromatographed on a 60 \times 2 cm column of silica gel, using increasing amounts of ether in hexane as eluent. Most fractions were oils with discouraging nmr spectra. One fraction (pure ether as eluent) partially crystallized on long standing. The solid was recrystallized from ether-pentane by the triangle scheme and afforded *erythro*-3, yield 1.8 g, mp 88.0-89.0° (lit.⁴⁰ mp 92°), and *threo*-3, yield 0.2 g, mp 52.2-53.2° (lit.^{14,40} mp 52°). A total of 0.5 g less pure *threo* isomer was obtained.

Compound *threo*-4 was prepared by the method of Zincke.⁴¹ The oily product was distilled over a short-pass still head, bp 125-129° (0.5 mm). The nmr spectra indicated no extraneous peaks.

Compound *erythro*-4 was prepared by the method of Bonner and Raunio⁴² from iodine, silver acetate, and 1-phenyl-1-butene, hereafter called procedure A. The product showed a melting point of 42-44° (lit.⁴⁰ mp 41°).

Compound *threo*-5 was prepared by a variant of procedure A as described below, mp 73.6-74.2° (lit.⁴⁰ mp 81°). The nmr spectrum disclosed no impurities.

Compound *erythro*-5 was prepared by a variant of procedure A. The intermediate ester was cleaved with dilute sodium hydroxide in water, yielding a nonhydroxylic oil, probably an epoxide. This material was stirred with 0.3 ml of formic acid in 10 ml of water overnight. The crude product was extracted with ether and dried over magnesium sulfate, and the solvent was evaporated. The product crystallized on long standing and was recrystallized twice from ether-hexane, mp 103.2-103.9° (lit.⁴⁰ mp 108°). No impurities were evident in the nmr spectrum.

Compound *threo*-6 was prepared similarly to *erythro*-5 described above. The reaction in this case was markedly nonstereospecific, with a mixture of epoxides being formed from either pure *cis*- or mostly *trans*-3,3-dimethyl-1-phenyl-1-butene. The cleavage of the mixture of epoxides, however, yielded predominantly a single diol 6 plus much ketonic material. The diol 6 was re-

(39) Conformers T_{G_1} and E_{G_1} are unlikely in 5 and 8 owing to severe 1,3 interactions (see ref 22).

(40) M. Tiffeneau, J. Levy, and P. Weill, *Bull. Soc. Chim. Fr.*, **49**, 1606 (1931).

(41) T. Zincke and K. Zahn, *Chem. Ber.*, **43**, 849 (1910).

(42) W. A. Bonner and T. Raunio, *J. Org. Chem.*, **31**, 291 (1966).

crystallized as before, mp 93–94°. Similar results to the above were obtained beginning with mostly *trans* olefin. Only traces of the second diol were evident. Owing to the similarities in infrared hydrogen bonding spectra and similar nmr dilution shifts with the above *threo* materials, this material, mp 94°, is assigned the *threo* configuration.

Anal. Calcd for C₁₂H₁₈O₂: C, 74.20; H, 9.30. Found: C, 74.08; H, 9.36.

Compound *erythro*-6 was finally prepared by oxidizing the *cis* olefin with potassium permanganate according to the procedure of Bonner and Raunio,⁴² mp 80.1–80.6°.

Anal. Calcd for C₁₂H₁₈O₂: C, 74.20; H, 9.30. Found: C, 73.98; H, 9.44.

Compound *threo*-7 was prepared by procedure A, mp 62–64° (lit.⁴² mp 64°).

Compound *threo*-8 was prepared by the procedure of Lucas and coworkers.^{43,44} To *cis*-4-methyl-2-pentene (26 g 0.31 mol) stirred in 150 ml of water, 100 ml of acetic acid, and 2 ml of sulfuric acid was added N-bromosuccinimide (71 g, 0.4 mol). The reaction mixture was stirred overnight and then extracted several times with ether. The ether layers were extracted with an equal volume of water, dilute sodium carbonate, and water, and dried over magnesium sulfate. The solvent was evaporated and the remaining oil was distilled over a Vigreux column at 17 mm. The fractions collected from 74–82° (27.1 g) were the mixed bromohydrins.

The bromohydrin (33.5 g, 0.185 mol) was stirred in 150 ml of water, and a solution of 8 g of sodium hydroxide in 30 ml of water was added dropwise. The final solution was gently heated. Upon cooling the solution was extracted with ether as before and dried, solvent was evaporated, and the epoxide was distilled through a 30-cm Podbielniak column, yield 9.2 g (50%), bp 98–103°.

The epoxide (2.3 g, 0.021 mol) was placed in 15 ml of acetic acid, 40 ml of water, and 0.5 ml of perchloric acid and stirred at room temperature for ca. 16 hr. The solution was saturated with ammonium chloride and extracted many times with ether. The ether layers were extracted with an ammonium chloride solution and dried over magnesium sulfate, and the solvent was evaporated. The residue was recrystallized from ether–hexane, mp 55.3–56.4° (lit.⁴⁵ mp 59.7°).

Compound *erythro*-8 was prepared similarly from the commercial *trans* olefin, mp 51.5–52.5° (lit.⁴⁶ mp 49.6°).

Compound *threo*-9 was prepared similarly, mp 81.1–82.0° (lit.⁴⁶ mp 78.5°).

Compound *erythro*-9 was prepared similarly, mp 73.8–74.6°.

Anal. Calcd for C₇H₁₆O₂: C, 63.59; H, 12.19. Found: C, 63.72; H, 12.06.

The 3-methyl-*trans*-1,2-cyclohexanediols were prepared by the procedure of Adkins and Roebuck.⁴⁶ The solid isomer 11 was

recrystallized twice from methylene chloride–carbon tetrachloride, mp 95.5–97.0° (lit.⁴⁶ mp 96°). The remaining oil was distilled over a short pass head, bp 104–113° (ca. 4 mm). However, the nmr spectrum indicated extensive contamination. The *trans*-diol 12 was obtained by preparative vpc on a 5 ft × 0.375 in. 10% LAC 446 acid-washed Chromosorb W column. At a column temperature of 190° and a flow rate of 50 ml/min, the retention time was 8.2 min. The nmr spectrum still indicated slight impurity.

The 3-methyl-*cis*-1,2-cyclohexanediol (10) was prepared by the permanganate oxidation method of Bonner and Raunio,⁴² mp 82–83° (lit.⁴⁷ mp 81–82°).

The nmr data were obtained on a Varian A-60D instrument *vs.* tetramethylsilane as internal standard. A trace of trifluoroacetic acid was added to promote rapid exchange. The coupling constants were taken by averaging the data from three to five 500-sec 100-Hz sweeps in either direction at each concentration (precision ±0.1 Hz). The spectrum of each compound was run at least twice using fresh solutions. The trends in *J* values were always as indicated in Table I, although the absolute values varied slightly from run to run (±0.2 Hz). The time-average spectra of 5 were obtained with a Varian HA-100 instrument at concentration of 0.1% (50-fold accumulation). It was impossible to go to lower concentrations without adding macro quantities of trifluoroacetic acid to catalyze exchange. The above spectra were simulated at one concentration using the LAOCOON III program with a Calcomp plotter trace of the spectrum. The simulations were run until the plot was superimposed with the original. However, the observed line separations were very close to the actual coupling constants, with the exception of 11.

The infrared data were obtained on a Perkin-Elmer Model 237 instrument and standardized against known polystyrene absorptions. The solvents used were reagent grade in each case; however, carbon tetrachloride was dried over Linde Molecular Sieve 4A before use. The infrared data is considered good to ±5 cm⁻¹.

Registry No.—*erythro*-3, 1075-04-3; *threo*-3, 1075-05-4; *erythro*-4, 19774-62-0; *threo*-4, 19774-63-1; *erythro*-5, 19776-13-7; *threo*-5, 19776-14-8; *erythro*-6, 23570-91-4; *threo*-6, 23646-54-0; *threo*-7, 5565-57-1; *erythro*-8, 6702-10-9; *threo*-8, 6464-40-0; *erythro*-9, 23646-57-3; *threo*-9, 23646-58-4.

Acknowledgment.—Initial support by the NSF was appreciated. Dr. M. E. Munk is thanked for a preprint of his interesting related work. Professor R. W. King is especially thanked for his efforts in obtaining the 100-MHz spectra.

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