[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

Studies in Stereochemistry. XXXI. Conformation, Configuration and Physical Properties of Open-chain Diastereomers[1]

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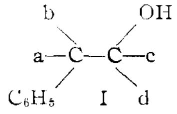
The physical properties of seven diastereomeric pairs of alcohols of the type $C_6H_5\overset{|}{\underset{|}{C}}{}^*-\overset{|}{\underset{|}{C}}{}^*OH$ have been examined, and correlations have been found between their infrared, ultraviolet and nuclear magnetic resonance spectra on the one hand, and their configurations and principal conformations on the other. Other properties such as optical rotatory dispersion, refractive index, densities and melting points were also examined, but good correlations were not found.

In the course of investigations reported in this series of papers, seven diastereomeric pairs of alcohols have been prepared which possess the general structure I, in which a, b, c and d are hydrogen, alkyl or phenyl groups. The relative configurations of the two asymmetric carbon atoms in all of these compounds have been determined through chemical reactions, and in many cases, the absolute configurations of the optically active forms have been established.[3] The availability of these compounds of known configuration provides an opportunity for a systematic study to be made between the relationship of the physical properties of these compounds and their configurations. Accordingly, the infrared, nuclear magnetic resonance and rotatory dispersion spectra of these fourteen compounds have been examined.



I

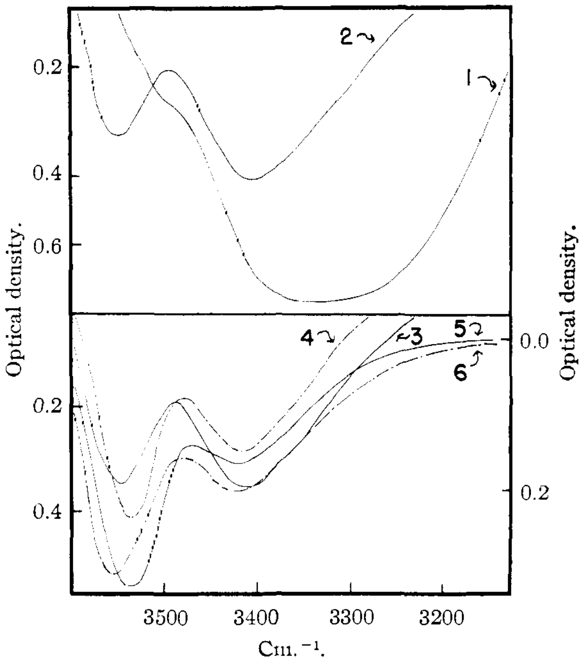


Fig. 1.—Infrared spectra, sodium chloride optics, Perkin-Elmer model 21 double beam spectrophotometer: curve 1, *erythro*-3-phenyl-2-pentanol, liquid film, 0.028-mm. cell; curve 2, *erythro*-3-phenyl-2-pentanol in 1.45 *M* chloroform solution in 0.11-mm. cell; curve 3, *erythro*-3-phenyl-2-pentanol in 1.0 *M* chloroform solution, 0.11-mm. cell; curve 4, *threo*-3-phenyl-2-pentanol in 1.0 *M* chloroform solution, 0.11-mm. cell; curve 5, *erythro*-1,2-diphenyl-1-propanol in 1.0 *M* chloroform solution, 0.11-mm. cell, optical density scale on right; curve 6, *threo*-1,2-diphenyl-1-propanol in 1.0 *M* chloroform solution, 0.11-mm. cell, optical density scale on right.

Infrared Spectra.—Considerable differences are found in the infrared spectra of these diastereomers, particularly in the 3400–3600 cm.$^{-1}$ region, which is associated with the O–H stretching vibration.[4] Although other differences are visible and have been used for analyses of diastereomeric mixtures, no attempt to interpret them will be made. For instance, the bands associated with C–O stretching (1125 to 1205 cm.$^{-1}$) for a pair of diastereomers are spaced 5 to 15 cm.$^{-1}$ from one another. No correlation could be found between configuration and the frequenceis of these bands, however. Correlations are found for the positions of the O–H stretching bands, and attention will be focused on these.

In each of the fourteen compounds studied, two bands are found in the O–H stretching region, one associated with the free hydroxyl group (3620 to 3570 cm.$^{-1}$) and the other with dimeric hydrogen-bonded hydroxyl groups (3470 to 3440 cm.$^{-1}$). Polymeric structures usually exhibit a third band in the 3380 to 3300 cm.$^{-1}$ region, but no such absorption is found for these compounds, presumably for steric reasons. As expected, the band associated with intermolecular hydrogen-bonding is sensitive to changes in concentration. Figure 1 records

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(1) This work was sponsored in part by the Office of Ordnance Research, U. S. Army.

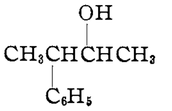
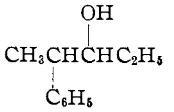
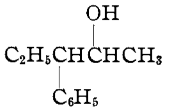
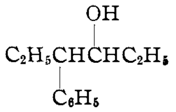
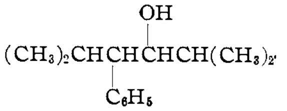
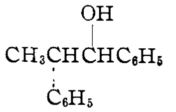
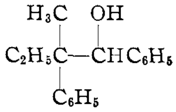
(2) Rockefeller Postdoctoral Fellow at U.C.L.A., 1957–1958.

(3) The preparation and determination of the configurations of these compounds were reported as follows: 3-phenyl-2-butanol, (a) D. J. Cram, THIS JOURNAL, **71**, 3863, 3883 (1949); (b) **74**, 2129, 2137, 2149 (1952); 3-phenyl-2-pentanol and 2-phenyl-3-pentanol, (c) D. J. Cram and R. Davis, *ibid.*, **71**, 3871 (1949); (d) D. J. Cram, *ibid.*, **71**, 3875 (1949); (e) D. J. Cram, *ibid.*, **74**, 2152, 2159 (1952); 4-phenyl-3-hexanol, (f) D. J. Cram, F. A. Abd Elhafez and H. Weingarten, *ibid.*, **75**, 2293 (1953); (g) D. J. Cram and F. A. Abd Elhafez, *ibid.*, **75**, 3189 (1953); 2,5-dimethyl-4-phenyl-3-hexanol, (h) D. J. Cram, F. A. Abd Elhafez and H. L. Nyquist, *ibid.*, **76**, 22 (1954); (i) D. J. Cram, H. L. Nyquist and F. A. Abd Elhafez, *ibid.*, **79**, 2875 (1957); 1,2-diphenyl-1-propanol, (j) D. J. Cram and F. A. Abd Elhafez, *ibid.*, **74**, 5828 (1952); (k) D. J. Cram and F. A. Abd Elhafez, *ibid.*, **74**, 5846 (1952); 1,2-diphenyl-2-methyl-1-butanol, (l) D. J. Cram and J. Allinger, *ibid.*, **76**, 4516 (1954); (m) D. J. Cram and J. Allinger, *ibid.*, **79**, 2858 (1957); 3,4-dimethyl-4-phenyl-3-hexanol, (n) D. J. Cram and J. D. Knight, *ibid.*, **74**, 5835, 5839 (1952); 3-phenyl-2-butanol-3-*d*, (o) D. J. Cram and J. Tadanier, *ibid.*, **81**, 2737 (1959).

(4) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1954, Chapt. 6.

TABLE I

INFRARED DATA ASSOCIATED WITH HYDROGEN–OXYGEN STRETCHING FREQUENCIES IN DIASTEREOMERIC ALCOHOLS[a]

Structure	Compd.	Isomer	Free hydroxyl ν, cm.$^{-1}$	Free hydroxyl ϵ^{b}	Hydrogen-bonded hydroxyl ν, cm.$^{-1}$	Hydrogen-bonded hydroxyl ϵ^{b}	$\Delta\nu$, cm.$^{-1}$	OH...O length in Å.
 $CH_3CH(C_6H_5)CH(OH)CH_3$	II	*erythro*	3595	22.8	3451	28.4	140	1.17
	II	*threo*	3540	27.1	3454	21.8	125	1.26
 $CH_3CH(C_6H_5)CH(OH)C_2H_5$	III	*erythro*	3591	21.2	3451	22.1	136	1.19
	III	*threo*	3580	25.4	3454	17.1	122	1.28
 $C_2H_5CH(C_6H_5)CH(OH)CH_3$	IV	*erythro*	3595	20.1	3444	26.1	147	1.13
	IV	*threo*	3578	24.6	3454	21.2	120	1.29
 $C_2H_5CH(C_6H_5)CH(OH)C_2H_5$	V	*erythro*	3594	21.6	3451	22.3	139	1.17
	V	*threo*	3576	26.1	3454	15.8	118	1.30
 $(CH_3)_2CHCH(C_6H_5)CH(OH)CH(CH_3)_2$	VI	*erythro*	3623	23.8	3474	22.3	145	1.14
	VI	*threo*	3593	20.8	3479	15.8	110	1.36
 $CH_3CH(C_6H_5)CH(OH)C_6H_5$	VII	*erythro*	3578	34.4	3454	15.4	120	1.29
	VII	*threo*	3595	32.0	3454	18.9	137	1.19
 $C_2H_5C(CH_3)(C_6H_5)CH(OH)C_6H_5$	VIII	*erythro*	3570	30.2	3464	13.9	102	1.42
	VIII	*threo*	3593	29.8	3464	16.7	125	1.26

[a] Spectra were measured on a Perkin–Elmer model 21 double beam spectrophotometer with a sodium chloride prism and cells. All determinations were made in 1 *M* chloroform solutions, and cells of 0.11 mm. thickness were used. The scale was increased to have 100 cm.$^{-1}$ in 4 cm. of chart paper. Corrections in the positions of the absorption bands were applied from a calibration curve made for this instrument. The positions of the absorption maximums are correct within a limit of ±5 cm.$^{-1}$. [b] Molecular extinction coefficients.

the spectra of *erythro*-3-phenyl-2-pentanol as a liquid film and in chloroform solution, and in the latter the intensity of the free O–H absorption increases at the expense of that of dimeric form. Similar patterns were observed in the spectra of the other isomers.

The same figure records the spectra of both diastereomers of 2-phenyl-3-pentanol and of 1,2-diphenyl-1-propanol. These spectra are representative. Differences between diastereomers are visible for each band, both in intensity of absorption and frequency. Table I gives the frequencies of these bands, their intensities and the difference in frequencies between the free and hydrogen-bonded bands ($\Delta\nu$, in cm.$^{-1}$).

The studies of Badger,[5] Lord[6] and Kuhn[7] have demonstrated that $\Delta\nu$ for the free and associated hydroxyl band represents a measure of the force constant of the $-\mathrm{OH}\cdots\overset{|}{\mathrm{O}}-$ bond, the greater the separation between the two bands, the stronger the hydrogen-bonding. The empirical relationship (1) where L = O· ·H distance in cm., employed[7] to calculate the length of the hydrogen bond in cyclopentanediols and cyclohexanediols can be used to obtain the *relative lengths of the intermolecular bond* in dimeric alcohols of the type studied in the present investigation. These lengths were calculated for the diastereomeric alcohols, and the values are recorded in Table I.

$$\Delta\nu = ((250 \times 10^{-8})/L) - 74 \qquad (1)$$

The values obtained for L range from 1.1 to 1.4 Å., which compare with those of 1.2 to 1.3 Å., obtained by Kuhn[7] for dimeric, monohydric alcohols in carbon tetrachloride solutions. As previously indicated,[7] these values are lower than expected. The values obtained in the present investigation will only be employed to *compare the relative lengths of hydrogen bonds in the compounds studied*, and no significance will be attached to the absolute values obtained.[8]

In II–VIII (Table I) the only effects to consider are the attractive forces between the hydroxyl groups and the repulsive forces between non-bonded atoms. Since the attractive forces between hydroxyl groups of two diastereomerically related alcohols must be approximately equal, the dif-

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[5] R. M. Badger, *J. Chem. Phys.*, **8**, 288 (1940).

[6] R. C. Lord and R. E. Merrifield, *ibid.*, **21**, 166 (1953).

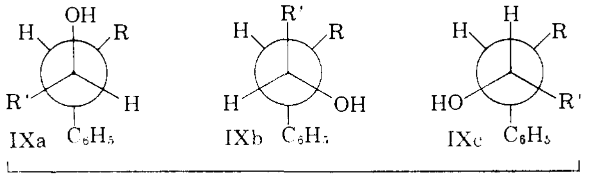
[7] L. P. Kuhn, THIS JOURNAL, **74**, 2493 (1952).

[8] Equation 1 was derived (ref. 7) for calculating lengths of intramolecular hydrogen bonds in dihydric alcohols or intermolecular hydrogen bonds in dimeric, monohydric alcohols in solutions of carbon tetrachloride. Although chloroform was used in the present investigation, the values of L obtained for dimeric, monohydric alcohols are in the same range as those found in the previous work (ref. 7).

ferences in L between diastereomers are due to the differences in steric environment of these groups in the isomers. Thus the lower value of L associated with one of the two diastereomers in each pair can be used to tell which isomer possesses the least hindered hydroxyl group.

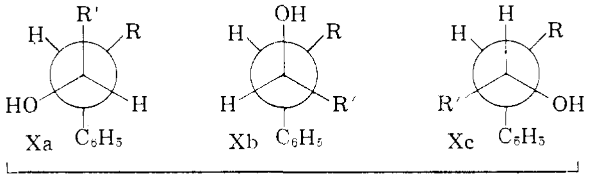
An *independent measure* of the same steric factor is found in the relative intensities of absorption of the monomeric and dimeric bands. The less hindered isomer in each set should be more hydrogen-bonded, and therefore the intensity of the band due to unassociated hydroxyl groups is expected to be lower. The data of Table I indicate that the two criteria always point to the same diastereomer as containing the least hindered hydroxyl group.

The spectrum of each compound is actually a composite of three rotomers, each of which contains the hydroxyl group in a differently hindered conformation. Although these rotomers are in equilibrium with one another, undoubtedly one predominates in the mixture for internal steric reasons.[9] Selection of the most stable rotomer can be made on the following basis. In compounds II–VI, $C_6H_5 > R > H$ in bulk on one asymmetric carbon and $R' > OH > H$, on the other.



IXa IXb IXc

erythro-configuration, compounds II–VI



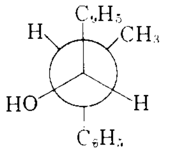
Xa Xb Xc

threo-configuration, compounds II–VI

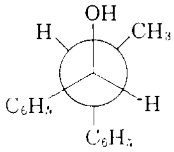
In the *threo* isomer, Xa can be selected *a priori* as the more stable rotomer on the following basis. (1) The largest groups (C_6H_5 and R′) on the two asymmetric carbon atoms are oriented 180° from one another, and are distributed between the two smallest groups on the other asymmetric carbon atom. (2) The two smallest groups (H) are oriented 180° from one another, and the four largest groups are divided into two pairs, separated by two hydrogens. Thus the steric factors tend to reinforce one another in stabilizing one rotomer at the expense of the other two. In the *erythro* isomer, the selection is more ambiguous. Clearly, IXc is less stable than IXa or IXb on both counts. On the basis of (1), IXb would appear to be the most stable, whereas IXa would be selected from consideration of (2). Thus selection of IXa or IXb as being the prominent rotomer depends on the relative importance of (1) on the one hand and (2) on the other.

The data of Table I are only compatible with IXa being more stable than IXb. The *erythro* isomers of compounds II–VI are more hydrogen-bonded and the bonds are shorter than for the corresponding *threo* isomers. Therefore, the hydroxyl groups in the *erythro* isomers must be less hindered than in the *threo* isomers. In rotomer Xa of the *threo* isomers, hydroxyl is between hydrogen and phenyl. In the *erythro* isomers, rotomer IXa has hydroxyl between hydrogen and R, and in rotomer IXb hydroxyl is between R and phenyl. Of these three rotomers, IXa < Xa < IXb in hindrance of the hydroxyl group. Thus for the *erythro* isomer alone, IXa > IXb > IXc in stability, and the steric factors associated with (2) must outweigh those associated with (1) in these kinds of systems.[10]

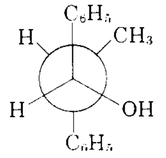
Further support for these interpretations is found in the relationships between conformations, configurations and hydrogen-bonding data for compounds VII and VIII. In these substances, the *threo* isomers are more highly hydrogen-bonded and the bond is shorter than in the corresponding *erythro* isomer (see Table I). These data are consistent with the orders of rotomer stability: VIIa > VIIb > VIIc, and VIIIa > VIIIb > VIIIc. In VIIb (*threo*), the hydroxyl is flanked by methyl and hydrogen and is therefore less hindered than in VIIa, where hydroxyl is between phenyl and hydrogen. In VIIIb (*threo*), hydroxyl is flanked by ethyl and methyl, which is less hindered than in VIIIa (*erythro*), where hydroxyl is between methyl and phenyl.



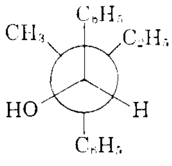
VIIa, (*erythro*)



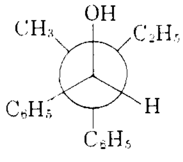
VIIb, (*threo*)



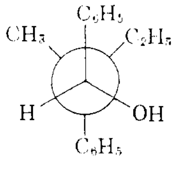
VIIc, (*threo*)



VIIIa, (*erythro*)



VIIIb, (*threo*)



VIIIc, (*threo*)

The above data suggest generalizations that might apply to rotomer stability in systems which possess two asymmetric carbon atoms and which do not carry groups that give rise to important dipole–dipole interactions. The order of rotomer stability shown in Chart I seems the most probable, although exceptions are conceivable. Below each formula is summarized the steric relationships associated with that structure. This order is

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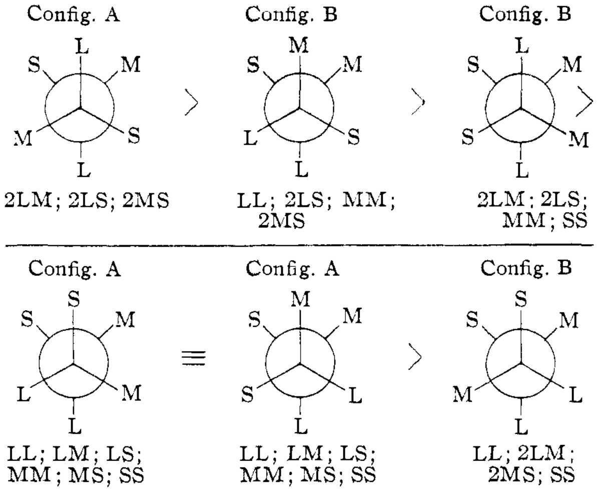
(9) In these molecules, dipole–dipole interactions probably play only a minor role in determining the more stable conformation since only one polar bond (C–O) is found in the molecule.

(10) A similar conclusion was reached on entirely different grounds in the 3-phenyl-2-butylamine system, which is sterically similar to 3-phenyl-2-butanol (II). In the deamination of this amine [D. J. Cram and J. E. McCarty, This Journal, **79**, 2866 (1957)], the migrating group was conformationally controlled, and a rough measure of the relative amounts of each conformation was obtained from the yields of the three products of neighboring-group migration. On this basis, conformations corresponding to those of IX and X arranged themselves in the order, Xa > IXa > IXb with respect to their relative stabilities.

CHART I



compatible with conclusions drawn earlier[11,31] with respect to which *diastereomer is the more thermodynamically stable* (diastereomer A of Chart I).

A number of other trends in Table I are also of interest. In the *erythro* isomers of compounds II–VI and the *threo* isomer of VII in which the hydroxyl is mainly between alkyl and hydrogen, the lengths of the hydrogen bonds are about equal (1.16 ± 0.03 Å.). In the *threo* isomers of compounds II–VI and the *erythro* isomer of VII in which hydroxyl is flanked mainly by phenyl and hydrogen, the lengths of the hydrogen bonds are also about equal (1.30 ± 0.06 Å.). In the *threo* isomer of VIII in which hydroxyl is mainly between methyl and ethyl, the bond length is 1.26 Å., and in the *erythro* isomer of VIII in which hydroxyl is mainly between phenyl and methyl, the length is 1.42 Å. These data correlate with the bulks of the groups involved and with what has been observed previously as to the relationships between hydrogen bonds and steric factors in open-chain alcohols.[12]

Nuclear Magnetic Resonance Spectra.—Nuclear magnetic resonance spectra have been used in studies of alcohols, and shifts of the proton frequency of the hydroxyl group with changes of concentration have been interpreted in terms of changes in hydrogen bonding.[13] In general, the more strongly hydrogen-bonded a proton of a hydroxyl group, the less shielded is that proton and the lower the field at which it absorbs. Thus the use of n.m.r. spectral data provides a potential criterion for the relative strengths of hydrogen bonds in the diastereomeric alcohols of the present investigation.

The n.m.r. spectra of alcohols II–VIII were determined in 1 *M* solutions of carbon tetrachloride with water as an internal standard. Figure 2 records the spectra of the two diastereomeric 3-phenyl-2-butanols, which are representative of those of alcohols II–VIII. Table II reports the displacements of the hydroxyl protons of the 14 alcohols from that of water. In alcohols II–VI, the *erythro* isomers absorb at lower fields than the corresponding *threo* isomers, and in alcohols VII and VIII, the *threo* isomers absorb at lower fields than the corresponding *erythro* isomers. Thus the protons are less shielded, the alcohols more strongly hydrogen-bonded, and therefore the hydroxyl is less sterically hindered in the *erythro* diastereomers of compounds II–VI, and in the *threo* diastereomers of compounds VII and VIII. These conclusions are in full accord with those drawn on the basis of the infrared data in the previous section, and provide strong support for the interpretations given there.

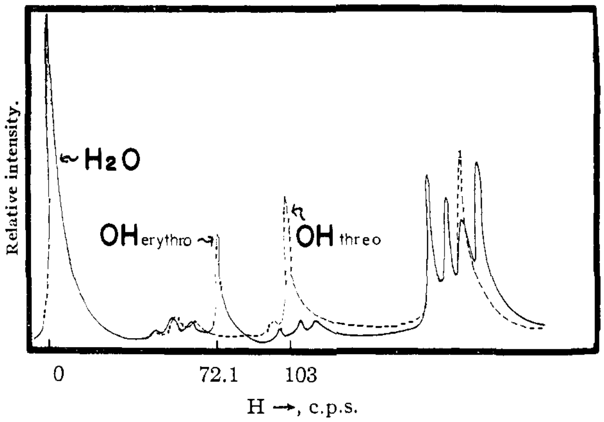


Fig. 2.—Nuclear magnetic resonance spectra (see footnote *a* of Table II for conditions): solid line, *erythro*-3-phenyl-2-butanol; broken line, *threo*-3-phenyl-2-butanol.

TABLE II

PROTON ABSORPTION OF PROTONS OF HYDROXYL GROUPS OF DIASTEREOMERIC ALCOHOLS[a]

Compound			Distance in c.p.s. from water peak
Name	No.	Config.	
3-Phenyl-2-butanol	II	*erythro*	72
3-Phenyl-2-butanol	II	*threo*	103
2-Phenyl-3-pentanol	III	*erythro*	98
2-Phenyl-3-pentanol	III	*threo*	120
3-Phenyl-2-pentanol	IV	*erythro*	48
3-Phenyl-2-pentanol	IV	*threo*	87
4-Phenyl-3-hexanol	V	*erythro*	63
4-Phenyl-3-hexanol	V	*threo*	102
2,5-Dimethyl-4-phenyl-3-hexanol	VI	*erythro*	116
	VI	*threo*	159
1,2-Diphenyl-1-propanol	VII	*erythro*	127
1,2-Diphenyl-1-propanol	VII	*threo*	108
1,2-Diphenyl-2-methyl-1-butanol	VIII	*erythro*	121
	VIII	*threo*	98

[a] Measurements were made in a Varian V-4300-B high resolution spectrometer equipped with a 12-inch magnet and superstabilizer. The frequency was fixed at 40 Mc./sec., and a magnetic field of about 9400 gauss was used. Determinations were made in 1 *M* CCl_4. Sample tubes of 5-mm. outside diameter were used, and a sealed capillary tube of about 1-mm. diameter filled with distilled water was placed inside the sample tube. The line of the water peak was used as reference to measure shifts. The distance between toluene peaks (196 c.p.s.) was used to calculate the separation between peaks. The samples were all spun while the measurements were made.

Ultraviolet Absorption Spectra.—The ultraviolet absorption spectra of the diastereomers of com-

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[11] (a) D. J. Cram and F. A. Abd Elhafez, THIS JOURNAL, **75**, 339 (1953); (b) D. J. Cram and F. D. Greene, *ibid.*, **75**, 6005 (1953).

[12] (a) F. A. Smith and E. C. Creitz, *J. Research Natl. Bur. Standards*, **46**, 145 (1951); (b) R. N. Jones and C. Sandorfy, "Technique of Organic Chemistry," Vol. IX, "Chemical Applications of Spectroscopy," Interscience Publishers, Inc., New York, N. Y., pp. 419–422.

[13] (a) E. D. Becker, U. Liddel and J. N. Shoolery, *J. Molec. Spectros.*, **2**, 1 (1958).

TABLE III

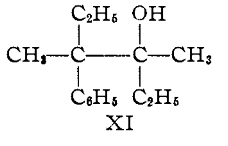
VARIATION IN INTENSITIES OF ABSORPTION OF DIASTEREOMERIC PAIRS IN THE ULTRAVIOLET[a]

Compound	Relationship of ϵ's	λ_{max}, mμ 242–243	247.5–248.5	252.5–253.5	258–259	260.5–262	264–264.8	267.5–268.5
3-Phenyl-2-butanol (II)	$\epsilon_{erythro}/\epsilon_{threo}$	1.22	1.15	1.13	1.11	1.19	1.19	1.39
3-Phenyl-2-butanol-3-*d* and	ϵ_h/ϵ_d for *threo*[b]	1.00	1.00	0.99	0.99	0.98	0.99	0.98
3-Phenyl-2-butanol-3-*h*	ϵ_h/ϵ_d for *erythro*[b]	1.07	1.07	1.05	1.03	1.12	1.05	1.21
3-Phenyl-2-butanol (II) in	ϵ_e/ϵ_c for *threo*[c]	1.00	1.01	0.99	0.98	0.99	0.98	1.00
ethanol and cyclohexane	ϵ_e/ϵ_c for *erythro*[c]	1.16	1.10	1.08	1.06	1.10	1.12	1.21
2-Phenylbutane and 2-phenylbutane-3-*d*	ϵ_h/ϵ_d	0.99	0.98	0.99	0.98	0.98	0.99	0.98
2-Phenyl-3-pentanol (III)	$\epsilon_{erythro}/\epsilon_{threo}$	.99	1.03	1.04	1.04	1.13	1.07	1.27
3-Phenyl-2-pentanol (IV)	$\epsilon_{erythro}/\epsilon_{threo}$	.99	1.00	1.00	1.00	1.08	1.02	1.18
4-Phenyl-3-hexanol (V)	$\epsilon_{erythro}/\epsilon_{threo}$	1.09	1.10	1.10	1.09	1.23	1.11	1.39
2,5-Dimethyl-4-phenyl-3-hexanol (VI)	$\epsilon_{erythro}/\epsilon_{threo}$	0.95	0.96	0.97	0.99	1.01	1.01	1.05
1,2-Diphenyl-1-propanol (VII)	$\epsilon_{erythro}/\epsilon_{threo}$	.94	.81	1.00	1.04	1.02	1.03	1.01
1,2-Diphenyl-2-methyl-1-propanol (VIII)	$\epsilon_{erythro}/\epsilon_{threo}$	.56	.63	0.73	0.84	..	0.83	0.71
3,4-Dimethyl-4-phenyl-3-hexanol (XI)	$\epsilon_{erythro}/\epsilon_{threo}$	1.09	1.03	1.00	1.01	..	1.01	..

[a] Cary recording spectrophotometer, model 11 MPS, spectra taken in 95% ethanol unless otherwise specified, and in quartz cells. [b] $\epsilon_{3\text{-hydrogen}}/\epsilon_{3\text{-deuterium}}$. [c] $\epsilon_{ethanol}/\epsilon_{cyclohexane}$.

pounds II–VIII, XI and of 3-phenyl-2-butanol-3-*d* were determined in 95% ethanol, and those of 3-phenyl-2-butanol (II) in cyclohexane. The wave lengths of the corresponding series of peaks ranging from 242 to 269 mμ vary a maximum of 1 mμ and as much as 80% in intensity within a diastereomeric pair. The ratios of intensities of absorption of the seven λ_{max}'s for the diastereomeric pairs and for deuterated and non-deuterated pairs are recorded in Table III, along with the ratio for 2-phenylbutane and 2-phenylbutane-2-*d*.

For 3-phenyl-2-butanol (II), $\epsilon_{erythro}/\epsilon_{threo}$ ranges from 1.11 to 1.39, depending on λ_{max}, the largest difference being associated with the longest wave length band. The intensity relationship, ϵ_h/ϵ_d, is equal to unity within experimental error for *threo*-II, and for the model compound, 2-phenylbutane. However, for *erythro*-II, ϵ_h/ϵ_d ranges from 1.03 to 1.21, again the longest wave length band showing the largest values. Thus, the intensity of absorption of *threo*-II shows no isotope effect while that of *erythro* shows an effect as high as 20%. When the benzyl hydrogen of II is replaced with an ethyl group as in XI, the longest wave length band cannot be distinguished, and $\epsilon_{erythro}/\epsilon_{threo}$ approaches unity for the other bands. For *erythro*-II but not for *threo*-II, the intensity of the seven bands are sensitive to solvent. Thus for *threo*-II, $\epsilon_{ethanol}/\epsilon_{cyclohexane} = 1$ for the seven bands, but range from 1.06 to 1.21 for *erythro*-II, and the longest wave length band gives the largest departure from unity.



$$\mathrm{CH_3-\underset{C_6H_5}{\overset{C_2H_5}{C}}-\underset{C_2H_5}{\overset{OH}{C}}-CH_3}$$

XI

In passing from II to III, IV and V, the values of $\epsilon_{erythro}/\epsilon_{threo}$ get closer to unity, and except for the lower wave length bands of VI, are always greater than unity. Throughout the series, the ratio has the largest value for the band at the longest wave length. The largest values of this ratio are always associated with the largest differences in values of λ_{max} for the various bands, although $\Delta\lambda_{max}$, is never greater than unity. These results will be interpreted in a later paper of this series.

Optical Rotatory Dispersion.—The optical rotatory dispersions of certain cyclic systems such as steroidal ketones have proved to be a powerful tool in characterization, and structure determination.[14] This method has been limited to compounds that possess strong optically active chromophores like the carbonyl group. This function absorbs in a convenient position in the ultraviolet, and absorbs at low enough intensity to permit good measurements of the dispersion peak. It seemed possible that some empirical correlation might also be found between the shapes of the dispersion curves and the configurations of alcohols II–VIII of the present investigation, particularly since in these compounds phenyl is attached to one of the two asymmetric centers.

Optically pure diastereomers prepared previously were used in each case,[3] and measurements were made from about 300 to 650 mμ in 0.1 to 1.1% solutions of the alcohols in dioxane. Over this range of concentration, the dispersion spectrum of (+)-*erythro*-1,2-diphenyl-1-propanol did not change appreciably. However, the curves of (+)-*threo* and (+)-*erythro*-1,2-diphenyl-1-propanol did change somewhat (see Fig. 3) in passing from ethanol to dioxane to chloroform, possibly due to differences in hydrogen bonding in these three solvents.

Figure 3 records the rotatory dispersion curves of the isomers of compounds II–VIII in dioxane. Although no general correlation between the configurations of these compounds and the shapes of these curves is evident, a few relationships are worth pointing out. In the series of alcohols whose two asymmetric centers are substituted with the same alkyl groups (3-phenyl-2-butanol, 4-phenyl-3-hexanol and 2,5-dimethyl-4-phenyl-3-hexanol), the curve for the *threo* isomer passes through a maximum at between 310 and 340 mμ, whereas the *erythro* isomers possess no maximum

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(14) C. Djerassi, J. Osiecki, R. Riniker and B. Riniker, THIS JOURNAL, **80**, 1216 (1958), and earlier papers of this series.

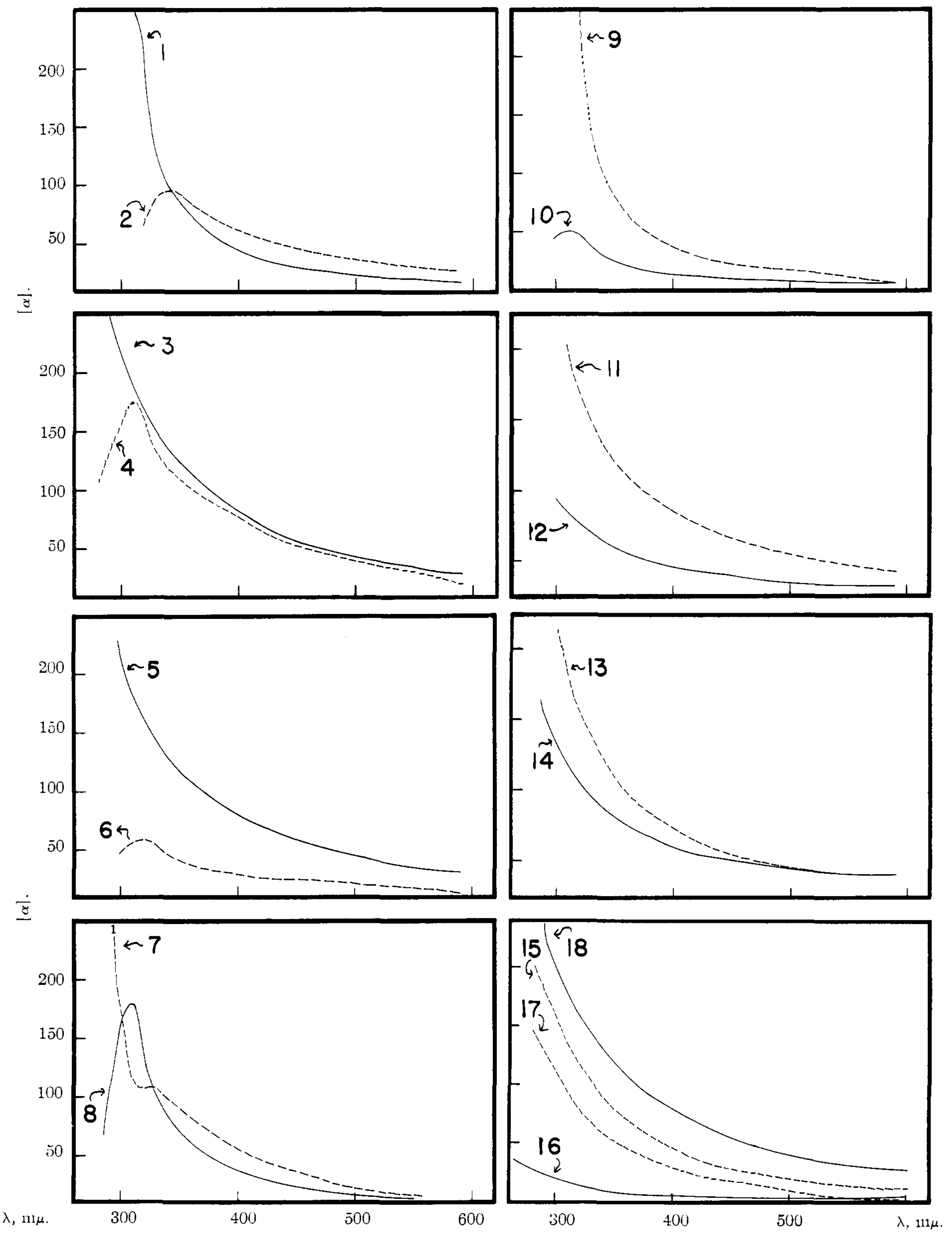

Fig. 3.—Optical rotatory dispersion curves (see Experimental for conditions): curves 1–14 were determined 0.5% by weight in dioxane solution, curves 15 and 16, 0.15% by weight in ethanol, and curves 17 and 18, 0.1% by weight in chloroform. Curve 1, *erythro-* and 2, *threo*-3-phenyl-2-butanol; curve 3, *erythro-* and 4, *threo*-4-phenyl-3-hexanol; curve 5, *erythro-* and 6, *threo*-2,5-dimethyl-4-phenyl-3-hexanol; curve 7, *threo-* and 8, *erythro*-2-phenyl-3-pentanol; curve 9, *threo-* and 10, *erythro*-3-phenyl-2-pentanol; curve 11, *threo-* and 12, *erythro*-1,2-diphenyl-2-methyl-1-butanol; curve 13, *threo-* and 14, *erythro*-1,2-diphenyl-1-propanol; curve 15, *threo-* and 16, *erythro*-1,2-diphenyl-1-propanol; curve 17, *threo-* and 18, *erythro*-1,2-diphenyl-1-propanol.

above 300 mμ.[15] In those alcohols in which one asymmetric carbon carried a methyl and the other an ethyl (3-phenyl-2-pentanol and 2-phenyl-3-pentanol), the situation is reversed, and the *erythro* isomer possesses a maximum above 300 mμ and the *threo* none. For the alcohols in which a phenyl is attached to each asymmetric carbon (1,2-diphenyl-1-propanol and 1,2-diphenyl-2-methyl-1-butanol), neither diastereomer possesses a maximum, and for most of the region examined, the *threo* isomers have higher rotations than the *erythro*. Plots of the inverse of $[\alpha]$ against λ^2 for representative compounds gave lines which were not straight, but deviations from linearity were small.

Other Physical Properties.—The refractive indices of those diastereomers that are liquids at room temperature (compounds II–V and VIII) were taken, and are recorded in Table III. In all compounds measured the *erythro* isomers possess the higher refractive index.

Enough densities of these alcohols were determined to establish that no generalizations could be made correlating density and configuration. It is noted that in most cases the melting points of the *erythro*-alcohols[3] and their esters[3] tend to be higher than those of the *threo*-alcohols, but enough exceptions are known to prevent this generalization to be used for diagnostic purposes.

TABLE III

INDICES OF REFRACTION OF DIASTEREOMERIC ALCOHOLS

Compound	Configuration	$n^{25}D$
3-Phenyl-2-butanol (II)	*erythro*	1.5167
3-Phenyl-2-butanol (II)	*threo*	1.5159
2-Phenyl-3-pentanol (III)	*erythro*	1.5121
2-Phenyl-3-pentanol (III)	*threo*	1.5113
3-Phenyl-2-pentanol (IV)	*erythro*	1.5106
3-Phenyl-2-pentanol (IV)	*threo*	1.5097
4-Phenyl-3-hexanol (V)	*erythro*	1.5088
4-Phenyl-3-hexanol (V)	*threo*	1.5072
1,2-Diphenyl-2-methyl-1-butanol (VIII)	*erythro*	1.5698
	threo	1.5694

Experimental

The footnotes of Tables I, II and III indicate the types of instruments, solvents and conditions of measurement for the infrared and n.m.r. studies. The data for the rotatory dispersion curves were taken in a Rudolph photoelectric spectropolarimeter model 200 S-80 equipped with a RCA IP 28 photomultiplier tube and a Xenon arc lamp. Readings were taken at 700, 650, 589 and 550 mμ, each 20 mμ's from 520 to 380, and each 10 or 5 mμ from 380 to 300 mμ. The polarimeter tube was 0.5 dm. with quartz windows. The slit width of the Beckman spectrometer was increased gradually to give approximately constant readings, which were taken by the symmetrical angles method.[16]

The 2-phenylbutane-3-*d* used in this investigation contained 91% deuterium, and its preparation and analysis will be reported in a future publication.

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[15] Measurements could not be made lower than 300 mμ because of the considerable light absorption of the aromatic system. The shapes of the dispersion curves without maxima above 300 mμ suggest that maxima do appear at somewhat lower wave lengths.

[16] W. Heller in A. Weissberger's "Physical Methods of Organic Chemistry," Interscience Publishers, Inc., New York, N. Y., 1949, 2nd edition, Vol. 1, Chapter 23.

LOS ANGELES, CALIF.

[CONTRIBUTION FROM THE RESEARCH DIVISION OF ETHICON, INC.]

Stereochemistry of Diels–Alder Adducts. III. The Preparation and Rearrangement of Some Brominated Derivatives of Norbornanecarboxylic Acids

BY WERNER R. BOEHME

RECEIVED JUNE 26, 1958

2-*exo*-Bromonorbornane-2-*endo*-carboxylic acid and its derivatives were obtained *via* the Diels–Alder reaction of cyclopentadiene with α-bromoacrylic acid and subsequent reduction of the double bond or by bromination of norbornane-2-*endo*-carbonyl chloride. Bromination of norbornane-2-*endo*-carboxylic acid, however, gave the rearranged 2-*exo*-bromonorbornane-1-carboxylic acid as the sole product. 2-*exo*-Bromonorbornane-2-*endo*-carboxamide undergoes rearrangement upon heating above its melting point or upon treatment with dilute alcoholic alkali to form 2-*exo*-bromonorbornane-1-carboxamide. Catalytic or chemical hydrogenolysis of the isomeric bromoamides gives norbornane-2-*endo*-carboxamide and norbornane-1-carboxamide, respectively.

As part of a program designed to synthesize highly hindered trisubstituted acetic acids of bicyclic systems,[1] we have studied the stereochemistry of some halogenated norbornanecarboxylic acids and the rearrangement of 2-*exo*-bromonorbornane-2-*endo*-carboxamide.[2]

The rearrangement of 2-*exo*-bromonorbornane-2-*endo*-carboxylic acid (I, R = OH) and its methyl ester (I, R = OCH_3) upon hydrogenolysis has been described by Kwart and Null.[3] These authors reported the formation of norbornane-1-carboxylic acid (IV, R = OH) upon catalytic hydrogenation of 2-*exo*-bromonorbornane-2-*endo*-carboxylic acid in the presence of dilute methanolic potassium hydroxide and palladium–charcoal catalyst and the formation of 1-carbomethoxynorbornane (IV, R = OCH_3) upon chemical reduction of 2-*exo*-bromo-2-*endo*-carbomethoxynorbornane (I, R = OCH_3) with zinc and acetic acid. It has been shown[2] recently that no rearrangement takes place upon either catalytic or chemical hydrogenolysis and that the bromonorbornanecarboxylic acid and its ester reported by Kwart and Null were already rearranged prior to hydrogenolysis.

Bromination of norbornane-2-*endo*-carbonyl chloride (III, R = Cl)[4] in boiling thionyl chloride solu-

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[1] W. R. Boehme, E. Schipper, W. G. Scharpf and J. Nichols, THIS JOURNAL, **80**, 5488 (1958).

[2] For a preliminary communication describing this rearrangement see W. R. Boehme, *ibid.*, **80**, 4740 (1958).

[3] H. Kwart and G. Null, *ibid.*, **80**, 248 (1958).

[4] K. Alder, G. Stein, M. Liebmann and E. Rolland, *Ann.*, **514**, 197 (1934).