least-squares fits from visually determined start and end points, and are extrapolated to the center of the peak.

Registry No.—**1a**, 35619-91-1; **1b**, 35619-92-2; **1c**, 35619-93-3; **1d**, 35619-94-4; **1e**, 35619-95-5; **1f**, 35619-96-6; **1g**, 35619-97-7; **1h**, 35619-98-8; **1i**, 35619-99-9; **1j**, 35620-00-9; **1k**, 35620-01-0; **5a**, 35620-02-1; **5b**, 35620-03-2; **5c**, 35620-04-3; **5d**, 35620-05-4; **5e**, 35620-06-5.

Acknowledgments.—We wish to thank Harold A. Huggins, who performed the microscopy and the calorimetric measurements. We are also pleased to acknowledge the contributions of A. L. Bednowitz, R. V. Dobransky, and N. C. Hien, who designed and built the DSC-computer interface and performed the major share of the necessary programming. We thank M. J. Freiser and D. T. Teaney for helpful discussions.

2,3-Di(2-pyridyl)-2,3-butanediol. A Crystal and Molecular Structure Study of the Meso Form with Ancillary Proton Magnetic Resonance Data

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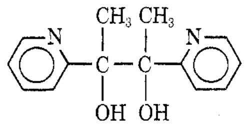
The crystal and molecular structure of 2,3-di(2-pyridyl)-2,3-butanediol ($C_{14}H_{16}N_2O_2$) has been determined by a single-crystal, X-ray diffraction study. The compound crystallizes with four molecules in a monoclinic cell ($P2_1/c$) of dimensions $a = 9.293$, $b = 11.885$, $c = 13.615 \pm 0.001$ Å, and $\beta = 123.98 \pm 0.01°$. The structure was solved by direct methods and the 1097 statistically significant reflections were refined to a final value of $R = 0.05$. Estimated standard deviations were less than 0.008 Å for bond distances and 0.5° for bond angles for those bonds not involving hydrogen atoms. The configuration was established as the meso compound, and, furthermore, the conformation was shown to be that involving hydrogen bridging between each of the pyridyl nitrogens and the more distant oxygen forming additional six-membered rings. Although not required by crystallographic symmetry, the molecule possesses a center of symmetry well within the estimated standard deviation. Pmr data for an additional ten compounds with analogous five-, six-, and seven-membered hydrogen-bonded ring possibilities are given and evaluated, and effectively underscore the uniqueness of the title compound. A comparison of the pmr data with a limited set of corresponding infrared data casts doubt on the reliability of the predictions from the infrared data regarding intramolecular hydrogen bonding.

Unequivocal assignment of the stereochemical identities of the two diastereomeric pinacols (I) resulting



I (meso, *dl* forms)

from the electropinacolization of 2-acetylpyridine was necessary as part of a continuing study[2] of the stereochemical consequences of this type of electrochemical bimolecular reduction. Such assignments may be made by the tedious and often unsuccessful procedures of absolute synthesis or enantiomeric resolution. More equivocal but often adequate approaches include differences in gross crystal structure, melting point comparisons, and infrared and pmr analysis of the hydroxyl group, particularly where several of these methods reinforce each other. In the present case, these convenient techniques were precluded; the two diastereomers have identical melting points, no free hydroxyl stretching bands in the infrared, and essentially identical hydroxylic proton resonances buried in the aromatic area.[3] A tentative assignment was made, however, on the basis of the degree of shielding encountered by the methyl groups as based on the apparent most favorable conformations for the several different forms possible for each diastereomer as determined from molecular models.[2] To establish this assignment unequivocally, an X-ray crystallographic study was undertaken on the diastereomer that had tentatively been assigned the meso form. Additional pmr studies of related compounds were also undertaken to consider the relative degrees of hydrogen bonding encountered in such compounds. The data are brought together and evaluated in this report.

Crystallographic Studies

Obtaining crystals of suitable quality for an X-ray structure study proved to be exceedingly difficult and time consuming. First, the compound crystallized in more than one space group, depending on solvent and experimental conditions; *i.e.*, monoclinic crystals in space group $P2_1$ (or $P2_1/m$) were obtained from hot carbon tetrachloride, while crystals in space group $P2_1/c$ were obtained from warm hexane solutions. Second, all of the crystals exhibited extreme layering perpendicular to the b axis. Intensity differences of 5:1 (or greater) in a φ scan at $\chi = 90°$ on a General Electric XRD-5 diffractometer were obtained repeatedly. Finally, a crystal of dimensions 0.10 × 0.15 × 0.23 mm was recrystallized from one of the hexane solutions and exhibited an intensity ratio of 1.13:1.00. Extinctions [$k = 2n + 1$ for the $(0k0)$ reflections and $l = 2n + 1$ for the $(h0l)$ reflections] uniquely characterized the space group as $P2_1/c$.

Lattice constants were determined by a least-squares fit of 16 carefully measured 2θ values (1° take-off angle

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[1] (a) Address pmr inquiries to J. H. S., crystallographic inquiries to L. M. T. (b) Tables of structure factor data and refined coordinates and temperature factors will appear following these pages in the microfilm edition of this volume of the journal. Single copies may be obtained from the Business Operations Office, Books and Journals Division, American Chemical Society, 1155 Sixteenth St., N.W., Washington, D. C. 20036, by referring to code number JOC-72-3712. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche.

[2] J. H. Stocker and R. M. Jenevein, *J. Org. Chem.*, **34**, 2807 (1969).

[3] For a more detailed discussion of these several approaches, with suitable references, see ref 2.

and 0.05° slit) at $2\theta > 66°$ where the Cu Kα_1 and Cu Kα_2 doublet is resolvable. The resultant lattice constants and their estimated standard deviations are a = 9.293 ± 0.001 Å; b = 11.885 ± 0.001 Å; c = 13.615 ± 0.001 Å; β = 123.98 ± 0.01°.

The experimental density of 1.29 ± 0.01 g/cm^3 agrees with the calculated density of 1.29 g/cm^3 assuming four molecules per unit cell.

Three-dimensional intensity data were collected on a General Electric XRD-490 fully automated diffractometer by the stationary-counter, stationary-crystal method using balanced nickel and cobalt filters and Cu Kα radiation. A total of 2135 independent reflections were measured to a 2θ maximum of 140° (d = 0.82 Å). Of these, 1097 reflections (51%) were considered statistically acceptable by the criterion $[I_{\text{Ni}} - 2\sigma(I_{\text{Ni}})] - [I_{\text{Co}} + 2\sigma(I_{\text{Co}})] > 100$ counts (10-sec counting times; σ based on counting statistics).

The data were corrected for α_1–α_2 splitting[4] as a function of 2θ and for absorption as a function of φ (linear μ = 7.2 cm^{-1} and a maximum difference of 13% in the φ scan at χ = 90°). An irregular crystal decay of 17% was observed during data collection and corrected by multiplicative factors as a function of time. Lorentz-polarization corrections were made and the intensities were reduced to structure amplitudes in the usual manner.

Structure Determination

The structure was solved by direct methods. After conversion to normalized structure magnitudes ($|E|$'s) and appropriate scaling using a k curve,[5] 279 reflections with $|E|$ values greater than 1.5 were obtained. Using only three-dimensional data, an origin and four other $|E|$'s were chosen from among the 15 largest $|E|$ values. The phases of these additional four were permuted, resulting in 16 combinations. Five of the 16 combinations resulted in the phasing of approximately 190 reflections each and these five also had consistency indices[6] significantly greater than the other 11. Of these five, only one had the combination (200) = − and (400) = + (both of which have large $|E|$'s, which would be anticipated if the molecule did not utilize the inversion center of the unit cell). An $|E|$ map was calculated for this case and 16 peaks were found, consistent with our expectations on chemical grounds. Five cycles of block-diagonal, least-squares isotropic refinement using $\sigma^{1/2}$ weights and approximating all of the peaks as carbon atoms resulted in a value of the reliability index, R = 0.31.[7] A new electron-density map phased by these 16 atoms clearly indicated the remaining two peaks anticipated. The relative heights of two of the peaks, combined with their small temperature factors in the least-squares refinement, made the assignment of the oxygen atoms on crystallographic grounds relatively simple. Since this was not the case for the nitrogens, all other atoms were left as carbons. Additional isotropic least-squares refinement resulted in a value of R = 0.14. At this stage, the temperature factors clearly indicated the nitrogens and thus all of the atoms were assigned appropriate scattering factors. After conversion to anisotropic temperature factors, refinement was continued for ten more cycles, resulting in a value of R = 0.09.

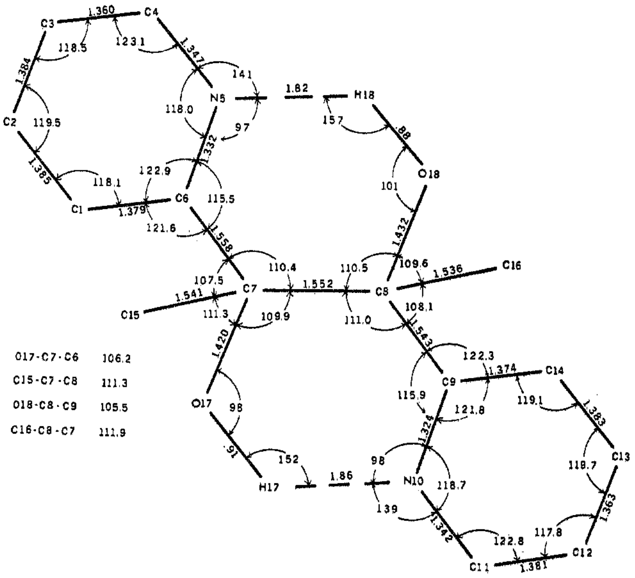


Figure 1.—Schematic drawing of the molecule showing bond distances and bond angles. Proposed intramolecular hydrogen bonding scheme indicated on the drawing.

The hydrogen atoms were located from a difference electron-density map and proved to be the only peaks with an electron density greater than 0.2 e/Å^3 (the hydrogen positions had peak heights ranging from 0.6 to 0.9 e/Å^3). A final series of similar least-squares was carried out varying the coordinates of all atoms (including the hydrogens). The anisotropic temperature factors of the nonhydrogens were also varied, but the isotropic temperature factors of the hydrogens were held fixed at a value of 4.0 Å^2. The refinement converged to a final value of $R = 0.05_2$ with the shifts of all of the parameters varied being significantly less than one-tenth of the estimated standard deviation of the respective parameter.

Crystallographic Results

Table I[1b] lists the final coordinates and temperature factors for the nonhydrogen atoms together with their estimated standard deviations (ESD's). Table II[1b] lists the analogous data for the refined hydrogen coordinates with the exception that the hydrogen positions were refined with fixed isotropic temperature factors of 4.0 A^2. Figure 1 is a schematic drawing of the molecule with bond angles and bond distances indicated on the drawing. ESD values for bond distances and bond angles (for the nonhydrogen bonds) are less than 0.00_8 Å and 0.5°, respectively. For those bond distances and bond angles involving hydrogen, the ESD's were significantly higher at values less than 0.04 Å and 3.0°, respectively. The refined hydrogen distances are available[1b] in tabular form.

(4) A. Tulinsky, C. Worthington, and E. Pignataro, *Acta Crystallogr.*, **12**, 623 (1959).

(5) J. Karle, H. Hauptman, and C. L. Christ, *ibid.*, **11**, 757 (1958).

(6) The consistency index was defined as $C = \Sigma_h(T_t - T_a)/\Sigma_h(T_t + T_a)$, where T_t = sum of triple products contributing towards the accepted phases and T_a = sum of triple products contributing against the accepted phases.

(7) The conventional reliability index $R = \Sigma w||kF|_o - F_c||/\Sigma w|F_o|$ is cited throughout the paper. Scattering factors for carbon, nitrogen, and oxygen are taken from the paper by D. Cromer and J. Waber, *Acta Crystallogr.*, **18**, 104 (1965), while that for hydrogen is from "International Tables for X-Ray Crystallography," Vol. III, Kynoch Press, Birmingham, England, 1968.

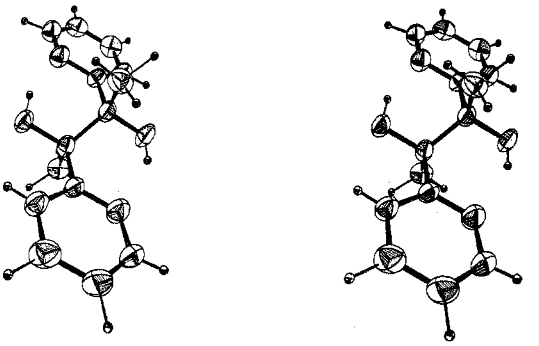


Figure 2.—ORTEP stereodrawing of the molecule.

The *meso*-pinacol may be considered to consist of two α-methyl-2-pyridylcarbinol groups bonded through the C7–C8 bond and held essentially rigid in the indicated conformation (Figure 1) by the hydrogen bridging between each of the pyridyl nitrogens and the more distant oxygen. The compound does not utilize the crystallographic center of symmetry in space group $P2_1/c$, hence affording two independent measurements of each parameter. However, within the ESD values observed in the parameters, the molecule does, in fact, possess a center of symmetry. All bond distances (including the N to O distances) are centrosymmetrically disposed within 2 ESD's and all bond angles within 3 ESD's. It is thus reasonable to compare parameters averaged over all of the molecule with analogous values found in the literature.

Within the pyridyl ring itself, the C–N distances average to $1.33_6 \pm 0.01_2$ Å, a value in agreement with the analogous value reported by Bak, *et al.*,[8] for pyridine (1.34 Å), and by Seff and Trueblood[9] for a substituted pyridine (1.34_6 Å). Similarly the C–C distances in this study average to $1.37_6 \pm 0.00_8$ Å compared to 1.39[8] and 1.38[9] in the aforementioned studies. A close parallel also exists between the pyridyl angles reported here and those reported by Trueblood:[9] *i.e.*, CNC = 118.3° (*vs.* 117.0°), CCC = 118.8° (*vs.* 118.7°), and NCC = 122.7° (*vs.* 123.5°).

A least-squares fit to the best planes indicates that each pyridyl ring (atoms 1–6 and 9–14) is planar within 0.005 Å. If one includes the immediately adjacent carbon in each case (C7 to pyridyl ring C1–C6 and C8 to pyridyl ring C9–C14), each seven-atom structure is still planar within 0.012 Å. The meso compound then consists of these two centrosymmetrically related planes bonded together at C7–C8 with an overall deviation from total plarity of 2.6°. The hydroxylic oxygens of each segment are in sufficiently close proximity to the nitrogen atom of the *other* segment to permit hydrogen bonding resulting in two additional six-membered rings which effectively fix the meso compound in the structure indicated in the ORTEP stereodrawing (Figure 2). The N to O distances of 2.66 and 2.70 Å lead to hydrogen-bonding distances of 1.82 and 1.86 Å with NHO angles of 152 and 157°, respectively.

In addition to the intramolecular hydrogen bonding already discussed, there exist a limited number of intermolecular close contacts. These lie in the range of 3.40–3.48 Å and consequently represent, at best, very weak interactions. Figure 3 shows the contents of the unit cell projected down the *b* axis and indicates these contacts. One of the pyridyl carbons (C2) has two close contacts (with an O18 at 3.43 Å and a C11 at 3.48 Å). The chemically related carbon in the other pyridyl ring (C13) has two analogous close contacts (with an O17 at 3.48 Å and a C4 at 3.40 Å).

Experimental Section

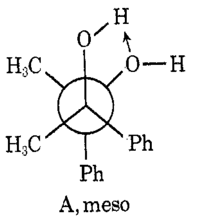
meso- and *dl*-acetophenone pinacols were synthesized as previously reported,[10] mp 121° (meso), 125° (*dl*). The two diastereomeric pinacols of 2-acetylpyridine have also been reported and were correspondingly prepared.[2] Hydropyridoin was purchased from the Aldrich Chemical Co. The 2-pyridoin and the several 2-pyridylalkanols were purchased from the J. T. Baker Co. The α-methyl-2-pyridylcarbinol [1-(2-pyridyl)ethanol] was synthesized by the routine $NaBH_4$ reduction of 2-acetylpyridine.

2,3-Di(2-pyridyl)-2-butanol was prepared by a modification of the published preparation for 1,2-di(2-pyridyl)ethene.[11] To a stirred ether solution of phenyllithium prepared from 14.8 ml of bromobenzene and 2.0 g of Li wire was added 15.7 g of ethylpyridine in 10 ml of anhydrous ether and the mixture was refluxed for 1 hr. After the reaction mixture was cooled to −10°, a solution of 13.4 g of 2-acetylpyridine in 10 ml of anhydrous ether was added dropwise with stirring and the stirring was continued for 1 hr at −10°. Water (50 ml) was added, and, after agitation, the reaction was transferred to a separatory funnel. The organic layer was extracted successively with 50 and 50 ml of H_2O, 18 and 10 ml of concentrated HCl. The collected aqueous extractions were neutralized with sodium bicarbonate and multiply extracted with ether. The ether extracts were dried and evaporated to yield 16.9 g of a dark oil. A fraction of this was distilled at reduced pressure, bp 125–130° (1 mm), to yield a colorless liquid that solidified on standing, mp 97°, uv 262 nm (ε 9000).

Nmr spectra were determined on an A-60 (Varian) instrument in deuterochloroform solution.

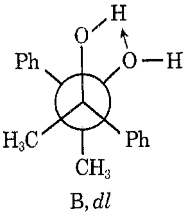
Nmr Studies

Conformational analysis of simple diastereomeric alkyl phenyl pinacols indicates that intramolecular hydrogen bonding should occur more favorably in the *dl* diastereomer, *e.g.*, for the acetophenone pinacols A and B, considering only those major conformations allowing such bonding



A, meso

one of two conformational forms; maximum nonbonded interactions



B, *dl*

one of two conformation forms; minimum nonbonded interactions

This is reflected in the greater degree of hydrogen bonding displayed by the *dl* form in the infrared,[12] and the greater downfield shift of the hydroxylic protons of this diastereomer. This latter phenomenon has been observed for a number of related pinacols[13] and has

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[8] B. Bak, L. Hansen-Nygaard, and J. Rastrup-Andersen, *J. Mol. Spectrosc.*, **2**, 361 (1958).

[9] K. Seff and K. N. Trueblood, *Acta Crystallogr., Sect. B*, **24**, 1406 (1968).

[10] J. H. Stocker and R. M. Jenevein, *J. Org. Chem.*, **33**, 294 (1968).

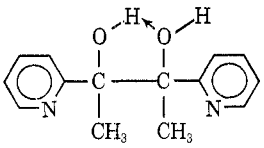
[11] C. S. Marvel, A. T. Tweedie, and J. Economy, *ibid.*, **21**, 1420 (1956).

[12] W. A. Mosher and N. D. Heindel, *ibid.*, **28**, 2154 (1963); L. P. Kuhn, *J. Amer. Chem. Soc.*, **80**, 5950 (1958).

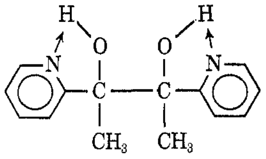
[13] J. H. Stocker, D. H. Kern, and R. M. Jenevein, *J. Org. Chem.*, **33**, 412 (1968); A. D. Thomsen and H. Lund, *Acta Chem. Scand.*, **23**, 3582 (1970).

been utilized previously for stereochemical assignment.[14]

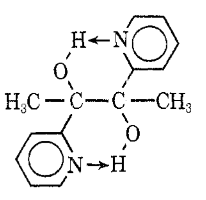
The 2-acetylpyridine pinacols present an unique case in which consideration of hydrogen bonding possibilities includes not only forms analogous to A and B (structure C) but, among others,[15] *two* additional five-membered ring forms (D, meso and *dl*) and two further



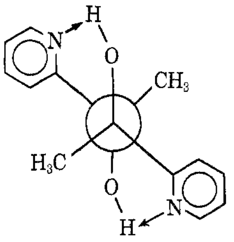
C



D



E



F

six-membered ring forms (E, meso and *dl*). Structure F provides a conformational analysis of hydrogen bridging in the meso form according to E (as well as the conclusions from the subsequent crystallographic study).

There is, of course, nothing to preclude one diastereomer from adopting preferentially a ring structure different from the other diastereomer.

Pmr data for 11 compounds appear in Table III. These compounds, all but two 2-pyridyl derivatives, were selected to permit hydrogen-bonding comparisons that involved five-, six-, and seven-membered rings, primary, secondary and tertiary carbinols, pinacols, and an enediol. The data may be summarized briefly as follows.

(1) The concentration independence of the hydroxylic proton resonance for the meso and *dl* forms underscores the intramolecular nature of the hydrogen bonding.

(2) The simplest pyridine glycol (hydropyridoin, no. 6) shows the effects of intramolecular bonding but in somewhat lesser degree than the title compound (3) (contrast δ 5.58 with 7.25).

(3) The maximum deshielding observed for hydroxylic protons involves a tertiary carbinol adjacent to a tertiary carbon atom, with both five- and six-membered ring possibilities (3, 4, 5) (excepting compound 7, *vide infra*).

(4) The simple carbinols (8–11) do not display the strong hydrogen bonded effects shown by the title compound and its diastereomer. The resonance position of the hydroxylic proton in these simple carbinols is strongly concentration dependent, suggesting that hydrogen bonding at higher concentrations is maximally intermolecular. The most dilute solutions

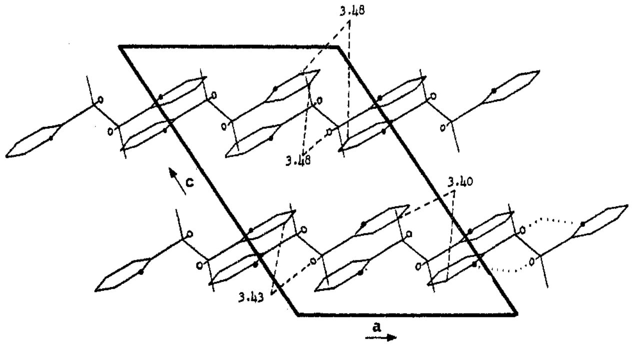


Figure 3.—Drawing of the unit cell projected down the *b* axis. Closest contacts (less than 3.50 Å) indicated.

have values comparable to the acetophenone pinacols 1 and 2.

(5) Only one compound, "pyridoin"[16] (7), showed a hydroxylic proton resonance more downfield than the title compound.

Additional General Comments

While the specific intent of the research reported here was to establish the diastereomeric identities of compound I, the data derived, taken in conjunction with selected pmr, crystallographic, and infrared information about hydrogen bonding in the same or related compounds from the literature, permit some additional comments placing the diastereomers of compound I in a larger framework, and allow some useful contrasts and comparisons.

Range of Pmr Values.—An impressively large range of intramolecularly bonded hydrogen values have been observed.

Fields and Regan[17] studied compound III, sterically a very crowded molecule, and reported that it displayed a hydroxylic proton resonance at δ 12.5–13.0 (broad singlet, concentration independent).

Vogt and Werth[18] reported the crystallographic structure of IV and suggested that there was a considerable resonance contribution by the quinoid-type structure indicated.

Compounds II, III, and IV may reasonably be considered to represent examples of extreme intramolec-

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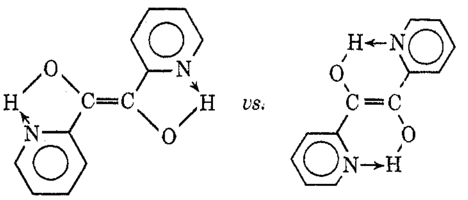
[14] J. H. Stocker, *J. Amer. Chem. Soc.*, **88**, 2878 (1966).

[15] For example, hydrogen bonding of the nonbridging hydroxylic proton in the pyridine analogs of A and B with a ring nitrogen may be considered less important.

[16] "Pyridoin" has been clearly established [see C. A. Buehler, *Chem. Rev.*, **64**, 7 (1964)] as being 1,2-di(2-pyridyl)-1,2-eth*ene*diol by infrared studies. Pmr data for this compound apparently have not been reported. The trans, double six-membered ring structure has been proposed (see above reference) as being the most reasonable hydrogen-bonded form, without additional data or consideration of alternate five-membered ring structures.



II

The name "pyridoin" appears to persist and is used routinely in the chemical catalogs.

[17] D. L. Fields and T. H. Regan, *J. Org. Chem.*, **36**, 2991 (1971).

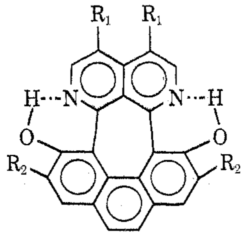
[18] L. H. Vogt, Jr., and J. G. Werth, *J. Amer. Chem. Soc.*, **93**, 5402 (1971).

TABLE III

PMR SPECTRA OF VARIOUS CARBINOLS AND GLYCOLS[a]

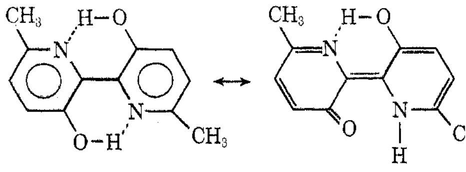
Registry no.	No.	Compd[b]	Concn[c]	Aromatic	Alkyl[d] α	β	γ	Hydroxy
4217-65-6	1	*meso*-PhC(CH$_3$)(OH)C(CH$_3$)(OH)Ph	3.3	7.25 (s)		1.59 (s)		2.28
			1.67	7.25		1.59		2.25
			0.83	7.24		1.60		2.25
22985-90-6	2	*dl*-1	3.3	7.25 (s)		1.50 (s)		2.60
			1.67	7.25		1.51		2.55
			0.83	7.24		1.51		2.54
20445-38-9	3	*meso*-PyC(CH$_3$)(OH)C(CH$_3$)(OH)Py	3.3	7.05–8.60 (m)		1.27		7.25
			1.67	7.05–8.60		1.27		7.25
			0.83	7.05–8.60		1.27		7.25
20445-39-0	4	*dl*-3	3.3	6.75–8.25		1.68		6.98
			1.67	6.75–8.24		1.68		6.97
			0.83	6.75–8.24		1.68		6.98
35657-31-9	5	PyC(CH$_3$)(OH)CH(CH$_3$)Py	13.3	6.90–8.70 (m)	1.35 (s)	3.68 (q)	1.00 (d)	6.30
			6.7	6.90–8.70	1.35	3.58	1.00	6.16
			3.3	6.90–8.70	1.35	3.57	1.00	6.03
1141-05-5	6	PyCH(OH)CH(OH)Py	6.7	7.00–8.70 (m)	4.96 (s)			5.59
			3.3	7.00–8.70	4.95			5.58
			1.67	7.00–8.70	4.94			5.58
			0.83	7.00–8.70	4.94			(5.58)
1141-06-6	7	PyCOCH(OH)Py	3.3	7.00–8.60 (m)				12.8
			1.67	7.00–8.60				12.8
586-98-1	8	PyCH$_2$OH	13.3	7.00–8.60 (m)	4.76 (s)			5.20
			6.7	7.00–8.60	4.76			4.55
			3.3	7.00–8.60	4.78			4.03
			1.67	7.00–8.60	4.77			3.12
			0.83	7.00–8.60	4.77			2.30
103-74-2	9	PyCH$_2$CH$_2$OH	13.3	6.95–8.60 (m)	3.02 (t)	4.01 (t)		4.63
			6.7	6.95–8.60	3.03	4.03		4.27
			1.67	6.95–8.60	3.02	4.03		3.44
			0.83	6.95–8.60	3.02	4.03		3.07
2589-68-9	10	PyCH$_2$CH$_2$CH$_2$OH	13.3	6.95–8.60 (m)	2.96 (t)	2.00 (m)	3.72 (t)	4.98
			6.7	6.95–8.60	2.96	2.00	3.71	4.59
			1.67	6.95–8.60	2.96	1.98	3.70	3.27
			0.83	6.95–8.60	2.96	1.98	3.70	2.85
18728-61-5	11	PyCH(OH)CH$_3$	13.3	6.90–8.70 (m)	4.93 (q)	1.50 (d)		4.54
			6.7	6.90–8.70	4.93	1.52		4.06
			1.67	6.90–8.70	4.91	1.51		3.15
			0.83	6.90–8.70	4.91	1.51		2.80

[a] In CDCl$_3$; all chemicals shifts (δ) are given with respect to TMS. [b] Ph = phenyl, Py = 2-pyridyl. [c] w/w, as per cent. [d] α, β, and γ are with respect to the hydroxylic carbon.



R$_1$R$_2$ = H, alkyl

III

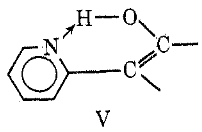


IV

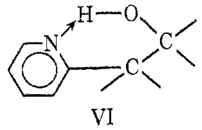
N–H, 1.69 Å N–O (closest), 2.568 Å

O–H, 0.69 Å NHO, 150.9°

ular hydrogen bonding for the type of system under consideration here. Two of the three compounds (II and III) display essentially identical hydroxylic proton resonance values (12.8 *vs.* 12.5–13.0). All three compounds permit a partial formulation as V. Such enolic



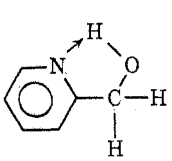
V

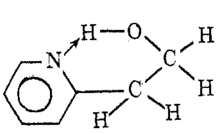


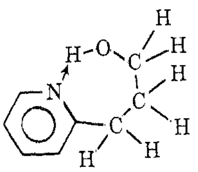
VI

structures have notably more deshielded hydroxylic protons and the pmr values are not unprecedented.

Compound I, as well as VII, VIII, and IX (compounds 8, 9, and 10, Table III) may be partially formulated as VI or an analog and cannot display the enolic







	VII	VIII	XI
OH (concd), δ	5.20	4.63	4.98
OH (dilute), δ	2.30	3.07	2.85

formulation V. It will be noted in the present studies that the hydroxylic proton resonance values of such compounds vary from the most deshielded, I, concentration independent at δ 7.25, to dilute solution values of 2.30 for VII, 2.85 for IX, and 3.07 for VIII (the most comparable to VI), *an overall range of almost five δ units.* The total range of contrast between V and VI is almost ten such units.

Crystallographic Comparisons.—Contrasting the crystallographic data for the title compound (I, average values, N–H 1.84 Å, N–O 2.68 Å, and NHO 155°) with that published for IV (see under structure) it will be noted that the enolic structure type V has the shorter distances, correlating with the tighter hydrogen bonding as reflected in the more deshielded proton. If the observed differences in NHO angles of 4° is significant, the more tightly bound structure IV has the more acute angle, in contrast to the presumed maximum favorability of linear overlap.[19]

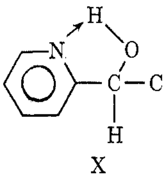
In comparing such crystallographic data for solids with pmr solution data, separating the contributions of intramolecular, intermolecular, and π-type hydrogen bonding is always difficult, since the observed pmr resonances reflect a total of such contributions. It may be pointed out that crystal studies should reflect an irreducible minimum of such *intra*molecular bonding; *i.e.*, if essentially complete intramolecular hydrogen bonding prevails in the presence of closely packed molecules, no less than this should be found in solution, assuming negligible solvent interactions. It is then pertinent to underscore the fact that, in both of the molecules for which crystallographic data are considered here, the minimum *inter*molecular potential hydrogen bonding contact is greater than 3.4 Å, well beyond the accepted distance. The point being made is that the solution pmr values do, in fact, reflect an effective measure of such intramolecular hydrogen bonding.

Pmr and Infrared Contrasts.—The available data do not lead to the same conclusions. This point is emphasized for the following reasons. Much of the assessment of such hydrogen bonding is customarily by infrared techniques.[12] In tightly *intra*molecularly bonded species, no free O–H stretching is observed in the infrared, and diagnostic values of $\Delta\bar{\nu}$, the frequency difference between the free and bonded forms, cannot be determined. Pmr approaches should be of particular value in such cases. Further, the use of $\Delta\bar{\nu}$ as a measure of the strength or distance of hydrogen bonding has been seriously challenged.[20]

Since infrared data have been published for three compounds considered in this present report, a formal comparison between the two techniques is possible. Kuhn,[19] *et al.*, interpreted infrared data for VII, VIII, and IX as reflecting "strong intramolecular hydrogen bonds." Based on $\Delta\bar{\nu}$ values for very dilute solutions, the order of strength of bonding was found to be IX (seven-membered ring) > VIII (six-membered ring) > VII (five-membered ring), with the last being somewhat more strongly bonded than anticipated. The use of Dreiding model comparisons of static conformations, leading to maximum intramolecular hydrogen bonding for each of these molecules, led to the conclusion that IX, with its seven-membered ring, in accord with the infrared data, should display the most favorable intramolecular hydrogen bonding. Assuming in the present study that the extreme concentration dependence of the hydroxylic proton resonances for these compounds reflects appropriate interplays of inter- and intramolecular bonding, the corresponding ratings for those concentrations involving appreciably intermolecularly bonded species would be VII > IX > VIII. The reverse order is suggested for the most dilute solutions, VIII > IX > VII, *i.e.*, the six-membered ring would appear to be the most favored arrangement, *in contrast to* the infrared data. Perhaps, more to the point, these values in very dilute solution would *not* appear to reflect *strong intra*molecular hydrogen bonding forces, whether considered simply as distinctly "upfield" values or when contrasted to the resonances observed for compound I. The use of model analogies for what is clearly a very dynamic situation is undoubtedly misleading. *Most important, however,* is that the infrared and pmr data do not lead to the same conclusions.

Meilahn and Munk[21] have commented briefly and succinctly on the differences in pmr and infrared approaches to conformational evaluation. In a pair of papers[21,22] dealing with the conformational equilibria of diastereomeric 1,2-amino- and substituted amino alcohols, their results underscore the importance of intramolecular hydrogen bonding. Of particular pertinence here is that for such bonding (NHO) giving rise to a five-membered ring, hydroxylic proton resonances for 15% $CDCl_3$ solutions appeared between *ca.* δ 3.3 and 5, essentially analogous for the corresponding concentrations to those observed in the present study for compounds VII–X. These values and the general discussion above serve to further emphasize the unique degree of intramolecular hydrogen bonding reflected in the δ 7.25 value for compound I.

The presence of the methyl group in X, as contrasted to its absence in VII, would appear to decrease the total hydrogen bonding, presumably by steric interference with intermolecular activity, while increasing the intramolecular bonding as demonstrated by the downfield shift in dilute solution. This parallels the influence of the two methyl groups in I when compared to simple hydropyridoin (compound 6, Table I).



X

OH (concd), δ 4.54

OH (dilute), δ 2.80

Acknowledgments.—J. N. B. and L. M. T. wish to express their gratitude to the National Science Foundation (GU 2632) for financial support, to the Depart-

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[19] L. P. Kuhn, R. A. Wires, W. Ruoff, and H. Kwart, *J. Amer. Chem. Soc.*, **91**, 4790 (1969).

[20] *E.g.*, see E. L. Eliel and H. D. Banks, *ibid.*, **94**, 171 (1971), for a brief but useful summary of this problem: ". . . attempted correlations of $\Delta\bar{\nu}$ with molecular geometry have tended to be empirical."

[21] M. K. Meilahn and M. E. Munk, *J. Org. Chem.*, **34**, 1440 (1969).

[22] M. E. Munk and M. K. Meilahn, *ibid.*, **33**, 3480 (1968).

ment of Health, Education and Welfare for a NDEA Fellowship (to J. N. B.), and to the computer center at LSUNO. The center's advanced computer facilities were partially provided by NSF under GJ 131. R. M. J. and J. H. S. acknowledge, with thanks, a Petroleum Research Fund (ACS) Graduate Fellowship (GF 14) to R. M. J. The pmr instrument was awarded to LSUNO by NSF under GP-3674.

The Stereochemistry of the Conjugate Addition of Derivatives of *endo*-2-Norbornylcopper(I) to Mesityl Oxide[1a]

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Reaction between mesityl oxide and the ate complex formed by mixing *endo*-2-norbornyl(tri-*n*-butylphosphine)copper(I) (*endo*-**2**) and *tert*-butyllithium yields the conjugate adduct, 4-methyl-4-(*endo*-2-norbornyl)pentan-2-one (**3**), with high stereoselectivity; no detectable 4-methyl-4-(*exo*-2-norbornyl)pentan-2-one (**4**) is formed. This stereochemical outcome excludes a free norbornyl radical as an intermediate in this particular conjugate addition reaction. Similar stereochemical results are obtained using either the analogous trimethyl phosphite complex or the ate complex formed by mixing *endo*-**2** with methyllithium; the same mechanistic conclusion can be drawn concerning these reactions. The copper-catalyzed conjugate addition of *endo*-2-norbornylmagnesium bromide (*endo*-**1**) to mesityl oxide yields an 81:19 ratio of endo and exo conjugate adducts; the conjugate addition of **2** itself occurs with extensive loss of stereochemistry. Mechanistic interpretation of these latter reactions is complicated both by the formation of conjugate adduct in relatively low yields, and by the two possibilities that epimerization of the copper reagents competes with their conjugate additions and that the endo and exo organometallic reagents differ in their reactivity in these additions. A comparison of the combined yields of **3** and **4** obtained on reaction of mesityl oxide with **1** in a copper-catalyzed reaction, with **2**, and with a number of ate complexes containing **2** and primary, secondary, tertiary, and aromatic lithium reagents indicates that the mixed ate complex of **2** and *tert*-butyllithium is uniquely active in the transfer of the 2-norbornyl group in the conjugate addition.

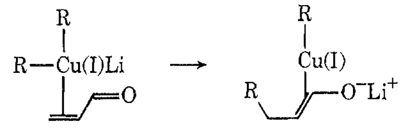
Both the copper-catalyzed conjugate addition of organomagnesium and -lithium reagents to α,β-unsaturated ketones and the rapid stoichiometric conjugate addition of lithium dialkylcuprates to these substances are well established and synthetically important reactions.[2] However, the mechanism by which the copper ion encourages addition of the anionic organic moiety to the β-carbon atom of the unsaturated ketone moiety at the expense of addition to the carbonyl group is not understood.[3] Several experimental generalizations known or believed to be true for it follow.

(a) Copper(I) is the valence state that is active in the conjugate addition; further, the copper(I) is apparently not oxidized or reduced irreversibly during the course of the reaction.[4]

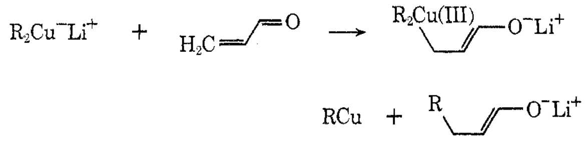
(b) Copper(I) alkyls add to a number of types of carbon–carbon multiple bonds in the absence of a conjugating carbonyl moiety; in particular, lithium dialkylcuprates add smoothly to α,β-unsaturated epoxides[6] and ethynylcarbinyl acetates,[7] and organocopper(I) compounds themselves add to terminal acetylenes[8] and nitroaromatics.[9] Thus, the presence of a conjugating carbonyl group is not necessary for the addition of an organic moiety bonded to copper to a carbon–carbon multiple bond.

(c) Conjugate addition can occur successfully to α,β-unsaturated ketones confined to a transoid configuration; a cyclic transition state for the addition, involving a cisoid conformation for the ketone, is thus not required.[3,10,11]

Four basic classes of mechanisms have been proposed to account for the influence of copper on reactions of organometallic reagents with α,β-unsaturated ketones. First, the reaction has been suggested to involve as its basic step the nucleophilic addition of an anionic alkyl group to the carbon–carbon double bond. In this mechanism (represented schematically by eq 1), the copper atom might serve either to orient the alkyl group in a position favorable for attack on the β-carbon atom of the enone moiety by coordination with the double bond, or to activate this bond for



(1)



(2)

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[1] (a) Supported by the National Science Foundation, Grants GP-28586X and GP-14247, and by the International Copper Research Association; (b) National Science Foundation Trainee, 1970–1971.

[2] For reviews and references, see (a) H. O. House, W. L. Respess, and G. M. Whitesides, *J. Org. Chem.*, **31**, 3128 (1966); (b) H. O. House and W. F. Fischer, Jr., *ibid.*, **33**, 949 (1968).

[3] The catalytic activity of copper in organic reactions has been reviewed: R. G. R. Bacon and H. A. O. Hill, *Quart. Rev., Chem. Soc.*, **19**, 95 (1965); O. A. Chaltykian, "Copper-Catalytic Reactions," A. E. Stubbs, Translator, Consultants Bureau, New York, N. Y., 1966.

[4] Alkylcopper(I) compounds frequently precipitate on reaction of the corresponding lithium dialkylcuprates with α,β-unsaturated ketones.[2b,5]

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[6] R. W. Herr and C. R. Johnson, *J. Amer. Chem. Soc.*, **92**, 4979 (1970); R. J. Anderson, *ibid.*, **92**, 4978 (1970).

[7] P. Rona and P. Crabbé, *ibid.*, **91**, 3289 (1969).

[8] J. F. Normant and M. Bourgain, *Tetrahedron Lett.*, 2583 (1971).

[9] M. Nilsson, C. Ullenius, and O. Wennerström, *ibid.*, 2713 (1971).

[10] H. O. House, R. A. Latham, and C. D. Slater, *J. Org. Chem.*, **31**, 2667 (1966).

[11] C. P. Casey and R. A. Boggs, *Tetrahedron Lett.*, 2455 (1971).