TABLE I

COMPOSITION OF THIOL–ALCOHOL MIXTURES[a] FROM THE REDUCTION OF THIO ACIDS (RCOSH)

R	Registry no.	Reducing agent $LiAlH_4$[b]	 $LiAlH_4$–BF_3[c]	 $NaBH_4$–$AlCl_3$
C_6H_5	98-91-9	56	70	86[d]
p-ClC_6H_4	31143-03-0	56	67	78
p-$MeOC_6H_4$	6279-44-3	53	76	95
n-C_5H_{11}	7530-91-8	45	60	
C_2H_5	1892-31-5	51		81

[a] Expressed as mole pecentage of thiol in the thiol–alcohol mixture. [b] Thio acid was added to the hydride. Inverse addition produced 45, 40, and 40% thiol from C_6H_5COSH, p-$MeOC_6H_4COSH$, and n-$C_5H_{11}COSH$, respectively. [c] Hydride was added to the mixtures of thio acid and boron fluoride etherate; $LiAlH_4$:BF_3:thio acid mole ratios, 1:0.8:0.8. [d] The mole percentage of thiol was 84 when $AlCl_3$ was omitted.

under a variety of conditions. Lithium aluminum hydride reduction occurs rapidly to give high yields (86–100%) of alcohol–thiol mixtures. As indicated in Table I, alcohol and thiol are formed in nearly equal amounts and the ratio is not significantly different for aliphatic, aromatic, and substituted aromatic acids. Also, the ratio was not affected by variation in the hydride concentration from 1 to 2 M or by changes in the $LiAlH_4$:thio acid mole ratio from 1.2 to 2.5. Slow, inverse addition of hydride results in a small but consistent increase in the proportion of alcohol formation over that observed when the thio acid was added to the hydride.

The data show that when boron fluoride etherate[5] and the thio acid are present in a 1:1 molar ratio, a significant increase in the proportion of oxide displacement (thiol formation) occurs. These reductions occurred rapidly and completely with yields in the range of 67–85%. A large excess (15:1) of boron fluoride etherate as described for the conversion of thiol esters to thioethers[2] reduced the total yield but did not result in further increase in the amount of benzyl mercaptan produced from thiobenzoic acid.

Sodium borohydride reduction of the thioacids in diglyme was investigated. Reduction of thiobenzoic acid with sodium borohydride alone was only about half complete after 2 days, but the sodium borohydride–aluminum chloride reagent described by Brown[6] caused essentially complete reduction in 0.5 hr with yields in the range of 78–95%. As seen in Table I, the proportion of oxygen displacement (thiol formation) is much higher than with the other reductants studied. In two cases investigated (thiobenzoic and thiopropanoic) the thio–alcohol ratio was nearly the same when $AlCl_3$ was omitted.

Experimental Section

Materials.—All compounds used in the study have been described previously. Authentic samples were either commercially available or prepared by standard procedures. Thiobenzoic acid was supplied by Evans Chemical Co.; the other thio acids were prepared from the corresponding acyl chlorides.[7] Equivalent weights of the thio acids were determined by iodine titration and found to be within at least 5% of the calculated values in all cases.

Methods of Analysis.—The mixtures of alcohols and thiols obtained by reduction of the thio acids were analyzed by vpc using an F & M Model 700 chromatograph. All analyses were done with a 4 ft × 0.25 in. aluminum column containing 15% Carbowax 20M on 60–80 mesh Chromosorb W (HMDS treated). Column temperatures were varied between 45 and 190° and flow rates from 60 to 120 ml/min so that short retention times were obtained (1.2–2.5 min for the alcohols). In all alcohol–thiol mixtures the thiol had the shorter retention time. Analysis was based on peak-height ratios. An average of six standard mixtures was prepared from the pure alcohol and thiol for each analysis. To assure accuracy of the peak-height analysis, slight adjustment of the flow rate was sometimes made, so as to reproduce identical retention times between runs. Yields were determined by addition of internal standards.

Lithium Aluminum Hydride Reductions.—In typical reductions 0.025 mol of the thio acid dissolved in 20 ml of ether was allowed to react with 0.031 mol of *ca.* 1 M, standardized $LiAlH_4$ solution. Solutions refluxed during addition and reaction was complete in less than 15 min. After hydrolysis with acid the ether solutions were analyzed directly by vpc. In a typical run using boron fluoride, 0.016 mol of *ca.* 1 M $LiAlH_4$ solution was added to a mixture of 0.0125 mol of the thio acid and 1.8 g (0.0125 mol) of redistilled boron fluoride etherate in 15 ml of ether.

Sodium Borohydride Reductions.—To 15 ml of a 1.04 M solution (0.016 mol) of $NaBH_4$ in diglyme, thio acid (0.0125 mol) in 5 ml of diglyme was added, followed by a solution of 0.005 mol of sublimed $AlCl_3$ in 5 ml of diglyme. The mixture was then stirred and heated at 75° for 30 min under nitrogen. The thiol–alcohol mixture was isolated by hydrolysis with acid and extraction with ether. The quantity of unreacted thio acid as determined by iodine titration after bicarbonate extraction of the ether solution was usually about 5%. In an experiment carried out under the same conditions but with the $AlCl_3$ omitted, 47% of thiobenzoic acid remained after 44 hr.

Registry No.—$LiAlH_4$, 16853-85-3; $NaBH_4$, 16940-66-2.

Acknowledgment.—Acknowledgment is made to the National Science Foundation (Academic Year Extension of the Research Participation Program for College Teachers) for support of this research.

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(5) Aluminum chloride as catalyst under the same conditions gave 50% thiol from thiobenzoic acid and 51% thiol from thiohexanoic acid, in combined thiol–alcohol yields of 83 and 65%, respectively. Extensive side reactions evidently occur at other conditions (increase in $AlCl_3$:$LiAlH_4$ ratios up to 3.2; mode of reagent addition changed), so that yields as low as 50% from thiobenzoic acid and 30% from thiohexanoic acid were observed. However, the mole percentage of thiol produced did not vary extensively: for thiobenzoic acid 34–57% and thiohexanoic acid, 48–60%.

(6) H. C. Brown and B. C. Subba Rao, *J. Amer. Chem. Soc.*, **78**, 2582 (1956).

(7) P. Noble, Jr., and D. S. Tarbell, "Organic Syntheses," Collect Vol. IV, N. Rabjohn, Ed., Wiley, New York, N. Y., 1963, p 924.

Intramolecular Hydrogen Bonding in the 1,2-Diphenylethanol System

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The use of infrared spectroscopy to show the presence of intramolecular hydrogen bonding between hydroxyl groups and π electrons is well documented.[2] Of special interest is the work of Oki and Iwamura, who demonstrated, *via* ir, that benzyl alcohols undergo a type of intramolecular hydrogen bonding as in I.[3]

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(1) NSF Undergraduate Fellow, 1970.

(2) L. H. Bellamy, "The Infra-red Spectra of Complex Molecules," Wiley, New York, N. Y., 1966, p 95.

(3) (a) M. Oki and H. Iwamura, *Bull. Chem. Soc. Jap.*, **32**, 955 (1959); (b) M. Oki and H. Iwamura, *ibid.*, **35**, 1552 (1962).

TABLE I

NEAR-INFRARED ABSORPTIONS FOR THE 4-SUBSTITUTED 1,2-DIPHENYLETHANOLS

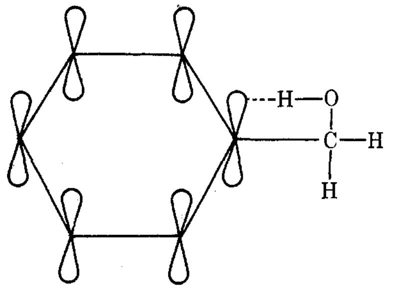
Substituent	Absorption bands in 0.5% CCl_4, μ		Δ	σ	Absorption bands in 0.5% benzene, μ
NMe_2 (V)	1.4160	1.4278	0.0118	−0.600	1.4270
OMe (VI)	1.4160	1.4275	0.0115	−0.268	1.4270
Me (VII)	1.4163	1.4273	0.0110	−0.170	1.4270
H (VIII)	1.4165	1.4258	0.0093	0.0000	1.4269
C_6H_5 (IX)	1.4166	1.4268	0.0102	+0.009	1.4270
F (X)	1.4165	1.4265	0.0100	+0.062	1.4272
Cl (XI)	1.4165	1.4255	0.0090	+0.226	1.4270
Br (XII)	1.4165	1.4255	0.0090	+0.232	1.4270
NO_2 (XIII)	1.4170			+0.778	1.4267

Using the 1.4-μ[4] region of the near infrared, Goldman and Crisler showed that an intramolecular hydrogen bond of type II exists in certain β-phenethyl alcohols.[5]

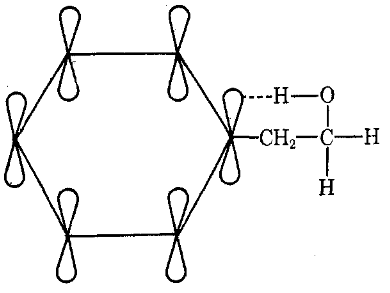
A system which has not been extensively studied with regard to hydrogen bonding is that of 1,2-diphenylethanol, which can be viewed as a derivative of either benzyl alcohol or β-phenethyl alcohol. Since in dilute solution the potential for two different types of intramolecular hydrogen bonding (III and IV) exists in this system, we prepared a number of 4-substituted 1,2-diphenylethanols and examined their spectrum in the 1.4-μ region of the near infrared to see if we could find any evidence of hydrogen bonding.

The results, which are listed in Table I, revealed that all the alcohols, with the exception of the *p*-nitro derivative, showed a strong band in the 1.4165-μ region and a discernible shoulder in the 1.4270-μ region. The ratio of the intensities of the two peaks was shown to be independent of concentration at several low concentrations (5–0.5% in carbon tetrachloride).

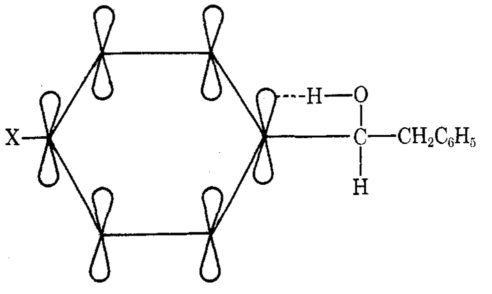
It is well known that, in benzene solution, alcohols form intermolecular hydrogen bonds between the hydrogen of the hydroxyl group and the π electrons of the benzene ring. This bonding occurs to such a large extent that in dilute solution the presence of the band for the free hydroxyl group is not detectable in the near-infrared region. In the case of benzyl alcohols and β-phenethyl alcohols the region in the near infrared, in which the intermolecular hydrogen bond absorbed in benzene solution, was found to be nearly identical with that in which the intramolecular hydrogen bond absorbed in CCl_4 solution.[4] For the 1,2-diphenylethanol system the near ir spectrum of each alcohol in benzene showed only one band in the 1.4270-μ region. We thus ascribe the absorption in the 1.4270-μ region for the 1,-2-diphenylethanols run in CCl_4 solution to be due to the presence of a hydrogen bond. The fact that the band continued to appear in CCl_4 even at low concentrations strongly mitigates against the possibility of intermolecular hydrogen bonding. The band in the region of 1.4165 μ which appeared only in CCl_4 solution is ascribed to the presence of a free hydroxyl group.



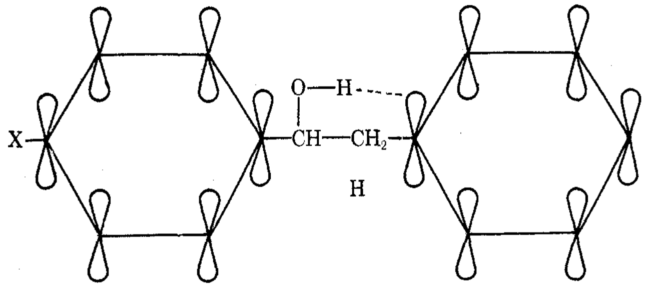
I



II



III



IV

In order to gain some insight into the nature of the intramolecular hydrogen bond that exists in the 1,2-diphenylethanol system, we compared the value of Δ[6] for each alcohol with the Hammett σ value.[7] The data in Table I clearly showed that the value of Δ decreased as the electron-withdrawing ability of the sub-

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(4) The 1.4-μ region, which is the area for the first overtone of the fundamental stretching vibration of the hydroxyl group, has been frequently used for hydrogen bonding studies on compounds containing a hydroxyl group. See L. Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 1940, p 316; also ref 2, p 104.

(5) I. M. Goldman and R. O. Crisler, *J. Org. Chem.*, **23**, 751 (1958).

(6) Δ = distance in microns between the peaks of each alcohol.

(7) J. Hine, "Physical Organic Chemistry," McGraw-Hill, New York, N. Y., 1962, p 90.

TABLE II

PHYSICAL PROPERTIES OF THE 4-SUBSTITUTED 1,2-DIPHENYLETHANOLS

Compd	Mp, °C	Lit. mp, °C	Ref	Calcd, % C	Calcd, % H	Found, % C	Found, % H
V	59–60	59–60	*a*				
VI	57–58	57–58	*b*				
VII	67–68	67–68	*c*				
VIII	67–68	67–68	*d*				
IX	156–157			87.56	7.35	87.42	7.44
X	43–44			77.76	6.06	77.88	6.18
XI	53–54	52–53	*c*				
XII	51–52	51–52	*e*				
XIII	109–110	109–110	*e*				

[a] F. Sachs and L. Sachs, *Ber.*, **38**, 515 (1905). [b] A. Orekhoff and M. Tiffeneau, *Bull. Soc. Chim. Fr.*, **37**, 1410 (1925). [c] A. Feldstein and C. van der Werf, *J. Amer. Chem. Soc.*, **76**, 1621 (1954). [d] Reference 4. [e] Reference 9.

stituent, as measured by σ, increased. This was what would have been expected for an intramolecular hydrogen bond of type III. If the bonding was of type IV, one would have expected either no change in Δ with σ or that the order of Δ with σ would have been opposite to what was found.[8]

In summary, the data tend to indicate that in dilute solution, a form of intramolecular hydrogen bonding resembling III exists for several derivatives of the 1,2-diphenylethanol system. Why this particular type of hydrogen bonding occurs can only be speculated on. However, the answer may lie in the fact that all the substituents studied, with the exception of the nitro group, possess the ability to donate electron density to the ring either by induction or resonance. This donation of electron density may be the driving force which enables the OH to bond with the phenyl ring possessing the substituent. It is noteworthy that the NO_2-substituted alcohol is the only one which fails to give a second band in the near ir. More information is currently needed before a complete picture can be developed. Further work is continuing in our laboratories.

Experimental Section

Instrumentation.—Near-infrared spectra were recorded on a Cary 14 recording spectrophotometer. Melting points were taken on a Hoover capillary melting point apparatus and are uncorrected.

Preparation of Compounds.—Compounds V–XII were prepared using the procedure illustrated by the preparation of 4-fluoro-1,2-diphenylethanol below. Compound XIII was prepared according to the procedure of Noyce.[9] All the physical data for compounds V–XIII is summed up in Table II.

Preparation of 4-Fluoro-1,2-diphenylethanol.—In a 500-ml, round-bottom flask equipped with a reflux condenser and a mechanical stirrer, a solution of benzylmagnesium chloride was made by adding benzyl chloride (13 g, 0.11 mol) to magnesium (2.4 g, 0.1 g-atom) in 100 ml of ether. A solution of 4-fluorobenzaldehyde (12.4 g, 0.1 mol) in 50 ml of ether was added over a 10-min period with stirring. After stirring for 2 hr the solution was hydrolyzed using a saturated ammonium chloride solution. The ether layer was filtered off. After the ether was removed under reduced pressure, the remaining solid was taken up in heptane and crystallized, mp 43–44°. The yield was 0.064 mol (64%).

Registry No.—V, 31233-60-0; VI, 5422-47-9; VII, 20498-63-9; VIII, 614-29-9; IX, 31233-64-4; X, 23096-47-1; XI, 31233-66-6; XII, 20498-64-0; XIII, 20498-66-2.

(8) Electron-withdrawing substituents on benzyl alcohols have been shown to strengthen the proton donor ability of the OH, resulting in a lower frequency of absorption for the OH when it forms a bond with any species besides the phenyl ring. See ref 3b.

(9) D. S. Noyce, D. R. Hartter, and R. M. Pollack, *J. Amer. Chem. Soc.*, **90**, 3794 (1968).

Formylation of Amines with Phenyl Formate

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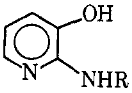
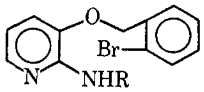
Conventional formylation procedures with 2-amino-3-pyridinol (**1**) or 2-amino-3-(*o*-bromobenzyloxy)pyridine (**2**) gave principally the formic acid salts **3** and **4**, respectively, and attempts, under a variety of conditions, to dehydrate **3** or **4** yielded tars rather than the corresponding *N*-formyl derivatives **5** and **6**. Eventually, **6** was prepared in 50% yield from **2**, HCO_2H, and dicyclohexylcarbodiimide;[1] the same procedure with **1**, however, failed to give **5**.



1, R = H
3, R = $H \cdot HCO_2H$
5, R = CHO
8, R = CH_3CO



2, R = H
4, R = $H \cdot HCO_2H$
6, R = CHO

In the search that ensued to uncover other formylation procedures for both **1** and **2**, it was found that phenyl formate (**7**) was a uniquely effective reagent that converted both **1** and **2** to **5** and **6**, respectively, in very high yields. The same reagent was also useful for converting a variety of aliphatic, aromatic, and heterocyclic amines to their *N*-formyl derivatives.[2]

In this procedure, the amine was mixed with a slight excess of **7** that had been cooled to 0°. Reaction was spontaneous, even at 0°, and sufficiently exothermic to raise the temperature of the mixture to 20–30°. In some instances the product crystallized from the reaction mixture and could be isolated by filtration. When the product was soluble, the mixture of phenol and any unreacted **7** was distilled *in vacuo* and the product isolated from the residue. The yields ranged from 60 to 95%.

(1) H. L. Yale and J. Pluscec, *J. Org. Chem.*, **35**, 4254 (1970).

(2) There are no reports in the literature of the use of phenyl formate as a formylating agent.