# Chemistry of Enolates. VI. An Acidity Scale for Ketones. Effect of Enolate Basicity in Elimination Reactions of Halides[1]

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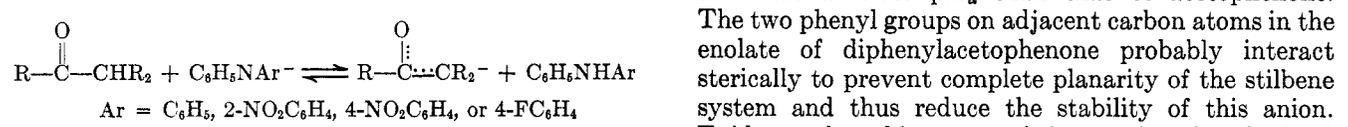
Relative acidities of dialkyl and alkyl phenyl ketones were determined by equilibration with one or more sodium diarylamides in polyether solvents. An acidity scale based on 4-nitrodiphenylamine, $pK_a$ = 15.9, was constructed for ketones ranging from deoxybenzoin, $pK_a$ = 16.1, to pentamethylacetone, $pK_a$ = 23.5. The equilibrium acidities did not parallel reported kinetic acidities from base-catalyzed proton exchange. In reactions of the conjugate sodium enolates with alkyl halides, the percentage of elimination accompanying alkylation increased markedly with the relative basicity of the enolate. Crystals of sodiodeoxybenzoin isolated from monoglyme were shown to contain one molecule of solvent per ion pair.

The determination of relative acidities of hydrocarbons by kinetic methods has received much recent attention, and the use of polar organic solvents containing varying amounts of water has permitted quantitative extensions of acidity scales from the pH region to a $pK_a$ of 19 for amines and alcohols.[2] The need for a basis for comparison of kinetic acidities determined by isotope exchange techniques has revived interest in the Conant–Wheland–McEwen scale of equilibrium acidities.[3]

Notably absent in these studies has been a comparison of acidities of carbonyl compounds. For their scale, Conant and Wheland chose acetophenone as the reference compound assigning to it a $pK_a$ of 20, but other ketones were not included. Acetone, also with a $pK_a$ of 20, was the least acidic compound and only simple ketone among a number of weak acids for which kinetic and thermodynamic acidities have been compared.[4] In an earlier publication from this laboratory, we reported a significant reduction in the acidity of butyrophenone resulting from alkyl substitution in the $\alpha$ position.[5]

The present paper describes a series of equilibrium studies from which an acidity scale is developed for dialkyl and alkyl aryl ketones in polyether solvents. The relative basicities of the conjugate enolate ions in typical alkylation reactions are then demonstrated by a correlation between the extent of dehydrohalogenation of the alkyl halide and the $pK_a$ of the ketone.

Relative acidities of eighteen ketones were compared by equilibration with one or more of four diarylamide ions of appropriate basicity. The ketone was allowed to react with the sodium salt of the diarylamine



$$R-\overset{\overset{O}{\|}}{C}-CHR_2 + C_6H_5NAr^- \rightleftharpoons R-\overset{\overset{O}{|}}{C}{=}CR_2^- + C_6H_5NHAr$$

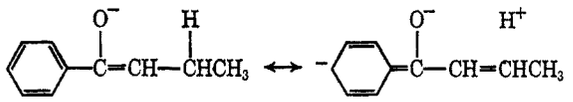
Ar = $C_6H_5$, 2-$NO_2C_6H_4$, 4-$NO_2C_6H_4$, or 4-$FC_6H_4$

in monoglyme or diglyme solution. Equilibrium concentrations of ketone and amine were determined by infrared (ir) spectroscopy.

## Results and Discussion

**Acidity Scale.**—The $pK_a$ values of deoxybenzoin and diphenylacetophenone were determined as 16.1 and 16.6, respectively, relative to that of 4-nitrodiphenylamine ($pK_a$ = 15.9).[6] These values were next used to assign a $pK_a$ of 17.1 to 2-nitrodiphenylamine in diglyme solution and this amine, in turn, to assign values of 18.6 and 19.5, respectively, to butyrophenone and isobutyrophenone. The link from these ketones to diphenylamine was established both directly and through 4-fluorodiphenylamine ($pK_a$ = 20.5) and pinacolone ($pK_a$ = 20.8). The $pK_a$ of 21.4 for diphenylamine obtained by this indirect route from the acidity scale of Stewart and O'Donnell is in agreement with the value of 21 assigned to this amine in the original Conant–Wheland scale.[3,7]

The relative acidities for eighteen ketones spanning a $pK_a$ range of seven units are listed in Table I. In general, the results are in accord with theory. $\alpha$ substitution by electron-releasing alkyl groups leads to lower acidities and phenyl substitution to higher acidities. Localization of the charge on oxygen in the enolate ions makes possible styrene and stilbene systems in the phenyl-substituted enolates and accounts for the increased stability of these anions. Also, this system permits stabilization of butyrophenone enolate by



hyperconjugation, which may explain why this ketone has a lower $pK_a$ than that of acetophenone. The two phenyl groups on adjacent carbon atoms in the enolate of diphenylacetophenone probably interact sterically to prevent complete planarity of the stilbene system and thus reduce the stability of this anion. Evidence for this type of interaction is obtained from the ultraviolet (uv) spectrum of the analogous triphenylethylene systems.[8]

Most of the ketones are either symmetrical or capable of producing only one enolate. Among the exceptions is methyl neopentyl ketone which has a $pK_a$ of 20.2, near that of methyl *t*-butyl ketone ($pK_a$ = 20.8) and

(1) We gratefully acknowledge grants from the National Science Foundation in support of this work and to the Department of Chemistry for the A-60 nmr spectrometer.

(2) D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press Inc., New York, N. Y., 1965.

(3) J. B. Conant and G. H. Wheland, *J. Amer. Chem. Soc.*, **54**, 1212 (1932); W. K. McEwen, *ibid.*, **58**, 1124 (1936).

(4) R. G. Pearson and R. L. Dillon, *ibid.*, **75**, 2439 (1953).

(5) W. L. Rellahan, W. L. Gumby, and H. D. Zook, *J. Org. Chem.*, **24**, 709 (1959).

(6) R. Stewart and J. P. O'Donnell, *Can. J. Chem.*, **42**, 1688 (1964).

(7) On the McEwen scale, the $pK_a$ of diphenylamine is 23; however, on that scale the $pK_a$ of ethanol is 18, two units higher than a value more recently determined from conductivity measurements: P. Ballanger and F. A. Long, *J. Amer. Chem. Soc.*, **82**, 795 (1960).

(8) H. Suzuki, *Bull. Soc. Chem. Jap.*, **33**, 389 (1960); *Chem. Abstr.*, **54**, 20471 (1960).

TABLE I

RELATIVE ACIDITIES OF KETONES

| Registry no. | RCOR′ R | R′ | [K]$_0$ | $XC_6H_4NC_6H_5^-$ X | [Am]$_0$ | $Q^a$ | p$K_a$ |
|---|---|---|---|---|---|---|---|
| 451-40-1 | Phenyl | Benzyl | 0.104–0.147 | 4-$NO_2$ | 0.122 | 0.63 ± 0.01 (2) | 16.1 |
| | | | 0.137 | 2-$NO_2$ | 0.145 | 10.0 | |
| 1733-63-7 | Phenyl | Benzhydryl | 0.124 | 4-$NO_2$ | 0.122 | 0.20 | 16.6 |
| | | | 0.123–0.151 | 2-$NO_2$ | 0.145 | 2.8 ± 0.3 (3) | |
| 102-04-5 | Benzyl | Benzyl | 0.125 | 4-$NO_2$ | 0.122 | 0.10 | 16.9 |
| 495-40-9 | Phenyl | *n*-Propyl | 0.131–0.134 | 2-$NO_2$ | 0.145 | 0.038 ± 0.006 (2) | 18.6 |
| | | | 0.142 | 4-F | 0.158 | 91 | |
| 98-86-2 | Phenyl | Methyl | 0.137–0.160 | 2-$NO_2$ | 0.145 | 0.006 ± 0.003 (3) | 19.1 |
| | | | 0.141 | 4-F | 0.158 | 57 | |
| 611-70-1 | Phenyl | Isopropyl | 0.165 | 2-$NO_2$ | 0.145 | 0.0038 | |
| | | | 0.124–0.132 | 4-F | 0.158 | 9.4 ± 0.4 (2) | 19.5 |
| | | | 0.149 | H | 0.166 | 56 ± 9 (2) | |
| 108-10-1 | Methyl | Isobutyl | 0.139–0.141 | H | 0.144 | 60 ± 2 (2) | |
| 590-50-1 | Methyl | Neopentyl | 0.134–0.173 | H | 0.150 | 15 ± 1 (2) | 20.2 |
| 5682-46-2 | Phenyl | Diethylcarbinyl | 0.137 | 4-F | 0.158 | 1.6 | 20.3 |
| 75-97-8 | *t*-Butyl | Methyl | 0.118–0.132 | 4-F | 0.158 | 0.54 ± 0.04 (2) | 20.8 |
| | | | 0.155–0.177 | H | 0.145 | 5.2 ± 0.6 (8) | |
| 108-83-8 | Isobutyl | Isobutyl | 0.186 | H | 0.164 | 2.5 ± 0.0 (2) | 21.0 |
| 1762-19-2 | Neopentyl | *n*-Propyl | 0.164–0.193 | H | 0.151 | 2.2 ± 0.1 (4) | 21.0 |
| 564-04-5 | *t*-Butyl | Ethyl | 0.101–0.258 | H | 0.161 | 1.3 ± 0.2 (5) | 21.3 |
| 5340-30-7 | Neopentyl | Ethyl | 0.201 | H | 0.064 | 1.2 | 21.3 |
| 5405-79-8 | *t*-Butyl | *n*-Propyl | 0.083–0.340 | H | 0.161 | 0.62 ± 0.16 (9) | 21.6 |
| 565-80-0 | Isopropyl | Isopropyl | 0.136–0.277 | H | 0.145 | 0.38 ± 0.04 (7) | 21.8 |
| 268-91-7 | *t*-Butyl | Neopentyl | 0.234 | H | 0.162 | 0.014 | 23.3 |
| 5857-36-3 | *t*-Butyl | Isopropyl | 0.121–0.156 | H | 0.151 | 0.009 ± 0.001 (2) | 23.5 |

[a] Equilibrium quotient at 32° for the reaction: ketone + sodium diarylamide. Average deviations are for the number of runs shown in parentheses. Dialkyl ketones were measured in monoglyme and alkyl aryl ketones in diglyme. Phenyl benzhydryl ketone and sodium 4-nitrodiphenylamide gave the same value for $Q$ in both solvents.

other methyl ketones but 3.1 p$K_a$ units lower than that of neopentyl *t*-butyl ketone. These results suggest that enolization involves the methyl group rather than the neopentyl group of this ketone and are in accord with deuterium quenching experiments which show 82% proton abstraction from the methyl group of methyl isobutyl ketone.[9]

Kinetic acidities obtained from rates of proton exchange have been compared for many weak acids including one series of ketones.[10] A linear relationship between kinetic and equilibrium acidities has a theoretical basis and is supported by experiment;[11] however, the correlation is of limited scope and not without exception.[2,4] The few available data for ketones are compared in Table II. Clearly, no correlation exists between equilibrium acidity and rates of base-catalyzed proton exchange. The latter appear to reflect steric hindrance at the $\alpha$-carbon atom.

TABLE II

COMPARISON OF KINETIC AND EQUILIBRIUM ACIDITIES

| Ketone | Hydrogen exchange rate × $10^7$ | p$K_a$ |
|---|---|---|
| Diisopropyl ketone | 0.6 | 21.8 |
| Isobutyrophenone | 0.7 | 19.5 |
| Acetophenone | 2200 | 19.1 |
| Propiophenone | 490 | |
| Butyrophenone | | 18.4 |

The significance of the p$K_a$ scale in polyether solvents is somewhat questionable. The aggregation number of sodium diphenylamide determined from boiling point elevations of 0.1 to 0.4 $M$ monoglyme solutions varies from 1.2 to 1.4 (see Experimental Section). In contrast, sodiobutyrophenone is trimeric over a wide range of concentrations in ether, and aggregation numbers of 2.5–2.7 have been measured in monoglyme.[12] The simplifying assumption that the equilibria may be formulated in terms of monomer ion pairs for which the activity quotient does not change markedly with solvent is justified only by the consistency of the results *e.g.*, diphenylamine, p$K_a$ = 21, in this study from 4-nitrodiphenylamine by way of three amines and three ketones in polyether solvents or by the McEwen route from methanol by way of two alcohols and a hydrocarbon. A precise thermodynamic treatment in the usual solvents for enolates would be difficult to achieve and would add little to the practical use of the acidity scale, *i.e.*, to estimate the extent of proton transfer among species in these solvents. Solvent effects in aqueous organic media have been noted in connection with the $H_-$ scale of Stewart and O'Donnell.[6] Larger solvent effects might be expected in nonaqueous media, particularly when functional groups capable of hydrogen bonding are present. For example, the p$K_a$ of 2-nitrodiphenylamine in diglyme is 17.1 compared with a value of 17.6 in sulfolane–water solution. The higher acidity of this *ortho* compound in diglyme is in accord

(9) H. O. House and V. Kramar, *J. Org. Chem.*, **28**, 3362 (1963).

(10) A. Streitwieser, Jr., D. E. Van Sickle and W. C. Langworthy, *J. Amer. Chem. Soc.*, **84**, 244 (1962); A. Streitwieser, Jr., W. C. Langworthy, and J. I. Brauman, *ibid.*, **85**, 1761 (1963); A. Streitwieser, Jr., and H. F. Koch, *ibid.*, **86**, 404 (1964); J. E. Hofmann, R. J. Muller, and A. Schriesheim, *ibid.*, **85**, 3002 (1963); A. I. Shatenshtein, *Advan. Phys. Org. Chem.*, **1**, 156 (1963); R. E. Dessy, Y. Okuzumi, and A. Chen, *J. Amer. Chem. Soc.*, **84**, 2899 (1962); H. Shechter, M. J. Collis, R. E. Dessy, Y. Okuzumi, and A. Chen, *ibid.*, **84**, 2905 (1962).

(11) G. S. Hammond, *ibid.*, **77**, 334 (1955); J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions" John Wiley and Sons, Inc., New York, N. Y., 1963, pp 235–242.

(12) H. D. Zook and W. L. Gumby, *J. Amer. Chem. Soc.*, **82**, 1386 (1960); H. D. Zook and T. J. Russo, *ibid.*, **82**, 1258 (1960).

with a predicted lowering of activity of the free amine by intramolecular hydrogen bonding in this solvent.

**Elimination Studies.**—Although much information is available concerning orientation, kinetics, and solvent effects in the alkylation reaction of enolates by alkyl halides, no quantitative data for the accompanying elimination reaction have been reported. In Table III are listed the percentages of elimination products

TABLE III
DEHYDROHALOGENATION BY ENOLATES

| Alkyl halide R | Alkyl halide X | Percentage elimination: Sodio-deoxybenzoin, $pK_a$ = 16.1 | Sodio-butyrophenone, $pK_a$ = 18.6 | Sodio-pinacolone, $pK_a$ = 20.8 |
|---|---|---|---|---|
| *n*-Propyl | Cl[a] | 7 | 22 | 99 |
| *n*-Propyl | Br | 4 | 16 | 92 |
| *n*-Propyl | I | 4 | 11 | 99 |
| Isopropyl | Br | 7 | 88 | 100 |
| Isopropyl | I | 5 | 75 | 100 |
| *n*-Butyl | Br | 7 | 12 | 76 |
| *s*-Butyl | Br | 20 | 93 | 100 |
| *t*-Butyl | Br | 100 | 99 | 100 |

[a] The alkyl chloride reactions were conducted at 45°, the others at room temperature.

from the reactions of eight halides and three enolates of widely different basicity and in Table IV the composition of the gaseous products from each of these eliminations. The secondary halides exhibit more elimination with all enolates than do the primary isomers, while *t*-butyl bromide gives virtually complete elimination in every case. Variation of the halogen atom produces negligible change in product composition.

TABLE IV
COMPOSITION OF GASES FROM DEHYDROHALOGENATION EXPERIMENTS

| Halide | Hydrocarbon | Enolate, %: Deoxybenzoin | Butyrophenone | Pinacolone |
|---|---|---|---|---|
| *n*-Propyl Cl | Propane | 12 | 8 | 0 |
| | Propene | 88 | 92 | 100 |
| *n*-Propyl Br | Propane | 13 | 17 | 0 |
| | Propene | 87 | 83 | 100 |
| *n*-Propyl I | Propane | 11 | 11 | 0 |
| | Propene | 89 | 89 | 100 |
| Isopropyl Br | Propane | 2 | 8 | 0 |
| | Propene | 98 | 92 | 100 |
| Isopropyl I | Propane | 5 | 4 | 0 |
| | Propene | 95 | 96 | 100 |
| *n*-Butyl Br | Butane | 8 | 28 | 0 |
| | 1-Butene | 92 | 72 | 100 |
| *s*-Butyl Br | Butane | 1 | 11 | 0 |
| | 1-Butene | 20 | 32 | 42 |
| | *cis*-2-Butene | 14 | 9 | 8 |
| | *trans*-2-Butene | 65 | 49 | 50 |
| *t*-Butyl Br | Isobutane | 0 | 13 | 1 |
| | Isobutylene | 100 | 87 | 99 |

The ratio of elimination to substitution is extremely sensitive to the basicity of the enolate. As the $pK_a$ of the ketone is raised from 16.1 to 20.8 the amount of elimination increases for most halides from less than 10 to more than 90%. This strong dependence on enolate basicity and the large ratio to *trans*- to *cis*-2-butene from *s*-butyl bromide suggests an E2 mechanism for the elimination reactions. Small quantities of alkanes accompany the alkenes from the reactions of butyrophenone and deoxybenzoin enolates. A possible origin of these products is an electron-transfer reaction similar to that observed in the reduction of halides by methylmagnesium bromide.[13] Propiophenone enolate is an excellent electron donor in certain reactions of this type.[14]

**Deoxybenzoin Enolate.**—The sodium enolate of deoxybenzoin was isolated as yellow crystals from a monoglyme solution. Equivalent weight determinations indicated the presence of one monoglyme molecule per ion pair of sodiodeoxybenzoin. The presence of monoglyme was confirmed by nmr measurements in benzene and dimethyl sulfoxide. In the latter solvent the monoglyme was displaced and identified by the two singlets at δ 3.24 and 3.42 with relative areas of 3:2. In benzene solution the coordinated monoglyme appeared as a broad peak at δ 2.92 signifying increased shielding compared with that in the free state. Because electron withdrawal due to coordination with sodium ion should result in deshielding, the coordinated monoglyme must be located in a position such that it is affected by ring currents of the benzene nuclei in the enolate. A similar effect has been observed for fluorenyl–lithium complexes with various solvents.[15] The above data together with the results of conductance, ir, kinetic, and ebulliometric studies[16] suggest a trimeric structure in which each sodium ion is coordinated by two enolate ions and one molecule of monoglyme.

## Experimental Section

**Materials.**—Mallinkrodt reagent grade ether and Ansul monoglyme were fractionally distilled through a column from lithium aluminum hydride. Ansul diglyme was stirred with the hydride before fractional distillation: bp 58° (13 mm). The solvents were transferred and stored under nitrogen.

Ketones and amines were the highest purity commercially available or were prepared by published methods. Liquid ketones and halides were fractionally distilled through efficient columns, and the purity of each was confirmed by vapor phase chromatography. Eastman deoxybenzoin was recrystallized twice from methanol: mp 55–56°. α,α-Diphenylacetophenone[16] was recrystallized from ethanol: mp 135–137°. Eastman diphenylamine was recrystallized twice from petroleum ether: 52.5–53.0°. Eastman 2-nitrodiphenylamine, mp 73–75°, and K & K 4-nitrodiphenylamine, mp 128–130°, were used without further purification. 4-Fluorodiphenylamine was prepared from *p*-fluorobromobenzene[17] and acetanilide.[18] Two recrystallizations from petroleum ether gave white crystals, mp 34–36° in agreement with the reported melting point.[19]

**Sodium Diarylamide Solutions.**—All apparatus was baked overnight at 130° and swept with dry nitrogen. The mineral oil was washed from 4.5 g of a 55% dispersion of sodium hydride with three 50-ml portions of dry pentane. The washed hydride was stirred with 250 ml of diglyme and 0.03 mol of diarylamine. Although rapid evolution of hydrogen occurred immediately, the mixtures were stirred for at least 24 hr and allowed to settle overnight. The 4-fluorodiphenylamine solution was heated at 45° with stirring for 2 days. Solutions of sodium diphenylamide and 4-nitrodiphenylamide also were prepared in monoglyme. Free amine was shown to be absent by ir analysis. Concentra-

(13) D. Seyferth and B. Prokai, *J. Org. Chem.*, **31**, 1702 (1966).
(14) G. A. Russell, E. G. Janzen, and E. T. Strom, *J. Amer. Chem. Soc.*, **86**, 1807 (1964).
(15) J. A. Dixon, P. A. Gwinner, and D. C. Lini, *ibid.*, **87**, 1379 (1965); L. L. Chan and J. Smid, *ibid.*, **89**, 4547 (1967).
(16) H. D. Zook, T. J. Russo, E. F. Ferrand, and D. S. Stotz, *J. Org. Chem.*, **33**, 2222 (1968).
(17) G. Olah, *J. Chem. Soc.*, 1828 (1957).
(18) A. J. Roe and W. E. Little, *J. Org. Chem.*, **20**, 1577 (1955).
(19) N. L. Smith, *ibid.*, **16**, 415 (1951).

tions were determined by titration of 10-ml aliquots with standard acid to a phenolphthalein end point.

**Equilibrium Studies.**—Solutions were prepared in heavy-walled tubes fitted with metal caps with butyl rubber liners or in glass tubes fitted with serum caps. The tubes were baked for 2 days at 130°, capped, evacuated, and filled with dry nitrogen through a hypodermic needle. Liquid ketone, followed by 10.0 ml of sodium diarylamide solution, was introduced by means of a dry syringe. The amount of ketone was determined by direct weighing of the capped tube.

Spectra were measured in a 0.016-cm cell at 32° by a Model 21 Perkin-Elmer ir spectrophotometer. Monoglyme and diglyme solutions of the amines and ketones obeyed Beer's Law at the C=O and N—H stretching bands. No appreciable absorbance was exhibited at these frequencies by the corresponding anions. Equilibrium concentrations were obtained from the Beer's Law plots and initial concentrations. Data are listed in Table I.

**Elimination Studies.**—Enolate solutions were prepared in a manner similar to that for sodium diarylamide solutions from 5 g of sodium hydride dispersion, 0.04 mol of ketone, and 250 ml of dry solvent. Sodiodeoxybenzoin was prepared in both monoglyme and diglyme, other enolates in diglyme only. Stirring at room temperature was continued until absorbance in the carbonyl region was negligible.

The elimination reactions were conducted in glass tubes by the technique described for the equilibrium studies. Halide (1 ml) and 10 ml of 0.15 *M* enolate were allowed to stand at room temperature until reaction was complete. Reactions with *n*-propyl chloride were carried out at 45°. The vapor over the reaction mixture was analyzed at 30° on a 20-ft column packed with 30% hexamethylphosphoramide on Chromosorb P. Hydrocarbons were identified by relative retention times with respect to pentane which was added to each sample. The liquid mixtures were diluted with 100 ml of water and extracted with *n*-butyl bromide. The bromide layer was washed with water to remove most of the diglyme and analyzed by glpc on a column of phenyl silicon on Gas-Chrom Z. The percentage of elimination was calculated from the areas under the peaks corresponding to alkylated ketone and original ketone. Thermal response values for homologous ketones have been shown to be equal within experimental error.[16]

**Ebulliometric Studies.**—Boiling point elevations were determined in a differential ebulliometer as described previously.[12] Reproducible temperatures were obtained quickly by forcing the stream of dry nitrogen through a bubbler containing mineral oil and then removing the bubbler to restore atmospheric pressure. The molal boiling point constant for monoglyme was determined for solutions of triphenylmethane in this solvent. A plot of $\Delta T$ *vs.* molality was linear and passed through the origin. The slope of the line $\Delta T/m = k = 3.05 \pm 0.04$. The constant was checked by a determination of the molecular weight of benzil. Also, the boiling point elevation of a 0.146 *M* (0.172 *m*) monoglyme solution of potassium *t*-butoxide was 0.153° indicating an aggregation number of 3.4, only slightly lower than that reported for 0.0077–0.0971 *M* solutions in benzene (3.6–3.9) where a structure with four *t*-butoxide ions at four corners of a cube has been suggested as a somewhat stable entity.[20] Boiling point elevations for 0.112, 0.173, and 0.407 *M* solutions of sodium diphenylamide were 0.337, 0.511, and 1.096° corresponding to aggregation numbers of 1.18, 1.24, and 1.41. Free amine could not be detected by ir analysis in the solutions following the ebulliometric measurements

**Registry No.**—*n*-Propyl chloride, 540-54-5; *n*-propyl bromide, 106-94-5; *n*-propyl iodide, 107-08-4; isopropyl bromide, 75-26-3; isopropyl iodide, 75-30-9; *n*-butyl bromide, 109-65-9; *s*-butyl bromide, 78-76-2; *t*-butyl bromide, 507-19-7; sodiodeoxybenzoin, 17003-50-8; sodiobutyrophenone, 17003-51-9; sodiopinacolone, 17003-52-0; sodiodeoxybenzoin with monoglyme, 17010-22-9.

(20) W. von E. Doering and R. S. Urban, *J. Amer. Chem. Soc.*, **78**, 5940 (1956).

# Conformational Equilibria in the 2-Amino-1,2-diphenylethanol System. I. Nuclear Magnetic Resonance Studies

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Conformational preferences in a series of 2-(N,N-dialkylamino)-1,2-diphenylethanols and their derivatives have been investigated utilizing the relationship between the vicinal coupling constant and the dihedral angle described by H–C–C–H of the ethane backbone. For the N,N-dialkylamino groups considered, *i.e.*, morpholino, piperidino, pyrrolidino and dimethylamino, the *anti* rotamer A is dominant in all compounds of the *threo* series and in all but eight compounds of the *erythro* series. This observation serves to emphasize the important stabilizing influence of the division of the four bulkiest groups into two pairs separated from one another by hydrogens. An examination of those *erythro* compounds in which the *gauche* rotamer (eB) dominates suggests the importance of (1) intramolecular hydrogen bonding (OH···N) in the *erythro* amino alcohols **1a–d**, (2) the large steric requirement of the N-methylpiperidino group in the *erythro* methiodides **5** and **6**, and (3) the special steric requirements of the pyrrolidino group.

In the preparation of the isomeric enamines, *cis*- and *trans*-1-(4-morpholino)-1,2-diphenylethylene, rather striking differences were noted in the reactivity of the precursors, *dl-erythro*- and *dl-threo*-2-(4-morpholino)-1,2-diphenylethyl mesitoate, respectively, toward strong base.[2] The amino alcohols from which these esters were derived also demonstrated some marked differences in reactivity. Observations such as these prompted, as part of a larger study, an investigation of the factors controlling the position of conformational equilibria in the 2-amino-1,2-diphenylethanol system.

The diastereomeric N,N-dialkylamino alcohols, *threo* and *erythro*[3] **1a–d** (Table I), possessing a high degree of configurational homogeneity, were prepared *via* nucleophilic scission of the C–O bond of *cis*- and *trans*-stilbene oxide, respectively, by the appropriate amine. The *trans* nature of the epoxide opening[4] was verified by the conversion of *threo* and *erythro* amino alcohols **1a** and **1b** back into the epoxides from which they were derived by treatment of the corresponding methiodides with sodium hydride in tetrahydrofuran.[5]

(1) (a) NDEA Fellow 1963–1966. (b) Participant in the Undergraduate Research Program supported by National Science Foundation Grant No. GY-817.

(2) M. E. Munk and Y. K. Kim, *J. Org. Chem.*, **30**, 3705 (1965).

(3) The terms *threo* and *erythro* as used in this paper indicate *dl-threo* and *dl-erythro*.

(4) (a) R. E. Lutz, J. A. Freek, and R. S. Murphy, *J. Amer. Chem. Soc.*, **70**, 2015 (1948); (b) W. Stuhmer and G. Messwarb, *Arch. Pharm.*, **286**, 19 (1953).

(5) The *trans* nature of the ring closure is well documented. See A. C. Cope and E. R. Trumbull, *Org. Reactions*, **11**, 317 (1960).