**1-Phenyl-1-(3-propenoxy)ethene (12):** method A, 50%; ^{1}H NMR (CCl$_4$) δ 4.15 (d, 1, J = 3 Hz), 4.4 (m, 2), 4.65 (d, 1, J = 3 Hz), 5.1–5.6 (m, 2), 5.8–6.3 (m, 1), 6.2–6.8 (m, 5). Anal. (C$_{11}$H$_{12}$O) C, H.

**2-Ethoxy-1,3,5-heptatriene (14):** method A, 54%; ^{1}H NMR (CCl$_4$) δ 1.35 (t, 3, J = 7 Hz), 1.75 (d, 3, J = 5 Hz), 3.75 (q, 2, J = 7 Hz), 3.95 (s, 2), 5.4–6.6 (m, 4). Anal. (C$_9$H$_{14}$O) C, H.

**2-Ethoxy-3-phenylpropene (16):**[8] method A, 90%; ^{1}H NMR (CDCl$_3$) δ 1.2 (t, 3, J = 8 Hz), 3.3 (s, 2), 3.7 (q, 2, J = 8 Hz), 3.8 (d, 1, J = 2 Hz), 3.9 (d, 1, J = 2 Hz), 7.2 (s, 5).

**2-Ethoxy-1-phenylpropene (17):**[24] from isomerization of **16** in CDCl$_3$ to give 83% of a mixture of 70% E and 30% Z isomers; ^{1}H NMR (CDCl$_3$) δ 1.3 (t, 3, J = 7 HZ), 1.9 (s, 3), 3.75 (q, 2, J = 7 Hz), 5.2 (s, 0.3), 5.5 (s, 0.7), 6.8–7.3 (m, 5).

**1-Methyl-1-phenylethene (19a):**[25] method A, 88%; ^{1}H NMR (CCl$_4$) δ 2.05 (s, 3), 4.95 (br s, 1), 5.25 (br s, 1), 7.0–7.4 (m, 5).

**1,1-Diphenylethene (19b):**[26] method A, 97%; ^{1}H NMR (CCl$_4$) δ 5.3 (s, 2), 7.1 (s, 10).

**3,3-Dimethyl-2-phenyl-1-butene (19c):** method A, 96%; ^{1}H NMR (CCl$_4$) δ 1.1 (s, 9), 4.65 (d, 1, J = 2 Hz), 5.05 (d, 1, J = 2 Hz), 6.8–7.1 (m, 5). Anal. (C$_{12}$H$_{16}$) mass spectrum.

**3,3,3-Trifluoro-2-phenylpropene (19d):** method A, 50%; ^{1}H NMR (CCl$_4$) δ 5.6 (d, 1, J = 1 Hz), 5.8 (d, 1, J = 1 Hz), 7.2 (s, 5). Anal. (C$_9$H$_7$F$_3$) mass spectrum.

**1-Methylene-1,2,3,4-tetrahydronaphthalene (21):**[27] method A, 73%; ^{1}H NMR (CCl$_4$) δ 1.8 (m, 2), 2.5 (m, 2), 2.8 (t, 2, J = 6 Hz), 4.8 (d, 1, J = 1 Hz), 5.3 (d, 1, J = 1 Hz), 6.9 (m, 3), 7.5 (m, 1).

**2-Methylene-1,2,3,4-tetrahydronaphthalene (23):**[28] method A, 40%, separated from **24** via chromatography; ^{1}H NMR (CCl$_4$) δ 2.45 (t, 2, J = 7 Hz), 2.85 (t, 2, J = 7 Hz), 3.5 (s, 2), 4.75 (br s, 2), 6.9 (s, 4).

**2,2-Dimethyl-1,2,3,4-tetrahydronaphthalene (24):**[29] method A, 15%, separated from **23** via chromatography; ^{1}H NMR (CCl$_4$) δ 0.95 (s, 6), 1.5 (t, 2, J = 6 Hz), 2.45 (s, 2), 2.7 (t, 2, J = 6 Hz), 6.8 (br s, 4).

**Methyl 2-(1-methoxyethenyl)benzoate (26):** method A, 45%, separated from **27** via chromatography; ^{1}H NMR (CCl$_4$) δ 3.55 (s, 3), 3.7 (s, 3), 4.1 (d, 1, J = 2 Hz), 4.2 (d, 1, J = 2 Hz), 7.0–7.4 (m, 3), 7.4–7.6 (m, 1). Anal. (C$_{11}$H$_{12}$O$_3$) C, H.

**1,2-Bis(1-methoxyethenyl)benzene (27):** method A, 65%, using 2 equiv of **1**; ^{1}H NMR (CCl$_4$) δ 3.5 (s, 6), 4.1 (d, 2, J = 2

Hz), 4.2 (d, 2, J = 2 Hz), 6.9–7.3 (m, 4). Anal. (C$_{12}$H$_{14}$O$_2$) C, H.

**Ethyl 2-(2-methylenecyclohexyl)acetate (29):** method A, 67%; ^{1}H NMR (CCl$_4$) δ 1.15 (t, 3, J = 7 Hz), 1.4–2.6 (m, 11), 4.0 (q, 2, J = 7 Hz), 4.4 (s, 1), 4.5 (s, 1). Anal. (C$_{11}$H$_{18}$O$_2$) mass spectrum.

**Methyl 2-phenyl-2-propenoate (31):** method A, 72%; ^{1}H NMR (CCl$_4$) δ 3.7 (s, 3), 5.7 (d, 1 J = 1 Hz), 6.2 (d, 1, J = 1 Hz) 7.1–7.4 (m, 5). Anal. (C$_{10}$H$_{10}$O$_2$) mass spectrum.

**2-Methoxy-3-phenyl-1,3-butadiene (32):** method A, 45%; ^{1}H NMR (CCl$_4$) δ 3.6 (s, 3), 4.0 (d, 1, J = 2 Hz), 4.1 (br s, 1), 5.05 (br s, 1), 5.55 (d, 1, J = 2 Hz), 7.1 (s, 5). Anal. (C$_{11}$H$_{12}$O) mass spectrum.

**1-(1-Phenylethenyl)piperidine (33):**[30] method B, D, 76% (by NMR); ^{1}H NMR (CCl$_4$) δ 1.6 (m, 6), 2.8 (m, 4), 4.0 (s, 1), 4.1 (s, 1), 7.1–7.4 (m, 5).

**4-(1-Phenylethenyl)morpholine (34):**[31] method D, 67% (by NMR); ^{1}H NMR (C$_6$D$_6$) δ 2.8 (m, 4), 3.7 (m, 4), 4.3 (s, 1), 4.6 (s, 1), 7.0–7.8 (m, 5). Anal. (C$_{12}$H$_{15}$NO) mass spectrum.

**1-(1-Phenylethenyl)pyrrolidine (35):**[30] method D, 80% (by NMR); ^{1}H NMR (C$_6$D$_6$) δ 1.7 (m, 4), 3.1 (m, 4), 4.2 (s, 1), 4.35 (s, 1), 7.1–7.8 (m, 5).

**N-Methyl-N-2-propenylbenzenamine (36):**[32] method D, 97% (by NMR); ^{1}H NMR (C$_6$D$_6$) δ 1.9 (s, 3), 3.0, (s, 3), 4.3 (s, 1), 4.35 (s, 1), 6.9–7.4 (m, 5).

**N-N-Dimethyl-2-propenamine (37):**[32] method D; ^{1}H NMR (C$_6$D$_6$) δ 1.9 (s, 3), 2.6 (s, 6), 3.85 (s, 1), 3.95 (s, 1).

**Registry No.** 1, 67719-69-1; **2a**, 93-58-3; **3b**, 99-75-2; **3c**, 121-98-2; **3d**, 1126-46-1; **4a**, 4747-13-1; **4b**, 51440-57-4; **4c**, 51440-56-3; **4d**, 67471-39-0; **5a**, 939-48-0; **5b**, 120-51-4; **5c**, 93-99-2; **5d**, 774-65-2; **6a**, 42237-98-9; **6b**, 25109-98-2; **6c**, 19928-57-5; **6d**, 78386-38-6; **7a**, 553-86-6; **7b**, 119-84-6; **8a**, 74104-12-4; **8b**, 74104-13-5; **9a**, 103-26-4; **9b**, 103-36-6; **9c**, 103-41-3; **10a**, 95045-97-9; **10b**, 77882-39-4; **10c**, 95045-98-0; **11**, 583-04-0; **12**, 40815-73-4; **13**, 2396-84-1; **14**, 95045-99-1; **15**, 101-97-3; **16**, 74104-11-3; (E)-**17**, 71094-33-2; (Z)-**17**, 71094-47-8; **18a**, 98-86-2; **18b**, 119-61-9; **18c**, 938-16-9; **18d**, 434-45-7; **19a**, 98-83-9; **19b**, 530-48-3; **19c**, 5676-29-9; **19d**, 384-64-5; **20**, 529-34-0; **21**, 25108-63-8; **22**, 530-93-8; **23**, 66448-77-9; **24**, 13556-55-3; **25**, 131-11-3; **26**, 51440-54-1; **27**, 95046-00-7; **28**, 24731-17-7; **29**, 53544-45-9; **30**, 15206-55-0; **31**, 1865-29-8; **32**, 95046-01-8; **33**, 14990-66-0; **34**, 7196-01-2; **35**, 3433-56-5; **36**, 21267-55-0; **37**, 22499-75-8; N-methylacetanilide, 579-10-2; 4-benzoylmorpholine, 1468-28-6; 1-benzoylpyrrolidine, 3389-54-6; dimethylacetamide, 127-19-5; 1-benzoylpiperidine, 776-75-0.

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# Solvent Effects on Keto–Enol Equilibria: Tests of Quantitative Models

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The effect of solvent on the equilibrium constants between selected keto–enol isomer pairs has been determined. The protomeric systems studied are 5,5-dimethyl-1,3-cyclohexanedione (1), 2-methyl-1,3-cyclohexanedione (3), 3-oxabicyclo[4.3.0]-2,9-dioxononane (5), 2,4-pentanedione (7), ethyl 3-oxobutanoate (9), and 9-anthracenone (11). A wide variety of theoretical and empirical solvation parameters have been tested in a multiparameter linear free energy format to model the changes in equilibria. The most successful correlations are obtained with the Kamlet–Taft polarity–polarizability and hydrogen-bonding terms, although the Swain A and B factors have advantages in some cases. In general, for the isomer pairs in which the enol cannot form an internal hydrogen bond (1–2, 3–4, and 11–12), the equilibria appear to be controlled almost completely by the hydrogen-bonding basicity of the solvent. For the isomer pairs 5–6, 7–8, and 9–10, in which intramolecular hydrogen bonding is possible, the polarity–polarizability effect dominates, although differential stabilization of the isomers by hydrogen bonding remains significant.
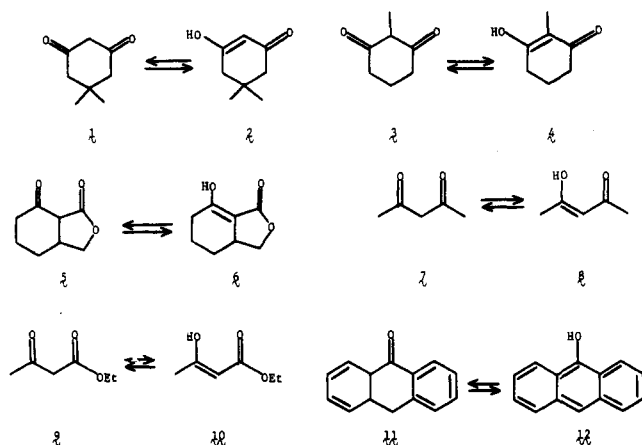
The effect of solvent on the relative energies of hydroxypyridine–pyridone and mercaptopyridine–thio-

pyridone isomers is quantitatively correlated by an approach that models the differential interactions of the

**Scheme I**
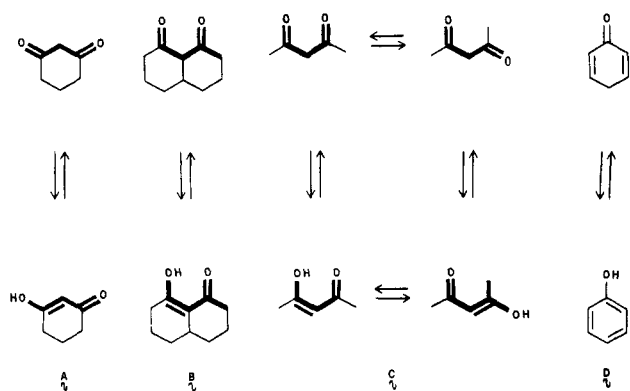


**Scheme II**



protomers with their molecular environment in terms of reaction field and hydrogen-bonding terms.[1-3] In order to determine if a general description of solvent effects on protomeric equilibria is provided by this model we have extended the analysis to structurally defined keto–enol promoters. In Scheme I examples of four major classes of tautomeric systems are illustrated, with heavy lines used to emphasize the relative orientation of the two carbonyl (or enol) moieties in the first three types. Catogory A refers to anti-fixed systems and B to syn-fixed systems, while conformationally flexible systems make up C. Phenol–cyclohexadienone tautomerism is represented by D. In Scheme II the specific isomer pairs we have investigated are shown. The positions of equilibria have been determined for these systems in a wide range of solvents and the relative energies have been tested against a number of models.

Solvent effects on β-dicarbonyl keto–enol equilibria have been thoroughly discussed and a number of the above systems have been previously investigated.[4,5] In our work

we found some disagreement with literature values, attributable perhaps to impurities in solvents, slow equilibration, or failure to achieve conditions of infinite dilution. All linear free energy correlations discussed in the present study are based on work done in our laboratory except as noted for 11–12 in two solvents and 9–10 in one solvent. The best correlations are obtained with the Kamlet–Taft polarity–polarizability–hydrogen-bonding approach, a result that provides useful insight into the dominant interactions of the promoters with their environment.[6]

### Results

The equilibrium constants $K_T$ were measured in each system by ultraviolet and/or NMR spectroscopy in a series of solvents. Concentrations used for the NMR work were generally $10^{-3}$ to $10^{-2}$ M and were shown to be below the range where self-association occurs.[5,7] The results are summarized in Table I, along with literature values.

**Equilibrium Constants for 1–2 and 3–4.** For ultraviolet measurements the methyl enol ethers corresponding to 2 and 4 were used as models and found to have $\lambda_{max}$ within 10 nm of the enols. The NMR measurements were made by comparing area ratios of corresponding protons in solutions that are less than $7 \times 10^{-3}$ M in the non-hydroxylic solvents.

**Equilibrium Constants for 5–6.** The synthesis of 5–6 was achieved by the method of Goldsmith et al. and the equilibration constants in Table I determined by integration of the nonequivalent methylene protons adjacent to oxygen of each protomer.[8] Observation of the doublet due to the proton between the two carbonyl groups and decoupling experiments allowed assignment of the appropriate methylene protons to 5. In an effort to find other syn-fixed systems that would have measurable equilibrium constants we prepared 13, 14, and 15.[9] Although we find
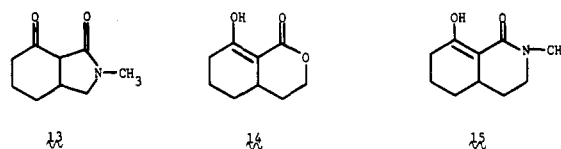


evidence from $^1$H and $^{13}$C NMR studies for an equilibrium constant of ca. 0.2 for 13 in chloroform, we were unable to obtain quantitative information in other solvents. In the cases of 14 and 15 we find these compounds to be greater than 95% in the enol form in a variety of solvents.

**Equilibrium Constants for 7–8 and 9–10.** The equilibrium constants of acetylacetone and ethyl acetoacetate were determined from NMR spectroscopy at concentrations from $2 \times 10^{-3}$ M in nonpolar solvents to $2 \times 10^{-2}$ M in polar solvents, generally by comparison of the methyl signals of the different promoters. The rates of

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(9) The details are presented in supplementary material. Ordering information is given on any current masthead page.

Table I. Equilibrium Constants for Protomeric Isomer Pairs $K_T$ = [Enol]/[Keto]

| solvent | 1–2 UV$^a$ | 1–2 NMR$^{a,b}$ | 1–2 lit. | 3–4 UV$^a$ | 3–4 NMR$^{a,b}$ | 5–6 NMR$^{a,b}$ | 7–8 NMR$^{a,b}$ | 7–8 lit. | 9–10 NMR$^{a,b}$ | 9–10 lit. | 11–12 UV$^{a,b}$ | 11–12 lit. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| water | ≥19 | 19 | | ≥19 | | 0.024 | 0.23 | 0.19,$^c$ 0.21$^d$ | | 0.07 | | |
| dimethyl sulfoxide | | 94 | ≥21$^e$ | | | 0.14 | 2.0 | 1.6,$^f$ 1.6,$^c$ 1.5$^g$ | 0.05 | 0.02$^f$ | 1.6 ± 1 | 2.8$^h$ |
| dimethylformamide | | 85 | 13$^e$ | | 1.3 | 0.053 | | | | | 1.3 ± 0.1 | 0.08$^h$ |
| dimethylacetamide | | | | | | | | 1.9$^c$ | | | 1.8 ± 0.5 | |
| ethyl acetate | | | | | | | | | | | 0.06 ± 0.01 | |
| acetonitrile | 2.3 ± 0.3 | | | 2.5 ± 0.5 | | 0.027 | 1.2 | 1.6,$^f$ 1.5$^d$ | 0.13 | 0.05,$^f$ 0.06$^d$ | | 0.22$^h$ |
| acetone | | 4.2 | 3.9$^e$ | | | 0.048 | 2.9 | 2.7,$^f$ 2.8,$^c$ 3.3$^d$ | 0.07 | 0.06,$^f$ 0.09$^d$ | 0.1 ± 0.03 | |
| methanol | ≥19 | 148 | | ≥19 | | 0.09 | 5.8 | 4.6$^f$ | 0.14 | 0.1,$^f$ 0.16,$^i$ 0.11$^d$ | 0.15 ± 0.03 | |
| ethanol | ≥19 | 169 | | | | 0.19 | 6.8 | 12.6$^d$ | 0.17 | 0.18$^d$ | 0.11 ± 0.05 | |
| 2-propanol | ≥19 | | | ≥19 | | | | | | | 0.1 ± 0.01 | |
| 1-butanol | ≥19 | | | ≥19 | | 0.074 | | | | | | 0.16$^h$ |
| methylene chloride | 0.07 ± 0.02 | | | 0.45 ± 0.1 | | 0.08 | 4.2 | | 0.09 | | ≤0.001 | |
| 1,2-dichloroethane | 0.04 ± 0.005 | | | 0.39 ± 0.5 | | | | | | | ≤0.001 | |
| chloroform | | 0.05 | 0.18,$^j$ 0.05$^e$ | | 0.2 | 0.2 | 5.94 | 6.4$^f$ | 0.09 | 0.08$^f$ | ≤0.001 | 0.13$^h$ |
| carbon tetrachloride | | | | | | 0.97 | 29 | 23,$^f$ 18,$^g$ 19$^c$ | 0.29 | 0.38$^f$ | ≤0.001 | |
| diethyl ether | 3.2 ± 0.5 | | 10.6$^e$ | 19 ± 10 | | 0.14 | 7.2 | 18/13$^d$ | 0.40 | 0.28,$^f$ 0.51$^d$ | 0.06 ± 0.02 | |
| tetrahydrofuran | 4.5 ± 0.1 | | 7.4 | 30 ± 10 | | 0.18 | 4.8 | 4.6/3.9$^d$ | 0.13 | 0.11,$^f$ 0.11$^d$ | 0.2 ± 0.1 | |
| 1,4-dioxane | 2.4 ± 0.4 | 2.8 | | 13 ± 5 | 12 | | | ≥160$^k$ | | | 0.07 ± 0.02 | |
| triethylamine | | | | | | | | | | | 1.1 ± 0.5 | 1.0$^h$ |
| pyridine | | | | | | 0.25 | 3.7 | 7.6$^f$ | 0.10 | 0.18$^f$ | 1.4 ± 0.5 | |
| benzene | | 0.12 | | | | 0.22 | 14.7 | | 0.26 | | | |
| toluene | | 0.08 | | | | 0.22 | 10 | | 0.39 | | 0.0025 ± 0.0005 | 0.003$^l$ |
| cyclohexane | | | 0.017$^e$ | | | 1.88 | 42 | 9,$^k$ 21,$^g$ 32,$^c$ 25$^d$ | 1.65 | 1.5$^d$ | ≥0.001 | |

$^a$ This work. $^b$ Deuterated solvents; error estimated as ±20%. $^c$ Reference 10g, by NMR. $^d$ Reference 10b, by NMR. $^e$ Reference 7d, by UV. $^f$ Reference 10d, by NMR. $^g$ Reference 10e, by NMR. $^h$ Reference 12b, by NMR. $^i$ Reference 10a, by UV and bromine titration. $^j$ Reference 7e, by NMR. $^k$ Reference 10c, by NMR. $^l$ Reference 12a, by UV.

Table II. Temperature Dependence and Thermodynamic Parameters of the Equilibrium of 7–8 in Various Solvents$^a$

| T, °C | methanol | ethanol | tetrahydrofuran | toluene | chloroform | dimethyl sulfoxide | cyclohexane |
|---|---|---|---|---|---|---|---|
| −60 | 15 | 33 | 35 | 60 | 21 | | |
| −40 | 9 | 18 | 14 | 34 | 14 | | |
| −20 | 6.6 | 10.5 | | 25 | 10 | | |
| 0 | 4 | 7.5 | 11 | 17 | 7.9 | | |
| 20 | 2.9 | 5.6 | 6.6 | 11 | 5.8 | 1.95 | 42 |
| 40 | 2.14 | 3.6 | 4.3 | 9.7 | 5.3 | | |
| 60 | 1.6 | | 4.2 | 6.7 | 4.0 | 1.07 | 16 |
| 80 | | 2.1 | 4.2 | 4.4 | | 0.97 | 13 |
| free energy$^{b,c}$ | −0.06 | −1.02 | −1.15 | −1.46 | −1.03 | −0.39 | −2.18 |
| enthalpy$^b$ | −2.9 | −2.9 | −2.4 | −2.6 | −1.9 | −2.5 | −4.1 |
| entropy$^d$ | −6.6 | −6.6 | −4.4 | −4.2 | −2.9 | −7.2 | −6.7 |
| correlation coefficient | 0.998 | 0.998 | 0.97 | 0.994 | 0.998 | 0.987 | 0.992 |

$^a$ $K_T$ deuterated solvents. $^b$ kcal/mol. $^c$ For 25 °C. $^d$ Entropy units, error estimated as ±20% for $K_T$ between 1 and 10 and ±35% for $K_T$ greater than 10.

equilibrations were slower then anticipated; for example, equilibration of **7–8** in methanol required 15 h and equilibration of **9–10** in carbon tetrachloride took 120 h. The data we obtain agree reasonably well with most of the many previous studies of these systems.[10] The present work was done under conditions unperturbed by self-association, which has been a complicating factor in some of the previous work.[7] The evidence in favor of predominant intramolecular hydrogen bonding in all neutral solution environments seem convincing, particularly the work of Egan et al., although a contrary view has recently been expressed by Spencer et al.[4,10,11]

**Equilibrium Constants for 11–12.** Determination of accurate equilibrium constants for these isomers was difficult because of a sensitivity to oxidation and the slow equilibrations in nonpolar solvents, both of which have been noted in previous studies.[12] The UV spectra used to obtain the equilibrium constants in Table I are corrected for the presence of 2–10% anthraquinone.

**Temperature Studies of the Equilibria of 7–8.** The change in $K_T$ for **7–8** as a function of temperature and solvent was investigated from –60 to 80 °C at ca. $10^{-2}$ M. Equilibration was very slow at lower temperatures requiring approximately 2 months to reach a constant value in most cases.[13] The data and the resultant thermodynamic parameters are summarized in Table II.

## Discussion

Quantitative analyses of the effect of solvent on a wide variety of chemical phenomena have been carried out by approaches that range from the wholly theoretical to the plainly empirical.[4d] Linear solvation energy relationships, which are seen in favorable cases, have been widely studied and broadly applied, although a proliferation of parameters used to improve correlations has led to criticism concerning the generality of this approach.[14] Recent analyses indicate that to a large degree, differently derived parameters can be dissected into linear combinations of one another.[6,15] This suggests that a solvent model that adequately represents fundamentally different properties would be useful for discussion of many solvation phenomena. We have used that well-precedented approach to analyze the major differences in the interactions of each isomer of the pair with the environment provided by the solvent.

In eq 1 is given one dissection of solvent effects[1,16] where

$$\Delta G_s^\circ - \Delta G_v^\circ =$$
$$\Delta G_{el}^\circ + \Delta G_{hb}^\circ + \Delta G_{cav}^\circ + \Delta G_{str}^\circ + \Delta G_{vdw}^\circ \quad (1)$$

the differences in energies of isomers in solution and in

the vapor $(\Delta G_s^\circ - \Delta G_r^\circ)$ are expressed as a linear combination of terms representing reaction field effects $(\Delta G_{el}^\circ)$, hydrogen bonding $(\Delta G_{hb}^\circ)$, cavitation energies $(\Delta G_{cav}^\circ)$, solvent structure $(\Delta G_{str}^\circ)$, and Van der Waals interactions $(\Delta G_{vdw}^\circ)$. We have suggested earlier that differences in energies between heterocyclic protomeric isomers can be expressed by eq 2, where the first two terms are retained

$$\Delta G_s^\circ = k\left(\frac{\epsilon - 1}{2\epsilon + 1}\right) + a\alpha + b\beta + \Delta G_v^\circ \quad (2)$$

and the effects of cavitation, solvent structure, and van der Waals interactions are assumed to be negligible.[1] The term $(\epsilon - 1)/(2\epsilon + 1)$ is the well-known Kirkwood–Onsager expression for estimating the energy of a dipole placed in a medium of dielectric constant $\epsilon$,[17] the parameters $\alpha$ and $\beta$ are empirical parameters designed by Kamlet and Taft to measure the hydrogen-bond-donating and accepting ability, respectively, of a given solvent,[6,18,20] and $k$, $a$, and $b$ are regression coefficients obtained from the multiparameter linear correlation analysis.[21] Correlations with the $(\epsilon - 1)/(2\epsilon + 1)$ term should provide a value for $k$ which is in principle equal to $\mu_x^2/a_x^3 - \mu_y^2/a_y^3$, where $\mu$ and $a$ refer to the dipole moments and molecular volumes of the protomers x and y, respectively.[17] This approach also provides an intercept which is $\Delta G_v^\circ$, the free energy difference between the isomers in the vapor phase.

In the present study, early results indicated that although the hydrogen bonding parameters were clearly useful, the Kirkwood–Onsager reaction-field term was less so. Because of its clear theoretical interpretation and because our previous studies employed it, we have included here results obtained with the reaction-field term.[1] Since our earlier work was completed, two empirical measures of solvent polarity have gained prominence, the Kamlet–Taft $\pi^*$ term[6,19] and the Swain $A$ and $B$ parameters.[15] We have tested these against our data. Kamlet and Taft constructed $\pi^*$ to be used in conjunction with $\alpha$ and $\beta$, and we employed it in that fashion by substituting it for $(\epsilon - 1)/(2\epsilon + 1)$ in eq 2. When this is done, the intercept no longer represents the gas-phase free energy value but is the $\Delta G^\circ$ value in cyclohexane, a solvent for which $\pi^*$ is zero. On the other hand, Swain and co-workers designed $A$ and $B$, separately or in combination as $A + B$, as measures of all solvent effects, so that correlation with the Swain parameters should take the forms shown in eq 3 or 4. Here $\Delta G_{hc}^\circ$ refers to the free energy value in heptane, for which $A = B = 0$.

$$\Delta G_2^\circ = aA + bB + \Delta G_{hc}^\circ \quad (3)$$

$$\Delta G_2^\circ = k(A + B) + \Delta G_{hc}^\circ \quad (4)$$

Recently, both Kamlet and Taft[22] and Swain[23] have exchanged criticisms of one anothers' solvent scale. In part, Kamlet and Taft suggested that the $A$ and $B$ scale

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(11) (a) Eistert, B.; Reiss, W. *Chem. Ber.* **1954**, *87*, 108. (b) Burdett, J. L.; Rogers, M. T. *J. Phys. Chem.* **1969**, *70*, 939. (c) Egan, W.; Gunnarson, G.; Bull, T. E.; Forsen, S. *J. Am. Chem. Soc.* **1977**, *99*, 4568.

(12) (a) Baba, H.; Takemura, T. *Tetrahedron* **1968**, *24*, 4779, 5311. (b) Sterk, H. *Monatsh. Chem.* **1969**, *100*, 916. (c) Beak, P.; Fry, F. S.; Lee, J.; Steele, F. *J. Am. Chem. Soc.* **1976**, *98*, 171.

(13) Equilibrium seemed to be exceptionally slow in acetonitrile. If samples at –20, and 0, and 20 °C that have been standing 14, 12, and 7 days are taken to be at equilibrium at $\Delta H^\circ$ of –3.3 kcal/mol and a $\Delta S^\circ$ of –11 eV can be obtained.

(14) Chapman, N. B., Shorter, J., Eds. "Advances in Linear Free Energy Relationships"; Plenum: London, 1972. Sjostrom, M.; Wold, S. *Acta Chem. Scand., Ser. B* **1981**, *B 35*, 537.

(15) Swain, C. G.; Swain, M. S.; Powell, A. L.; Alunni, S. *J. Am. Chem. Soc.* **1983**, *105*, 502.

(16) Sinanoglu, O. "Molecular Associations in Biology"; Pullman, E. B., Ed., Academic Press: New York, 1967; p 427.

(17) Onsager, L. *J. Am. Chem. Soc.* **1936**, *58*, 1486. Kirkwood, J. G. *J. Chem. Phys.* **1936**, 2. Powling, J.; Bernstein, H. J. *J. Am. Chem. Soc.* **1951**, *73*, 1815, 4353. Abraham, R. J.; Banks, H. D.; Eliel, E. L.; Hofer, D.; Kaldustian, M. K. *J. Am. Chem. Soc.* **1972**, *94*, 1913. Stein, M.-L.; Claessens, M.; Lopez, A.; Reisse, J. *J. Am. Chem. Soc.* **1982**, *104*, 5902 and references cited therein.

(18) Kamlet, M. J.; Taft, R. W. *J. Am. Chem. Soc.* **1976**, *98*, 377.

(19) Kamlet, M. J.; Abboud, J. L.; Taft, R. W. *J. Am. Chem. Soc.* **1977**, *99*, 6027.

(20) We have tested $\beta$ and $\beta'$ values. The latter, which are based on phenolic hydrogen bonding and differ from $\beta$ values only for water, methanol, isopropyl alcohol, and ethanol, generally provide better correlations and are used in the present work.

(21) Avner, R. A. "A Basic Statistical Service Package", 11th ed.; Control Data Corporation: Minneapolis, MN, 1980.

### Table III. Data for Multivariable Free Energy Correlations for 1-2 and 3-4

| | | | | isomers | | | |
| | | | | 1-2 | | 3-4 | |
| solvent | $\dfrac{\epsilon - 1}{2\epsilon + 1}$ | $\alpha$ | $\beta$ | $\Delta G_{\text{exptl}}^{\circ\ a}$ | $\Delta G_{\text{calc}}^{\circ\ a,b}$ | $\Delta G_{\text{exptl}}^{\circ\ a}$ | $\Delta G_{\text{calc}}^{\circ\ c}$ |
|---|---|---|---|---|---|---|---|
| water | 0.49 | 1.02 | 0.14[d] | -1.75 | -1.62 | ≤-3.3[g] | |
| methanol | 0.48 | 0.98 | 0.62[e] | -2.91 | -2.97 | ≤-3.24 | |
| ethanol | 0.47 | 0.826 | 0.77[f] | -2.99 | -3.06 | ≤-1.71 | |
| acetonitrile | 0.48 | 0.27 | 0.31 | -0.51 | -0.25 | -0.59 | -0.60 |
| acetone | 0.47 | 0 | 0.48 | -0.83 | -1.12 | ≤-3.2 | |
| Me₂SO | 0.48 | 0 | 0.75 | -3.0 | -3.15 | | |
| 1,4-dioxane | 0.22 | 0 | 0.37 | -0.62 | -.037 | -1.47 | -1.35 |
| diethyl ether | 0.35 | 0 | 0.47 | -0.68 | -0.97 | -1.71 | -1.72 |
| THF | 0.40 | 0 | 0.52 | -1.17 | -1.29 | -1.99 | -2.04 |
| benzene | 0.23 | 0 | 0.1 | 1.22 | 1.34 | -0.05 | -0.12 |
| toluene | 0.24 | 0 | 0.11 | 1.45 | 1.27 | | |
| 1,2-dichloroethane | 0.43 | 0 | 0 | 1.82 | 1.79 | 0.54 | 0.47 |
| chloroform | 0.36 | 0.34 | 0 | 1.74 | 1.48 | 0.94 | 0.79 |
| dichloromethane | 0.42 | 0.22 | 0 | 1.59 | 1.68 | 0.46 | 0.71 |
| DMF | 0.48 | 0 | 0.69 | -2.59 | -2.38 | <-3.1 | |

[a] Units of kcal/mol, ± 0.2. [b] Calculated from eq 5. [c] Calculated from eq 7. [d] $\beta' = 0.47$. [e] $\beta' = 0.70$. [f] $\beta' = 0.73$. [g] Limit values are based on the assumption the $S/N$ ratio provides the limit of detectability.

was deficient in dealing with solvation phenomena in which hydrogen bonding played a primary role,[22] while Swain has repeatedly asserted that $A$ and $B$ account satisfactorily for this effect.[15,23] Since our results do not generally correlate well with either $(\epsilon - 1)/(2\epsilon + 1)$ or $\pi^*$ alone, these data seem to be a useful test of parameters that purport to measure hydrogen bonding as well as more general solvent effects.

Toward this end, we carried out a large number of correlations with these and other solvent parameters and these are available as supplementary material.[9] In the present work, we generally limit detailed discussion to cases that have coefficients of multiple regression ($R$ values) of greater than 0.95 and a probability that a correlation could be due solely to chance ($P$ values) of less than one in $5 \times 10^{-3}$. We also give the standard error of estimate (SE) expressed as a percent range of the $\Delta G_s^{\circ}$ value. We have, at the editors request, included a few cases of unsatisfactory correlations to provide comparisons of the Kamlet and Taft and Swain correlations.

**Equilibrium for 1-2 and 3-4.** A multiparameter correlation of the solvent effect on the tautomeric equilibrium of 1-2 using the Kirkwood–Onsager term and the Kamlet–Taft hydrogen-bonding parameters is given by eq 5. The relevant data are presented in Table III. For this

$$\Delta G_s^{\circ} = -0.75(\epsilon - 1)/(2\epsilon + 1) - 0.53\alpha - 6.0\beta + 2.11 \quad (5)$$

correlation, $R$ is 0.9929, and there is less than once chance in $10^9$ that the correlation obtains from chance. The standard error of 0.22 kcal/mol is 4% of the total range of $\Delta G_s^{\circ}$. The statistical tests indicate this is a very good correlation. Moreover, since the Kirkwood–Onsager term is used an independent test of the coefficient is available. From the dipole moments of 2,2,5,5-tetramethyl-1,3-cyclohexanedione and of 5,5-dimethyl-3-ethoxy-2-cyclohex-1-one of 3.23 and 3.76 D, respectively,[24] a value of -0.80 can be calculated for $k$. This value compares well with the value of -0.75 from the correlation,[25] although it should be noted this term does not carry much of the correlation

so the correspondence may well be fortuitous. Although the gas-phase value of the equilibrium constant has not been determined quantitatively, photoelectron spectroscopic studies have shown that the diketone form predominates in the vapor phase.[26] In cyclohexane at low concentration a $K_T$ value of 0.016 corresponding to a $\Delta G_{hcb}^{\circ}$ of 2.39 kcal/mol has been reported.[7d] This is consistent with the estimated gas-phase value of 2.11 kcal/mol, in favor of the diketone form.

The coefficient of the $\beta$ term of -6.0 makes this term dominant and implies that the enol form is stabilized preferentially by hydrogen-bonding-acceptor solvents. The much smaller coefficient of $\alpha$ of -0.53 indicates substantially less stabilization of the same form by hydrogen-bond-donor solvents.

If other nonspecific parameters are used in place of the Kirkwood–Onsager term, good correlations also result. Thus, when $\pi^*$ is used eq 6 results with a correlation

$$\Delta G_s^{\circ} = -0.75\pi^* - 0.49\alpha - 6.1\beta' + 2.38 \quad (6)$$

coefficient of 0.9957. There is less than one chance in $10^9$ that the correlation results from chance and the SE is 0.17 kcal/mol. When no polarity–polarizability terms are included in the correlation, an equation with $a = -0.6$ and $b = -6.1$ results with $R$ equal to 0.9923, $P \leq 10^{-9}$, and a SE -0.22 kcal/mol. Both equations show that nearly the whole weight of the correlation is carried by the hydrogen-bonding terms.[27] Indeed, when $\beta'$ alone is correlated against the data set, $R = 0.985$. Correlation with $A$ and $B$ does not give satisfactory results: $R = 0.460$; statistical data are summarized in Table VI.

Correlation of the equilibrium for 3-4 using the Kirkwood–Onsager polarity term or the $\pi^*$ polarity–polarizability in conjunction with $\alpha$ and $\beta$ terms results in eq 7 and 8.

$$\Delta G_s^{\circ} = 0.70\left(\frac{\epsilon - 1}{2\epsilon + 1}\right) + 1.1\alpha - 4.53\beta + 0.17 \quad (7)$$

$$\Delta G_s^{\circ} = 0.17\pi^* + 1.2\alpha - 4.4\beta + 0.27 \quad (8)$$

It is again clear that the $\beta$ term carries the correlation

(22) Taft, R. W.; Abboud, J. L.; Kamlet, M. J. *J. Org. Chem.* **1984**, *49*, 2001.

(23) Swain, C. G. *J. Org. Chem.* **1984**, *49*, 2005.

(24) Hukins, A. A.; LeFevre, R. J. W. *J. Chem. Soc.* **1960**, 898. McClellan, A. L. "Tables of Experimental Dipole Moments"; W. H. Freeman and Co.: San Francisco, CA, 1970.

(25) The calculation is not very sensitive to the value chose for molecular volume.

(26) Houk, K. N.; Davis, L. P.; Newcome, G. R.; Duke, R. E., Jr.; Naumad, R. V. *J. Am. Chem. Soc.* **1973**, *95*, 8364.

(27) Almost all correlations are successful if $\beta'$ terms are used. For example when $A + B$ is used as dual parameters a correlation with $R = 0.47$ results. However, if $A + B$ is used along with $\alpha$ and $\beta'$ a correlation with $R = 0.9955$ obtains. The intercept and regression coefficients for $\beta'$ do not change significantly in any of the correlations.

**Table VI. Summary of Statistical Data**

| | 1–2 | 3–4 | 5–6 | 7–8 | 9–10 | 11–12 |
|---|---|---|---|---|---|---|
| $\Delta G_s^\circ = \Delta G_{hc}^\circ +$ $S\pi^* + a\alpha + b\beta$ | | | | | | |
| $\Delta G_{hc}^\circ$ | 2.4 | 0.27 | −0.51 | −2.4 | −0.26 | 4.0 |
| $S$ | −0.75 | 0.17 | 2.43 | 2.1 | 2.1 | −0.33 |
| $a$ | −0.49 | 1.2 | −0.06 | 0.6 | 0.7 | 1.8 |
| $b$ | −6.1 | −4.4 | 0.51 | −0.6 | −0.3 | −5.4 |
| $R$ | 0.9957 | 0.9928 | 0.944 | 0.937 | 0.954 | 0.9739 |
| SE | 0.17 | 0.14 | 0.23 | 0.25 | 0.21 | 0.31 |
| $\Delta G_s^\circ = \Delta G_{hc}^\circ +$ $a\alpha + b\beta$ | 1.87 | 0.39 | 0.9 | −1.3 | 0.86 | 4.0 |
| $\Delta G_{hc}^\circ$ | −0.58 | 1.33 | 0.5 | 0.9 | 1.0 | 1.85 |
| $b$ | −6.1 | −4.5 | 0.7 | 0.2 | 0.0 | −5.6 |
| $R$ | 0.9923 | 0.9926 | 0.45 | 0.55 | 0.58 | 0.9723 |
| SE | 0.22 | 0.14 | 0.62 | 0.6 | 0.57 | 0.32 |
| $\Delta G_s^\circ = \Delta G_{hc}^\circ +$ $aA + bB$ | | | | | | |
| $\Delta G_{hc}^\circ$ | +0.65 | −2.2 | −0.54 | −2.5 | −0.38 | 3.2 |
| $a$ | −3.28 | 7.78 | 0.65 | 1.45 | 1.53 | −0.95 |
| $b$ | −0.09 | −0.38 | 2.29 | 1.68 | 1.53 | −2.47 |
| $R$ | 0.4596 | 0.7336 | 0.9379 | 0.9536 | 0.9604 | 0.4809 |
| SE | 1.61 | 0.77 | 0.242 | 0.22 | 0.20 | 1.19 |

indicating dominance by hydrogen-bond acceptance by the solvent. If only hydrogen-bonding terms are included, eq 9 results, where $R$ is 0.9926, $P$ is $6 \times 10^{-6}$, and SE is 0.14

$$\Delta G_s^\circ = 1.3\alpha - 4.5\beta + 0.38 \qquad (9)$$

kcal/mol. With $\beta$ alone a correlation coefficient of 0.9802 is obtained. The effect of the $\alpha$ term is not clear cut in this case, because no data in solvents with heteroatom-bound protons are available, and the $\alpha$ values of acetonitrile, chloroform, and methylene chloride are known to be uncertain.[5] Our failure to observe **3** in solvents with high $\beta$ values is suggested from the correlation results. For **1–2**, strong hydrogen-bond acceptor solvents shift the equilibrium toward the enol so that the dicarbonyl form is barely detectable. If these solvents have the same effect on **3–4**, a pair in which there is an additional 2 kcal/mol favoring the enol, the dicarbonyl form would be below our detection limits. When $A$ and $B$ are used as parameters, a correlation coefficient of 0.734 results; statistical data are summarized in Table VI.

As for **1–2**, an independent $\Delta G_v^\circ$ value is not available, although it has been noted by photoelectron spectroscopy that 2-methyl substitution in 1,3-cyclohexanediones does increase the amount of the enol relative to the unsubstituted species, in agreement with the present correlations.[26] The value of $k$ given in eq 7 implies that the tautomer with the higher dipole moment is the diketo form. While this is different from the case of **1–2**, experimental dipole moments are not available for models of the two tautomers and the small magnitude of the $k$ term is reasonable. However, as will be shown in the discussion of **11–12** this term can become unreliable if the data have a significant error range, and that also may be the situation with **3–4**. In any case, the dominant role of the hydrogen-bond-accepting function of the solvents in the tautomerism of **1–2** and **3–4** is consistent with expectation based on the similar dipole moments of the isomers and the impossibility of intramolecular hydrogen bonding in **2** and **4**.

**Equilibrium of 5–6.** The isomers **5–6** provide a system in which the enol is fixed syn to the carbonyl group, intramolecular hydrogen bonding is possible, and the two protomers should not differ greatly in dipole moment. The change in the relative free energies of the protomers in 17 solvents covers a range of 2.5 kcal/mol from cyclohexane to water. However, all of our attempts to correlate this

full data set with established parameters have failed.[28] If dimethyl sulfoxide and pyridine, which we found contain water, are removed from the data set the correlation with $p^*$, $\alpha$, and $\beta$ given by eq 10 is obtained. In this case the $R$ value is 0.9443, the $P$ value is $6 \times 10^{-9}$ and SE is 0.23 kcal/mol. Correlations with more acceptable $R$ values can be obtained if solvents are separated into aromatic, chlorinated, and aliphatic types based on polarizability, with chloroform and dimethyl sulfoxide excluded.[6] Indeed, eq 11 which has an $R$ value of 0.9744, a $P$ of $10^{-3}$, and SE of 0.17 kcal/mol is obtained for the nine aliphatic solvents.

The use of $A$ and $B$ for the data set without dimethyl sulfoxide and pyridine gave eq 12 with $R = 0.938$. When

$$\Delta G_s^\circ = 2.42 \ \pi^* - 0.07\alpha \ p \ 0.51\beta - 0.51 \qquad (10)$$

$$\Delta G_s^\circ = 2.5\pi^* - 0.26\alpha - 0.05\beta - 0.17 \qquad (11)$$

$$\Delta G_s^\circ = 0.65A + 2.29B - 0.54 \qquad (12)$$

the parameter $A + B$, which Swain designated as "polarity",[15] is correlated against the data set, $R = 0.87$.

Although a quantitative interpretation is not warranted, these results can be taken to indicate that both polarity-polarizability and hydrogen bonding have significant effects on the equilibria of **5–6**.

**Equilibria of 7–8 and 9–10.** The isomer pairs **7–8** and **9–10**, depending on their conformation, could have the enol and carbonyl groups syn or anti, hydrogen bonding could be internal or external, and dipole moment differences could be large or small. As is the case for **5–6** the best correlations are obtained if the solvents are divided into polarizability classes. For the case of **7–8** with three chlorinated solvents eq 13, which has a $R$ value of 0.996,

$$\Delta G_s^\circ = 2.08\pi^* - 2.56 \qquad (13)$$

$$\Delta G_s^\circ = 2.05\pi^* - 2.55 \qquad (14)$$

is obtained; with the three aromatic solvents eq 14, which has a $R$ value of 0.96, results. Although the equations should not be given much significance in view of the limited data set, both indicate that the polarity–polarizability term is dominant and intermolecular hydrogen bonding is not important in these solvents.

With the nine aliphatic solvents, inclusion of the hydrogen bonding terms is necessary to provide eq 15, which

$$\Delta G_s^\circ = 2.4\pi^* + 0.47\alpha - 0.7\beta - 2.1 \qquad (15)$$

gives a satisfactory correlation of the equilibrium for **7–8**. The $R$ value is 0.998 the $P$ value is $10^{-4}$, and the standard error is 0.12 kcal/mol.[29]

In the case of **9–10** the use of $\pi^*$ and hydrogen-bonding terms with all solvents gives eq 16, which has a minimally

$$\Delta G_s^\circ = 2.1\pi^* + 0.68\alpha - 0.26\beta - 0.26 \qquad (16)$$

acceptable $R$ value of 0.954, a $P$ value of $2 \times 10^{-7}$, and an SE of 0.21. As would be expected, separation into polarizability classes, as shown above, results in better correlations.[30]

The correlations provide $\Delta G_{hcb}^\circ$ of −.21 kcal/mol for **7–8** and −0.25 kcal/mol for **9–10**, which are comparable to gas-phase values of −1.6 and 0 kcal/mol, respectively.[31] The importance of the $\pi^*$ term is consistent within the series. In addition the hydrogen-bonding terms suggest

(28) The use of $A + B$ was not satisfactory and $A$ and $B$ as separate parameters gave an equation with a $R$ value of 0.825.

(29) Attempted correlations of all solvents provided $\Delta G_s^\circ = 2.1\pi^* + 0.61\alpha - 0.07\beta - 2.44$ with a $R$ value of 0.937.

(30) With aromatic solvents $\Delta G_s^\circ = 2.28\pi^* - 0.62$ and $R = 0.983$ for three solvents, with chlorinated solvents $\Delta G_s^\circ = 1.42\pi^* + 0.31$ and $R = 1.00$ for three solvents. With aliphatic solvents $\Delta G_s^\circ = 2.4\pi^* + 0.64\alpha - 0.45\beta - 0.25$ with $R = 0.980$ for nine solvents.

hydrogen bond donation by the solute stabilizes the enol form as expected. The hydrogen-bond acceptance term, on the other hand, favors the dicarbonyl isomers in both cases. The similarity of the terms in eq 16 to those in eq 11 suggests that 7-8 and 9-10, like 5-6, have the syn form for the enol consistent with earlier assignments.[4]

Although Swain's *A* and *B* parameters did not provide satisfactory correlation in other cases, the solvent effects on the equilibria of 7-8 and 9-10 are correlated best by that approach. Thus for 7-8 eq 17 results, with an *R* value

$$\Delta G_s^{\circ} = 1.45A + 1.68B - 2.54 \qquad (17)$$

$$\Delta G_s^{\circ} = 1.53A + 1.53B - 0.38 \qquad (18)$$

$$\Delta G_s^{\circ} = 1.57(A + B) - 2.51 \qquad (19)$$

$$\Delta G_s^{\circ} = 1.54(A + B) - 0.38 \qquad (20)$$

of 0.54, a *P* value of $2.4 \times 10^{-8}$, and an SE of 0.22 kcal/mol. In the case of 9-10 eq 18 is obtained, which has an *R* value of 0.960, a *P* value of $9.3 \times 10^{-9}$, and an SE of 0.20 kcal/mol. Since the coefficients of *A* and *B* in each case are rather similar, successful correlations with *A* + *B* would be expected. Indeed, for 7-8 with *A* + *B*, eq 19 results, with *R* = 0.952, a *P* value of $5 \times 10^{-9}$, and an SE of 0.22 kcal/mol. For 9-10, eq 20 results, with an *R* value of 0.9602, a *P* value of less than $10^{-9}$, and an SE of 0.20 kcal/mol. These correlations are summarized in Table IV of supplementary material.

**Equilibrium for 11-12.** The keto-enol equilibrium represented by 11-12 provides a comparison involving an aromatic system. Although *A* and *B* do not provide a satisfactory correlation, with *A* and *BR* = 0.481, an acceptable correlation is obtained with the Kirkwood-Onsager and hydrogen-bonding terms as shown for eq 21 and

$$\Delta G_s^{\circ} = -1.45(\epsilon - \tfrac{1}{2}\epsilon + 1) + 1.87\alpha - 5.5\beta' + 4.0 \qquad (21)$$

in Table V of supplementary material. The *R* value is 0.9725, *P* is $10^{-8}$, and SE is 0.32 kcal/mol. It should be noted that a similarly acceptable correlation is obtained when the dielectric constant term is deleted. The fact that this term is not important is also indicated by the fact that the value for *k*, calculated from dipole moments of anthrol and anthrone[12] of 1.3, is considerably different from the -0.45 of the correlation. The $G_v^{\circ}$ obtained from the correlation of 4 kcal/mol is in qualitative agreement with ultraviolet spectroscopy which shows anthrone to be the only detectable tautomer in the gas phase.[12c]

**Temperature Effects on the Equilibria.** The comparison of $\Delta G^{\circ}$, $\Delta H^{\circ}$, and $\Delta S^{\circ}$ for 7-8 is shown in Table II. Inspection of the table shows that neither $\Delta\Delta H^{\circ}$ or $\Delta\Delta S^{\circ}$ terms are small. Accordingly neither kinetic nor potential energy terms dominate and $G_v^{\circ}$ is the result of compensation.[2,32] For the present it appears that discussion of free energies offers the best opportunity for insight into the major interactions of protomers with their environent.

**Comparison and Classification of Solvent Effects**

**on Tautomeric Equilibria.** The above correlations reveal two types of sensitivity of protomeric equilibria to changes in solvent. The anti-fixed enol bond systems 1-2, 3-4, and phenol-cyclohexadienone pair 11-12 of catagories A and D give good correlations with polarity and hydrogen-bonding terms. The *R* values are greater than 0.965, and all *P* values are less than $5 \times 10^{-3}$. The regression coefficients computed by this method are independently testable in some cases and the correlations provide $\Delta G_v^{\circ}$ values in agreement with experimental observation.[33] The dominance of the correlations by the $\beta$ term indicates the major differential interaction of the isomers with their environment is the ability of the enolic forms to act as a hydrogen-bond donor to a basic solvent. Values for the $\beta$ term are -6.0, -4.5, and -5.5 kcal/mol for 1-2, 3-4, and 11-12, respectively. Although any generalization will need to be tested, these results do suggest a $\beta$ term value of approximately -5 kcal/mol might be assigned to correlate equilibria for tautomeric systems in which one form has an active externally hydrogen-bonding proton.[34]

On the other hand, the equilibria of categories B and C represented by 5-6, 7-8, and 9-10 are much more dependent on polarity-polarizability interactions with the molecular environment. The best correlations result from parsing the data into the polarizability subsets suggested by Kamlet and Taft, who have also pointed out that the best analysis of solvent effects comes from the use of "select solvents", i.e., the monofunctional alphatic set.[6,35] The $\pi^*$ term is the major parameter in each case; indeed the regression coefficient for $\pi^*$ is similar in these three cases, although the $\alpha$ and $\beta$ terms do make some contribution. Although it is premature to assert that such a relationship will hold generally for cases of syn-fixed enols of $\beta$-dicarbonyl compounds, that seems a useful working hypothesis.

In Table VI are summarized correlations with the Swain and Kamlet-Taft parameters. Although the Swain *A* and *B* parameters perform satisfactorily for 5-6, 7-8, and 9-10, inadequate correlations are observed for 1-2, 3-4, and 11-12, consistent with the suggestion by Taft et al.[22] that these parameters do not deal effectively with cases in which hydrogen-bond basicity of the solvent is a controlling factor. The reasonable success of *A* and *B* with 5-6, 7-8, and 9-10 is interesting but difficult to dissect. Swain refers to *A* and *B* as representing anion and cation solvating ability, but it is not clear how such effects can account for the correlation seen here.[36]

Of the wide variety of solvent parameter sets that have

(31) Briegleb, G.; Strohmeir, W.; *Agnew. Chem.* **1952**, 409. Funcke, E.; Mecke, R. In "Hydrogen Bonding"; Pergamon Press: London, 1959; p 433. Mines, G. W.; Thompson, H. *Proc. R. Soc. London, Ser. A* **1975**, *342*, 327. Nakanishi, H.; Morita, H.; Nagakura, S. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 2255. Melia, T. P.; Merrifield, R.; *J. Appl. Chem.* **1969**, *19*, 79. Bogolyubov, G. M.; Galperin, Ya. V.; Grishin, N. N. *Zh. Obsh. Khim.* **1975**, *3*, 599.

(32) The data do not show an isokinetic relationship although the limited data, the relatively large errors, and the large differences in the solvents and possible interactions make that test problematic. Amis, E. A.; Hinton, J. F. "Solvent Effects on Chemical Phenomena"; Academic Press: New York, 1973; Chapter 4 Leffler, J. E.; Grunwald, E. "Rates and Equilibrium of Organic Reactions"; Wiley: New York, 1963; Chapter 4 and 5.

(33) Also of interest are the coefficients of $\alpha$ obtained from the correlations. For 11-12 an $\alpha$ value of 1.8 kcal/mol is found, while for 1-2 it is equal to -0.8 kcal/mol. These terms represent the differential stabilization of the tautomers by hydrogen bonds donated by the solvent and indicate that for 11-12 the ketone is more stabilized by accepting a hydrogen bond, while in 1-2 the enol form is more stabilized by accepting a hydrogen bond. These results may be related to the dipole moments in both cases, if it is the more polar form that most effectively acts as a hydrogen-bonding base.

(34) Support for this supposition comes from the work of Pipkin and Stella (Pipkin, J. D.; Stella, V. J. *J. Am. Chem. Soc.* **1982**, *104*, 6672). who examined the formation constants of hydrogen-bonded complexes of 2-phenyl-1,3-indandione with dipolar aprotic solvents in cyclohexane. For the 1:1 complexes, they observed a correlation of $\beta$ and ln *k* with a *b* value is about 7. Although not directly comparable to the equilibrium studies performed here, this result is consistent in sign and magnitude with the values we observe.

(35) It is noteworthy that Kamlet and Taft exclude alcohols from their select solvent set, primarily because they observed complex behavior in many systems where both solvents and solutes have active hydrogens.[6] They attribute these difficulties to differential degrees of alcohol self-association, whey they suggest can change the effective hydrogen-bonding species that the solute encounters. In our case incorporation of these solvents does not appear to degrade the correlations, even in situations where hydrogen bonding is a secondary, but significant, effect.

been explored in the present work, it seems clear that the most generally useful consists of $\pi^*$, $\alpha$, and $\beta$. For the cases of 1-2, 3-4, and 11-12, there is no difficulty in using this approach since the equilibria depend primarily on $\beta$. For 5-6, 7-8, and 9-10, this approach is also effective, although separation of solvents into polarity types is required to obtain good correlations.

Comparisons of these results with previous work emphasizes the importance of dipole moment difference and net hydrogen-bonding ability in accounting for solvent effects on protomeric equilibria. All the heterocyclic cases of our earlier report[1] have active protons on both tautomers. Hence the potentially significant role of the $\beta$ term must be largely compensated and the large differences in dipole moments between the tautomers remains dominant, so that the polarity term of the Kirkwood-Onsager model becomes important. Such cases are qualitatively distinct from the present systems in which only one isomer has a prospectively active hydrogen for hydrogen bonding.

The possibility of predicting solvent effects in keto-enol and related equilibria is suggested by these correlations. If there exists a substantial dipole moment difference between the protomers and both forms can donate a hydrogen from a heteroatom for hydrogen bonding to solvent, the polarity term should dominate. If only one protomer has a heteroatom-bonded hydrogen and if that is available for external hydrogen bonding the $\beta'$ term should determine the effect of solvent on the equilibrium. If an internal hydrogen bond is possible the polarity-polarizability term should prove of most importance. Quantitative application of these criteria will await availability of chemical systems that are well-characterized in solvent sensitivity, dipole moments, and vapor-phase equilibria, but semiquantitative applications may be possible.

## Experimental[37] Section

**Materials.** All manipulations with solvents, and UV and NMR samples, were performed in a glovebag flushed with dry nitrogen. Precautions were taken at all times to prevent purified solvents were coming in contact with the atmosphere.

The following NMR solvents were obtained from either Merck and Co., Isotopes, or Aldrich and were used as received: acetone-$d_6$, acetonitrile-$d_3$, benzene-$d_6$, chloroform-$d$, cyclohexane-$d_{12}$, deuterium oxide, 1,2-dichloroethane-$d_4$, dimethylformamide-$d_7$, dimethyl sulfoxide-$d_6$, 1,4-dioxane-$d_8$, ethanol-$d_6$, methanol-$d_4$, methylene chloride-$d_2$, 2-propanol-$d_8$, pyridine-$d_5$, tetrahydrofuran-$d_8$, and toluene-$d_8$.

The solvents for UV studies were purified separately for 11-12, for the monocyclic $\beta$-diketones 1-2 and 3-4 and for 5-6. With few exceptions (vide infra) purified solvents were not monitored for UV transparency, since the commercially available solvents were generally of UV grade; purification was effected to remove UV-transparent polar impurities. All distillations were done under dry nitrogen.

**11-12.** $CCl_4$ was passed through activated alumina and then degassed with $N_2$. Chloroform was washed with $H_2SO_4$ and then

water, dried over $CaCl_2$, and then distilled. 1,2-Dichloroethane was stored over NaOH and distilled from $P_2O_5$. Dichloromethane was washed with $H_2SO_4$, 5% $Na_2CO_3$, and then water, dried over $CaCl_2$, and then distilled from $P_2O_5$. Distilled in glass, cyclohexane was washed several times with $H_2SO_4$, 10% $NaHCO_3$, and water and then dried over $MgSO_4$ and distilled from $P_2O_5$. Triethylamine was dried over NaOH and fractionally distilled from phenyl isocyanate. Toluene was fractionally distilled. Ethyl acetate was washed with 5% $Na_2CO_3$ and saturated aqueous $CaCl_2$, dried over $K_2CO_3$ (2 h), and twice distilled from $P_2O_5$. Dimethylformamide was shaken with KOH and distilled from either BaO or CaO. 1-Butanol was distilled from $CaH_2$. 2-Propanol was distilled from Mg metal. Tetrahydrofuran was distilled from benzophenone ketyl. 1,4-Dioxane was allowed to reflux with 5% by volume of 1 N aqueous HCl overnight. The solution was then dried over KOH and then refluxed over and distilled from Na. Diethyl ether (anhydrous) was distilled from $CaH_2$. *N,N*-Dimethylacetamide was distilled from KOH. Pyridine was dried over KOH and distilled from CaO. Dimethyl sulfoxide was stored over NaOH and then distilled from NaOH under reduced pressure.

**1-2 and 3-4.** In all distillations at least the first and last 5% was discarded. Water (deionized) was degassed with $N_2$ and then distilled, the first half being discarded. Dichloromethane was purified as above, except that the first 25% was discarded. Methanol was either distilled from magnesium methoxide or allowed to reflux over sulfanilic acid before being distilled. Cyclohexane was purified as above. 1,2-Dichloroethane was shaken with basic alumina, filtered, refluxed over $P_2O_5$, and fractionally distilled. Absolute ethanol was refluxed over CaO for several hours and then fractionally distilled. Tetrahydrofuran displayed a UV-active impurity ($\lambda_{max}$ 220 nm) that was not removed by reflux over LiAlH$_4$, Na, or benzophenone kethyl. Treatment of the tetrahydrofuran with $O_3$ at -20 °C (8 mmol/500 mL), followed by reflux over and fractional distillation from LiAlH$_4$, gave satisfactory material. Diethyl ether was refluxed over Na and then over $CaH_2$, from which it was fractionally distilled. Acetonitrile was purified according to Riddick and Bunger, procedure I:[38] careful fractional distillation was required to remove a UV-active impurity at 210-220 nm. 2-Propanol was allowed to reflux over Mg, from which it was fractionally distilled, the first 15% being discarded. 1-Butanol was refluxed was refluxed over CaO, decanted, and then refluxed over and fractionally distilled from Mg. 1,4-Dioxane was purified according to the literature method,[38] except that the last step of recrystallization was omitted.

For 5-6, solvent purification was performed as follows: Methanol was refluxed over and distilled from Mg. Cyclohexane was refluxed over and distilled from either $P_2O_5$ or Na. Dichloromethane was distilled from $P_2O_5$. Acetonitrile was distilled from $P_2O_5$. Water was deionized grade. Acetylacetone (7-8) and ethyl acetoacetate (9-10) were redistilled to analytical purity prior to use. Dimedone (1-2) from Aldrich was analytically pure, displayed a sharp melting point, and was used as obtained. 2-Methyl-1,3-cyclohexanedione (3-4) was recrystallized to analytical purity from ethanol. Anthrone (11-12) was purified as follows: The material (in $CHCl_3$/hexane) was run quickly through a short silica column to remove high-melting impurities. The material obtained was then carefully run through a $^1/_2$ in., 3-ft MPLC silica column, using a 2:1 $CHCl_3$/hexane solvent system. The first portions of the major peak were removed and purity was established by melting point (154-155 °C (lit. 155 °C)) and elemental analysis. Impure material gave higher and broader melting points and unsatisfactory elemental analysis, consistent with the presence of anthraquinone as the impurity. 3-Oxabicyclo[3.30]-2,9-dioxononane (5-6). The synthesis of 5-6 was performed according to the procedures of Goldsmith et al.[10] with the exception of the synthesis described below. Elemental analysis, IR, and $^1$H and $^{13}$C NMR were consistent with the assigned structure and with literature values.[8]

***cis*-3-(Hydroxymethyl)cyclohexanol.** To a stirring solution of 1 g (5.8 mmol) of ketone in dry THF under $N_2$ was added 0.41 g (10.8 mmol) lithium aluminum hydride in 14 mL of THF dropwise over 10 min at room temperature. Stirring was continued

(36) The coefficient of a 1.6 is much smaller than the values of $a$ and $b$ that Swain et al. commonly observe for $S_N1$ and $S_N2$ reactions, which range from 3 to 13,[15] so that some degree of ionic contribution may be used to rationalize the fit. Alternatively, the $A + B$ term can be treated simply as an empirical parameter with an exceptionally wide data base; future analyses may clarify its ability to deal with tautomeric equilibria and provide insight into the solvation processes involved.

(37) Proton nuclear magnetic resonance spectra were obtained on either Varian EM-390 or Nicolet NT-360 spectrometers; carbon-13 spectra were recorded on the Nicolet instrument. For the Nicolet instrument, proton spectra were taken using 16K data points and a 4000-Hz spectral window; carbon-13 spectra were performed with 32K data points and a 20 000 Hz window. Chemical shifts are reported in $\delta$ (ppm) downfield from an internal tetramethylsilane standard. Ultraviolet spectra were obtained on Perkin-Elmer 13, Perkin-Elmer 202, Cary 14, or Beckman Acta MVI spectrometers, using UV cells of 1.00-cm path length. All measurements were made at ambient temperature.

(38) Riddick, J. A.; Bunger, W. B. "Techniques of Chemistry", 3rd ed.; Wiley-Interscience: New York, 1970; Vol. II.

for 12 h, after which excess LAH was destroyed by the addition of a thick aqueous slurry of $Na_2SO_4$. The solution was filtered and the combined ethereal layers were evaporated under reduced pressure to give thick yellow oil. This was distilled in a Kugelrohr appratus (120 °C (0.2 mm) to give 0.48 g (90%) of product as a very viscous colorless oil, which was homogeneous by TLC ($CHCl_3$:EtOAc 5:1) and used without further purification.

**UV Studies.** For **11–12** the spectrum taken immediately after dissolution in a nonpolar solvent was used as the standard spectrum of the anthrone tautomer. Under these conditions the rate of isomerization was sufficiently slow that no detectable contribution from the anthrol tautomer was present. The spectrum of anthrol and the spectrum of anthrol–triethylamine complex in benzene, as reported by Baba and Takemura,[12] were jointly used as the standard spectrum for anthrol. The UV spectrum of reagent grade anthraquinone (the impurity in anthrone) was taken in several solvents and used whenever its inclusion provided a better fit to the observed spectrum. Model spectra were shifted in wavelength whenever necessary to provide a better fit to the experimental spectrum. The spectra of anthrone and anthrol are easily differentiated and have regions of essentially no overlap.

**NMR Temperature Studies.** Temperature studies were performed on the Nicolet NT-360. Temperature control on the instrument was achieved by calibration of the variable-temperature unit with a Doric Trendicator 400A. However, work at temperatures below 0 °C were generally done 5–10 °C below the indicated temperature. The kinetics of equilibration (vide infra) clearly showed negligible change occurred under these conditions. All work at or above 0 °C was performed within 1 °C of the indicated temperature.

Samples were prepared in 528-size 5-mm NMR tubes modified with a ground-glass joint for attachment to a vacuum line. The solutions were prepared under dry $N_2$ and sealed under partial vacuum, but not attempt was made to rigously degas them.

The low-temperature studies on **7–8** were shown to require extended lengths of time for satisfactory equilibration (vide infra). For the –20 and the 0 °C points a freezer and an ice bath in a refrigerator, respectively, served as temperature baths. For the –40 and –60 °C data, a Cryocool Immersion Cooler (CC-100, Neslab) was used to cool a mechanically stirred bath in a Dewar. Temperature control was generally ±1 °C. When spectra were to be taken on these samples, they were transferred to a small Dewar containing a dry-ice slush near the required temperature. When the sample was to be placed in the probe it was quickly wiped dry and allowed to descend into the precooled probe, taking care to keep the time that the sample was exposed to ambient temperature to 5–20 s.

High-temperature samples were equilibrated in a beaker containing ethylene glycol which itself was placed in an oil bath. When care was taken to avoid drafts, temperature control to ±1 °C was achieved. The samples were transferred via a Dewar containing water and a heating element, and the temperature was regulated at all times to ±2 °C of the desired temperature. Again, rapid transfers were effected to minimize loss of equilibration.

Low-temperature studies, which were performed exclusively on **7–8**, were extended to a period of several months. The –60 °C work was ultimately extended to 2 months, the –40 °C experiments to about 17 days, and the –20 °C experiments to about 5 days. It appears that at –60 °C the $CDCl_3$ and THF-$d_8$ solutions were equilibrated within 2 weeks, the ethanol-$d_6$ and methanol-$d_4$ solutions within 6 weeks, and the toluene-$d_8$ solution within 7 weeks. The data is presented in the supplementary material.

**Supplementary Material Available:** Syntheses and analyses of **13**, **14**, and **15** and tables of $\Delta G°$ observed and calculated for **7–8**, **9–10**, and **11–12**, NMR data for **7–8** as a function of solvent and temperature, and correlation analyses of solvent effects on protomeric equilibria for **1–2**, **3–4**, **5–6**, **7–8**, **9–10**, and **11–12** (17 pages). Ordering information is given on any current masthead page.