Structural Effects on Charge Delocalization in Benzylic Anions

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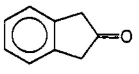
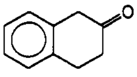
The pK_a's of the benzylic ketones 2-indanone (1), 2-tetralone (2), and 2-benzosuberone (3) were determined in DMSO (16.70, 17.64, and 19.4, respectively), along with the ^{13}C chemical shifts of the neutral species and the anions. Good correlations were observed between the pK_a's and the chemical shifts of the *para* carbons and one of the *ortho* carbons of the anions. These correlations indicate that the order of negative charge delocalization into the ring for the anions is 1 > 2 > 3. This conclusion agrees with calculations of increments of negative charge distribution in the anions. It appears that the anions of 2-tetralone and 2-benzosuberone prefer to bend out of the plane of the aromatic ring at the expense of orbital overlap rather than remain planar at the expense of increased internal strain energy.

A knowledge of structural effects on the acidity of organic molecules is of fundamental importance for an understanding of chemical reactivity. We have been particularly interested in the acid-strengthening effects of phenyl and vinyl substituents on protons adjacent to carbonyl groups.[1-5] These substituents are capable of increasing the aqueous acidity of ketones by up to 10^6–10^7-fold. In the case of phenyl substituents, the magnitude of this effect depends upon the ability of the phenyl group to delocalize the charge of the anion by resonance. The aqueous pK_a's for the cyclic benzyl ketones 2-indanone (1), 2-tetralone (2), and 2-benzosuberone (3) are 12.19, 12.88, and 14.9 respectively.[2,4] 2-Indanone is about 4 orders of magnitude more acidic than benzyl methyl ketone (4) (p$K_a^{H_2O} \approx 16$)[6,7] and about 7 orders of magnitude more acidic than acetone (p$K_a^{H_2O}$ = 19.2).[8] Thus, the intrinsic electronic effect of a phenyl group on the aqueous acidity of a ketone is approximately 10^7-fold.


1
pK_a = 12.2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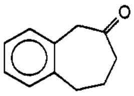
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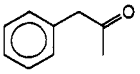
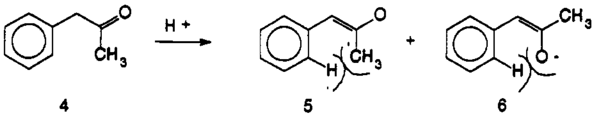

4
pK_a = 16.2

The lower acidity of benzyl methyl ketone compared to the cyclic ketones may be explained by an inability of the phenyl ring in the anion of benzyl methyl ketone to stabilize the negative charge as effectively. Delocalization of the negative charge into the phenyl ring in the enolate of benzyl methyl ketone requires that the anion be in conformation 5 or 6, both of which have significant steric interactions between an *ortho* hydrogen of the phenyl ring and either the methyl group or the alkoxide oxygen. In polar solvents, conformation 5 may be preferred due to inhibition of solvation of the negatively charged oxygen in 6 by the *ortho* hydrogen of the phenyl ring. Guthrie[9] has argued that enolates assume conformations that minimize interference with solvation of the oxyanion and that an enolate oxygen is larger than a methyl group.



An examination of models of the anion of benzyl methyl ketone suggests that the anion would suffer considerable steric strain in the planar conformation, and therefore, the lowered acidity of benzyl methyl ketone relative to the cyclic benzyl ketones might be due to decreased resonance. Although a twist in the dihedral angle between the double bond and the plane of the phenyl ring would ease crowding in the molecule, this twist would be at the expense of optimum π-orbital overlap in the anion. Alternatively, the anion of benzyl methyl ketone might maximize orbital overlap by assuming a planar conformation. In this case, the energy of the anion would be raised by adverse steric interactions. Molecular mechanics calculations[4] suggest that an increase in ring size induces a decrease in the planarity of the ions, which leads to inhibition of charge delocalization.

In order to independently assess the amount of negative charge of the anions of 1–4 that is delocalized into the ring, we have determined the *para* ^{13}C chemical shifts of these enolate ions in DMSO and used these results to estimate the increase in charge upon ionization. ^{13}C NMR has been employed as a tool for the measurement of the

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[1] Pollack, R. M.; Mack, J. P. G.; Eldin, S. *J. Am. Chem. Soc.* **1987**, *109*, 5048.

[2] Ross, A. M.; Whalen, D. L.; Eldin, S.; Pollack, R. M. *J. Am. Chem. Soc.* **1988**, *110*, 1981.

[3] Pollack, R. M.; Zeng, B.; Mack, J. P. G.; Eldin, S. *J. Am. Chem. Soc.* **1989**, *111*, 6419.

[4] Eldin, S.; Pollack, R. M.; Whalen, D. L. *J. Am. Chem. Soc.* **1991**, *113*, 1344.

[5] Dzingeleski, G. D.; Blotny, G.; Pollack, R. M., *J. Org. Chem.*, **1990**, *55*, 1019.

[6] Keeffe, J. R.; Kresge, A. J.; Yin, Y. *J. Am. Chem. Soc.*, **1988**, *110*, 8201.

[7] Guthrie, J. P. *Can. J. Chem.* **1979**, *57*, 1177.

[8] Chiang, Y.; Kresge, A. J.; Tang, Y. S.; Wirz, J. *J. Am. Chem. Soc.* **1984**, *106*, 460.

[9] Guthrie, J. P. *J. Am. Chem. Soc.* **1991**, *113*, 7249.

0022-3263/93/1958-3490$04.00/0

Table I. Ketone pK_a's (± standard deviation) in DMSO[a] and in H_2O[b]

ketone	pK_a^{DMSO}	$pK_a^{H_2O}$
2-indanone (1)	16.70 ± 0.09[c]	12.19 ± 0.03
2-tetralone (2)	17.64 ± 0.15	12.88 ± 0.08
2-benzosuberone (3)	19.41 ± 0.11	14.90 ± 0.02

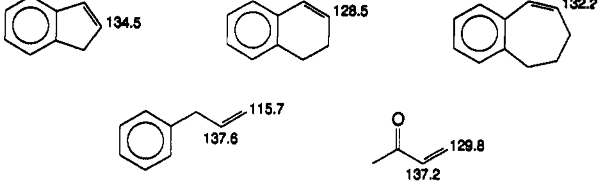
[a] This work. [b] Reference 4. [c] Previously reported as 16.95 (Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456).

extent of charge delocalization in a variety of systems.[10-14] Excellent correlations of calculated total charge density and charge density of the carbon *para* to the substituent vs the ^{13}C chemical shift of the *para* carbon were reported for monosubstituted benzenes, although ^{13}C chemical shifts for *meta* or *ortho* carbons did not correlate well with calculated charge densities.[15,16] In this paper we report correlations of the ^{13}C chemical shifts of the *para* carbons and one of the *ortho* carbons of the enolate anions derived from 1–4 with the acidities of the corresponding ketones. These correlations indicate that the amount of negative charge delocalization into the phenyl ring is greatest for 1 and least for 3 and suggest that the enolate of 2-indanone is indeed the most planar of the cyclic ketones, followed by the enolates of 2-tetralone and 2-benzosuberone, respectively.

Results

pK_a (DMSO) Measurements. pK_a values for the benzylic ketones 2-indanone (1), 2-tetralone (2), and 2-benzosuberone (3) were measured in DMSO (pK_a^{DMSO}) by the indicator method of Bordwell and co-workers[17] (Table I). This procedure is based on titrating a solution containing a known concentration of an indicator anion with a second solution containing the ketone. The success of this procedure depends on an appropriate choice of indicator; the pK_a's of the indicator used should be within two pK_a units of the ketone so that at equilibrium the ratio between the ionized ketone and the unionized ketone does not exceed 100-fold. 9-Phenylfluorene (pK_a^{DMSO} 17.9) was used for the determination of the pK_a's of 2-indanone and 2-tetralone, with the reactions monitored at 540 nm. 4-Chloro-2-nitroaniline (pK_a^{DMSO} 18.9) was used with 2-benzosuberone, and the reaction was monitored at 580 nm. As a control, the pK_a of imidazole was determined with the indicator 4-chloro-2-nitroaniline. The measured pK_a of imidazole (18.5 ± 0.3) is within experimental error of the literature value (18.6).[18]

NMR Studies. The hydrogen (δ_H) and carbon (δ_C) chemical shifts of 1–4 and their anions were determined in DMSO (Table II). The hydrogen and carbon chemical shifts for 1, 2, and 4 are available,[19,20] as are the δ_C chemical shifts for the anions of 2-indanone[21] and benzyl methyl ketone;[22] these are consistent with our values and assignments. The assignment of chemical shifts for relatively simple compounds such as methyl vinyl ketone, 2-indanone, 2-indanone anion, 2-tetralone, benzyl methyl ketone, and benzyl methyl ketone anion were made by inspection, decoupling experiments (in the case of carbon shifts), and/or comparisons with literature values. For more complicated systems, 2D NMR techniques were employed. The chemical shifts for 2-benzosuberone and the anions of 2-benzosuberone and 2-tetralone were assigned by heteronuclear multiple-bond correlation (HMBC)[23] experiments. For the vinylic carbons of allylbenzene, indene, 1,2-dihydronaphthalene, and 1,2-benzo-1,3-cycloheptadiene, the assignment of the proton chemical shifts is straightforward and was done by inspection. Chemical shifts for vinylic carbons were assigned by 2D one-bond ^1H–^{13}C coupled correlation (HMQC) experiments.[24]



Discussion

Relative Charge Density Distribution. The pK_a^{DMSO} values for cyclic benzylic ketones 1–3 follow the same trend as the $pK_a^{H_2O}$ values; both increase with increasing ring size (Table I). The difference $pK_a^{DMSO} - pK_a^{H_2O}$ is similar for each of the ketones, ranging from 4.5 to 4.8 pK_a units. We have previously suggested[4] that an increase in ring size causes deviations from planarity in the anions, resulting in poor π-orbital overlap between the phenyl ring and enolate moiety. Consequently, negative charge delocalization from the enolate portion of the ion into the phenyl group will be inhibited as the ring size increases. The extent of charge delocalization into the phenyl ring should be reflected in the difference of the *para* ^{13}C chemical shifts of the ketone and the corresponding anion.

Bradamante and Pagani[12] have shown that for a series of substituted benzylic anions of the structure $PhCH_2X$ (X = Ph, 3-C_5H_4N, 2-C_5H_4N, 4-C_5H_4N, SOMe, SO_2Me, SO_2Ph, $PO(OEt)_2$, $CONMe_2$, CO_2Me, COMe, COPh, NO_2), the ^{13}C chemical shifts of the *para* carbons (C_{para}) in DMSO are linearly related to the pK_a^{DMSO} values of the corresponding carbon acids (Figure 1). The experimental data point for the substituent X = CN falls below the line, indicating the $PhCH_2CN$ is ca. 7 orders of magnitude more acidic than predicted from the correlation line. Alternatively, C_{para} for $PhCH_2CN$ may be viewed as appearing

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(10) For a review, see: Young, R. N. *Prog. Nucl. Magn. Reson. Spectrosc.* **1979**, *12*, 261.

(11) McNab, H. *J. Chem. Soc., Perkin Trans. 2*, **1981**, 1287.

(12) Bradamante, S.; Pagani, G. A. *J. Chem. Soc., Perkin Trans. 2* **1986**, 1035.

(13) Hunadi, R. J. *J. Am. Chem. Soc.* **1983**, *105*, 6889.

(14) Bates, R. B.; Brenner, S.; Cole, C. M.; Davidson, E. W.; Forsythe, G. D.; McCombs, D. A.; Roth, A. S. *J. Am. Chem. Soc.* **1973**, *95*, 926.

(15) Nelson, G. L.; Levy, G. C.; Cargioli, J. D. *J. Am. Chem. Soc.* **1972**, *94*, 3089.

(16) Olah, G. A.; Westerman, P. W.; Forsyth, D. A. *J. Am. Chem. Soc.* **1975**, *97*, 3419.

(17) Matthews, W. S.; Bares, J. E.; Bartmess, J. E.; Bordwell, F. G.; Cornforth, F. J.; Drucker, G. E.; Margolin, Z.; McCallum, R. J.; McCallum, G. J.; Vanier, N. R. *J. Am. Chem. Soc.* **1975**, *97*, 7006.

(18) Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456.

(19) Pouchert, J. C.; Campbell, J. R. *The Aldrich Library of NMR Spectra*; Aldrich: Milwaukee, WI, 1974; Vol. 6.

(20) *Carbon-13 NMR*; Sadtler Research Laboratories, Division of Bio-Rad Laboratories, Inc., 1982.

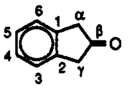
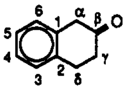
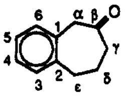
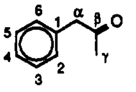
(21) Carbon chemical shifts for 2-indanone anion have been previously reported by Lambert and co-workers (Lambert, J. B.; Wharry, S. M. *J. Am. Chem. Soc.* **1982**, *104*, 5857), and their data are consistent withour interpretation. The reported assignments of 2-indanone anion carbon chemical shifts in that work, however, were incorrectly tabulated (Lambert, J. B., personal communication).

(22) House, H. O.; Prabhu, A. V.; Phillips, W. V. *J. Org. Chem.* **1976**, *41*, 1209.

(23) Bax, A.; Summers, M. F. *J. Am. Chem. Soc.* **1986**, *108*, 2093.

(24) Bax, A.; Subramanian, S. *J. Magn. Reson.* **1986**, *67*, 565.

Table II. Carbon and Hydrogen Chemical Shifts of Ketones and Their Anions in DMSO (Relative to TMS in ppm)

ketone		α-CH	α-CH$_2$	β-C	γ-CH	δ-CH	ε-CH	C$_1$	C$_2$	C$_3$	C$_4$	C$_5$	C$_6$
	δ_C, neutral		44.54	217.33	44.54			138.85	138.85	127.98	125.76	125.76	127.97
	δ_C, anion	89.10		184.22				154.80	133.59	125.43	110.68	121.25	113.09
	δ_H, neutral		3.4		3.4					7.2	7.2	7.2	7.2
	δ_H, anion	4.39								6.63	6.15	6.63	6.26
	δ_C, neutral		44.99	210.95	37.74	27.77		133.23	137.76	127.63	126.87	126.87	128.27
	δ_C, anion	89.95		175.05	35.57	30.65		144.81	128.16	126.05	115.51	126.05	118.55
	δ_H, neutral		3.50		2.40	2.95				7.15	7.15	7.15	7.15
	δ_H, anion	4.68			1.97	2.60				6.69	6.25	6.69	6.29
	δ_C, neutral		49.58	207.41	44.10	26.27	32.52	133.67	140.96	129.14	126.81	127.18	129.32
	δ_C, anion	95.65		175.63	41.84	25.82	36.79	143.07	134.47	128.24	116.26	125.27	124.20
	δ_H, neutral		4.44		3.23	2.54	3.64			7.86	7.86	7.86	7.86
	δ_H, anion	4.89			2.24	1.72	2.57			6.67	6.30	6.67	6.54
	δ_C, neutral		49.55	205.53	29.17			134.76	129.33	128.12	126.33	128.12	129.33
	δ_C, anion	88.86		171.74	29.61			145.85	121.50	127.00	115.37	127.00	121.50
	δ_H, neutral		3.68		2.24					7.25	7.25	7.25	7.25
	δ_H, anion	4.39			1.58					7.45	6.30	7.45	6.78

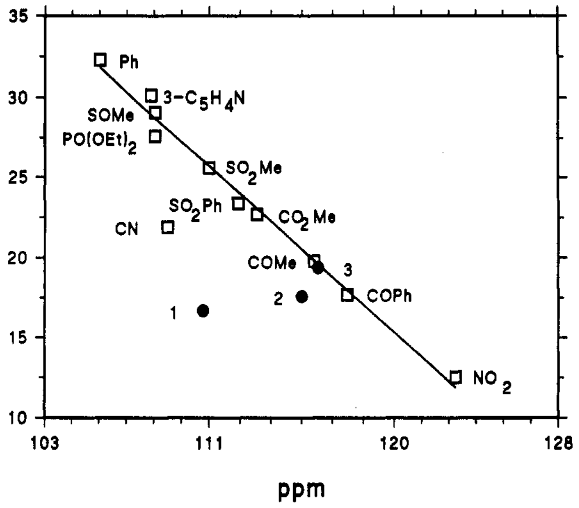


Figure 1. Plot of the chemical shifts for the *para* carbons of the anions of PhCHX[12] and 1–3 vs the pK_a of the ketone in DMSO (where X represents the substituents in the plot).

at a higher field than predicted, indicating a greater negative charge density on that carbon than expected for its pK_a. Bradamante and Pagani[12] argued that this deviation is due to (1) a lesser degree of resonance delocalization of the charge onto the α-substituent (CN) for the phenyl acetonitrile anion than for the other anions, leaving more charge available for delocalization into the phenyl ring, and (2) the planarity of the phenyl acetonitrile anion, in contrast to the other substituted benzyl anions, which have steric interactions that would exert some twisting of the bond between the anionic carbon and the phenyl ring. This planarity enables the negative charge to be most efficiently delocalized into the phenyl ring for the anion of phenyl acetonitrile, leading to a higher charge density at the *para* position than predicted from the pK_a^{DMSO} value.

Addition of the anions of the cyclic benzylic ketones 1–3 to this set of benzylic anions gives insight into the relative extent of charge delocalization into the phenyl ring (charge density at the *para* position) for anions 1–3. The deviation of these points from the line is indicative of the planarity of the anions. The measured C_{para} chemical shifts of the anions and the pK_a^{DMSO}'s for 2-indanone (1), 2-tetralone (2), and 2-benzosuberone (3) are plotted along with the compounds studied by Bradamante and Pagani (Figure 1).[12,25] Among the benzylic ketones 1–3, the point for 2-benzosuberone is close to the line, whereas that of 2-tetralone is further from it, and that of 2-indanone is the farthest away. The deviations of the *para* carbon chemical shifts of 2-indanone anion and 2-tetralone anion from the line reflect the increased charge density at the *para* position, due to optimum π-orbital overlap, achieved by system planarity.

It is important to note that the substituted benzylic anions studied by Bradamante and Pagani (Figure 1) are monosubstituted benzenes, which are being compared with cyclic benzylic ketones that are disubstituted benzenes. However, these alkyl groups are expected to have only minor effects on the chemical shifts of the *para* carbon atoms,[26] consistent with the small difference between the chemical shifts of benzyl methyl ketone (126.3 ppm) and 2-indanone (125.8 ppm). Thus, the C_{para}/pK_a relationship of monophenyl-substituted benzylic anions can be confidently extended to include the cyclic benzylic ketones 1–3.

Calculation of Negative Charge Distribution in the Phenyl Ring. The π-charge distribution in the phenyl ring of the anions of benzylic ketones 1–4 can be calculated by an empirical formula based on the work of Spiesecke and Schneider (eq 1).[27] Chemical shifts for ring carbons

$$(\delta_n - \delta_-)/160 = q \tag{1}$$

have been shown to be proportional to π-electron density, with a proportionality constant in delocalized π-systems of ca. 160 ppm/electron.[27–30] The fraction of negative charge (q) introduced at a carbon atom upon ionization may be calculated from the difference between the chemical shifts at that carbon before (δ_n) and after ionization (δ_-), divided by 160 ppm/e[12,21] (eq 1). Negative charges for the phenyl carbons of the anions are given in Table III.

Calculation of Charge on the α-Carbons of Enolates 1–4. Negative charge densities on the α-carbons of the

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[25] Bradamante and Pagani[12] reported chemical shifts in the presence and absence of [2.2.1]cryptand. Chemical shifts are very similar with and without the cryptand. We use the values without the added cryptand in the plot as we did not use cryptand in our experiments.

[26] Silverstein, R. M., Bassler, G. C., Morrill, T. C. *Spectrophotometric Identification of Organic Compounds*, 5th ed.; Wiley: New York, 1991; p 240.

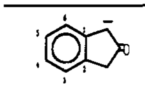
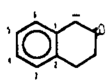
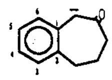
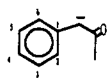
[27] Spiesecke, H.; Schneider, W. G. *Tetrahedron Lett.* **1961**, 468.

[28] O'Brien, D. H.; Hart, A. J.; Russell, C. R. *J. Am. Chem. Soc.* **1975**, *97*, 4410.

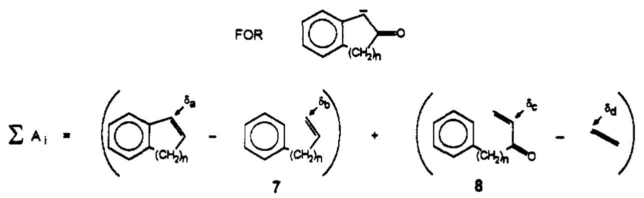
[29] Stothers, J. B. *Carbon-13 NMR Spectroscopy*; Academic Press: New York, 1972; p 91.

[30] Breitmaier, E.; Voelter, W. *Carbon-13 NMR Spectroscopy*; VCH: New York, 1987; p 254.

Table III. Fraction of Charge Densities for Carbons of the Anions of Aromatic Ketones

ketone	q_1	q_2	q_3	q_4	q_5	q_6	q_{ph}	q_α	q_x
	−0.099	0.033	0.016	0.094	0.028	0.093	0.164	0.390	0.446
	−0.072	0.060	0.010	0.071	0.005	0.061	0.135	0.360	0.505
	−0.063	0.041	0.006	0.066	0.012	0.032	0.094	0.336	0.570
	−0.069	0.041	0.014	0.068	0.014	0.041	0.109	0.386	0.505

Scheme I



enolate ions of 1–4 were also calculated from the ^{13}C chemical shifts. Although eq 1 is appropriate for calculation of fractional charge densities on the phenyl ring carbons of the anion, the chemical shift for the neutral carbon atom cannot be used as the δ_n value for carbon atoms that undergo a change in hybridization upon ionization.

The model of Scheme I was used to calculate an appropriate value for δ_n for the α-carbon of cyclic benzylic ketones. This scheme is a slight modification of that used by Bradamante and Pagani[31] for calculating values of δ_n for monosubstituted benzenes and takes into account that 1–3 are disubstituted benzenes.[32] The chemical shift of a substituted sp^2 carbon atom can be viewed as the chemical shift of an unsubstituted sp^2 carbon atom in ethylene (δ_d) corrected for the contribution of the substituent. The shielding contribution of a substituent on the chemical shift (A_i) is equal to the chemical shift of a substituted sp^2 carbon minus the chemical shift of ethylene. The first term in Scheme I gives the change in chemical shift expected upon the addition of a phenyl ring to an olefinic carbon and placing it into a cyclic system. The second term corrects for the effect of an acyl moiety on the chemical shift. The summation of shielding contributions can then be used in eq 2 to calculate an appropriate δ_n to use for the α-benzylic carbons.

$$\delta_n = \delta_d + \sum A_i = \delta_a - \delta_b + \delta_c \tag{2}$$

According to Scheme I carbon chemical shifts for compounds 7 and 8, where n equals 2 and 3, should be used for the 2-tetralone and 2-benzosuberone systems, respectively. Compounds 7 and 8 for n = 2, 3 were unavailable, so approximations were utilized to obtain the needed chemical shifts. Since the structural differences within this series are small and remote from the terminal vinylic carbon, the chemical shift of the terminal carbon of allylbenzene, 7 (n = 1), was used for n equal to 2 and 3. Using the same reasoning, the carbon chemical shifts for the vinyl carbons α to the carbonyl group are expected to be the same for 8 with n = 1–3. The α-vinylic carbon chemical shift for 8 (n = 1) was estimated by assuming that the effect of phenyl substitution on the α-vinylic carbon chemical shift for methyl vinyl ketone is similar to that for acetone.[33]

Summary of Results and Conclusions

Calculated negative charge distributions at the aromatic ring carbon atoms (q_n) and at the α-carbon atom (q_α) for the anions of 1–4 are given in Table III. The total charge transferred into the phenyl ring upon anion formation (q_{ph}) equals the sum of the charge densities of the aromatic ring carbons. The charge delocalized into the carbonyl functionality (q_x) is to $1 - (q_{ph} + q_\alpha)$.

The calculated negative charges at the *para* carbons (q_4) and *ortho* carbons (q_6) and total negative charge of the phenyl rings (q_{ph}) of the enolates from 1–4 correlate well with the pK_a's of the corresponding ketones. The fraction of negative charge delocalized into the phenyl ring is calculated to be 16.4%, 13.5%, and 9.4% for the anions of 2-indanone, 2-tetralone, and 2-benzosuberone, respectively. We interpret these results to mean that charge density is most efficiently transferred from the α-carbon into the phenyl ring in the 2-indanone anion, followed by the 2-tetralone and 2-benzosuberone anions. This order is expected for inhibition of resonance due to poorer overlap of the anion's p-orbitals with increasing ring size. These results are consistent with our previous conclusion[4] that the 2-indanone anion has the least structural twisting from planarity (if any) followed by the 2-tetralone and 2-benzosuberone anions.

It should be noted from Table III that rather poor correlations between pK_a's of 1–4 and calculated negative charges at the 1-, 2-, 3-, 5-, and α-carbons of the enolate ions exist. The lack of correlations between pK_a and calculated charge densities based on ^{13}C NMR chemical shifts for the 3- and 5-carbons is not surprising on the basis of earlier results that showed poor correlations between ^{13}C chemical shifts of *meta* carbons in monosubstituted benzenes and calculated negative charge

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(31) Bradamante, S.; Pagani, G. A. *J. Org. Chem.* 1984, *49*, 2863.

(32) This problem has been also been addressed by House[22] and Lambert[21] and their co-workers, who used a fixed model (enol acetates) to estimate the chemical shift of a neutral carbon atom with a hybridization and magnetic environment similar to that of the corresponding atom in the charged molecule. Although the influence of substituents was ignored by both House[22] and Lambert,[21] the identity of this group appears to have a significant effect on δ_n. For example, the vinylic carbon chemical shifts of methyl vinyl ether and vinyl acetate differ by about 12 ppm (Kalinowski, H.; Berger, S.; Braun, S. *Carbon-13 NMR Spectroscopy*; John Wiley & Sons: New York, 1988; p 291).

(33) The difference in chemical shifts for the methyl carbons of acetone and benzyl methyl ketone is $\Delta\delta$ = 1.5 ppm.

densities.[15,16] Carbon-2, although *ortho*, is in a different chemical environment for each substrate and thus a correlation of q_2 with pK_a might not be expected.

The calculated negative charge on the α-anionic carbon is highest for 2-indanone and decreases slightly with increasing ring size. The percent change in calculated charge at this carbon is quite small, however, and thus no conclusions are drawn. In the absence of molecular orbital calculations or other experimental data, it is unclear whether negative charge on the α-carbon increases as the system becomes more planar. It has been reported by Bradamante and Pagani[12] that the anion of phenylacetonitrile has a relatively high calculated charge density at the α-carbanionic atom compared to the other nonplanar benzylic anion systems that they have studied.

The charge distribution for the acetone anion in THF[34] was calculated from ^{13}C measurements for comparison with the benzylic anions, in order to study the effect of phenyl substitution. The negative charge residing on the α-carbon[35] of the acetone anion in THF is 42.4%, with 57.6% in the carbonyl functionality. For phenylacetone anion, 10.9% of the negative charge is transferred into the phenyl ring (in DMSO), with no major change in the charge distribution ratios between the α-carbon and the carbonyl functionality. It should be noted, however, that the nature of the solvation of the anions may be quite different in the two solvents. Although the cation in both solvent systems was potassium, ion pairing is more likely in THF than DMSO.

In our previous study[4] of the aqueous acidity of **1**–**3**, we observed an increase in pK_a with ring size. This trend was explained in terms of a decrease in charge delocalization with ring size, consistent with molecular mechanics calculations that predict that the enolates would become less planar as the ring size gets larger. The enolates must either remain planar at the expense of an increased internal strain energy or bend out of plane at the cost of optimum π-orbital overlap and charge delocalization. The results in this study indicate that the enolates of **1**–**3** prefer to bend out of plane with an increase in ring size in order to relieve the internal strain energy, rather than to maintain planarity at the cost of internal strain energy.

From a comparison of the aqueous acidities of 2-indanone (p$K_a^{H_2O}$ = 12.2),[2] acetone (p$K_a^{H_2O}$ = 19.2),[8] and cyclopentanone (p$K_a^{H_2O}$ = 20),[36] the intrinsic electronic effect of a phenyl group on the aqueous acidity of a ketone can be estimated to be about 10^7-fold.[2] The effect in DMSO calculated in the same manner is about 10^{9-10}-fold (acetone pK_a^{DMSO} = 26.5, cyclopentanone pK_a^{DMSO} = 25.8, 2-indanone pK_a^{DMSO} = 16.7).[18] The greater effect of a phenyl group on the acidity of a ketone in DMSO than in aqueous solution is expected as the negative charge on the oxygen in the anion should be better solvated in aqueous solution than in DMSO. Thus, the extent of charge delocalization into the phenyl ring is a greater contributor to the stability of the anion in DMSO than in aqueous solution.

Experimental Section

Materials. Unless otherwise indicated, reagents were purchased from commercial suppliers and used without further purification. Anhydrous diethyl ether was refluxed over sodium–benzophenone ketyl followed by distillation. 4-Chloro-2-nitroaniline was recrystallized from ethanol (mp 115.5–116 °C (lit.[37] mp 116–117 °C)). Imidazole was recrystallized from $CHCl_3$ (mp 89 °C (lit.[37] mp 90–91 °C)). Argon gas was dried by passing it in turn through anhydrous calcium sulfate, a concentrated sulfuric acid bubbler, and sodium hydroxide pellets and was then deoxygenated by passing it through an inline Oxiclear oxygen scavenger (VWR). 2-Indanone was purified by sublimation under vacuum, mp 57 °C (lit.[38] mp 57–58 °C). The ketone showed only one spot on TLC (silica, 1:1 hexane/ethyl acetate) and only one peak on HPLC (C_{18}, 40% acetonitrile in H_2O). 2-Tetralone was purified by vacuum distillation: bp (1.75 mmHg) 100–115 °C. Only one peak was observed upon analysis by HPLC (C_{18}, 25% acetonitrile in H_2O). 2-Benzosuberone and 1,2-benzo-1,3-cycloheptadiene have been previously prepared in our laboratory.[4] Aqueous solutions were prepared with doubly distilled water.

Benzyl methyl ketone was prepared according to the procedure of Hauser and co-workers[39] by the Grignard reaction of benzyl bromide with anhydrous acetonitrile, followed by hydrolysis of the ketimine. The ketone was purified by column chromatography (silica, 9:1 hexane/ethyl acetate) to give a clear liquid with spectroscopic properties that matched literature IR[40] and NMR[19] values for benzyl methyl ketone.

Dimethyl Sulfoxide. DMSO (99.9%, ACS spectroscopic grade) was stirred with sodium hydride and several mg of triphenylmethane at 65–70 °C under argon until the red color of the triphenylmethyl anion appeared. The DMSO was then distilled at reduced pressure (bp 43 °C, 1 mmHg) under dry, deoxygenated argon. The distillate was stored under argon until used. DMSO-d_6 (99.5% D) was purified by a similar procedure. **CAUTION**: Sodium hydride should be used with care in this procedure, as it has been reported that solutions of dimsyl sodium in DMSO may explode after about 1 h.[41] When CaH_2 was used to dry the DMSO, no red indicator color appeared even after several hours of heating. Addition of KH to DMSO distilled from CaH_2 resulted in a violent evolution of hydrogen gas.

Potassium Dimsyl (K^+/DMSYL$^-$). The DMSO/K^+DMSYL$^-$ solutions were prepared according to the procedure of Bordwell and co-workers[17] by transfer of 0.1-1 g of KH (35% dispersion in mineral oil) into a dry fritted funnel connected via a side arm above the frit to a vacuum/argon line. The KH was washed several times with pentane freshly distilled from P_2O_3, and the pentane/oil wash was drained out through the frit. The system was then evacuated and purged with argon several times. DMSO or DMSO-d_6 (20-60 mL) was added dropwise under a positive argon pressure. The DMSO/K^+DMSYL$^-$ solution was filtered through the frit into a dry Schlenk storage tube. Dilute DMSO/K^+DMSYL$^-$ solutions are clear and colorless, whereas concentrated solutions are clear and slightly pink. Exposure to air turns the solutions yellow-gray and then black.

pK_a Measurements in DMSO. The pK_a's of the benzylic ketones **1**–**3** were measured by spectrophotometric titration (indicator method) according to the procedure of Bordwell and co-workers.[17] The indicator 9-phenylfluorene (pK_a 17.9) was used in the pK_a determinations of 2-indanone and 2-tetralone, with indicator absorbances measured at 540 nm. The indicator

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[34] The enolate of acetone seemed to be the least stable among anions formed, possibly due to ease of formation of aldol adducts, and was difficult to obtain in DMSO. Thus, the calculated charge density is for the potassium salt of the anion in THF.

[35] Calculated from adding the shielding contribution of an acetyl group (15.8 ppm) to the carbon chemical shift of ethylene (122.8 ppm) and subtracting the chemical shift of the α-carbanionic atom (70.65 ppm), all divided by 160 ppm/electron.

[36] The aqueous pK_a of cyclopentanone can be estimated from the keto–enol equilibrium constant (pK_E = 7.94: Kresge, A. J. *Acc. Chem. Res.* **1990**, *23*, 43) and an estimate of the pK_a of the enol (12 ± 1: Guthrie, J. P.; Cullimore, P. *Can. J. Chem.* **1979**, *57*, 240).

[37] *CRC Handbook of Chemistry and Physics*, 66th ed.; Weast, R. C., Ed.; CRC Press: Boca Raton, FL, 1985.

[38] Horan, J. E.; Scheissler, R. W. *Organic Syntheses*; Wiley: New York, 1973; Collect. Vol. V, p 647.

[39] Hauser, C. R.; Humphlett, W. J.; Weiss, M. J. *J. Am. Chem. Soc.* **1948**, *70*, 426.

[40] Pouchert, C. J. *The Aldrich Library of Infrared Spectra*; Aldrich Chemical Co., Inc.: Milwaukee, WI, 1970; p 627.

[41] Furniss, B. S.; Hannaford, A. J.; Rogers, V.; Smith, P. W. G.; Tatchell, A. R. *Vogel's Textbook of Practical Organic Chemistry*, 4th ed.; John Wiley & Sons: New York, 1978, p 278.

4-chloro-2-nitroaniline (pK_a 18.9) was used in the pK_a determination of 2-benzosuberone, and the indicator absorbances were measured at 580 nm.

In a representative procedure, a cuvette connected to a stopcock fitted with a septum was evacuated, purged with argon, and weighed. About 1 g of DMSO was added to the cuvette via an air-tight syringe through the septum and stopcock. The cuvette was reweighed to determine accurately the amount of DMSO added. A small amount of DMSO/K^+DMSYL$^-$ solution (0.01–0.1 g) was added via an air-tight syringe. The cuvette was weighed once more to determine the amount of DMSO/K^+DMSYL$^-$ solution added. Aliquots (7-50 mg) of indicator solutions in DMSO of known concentration (from 6.7×10^{-3} to 2.7×10^{-2} molal) were added via an air-tight syringe through the septum and stopcock to the DMSO/K^+DMSYL$^-$ solution in the cuvette. The cuvette was weighed, and the absorbance was measured after each addition of indicator solution. At less than complete ionization of the indicator, a plot of absorbance vs indicator concentration is linear; the slope is equal to the extinction coefficient of the ionized indicator (for 9-phenylfluorene, $\epsilon_{540} = 630 \pm 70$, and for 4-chloro-2-nitroaniline, $\epsilon_{580} = 2500 \pm 200$). The concentration at which the plot of absorbance versus indicator concentration levels off is the concentration of base in the cuvette (from 0.001 to 0.003 molal). The addition of additional indicator solution after all the base is consumed causes no further ionization of the indicator, but rather a slight decrease in absorbance due to dilution.

Aliquots of 21-210 mg of the ketone solution in DMSO (from 5.6×10^{-3} to 3.2×10^{-2} molal) were added to the cuvette.[42] The cuvette was weighed to determine the amount of ketone added, and the absorbance was measured after each addition. The drop in absorbance after addition of ketone (with a correction for dilution) reflects the amount of indicator anion protonated by the ketone. Thus, the absorbance of the solution before the ketone addition was used to calculate the fraction of indicator initially in its ionized form and the absorbance of the solution after the ketone addition was used to calculate the fractions of both indicator and ketone in their ionized forms after ketone addition. pK_a's were calculated after each addition of ketone and averaged. Deviations from the averages were random.

NMR Measurements. NMR experiments were performed on a GE GN-500 spectrometer thermostated at 25 °C. For samples in DMSO-d_6 or DMSO-d_6/K^+DMSYL$^-$-d_5, the solvent peaks at 2.49[43] and 39.6[44] ppm were used as the reference points for ^{1}H and ^{13}C spectra, respectively. For samples in DMSO/K^+DMSYL$^-$ (15% DMSO-d_6), the DMSO solvent peaks at 2.49 and 40.5[44] ppm were used as the reference points for ^{1}H and ^{13}C spectra, respectively. The carbon chemical shifts of phenyl acetic acid methyl ester anion were measured and found to be consistent with the literature values.[12] Heteronuclear multiple bond correlation[23] (HMBC) experiments were employed for the assignment of chemical shifts for 2-benzosuberone and the anions of 2-benzosuberone and 2-tetralone. A small amount (<1 mg) of triphenylmethane was added to NMR solvent used to prepare ketone enolates, and the deep red color of its anion served as a marker for complete ionization of the ketones. 2D ^{1}H–^{13}C correlation (HMQC) NMR experiments were conducted for indene, 1,2-dihydronaphthalene, 1,2-benzo-1,3-cycloheptadiene, and allylbenzene in order to accurately assign the vinylic carbon chemical shifts.

Allylbenzene spectral data: ^{1}H NMR (DMSO-d_6) δ 3.35 (d, 2H), 5.05 (t, 2H), 5.95 (m, 1H), 7.18 (m, 3H), 7.28 (m, 2H); ^{13}C NMR (DMSO-d_6) δ 39.4, 115.71, 125.97, 128.34, 128.40, 137.64, 139.71.

Indene spectral data: ^{1}H NMR (DMSO-d_6) δ 3.34 (broad s, 2H), 6.60 (m, 1H), 6.92 (m, 1H), 7.20 (dt, 2H), 7.44 (dd, 2H); ^{13}C NMR (DMSO-d_6) δ 38.63, 120.65, 123.54, 124.29, 125.96, 131.59, 134.48, 143.24, 144.27.

1,2-Dihydronaphthalene spectra data: ^{1}H NMR (DMSO-d_6) δ 2.25 (broad s, 2H), 2.72 (t, 2H), 6.03 (m, 1H), 6.47 (d, 1H), 7.02 (d, 2H), 7.10 (m, 2H); ^{13}C NMR (DMSO-d_6) δ 22.64, 26.73, 125.67, 126.35, 126.82, 127.34, 127.48, 128.56, 133.58, 134.84.

1,2-Benzo-1,3-cycloheptadiene spectral data: ^{1}H NMR (DMSO-d_6) δ 1.86 (m, 2H), 2.38 (broad d, 2H), 2.79 (t, 2H), 5.88 (m, 1H), 6.39 (d, 1H), 7.14 (m, 4H); ^{13}C NMR (DMSO-d_6) δ 26.33, 32.09, 35.46, 125.88, 126.58, 128.85, 129.44, 130.70, 132.18, 135.68, 141.12.

Ketone Enolates. The anions of 2-tetralone and 2-benzosuberone were prepared in dry argon-filled NMR tubes capped with rubber septa. Potassium dimsyl solution (0.5 mL, about 0.6 M), containing 15% DMSO-d_6 for NMR signal locking) with <1 mg of triphenylmethane as indicator, was added with an air-tight syringe. The solutions were subjected to several cycles of freezing, evacuating, and purging with argon. About 15-25 mg of the ketone was added to the NMR tube to form the anion. In the preparation of benzyl methyl ketone, 99.5% deuterated DMSO/K^+DMSYL$^-$ solution was added to 10 mg of the ketone until a deep red color formed.

When this procedure (with an excess of K^+/DMSYL$^-$ present) was used to prepare the enolate of 2-indanone, the aromatic dianion was formed.[45] To determine how much K^+/DMSYL$^-$ solution was necessary to form the monoanion, 10 mg of 2-indanone and less than 1 mg triphenylmethane were added to a test tube, followed by DMSO-d_6/K^+DMSYL$^-$-d_5 solution until the solution turned red, indicating the formation of the dianion. To generate the monoanion, 10 mg of 2-indanone was added to an NMR tube, followed by the addition of half the amount of DMSO-d_6/K^+DMSYL$^-$-d_5 needed to form the dianion.

Acetone enolate was obtained by the reaction of acetone with KH in THF.[46] About 8 mL of pentane (freshly distilled from P_2O_5) was added to KH (200-300 mg) in mineral oil in a dry three-necked 50-mL flask, and the mixture was stirred magnetically. The pentane was then removed by a syringe. This process was repeated several times, and the system was evacuated. After complete evaporation of the pentane, the system was purged with argon, and 0.5 mL of THF-d_8 was added. The system was evacuated once more to remove the THF-d_8. The system was purged with argon, and 2 mL of THF-d_8 was added to the flask. Twenty μL of acetone was added dropwise with stirring (hydrogen evolution was noticeable). After hydrogen evolution had ceased, 0.5 mL of the THF-d_8 solution containing the anion was transferred to an NMR tube via an air-tight syringe for ^{1}H and ^{13}C NMR scans. Acetone spectral data: ^{13}C NMR (THF-d_8) δ 30.36, 204.58 ppm; ^{13}C NMR (DMSO-d_6) δ 30.69, 206.44 ppm. Acetone anion spectral data: ^{1}H NMR (THF-d_8) δ 1.62 (s, 3H), 2.85 (s, 1H), 2.99 (s, 1H); ^{13}C NMR (THF-d_8) δ 171.51, 70.65, 27.19 ppm.

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[42] The enolate of 2-tetralone is not very stable in aqueous solution, and the colorless reaction solution turns blue within a couple of minutes of enolate formation. The same instability of the 2-tetralone enolate is observed in DMSO. For 2-tetralone, only one to four 2-tetralone additions were used in each run, during which time there was no observable change in color.

[43] Table for reference data on NMR solvents, MERCK & CO., St. Louis, MO 63116.

[44] Levy, G. C.; Lichter, R. L.; Nelson, G. L. *Carbon-13 Nuclear Magnetic Resonance Spectroscopy*, 2nd ed.; John Wiley & Sons: New York, 1980.

[45] The symmetrical 2-indanone dianion has been reported to show only five peaks at 77.62, 106.77, 109.10, 129.34, and 168.70 ppm.[21]

[46] Brown, C. A. *J. Org. Chem.* 1974, *39*, 3913.