were placed in a constant-temperature oil bath, and the contents were allowed to equilibrate, and an accurate timer was started. Individual tubes were removed at various times and opened, and the contents placed in a polarimeter cell (1 dm). Optical rotations were measured at 365 nm. Some representative results are collected in Table I.

Thermal Stability Study of (±)-15. A freshly prepared sample of (±)-**15** (8 mg) was dissolved in diglyme-d_{14} (1 g) and placed in an NMR tube. The ^{1}H NMR spectrum was recorded and integrated with respect to internal protiated diglyme. The tube was placed in a constant-temperature oil bath (158.0 ± 0.15 °C) for 22.75 h. At the completion of the experiment, the ^{1}H NMR spectrum was again recorded and integrated. An approximate 7% decrease in the intensity of the olefinic proton absorption was noted. No characteristic new signals appeared in their stead.

Acknowledgment. The financial support of the National Science Foundation is gratefully acknowledged.

Registry No. 8, 10412-04-1; (±)-**9**, 106286-14-0; (±)-**10a**, 117021-90-6; (±)-**10b**, 117021-91-7; (±)-**11**, 106286-15-1; (±)-**11** (sulfone), 117021-92-8; (±)-**12**, 117021-93-9; (±)-**13**, 106286-16-2; (±)-**14**, 106286-17-3; (±)-**15**, 106313-33-1; (−)-**15**, 106286-19-5; (+)-**15**, 106313-32-0; **16**, 106286-18-4; **17**, 106357-98-6; isoprene, 78-79-5; (−)-*endo*-bornyl-1,2,4-triazolinedione, 117066-40-7.

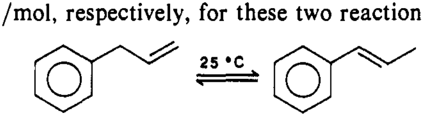
2-Indanone and Its Enol. The Effect of a Conjugated Phenyl Group on Enol and Enolate Stability

J. R. Keeffe,*,† A. J. Kresge,*,‡ and Y. Yin‡

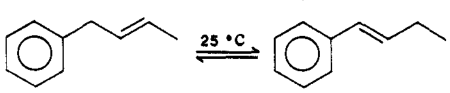
Contribution from the Department of Chemistry, University of Toronto, Toronto, Ontario M5S 1A1, Canada. *Received May 9, 1988*

Abstract: Rate and equilibrium constants for the interconversion of 2-indanone with its enol and enolate ion have been determined in dilute aqueous acid and base solution (ionic strength = 0.10 M) at 25 °C. These measurements provide the keto–enol equilibrium constant, $pK_E = 3.84 \pm 0.04$; the acidity constant of the ketone ionizing as a carbon acid, $pK_a^K = 12.20 \pm 0.08$; and the acidity constant of the enol ionizing as an oxygen acid, $pK_a^E = 8.36 \pm 0.09$. Comparison of these results with values for acetone show that the effects of the benzene ring are large: a factor of $10^{4.4}$ on K_E, $10^{7.0}$ on K_a^K, and $10^{2.6}$ on K_a^E. Considerably smaller phenyl effects are estimated for the acyclic model ketone phenylacetone; reduced coplanarity in the latter is suggested as the major reason for the reduced effects. In terms of rate constants, the greater enol content of 2-indanone relative to acetone manifests itself in the acid-catalyzed reaction mainly as a largely reduced rate of enol ketonization and in the "uncatalyzed" reaction entirely by an increased rate of enolization. For hydroxide ion promoted enolate formation the phenyl effect appears roughly equally as an increase in the rate of enolate formation and a decrease in ketonization rate. It is suggested that the effects of a conjugated benzene ring on enol and enolate stability are fully expressed by the reactions of 2-indanone.

It is well established that replacement of a hydrogen atom or an alkyl group by phenyl stabilizes an attached carbon–carbon double bond. Hine's empirically based double bond stabilization parameters give $\Delta G = -4.9$ and -1.7 kcal/mol, respectively, for reactions 1 and 2.(1) Similarly, Benson's additivity parameters, also empirically based, give gas phase ΔG°_{298} values of −4.1 and −1.5 kcal/mol, respectively, for these two reactions.(2)



(1)



(2)

The influence of a conjugated phenyl group on double bond stabilization also has kinetic manifestations. Reactions 3 and 4, both examples of rate-controlling proton transfer to the double bond, give rate constant ratios k_{Ph}/k_{CH_3}, which are less than unity.(3,4) These results can be rationalized (in part) by invocation of superior initial-state stabilization by phenyl.(5)

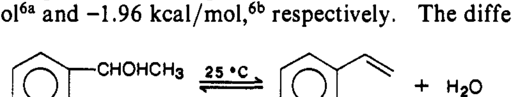
$$CH_2{=}C(R)CH_3 \xrightarrow{H^+} CH_3\overset{+}{C}(R)CH_3 \xrightarrow{H_2O} CH_3C(OH)(R)CH_3 \quad (3)$$

$$R = Ph, CH_3$$

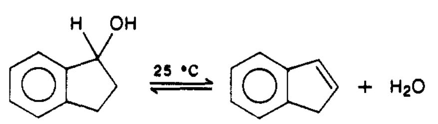
$$CH_2{=}C(R)OC_2H_5 \xrightarrow{H^+} CH_3\overset{+}{C}(R)OC_2H_5 \xrightarrow{H_2O} CH_3C(O)R \quad (4)$$

$$R = Ph, CH_3$$

Incorporation of a double bond into a five-membered ring exalts this stabilizing effect of a conjugated phenyl group: for reactions 5 and 6, equilibrated in aqueous acid solution, $\Delta G = +2.19$ kcal/mol(6a) and −1.96 kcal/mol,(6b) respectively. The difference



(5)



(6)

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† Present address: Department of Chemistry and Biochemistry, San Francisco State University, 1600 Holloway Avenue, San Francisco, California 94132.

‡ University of Toronto.

(1) Hine, J.; Flachskam, N. W. *J. Am. Chem. Soc.* **1973**, *95*, 1179–1185. Hine, J. *Structural Effects on Equilibria in Organic Chemistry*; Wiley: New York, 1975; pp 270–276.

(2) Benson, S. W. *Thermochemical Kinetics*; Wiley: New York, 1968.

(3) (a) Oyama, K.; Tidwell, T. T. *J. Am. Chem. Soc.* **1976**, *98*, 947–951. (b) Ciapetta, F. G.; Kilpatrick, M. L. *J. Am. Chem. Soc.* **1948**, *70*, 639–646.

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(5) Chiang, Y.; Chwang, W. K.; Kresge, A. J.; Robinson, L. H.; Sagatys, D. S.; Young, C. I. *Can. J. Chem.* **1978**, *56*, 456–460.

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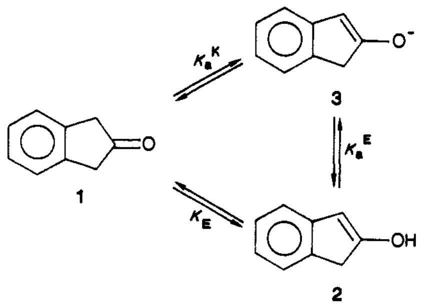
must be corrected for the different degrees of alkylation on the double bond, but a 2.6 kcal/mol correction[7] still leaves ca. a 1.6 kcal/mol superiority for the cyclic system. Other models[2,8] give slightly different numbers, but the qualitative exaltation remains.[9]

The effects described above are for hydrocarbons. Our interest in the effects of structure on enol and enolate stability led us to investigate 2-indanone, for which the enol and enolate forms have a benzene ring conjugated with a double bond, the latter also bearing a trans OH or O$^-$ substituent (see eq 7). We,[10] as well as Ross et al.,[8] have previously determined that 2-indanone is remarkably acidic for a monofunctional ketone bearing neither heteroatom nor proaromatic activators: pK_a^K = 12.2. Here we report all the equilibrium constants for eq 7, as well as individual rate constants for the paths connecting species **1**–**3**. All measurements were made at 25 °C in dilute aqueous solution, ionic strength = 0.10 M.



(7)

Experimental Section

Materials. Inorganic reagents (concentrated HBr, HCl, NaBr, NaCl, Br_2, NaOH) were the best available commercial grade; the salts were dried at 110 °C before use. Stock solutions were prepared from these reagents and doubly distilled, deionized water. The stock HCl, HBr, and NaOH solutions were standardized and further diluted as needed.

2-Indanone (1). The ketone was prepared by a Jones oxidation[11] of 2-indanol. After recrystallization from methanol, the solid melted at 52.5–53.5 °C (lit.[12] mp 57–58 °C) and was shown to be pure by 60-MHz ^{1}H NMR spectroscopy. 2-Indanone is sensitive to air, especially in neutral or basic solution; it was stored cold under argon.

2-Methoxyindene (2-OMe). The enol ether was synthesized from 2-indanone and trimethyl orthoformate in methanolic *p*-toluenesulfonic acid solution. After purification by preparative GLPC, the 60-MHz ^{1}H NMR spectrum ($CDCl_3$) showed δ 7.05 (complex, 4 H), 5.64 (s, 1 H), 3.77 (s, 3 H), 3.35 (s, 2 H). The resonances at 5.64 and 3.35 ppm were slightly broadened. The UV spectrum had a strong maximum at 266 nm (THF) or 265 nm (H_2O). These data are expected for the enol ether. Indene itself has λ_{max} = 248 nm (H_2O),[6b] and the 18-nm shift upon substitution of OR for H agrees with known effects.[13] A ^{13}C spectrum has been reported for **2-OMe**.[14]

2-[(Trimethylsilyl)oxy]indene (2-OTMS). In a three-necked flask fitted with a condenser and dropping funnel were placed 2 mL (0.015 mol) of dry triethylamine and 30 mL of dry ether. The solution was stirred under argon and cooled with an ice–salt bath. Through the dropping funnel was added 1.97 g (0.015 mol) of 2-indanone in 20 mL of dry ether and then, dropwise, 1.3 mL (0.016 mol) of trimethylsilyl chloride. A white precipitate formed immediately, and the mixture was stirred for another 3 h while warming to room temperature. The mixture was then filtered through Celite and the ether removed from the filtrate. ^{1}H NMR and GLPC (OV-17 column) analysis showed the residue to be a mixture of 2-indanone and **2-OTMS** in a ratio of 2:1. Spectroscopic data for the silyl ether are very similar to those for the methyl ether and include the following: 60-MHz ^{1}H NMR ($CDCl_3$) δ 7.0 (complex, 4 H), 5.63 (s, 1 H), 3.18 (s, 2 H), 0.22 (s, 9 H). The resonances at 5.63 and 3.18 ppm were slightly broadened. The UV spectrum had a strong maximum at 268 nm (THF). The silyl ether rapidly hydrolyses to 2-indanone, hence the ketone–silyl ether mixture was used for kinetic studies without further purification.

Table I. Experimental First-Order Rate Constants and Molar Absorptivities of Product Solutions for the Interconversion of 2-Indanone and Its Enolate in Dilute Aqueous NaOH[a]

$[OH^-]$, *M*	k_{exp}, s^{-1} [b]	ϵ_∞, M^{-1} cm^{-1} [c]
0.00179	6.0 ± 0.3	1660 ± 30
0.00380	6.68 ± 0.04	2820 ± 25
0.00580	7.56 ± 0.09	3820 ± 30
0.00781	7.95 ± 0.04	4610 ± 25
0.0128	9.62 ± 0.05	6210 ± 20
0.0178	10.85 ± 0.04	7390 ± 20
0.0279	13.34 ± 0.07	9100 ± 60
0.0379	15.71 ± 0.20	10180 ± 60
0.0479	18.23 ± 0.23	11050 ± 30
0.0731	23.29 ± 0.16	12290 ± 30
0.0982	28.79 ± 0.17	12980 ± 20

[a] At 25 °C, ionic strength = 0.10 M (NaBr). [b] Average values from a total of 64 runs. [c] Average values from a total of 70 runs.

Table II. Experimental First-Order Rate Constants for the Monobromination of 2-Indanone in Dilute Aqueous HBr[a]

$[H^+]$, M	$k_{exp}/10^{-5}$, s^{-1}	$[H^+]$, M	$k_{exp}/10^{-5}$, s^{-1}
0.0196	4.15	0.0784	6.64
0.0199	4.26	0.0794	6.73
0.0397	4.72	0.0994	7.72
0.0596	5.81	0.0999	7.54

[a] At 25 °C, ionic strength = 0.10 M (NaBr).

Table III. Experimental First-Order Rate Constants for the Ketonization of 2-Hydroxyindene (**2**) in Dilute Aqueous HBr[a]

$[H^+]$, M	k_{exp}, s^{-1} [b]	$[H^+]$, M	k_{exp}, s^{-1} [b]
0.00451	0.233 ± 0.003	0.0294	0.305 ± 0.006
0.00945	0.240 ± 0.005	0.0344	0.324 ± 0.001
0.0144	0.252 ± 0.003	0.0393	0.340 ± 0.001
0.0193	0.273 ± 0.002	0.0443	0.354 ± 0.013
0.0243	0.289 ± 0.004		

[a] At 25 °C, ionic strength = 0.10 M (NaBr). [b] Average values from a total of 49 runs.

Kinetic Measurements. Reversible formation of enolate **3** from ketone **1** was monitored at 287 nm upon stopped-flow mixing of aqueous **1** (pH 2.4) with aqueous NaOH solutions.[10] Traces were analyzed by least-squares fit to the logarithmic form of the first-order rate equation and in some cases by the Guggenheim method.[15] The first-order rate constants (average values from 64 runs) are tabulated in Table I against corrected hydroxide concentration. Also listed there are the molar absorptivities of each solution at 8–10 half-lives (ϵ_∞).

Enolization of **1** in dilute acid was monitored by scavenging enol **2** with bromine. In our first experiments, we examined the initial rates of disappearance of Br_2 in the presence of HBr and excess ketone.[16] Kinetic irregularities and interference by precipitation of a product which has no aliphatic hydrogens by ^{1}H NMR indicate that the successive bromination steps are not kinetically separable enough to allow a clean zero-order study.

A successful enolization study was accomplished by using HPLC (300 × 3.9 mm C_{18} column) to monitor the disappearance of 2-indanone from

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[7] Hine, J. *Structural Effects on Equilibria in Organic Chemistry*; Wiley: New York, 1975; pp 265–270.

[8] Ross, A. M.; Whalen, D. L.; Eldin, S.; Pollack, R. M. *J. Am. Chem. Soc.* **1988**, *110*, 1981–1982. These authors argue that in the acyclic system repulsion between an ortho hydrogen and a cis methyl group prevents coplanarity of the alkene and phenyl π orbitals. In support of this contention, we report that force field calculations (MMPMI) indicate that the deviation from coplanarity of these two π systems in 1,1-dimethyl-2-phenylethene is ca. 55°. We thank Norman P. Schepp for this calculation.

[9] Gas-phase $\Delta G°_{298}$ values can be computed for the dehydrogenation of phenylpropane to *cis*-1-phenylpropane and for the dehydrogenation of indan to indene.[2] The results favor indan → indene by ca. 1.2 kcal/mol. A larger exaltation (3.8 kcal/mol) was computed by Ross et al.[8] with gas-phase data for the dehydrogenation of phenylpropane and liquid-phase data for indan → indene.

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[15] Guggenheim, E. A. *Philos. Mag.* **1926**, *2*, 538–543.

[16] Keeffe, J. R.; Kresge, A. J.; Toullec, J. *Can. J. Chem.* **1986**, *64*, 1224–1227.

Table IV. Experimental First-Order Rate Constants for the Hydrolysis of 2-[(Trimethylsilyl)oxy]indene (**2**-OTMS) in Dilute Aqueous HCl[a]

$[H^+]$, M	k_{exp}, s^{-1}
0.004	0.143, 0.142, 0.141
0.008	0.170, 0.173, 0.171
0.012	0.180, 0.189, 0.187
0.016	0.197, 0.192, 0.187
0.020	0.206, 0.203
0.030	0.219, 0.236, 0.219

[a] At 25 °C, ionic strength = 0.10 M (NaCl).

Table V. Experimental First-Order Rate Constants for the Hydrolysis of 2-Methoxyindene (**2**-OMe) in Dilute Aqueous HCl[a]

$[H^+]$, M	$k_{exp}/10^{-3}$, s^{-1}
0.02	0.792, 0.791
0.04	1.60, 1.60, 1.59
0.06	2.29, 2.40
0.08	3.07, 3.15, 3.09
0.10	4.07, 4.02, 3.90

[a] At 25 °C, ionic strength = 0.10 M (NaCl).

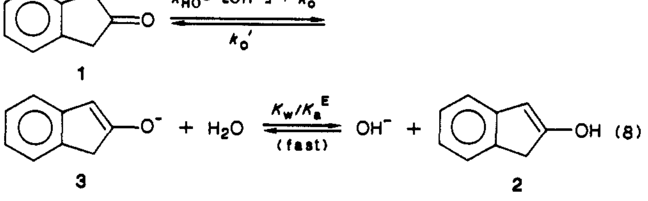
aqueous HBr/Br_2 solutions ($[Br_2]_0/[\mathbf{1}]_0 = 4.7$). Good separation was achieved by gradient elution with methanol-water. The integrated areas of the 2-indanone peaks (UV detection at 268 nm) were analyzed by least-squares fit; good first-order behavior was observed for 2-3 half-lives. The resulting rate constants are given in Table II.

Ketonization of enol **2** in dilute acid was measured in two ways: by stopped-flow mixing of enolate and acid solutions and by hydrolysis of the silyl enol ether **2**-OTMS. In the first method, an enolate solution was prepared and immediately placed in the stopped-flow apparatus where it was mixed with an aqueous HBr/NaBr solution. Loss of absorbance at 275 nm was monitored and analyzed with the logarithmic first-order rate equation. The averaged rate constants from 49 runs are given in Table III. In the second method 10 μL of a THF solution of **2**-OTMS was injected into 3 mL of dilute aqueous HCl in the thermostated cell compartment of a Hewlett-Packard 8451A diode-array spectrophotometer. Immediate formation of an intense band, λ_{max} = 266 nm, was followed by its disappearance over a minute or so, the rate of disappearance depending on $[H^+]$. The final weak spectrum was identical with that of 2-indanone. We attribute the band at 266 nm to enol **2** by analogy with the spectra of 2-methoxyindene and **2**-OTMS. We estimate that we missed the first 2-3 half-lives of reaction; nevertheless good first-order behavior was seen; the derived rate constants are listed in Table IV.

Acid-catalyzed hydrolysis of 2-methoxyindene was observed in a conventional manner by measuring the decrease in absorption at 266 nm of dilute HCl solutions of the enol ether. The first-order experimental rate constants are found in Table V.

Results

Enolization of 2-Indanone in Aqueous Base. Equation 8 describes the first-order approach to equilibrium when 2-indanone reacts with dilute hydroxide ion solutions. The experimental first-order rate constants (Table I) are sums of the forward and reverse constants: k_{exp} (s^{-1}) = $k_f + k_r$, where $k_f = (k_{HO^-}{}^E[OH^-] + k_0{}^E)$ and $k_r = (k_0' K_a{}^E[OH^-])/(K_w + K_a{}^E[OH^-])$. In these equations $K_a{}^E$ is the acid dissociation constant of the enol and K_w, the autoprotolysis constant of water, is assigned the value 1.59×10^{-14} M^2 at μ = 0.10 M which was calculated with the activity coefficients for H^+ and OH^- recommended by Bates.[17] The uncatalyzed rate of enolization, $k_0{}^E$, is negligible under these conditions (see below), as is the rate of carbon protonation of the enolate by H^+; hence k_{exp} is given by eq 9, which simplifies to eq 10 for $K_a{}^E[OH^-] \gg K_w$. Under our experimental conditions eq 10 is valid. Least-squares evaluation of the data at the seven highest $[OH^-]$ yielded $k_{HO^-}{}^E = (2.25 \pm 0.02) \times 10^2$ M^{-1} s^{-1} for the deprotonation of 2-indanone by hydroxide ion and $k_0' = 6.95 \pm 0.09$ s^{-1} for the protonation of enolate by water.[18] These and the other constants found in this work are summarized in Table VI.



$$k_{exp} = k_{HO^-}{}^E[OH^-] + k_0' K_a{}^E[OH^-]/(K_w + K_a{}^E[OH^-]) \tag{9}$$

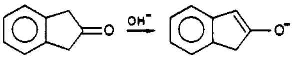
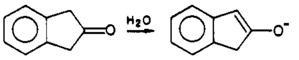
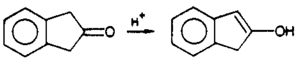
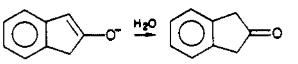
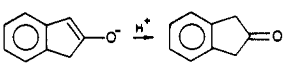
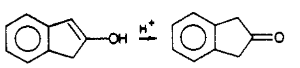
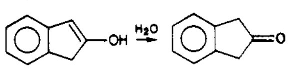
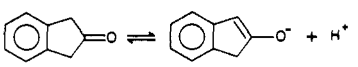
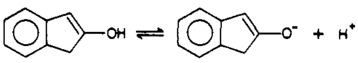
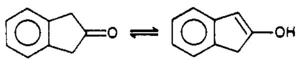
$$k_{exp} = k_{HO^-}{}^E[OH^-] + k_0' \tag{10}$$

The data in aqueous base allow calculation of $K_a{}^K$, the acid ionization constant of 2-indanone, in two ways.[10] The "infinite time" molar absorptivities, ϵ_∞, depend on $[OH^-]$ according to eq 11, in which ϵ_E, ϵ_K, and ϵ_{E^-} are the molar absorptivities of enol, ketone, and enolate, respectively. Least-squares fit[19] of the data to eq 11 yields a value for $K_a{}^K$ which is concordant with the value calculated from our kinetic data. Averaging the two gives $K_a{}^K = (6.3 \pm 1.1) \times 10^{-13}$ M and $pK_a{}^K = 12.20 \pm 0.08$.[20-22]

$$\epsilon_\infty = \frac{(\epsilon_E K_E + \epsilon_K) + \epsilon_{E^-}(K_a{}^E/K_w)[OH^-]}{1 + (K_a{}^K/K_w)[OH^-]} \tag{11}$$

Enolization of 2-Indanone (1) in Aqueous Acid. The disappearance of 2-indanone in aqueous HBr/Br_2 solutions gave good

Table VI. Summary of Rate and Equilibrium Constants for the Keto-Enol Interconversion of 2-Indanone in Dilute Aqueous Solution at 25 °C, Ionic Strength = 0.10 M[a]

	$k_{HO^-}{}^E = 2.25 \times 10^2$ M^{-1} s^{-1}
	$k_0{}^E = 3.2 \times 10^{-5}$ s^{-1}
	$k_{H^+}{}^E = 4.4 \times 10^{-4}$ M^{-1} s^{-1}
	$k_0' = 6.95$ s^{-1}
	$k_{H^+}' = 4.9 \times 10^7$ M^{-1} s^{-1}
	$k_{H^+}{}^K = 3.36$ M^{-1} s^{-1}
	$k_0{}^K = 0.207$ s^{-1}
	$K_a{}^K = 6.3 \times 10^{-13}$ M; $pK_a{}^K$ = 12.20
	$K_a{}^E = 4.4 \times 10^{-9}$ M; $pK_a{}^E$ = 8.36
	$K_E = 1.43 \times 10^{-4}$; pK_E = 3.84

[a] The equilibrium constants are concentration quotients appropriate to this ionic strength.

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(17) Bates, R. G. *Determination of pH. Theory and Practice*; Wiley: New York, 1973; p 49.

(18) First-order behavior of the traces at lower $[OH^-]$ was slightly poorer than at higher $[OH^-]$. Nevertheless evaluation[19] of all the data using eq 9 gave good agreement with eq 10: $k_{HO^-}{}^E = (2.28 \pm 0.04) \times 10^2$ M^{-1} s^{-1} and $k_0' = 6.88 \pm 0.20$ s^{-1}. Lack of data at sufficiently low $[OH^-]$ prevented a reliable calculation of $K_a{}^E$ by this method.

(19) Bevington, P. R. *Data Reduction and Error Analysis for the Physical Sciences*; McGraw-Hill: New York, 1969; pp 237-242.

(20) The molar absorptivity of enolate **3** at 287 nm is calculated to be $\epsilon_{E^-} = 15700 \pm 62$ M^{-1} cm^{-1}, and $(\epsilon_E K_E + \epsilon_K)$ is calculated to be 537 ± 41 M^{-1} cm^{-1} at the same wavelength. Once again there were insufficient data at low $[OH^-]$ for a reliable calculation of all parameters; K_E could not be obtained from eq 11.

(21) This equilibrium constant is a concentration quotient appropriate to ionic strength = 0.10 M.

(22) The difference between the two numbers is greater than the sum of the standard deviations, indicating the incursion of systematic errors. Nevertheless, the difference is acceptably small.

first-order kinetics. This shows that enolization of **1** was rate determining under our conditions; that is, scavenging of the enol by Br_2/Br_3^- was much faster than ketonization over the entire range of [H^+] used. Equation 12, the first-order rate law, was used to fit the data of Table II by least-squares analysis. This

$$k_{exp}\ (s^{-1}) = k_0^E + k_{H^+}^E[H^+] \qquad (12)$$

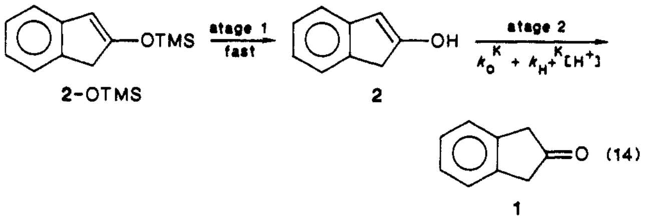
yields $k_0^E = (3.24 \pm 0.11) \times 10^{-5}\ s^{-1}$ for uncatalyzed enolization and $k_{H^+}^E = (4.37 \pm 0.16) \times 10^{-4}\ M^{-1}\ s^{-1}$ as the rate constant for hydrogen ion catalysis.

Ketonization of 2-Hydroxyindene (2) in Aqueous Acid. The data from Table III were fitted to the rate law given in eq 13.

$$k_{exp}\ (s^{-1}) = k_0^K + k_{H^+}^K[H^+] \qquad (13)$$

Least-squares evaluation gave $k_0^K = 0.207 \pm 0.002\ s^{-1}$ for the pH-independent ketonization reaction and $k_{H^+}^K = 3.36 \pm 0.08\ M^{-1}\ s^{-1}$ for the hydrogen ion catalyzed process. This last number is in good agreement with a value, $k_{H^+}^K = 3.48\ M^{-1}\ s^{-1}$, recently reported by Capon and Kwok.[23]

Acid-catalyzed ketonization of **2** was also studied by measuring the rates of hydrolysis of the trimethylsilyl ether of **2**. We picture this process as occurring in two stages, shown by eq 14. Rates of stage 1 have been measured for other trimethylsilyl enol ethers.[24] Reactions relevant to the present case include the hydrolysis of the TMS ether of acetophenone, for which $k_{H^+} = 96\ M^{-1}\ s^{-1}$, and the hydrolysis of the TMS ether of 2-phenylethenol, for which $k_{H^+} > 100\ M^{-1}\ s^{-1}$.[24b] These constants are so large that we are assured of the correctness of eq 14. Least-squares fit of the data in Table IV to the rate law shown for stage 2 gives $k_0^K = 0.143 \pm 0.004\ s^{-1}$ and $k_{H^+}^K = 2.92 \pm 0.25\ M^{-1}\ s^{-1}$. The results do not have the precision of the first method, but they do confirm the identity of the reaction studied by that method.

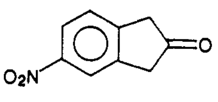


Hydrolysis of 2-Methoxyindene (2-OMe) in Aqueous Acid. Alkyl enol ethers are known to hydrolyze in H^+/H_2O solutions according to the rate law $k_{exp}\ (s^{-1}) = k_0 + k_{H^+}[H^+]$.[25] The data in Table V were fitted to this equation, yielding $k_0 = (9.1 \pm 4.2) \times 10^{-6}\ s^{-1}$ and $k_{H^+} = (3.96 \pm 0.06) \times 10^{-2}\ M^{-1}\ s^{-1}$. The ratio of our ketonization rate constant (see above) to this enol ether constant is $k_{H^+}^K/k_{H^+} = 85$. Methyl enol ethers are known to be protonated by hydrogen ions ca. 20–100 tims more slowly than are the corresponding enols.[25d] This fact gives us further confidence in our ketonization results.

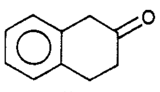
Discussion

Ketone ⇄ Enolate. The phenyl effect on K_a^K for 2-indanone is very large. Acetone has $pK_a^K = 19.16 \pm 0.02$,[26] so the acid-strengthening effect of the benzene ring on the ionization of **1** is $\delta\Delta G = 9.5 \pm 0.1$ kcal/mol. Since the effect of phenyl, relative to hydrogen, in stabilizing a double bond is about 4.9 kcal/mol,[1] the additional effect is most likely due to delocalization of the negative charge through the double bond and into the benzene ring. In support of this idea we note that a pK_a^K value of 8.94 has been reported for 5-nitro-2-indanone (**4**).[27] If we assume predominant ionization at the carbon para to the nitro group, and allow for the additional acidic site on 2-indanone, a two-point ρ^- value of ca. 2.8 may be estimated.

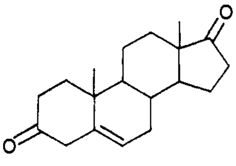
The acidity of 2-indanone is similar to that of 2-tetralone (**5**)[8] and 5-androstene-3,17-dione (**6**),[28] the pK_a values for which are 12.9 and 12.7, respectively. These results show that conjugation of phenyl with C=C—O⁻ is similar whether the latter moiety is part of a 5- or 6-membered ring. They also indicate that the activating effect of a C=C unit is much like that of phenyl.



4, $pK_a^K = 8.94$

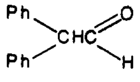


5, $pK_a^K = 12.92$

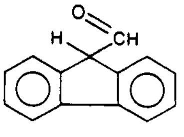


6, $pK_a^K = 12.7$

However, if the acid-strengthening phenyl group is not fused to a ring containing the enolate functionality, its effect is much smaller, a result reminiscent of the comparison made between reactions 5 and 6 in the introduction. In our earlier communication[10] we noted that diphenylacetaldehyde (**7**), $pK_a^K = 10.42$,[29] is only 6.3 pK units more acidic than acetaldehyde,[30] corresponding to an effect of only 4.3 kcal/mol per phenyl group. Even 9-formylfluorene (**8**), $pK_a^K = 6.2$,[31] shows an effect per benzene ring of "only" 7.2 kcal/mol relative to acetaldehyde, this despite the proaromatic nature of the 9-fluorenyl group.

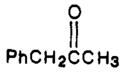


7, $pK_a^K = 10.42$



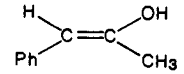
8, $pK_a^K = 6.2$

In light of the above it is instructive to compare 2-indanone with the acyclic model ketone phenylacetone (**9**). In order to make the comparison we need an estimate for the pK_a^K of **9**. We make this estimate by way of a thermodynamic cycle which includes the keto–enol constant for phenylacetone and the acidity constant of its E enol (**10**), as follows. Acid-catalyzed enolization of phenylacetone at the benzylic carbon has $k^E = 5.0 \times 10^{-5}\ M^{-1}\ s^{-1}$.[32] Carbon protonation of the methyl ether of **10** has $k_{H^+} = 1.67\ M^{-1}\ s^{-1}$,[33] a value 42 times greater than that for the methyl ether of 2-indanone (see above). We take ketonization of enol **10** therefore to be ca. 42 times faster than that of the enol of 2-indanone; that is, we estimate $k_{H^+}^K \cong 140\ M^{-1}\ s^{-1}$ for enol **10**. Combination of this value with the experimental enolization rate constant leads to our estimate that $K_E = k_{H^+}^E/k_{H^+}^K \cong 3.6 \times 10^{-7}$ (p$K_E \cong 6.4$) for phenylacetone isomerizing to its E enol, **10**. To



$PhCH_2\overset{\overset{O}{\|}}{C}CH_3$

9



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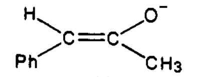

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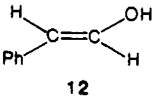

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obtain the acidity constant for enol **10** we first note that acid dissociation constants of enols are not very sensitive to replacement of H by CH_3 at the C–O carbon: pK_a^E for vinyl alcohol is 10.50,[30] while that for 2-hydroxypropene is 10.94,[26] a difference of 0.44 unit. The pK_a^K for (*E*)-2-phenylvinyl alcohol (**12**) is 9.31;[24b] hence we take pK_a^E for **10** to be $9.31 + 0.44 = 9.75$. Finally we combine our estimates to get $pK_a^E = pK_E + pK_a^E = 16.2$ for phenylacetone. This estimate cannot be high by much if at all: Ross et al. note that phenylacetone in 1.0 M NaOH solution gives no observable spectral change.[8] Therefore, relative to acetone the (statistically corrected) effect of the phenyl group on the acidity of phenylacetone is $\delta\Delta G \cong 4.4$ kcal/mol, less than half the effect shown by 2-indanone.

Why is phenylacetone so much less acidic than 2-indanone? Possible factors include improved π overlap and charge delocalization in the enolate of 2-indanone compared with that of phenylacetone. In the former ion, coplanarity of the π systems is enforced, while for the latter, a noncoplanar alignment of the phenyl and enolate π systems is not only possible but might be dictated by steric repulsion between an ortho hydrogen and either the methyl group (in the *E* enolate **11**)[8] or the negative oxygen atom (in the *Z* enolate). A compromise between π overlap and minimization of steric repulsion would produce less than optimal stabilization. It is also conceivable that enolate formation from 2-indanone, an already planar molecule, is less unfavorable entropically than enolate formation from phenylacetone. However Bors et al. have determined that freezing rotation about one C–phenyl bond costs about 3.0 cal/(deg·mol).[34] At 298 K this amounts to a 0.9 kcal/mol contribution to ΔG, less than 20% of the difference between the statistically corrected phenyl group effects on the acidities of 2-indanone and phenylacetone. Thus, reduced coplanarity of the π systems in the enolate(s) of phenylacetone diminishes the effect of the phenyl group on its acidity. We suggest that the 2-indanone system fully expresses the effect of a conjugated benzene ring on enolate stability. Similar arguments rationalize the failure of diphenylacetaldehyde to be more acidic than it is relative to acetaldehyde.

Ketone $\rightleftarrows$ Enol. The keto–enol equilibrium constant for 2-indanone can be calculated from our kinetic data. From the acid-catalyzed enolization and ketonization rates we get $K_E = k_{H^+}^E/k_{H^+}^K = (1.30 \pm 0.05) \times 10^{-4}$; from the uncatalyzed reactions we get $K_E = k_0^E/k_0^K = (1.57 \pm 0.06) \times 10^{-4}$. Averaging these results gives $K_E = (1.43 \pm 0.13) \times 10^{-4}$; $pK_E = 3.84 \pm 0.04$. This represents a large phenyl-group effect. The purely aliphatic models, acetone and cyclopentanone, have pK_E values of 8.22[26] and 7.94,[35] respectively; thus the phenyl effect on K_E is $\delta\Delta G$ = 5.6–6.0 kcal/mol. Capon and Kwok have reported a similar value, $pK_E = 4.09$, for 2-indanone.[23]

Again it is useful to compare 2-indanone with the acyclic benzyl ketone phenylacetone (**9**). Our estimate for this compound (see above) is $pK_E \cong 6.4$. Relative to acetone a statistically corrected phenyl effect of ca. 2.9 kcal/mol is calculated. As with the ketone acidity constants, the phenyl effect on K_E is considerably larger for 2-indanone than for phenylacetone. The same factors which diminish the acidity of phenylacetone relative to 2-indanone are probably at work (somewhat attenuated) in decreasing the enol content of phenylacetone relative to that of 2-indanone (see discussion above).

Enol $\rightleftarrows$ Enolate. The acid dissociation constant of 2-hydroxyindene is the third leg of the thermodynamic triangle shown in eq 7. It can therefore be computed from knowledge of the other two equilibrium constants. The result is $K_a^E = K_a^K/K_E = (4.4 \pm 0.9) \times 10^{-9}$ M and $pK_a^E = 8.36 \pm 0.09$. Ordinarily the acidity of enols is not very sensitive to structural effects.[36] A β-phenyl group does, however, have a significant acid strengthening effect: acetone enol, phenylacetone enol (**10**), and 2-hydroxyindene (**2**) have pK_a^E values of 10.94,[26] 9.75 (estimated, see above), and 8.36, respectively. The polar effect of phenyl is electron withdrawing and this factor doubtless plays a role in stabilizing the enolate relative to the enol. Yet the apparently greater acidity of **2** over **10** argues that there is a resonance effect as well, that this effect is more pronounced in the enolate than the enol, and that it is manifested more strongly in the planar indene system than in the acyclic system.

Table VII. Medium Effects on the Acidities of Acetone, Phenylacetone, and 2-Indanone

ketone	pK_a^K (H_2O)	pK_a^K (DMSO)	$-\delta\Delta G$ (g)	$-\delta\Delta G$- (DMSO)[a]	$-\delta\Delta G$- (H_2O)[a]
acetone	19.16[b]	26.5[e]	(0.0)	(0.0)	(0.0)
phenylacetone	~16.2[c]	19.8[e]	~17	9.8	~4.4
2-indanone	12.20[d]	16.9[f]		13.4	9.5

[a] Statistically corrected: two acidic sites on acetone and 2-indanone, one on phenylacetone. [b] Reference 26. [c] Estimate (see text). [d] This work. [e] Reference 38a. [f] Reference 38b.

The Phenyl Effect on Ketone Acidity. Medium Dependence. Acidity constants, pK_a^K, have been reported for acetone and phenylacetone in the gas phase[37] and in DMSO.[38a] A value for 2-indanone in DMSO, $pK_a = 16.9$, has also been measured.[38b] These values and the medium effects on acidity ($-\delta\Delta G$) are collected in Table VII. The attenuating effect of solvent on $\delta\Delta G$ is not surprising for acids which have conjugate bases with considerable negative charge on an oxygen atom.[37b,38c,39] Strong solvation, especially by hydroxylic solvents, is expected whether or not a phenyl group is present. Since 2-indanone in water and in DMSO displays a substantially larger phenyl effect on pK_a^K than does phenylacetone, we believe that its gas-phase acidity will be found to be unusually high.

Dissection of the Phenyl Effect into Kinetic Contributions. Examination of the rate constants for the base-promoted interconversion of 2-indanone and its enolate shows that the equilibrium constant for this reaction, K_a^K/K_w, owes its $\sim 10^7$ increase relative to acetone both to a substantial increase in the rate of enolate formation ($k_{HO^-}^E$ is ca. 10^3 larger than for acetone[26]) and to a large decrease in the rate at which the enolate is ketonized by water (k_0' is 7.2×10^3 smaller than for that of acetone enolate[30]). We forego discussion of a Brønsted correlation between $k_{HO^-}^E$ and K_a^K on the grounds that lack of structural coherence between cyclic and acyclic ketones makes conclusions uncertain.[40] Instead we observe only that the comparative rate constants suggest that the transition state for this reaction is almost central with respect to the extent of proton transfer. This idea accords with the Leffler–Hammond postulate[41] for an almost ergoneutral reaction $K_a^K/K_w = 40\ M^{-1}$).

The enol content of 2-indanone (**1**) is $10^{4.4}$ greater than that of acetone[26] and $10^{4.1}$ greater than that of cyclopentanone.[35] This augmentation occurs despite the fact that acid-catalyzed enolization of **1** is only 15 times faster than enolization of acetone[42] and 7 times faster than enolization of cyclopentanone.[35] Rather, it is the 1600-fold reduction in the ketonization rate constant, $k_{H^+}^K$, which, from the kinetic point of view, largely enhances the enol content of 2-indanone. This result too is reasonable. We assume the Pedersen mechanism[43] for enolization expressed as eq 15. The

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(40) Combination of data for acetone,[26] acetophenone,[16] and acetaldehyde[30] with the present results yields a Brønsted $\alpha = 0.44 \pm 0.02$. A statistical correction for two acidic sites was applied to the constants for acetone and 2-indanone.

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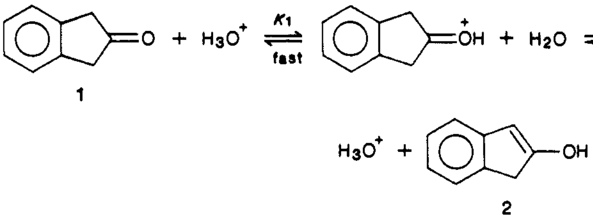
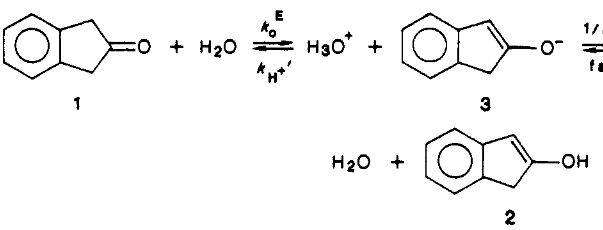


(15)

polar effect of the benzene ring will reduce K_1 for 2-indanone relative to acetone. This fact compensates for the increased rate of step two, a step in which, moreover, the ability of the benzene ring to stabilize the enol is only partly realized at the transition state. In the reverse direction protonation of 2-hydroxyindene is strongly retarded relative to acetone enol because the stabilizing effect of the benzene ring is substantially lost at the transition state.

The kinetics of the *uncatalyzed* keto–enol interconversion tell a different story. The analysis given below shows that the $10^{4.4}$ greater enol content of 2-indanone compared with acetone is, by this pathway, entirely expressed by the differing rate constants for enolization. We take eq 16 as the mechanism for this reaction.[44] For enolization, acetone has $k_0^E = 4.6 \times 10^{-10}\ s^{-1}$.[45] Thus



(16)

the ratio of enolization constants, that of 2-indanone over that of acetone, is about 7.0×10^4 or $10^{4.8}$. The uncatalyzed rate constant for ketonization according to this mechanism is $k_0^K = (K_a^E\ k_{H^+}')$. For enol **2**, $k_0^K = 0.207\ s^{-1}$ while for acetone enol it is actually smaller: $k_0^K = 0.077\ s^{-1}$.[44] The reason that uncatalyzed ketonization of 2-hydroxyindene is faster than that of acetone enol is the greater acidity of the former: K_a^E is 380 times larger than for acetone enol. This enhancement is not quite compensated by a smaller value of k_{H^+}' (see eq 16) so that the product, $(K_a^E k_{H^+}') = k_0^K$, is slightly larger for 2-hydroxindene.

Knowledge of k_0^K and K_a^E allows us to calculate the rate constant for protonation of enolate **3**, on carbon, by hydrogen ions: $k_{H^+}' = k_0^K/k_a^E = (4.7 \pm 1.0) \times 10^7\ M^{-1}\ s^{-1}$. A second estimate is available from combination of the rate constant for uncatalyzed enolization and the acid ionization constant of the ketone: $k_0^E/K_a^K = (5.14 \pm 0.90) \times 10^7\ M^{-1}\ s^{-1}$. The two estimates are in accord and average to $k_{H^+}' = (4.9 \pm 0.9) \times 10^7\ M^{-1}\ s^{-1}$. Large as this number is, it is about 10^2 smaller than k_{H^+}' for the enolates of ordinary, less acidic ketones,[44] and is also smaller than the value for isobutyrophenone enolate.[46] Thus the ability of the conjugated benzene ring to stabilize an enolate ion remains significant even on the rate of a highly exergonic reaction.

Uncatalyzed vs Acid-Catalyzed Enolization. Our studies of the acid-catalyzed bromination of 2-indanone revealed two interesting features. First, the uncatalyzed reaction makes an unusually large contribution to the total rate in dilute aqueous acid: the ratio, $k_{H^+}^E/k_0^E$, is only 13.5 M^{-1}, whereas less reactive ketones such as acetone,[42,45] other aliphatic ketones,[35] and acetophenone[16] have $k_{H^+}^E/k_0^E$ ratios of 10^3 or more. Second, the bromination steps following monobromination are competitive with the initial bromination even when the ketone is in excess. These observations have a common explanation, as follows. The more acidic the ketone, the more rapid is its deprotonation by water. The 10^7 increase in acidity of 2-indanone over acetone is reflected in an almost 10^5 increase in k_0^E. On the other hand, the acid-catalyzed enolization of 2-indanone is only 15 times faster than that of acetone. As discussed above, this result is attributable to the reduced basicity of 2-indanone relative to acetone. The same structural features (electron-withdrawing groups) which increase the acidity of a ketone are those which decrease its basicity. As 2-indanone becomes brominated its acidity rises as does k_0^E. However, its basicity declines, hence $k_{H^+}^E$ is not strongly affected. Polybrominated 2-indanones, ever more reactive toward enolization by water, compete with unbrominated starting material for the remaining bromine. These arguments lead to the expectation that as increasingly electron withdrawing substituents are attached to the aromatic ring of 2-indanone, we will find acid-catalyzed enolization more difficult to detect over the background of the uncatalyzed reaction.

An extreme example of the considerations expressed above is the enolization of the very acidic β-diketone acetylacetone, for which $k_0^E = 1.5 \times 10^{-2}\ s^{-1}$.[47] Here the uncatalyzed reaction is so efficient that proton catalysis is not even seen.[48] It is of interest in this context that although catalysis by hydrogen ions has not been demonstrated for acetylacetone, catalysis by divalent metals (Cu(II) and Fe(II)) is easily seen for this compound[49] as well as for ethyl acetoacetate.[50] These catalysts, able to coordinate with both keto oxygens, induce a favorable conformational geometry prior to formation of the resonance-stabilized enolate chelate.[49a] Hydrogen ions cannot perform this function nearly so well.

Conclusions

The ability of a conjugated benzene ring to stabilize an enol or enolate in aqueous solution is probably fully expressed by the reactions of 2-indanone (eq 7). Relative to acetone this phenyl effect manifests itself most strongly on K_a^K (a factor of $10^{7.0}$), next on K_E (a factor of $10^{4.4}$), and least strongly on K_a^E (still a factor of $10^{2.6}$). The acyclic analogue, phenylacetone, displays the phenyl effect to a much smaller degree. However in 2-tetralone[8] and 5-androstene-3,17-dione,[28] the phenyl effect and "vinyl effect", respectively, on K_a^K are almost as large as in 2-indanone. Enforced coplanarity of the π systems in the cyclic compounds appears to be the main reason for the larger effects.

In terms of rate constants, the enol content of 2-indanone in acid solution is greater than that of acetone principally because of a strongly decreased rate of ketonization of the enol form. However in the uncatalyzed keto–enol interconversion reactions it is the greater enolization rate of 2-indanone which accounts entirely for its larger enol content. The phenyl effect on hydroxide-promoted enolate formation is an intermediate case: both an increased rate of enolate formation and a smaller rate of ketonization are important.

Highly acidic ketones have significantly increased rates of uncatalyzed enolization compared with ordinary ketones. On the other hand, their acid-catalyzed enolization rates are not greatly increased, a consequence of their weaker basicity. These facts mean that the more acidic a ketone is, the more difficult it is to detect acid catalysis above the background of the uncatalyzed reaction, at least in dilute aqueous acid.

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