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Structural Effects on the Energetics of s-Cis and s-Trans Dienolates

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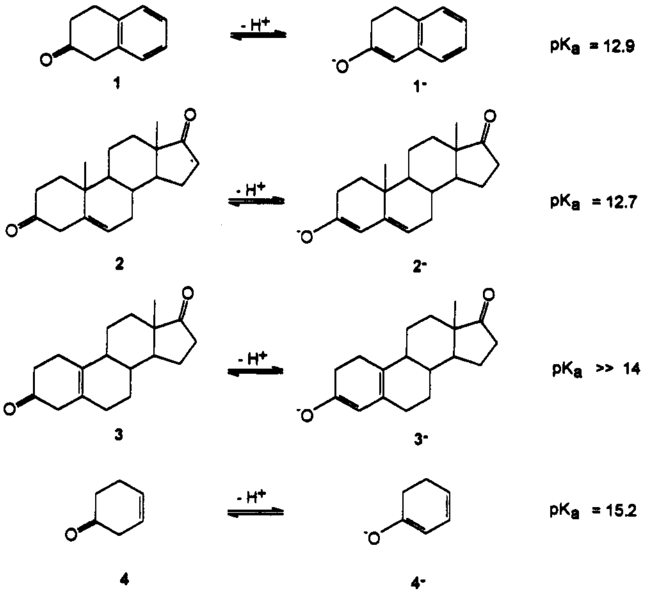
The rates of deuterium exchange of the cis and trans γ protons of 2-cyclopentylidenecyclopentanone were determined in 90% CD_3OD/10% D_2O with NaOD concentrations varying from 0.020 M to 0.352 M. The trans protons were observed to exchange 2.4-fold more rapidly than the cis protons. Similarly, when a solution of the dienolate of 2-cyclopentylidenecyclopentanone in DMSO is quenched in D_2O, incorporation of deuterium at the trans carbon is 4-fold greater than at the cis carbon. Both the kinetic and quenching experiments indicate that the transition state for the formation of the s-cis dienolate is higher in energy than that for the formation of the s-trans dienolate by a factor of *ca.* 4-fold. These results combined with an estimate of the Brönsted β value for deprotonation give an energy difference between these dienolate ions of *ca.* 1.7 kcal/mol.

Much attention has been given recently to the determination of rate and equilibrium constants for enolate formation by the loss of protons α to a carbonyl group.[1] These enolates are intermediates in a variety of chemical and enzymatic reactions, including eliminations, aldol condensations, and alkylations.[2,3] Although studies on the acid- and base-catalyzed conversion of aldehydes and ketones to their enols were reported as early as the 1900's,[4] the inaccessibility of these enols in aqueous solution hindered the study of their ketonizations. In the early 1980's, Kresge,[5] Capon,[6] and their co-workers developed techniques for producing enols in sufficiently high concentration to enable their ketonization reactions to be examined. These studies, and those of others,[1] have provided a great deal of insight into the effect of structure of the carbonyl compound on the reactivity and the equilibrium constants for these reactions. Aqueous pK_a's, keto-enol equilibrium constants, and rate constants for keto-enol interconversions are now available for a variety of aldehydes and ketones.[5,7]

Scheme I



We have been examining the acidifying effect of the substitution of a phenyl group and of a vinyl group at the α-carbon of a carbonyl compound.[8-12] Both a phenyl substituent and a vinyl substituent can increase the aqueous acidity of a simple ketone by as much as 10^7-fold. The aqueous acidities of 2-tetralone (**1**, pK_a 12.9[8] and 5-androstene-3,17-dione (**2**, pK_a 12.7)[9] are comparable (Scheme I), implying a similar acidifying effect for a phenyl group and a double bond on the α-carbon of carbonyl compounds.

However, the double bonds in the β,γ-unsaturated ketones 5(10)-androstene-3,17-dione (**3**, p$K_a \gg 14$[13]) and 3-cyclohexenone (**4**, p$K \approx 15.2$[10]) are approximately 10^2- to 10^3-fold less effective in promoting the ionization of the α-hydrogen than in compound **2** (pK_a = 12.7). There are several structural factors that might account for the striking difference in acidities between these compounds. The most obvious differences between the enolate from **2** and those from **3** and **4** are as follows: (1) 2^- has an s-trans conformation of the double bonds, whereas the anions of the other two ketones possess an s-cis geometry, and (2) 2^- has an exocyclic double bond that is not present in the anions of **3** or **4**.

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(1) For an excellent monograph on this subject, see: *The Chemistry of Enols;* Rappoport, Z., Ed.; John Wiley and Sons: Chichester, 1990.

(2) (a) d'Angelo, J. *Tetrahedron,* **1975,** *32,* 2979. (b) House, H. O. *Modern Synthetic Reactions,* 2nd ed.; W. A. Benjamin; Menlo Park, CA, 1972; Chapter 9.

(3) Gerlt, J. A; Kozarich, J. W.; Kenyon, G. L.; Gassman, P. G. *J. Am. Chem. Soc.* **1991,** *113,* 9667.

(4) For reviews, see: (a) Bell, R. P. *The Proton in Chemistry,* 2nd ed.; Cornell University Press: Ithaca, NY, 1973. (b) Lamaty, G. In *Isotopes in Organic Chemistry;* Buncel, E., Lee, C. C., Eds.; Elsevier: Amsterdam, 1976; Vol. 2, pp 157-240. (c) Toullec, J. *Adv. Phys. Org. Chem.* **1982,** *18,* 1-77. (d) Pollack, R. M. *Tetrahedron* **1989,** *45,* 4913.

(5) Keeffe, J. R.; Kresge A. J. ref 1, Chapter 7.

(6) Capon, B. ref 1, Chapter 5.

(7) Toullec, J. ref 1, Chapter 6.

(8) Ross, A. M.; Whalen, D. L.; Eldin, S.; Pollack, R. M. *J. Am. Chem. Soc.* **1988,** *110,* 1981.

(9) Pollack, R. M.; Zeng, B.; Mack, J. P. G.; Eldin, S. *J. Am. Chem. Soc.* **1989,** *111,* 6419.

(10) Dzingeleski, G. D.; Blotny, G.; Pollack, R. M. *J. Org. Chem.* **1990,** *55,* 1019.

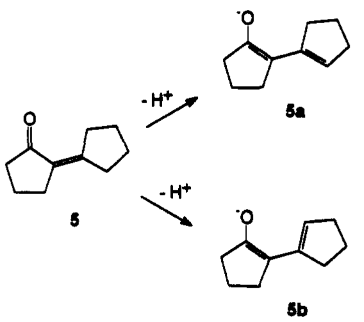
(11) Eldin, S.; Pollack, R. M.;. Whalen, D. L. *J. Am. Chem. Soc.* **1991,** *113,* 1344.

(12) Zeng, B.; Pollack, R. M. *J. Am. Chem. Soc.* **1991,** *113,* 3838.

(13) No spectral changes attributed to the dienolate can be observed in 1 N NaOH solutions; therefore, the pK_a of **3** must be substantially greater than 14.

0022-3263/93/1958-7100$04.00/0

Scheme II



We report here an ^{1}H NMR investigation of the relative kinetic acidities of the cis and trans γ-protons of 2-cyclopentylidenecyclopentanone (5) (Scheme II). In this system the influence of endo- vs exocyclic double bonds is eliminated. Thus, it should be possible to isolate the effect of orientation of the double bonds of a dienolate ion (s-cis vs s-trans) on the acidifying effect of a β,γ-double bond.

Results

Assignment of ^{1}H NMR Peaks of 5. The proton NMR of 2-cyclopentylidenecyclopentanone (5) in CD_3OD (Figure 1a) shows a set of six peaks at δ 1.66 (m, 4H), 1.85 (q, 2H), 2.23 (t, 2H), 2.28 (m, 2H), 2.52 (m, 2H), and 2.68 (m, 2H). The COSY plot (not shown) shows that the protons at 1.85 ppm couple with those at 2.23 and 2.52 ppm and that the protons at 1.66 ppm couple with those at 2.28 and 2.68 ppm. Since 5 contains two rings, the 1.85, 2.23, and 2.52 ppm protons (six hydrogens) are those of the carbonyl-containing ring, and the 1.66, 2.28, and 2.68 ppm protons (eight hydrogens) may be assigned to the other ring. The 1.85 ppm protons show cross peaks with two sets of protons (2.23 and 2.52 ppm), indicating that the 1.85 ppm protons are located between these two sets of protons. Similarly, the 1.66 ppm protons show cross peaks with two sets of protons (2.28 and 2.68 ppm), showing that the 1.66 ppm protons are located between these two sets of protons. Therefore, the protons appearing at 1.85 ppm belong to carbon f, and the 1.66 ppm protons are those of carbons b and c (Chart I).

A deuterium-exchange experiment enabled the 2.23 ppm peaks to be assigned to the α-protons of cyclopentylidenecyclopentanone. The ketone in 80% CD_3OD/D_2O was treated with 0.08 M NaOD. Under these conditions, only the three sets of protons appearing at 2.23, 2.28, and 2.68 ppm exchange with deuterium. These exchange at different rates, with the two protons at 2.23 ppm exchanging the most rapidly. Since the protons of carbon g are the only exchangeable protons in the carbonyl-containing ring, these must be the 2.23 ppm protons. Prolonged reaction of the ketone with base (ca. 24 h) does not cause any exchange of either the 2.52 or 1.66 ppm protons, indicating that they are attached to carbons e and b/c, respectively.

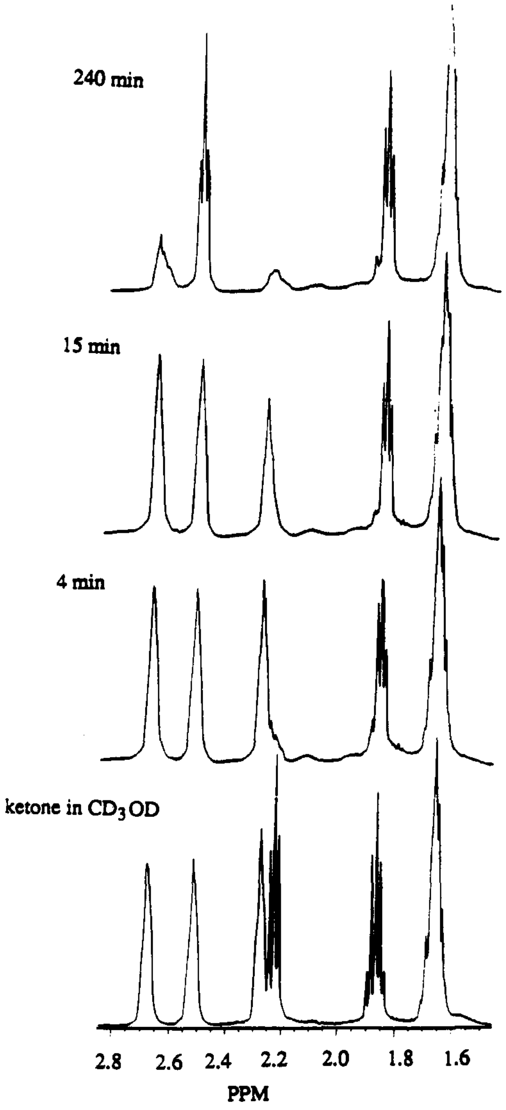


Figure 1. ^{1}H NMR of 2-cyclopentylidenecyclopentanone in CD_3OD (a) and in 0.116 M NaOD (90% CD_3OD/D_2O) at different time intervals (b–d).

Structural effects on the magnetic environment in α,β-unsaturated ketones[14–16] were used to assign the 2.68 ppm peak and the 2.28 ppm peak to carbons a and d, respectively. s-Cis α,β-unsaturated ketones have an imaginary plane running across the molecule (Chart II); protons that are above this plane are deshielded and those below the plane are shielded.[14–16] Accordingly, the protons of carbon a are expected to be deshielded, whereas those of carbon d should be shielded. Therefore, the protons at 2.68 and 2.28 ppm can be assigned to carbons a and d, respectively.[17–19]

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(14) Williams, D. H. *Tetrahedron Lett.* **1965**, 2305.

(15) Timmons, C. J. *J. Chem. Soc., Chem. Commun.* **1965**, 576.

(16) Gottlieb, H. E. In *The Chemistry of Enones;* Patai, S., Rappoport, Z., Eds.; John Wiley and Sons: Chichester, 1989; Chapter 5.

(17) Jedlinski and co-workers[18] have reported IR vibrational frequencies and ^{1}H NMR chemical shifts in $CDCl_3$ relative to TMS for 2-cyclopentylidenecyclopentanone. Their IR data and NMR chemical shifts are almost identical to the present data. However, their reported integrations for the 1.90 and 2.30 ppm peaks differ from this work, as they report that the 1.90 and 2.30 ppm peaks integrate for four and two protons, respectively. In this work, the 1.90 ppm peak (belonging to carbon f) appears as a quintet and integrates for two protons. The splitting pattern and integration of the 1.90 ppm peak is the same in different solvents ($CDCl_3$, DMSO-d_6 and CD_3OD). The 2.30 ppm peak (belonging to carbons d and g) appears as a multiplet in $CDCl_3$ and integrates for four protons. The 2.30 ppm peak however, splits into two distinct peaks in DMSO and in CD_3OD, a triplet at 2.23 ppm (CD_3OD) or 2.13 ppm (DMSO-d_6) for carbon g protons (rapidly collapsing upon the reaction of ketone with deuterated base), and a broad singlet at 2.68 ppm (CD_3OD) or 2.19 ppm (DMSO), each integrating for two protons.

(18) Jedlinski, Z.; Misiolek, A.; Glowkowski, W.; Janeczek, H.; Wolinska, A. *Tetrahedron*, **1990**, 46, 3547.

(19) In an attempt to confirm this assignment an NOE difference spectrum with irradiation of the 2.52 peak was run. However, no enhancement was observed for the peaks at either 2.28 or2.68 ppm.

Chart I

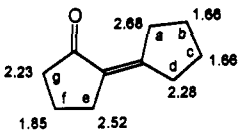

Chart II

Table I. Observed Pseudo-First-Order Rate Constants for the Rate of Deuterium Exchange of the C_d Trans Protons (k_1) and the C_a Cis Protons (k_2) at Different Base Concentrations

[NaOD], M	$10^2k_1^{obs}$, min^{-1}	$10^2k_2^{obs}$, min^{-1}
0.020	0.30 ± 0.07	*a*
0.075	1.26 ± 0.09	0.32 ± 0.02
0.116	1.73 ± 0.13	0.46 ± 0.03
0.195	2.63 ± 0.41	1.04 ± 0.09
0.218	3.11 ± 0.42	1.25 ± 0.09
0.298	4.86 ± 0.33	1.80 ± 0.13
0.352	5.31 ± 0.68	2.22 ± 0.19

[a] Rate of reaction is too slow to be monitored by this technique (estimated $t_{1/2} \approx 9$ h and $k_2 \approx 1.3 \times 10^{-3}$ min^{-1}).

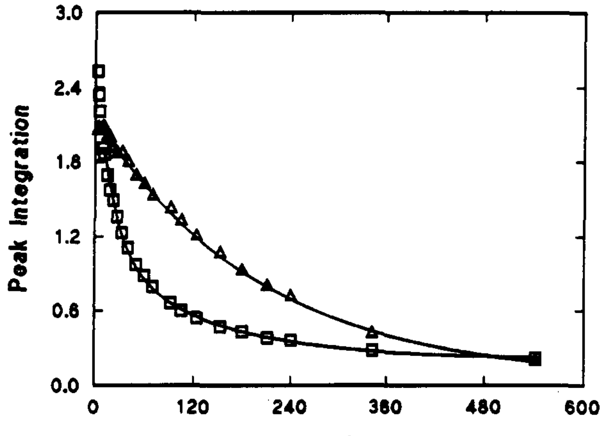

Figure 2. Plot of absolute proton peak area integrations for the γ-carbons on C_d (□) and on C_a (△) *vs* time at 25.0 °C in 0.116 M NaOD. The data were fit with a nonlinear least-squares computer program to a single exponential decay.

Rate of Deuterium Exchange. The rate of exchange of the γ-protons of 2-cyclopentylidenecyclopentanone with deuterium in $CD_3OD/D_2O/OD^-$ was monitored by ^1H NMR under pseudo-first-order conditions (Figure 1). Twenty-six mg of the ketone was dissolved in 90% CD_3OD/10% D_2O (0.5 mL) with NaOD ranging in concentration from 0.020 to 0.352 M. Pseudo-first-order rate constants (k_{obs}) were obtained from a non-linear least-squares single exponential fit[20] of proton peak area integration *vs* time (Table I). A plot of k_{obs} *vs* [OD^-] is linear for the disappearance of both sets of γ protons (Figure 3).

Apparent second-order rate constants for the reactions of the trans and cis γ protons with base (k_1 and k_2, respectively) were calculated using a weighted linear least-squares analysis of the data, according to eqs 1 and 2. The ratio of the apparent rate constant for exchange of the trans γ protons to that for the cis γ protons (k_1/k_2) is 2.4 ± 0.2 ($k_1 = 0.148 \pm 0.007$ and $k_2 = 0.064 \pm 0.004$ M^{-1} min^{-1}). Due to the large excess of D_2O over HOD, the reverse rate constants k_{-1}, and k_{-2} are indistinguishable from zero.

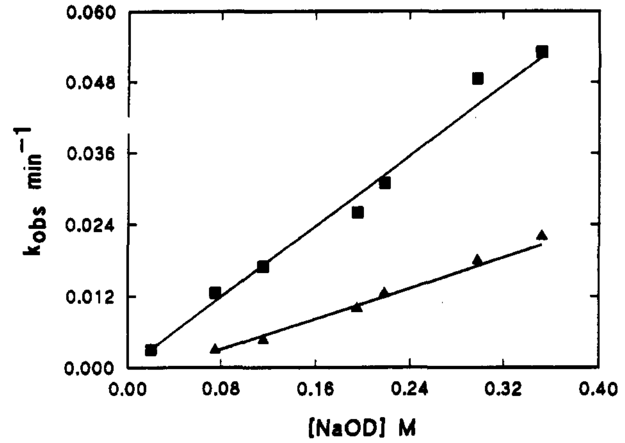

Figure 3. Plot of k_{obs} *vs* [NaOD] for exchange of protons on C_d (■) and C_a(▲).

$$k_1^{obs} = k_1[OD^-] + k_{-1} \quad (1)$$

$$k_2^{obs} = k_2[OD^-] + k_{-2} \quad (2)$$

γ-Protonation of the Dienolate Anion. 2-Cyclopentylidenecyclopentanone (**5**) was allowed to react with K^+/$DMSYL^-$ (ca. 0.6 *m*) to form a mixture of dienolates **5a** and **5b** (Scheme II). After equilibration for 5 h, the solution was quenched with D_2O and the product was purified by column chromatography (silica, CH_3Cl). To avoid possible interference in the analysis caused by the remaining α protons (*ca.* 20%) with determination of the residual C_γ protons, the ketone was treated with 0.195 M NaOD for 4.5 min. Previous kinetic runs at 0.195 M NaOD indicated that 4.5 min would be sufficient to exchange all the α-carbon protons, with ≤3 % exchange of the trans and cis C_γ protons. ^1H NMR integrations of the trans and cis C_γ protons after exchange of the α protons showed 1.19 and 1.76 protons, respectively. Thus, 0.81 and 0.24 protons of the trans C_γ and the cis C_γ carbons, respectively, were exchanged with solvent deuterium. With the assumption that the NMR integrations have an error of ±5%, the ratio of protonation at the trans carbon to that of the cis carbon of the dienolate is 4 ± 2.

As a control, the quenching experiment was duplicated under the same conditions except that the ketone was added after D_2O quenching of the $K^+/DMSYL^-$ solution. ^1H NMR analysis of the ketone product showed that, within experimental error, all of the α-carbon protons and none of the trans C_γ or cis C_γ protons had exchanged with deuterium, showing that treatment of the ketone with 0.195 M NaOD does not exchange the protons on the γ carbon atoms.

NMR of the Dienolate. The ^1H NMR of 2-cyclopentylidenecyclopentanone in DMSO exhibits six sets of peaks at δ 1.56 (m, 4H), 1.76 (q, 2H), 2.13 (t, 2H), 2.19 (m, 2H), 2.42 (m, 2H), and 2.58 (m, 2H). In $K^+/DMSYL^-$ the anion also shows six sets of peaks: δ 1.56 (m, 2H), 1.64 (m, 2H), 1.82 (m, 2H), 2.18 (m, 4H), 2.62 (m, 2H), 4.23 (bs, 1H). The spectrum of the anion shows only one vinylic peak, which strongly suggests that rotation around the single bond

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[20] To avoid any interference between the deuterium exchange of the more labile α protons and those of the γ-trans protons (all appearing at 2.30 ppm) only points after the 2.30 ppm peak integrated for two protons were used. The kinetic data at 0.020 M NaOD were fit to a double-exponential equation.

between the two conjugated double bonds is rapid on the NMR time scale.

Discussion

Energetics of s-Trans *vs* s-Cis Dienolates. In order to relate the observed results to the relative stabilities of the cis and trans dienolates, it is necessary to determine whether bond rotation around the bond connecting the two rings of the anion is faster or slower than protonation at the γ carbon atoms. If rotation is slower than protonation, both the quenching ratio and the kinetic ratio give the relative stabilities of the conformers. However, if bond rotation is rapid, the relative stabilities of these two conformations (**5a** and **5b**) cannot be obtained directly. Rather, the ratios of protonation are related to the stabilities of the corresponding transition states for protonation. Since rotation around the single bond connecting the two rings of the anion is fast on the NMR time scale at room temperature, the latter condition is likely to hold.

Additional evidence supporting rapid bond rotation is provided by the observation that protonation at the α-carbon in dienolate ions is invariably more rapid than protonation at the γ-carbon.[21] Protonation at the α-carbon of either **5a** or **5b** yields a β,γ-unsaturated ketone with a single bond between the rings. Formation of this ketone, with ensuing bond rotation, is thus more rapid than protonation at the γ-carbon atoms. This ketone then is converted to the product through an equilibrium mixture of **5a** and **5b**.

Since rotation about the bond joining the two rings is rapid, the ratio of products deuterated at the cis and trans γ positions (C_a and C_d, respectively) from quenching of the dienolate ion of 2-cyclopentylidenecyclopentanone reflects the relative barrier heights of the transition states for deuteration of the corresponding carbons. The principle of microscopic reversibility dictates that this ratio also represents the relative transition state barrier heights for loss of the C_a and C_d protons.

Analysis of the kinetics of proton exchange is complicated by the rapid bond rotation in the dienolate ion and the existence of two hydrogens at both the cis and trans sites. Although loss of both the cis and trans protons shows acceptable pseudo-first-order kinetic behavior (Figure 2), these processes consist of the interconversion of approximately 20 different partially deuterated species, including neutral ketones and dienolate ions. The complete kinetic scheme was modeled by the KINSIM program of Frieden,[22] which calculates the concentrations of all species in a reaction as a function of time for specific values of rate constants. Using the trans/cis ratio of 4 as the relative deprotonation rate for protons on these carbons and an estimated primary deuterium kinetic isotope effect of 6 for protonation of the carbanion, the KINSIM program shows that the observed kinetic behavior for loss of the cis and trans protons differs only slightly from pseudo-first-order kinetics. However, the apparent rate constants are not those for loss of the appropriate protons; rather, the apparent rate constant for the faster process is lower than the true value, and that for the slower process is higher. When these simulated data are fit to simple pseudo-first-order kinetics, the calculated rate constant for loss of the trans proton is greater than that for the cis proton by a factor of 2. Thus, the observed quenching ratio (4 ± 2) and the kinetic ratio (2.4 ± 0.2) are both consistent with a ratio of microscopic rate constants of 4.

Both the kinetic and quenching experiments indicate that the transition state for the formation of the s-cis dienolate (**5b**) is higher than that for the s-trans dienolate (**5a**) by a factor of about 4-fold (ca. 0.8 kcal/mol). Whalen et al.[23] have shown that the Brönsted β values for the protonation of the γ-carbon in the dienolate ions of 3-cyclohexenone and 3-cyclopentenone are approximately 0.5. If similar transition states are assumed for the formation of **5a** and **5b**, then the difference in rates of the cis and trans protons can be related to the difference in their pK_a's by eq 3. An estimate of the relative stabilities of the s-cis and s-trans conformations of the dienolate ion may then be obtained. This assumption leads to the conclusion that the s-trans dienolate is about 1.7 kcal/mol more stable than the s-cis dienolate, corresponding to a difference in pK_a of 1.2 units.

$$\Delta \log k = 0.5\Delta \log K_a \qquad (3)$$

This energy difference, however, is sufficient to explain only part of the greater acidity of **2** (pK_a 12.7) than **3** (pK_a $\gg$ 14) and **4** (pK_a 15.2). Thus, this difference is probably not solely an effect arising from the orientation of the two double bonds of the dienolates.

Strain Caused by the Insertion of Exo- and Endocyclic Double Bonds in Cyclohexenes. In an effort to evaluate the differential effect of exo and endo double bonds on acidity, we examined the stabilities of several systems by molecular mechanics calculations. Table II lists calculated heats of formation for a number of unconjugated ketones and their corresponding dienolates.[24] The differences between the heats of formation of the s-trans dienolates and their corresponding ketones (**6**, **8**, and **10**) are 8.0, 9.0, and 4.6 kcal/mol, respectively. In contrast, the differences between the heats of formation of the s-cis dienolates and their corresponding ketones **3**, **7**, and **9** are substantially larger, 16.8, 18.5, and 15.9 kcal/mol, respectively. Molecular mechanics calculations of the heats of formation of the s-cis and s-trans dienolate conformations of **5** indicate that the s-cis dienolate is less stable than the s-trans form by 3.35 kcal/mol.

Both the similarity in the rates of exchange of the cis and trans protons of **5** and the small difference in stability of the s-cis and s-trans isomers **5a** and **5b** calculated by molecular mechanics suggest that the inherent stabilities of s-cis and s-trans dienolates in acyclic systems are comparable. Some other factor, such as introduction of ring strain upon enolization, must therefore be primarily responsible for the greater acidity of **2** compared to **3**. In the systems in which an s-cis dienolate is formed, the two double bonds are endocyclic, whereas in systems in which an s-trans dienolate is formed, one of the two double bonds is endocyclic and the other exocyclic. Introduction of the second double bond in the ketone ring might be the source of increased strain upon enolization of **3** and **4** to the cyclic s-cis dienolate ions 3^- and 4^-, respectively, compared to

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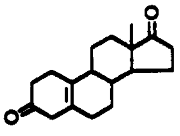
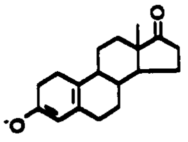
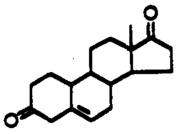
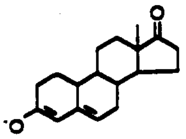
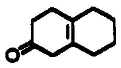
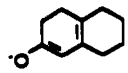
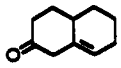
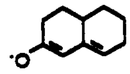
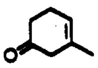
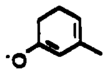
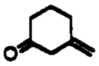
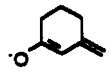
[21] Pollack, R. M.; Bounds, P. L.; Bevins, C. L. In *The Chemistry of Enones;* Patai, S., Rappoport, Z., Eds.; John Wiley and Sons: Chichester, 1989; Chapter 13.

[22] Frieden, C. *Trends Biochem. Sci.* **1993**, *18*, 58.

[23] Whalen, D. L.; Weimaster, J. F.; Ross, A. M.; Radhe, R. *J. Am. Chem. Soc.* **1976**, *98*, 7319.

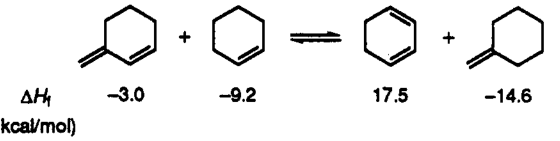
[24] Molecular mechanics calculations were performed using PC-MODEL PI, which uses MMX, an enhanced version of the MM2 and MMP programs (Serena software, Box 3076, Bloomington, IN 47402-3076).

Table II. Calculated Heats of Formation for Selected Ketones and Their Enolates

ketone	$-\Delta H_f$, kcal/mol	enolate	$-\Delta H_f$, kcal/mol	$\Delta\Delta H_f$, kcal/mol
 **3**	-92.3	 **3^-**	-75.5	16.8
 **6**	-92.0	 **6^-**	-84.0	8.0
 **7**	-49.8	 **7^-**	-31.3	18.5
 **8**	-47.0	 **8^-**	-38.0	9.0
 **9**	-41.2	 **9^-**	-25.3	15.9
 **10**	-35.4	 **10^-**	-30.8	4.6

that for enolization of **2**, which results in the introduction of an exocyclic double bond.

Alternatively, there may be a substituent effect on the acidity due to the difference in substitution patterns at the γ carbon for the s-cis and s-trans dienolates. Each of the three s-cis dienolate ions (3^-, 7^-, and 9^-) is more substituted at the γ carbon than the corresponding s-trans dienolate. Although this effect is mitigated by the similar substitution patterns in the starting ketones, it may affect the pK_a's. In order to try to eliminate this effect from consideration, we have examined the heats of formation for the reaction of eq 4. In this system the total substitution



(4)

pattern is similar for reactants and products. A comparison of the heats of formation[25] for the compounds in the right hand side of eq 4 with the compounds on the left hand side should give an insight on the relative stabilities of two endocyclic double bonds vs an endocyclic and an exocyclic double bond in 6-membered ring systems. The calculated difference in the heats of formation for the reaction of eq 4 is 15.1 kcal/mol. Thus, the introduction of a second endocyclic double bond in a six-membered ring appears to impart a significantly higher energy to the system. If so, then a homoannular dienolate ion derived from a cyclohexenone would also be expected to be of higher energy than an isomeric heteroannular dienolate ion. Thus, it appears that cyclic s-cis dienolates are considerably less stable than their corresponding s-trans dienolates due to two factors: (1) greater strain caused by the presence of two double bonds in the same ring for the s-cis dienolate and (2) an inherent energy difference between s-cis and s-trans geometries, with the first factor likely the major one.

Experimental Section

Materials. 2-Cyclopentylidenecyclopentanone (**5**) was purchased from Lancaster and used as received (one spot on TLC, silica, 2:1 hexane/ethyl acetate). Deuterated and nondeuterated solvents were commercial and also used without purification; D_2O (99.9% atom D) and NaOD (40% wt, 99+ atom D). Solutions of potassium methylsulfinylmethide (dimsylpotassium) were prepared according to a previously described procedure.[26]

Kinetic Measurements. NMR experiments were performed on a General Electric GN-500 spectrometer (500.11 MHz, ^{1}H) equipped with a variable-temperature probe set at 25.0 °C. In an NMR tube, 0.05 mL of an NaOD solution in D_2O ranging in concentration from 0.20 to 3.52 M was added to 0.025 mL of ketone dissolved in 0.425 mL of CD_3OD. The total volume of the 90% CD_3OD/10% D_2O solution in the NMR tube was 0.5 mL, and the final base concentration ranged from 0.020 to 0.352 M. About 5 μL of TMS was added to the NMR tube as a standard reference.

First-order rates of exchange of the γ-carbon protons with solvent deuterium were measured by monitoring the loss of the corresponding proton signals with time. Integrations were carried out at approximately 20 equally spaced time intervals over periods of 3–11 half-lives. Peak areas of exchangeable protons were

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[25] Heats of formation utilized are for the liquid phase. (Pedley, J. B.; Naylor, R. D.; Kirby, S. P. *Thermochemical Data of Organic Compounds*; Chapman and Hall: London, 1986).

[26] Eldin, S.; Whalen, D. L.; Pollack, R. M. *J. Org. Chem.* **1993**, *58*, 3490.

digitally integrated and calibrated against peak areas of nonexchangeable protons. Pseudo-first-order rate constants were calculated with a nonlinear least-squares regression program. Second-order rate constants were obtained from the slopes of weighted least-squares plots of the observed rate constants *vs* deuteroxide ion concentration.

Ratio of s-Trans/s-Cis Protonation of the Dienolate Anion from 5. Ten mL of freshly distilled DMSO and about 1 mg of triphenylmethane (acting as an indicator for complete ionization of the ketone) were added under argon to a 125-mL round-bottomed flask. The flask was sealed with a septum through which the system was evacuated and purged with argon several times to remove dissolved oxygen in the solution. Ten mL of a solution of dimsylpotassium in DMSO (*ca.* 0.6 M) was added from a syringe to the round bottomed flask *via* the septum. 2-Cyclopentylidenecyclopentanone (**5**) (0.5 mL) was added, and the resulting solution was stirred magnetically for 4 h. During this time the red coloration due to triphenylmethyl anion persisted. The reaction mixture was then quenched with 100 mL of D_2O with rapid stirring, and the ketone was immediately extracted into methylene chloride. The methylene chloride solution was washed several times with D_2O and dried over anhydrous magnesium sulfate.

NMR of the Dienolate Anion from 5. About 0.5 mL of a solution of potassium dimsyl-d_5 in DMSO (*ca.* 0.6 M) was added through a rubber septum to an NMR tube containing ca. 1 mg of triphenylmethane indicator under argon. The NMR tube was evacuated and purged several times with dried/deoxygenated argon gas. The ketone (10–25 mg) and 5 μL of TMS were added through the septum to the contents of the NMR tube. In cases where a persistent red color was not obtained due to insufficient base, more potassium-d_5 dimsyl solution was added until the deep red coloration persisted. ^{1}H NMR spectra were then recorded.

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