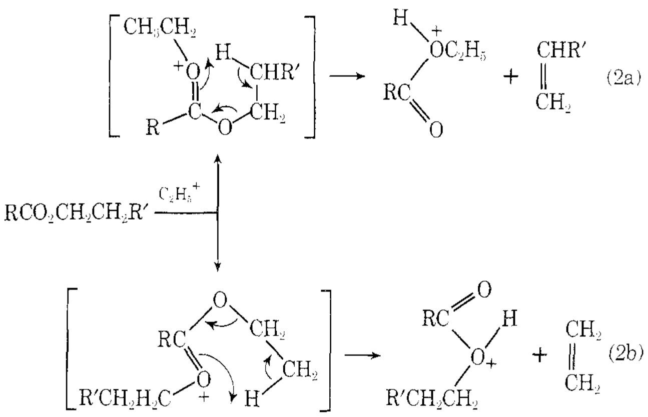

In the CH_4 CI spectrum of the α-dideuterioethyl ester, the abundance of the ion at *m/e* 89, although small, is significantly higher than the value for $(M - H)^+$ ions in the spectrum of the undeuterated ethyl acetate, *m/e* 87. This increase in abundance at *m/e* 89 in the spectrum of $CH_3CO_2CD_2CH_3$ is due to reaction 2a.

The ions expected from reaction 2a with $CH_3CO_2CD_2CD_3$ are observed at *m/e* 90 and the relative abundance, 2.4% in Table I, is consistent with the amount of reaction 2a observed for $CH_3CO_2CD_2CH_3$, 2.9%.

The difference in relative abundances of $(M + H)^+$ and protonated acid ions between the C_2D_5 ester and the other two esters can be attributed to a lower inlet temperature. It was necessary to use lower temperatures for the C_2D_5 ester than for the others to reduce surface-catalyzed exchange reactions, which were demonstrated by significant abundances of ions at *m/e* 89 and 61 from $CH_3COOC_2D_5$ and by the observation of changes in the abundances of these ions with temperature. A decrease in abundance of $(M + H)^+$ and an increase in abundance of $CH_3CO_2H_2^+$ with increasing temperature were observed previously[1] and were also noted in these studies.

In chemical ionization mass spectrometry, the reagent ions may also be labeled in order to study mechanisms. Such experiments have been reported with CD_4,[4] ND_3,[5] D_2O,[6] and C_4D_{10}.[7] We have obtained spectra with CD_4 of the three labeled ethyl acetates. These perdeuteriomethane spectra are not reported, however, because small amounts of partially deuterated methane and traces of water are present in the reagent and these impurities caused significant amounts of $(M + H)^+$ ions to be present in the spectra. In spite of this complication, several of the postulated[1] reactions can be confirmed.

In our CD_4 spectra, predominately $(M + D)^+$ ions are observed. This indicates that the protonated ethyl acetate obtains a hydrogen from the reactant ions. The observation of predominately $CH_3CO_2HD^-$ for $CH_3COOCH_2CH_3$ and $CH_3COOCD_2CH_3$ and of predominately $CH_3CO_2D_2^+$ for $CH_3COOCD_2CD_3$ indicates that one hydrogen of the protonated acid comes from the reactant ion and the other from the alkyl group as predicted by reaction 1. Small amounts of CH_3CO^+, *m/e* 43, are observed (~5%) in the CD_4 spectra of the ethyl acetates. This confirms the observations of CH_3CO^+ made under high resolution in CH_4 CI spectra. Reaction 2a is indicated by the formation of small amounts of $CH_3COHOC_2D_5^+$ ions, *m/e* 94, in the CD_4 spectra of $CH_3COOCH_2CH_3$ and $CH_3COOCD_2CH_3$.

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References and Notes

(1) M. S. B. Munson and F. H. Field, *J. Amer. Chem. Soc.*, **88**, 4337 (1966).
(2) An equivalent mechanism can be written involving alkyl-oxygen protonation, which cannot be distinguished from 1.
(3) E. W. Godbole and P. Kebarle, *Trans. Faraday Soc.*, **58**, 1897 (1962).
(4) M. S. Wilson, I. Dzidic, and J. A. McCloskey, *Biochim. Biophys. Acta*, **240**, 623 (1971).
(5) D. F. Hunt, C. N. McEwen, and R. A. Upham, *Tetrahedron Lett.*, 4539 (1967).
(6) D. F. Hunt, C. N. McEwen, and R. A. Upham, *Anal. Chem.*, **44**, 1292 (1972).
(7) S. G. Lias, A. Viscomi, and F. H. Field, *J. Amer. Chem. Soc.*, **96**, 359 (1974).

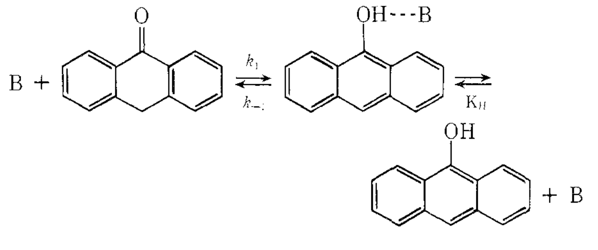
Communications

Proton Migration in an Aprotic Solvent Catalyzed by Very Weak Bases

Summary: Amides and other weak aqueous bases can in an aprotic solvent effectively catalyze an intramolecular migration of a proton from a carbon atom to a distant oxygen.

Sir: Association constants for complexation between *p*-fluorophenol and a wide variety of bases have provided a measure of base strength in CCl_4.[1] The logarithms of these constants (pK_{HB}'s) do not correlate with pK_a values in water.[2] This has been attributed to a relatively small degree of proton transfer (<30%) within the hydrogen-bonded complexes.[1-3] An alternate explanation for the lack of correlation, namely hydration effects on aqueous basicity, has been rejected.[3,4] The strongest support for the "extent of transfer" hypothesis comes from the observation that upfield F nmr shifts of hydrogen-bonded ion pairs, formed between organic bases and *p*-fluorobenzenesulfonic acid in CH_2Cl_2, parallel pK_a rather than pK_{HB}.[3]

We have found that extremely weak aqueous bases can assist proton removal from carbon acids in aprotic solvents. Thus, acetamide catalyzes the tautomerization of anthrone to anthranol in acetonitrile. The simplest mechanism for this reaction consistent with the kinetic data is given in eq 1.[5,6] Each of the following reaction variables was determined independently[7] for a variety of bases: k_1 (the rate of the base-catalyzed proton removal from the



(1)

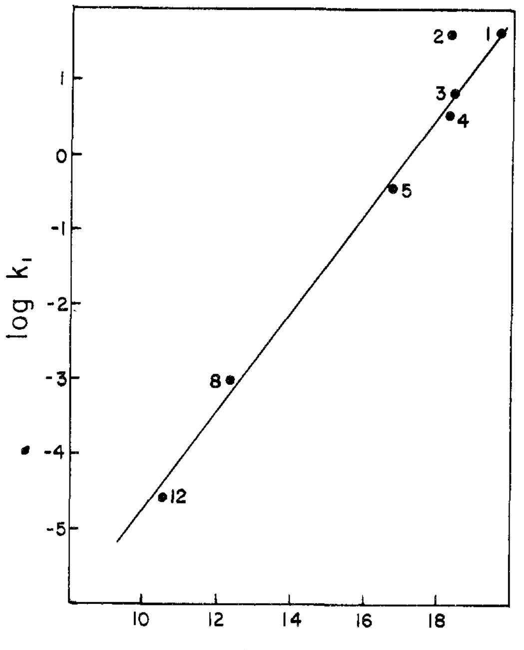


Figure 1. Plot of log k_1 (M^{-1} sec^{-1}) for the base-catalyzed anthrone tautomerization in acetonitrile at 25.0° *vs.* pK_a of the bases in acetonitrile. The numbers refer to the bases in Table I.

carbon acid); $K_1 = k_1/k_{-1}$ (the equilibrium constant relating anthrone with hydrogen-bonded anthranol); and K_H (the association constant for hydrogen bonding between base and anthranol). Acetonitrile was selected as the solvent because this is the only aprotic medium in which pK_a values for several nitrogen and oxygen bases are known.[8-10] Thus, we could compare the response of each of the reaction parameters to basicity as measured by the pK_a in water, pK_a in acetonitrile, and pK_{HB} in carbon tetrachloride.[11] The data are presented in Table I, and the important relationships are summarized below.

1. A plot of log k_1 *vs.* pK_a in CH_3CN for *nitrogen* bases is linear with a slope β equal to 0.67 (Figure 1).[12] This value of β approximates (if the classical treatment is correct[13]) the extent to which the transition state resembles the ion-pair intermediate believed involved in the anthrone tautomerism.[6]

2. There is no correlation between log k_1 and pK_{HB} even if one restricts the comparison to nitrogen bases. For example, *n*-butylamine and pyridine have rates differing by 3.56 log units, and yet their pK_{HB} values are similar (2.11 and 1.88, respectively[1]). These results reflect more extensive proton transfer in the transition state of the k_1 step relative to that occurring during hydrogen bonding in CCl_4.[1-3]

3. Weak oxygen bases such as dimethyl sulfoxide (pK_a = −2.6 in water[2]) and *N,N*-dimethylacetamide (pK_a = −0.39 in water[14]) are surprisingly effective in removing the labile proton from the carbon acid.[15] For example, acetamide is a better catalyst than pyridine, although acetamide is a much weaker base than pyridine in both water and acetonitrile (Table I). A two-point Brønsted plot utilizing k_1 and pK_a data in Table I for acetamide and benzamide (two bases of the same "family") shows that β is near unity. This implies a large degree of proton transfer in the transition state for the amide-catalyzed proton migration in the aprotic solvent.

4. On the basis of rather limited data, it appears that log k_1 for weak bases is unrelated to ion-pair Δ values[3] (secured from F nmr shifts of *p*-fluorobenzenesulfonic acid ion paired with organic bases in CH_2Cl_2). Thus, although *N,N*-dimethylacetamide is a slightly better catalyst than pyridine, the pyridine ion pair displays a chemical shift 1.47 ppm larger than that of the amide.[3,16] The lack of a positive correlation is observed despite the fact that both k_1 and Δ describe ion-pair processes. Clearly, the relationship between basicity and catalytic activity in nonaqueous systems (where solvation does not exert a large leveling effect) can be extraordinarily complex.

Table I
Dependence on Base of the Reaction Parameters for the Catalyzed Tautomerism of Anthrone in Acetonitrile at 25.0°

Base	k_1, M^{-1} sec^{-1}	K_1, M^{-1}	K_H, M^{-1}	pK_A (CH_3CN)
Pyrrolidine	49	36	1400	19.58[b]
Dabco[a]	45	88	3500	18.29[b]
Triethylamine	7.3	0.21	7.7	18.46[b]
n-Butylamine	3.6	33	1000	18.26[b]
Benzylamine	3.9×10^{-1}	8.1	340	16.76[b]
Acetamide	2.2×10^{-2}	0.061	2.3	6.0[c]
N,N-Dimethylacetamide	1.8×10^{-3}	0.036	2.1	
Pyridine	1.0×10^{-3}	0.13	4.7	12.33[b]
Dimethylsulfoxide	5.5×10^{-4}	0.072	2.7	5.8[c]
N,N-Dimethylaniline	1.3×10^{-4}	0.078	3.8	
Benzamide	1.2×10^{-4}	0.074	2.8	3.8[c]
Aniline	2.7×10^{-5}	0.024	1.7	10.56[b]

[a] Triethylenediamine. [b] Reference 8. [c] Reference 9.

5. Plots of log K_1 and log K_H *vs.* pK_a of nitrogen bases in CH_3CN are linear and have slopes of 0.38 ± 0.05. These slopes, which indicate only moderate proton transfer from hydroxyl groups to amine, seem reasonable in light of previous work on acid-base behavior in acetonitrile.[17,18] Plots of log K_1 and log K_H *vs.* pK_a show large positive and negative deviations for Dabco and triethylamine, respectively. Undoubtedly, the peri hydrogens in proximity to the hydroxyl group of anthranol enhance the sensitivity of the hydrogen bonding to the steric properties of the bases.

In summary, we have found that weak aqueous bases in an aprotic solvent can effectively catalyze the migration of a proton from a carbon atom to a distant oxygen. The reaction occurs with considerable proton transfer to the bases. We presume that the bases associate with the labile proton as the proton migrates intramolecularly[6] along the anthrone orbitals from carbon to oxygen. The remarkable ability of extremely poor aqueous bases such as amides to promote the anthrone tautomerism supports the idea that weak bases might function catalytically at hydrophobic sites of enzymes.[11,19]

Acknowledgment. This work was supported in part by grants from the National Science Foundation and the National Institutes of Health.

References and Notes

(1) R. W. Taft, D. Gurka, L. Joris, P. v. R. Schleyer, and J. W. Rakshys, *J. Amer. Chem. Soc.*, **91**, 4801 (1969).
(2) D. Gurka and R. W. Taft, *J. Amer. Chem. Soc.*, **91**, 4794 (1969).
(3) H. B. Yang and R. W. Taft, *J. Amer. Chem. Soc.*, **93**, 1310 (1971).
(4) E. M. Arnett and E. J. Mitchell, *J. Amer. Chem. Soc.*, **93**, 4052 (1971).
(5) H. Baba and T. Takemura, *Tetrahedron*, **24**, 4779 (1968).
(6) T. Takemura and H. Baba, *Tetrahedron.*, **24**, 5311 (1968).
(7) Full details of the rather complicated methods for evaluating the parameters in eq 1 can be found in the Ph.D. thesis of R. F. Williams entitled "Bile Salt Micelles (Part I) and Kinetics of Base-Catalyzed Anthrone–Anthranol Tautomeric Equilibrium (Part II). For example, k_1 was determined from the following relationship where A, t, and B are the absorbance, time, and initial concentrations of base, respectively; ϵ_e and ϵ_K are the extinction coefficients of anthranol and anthrone; C_K and d are the initial anthrone concentration and cell length. All reactions are first order in catalyst.

$$\frac{1}{(\epsilon_e - \epsilon_K)C_K d}\left(\frac{dA}{dt}\right)_{t=0} = k_1 B$$

(8) J. F. Coetzee and G. R. Padmanabhan, *J. Amer. Chem. Soc.*, **87**, 5005 (1965).
(9) I. M. Kolthoff and M. K. Chantooni, *J. Amer. Chem. Soc.*, **95**, 8539 (1973).
(10) On the other hand, acetonitrile has two (surmountable) disadvantages: anthrone tautomerizes spontaneously in this solvent and anthranol hydrogen bonds weakly to acetonitrile.
(11) See also P. W. Arana, C. W. Su, and J. W. Watson, *Chem. Commun.*, 363 (1970).
(12) No statistical correction for Dabco was made.
(13) F. G. Bordwell and W. J. Boyle, *J. Amer. Chem. Soc.*, **93**, 511 (1971).
(14) P. Haake, R. D. Cook, and G. H. Hurst, *J. Amer. Chem. Soc.*, **89**, 2650 (1967).
(15) A qualitative explanation for the reactivity of weak oxygen bases in terms of Linnett theory may be found in the Ph.D. thesis of R. F. Williams (see footnote 7).
(16) The magnitude of 1.47 ppm may be gauged from the 2.57-ppm shift of *sym*-tetramethylguanidine relative to that of *N,N*-dimethylacetamide (the strongest and weakest bases recorded in ref 3).
(17) Phenoxide is a stronger base than triethylamine in acetonitrile by more than 8 pK_a units: J. F. Coetzee, *Progr. Phys. Org. Chem.*, **4**, 45 (1967).
(18) H. Baba, A. Matsuyama, and H. Kokubun, *Spectrochim. Acta*, **25A**, 1709 (1969), have found that *p*-nitrophenol and triethylamine form solvent-separated ion pairs in acetonitrile. However, anthranol (with a pK_a in acetonitrile probably six units greater than that of *p*-nitrophenol)[17] would not be expected to form ion pairs.
(19) F. M. Menger and A. C. Vitale, *J. Amer. Chem. Soc.*, **95**, 4931 (1973).
(20) Recipient of a Camille and Henry Dreyfus Foundation Teacher-Scholar Grant and a National Institutes of Health Research Career Development Award.

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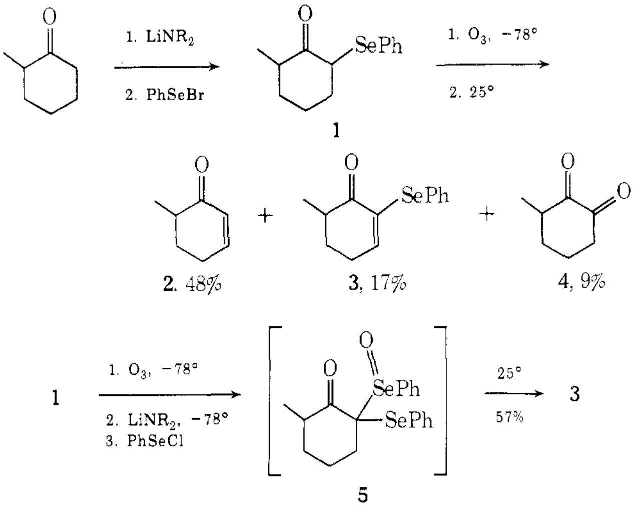
Organoselenium Chemistry. Conversion of Cyclic Ketones and β-Dicarbonyl Compounds to Enones

Summary: The selenoxide syn elimination method for the synthesis of enones has been extended to the preparation of β-dicarbonyl enones, cyclobutenones, and enone ketals; and an important limitation to the method has been found.

Sir: The syn elimination of selenoxides has been shown to be a convenient, mild, and high-yield method for the preparation of α,β-unsaturated carbonyl compounds.[1,2] The precursor α-phenylselenocarbonyl compounds can be prepared from ketones, aldehydes, and esters,[1,2] as well as from enol acetates[1b,2b] and acetylenes.[1b] We describe here some limitations of the method not heretofore recognized, as well as extensions to four-membered rings and β-dicarbonyl compounds.

The necessity for achieving a cyclic transition state in the selenoxide elimination[3] may impose conflicting conformational demands on cyclic systems, and in fact only a limited range of cyclic enones (five- and six-membered rings) have been prepared. Our inability to achieve a high yield transformation of 2-methyl-6-phenylselenocylohexanone (1) to the enone (2)[1a] led us to examine this reaction in more detail (Scheme I). The formation of by-products 3 and 4 can be rationalized as resulting from a Pummerer-like reaction of the ketoselenoxide. 2-Phenyl-6-phenylselenocyclohexanone[6] also gives only a fair yield of enone, but the isomeric 2-phenylseleno compound, in which the phenyl substituent prevents the Pummerer reaction, gives enone in high yield (Table I). Scheme I also presents an alternate synthesis of the vinyl selenide 3 by selenenylation of the ketoselenoxide.

Scheme I



Both 2-phenylselenocycloheptanone and -cyclooctanone give only small amounts of enone (5–15%) under all conditions we have tried. If the oxidation is carried out using sodium metaperiodate buffered with sodium bicarbonate, 33 and 48%, respectively, of the vinyl selenides analogous to 3 are formed.

The occurrence of a facile Pummerer reaction depends on the acidifying effect of the carbonyl group on the α proton. Hence it is not surprising that the ketal 6 undergoes oxidation[8a] and elimination[8b] to enone ketal 7 in good yield. 2-Phenylselenocycloheptanone can similarly be converted to the ethylene ketal of cycloheptenone in 68% yield.

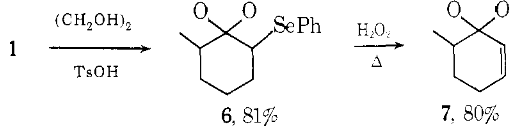
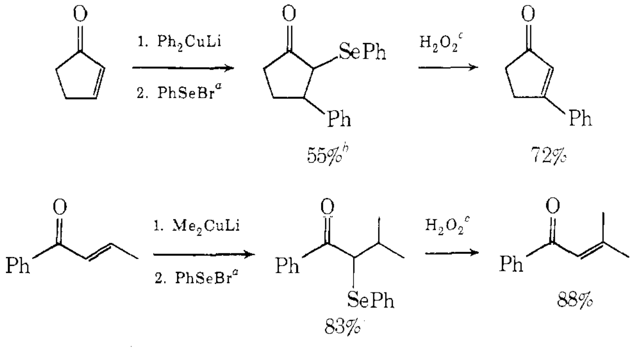


Table I shows several examples of the preparation of cyclopentenones[9a] and cyclobutenes. The great facility with which cyclobutanones undergo Baeyer–Villiger oxidation necessitates the use of ozone as oxidant[10] for the preparation of 3-phenyl-2-cyclobutenone.[11] Scheme II presents two examples which illustrate the ability to trap copper enolates with PhSeBr for the synthesis of β-substituted enones.

The extension of the selenoxide elimination to the synthesis of enediones from β-dicarbonyl compounds is an important one, since such transformations are difficult using classical methods.[12] The dehydrohalogenation in particular often fails because of instability of halodicar-

Scheme II



[a] Total quantity of PhSeBr used was 10% excess over RLi used in the preparation of the cuprate. A small amount of Ph_2Se_2 was added to suppress formation of α-halo ketones. [b] Both cis and trans isomers (1:4.5) appeared to give enone. [c] Reference 8a.