was determined as a function of concentration [(0.94 − 25.16) × 10^{-2} M] relative to the chloroform signal at τ 2.73 (727 Hz downfield from TMS) (Figure 4). The spectra of the acetates (I and II, R = Ac) also were obtained in carbon tetrachloride and benzene-d_6 (0.50–0.93 M). In general, all spectra were recorded under identical conditions and were reproducible. Chemical shifts and coupling constants were determined either from first-order analyses or from appropriate ABX approximations.[53]

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[53] J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill, New York, N. Y., 1959, Chapter 6.

Nuclear Magnetic Resonance Determination of Ketone Basicity and the Use of Ketones as Indicators for Evaluation of Medium Acidity

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Abstract: Basicity constants determined by proton nmr are reported for several types of ketones. Carbonyl substituent chemical shifts are plotted against Hammett acidity (H_0) yielding half-protonation values that reproduce spectrophotometric basicity constants. The nmr method facilitates basicity measurements for extremely weak ketone bases in superacid media. Basicity constants for several α-halogen substituted acetones are reported. Fluoro, chloro, and bromo substituents all reduce ketone basicity substantially. The three halogens are approximately equal in their effect. Carbonyl compounds that are not stable enough for spectrophotometric basicity studies may be evaluated by nmr. The nmr basicity constant for acetaldehyde (pK = −10.2) indicates that the aldehyde is far less basic than expected. Several ketones are used as a set of indicators for rapid evaluation of (Hammett) medium acidity by nmr. Applicability of the nmr method for acidity evaluation over the entire Hammett scale (currently H_0 = 0 to −17.5) allows facile measurements in both superacid and conventional acid systems.

The quantitative study of ketones as weak organic bases has occupied various groups of chemists during the past decade. A review article by Arnett, published in 1963, gives an excellent account of the earlier work.[1] Ketone basicity values published since 1963 have primarily been reevaluations and interpretations of the earlier results.

In the last few years, it has been shown that ketones do not behave as true Hammett bases[2] and that the pK_a values reported in earlier investigations were not actually thermodynamically defined constants but, instead H_0 acidity values for half-protonation. Nevertheless, it has been shown that useful correlations of these half-protonation basicity values with other reactivity parameters exist for various structurally related bases.[3] For ketone bases the observed deviations from ideal Hammett behavior are due in part to the hydrogen-bonding interactions of ketones in the acid media.

The usual experimental method employed for measurement of ketone basicity constants is spectrophotometric, utilizing visible and/or ultraviolet absorptions of the protonated and unprotonated base.[4,5] Difficulties often arise in separating the affects of protonation and hydrogen bonding on the observed spectra.[1,2,5]

Nuclear magnetic resonance has been utillized in a few instances for basicity determinations.[6,7] Taft studied fluorine magnetic resonance of *para*-fluorinated aryl bases in acid media.[6] His method was limited by the choice of fluorinated bases and solubility considerations. Deno reported a pK[8] value for acetone using the proton nmr chemical shift of the methyl group relative to the resonance of external benzene.[7] Proton nmr has been used in several attempts to determine basicity constants for amides, alcohols, and ethers.[7,9,10] These attempts were quantitatively unsuccessful due to the relatively large effect of hydrogen bonding (between the protonated base and the medium) on the nmr chemical shifts studied.

In this paper, a proton nmr method will be presented and substantiated with nmr determined basicity constants for ketones of known basicity. This method allows basicity determinations for ketones that have not previously been studied: for example, α-halo ketones.[11] In addition, ketone systems of limited stability can be investigated.

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[1] E. M. Arnett, *Progr. Phys. Org. Chem.*, 1, 223 (1963).

[2] (a) C. C. Greig and C. D. Johnson, *J. Amer. Chem. Soc.*, 90, 6453 (1968); (b) T. G. Bonner and J. Phillips, *J. Chem. Soc. B*, 650 (1966).

[3] E. M. Arnett, R. P. Quirk, and J. W. Larson, *J. Amer. Chem. Soc.*, 92, 3977 (1970).

[4] L. A. Flexser, L. P. Hammett, and A. Dingwall, *ibid.*, 57, 2103 (1935); (b) R. Stewart and K. Yates, *ibid.*, 80, 6355 (1958); 82, 4059 (1960); R. Stewart and M. R. Granger, *Can. J. Chem.*, 39, 2508 (1961); K. Yates and R. Stewart, *ibid.*, 37, 664 (1959).

[5] H. J. Campbell and J. T. Edward, *ibid.*, 38, 2109 (1960).

[6] R. W. Taft, Jr., and P. L. Levins, *Anal. Chem.*, 34, 436 (1962).

[7] (a) N. C. Deno and M. J. Wisotsky, *J. Amer. Chem. Soc.*, 85, 1735 (1963); (b) D. G. Lee, *Can. J. Chem.*, 48, 1919 (1970).

[8] Throughout this paper "pK value" or "pK" will be taken as equivalent to the (Hammett) H_0 value at half-protonation of the base; "pK_a" will refer only to thermodynamically secure basicity constants.

[9] J. T. Edward, J. B. Leane, and I. C. Wang, *Can. J. Chem.*, 40, 1521 (1962).

[10] E. Grunwald, A. Loewenstein, and S. Meiboom, *J. Chem. Phys.*, 27, 641 (1957).

[11] Preliminary results reported: G. C. Levy, *Chem. Commun.*, 1257 (1969).

Table I. Limitations and Advantages of the Nmr Method Compared with Spectrophotometric Procedures

Limitations	Advantages
A. Ketone Basicity Determinations	
1. Relatively low sensitivity; pK values ± 0.2–± 0.3 H_0 unit	1. Rapid determinations
2. Possibility of ketones undergoing side reactions in acid media	2. Some ketone decomposition will not invalidate pK values
	3. Low-temperature studies simplified for relatively unstable systems
B. Medium Acidity Evaluation	
1. Relatively low sensitivity; medium acidity ± 0.3–± 0.5 H_0 unit	1. Range of measurement covers all known strong acid systems ($-H_0 = 0$–17.5)
	2. Rapid procedure
	3. No "color purity" requirement
	4. Multiple-phase media can be routinely evaluated
	5. Significant decomposition of ketone indicator will not normally interfere with acidity determinations

Introduction and General Discussion

The nmr chemical shift method relies on the sensitivity of substituent chemical shifts to changes in the polarity of the C–O bond when the carbonyl group is protonated. Protons on α-carbon atoms in protonated ketones are deshielded by 0.4–1.0 ppm relative to the same protons in the unprotonated ketone (chemical shifts of protons more distant from the carbonyl group are deshielded to a lesser extent). Since the nmr time scale is relatively long[12] and protonation–deprotonation of ketones is extremely rapid under near equilibrium conditions[13] a time- and species-averaged chemical shift is observed for a given proton resonance. Thus, at the medium acidity corresponding to half-protonation, a given proton has a chemical shift midway between the shifts observed for the protonated ketone and the unprotonated compound. The curve obtained when α-substituent chemical shifts are plotted against H_0 gives a rough measure of the ratio $(BH^+)/(B)$. The representation is especially good where $(BH^+)/(B)$ is close to 1.

The equivalence of the experimental curve to that predicted by theory is limited by (1) chemical-shift standardization, (2) the structure of the base and the presence of other functional groups, and (3) the presence of large medium effects.

(1) Internal standardization is required to give an accurate measure of ketone chemical-shift changes as a result of protonation rather than as a result of changes in magnetic environment. Cyclohexane was used in this study wherever possible but stability and solubility considerations required the use of tetramethylammonium chloride (TMAC) in both extremely strong acid systems and dilute aqueous acids.[14]

(2) In nmr ketone basicity studies, the chemical structure of the base is generally the limiting factor controlling the accuracy of determinations. Two variables are important.

First, the carbonyl substituent to be monitored may be an easily identifiable methyl group, another α substituent, or a more distant group (α-methyl protons are used in preference to other signals due to increased sensitivity to carbonyl protonation).

Second, presence of other functional groups capable of protonating or hydrogen bonding strongly to the solvent can obscure protonation of the carbonyl group.

(3) Medium effects, such as hydrogen bonding, do not usually interfere significantly with nmr ketone basicity determinations except in cases as noted in (2). Unlike the situation with ethers and alcohols, *protonated* ketone chemical shifts remain constant as acidity increases. This results in a level top to the "titration curve."[15] The base line of the curve is subject to more fluctuation from hydrogen bonding interactions and other medium changes; however, the error introduced to *the determined pK value* is usually small.

Summary of the Advantages and Limitations of the Nmr Method. Half-protonation values for ketones determined by the nmr method can be considered accurate to ± 0.1 only in near ideal cases. A more realistic error limit for most determinations would be ± 0.3 pK unit (H_0 unit). The principal advantages and limitations of the nmr method are shown in Table IA.

As is indicated in Table IA, the nmr method cannot compete in accuracy with spectrophotometric basicity determinations. Nevertheless, in many cases the nmr method is the only procedure that can be used.

Once a ketone's basicity has been determined by nmr, that ketone may serve as an indicator for measurement of medium acidity. Thus, a series of ketones whose equilibrium protonation occurs over the acidity range of interest can serve as a complete set of indicators.

Ketone basicities are determined independently in precalibrated acid systems. The acid systems are evaluated by classical Hammett methods and checked where possible against literature values. For determinations in acids weaker than 100% H_2SO_4, accurate experimental values are available. For the FSO_3H–SbF_5 system (which is used as the calibrating acid for all super acid media) newely determined spectrophotometric values from Gillespie, *et al.*,[16] are used to define the indicator basicity constants.

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(12) (a) F. A. L. Anet and A. J. R. Bourn, *J. Amer. Chem. Soc.*, 89, 760 (1967); (b) C. S. Johnson, Jr., *Advan. Magn. Resonance*, 1, 33 (1965).

(13) In superacid media such as the FSO_3H–SbF_5 system, most ketones are virtually 100% protonated and proton exchange with the acid pool is slow on the nmr time scale. See G. C. Levy, Ph.D. Dissertation, U.C.L.A., Los Angeles, Calif., 1968.

(14) Both cyclohexane and TMAC are actually secondary standards, referred to TMS = δ 0.00. Where it was practical, the chemical shifts of the secondary standards were confirmed.

(15) For equilibrium mixtures in which the ketone is nearly 100% protonated, all chemical shifts reproduce the chemical shifts observed for the pure protonated ketone in superacid media (allowing for drastic changes in medium).

(16) R. J. Gillespie and T. Peel (McMaster University), unpublished data. The H_0 values for FSO_3H–SbF_5 solutions may be modified prior to publication by Dr. Gillespie. Minor revision would not affect the conclusions of this paper.

Eight ketones were chosen as a general set of indicators for acidity evaluation; they are listed in a later section. Choice of these compounds was made on a basis of (1) ease of nmr observation, (2) relative stability, and (3) commercial availability.

The advantages and limitations of acidity evaluation by nmr are listed in Table IB.

Results

Evaluation of Ketone Basicity. Several ketones of known basicity were reevaluated using the nmr method. The results, shown in Table II, indicate that the nmr method provides accurate pK values[17] over a wide range of basicities (acid strengths). For the six ketones listed in Table II, only the pK value of cyclobutanone differs significantly from the spectrophotometric value in the literature. The literature value for cyclobutanone was not accompanied by sufficient experimental data to ascertain the error limitation of the measurement.[5]

Table II. Comparison of Nmr Basicity Values and Literature (Spectrophotometric) Values

Ketone	Nmr pK^a	Corrected lit. pK^b
2,6-Dimethyl-γ-pyrone	0.3	0.34
p-Methoxyacetophenone	−4.9	−4.83
Acetophenone	−6.3	−6.4
Acetone	−7.5	−7.6
p-Nitroacetophenone	−8.5	−8.5
Cyclobutanone	−9.5	−10.6

[a] H_0 at half-protonation (H_2SO_4–H_2O system), 26°. [b] pK values collected from ref 1. They are corrected to the H_0 scale as evaluated by Jorgenson and Hartter, ref 17.

The basicities of several ketones were determined in a second acid system in order to define further the accuracy limitations of the nmr method. The CF_3COOH (hereafter, TFA)–H_2SO_4 system was chosen because of its ease of preparation, range of acidities, and lack of H_2O as a component. The TFA–H_2SO_4 system has previously been evaluated by spectrophotometric methods.[18,19] We repeated the spectrophotometric evaluation to confirm the earlier values. The acidity of each acid mixture used for a data point in an nmr determination was separately evaluated. The basicity constants for acetone and the three acetophenones as determined in TFA–H_2SO_4 reproduced the H_2SO_4–H_2O values very well. The largest deviation was for *p*-methoxyacetophenone. Its pK in TFA–H_2SO_4 was −5.2, compared with −4.9 in H_2SO_4–H_2O. For acetone, acetophenone, and *p*-nitroacetophenone, the TFA–H_2SO_4 values were −7.4, −6.4, and −8.5, respectively (deviations of 0.1, 0.1, and 0.0 from the H_2SO_4–H_2O values).

Evaluation of Ketone Basicity in Super Acid Systems; α-Halogen Substituted Acetones. Ketone basicity constants in the literature fall within the range of basicities given in Table II. No pK values have been measured for extremely nonbasic ketones since those determinations would require the use of acids stronger than 100% H_2SO_4.

Although several super acid systems have been increasingly studied in recent years, experimental difficulties have discouraged attempts to utilize them in spectrophotometric equilibrium studies. Most of the difficulties encountered arise from small impurities present in the superacid media and also from impurities generated during the basicity determinations. In addition, several super acid systems contain HF as a constituent. This readily attacks and dissolves silica-based spectrophotometric cells.

Use of the nmr method circumvents these difficulties because of the impartiality of magnetic resonance to minor impurities.[20] Equilibria in media containing HF can be studied using commercially available Teflon inserts to protect the glass sample tubes.[21]

Using the nmr method, we have now determined the basicities of several α-halogen substituted acetones.[11] Several authors have previously noted the weakly basic character of α-halo ketones, but no quantitative measure of their basicity has been available.[22,23]

Our findings are summarized in Table III. It is interesting to note that even monohalogenated ketones are extremely weakly basic. The reduction in the basicity of acetone due to monohalogen substitution is is comparable to the change in basicity observed when a *para*-nitro group is substituted for a *para*-methoxy group in the acetophenone series (*ca.* 3–3.5 H_0 units; see Table II). Multiple halogen substitution produces a further, approximately linear, decrease in ketone basicity (~2 H_0 units per halogen).

Table III. Basicity Constants for α-Halogen Substituted Acetones

Compd	−pK^a
FCH_2COCH_3	10.8
$ClCH_2COCH_3$	10.7
$BrCH_2COCH_3$	10.7^b
FCH_2COCH_2F	12.9^c
F_3CCOCH_3	14.9
Cl_3CCOCH_3	14.8
$F_2CHCOCHF_2$	*Ca.* 17^d

[a] $-H_0$ at half-protonation, 26° (±2°). Estimated maximum error ±0.3 unit. Probable error <0.2. New H_0 values for FSO_3H-SbF_5 system, R. J. Gillespie, ref 16. [b] Decomposes readily. Determination checked at 0°. [c] Estimated error <±0.5. [d] Cannot be fully protonated.

It is clear from the data (Table III) that bromo and chloro ketones are not significantly more basic than fluoro ketones. This is shown graphically in Figure 1. It is somewhat surprising that the three halogens are almost equivalent in their effect on ketone basicity; however, this is consistent with the similar Taft, σ_I, constants for monohalogenated substituents.[24]

The previous data indicate that mechanisms involving reaction with protonated halo ketone intermediates are unlikely in normal acid media. In most reactions of halo ketones, nucleophilic attack on the

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(17) In this paper, all pK and H_0 values are corrected to the H_0 scale as evaluated by: M. J. Jorgenson and D. R. Hartter, *J. Amer. Chem. Soc.*, **85**, 878 (1963).

(18) G. Dallinga and G. ter Maten, *Recl. Trav. Chim. Pays-Bas*, **79**, 737 (1960).

(19) E. L. Mackor, P. J. Smit, and J. H. van der Waals, *Trans. Faraday Soc.*, **53**, 1309 (1957).

(20) Paramagnetic species excluded.

(21) NMR Specialties Co., New Kensington, Pa.

(22) G. E. Maciel and J. J. Natterstad, *J. Chem. Phys.*, **42**, 2752 (1965).

(23) D. Cook, *J. Amer. Chem. Soc.*, **80**, 49 (1958).

(24) R. W. Taft and I. C. Lewis, *ibid.*, **80**, 2441 (1958).

carbonyl carbon can successfully compete with oxygen protonation. Our basicity data confirm some recent work on a mechanism for hydration of halogenated and nonhalogenated acetones.[25] Greenzaid, Luz, and Samuel indicated that it was likely that halogen-substituted ketones hydrated by a mechanism not involving protonation of the carbonyl group. Similarly, the mechanism recently proposed[26] for acid-catalyzed reaction of α-halobenzyl phenyl ketones with triphenylphosphine may need modification since the authors invoke protonation of the carbonyl group in dilute acid.

Basicity Determinations for Representative Cyclopropyl, Olefinic, and Polyketones. Using the nmr method, we have determined the basicity constants for several ketones of interest to the organic chemist.

The first of these compounds is methyl cyclopropyl ketone. Protonation of this compound gives a hydroxy cation stabilized by the α-cyclopropyl group. The effect of this cyclopropyl "conjugation" has been compared with the result of α-phenyl stabilization in acetophenone.[27] The criterion used was the C=O—H proton chemical shift of the cation in FSO_3H-SbF_5-SO_2 media.

Analysis of the C=O—H chemical shifts for methyl cyclopropyl ketone, several other cyclopropyl ketones, and several phenyl ketones, indicates that the cyclopropyl group is at least as effective as phenyl in stabilizing the cation by conjugative withdrawal of charge. On the basis of ^{13}C nmr evidence, Olah, *et al.*, disagree with this conclusion.[28] The basicity constant for methyl cyclopropyl ketone determined by nmr supports the earlier conclusion based on C=O—H chemical shifts. Methyl cyclopropyl ketone at pK -5.9 is far more basic than methyl isopropyl ketone (pK -7.4),[1,17] and significantly more basic than acetophenone (pK -6.4). Our basicity constant for methyl cyclopropyl ketone is based on the average of several determinations in H_2SO_4-H_2O and TFA-H_2SO_4.[29]

In addition to phenyl and cyclopropyl conjugation, the organic chemist is interested in olefinic conjugation and its affect on cation stability. In our work, we utilized 3-methylcyclohex-2-enone (I) because of the easily identifiable methyl resonance. Although this group is relatively distant, its (chemical shift) sensitivity to carbonyl group protonation (0.4 ppm) is high enough to allow accurate basicity determination. The pK of I at -3.8 indicates that simple olefinic conjugation can be more effective for stabilizing cations than either phenyl or cyclopropyl conjugation. The monoolefinic ketone I can be compared with 2,6-dimethyl-γ-pyrone (II), a fully conjugated olefinic system with "heteroaromatic stabilization." The pK value for II is $+0.3$. A recent paper by Zalewski and Dunn lists spectrophotometric basicity constants for a series of α,β-unsaturated alicyclic ketones.[30] Their values are based on the H_A (amide) acidity function. Conversion of their constant for I to the H_0 scale gives pK -3.96, in good agreement with our value.

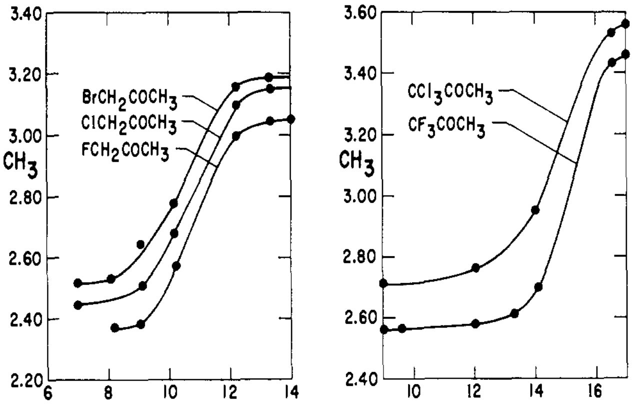
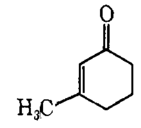
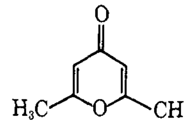


Figure 1. Protonation curves for α-halogen substituted acetones.



I

pK = -3.8



II

pK = $+0.3$

Ketones as basic as I follow the H_A scale reasonably well. For less basic ketones it appears that this correlation degrades.[2a] Whether H_A or H_0 is more closely followed, the basis for thermodynamic extrapolation from strong (especially nonaqueous) acid systems to dilute aqueous acids is doubtful. For this reason, it is important to recognize the limitations inherent in basicity constants assigned to one or another scale. Several authors[2a,31] prefer to relate the protonation of all bases to the Hammett (H_0) scale, utilizing experimentally observed relationships between H_0 and the other functions. Whatever the mode of presentation, significant correlations between structure and reactivity can be derived within a relatively homogeneous set of bases.

Polyketones. Our attempts to determine the basicity constants of several polyketones have not been successful, failing at separation of the successive multiple protonations. The experimental curve observed for protonation of m-diacetylbenzene, for example, gives an elongated acidity range in which the methyl group chemical shifts are increasingly deshielded. Nevertheless, the top of the experimental curve (Figure 2) corresponds to the chemical shift observed for the pure dication in FSO_3H-SbF_5 (δ_{CH_3} = 3.52). It was hoped that a discontinuous experimental curve would be observed, allowing estimation of the first and second protonations. This still may be possible in polyketone systems where there is a large difference in basicity between the carbonyl groups.

Protonation of m-diacetylbenzene occurs over the H_0 range -7.5 to -10. The triketone 1,3,5-triacetylbenzene protonates over the H_0 range -8.5 to -11. At H_0 = -11 the triketone is completely

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(25) P. Greenzaid, Z. Luz and D. Samuel, *Trans. Faraday Soc.*, **64**, 2780, 2787 (1968).

(26) I. J. Borowitz, P. E. Rusek, and R. Virkhaus, *J. Org. Chem.*, **34**, 1595 (1969).

(27) (a) G. C. Levy, Ph.D. Dissertation, University of California, Los Angeles, Calif., 1968; (b) M. Brookhart, G. C. Levy, and S. Winstein, *J. Amer. Chem. Soc.*, 89, 1735 (1967).

(28) G. A. Olah and A. M. White, *ibid.*, **91**, 5801 (1969).

(29) In a personal communication, H. G. Richey, (Pennsylvania State University) reports a spectrophotometric value for methyl cyclopropyl ketone, p$K \cong -5.7$ (solvent band shifts precluded more accurate measurement).

(30) R. I. Zalewski and G. E. Dunn, *Can. J. Chem.*, 47, 2263 (1969).

(31) J. F. Bunnett and F. P. Olson, *ibid.*, **44**, 1899 (1966).

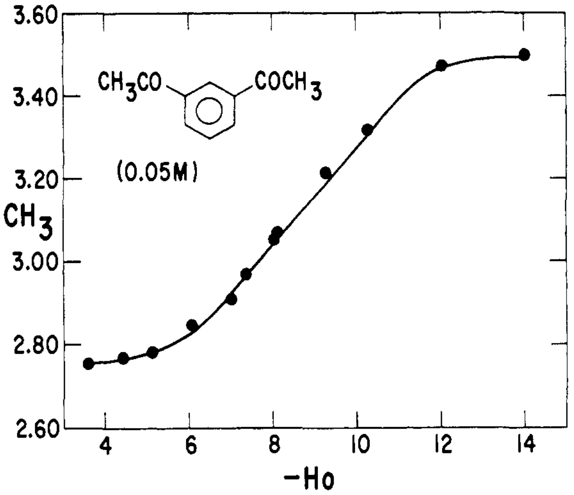


Figure 2. Protonation curve for *m*-diacetylbenzene.

protonated (three equivalent C=O—H protons observed in FSO_3H-SbF_5).

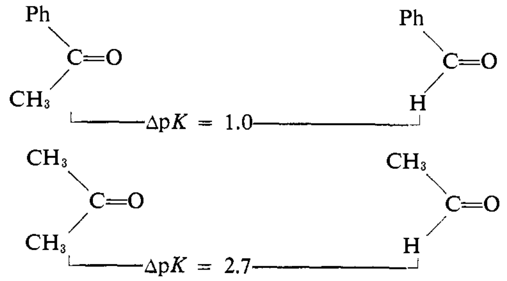
Basicity Determinations for Acetaldehyde. Using the acid systems TFA-H_2SO_4 and TFA-CF_3SO_3H,[32] we have determined a basicity constant (H_0 at half-protonation) for acetaldehyde. Nonaqueous media were required because of the rapid hydration of acetaldehyde in acids containing appreciable H_2O. Spectrophotometric determination of the basicity of acetaldehyde has not been reported.

In acid systems strong enough to protonate acetaldehyde, condensation reaction products begin forming rapidly at room temperature. Thus, in the present work acetaldehyde was added to the different acid media at 0°, and then warmed to 26° in the probe of the nmr spectrometer. The spectra were taken within 3–5 min. Nevertheless, some condensation products were observed in the strongest acids utilized in this study.[33]

The experimental points are plotted in Figure 3. The observed p*K* for acetaldehyde at -10.2 indicates that acetaldehyde is far less basic than expected. Predictions of the basicity constant for acetaldehyde based on the constant observed for acetone and the analogous structural difference between benzaldehyde and acetophenone has led to an estimate for acetaldehyde, p*K* *ca.* -8.5.[1,17,34]

The large discrepancy between prediction and observation is difficult to explain. Increased conjugation (ring–carbonyl group coplanarity) of the phenyl ring in benzaldehyde relative to acetophenone would explain part of the difference. However, the Δp*K* for acetaldehyde and acetone is 2.7 (H_0) units, and it is unlikely that a small change in coplanarity could stabilize the protonated benzaldehyde cation enough to reduce Δp*K* to 1.0.

It could be argued that nonaqueous basicity constants are not comparable to basicity constants determined in H_2SO_4–H_2O. However, nmr data suggest that at high acidity there is no significant difference in ketone protonation behavior in partially aqueous or nonaqueous media. Thus, the experimental curves for *p*-nitroacetophenone in H_2SO_4–H_2O and TFA–H_2SO_4 are nearly equivalent (see below).



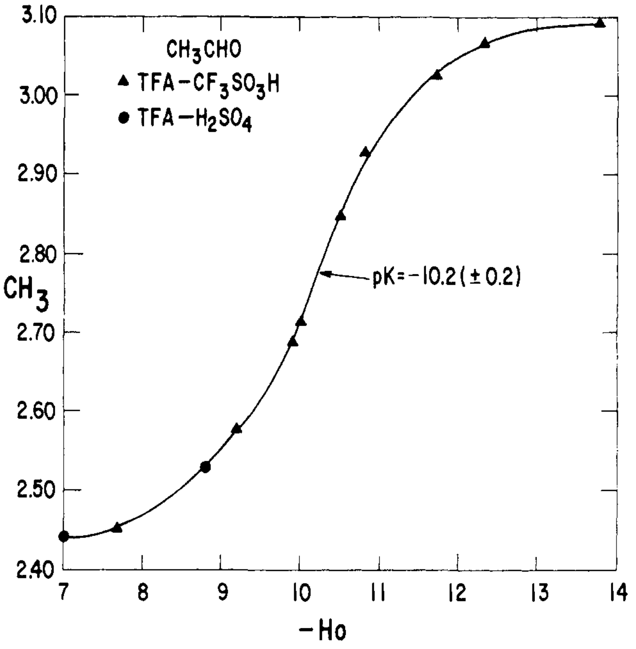


Figure 3. Protonation curve for acetaldehyde.

The newly determined basicity value for acetaldehyde supports the nonprotonation mechanism proposed by Pocker and Dickerson[35] for hydration of acetaldehyde (and other aliphatic aldehydes) in dilute aqueous acids. The low basicity of acetaldehyde helps to confirm that mechanisms such as that proposed by Gruen and McTigre[36] are not tenable.

Ketone Basicity Equilibria; Deviations from Hammett Behavior. Deviations from true Hammett behavior (based on protonation of primary amines) occur with ketones at both ends of the basicity scale. The deviations seem largest for the more basic compounds such as aromatic ketones and amides. In the region of protonation for aromatic ketones, the amide acidity function, H_A, has a slope nearly half that of the H_0 function.[30] This means that in an acid system that is 1 H_A unit (~2 H_0 units) more acidic than a given ketone half-protonation mixture, the ketone will be either ~90% protonated if it follows H_A or ~99% protonated if H_0 more nearly describes the equilibrium.

Although the amide acidity function H_A adequately describes protonation equilibria for amides and very basic ketones, it is doubtful whether it is accurate for less basic carbonyl compounds. In particular, rel-

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[32] Evaluation of this acid system reported below.

[33] The half-life of the acetaldehyde–protonated acetaldehyde mixture in TFA-CF_3SO_3H (H_0, -10.7) was *ca.* 15 min. In TFA-H_2SO_4 (H_0, -5.5), $\tau_{1/2}$ was *ca.* 15 hr (both at room temperature).

[34] M. L. Ahrens and H. Strehlow, *Discuss. Faraday Soc.*, **39**, 112 (1965).

[35] Y. Pocker and D. G. Dickerson, *J. Phys. Chem.*, **73**, 4005 (1969).

[36] L. C. Gruen and P. T. McTigre, *J Chem. Soc.*, 5224 (1963).

Table IV. Suggested List of Nmr Indicators for Evaluation of Medium Acidity (H_0)

		$-H_0$ (half-protonation)	Indicator range ($-H_0$)
	Indicators		
1.	2,6-Dimethyl-γ-pyrone	-0.3	0–2.0
2.	3-Methylcyclohex-2-enone	3.8	2.3–5.0
3.	Methyl cyclopropyl ketone	5.9	5.1–7.0
4.	Acetone	7.5	6.0–8.5
5.	1,3,5-Triacetylbenzene	9.9	7.5–11.5
6.	1,3-Difluoroacetone[a,b]	~13	12.0–14.0
7.	1,1,1-Trifluoroacetone	14.9	13.4–16.0
8.	1,1,2,2-Tetrafluoroacetone[a]	~17	16.5–18(?)
	Alternate Indicators		
9.	Acetophenone	6.4	5.5–7.3
10.	p-Nitroacetophenone	8.5	7.3–10.0
11.	Cyclobutanone	9.5	8.0–11.0
12.	Monofluoroacetone[b]	10.8	9.5–11.8

[a] Accuracy *ca.* ±0.5 H_0 unit. [b] Poisonous!

Table V. Chemical Shifts for Indicators in H_2SO_4–H_2O and FSO_3H Media[a]

	$-H_0$ (Hammett acidity)																	
Ind	0.0	1.0	2.0	3.0	4.0	5.0	6.0	7.0	8.0	9.0	10.0	11.0	12.0	13.0	14.0	15.0	16.0	17.0
1	2.55	2.64	2.68															
2		2.02	2.06	2.14	2.24	2.32	2.40											
3					2.34	2.40	2.56	2.68	2.73									
4						2.40	2.44	2.58	2.73	2.87	2.95							
5							2.88	2.92	3.00	3.11	3.24	3.41	3.55	3.58	3.59			
6[b]											5.33	5.34	5.38	5.61	5.78			
7													2.57	2.60	2.70	3.02	3.34	3.44
8[c]														6.27	6.27	6.28	6.30	6.44
9				2.68	2.72	2.79	2.90	3.09	3.21	3.24								
10							2.84	2.87	3.00	3.19	3.33	3.37	3.40					
11[d]							3.25	3.27	3.34	3.46	3.59	3.71	3.78	3.80				
12										2.38	2.50	2.77	2.99	3.04	3.05			

[a] TMAC standard; CH_3 resonances at 26°. [b] CH_2F resonance. [c] CHF_2 resonance. [d] α-CH_2 resonance.

atively basic aromatic ketones may[37] or may not[2a] follow H_A.

It must be stressed that whether or not any particular acidity function is followed, basicity constants obtained as half-protonation values can be valuable for precise comparisons between closely related compounds and also for rough correlations over a broader range of bases.

The shapes of experimental curves observed in the present nmr work indicate that as ketone basicity decreases, the equilibria may be more closely represented by H_0. This should be independently confirmed since it is not clear whether the experimental nmr curves measure only species averaged protonation equilibria or whether they are affected by hydrogen bonding shifts and other parameters. For example, in dilute aqueous acid, ^{13}C nmr experiments[38] indicate that base line deviations in the experimental curves occur as a result of large changes in the activity coefficients of H_2O and/or H_3O^+. These large medium changes also cause difficulties in spectrophotometric measurements.[39] To avoid this experimental problem, nmr measurements for ketones more basic than p-nitroacetophenone and less basic than 3-methylcyclohex-2-enone are preferentially made in the TFA–H_2SO_4 system. Curves generated from these experiments are not perturbed by medium changes. For weakly basic ketones the H_2SO_4–H_2O system and several nonaqueous media all generate good curves.

Use of Ketones as Indicators for Evaluation of Medium Acidity. Earlier in this paper an nmr method for evaluation of medium acidity was outlined. The procedure utilizes eight ketones of known basicity as a set of "indicators" for the entire H_0 scale. These eight compounds are listed in Table IV, along with their pK values and effective indicator ranges. Experimental protonation curves for the indicators are given in Figure 4.

Unfortunately, there are several short breaks between indicator covered ranges. Nevertheless, within the normal accuracy limitations of the method these eight compounds give complete coverage of the H_0 scale.

Table IV contains data on four alternate indicators that can be used interchangeably with the first eight. (Protonation curves for these ketones are also shown in Figure 4.)

The protonation curves in Figure 4 may be used for rapid, approximate determinations of medium acidity. However, for higher accuracy measurements it is recommended that experimenters reproduce appropriate protonation curves.

Indicator chemical shifts in H_2SO_4–H_2O and FSO_3H media are extracted from the protonation curves and listed in Table V.

Experimental Section

All nmr measurements were made on a Varian A-60 spectrometer equipped with variable temperature control. The probe temperature was kept at 26–28° by passing dry N_2 through the heat exchanger (which was exposed to ambient conditions). The electrical control system was not required.

Reagents. All compounds utilized in the study were available commercially[40] except for CF_3SO_3H, which was given to us by the Minnesota Mining and Manufacturing Company. The ketone bases were checked for purity by nmr; no purification was required. Preparation of the various acid solutions was accomplished by diluting several freshly prepared stock solutions. ACS Reagent grade H_2SO_4 was used for all H_2SO_4–H_2O solutions below 98 wt % acid. Commercial 100% (nominal) H_2SO_4 was purchased from G. Frederick Smith Chemical Co. CF_3COOH was obtained from Halocarbon Co. and distilled from 5–10% $(CF_3CO)_2O$. Allied Chemical Co. technical grade FSO_3H was distilled prior to use and

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(37) R. I. Zalewski and G. E. Dunn, *Can. J. Chem.*, 46, 2469 (1968).

(38) Unpublished work with W. L. Wilson of Varian Associates, Palo Alto, Calif.

(39) R. S. Ryabora, I. M. Medvetskaya, and M. I. Vinnik, *Russ J. Phys. Chem.*, 40, 182 (1966).

(40) 1,1,2,2-Tetrafluoroacetone, Pierce Chemical Co.; all other ketones, Aldrich Chemical Co., etc.

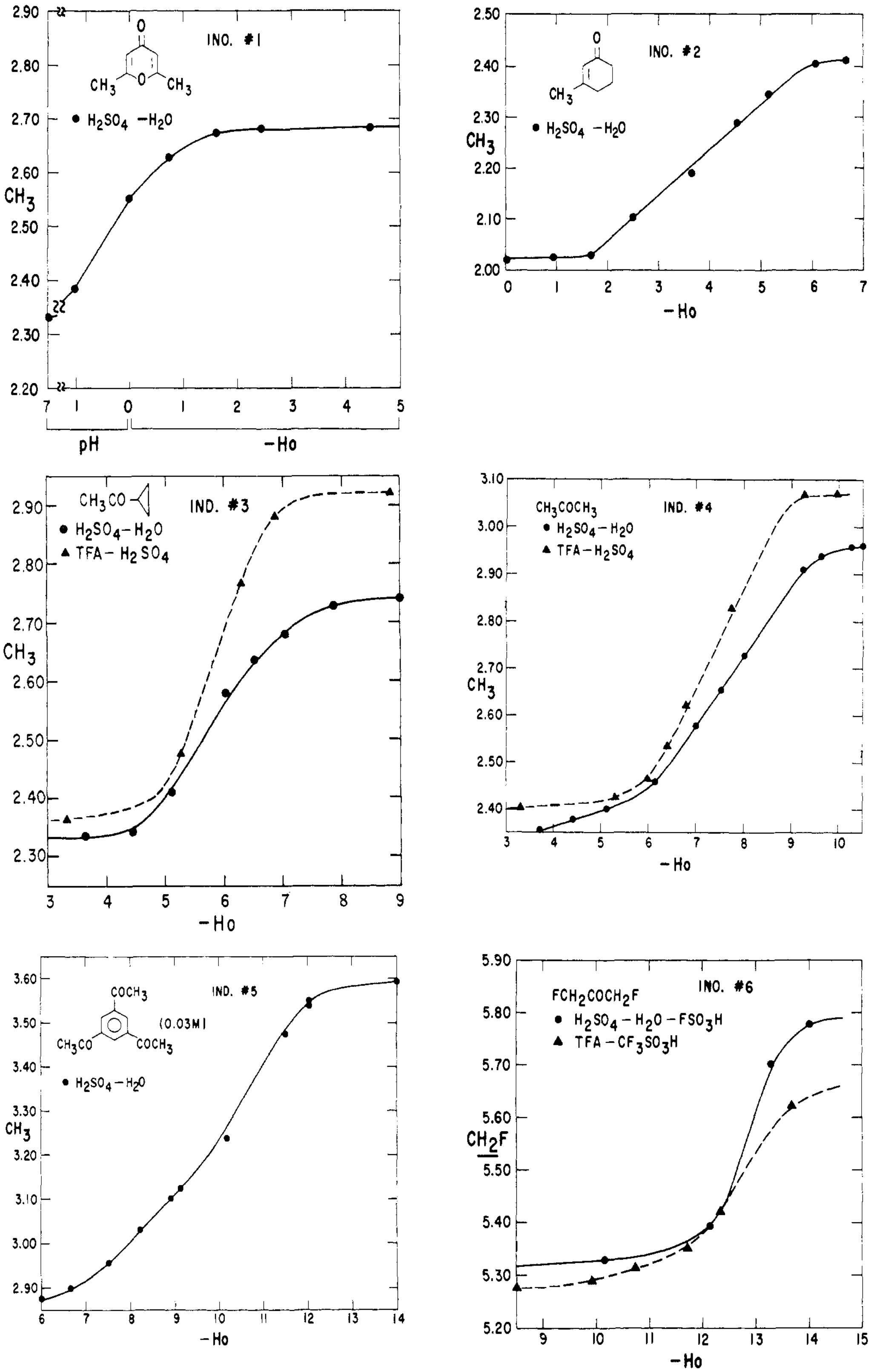

Figure 4. Protonation curves for nmr indicators (on this and opposite page): 26° (±2°); nmr standards: cyclohexane used in TFA media; TMAC used in all other acid systems.

then sealed in glass ampoules. Stock solutions of FSO_3H-SbF_5 were prepared and kept in Teflon bottles (the SbF_5 had been distilled through a Vycor apparatus).

Calibration of Acid Media. The acidities of H_2SO_4-H_2O and TFA-H_2SO_4 media were confirmed spectrophotometrically, utilizing primary aniline indicators according to Jorgenson and Hartter.[17] The acidity of the commercial 100% H_2SO_4 was evaluated by specific dilution with H_2O and subsequent nmr measurements. Acidity values for H_2SO_4-FSO_3H and FSO_3H-SbF_5 were determined spectrophotometrically using nitro compounds as indicators (Gillespie, ref 16).[41] The TFA-CF_3SO_3H acid system was evaluated by nmr (indicators 4-6, 10-12—Table IV).

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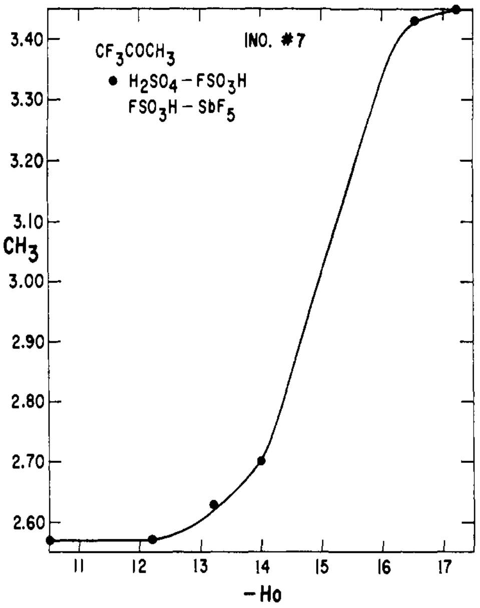
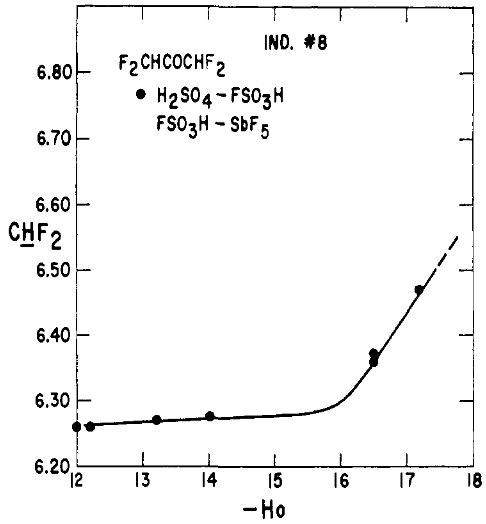
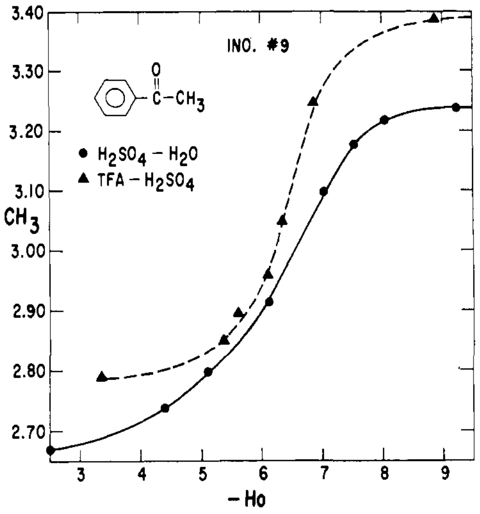
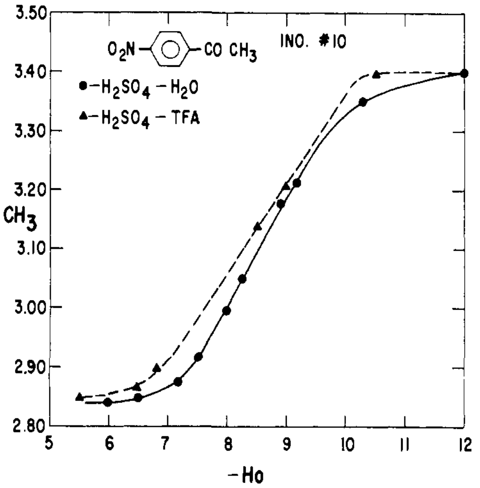
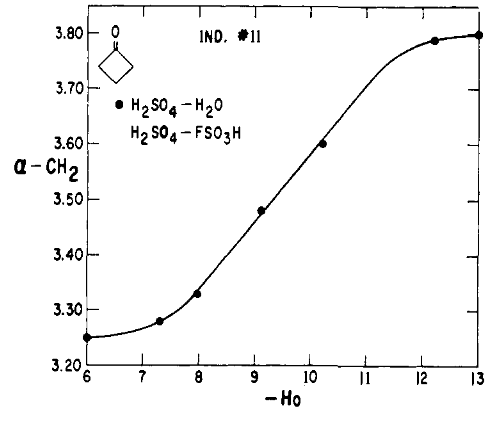
[41] R. J. Gillespie finds H_0 for 100.0% FSO_3H to be $\cong -14.5$. FSO_3H-SbF_5 (SbF_5 > 15 mol %) has an acidity of $H_0 \sim -17.5$.

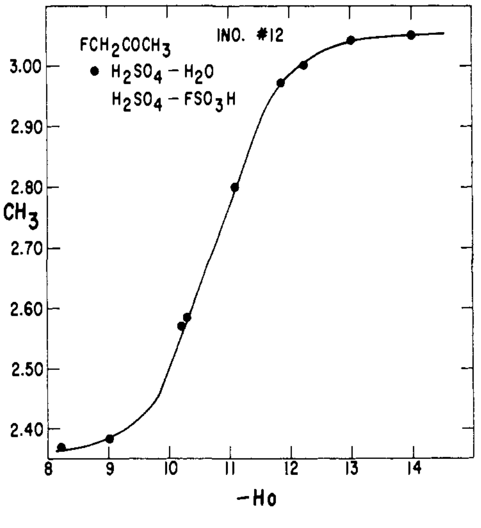












Ketone Concentrations. When ketone concentration was lower than 0.5 *M*, further dilution had little effect on chemical shifts. In actual determinations, ketone concentrations were kept between 0.1 and 0.15 *M*. Some experiments were performed with ketone concentrations as low as 5×10^{-3} *M*.

Nmr Standards. All chemical shifts are given in parts per million downfield from TMS, which is set δ 0.00. Cyclohexane is used as the internal standard (δ 1.45) in nonaqueous acid systems containing TFA. Cyclohexane is not stable in superacids.

Tetramethylammonium chloride (TMAC) was used as an internal standard in aqueous acid and super acid media. The chemical shift of TMAC does not remain constant relative to TMS or DSS [(3-trimethylsilyl)-1-propanesulfonic acid sodium salt] even in H_2SO_4-H_2O media. TMAC varies from δ 3.20 in H_2O or very

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For the present work we assumed $H_0 = -14$ for once distilled FSO_3H and $H_0 = -17.2$ for our prepared FSO_3H-SbF_6.

Table VI

H_2SO_4-H_2O	
Wt % H_2SO_4	δCH_3 (TMAC)
0–20	3.20
25–60	3.18
65	3.17
70	3.16
75	3.14
80	3.12
90–100	3.10

dilute acid to δ 3.10 in 90–100 wt % H_2SO_4 (see Table VI). TMAC in all superacid media sssumed $\delta = 3.10$.

Low-Temperature Protonations. It is advantageous to protonate labile (*e.g.*, $CH_2BrCOCH_3$, CH_3CHO) carbonyl compounds below room temperature in order to minimize decomposition and side reactions. In these cases the base is added to the acid medium just below the freezing point of the acid. The nmr tube is then removed from the cold bath (dewar) and mixed thoroughly as the ketone and/or acid melt. Before the nmr tube warms completely it is placed in the spectrometer probe. A spectrum can be taken in 3–5 min.

Evaluation of Unknown Acid Systems. Simple measurement of a ketone chemical shift gives only an approximate acidity value in the typical experiment. In cases where the acid to be evaluated is not closely related to a calibrating acid system, individual nmr chemical shifts can be misleading. Thus, for most accurate measurements it is necessary to get more than one point on the protonation curve for the acid system to be evaluated. This can be done by (1) adding small amounts (2–3 drops) of a stronger acid or (2) adding small amounts of a strong base. In this way the chemical-shift dependence of the ketone indicator in a given acid system can be best visualized. Thus, addition of small amounts of a sufficiently strong acid will give a substituent chemical shift corresponding to "full protonation" in that acid medium. Likewise, addition of strong base will allow measurement of the unprotonated carbonyl substituent chemical shift.

For example, in evaluation of CH_3SO_3H–CH_3NO_2 solutions (CD_3NO_2 is used for nmr purposes) OH^- or H_2O may serve as the base and FSO_3H, CF_3SO_3H, or 100% H_2SO_4 act as strong acids. The best choices are OH^- and FSO_3H since these will cause the largest changes in medium acidity.

Acknowledgment. The authors wish to thank Professor R. J. Gillespie for making available unpublished acidity data on H_2SO_4-FSO_3H and FSO_3H-SbF_5 media.

Acid-Catalyzed Sigmatropic Shifts of Allyl Groups in Cyclohexa-2,4-dien-1-ones. The Possibility of Differing Reactions from n- and π-Protonated Ketones[1]

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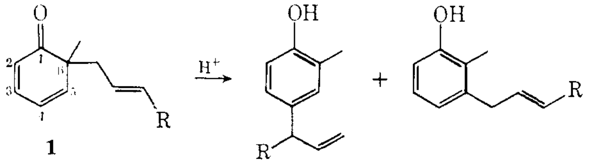
Abstract: Acid-catalyzed rearrangements of allyl-substituted cyclohexa-2,4-dien-1-ones can result in five different types of migrations. These are (starting with structure **1**) [1,2] migration of the allyl group to C-5, [3,3] migration to C-4, [3,3] migration to oxygen, [1,5] migration to C-2, and [3,5] migration to C-2. No one dienone exhibits all of these types of migrations, the occurrence of which depends on the substitution pattern on the ring. The large number of migration types observed can be reconciled with the requirements of the conservation of orbital symmetry if the assumption is made that the rearrangements proceed through both n- and π-protonated ketones.

Acid-catalyzed rearrangements of linearly conjugated dienones, such as **1**, have been reported to result principally in migration of the allyl group to C-4 of the dienone.[2–4] In earlier work[2] we have shown that these migrations proceed *via* [3,3] sigmatropic shifts[5] involving inversion of the allyl group. In one instance, a "normal" [1,2] shift of the allyl group to C-5 was reported to occur along with the migration to C-4.[3]



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We have now found that when the cyclohexadienone molecule is so substituted as to inhibit effectively either of the above migrations, acid-catalyzed reverse-Claisen migration to oxygen and [1,5][6] shifts of the allyl group to C-2 can become major rearrangement paths. Finally, an apparent [3,5][6] shift of the allyl group to C-2 with inversion has been observed, but it cannot yet be determined whether this migration proceeds in a single step or by a sequence of other migrations.

The occurrence of such a large number of migration types does not seem consistent with predictions from the Woodward–Hoffmann rules.[5] A possible way of reconciling these rules with our observations will be offered in the discussion section.

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(1) (a) Reactions of Cyclohexadienones. XXIV. Part XXIII: B. Miller, *J. Amer. Chem. Soc.*, **92**, 432 (1970). (b) A preliminary account of part of this work has been published: *ibid.*, **91**, 2170 (1969).

(2) B. Miller, *ibid.*, 87, 5115 (1965).

(3) P. Fahrni, A. Habich, and H. Schmid, *Helv. Chim. Acta*, **43**, 448 (1960).

(4) J. Leitich, *Monatsh.*, **92**, 1167 (1961).

(5) R. B. Woodward and R. Hoffmann, *J. Amer. Chem. Soc.*, **87**, 2511 (1965); *Accounts Chem. Res.*, **1**, 17 (1968).

(6) The proper designations for sigmatropic shifts in cyclic systems of π orbitals seems somewhat ambiguous. Although a shift of a group from C-6 to C-2 of a dienone could be designated as a [1,3] shift, we have chosen to count along the system of double bonds, rather than through the carbonyl group, in order to have the allowed and forbidden migrations be consistent with those in the acyclic examples.