Relative Rates of Base-Catalyzed Enolization of Methyl Alkyl Ketones in Aqueous Dioxane[1]

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Abstract: The effects of substituting methyl groups for hydrogen, at one methyl group of acetone and at C_1 of 2-butanone, on relative rates of hydroxide-catalyzed H–D exchange at C_1 and C_3, have been determined by nmr. Rates were measured at 32°, with solutions made from 2:1 dioxane–D_2O (90 or 95 parts) and ketone (5 or 10 parts), all ratios referring to volumes. It was found that, for the α-substituted series beginning with acetone and ending with pinacolone as well as for the β-substituted series beginning with 2-butanone and ending with methyl neopentyl ketone, substitution reduces the rates of enolization of both reactive sites in a ketone.

Rates of enolization of ketones have been determined through studies of their halogenation, racemization, and hydrogen–deuterium exchange. The usual effect of an α-alkyl substituent is to accelerate acid-catalyzed enolization and to retard base-catalyzed enolization, relative to the corresponding rates for unsubstituted ketone. This generalization was formulated early on the basis of measurements of rates of enolization of aryl alkyl ketones,[3] dialkyl ketones,[4–6] and ring-substituted acetophenones[7–10] as well as on experiments in which relative rates of exchange at two sites in an unsymmetrical ketone were determined.[11–13] Measurements of the latter type can now be made conveniently, although not very accurately, by nmr, and several papers on the subject have appeared in the last few years.[14–16]

There is no doubt that, in general, alkyl substitution at the α carbons of a ketone retards the rate of base-catalyzed enolization. One explanation for the effect, namely, that alkyl groups inductively destabilize an enolate-like transition state, was questioned recently[15] when it was found that there is at least one exception. The methylene protons of 2-butanone are exchanged as fast as, or faster than, the α-methyl protons by several bases in D_2O.[14c,15,16]

It seemed important to study rates of exchange of other dialkyl ketones which is the subject of this report.

(1) This work was supported by the National Research Council of Canada.

(2) National Research Council of Canada Postdoctoral Fellow, 1965–1966.

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Experimental Section

Ketones. The commercially-available ketones were shaken with saturated aqueous sodium carbonate to remove acidic impurities. They were then dried over anhydrous potassium carbonate or sodium sulfate prior to distillation. Center cuts were redistilled, if necessary, to attain glpc purity. All samples were checked for extraneous signals in the nmr, using neat samples. Samples used for exchange kinetics were clear and colorless, except for methyl neopentyl ketone which was pale yellow.

Methyl 1,1,1,3,3,3-Hexadeuterio-2-propyl Ketone. Hexadeuterioacetone was reduced with $LiAlH_4$ in ether. The resulting hexadeuterio-2-propanol was converted to the bromide with PBr_3 at −10°, and the bromide was converted to the corresponding Grignard reagent in the usual way. Addition of the Grignard reagent to an ethereal solution of acetic anhydride (twofold excess) at −70° afforded the title compound. It was isolated by extraction of the ethereal solution with water and aqueous carbonate, followed by drying and distillation of the ether. Residual material was fractionated with a spinning-band column after addition of toluene to act as chaser. The fraction collected boiled at 93–94° and contained about 15% toluene (glpc). This impurity was desirable as it provided a convenient reference signal (CH_3) for the kinetic measurements. In the nmr, the methine signal from the ketone was a broadened singlet and there was no evidence of β-hydrogen except at high spectrum amplitudes.

Dioxane. Fisher's laboratory grade dioxane was purified by a procedure described by Fieser[17] and it was stored under argon. The nmr spectrum had no peaks other than the expected singlet and the ^{13}C–H multiplets symmetrically disposed at 72 cps on both sides of the main peak.

Basic Dioxane–D_2O Solutions. For procedure B (see below) a small pellet of reagent grade NaOH was weighed in a glass-stoppered bottle. It was dissolved in a suitable volume of 2:1 (v/v) dioxane–D_2O to make a solution about 0.05 *N* in base. This stock solution was diluted with 2:1 dioxane–D_2O to prepare more dilute solutions. Base strength of the dilute solution was determined titrimetrically, using mixed indicator (0.1% screened neutral red and 0.1% methylene blue in 95% EtOH). Solutions were kept for a few days only, when new ones were prepared.

For procedure A, a series of concentrated solutions of NaOH in D_2O–dioxane were prepared and titrated to the phenolphthalein end point. The concentrations were such that by addition of about 0.05 ml of the appropriate solution to 0.5 ml of D_2O–dioxane–ketone solution, final base concentrations of about 0.01, 0.02, 0.03, 0.04, and 0.05 *N* could be achieved.

Temperature. The methanol sample supplied with the A-60 nmr spectrometer (Varian Associates) was allowed to come to equilibrium with a controlled water bath at 32°. Line separation was determined immediately after transfer of the tube to the cavity of the instrument. When the value of line separation had been determined several times, the cavity of the instrument was cooled to 32° by passing ice-cooled nitrogen through the temperature controller accessory. Adjustment of temperature was made by changing the flow rate slightly, the heater-sensor circuit being kept

(17) L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., Boston, Mass., 1955, p 285, procedure a.

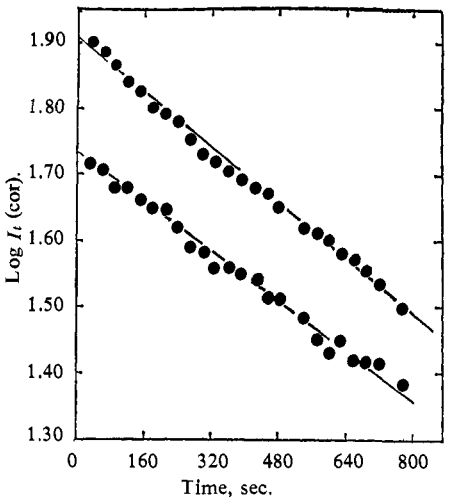

Figure 1. Plot of log integral amplitude (mm), corrected for ^{13}C signal from dioxane, against time for exchange in $CH_3COCH_2CH_3$. Upper curve, CH_3; lower curve, CH_2.

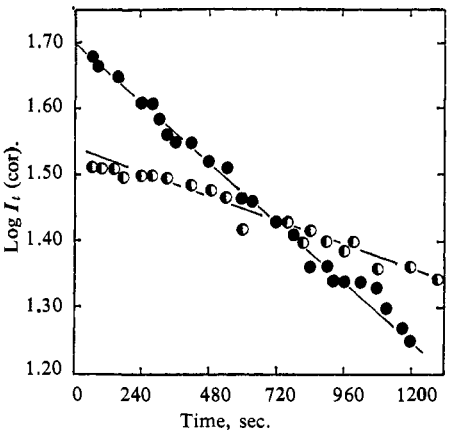

Figure 2. Plot of log integral amplitude (mm), corrected for ^{13}C signal from dioxane, against time for exchange in $CH_3COCH_2CH(CH_3)_2$. The solid circles pertain to the methyl group and half-filled circles represent the methylene group.

inoperative. Temperature stability, as measured by the separation of the methanol lines at 250-cps sweep width, was better than ±0.5° over a period of several hours and the temperature could be reproduced from day to day. The line separation corresponding to 32° (calibrated thermometer), corresponded to about 31.5° on the calibration chart (methanol) supplied with the A-60 and the higher temperature was taken as the true value.

Rate Measurements. Two techniques were employed. In procedure A, the D_2O–dioxane solvent and the ketone were introduced into a calibrated nmr tube from calibrated syringes. The tube was brought to 32°, and the integral was swept three or four times after initial adjustments for drift. A small volume of concentrated OD^- in D_2O–dioxane, also at 32°, was introduced so as to achieve the desired base strength. The tube was shaken vigorously to mix the contents, the stopwatch was started, and integrals were recorded at about 30-sec intervals. All ketones except acetone, 2-butanone, and pinacolone were examined by procedure A, and each exchange was followed for five different base concentrations lying between 0.01 and 0.05 *N*. During that series of measurements the spectrometer was relatively insensitive, with signal:noise ≅ 5, and all ketone concentrations were 10% by volume.

In procedure B, a clean, dry nmr tube was rinsed once with basic solvent of the concentration to be used in the run. It was then filled to a calibration mark at 0.45 ml, capped with a tight-fitting plastic cap, and placed in the water bath. After 10 min or more it was transferred to the probe, and the spectrum, as well as several integrals of the high-field branch of the ^{13}C–H satellites of dioxane, was recorded. Ketone (0.025 ml) was then injected from a Hamilton syringe and after mixing the scanning proceeded as in procedure A. All sweeps were started below the ^{13}C–H satellite of dioxane and continued through the ketonic signals. The signal-to-noise ratio during the series B runs was better than 12:1, so that ketone concentrations near 5% gave adequate signals. Successive sweeps were kept separate by moving the paper after each sweep. All of the ketones were studied by procedure B.

In both procedures, fast exchanges ($t_{1/2} < 1$ hr) were followed to at least one half-life with the sample in the probe. Slow rates, such as the methylene rate in the case of methyl neopentyl ketone, were obtained by transferring the sample from the water bath to the probe once every hour or half hour and then returning it to the bath after several integrals had been recorded.

Integrations were performed at radiofrequency level 0.1, spectrum amplitude 10, and integral amplitude 80. The sweep width was 500 cps throughout, and the sweep rate was 50. With the instrument working under optimum conditions (signal:noise > 12:1), only slight adjustments for drift, or none at all, were required during a run.

Procedures A and B gave results in good agreement except in a few cases. In case of disagreement the results of procedure B were chosen.

Treatment of Experimental Results. Exchange was treated as effectively irreversible during the first half-life. Accordingly, pseudo-first-order kinetic behavior was assumed, and log I_t was plotted against time, where I_t is the integral amplitude, at time t, corresponding to the reacting site in question, normalized with reference to a nonexchanging internal standard.

Internal standards were the signals from β- or γ-hydrogen, in general. In the cases of acetone and pinacolone, the ^{13}C–H signal of dioxane was the most convenient internal standard and, in the case of $CH_3COCH(CD_3)_2$, it was the CH_3 signal from the toluene impurity which had been deliberately introduced for that purpose (*vide supra*).

Plots were generally linear to about one half-life when originating from procedure A (10% ketone) and to one or two half-lives when derived from procedure B (5% ketone). The observed pseudo-first-order constant, k_R^{obsd}, and the bimolecular rate constant, k_R^H, were obtained from the slope of such a plot and from the base concentration by means of the equations $k_R^{obsd} = 2.303 \times$ slope and $k_R^H = k_R^{obsd}/[OD^-]$. Slopes were obtained by feeding data to one half-life into a linear, least-squares program for the IBM 7040 computer, although many graphs could be drawn confidently by eye. The program also gave the standard deviations of the slope.

Some of the integral amplitudes, I_t, had to be corrected for underlying extraneous signals. One such correction was for the integral arising from the high-field ^{13}C–H satellite of dioxane. In procedure B the latter was always recorded, as already stated, prior to addition of the ketone so that it could readily be subtracted from the total signal in the α-methylene and α-methine regions, both of which overlap with that occupied by the ^{13}C–H multiplet. In procedure A the total integral was recorded prior to addition of base, and the correction was based on the excess value of the methylene or methine integral as determined from the other signals in the spectrum. The ^{13}C–H corrections were not adjusted for the small changes in concentration accompanying addition of base (procedure A) or of ketone (procedure B).

In the case of methyl isobutyl ketone an additional correction was required. The highly-split methine signal is broad enough to make detection difficult and it runs into both the methylene peak and the α-methyl peak. A well-defined plateau exists in the integral, between the methylene and methyl regions so that there are two readily measurable amplitudes both of which need correction for a fraction of the one-proton equivalent. Two ways of splitting up the correction were examined. First, the integral of neat ketone was taken, with the *gem*-dimethyl doublet defining the integral amplitude per hydrogen. It was found that the methylene area needed to be reduced by 0.25 of the proton equivalent to give it relative area 2 while the methyl area required subtraction of 0.75 of that equivalent to bring it to relative area 3. In the second method, the spectrum of highly exchanged ketone (*i.e.*, $CD_3COCD_2CH(CH_3)_2$) was examined to locate the center of the broad methine multiplet relative to the center of the *gem*-dimethyl doublet. It was found that 0.23 of the multiplet would overlap with the CH_2 signal of protio ketone and 0.77 of the multiplet would contain the α-CH_3 signal, assuming that, in the protio ketone, the methine signal is symmetrically disposed about its center and that the center is unshifted by exchange. It is well known that chemical shifts from deuterium substitution are very small[18] so that the assumption

Table I. Effects of α Substitution. Rates of Exchange in CH_3COR[a]

R	$k_{CH_3}^H \times 10^2$ M^{-1}, sec^{-1}	$k_R^H \times 10^2$ M^{-1}, sec^{-1}	$k_{CH_3}^H(R)/k_{acetone}^H$	$k_R^H/k_{acetone}^H$	$k_{CH_3}^H/k_R^H$
CH_3	25.9 ± 0.6				
	27.7 ± 0.4				
	24.6 ± 0.5				
	23.3 ± 0.8				
	Mean 25.4		1	1	1
CH_2CH_3	14.2 ± 0.2	12.5 ± 0.7			
	9.98 ± 0.20	8.52 ± 0.26			
	13.2 ± 0.2	11.4 ± 0.7			
	13.8 ± 0.4	11.5 ± 0.5			
	Mean 12.8	Mean 11.0	0.50	0.43	1.16
			(0.45)[b]	(0.41)[b]	(1.09)[b]
$CH(CD_3)_2$	9.36 ± 0.13	0.704 ± 0.071			
	8.82 ± 0.15	0.716 ± 0.080			
	8.50 ± 0.10	0.620 ± 0.054			
	8.71 ± 0.12	0.651 ± 0.062			
$CH(CH_3)_2$	7.91 ± 0.09	1.29 ± 0.23			
	8.36 ± 0.13	1.05 ± 0.21			
	Mean 8.61	Mean 0.673[c]	0.34	0.026	12.8
			(0.45)[b]	(<0.0028)[b]	(<163)[b]
$C(CH_3)_3$	4.73 ± 0.13				
	4.11 ± 0.07				
	3.49 ± 0.14				
	3.25 ± 0.08				
	5.26 ± 0.10				
	Mean 4.17		0.16		
			(0.28)[b]		

[a] The precision limit for a given experiment is given as the standard deviation. [b] Data of Rappe and Sachs,[14a] converted to the *per hydrogen* basis. A possible reason for lack of agreement is mentioned in the text. [c] The values obtained from the protio ketone are less reliable and are not included in the average.

should be good. The agreement between the two estimates of the methine corrections suggests that little error is introduced in making them.

Methyl isopropyl ketone gave badly scattered results for the methine rate, presumably because of the difficulty in measuring the integral from a highly-split signal accurately. Use of the β-deuterio analog made integration of the methine signal, a broadened singlet, more reliable.

Discussion

Before considering rates and relative rates of exchange in ketones we devote some attention to definitions of "reactivity" and "rate constant." These can be defined on the *per hydrogen* basis or on the *per group* basis. The former basis is the one of choice for discussion of substituent effects. Thus, to consider how the β-methyl group of 2-butanone affects enolization *chemically*, we must compare the reacting sites under identical conditions. Obviously the concentrations must be considered and rate constants must be put on the unit basis; *i.e., per hydrogen.*

On the other hand, the total effect of the β-methyl group is often of interest. If one wished to estimate the initial ratio of the two monodeuterio ketones from exchange of 2-butanone one would need to multiply the intrinsic (per H) reactivity at a given site by the number of hydrogens at that site. Such concentration-corrected values measure reactivity *per group* and contain the sum of *chemical* and *statistical* factors. If k_R^H is defined as the rate constant per hydrogen in a group R containing n hydrogen atoms and if k_R is defined as the rate constant *per group*, then the relationship between the two measures of reactivity is given by the equation $k_R = nk_R^H$. In the following discussion we define rate constants on the *per hydrogen* basis as before[15] and we use the term "reactivity" in the same sense. Others[14,16] have chosen to use *per group* values, a matter that must be kept in mind in comparing results.

Figures 1 and 2 show some representative plots of exchange data while Tables I and II give the rates and the rate relationships, as well as results of another group. The errors in the absolute rates are quite large (about 15%) while those in the relative rates of reaction in the same molecule are probably less than 10% because they are less sensitive to fluctuations of temperature. In view of the error inherent in the nmr method, very detailed discussion is not warranted at this time. However, the errors are not large enough to accommodate the difference between some of our results and those of Rappe and Sachs[14g] (Tables I and II). A possible source of error in the latter work concerns the ^{13}C–H satellite peaks of dioxane. A correction for the integral of the high-field branch is not mentioned.[14f,g] For relatively insoluble ketones in 60% dioxane, that integral is large relative to ketonic signals. The total high-field integral could then decrease very little as a result of exchange, leading to low apparent rate constants and early apparent deviation from pseudo-first-order kinetics, particularly for CH_2 and CH groups.

From Table I it is clear that substitution at one α site with methyl groups has a considerable retarding effect on the rate of enolization of the unsubstituted α site as well as on that of the site of substitution.[16] Thus, the methyl hydrogens of 2-butanone are only half as reactive as those of acetone and the trend continues to methyl *t*-butyl ketone, which is about $^1/_6$ as reactive as acetone. We can explain this only in terms of a steric factor since any electronic effect through the four bonds separating α-methyl hydrogens from the substituent methyls must be very small.

Table I also shows the effects of α substitution on

(18) O. S. Tee and J. Warkentin, *Can. J. Chem.*, 43, 2424 (1965), and references therein.

Table II. Effects of β Substitution. Rates of Exchange in CH_3COCH_2R[a]

R	$k_{CH_3}^H \times 10^2$ M^{-1}, sec^{-1}	$k_{CH_2}^H \times 10^2$ M^{-1}, sec^{-1}	$k_{CH_3}^H$(R)/ $k_{CH_3}^H$(butanone)	$k_{CH_2}^H$(R)/ $k_{CH_2}^H$(butanone)	$k_{CH_3}^H/k_{CH_2}^H$
CH_3[b]	Mean 12.8	Mean 11.0	1	1	1.16
CH_2CH_3	9.75 ± 0.16	5.04 ± 0.22			
	9.42 ± 0.21	6.16 ± 0.23			
	8.15 ± 0.27	4.45 ± 0.47			
	7.89 ± 0.34	4.91 ± 0.33			
	9.01 ± 0.37	4.45 ± 0.18			
	Mean 8.84	Mean 5.00	0.69	0.45	1.77
$CH(CH_3)_2$	6.74 ± 0.10	2.79 ± 0.21			
	7.33 ± 0.22	2.96 ± 0.21			
	6.23 ± 0.12	2.42 ± 0.18			
	7.48 ± 0.09	3.20 ± 0.11			
	6.70 ± 0.14	3.14 ± 0.19			
	Mean 6.90	Mean 2.90	0.54	0.26	2.38
$C(CH_3)_3$	5.34 ± 0.07	0.374 ± 0.043			
	5.83 ± 0.11	0.254 ± 0.054			
	5.26 ± 0.10	0.283 ± 0.051			
	5.20 ± 0.09	0.242 ± 0.040			
	5.04 ± 0.12	0.231 ± 0.044			
	Mean 5.33	Mean 0.277	0.42	0.025	19.2
			(0.11)[c]	(0.01)[c]	(12.2)[c]

[a] The precision limit for a given experiment is given as the standard deviation. [b] Carried over from Table I. [c] Data of Rappe and Sachs,[14a] converted to the *per hydrogen* basis. A possible reason for the disagreement is discussed in the text.

rates at the substituted sites. A methylene hydrogen of 2-butanone is only about 0.4 as reactive as a hydrogen of acetone (column 5) while the methine hydrogen of methyl isopropyl ketone is less than $^1/_{30}$ as reactive as a hydrogen of acetone.[19] The interpretation is not

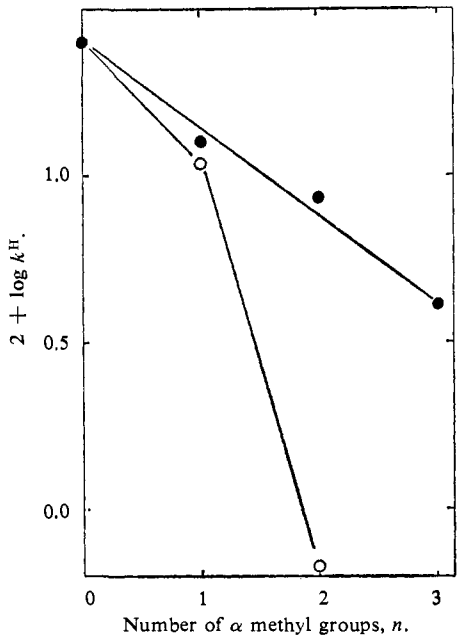

Figure 3. Dependence of rate constant for base-promoted exchange in $CH_3COCH_{3-n}(CH_3)_n$ on n; methyl group, ●; methylene or methine group, ○.

as simple in this case because both steric and polar effects are conceivable at substituted sites, where the substituent is bonded to sp^3 carbon in the ketone and to sp^2 carbon in the enol or enolate ion.

It is easily seen though, that the facts cannot be explained satisfactorily in terms of a polar effect alone. Without worrying for the moment about the direction of such an effect, one would expect it to be approximately additive. There is no doubt, however, that two methyl groups have a much larger effect at the substituted site than twice that of one methyl group. Thus inductive effects, if present, must play a minor role.

The major factor determining the enolization rates appears to be steric hindrance, which is probably a composite of terms including internal, nonbonded interactions and solvation. That effect is large enough to make smaller, polar effects hard to separate from the total. The data for 2-butanone do suggest the existence of an accelerating, polar effect. Figure 3 demonstrates the pronounced effect of α substitution on rates at substituted sites, relative to the effect of such substitution on methyl reactivity. However, in pure D_2O and with OD^- as base the points for $n = 1$ (Figure 3) are coincident[20] and for catalysis by acetate in D_2O at 59°, $k_{CH_3}^H/k_{CH_2}^H$ is about 0.5 for 2-butanone.[21,22] This suggests that curves such as those in Figure 3, but pertaining to acetate catalysis in water, would cross.[23] The easiest way to account for such a phenomenon is to invoke a polar effect which opposes the steric effect and is swamped by it in all the ketones except butanone. Such a polar effect could itself be accounted for if the transition state for enolization in water were enol-like, as suggested earlier.[15] An alkyl group could stabilize such a transition state for the same reasons that make nonterminal olefins more stable than terminal olefins.

(19) The rate was actually determined for methyl hexadeuterioisopropyl ketone. β deuterium should have a small effect only so that the values are assumed to apply fairly well to the protio analog.

(20) In pure D_2O the two rate constants are equal,[15] but addition of dioxane shifts the ratio of constants in favor of $k_{CH_3}^H$. Our previous value for 60% dioxane, $k_{CH_3}^H/k_{CH_2}^H = 1.6$, is too large however, because we had neglected to correct for the mounting ^{13}C–H satellite of dioxane as the concentration of dioxane was raised (*cf.* Experimental Section of this paper).

(21) We have recently confirmed this ratio, reported earlier,[15b] by another method. It was also shown that, for catalysis by OD^- in D_2O, $k_{CH_3}^H/k_{CH_2}^H$ increases slightly as the temperature is increased from 0 to 55°. The low ratio for acetate catalysis is therefore not likely to result from the higher temperature at which the acetate work was done.[22]

(22) J. Warkentin and R. A. Cox, *J. Org. Chem.*, 33, 1301 (1968).

(23) Low solubilities preclude such measurements by nmr at this time. It is most unlikely, however, that the relative heights of the points at $n = 2$, would change for D_2O–AcO^- conditions.

On the other hand, an enolate-like transition state might be destabilized by an α-methyl group.[24] Further work is needed to establish firmly the existence of polar effects of alkyl groups in enolization. It is to be expected that the importance of such effects will depend on such factors as the strength of the catalyzing base, the acidity of the ketone (*i.e.*, other substituents), and the solvent.

We return now to discussion of the over-all effects, to which steric factors contribute strongly.[13] Table II holds the rates and rate relationships pertaining to β substitution. Considering first the methyl reactivities, we see that three β-methyl groups reduce α-methyl reactivity by a factor of 2.4 only (column 4), a 2.6-fold smaller effect than that from similar α substitution (Table I). This is not unexpected, for the β substituents can get far away from the α-methyl group, at least in some conformations. Thus $k_{CH_3}{}^H(R = CH_2C(CH_3)_3) > k_{CH_3}{}^H(R = C(CH_3)_3)$ is not surprising.

At the methylene positions (Table II) the effects are larger, with a total 40-fold drop from 2-butanone to methyl neopentyl ketone. These effects are far from linear in the number of substituents, for they vary from a factor near 2 for the first methyl to a factor of 10 between the second and the third. Such behavior is well known in ester hydrolysis, where the steric substituent parameters (E_s) show a similar trend.[25]

Finally, we come briefly to the relative reactivities of two sites in the same molecule. These are in the last columns of Tables I and II and express the relative chances of reaction of a given hydrogen at each site. The maximum effect per substituent methyl group is, by a small margin, in the α series where the value is 6.4 (*i.e.*, 12.8/2) compared to the β series where it is 5.5 (*i.e.*, 19.2/1.16 × 3). To get from the inherent relative reactivities in the tables to numbers which predict the relative rates of reaction at the two sites, statistical factors must be included. For example, if halogenation is analogous to exchange,[26] then the relative amounts of monobromides, from monobromination of 2-butanone under comparable conditions, should be about: $CH_2BrCOCH_2CH_3/CH_3COCHBrCH_3 = 1.16 \times 3/2 = 1.74$.

Acknowledgment. We are grateful to the National Research Council of Canada for financial assistance, including a Postdoctoral Fellowship to C. B.

(24) Although *m*- or *p*-methyl in benzoic acid and in phenol is acid weakening, those equilibria are not perfect models for the enolization reaction, which involves rehybridization at the seat of substitution. For data which suggest that the methyl group, relative to hydrogen, is electron donating toward sp^2 carbon and electron withdrawing from sp^3 carbon, in uncharged systems, see (a) H. D. Holtz and L. M. Stock, *J. Am. Chem. Soc.*, **87**, 2404 (1965) and (b) V. W. Laurie and J. S. Muenter, *ibid.*, **88**, 2884 (1966), as well as references cited therein.

(25) R. W. Taft in "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p 601.

(26) Recent work by Rappe has been taken to indicate that there are halogenation mechanisms which do not have analogs in exchange processes. See ref 14d and also C. Rappe, *Acta Chem. Scand.*, **21**, 857 (1967).

The Kinetics and Mechanism of the Acid-Catalyzed Isomerization of *cis*-Stilbene[1,2]

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Abstract: The isomerization of *cis*-stilbene to *trans*-stilbene as catalyzed by sulfuric acid involves the rate-limiting transfer of a proton to the double bond. The isomerization rate correlates well with the acidity of the medium, a plot of log k *vs.* H_0 being linear with a slope of -1.25. In deuteriosulfuric acid the rate of isomerization is diminished at the same acidity. The rates of isomerization of 11 substituted *cis*-stilbenes correlated well with Hammett's equation: $\log k_{X,Y} = -4.46 - 3.30(\sigma_X^+ + 0.29\sigma_Y)$. Examination of the rates of isomerization of *cis*-4,4′-dimethoxystilbene, *cis*-stilbene, and *cis*-3,3′-dichlorostilbene do not provide any indication for the intervention of an olefin π complex during the isomerization reaction.

The isomerization of *cis*-stilbene to *trans*-stilbene may be catalyzed by a wide variety of reagents, including radical sources,[5,6] light,[7,8] and mineral acids[9] and Lewis acids.[10]

We have undertaken a study of the acid-catalyzed isomerization in aqueous acids in order to gain more information regarding mechanisms of proton transfer. The hydration of isobutylene[11] and of styrene[12,13]

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