Steric Effects on Equilibrium Basicity of Alkoxides. Potassium Tri-s-alkylmethoxides, Alkoxides of Enhanced Basicity

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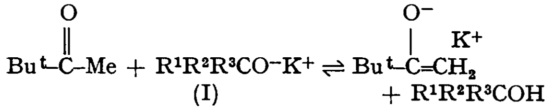
Summary Increases in the size of the alkyl group of alkoxides, raise the basicity measured against ketone indicators; extremely hindered alkoxides derived from tri-s-alkylmethanols exhibit markedly enhanced basicity sufficient to convert a variety of ketones essentially quantitativity into their respective enolates.

Alkoxides ($R^1R^2R^3CO^-M^+$) are subject to structural variation by altering R^n in the precursor alcohols. Recently, the range of alkyl group size available has been substantially extended *via* organoborane synthesis.[1] Although alkali-metal salts of lower tertiary alcohols have been widely used[2] the effects of increased alkyl group size upon alkoxide basicity (or, conversely, alcohol acidity) have not been studied extensively. Since hindered potassium alkoxides are now readily available *via* metallation with potassium hydride,[3] we investigated this question, especially in view of continued discussion of the roles of steric hindrance and basicity in elimination reactions.[4,5]

Alkoxides have been shown to exhibit greatly enhanced kinetic[6] and thermodynamic[7] basicity in solutions of dipolar aprotic solvents (*e.g.* Me_2SO) compared to ethereal and hydroxylic media. This phenomena has generally attributed to the greater degree of aggregation, association with solvent, and ion pairing of strong bases in the latter solvents.[6b,8] Increasing the bulk of R^n in (I), *i.e.* increasing steric hindrance, should interfere with aggregation, *etc.*, as well as with cation solvation in the ion pair, and might be expected, *a priori*, to result in significantly increased alkoxide basicity. This effect has now been observed directly in tetrahydrofuran, using pinacolone ($pK_A = 20{\cdot}8^{9a}$) as an i.r. indicator ($\nu_{C=O}$ 1708 cm^{-1}, $\nu_{enolate}$ 1568 cm^{-1}).

Aliphatic ketones are generally considered to be somewhat less acidic than alcohols;[9] thus it is surprising that equilibrium (1) lies to the right, even with a primary alcohol. As the size of R^n, and steric hindrance of the alkoxide, is increased, equilibrium (1) lies further to the right



$$\mathrm{Bu^t\!-\!C(=O)\!-\!Me} + \mathrm{R^1R^2R^3CO^-K^+} \rightleftharpoons \mathrm{Bu^t\!-\!C(O^-)\!=\!CH_2\;K^+} + \mathrm{R^1R^2R^3COH} \qquad (1)$$

(I)

TABLE

Effect of R^n upon K_{eq} for reaction (1)

R^1	R^2	R^3	K[a,b]
Pr^i	H	H	1·7
$-[CH_2]_5-$		H	1·9
Me	Me	Me	6·7
Et	Me	Me	10
Et	Et	Me[c]	23[d]
Et	Et	Et	57
Cx[e]	Cx	Cx[f]	710

[a] Determined by i.r. spectroscopy upon 1:1 mixtures of alkoxide and ketone and upon 1:1 mixtures of alcohol and enolate. [b] Estimated ±25%. Results generally exhibited substantially higher precision. [c] With a series of aliphatic ketones including primary, secondary, and tertiary α-hydrogens, K_{eq} values in the range 10—25 were observed. [d] Mixtures containing 100% excess of alcohol showed a small decrease in K_{eq}. [e] Cx = cyclohexyl. [f] Similar results are observed with other tri-s-alkylmethanols.

(Table). Of particular interest is the considerably enhanced basicity of the highly hindered tricyclohexylmethanol, pK_A of *ca.* 24, approaching the values reported for tertiary alcohols in Me_2SO.[7] The basicity of this and related tri-s-alkyl methoxide bases is sufficiently high to allow complete conversion of a variety of ketones into their enolates. Thus addition of various ketones, (pentan-3-one, 2,4-dimethylpentan-3-one, 2-methylcyclohexanone, and 2,6-dimethylcyclohexanone) to 1·05—1·1 equiv. of alkoxide resulted rapidly (<1 min) in complete conversion of ketone into enolate; CO i.r. absorption was not detected (<1%) in 0·4—0·5 M solutions.

Bartsch and his co-workers have recently reported an excellent correlation between base strength and $\Delta\Delta F^{\ddagger}$ for elimination of 2-butyl halides[5] in Me_2SO. Product ratios have also been reported for various alkoxides bases in low dielectric media.[10] Using the alkoxide basicities in a low dielectric solvent reported here, it is found that the proportion of but-1-ene increases far faster as R^n size increases than predicted from the slope of Bartsch's correlations. These results support the position that steric effects, considerably amplified by aggregation, *etc.*,[10] play a major role in promoting Hofmann elimination.

(*Received*, 3*rd May* 1974; *Com.* 508.)

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