Table I. Relative Rate Ratios Z_p/Z_m for the M − H Reaction of Substituted Toluenes (I)

X^a	Z_p/Z_m at								
	70^d	50^d	30^d	25^d	20^d	15^d	12^d	11^d	10^d
$OCH_3{}^c$	2.94	2.91	2.83	2.85	2.74	2.65	2.22	1.80	1.1^b
CH_3	1.04	1.02	1.04	0.99	1.00	0.94	0.91	0.95	0.9^b
F	0.99	1.03	1.02	1.00	1.02	0.98	1.00	1.00	
Cl	1.47	1.47	1.39	1.40	1.36	1.49	1.5^b		
Br	1.75	1.85	1.81	1.77	1.70	1.78	1.7^b		
CN	1.00	1.00	0.98	0.99	0.98	0.97	1.00	1.0^b	

[a] X = NO_2 and $COCH_3$ did not show M − H peaks. [b] Measurements made from very low rates. [c] M − H measurements made from methoxytoluenes-d_3. [d] Electron volts.

(except for X = OCH_3) are identical, which in turn is most simply interpreted in terms of transition states of the same structure (tropylium-like, II or III → IV) for each *m*- and *p*-X pair (except for X = OCH_3), and (ii) that the distribution and population of reactive excited states over the entire electron energy range must be very similar for each *m*- and *p*-X substituted isomer pairs of molecular ions.

For substituents X = CH_3, F, and CN, the identical rates $Z_p = Z_m$ imply identical "energies of activation"[3] for each *m*- and *p*-X pair (see ref 1, energy diagram C), which in turn suggests either unrearranged[13] (*e.g.*, III) or rearranged[15] (*e.g.*, II) molecular ions of the same energy. For substituents X = Cl, Br, the different rates $Z_p > Z_m$ indicate different energies of activation ($E_m > E_p$) for each *m*- and *p*-X pair (see ref 1, energy diagram A), which in turn argues for unrearranged (III) molecular ions of differing energies. However, as suggested by the voltage independence of Z_p/Z_m, the transition states for the M − H reaction still have the same energy for each *m*- and *p*-X pair, and therefore in all probability, the same tropylium-like structures, leading to M − H ions IV (X = Cl, Br).

For substituents X = OCH_3, Z_p/Z_m decreases with decreasing electron energy as the threshold is approached (Table I), betraying the higher transition-state energy for the *para* isomer. Also $Z_p > Z_m$, and therefore the "energy of activation"[3] is lower for the *para* isomer in this instance. This information permits assignment of unrearranged (benzylic) structures to both transition states and molecular ions (III → V, X = OCH_3).

With all the substituents studied, the nature of the molecular ion and the transition state for the M − H reaction are thus found to be strongly substituent dependent, and it is not surprising that no correlation of over-all rate (log Z/Z_0)[4] with either σ or σ^+ constants is observed.

Table II. Metastable Ion Characteristics for Decomposition Reactions in Substituted Toluenes (I) at 70 eV[18]

X	Transition	Metastable	$\frac{[\text{Metastable}]}{[\text{parent}]} \times 10^3$	
			m-X	*p*-X
OCH_3	$M \rightarrow M - CH_2O$	69.3	1.1	0.33
	$M - 1 \rightarrow M - CH_3O$	68.4	1.3	0.42
CH_3	$M \rightarrow M - CH_3$	78.2	6.3	6.0
	$M - H \rightarrow M - C_2H_3$	59.5	0.80	0.80
F	$M - H \rightarrow M - C_2H_3$	63.2	0.98	0.93
Cl	$M \rightarrow M - Cl$	65.8	4.3	2.3
Br	$M \rightarrow M - Br$	48.2	1.1	1.6
CN	$M \rightarrow M - HCN$	69.2	4.7	4.6
	$M - H \rightarrow M - H_2CN$	68.2	1.6	1.7

Metastable ion characteristics[17] (Table II) have been recorded for decompositions of the molecular ions and the M − H species and are found to be in accord with the kinetic results. Thus identical metastable abundances[18] for decompositions of *m*- and *p*-X pairs of molecular ions when X = CH_3 and CN demonstrate the existence of common, rearranged parent ions (*e.g.*, II), whereas different metastable abundances[18] when X = OCH_3,[19] Cl, and Br militate for unrearranged parent ions (*e.g.*, III). As before,[6] identical metastable abundances for decomposition of *m*- and *p*-X derived M − H ions provide support for the symmetrical tropylium structure (IV) for all substituents except X = OCH_3, when at least the *para* isomer is benzylic (V).[20]

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[13] Ionization potentials of 9.05 and 8.99 eV have been reported[14] for *m*- and *p*-xylene, respectively, but similar data apparently are not presently available for *meta* and *para* isomers of I, X = F or CN.

[14] G. F. Crable and G. L. Kearns, *J. Phys. Chem.*, **66**, 436 (1962).

[15] Randomization of hydrogens over the molecule by a series of 1,5-sigmatropic shifts is known to occur in thermally excited cycloheptatriene.[16]

[16] J. A. Berson and M. R. Willcott, *J. Amer. Chem. Soc.*, **88**, 2494 (1966), and references cited therein.

[17] T. W. Shannon and F. W. McLafferty, *ibid.*, **88**, 5021 (1966), and subsequent papers in this series.

[18] Metastable abundances were measured over the energy range 70–12 eV, below which their intensities were too low for accurate measurement.

[19] In I, X = OCH_3, however, identical[18] metastable ion characteristics for the *meta* and *para* isomers for an M − CH_3 process (M − CD_3 in I, X = OCD_3) were observed, which means that at least some molecular ion rearrangement is occurring in this case. Together with the kinetic data, this directly implicates at least two different molecular ions (*e.g.*, II and III, X = OCH_3) in unknown proportions, one rearranged and the other not, for each *m*- and *p*-OCH_3 isomer.

[20] J. M. S. Tait, T. W. Shannon, and A. G. Harrison, *J. Amer. Chem. Soc.*, **84**, 4 (1962).

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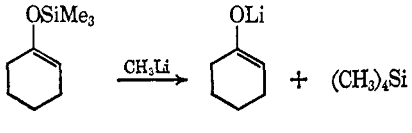
Isolation of Ketone Enolates as Trialkylsilyl Ethers

Sir:

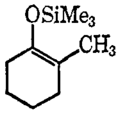
Enolate ions occupy a central place in the chemistry of carbonyl compounds. In connection with our continuing interest in the alkylation of ketones and aldehydes, it became desirable to find a method of trapping metal enolates as isolable derivatives from which they could be regenerated readily.

We have used trialkylsilyl enol ethers to these ends for some time[1] and report here on our experience with these substances. Our interest in trialkylsilyl enol ethers was first aroused by the expectation that they would be readily cleaved by organometallic reagents. In the specific case of a trimethylsilyl enol ether and methyllithium, the products should be the lithium enolate and tetramethylsilane (TMS). The latter does not exchange its hydrogens under the conditions of the reaction and is a useful internal standard for nmr investigation of these enolate solutions.

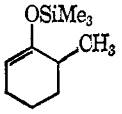


We report here (1) on a generally useful method for the isolation of trialkylsilyl enol ethers, (2) on their properties and hydrolytic stability, and (3) on the value of these derivatives in the isolation of enolates produced in a structure-specific manner.

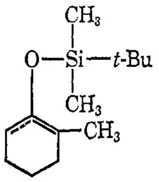
Trimethylsilyl enol ethers are rapidly hydrolyzed by water. They can in some cases be isolated by direct distillation following silylation,[2] but a more generally applicable and satisfactory procedure was eventually found which allowed aqueous work-up. This is illustrated with 2-methylcyclohexanone. The latter (1.2 g) was refluxed in 20 ml of glyme for 3 hr with 1.0 g of 60% sodium hydride dispersion. After cooling, triethylamine and trimethylsilyl chloride (50% excess of each) were added, followed after *ca.* 15 min by dilution with pentane, washing successively with 5% hydrochloric acid and with aqueous sodium bicarbonate.[3] Drying and examination by vpc showed a mixture of I and II in a 27:73 ratio. Less than 2% of ketone was present. The two isomeric enol silyl ethers are easily separated by preparative vpc on 10-ft SF-96 columns at 100°. (Retention times of I and II are 7.5 and 9.3 min, respectively, at a flow rate of 100 ml/min). Pure II could readily be obtained also by distillation through a spinning-band column. It had bp 78–79° (17 mm); ir 1686 cm^{-1}; nmr δ 1.55 (broad singlet, 3 H) and 0.16 (singlet, 9 H); mass spectrum (major peaks): 184 (M), 169 (M $-$ CH$_3$), 141 (156 $-$ CH$_3$), 75 (M $-$ Me$_2$SiOH), 73 (M $-$ Me$_3$Si), 45 (MeSiH$_2^+$). The minor isomer I has ir 1661 cm^{-1}; nmr δ 4.65 (M, 1 H), 0.97 (d, 3 H), and 0.15 (s, 9 H). Acid-catalyzed equilibration (*p*-toluenesulfonic acid in carbon tetrachloride at 85° for 16 hr) gave the equilibrium mixture consisting of 9% I and 91% II.[4]



II



I



III

The hydrolytically more stable *t*-butyldimethylsilyl enol ethers (*cf.* III) could be prepared similarly from the corresponding silyl chloride.[6] Reaction in such cases was allowed to take place for 0.5 hr at room temperature. These silyl ethers could be submitted to the usual aqueous work-up without special precautions.

The silyl enol ethers from six- and five-membered ketones showed double bond stretching frequencies at 1664 ± 6 (six-membered ring) and ~1645 cm^{-1} (five-membered ring) for trisubstituted double bonds and at 1679 ± 7 (six-membered ring) and ~1692 cm^{-1} (five-membered ring) for tetrasubstituted ones. These values are almost identical with those reported for the corresponding ethyl enol ethers.[5] The vinyl hydrogen (*cf.* I) however has its absorption in the nmr at lower field than alkyl enol ethers: δ 4.75 (CCl$_4$) *vs.* 4.43 for the latter, presumably reflecting decreased electron availability due to back-bonding from oxygen to silicon.

Trimethylsilyl enol ethers are rapidly hydrolyzed in either basic or acidic media while the *t*-butyldimethylsilyl ethers are, as expected,[7] much more stable. Some results with II and III are typical. Within 0.5 min at room temperature, hydrolysis of II was complete with 2% aqueous methanolic *p*-toluenesulfonic acid (III showed no cleavage in 4 min and 80% in 4 hr). With 2% aqueous methanolic methoxide hydrolysis of II was 90% complete in 0.5 min (III showed no cleavage in 3 hr, 15% in 26 hr). Aqueous methanolic sodium chloride gave no hydrolysis of II in 3 min, while in the same time sodium bicarbonate (~7%) produced 5% cleavage.

We have examined the ratios (obtained by vpc and nmr) of the less to the more substituted enolates of a number of ketones: **2-methylcyclohexanone**: NaH, equilibrium conditions, 26/74; (C$_6$H$_5$)$_3$CK, kinetic conditions, 67/33; (C$_6$H$_5$)CK, equilibrium conditions, 38/62 (reported[6] 35/65); **2-methylcyclopentanone**: NaH, equilibrium conditions, 29/71; (C$_6$H$_5$)$_3$CK, equilibrium conditions, ~30/70 (reported[8] 22/78); **2-heptanone**: (C$_6$H$_5$)$_3$CK, kinetic conditions, 50/50 (reported[8] 54/46); equilibrium conditions, 42/58 (reported[8] 42/58); **1-decalone**: NaH, equilibrium conditions, 50/50.

The excellent agreement, when comparison is available with the results of House, using acetic anhydride trapping,[5,8] shows that the structures of trimethylsilyl enol ethers isolated correspond accurately to those of the enolates in a given mixture, and it is therefore possible to use the method in the trapping of enolates kinetically generated so as to have a specific structure, *e.g.*, by conjugate addition of Grignard reagents to α,β-unsaturated ketones. The mixture obtained by adding 2.0 g of piperitone IV to an ice-cold solution of 10 ml of 2 *M* methylmagnesium bromide in 10 ml of ether, in the presence of 200 mg of cuprous chloride, was treated, after 5 min, with 4 ml of trimethylsilyl chloride, 5 ml of triethylamine, and 2.5 ml of hexamethylphosphoramide and gave, after 1 hr at room temperature, followed by the usual work-up, 2.9 g of silyl

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[1] *Cf. Chem. Eng. News*, **45**, 138 (Feb 20, 1967).

[2] *Cf.* C. R. Krüger and E. G. Rochow, *J. Organometal. Chem.* (Amsterdam), **1**, 476 (1964); R. Bouchis and E. Frainnet, *Bull. Soc. Chim. France*, 3552 (1967).

[3] Other work in this laboratory has shown that it is often possible merely to add trimethylsilyl chloride in slight excess to the enolate, followed after reaction by removal of solvent and excess silyl chloride *in vacuo* and taking up of the silyl ether in hexane.

[4] The silyl ethers thus fall between enol acetates and enol ethers; *cf.* ref 5.

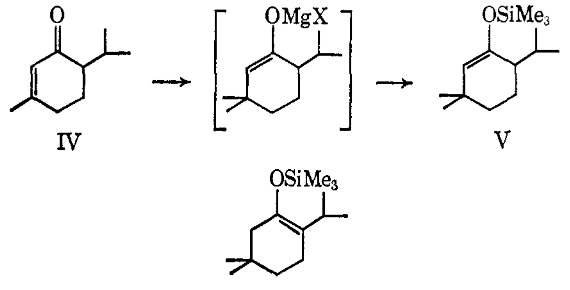
[5] H. O. House and J. Kramer, *J. Org. Chem.*, **28**, 3362 (1963).

[6] L. H. Sommer and L. J. Tyler, *J. Am. Chem. Soc.*, **76**, 1030 (1964).

[7] E. Åckerman, *Acta Chem. Scand.*, **11**, 373 (1957).

[8] H. O. House and B. M. Trost, *J. Org. Chem.*, 30, 2502 (1965).

ether V (ir 1660 cm^{-1}; nmr δ 4.6 (broad singlet, 1 H)). The isomeric enol ether Va with a tetrasubstituted double bond could be obtained by anhydrous acid isomerization of V and has λ_{max} 1672 cm^{-1}.[9]



IV V

Va

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[9] The retention times of V and Va were 7.0 and 7.3 min, respectively, on 10-ft SE-30 columns at 140° (100 ml/min).

[10] We thank the National Science Foundation for the support of this work.

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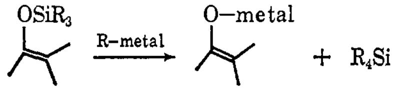
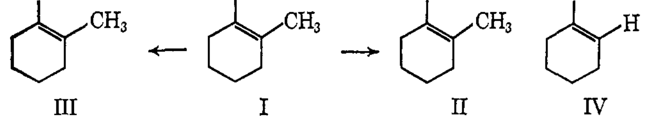
Generation, Nuclear Magnetic Resonance Spectra, and Alkylation of Enolates from Trialkylsilyl Enol Ethers

Sir:

We have found trialkylsilyl enol ethers[1] ideally suited to the generation of a variety of metal enolates *via* reaction with organometallic reagents. The major advantage of this method is that the only extraneous substance formed in the process is an inert tetraalkylsilane (*e.g.*, tetramethylsilane).



The rate of cleavage of silyl enol ethers is strongly dependent on the specific organometallic reagent, the solvent, and the nature of the trialkylsilyl group. For instance, at room temperature, methyllithium completely transforms the trimethylsilyl enol ether of 2-methylcyclohexanone (I) into the lithium enolate II within 6 min in glyme and in about 1 hr in ether, while in benzene, cleavage with butyllithium is only about 15% complete within 1 hr. Complete cleavage is achieved by refluxing for 1 hr. Transformation into the magnesium enolate III *via* methylmagnesium bromide requires refluxing in glyme for 24 hr. It is worth noting that hindered silyl ethers such as *t*-butyldimethylsilyl enol ethers are only cleaved to the extent of 1% in 24 hr by methylmagnesium bromide in refluxing glyme and are stable for 1 day to methyllithium in ether at room temperature. Cleavage may, however, be accomplished quantitatively in 20 hr at room temperature with methyllithium in glyme.



III I II IV

The generation of enolate ions from the corresponding silyl enol ethers allows determination of the effect of the metal ion and solvent composition on the nature of these species. We have now carried out an examination of some of the metal enolates of cyclohexanone with respect to the position of their vinyl protons in the nmr. In THF-d_8, the vinyl proton appeared as a triplet centered at δ 4.16 in the lithium enolate IV, R = Li, and at δ 4.78 for the magnesium enolate IV, R = MgBr. In glyme, in which the vinyl proton of the lithium enolate appears at δ 4.24, that of the potassium enolate IV, R = K, is at δ $\sim$3.9. For comparison, the proton in the trimethylsilyl enol ether IV, R = $SiMe_3$, is at 4.83 in THF-d_8 and 4.75 in CCl_4, a solvent in which the enol acetate, ethyl enol ether, and pyrrolidine enamine of cyclohexanone (IV, R = Ac, Et, pyrrolidinyl) show their vinyl protons at δ 5.27, 4.43, and 4.13, respectively.

This last sequence, in which the proton is progressively more shielded as electron availability on the double bond is increased, allows the reasonable assumption that the position of the vinyl proton absorption reflects electron availability at the β carbon of the enolate salt and that the chemical shift of that proton gives a rough indication of the looseness of the oxygen–metal bond. This last property should be related to the ability of the enolate to function as a base toward protons α to a carbonyl group, and thus, to participate in the proton transfer reactions which are responsible for the loss of structural specificity in enolate reactions, as well as for undesirable polyalkylation.

Fortunately, tightness of the oxygen–metal bond sufficient to prevent proton transfer is not prohibitive with respect to reaction with sufficiently active electrophilic agents, *e.g.*, methyl iodide. These were, of course, the considerations which had led us to introduce the use of lithium enolates, rather than their sodium or potassium analogs, in the alkylation of specifically generated enolates.[2]

The remarkable observation has been made that addition of hexamethylphosphoramide (HMP) has very little effect on the position of the vinyl proton absorption in these enolates. The lithium enolate of cyclohexanone shows practically no shift from THF-d_8 to THF-d_8 containing 40% HMP. The magnesium enolate shows some upfield shift from δ 4.78 to 4.62 with 50% HMP, and the vinyl proton of the potassium salt which absorbs at δ $\sim$3.9 in glyme shifts $\sim$3.72 in glyme–30% HMP.

We could not detect an appreciable solvent effect of HMP on the position of the olefinic proton of vinyl ethers, enamines, or enol silyl ethers, and since, in any event, the addition of HMP did not lead to the same position of the vinyl hydrogen starting with enolates from different metals, it is clear that most metal enolates are not transformed into free ions by this dipolar aprotic solvent.[3]

The preparation of lithium or magnesium enolates *via* silyl enol ethers has considerable synthetic utility, since they are produced free of substances (such as

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[1] G. Stork and P. Hudrlik, *J. Am. Chem. Soc.*, 90, 4462 (1968).

[2] G. Stork, P. Rosen, and N. L. Goldman, *ibid.*, **83**, 2965 (1961); G. Stork, P. Rosen, N. L. Goldman, R. V. Coombs, and J. Tsuji, *ibid.*, **87**, 275 (1965).

[3] Compare H. E. Zaugg and A. D. Schaefer, *ibid.*, **87**, 1857 (1965).