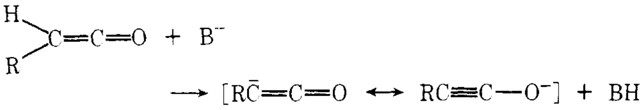
Reaction of Trimethylsilylketene with Strong Base. Evidence for Ketene Enolate Formation

Summary: Evidence for the formation of a ketene enolate of trimethylsilylketene, based on trapping experiments with trimethylchlorosilane, is described.

Sir: The β hydrogens of aldoketenes are potentially acidic and it is possible to conceive of base-promoted ketene enolate formation in a fashion analogous to that for the familiar aldehyde or ketone enolates. Indeed, Bryce-Smith obtained insoluble, presumably polymeric materials on treatment of ketene with copper or silver salts in the presence of weak bases.[1] The products were formulated as metal ketenides, $M_2C{=}C{=}O$ ($M = Cu^I, Ag^I$). We present here evidence for the formation of a lithium enolate derived from trimethylsilylketene (1).



$$\text{H(R)C}{=}C{=}O + B^- \longrightarrow [R\bar{C}{=}C{=}O \longleftrightarrow RC{\equiv}C{-}O^-] + BH$$

The reaction of bis(trimethylsilyl)ketene (2) with n-butyllithium proceeds normally, if somewhat sluggishly, at room temperature. The reaction mixture remains colorless and quenching gives good yields of the expected addition product 3. In contrast, when n-butyllithium was added to 1 under the same conditions, the solution turned black immediately and quenching after periods of 5 min to 24 h gave trimethylsilylcarbinol as the only GLC mobile product of longer retention time than the solvent. The complete absence of the following addition products was established: $(CH_3)_3SiCH_2CO\text{-}n\text{-}C_4H_9$, $(CH_3)_3SiCH_2COH(n\text{-}C_4H_9)_2$, $CH_3CO\text{-}n\text{-}C_4H_9$, and $CH_3COH(C_4H_9)_2$.

$$\underset{\textbf{2}}{[(CH_3)_3Si]_2C{=}C{=}O} + n\text{-}C_4H_9Li \xrightarrow[2.\ H_3O^+]{1.\ THF,\ 25\ °C,\ 8\ h} \underset{\textbf{3}\ (85\%)}{[(CH_3)_3Si]_2CHCO\text{-}n\text{-}C_4H_9}$$

Addition of 1 equiv of 1 to a 0.5 M THF solution of n-butyllithium at −78 °C gave a colorless solution. Quenching this solution after 5 min with an equivalent amount of trimethylchlorosilane gave a 23% yield of 2, presumably by formation of the ketene enolate 4.

$$\underset{\textbf{1}}{(CH_3)_3SiHC{=}C{=}O} + n\text{-}C_4H_9Li \xrightarrow{-78\ °C} \underset{\textbf{4}}{(CH_3)_3SiC{\equiv}COLi} \xrightarrow{(CH_3)_3SiCl} \underset{(23\%,\ GLC)}{\textbf{2}}$$

Addition of 1 to solutions of n-butyllithium at −100 °C increased the yield of 2 to 60–65%. Finally, addition of 1 to 0.1 M solutions of n-butyllithium at −100 °C gave 80–90% yields of 2. Reaction mixtures obtained by this latter procedure turned black when allowed to warm to 0 °C for 15 min prior to the addition of trimethylchlorosilane and only 15–20% yields of 2 were obtained.

Similar results were obtained using other bases, although somewhat lower yields of 2 were obtained. The red color of trityllithium is rapidly discharged by 1 and, though the yield of 2 is small, triphenylmethane was recovered quantitatively. This is additional evidence that the sequence leading to 2 involves a simple acid–base reaction.

$$\textbf{1} + BLi \xrightarrow[2.\ (CH_3)_3SiCl]{1.\ -100\ °C,\ THF} [(CH_3)_3Si]_2C{=}C{=}O$$

$$20\text{–}30\%,\ B = tert\text{-}C_4H_9;\quad 15\text{–}20\%,\ B = C(C_6H_5)_3;\quad 15\%,\ B = N[CH(CH_3)_2]_2$$

Attempts to trap the enolate 4 with other electrophiles, ϵ^+, have so far been unsuccessful. No GLC mobile products were obtained by quenching reaction mixtures of 1 and n-butyllithium with methyl iodide, benzyl bromide, acetone, or acetic anhydride. In addition, quenching with a variety of proton acids including water, acetic acid, or methanesulfonic acid returned only trace amounts of 1. These negative results may simply be due to the instability of 4 or the instability of the product alkynol ethers 5 or ketenes 6.

$$\underset{\textbf{4}}{(CH_3)_3SiC{\equiv}COLi} + \epsilon^+ \rightarrow \underset{\textbf{5}}{(CH_3)_3SiC{\equiv}CO\epsilon} + \underset{\textbf{6}}{(CH_3)_3Si(\epsilon)C{=}C{=}O}$$

The following procedure describes a typical trapping experiment using trimethylchlorosilane. A 50-mL flask equipped with septum inlet, mercury bubbler, and magnetic stirrer was flushed with argon and immersed in a −100 °C cooling bath (liquid nitrogen and ethanol). The flask was charged with 10 mL of THF followed by 0.67 mL (1.0 mmol) of a 1.5 M solution of n-butyllithium in hexane. After 15 min of stirring, 0.114 g (1.0 mmol) of trimethylsilylketene[2] was injected over a 5-min period. The colorless solution was stirred an additional 15 min and then 0.131 g (1.2 mmol) of trimethylchlorosilane was injected all at once. The solution was allowed to reach room temperature and analyzed by GLC (6 ft × 0.25 in. Carbowax 20 M column). The presence of 0.9 mmol (90%) of bis(trimethylsilyl)ketene[3] was established. Evaporation of the solvent at 25 °C gave a residue (0.16 g, 85%) of pure 2 based on either ^1H NMR [δ 0.25 (s)] or IR [2085, 1295 cm^{-1} (lit.[4] 2085, 1295 cm^{-1})] spectral examination.

Acknowledgment is made to the National Science Foundation for partial support of this research.

References and Notes

(1) (a) E. T. Blues, D. Bryce-Smith, H. Hirsch, and M. J. Simons, *Chem. Commun.*, 699 (1970); (b) E. T. Blues, D. Bryce-Smith, B. Kettlewell, and M. Roy, *J. Chem. Soc., Chem. Commun.*, 921 (1973).

(2) Trimethylsilylketene was prepared as described by R. A. Ruden, *J. Org. Chem.*, **39**, 3607 (1974).

(3) Authentic samples of bis(trimethylsilyl)ketene were available from an earlier study: D. F. Sullivan, R. P. Woodbury, and M. W. Rathke, *J. Org. Chem.*, **42**, 2038 (1977).

(4) L. L. Shchukovskaya, A. I. Koltsov, A. N. Lazarev, and R. I. Palchick, *Dokl. Akad. Nauk, SSSR*, **179**, 892 (1968).

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Received September 22, 1977

An Approach to Cytochalasins: Diels–Alder Addition of α,β-Unsaturated Imides

Summary: Diels–Alder reactions of α,β-unsaturated imides are considerably accelerated relative to the reaction of the parent amides. This activating effect is used for the synthesis of a cytochalasin precursor.

Sir: Weinreb and Auerbach have described an elegant synthetic approach[1] to cytochalasins[2] by internal Diels–Alder addition of the diene ester 3. This interesting reaction controls the regiochemistry of cycloaddition and defines four asymmetric centers in the adduct 4. However, the problem of C-3 benzyl stereochemistry and the correct C-3 oxidation level remains unsolved.