Reaction of (Trimethylsilyl)ketene with Silylated Ketene Acetals

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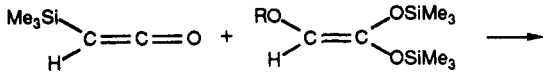
We have reported on the [2 + 2] cycloaddition of (trimethylsilyl)ketene with electron-rich tetraalkoxyethylenes to yield products that on hydrolysis give semisquaric acid.[1] The cycloaddition of this ketene with dimethyl- and diethylketene acetals under rather vigorous conditions gave silicon-containing cyclobutanones.[2] It is pertinent to realize that ketene acetals are electron-rich olefins and well suited for cycloaddition reactions with this isolable and stable ketene. We now wish to describe the reaction of (trimethylsilyl)ketene (1), with some readily available O-silylated ketene acetals to yield acyclic unsaturated esters.



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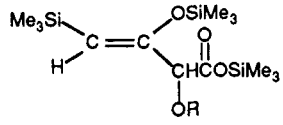
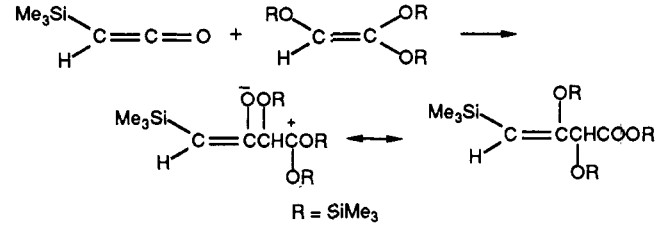


2, R = Me
3, R = $SiMe_3$

The reaction of equimolar quantities of 1 and (trimethylsiloxy)ketene bis(trimethylsilyl) acetal under a nitrogen atmosphere at ambient temperature resulted in a 95% yield of trimethylsilyl 2,3-bis(trimethylsiloxy)-4-(trimethylsilyl)-3-butenoate (3) after 24 h. The proton nuclear magnetic resonance spectrum of this unsaturated ester was interesting in that four singlets appeared with the same ratios for the four different trimethylsilyl substituents and also two singlets for the vinyl and allylic protons. The ester revealed a carbonyl band at 1740 cm^{-1} and a carbon–carbon double bond signal at 1620 cm^{-1} in the infrared spectrum. The NMR spectrum and the vapor-phase chromatography data suggested that only a single isomer had been formed. This would be expected to be the *E* isomer on the basis of the large steric requirements of the two substituents bonded to the vinyl system.

The reaction of equimolar quantities of 1 and methoxyketene bis(trimethylsilyl) acetal under a nitrogen atmosphere at ambient temperature resulted in a 95% yield of trimethylsilyl 2-methoxy-3-(trimethylsiloxy)-4-(trimethylsilyl)-3-butenoate (2). The proton NMR spectrum revealed three singlets with the same ratios for the three different trimethylsilyl substituents and also a singlet for three protons for the methyl group and a singlet for the vinyl proton. Also, a carbonyl band at 1740 cm^{-1} and a carbon–carbon double bond signal at 1620 cm^{-1}. The NMR spectrum and the VPC data suggested that only a single isomer had been formed.

The above results are consistent with a two-step mechanistic pathway involving a dipolar intermediate as originally proposed by Scarpati and co-workers.[3] The dipolar intermediates achieves stabilization by a 1,5-silyl migration to yield the unsaturated ester.



R = $SiMe_3$

The attempted reaction of 1 with simple olefins and silyl enol ethers has been unsuccessful. Since the trimethylsilyl substituent may function as either an electron donor or electron acceptor, firm conclusions regarding electronic effects are difficult to make.

(Trimethylsilyl)ketene is a colorless liquid that boils at 82 °C, is very stable (and yet an aldoketene, which is most unusual), does not dimerize upon heating, and can be stored for long periods of time.[4] *tert*-Butylketene is much more reactive than 1. The trimethylsilyl substituent is bulkier than the *tert*-butyl group due to the longer silicon–carbon bond (1.84 Å) vs the carbon–carbon single bond (1.54 Å). Thus, the methyl groups on silicon are further from the (trimethylsilyl)ketene functionality compared to *tert*-butylketene. Another measure of reactivity is the cone angle, which is the apex angle of a cylindrical cone, centered 1.84 Å from the center of the silicon atom that just touches the van der Waals radii of the hydrogen of the methyl group. The cone angle in (trimethylsilyl)-ketene is smaller than that in *tert*-butylketene. Therefore, on the basis of the cone angle and steric hinderance, *tert*-butylketene would be expected to be less reactive than (trimethylsilyl)ketene.

The chemical shift for the sp^2-hybridized carbon atom resonance in the carbon-13 NMR spectrum of 1 is found at the extremely high field position of 0.7 ppm. This is the most shielded sp^2 carbon atom observed. This high field position is indicative of an electron-donating silyl group in this particular environment. Ths shielding of the heteroatom increases in the order of Si < Ge < Sn.[5] In contrast, it is interesting to note that vinyltrimethylsilane, an electron-efficient olefin, has low reactivity in cycloaddition reactions with ketenes. Furthermore, the addition of hydrogen halides to vinyltrimethylsilane occurs anti-Markovnikov. These results suggest the trimethylsilyl substituent in this environment is electron withdrawing through the Pπ–dπ bonding between the vinyl group and the silicon atom.

Experimental Section

The proton NMR spectra were recorded on a Perkin-Elmer R-24B nuclear magnetic resonance spectrometer employing carbon tetrachloride as the solvent and chloroform as the internal standard. Analytical and spectroscopic samples were obtained by VPC on a Perkin-Elmer Model 3920-B gas chromatograph using either a 6 ft × $^1/_4$ in. column packed with 10% SE-30 on an acid-washed Chromosorb W (80/100 mesh) support or a 10 ft × $^1/_4$ in. column packed with 10% QF-1 on acid-washed Chromosorb W (30/100 mesh) support. The infrared spectra were

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obtained on a Beckman IR 33 spectrometer. Mass spectra were obtained on a Hitachi-Perkin-Elmer RMU-6E double focusing mass spectrometer and a Finnigan GC/MS 3200 with a 6100 data system. Ethoxyacetylene was commercially available and also was prepared by bromination of ethyl vinyl ether, dehydrohalogenation with *n*-butylamine, and KOH, respectively.[6]

(Trimethylsilyl)ketene was prepared by a procedure similar to that of Ruden.[4] (Trimethylsiloxy)ketene bis(trimethylsilyl) acetal and methoxyketene bis(trimethylsilyl) acetal were prepared according to a procedure described by Wissner.[7]

Typical Procedure for Reaction of (Trimethylsilyl)ketene with Ketene Bis(trimethylsilyl) Acetal. A 17.5-mmol (2-g) portion of (trimethylsilyl)ketene was added dropwise over 2 h to a stirred solution of 17.5 mmol of ketene bis(trimethylsilyl) acetals at room temperature under a nitrogen atmosphere. After the addition was complete the mixture was stirred until the ketene had been consumed as evidenced by the disappearance of the ketene band in the IR spectrum (24 h). The adduct was vacuum distilled and further purified by VPC.

Trimethyl 2,3-Bis(trimethylsiloxy)-4-(trimethylsilyl)-3-butenoate (3). From a 17.5-mmol (2-g) portion of (trimethylsilyl)ketene, 17.5 mmol (5.12 g) of (trimethylsiloxy)ketene bis(trimethylsilyl) acetal was isolated 6.7 g (94%) of **3**, which distilled at 75–80 °C (0.05 Torr): IR (neat) sharp bands at 2980, 1740 (C=O), 1620 cm^{-1} (C=C); NMR (CCl_4 with $CHCl_3$ as reference) δ 0.15 (s, 9 H), 0.20 (s, 9 H), 0.26 (s, 9 H), 0.30 (s, 9 H), 4.35 (s, 1 H), 4.50 (s, 1 H); mass spectrum, parent peak *m/e* at 406, 407 (M + 1), 408 (M + 2), 409 (M + 3), 391 (M - 15), 292, 221, 147, base peak at *m/e* 73.

Anal. Calcd for $C_{16}H_{38}O_4Si_4$: C, 47.29; H, 9.36. Found: C, 47.01; H, 9.74.

Trimethylsilyl 2-Methoxy-3-(trimethylsiloxy)-4-(trimethylsilyl)-3-butenoate (2). A 17.5-mmol (2.0-g) portion of (trimethylsilyl)ketene and 17.5 mmol (4.1 g) of methoxyketene bis(trimethylsilyl) acetal were reacted to give 5.8 g (95%) of **2**, bp 60–65 °C (0.05 Torr): IR (neat) sharp bands at 2980, 1740 (C=O), 1620 cm^{-1} (C=C); NMR (CCl_4 with $CHCl_3$ as reference) δ 0.15 (s, 9 H), 0.26 (s, 9 H), 0.34 (s, 9 H), 3.95 (s, 3 H), 4.52 (s, 1 H); mass spectrum parent peak *m/e* at 348, 349 (M + 1), 350 (M + 2), 351 (M + 3), 333 (M - 15), 317, 234, 231, 186, 147, base peak at *m/e* 73.

Anal. Calcd for $C_{14}H_{32}O_4Si_3$: C, 48.3; H, 9.20. Found: C, 47.97; H, 9.42.

Acknowledgment. We are grateful to the Robert A. Welch Foundation for support of this work.

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Synthesis of (*S*)-β,β,β-Trifluorolactic Acid and (*S*)-α-Methoxy-α-(trifluoromethyl)phenylacetic Acid from (*R*)-Methyl *p*-Tolyl Sulfoxide

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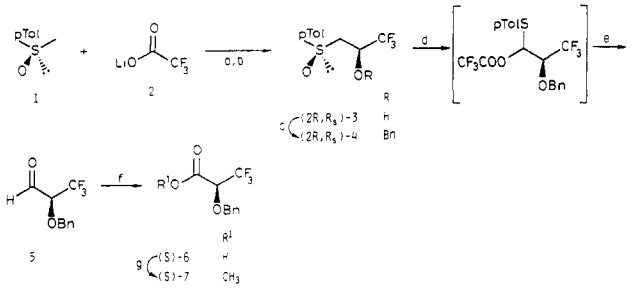
Selectively fluorinated organic compounds are finding increasing applications in several fields.[1] Fluorinated substances most commonly employed in analytical,[2] biological,[3] and medicinal chemistry[4] contain a single fluorine atom or a trifluoromethyl group. We have already reported the preparation of some chiral and nonracemic monofluorinated products.[5]

In this paper we describe the asymmetric synthesis of two interesting trifluoromethyl-substituted products: the (*S*)-methyl *O*-benzyl-β,β,β-trifluorolactate (**6**) (a compound that has been used in racemic form in medicinal and biological chemistry)[6] and the (*S*)-α-methoxy-α-(trifluoromethyl)phenylacetic acid (**10**) (a reagent commonly employed in analytical chemistry).[7]

Scheme I. Synthesis of (*S*)-Methyl *O*-Benzyl-β,β,β-trifluorolactate[a]



[a] Reagent and conditions: (a) LDA, THF, −78 °C; (b) $NaBH_4$, MeOH, NH_4OH, −40 °C; (c) NaH, BnBr DMF, 0 °C; (d) $(CF_3CO)_2O$, 2,4,6-trimethylpyridine, acetonitrile, 0 °C; (e) $HgCl_2$, H_2O, room temperature; (f) $NaClO_2$, KH_2PO_4, *tert*-butyl alcohol, 2-methyl-2-butene; (g) CH_2N_2, Et_2O, room temperature.

In our synthetic procedure, (2*R*)-1,1,1-trifluoro-3(*R*)-[(4-methylphenyl)sulfinyl]propan-2-ol (**3**), obtained through acylation of the lithium derivative of (*R*)-methyl 4-methylphenyl sulfoxide[8] (**1**) with lithium trifluoroacetate (**2**) and selective reduction of the so-formed trifluorosulfinylpropanone,[9] was *O*-benzylated in high yield by using proper reaction conditions (Scheme I). The so-formed (2*R*,R_S)-(benzyloxy)sulfinyl derivative **4** was treated with trifluoroacetic anhydride and 2,4,6-trimethylpyridine.[10] A clean Pummerer rearrangement occurred and gave an intermediate, (2*R*)-2-(benzyloxy)-1,1,1-trifluoro-3-[(trifluoroacetyl)oxy]-3-[(4-methylphenyl)thio]-propane, which was not isolated but directly hydrolyzed with mercury(II) chloride. (*S*)-*O*-Benzyl-β,β,β-trifluorolactic aldehyde (**5**) was thus produced and directly oxidized with sodium chlorite[11] to the correspondign (*S*)-β,β,β-trifluorolactic acid **6**, which afforded the ester **7** by treatment with diazomethane.

Similarly, the 1,1,1-trifluoro-2-phenyl-3(*R*)-[(4-methylphenyl)sulfinyl]propan-2-ol (**9**) was obtained as a 3:1 mixture of the 2*R*,R_S and 2*S*,R_S diastereoisomers (Scheme II) through hydroxyalkylation of the lithium derivative of (*R*)-methyl *p*-tolyl sulfoxide (**1**) with 1,1,1-trifluoroacetophenone (**8**). Single diastereoisomers were easily obtained

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