1-Trimethylsilyloxy-1-cyclopropylethylene: A Useful Reagent for the Preparation of β-Cyclopropyl-α,β-unsaturated Ketones

Paul A. Grieco*[1] and Yasufumi Ohfune

*Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15260*

We report below the preparation of 1-trimethylsilyloxy-1-cyclopropylethylene (1) and its application to the synthesis of β-cyclopropyl-α,β-unsaturated ketones (vinylcyclopropanes), which are currently of interest from a synthetic viewpoint.[2] The preparation and thermal rearrangement of β-cyclopropyl-α,β-unsaturated ketones have been the subject of several recent accounts in the literature.

β-Cyclopropyl-α,β-unsaturated ketones have previously been prepared by 1,4-conjugate addition of either lithium phenylthio(cyclopropyl)cuprate or lithium dicyclopropylcuprate to β-halo-α,β-unsaturated ketones (eq 1).[2a,3] β-Vinyl-

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$$(2)$$
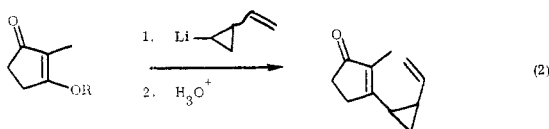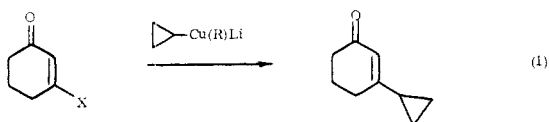
cyclopropyl enones have been prepared by 1,2 addition of 1-lithio-2-vinylcyclopropane to 3-alkoxy enones as illustrated in eq 2.[4-6] Finally, Marino has reported a route to functionalized β-cyclopropyl enones employing 2-methylcyclopentenone 3-dimethylsulfoxonium methylide (eq 3).[7]

$$(3)$$
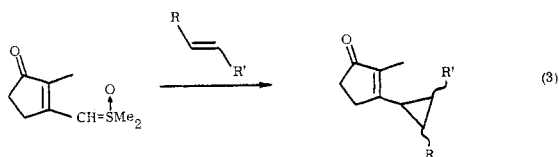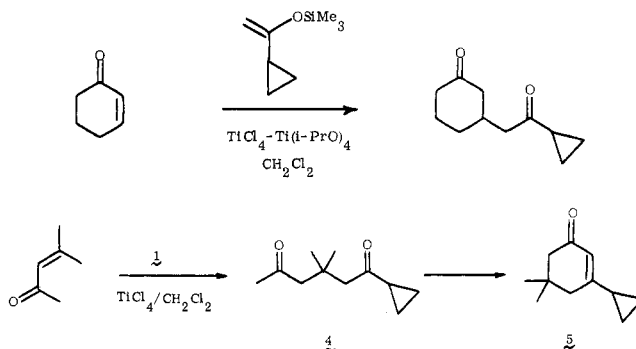
We wish to report an efficient, convenient two-step synthesis of β-cyclopropyl enones which complements existing synthetic methodology. Our method employs the 1,4 addition of 1-trimethylsilyloxy-1-cyclopropylethylene (1) to Michael acceptors followed by aldol cyclization. The method as applied to α,β-unsaturated ketones is depicted in eq 4.


$$(4)$$
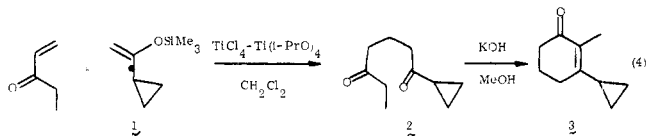
The required 1-trimethylsilyloxy-1-cyclopropylethylene (1) can, in principle, be prepared directly by silylating cyclopropyl methyl ketone employing triethylamine–chlorotrimethylsilane or indirectly via silylation of its corresponding enolate employing chlorotrimethylsilane. Using the latter approach, commercially available cyclopropyl methyl ketone upon treatment at −78 °C with lithium diisopropylamide in tetrahydrofuran followed by addition of chlorotrimethylsilane gave a 78% yield after distillation of 1-trimethylsilyloxy-1-cyclopropylethylene as a colorless liquid (see Experimental Section).

In a preliminary experiment we observed the smooth Michael addition (92%) of silyl enol ether 1 to cyclohexenone in methylene chloride using 1.1 equiv of titanium tetrachloride and 0.55 equiv of titanium tetraisopropoxide.[8] Similar treat-

ment of ethyl vinyl ketone with silyl enol ether 1 gave a 66% yield of 1,5-diketone 2, which upon treatment with methanolic potassium hydroxide gave rise to an 83% yield of β-cyclopropyl enone 3 (eq 4). Mesityl oxide underwent a smooth reaction in 93% yield with 1 in methylene chloride employing only titanium tetrachloride. The resulting diketone 4 upon cyclization (KOH/MeOH) generated the β-cyclopropyl enone 5.

The Michael reaction of compound 1 with 2-nitro-1-butene[9] [TiCl₄ (1.1 equiv)–Ti(i-PrO)₄ (0.55 equiv), methylene chloride, −78 °C] followed by aqueous treatment at 60–65 °C and aldol cyclization [KO-t-Bu, t-BuOH–benzene (2:1), 15 min] demonstrates the potential of this reaction sequence for the synthesis of β-cyclopropylcyclopentenones of type 6 (eq 5).

$$(5)$$
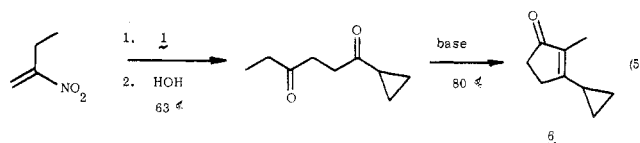
Experimental Section

All melting points and boiling points are uncorrected. Infrared (IR) spectra were determined on a Perkin-Elmer 247 grating infrared spectrometer. Nuclear magnetic resonance (NMR) spectra were recorded at 60 MHz (Varian A-60D or T-60 spectrometer). Chemical shifts were reported in parts per million (δ) relative to tetramethylsilane (Me₄Si) (δ_{Me_4Si} 0.00 ppm) as an internal standard. Low-resolution mass spectra were recorded on an LKB-9000 instrument. High-resolution spectra were recorded on a Varian MAT CH5-DF instrument.

Reactions were run under an atmosphere of nitrogen. "Dry" solvents were dried immediately before use. Tetrahydrofuran was distilled from lithium aluminum hydride. *tert*-Butyl alcohol was freshly distilled from potassium. Methylene chloride was passed through a column of alumina. Titanium tetrachloride was distilled prior to use.

1-Trimethylsilyloxy-1-cyclopropylethylene (1). A solution of 3.6 g (42.9 mmol) of cyclopropyl methyl ketone in 6.0 mL of anhydrous tetrahydrofuran was added dropwise over a period of 20 min to a cooled (−78 °C) solution of lithium diisopropylamide [prepared from diisopropylamine (10 mL, 72 mmol) and n-butyllithium (44 mL, 68 mmol)] in 70 mL of dry tetrahydrofuran. After the reaction mixture was stirred an additional 30 min at −78 °C, 12.5 mL (100 mmol) of chlorotrimethylsilane was added. Stirring was continued for 1 h. The reaction was quenched by the addition of water (10 mL) followed by 300 mL of pentane. The separated organic layer was washed with water and dried over anhydrous magnesium sulfate. Evaporation of the solvent under reduced pressure afforded a liquid which upon distillation gave 4.35 g (78%) of pure 1-trimethylsilyloxy-1-cyclopropylethylene: bp 38–40 °C (12 mmHg); IR (CCl₄) 1650 cm⁻¹; NMR (CCl₄) δ 4.02 (d, 1 H, J = 1.0 Hz), 3.91 (d, 1 H, J = 1.0 Hz), 1.25 (m, 1 H), 0.50 (m, 4 H), 0.19 (s, 9 H).

Addition of 1-Trimethylsilyloxy-1-cyclopropylethylene to Cyclohexenone. A solution of 418 mg (2.2 mmol) of titanium tetrachloride and 312 mg (1.1 mmol) of titanium tetraisopropoxide in 2.5 mL of methylene chloride was added dropwise (∼10 min) to a cooled solution (−78 °C) of 198 mg (2.0 mmol) of cyclohexenone and 342 mg (2.2 mmol) of 1-trimethylsilyloxy-1-cyclopropylethylene in 7.0 mL of methylene chloride. After 45 min at −78 °C the reaction was quenched with 10% aqueous potassium carbonate solution (2.0 mL). The organic layer was diluted with 30 mL of ether, separated, and dried over anhydrous magnesium sulfate. After filtration and removal

of the solvents in vacuo there was obtained an oil which was directly purified on 50 g of silica gel. Elution with hexane–ether (3:1) gave 333 mg (92%) of pure Michael adduct: bp 105 °C (bath temperature) (15 mmHg); IR (CCl$_4$) 3080, 1700, 1712 cm^{-1}; NMR (CCl$_4$) δ 0.64–1.00 (m, 4 H). Anal. Calcd for C$_{11}$H$_{16}$O$_2$: M$^+$ 180.11503. Found: M$^+$ 180.11523.

2-Methyl-3-cyclopropylcyclohex-2-enone (3). A solution of 418 mg (2.2 mmol) of titanium tetrachloride and 312 mg (1.1 mmol) of titanium tetraisopropoxide in 3.0 mL of methylene chloride was added dropwise over a period of 10 min to a solution of 168 mg (2.0 mmol) of ethyl vinyl ketone and 342 mg (2.2 mmol) of silyl enol ether 1 in 8 mL of methylene chloride cooled to −78 °C. Stirring at −78 °C was continued for 45 min. The reaction was quenched with 10% aqueous potassium carbonate solution and the resulting diketone was extracted with methylene chloride. The combined organic extracts were washed with brine, dried over anhydrous magnesium sulfate, and evaporated under reduced pressure. The resulting crude diketone was chromatographed on 40 g of silica gel. Elution with hexane–ether (3:1) gave 221 mg (66%) of diketone 2: bp 75 °C (bath temperature) (16 mm Hg); IR (CCl$_4$) 3088, 1712, 1698 cm^{-1}; NMR (CCl$_4$) δ 2.7–2.2 (m, 6 H), 2.1–1.5 (m, 3 H), 1.01 (t, 3 H, J = 7 Hz), 1.0–0.7 (m, 4 H).

The above diketone (160 mg, 0.95 mmol) was treated with potassium hydroxide (84 mg, 1.5 mmol) in 4.0 mL of methanol for 16 h at room temperature. The reaction mixture was quenched by the addition of a saturated ammonium chloride solution and the product was extracted with ether. The combined ethereal extracts were washed with brine, dried (MgSO$_4$), and evaporated in vacuo. Chromatography of the crude product on 20 g of silica gel afforded 120 mg (84%) of crystalline enone 3: mp 35 °C (lit.[2a] mp 36–37 °C); IR (CCl$_4$) 3080, 1665, 1616 cm^{-1}; NMR (CCl$_4$) δ 1.83 (s, 3 H), 0.6–0.9 (m, 4 H).

3-Cyclopropyl-5,5-dimethylcyclohex-2-enone (5). A solution of 625 mg (3.33 mmol) of titanium tetrachloride in 6.0 mL of methylene chloride was added dropwise over a period of 15 min to a cooled (−78 °C) solution of 300 mg (3.06 mmol) of mesityl oxide and 520 mg (3.33 mmol) of silyl enol ether 1 in 15 mL of methylene chloride. After an additional 30 min at −78 °C, the reaction was quenched by the addition of a 10% aqueous potassium carbonate solution. Extraction with chloroform followed by drying (MgSO$_4$) afforded 700 mg of crude diketone which was chromatographed on silica gel. Elution with ether–hexane (1:1) gave 508 mg (93%) of pure 1,5-diketone 4: bp 90 °C (bath temperature) (15 mmHg); IR (CHCl$_3$) 1710, 1695 cm^{-1}; NMR (CCl$_4$) δ 2.71 (s, 2 H), 2.57 (s, 2 H), 2.02 (s, 3 H), 1.60 (m, 1 H), 1.08 (s, 6 H), 0.82 (m, 4 H).

The above diketone (300 mg, 1.6 mmol) was treated with 108 mg (2.0 mmol) of potassium hydroxide in 2.0 mL of methanol at room temperature for 8 h. The reaction was quenched with saturated aqueous ammonium chloride solution and worked up as described above. Purification of the crude enone on silica gel gave 250 mg (93%) of pure 5: bp 70 °C (bath temperature) (15 mmHg); IR (CCl$_4$) 3080, 1665, 1621 cm^{-1}; NMR (CCl$_4$) δ 5.78 (bs, 1 H), 2.2–2.0 (m, 4 H), 1.45 (m, 1 H), 1.08 (s, 6 H), 1.0–0.6 (m, 4 H).

2-Methyl-3-cyclopropylcyclopent-2-enone (6). A solution of 418 mg (2.2 mmol) of titanium tetrachloride and 312 mg (1.1 mmol) of titanium tetraisopropoxide in 3.0 mL of methylene chloride was added slowly (10 min) to a cooled (−78 °C) solution of 202 mg (2.0 mmol) of 2-nitro-1-butene and 342 mg (2.2 mmol) of 1-trimethylsilyloxy-1-cyclopropylethylene in 7.0 mL of methylene chloride. After 1.5 h at −78 °C, 2.0 mL of water was added and the temperature of the reaction was gradually raised to 40 °C. The reaction mixture was refluxed for 5 h. The reaction was diluted with water and the product isolated by extraction with ether. The combined ether extracts were washed with saturated sodium bicarbonate solution and dried over anhydrous magnesium sulfate. Removal of the solvent under reduced pressure gave crude diketone which was chromatographed on silica gel. Elution with hexane–ether (4:1) gave 194 mg (63%) of pure cyclopropyl 3-oxopentyl ketone: bp 65 °C (bath temperature); IR (CCl$_4$) 3085, 1718, 1700 cm^{-1}; NMR (CCl$_4$) δ 2.9–2.2 (m, 6 H), 1.91 (m, 1 H), 1.1–0.6 (m, 4 H), 1.03 (t, 3 H, J = 7 Hz). Anal. Calcd for C$_9$H$_{14}$O$_2$: M$^+$ 154.09938. Found: M$^+$ 154.09912.

A solution of the above diketone (100 mg, 0.71 mmol) in 1.0 mL of dry benzene was added to a solution of potassium *tert*-butoxide in *tert*-butyl alcohol [prepared from 39 mg (1.0 mmol) of potassium in 2.0 mL of *tert*-butyl alcohol]. After 15 min the reaction was quenched by addition of aqueous ammonium chloride. The product was isolated by extraction with ether. The combined ether extracts were dried over anhydrous magnesium sulfate. Removal of the solvent in vacuo gave the crude product, which was directly chromatographed on 15 g of silica gel. Elution with hexane–ether (4:1) afforded 80 mg (82%) of pure cyclopentenone 6[2a,3] as an oil: bp 60 °C (bath temperature) (16 mmHg); IR (CCl$_4$) 3095, 1695, 1635 cm^{-1}; NMR (CCl$_4$) δ 0.75–1.20

(m, 4 H), 1.75 (bs, 3 H), 1.80–2.30 (m, 5 H). Anal. Calcd for C$_9$H$_{12}$O: M$^+$ 136.08882. Found: M$^+$ 136.08866.

Registry No.—1, 42161-96-6; 2, 66270-49-3; 3, 61765-56-8; 4, 66270-50-6; 5, 66270-51-7; 6, 59939-09-2; cyclopropyl methyl ketone, 765-43-5; chlorotrimethylsilane, 75-77-4; cyclohexenone, 930-68-7; cyclopropyl (3-oxocyclohexyl)methyl ketone, 66270-52-8; ethyl vinyl ketone, 1629-58-9; mesityl oxide, 141-79-7; 2-nitro-1-butene, 2783-12-2; cyclopropyl 3-oxopentyl ketone, 66270-53-9.

References and Notes

(1) Fellow of the Alfred P. Sloan Foundation.
(2) For recent applications of the thermal vinylcyclopropane rearrangement to organic synthesis see: (a) E. Piers, C. K. Lau, and I. Nagakura, *Tetrahedron Lett.*, 3233 (1976); (b) B. M. Trost and D. E. Kelley, *J. Am. Chem. Soc.*, **98** 248 (1976); (c) E. J. Corey and R. H. Wollenberg, *J. Org. Chem.*, **40**, 2265 (1975); (d) S. A. Monti, F. G. Cowherd, and T. W. McAninch, *ibid.*, **40**, 858 (1975); (e) B. M. Trost and M. J. Bogdanowicz, *J. Am. Chem. Soc.*, **95**, 5311 (1973); (f) E. J. Corey and S. W. Walinsky, *ibid.*, **94**, 8932 (1972).
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(4) J. P. Marino and L. J. Browne, *Tetrahedron Lett.*, 3245 (1976).
(5) P. A. Wender and M. P. Filosa, *J. Org. Chem.*, **41**, 3490 (1976).
(6) Cf. E. Piers and I. Nagakura, *Tetrahedron Lett.*, 3237 (1976); J. P. Marino and L. J. Browne, *ibid.*, 3241 (1976).
(7) J. P. Marino and T. Kaneko, *J. Org. Chem.*, **39**, 3175 (1974), and references cited therein.
(8) For reaction of silyl enol ethers with carbonyl compounds in the presence of titanium tetrachloride–titanium tetraisopropoxide see: T. Mukaiyama, K. Banno, and K. Narasaka, *J. Am. Chem. Soc.*, **96**, 7503 (1974); K. Saigo, M. Osaki, and T. Mukaiyama, *Chem. Lett.*, 163 (1976).
(9) For a recent report on the reaction of silyl enol ethers with nitro olefins in the presence of Lewis acids see: M. Miyashita, T. Yanami, and A. Yoshikoshi, *J. Am. Chem. Soc.*, **98**, 4679 (1976).

Reaction of Triarylvinyl Bromides with Lithium Aluminum Hydride[1]

Choi Chuck Lee* and Ursula Weber

Department of Chemistry and Chemical Engineering, University of Saskatchewan, Saskatoon, Saskatchewan, Canada S7N 0W0

Theoretical calculations have shown that the direct S$_N$2 displacement at a vinylic carbon is energetically unfavorable[2] and it has been pointed out in a recent review[3] that such a reaction has so far not been observed. Where an inversion component in solvolytic displacements with vinylic systems has been observed, the intervention of an ion pair with shielding effects rather than a backside S$_N$2 displacement is suggested as the mechanism.[4] In an early study on LiAlH$_4$ reductions, Trevoy and Brown[5] proposed a general mechanism for the reaction involving a nucleophilic attack on carbon by complex hydride ions. Among the reactions reported by Trevoy and Brown was the conversion of β-bromostyrene to styrene, and if the proposed mechanism applies, this would constitute a direct displacement on a vinylic carbon. In the present work, the reactions of LiAlH$_4$ with a number of triarylvinyl bromides were studied in order to obtain some mechanistic information on this reaction.

The triarylvinyl bromides used in the present study included triphenylvinyl, tri-p-tolylvinyl, tri-p-anisylvinyl, *cis*-2-phenyl-1,2-di-p-tolylvinyl, and *cis*-1,2-di-p-anisyl-2-phenylvinyl bromides (1, 2, 3, *cis*-4, and *cis*-5, respectively). These were available from earlier studies in this laboratory on degenerate rearrangements in triarylvinyl cations generated from solvolyses with these bromides as substrates.[6] Treatment of 1,[6a,b] 2,[6e] and 3[6c] with an excess of LiAlH$_4$ in ether gave the corresponding triphenylethylene (6), tri-p-tolylethylene (7), and tri-p-anisylethylene (8), respectively,