Synthesis of Acylcyclopropanes and Oxiranes from Vinylsulfonium Salts and Lithium Enolates

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Unsaturated onium salts have great synthetic utility as Michael acceptors and dipolarophiles as well as ylide precursors.[1,2] Of the salts, vinylphosphonium salts have been widely used for synthesis of heterocyclic compounds via Michael additions and subsequent Wittig reactions.[3] However, similar application of vinylsulfonium salts to synthetic chemistry has not been reported except for a few reactions with active methylene compounds such as malononitrile and diethyl malonate to give cyclopropanes.[4] Accordingly, in order to get further information on reactivities of vinylsulfonium salts, we have investigated the reaction between the salts and lithium enolates.

Dimethylstyrylsulfonium perchlorate (**2a**) was allowed to react with lithium acetophenone enolate (**1a**) in THF–DMF at room temperature to give *trans*-1-benzoyl-2-phenylcyclopropane (**3a**) in 70% yield. A similar reaction between other vinylsulfonium salts **2** and lithium enolates **1** gave the corresponding *trans*-acylcyclopropanes **3** in good yield (Table I).

On the other hand, similar treatment of **2** with other lithium enolates **4** produced oxiranes **5**, but none of the expected acylcyclopropanes were detected except for the reaction of **2a** with **4b** (Table II). The reaction of **2a** with lithium *p*-chloropropiophenone enolate (**4b**) gave *trans*-1-*p*-chlorobenzoyl-1-methyl-2-phenylcyclopropane (**3e**) in 66% yield instead of the oxirane corresponding to **5c**. For the establishment of the structure of **5a**, treatment of **5a** with Raney Ni gave 2,4-diphenyl-3-methyl-1-pentene (**6**) in 85% yield. The pentene **6** would be formed by ring opening of the oxirane, followed by dehydration.[6]

The formation of acylcyclopropanes **3** and oxiranes **5** would be considered as follows: The reaction of vinylsulfonium salts **2** with enolate anion **1** or **4** give betain A and/or ylide B. The betain A would easily decompose to acylcyclopropanes **3** with elimination of dimethyl sulfide. On the other hand, oxiranes **5** might be formed by the intramolecular reaction of the ylide B with the carbonyl group. Although the products depend on the substituents of lithium enolates, the difference of the two pathways is not clear at this stage.

Finally these results indicate that vinylsulfonium salts are versatile reagents, since selective formation of acylcyclopropanes and oxiranes is possible by the choice of nucleophiles.

Experimental Section

General. Melting points were determined on a Yanagimoto micro melting point apparatus and were uncorrected. IR, ^{1}H NMR, and mass spectra were obtained on a JASCO IR-E spectrometer, JEOR LMN-3H-60 and JNM-ps-100 spectrometer, and a Hitachi RMU-6E spectrometer, respectively.

Materials. Dimethylstyrylsulfonium perchlorate (**2a**) and dimethylisobutenylsulfonium perchlorate (**2b**) were prepared by the reaction of corresponding methyl *trans*-vinyl sulfides with methyl iodide in the presence of silver perchlorate. Trimethylsilyl enol ethers of acetophenone, *p*-chloroacetophenone, propiophenone, and diethyl ketone were prepared from the corresponding ketones and trimethylsilyl chloride according to the established method.[7]

Reaction of Vinylsulfonium Salts with Lithium Enolates. General Procedure A. To a solution of 12 mmol of methyllithium in 30 mL of dry THF was added an equimolar amount of trimethylsilyl enol ether of ketone with stirring under cooling. After 1 h, 10 mmol of vinylsulfonium salt in 30 mL of dry DMF was added dropwise, and allowed to stand at room temperature for 12–20 h. The reaction mixture was treated with 20 mL of water, extracted with chloroform, dried over sodium sulfate, and distilled in vacuo. This procedure was applied to the reactions of lithium enolates **1a, 1b, 4a,** and **4c.**

General Procedure B. To a solution of 12 mmol of lithium diisopropylamide in 30 mL of dry THF was added an equimolar amount of ketone with stirring at −78 °C. After 1 h, 10 mmol of vinylsulfonium salt in 30 mL of dry DMF was added dropwise. The reaction mixture was warmed to room temperature and allowed to stand for 15 h. The following workup method was similar to the procedure A. This procedure was applied to the reactions of lithium enolate **4b.**

***trans*-1-Benzoyl-2-phenylcyclopropane (3a):** mp 48.5–51.5 °C (lit.[5a] mp 45.5–50 °C); IR (Nujol) 1650 cm^{-1}; mass spectrum (70 eV) *m/e* 222 (M$^+$); NMR ($CDCl_3$) δ 1.41–1.64 (m, 1), 1.76–2.02 (m, 1), 2.56–3.00 (m, 2), 7.00–7.60 (m, 8, aromatic), 7.84–8.04 (m, 2, aromatic).

Anal. Calcd for $C_{16}H_{14}O$: C, 86.45; H, 6.35. Found: C, 86.36; H, 6.09.

***trans*-1-Benzoyl-2-isopropylcyclopropane (3b):** bp 122–123 °C (10 mm); IR (neat) 1650 cm^{-1}; mass spectrum (70 eV) *m/e* 188 (M$^+$); NMR ($CDCl_3$) δ 1.02 (d, 6, 2 CH_3, J = 6.1 Hz), 1.08–1.18 (m, 1), 1.36–1.56 (m, 2), 1.80 (m, 1), 2.36–2.60 (m, 1), 7.16–7.60 (m, 3, aromatic), 7.88–8.08 (m, 2, aromatic).

Anal. Calcd for $C_{13}H_{16}O$: C, 82.93; H, 8.57. Found: C, 82.96; H, 8.81.

***trans*-1-*p*-Chlorobenzoyl-2-phenylcyclopropane (3c):** bp 142–144 °C (1.5 mm); IR (neat) 1660 cm^{-1}; mass spectrum (70 eV)

Table I. Synthesis of Acylcyclopropanes from Vinylsulfonium Salts and Lithium Enolates

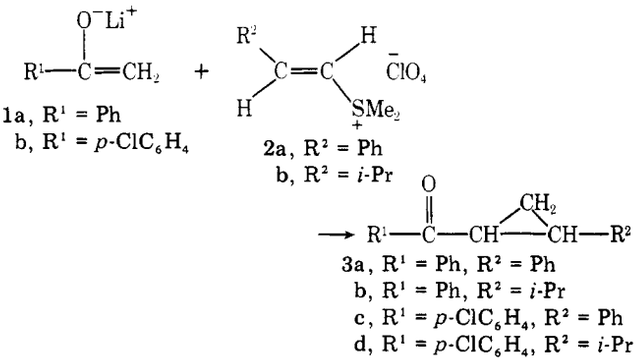
Enolate	Registry no.	Sulfonium salts	Registry no.	Reaction time, h	Product[a]	Registry no.	Yield, %
1a	35249-09-3	**2a**	38066-22-7	12	**3a**	1145-92-2	70
1a		**2b**	63016-90-0	17	**3b**	63016-91-1	80
1b	63016-88-6	**2a**		17	**3c**	63016-92-2	42
1b		**2b**		20	**3d**	63016-93-3	67

[a] All products were trans; **3a** and **3b** were identified with authentic samples and literature data.[5] The structure of **3c** and **3d** were confirmed by the NMR data, which were similar to those of **3a** and **3b,** respectively.

Table II. Synthesis of Oxiranes from Vinylsulfonium Salts and Lithium Enolates

Enolate	Registry no.	Sulfonium salt	Reaction time, h	Product[a]	Registry no.	Yield, %
4a	57204-88-3	**2a**	12	**5a**	63016-95-5	69
4a		**2b**	19	**5b**	63016-96-6	61
4b	63016-94-4	**2b**	15	**5c**	63016-97-7	37
4c	61501-43-7	**2a**	15	**5d**	63016-98-8	45
4c		**2b**	15	**5e**	63016-99-9	36

[a] Although the products may exist as four diastereoisomeric racemates, all the products gave only one peak on GLC and it was difficult to determine how many diastereomers they include.



1a, R^1 = Ph
b, R^1 = *p*-ClC_6H_4

2a, R^2 = Ph
b, R^2 = *i*-Pr

3a, R^1 = Ph, R^2 = Ph
b, R^1 = Ph, R^2 = *i*-Pr
c, R^1 = *p*-ClC_6H_4, R^2 = Ph
d, R^1 = *p*-ClC_6H_4, R^2 = *i*-Pr

m/e 256 (M^+); NMR ($CDCl_3$) δ 1.40–1.68 (m, 1), 1.72–2.40 (m, 1), 2.56–2.92 (m, 2), 7.04–7.48 (m, 7, aromatic), 7.80–8.00 (m, 2, aromatic).

Anal. Calcd for $C_{16}H_{13}OCl$: C, 74.85; H, 5.07; Cl, 13.84. Found: C, 74.95; H, 5.11; Cl, 13.74.

***trans*-1-*p*-Chlorobenzoyl-2-isopropylcyclopropane (3d):** bp 128–130 °C (2 mm); IR (neat) 1660 cm^{-1}; mass spectrum (70 eV) *m/e* 222 (M^+); NMR ($CDCl_3$) δ 1.03 (d, 6, 2 CH_3, *J* = 6.1 Hz), 0.92–1.20 (m, 1), 1.40–1.56 (m, 2), 1.64–1.88 (m, 1), 2.32–2.52 (m, 1), 7.20–7.58 (m, 2, aromatic), 7.82–8.08 (m, 2, aromatic).

Anal. Calcd for $C_{13}H_{15}OCl$: C, 70.11; H, 6.74; Cl, 15.96. Found: C, 70.28; H, 6.89; Cl, 16.20.

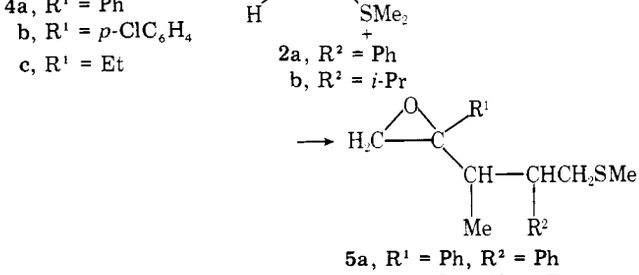
***trans*-1-*p*-Chlorobenzoyl-1-methyl-2-phenylcyclopropane (3e).** NMR analysis confirmed that the phenyl group is trans to the *p*-chlorobenzoyl group:[4a] bp 163–165 °C (1 mm); IR (neat) 1660 cm^{-1}; mass spectrum (70 eV) *m/e* 270 (M^+); NMR ($CDCl_3$) δ 1.16 (s, 3, CH_3), 1.28 (d of d, 1, *J* = 4.5 and 6.8 Hz), 1.95 (d of d, 1, *J* = 4.5 and 9.1 Hz), 2.66 (d of d, 1, *J* = 6.8 and 9.1 Hz), 7.08–7.48 (m, 7, aromatic), 7.60–7.80 (m, 2, aromatic).

Anal. Calcd for $C_{17}H_{15}OCl$: C, 75.42; H, 5.55; Cl, 13.12. Found: C, 75.12; H, 5.63; Cl, 13.43.

2,4-Diphenyl-3-methyl-5-methylthio-1-pentene oxide (5a): bp 155–158 °C (2 mm); IR (neat) 1280, 1250, 1220, 1150, 1070, 1020, 930, 905, 830, 760 cm^{-1}; mass spectrum (70 eV) *m/e* 298 (M^+), 151 ($PhCHCH_2SMe^+$), 147 ($H_2\overline{COC}(Ph)CHMe^+$); NMR ($CDCl_3$) δ 1.12 (d, 3, CH_3, *J* = 7.5 Hz), 1.80 (s, 3, SCH_3), 2.10–2.50 (m, 1), 2.55–2.96 (m, 5), 7.00–7.45 (m, 10, aromatic).

Anal. Calcd for $C_{19}H_{22}OS$: C, 76.48; H, 7.43; S, 10.73. Found: C, 76.65; H, 7.46; S, 10.69.

2-Phenyl-3-methyl-4-isopropyl-5-methyl-thio-1-pentene oxide (5b): bp 133–135 °C (2 mm); IR (neat) 1280, 1250, 1230, 1150, 1100, 1020, 940, 910, 830, 760 cm^{-1}; mass spectrum (70 eV) *m/e* 264 (M^+), 147 ($H_2\overline{COC}(Ph)CHMe^+$), 117 (*i*-$PrCHCH_2SMe^+$); NMR ($CDCl_3$) δ 0.80 (d, 6, 2 CH_3, *J* = 6.1 Hz), 1.04 (d, 3, CH_3, *J* = 7.6 Hz), 1.54 (m, 1, *J* = 6.1 Hz), 1.90 (s, 3, SCH_3), 1.80–2.14 (m, 2), 2.22 (d, 2, CH_2SMe, *J* = 5.8 Hz), 2.78 (d, 1, *J* = 5.3 Hz), 2.97 (d, 1, *J* = 5.3 Hz), 7.20–7.48 (m, 5, aromatic).



4a, R^1 = Ph
b, R^1 = *p*-ClC_6H_4
c, R^1 = Et

2a, R^2 = Ph
b, R^2 = *i*-Pr

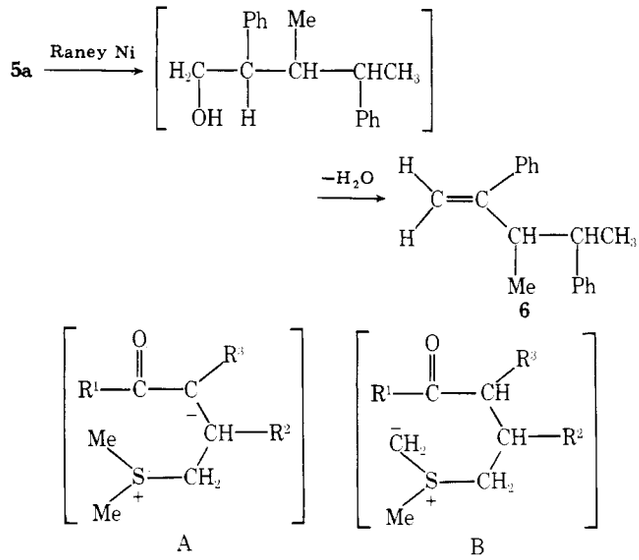
5a, R^1 = Ph, R^2 = Ph
b, R^1 = Ph, R^2 = *i*-Pr
c, R^1 = *p*-ClC_6H_4, R^2 = *i*-Pr
d, R^1 = Et, R^2 = Ph
e, R^1 = Et, R^2 = *i*-Pr

Anal. Calcd for $C_{16}H_{24}OS$: C, 72.69; H, 9.15; S, 12.11. Found: C, 72.29; H, 9.11; S, 11.77.

2-*p*-Chlorophenyl-3-methyl-4-isopropyl-5-methylthio-1-pentene oxide (5c): bp 122–124 °C (1 mm); IR (neat) 1250, 1150, 1090, 1005, 950, 830, 750 cm^{-1}; mass spectrum (70 eV) *m/e* 298 (M^+), 181 ($H_2COC(CHMe)C_6H_4Cl$-*p*$^+$), 116 (*i*-$PrCCH_2SMe^+$); NMR ($CDCl_3$) δ 0.85 (d, 6, 2 CH_3, *J* = 7.6 Hz), 1.02 (d, 3, CH_3, *J* = 6.1 Hz), 1.50–2.08 (m, 3), 1.97 (s, 3, SCH_3) 2.32–2.72 (m, 3, CH_2SMe and HHCOC), 3.68 (d, 1, HHCOC, *J* = 6.0 Hz), 7.05–7.50 (m, 4, aromatic).

Anal. Calcd for $C_{16}H_{23}OSCl$: C, 64.32; H, 7.71 Found: C, 64.05; H, 7.81.

2-Ethyl-3-methyl-4-phenyl-5-methylthio-1-pentene oxide (5d): bp 147–150 °C (4 mm); IR (neat) 1280, 1150, 1110, 1070, 910, 830, 760 cm^{-1}; mass spectrum (70 eV) *m/e* 250 (M^+), 151 ($PhCHCH_2SMe^+$); NMR ($CDCl_3$) δ 0.78 (t, 3, CH_3, *J* = 7.6 Hz), 0.98 (d, 3, CH_3, *J* = 7.3 Hz), 1.22 (m, 1), 1.58 (q, 2, CH_2CH_3, *J* = 7.6 Hz), 1.92 (s, 3, SCH_3), 2.22 (m, 1), 2.48 (s, 2), 2.84 (s, 2), 7.02–7.44 (m, 5, aromatic).



6

A

B

Anal. Calcd for $C_{15}H_{22}OS$: C, 71.97; H, 8.86; S, 12.78. Found: C, 71.75; H, 9.13; S, 12.43.

2-Ethyl-3-methyl-4-isopropyl-5-methylthio-1-pentene oxide (5e): bp 133–135 °C (15 mm); IR (neat) 1280, 1240, 1190, 1090, 1030, 950, 815, 750 cm^{-1}; mass spectrum (70 eV) *m/e* 216 (M^+), 99 ($H_2COC(Et)CHMe^+$); NMR ($CDCl_3$) δ 0.82–1.20 (m, 12, 4 CH_3), 1.34–1.96 (m, 5), 2.08 (s, 3, SCH_3), 2.42 (d, 2, CH_2SMe, *J* = 5.3 Hz), 2.56 (d, 1, *J* = 4.5 Hz), 2.62 (d, 1, *J* = 4.5 Hz).

Anal. Calcd for $C_{12}H_{24}OS$: C, 66.63, H, 11.18; S, 14.79. Found: C, 66.78; H, 11.35; S, 14.70.

2,4-Diphenyl-3-methyl-1-pentene (6). The suspension of 1.5 g of **5a** and Raney Ni in 30 mL of EtOH was refluxed for 11 h and Raney Ni was filtrated off. After removal of solvent, the residue was chromatographed on alumina (benzene–hexane, 1:1) to give 0.8 g of **6**: bp 60–62 °C (1.5 mm); IR (neat) 1615, 900 cm^{-1}; mass spectrum (70 eV) *m/e* 236 (M^+); NMR ($CDCl_3$) δ 1.04 (d, 3, CH_3, *J* = 6.1 Hz), 1.11 (d, 3, CH_3, *J* = 6.1 Hz), 2.68–3.16 (m, 2), 5.08 (d, 1, *J* = 15.2 Hz), 5.26 (d, 1, *J* = 15.2 Hz), 7.04–7.48 (m, 10, aromatic).

Anal. Calcd for $C_{18}H_{20}$: C, 91.47; H, 8.53. Found: C, 91.07; H, 8.40.

Registry No.—3e, 63017-00-5; **6,** 63017-01-6; *trans*-1-phenyl-2-methylthioethane, 15436-06-3; *trans*-1-methylthio-3-methylbut-1-ene, 25650-52-6; methyllithium, 917-54-4; 1-trimethylsilyloxy-1-phenylethene, 13735-81-4; 1-trimethylsilyloxy-1-*p*-chlorophenylethene, 58518-76-6; 1-trimethylsilyloxy-1-phenylpropene, 37471-46-8; 3-trimethylsilyloxy-pent-α-ene, 17510-47-3; lithium diisopropylamide, 4111-54-0; 4′-chloropropiophenone, 6285-05-8; methyl iodide, 74-88-4.

References and Notes

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