S-Alkyl-4-oxothianium Ions for the Synthesis of Cyclopentenones. Acid-Catalyzed Cyclization of Divinyl Ketones

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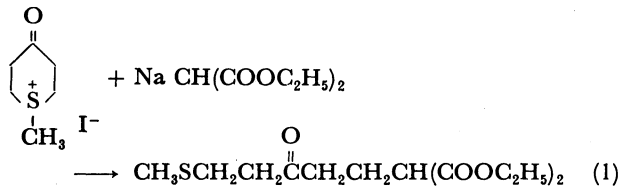
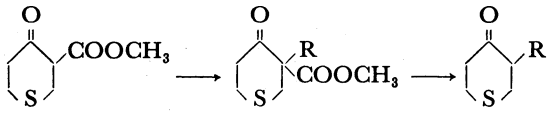
Synopsis. A new approach to 2-cyclopentenones via an acidic cyclization of divinyl ketones by the use of S-alkyl-4-oxothianium ions as key compounds is described.

Considerable attention has been focused in recent years on cyclic sulfur compounds for the synthesis of interesting organic compounds. 4-Thianone (**1**) (R=H) is constituted of 5 carbon units and a sulfur atom as an active functional group for a ring transformation. Recently, we reported a general synthesis of 2-alkyl-3-cyclopentenones via a Ramberg-Bäcklund reaction starting from **1** (R=alkyl) as a 5 C synthon.[1] In connection with the use of **1** for the synthesis of cyclopentenones, we examined the possible route to 2-cyclopentenones (**6**) from S-alkyl-4-oxothianium ions (**2**) as shown in Scheme 1.[2] Cardwell reported that S-methyl-4-oxothianium iodide reacted with a carbon nucleophile, such as sodium diethyl malonate, to give a ring-substitution product in good yield (Eq. 1).[3]



(1)

We found that sulfonium ions (**2**) reacted smoothly with sodium ethanethiolate to give **3** in good yield (Scheme 1). In this note we illustrate the utility of S-ethyl-4-oxothianium ions (**2**) for the synthesis of 2-alkyl-2-cyclopentenones (**6**). The starting materials, 3-alkyl-4-thianones (**1**) (R=alkyl), were prepared by the alkylation of 3-methoxycarbonyl-4-thianone with alkyl halides (R-X, NaH, *N*,*N*-dimethylformamide (DMF)), followed by demethoxycarbonylation (NaCl, wet dimethyl sulfoxide (DMSO), 150°C) (Eq. 2).[4] S-

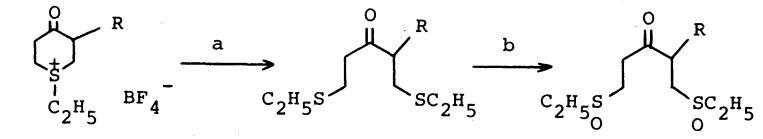


(2)

1

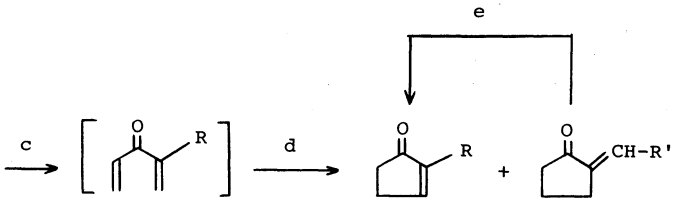
a : R=*n*-C_5H_{11}
b : R=$C_6H_5CH_2$

Ethyl-4-oxothianium tetrafluoroborate (**2**) was readily prepared from **1** with Meerwein's reagent (triethyloxonium tetrafluoroborate) in dichloromethane at room temperature. It underwent a clean substitution reaction with sodium ethanethiolate in methanol (room temperature for 20 h) to form 2-alkyl-1,5-bis(ethylthio)-3-pentanone **3** (**3a**: 89%; **3b**: 69%). **3** was oxidized with sodium periodate (2.2 equiv) in methanol (room temperature for 20 h) to give 2-alkyl-1,5-bis(ethylsulfinyl)-3-pentanone (**4**) (**4a**: 82%; **4b**: 80%). Divinyl ketone (**5**) was formed by refluxing a benzene solution of **4** in the presence of calcium carbonate (3 equiv). The IR spectrum of the benzene solution showed a strong absorp-



2 **3** **4**

a: R = *n*-C_5H_{11}
b: R = $C_6H_5CH_2$



5 **6** **7**

a: R = *n*-C_5H_{11} **a**: R' = *n*-C_4H_9
b: R = $C_6H_5CH_2$ **b**: R' = C_6H_5

a: C_2H_5SH-CH_3ONa-CH_3OH, **b**: $NaIO_4$-CH_3OH,
c: $CaCO_3$-C_6H_6, **d**: H_3PO_4-HCOOH (1:1),
e: HCl-1-C_4H_9OH

Scheme 1.

tion band of the carbonyl group at 1680 cm^{-1}, corresponding to the vinyl ketone. An acid-catalyzed cyclization (phosphoric acid–formic acid (1:1), reflux)[5] of the divinyl ketone (**5**) gave 2-alkyl-2-cyclopentenone (**6**) (**6a**: 34%; **6b**: 22%) and its *exo*-enone isomer (**7**) (**7a**: 20%; **7b**: 10%). In our reaction system, a chemical yield of 2-cyclopentenones can be 32 to 54% because the isomerization of **7** to **6** could be accomplished by heating **7** in HCl/1-butanol at 90 °C.[6]

In conclusion, as shown in Scheme 1, S-alkyl-4-oxothianium ions (**2**) are very interesting compounds for a ring transformation of a six-membered ketone (4-thianone, **1**) to a five-membered ketone (2-cyclopentenone, **6**).

Experimental

The IR spectra were determined on a Hitachi 260-10 spectrometer. The NMR spectra were recorded on Hitachi R-20B and JEOL FX-60 spectrometers, using TMS (tetramethylsilane) as an internal standard. The mass spectra were recorded with a JEOL DMX-300 mass spectrometer. Column chromatography was performed with silica gel Wakogel C-200 and preparative TLC was carried out using silica gel $60F_{254}$ PLC plates (Merck 5717).

3-Pentyl-4-thianone (1a). Granular sodium hydride (0.36 g, 15 mmol) was added to a solution of 3-methoxycarbonyl-4-thianone[3] (1.74 g, 10 mmol) and pentyl iodide (2.97 g, 15 mmol) in dry DMF (60 ml) under an atmosphere of dry nitrogen. The mixture was stirred at ambient temperature for 20 h and then poured into water (100 ml). A normal ether work-up followed by column chromatography (hexane: ether=5:1) gave 3-pentyl-3-methoxycarbonyl-4-thianone as a colourless oil (1.76 g, 72%); Bp 138 °C/2.5 mmHg (1 mmHg=133.322 Pa); IR (neat) 1740 and 1710 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.97 (3H, t), 1.00—1.50 (8H, m), and 2.84—3.46 (6H, m), 3.77 (3H, s); MS: *m/z* 244 (M^+).

A mixture of the β-keto ester (1.25 g, 5.1 mmol), anhydrous sodium chloride (0.33 g, 5.6 mmol) and water (0.3 ml) in DMSO (20 ml) was heated (oil bath temperature, 150 °C) for 20 h. After cooling the solution to room temperature, a normal ether work-up followed by column chromatography (hexane:ether=9:1) gave the ketone (**1a**) as a colourless oil (442 mg, 46%); IR (neat) 1705 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.90 (3H, br t), 1.29—1.33 (8H, m), 2.60—3.10 (7H, m); MS: *m/z* 186 (M^+).

3-Benzyl-4-thianone (1b). Granular sodium hydride (0.36 g, 15 mmol) was added to a solution of 3-methoxycarbonyl-4-thianone (1.74 g, 10 mmol) and benzyl bromide (1.88 g, 11 mmol) in dry DMF (60 ml) under an atmosphere of dry nitrogen. The mixture was stirred at ambient temperature for 2.5 h and then poured into water (100 ml). A normal ether work-up followed by column chromatography (hexane:ether=5:1) gave 3-benzyl-3-methoxycarbony-4-thianone as solids (2.16 g, 82%); Mp 64.5—65.3 °C; IR (KBr) 1750 and 1710 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=2.90 (5H, br s), 3.20—3.30 (3H, m), 3.69 (3H, s), 7.23 (5H, br s); ^{13}C NMR ($CDCl_3$) δ= 30.6, 37.9, 39.7, 43.4, 52.3, 64.2 (OCH_3), 126.9, 128.1, 130.4, 135.6, 170.5 (ester C=O), 204.7 (keto C=O); MS: *m/z* 264 (M^+). Anal. ($C_{14}H_{16}O_3S$) C, H.

A mixture of the β-keto ester (1.10 g, 4 mmol), anhydrous sodium chloride (0.26 g, 4.4 mmol) and water (0.22 ml) in DMSO (5 ml) was heated (oil bath temperature, 150 °C) for 20 h. After cooling the solution to room temperature, a normal ether work-up followed by column chromatography gave the ketone (**1b**) as a colourless oil (0.49 g, 60%); Bp 149 °C/2 mmHg; IR (neat) 1705 (C=O) and 1490 cm^{-1} (aryl); ^{1}H NMR ($CDCl_3$) δ=2.40—3.30 (9H, m), 7.24 (5H, br s); ^{13}C NMR ($CDCl_3$) δ=30.8, 35.0, 35.2, 43.9, 54.5, 126.3, 128.4, 129.0, 138.8, 205.5 (C=O); MS: *m/z* 206 (M^+).

2-Pentyl-1,5-bis(ethylthio)-3-pentanone (3a). A dichloromethane solution (20 ml) of 3-pentyl-4-thianone (**1a**) (408 mg, 2.2 mmol) and triethyloxonium tetrafluoroborate (500 mg, 2.6 mmol) was stirred for 20 h at room temperature. After the reaction solution was concentrated in vacuo, the residual oil was dissolved in dry methanol (10 ml). To a methanol solution (20 ml) of sodium ethanethiolate (2.8 mmol; 1.3 equiv) was added the above methanol solution of sulfonium salt (**2a**) and the mixture was stirred at room temperature for 21 h. After the removal of methanol in vacuo, a normal dichloromethane work-up to give an oil (**3a**) which was homogeneous on silica gel TLC (539 mg, 89%); IR (neat) 1710 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.90 (3H, t), 1.00—1.80 (14H, m containing t at 1.26 (J=7.2 Hz)), 2.30—3.00 (11H, m containing s at 2.76).

2-Benzyl-1,5-bis(ethylthio)-3-pentanone (3b). A dichloromethane solution (20 ml) of 3-benzyl-4-thianone (**1b**) (734 mg, 3.6 mmol) and triethyloxonium tetrafluoroborate (820 mg, 4.3 mmol) was stirred for 19 h at room temperature. After the dichloromethane solution was concentrated in vacuo, the residual oil was dissolved in dry methanol (10 ml). To a methanol solution (20 ml) of sodium ethanethiolate, which was prepared by the reaction between sodium metal (4.8 mmol) and ethanethiol (330 mg, 5.3 mmol), was added the above methanol solution of sulfonium salt (**2b**) and the mixture was stirred at room temperature for 22 h. After the methanol solution was concentrated in vacuo, a normal dichloromethane work-up to give an oil (**3b**) which was homogeneous on silica gel TLC (726 mg, 69%); IR (neat) 1705 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.20 (6H, t, J=6.6 Hz), 2.24—2.97 (3H, m), 7.19—7.21 (5H, m); ^{13}C NMR ($CDCl_3$) δ=14.67, 24.67, 25.97, 26.75, 32.86, 38.18; 44.80, 53.89, 126.49, 128.56, 128.81, 138.56, 210.89 (C=O).

2-Pentyl-1,5-bis(ethylsulfinyl)-3-pentanone (4a). 2-Pentyl-1,5-bis(ethylthio)-3-pentanone (**3a**) (539 mg, 2 mmol) was treated with sodium periodate (940 mg, 4.4 mmol) in methanol at room temperature for 21 h. After removal of insoluble solids, methanol solution was concentrated in vacuo and the residue was dissolved in chloroform to give **4a** (492 mg, 82%); IR (neat) 1710 (C=O), 1050 and 1020 cm^{-1} (S=O); ^{1}H NMR ($CDCl_3$) δ=0.90 (3H, br t), 1.20—1.90 (14H, m containing t at 1.35 (J=7.2 Hz)), 2.56—3.30 (11H, m containing t at 2.68 (J=7.2 Hz)).

2-Benzyl-1,5-bis(ethylsulfinyl)-3-pentanone (4b). 2-Benzyl-1,5-bis(ethylthio)-3-pentanone (**3b**) (193 mg, 0.56 mmol) was oxidized with sodium periodate (310 mg, 1.45 mmol) in methanol at room temperature for 20 h. After filtration of insoluble solids, methanol solution was concentrated in vacuo and the product was extracted with chloroform to give **4b** (151 mg, 71%); IR (neat) 1715 (C=O), 1050 and 1020 cm^{-1} (S=O).

2-Pentyl-2-cyclopentenone (6a). A benzene solution (10 ml) of **4a** (492 mg, 1.6 mmol) and calcium carbonate (480 mg, 4.8 mmol) was refluxed for 17 h. After filtration of the above solution, its IR spectrum showed a strong absorption band at 1680 cm^{-1} corresponding to vinyl ketone. After removal of benzene, phosphoric acid (8 ml) and formic acid (8 ml) were added to the residual oil and the solution was refluxed for 20 h (oil bath temperature, 100 °C). After cooling the solution to room temperature, a normal benzene work-up, followed by preparative TLC (hexane:ether=5:1) to give **6a** (83 mg, 34%) and its *exo*-enone isomer **7a** (48 mg, 20%); **6a**:[5] IR (neat) 1700 (C=O) and 1625 cm^{-1} (C=C); ^{1}H NMR ($CDCl_3$) δ=0.90 (3H, br t), 1.00—1.70 (6H, m), 2.00—2.26 (6H, m), 7.31 (1H, m); MS: *m/z* 152 (M^+). **7a**: IR (neat) 1715 (C=O) and 1645 (C=C) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.95 (3H, br t), 1.10—1.60 (4H, m), 1.60—2.73 (8H, m), 6.16—6.60 (1H, m). Authentic **7a** was also

prepared by cross-aldol reaction between enol silyl ether of cyclopentanone (2.60 g, 16.7 mmol) and pentanal (1.59 g, 18.5 mmol) in the presence of titanium tetrachloride (1.85 ml, 16.7 mmol) in dichloromethane at −78 °C for 4.5 h in 59% yield;[7] IR (neat) 1720 (C=O) and 1645 (C=C) cm^{-1}. **6a** was obtained by heating **7a** (1.496 g, 9.87 mmol) in HCl (1 ml)/1-butanol (40 ml) at 90 °C for 19 h in 87% yield;[6] Bp 79.5—82.0 °C/5 mmHg; IR (neat) 1700 and 1630 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.85 (3H, br t), 1.00—1.74 (6H, m), 1.86—2.66 (6H, m), 7.25 (1H, m).

2-Benzyl-2-cyclopentanone (6b). A benzene solution (5 ml) of **4b** (445 mg, 1.4 mmol) and calcium carbonate (410 mg, 4.1 mmol) was refluxed for 21 h. After filtration of the above solution, its IR spectrum showed a strong absorption band at 1680 cm^{-1} corresponding to vinyl ketone. After the removal of benzene, phosphoric acid (6 ml) and formic acid (6 ml) were added to the residual oil and the solution was refluxed for 23 h (oil bath temperature, 100 °C). After cooling the solution to room temperature, a normal benzene work-up, followed by preparative TLC (hexane:ether=1:1) to give **6b** (76 mg, 22%) and its *exo*-enone isomer **7b** (34 mg, 10%); **6b**: IR (neat) 1690 and 1630 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.40—2.60 (4H, m), 3.40—3.60 (2H, m), 7.10—7.30 (6H, m containing s at 7.25); MS: *m/z* 172 (M^+). **7b**: IR (CCl_4) 1710 and 1620 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.79—2.50 (4H, m), 2.85 (2H, t, d, *J*=6.6 and 3 Hz), 7.31—7.56 (6H, m). **7b** was prepared by aldol reaction between cyclopentanone (8.4 g, 0.10 mol) and benzaldehyde (3.56 g, 0.03 mol) in sodium hydroxide solution (sodium hydroxide (2.0 g, 0.05 mol) in 463 ml of water) at room temperature for 22 h in 53% yield;[8] Bp 115—117 °C/2 mmHg; IR (CCl_4) 1710 and 1620 cm^{-1}.

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