Stable Sulfur Ylides. X.[1a] Reactions of Carbonyl-Stabilized Sulfonium Ylides with Acetyl Chloride

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Highly stabilized sulfonium diacetylmethylides (1a—c) reacted with acetyl chloride to give a mixture of the enol acetates (2a—c) and the enol diacetates (3a—c). Similarly, sulfonium acetylcarbomethoxymethylides (5a, b) gave the enol acetates (6a, b). These enol acetates were hydrolyzed with HCl–MeOH to give 3-methylthio- (3-phenylthio-)2,4-pentanediones (4a, b) or methyl 2-methylthio- (2-phenylthio-)acetoacetates (7a, b).

Keywords stable sulfonium ylide; acetyl chloride; 1,3-dicarbonyl compound; enol acetate; enol diacetate; hydrolysis

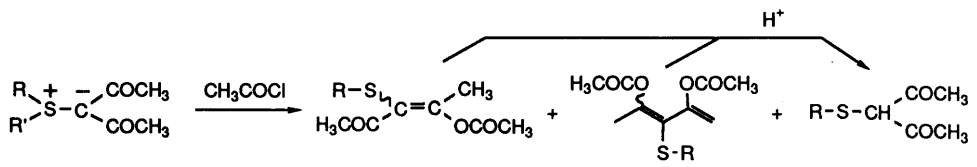
The sulfonium diacetylmethylides having two carbonyl substituents at the ylide carbon are well-known as fairly stable compounds[2] because the electrons on the ylide carbon are delocalized through the two carbonyl groups. Therefore their synthetic applications have been limited compared with common sulfur ylides such as dimethylsulfonium methylide and dimethylsulfonium benzoylmethylide.

In previous papers[1] of this series, we reported some synthetic utility of the stable sulfur ylides: the reaction of dimethylsulfonium diacetylmethylide (**1a**) with quinoline 1-oxide or isoquinoline 2-oxide in the presence of benzoyl chloride gave pyrido[1,2-*a*]quinoline[1b] or pyrido[2,1-*a*]-isoquinoline[1c] derivatives. Although the reaction mechanism was not clarified, it was presumed that the methyl moiety of an acetyl group on the ylide attacks as a nucleophile at the 2-position or 1-position of the aromatic amine *N*-oxide. Enol acylate can be considered as a nucleophile, so the reaction of the ylide (**1a**) with acetyl chloride was examined under various reaction conditions. When the reactions was carried out in the presence of triethylamine as a base, we obtained the enol diacetate (**3a**), of which the terminal methylene moiety, would be expected to react with aromatic amine *N*-oxides. However, we could not find satisfactory reaction conditions for the preparation of condensed heterocycles by the use of the enol diacetate.

In this paper, the reactions of highly stabilized sulfonium diacetylmethylides[3] (**1a—d**) and sulfonium acetylcarbomethoxymethylides[3] (**5a, b**) with acetyl chloride under mild conditions are described.

The reaction of **1a** with acetyl chloride in the presence of triethylamine gave an oil. This oil was found to consist of three components (**2a**, **3a**, and **4a**) by gas chromatographic (GLC) analysis, and these components were separated by fractional distillation under reduced pressure (Chart 1). The structures of these compounds were confirmed to be 2-acetoxy-3-methylthio-2-penten-4-one (**2a**), 2,4-diacetoxy-3-methylthio-1,3-pentadiene (**3a**), and 3-methylthio-2,4-pentanedione (**4a**) by analysis of their mass (MS), proton nuclear magnetic resonance (^{1}H-NMR), and infrared (IR) spectra (Table I). The ^{1}H-NMR spectrum of **3a** showed characteristic terminal methylene signals at δ 5.13 and 5.35. However, signals in the methyl proton region were too complicated to be assigned.

In a similar manner **1b** was treated with acetyl chloride to give a mixture of 2-acetoxy-3-phenylthio-2-penten-4-one (**2b**) and 2,4-diacetoxy-3-phenylthio-1,3-pentadiene (**3b**). The structures of the products were confirmed by spectral data. Sulfonium acetylcarbomethoxymethylides (**5a** and **5b**) were treated with acetyl chloride to give methyl 3-acetoxy-2-methylthio-2-butenoate (**6a**) and methyl 3-acetoxy-2-phenylthio-2-butenoate (**6b**), respectively, as sole products, which appear to be mixtures of geometric isomers from their ^{1}H-NMR spectra (Table I).

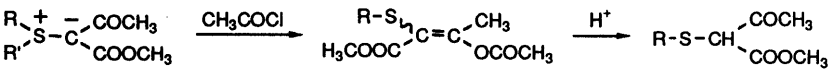


1a : R = R' = CH_3
1b : R = C_6H_5, R' = CH_3
1c : R = R' = $-(CH_2)_4-$
1d : R = R' = C_6H_5

2a : R = CH_3
2b : R = C_6H_5
2c : R = $-(CH_2)_4Cl$

3a : R = CH_3
3b : R = C_6H_5
3c : R = $-(CH_2)_4Cl$

4a : R = CH_3
4b : R = C_6H_5
4c : R = $-(CH_2)_4Cl$



5a : R = R' = CH_3
5b : R = C_6H_5, R' = CH_3

6a : R = CH_3
6b : R = C_6H_5

7a : R = CH_3
7b : R = C_6H_5

Chart 1

As mentioned above, when the ylides (**1a**, **b**, **5a**, and **5b**) were treated with acetyl chloride, the methyl group at the sulfur atom was removed in all cases. It is probably removed as methyl chloride; the phenyl group might be difficult to remove. To confirm this presumption, tetramethylenesulfonium ylide (**1c**) was treated with acetyl chloride under reaction conditions similar to those used in the reaction of **1a**. The reaction product was a mixture of the enol acetate (**2c**), the enol diacetate (**3c**), and **4c** which contain a chlorobutylthio group. When diphenylsulfonium diacetylmethylide (**1d**) was treated with acetyl chloride, no reaction occurred and the starting ylide was recovered almost quantitatively.

Compounds **2a**—**c** and **3a**—**c** were easily hydrolyzed with HCl–MeOH to give 3-methylthio-, 3-phenylthio-, and 3-(4-chlorobutylthio)-2,4-pentanedione (**4a**, **4b**, and **4c**) in satisfactory yields (Table II). The reaction of **4a** with hydrazine hydrate gave 3,5-dimethyl-4-methylthiopyrazole. Similarly, **6a** and **6b** were hydrolyzed to methyl 2-methylthio- and 2-phenylthioacetoacetate (**7a** and **7b**) which were also converted to the corresponding pyrazolone derivatives.

The procedure described above is a convenient method for the introduction of methylthio or phenylthio groups at the active methylene moiety of 1,3-dicarbonyl compounds as compared with other methods.[4] Finally, the reaction of **3a** with common dienophiles, such as naphthoquinone, maleic anhydride, and dimethyl acetylenedicarboxylate, did not give any cycloadducts under thermal conditions. The direct conversion of **1a** to a more reactive diene has been achieved in our laboratories and the results will be reported shortly.

Experimental

Melting points were taken on Yanaco micro melting point apparatus, and are uncorrected. IR spectra were measured with JASCO IR-810 or IRA-2 spectrophotometer. ^{1}H-NMR spectra were run on a Hitachi R-600, a JEOL JNM FX-90Q, or a JNM GX-400 spectrometer. Chemical shifts are given in ppm (δ) relative to tetramethylsilane as an internal standard. MS were taken with a JEOL JMS DX-303 spectrometer and a JEOL DA-5000 data processor.

Reaction of the Ylide 1a with Acetyl Chloride A solution of acetyl chloride (19.0 g, 0.24 mol) in CH_2Cl_2 (20 ml) was added dropwise with stirring to a solution of **1a** (16.0 g, 0.1 mol) and triethylamine (2.0 ml) in CH_2Cl_2 (100 ml) at room temperature. The mixture was stirred for an additional 12 h. After removal of the solvent, the residue was extracted with ether (3 times). The combined extract was washed with 5% $NaHCO_3$ and water, and then dried over Na_2SO_4. After evaporation of the solvent, 15.9 g (crude) of a pale yellow oil was obtained. This oil showed three peaks [**2a** (48.7%), **3a** (37.0%), and **4a** (3.3%)] by GLC analysis, and was separated into three components by fractional distillation under reduced pressure (Table I).

Reaction of the Ylide 1b with Acetyl Chloride The ylide **1b** (22.2 g, 0.1 mol) was treated with acetyl chloride under the same conditions as above to give 23.5 g of a brown oil. This oil showed two peaks [**2b** (50.5%) and **3b** (29.3%)] by GLC analysis, and **2b** (12.6 g) and **3b** (8.5 g) were isolated by fractional distillation under reduced pressure (Table I).

Reaction of Ylide 1c with Acetyl Chloride The ylide **1c** (1.9 g, 10 mmol) was treated with acetyl chloride to give 2.0 g of a brown oil. This oil was examined by GC-MS (GC conditions: 3% OV-1 on Uniport HP (80—100 mesh), 2.6 mm × 1 m glass column; column temperature, 120—320 °C (8 °C/min); N_2, 1.5 kg/cm^2). The chromatogram consisted of 3 peaks. The first peak, t_R = 4.24 min; **4c**, MS *m/z* (relative intensity): 224 and 222 (M^+ for $C_9H_{15}ClO_2S$, 17 and 49), 182 (7), 180 (7), 163 (6), 161 (15), 132 (27), 117 (19), 93 (33), 91 (100). The second peak, t_R = 5.49 min; **2c**, MS *m/z* (relative intensity): 266 and 264 (M^+ for $C_{11}H_{17}ClO_3S$, 6 and 18), 224 (38), 222 (100), 163 (5), 161 (16), 132 (28), 117 (13), 93 (27), 91 (87). The third peak, t_R = 7.33 min; **3c**, MS *m/z* (relative intensity): 308 and 306 (M^+ for $C_{13}H_{19}ClO_4S$, 6 and 18), 266 (11), 264 (39), 224 (36), 222 (100), 206 (10), 204 (28), 93 (22), 91 (61).

Reactions of 5a and 5b with Acetyl Chloride The ylide **5a** (35.2 g, 0.2 mol) was treated with acetyl chloride under the same conditions as above to give 28.3 g (69.4%) of **6a** as an oil. The same treatment of **5b** (4.76 g, 20 mmol) gave 4.4 g (82.3%) of **6b** as an oil (Table I).

Hydrolysis of Enol Acetates 3-Methylthio-2,4-pentanedione (**4a**): The oil (11.1 g, mixture of **2a**, **3a**, and **4a**) obtained from the reaction of **1a** with acetyl chloride, and 10% HCl–MeOH (20 ml) in MeOH (100 ml) was stirred for 12 h at room temperature. After evaporation of the solvent *in vacuo*, the residue was extracted with ether (3 times). The combined extract was washed with 5% $NaHCO_3$ and dried over Na_2SO_4. The solvent was removed and the oily residue was distilled to give **4a** (6.45 g) as a pale yellow oil; bp 85—90 °C/28 mmHg. (lit.,[4c] bp 75—75.7 °C/28 mmHg, 100% enol form).

3-Phenylthio-2,4-pentanedione (**4b**): The oil product (11.5 g, **2b** and **3b** mixture) gave **4b** (6.25 g) as a colorless oil (Table II).

3-(4-Chlorobutylthio)-2,4-pentanedione (**4c**): The oil product (1.50 g) gave **4c** (0.65 g) as a pale yellow oil (Table II).

Methyl 2-Methylthioacetoacetate (**7a**): Compound **6a** (20 g, 0.1 mol) gave **7a** (13.1 g) as a colorless oil (Table II).

Methyl 2-Phenylthioacetoacetate (**7b**): Compound **6b** (6.7 g, 25 mmol) gave **7b** (5.0 g) as a colorless oil; bp 102 °C/1.0 mmHg. (lit.,[4d] bp 115—120 °C/1.0 mmHg, 95% enol form).

Preparation of Pyrazoles A mixture of **4a** (0.3 g, 2.0 mmol), hydrazine hydrate (0.15 g, 3.0 mmol), and AcOH (1 drop) in EtOH (10 ml) was refluxed for 2 h. After removal of the solvent, the residue was recrystallized

TABLE I. Physical Data for Enol Acetates

Compd. No.	bp °C (mmHg)	IR (neat) cm^{-1}, C=O	MS (*m/z*)	Formula	Analysis (%) Calcd (Found) C	H	S	^{1}H-NMR ($CDCl_3$) ppm
2a	130—133 (22.0)	1760 1700	188 (M^+) 146, 131	$C_8H_{12}O_3S$	51.06 (51.29	6.43 6.27	17.00 16.71)	2.13—2.49 (12H, m, CH_3 × 4)
3a	146—150 (22.0)	1764 br	230 (M^+) 188, 146	$C_{10}H_{14}O_4S$	52.17 (51.58	6.13 6.18	13.90 14.03)	2.13—2.17 (12H, m, CH_3 × 4), 5.13 and 5.35 (2H, each br s, C=CH_2)
2b	125—127 (1.0)	1760 1690	250 (M^+) 208, 193	$C_{13}H_{14}O_3S$	62.38 (62.31	5.64 5.69	12.81 12.78)	2.00—2.33 (9H, m, CH_3 × 3), 7.0—7.4 (5H, m, Ph)
3b	133—135 (1.0)	1760 br	292 (M^+) 250, 208	$C_{15}H_{16}O_4S$	61.63 (61.14	5.52 5.55	10.97 11.07)	2.00—2.27 (9H, m, CH_3 × 3), 4.93—5.13 (2H, m, C=CH_2), 7.1—7.4 (5H, m, Ph)
6a[a]	136—137 (20.0)	1765 1720	204 (M^+) 162, 130	$C_8H_{12}O_4S$	47.05 (46.66	5.92 5.93	15.70 15.65)	2.15 (3H, s, S-CH_3), 2.23 and 2.24 (3H, each s, $COCH_3$), 2.25 and 2.26 (3H, each s, =C-CH_3), 3.77 and 3.82 (3H, each s, $COOCH_3$)
6b[b]	122 (2.0)	1760 1720	266 (M^+) 224, 192	$C_{13}H_{14}O_4S$	58.63 (58.48	5.30 5.29	12.04 11.94)	2.16 and 2.19 (3H, each s, $COCH_3$), 2.30 and 2.35 (3H, each s, =C-CH_3), 3.56 and 3.59 (3H, each s, $COOCH_3$), 7.16—7.40 (5H, m, Ph)

a) Approximately 3/1 mixture of *E*/*Z* (or *Z*/*E*) isomers by ^{1}H-NMR. *b*) Approximately 4/1 mixture of *E*/*Z* (or *Z*/*E*) isomers by ^{1}H-NMR.

TABLE II. Physical Data for **4b**, **4c**, and **7a**

Compd. No.	bp °C (mmHg)	IR (neat) cm^{-1}, C=O	MS (*m/z*)	Formula	Analysis (%) Calcd (Found) C	H	S	^{1}H-NMR ($CDCl_3$) ppm
4b	85—87 (0.8)	1580 br	208 (M^+) 193, 166	$C_{11}H_{12}O_2S$	63.44 (63.64	5.81 5.83	15.39 15.36)	2.33 (6H, s, $COCH_3 \times 2$), 7.0—7.4 (5H, m, Ph), 17.25 (1H, s, enol OH)
4c[a]	—	1580 br	224 and 222 (M^+) 207, 180	$C_9H_{15}ClO_2S$	48.54 (48.45	6.79 6.66	14.37 14.64)	1.60—2.20 (4H, m, CH_2CH_2), 2.43 (6H, s, $COCH_3 \times 2$), 2.53 (2H, t, $J=7$ Hz, SCH_2), 3.55 (2H, t, $J=7$ Hz, $ClCH_2$), 17.07 (1H, s, enol OH)
7a[b]	115 (20.0)	1750 1720 1595	162 (M^+) 130, 105	$C_6H_{10}O_3S$	44.43 (43.97	6.21 6.14	19.77 19.37)	2.12 (enol) and 2.15 (keto) (3H, each s, $C-CH_3$), 2.36 (3H, s, SCH_3), 3.27 (enol) and 3.32 (keto) (3H, each s, OCH_3), 4.10 (keto CH), and 13.30 (enol OH) (1H, each s)

a) Purified by column chromatography. *b*) Approximately 1 : 1 mixture of keto and enol forms by ^{1}H-NMR.

from ether–petroleum ether to give 3,5-dimethyl-4-methylthiopyrazole: mp 75—77 °C (from ether–petroleum ether). *Anal.* Calcd for $C_6H_{10}N_2S$: C, 50.69; H, 7.09; N, 19.71; S, 22.51. Found: C, 50.50; H, 7.12; N, 19.73; S, 22.59. MS *m/z*: 142 (M^+). Compounds **4b**, **4c**, **7a**, and **7b** were treated with hydrazine hydrate in the same way as above and gave the corresponding pyrazoles.

3,5-Dimethyl-4-phenylthiopyrazole (from **4b**): mp 120—122 °C (from benzene–hexane). *Anal.* Calcd for $C_{11}H_{12}N_2S$: C, 64.67; H, 5.92; N, 13.83; S, 15.69. Found: C, 64.74; H, 5.95; N, 13.71; S, 15.52. MS *m/z*: 204 (M^+). 4-(4-Chlorobutylthio)-3,5-dimethylpyrazole (from **4c**): mp 55—56 °C (from *n*-hexane). *Anal.* Calcd for $C_9H_{15}ClN_2S$: C, 49.43; H, 6.91; N, 12.80; S, 14.66. Found: C, 49.86; H, 7.03; N, 12.47; S, 15.04. MS *m/z*: 220 and 218 (M^+). 3-Methyl-4-methylthio-2-pyrazolin-5-one (from **7a**): mp 264—268 °C (dec.) (from MeOH). (lit.[4b] mp 265 °C dec.). *Anal.* Calcd for $C_5H_8N_2OS$: C, 41.65; H, 5.59; N, 19.43; S, 22.23. Found: C, 41.84; H, 5.59; N, 19.36; S, 22.51. MS *m/z*: 144 (M^+). 3-Methyl-4-phenylthio-2-pyrazolin-5-one (from **7b**): mp 294—296 °C (dec.) (from H_2O–EtOH). *Anal.* Calcd for $C_{10}H_{10}N_2OS$: C, 58.23; H, 4.87; N, 13.58; S, 15.54. Found: C, 58.05; H, 4.99; N, 13.46; S, 15.18. MS *m/z*: 206 (M^+).

Acknowledgments We are indebted to the staff of the Center for Instrumental Analysis of Nagasaki University for elemental analysis and spectral measurements. Thanks are also due to Misses S. Yoshida and S. Ohshige for their technical assistance.

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