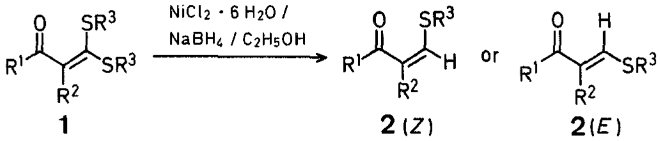
Partial Reductive Demethylthiolation of α-Ketoketene *S,S*-Acetals with Sodium Borohydride/Nickel Chloride: A New, General Method for 2-Methylthio-1-alkenyl Ketones[1]

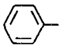
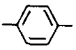
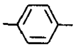
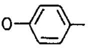
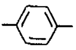
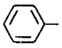
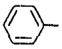
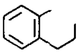
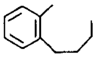
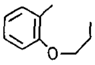
B. MYRBOH, L. W. SINGH, H. ILA*, H. JUNJAPPA*

Department of Chemistry, North-Eastern Hill University, Shillong 793003, Meghalaya, India

Alkylthiovinyl ketones, besides their use as a blocking group[2], have been shown to be versatile synthetic intermediates[3] in organic synthesis. Many recent publications have been concerned with their synthetic utility rather than methods of preparation. The most commonly employed method involves the treatment of formyl derivatives (or their tosylates) of alkyl ketones with butyl mercaptan[2,4,5]. The other methods involve either 1,4-addition of alkyl/aryl mercaptans to β-ketoacetylenes[6–9] or the displacement reaction of β-chlorovinyl ketones[10,11] with appropriate mercaptans. Although the latter two methods are useful, preparation of the starting materials involves inconvenient, multi-step synthetic operations[11]. Our interest in the synthetic utility of α-ketoketene *S,S*-acetals[12], derived from a variety of active methylene compounds in a one-pot reaction, prompted us to investigate whether they could be reduced selectively to give the title compounds in useful yields.

Our literature survey revealed that there is only one report on the electrochemical reduction[13] of **1a** which gave the corresponding methylthiovinyl ketone **2a** in 64% yield. We report here that partial reductive demethylthiolation of α-ketoketene *S,S*-acetals **1** with sodium borohydride/nickel chloride[14] gives the corresponding methylthio-2-alkenyl ketones **2** in good yields. Apparently, the reported methods require alkyl



1,2	R¹	R²	R³
a		H	CH$_3$
b	H$_3$C– 	H	CH$_3$
c	Cl– 	H	CH$_3$
d	C$_2$H$_5$O– 	H	CH$_3$
e	H$_3$CO– 	H	C$_2$H$_5$
f	H$_3$C– 	CH$_3$	CH$_3$
g		C$_2$H$_5$	CH$_3$
h		*n*-C$_3$H$_7$	CH$_3$
i	CH$_3$	H	CH$_3$
j			CH$_3$
k			CH$_3$
l			CH$_3$
m	—(CH$_2$)$_3$—		CH$_3$
n	—(CH$_2$)$_4$—		CH$_3$

Eingang: 17. August 1981

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[1] H. Hunsdiecker, *Ber. Dtsch. Chem. Ges.* **75**, 454 (1942).

[2] E. I. Nienhouse, R. M. Irwin, G. R. Finni, *J. Am. Chem. Soc.* **89**, 4557 (1967).
Y. Fukujama, T. Tokoroyama, Tekubota, *Tetrahedron Lett.* **1973**, 4869.
T. Cuvigny, M. Lercheveque, H. Normant, *Tetrahedron Lett.* **1974**, 1237.
R. M. Jacobson, R. A. Raths, J. H. McDonald, *J. Org. Chem.* **42**, 2545 (1977); hier weitere Literatur.
Vgl. auch:
B. M. Trost, F. W. Gowland, *J. Org. Chem.* **44**, 3448 (1979).
B. M. Trost, D. P. Curran, *J. Am. Chem. Soc.* **102**, 5699 (1980).
E. Pears, B. Abeysekera, J. R. Scheffer, *Tetrahedron Lett.* **1979**, 3279; hier weitere Literatur.

[3] R. M. Jacobson, A. Abbaspour, G. P. Lahm, *J. Org. Chem.* **43**, 4650 (1978).

[4] A. Dornow, H. D. Jordan, *Chem. Ber.* **94**, 76 (1961).
W. Oppolzer, M. Petrzilka, K. Bättig, *Helv. Chim. Acta* **60**, 2964 (1977).
T. L. Gilchrist, D. A. Lingham, T. G. Roberts, *J. Chem. Soc. Chem. Commun.* **1979**, 1089.

[5] A. Roedig, in: Houben-Weyl, *Methoden der Organischen Chemie*, 4. Auflage, herausgegeben von E. Müller, Band 5/4, Georg Thieme Verlag, Stuttgart, 1960, p. 601.

[6] D. Seebach et al., *Helv. Chim. Acta* **64**, 725, 727 (1981).

0039-7881/82/0432-0307 $ 03.00

Table. 2-Methylthio-1-alkenyl Ketones **2a–n**

Product	Reflux time [h]	Yield [%][a] by Method A	B	m.p. [°C] or b.p. [°C]/torr	Molecular formula[b] or Lit.m.p. or p.b.	I.R. (neat) ν [cm^{-1}]	^{1}H-N.M.R. (CCl$_4$) δ [ppm]	M.S. m/e (M$^+$)	Configuration
2a	30	62	—	oil: 140–142°/1	140°/1[13]	1643	2.32 (s, 3H); 6.70 (d, 1H, J=15 Hz); 7.4 (m, 3H); 7.7–7.9 (m, 3H)	178	*E*
2b	25	64	82	120–121°[c]	$C_{11}H_{12}OS$ (192.3)	1645	2.32 (s, 3H); 2.38 (s, 3H); 6.91 (d, 1H, J=9 Hz); 7.0–7.3 (m, 3H); 7.50–7.85 (d, 2H)	192	*Z*
2c	10	50	—	69–70°	$C_{10}H_9ClOS$ (212.7)	1632[d]	2.42 (s, 3H); 6.60 (d, 1H, J=15 Hz); 7.32 (d, 2H); 7.7–7.9 (m, 3H)	212.5	*E*
2d	37	45	—	127.5–128.5°[c]	$C_{12}H_{14}O_2S$ (222.3)	1625[d]	1.40 (t, 3H); 2.37 (s, 3H); 4.07 (q, 2H); 6.85 (d, 2H); 6.93 (d, 1H, J=9 Hz); 7.15 (d, 1H, J=9 Hz); 7.85 (d, 2H)	222	*Z*
2e	12	42	—	thick, viscous oil	$C_{12}H_{14}O_2S$ (222.3)	1640	1.28 (t, 3H); 2.68 (q, 2H); 3.75 (s, 3H); 6.71 (d, 2H); 6.82 (d, 1H, J=9 Hz): 7.12 (d, 1H, J=9 Hz); 7.80 (d, 2H)	222	*Z*
2f	8	56 (51)[e]	—	oil: 100–101°/1	$C_{12}H_{14}OS$ (206.3)	1635	1.90 (s, 3H); 2.30 (s, 3H); 2.35 (s, 3H); 6.81 (s, 1H); 7.0–7.6 (A_2B_2 m, 4H)	206	*Z*
2g	25	57 (52)[e]	—	oil: 129–130°/1	$C_{12}H_{14}OS$ (206.3)	1635	1.05 (t, 3H); 2.30 (s, 3H); 2.45 (q, 2H); 6.80 (s, 1H); 7.2–7.7 (m, 5H)	206	*Z*
2h	28	66 (55)[e]	—	oil: 135°/1	$C_{13}H_{16}OS$ (220.3)	1620	0.95 (t, 3H); 1.4 (m, 2H); 2.25 (s, 3H); 2.35 (t, 2H); 6.82 (s, 1H); 7.3–7.6 (m, 5H)	220	*Z*
2i	11	77 (65)[e]	85	56°/1; 37–38°[f]	C_5H_8OS (116.2)	1690	2.15 (s, 3H); 2.33 (s, 3H); 5.90 (d, 1H, J=15 Hz); 7.50 (d, 1H, J=15 Hz)	116	*E*
2j	9	58	—	68°	$C_{12}H_{12}OS$ (204.3)	1660[d]	2.48 (s, 3H); 2.80 (A_2B_2 q, 4H); 7.0–7.4 (m, 3H); 7.51 (s, 1H); 7.9 (m, 1H)	204	*E*
2k	10	60	—	thick, viscous oil	$C_{13}H_{14}OS$ (218.3)	1675, 1650	1.88 (A_2B_2 q, 2H); 2.25 (br t, 2H); 2.40 (s, 3H); 2.71 (t, 2H); 6.9–7.6 (m, 5H)	218	*E*
2l	12	57	—	thick, viscous oil	$C_{12}H_{12}O_2S$ (220.3)	1650	2.45 (s, 3H); 2.60 (t, 2H); 4.15 (t, 2H); 6.7–7.1 (m, 2H); 7.25 (s, 1H); 7.1–7.4 (m, 1H); 7.5–7.8 (m, 1H)	220	*E*
2m	16.5	66	75	47–48°	$C_7H_{10}OS$ (142.2)	1705[d]	1.6–2.5 (m, 6H); 2.45 (s, 3H); 7.10 (t, 1H, J=1.5 Hz)	142	*E*
2n	10	62 (56)[e]	72	oil: 95–97°/1	$C_8H_{12}OS$ (156.2)	1712	1.5–2.0 (m, 4H); 2.0–2.6 (m, 4H); 2.45 (s, 3H); 7.25 (br t, 1H)	156	*E*

[a] Yield of isolated, pure product.

[b] Satisfactory microanalyses obtained: C ±0.33, H ±0.26.

[c] Isolated as a viscous oil which solidifies after a few days.

[d] Nujol.

[e] Yield after distillation.

[f] Liquid solidifies after distillation.

mercaptans as one of the reactants, while the present method offers a convenient procedure for the synthesis of methylthioalkenyl ketones from the easily available ketene *S,S*-acetals.

When **1a** was refluxed with sodium borohydride and nickel chloride in alcohol, work-up and column chromatography of the reaction mixture gave **2a** in 62% yield. The ketene *S,S*-acetals **1b–e** similarly gave the corresponding **2b–e** in 42–64% overall yields. Reduction of ketene *S,S*-acetals **1f–h** bearing α-alkyl groups also gave the respective **2f–h** in 56–60% overall yields. The ketene *S,S*-acetal **1i** derived from acetone yielded the corresponding **2i** in 77% yield. When the cyclic ketene *S,S*-acetals **1j–n** were reduced under similar conditions, the respective **2j–n** were obtained in 57–66% overall yields.

When the reduction of **1a** was carried out in the presence of excess of nickel chloride (5 equiv), a complex mixture of propiophenone, **2a** and the saturated β-thioacetal was obtained. Similarly the reduction of **1a** in the presence of sodium borohydride and cobalt chloride yielded a mixture of partially and completely reduced products.

The configurations of the compounds **2a**–**2n** were assigned on the basis of their N.M.R. spectra. Compounds **2a**, **2c**, **2i** and **2b**, **2e** were assigned *trans*-(*E*) and *cis*-(*Z*) configurations, respectively, on the basis of coupling constants of the vinyl protons (Table). The vinyl proton *cis* to aroyl/acetyl group in **2a**, **2e**, and **2i** appears at $\delta = 7.5$ ppm or higher. Similarly, the lower chemical shifts of $\delta = 6.8$ ppm in the compounds **2f**–**2h** were assigned to the vinyl protons *trans* to the benzoyl group. The compounds **2j**–**2n**, which exhibited chemical shifts for vinyl protons of $\delta = 7.10$–7.50 ppm were also assigned the (*E*)-configuration. It may be noted that in all these reductions, the formation of only one predominant isomer is observed. The mechanism of the reduction in favour of one predominant isomer is interesting and will be discussed in a subsequent paper.

1-Alkylthio-2-alkenyl Ketones (2a–n); General Procedure:
To a stirred suspension of nickel chloride hexahydrate (38 g, 0.16 mol) in ethanol (150 ml), sodium borohydride (7.6 g, 0.2 mol) is slowly added (15 min) and the mixture is further stirred for 10 min. A solution of ketene *S*,*S*-acetal **1** (0.06 mol) in ethanol (50 ml) is added to the black suspension and the mixture is further stirred at room temperature for 10 min. It is then heated under reflux on an oil bath with stirring for the stated time (Table), until the starting material has disappeared completely (T.L.C.). The mixture is filtered hot through a sintered funnel and the black residue is washed with boiling chloroform (3 × 200 ml). The combined filtrate is washed with water (2 × 300 ml), the organic layer is dried with sodium sulfate, and evaporated to give a dark viscous liquid, which is passed through a silica gel column (Method A). Elution with hexane/benzene (9 : 1) (**2a–g**, **2m–2n**) or ethyl acetate/hexane (1 : 99) (**2h–l**) gives the methylthioalkenyl ketones **2a–n** as yellow viscous liquids/crystalline solids (T.L.C. single spot) (Table).

In a few cases (**1b**, **1i**, **1m**, and **1n**), ethanol from the reaction mixture obtained after refluxing, is removed under reduced pressure and the slurry is directly passed through a silica gel column (Method B). Elution with hexane/ethyl acetate (95 : 5) gives the corresponding **2b**, **2i**, **2m**, and **2n** in higher yields (Table) (T.L.C. single spot, N.M.R. shows 99% purity) though the products are darker in colour.

One of us (B. M.) thanks UGC, New Delhi, for a Junior Research Fellowship.

Received: September 23, 1981

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[1] Part XVIII; of the series; Part XVII: V. Aggarwal, G. Singh, H. Ila, H. Junjappa, *Synthesis* **1982**, 214.

[2] R. E. Ireland, J. A. Marshall, *J. Org. Chem.* **27**, 1615, 1620 (1962).

[3] T. Nishio, Y. Omote, *Synthesis* **1980**, 1013, and references therein.

[4] P. R. Bernstein, *Tetrahedron Lett.* **1979**, 1015.

[5] R. M. Coates, R. L. Sowerby, *J. Am. Chem. Soc.* **93**, 1027 (1971).

[6] E. N. Prilezhaeva, G. S. Vasil'ev, I. L. Mikhelashvili, V. S. Bogdanov, *Zh. Org. Khim.* **7**, 1349 (1971); *C. A.* **75**, 129023 (1971).

[7] K. Bowden, E. A. Braude, E. R. H. Jones, *J. Chem. Soc.* **1946**, 945.

[8] S. Akiyama, M. Iyoda, M. Nakagawa, *J. Am. Chem. Soc.* **98**, 6410 (1976).

[9] M. T. Omar, M. N. Basyouni, *Bull. Chem. Soc. Jpn.* **47**, 2325 (1974).

[0] S. Akiyama, S. Nakatsuji, T. Hamamura, M. Kataoka, M. Nakagawa, *Tetrahedron Lett.* **1979**, 2809, and references therein.

[1] A. E. Pohland, W. R. Benson, *Chem. Rev.* **66**, 161 (1966).

[2] A. Kumar, H. Ila, H. Junjappa, *J. Chem. Soc. Perkin Trans. 1* **1978**, 857, and references therein.

[3] H.-H. Ruttinger, W.-D. Rudorf, H. Matschiner, *J. Prakt. Chemie* **321**, 443 (1979).

[4] T. Nishio, Y. Omote, *Chem. Lett.* **1979**, 365.