CHEMISTRY LETTERS, pp. 953-956, 1982. © The Chemical Society of Japan 1982

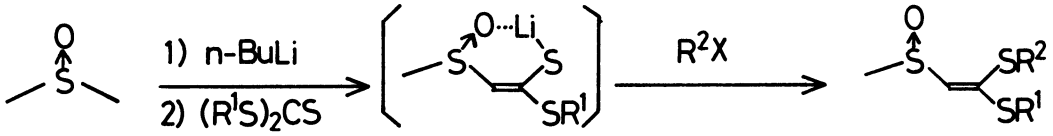
SYNTHESIS OF BIS[2,2-BIS(ETHYLTHIO)ETHENYL] SULFOXIDE

Masataka YOKOYAMA,* Masahiro HAYASHI, and Tsuneo IMAMOTO
Department of Chemistry, Faculty of Science, Chiba University
Yayoi-cho, Chiba City 260

(Methylsulfinyl)ketenedithioacetals (3) and alkyl (methylsulfinyl)-dithioacetates (4) were prepared from dimethyl sulfoxide. Next, the useful title compound (8) was synthesized from 4.

We have investigated the preparation of a variety of dithiocarboxylic acids and their application to the synthesis of heterocyclic compounds.[1] In connection with these studies, (methylsulfinyl)ketenedithioacetals (3) and alkyl (methylsulfinyl)dithioacetates (4) have become interesting as starting materials for synthesis of heterocycles because ketenedithioacetals conjugated with functional groups have been exploited in many synthetic applications.[2] In this paper we wish to report efficient methods for the syntheses of 3 and 4 from dimethyl sulfoxide and further bis[2,2-bis(ethylthio)ethenyl] sulfoxide (8) from 4.

The most simple approach to prepare 3 seemed to be the reaction of methylsulfinyl carbanion (dimsyl anion[3]) with carbon disulfide followed by alkylation. However, this attempt gave unacceptable yield of 3 because of competing polymerization. After several trials we found that 3 could be synthesized stereoselectively in good yield by the reaction of lithio-dimethyl sulfoxide with trithiocarbonic ester followed by alkylation. The results are summarized in Table 1.



1 2 3

A general experimental procedure is as follows; to a solution of DMSO (1.56 g, 20 mmol) in 60 ml of THF was added 15 % solution of n-BuLi in hexane (14 ml, 21 mmol) at -40 °C under nitrogen. After stirring for 30 min, trithiocarbonic ester (10 mmol) was added to the mixture and it was stirred for an additional 30 min. After addition of alkyl halide (22 mmol), the resulting mixture was stirred for 3 h at -10 °C, poured into 50 ml of water, and then extracted with benzene. The benzene extract was dried over sodium sulfate and rotary evaporated. The yellow oil obtained was purified by column chromatography on silica gel using AcOEt : MeOH (20 : 1) as an eluant to afford 3.

The structures of 3 were determined on the basis of elemental analyses and spectroscopic data, especially NMR analyses. In the NMR spectra of 3b and 3d, the magnetic nonequivalence, which was induced by the center of chiral sulfinyl group, was observed on the adjacent methylene protons of sulfur atom in R^2 group.[4]

Table 1. Preparation of 3

Compounds	R^1	R^2	Mp (°C) (recry. solv.)	Yield (%)
3a	Me	Me	——— a	74
3b	Me	Et	63-64(ether)	41
3c	Me	i-Pr	50-51(ether)	50
3d	Me	n-Bu	——— b	44
3e	Me	Bz	40-41(ether)	63
3f	Et	Me	——— c	82
3g	Et	Et	20-21(ether)	80
3h	n-Bu	Me	——— d	90

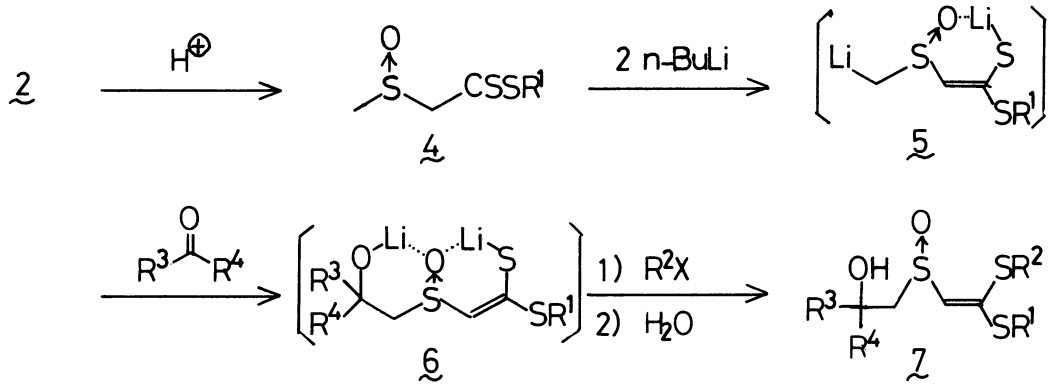
a. colorless oil, 125°C(dec); b. colorless oil, 209°C(dec); c. colorless oil, 149°C(dec); d. colorless oil, 155°C(dec)

On the other hand, this effect did not appear in those of 3f and 3h. This fact supports that both methylsulfinyl and R^2S groups of 3 exist in a cis form. In the case of open-chain compounds the significant effects of asymmetry have been reported for protons which are as many as seven bonds away from asymmetric center.[5] Our observation shows an interesting result that the effect of chirality appears on the protons through five bonds from a chiral center.

Compounds 3 were unchanged in crystalline state. However, it was observed on the basis of NMR spectrum that ca. 20 % of 3b changed to 3f on standing in chloroform solution at 0 °C for 1 week. When treated with 1 equiv of n-BuLi followed by benzylation, 3 (R^1= Me, R^2= Et) could afford (Z)-1-benzyl-1-(methylsulfinyl)-2-(ethylthio)-2-(methylthio)ethene[6] resulting from an intermediate metallated at vinyl position.

In addition, it was found that the present reaction to form 3 was performed using sodio-dimethyl sulfoxide instead of lithio-dimethyl sulfoxide to give an equal mixture of Z- and E-forms of 3.

Next, methyl (methylsulfinyl)dithioacetate[7] and ethyl (methylsulfinyl)dithioacetate[8] could be isolated by treatment with dil HCl in the place of alkyl halide in the present reaction. These compounds 4, which decomposed slowly at ambient temperature, reacted with phenylhydrazine to give (methylsulfinyl)thioaceto-ß-phenylhydrazide.[9] When treated with a n-BuLi (2 equiv)/ carbonyl compounds/ alkyl halides combination, 4 could afford 7[10] resulting from 5 in moderate yields.

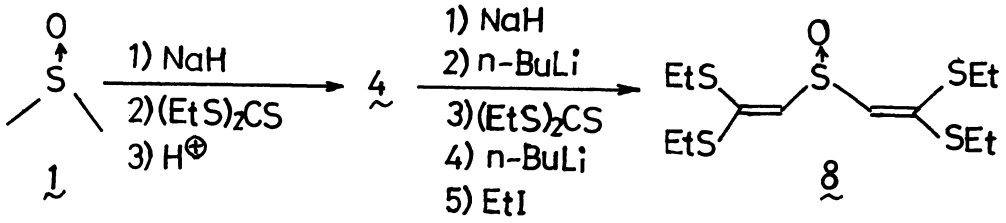


On the basis of the above result, the title compound 8 was synthesized as follows; to the dimsyl anion prepared from NaH (80 mmol) and DMSO (30 ml)[3] was

added THF (50 ml) and then dropwise diethyl trithiocarbonate (6.6 g, 40 mmol) with stirring under cooling in an ice-bath. After stirring for 30 min at room temperature, the reaction mixture was washed with benzene, made acid to pH 3 with dil HCl, and extracted with dichloromethane. The extract was washed with water and saturated NaCl, and purified by column chromatography on silica gel using AcOEt as an eluant to give 4 (R^1= Et) in 70 % yield. Compound 4 could be stored at -30 °C without decomposition.

To a slurry of NaH (7 mmol) and THF (30 ml) was added 3 ml of THF containing 4 (5 mmol) under cooling at 0 °C. The mixture was treated with a n-BuLi hexane solution (6 mmol) with 30 min's stirring/ diethyl trithiocarbonate (1.7 g) with 1 h's stirring/ n-BuLi hexane solution (6 mmol) with 10 min's stirring at ca. -50 °C. Ethyl iodide (2.5 g) was added to the resulting mixture, and it was stirred for 2 h at room temperature. Usual work up was performed and purification by column chromatography on silica gel using AcOEt as an eluant gave 8[11] as colorless needles (recry. from Et_2O) of mp 25 °C in 56 % yield.

The attempted method to prepare 8 from 1 in one pot was unsuccessful because of the contamination with large amounts of impurities. Further investigations into synthetic applications of 3, 4, and 8 are in progress in our laboratory.



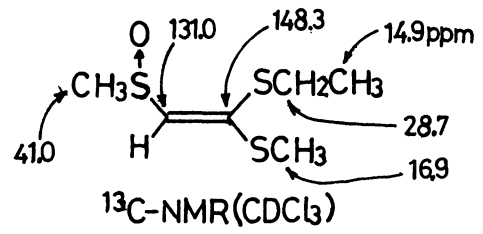
References

1) T.Takeshima,M.Yokoyama,T.Imamoto,M.Akano,and H.Asaba,J.Org.Chem.,34,730(1969) and references cited therein; T.Takeshima,M.Yokoyama,N.Fukada,and M.Akano,ibid., 35,2438(1970); M.Yokoyama,ibid.,35,283(1970); ibid.,36,2009(1971); M.Yokoyama,Y. Sawachi,and T.Isso,ibid.,38,802(1973); M.Yokoyama,Bull.Chem.Soc.Jpn.,43,2938 (1970); ibid.,44,1610(1971); ibid.,3195(1971); M.Yokoyama,T.Kondo,N.Miyase,and M.Torri,J.C.S.Perkin I,160(1975); M.Yokoyama,K.Motozawa,and T.Imamoto,ibid.,2499 (1981) and references cited therein; M.Yokoyama,M.Kurauchi,and T.Imamoto, Tetrahedron Lett.,22,2285(1981); M.Yokoyama,M.Nakamura,T.Imamoto,and K.Yamaguchi, J.C.S.Chem.Comm.,560(1981); M.Yokoyama,K.Hoshi,and T.Imamoto,Synthesis,908(1981).

2) B.T.Grobel and D.Seebach,Synthesis,357(1977); F.A.Carey and A.J.Court,J.Org. Chem.,37,4474(1972); R.K.Dieter,ibid.,46,5031(1981); M.Augustin and Ch.Groth, J.Prakt.Chem.,321,215(1979); M.Augustin,Ch.Groth,H.Kristen,K.Peseke,and Ch. Wiechmann,ibid.,321,205(1979); J.P.Marino and J.L.Kostusyk,Tetrahedron Lett., 2489,2493(1979); S.Masson and A.Thuillier,ibid.,4085(1980); E.J.Corey and R.H. K.Chen,ibid.,3817(1973); R.R.Schmidt,H.Speer,and B.Schmid,ibid.,4277(1979); K.T. Potts,M.J.Cipullo,P.Ralli,and G.Theodoridis,J.Am.Chem.Soc.,103,3584(1981); H.Okamura,Y.Mitsuhira,M.Miura,and H.Takei,Chem.Lett.,517(1978).

3) E.J.Corey and M.J.Chaykovsky,J.Am.Chem.Soc.,87,1345(1965).

4) NMR(CCl_4): 3b, δ6.20(s,1H,vinyl proton), 3.00(d,q,1H,C<u>H</u>$_2$,J_{gem}= 16Hz,J_{vic}= 7Hz), 2.93(d,q,1H,C<u>H</u>$_2$,J_{gem}= 16Hz,J_{vic}= 7Hz), 2.68(s,3H,C<u>H</u>$_3$SO),2.41(s,3H,SC<u>H</u>$_3$),1.32 (t,3H,C<u>H</u>$_3$,J= 7Hz); 3d,δ6.31(s,1H,vinyl proton),ca.2.93(two sets of triplets, 2H,SC<u>H</u>$_2$,J= ca.7Hz),2.63(s,3H,C<u>H</u>$_3$SO), 2.44(s,3H,SC<u>H</u>$_3$),1.58(m,4H,-C<u>H</u>$_2$C<u>H</u>$_2$-),0.93(m,3H,C<u>H</u>$_3$).



5) G.M.Whitesides,D.Holtz,and J.D.Roberts,J.Am.Chem.Soc.,86,2628(1964).

6) colorless needles (recry. from Et_2O); mp 56-58 °C; ir(KBr)3050(arom.CH),3000-2850(CH),and 1050 cm^{-1}(SO); NMR(CCl_4)δ7.50-7.10(m,5H,Ph),4.10(d,1H,PhC<u>H</u>$_2$,J_{gem}= 14Hz),4.00(d,1H,PhC<u>H</u>$_2$,J_{gem}= 14Hz),2.76(m,2H,C<u>H</u>$_2$CH$_3$),2.36(s,3H,SC<u>H</u>$_3$),2.30(s,3H, C<u>H</u>$_3$SO),1.23(t,3H,CH$_2$C<u>H</u>$_3$,J= 8Hz).

7) red oil; ir(neat)3000-2900(CH) and 1060 cm^{-1}(SO); NMR(CCl_4)δ4.41(s,2H,C<u>H</u>$_2$),2.66 (s,3H,C<u>H</u>$_3$SO),2.71(s,3H,SC<u>H</u>$_3$).

8) red needles; mp 18-19 °C, 135 °C(dec); ir(neat)2950-2850(CH),and 1060 cm^{-1}(SO); NMR(CCl_4)δ4.36(s,2H,C<u>H</u>$_2$),3.26(q,2H,C<u>H</u>$_2$CH$_3$,J= 7Hz),2.65(s,3H,C<u>H</u>$_3$SO),1.36(t,3H, CH$_2$C<u>H</u>$_3$,J= 7Hz).

9) colorless plates (recry. from EtOH); mp 145-146 °C; ir(KBr)3210,3150(NH),3040 (arom.CH),3000-2800(CH),and 1020 cm^{-1}(SO); NMR(DMSO-d_6)δ12.10(br,1H,N<u>H</u>),8.40 (br,1H,N<u>H</u>),7.40-6.70(m,5H,Ph),4.13(s,2H,C<u>H</u>$_2$),2.71(s,3H,C<u>H</u>$_3$).

10) 7a(R^1= Et; R^2= Me; R^3= Me; R^4= Me): colorless oil (63 % yield); 148 °C(dec); ir(neat)3300(OH),2950-2900(CH),and 1010 cm^{-1}(SO); NMR(CCl_4)δ6.47(s,1H,vinyl proton),4.50(br,1H,O<u>H</u>),3.12(d,1H,C<u>H</u>$_2$,J_{gem}= 14Hz),2.97(q,2H,C<u>H</u>$_2$CH$_3$,J= 8Hz),2.79 (d,1H,C<u>H</u>$_2$,J_{gem}= 14Hz),1.42(s,3H,C<u>H</u>$_3$),1.36(s,3H,C<u>H</u>$_3$),1.34(t,3H,CH$_2$C<u>H</u>$_3$,J= 8Hz); 7b (R^1= Et, R^2= Me, R^3= H, R^4= Ph): colorless prisms (recry. from CCl_4); mp 61 °C; 72 % yield; ir(KBr)3300-3150(OH),3030(arom.CH),3000-2850(CH),and 1010 cm^{-1}(SO); NMR($CDCl_3$)δ7.60-7.20(m,5H,Ph),6.32(s,0.40 H,C<u>H</u>),6.23(s,0.33 H,C<u>H</u>), 6.20(s,0.27 H,C<u>H</u>),5.50-5.20(m,1H,PhC<u>H</u>),4.72(br,1H,O<u>H</u>),3.30-2.70(m,4H,SC<u>H</u>$_2$, C<u>H</u>$_2$SO),2.40(m,3H,SC<u>H</u>$_3$),1.50-1.10(m,3H,CH$_2$C<u>H</u>$_3$); the NMR datum shows 7b to be an isomeric mixture.

11) ir(neat)3000-2850(CH),1030(SO); NMR(CCl_4)δ6.65(s,2H,C<u>H</u>),2.95(q,4H,C<u>H</u>$_2$CH$_3$,J= 8 Hz),2.90(q,4H,C<u>H</u>$_2$CH$_3$,J= 8Hz),1.33(t,12H,CH$_2$C<u>H</u>$_3$,J= 8Hz). Found: C,42.11;H,6.40 %. Calcd for $C_{12}H_{22}OS_5$: C,42.07;H,6.47 %.

(Received March 29, 1982)