B. **3-Phenyl-1-trimethylsilylpropyne (1).** A solution of 25 ml of 1.6 *M n*-butyllithium in hexane was added to 5 ml (0.04 mol) of 1-phenylpropyne and 1.4 ml (0.01 mol) of TMEDA. The mixture was heated at reflux for 20 min, cooled to −78°, and quenched with 7.5 ml (0.06 mol) of trimethylchlorosilane in 25 ml of THF. The product was added to 50 ml of water. The organic phase was separated, washed with two 25-ml portions of water, and distilled giving 3.5 g (50%) of **1** and 2.2 g of a mixture of **1** and **3**. See Table III for physical properties of **1**.

C. **3-Phenyl-1,3-bis(trimethylsilyl)propyne (3).** In the same manner described for **1**, 5 ml (0.04 mol) of 1-phenylpropyne was treated with 2.8 ml (0.02 mol) of TMEDA and 50 ml of 1.6 *M n*-butyllithium (0.08 mol) in hexane giving 7.2 g of a mixture of **1** (15%), **3** (70%), and **5** (15%) (gc area per cent), bp 80–120° (1 Torr). **3** was isolated from **1** and **5** by preparative gc and characterized (Table III).

D. **Phenyltris(trimethylsilyl)allene (5).** As above, metalation of 1-phenylpropyne (5.0 ml, 0.04 mol) with 3.2 ml (0.03 mol) of TMEDA and 75 ml of 1.6 *M n*-butyllithium in hexane followed by derivatization with 20 ml (0.16 mol) of trimethylchlorosilane in 75 ml of THF gave 10 g of a mixture of **5** and **3**, ratio 3:1, bp 95–125° (1 Torr). **5** was isolated pure by gc and characterized (Table III). Estimated yield of **5** was about 60%.

E. **3-(*p*-Trimethylsilylphenyl)-1,3-bis(trimethylsilyl)propyne (6).** A mixture of 2 ml (0.016 mol) of 1-phenylpropyne, 5.5 ml (0.40 mol) of TMEDA, and 100 ml of 1.6 *M n*-butyllithium in hexane was stirred at room temperature for 3 days. Derivatization with 25 ml (0.20 mol) of trimethylchlorosilane in 100 ml of THF at −78° followed by an aqueous work-up gave 4.3 g of oil, bp 150–165° (1.5 Torr). Gc showed this oil to be a mixture of **5** (20%), **6** (20%), and **7** (60%). **6** was isolated by preparative gc and characterized (Table III).

F. **1-Phenyl-3-trimethylsilylallene (2).** A solution of 1.8 g (0.01 mol) of 3-phenyl-1-trimethylsilylpropyne (**1**) and 14 ml of 1.6 *M n*-butyllithium in hexane was heated at reflux for 30 min to give a yellow solid. The mixture was added to 75 ml of 6 *N* hydrochloric acid. The organic phase was separated and concentrated. Gc showed only **1** and **2** to be present in the ratio 2:1. Allene **2** was isolated by preparative gc and characterized (Table III).

G. **1-Phenyl-1,3-bis(trimethylsilyl)allene (4).** A solution of 3.5 g (0.013 mol) of 3-phenyl-1,3-bis(trimethylsilyl)propyne (**3**) and 10 ml of 1.6 *M n*-butyllithium in hexane was heated at reflux for 30 min, then added to 25 ml of 6 *N* hydrochloric acid. The organic phase was separated and concentrated to give an equimolar mixture of **3** and **4**. Compound **4** was isolated by preparative gc and characterized (Table III).

3. **Infrared Spectra of Lithiated Phenylpropynes and -allenes.** A. **1-Lithio-3-phenylpropyne.** Addition of a solution of 1 ml of 1.6 *M n*-butyllithium in cyclohexane to 2 ml (16 mmol) of 3-phenylpropyne gave a reddish white solid. The solid was filtered under nitrogen and washed with three 1-ml portions of cyclohexane. The ir spectrum (Nujol) of the solid shows only a weak absorption at 2050 cm^{-1} in the region 1600–2200 cm^{-1}. Quenching with trimethylchlorosilane gives predominately **1**.

B. **1-Phenyl-1,3-dilithioallene.** Addition of a solution of 0.1 ml (0.8 mmol) of 3-phenylpropyne in 1 ml of cyclohexane to a solution of 1 ml of 1.6 *M n*-butyllithium in cyclohexane gave a yellow solid. This solid was isolated as described above. The ir spectrum (Nujol) showed a very strong band at 1900 cm^{-1}. Derivatization of the solid with trimethylchlorosilane gives predominantly **3**.

C. **Phenyltrilithioallene.** A solution of 0.2 ml (1.6 mmol) of 3-phenylpropyne in 1 ml of cyclohexane was added to 3.3 ml of 1.6 *M n*-butyllithium in cyclohexane. Immediately after mixing, ir analysis of the deep red solution showed a very strong band at 1900 cm^{-1}, Ph(Li)C=C=CHLi, and a weak band at 1780 cm^{-1}, Ph(Li)C=C=CLi_2. Gradually the 1900-cm^{-1} band disappeared and the 1780-cm^{-1} band became very strong.

D. **Lithium Derivatives of 3-Phenyl-1-trimethylsilylpropyne (1).** A solution of 0.2 g (1 mmol) of **1**, 2 ml of cyclohexane, and 0.6 ml of 1.6 *M n*-butyllithium in cyclohexane was heated briefly at reflux. The ir spectrum showed a weak band due to **1** at 2190 cm^{-1}, a strong broad absorption assigned to Ph(Li)C=C=$CHSiMe_3$ at 1870 cm^{-1}, and a weak band at 1790 cm^{-1} assigned to Ph(Li)C=C=C($SiMe_3$)Li. Another 1 ml of 1.6 *M n*-butyllithium solution was added. With time the 1870-cm^{-1} band became weaker and the 1790-cm^{-1} band grew stronger.

E. **Lithium Derivatives of 3-Phenyl-1,3-bis(trimethylsilyl)propyne (3).** A solution of 0.5 g (1.9 mmol) of **3**, 2 ml of cyclohexane, and 1.5 ml of 1.6 *M n*-butyllithium in cyclohexane was heated to reflux, cooled, and analyzed by ir spectrum showing two strong absorptions at 2000 and 1850 cm^{-1} of about equal intensity. These bands did not change with time. The 2000-cm^{-1} band is attributed to the species 3-phenyl-1,3-bis(trimethylsilyl)-3-lithiopropyne, Ph(Me_3Si)LiCC≡$CSiMe_3$, and the 1850-cm^{-1} band to the species 1-phenyl-1,3-bis(trimethylsilyl)-3-lithioallene, Ph(Me_3Si)C=C=C($SiMe_3$)Li.

A New Synthesis of α,β-Unsaturated Aldehydes Using 1,3-Bis(methylthio)allyllithium

E. J. Corey,* Bruce W. Erickson, and Ryozi Noyori

Contribution from the Department of Chemistry, Harvard University,
Cambridge, Massachusetts 02138. Received July 23, 1970

Abstract: Reaction of 1,3-bis(methylthio)-2-methoxypropane (**5**) (easily available in two steps from epichlorohydrin) with lithium diisopropylamide in tetrahydrofuran produces the lithio derivative of the 1,3-bis(methylthio)-allyl anion (**1**). The reagent **1** so generated has been shown to serve effectively as the equivalent of the unknown β-formylvinyl anion by the synthesis of a number of α,β-unsaturated aldehydes starting with alkyl halides, carbonyl compounds, or 1,2-epoxides. In the case of the last two substrates a trifunctional γ- or δ-hydroxy α,β-unsaturated aldehyde unit results. This is a unique and useful feature of the new method which has been exploited in a total synthesis of prostaglandin $F_{2\alpha}$. It is concluded from these studies that the use of the reagent **1** represents a significant new approach to the synthesis of conjugated aldehydes which should be advantageous in a wide range of synthetic problems.

The β-carbon atom of the unit –CH=CHCHO is a receptor for nucleophiles and free radicals, but not for electrophiles. The present paper reports a reagent which functions as the equivalent of this unit having inverted, *i.e.*, nucleophilic, reactivity. This inversion imparts a special applicability and utility in organic synthesis,[1] as is illustrated by a number of test cases.

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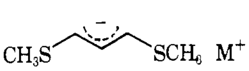
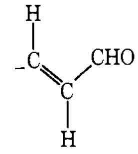
(1) For a discussion of other examples of the synthetic strategy of group equivalents having inverted reactivity, see (a) E. J. Corey, *Pure*

The 1,3-bis(methylthio)allyl anion (**1**) is an especially interesting synthetic equivalent of the presently unknown (and probably intrinsically unstable) anion **2**,



1



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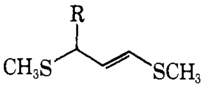
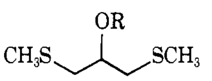
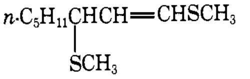


3

since it ought to be stabilized relative to the allyl system[1b,2] and since attachment of an electrophile R^+ to either terminal carbon would yield the same protected form (**3**) of the conjugated aldehyde $RCH{=}CHCHO$. The generation of the carbanion **1** as the lithio derivative was readily accomplished by a simple three-step sequence from epichlorohydrin. Reaction of epichlorohydrin with sodium methylthiolate gave 1,3-bis(methylthio)-2-propanol (**4**, 84%), which was converted to the sodio derivative (NaH) and methylated (CH_3I) to afford 1,3-bis(methylthio)-2-methoxypropane (**5**, 90%). Treatment of the methyl ether **5** with 1 equiv of lithium diisopropylamide in tetrahydrofuran resulted in the elimination of methanol to give 1,3-bis(methylthio)propene (88%). The same substance was prepared by an independent synthesis from methylthioacetaldehyde and the lithio derivative of diethyl methylthiomethylphosphonate, thereby confirming the structural assignment. Reaction of **5** with 2 equiv of lithium diisopropylamide in tetrahydrofuran at −15 to 0° under nitrogen furnished a deep purple solution of the lithio derivative of **1**. The lithio reagent **1** could be stored for 12 hr at 0° without appreciable decomposition. The formation of the anionic reagent **1** was verified by its characteristic behavior toward alkyl halides, carbonyl compounds, and epoxides.

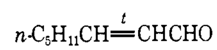


4, R = H
5, R = CH_3



$n\text{-}C_5H_{11}\underset{SCH_3}{CH}CH{=}CHSCH_3$

6

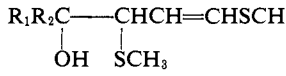


$n\text{-}C_5H_{11}CH\overset{t}{=}CHCHO$

7

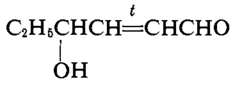
Reaction of **1** with 1-bromopentane for 2 hr at −75° furnished 1,3-bis(methylthio)-1-octene (**6**) in 90% yield. This bisthio ether was converted smoothly by hydrolysis using 4 equiv of mercuric chloride in aqueous acetonitrile for 4 hr at 50° to *trans*-2-octenal (**7**) in 84% yield. This sequence is shorter and more efficient than any of the five methods of synthesis which have been described.[3–7]

Reaction of 1,3-bis(methylthio)allyllithium with an aldehyde or ketone followed by hydrolysis of the 1,3-bis(methylthio)-1-alkene moiety furnishes a γ-hydroxy-α,β-unsaturated aldehyde. For example, addition of the allyllithium reagent to propanal formed 1,3-bis(methylthio)-1-hexen-4-ol (**8**) in 89% yield, which was hydrolyzed to *trans*-4-hydroxy-2-hexenal (**9**) using either mercuric chloride (41% yield) or silver nitrate (48% yield) to complex with the liberated methanethiol.



$R_1R_2\underset{OH}{C}—\underset{SCH_3}{C}HCH{=}CHSCH_3$

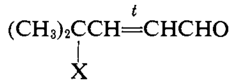
8, $R_1 = C_2H_5$; $R_2 = H$
10, $R_1 = R_2 = CH_3$
11, $R_1 = R_2 = C_6H_5$



$C_2H_5\underset{OH}{C}HCH\overset{t}{=}CHCHO$

9

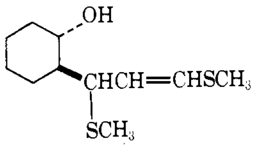
The adduct **10** was obtained from the reaction of the anion **1** with acetone in 97% yield, and similarly benzophenone afforded **11** in 95% yield despite its much lower electrophilicity. The acetone adduct could be converted to a variety of aldehyde derivatives including the γ-hydroxy, γ-methoxy, and γ-methylthio aldehydes **12–14**, respectively. The reactions involved in these conversions are described in detail in the Experimental Section.



$(CH_3)_2\underset{X}{C}CH\overset{t}{=}CHCHO$

12, X = OH
13, X = OCH_3
14, X = SCH_3

The reaction of the lithio reagent **1** with cyclohexene oxide produced the *trans*-cyclohexanol derivative **15**. Acetylation of **15** followed by mercuric ion promoted hydrolysis afforded the acetoxy aldehyde **16** in 82% yield overall from cyclohexene oxide. By a similar sequence cyclopentene oxide was transformed into the lower homolog of **16** and propylene oxide was converted to 5-acetoxy-*trans*-2-hexenal (**17**). The application of the lithio reagent **1** to the conversion of the oxido acetal **18** to the hydroxy aldehyde **19** as a key step in a total synthesis of prostaglandin $F_{2\alpha}$ (**20**) has recently been described.[8]



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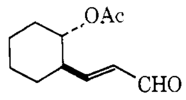

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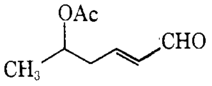

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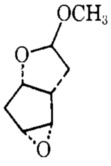

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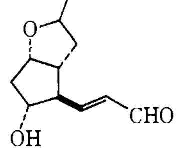

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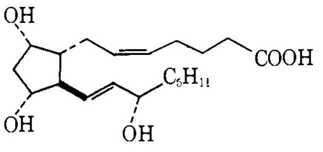

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(8) E. J. Corey and R. Noyori, *Tetrahedron Lett.*, 311 (1970).

Experimental Section

Melting points and boiling points are uncorrected. Analytical thin layer chromatography (tlc) was performed on Merck 0.25-mm precoated fluorescent silica gel plates; preparative tlc was conducted on 2.0-mm silica gel plates using one solvent development, unless otherwise stated. Analytical gas chromatography (glc) was performed with a Hewlett Packard (F & M) instrument equipped with flame ionization detectors. Column A was a 3 ft × 0.125 in. stainless steel column packed with 5% LAC-446 (cross-linked diethylene glycol–adipic ester) on Diatoport S; column B was a 1.5 ft × 0.125 in. column packed with 3% OV-7 (polydimethylsiloxane with phenyl groups replacing 20% of the methyl groups); column C was a 4 ft × 0.125 in. column packed with 3% OV-7 on silanized support. The carrier gas was prepurified nitrogen (30 ml/min for columns A and B, 60 ml/min for C). Retention time (t_R) is given in minutes.

Infrared (ir) data were obtained using a Perkin-Elmer Model 137 (Infracord) spectrophotometer. Nuclear magnetic resonance (nmr) spectra were measured with a Varian Associates A-60 or T-60 spectrometer; chemical shifts are expressed in parts per million downfield from internal tetramethylsilane. The ir and nmr spectra were observed in CCl_4 solution unless stated otherwise. Mass spectra were determined in these laboratories with an AEI-MS 9 spectrometer at 70 eV. Complete spectral data are contained in the Ph.D. dissertation of B. W. Erickson, Harvard University, 1970. *n*-Butyllithium in pentane was obtained from Foote Mineral Co. All reactions involving the use of strong bases were conducted under an atmosphere of dry nitrogen or argon.

1,3-Bis(methylthio)-2-propanol (4). Methanethiol was distilled into a solution of sodium hydroxide in methanol (4.4 *M;* 250 ml, 1.10 mol) until the latter was saturated at 20°. Epichlorohydrin (37.6 ml, 0.48 mol) was added to this solution dropwise over 10 min. The vigorous reaction was kept at 50–60° by external ice–water cooling. The resulting mixture, which contained much precipitated sodium chloride, was stirred for 1 hr and diluted with water. Ether extracts of this solution were washed with water until neutral, dried, and freed of solvent.

Short-path distillation of the residual liquid provided the analytically pure alcohol **4** (61.0 g, 84% yield) as a colorless liquid: bp 110–111° (7 Torr); tlc, R_f 0.40 ($CHCl_3$); glc, t_R 1.75 (column A, 140°); ir 2.92 (m, OH), 6.94 (s, SCH_2 bend), 6.99 and 7.07 (s, SCH_3 asym bend), 7.22 (s), 7.39 (m), 7.53 (m, SCH_3 sym bend), 7.81 (s, SCH_2 wag), 7.98 (m), 8.12 (m), 9.19 (m), 9.33 (s), 9.62 (s, C–O), and 10.33 μ (m, SCH_3 rock); nmr (ppm) $[(CH_3{}^aSCH_2{}^b)_2CH^cOH^d]$, 2.13 (s, 6 H, H^a), 2.63 (d, 4 H, J_{bc} = 6 Hz, H^b), 3.86 (p, 1 H, H^c), and 3.78 (s, 1 H, H^d); molecular ion, *m*/e 152.0334 (calcd for $C_5H_{12}OS_2$: 152.0330).

Anal. Calcd for $C_5H_{12}OS_2$: C, 39.44; H, 7.94. Found: C, 39.62; H, 7.93.

1,3-Bis(methylthio)-2-methoxypropane (5). 1,3-Bis(methylthio)-2-propanol (**4**; 1.568 g, 10.3 mmol) was added dropwise over 4 min to a slurry of oil-free sodium hydride (0.55 g, 23 mmol) in dry THF (10 ml) stirring under argon at 0°. The mixture was stirred at 0° until hydrogen evolution ceased (5 min), treated with neat iodomethane (0.69 ml, 11.1 mmol), and stirred at 0° for 1.0 hr. As much starting alcohol was present by tlc assay, the mixture was stirred at 25° for 1 hr, diluted with dry THF (10 ml), and stirred vigorously at 25° for 6 hr. The resulting slurry was diluted with ether, washed with 1.0 *M* aqueous ammonium chloride (foaming), water, and brine, dried, and freed of solvent.

Short-path distillation of the residual liquid furnished the analytically pure methyl ether **5** (1.415 g, 90% yield) as a colorless liquid: bp 96–97° (9 Torr), bp 59–60° (0.35 Torr); tlc, R_f 0.65 ($CHCl_3$); glc, t_R 0.67 (column A, 140°), t_R 1.00 (column A, 120°); ir 6.88 (w, OCH_3 asym bend), 6.96 (m), 7.02 (m), 7.12 (w), 7.45 (w), 7.59 (s, SCH_3 sym bend), 8.47 (w), 9.06 (vs, C–O asym stretch), 9.96 (w), and 10.44 μ (w, SCH_3 rock); nmr (ppm) $[(CH_3{}^aSCH_2{}^b)_2CH^cOCH_3{}^d]$, 2.13 (s, 6, H, H^a), 2.68 (d, 4 H, J_{bc} = 5.4 Hz, H^b), 3.41 (s, 3 H, H^d), and 3.50 (p, 1 H, H^c); molecular ion, *m/e* 166.0488 (calcd for $C_6H_{14}OS_2$: 166.0486).

Anal. Calcd for $C_6H_{14}OS_2$: C, 43.33; H, 8.49. Found: C, 43.58; H, 8.42.

1,3-Bis(methylthio)propene. A. From Diethyl Methylthiomethylphosphonate and Methylthioacetaldehyde. *n*-Butyllithium in pentane (1.30 *M;* 15.8 ml, 20.6 mmol) was added to a solution of diisopropylamine (3.08 ml, 21.4 mmol) in dry THF (30 ml) stirring under argon at −75°. Diethyl methylthiomethylphosphonate[9] (3.52 ml, 20.2 mmol) was added; after 11 hr at −15°, the clear orange solution was treated at −75° with methylthioacetaldehyde[10] (1.65 ml, 19.1 mmol) and stirred at −20° for 1 hr. Solvent was distilled from the solution at 1 atm until the vapors reached 60°; the solution was heated at reflux (60–65°) for 30 min, cooled, and poured into water. Ether extracts of this mixture were washed with 5 *M* aqueous ammonium chloride, 1 *M* aqueous sodium bicarbonate, and brine, dried, and freed of solvent at 35° (10 Torr).

The remaining liquid was evaporatively distilled (110–125°, 8 Torr) to provide 1,3-bis(methylthio)propene (0.793 g, 31%) as a colorless liquid: glc, t_R 0.36 (cis) and 0.44 (trans) (column A, 140°), t_R 0.45 (cis) and 0.55 (trans) (column A, 120°); ir 6.22 μ (m, C=C); nmr (ppm) $(CH_3{}^aSCH_2{}^cCH^d{=}CH^eSCH_3{}^b)$: trans 1.97 (s, 3 H, H^a), 2.23 (s, 3 H, H^b), 3.13 (d, 1 H, J_{cd} = 7.5 Hz, H^c), 5.33 (dt, 1 H, H^d), and 6.12 (d, 1 H, J_{de} = 15.0 Hz, H^e); cis 2.02 (s, 3 H, H^a), 2.26 (s, 3 H, H^b), 3.15 (d, 1 H, J_{cd} = 7.5 Hz, H^c), 5.53 (dt, 1 H, H^d), and 6.01 (d, 1 H, J_{de} = 9.0 Hz, H^e); molecular ion, *m/e* 134.0211 (calcd for $C_5H_{10}S_2$: 134.0224).

The residual liquid after distillation consisted of two diastereomers of diethyl 1,3-bis(methylthio)-2-hydroxypropylphosphonate (1.24 g, 23% yield): nmr (ppm) 1.34 (t, 6 H, CCH_3, *J* = 7 Hz), 2.13 (s, 3 H, SCH_3), 2.26 (s, 3 H, SCH_3), 2.3–3.5 (m, 4 H, $CHCHCH_2$), 4.2 (two p, OCH_2, *J* = 7 Hz), and 4.4 (bs, 1 H, OH).

B. From 1,3-Bis(methylthio)-2-methoxypropane. *n*-Butyllithium in pentane (1.24 *M;* 18.0 ml, 22.3 mmol) was added to a solution of diisopropylamine (2.29 g, 22.6 mmol) in dry THF (50 ml) stirring under argon at −75°. After the addition of 1,3-bis(methylthio)-2-methoxypropane (**5**, 1.915 g, 11.5 mmol) at −75°, the solution was stirred at 0° for 2.0 hr. Small portions were added to ethanol at intervals; glc assay of the product mixtures showed the following relative amounts of recovered methyl ether **5**: 16% after 10 min, 5% after 20 min, 0.5% after 60 min, and 0.3% after 120 min.

The reaction mixture was diluted with 1:1 pentane–dichloromethane, washed with 0.5 *M* aqueous sodium bicarbonate and brine, and dried. After the solvents were distilled off through a 10-cm Vigreux condenser, the residual liquid was distilled without column near 75° (10 Torr). The distillate (2.1 g) was evaporatively distilled to provide 1,3-bis(methylthio)propene [1.36 g, 88% yield; trans/cis = 64:36 (glc)], pure by nmr assay, as a colorless liquid: glc, t_R 0.98 (cis), 1.18 (trans) (column **B**, 80°); t_R 3.65 (cis) and 4.60 (trans) (column **B**, 50°).

When this reaction was repeated at 25° using lithium diisopropylamide and the methyl ether **5** in the ratio 1.05:1.00, respectively, 10% of the methyl ether remained after 6.3 hr and 4% was present after 18 hr.

1,3-Bis(methylthio)-1-octene (6). *n*-Butyllithium in pentane (1.24 *M;* 18.0 ml, 22.3 mmol) was added to a solution of diisopropylamine (2.35 g, 23.2 mmol) and 1,3-bis(methylthio)-2-methoxypropane (1.826 g, 11.0 mmol) in dry THF (33 ml) stirring under argon at −75°. The reaction solution was kept at −15° for 70 hr, treated at −75° with 1-bromopentane (2.155 g, 14.25 mmol), and kept at −75° for 2 hr. The alkylation was complete after 1 hr at −75°, for the acetone adduct **12** was absent by glc assay from a part of the reaction solution quenched with acetone. The solution was treated at −75° with methanol (1.0 ml), diluted with ether, washed with 5 *M* aqueous ammonium sulfate, water, 1 *M* aqueous sodium bicarbonate, and brine; the organic phase and ether extracts of the aqueous washings were dried and freed of solvent.

The residual liquid (2.15 g) consisted of 1,3-bis(methylthio)-propene (5 rel mol %; trans/cis = 68:32) and 1,3-bis(methylthio)-1-octene (**6**; 95 rel mol %; trans/cis = 80:20) by glc assay. It was evaporatively distilled at 130° (0.25 Torr) to furcish the octene (1.94 g, 90% yield) as a colorless liquid: glc, t_R 0.87 (cis) and 1.23 (trans) (column A, 140°), t_R 1.32 and 1.81 (column A, 120°); ir, 6.22 (m, C=C), 6.82 (s), 6.94 (s), 7.26 (m), 7.60 (m), 8.46 (m), 10.39 (s), and 10.64 μ (s); partial nmr (ppm) $[CH_3{}^bSCH^c{=}CH^dCH^e(SCH_3{}^a)C_5H_{11}]$; trans 1.92 (s, 3 H, H^a), 2.23 (s, 3 H, H^b), 3.1 (m, 1 H, H^e), 5.10 (dd, 1 H, J_{cd} = 15.0 Hz, J_{de} = 9.5 Hz, H^d) and 5.97 (d, 1 H, H^c); cis 1.98 (s, 3 H, H^a), 2.23 (s, 3 H, H^b), 3.5 (m, 1 H, H^e), 5.30 (dd, 1 H, J_{cd} = 9.5 Hz, J_{de} = 10.5 Hz, H^d), and 5.96 (d, 1 H, H^c); molecular ion, *m/e* 204.0984 (calcd for $C_{10}H_{20}S_2$: 204.1006).

***trans*-2-Octenal (7).** A solution of mercuric chloride (3.25 g, 12.0 mmol) in 8:1 acetonitrile–water (9 ml) was added to a solution of 1,3-bis(methylthio)-1-octene (**6**, 0.612 g, 3.00 mmol; trans/cis = 81:19) in the same solvent mixture (9 ml). A voluminous white

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[9] M. Green, *J. Chem. Soc.*, 1324 (1963).

[10] A. C. Cope, P. Kovacic, and M. Burg, *J. Amer. Chem. Soc.*, **71**, 3658 (1949).

Table I. Nmr Data for Eight *trans*-2-Alkenal Derivatives

Compd^a	Chemical shift (ppm), multiplicity^b a	b	c	d	e	f	g	*J*, Hz J_{ab}	J_{bc}	J_{bd}	J_{cd}	J_{de}	J_{ef}
7	9.47 d	6.01 ddd	6.81 dt	2.32 q	1.0–1.8 m	0.90 t		7.4	15.4	1.3	6.4		7
9	9.49 d	6.23 ddd	6.85 dd	4.30 m	1.2–1.9 m	0.96 t		7.6	15.5	1.0	4.3		7
12	9.55 d	6.23 dd	6.99 d	1.38 s			4.09 s	7.5	15.7				
13	9.50 d	6.08 dd	6.67 d	1.36 s			3.18 s	7.3	15.5				
14	9.51 d	5.84 dd	6.58 d	1.45 s			1.90 s	7.4	15.5				
16	9.40 d	6.10 dd	6.70 dd	1.1–2.8 m		4.70 m	2.00 s	7.5	15		7.5		
17	9.54 d	6.13 dd	6.85 dt	2.61 dd	5.11 m	1.28 d	2.05 s	7	16		7	6	6.5
22	9.55 d	6.12 dd	6.88 dd	2.86 m	1.5–2.4 m	4.96 m	2.05 s	7.5	15.5		7		

^{a} CCl_4 solution, except $CDCl_3$ for **16**, **17**, and **22**. ^{b} $O{=}CH^aCH^b{=}CH^cR$.

precipitate formed immediately. The mixture was stirred at 50° for 4 hr, cooled, and diluted with brine. Ether extracts of this mixture were washed with water, 1 *M* aqueous sodium bicarbonate, and brine, dried, and freed of solvent.

The residual liquid was submitted to preparative tlc using trichloromethane as eluent. The strongly uv-active band (R_f 0.46–0.65) afforded a liquid identified as unreacted octene **6** (0.186 g, 30% recovery, trans/cis = 68:32) by glc and nmr assay. The weakly uv-active band (R_f 0–0.46) furnished *trans*-2-octenal (0.220 g, 58% gross yield, 84% net yield). Evaporative distillation of the latter at 110° (19 Torr) provided a colorless liquid: glc, t_R 0.23 (column A, 120°); ir 3.55 and 3.66 (m, O=*CH*), 5.91 (vs, *C*=*O*), 6.11 (m, *C*=*C*), 6.86 (m), 8.78 (s), 9.14 (m), and 10.24 μ (s, trans-CH=CH); nmr (Table I) identical with that previously described;[11] molecular ion *m/e* 126.1043 (calcd for $C_8H_{14}O$: 126.1045).

1,3-Bis(methylthio)-1-hexen-4-ol (8). A solution of 1,3-bis-(methylthio)-2-methoxypropane (1.82 g, 10.9 mmol) and diisopropylamine (2.33 g, 23.0 mmol) in dry THF (35 ml) was stirred at −75° under argon, treated with 1.24 *M* *n*-butyllithium in pentane (18.0 ml, 22.4 mmol), and stirred at −15° for 21 hr. The deep red-purple solution was cooled to −75°, treated with freshly distilled propanal (0.579 g, 10.0 mmol), and stirred at −75° for 5 min and at 20° for 30 min. The solution was diluted with ether and washed with 5 *M* aqueous ammonium chloride, water, and brine; the organic phase and ether extracts of the aqueous washings were dried and freed of solvent.

Evaporative distillation (110°, 0.09 Torr) of the residual liquid provided an adduct mixture (1.71 g, 89% yield), which consisted of two diastereomers (E_1, E_2) of the trans alcohol *trans*-**8** and two diastereomers (Z_1, Z_2) of the cis alcohol *cis*-*8* in the ratio $E_1/E_2/Z_1/Z_2$ = 25:23:41:11 (nmr), as a colorless liquid: tlc, R_f 0.16 ($CHCl_3$), R_f 0.58 (9:1 $CHCl_3$–Et_2O); glc, t_R 3.08 (Z_1, Z_2), 3.69 (E_1), and 4.07 (E_2) (column A, 140°); ir 2.89 (w, OH), 6.24 (m, C=C), 6.85 (m), 6.98 (s), 7.20, 7.60, 7.72, 8.06, 8.86, 9.41, and 9.68 (all m), 10.22 (s), and 10.62 μ (s, *trans* CH=CH); molecular ion, *m/e* 192.0644 (calcd for $C_8H_{16}OS_2$: 192.0643).

Anal. Calcd for $C_8H_{16}OS_2$: C, 49.96; H, 8.39. Found: C, 50.39; H, 8.45.

***trans*-4-Hydroxy-2-hexenal (9). A. With Mercuric Chloride.** A solution of mercuric chloride (0.82 g, 3.0 mmol) in 7:2 THF–water (9 ml) was added to a solution of 1,3-bis(methylthio)-1-hexen-4-ol (**8**; 0.196 g, 1.02 mmol) in THF (4 ml) containing powdered calcium carbonate (0.30 g, 3.0 mmol). The opaque white mixture was stirred under nitrogen at 52° for 11.5 hr. After the addition of powdered sodium bicarbonate (0.1 g), the mixture was filtered through Super Cel using 1:1 pentane–dichloromethane to wash the filter cake. The filtrate was washed with brine; the organic phase and extracts of the brine wash were dried over a mixture of powdered sodium bicarbonate and anhydrous magnesium sulfate and freed of most solvent. The residual liquid (1 ml) was diluted with tetrachloromethane (1 ml), and filtered through a 1-cm column of Merck silicic acid using tetrachloromethane (4 ml) as eluent. The eluate was freed of solvent, slurried with tetrachloromethane (1 ml), and refiltered through the silicic acid column.

Evaporation of solvent from the second eluate afforded the aldehyde **9** (47 mg, 41% yield), pure by glc assay, as a light yellow liquid: glc, t_R 1.23 (column A, 140°); ir 2.87 (w, OH), 3.54 and 3.67 (w, O=*CH*), 5.89 (vs, C=O), 6.10 (w, C=C), 6.88 (m), 8.73 (m), 8.96 (s), 9.27 (m), 9.53 (m), 9.93 (m), and 10.21 μ (s); nmr, see Table I; molecular ion, *m/e* 114.0675 (calcd for $C_6H_{10}O_2$: 114.0681).

B. With Silver Nitrate. Silver nitrate (0.66 g, 3.9 mmol) in 4:1 acetonitrile–water (13 ml) was added to a solution of 1,3-bis-(methylthio)-1-hexen-4-ol (**8**; 0.187 g, 0.97 mmol) in acetonitrile (5 ml). The yellow solution was stirred at 67° for 26 hr. A sparse yellow precipitate formed after a few minutes, gradually turned black by the tenth hour, and was completely dissolved by the fifteenth hour. The clear yellow solution was shaken with brine (6 ml) and 1 *M* aqueous sodium bicarbonate (7 ml); the entire mixture was filtered through Super Cel and washed through with ether. The organic phase of the filtrate was washed with brine, dried, and freed of solvent. The residual liquid (153 mg) was submitted to preparative tlc using 4:1 trichloromethane–ether as eluent. The major band (R_f 0.09–0.21) furnished a liquid (114 mg) that was evaporatively distilled at 130° (10 Torr) to provide the aldehyde **9** (53 mg, 48% yield), pure by nmr assay, as a colorless liquid.

3,5-Bis(methylthio)-2-methyl-4-penten-2-ol (10). *n*-Butyllithium in pentane (1.30 *M*; 81 ml, 105 mmol) was added to a solution of 1,3-bis(methylthio)-2-methoxypropane (8.47 g, 50.9 mmol) and diisopropylamine (10.96 g, 108 mmol) in dry THF (170 ml) stirring at −75° under argon. The deep purple solution was stirred at 25° for 100 min, cooled to −75°, treated with freshly distilled acetone (2.73 g, 47.0 mmol), and stirred at −75° for 5 min. The deep emerald green solution was stirred at 18° for 5 min, diluted with ether, and washed with 5 *M* aqueous ammoniun chloride, water, and brine; the organic phase and ether extracts of the aqueous washings were dried and freed of solvent.

The residual orange liquid was distilled through a 5-cm Vigreux column to furnish the alcohol **10** [8.77 g, 97% yield; trans/cis = 57:43 (nmr)] as a colorless liquid: bp 91–92° (0.23 Torr); tlc, R_f 0.29 ($CHCl_3$); glc, t_R 2.34 (cis) and 2.82 (trans) (column A, 140°); ir 2.86 (m, OH), 6.23 (m, C=C), 6.85 (m, C*CH*$_3$), 6.96 and 7.01 (m, S*CH*$_3$), 7.23 and 7.30 [s, $C(CH_3)_2$], 7.48 (s), 7.58 (m), 8.29 (m), 8.61 (s, C–O), 9.03 (m), 10.20 (m), 10.39 (m), 10.61 (s, trans-CH=CH), 10.98 (m), and 14.30 μ (m). The analytical sample was prepared by preparative tlc and evaporative distillation: molecular ion *m/e* 192.0642 (calcd for $C_8H_{16}OS_2$: 192.0643).

Anal. Calcd for $C_8H_{16}OS_2$: C, 49.96; H, 8.39. Found: C, 49.92; H, 8.31.

A solution of the alcohol **10** (0.194 g, 1.00 mmol), 1.00 *M* aqueous hydrochloric acid (1.00 ml), and THF (4.0 ml) was stirred at 25° for 12 days. The liquid obtained on extractive work-up was the pure starting alcohol **10** (91% recovery) by tlc and nmr assay.

3,5-Bis(methylthio)-2-methyl-4-penten-2-yl Acetate. A solution of the alcohol **10** (0.81 g, 4.2 mmol; trans/cis = 60:40) in dry pyridine (1.25 ml, 15 mmol) and acetic anhydride (2.85 ml, 30 mmol) was stirred at 80–85° for 120 hr. As alcohol **10** was absent by tlc assay, the cooled mixture was diluted with ether and washed with 5 *M* aqueous ammonium chloride, water, 1 *M* aqueous ammonium bicarbonate, and brine; the organic phase plus ether extracts of the aqueous washes were dried and freed of solvent.

The residual red liquid was evaporatively distilled at 115° (0.45 Torr) to provide the title acetate (0.925 g, 94% yield; trans/cis = 65:35), pure by glc assay, as a colorless liquid: tlc, R_f 0.52–0.62 ($CHCl_3$); glc, t_R 2.34 (trans) and 2.68 (cis) (column A, 140°); ir 5.74 (s, C=O), 6.25 (w, C=C), 6.98 (m), 7.22 (m), 7.31 (s), 7.97 (s, CO), 8.30 (m), 8.56 (m), 8.88 (s, CO), 9.79 (m), and 10.6 μ (m); molecular ion, *m/e* 234.0739 (calcd for $C_{10}H_{18}O_2S_2$: 234.0748). The analytical sample was prepared by preparative tlc using 9:1 trichloromethane–ethyl acetate as eluent (R_f 0.55–0.74).

Anal. Calcd for $C_{10}H_{18}O_2S_2$: C, 51.25; H, 7.74. Found: C, 50.97; H, 7.96.

1,1,2-Tris(methylthio)-4-methyl-3-pentene. A solution of the alcohol **10** (0.186 g, 0.97 mmol; trans/cis = 1.35) and *p*-toluene-

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[11] J. J. Riehl and F. Jung, *Tetrahedron Lett.*, 3139 (1969).

sulfonic acid monohydrate (0.185 g, 0.97 mmol) in dry THF (2.0 ml) was stirred near 25° for 20 hr, diluted with ether (20 ml), washed with aqueous sodium bicarbonate and brine, dried, and freed of solvent. The residual liquid (0.17 g) was submitted to preparative tlc using trichloromethane as eluent.

The slower band (R_f 0.11–0.32) afforded only the cis alcohol **10** (46 mg, 25% recovery) by nmr and ir assay: ir 2.90 (w, OH), 6.26 (w, C=C), 6.88 (w), 6.99, 7.26, 7.32, 7.51, 7.63, 8.32, 8.64, 9.09, and 10.44 (all m), 11.04 (w), and 14.5 μ (w). Thus 60% of the cis isomer of alcohol **10** initially present was recovered.

The faster band (R_f 0.62–0.72) provided a liquid that was predominantly the title sulfide (37 mg, 17% gross yield, 23% net yield): glc, t_R 5.9 (column A, 140°); ir 6.95 and 7.03 (s), 7.26, 8.6, 10.39, 11.11 μ (all m); nmr (ppm) $[(CH_3{}^bS)_2CH^cCH^d(SCH_3{}^a)CH^e{=}C(CH_3{}^f)_2]$, 1.67 and 1.80 (two d, 6 H, J_{ef} = 1.3 Hz, H^f), 1.95 (s, 3 H, H^a), 2.10 and 2.12 (two s, 6 H, H^b), 3.69 (s, 1 H, H^c), 3.74 (d, 1 H, J_{de} = 2.5 Hz, H^d), and 5.18 (m, 1 H, H^e); molecular ion, *m/e* 222.0571 (calcd for $C_9H_{18}S_3$: 222.0571).

trans-**4-Hydroxy-4-methyl-2-pentenal (12). A. With Mercuric Chloride–Calcium Carbonate.** A mixture of the alcohol **10** (0.192 g, 1.00 mmol), mercuric chloride (0.82 g, 3.0 mmol), powdered calcium carbonate (0.30 g, 3.0 mmol), THF (11 ml), and water (2 ml) was heated at reflux (near 85°) for 4.0 hr. The crude product obtained on extractive work-up was submitted to preparative tlc using 3:1 trichloromethane–ethyl acetate as eluent (two developments). The aldehyde **12** (R_f 0.25–0.40; 47 mg, 41% yield) was isolated as a colorless liquid: glc, t_R 0.50 (column A, 140°); ir 3.00 (w, OH), 3.59 and 3.69 (w, O=*CH*), 5.89 (vs, C=O), 6.14 (m, C=C), 7.25 and 7.33 [w, $C(CH_3)_2$], 8.61 (m), 8.89 (m), 9.09 (s), and 10.25 μ (m); nmr, see Table I; molecular ion, *m/e* 128.0791 (calcd for $C_7H_{12}O_2$: 128.0837).

B. With Trifluoroacetic Acid. A solution of the alcohol **10** (0.202 g, 1.05 mmol) in neat trifluoroacetic acid (0.50 ml, 6.8 mmol) was stirred at 25° for 1.0 hr and freed of solvent. An ethereal solution of the residual liquid was washed with water, dried, and freed of solvent. The remaining liquid was submitted to preparative tlc using trichloromethane as eluent. The band at R_f 0.25–0.32 furnished a colorless liquid that was the pure aldehyde **12** (51 mg, 42% yield) by glc and nmr assay.

4-Hydroxy-4-methyl-2-pentenoic Acid Lactone. A solution of *trans*-4-hydroxy-4-methyl-2-pentenal (**12**; 0.123 g, 1.08 mmol) in pyridine (0.5 ml) was treated with a slurry of chromium trioxide (0.162 g, 1.62 mmol) in pyridine (2.0 ml); the mixture was stirred at 25° for 20 hr and poured into water (10 ml). Ether extracts of this mixture were washed with 3 *M* aqueous hydrochloric acid, 0.8 *M* aqueous sodium carbonate, and brine, dried, and freed of solvent. The residual liquid was evaporatively distilled at 110° (9 Torr) to furnish the title γ-lactone (0.042 g, 38% yield) as a colorless liquid: ir 5.66 μ (vs, C=O); nmr (ppm) $[CH^a{=}CH^b\text{-}C(CH_3{}^c)_2]$, 1.46 (s, 6 H, H^c), 5.87 (d, 1 H, J_{ab} = 5.5 Hz, H^a), and 7.48 (d, 1 H, H^b); molecular ion, *m/e* 112.0523 (calcd for $C_6H_8O_2$: 112.0524).

1,3-Bis(methylthio)-4-methoxy-4-methyl-1-pentene (21). A solution of the alcohol **10** (0.962 g, 5.00 mmol; trans/cis = 88:12) in dry THF (1.0 ml) was added to a suspension of oil-free sodium hydride (0.42 g, 10.0 mmol) in dry THF (4.0 ml). The mixture was stirred near 25° for 10 min, cooled to 0°, treated with neat iodomethane (0.40 ml, 6.0 mmol), and stirred near 5° for 30 hr in a glass-stoppered flask. The solidified reaction mixture was partitioned between ether and 2 *M* aqueous ammonium chloride; the organic phase was washed with water and brine, combined with ethereal extracts of the aqueous washings, dried, and freed of solvent.

The residual liquid was submitted to preparative tlc using dichloromethane as eluent. The slower component (R_f 0.12–0.33) was the alcohol **10** (0.150 g, 16% recovery). The faster component (R_f 0.33–0.65) was evaporatively distilled at 115° (3.4 Torr) to furnish mainly the methyl ether **21** (0.696 g, 70% gross yield, 83% net yield; trans/cis = 9:1) as a colorless liquid: tlc, R_f 0.54 ($CHCl_3$); glc, t_R 1.47 (trans) and 1.72 (cis) (column A, 140°); ir 6.25 (w, C=C), 6.85 (m), 6.98 (m), 7.05 (m), 7.26 and 7.35 [m, $C(CH_3)_2$], 7.66 (w), 8.19 (m), 8.46 (m), 8.82 (s), 9.28 (vs), 10.63 (m), 11.61 (w), and 14.33 μ (w); molecular ion, *m/e* 206.0794 (calcd for $C_9H_{18}OS_2$: 206.0799).

Anal. Calcd for $C_9H_{18}OS_2$: C, 52.38; H, 8.79. Found: C, 53.18; H, 8.69.

This liquid contained *ca.* 4% of the allylic isomer of **21**, 1,1-bis(methylthio)-4-methoxy-4-methyl-2-pentene, by nmr characterization and glc assay (t_R 1.22, column A, 140°). The proportion of this dithio ketal rose to 29% when the methylation was conducted for 20 hr at 25–30°.

trans-**4-Methoxy-4-methyl-2-pentenal (13).** A solution of mercuric chloride (0.820 g, 3.0 mmol) in 4:1 acetonitrile–water (3.0 ml) was added to a solution of the ether **21** (0.154 g, 0.75 mmol; trans/cis = 9:1) in the same solvent mixture (2.0 ml) stirring at 25°. A voluminous white precipitate formed immediately. After 3 min the liquid phase contained only the aldehyde **13** by glc assay. The mixture was stirred at 20–25° for 10 hr and filtered through Super Cel, using ether to wash the filter cake. The organic phase of the filtrate was washed with 1.0 *M* aqueous sodium bicarbonate and brine, combined with ether extracts of the aqueous washings, dried, and freed of solvent at 95° (1 atm). The residual liquid was submitted to preparative tlc using trichloromethane as eluent.

Ether extracts of the major band (R_f 0.07–0.36) were freed of solvent at 52° (1 atm) and evaporatively distilled at 120° (32 Torr) to furnish the aldehyde **13** (0.062 g, 65% yield), pure by glc assay, as a colorless liquid; glc, t_R 0.31 at 140°, 0.97 at 100° (column A); ir 3.59 and 3.71 (w, O=*CH*), 5.87 (vs, C=O), 6.12 (w, C=C), 6.85 (w), 7.28 and 7.34 [w, $C(CH_3)_2$], 8.03 (m), 8.51 (m), 8.70 (m), 9.05 (m), 9.29 (s), 9.95 (w), 10.19 (m), 10.8 (w), and 11.57 μ (w); nmr, see Table I; molecular ion, *m/e* 128.0791 (calcd for $C_7H_{12}O_2$: 128.0837).

trans-**4-Methylthio-4-methyl-2-pentenal (14).** A solution of the methyl ether **21** (58 mg, 0.28 mmol; trans/cis = 67:33) in trifluoroacetic acid (0.14 ml, 1.88 mmol) was kept at 25° for 40 min and freed of solvent. The residual liquid was shaken with ether and 1.0 *M* sodium bicarbonate; the organic phase plus ether extracts of the aqueous phase were dried and freed of solvent. The remaining liquid was submitted to preparative tlc using dichloromethane as eluent (two developments).

The faster moving band (R_f 0.55–0.67) furnished the dithioacetal of **14** (19 mg, 30% yield), 1,1,4-tris(methylthio)-4-methyl-2-pentene, as a colorless liquid: glc, t_R 2.48 (column A, 140°); ir 6.95 (m), 7.02 (m), 7.23 and 7.32 [w, $C(CH_3)_2$], 7.61 (w), 8.68 (w), 8.89 (m), and 10.33 μ (s); molecular ion, *m/e* 222.0565 (calcd for $C_9H_{18}S_3$: 222.0571).

Anal. Calcd for $C_3H_{18}S_3$: C, 48.60; H, 8.17. Found: C, 49.22; H, 8.32.

The slower moving band (R_f 0.32–0.51) afforded the aldehyde **14** (23 mg, 57% yield) as a colorless liquid: glc, t_R 0.44 (column A, 140°); ir 3.63 and 3.74 (w, O=*CH*), 5.89 (vs, C=O), 6.16 (m, C=C), 6.87 (w), 6.97 (w), 7.24 and 7.33 [w, $C(CH_3)_2$], 8.56 (m), 8.84 (m), 9.05 (s), 9.90 (w), 10.11 (wm), 10.22 (m), 10.42 (w), and 11.75 μ (w); nmr, see Table I; molecular ion, *m/e* 144.0610 (calcd for $C_7H_{12}OS$: 144.0609).

Anal. Calcd for $C_7H_{12}OS$: C, 58.29; H, 8.39. Found: C, 58.02; H, 8.51.

2,4-Bis(methylthio)-1,1-diphenyl-3-butenol (11). The preparation of the propanal adduct **8** was repeated, except that a solution of benzophenone (1.822 g, 10.0 mmol) in THF (10 ml) was used instead of propanol. Extractive work-up furnished a red liquid that was evaporatively distilled at 210° (0.07 Torr) to provide the alcohol **11** [2.99 g, 95% yield; trans/cis = 5:4 (nmr)], pure by nmr assay, as a colorless liquid: tlc, R_f 0.36–0.57 ($CHCl_3$). This material solidified to a wax on standing; it was crystallized from tetrachloromethane to give the cis isomer as white needles: mp 121.4–121.6°; ir[12] 2.83 (m, OH), 6.25 (m, C=C), 6.70 (m), 6.90 (s), 7.45 (m), 7.51 (m), 8.58 (s), 9.47 (s), 9.69 (s), 10.42 (s), and 14.33 μ (vs, C_6H_5); molecular ion, *m/e* 316.0950 (calcd for $C_{18}H_{20}OS_2$: 316.0956).

trans-**2-[1,3-Bis(methylthio)allyl]cyclohexanol (15).** *n*-**Butyllithium** in pentane (1.3 *M*; 8.6 ml, 11.2 mmol) was added to a solution of 1,3-bis(methylthio)-2-methoxypropane (0.911 g, 5.48 mmol) and diisopropylamine (1.16 g, 11.4 mmol) in dry THF (18 ml) stirring under argon at −75°. After being stored at −15° for 70 hr, the deep purple solution was cooled to −75°, treated with cyclohexene oxide (0.550 g, 5.60 mmol), and kept at −75° until the purple color was discharged (5 hr). Methanol (2 ml) and then 5 *M* aqueous ammonium chloride were added; ether extracts of the reaction mixture were washed with brine, dried, and freed of solvent.

The residual liquid (1.23 g, 96% yield) consisted of two diastereomers (E_1, E_2) of the trans alcohol and one diastereomer (Z) of the cis alcohol in the ratio $E_1/E_2/Z$ = 6:3:1 (nmr): tlc, R_f 0.37 (10:1 C_6H_6–EtOAc); ir ($CHCl_3$) 2.90 (OH) and 6.24 μ (C=C); nmr ($CDCl_3$) (ppm) $[CH_3{}^bSCH^c{=}CH^dCH^e(SCH_3{}^a)CH^fCH^gOH^h]$; E_1 0.8–2.1 [m, 9 H, H^f and $(CH_2)_4$], 2.02 (s, 3 H, H^a), 2.29 (s, 3 H, H^b), 2.32 (bs, 1 H, H^h), 3.0–3.5 (m, 1 H, H^g), 3.69 (dd, 1 H, J_{de} = 10

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[12] The moderate band at 10.57 μ (trans CH=CH) observed for the trans/cis mixture of alcohol **11** was absent.

Hz, J_{ef} = 6 Hz, H^{e}), 5.26 (dd, 1 H, J_{cd} = 15 Hz, H^{d}), and 6.14 (d, 1 H, H^{c}); E$_2$ 2.03 (s, H^{a}), 3.58 (dd, J_{de} = 10 Hz, J_{ef} = 5 Hz, H^{e}), and 5.40 (dd, J_{cd} = 15 Hz, H^{d}); Z 2.06 (s, H^{a}) and 6.25 (d, J_{cd} = 10 Hz, H^{c}); molecular ion, *m/e* 232.0956 (calcd for $C_{11}H_{20}OS_2$: 232.0956); base ion, *m/e* 87.

***trans*-2-[1,3-Bis(methylthio)allyl]cyclohexyl Acetate.** A solution of the alcohol **15** (0.204 g, 0.878 mmol) and acetic anhydride (0.60 ml, 6.4 mmol) in dry pyridine (1.0 ml, 12 mmol) was kept at room temperature for 4 hr and freed of solvents. The remaining viscous oil (0.240 g, 100% yield) consisted of two diastereomers (E$_1$, E$_2$) of the *trans*-acetate of **15** and one diastereomer (Z) of the *cis*-acetate of **15** in the ratio E$_1$/E$_2$/Z = 63:27:10 (nmr): tlc, R_f 0.33 (C_6H_6); ir ($CHCl_3$) 5.78 (s, C=O), 6.23 (m, C=C), 6.87 (m), 6.98 (m), 7.30 (s, *CH*$_3$CO), 8.15 (vs, *COC*=O asym), 9.70 (s, *COC*=O sym), 10.12 (m), 10.66 (m, trans CH=CH), and 11.0 μ (m); nmr ($CDCl_3$) (ppm) $[\mathrm{CH_3{}^bSCH^c{=}CH^dCH^e(SCH_3{}^a)CH^fCH^gOCOCH_3{}^h}]$; E$_1$ 0.8–2.2 [m, 9 H, H^{f} and $(CH_2)_4$], 1.96 (s, 3 H, H^{a}), 2.06 (s, 3 H, H^{h}), 2.32 (s, 3 H, H^{b}), 3.31 (dd, 1 H, J_{de} = 10 Hz, J_{ef} = 6 Hz, H^{e}), 4.4–4.9 (m, 1 H, H^{g}), 5.23 (dd, 1 H, J_{cd} = 15 Hz, H^{d}), and 5.99 (d, 1 H, H^{c}); E$_2$ 2.01 (s, H^{a}), 3.18 (dd, J_{de} = 10 Hz, J_{ef} = 6 Hz, H^{e}), 5.33 (dd, J_{cd} = 15 Hz, H^{d}), and 6.07 (d, H^{c}); Z 2.29 (s, H^{b}) and 6.11 (d, J_{cd} = 10 Hz, H^{c}): molecular ion, *m/e* 274.1070 (calcd for $C_{13}H_{22}O_2S_2$: 274.1061).

***trans*-3-(*trans*-2-Acetoxycyclohexyl)-2-propenal (16).** Powdered calcium carbonate (0.103 g, 1.0 mmol) and solid mercuric chloride (0.190 g, 0.70 mmol) were sequentially added to a solution of the acetate of **15** (48 mg, 0.175 mmol) in 4:1 acetonitrile–water (3.0 ml). The reaction mixture was stirred under argon at 50° for 6 hr and filtered through Super Cel, using ether to wash the filter cake. The organic phase of the filtrate was washed with water and brine, dried, and freed of solvent. The residual liquid (37 mg) was submitted to preparative tlc using 6:1 benzene–ethyl acetate as eluent (two developments).

The major band (R_f 0.39–0.50) provided the *trans*-aldehyde **16** (29 mg, 85% yield) as an oil that crystallized on standing. Recrystallization from cyclohexane–benzene afforded colorless needles: mp 114–116°; tlc, R_f 0.63 (4:1 C_6H_6–EtOAc); ir ($CHCl_3$) 3.57 and 3.72 (w, *HC*=O), 5.77 (s, CH$_3$*C*=*O*), 5.92 (vs, H*C*=*O*), 6.13 (w, C=C), 6.91 (w), 7.28 (m), 8.00 and 8.2 (s, *COC*=O asym), 8.60 (w), 9.09 (m), 9.63 (m, *COC*=O sym), 10.16 (m, trans CH=CH), and 10.92 μ (w); nmr, see Table I; molecular ion, *m/e* 196.1092 (calcd for $C_{11}H_{16}O_3$: 196.1099).

Conversion of Propylene Oxide to 5-Acetoxy-*trans*-2-hexenal (17). A solution of 1,3-bis(methylthio)-2-methoxypropane (530 mg, 3.19 mmol) and diisopropylamine (679 mg, 6.70 mmol) in dry THF (11 ml) was cooled to −75° under argon, treated with *n*-butyllithium in pentane (1.3 *M*; 5.0 ml, 6.5 mmol), kept at 0° for 8 hr, and treated at −75° with propylene oxide (222 mg, 3.83 mmol). The reaction solution was kept at −75° for 12 hr and poured into 5 *M* aqueous ammonium chloride. Ether extracts of this mixture were dried and freed of solvent to afford the olefinic stereoisomers of 4,6-bis(methylthio)-5-hexen-2-ol (592 mg, 97% yield) as a liquid: tlc, R_f 0.20 (10:1 C_6H_6–EtOAc); ir ($CHCl_3$) 2.90 (OH) and 6.24 μ (C=C); nmr ($CDCl_3$) (ppm) $[\mathrm{CH_3{}^bSCH^c{=}CH^dCH^e(SCH_3{}^a)CH_2{}^fCH^g(OH^h)CH_3{}^i}]$, 1.22 (d, 3 H, J_{gi} = 6 Hz, H^{i}), 1.72 (m, 2 H, H^{f}), 1.9–2.2 (m, 4 H, H^{a} and H^{h}), 2.29 (s, 3 H, H^{b}), 3.23 (m, 1 H, H^{e}), 3.88 (m, 1 H, H^{g}), 4.9–5.7 (m, 1 H, H^{d}), and 5.9–6.3 (m, 1 H, H^{c}).

A solution of this alcohol (603 mg, 3.13 mmol) in dry pyridine (4.0 ml, 50 mmol) and acetic anhydride (3.0 ml, 32 mmol) was kept at room temperature for 3 hr and freed of solvents to furnish the olefinic stereoisomers of 4,6-bis(methylthio)-5-hexen-2-yl acetate (731 mg, 100% yield) as a liquid: tlc, R_f 0.53 (10:1 C_6H_6–EtOAc); ir ($CHCl_3$) 5.76 (CH$_3$*C*=*O*), 6.24 (C=C), and 8.02 μ (*COC*=O); nmr ($CDCl_3$) (ppm) $[\mathrm{CH_3{}^bSCH^c{=}CH^dCH^e(SCH_3{}^a)CH_2{}^fCH^g(OCOCH_3{}^h)CH_3{}^i}]$, 1.22 (d, 3 H, J_{gi} = 6 **Hz,** H^{i}), 1.83 (m, 2 H, H^{f}), 1.95–2.10 (singlets, 6 H, H^{a} and H^{h}), 2.20–2.30 (singlet, 3 H, H^{b}), 3.22 (m, 1 H, H^{e}), 4.7–5.5 (m, 2 H, H^{d} and H^{g}), and 5.9–6.3 (m, 1 H, H^{c}).

A solution of this acetate (602 mg, 2.57 mmol) in 4:1 acetonitrile–water (30 ml) was treated with powdered calcium carbonate (1.55 g, 15.5 mmol) and mercuric chloride (2.87 g, 10.6 mmol); the mixture was stirred at 45° for 3 hr, cooled, and filtered through Super Cel. The filtrate was diluted with brine and extracted with ether; the extracts were dried and freed of solvent. The residual liquid (440 mg), which was homogeneous by glc (t_R 3.7, column C, 85°), was submitted to preparative tlc using 4:1 benzene–ethyl acetate as eluent (two developments). The band at R_f 0.40–0.60 afforded 5-acetoxy-*trans*-2-hexenal (324 mg, 81% yield) as a pale yellow liquid: tlc, R_f 0.37 (4:1 C_6H_6–EtOAc); ir ($CHCl_3$) 5.74 (CH$_3$*C*=*O*), 5.90 (H*C*=*O*), 6.07 (C=C), 8.0–8.3 (*COC*=O), and 10.26 μ (trans CH=CH); nmr, see Table I; molecular ion, *m/e* 156.0787 (calcd for $C_8H_{12}O_3$: 156.0786); fragment ions, *m/e* 112, 87 $[(\mathrm{CH_3CHOCOCH_3})^+]$, 70 (base), and 68.

Conversion of Cyclopentene Oxide to *trans*-3-(*trans*-2-Acetoxycyclopentyl)-2-propenal (22). *n*-Butyllithium in pentane (1.3 *M*; 5.0 ml, 6.5 mmol) was added over 5 min to a solution of 1,3-bis(methylthio)-2-methoxypropane (530 mg, 3.19 mmol) and diisopropylamine (679 mg, 6.70 mmol) in dry THF (14 ml) stirring under argon at −75°. The resulting dark purple solution was kept at 0° for 8 hr and treated at −75° with cyclopentene oxide (403 mg, 4.80 mmol); after being stored at −20° for 15 hr and at 0° for 2 hr, the solution was poured into 5 *M* aqueous ammonium chloride. Ether extracts of this solution were dried and freed of solvent to provide the olefinic stereoisomers of *trans*-2-[1,3-bis(methylthio)allyl]cyclopentanol (693 mg, 99% yield) as an orange-yellow oil: tlc, R_f 0.23 (10:1 C_6H_6–EtOAc); ir ($CHCl_3$) 2.90 (OH) and 6.24 μ (C=C); nmr ($CDCl_3$) (ppm) $[\mathrm{CH_3{}^bSCH^c{=}CH^dCH^e(SCH_3{}^a)CH^fCH^gOH^h}]$, 1.4–2.8 [m, 8 H, H^{f}, H^{h}, $(CH_2)_3$], 2.0–2.2 (singlet, 3 H, H^{a}), 2.29 (s, 3 H, H^{b}), 2.9–3.8 (m, 1 H, H^{e}), 4.08 (m, 1 H, H^{g}), 5.0–5.6 (m, 1 H, H^{d}), and 5.9–6.5 (m, 1 H, H^{c}).

A solution of this alcohol (640 mg, 2.93 mmol) in dry pyridine (4.0 ml, 50 mmol) and acetic anhydride (3.0 ml, 32 mmol) was kept at room temperature for 4 hr and freed of solvents to furnish the olefinic stereoisomers of *trans*-2-[1,3-bis(methylthio)allyl]cyclopentyl acetate (702 mg, 92% yield) as an oil: tlc, R_f 0.50 (10:1 C_6H_6–EtOAc); ir ($CHCl_3$) 5.77 (CH$_3$*C*=*O*), 6.24 (C=C), and 7.98 μ (*COC*=O); nmr ($CDCl_3$) (ppm) $[\mathrm{CH_3{}^bSCH^c{=}CH^dCH^e(SCH_3{}^a)CH^fCH^gOCOCH_3{}^h}]$, 1.4–2.7 [m, 7 H, H^{f} and $(CH_2)_3$], 1.9–2.1 (singlets, 6 H, H^{a} and H^{h}), 2.28 (s, 3 H, H^{b}), 3.0–3.5 (m, 1 H, H^{e}), 4.8–5.7 (m, 2 H, H^{d} and H^{g}), and 5.9–6.7 (m, 1 H, H^{c}).

A solution of this acetate (580 mg, 2.22 mmol) in 4:1 acetonitrile–water (30 ml) was treated with powdered calcium carbonate (1.33 g, 13.3 mmol) and then mercuric chloride (2.42 g, 8.90 mmol); the resulting mixture was stirred under argon at 45° for 3.5 hr, cooled, and filtered through Super Cel. The filtrate was diluted with brine and extracted with ether; the extracts were dried and freed of solvent to give an oil that was submitted to preparative tlc using 5:1 benzene–ethyl acetate as eluent (two developments). The band at R_f 0.53–0.63 provided the enal **22** (240 mg, 59% yield) as a pale yellow oil: tlc, R_f 0.42 (4:1 C_6H_6–EtOAc); ir ($CHCl_3$) 5.77 (CH$_3$*C*=*O*), 5.90 (H*C*=*O*), 8.0–8.4 (*COC*=O), and 10.22 μ (trans CH=CH); nmr, see Table I; molecular ion, *m/e* 182.0950 (calcd for $C_{10}H_{14}O_3$: 182.0943); fragment ions, *m/e* 140 and 96 (base).

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