Stereoselective Ring Opening Reaction of 2-[(Phenylthio)methyl]cycloalkanols Mediated by *N*-Chlorosuccinimide and Triethylamine

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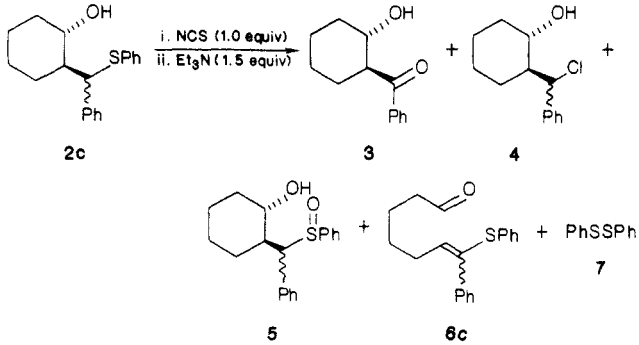
Received August 11, 1986

Treatment of 2-[1-(phenylthio)benzyl]cyclohexanol (**2c**) with *N*-chlorosuccinimide (NCS) and triethylamine gave various products **3–6c** depending on reaction conditions. Exclusive ring-opening reation of **2c** was achieved by temperature control. Thus, five-, six-, and seven-membered cycloalkanols **2a–g** were converted to ω-oxo-α,β-unsaturated sulfides **6a–g** in good yields. The stereochemistry of the reaction was determined by using four diastereomers **10a–d**; *trans-erythro*-**10b** and *cis-threo*-**10c** afforded (*E*)- and (*Z*)-heptenals **6c** as a single isomer, respectively, while a mixture of the two isomers **6c** (60:40 or 40:60) was obtained from *trans-threo*-**10a** and *cis-erythro*-**10d**. Allyl-, propargyl-, and [(trimethylsilyl)methyl]cyclohexanols **23**, **25**, and **27** also yielded corresponding unsaturated sulfides **24**, **26**, and **28**.

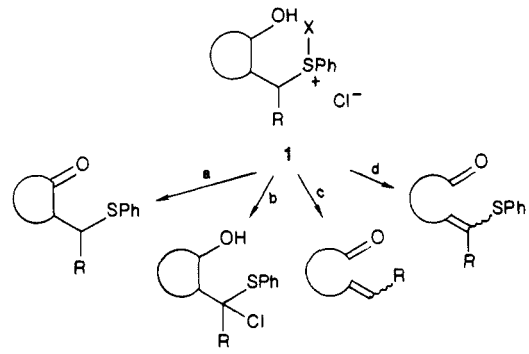
Although sulfide–NCS complexes are readily available precursors of oxy- and azasulfonium salts[1] and have been used in many reactions, particularly alcohol oxidation,[2] these examples are only limited to intermolecular reactions. A chemical behavior of the complexes having internal hydroxy and amino groups has been rarely investigated. Previously we reported the reaction of 2-[1-(phenylseleno)benzyl]cyclohexanol with NCS and 1,8-diazabicyclo[5.4.0]undec-7-ene to give 2-benzylidenecyclohexanol.[3] In connection with this result, it is of interest to study a chemical property of the complexes **1** derived from 2-[(phenylthio)methyl]cycloalkanols, since **1** would be changed to various products depending on their reaction fashions, that is, oxidation of the hydroxy group (Scheme I, path a), Pummerer reaction (b), and Grob fragmentation (c). We report herein a full detail of a new ring-opening reaction of **1** (d) focusing on its stereochemistry.[4]

A reaction of *trans*-2-[1-(phenylthio)benzyl]cyclohexanol (**2c**) with NCS and triethylamine was complicated as



shown in Table I. No reaction took place in toluene (entry 1) and keto cyclohexanol **3** was obtained in chloroform along with diphenyl disulfide (entry 2). The product **3** was presumably derived from the Pummerer product, 2-[1-chloro-1-(phenylthio)benzyl]cyclohexanol by hydrolysis.[5] ω-Oxo-α,β-unsaturated sulfide **6c** was isolated in dichloromethane, but careful temperature control was necessary. When the reaction was carried out at 0 °C, substitution of the phenylthio group by chloride took place

Scheme I[a]



[a] X = succinimidyl.

Table I. Reaction of *trans*-2-[1-(Phenylthio)benzyl]cyclohexanol (2c) with NCS and Triethylamine

		temp (°C), time (h)		
entry	solvent	step i	step ii	product (yield,[a] %)
1	$C_6H_5CH_3$	0–rt, 1	rt, 3	**2c**
2	$CHCl_3$	rt, 3	rt, 3	**3** (30) + **7** (40)
3	CH_2Cl_2	0, 2	0, 2	**4** (11) + **6c** (40) + **7** (26)
4	CH_2Cl_2	−20, 2	−20, 2	**5** (45) + **6c** (32) + **7** (12)
5	CH_2Cl_2	−40 to −20, 3	−10–rt, 3	**6c** (66–85)

[a] Isolated yields. [b] rt = room temperature.

(probably via oxysulfonium intermediate **13** in Scheme III) to give chlorocyclohexanol **4** (entry 3). In contrast, **13** remained at −20 °C and hydrolyzed to sulfoxide **5** (entry 4). Exclusive formation of **6c** was achieved by keeping the first step below −20 °C and warming the mixture up to room temperature after addition of triethylamine (entry 5). The structure of **6c** was confirmed by comparison of its spectral data with those of an authentic sample prepared from 5-(ethoxycarbonyl)valeraldehyde (see Experimental Section).

The ring-opening reaction was performed for various cycloalkanols **2** under similar conditions described above (Table II). Secondary (R = H) and tertiary (R = Me) substrates **2** were converted to the corresponding ω-oxo-α,β-unsaturated sulfides **6** in good yields except for *trans*-cyclopentanols **2a** and **2b**.[6] Stereochemistry of the

(1) (a) Vilsmaier, E.; Sprugel, W. *Liebigs Ann. Chem.* **1971**, *747*, 151; (b) *Tetrahedron Lett.* **1972**, 625.
(2) Corey, E. J.; Kim, C. U. *J. Am. Chem. Soc.* **1972**, *94*, 7586.
(3) Takaki, K.; Yasumura, M.; Negoro, K. *J. Org. Chem.* **1983**, *48*, 54.
(4) Yasumura, M.; Takaki, K.; Tamura, T.; Negoro, K. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 317.
(5) Bakuzis, P. G.; Bakuzis, M. L. F.; Fortes, C. C.; Santos, R. *J. Org. Chem.* **1976**, *41*, 2769.

(6) Low yields for **2a** and **2b** may be attributed to their longer distances between the hydroxy and phenylthio groups than in other substrates as shown by molecular model.

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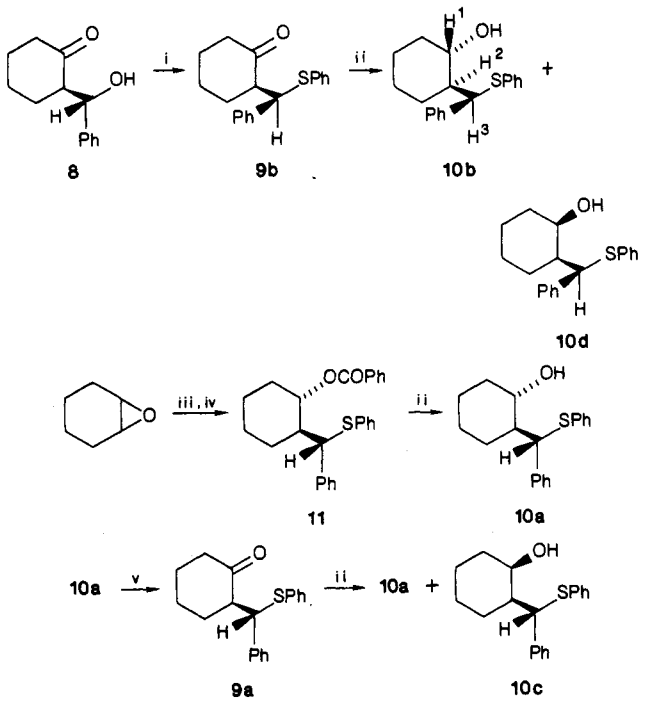
Table II. Synthesis of ω-Oxo-α,β-unsaturated Sulfides 6 from 2-[1-(Phenylthio)benzyl]cycloalkanols 2

substrate	n	R	stereochemistry[a] C_1–C_2 (trans or cis)[b]	stereochemistry[a] C_2–C_3 (threo:erythro)	product	yield[c] (%)	E:Z[a]
2a	3	H	trans	60:40	**6a**	10	75:25
2b	3	Me	trans	67:33	**6b**	36	67:33
2c	4	H	trans	67:33	**6c**	76	70:30
2d	5	H	trans	50:50	**6d**	64	60:40
2e	5	Me	trans	60:40	**6e**	63	60:40
2f	3	H	cis	50:50	**6a**	60	25:75
2g	4	Me	cis	25:75	**6g**	68	25:75

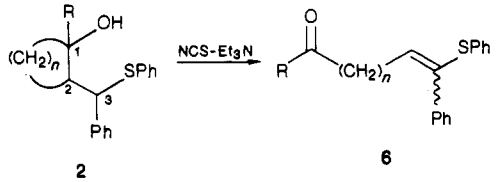
[a] Determined by NMR. [b] Stereochemistry between the hydroxy and benzyl substituents. [c] Isolated yeilds.

Scheme II[a]



[a] (i) *N*-(Phenylthio)succinimide/*n*-Bu_3P/PhH; (ii) $LiAlH_4$/ether or dioxane; (iii) PhSCH(Li)Ph/THF; (iv) PhCOCl; (v) PCC/CH_2Cl_2.

products **6** were determined by ^1H NMR. For example, **6c** shows two doublets at 6.02 and 6.35 ppm for the olefinic protons. The former was assigned to the *E* isomer on the basis of calculation of the chemical shift[7] and literature data.[8] The reaction of *trans*-cycloalkanols **2a–e** gave mainly *E* isomers **6**, whereas *Z* isomers **6** were obtained as major products from *cis*-cycloalkanols **2f** and **2g**. But selectivity was not high, because all substrates **2** were mixtures of threo and erythro.



Then we decided to prepare four diastereomers of 2-[1-(phenylthio)benzyl]cyclohexanol (**10a–d**)[9] in order to examine stereochemistry of the reaction (Scheme II). Threo aldol **8**[10] was converted to erythro keto sulfide **9b** with inversion.[11] Reduction of **9b** with LAH and separation by MPLC[12] gave *trans-erythro*-**10b** and *cis-erythro*-**10d** in 37% and 21% yields, respectively. Trans addition of [1-(phenylthio)benzyl]lithium to cyclohexene oxide[13] afforded **2c**, a mixture of *trans-threo*-**10a** and *trans-erythro*-**10b** (ratio, 67:33), whose minor product was identified with **10b** prepared from **8**. The addition reaction followed by quenching with benzoyl chloride gave benzoate of **2c**. Fortunately, the major isomer **11** was crystallized and isolated from the mixture in 70% yield. *trans-threo*-**10a** was obtained by reduction of **11** with LAH (60%). Oxidation of **10a** with PCC gave threo keto sulfide **9a** (60%), which was reduced again with LAH and separated by MPLC to afford *trans-threo*-**10a** and *cis-threo*-**10c** in 46% and 53% yields, respectively. ^1H NMR spectra of the four diastereomers **10a–d** (Table IV) provide an additional proof for their structures. Since H^1 protons of the trans isomers **10a** and **10b** occupy axial positions, large $W_{1/2}$ of the protons are observed (18 Hz for **10a** and 17 Hz for **10b**). In contrast, those of *cis-threo*-**10c** and *cis-erythro*-**10d** are 8 Hz and 6 Hz, respectively. Differentiation between the threo and erythro isomers is also possible. Coupling constants $J_{2,3}$ of the threo isomers are always larger than those of the erythro ones (4.0 Hz for **10a** vs. 2.6 Hz for **10b**; 10.2 Hz for **10c** vs. 9.4 Hz for **10d**). This result may be accounted for by the conformers that strong hydrogen bonding to the phenylthio group is attained.[14]

Table III. Synthesis of 7-Phenyl-7-(phenylthio)hept-6-enal (6c) from 2-[1-(Phenylthio)benzyl]cyclohexanols 10a–d

substr	stereochem	yield[a] (%)	ratio of E/Z
10a	*trans-threo*	85	60:40
10b	*trans-erythro*	30	100:0
10c	*cis-threo*	60	0:100
10d	*cis-erythro*	60	40:60

[a] Isolated yields.

Ring-opening reactions of the four diastereomers **10a–d** are summarized in Table III. *trans-erythro*-**10b** and *cis-threo*-**10c** gave exclusively *E* and *Z* sulfides **6c**, respectively. Selectivity in *trans-threo*-**10a** and *cis-erythro*-**10d** was low, but the ratio was just reversed. The *trans*-cyclohexanol **2c** (threo/erythro, 67:33) was calculated to afford a 73:27 mixture of (*E*)- and (*Z*)-**6c** on the basis of the ratios of **10a** and **10b**, which agreed with the observed result (70:30). Interestingly, calculated *E*/*Z* ratios

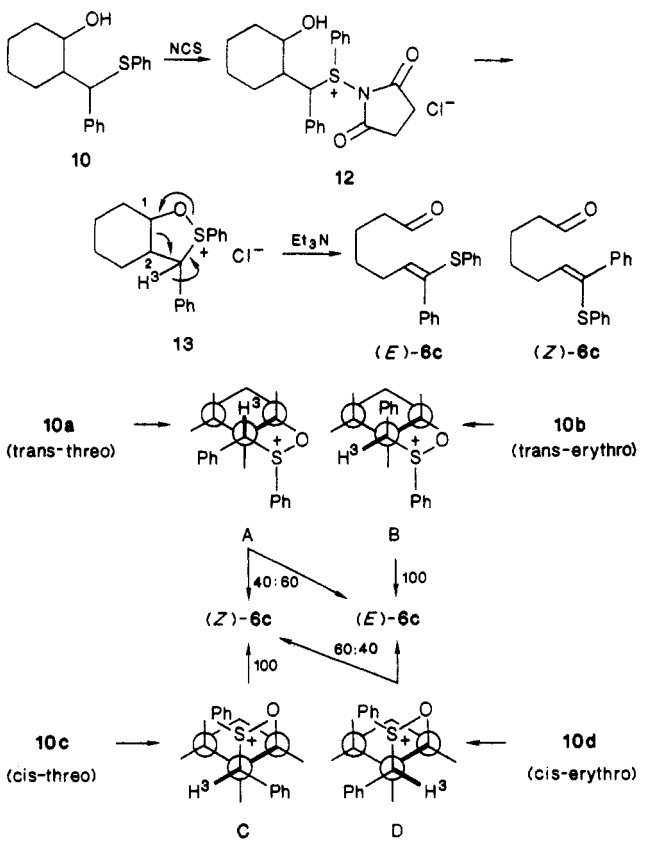
(7) (a) Pascual, C.; Meier, J.; Simon, W. *Helv. Chim. Acta* **1966**, *49*, 165. (b) Matter, U. E.; Pascual, C.; Pretsch, E.; Press, A.; Simon, W.; Sternhell, S. *Tetrahedron* **1969**, *25*, 691.
(8) Milolajczyk, M.; Grzejszczak, S.; Chefczynska, A.; Zatorski, A. *J. Org. Chem.* **1979**, *44*, 2967.
(9) Stereochemistry of the cycloalkanols (trans-cis, threo-erythro) was defined as indicated in Table II.
(10) Mukaiyama, T.; Banno, K.; Narasaka, K. *J. Am. Chem. Soc.* **1974**, *96*, 7503.
(11) Walker, K. A. M. *Tetrahedron Lett.* **1977**, 4475.
(12) MPLC separates the mixture into cis and trans isomers, but not into threo and erythro ones.
(13) (a) Song, S.; Shiono, M.; Mukaiyama, T. *Chem. Lett.* **1974**, 1161. (b) Smith, J. G. *Synthesis* **1984**, 629.
(14) Kingsbury, C. A. *J. Org. Chem.* **1972**, *37*, 102.

Table IV. ^{1}H NMR and IR Spectral Data for 2-[1-(Phenylthio)benzyl]cyclohexanols (10a–d)

diastereomer[a]	^{1}H NMR ($CDCl_3$, δ)	IR (CCl_4, cm^{-1})
trans-threo-**10a**	0.52–2.25 (m, 10 H), 2.82–3.38 (m, 1 H), 4.92 (d, J = 4.0 Hz, 1 H), 6.98–7.52 (m, 10 H)	3600, 3440, 2950, 2870, 1580, 1480, 1450, 1060, 1020
trans-erythro-**10b**	0.72–2.29 (m, 10 H), 3.55–4.09 (m, 1 H), 4.89 (d, J = 2.6 Hz, 1 H), 6.82–7.62 (m, 10 H)	3595, 3435, 2940, 2860, 1580, 1480, 1450, 1200, 1060
cis-threo-**10c**	0.95–2.15 (m, 10 H), 4.14 (d, J = 10.2 Hz, 1 H), 4.53–4.72 (m, 1 H), 7.12 (br s, 10 H)	3570, 3440, 3060, 3040, 2940, 2860, 1585, 1480, 1440, 970
cis-erythro-**10d**	0.90–2.07 (m, 10 H), 3.40–3.57 (m, 1 H), 4.13 (d, J = 9.4 Hz, 1 H), 7.07 (br s, 10 H)	3550, 3445, 2925, 2800, 1580, 1480, 1440, 965

[a] **10a**: colorless prisms from hexane–ether; mp 95.5–96 °C. **10b**: white powdery solid from hexane; mp 83.5–84 °C. **10c**: colorless oil. **10d**: colorless oil.

Scheme III



for **2a–g** using the results in Table III[15] were in good accordance with those in Table II (±6) except for the cycloheptanols **2d** and **2e** (±20), suggesting that similar selectivity would be observed in other five- and six-membered cycloalkanols.

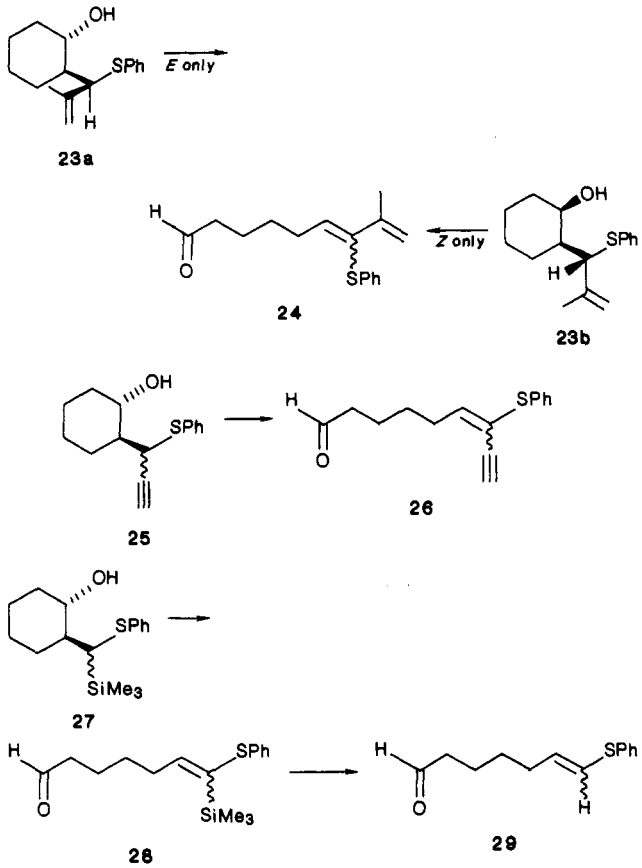
The results are explained as follows (Scheme III). The cyclohexanol **10** reacted with NCS to give complex **12**,[1] which was subsequently converted to oxysulfonium salt **13** by intramolecular substitution of the hydroxy group.[16] Proton abstraction (H^3) initiated ring-opening reaction to afford the product **6c**.[17] The structure of the oxysulfonium salt **13** seems to be a key point to account for the stereochemistry of the reaction. *trans-erythro*-**10b** gave the intermediate B, where the proton H^3 was antiperiplanar to the disconnecting bond (C_1–C_2).[18] Therefore (*E*)-**6c** was formed selectively, whereas the oxysulfonium salt A derived from *trans-threo*-**10a** was not anticipated to exist in such a conformer, giving rise to a mixture of (*E*)- and (*Z*)-**6c** (60:40) by rotation of the C_2–C_3 bond. A similar explanation is also possible for cis isomers **10c** and **10d** as depicted in Scheme III (C and D).

We next undertook the reaction of *trans*-2-[bis(phenylthio)methyl]cyclohexanol (**14**) with NCS–triethylamine, because Grob fragmentation of the similar system with copper(II) triflate has been reported to give an ω-oxo-α,-β-unsaturated sulfide.[19] Ketene thioacetal **15**[20] and 7-chloroheptanal **16** were obtained in 14% yields under standard conditions (Scheme IV). Formation of **16** indicated the Grob fragmentation of sulfonium salt **17** to α,β-unsaturated sulfide **18**, which reacted with eliminated phenylsulfenyl chloride to give **16**. The ketene thioacetal **15** would be formed via cyclic oxysulfonium salt like **13**. Alternatively dehydrochlorination of the other regioisomer **19** corresponding to **16** may produce the ketene thioacetal **15**. The latter is unlikely because addition of phenylsulfenyl chloride to **18** could produce the sulfide **16** selectively.[21] In fact, treatment of protected α,β-unsaturated sulfide **20** with phenylsulfenyl chloride afforded **22** in 60% yield, and regioisomers of **21** and its derivatives were not detected. Thus two reaction paths are competing in the reaction of bis(phenylthio)cyclohexanol **14**.

The present method is also applicable to 2-allylic, propargylic, and trimethylsilylated cyclohexanols **23**, **25**, and **27**. *trans-erythro*-Allylcyclohexanol (**23a**) reacted with NCS and triethylamine to give selectively (*E*)-1,3-dienyl sulfide **24** in 48% yield. On the other hand, *Z* isomer **24** was obtained from *cis-threo*-**23b** in 44% yield. This stereochemical result is perfectly consistent with the previous one in Table III. A trans mixture (73:27) of propargylcyclohexanol **25** gave the expected product **26** in 75% yield, but stereochemistry of both compounds was not determined unambiguously. Similarly *trans*-[(trimethylsilyl)-methyl]cyclohexanol **27** (threo/erythro, 50:50) was changed to silylated α,β-unsaturated sulfide **28** (*E*/*Z*, 80:20) in 80% yield. Excessive addition of NCS caused protiodesilylation[22] of **28** to give **29**.

In summary, temperature control in the reaction of 2-[(phenylthio)methyl]cycloalkanols with NCS and triethylamine permitted a new ring-opening reaction to yield ω-oxo-α,β-unsaturated sulfides. Stereochemistry of the product depended on that of the starting cycloalkanols, particularly trans-erythro and cis-threo isomers gave se-

(15) The ratios were calculated neglecting the yields.
(16) (a) Marino, J. P. In *Topics in Sulfur Chemistry*; Senning, A., Ed.; Georg Thieme Publishers: Stuttgart, 1976; Vol. 1, pp 53–81. (b) Glass, R. S.; Hojjatie, M.; Setzer, W. N.; Wilson, G. S. *J. Org. Chem.* **1986**, *51*, 1815.
(17) In the reaction of *trans*-2-[1-(phenylseleno)benzyl]cyclohexanol, a selenium analogue of **10**, with NCS and BDU, a proton (H^2) of the similar intermediate was abstracted exclusively to give 2-benzylidenecyclohexanol in 97% yield.[3] But the difference between them remains ambiguous.
(18) Anti transition states were also observed in Grob fragmentation: (a) Grob, C. A.; Schiess, P. W. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 1. (b) Semmelhack, M. F.; Tomesch, J. C. *J. Org. Chem.* **1977**, *42*, 2657.
(19) Reference 18b.
(20) The products **15**, **24**, **26**, and **28** are labile and gradually decomposed during workup.
(21) Toyoshima, K.; Okuyama, T.; Fueno, T. *J. Org. Chem.* **1978**, *43*, 2789.
(22) Colvin, E. In *Silicon in Organic Synthesis*; Butterworths: London, 1981; pp 64–66.



lectively *E* and *Z* unsaturated sulfides, respectively. Coupled with easy preparation of diastereomerically pure cycloalkanols, this simple method could be applied to selective synthesis of various vinyl and 1,3-dienyl sulfides.

Experimental Section

Melting points were measured with a Yanagimoto micro melting point apparatus and are uncorrected. IR spectra were recorded with a Hitachi 215 spectrophotometer. ^1H and ^{13}C NMR spectra were obtained from a JEOL PMX-60 and a JEOL FX-900 spectrometer, and chemical shifts are reported in parts per million on the δ scale from internal tetramethylsilane. Mass spectra were taken with a Hitachi RMU-6D mass spectrometer. Microanalyses were determined on a Yanagimoto CHN-Corder, Type II. Medium pressure liquid chromatography (MPLC) was performed by using Merck Kieselgel 60 (230–400-mesh ASTM).

***trans*-2-[1-(Phenylthio)benzyl]cycloalkanols and *trans*-1-Methyl-2-[1-(phenylthio)benzyl]cycloalkanols 2a–e.** The *trans*-cycloakanols **2a–e** (threo-erythro mixtures) were prepared from [1-(phenylthio)benzyl]lithium and the corresponding cycloalkene oxides[13] (80% yields, method A). **2a**: IR (neat) 3680–3120, 3060, 3040, 2960, 2875, 1580, 1480, 1440 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.75–2.62 (m, 8 H), 3.93 (d, J = 10.3 Hz, 0.6 H), 4.05 (d, J = 8.2 Hz, 0.4 H) (threo/erythro = 60:40), 3.93–4.42 (br, 1 H), 6.78–7.82 (m, 10 H). Anal. Calcd for $C_{18}H_{20}OS$: C, 76.01; H, 7.09. Found: C, 75.68; H, 6.95. **2b**: IR (neat) 3610, 3490, 3080, 3050, 2980, 2890, 1585, 1485, 1460, 1440 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.83–2.48 (m, 11 H), 4.30 (d, J = 4.0 Hz, 0.33 H), 4.37 (d, J = 5.0 Hz, 0.67 H) (threo/erythro = 67:33), 6.87–7.43 (m, 10 H). Anal. Calcd for $C_{19}H_{22}OS$: C, 76.35; H, 7.43. Found: C, 76.35; H, 7.38. **2c**: bp 202 °C (5 mm, Kugelrohr); IR (neat) 3650–3150, 3060, 3030, 2940, 2855, 1600, 1585, 1495, 1480, 1450 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.52–2.29 (m, 10 H), 2.82–3.40 (m, 0.67 H), 3.60–4.07 (m, 0.33 H) (threo/erythro = 67:33), 4.90 (two d, 1 H), 6.97–7.60 (m, 10 H); MS, m/e 298 (M^+). Anal. Calcd for $C_{19}H_{22}OS$: C, 76.47; H, 7.43. Found: C, 76.47; H, 7.32. **2d**: IR (neat) 3650–3150, 3075, 3040, 2940, 2850, 1600, 1590, 1500, 1490, 1455, 1440 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.73–2.33 (m, 12 H), 3.26–3.80 (m, 0.5 H), 3.80–4.26 (m, 0.5 H), 4.65 (d, J = 5.5 Hz, 0.5 H), 4.73 (d, J = 4.0 Hz, 0.5 H) (threo/erytro = 50:50), 6.90–7.56 (m, 10 H); MS, m/e 312 (M^+). **2e**: IR (neat) 3630–3200, 3060, 3040, 2940, 2850, 1600, 1580, 1495, 1480, 1450, 1435 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.07–2.05 (m, 15 H), 4.00 (d, J = 10.6 Hz, 0.6 H), 4.53 (d, J = 4.0 Hz, 0.4 Hz) (threo/erythro = 60:40), 6.97–7.47 (m, 10 H). Anal. Calcd for $C_{21}H_{26}OS$: C, 77.25; H, 8.03. Found: C, 77.20; H, 8.00.

***cis*-2-[1-(Phenylthio)benzyl]cyclopentanol (2f) and *cis*-1-Methyl-2-[1-(phenylthio)benzyl]cyclohexanol (2g).** Addition of thiophenol to 2-benzylidenecycloalkanones, followed by reduction with sodium borohydride (for the cyclopentanone) or by reaction with methylmagnesium iodide (for the cyclohexanone), gave the corresponding cycloalkanols containing four diastereomers. Less polar cis mixtures **2f** and **2g** were separated from trans mixtures by MPLC in 43% and 14% yields, respectively[12] (method B). **2f**: IR (neat) 3650–3200, 3070, 3035, 2950, 2875, 1585, 1495, 1480, 1450, 1440 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.02–2.65 (m, 8 H), 3.65–3.85 (m, 1 H), 4.20 (d, J = 11.0 Hz, 0.5 H), 4.24 (d, J = 10.0 Hz, 0.5 H) (threo/erythro = 50:50), 6.85–7.33, (m, 10 H). Anal. Calcd for $C_{18}H_{20}OS$: C, 76.01; H, 7.09. Found: C, 75.95; H, 7.03. **2g**: IR (neat) 3620–3200, 3050, 3020, 2930, 2850, 1580, 1480, 1440 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85–2.28 (m, 13 H), 4.53 (d, J = 2.4 Hz, 0.75 H), 4.71 (d, J = 3.0 Hz, 0.25 H) (threo/erythro = 25:75), 6.86–7.60 (m, 10 H). Anal. Calcd for $C_{20}H_{24}OS$: C, 76.88; H, 7.74. Found: C, 76.89; H, 7.72.

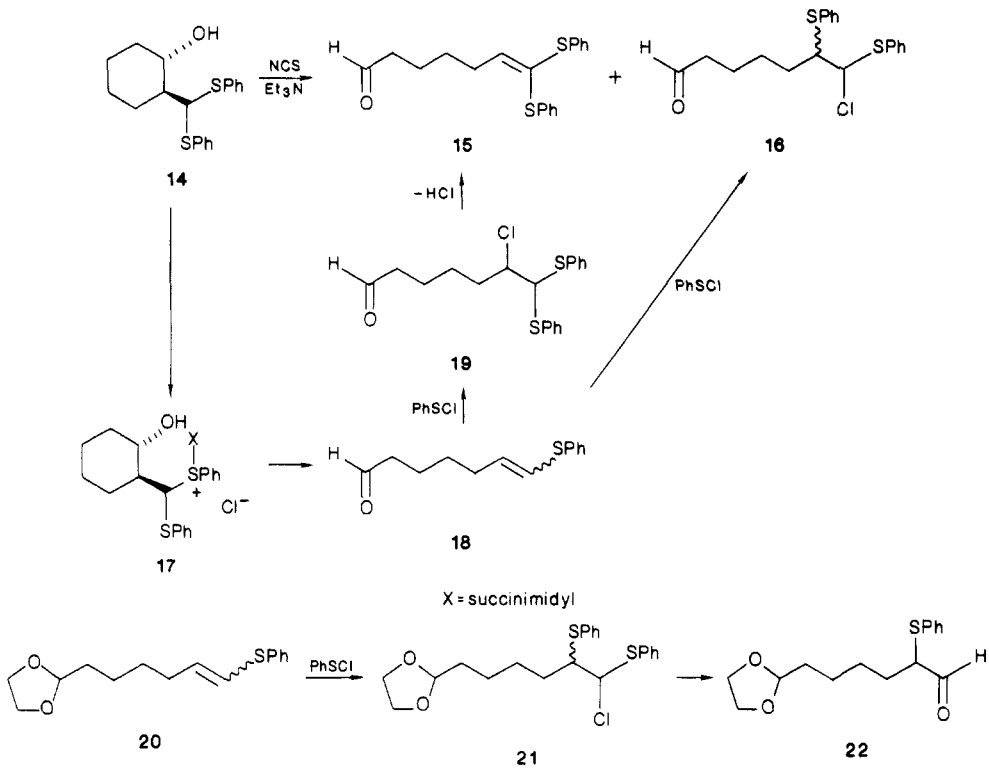
***trans*-threo-, *trans*-erythro-, *cis*-threo-, and *cis*-erythro-2-[1-(Phenylthio)benzyl]cyclohexanol (10a–d).** *threo*-2-[1-(Hydroxy)benzyl]cyclohexanone (8)[10] was treated with equimolar amounts of *N*-(phenylthio)succinimide and tributylphosphine in dry benzene[11] to afford *erythro*-2-[1-(phenylthio)-benzyl]cyclohexanone (**9b**) in 43% yield: colorless oil; IR (Nujol) 3050, 2950, 2860, 1720, 1580, 1480, 1450, 1440 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.23–3.07 (m, 9 H), 4.69 (d, J = 6.8 Hz, 1 H), 6.97–7.30 (m, 10 H). Reduction of **9b** with lithium aluminum hydride (LAH) in dry 1,4-dioxane and separation by MPLC using benzene–ethyl acetate (5:1) gave *cis-erythro*-**10d** and *trans-erythro*-**10b** in 21% and 37% yields, respectively (method C). On the other hand, cyclohexene oxide was added at −78 °C to a solution of [1-(phenylthio)benzyl]lithium, prepared from benzyl phenyl sulfide (1.0 equiv) and butyllithium (1.0 equiv) in dry THF (~0.6 M), and stirred for 3 h at −30 °C under nitrogen. Then benzoyl chloride (1.0 equiv) was added to the solution at −78 °C and stirred overnight. After the usual workup, *trans*-1-(benzoyloxy)-2-[*threo*-1-(phenylthio)benzyl]cyclohexane (**11**) was crystallized by addition of hexane to the reaction mixture and isolated (method D): 70% yield; mp 100.5–101.5 °C (benzene–hexane); IR (Nujol) 1715 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.80–2.63 (m, 9 H), 4.35–4.93 (m, 1 H), 4.72 (d, J = 4.0 Hz, 1 H), 6.80–7 .65 (m, 13 H), 7.90–8.27 (m, 2 H). Anal. Calcd for $C_{26}H_{26}O_2S$: C, 77.58; H, 6.51. Found: C, 77.40; H, 6.46. Reduction of **11** with LAH in boiling 1,4-dioxane gave *trans-threo*-**10a** (60%) as a single isomer. Then, **10a** was oxidized with pyridinium chlorochromate (PCC) in dichloromethane to *threo*-2-[1-(phenylthio)benzyl]cyclohexanone (**9a**) in 60% yield: colorless needles; mp 82 °C (ether); IR (Nujol) 3060, 3040, 2950, 2870, 1718, 1582, 1480, 1450, 1440 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.87–3.10 (m, 9 H), 4.65 (d, J = 8.0 Hz, 1 H), 6.97–7.38 (m, 10 H). Reduction of **9a** with LAH in boiling 1,4-dioxane afforded a mixture of *cis-threo*-**10c** and *trans-threo*-**10a**, which was separated by MPLC using benzene–ethyl acetate (5:1) (53% and 46% yields). Spectral data for **10a–d** are summarized in Table IV.

***trans*-2-[Bis(phenylthio)methyl]cyclohexanol (14).** Cyclohexanol **14** was prepared from cyclohexene oxide and [bis-(phenylthio)methyl]lithium[23] (method A). **14**: IR (neat) 3630–3200, 3060, 2940, 2860, 1585; ^1H NMR ($CDCl_3$) δ 0.97–0.24 (m, 10 H), 3.57–4.10 (m, 1 H), 5.10 (d, J = 2.0 Hz, 1 H), 7.07–7.55 (m, 10 H); MS, m/e 330 (M^+). Anal. Calcd for $C_{19}H_{22}OS_2$: C, 69.05; H, 6.71. Found: C, 69.01; H, 6.57.

***trans*-2-[*erythro*-2-Methyl-1-(phenylthio)allyl]cyclohexanol (23a) and *cis*-2-[*threo*-2-Methyl-1-(phenylthio)allyl]cyclohexanol (23b).** Reaction of cyclohexene oxide with [2-methyl-1-(phenylthio)allyl]lithium, followed by quenching with benzoyl chloride, gave a mixture of benzoates (method D). The major benzoate of *trans-threo*-cyclohexanol was obtained by recrystallization from ether–hexane (40%): mp 74–76 °C; ^1H NMR ($CDCl_3$) δ 1.05–2.41 (m, 9 H), 1.79 (s, 3 H), 4.01 (d, J = 6.6 Hz,

(23) Corey, E. J.; Seebach, D. *J. Org. Chem.* **1966**, *31*, 4097.

Scheme IV



1 H), 4.51–4.82 (m, 2 H), 4.97–5.43 (m, 1 H), 7.01–7.51 (m, 8 H), 7.86–8.09 (m, 2 H). MPLC of the mother liquid gave the minor benzoate of *trans-erythro*-**23a** as an oil (8%): IR (neat) 3060, 2940, 2860, 1730, 1710, 1640, 1600, 1585, 1480 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.03–2.46 (m, 9 H), 1.87 (s, 3 H), 3.84 (d, J = 6.2 Hz, 1 H), 4.51–4.81 (m, 2 H), 4.91–5.36 (m, 1 H), 6.99–7.53 (m, 8 H), 7.99–8.09 (m, 2 H). The major benzoate was converted to the *cis-threo*-cyclohexanol **23b** in a similar way to **10c** (56% yield). *trans-erythro*-**23a** was obtained from the minor benzoate by LAH reduction (56% yield). **23a**: IR (neat) 3650–3150, 3080, 2950, 2870, 1650, 1590, 1490, 1450 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.93–2.16 (m, 10 H), 1.86 (s, 3 H) 3.46–3.96 (m, 1 H), 4.12 (d, J = 4.0 Hz, 1 H), 4.83–5.16 (m, 2 H), 7.03–7.43 (m, 5 H). Anal. Calcd for $C_{16}H_{22}OS$: C, 73.24; H, 8.45. Found: C, 73.21; H, 8.25. **23b**: IR (neat) 3660–3100, 3070, 3040, 2930, 2850, 1635, 1580, 1475, 1450 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.83–2.13 (m, 9 H), 1.83 (s, 3 H), 2.70–3.17 (m, 1 H), 3.40–3.83 (m, 1 H), 3.89 (d, J = 7.0 Hz, 1 H), 4.63–4.83 (m, 2 H), 7.07–7.43 (m, 5 H). Anal. Calcd for $C_{16}H_{22}OS$: C, 73.24; H, 8.45. Found: C, 73.00; H, 8.30.

***trans*-2-[1-(Phenylthio)propargyl]cyclohexanol (25).** *trans*-Cyclohexanol **25** (threo-erythro mixture) was prepared in 41% yield from cyclohexene oxide and dianion of propargyl phenyl sulfide, generated by the treatment with butyllithium (2.0 equiv) in THF and TMEDA (method A). **25**: IR (neat) 3650–3100, 3300, 3070, 2940, 2870, 1590, 1480, 1450 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.82–2.50 (m, 11 H), 3.31–3.88 (m, 1 H) 4.29 (dd, J = 2.6 and 1.8 Hz, 0.27 H), 4.51 (dd, J = 2.6 and 1.9 Hz, 0.73 H), 7.12–7.70 (m, 5 H); ^{13}C NMR ($CDCl_3$) ppm (major isomer) 24.7, 25.2, 26.0, 35.9, 40.5, 49.1, 71.8, 73.5, 81.9, 127.1, 128.7, 131.7, 135.2; (minor isomer) 24.7, 25.5, 27.7, 35.4, 41.8, 49.9, 71.0, 72.8, 83.7, 127.1, 128.2, 132.0, 135.2; MS, m/e 246 (M^+). Anal. Calcd for $C_{15}H_{18}OS$: C, 73.14; H, 7.37. Found: C, 72.76, H, 7.28. Ratio of the major and minor isomers is 73:27 on the basis of ^1H and ^{13}C NMR spectra, but it is difficult to assign which is which.

***trans*-2-[(Phenylthio)(trimethylsilyl)methyl]cyclohexanol (27).** Reaction of cyclohexene oxide with [(phenylthio)(trimethylsilyl)methyl]lithium[24] gave the cyclohexanol **27** in 84% yield (method A): IR (neat) 3650, 3250, 3050, 2920, 2850, 1580, 1240, 850 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.18 (s, 4.5 H), 0.20 (s, 4.5 H) (threo/erythro = 1:1), 0.88–2.15 (m, 10 H), 3.02–3.18 (m, 1 H), 3.22–3.78 (m, 1 H), 6.98–7.62 (m, 5 H). Anal. Calcd for $C_{16}H_{26}OSSi$: C, 65.25; H, 8.90. Found: C, 64.91; H, 8.79.

Reaction of *trans*-2-[1-(Phenylthio)benzyl]cyclohexanol (2c) with *N*-Chlorosuccinimide and Triethylamine. General Procedure for the Ring-Opening Reaction. The cyclohexanol **2c** (2.98 g, 10.0 mmol) was added under nitrogen to a solution of NCS (1.34 g, 10.0 mmol) in dry dichloromethane (40 mL) below −20 °C and stirred for 3 h at −20 °C. Then triethylamine (1.52 g, 15.0 mmol) was added to the mixture and it was allowed to warm to room temperature. After being stirred for 3 h, the mixture was quenched with water (20 mL), extracted with ether, washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The residual oil was purified by MPLC using benzene–ethyl acetate (10:1) to give 7-phenyl-7-(phenylthio)hept-6-enal (**6c**) (2.25 g, 76%): oil; IR (neat) 1730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.17–1.90 (m, 4 H), 1.97–2.90 (m, 4 H), 6.02 (t, J = 7.0 Hz, 0.7 H), 6.35 (t, J = 7.0 Hz, 0.3 H) (E/Z = 70:30) 6.77–7.42 (m, 10 H), 9.53–9.77 (m, 1 H); MS, m/e 296 (M^+). Anal. Calcd for $C_{19}H_{20}OS$: C, 76.99; H, 6.80. Found: C, 76.70; H, 7.10. When the reaction was carried out under the different conditions indicated in the Table I (entries 2–4), undesirable byproducts **3–5** were formed. *trans*-2-Benzoylcyclohexanol (**3**): IR (neat) 3500, 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.07–2.93 (m, 9 H), 3.43–3.97 (m, 1 H), 3.51 (s, 1 H), 7.20–7.53 (m, 3 H), 7.53–7.87 (m, 2 H). *trans*-2-(1-Chlorobenzyl)cyclohexanol (**4**): IR (neat) 3530–3190, 3050, 2940, 2850, 1450, 760 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.80–2.30 (m, 10 H), 2.87–3.38 (m, 0.8 H), 3.38–3.97 (m, 0.2 H), 5.57 (d, J = 4.0 Hz, 0.8 H), 6.27 (d, J = 4.0 Hz, 0.2 H), 7.13–7.33 (m, 5 H). *trans*-2-[1-(Phenylsulfinyl)-benzyl]cyclohexanol (**5**): IR (neat) 3530–3100, 1010 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.93–2.37 (m, 10 H), 3.20–3.67 (m, 1 H), 3.88 (d, J = 6.0 Hz, 1 H), 7.07–7.43 (m, 10 H); MS, m/e 189 (M^+ − SOPh), 171 (M^+ − SOPh − H_2O). Anal. Calcd for $C_{19}H_{22}O_2S$: C, 72.58; H, 7.05. Found: C, 72.50; H, 7.01. The heptenal **6c** was prepared independantly as follows. Reaction of 5-(ethoxycarbonyl)valeraldehyde with [1-(phenylthio)-1-(trimethylsilyl)benzyl]lithium gave 6-(ethoxycarbonyl)-1-phenyl-1-(phenylthio)hex-1-ene (30% yield, E/Z mixture): ^1H NMR ($CDCl_3$) δ 1.07–2.73 (m, 8 H), 1.23 (t, J = 7.0 Hz, 3 H), 4.08 (q, J = 7.0 Hz, 2 H), 6.02 (t, J = 7.0 Hz, 0.33 H), 6.33 (t, J = 7.0 Hz, 0.67 H), 6.97–7.30 (m, 10 H). This hexene was converted to the heptenal **6c** (E/Z = 10:90) by reduction with LAH (80%) and subsequent oxidation with PCC (80%), which was identified with the sample prepared from the cyclohexanol **2c**. The ring-opening reaction of pure diastereomers

(24) (a) Kocienski, P. J. *Tetrahedron Lett.* **1980**, *21*, 1559. (b) Ager, D. J. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1131.

10a–d was performed under similar conditions as described above and the result was summarized in Table III.

6-Phenyl-6-(phenylthio)hex-5-enal (6a): IR (neat) 1730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.42–2.87 (m, 6 H), 5.93 (t, J = 7.0 Hz, 0.75 H), 6.33 (t, J = 7.0 Hz, 0.25 H), (E/Z = 75:25) 6.82–7.65 (m, 10 H), 9.45–9.78 (m, 1 H); MS, m/e 282 (M^+). Anal. Calcd for $C_{18}H_{18}OS$: C, 76.56; H, 6.42. Found: C, 76.38; H, 6.32.

7-Phenyl-7-(phenylthio)hept-6-en-2-one (6b): IR (neat) 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.08–2.61 (m, 9 H), 6.30 (t, J = 7.0 Hz, 0.67 H), 6.78 (t, J = 5.0 Hz, 0.33 H) (E/Z = 67:33), 6.42–7.72 (m, 10 H); MS, m/e 296 (M^+). Anal. Calcd for $C_{19}H_{20}OS$: C, 76.99; H, 6.80. Found: C, 76.54; H, 6.77.

8-Phenyl-8-(phenylthio)oct-7-enal (6d): IR (neat) 1730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.12–1.92 (m, 6 H), 1.92–2.78 (m, 4 H), 6.05 (t, J = 7.5 Hz, 0.6 H), 6.35 (t, J = 7.5 Hz, 0.4 H) (E/Z = 60:40), 6.92–7.40 (m, 10 H), 9.55–9.75 (m, 1 H); MS, m/e 310 (M^+). Anal. Calcd for $C_{20}H_{22}OS$; C, 77.38; H, 7.14. Found: C, 77.38; H, 7.13.

9-Phenyl-9-(phenylthio)non-8-en-2-one (6e): IR (neat) 1715 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.86–2.73 (m, 13 H), 6.06 (t, J = 7.0 Hz, 0.6 H), 6.36 (t, J = 7.0 Hz, 0.4 H) (E/Z = 60:40), 6.73–7.66 (m, 10 H); MS, m/e 324 (M^+). Anal. Calcd for $C_{21}H_{24}OS$: C, 77.73; H, 7.45. Found: C, 77.70; H, 7.42.

8-Phenyl-8-(phenylthio)oct-7-en-2-one (6g): IR (neat) 1715 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.27–2.80 (m, 11 H), 6.03 (t, J = 7.0 Hz, 0.25 H), 6.35 (t, J = 7.0 Hz, 0.75 H) (E/Z = 25:75), 7.00–7.42 (m, 10 H), MS, m/e 310 (M^+). Anal. Calcd for $C_{20}H_{22}OS$: C, 77.38; H, 7.14. Found: C, 77.17; H, 7.11.

Ring-Opening Reaction of *trans*-2-[Bis(phenylthio)-methyl]cyclohexanol (14). Cyclohexanol 14 was treated with NCS and triethylamine under typical conditions as described above and the reaction mixture was separated by MPLC using benzene to give 7,7-bis(phenylthio)hept-6-enal (**15**) (14%)[20] and 6,7-bis(phenylthio)-7-chloroheptanol (**16**) (14%). **15**: IR (neat) 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.35–1.81 (m, 4 H), 2.20–2.64 (m, 4 H), 6.23 (t, J = 7.4 Hz, 1 H), 7.04–7.40 (m, 10 H), 9.62 (t, J = 1.5 Hz, 1 H); MS, m/e 328 (M^+). Anal. Calcd for $C_{19}H_{20}OS_2$: C, 69.47; H, 6.14. Found: C, 69.29; H, 6.05. This compound was identified with an authentic sample prepared by the reaction of 5-(ethoxycarbonyl)valeraldehyde with [bis(phenylthio)(trimethylsilyl)methyl]lithium, followed by reduction (LAH) and oxidation (PPC). **16**: IR (neat) 1730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.50–1.87 (m, 6 H), 2.24–2.67 (m, 2 H), 2.77–3.14 (m, 2 H), 6.87–7.40 (m, 10 H), 9.69 (m, 1 H); MS, m/e 362 (M^+). Anal. Calcd for $C_{19}H_{21}ClOS_2$: C, 62.53; H, 5.80. Found: C, 62.67; H, 6.07.

Reaction of 7-(Phenylthio)hept-6-enal Ethylene Acetal (20) with Phenylsulfenyl Chloride. Phenylsulfenyl chloride (0.29 g, 2.0 mmol) was added to a solution of the ethylene acetal **20** (0.53 g, 2.0 mmol) in dry dichloromethane (20 mL) at −10 °C under nitrogen and stirred for 1 h. The mixture was quenched with water (10 mL), extracted with ether, washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by MPLC using benzene to give 7-oxo-6-(phenylthio)heptanal ethylene acetal (**22**) (0.33 g, 60%); IR (neat) 1730, 1585, 1480, 1442, 1140, 1030 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.27–1.93 (m, 8 H), 3.13–3.73 (m, 1 H), 3.73–4.03 (m, 4 H), 4.16 (t, J = 4.2 Hz, 1 H), 7.13–7.47 (m, 5 H), 9.34 (d, J = 4.1 Hz, 1 H). Anal. Calcd for $C_{15}H_{20}O_3S$: C, 64.26; H, 7.19. Found: C, 64.10; H, 7.01.

8-Methyl-7-(phenylthio)nona-6(*E* or *Z*),8-dienal (24). The *E* and *Z* dienals **24** were prepared from *trans-erythro*-cyclohexanol **23a** and the cis-threo isomer **23b**, respectively, according to the general procedure (*E*, 48%, and *Z*, 44% yields):[20] IR (neat) 3060, 2940, 2860, 1730, 1580, 1480, 1440 cm^{-1}; ^1H NMR ($CDCl_3$) δ (*E* isomer) 1.02–2.58 (m, 8 H), 1.80 (s, 3 H), 4.65–5.02 (m, 2 H), 5.81 (t, J = 1.8 Hz, 1 H), 6.98–7.68 (m, 5 H), 9.60 (t, J = 1.8 Hz, 1 H), (*Z* isomer) 1.03–2.67 (m, 8 H), 1.93 (s, 3 H), 4.80–5.10 (m, 2 H), 6.22 (t, J = 2.0 Hz, 1 H), 7.23–7.68 (m, 5 H), 9.57 (t, J = 2.0 Hz, 1 H); MS, m/e 260 (M^+).

7-(Phenylthio)non-6-en-8-yn-1-al (26): 75% yield by NMR, 25% isolated yield;[20] IR (neat) 3700–3100, 2950, 2870, 1720, 1580, 1480, 1440 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25–1.95 (m, 4 H), 2.22–2.65 (m, 4 H), 3.12 (s, 1 H), 6.32 (t, J = 7.6 Hz, 1 H), 7.12–7.48 (m, 5 H), 9.72 (t, J = 1.6 Hz, 1 H); MS, m/e 244 (M^+).

7-(Phenylthio)-7-(trimethylsilyl)hept-6-enal (28). A mixture of (*E*)- and (*Z*)-heptenals **28**[20] was obtained in 80% yield, which was separeted into pure isomers (ratio, 80:20) by MPLC using benzene. *E* isomer: IR (neat) 3070, 2950, 1735, 1580, 1480, 1440, 1250, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.10 (s, 9 H), 1.32–1.85 (m, 4 H), 2.22–2.68 (m, 4 H), 6.54 (t, J = 6.8 Hz, 1 H), 7.17 (br s, 5 H), 9.68 (m, 1 H); MS, m/e 292 (M^+). Anal. Calcd for $C_{16}H_{24}OSSi$: C, 65.92; H, 8.30. Found: C, 65.61; H, 8.28. *Z* isomer: IR (neat) 3070, 2950, 1730, 1580, 1480, 1250, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.07 (s, 9 H), 1.40–1.90 (m, 4 H), 2.07–2.64 (m, 4 H), 6.09 (t, J = 5.0 Hz, 1 H), 7.27 (br s, 5 H), 9.62 (t, J = 2.0 Hz, 1 H); MS, m/e 292 (M^+). Anal. Calcd for $C_{16}H_{24}OSSi$: C, 65.92; H, 8.30. Found: C, 66.34; H, 8.31. The minor (*Z*)-**28** was gradually isomerized to (*E*)-**28** on standing at room temperature. When the ring-opening reaction was performed by using an excessive amount of NCS (1.5 equiv), 7-(phenylthio)hept-6(*E*)-enal (**29**) was isolated as nearly one stereoisomer in 60% yield: IR (neat) 2940, 1730, 1585, 1480, 1440 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.37–1.77 (m, 4 H), 2.10–2.57 (m, 4 H), 5.60–6.30 (m, 2 H), 7.20 (br s, 5 H), 9.63 (t, J = 2.0 Hz, 1 H). Anal. Calcd for $C_{13}H_{16}OS$: C, 70.87; H, 7.32. Found: C, 70.63; H, 7.20. This heptenal **29** was oxidized to the sulfone (2.6 equiv of MCPBA, CH_2Cl_2, room temperature, 6 h) to determine its stereochemistry by using the coupling constant between the olefinic protons: IR (neat) 1735, 1630, 1320, 1150 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.33–1.97 (m, 4 H), 2.13–2.68 (m, 4 H), 6.31 (dt, J = 15.0 and 1.2 Hz, 1 H), 6.98 (dt, J = 15.0 and 6.6 Hz, 1 H), 7.43–7.70 (m, 3 H), 7.77–8.03 (m, 2 H), 9.70 (t, J = 2.0 Hz, 1 H).

Stereochemistry in the Reactions of (*Z*)- and (*E*)-Allyltributylstannyl Reagents with Quinones

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Received July 30, 1986

In the BF_3-catalyzed allylation of quinones with allylstanyl reagents, (*Z*)-2-hexenyltributylstannane (**3**) is introduced with no retention of the original double-bond stereochemistry, and neryl reagent (**5**) is introduced with partial loss of olefin stereochemistry. In contrast, (*E*)-2-hexenyltributylstannane (**4**) and geranyltributylstannane (**6**) are introduced with complete retention of their olefin geometries.

The stereochemical fate of an introduced moiety into an aromatic nucleus is of current importance in synthetic organic chemistry. Because of high interest in the synthesis of naturally occurring quinones, the stereoselective introduction of all (*E*)-prenyl functions into the *p*-quinone nucleus has been extensively investigated.[1] Naruta and

0022-3263/87/1952-1261$01.50/0