The Use of 4,4-Disubstituted Nopinones for Natural-Product Synthesis. Synthesis of Elemanoid Sesquiterpenes

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A general and convenient synthetic route to 4,4-disubstituted nopinones **14** from (+)-nopinone (**1**) is developed and applied to the asymmetric synthesis of some representative elemanoid sesquiterpenes. Phenylsulfenylation of **1** provided sulfide **6** in high yield. A convenient transformation of **6** to 3-(phenylsulfonyl)-4,4-disubstituted-nopinones **13** was accomplished by (i) *m*-CPBA oxidation of a sulfide compound followed by the Pummerer rearrangement and (ii) the conjugate addition of carbon nucleophiles to the resulting enones, **6** → **8** → **9** and **9** → **10**,**11** → **13**. Subsequent reductive desulfurization of the adducts **13** provided **14** in good overall yield from **1**. Bicyclic ketones **14** are envisioned as promising intermediates for natural product synthesis. As examples, syntheses of two elemanoid sesquiterpenes, β-elemenone (**16**) and eleman-8β,12-olide (**17**) in optically active form from (1*R*,4*S*,5*S*)-4,6,6-trimethyl-4-vinylbicyclo[3.1.1]heptan-2-one (**14a**) were carried out.

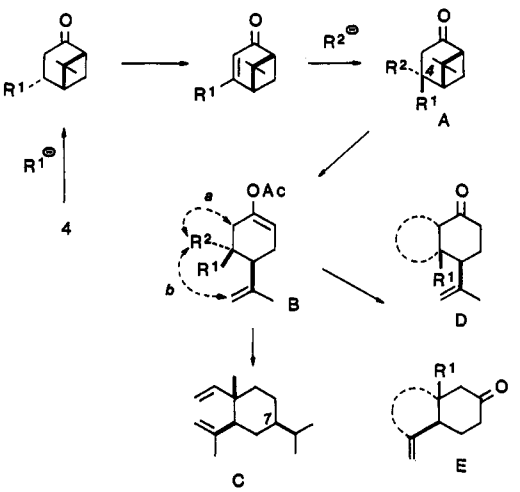
Introduction

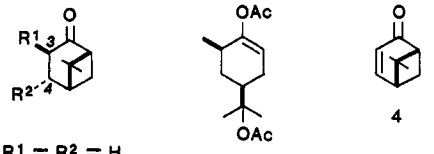
(+)-Nopinone (**1**),[1] readily obtainable in large quantities by ozonolysis of (−)-β-pinene, is a useful chiral source for natural product synthesis. Although some elegant total syntheses starting with **1** have been reported,[2] (+)-nopinone is employed as a chiral starting material rather infrequently in comparison with (−)-carvone which is as abundant as (−)-β-pinene in nature.[2]

This can be attributed to the following two reasons: First, protic acid promoted cleavage of the cyclobutane ring in both **1** and its homologue such as (+)-*cis*-3-methylnopinone (**2**)[3] afforded cyclohexanones which were almost completely racemized at the position bearing the isopropyl group.[1a,4] These ring-opened compounds would be useful for asymmetric synthesis of natural products, provided that the ring cleavage can be achieved without loss of optical purity. Second, practical preparation of 3-alkylnopinones by direct alkylation of **1** with alkyl halides other than methyl iodide seems not to be feasible probably because of steric hindrance from the *gem*-dimethyl group in **1**. Furthermore, few efficient synthetic approaches to 3,3-dialkylnopinones have been reported even though these compounds would be promising intermediates for the construction of some bicyclic compounds, as seen, for example, in the nootkatone synthesis.[5]

We have recently reported that the combined reagent, BF_3·OEt_2–$Zn(OAc)_2$–acetic anhydride, provides an effective solution to the first problem; thus, treatment of **2** with this reagent afforded the optically pure diacetate **3** in high yield.[6,7] The main features of this reaction are (i) cleavage of the cyclobutane ring with little loss of optical integrity, (ii) regioselective formation of an enol acetate function suitable for further regioselective manipulation, and (iii) mild reaction conditions.[8]

Scheme I





1 $R^1 = R^2 = H$

2 R^1 = Me, R^2 = H

5 R^1 = H, R^2 = Me

To solve the second problem, we focused our attention on the reaction at the C(4) of nopinone derivatives having a conjugated enone. It is known that the conjugate addition of lithium dimethylcuprate to enone **4** proceeds stereoselectively to give 4(*R*)-methylnopinone (**5**) in high yield.[3c,9] This stereoselectivity is based on the well-known reactivity characteristic of pinane-type compounds; in this

(1) (a) Van Der Gen, A.; Van Der Linde, L. M.; Witteveen, J. G.; Boelens, H. *Recl. Trav. Chim. Pay-Bas.* **1971**, *90*, 1031. (b) Banthorpe, D. V.; Wittaker, D. *Chem. Rev.* **1966**, *66*, 647.

(2) (Reviews) Heathcock, C. H. The Total Synthesis of Sesquiterpenes. In *The Total Synthesis of Natural Products*, ApSimon, J., Ed.; Wiley-Interscience: New York, 1973; Vol. 2, pp 197–558. Heathcock, C. H.; Graham, S. L.; Pirrung, M. C.; Plavac, F.; White, C. T. Total Synthesis of Sesquiterpenes 1970–79. In *The Total Synthesis of Natural Products*, ApSimon, J., Ed.; John-Wiley & Sons, Inc.: New York, 1983; Vol. 5.

(3) (a) Yoshikoshi, A.; Takagi, Y.; Nishimura, T.; Iwamoto, M.; Kojo, K. (T. Hasegawa, Co.) Jpn. Kokai Tokkyo Koho 78,132,541, 1978; *Chem. Abstr.* **1979**, *90*, 187171e. (b) Konopelski, J. P.; Djerassi, C. *J. Org. Chem.* **1980**, *45*, 2297. (c) Konopelski, J. P.; Sundararaman, P.; Barth, G.; Djerassi, C. *Ibid.* **1980**, *102*, 2737.

(4) With $EtAlCl_2$: Snider, B. B.; Rodini, D. J.; van Straten, J. *J. Am. Chem. Soc.* **1980**, *102*, 5872. With FSO_3H: Coxon, J. M.; Hydes, G. J.; Steel, P. J. *Tetrahedron* **1985**, *41*, 5213.

(5) Yanami, T.; Miyashita, M.; Yoshikoshi, A. *J. Org. Chem.* **1980**, *45*, 607. Inokuchi, T.; Asanuma, G.; Torii, S. *Ibid.* **1982**, *47*, 4622.

(6) Kato, M.; Kamat, V. P.; Tooyama, Y.; Yoshikoshi, A. *J. Org. Chem.* **1989**, *54*, 1536.

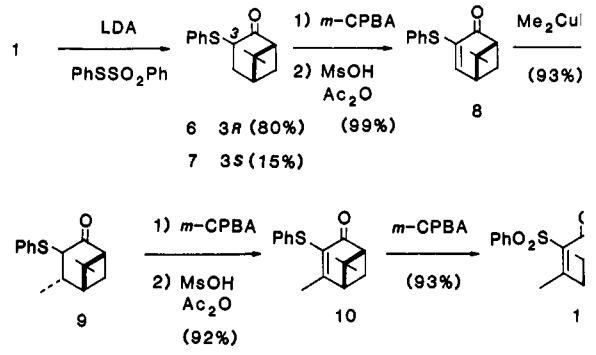
(7) Similarly, BF_3·OEt_2-promoted cyclobutane ring cleavage of **1** provided the expected diacetate. Kato, M.; Watanabe, M.; Vogler, B.; Tooyama, Y.; Yoshikoshi, A. *J. Chem. Soc., Chem. Commun.* **1990**, 1706.

(8) (Other recent reports for preparation of optically active cyclobutane-opened products) Levine, S. G.; Gopalakrishnan, B. *Tetrahedron Lett.* **1971**, 966. Boger, D. L.; Mullican, M. D.; Hellberg, M. R.; Patel, M. *J. Org. Chem.* **1985**, *50*, 1904. References 3b,c.

(9) Nishino, C.; Takayanagi, H. *Agric. Biol. Chem.* **1979**, *43*, 1967.

0022-3263/91/1956-7071$02.50/0

Scheme II



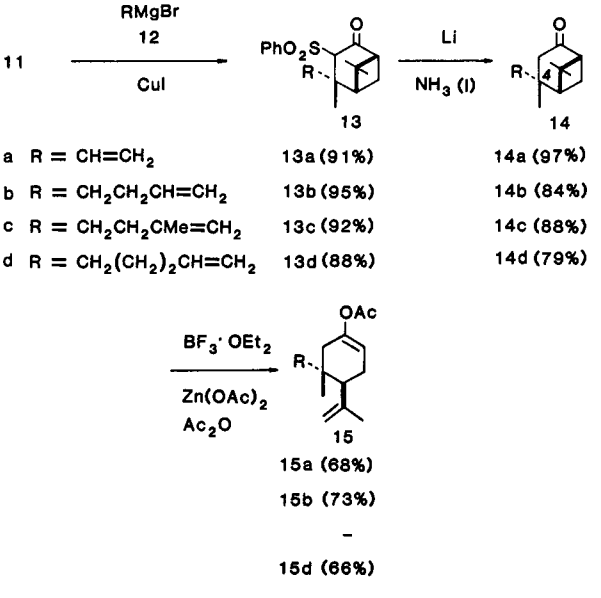
case, the nucleophile approaches from the less hindered side away from the *gem*-dimethyl bridge. In planning the synthesis of 4,4-disubstituted nopinones A, stereoselective introduction of two kinds of substituents, R^1 and R^2, at C(4) could be realized by two successive conjugate addition reactions starting from **4** (Scheme I). Moreover, the cyclobutane opened product B derived from A appears to be a suitable intermediate not only for the synthesis of elemanoid sesquiterpenes C, but also for preparation of two types of bicyclic compounds D and E via cyclizations of *a* and *b*, respectively. Compounds D and E could act as precursors for the synthesis of bicyclic natural products. We wish to describe herein preparation of 4,4-dialkylnopinones as well as the synthesis of some representative elemanoid sesquiterpenes,[10] as the first part of our project mentioned above.[11]

Results and Discussion

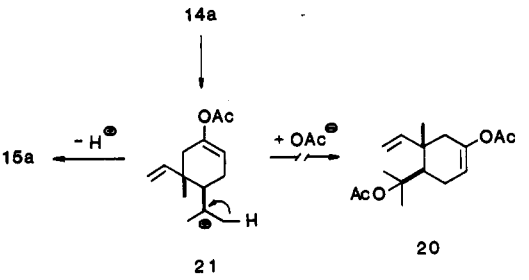
Our synthetic study began with the preparation of α-phenylthio enone **8**, which was expected to be more reactive than enone **4** in conjugate addition reactions.[12] Furthermore the phenylthio group would allow subsequent introduction of an enone into the adduct obtained (Scheme II). Treatment of the lithium enolate derived from nopinone (**1**) with *S*-phenyl benzenethiosulfonate[13] at −78 °C followed by warming to room temperature for several hours provided the thermodynamically stable 3(*R*)-(phenylthio)nopinone **6** as the major product (>80%), along with the kinetically controlled 3(*S*)-(phenylthio)nopinone (**7**) as the minor product. TLC monitoring showed that **6** was formed via **7**, indicating that epimerization of the phenylthio group in **7** occurs while the sulfenylation proceeds. In fact, a significant amount of **7** was obtained, when the reaction mixture was quenched after 5 h. Furthermore, it was confirmed that **7** readily isomerized to **6** with base.[14]

Compound **6** was then oxidized with an equimolar amount of *m*-CPBA, and the resulting sulfoxide was submitted to the Pummerer rearrangement with acetic anhydride containing a small amount of methanesulfonic acid, giving the first enone acceptor **8** in 94% overall yield from **1**. Conjugate addition with lithium dimethylcuprate in THF proceeded in a stereoselective fashion to give 4-(*S*)-methylnopinone **9**[15] as the sole product. Configurational assignment of the newly introduced methyl group was based on the aforementioned stereoselectivity common to pinane derivatives. Transformation of **9** into enone **10** was accomplished by repetition of the two-step sequence of reactions employed above: oxidation of **9** with *m*-CPBA followed by Pummerer rearrangement with acetic anhydride containing methanesulfonic acid, affording enone **10**. Finally, in order to increase the electron-withdrawing effect of the activator, the phenylthio group in **10** was oxidized with *m*-CPBA (2 equiv) to obtain sulfone **11**, the second enone acceptor, in 80 and 75% overall yields from **8** and **1**, respectively.

Scheme III



Scheme IV



The conjugate addition reactions of **11** with some Grignard reagents in the presence of copper(I) iodide were examined next (Scheme III). Commercially available vinylmagnesium bromide (**12a**) was chosen first for the synthesis of elemanoid sesquiterpenes. 3-Butenyl- and 4-pentenylmagnesium bromides, **12b,d**, and (3-(3-methylbutenyl))magnesium bromide **12c** were also employed because their double bonds are convertible by ozonolysis, at a later stage, to the formyl and methyl ketone groups necessary for aldol cyclization reactions.

All conjugate addition reactions proceeded smoothly to give the adducts **13a–d**[15] in high to excellent yields, and no formation of stereoisomers at the C(4) position was detected. Finally, the desired 4,4-disubstituted nopinones **14a–d** were obtained by reductive desulfurization of **13a–d** with lithium in liquid ammonia.

With (4*S*)-4-methyl-4-vinylnopinone (**14a**) available, attention was focused on the utility of **14a** in the asymmetric synthesis of the elemanoid sesquiterpenes, β-elem-

(10) Reported in part in a preliminary communication: Kato, M.; Vogler, B.; Tooyama, Y.; Yoshikoshi, A. *Chem. Lett.* **1990**, 151.

(11) Synthetic studies toward some sesqui- and diterpenes starting with bicyclic compounds corresponding to the compounds D and E are now in progress and will be published in due course.

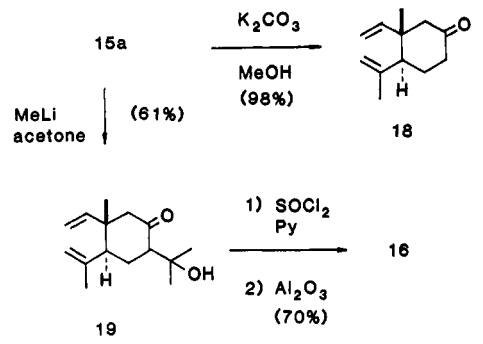
(12) The use of the phenylthio group as an activator: Iwai, K.; Kosugi, H.; Uda, H. *Chem. Lett.* **1974**, 1237. Monterio, H. *J. Org. Chem.* **1977**, *42*, 2324. Kido, F.; Noda, Y.; Yoshikoshi, A. *J. Am. Chem. Soc.* **1982**, *104*, 5509. Kato, M.; Ouchi, A.; Yoshikoshi, A. *Chem. Lett.* **1983**, 1511.

(13) Trost, B. M.; Massiot, G. S. *J. Am. Chem. Soc.* **1977**, *99*, 4405.

(14) An analogous trend was observed in methylation of **1**. See ref 3b,c.

(15) Compounds **9** and **13** are epimeric mixtures with respect to the phenylthio and phenylsulfonyl groups.

Scheme V



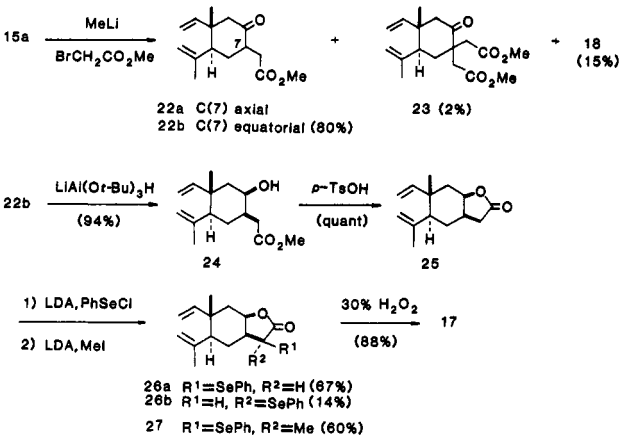
enone (**16**)[16] and eleman-8β,12-olide (**17**).[16] These natural products have been isolated from the essential oils of *Geranium macrorhizum* L,[17a] *Rhododendron adamsii* Rend,[17b] *Mirica gale*,[17c] and *Ledum palustre*[17d] and from the essential oils of *Liatris platylepis*[18a] and *Spilanthes leiocarpa*,[18b] respectively.

The cyclobutane opening reaction of **14a** under our reaction conditions, $BF_3{\cdot}OEt_2$ (0.1–0.2 equiv) and $Zn(OAc)_2$ (1.0 equiv) in acetic anhydride at room temperature for 48 h,[6] followed by aqueous workup provided, as the sole ring-opened product, enol acetate **15a** in 68% yield (Scheme III). Formation of diacetate **20**, which would be predicted from the aforementioned ring-opening reaction of **2**, was not observed. This result can be attributed to the steric interactions between the substituents at C(5) and acetate ion in the transition state for nucleophilic capture leading to **20** (Scheme IV). Analogous results were observed in the cyclobutane opening of **14b,d**, which afforded isopropenyl enol acetates **15b,d** as the only products.

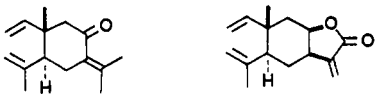
The stereostructure of **15a** was confirmed by hydrolysis with methanolic K_2CO_3 to the known cyclohexanone **18**, $[\alpha]^{21}_D$ −29.2° (*c* 1.44, $CHCl_3$) [lit.[19a] $[\alpha]^{23}_D$ −26.2° (*c* 1.05, $CHCl_3$)], which has been evaluated as a potential intermediate for elemanoid sesquiterpene synthesis[19a] (Scheme V). This correlation proved that introduction of the vinyl group in **11** by conjugate addition occurred as expected from the less hindered α face of the molecule.

When considering that elemanoid sesquiterpenes have a functionalized isopropyl unit commonly at the C(7) position, enol acetate **15a** was envisioned as a common synthetic intermediate, because the enol acetate function is synthetically equivalent to an enolate anion and would play an important role in regioselective introduction of the isopropyl unit. The lithium enolate derived from **15a** with methyllithium (2 equiv) in ether at −78 °C was treated with acetone in the presence of $ZnCl_2$, the kinetically controlled aldol reaction proceeding regioselectively to give hydroxy ketone **19**[20] as the sole condensation product along with a small amount of **18** (Scheme V). Dehydration of **19** with thionyl chloride in pyridine, followed by active Al_2O_3 in

Scheme VI



benzene provided (+)-β-elemenone (**16**), $[\alpha]^{18}_D$ +46.0° (*c* 0.80, $CHCl_3$) [lit.[19a] $[\alpha]^{23}_D$ +39.3° (*c* 1.02, $CHCl_3$)], whose spectral data are identical in all respects with those of the authentic sample.[19a,b]



16 17

The racemic synthesis of eleman-8β,12-olide (**17**) starting with (±)-**18** has been reported by Bohlmann and coworkers.[19c] We examined the asymmetric synthesis of **17** from **15a** with a slight modification of the reported method.[19c] Regioselective introduction of a (methoxycarbonyl)methyl group in **15a** was carried out by treatment of **15a** with methyllithium (2 equiv) in the presence of HMPA at −78 °C followed by addition of methyl bromoacetate. The reaction provided, along with **18** (15%) and dialkylation product **23** (3%), the thermodynamically stable keto ester **22b** (80%) which was produced by isomerization of the initially formed **22a** with lithium *tert*-butoxide present in the medium[21] (Scheme VI). In fact, treatment of keto ester **22b** with sodium methoxide in methanol resulted in no change, thus confirming the thermodynamic stability of this isomer. Reduction of **22b** with lithium tri-*tert*-butoxyaluminum hydride in THF at low temperature gave a single hydroxy ester **24** by exclusive attack of the hydride from the less hindered α side. Lactonization of the latter proceeded smoothly upon treatment with *p*-toluenesulfonic acid in CH_2Cl_2 for 30 min, giving γ-lactone **25** quantitatively.

Conversion of **25** into the *exo*-methylene γ-lactone **17** was performed by a sequence of conventional reactions; (i) phenylselenenylation of **25**, followed by methylation of the resulting selenide **26** with formation of **27**, and (ii) oxidation of **27** with 30% H_2O_2 followed by selenoxide fragmentation. The ^1H NMR (400 MHz) and IR spectra of the synthetic **17**, $[\alpha]^{20}_D$ +100.9° (*c* 0.65, $CHCl_3$), are identical with those of natural eleman-8β,12-olide.[19c]

Syntheses of decalones corresponding to structures D and E (Scheme I), starting with **14b–d**, and their applications to natural product synthesis are in progress.

Experimental Section

Melting points are uncorrected. ^1H NMR spectra were recorded at 90 MHz. All reactions were carried out under dry N_2 or Ar atmosphere with use of standard procedures for the exclusion of

(16) The sesquiterpenes, **16** and **17**, themselves are not known to occur in nature in optically active form.

(17) (a) Ognjanov, I.; Herout, V.; Horak, M.; Sorm, F. *Collect. Czech., Chem. Commun.* **1959**, *24*, 2371. (b) Pizulerskii, G. V.; Belova, N. V. *Zh. Obsch. Khim.* **1964**, *34*, 1345. (c) Tattje, D. H. E.; Bos, R. *Pharm. Weekbl.* **1974**, *109*, 1189; *Chem. Abstr.* **1975**, *83*, 103117m. (d) Naya, Y.; Nagahama, Y.; Kotake, M. *Heterocycles* **1978**, *10*, 29.

(18) (a) Bohlmann, F.; Dutta, L. *Phytochemistry* **1979**, *18*, 1228. (b) Bohlmann, F.; Jakupovic, J.; Hartono, L.; King, R. M.; Robinson, H. *Ibid.* **1985**, *24*, 1100.

(19) (a) Syntheses of optically active **16** and **18**: Sato, T.; Gotoh, Y.; Watanabe, M.; Fujisawa, T. *Chem. Lett.* **1983**, 1533. (b) Syntheses of racemic **16** and **18**: Majetich, G.; Grieco, P. A.; Nishizawa, M. *J. Org. Chem.* **1977**, *42*, 2327. (c) Syntheses of racemic **17** and **18**: Friedrich, D.; Bohlmann, F. *Tetrahedron* **1988**, *44*, 1369.

(20) The stereochemistry of the 2-hydroxypropyl group is tentatively assigned as α axial.

(21) It was reported that methoxycarbonylmethylation of racemic **18** with methyl bromoacetate under the kinetically controlled conditions gave racemic **22a** exclusively. See ref 19c.

moisture. Extracts obtained on aqueous workup of the reaction mixtures were washed successively with water and brine and dried over $MgSO_4$, unless otherwise stated. Column and flash column chromatography were performed on 70–230- and 230–400-mesh silica gel (Merck), respectively, and Kieselgel GF_{254} was employed for preparative TLC. Solvents for elution are shown in parentheses.

(+)-Nopinone (1). This ketone, $[\alpha]^{23}_D$ +36.9° (*c* 4.2, MeOH; 92% optical purity),[22] was prepared from (−)-β-pinene (Aldrich Chemical Co.) according to the published procedure[23] with a slight modification. Ozone was bubbled through a solution of (−)-β-pinene (60.0 g, 0.44 mol) in CH_2Cl_2 (600 mL) at −78 °C until the medium turned dark blue. Excess ozone was purged by N_2, and 50% aqueous MeOH (400 mL) was added. After CH_2Cl_2 was gradually distilled off insofar as possible in an oil bath (75–80 °C) over a period of 3 h, additional water (300 mL) was added. The resulting solution was concentrated approximately two-thirds by azeotropic distillation with decomposition of the ozonide in an oil bath (100–120 °C) over a period of 8 h, and after cooling, it was extracted with hexane. The distillate was diluted with water and extracted with CH_2Cl_2. The combined extracts were dried and evaporated. The residue was carefully distilled, and the fraction boiling at 63–75 °C (4 Torr) was further purified by redistillation, giving 1 (37.6 g, 63%), bp 63–67 °C (4 Torr).[24]

(1*R*,3*R*,5*R*)-6,6-Dimethyl-3-(phenylthio)bicyclo[3.1.1]heptan-2-one (6) and Its C(3)-Epimer (7). To a stirred solution of diisopropylamine (4.21 mL, 30.0 mmol) in THF (30 mL) at −78 °C was added dropwise a 1.49 M solution of BuLi in hexane (18.5 mL, 27.5 mmol). The bath was replaced by an ice bath, and the mixture was stirred for 30 min and then recooled to −78 °C. A solution of (+)-nopinone (1) (3.45 g, 25.0 mmol) in THF (10 mL) was added dropwise, and the mixture was stirred at −78 °C for 30 min, at 0 °C for 30 min, and recooled to −78 °C. A solution of *S*-phenyl benzenethiosulfonate[13] (6.89 g, 27.5 mmol) in THF (10 mL) was added dropwise. The resulting solution was stirred at −78 °C for 20 min and allowed to warm to rt over 5 h. After an additional 15 h, the reaction mixture was quenched with 10% HCl and extracted with ether. The combined extracts were washed successively with aqueous $NaHCO_3$ and brine and dried. Filtration followed by evaporation of the filtrate gave an oil, filtration of which through a short silica gel column with CH_2Cl_2 provided semicrystals. Recrystallization (hexane–ether, 4:1) gave **6** (3.22 g). A crystalline residue obtained from concentration of the filtrate was chromatographed on silica gel (hexane–ether, 4:1) to give **6** (1.69 g) and oily **7** (943 mg, 15%). The total yield of **6** was 4.92 g (80%).

6: needles; mp 97–98 °C; $[\alpha]^{20}_D$ +10.3° (*c* 1.01, $CHCl_3$); IR (KBr) 1705, 1590, 1490, 740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.83 (s, 3 H), 1.35 (s, 3 H), 1.4–2.8 (m, 6 H), 4.18 (dd, 1 H, *J* = 10.8, 7.6 Hz), 7.2–7.6 (m, 5 H). Anal. Calcd for $C_{15}H_{18}OS$: C, 73.14; H, 7.37; S, 12.99. Found: C, 72.90; H, 7.26; S, 12.66.

7: an oil; IR (film) 1710, 1590 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85 (s, 3 H), 1.36 (s, 3 H), 1.2–2.8 (m, 6 H), 3.74 (dd, 1 H, *J* = 9.0, 2.9 Hz), 7.2–7.7 (m, 5 H). Anal. Calcd for $C_{15}H_{18}OS$: C, 73.14; H, 7.37; S, 12.99. Found: C, 73.38; H, 7.48; S, 13.22.

(1*R*,5*R*)-6,6-Dimethyl-3-(phenylthio)bicyclo[3.1.1]hept-3-en-2-one (8). To a stirred solution of **6** (6.00 g, 24.4 mmol) in CH_2Cl_2 (100 mL) was added dropwise at 0 °C a solution of *m*-CPBA (80% purity; 5.26 g, 24.4 mmol) in CH_2Cl_2 (50 mL), and stirring was continued at 0 °C for 1 h and then at rt for 10 h. The precipitate was filtered, and the filtrate was washed successively with aqueous $Na_2S_2O_3$, aqueous $NaHCO_3$, brine, dried, and filtered. To the CH_2Cl_2 solution was added acetic anhydride (4.5 mL, 47.1 mmol) and methanesulfonic acid (1.0 mL, 15.7 mmol). The resulting solution was stirred at 0 °C for 1 h, allowed to warm to rt, and stirred for an additional 15 h. Water (30 mL) was added, the mixture was stirred for 30 min, and the aqueous layer was separated and extracted with CH_2Cl_2. The combined extracts were washed successively with $NaHCO_3$ and brine and dried. Removal of the solvent followed by chromatography of an oily residue on silica gel (hexane–ether, 4:1) afforded **8** (5.9 g, 99%) as crystals: mp 52–53 °C; $[\alpha]^{20}_D$ +91.8° (*c* 1.34, $CHCl_3$); IR ($CHCl_3$) 1680, 1590, 1580 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.10 (s, 3 H), 1.48 (s, 3 H), 2.0–2.3 (m, 1 H), 2.45–2.7 (m, 1 H), 2.7–2.98 (m, 2 H), 6.95 (d, 1 H, *J* = 6.5 Hz), 7.2–7.6 (m, 5 H). Anal. Calcd for $C_{15}H_{16}OS$: C, 73.75; H, 6.60; S, 13.11. Found: C, 73.66; H, 6.67; S, 12.86.

(1*R*,3*RS*,4*S*,5*R*)-4,6,6-Trimethyl-3-(phenylthio)bicyclo[3.1.1]heptan-2-one (9). To a stirred mixture of CuBr·Me_2S (1.99 g, 9.7 mmol) in THF (20 mL) at −78 °C was added a solution of 1.05 M MeLi in ether (18.5 mL, 19.4 mmol). Stirring was continued at −78 to −40 °C for 1 h. After recooling to −78 °C, a solution of **8** (1.97 g, 8.1 mmol) in THF (20 mL) was added and the resulting mixture was allowed to warm to −10 °C over 7 h. The reaction mixture was quenched by addition of aqueous NH_4Cl, and the product was extracted with ether. Removal of the solvent left an oil which was chromatographed on silica gel (hexane–ether, 4:1) to give **9** (1.96 g, 93%) as an oil: IR (film) 1715 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.76 (s, 3 H), 1.22 (d, 3 H, *J* = 6.5 Hz), 1.35 (s, 3 H), 1.5–2.8 (m, 5 H), 3.38 (d, 1 H, *J* = 7.9 Hz), 7.2–7.6 (m, 5 H). Anal. Calcd for $C_{16}H_{20}OS$: C, 73.82; H, 7.74; S, 12.30. Found: C, 73.68; H, 7.74; S, 12.05.

(1*R*,5*S*)-4,6,6-Trimethyl-3-(phenylthio)bicyclo[3.1.1]hept-3-en-2-one (10). According to the procedure described for preparation of **8**, **9** (1.50 g, 5.8 mmol) was treated with *m*-CPBA (80% purity, 1.30 g, 6.0 mmol) in CH_2Cl_2 (25 mL) to give the corresponding sulfoxide as a viscous oil, which was reacted with acetic anhydride (1.08 mL, 11.5 mmol) and methanesulfonic acid (0.2 mL, 2.9 mmol) in CH_2Cl_2 (20 mL), giving **10** (1.37 g, 92%) as crystals: mp 64–65 °C; $[\alpha]^{24}_D$ +144.0° (*c* 0.99, $CHCl_3$); IR (KBr) 1690, 1590, 1580, 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00 (s, 3 H), 1.50 (s, 3 H), 2.1–2.3 (m, 1 H), 2.33 (s, 3 H), 2.55–2.9 (m, 3 H), 7.1–7.5 (m, 5 H). Anal. Calcd for $C_{16}H_{18}OS$: C, 74.40; H, 7.02; S, 12.40. Found: C, 74.54; H, 7.13; S, 12.78.

(1*R*,5*S*)-4,6,6-Trimethyl-3-(phenylsulfonyl)bicyclo[3.1.1]hept-3-en-2-one (11). To a stirred solution of **10** (3.10 g, 12.0 mmol) in CH_2Cl_2 (20 mL) was added at 0 °C a solution of *m*-CPBA (80% purity, 6.75 g, 31.3 mmol) in CH_2Cl_2 (70 mL), and the resulting mixture was stirred at 0 °C for 30 min and then at rt for 2 h. Workup according to the procedure for preparation of **8** provided a crystalline residue which was filtered through a *short* silica gel column (CH_2Cl_2) to give **11** (3.37 g, 93%) as crystals: mp 113–114 °C; $[\alpha]^{20}_D$ +172.8° (*c* 1.03, $CHCl_3$); IR (KBr) 1690, 1580, 1305, 1145, 720, 680, 630 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.82 (s, 3 H), 1.44 (s, 3 H), 2.06 (m, 1 H), 2.5–2.9 (m, 3 H), 2.70 (s, 3 H), 7.3–7.7 (m, 3 H), 7.9–8.2 (m, 2 H). Anal. Calcd for $C_{16}H_{18}O_3S$: C, 66.19; H, 6.25; S, 11.02. Found: C, 65.97; H, 6.30; S, 11.37.

Preparation of 3-(Phenylsulfonyl)-4,4-disubstituted-nopinones 13a–d. (i) Preparation of the Grignard Reagents (General Procedure). To a stirred suspension of magnesium turnings (1.0 molar equiv) in THF was added dropwise at rt a solution of alkenyl bromide (1.05 molar equiv) in THF at a rate so as to maintain a gentle reflux, and after addition was complete, stirring was continued for an additional 1 h at rt. The molar concentration of the resulting Grignard reagent was obtained from titration with a 1.00 M 2-propanol in toluene using 1,10-phenanthroline as an indicator.

(ii) (1*R*,3*RS*,4*S*,5*R*)-4,6,6-Trimethyl-3-(phenylsulfonyl)-4-vinylbicyclo[3.1.1]heptan-2-one (13a) (Representative Procedure). To a stirred mixture of CuI (515 mg, 2.70 mmol) in THF (15 mL) was added dropwise at −50 °C a 1.01 M solution of vinylmagnesium bromide in THF (13.0 mL, 13.0 mmol), and the resulting mixture was stirred for 30 min. A solution of **11** (1.52 g, 5.4 mmol) in THF (15 mL) was added dropwise, and stirring was continued for an additional 1.5 h at −50 °C. The reaction mixture was quenched by addition of aqueous NH_4Cl and extracted with a mixed solvent of ether and CH_2Cl_2 (4:1). Evaporation followed by purification of the oily residue by chromatography on silica gel (hexane–AcOEt, 6:1) gave a diastereomeric mixture of **13a** (1.32 g, 79%) and recovered **11** (194 mg, 12%). **13a**: an oil; IR ($CHCl_3$) 3080, 1720, 1640, 1590, 1320, 1150 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.08 and 1.20 (s each, 3 H in total, ca. 1:1 ratio by integration), 1.33 and 1.38 (s each, 3 H in total), 1.80 and 2.04 (s each, 3 H in total, ca. 1:1 ratio by integration), 2.0–2.6 (m, 4 H), 4.06 and 4.29 (s each, 1 H in total, ca. 1:1 by

(22) The $[\alpha]_D$ value of optically pure **1** has been estimated. Grimshaw, J.; Grimshaw, J. T.; Junega, H. R. *J. Chem. Soc., Perkin Trans. 1* **1972**, 50.

(23) Lewis, K. G.; Williams, G. J. *Aust. J. Chem.* **1968**, *21*, 2467.

(24) It was reported that decomposition of the ozonide with Me_2S was frequently insufficient to cause explosion on distillation of the extract. Gordon, P. M. *Chem. Eng. News* **1990**, *68*, 2.

integration, SCH), 4.9–5.55 (m, 2 H), 5.92–6.40 (m, 1 H). Anal. Calcd for $C_{18}H_{22}O_3S$: C, 67.91; H, 6.97; S, 10.05. Found: C, 67.89; H, 6.76; S, 10.18.

The following compounds were prepared in a similar manner. Starting material, reagents, yields, physical data, and elemental analyses are as follows.

(1*R*,3*RS*,4*S*,5*S*)-4-(3-Butenyl)-4,6,6-trimethyl-3-(phenylsulfonyl)bicyclo[3.1.1]heptan-2-one (13b). **11** (1.04 g, 3.6 mmol), CuI (343 mg, 1.81 mmol), and a 1.2 M solution of 3-butenylmagnesium bromide in THF (7.5 mL, 9.0 mmol) produced a diastereomeric mixture of **13b** (1.19 g, 95%): ^{1}H NMR ($CDCl_3$) δ 3.95 and 4.0 (s each, 1 H in total, ca. 5:1 ratio by integration, SCH). Purification of the mixture **13b** by flash column chromatography on silica gel (hexane–AcOEt, 8:1) gave the major epimer of **13b** as crystals: mp 141–142 °C; IR ($CHCl_3$) 3050, 1720, 1640, 1310, 1210 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.17 (s, 3 H), 1.37 (s, 3 H), 1.73 (s, 3 H), 1.5–2.6 (m, 8 H), 3.95 (s, 1 H), 4.95–5.20 (m, 2 H), 5.60–6.10 (m, 1 H). Anal. Calcd for $C_{20}H_{26}O_3S$: C, 69.34; H, 7.57; S, 9.23. Found: C, 69.52; H, 7.35; S, 9.54.

(1*R*,3*RS*,4*S*,5*S*)-4,6,6-Trimethyl-4-(3-methyl-3-butenyl)-3-(phenylsulfonyl)bicyclo[3.1.1]heptan-2-one (13c). **11** (2.04 g, 7.0 mmol), CuI (533 mg, 2.81 mmol), and a 0.8 M solution of (3-(3-methylbutenyl))magnesium bromide in THF (18 mL, 14.4 mmol) gave a diastereomeric mixture of **13c** (2.32 g, 92%): ^{1}H NMR ($CDCl_3$) δ 3.95 and 3.99 (s each, 1 H in total, ca. 5:1 ratio by integration, SCH). Purification of the mixture **13c** by flash column chromatography on silica gel (hexane–AcOEt, 8:1) gave the major epimer of **13c** as an oil: IR ($CHCl_3$) 3050, 1720, 1650, 1310, 1150, 900 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.18 (s, 3 H), 1.35 (s, 3 H), 1.72 (s, 3 H), 1.78 (s, 3 H), 1.5–2.6 (m, 8 H), 3.95 (s, 1 H), 4.72 (br s, 2 H). Anal. Calcd for $C_{21}H_{28}O_3S$: C, 69.96; H, 7.82; S, 8.89. Found: C, 70.13; H, 7.89; S, 8.67.

(1*R*,3*RS*,4*S*,5*S*)-4,6,6-Trimethyl-3-(phenylsulfonyl)-4-(4-pentenyl)bicyclo[3.1.1]heptan-2-one (13d). **11** (830 mg, 2.86 mmol), CuI (280 mg, 1.47 mmol), and a 0.7 M solution of 4-pentenylmagnesium bromide in THF (9.5 mL, 6.7 mmol) gave a diastereomeric mixture of **13d** (909 mg, 88%): ^{1}H NMR ($CDCl_3$) δ 3.92 and 4.0 (s each, 1 H in total, ca. 5:1 ratio by integration, SCH). Purification of the mixture of **13d** by flash chromatography on silica gel (hexane–AcOEt, 8:1) gave the major epimer of **13d** as crystals: mp 135–136 °C; IR ($CHCl_3$) 3050, 1720, 1640, 1590, 1310, 1150, 910 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.15 (s, 3 H), 1.34 (s, 3 H), 1.70 (s, 3 H), 1.2–1.8 (m, 4 H), 1.9–2.6 (m, 6 H), 3.92 (s, 1 H), 4.86–5.15 (m, 2 H), 5.60–6.00 (m, 1 H). Anal. Calcd for $C_{21}H_{28}O_3S$: C, 69.96; H, 7.85; S, 8.89. Found: C, 69.77; H, 7.81; S, 8.64.

Reductive Desulfurization of 13a–d with Lithium in Liquid Ammonia. (1*R*,4*S*,5*S*)-4,6,6-Trimethyl-4-vinylbicyclo[3.1.1]heptan-2-one (14a) (Representative Procedure). Anhydrous liquid NH_3 (80 mL) distilled from Li wire was stirred and cooled at −78 °C as a solution of **13a** (1.42 g, 4.5 mmol) in THF (7 mL) was added. After brief stirring, Li wire (103 mg, 0.02 g-atom) cut into small pieces was added, and stirring was continued for an additional 30 min. Excess NH_4Cl (solid) was added cautiously, and the NH_3 was mostly removed at rt. Water was added, and the product was extracted with ether. Removal of the solvent gave an oily residue which was chromatographed on silica gel (hexane–ether, 4:1) to give **14a** (792 mg, 97%) as an oil: $[\alpha]^{21}_D$ +87.9° (*c* 2.15, $CHCl_3$); IR (film) 3070, 1710, 1640, 915 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.08 (s, 3 H), 1.23 (s, 3 H), 1.38 (s, 3 H), 1.4–1.7 (m, 1 H), 1.9–2.1 (m, 1 H), 4.92 (d, 1 H, J = 17.1 Hz), 4.99 (d, 1 H, J = 9.9 Hz with fine splittings), 5.78 (dd, J = 17.1, 9.9 Hz). Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.64; H, 9.92.

The following compounds were prepared in a similar manner. Starting material, reagents, yield, physical data, and elemental analyses of the products are as follows.

(1*R*,4*R*,5*R*)-4-(3-Butenyl)-4,6,6-trimethylbicyclo[3.1.1]heptan-2-one (14b). **13b** (1.18 g, 3.4 mmol), Li (90 mg, 0.013 g-atom), and NH_3 (150 mL) gave **14b** (595 mg, 84%): oil; $[\alpha]^{20}_D$ +34.6° (*c* 1.04, $CHCl_3$); IR (film) 3080, 1715, 1640, 910 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.05 (s, 3 H), 1.17 (s, 3 H), 1.37 (s, 3 H), 1.3–2.62 (m, 10 H), 4.83–5.12 (m, 2 H), 5.58–6.02 (m, 1 H). Anal. Calcd for $C_{14}H_{22}O$: C, 81.49; H, 10.75. Found: 81.35; H, 10.92.

(1*R*,4*R*,5*R*)-4-(3-Methyl-3-butenyl)-4,6,6-trimethylbicyclo[3.1.1]heptan-2-one (14c). **13c** (1.20 g, 3.3 mmol), Li (90 mg, 0.013 g-atom), and NH_3 (150 mL) gave **14c** (644 mg, 88%): oil; $[\alpha]^{20}_D$ +32.8° (*c* 1.05, $CHCl_3$); IR (film) 3080, 1715, 1630, 890 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.03 (s, 3 H), 1.18 (s, 3 H), 1.36 (s, 3 H), 1.72 (s, 3 H), 1.4–2.1 (m, 6 H), 2.3–2.62 (m, 4 H), 4.68 (br s, 2 H). Anal. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.96; H, 11.16.

(1*R*,4*R*,5*R*)-4-(4-Pentenyl)-4,6,6-trimethylbicyclo[3.1.1]heptan-2-one (14d). **13d** (763 mg, 2.12 mmol), Li (65 mg, 0.01 g-atom), and NH_3 (100 mL) gave **14d** (370 mg, 79%): oil; $[\alpha]^{20}_D$ +36.3° (*c* 1.16, $CHCl_3$); IR (film) 3080, 1710, 1640, 915 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.03 (s, 3 H), 1.14 (s, 3 H), 1.35 (s, 3 H), 1.25–1.75 (m, 4 H), 1.80–2.15 (m, 4 H), 2.23–2.60 (m, 4 H), 4.85–5.13 (m, 2 H), 5.57–6.0 (m, 1 H). Anal. Calcd for $C_{14}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.96; H, 10.99.

(4*S*,5*S*)-1-Acetoxy-4-isopropyl-5-methyl-5-vinyl-1-cyclohexene (15a). A mixture of **14a** (362 mg, 2.03 mmol), freshly distilled BF_3·OEt_2 (0.04 mL, 0.4 mmol), $Zn(OAc)_2$ (372 mg, 2.03 mmol), and acetic anhydride (3 mL) was allowed to stir at rt for 48 h. The reaction mixture was diluted with water (20 mL), and stirring was continued for an additional 30 min at rt. The product was extracted with ether, and the combined extracts were washed successively with $NaHCO_3$, water, and brine and dried. Evaporation of the solvent left an oil, which was chromatographed on silica gel (hexane–ether, 9:1) to give **15a** (304 mg, 68%) along with a small amount of recovered **14a**. **15a**: oil; $[\alpha]^{19}_D$ −7.6° (*c* 0.48, $CHCl_3$); IR (film) 3080, 1760, 1695, 1640, 910, 900 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.08 (s, 3 H), 1.74 (s, 3 H), 2.10 (s, 3 H), 1.9–2.3 (m, 4 H), 4.75–5.1 (m, 4 H), 5.35 (br s, 1 H), 5.83 (dd, 1 H, J = 18.0, 10.0 Hz). Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.32; H, 9.15. Found: C, 76.21; H, 9.31.

(3*S*,4*S*)-3-Methyl-4-isopropyl-3-vinyl-1-cyclohexanone (18). A mixture of **15a** (133 mg, 0.60 mmol), anhydrous K_2CO_3 (82 mg, 0.60 mmol), and MeOH (5 mL) was stirred at 0 °C for 2 h. The solvent was removed under reduced pressure, water was added, and the product was extracted with ether. The oil obtained by concentration was chromatographed on silica gel (hexane–ether, 5:1) to give **18** (105 mg, 98%) as an oil: $[\alpha]^{20}_D$ −29.2° (*c* 1.44, $CHCl_3$) [lit.[19a] $[\alpha]^{23}_D$ −26.2° ($CHCl_3$)]. The IR and ^{1}H NMR spectra were identical with those of **18** reported in the literature.[19a]

(+)-β-Elemenone (16). To a stirred 1.11 M solution of MeLi in ether (1.1 mL, 1.2 mmol) was added dropwise at −78 °C a solution of **15a** (119 mg, 0.54 mmol) in ether (2 mL). After brief stirring for 20 min, a solution of $ZnCl_2$ (74 mg, 0.54 mmol) in ether (5 mL) was added dropwise, and the reaction mixture was stirred at −78 °C for 20 min. To this was added dropwise freshly distilled acetone (0.4 mL), and stirring was continued for an additional 10 min. The reaction was quenched by addition of aqueous NH_4Cl, and the product was extracted with ether. Evaporation of the solvent left an oil which was chromatographed on silica gel (hexane–ether, 2:1) to give **18** (18 mg, 15%) and **19** (78 mg, 61%): IR (film) 3400, 1700, 1640, 920, 900 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.05 (s, 3 H), 1.18 (s, 3 H), 1.20 (s, 3 H), 1.87 (s, 3 H), 1.5–2.05 (m, 2 H), 2.10–2.80 (m, 4 H), 3.97 (br s, 1 H, exchangeable with D_2O), 4.7–5.1 (m, 4 H), 5.78 (dd, 1 H, J = 17.3, 10.8 Hz).

To a stirred solution of **19** (78 mg, 0.33 mmol) in pyridine (1 mL) was added at 0 °C $SOCl_2$ (0.1 mL), and stirring was continued at 0 °C for 2 h and then at rt for 2 h. Ether (10 mL) was added, and the resulting solution was washed successively with aqueous $CuSO_4$, water, and brine and then dried. The oily residue obtained from concentration was dissolved in benzene (2 mL), active Al_2O_3 (100 mg) was added, and the resulting suspension was stirred at rt for 4 h. Filtration followed by concentration left an oil which was purified by preparative TLC (hexane–ether, 4:1) to give **16** (50 mg, 72%) as an oil: $[\alpha]^{18}_D$ +46.0° (*c* 0.80, $CHCl_3$) [lit.[19a] $[\alpha]^{23}_D$ +39.3° (*c* 1.02, $CHCl_3$)]. The IR and ^{1}H NMR spectra were identical with those of the authentic sample.[19a]

Methyl [(2*R*,4*S*,5*S*)-2-(4-Isopropenyl-5-methyl-5-vinyl-1-oxocyclohexyl)]acetate (22b).[25] A 0.99 M solution of MeLi in ether (2.2 mL, 2.2 mmol) was stirred and cooled at −78 °C as a solution of **15a** (220 mg, 1.00 mmol) in THF (2 mL) was added dropwise. After 20 min, a solution of methyl bromoacetate (168 mg, 1.1 mmol) in THF (2 mL) followed by HMPA (0.3 mL) was added, and the resulting mixture was stirred at −78 °C for 1 h

(25) For preparation of the racemate and its IR and ^{1}H NMR (400 MHz) data, see ref 19c.

and allowed to warm to rt. After an additional 15 h, the reaction mixture was quenched by addition of aqueous NH_4Cl and extracted with ether. Removal of the solvent left an oil which was purified by preparative TLC (hexane–ether, 3:1) to give **22b** (200 mg, 80%), **23** (8 mg, 2%), and **18** (37 mg, 15%).

22b: crystals; mp 58–59 °C; $[\alpha]^{24}_D$ -2.7° (*c* 0.83, $CHCl_3$); IR (KBr) 3080, 1740, 1720, 1640, 920, 910 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.98 (s, 3 H), 1.78 (s, 3 H), 1.5–3.1 (m, 8 H), 3.70 (s, 3 H), 4.65–5.10 (m, 4 H), 5.85 (dd, J = 17.3, 10.8 Hz, 1 H).

23: crystals; mp 97–98 °C; IR (film) 3070, 1740, 1730, 1640, 1210, 1165, 990, 900 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.87 (s, 3 H), 1.72 (s, 3 H), 1.4–2.2 (m, 7 H), 2.50–2.66 (m, 2 H), 3.67 (s, 3 H), 3.78 (s, 3 H), 4.63–5.05 (m, 4 H), 5.80 (dd, J = 17.3, 11.0 Hz, 1 H).

13-Noreleman-8β,12-olide (25).[25] A suspension of lithium tri-*tert*-butoxyaluminium hydride (254 mg, 1.00 mmol) in THF (1 mL) was stirred and cooled to -78 °C as a solution of **22b** (63 mg, 0.25 mmol) in THF (4 mL) was added dropwise. After stirring for 30 min at -78 °C, the reaction temperature was raised to rt over 7 h. Excess hydride reagent was decomposed by addition of wet ether followed by aqueous HCl, and the product was extracted with ether. Removal of the solvent followed by filtration of an oily residue through a short silica gel column (hexane–ether, 1:1) gave **24** (59 mg, 94%) as an oil: ^1H NMR ($CDCl_3$) δ 1.17 (s, 3 H), 1.75 (s, 3 H), 1.3–2.1 (m, 7 H), 2.31–2.55 (m, 2 H), 3.68 (s, 3 H), 3.97 (br s, 1 H), 4.6–5.05 (m, 4 H), 5.75 (dd, J = 17.5, 10.5 Hz, 1 H).

A mixture of **24** (25 mg, 0.1 mmol), *p*-toluenesulfonic acid (5 mg), and CH_2Cl_2 (7 mL) was stirred at rt for 3 h, washed with brine, and dried. Concentration followed by purification of a crystalline residue by preparative TLC (hexane–ether, 1:1) gave **25** (21 mg, quantitative) as crystals: mp 79–80 °C; $[\alpha]^{25}_D$ +16.3° (*c* 0.51, $CHCl_3$); IR (KBr) 3060, 1760, 1156, 950, 890 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.07 (s, 3 H), 1.72 (s with fine splittings, 3 H), 1.4–2.9 (m, 8 H), 4.51–4.67 (m, 2 H), 4.80–4.98 (m, 2 H), 5.02 (s with fine splittings, 1 H), 5.75 (dd, J = 17.5, 10.5 Hz, 1 H).

Eleman-8β,12-olide (17).[25] The lithium enolate of **25** prepared from LDA, generated from a 1.5 M solution of BuLi in THF (0.46 mL, 0.71 mmol) and diisopropylamine (110 μ L, 0.79 mmol) in THF (6 mL), and **25** (128 mg, 0.58 mmol) was treated with phenylselenenyl chloride (126 mg, 1.03 mmol) in THF (3 mL) at -78 °C to give **26a** (147 mg, 67%), **26b** (30 mg, 14%), and recovered **25** (23 mg, 18%).

26a: oil; IR ($CHCl_3$) 3080, 1770, 1640, 1580, 1180 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.03 (s, 3 H), 1.68 (s, 3 H), 1.2–2.45 (m, 6 H), 3.70 (s, 1 H), 4.56 and 5.00 (s, 1 H each), 4.75 (m, 1 H), 4.8–4.9 (m, 2 H), 5.72 (dd, J = 17.5, 10.5 Hz, 1 H), 7.2–7.38 (m, 3 H), 7.48–7.55 (m, 2 H).

26b: crystals; mp 119–120 °C; IR ($CHCl_3$) 3080, 1780, 1640, 1580, 1160 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.04 (s, 3 H), 1.72 (s, 3 H), 1.2–2.7 (m, 6 H), 4.50 (d, J = 5.6 Hz, 1 H), 4.5 (m, 1 H), 4.62–5.01 (m, 4 H), 5.72 (dd, J = 17.0, 10.5 Hz, 1 H), 7.2–7.35 (m, 3 H), 7.5–7.75 (m, 2 H).

The lithium enolate of **26a** prepared from LDA, generated from a 1.59 M solution of BuLi in THF (1.59 mL, 0.7 mmol) and diisopropylamine (160 μL, 1.1 mmol) in THF (6 mL), and **26a** (156 mg, 0.42 mmol) were treated with MeI (71 mg, 0.50 mmol) to give **27** (97 mg, 60%) as crystals: mp 134.5–135 °C; IR ($CHCl_3$) 3080, 1765, 1620, 1580, 1090 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.02 (s, 3 H), 1.35 (s, 3 H), 1.68 (s, 3 H), 1.4–2.5 (m, 6 H), 4.60–5.05 (m, 5 H), 4.78 (dd, J = 17.5, 10.8 Hz, 1 H), 7.2–7.43 (m, 3 H), 7.6–7.8 (m, 2 H).

A solution of **27** (88 mg, 0.23 mmol) and pyridine (0.1 mL) in THF (3 mL) was stirred and cooled at 0 °C as 30% H_2O_2 (0.5 mL) was added, and the resulting solution was stirred at rt for 30 min. Workup gave **17** (46 mg, 88%) as an oil: $[\alpha]^{20}_D$ +100.9° (*c* 0.65, $CHCl_3$); HRMS calcd for $C_{15}H_{20}O_2$ *m/z* 232.1465, found *m/z* 232.1469. The ^1H NMR (400 MHz) spectral data of the synthetic **17** are identical with those reported for racemic **17**.[19c]

Registry No. **1**, 38651-65-9; **6**, 128261-63-2; **7**, 128301-59-7; **8**, 128261-64-3; (3*R*)-**9**, 128261-70-1;)3*S*)-**9**, 128261-65-4; **9** sulfoxide, 137041-00-0; **10**, 128261-66-5; **11**, 128261-67-6; **12a**, 1826-67-1; **12b**, 7103-09-5; **12c**, 97344-88-2; **12d**, 34164-50-6; (3*R*)-**13a**, 137041-01-1; (3*S*)-**13a**, 137041-21-5; (3*R*)-**13b**, 137041-02-2; (3*S*)-**13b**, 137041-22-6; (3*R*)-**13c**, 137041-03-3; (3*S*)-**13c**, 137041-23-7; (3*R*)-**13d**, 137041-04-4; (3*S*)-**13d**, 137041-24-8; **14a**, 128261-62-1; **14b**, 137041-05-5; **14c**, 137041-06-6; **14d**, 137041-07-7; **15a**, 128261-61-0; **15b**, 137041-08-8; **15d**, 137041-09-9; **16**, 137041-12-4; **17**, 137041-20-4; **18**, 137041-10-2; **19**, 137041-11-3; **22b**, 137041-13-5; **23**, 137041-14-6; **24**, 137041-15-7; **25**, 137041-16-8; **26a**, 137041-17-9; **26b**, 137041-18-0; **27**, 137041-19-1; (-)-β-pinone, 18172-67-3.

Supplementary Material Available: Full experimental and physical data ($[\alpha]^{20}_D$, IR, ^1H NMR) of compounds **15b,d** (2 pages). Ordering information is given on any current masthead page.

Thermal Rearrangements of α-(Acyloxy)silanes. 2. Formation of Chiral Precursors and Migratory Preference of Silicon-Based Groups

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The asymmetric reduction of acylsilanes to chiral α-hydroxysilanes and the thermal rearrangement of the corresponding chiral α-acetoxysilanes was explored. Ipc_2BCl reduces many acylsilanes in >95% ee. The rate of the thermal rearrangement of the α-acetoxysilanes was dependent upon the substituents at both silicon and carbon. Evidence is presented to indicate there is electron deficiency at the α-carbon in the transition state. Migratory aptitudes follow those expected on the basis of the migrating group assuming an apical migratory group at a pentacoordinate silicon. A previously unreported hydrolytic transformation of a proposed acylsilyl hydride to a stable 1-sila-1,2-diol was observed.

Brook,[1] Reetz,[2] and Tacke[3] have demonstrated that α-acetoxysilanes (e.g., **2**) can be thermally rearranged to the corresponding silyl acetates with concurrent migration of one aryl group from silicon to carbon (as shown). Larson[4] studied the stereochemistry of a similar rearrangement of α-chlorosilanes. We recently reported a thermal rearrangement of α-acetoxysilanes which can be incorporated into synthetic methodology leading to the preparation of chiral non-silicon-containing secondary alcohols in reasonably high enantiomeric excess (Scheme

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