Enantiospecific Synthesis of a Chrysanthemic Acid Precursor

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1,4 Addition of the lithium anion of allyl phenyl sulfide to 3,3-dimethylacrylonitrile and to methyl 3,3-dimethyl acrylate occurred at the α position of the carbanion. The resulting adducts **5** and **6** were converted to the allylic alcohols **1** and **9** by [2,3] sigmatropic shift of the sulfoxides, obtained by oxidation. Besides sulfoxide **7**, sulfenate **13** arising from [2,3] sigmatropic shift and sulfinate **10** were detected. Alcohol **1** was epoxidized according to the Katsuki–Sharpless procedure to the (4*S*,5*R*) epoxy alcohol **17** with an ee > 94%. Its silyl ether **19** was converted to a mixture of cis and trans cyclopropylnitriles by the Stork cyclization. After removal of the silyl group and periodate cleavage, trans and cis aldehydes **24** and **25** were separated. The trans aldehyde **24** was converted to (1*R*,3*R*)-*trans*-chrysanthemic nitrile **26** (ee 92%).

Pyrethroids and synthetic chrysanthemic acid derivatives are very potent insecticides.[1] This activity is restricted to one of the diastereomers. Thus, methods for enantiospecific synthesis of chrysanthemic acid are of interest.[2] Several asymmetric syntheses have been published.[3-11] We present here a synthesis combining the asymmetric Katsuki–Sharpless epoxidation[12] and a regiospecific alkylation (Stork cyclization).[13,14]

The planned synthesis required nitrile **1**. The 1,4 addition of carbanion **2** to 3,3-dimethylacrylonitrile occurred already at −78 °C in THF (experiment 1) and appeared to be fast by observing the color change of the reaction media. Variation of the experimental conditions such as quantities of 3,3-dimethylacrylonitrile and HMPA and addition of lithium bromide led to the desired 1,4-adduct **5** in 75% yield (see Table I). A satisfactory yield (experiment 6) was finally obtained with an excess of electrophile (1.5 equiv), in the presence of lithium bromide and HMPA. The 1,4 addition occurred at the position α to the thioether. The 1,4 addition of the anion **2** to methyl 3,3-dimethyl acrylate **4** gave ester **6** (65% yield), the experimental conditions were not optimized).

The 1,4 addition to α,β-unsaturated nitrile **3** appears to be a new observation. 1,4 Additions to α,β-unsaturated esters[15,16] and ketones[17] have been described. The fact that lithium carbanion undergoes 1,4 addition in THF, even in the absence of HMPA, is noteworthy and shows that the α,β-unsaturated nitrile **3** is a good Michael acceptor.

Table I. Optimization of the Yield of 1,4 Adduct 5 from Carbanion 2 to Dimethylacrylonitrile

exp	nitrile **3** (eq)	HMPA (equiv)	LiBr (equiv)	% yield of **5**[a]
1	1	0	0	25
2	1	0	0	10
3	1	1	0	20[b]
4	1.5	0	0	50
5	1	3	2	30 (<10)[c]
6	1.5	3	2	75
7	2	3	2	65

[a] Yield of isolated nitrile **5**, experiments run at −78 °C for 2 h. [b] Reaction quenched at −78 °C, 15 min after addition of **3**. [c] Run at −40 °C, yield estimated by ^{H} NMR spectroscopy.

The next step was the conversion of thioether **5** to the allylic alcohol **1** through the well-known [2,3] sigmatropic shift of the sulfoxide **7**. Oxidation of **5** with *m*-chloroperbenzoic acid at −78 °C afforded sulfoxide **7** which was directly converted to the alcohol **1** at 60 °C, in the presence of diethylamine (86% yield from thioether **5**). By the same procedure, thioether **6** was converted to the ester alcohol **9** (77% yield from thioether **6**). The *E* configuration of the double bond was confirmed by the coupling constants for the vinylic protons.

When the oxidation product of thioether **5** was examined by ^{1}H NMR spectroscopy, it was found to be a mixture of sulfoxide **7**, byproduct A, and a minor byproduct B. With time, the ratio of A to the sulfoxide increased to 1/2. The ^{1}H NMR spectrum of A shows an AB(X) system at δ 4.13 and 4.52, implying the presence of a methylene group next to an asymmetric center.

Two structures were considered for product A: sulfoxide **12** arising from [1,3] allylic migration and sulfinate **10**. The ^{1}H NMR spectrum is more consistent with the latter. Both were prepared independently from alcohol **1** as illustrated in Figure 2.[18] The NMR spectrum of the sulfinate is identical to that of byproduct A.

The ^{1}H NMR spectrum of byproduct B showed a doublet at δ 4.24. B could be the sulfenate **13** in equilib-

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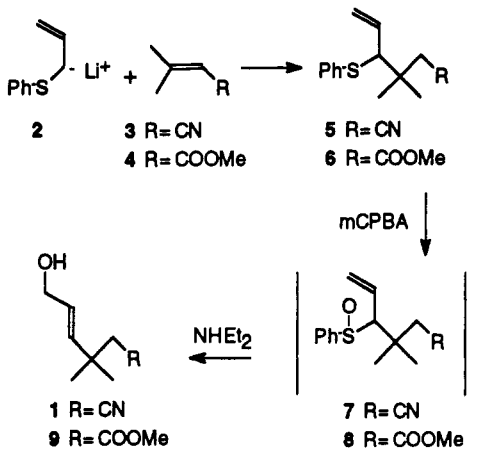

Figure 1.

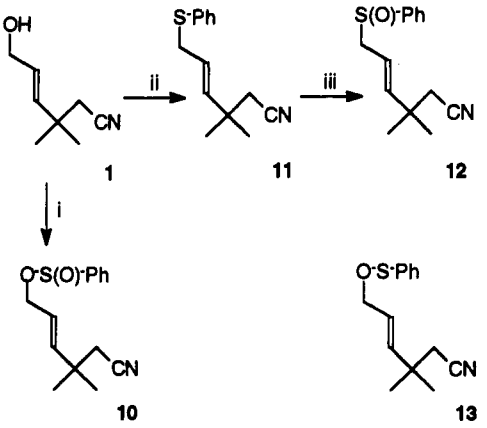

Figure 2. Key: (i) DMAP, NEt_3, PhSOCl, CH_2Cl_2; (ii) (a) MeLi, pTsCl, ether/HMPA, (b) PhSLi, ether; (iii) *m*-CPBA, CH_2Cl_2.

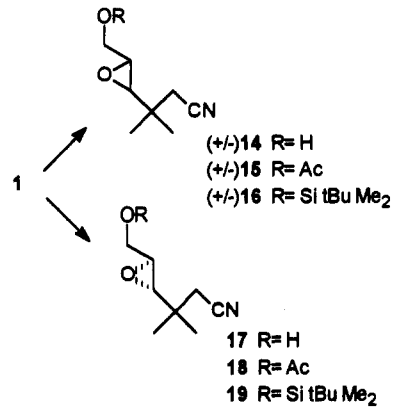

Figure 3.

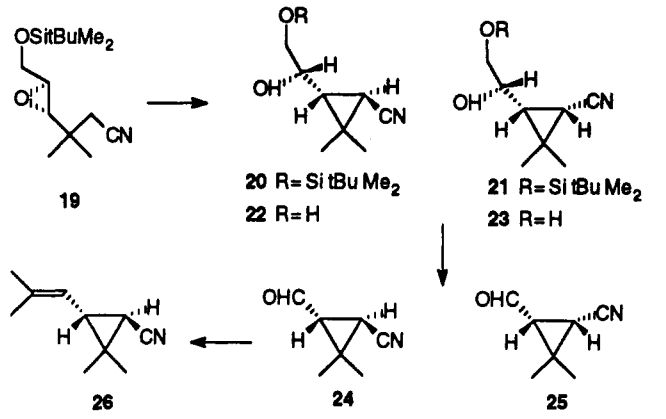

Figure 4.

rium with the sulfoxide **7**. Similar results were obtained starting with the ester thioether **6**. The steric crowding of sulfoxide **7** may be responsible for shifting the normal sulfoxide-sulfenate equilibrium toward the sulfenate enough to allow its detection by ^1H NMR. Some allylic sulfenates have been detected or even found to be stable.[19,20]

The presence of the sulfinate ester **10** was unexpected. But its reaction with diethylamine gave alcohol **1** in high yield, likely via attack of the amine to the sulfur.[21,22] The sulfinate **10** could well be generated during the oxidation of the sulfide to the sulfoxide, the peracid being present in a slight excess (1.1 equiv). The facile rearrangement of the sulfoxide to the sulfenate and the oxidation of the latter by the peracid to the sulfinate could be the origin of the sulfinate. The apparent increase of the ratio sulfinate over sulfoxide on storage could come from oxidation by molecular oxygen, acting as a trapping agent of the sulfenate.[23] Further studies should clarify these points and the steric effect on the racemization of sterically hindered sulfoxides.

The allylic alcohol **1** was converted to the epoxide **14** with *m*-chloroperbenzoic acid. This epoxide was unstable, and even chromatography on triethylamine-treated silica gel lowered the yield. When the crude reaction product was silylated with *tert*-butyldimethylsilyl chloride in the presence of triethylamine and *p*-(dimethylamino)pyridine, the silylated epoxide **16** was isolated in high yield. The asymmetric Katsuki–Sharpless epoxidation was used to prepare the enantiomer **17** of epoxide **14** required for the (+)-(1*R*,3*R*)-chrysanthemic acid. In general, trans allylic alcohols are rather slow to react so that more catalyst had to be used.[24-27] The best result was obtained with 0.3 equiv of catalyst; the reaction was complete after 48 h at −8 °C. Compound **19** was obtained in 62% yield (>94% ee) after protection of alcohol **17**. When 0.2 equiv of catalyst was used, the yield was the same but the ee was lower (88%). The ee of epoxy alcohol **17** was determined by conversion to its acetate **18** (see Experimental Section) and ^1H NMR analysis in the presence of the chiral europium shift reagent $Eu(hfc)_3$ in deuterated benzene.[28] The ee of the epoxy alcohol was higher than 94%, the estimated detection limit.

The cyclization of the protected epoxynitriles **16** and **19** was performed according to Stork and Cohen.[13,29,30] The nitrile enolate was prepared at −20 °C with LDA, and the cyclization occurred at 20 °C in 3 h (86% yield) with a *cis*-**21**/*trans*-**20** ratio of 1/2, as determined by ^1H NMR analysis. The silyl ether was removed with tetrabutylammonium fluoride to afford diols **22** and **23** (89% yield). The diols **22** and **23** as a cis–trans isomer mixture were cleaved by sodium periodate to aldehydes **24** and **25** (45% yield). The low yield was due in part to autoxidation of

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the aldehydes. The trans and cis aldehydes **24** and **25** were separated by chromatography on silica gel.[31]

The Wittig reaction of aldehyde **24** with the ylide of isopropyl triphenylphosphonium iodide[32] gave the (1*R*,3*R*)-*trans*-chrysanthemic nitrile **26** $[\alpha]_D$ +27°. This nitrile prepared from pantolactone (**29**) has been described with $[\alpha]_D$ +29.3°. Thus, the nitrile **26** prepared from the aldehyde **24** has an ee of 92%.

Experimental Section

General methods. ^1H NMR spectra were obtained in $CDCl_3$ at 200 MHz. Merck silica gel, grade 7734 (70–230 mesh), was used for the flash chromatographic separation. 3,3-Dimethylacrylonitrile **3** and methyl 3,3-dimethylacrylate **4** were supplied by Roussel-Uclaf.

3,3-Dimethyl-4-(phenylthio)-5-hexenenitrile (5). To a cold (−78 °C) solution of allyl phenyl sulfide (1.2 g, 8 mmol), anhydrous LiBr (1.4 g, 16 mmol), and HMPA (4.2 mL, 24 mmol) in THF (25 mL) under argon was added dropwise a 1.3 M solution of butyllithium in hexane (7 mL, 8.8 mmol). After 20 min nitrile **3** (1.17 mL, 12 mmol) was added dropwise. The solution was stirred at −78 °C for 45 min, the temperature was raised to −20 °C for 1 h, and a saturated aqueous NH_4Cl solution was added. The aqueous layer was extracted with ether (3 × 25 mL), and the combined extracts were washed with brine, dried ($MgSO_4$), concentrated, and column chromatographed on silica gel (100 g, hexane–7% ether) to give 1.4 g (76% yield) of **5** as a colorless oil. ^1H NMR: δ 1.25 (s, 3 H), 1.19 (s, 3 H), 2.48 and 2.58 (q, J_{AB} = 16 Hz, 2 H), 3.45 (d, J = 10 Hz, 1 H), 4.80 (d, J = 7 Hz, 1 H), 4.98 (d, J = 10 Hz, 1 H), 7.26–7.45 (m, 5 H). Anal. Calcd for $C_{14}H_{17}NS$: C, 72.68; H, 7.41; N, 6.05. Found: C, 72.7; H, 7.4; N, 6.1.

Methyl 3,3-Dimethyl-4-(phenylthio)-5-hexenoate (6). To a cold (−78 °C) solution of allyl phenyl sulfide (0.60 g, 4 mmol) and anhydrous LiBr (0.7 g, 8 mmol) in THF (15 mL) under argon was added dropwise a 1.4 M solution of *sec*-butyllithium in hexane (3.1 mL, 4.4 mmol) followed by HMPA (2.1 mL, 12 mmol). After 30 min acrylate **4** (0.7 g, 6 mmol) was added dropwise. The solution was stirred at −78 °C for 45 min, the temperature was raised to 0 °C in 10 min, and a saturated aqueous NH_4Cl solution was added. The aqueous layer was extracted twice with hexane, and the combined extracts were washed with water and then brine, dried (Na_2SO_4), concentrated, and column chromatographed on silica gel (60 g, hexane–1% ethyl acetate) to give 0.685 g (65% yield) of **6** as a pale yellow oil. ^1H NMR: δ 1.13 (s, 3 H), 1.19 (s, 3 H), 2.42 and 2.65 (q, J_{AB} = 14.5 Hz, 2 H), 3.66 (s, 3 H), 3.70 (d, J = 10.0 Hz, 1 H), 4.72 (d, J = 1.7 Hz, 16.8 Hz, 1 H), 4.91 (d, J = 1.7 Hz, 10 Hz, 1 H), 5.81 (dt, J_{trans} = 19.9 Hz, J_{cis} = 10.0 Hz, 1 H), 7.20–7.42 (m, 5 H). Anal. Calcd for $C_{15}H_{20}O_2S$: C, 68.2; H, 7.62. Found: C, 68.1; H, 7.7.

3,3-Dimethyl-6-hydroxy-4(*E*)-hexenenitrile (1). A solution of nitrile **5** (0.32 g, 1.38 mmol) and *m*-CPBA (0.38 g, 1.52 mmol) in CH_2Cl_2 (15 mL) was stirred at −78 °C for 15 h. The reaction was hydrolyzed with a saturated aqueous $NaHCO_3$ solution and extracted with CH_2Cl_2 (3 × 20 mL), and the combined extracts were dried ($MgSO_4$) and evaporated to give 364 mg of a yellow oil. The crude product was dissolved in methanol (15 mL) in the presence of diethylamine (0.73 g, 10 mmol) and heated at reflux for 20 h. Solvents were removed under reduced pressure, and the residue was diluted with ether (20 mL), washed with water (2 × 20 mL), dried ($MgSO_4$), evaporated, and column chromatographed on silica gel (15 g, hexane–50% ether) to give 0.165 g (86% from nitrile **5**) of alcohol **1** as a pale yellow oil. ^1H NMR: δ 1.20 (s, 6 H), 1.75 (s, 1 H), 2.35 (s, 2 H), 4.15 (d, J = 2.1 Hz, 2 H), 5.68–5.70 (m, 2 H). Anal. Calcd for $C_8H_{13}NO$: C, 69.03; H, 9.41; N, 10.06. Found: C, 69.2; H, 9.6; N, 9.8.

Before, the treatment with diethylamine, ^1H NMR signals corresponding to the sulfoxide **7** and the sulfenate **13**, besides those of the sulfinate **10**, were observed.

7: δ 1.24 (s, 3 H), 1.49 (s, 3 H), 2.55 and 3.25 (q, J_{AB} = 16.7 Hz, 2 H).

13: δ 1.16 (s, 6 H), 2.27 (s, 2 H), 4.29 (d, J = 5.4 Hz, 2 H), 5.5–6.05 (m, 2 H), 7.4–7.6 (m, 5 H).

Characterization data for sulfinate **10** are given below.

Methyl 3,3-Dimethyl-6-hydroxy-4(*E*)-hexenoate (9). A solution of ester **5** (0.53 g, 2 mmol) and *m*-CPBA (0.49 g, 2.1 mmol) in CH_2Cl_2 (20 mL) was stirred at −78 °C for 7 h and then warmed up to room temperature. The reaction was hydrolyzed with a saturated aqueous $NaHCO_3$ solution and extracted with CH_2Cl_2 (2 × 30 mL), and the combined extracts were washed with water, dried (Na_2SO_4), and evaporated to give 540 mg of a yellow oil. The crude product was dissolved in methanol (20 mL) in the presence of diethylamine (0.59 g, 8 mmol) and heated at reflux for 12 h. Solvents were removed under reduced pressure, and the residue was diluted with ether (30 mL), washed with water, dried (Na_2SO_4), evaporated, and column chromatographed on silica gel (30 g, hexane–10% ethyl acetate) to give 0.26 g (77% from ester **6**) of alcohol **9** as a colorless oil. ^1H NMR: δ 1.14 (s, 6 H), 1.75 (s, 1 H), 2.31 (s, 2 H), 3.64 (s, 1 H), 4.11 (dd, J = 1.0, 5.5 Hz, 2 H), 5.58 (dt, J = 5.5, 15.7 Hz, 1 H), 5.77 (dt, J = 15.7, 5.5 Hz, 1 H). Anal. Calcd for $C_9H_{16}O_3$: C, 62.77; H, 9.36. Found: C, 62.7; H, 9.5.

3,3-Dimethyl-6-[(phenylsulfinyl)oxy]hexenenitrile (10). To a solution of alcohol **1** (0.1 g, 0.7 mmol) in CH_2Cl_2 (5 mL) was added *p*-(dimethylamino)pyridine (0.05 g, 0.4 mmol), NEt_3 (1 mL), and benzenesulfinyl chloride (0.2 mL, prepared from benzenesulfinic acid and thionyl chloride). After 2 h at 20 °C water was added, the aqueous layer was extracted with CH_2Cl (2 × 10 mL), and the combined extracts were washed with water, dried ($MgSO_4$), evaporated, and chromatographed on a 2.5-mm Merck preparative TLC (hexane–40% ether) to give 0.05 g (30%) of sulfinate **10** as an oil. ^1H NMR: δ 1.17 (s, 6 H), 2.29 (s, 2 H), 4.14 and 5.52 (2 q, J_{AB} = 11.7 Hz, J = 6 Hz, 2 H), 5.55 (dt, J = 15.7, 15 Hz, 1 H), 5.72 (d, J = 15.7 Hz, 1 H), 7.5–7.85 (m, 5 H).

3,3-Dimethyl-6-(phenylthio)-4-hexenenitrile (11). To a solution of alcohol **1** (0.14 g, 1 mmol) in ether (10 mL) and HMPA (3.5 mL) at 0 °C was added a 1.5 M solution of methyllithium in ether (0.7 mL, 1.1 mmol). After 0.5 h, a solution of *p*-toluenesulfonyl chloride (0.19 g, 1 mmol) in ether (10 mL) was added, followed by a solution of lithium phenylthiolate (prepared from thiophenol (0.1 g, 0.9 mmol) and methyllithium (0.6 mL, 0.9 mmol) in ether). After 3 h at 20 °C, a saturated aqueous NH_4Cl solution was added (20 mL), the aqueous layer was extracted with ether (3 × 20 mL), and the combined extracts were washed with water and brine, dried ($MgSO_4$), evaporated, and column chromatographed on silica gel (40 g, hexane–10% ether) to give 0.145 g (63%) of thioether **11** as an oil. ^1H NMR: δ 1.09 (s, 6 H), 2.18 (s, 2 H), 3.51 (d, J = 15.5 Hz, 2 H), 5.38–5.53 (m, 2 H), 7.22–7.37 (m, 5 H). Anal. Calcd for $C_{14}H_{17}NS$: C, 72.68; H, 7.41; N, 6.05. Found: C, 72.7; H, 7.6; N, 5.8.

Corresponding sulfoxide **12**. The same procedure as described for the preparation of sulfoxide **7** afforded **12** (yield 95%). ^1H NMR: δ 1.07 (s, 6 H), 2.18 (s, 2 H), 3.43 and 3.59 (qd, J_{AB} = 13, 6.8 Hz, 2 H), 5.3–5.53 (m, 2 H), 7.45–7.68 (m, 5 H).

(±)-3,3-Dimethyl-4,5-epoxy-6-hydroxyhexanenitrile (14). A solution of alcohol **1** (0.65 g, 1.18 mmol) and *m*-CPBA (0.31 g, 2.53 mmol) in CH_2Cl_2 (10 mL) was left at 20 °C for 20 h. The reaction was hydrolyzed with a saturated aqueous $NaHCO_3$ solution and extracted with CH_2Cl_2 (2 × 20 mL), and the combined extracts were dried ($MgSO_4$), evaporated, and column chromatographed on silica gel (50 g, hexane–30% ethyl acetate) to give 0.114 g (60%) of epoxide **14**. ^1H NMR: δ 1.06 (s, 3 H), 1.11 (s, 3 H), 2.29 and 2.38 (q, J_{AB} = 16.7 Hz, 2 H) 2.91 (d, J = 2.3 Hz, 1 H), 3.13 (ddd, J = 2.6, 4.0, 2.3 Hz, 1 H), 3.68 and 3.95 (qd, J_{AB} = 12.7, 2.6, 4.0 Hz, 2 H). Anal. Calcd for $C_8H_{13}NO_2$: C, 61.91; H, 8.44. Found: C, 61.7; H, 8.5.

Acetate of (±)-3,3-Dimethyl-4,5-epoxy-6-hydroxyhexanenitrile (15). To a solution of (±)-epoxide **14** (50 mg of crude product), DMAP (50 mg, 0.4 mmol), and NEt_3 (1 mL) in CH_2Cl_2 (10 mL) was added an excess of acetic anhydride (1 mL). After 12 h at 20 °C the reaction was hydrolyzed, and the organic layer

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was dried ($MgSO_4$), evaporated, and column chromatographed on silica gel (20 g, hexane–5% ether) to give 54 mg of acetate 15. ^1H NMR: δ 1.05 (s, 3 H), 1.11 (s, 3 H), 2.08 (s, 3 H), 2.27 and 2.37 (q, J_{AB} = 16.6 Hz, 2 H), 2.79 (d, J = 2.2 Hz, 1 H), 3.15 (m, 1 H), 3.96 and 4.33 (qd, J_{AB} = 12.3 Hz, J = 2.6, 4.0 Hz, 2 H). Anal. Calcd for $C_{10}H_{15}NO_3$: C, 60.9; H, 7.67; N, 7.10. Found: C, 61.1; H, 7.8; N, 6.9. In solution in deuterated benzene, in the presence of Eu(hfc)$_3$, the signal at δ 2.79 gives rise to two doublets for the (±)-acetate.

(4*S*,5*S*)-3,3-Dimethyl-4,5-epoxy-6-hydroxyhexenenitrile (17). To a suspension of 4-Å molecular sieves (0.5 g) in freshly distilled CH_2Cl_2 (50 mL) cooled to −20 °C were added neat titanium isopropoxide (0.65 mL, 2.17 mmol) and later diethyl L-tartrate (0.52 g, 2.53 mmol) in solution in CH_2Cl_2 (3 mL). *tert*-Butyl hydroperoxide (0.74 mL, 6 mmol) in solution in *tert*-butyl peroxide (dried for 5 min over molecular sieves) was added. After 0.5 h at −20 °C, a solution of the allylic alcohol 1 (1.0 g, 7.23 mmol) in CH_2Cl_2 (15 mL), dried for 15 over molecular sieves, was added. The reaction mixture was stirred for 48 h at −10 °C, and then water and 0.5 N NaOH (5 mL) were added. After 0.5 h the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). During the extraction an emulsion appeared, and it was broken up by the addition of methanol (about 10 mL). The combined extracts were washed with water, dried (Na_2SO_4), and evaporated to give 1.09 g of a yellow oil. By TLC the epoxide 17 appears almost pure; on purification trials, great loss of this epoxide occurred. ^1H NMR as above for 14.

The acetate 18 was prepared from epoxide 17 with the same method as for 15.

(4*S*,5*R*)-3,3-Dimethyl-4,5-epoxy-6-[(*tert*-butyldimethylsilyl)oxy]hexanenitrile (19). The product of the asymmetric epoxidation reaction from allylic alcohol 1 (1.09 g) in solution in CH_2Cl_2 (20 mL) was treated with *tert*-butyldimethylsilyl chloride (1.3 g, 8.7 mmol) in the presence of NEt_3 (1 mL) and DMAP (0.62 g, 2.1 mmol) at 4 °C for 18 h. The reaction was hydrolyzed and extracted with CH_2Cl_2 (2 × 15 mL), and the combined extracts were dried ($MgSO_4$), evaporated, and column chromatographed on silica gel to give 1.215 g (62% from allylic alcohol 1) of the title compound as an oil. $[\alpha]_D$: −8.3° (*c* 10, $CHCl_3$). ^1H NMR: δ 0.07 (s, 3 H), 0.08 (s, 3 H), 0.9 (s, 9 H), 1.06 (s, 3 H), 1.13 (s, 3 H), 2.27 and 2.38 (q, J_{AB} = 14.5 Hz, 2 H), 2.78 (d, J = 2.2 Hz, 1 H), 3.4 (m, 1 H), 3.67 and 3.84 (qd, J_{AB} = 11.9 Hz, J = 3.2, 4.7 Hz, 2 H). Anal. Calcd for $C_{14}H_{27}NO_2Si$: C, 62.40; H, 10.10; N, 5.20. Found: C, 62.3; H, 10.0; N, 5.1.

(1*R*,3*R*)- and (1*S*,3*R*)-1-Cyano-2,2-dimethyl-3-[2′-[(*tert*-butyldimethylsilyl)oxy]-1′-hydroxyethyl]cyclopropane (20 and 21). A solution of the epoxide 19 (1.21 g, 4.5 mmol) in THF (15 mL) was added at −20 °C to solution of LDA (9 mmol) in THF (5 mL). After 10 h at 20 °C, an aqueous solution of NH_4Cl was added. The aqueous layer was extracted with ether (3 × 50 mL), and the combined extracts were washed with brine, dried ($MgSO_4$), evaporated, and column chromatographed on silica gel (80 g, hexane–10% ethyl acetate) to give 1.07 g (88%) of a mixture of the title compounds as an oil, with a cis/trans ratio close to 1/2. ^1H NMR: δ 0.11 (s, 6 H), 0.91 (s, 9 H), 1.06 (s, 3 H), 1.06 (d, J = 5.2 Hz), 1.21 and 1.41 (2s), 1.28 and 1.36 (2s), 3.23–3.33 (m), 3.54–3.63 (m), 3.72–3.86 (m). MS (70 eV): 269 (M^+), 212, 194, 175, 120, 94. Anal. Calcd for $C_{14}H_{27}NO_2Si$: C, 62.40; H, 10.10; N, 5.20. Found: C, 62.4; H, 10.12; N, 4.9.

(1*R*,3*R*)- and (1*S*,3*R*)-1-Cyano-2,2-dimethyl-3-(1′,2′-dihydroxyethyl)cyclopropane (22 and 23). A solution of the silyl ethers 20 and 21 (58 mg, 0.22 mmol) in THF (5 mL) was added to a 1.1 M solution of tetrabutylammonium fluoride in THF (0.57 mL, 0.63 mmol). After 12 h at 20 °C, the solvent was removed and chromatography on silica gel (10 g, ethyl acetate) gave 29 mg (89%) of the diols 22 and 23 as a visquous oil. ^1H NMR: δ 1.09 (d, J = 5.31 Hz, trans), 1.20 (s, cis) and 1.39 (s, cis), 1.27 (s, trans), 1.35 (s, trans), 3.30–3.39 (m), 3.57–3.66 (m), 3.73–3.86 (m).

(1*R*,3*R*)- and (1*R*,3*S*)-1-Cyano-2,2-dimethyl-3-formylcyclopropane (24 and 25). A solution of sodium metaperiodate (1.71 g, 8 mmol) in water (40 mL) was added to a solution of the diols 22 and 23 (0.62 g, 3.97 mmol) in methanol (5 mL). After 24 h, methanol was evaporated and extraction with ether was performed. The organic layer was dried ($MgSO_4$), evaporated, and column chromatographed on silica gel (30 g, hexane–20% ethyl acetate) to give 0.125 g of the aldehyde 24 and 0.096 g of the aldehyde 25 (45% yield) as oils.

24. $[\alpha]_D$: +85° (*c* 12.5, $CHCl_3$). ^1H NMR: δ 1.24 (s, 3 H), 1.48 (s, 3 H), 2.33 (d, J = 5.3 Hz, 1 H), 2.41 (dd, J = 2.3, 5.3 Hz, 1 H), 9.69 (d, J = 2.4 Hz, 1 H). Anal. Calcd for C_7H_9NO: C, 68.27; H, 7.36. Found: C, 68.2; H, 6.8.

25. $[\alpha]_D$: −34° (*c* 9.6, $CHCl_3$). ^1H NMR: δ 1.30 (s, 3 H), 1.54 (s, 3 H), 1.92 (d, J = 8.1 Hz, 1 H), 2.01 (dd, J = 5.2, 8.1 Hz, 1 H), 9.52 (d, J = 5.2 Hz, 1 H).

(1*R*,3*R*)-*trans*-Chrysanthemic nitrile (26) was synthesized according to a literature procedure.[29] To a solution of isopropyltriphenylphosphonium iodide (0,55 g, 1.3 mmol) in THF (20 mL) and HMPA (1 mL) was added a 1 M solution of butyllithium in hexane (0.8 mL, 0.8 mmol). After 2 h at 20 °C aldehyde 24 (0.13 g, 1.05 mmol) in THF (5 mL) was added via syringe. The reaction was hydrolyzed after 24 h. The aqueous layer was extracted with ether (2 × 10 mL), and the combined extracts were dried ($MgSO_4$), evaporated, and column chromatographed on silica gel (30 g, hexane–10% ether) to give 42 mg (30%) of the nitrile 26 as an oil. $[\alpha]_D$: +27° (*c* 12.5, EtOH) (lit.[29] $[\alpha]_D$ +29.3° (*c* 1.31, EtOH). ^1H NMR[32] δ 1.04 (d, J = 5.15 Hz, 1 H), 1.13 (s, 3 H), 1.35 (s, 3 H), 1.73 (s, 3 H), 1.74 (s, 3 H), 1.88 (dd, J = 5.1, 7.6 Hz, 1 H), 4.82 (m, 1 H).

Registry No. 1, 134812-57-0; 3, 4786-24-7; 4, 924-50-5; (±)-5, 134812-55-8; (±)-6, 143706-93-8; 7, 134812-56-9; 9, 143706-94-9; (±)-10, 143706-95-0; 11, 143706-96-1; (±)-12, 143706-97-2; 13, 143706-98-3; (±)-14, 143788-63-0; (±)-15, 143706-99-4; 17, 134812-58-1; 18, 143707-00-0; 19, 134812-60-5; 20, 143788-64-1; 21, 143788-65-2; 22, 143788-66-3; 23, 143788-67-4; 24, 134929-79-6; 25, 134929-78-5; 26, 134929-80-9; $PhSCH_2CH{=}CH_2$, 5296-64-0.