Nucleophilic Addition to 2,3-Disubstituted Butanal Derivatives and Their Application to Natural Product Synthesis

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The reaction of 2,3-*anti*-2-*tert*-butyldimethylsiloxy-3-substituted butanal derivative [*anti*-B, (±)-10 and (±)-16] derived from *trans*-(2,3)-epoxy butanoate (1) with carbon nucleophiles [α-furyl anion, acetate anion, and indium (In)-assisted allyl anion] has been investigated to give selectively the *anti*-, *anti*-adduct D. This *anti*-stereoselection could be explained by the Felkin–Anh transition state model. Thus obtained *anti*-, *anti*-adducts (±)-17 and (±)-38 were formally converted to natural products, (±)-asperlin (2) and (±)-olivose (4), respectively. The major *anti*-, *anti*-adduct (±)-26 was converted to (±)-digitoxose (3), while the minor *anti*-, *syn*-adduct (±)-27 was also converted to (±)-olivose (4). The reaction of (±)-10 with *tert*-butyl acetate anion gave predominantly afforded the *anti*-, *anti*-adduct (±)-23, which was converted to (±)-1,5-dideoxyhexitol (25). Alternately, the reaction of 2,3-*syn*-2-*tert*-butyldimethylsiloxy-3-*p*-methoxyphenoxy butanal derivative [*syn*-B, (±)-14] derived from *trans*-(2,3)-epoxy butanoate (1) with carbon nucleophile (In-assisted allyl anion) afforded a *ca.* 1 : 1 mixture of the *syn*-, *anti*-adduct E [(±)-32 or (±)-34] and *syn*-, *syn*-adduct F [(±)-33 or (±)-35]. After separation of this mixture, (±)-34 and (±)-35 were separately converted to (±)-oliose (5) and (±)-boivinose (6), respectively.

Key words (±)-asperlin; (±)-digitoxose; (±)-olivose; (±)-oliose; (±)-boivinose; selective 1,2-*anti*-addition

Previously we reported the syntheses of natural products such as oudemansins,[1] indolmycin,[2] cystothiazoles,[3] and chuangxinmycin,[4] starting from *trans*-(2,3)-epoxy butanoate (**1**). In connection with these studies, the synthesis of 2,3-*anti*-disubstituted butanal derivative *anti*-**B** (Chart 1) derived from (2,3)-*anti*-2-hydroxy ester *anti*-**A** and the synthesis of 2,3-*syn*-disubstituted butanal derivative *syn*-**B** (Chart 1) derived from (2,3)-*syn*-2-hydroxy ester *syn*-**A** aroused our interest. Nucleophilic addition of a carbanion to *anti*-**B** would give the building blocks **C** or **D** possessing three continuous chiral centers, while nucleophilic addition of carbanion to *syn*-**B** would afford the building blocks **E** or **F** possessing three continuous chiral centers as shown in Chart 1. These synthons could be converted to asperlin (**2**) exhibiting antitumour and antibacterial activity, and rare deoxysugar such as D-digitoxose (**3**), D-olivose (**4**), D-oliose (**5**) and D-boivinose (**6**). Rare monosaccharides are important structural constituents of numerous antibiotics. Herein we report the selective synthesis of the above-mentioned synthons (**C**, **D**, **E** and **F**) and their application to the synthesis of the above-men-

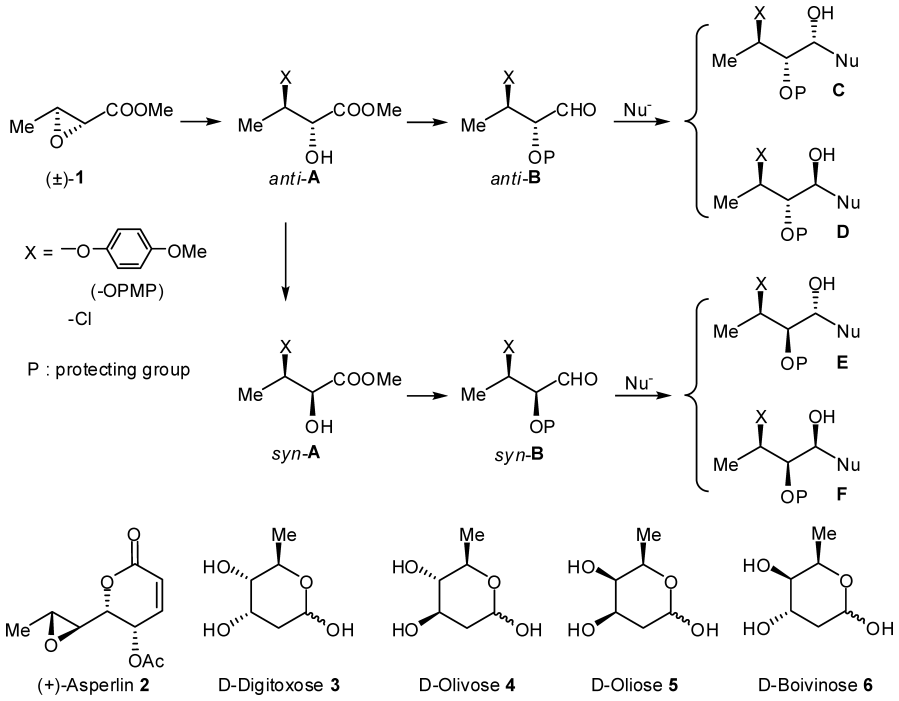

Chart 1

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tioned natural products.

Synthesis of (±)-2,3-Disubstituted Butanal Derivative (*anti*-B and *syn*-B) The staring (±)-2,3-*anti*-2-hydroxy-3-*p*-methoxyphenoxybutanal (**7**) was previously obtained by the $BF_3 \cdot Et_2O$ assisted reaction of (±)-**1** and *p*-methoxyphenol.[2] Silylation of (±)-**7** with *tert*-butyldimethylsilyl chloride (TBDMSCl) gave the corresponding silyl ether (±)-**8** (88%), which was reduced with diisobutylaluminum hydride (Dibal-H) to afford alcohol (±)-**9** in 77% yield. Pyridinium chlorochromate (PCC) oxidation of (±)-**9** gave the desired aldehyde (±)-**10** (75%) as shown in Chart 2. Alternately, the reaction of (±)-**7** with benzoic acid in the presence of triphenylphosphine (Ph_3P) and diisopropylazodicarboxylate gave (±)-2,3-*syn*-2-benzoloxy-3-*p*-methoxyphenoxybutanoate, which was subjected to hydrolysis to afford (±)-2,3-*syn*-2-hydroxy-3-*p*-methoxyphenoxybutanoate **11** (58% yield). Thus obtained (±)-**11** was converted to 2,3-*syn*-disubstituted butanal derivative (±)-**14** in a similar manner as the synthesis of (±)-**10** [(±)-**12**: 92%, (±)-**13**: 88%, and (±)-**14**: 79%]. (±)-3-Chloro-2-*tert*-butyldimethylsilyloxybutanal (**16**) was obtained by the reported procedure from (±)-**1**.[5]

Formal Synthesis of (±)-Asperlin (2) (+)-Asperlin (**2**), isolated from *Aspergillus nidulans* and *Aspergillus caespiyosus*, has been shown to exhibit antitumour and antibacterial activity. Its structure, including the absolute configuration, was determined by spectroscopic and chemical studies.[6—8] Because of its interesting bioactivity, the synthesis of natural product (**2**) and its related compounds has been reported by several groups.[9—11] The formal synthesis of (±)-asperlin (**2**) from (±)-**10** is shown in Chart 3. The reaction of (±)-**10** with α-furyl anion gave major product (±)-**17** (77% yield) and minor product (±)-**18** (17% yield). To confirm the stereochemistry of (±)-**17**, it was converted to the known synthetic intermediate, epoxy-alcohol (±)-**22**,[12,13] for the synthesis of (±)-**2**. Protection of the secondary alcohol group of (±)-**17** as a benzoyl group followed by deprotection of the *p*-methoxyphenyl group with ceric ammonium nitrate (CAN) afforded (±)-**20** (57%). Tosylation of (±)-**20** gave the corresponding tosylate (±)-**21** (86%), which was subjected to consecutive desilylation and K_2CO_3 treatment to afford epoxide (±)-**22** in 61% yield. Spectral data (^{1}H- and ^{13}C-NMR) of the synthetic (±)-**22** were identical with those of the reported (±)-**22**.[12] The synthesis of (±)-asperlin (**2**) from (±)-**22** was already achieved by Honda *et al.*[12] Consequently, the stereochemistry of (±)-**17** was determined to be 1,2-*anti*- and 2,3-*anti*-structures, and that of minor component (±)-**18** was determined to be 1,2-*syn*- and 2,3-*anti*. The stereoselective formation of (±)-**17** from (±)-**10** is explained

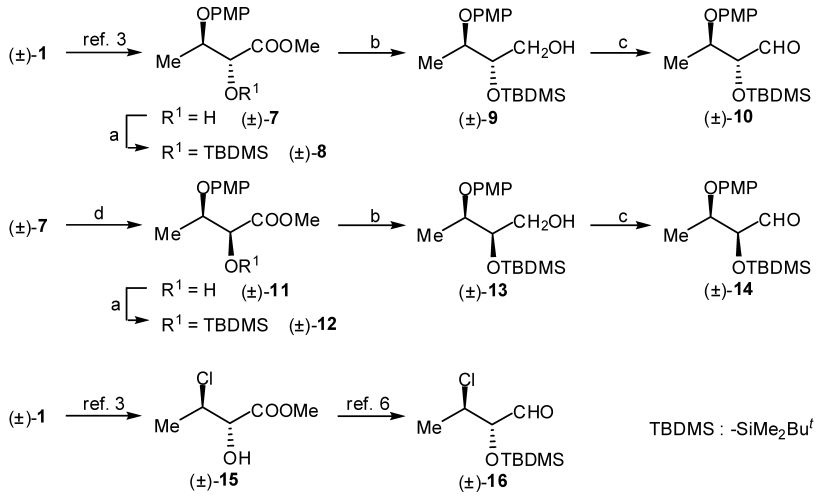


Chart 2

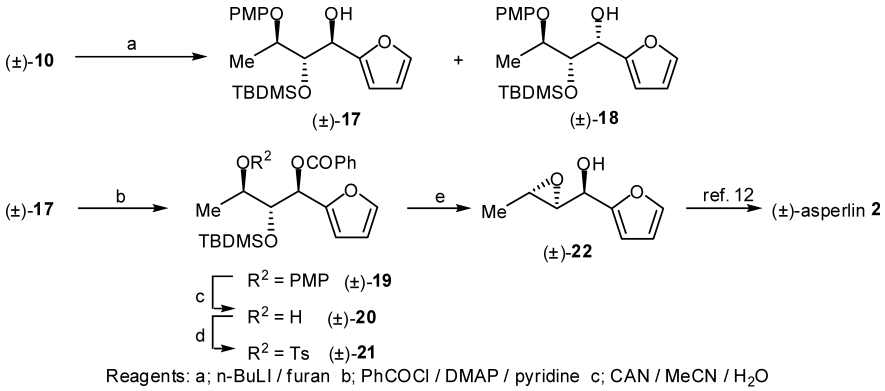


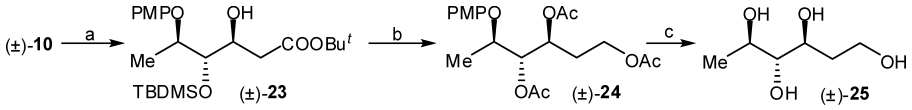
Chart 3

later in the text.

Synthesis of (±)-1,5-Dideoxyhexitol (25) The reaction of (±)-**10** with *tert*-butyl acetate anion gave β-hydroxy ester (±)-**23** (83%) as a single diastereoisomer as shown in Chart 4. To confirm the stereochemistry of (±)-**23**, it was converted to the known (±)-1,5-dideoxyhexitol (**25**).[14] Reduction of (±)-**23** with $LiAlH_4$ followed by consecutive desilylation and acetylation gave triacetate (±)-**24** in 78% yield, which was subjected to consecutive desilylation and K_2CO_3 treatment to afford tetraol (±)-**25** in 95% yield. Spectral data (^{1}H- and ^{13}C-NMR) of the synthetic (±)-**25** were identical with those of the reported (±)-**25**.[14] Consequently, the stereochemistry of (±)-**25** was determined to be 3,4-*anti*- and 4,5-*anti*. The stereoselective formation of (±)-**23** from (±)-**10** is explained later in the text.

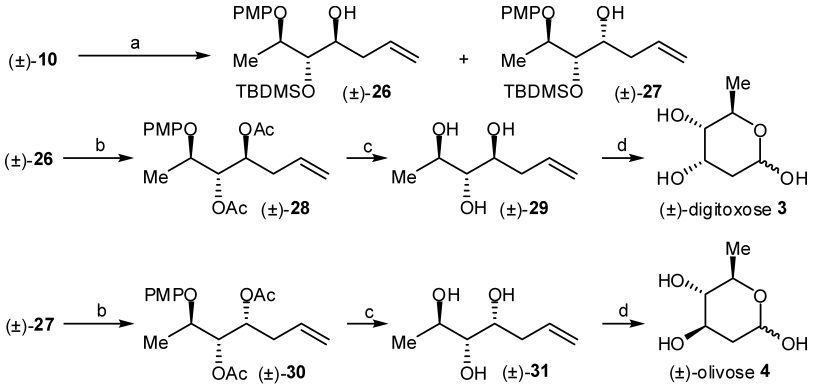
Synthesis of (±)-Digitoxose (3) and (±)-Olivose (4) The metal indium (In) has recently been found to provide intriguing advantages for effecting carbon–carbon bond formation under aqueous condition.[15,16] The reaction of (±)-**10** with allyl bromide in the presence of In gave major product (±)-**26** (86% yield) and minor product (±)-**27** (11% yield) as shown in Chart 5. To confirm the stereochemistry of (±)-**26**, it was converted to (±)-digitoxose (**3**). Deprotection of the silyl group of (±)-**26** followed by acetylation afforded diacetate (±)-**28** (74%), which was subjected to consecutive deprotection of the *p*-methoxyphenyl group with CAN and K_2CO_3 treatment to afford triol (±)-**29** in 73% yield. Ozonolysis of (±)-**29** followed by reductive treatment with dimethyl sulfide (Me_2S) afforded a 3.9:1 diastereomeric mixture (β-isomer : α-isomer=3.9 : 1) of (±)-**3** (73%). Spectral data (^{1}H- and ^{13}C-NMR) of the synthetic (±)-**3** were identical with those of the reported (±)-**3**.[17] To confirm the stereochemistry of (±)-**27**, it was converted to (±)-olivose (**4**). Deprotection of the silyl group of (±)-**27** followed by acetylation afforded diacetate (±)-**30** (76%), which was subjected to consecutive deprotection of the *p*-methoxyphenyl group with CAN and K_2CO_3 treatment to afford triol (±)-**31** in 73% yield. Ozonolysis of (±)-**31** followed by reductive treatment with Me_2S afforded a 4 : 3 diastereomeric mixture (β-isomer : α-isomer=4 : 3) of (±)-olivose (**4**). Spectral data (^{1}H- and ^{13}C-NMR) of the synthetic (±)-**4** were identical with those of the reported (±)-**4**.[17] Consequently, the stereochemistry of (±)-**26** was determined to be 4,5-*anti*- and 5,6-*anti*, and that of minor component (±)-**27** was determined to be 4,5-*syn*- and 5,6-*anti*. The stereoselective formation of (±)-**26** from (±)-**10** is explained later in the text.

Synthesis of (±)-Oliose (5) and (±)-Boivinose (6) The reaction of (±)-**14** with allyl bromide in the presence of In gave an inseparable 1.2 : 1 diastereomeric mixture of (±)-**32** and (±)-**33** (99% yield) as shown in Chart 6. This mixture was subjected to consecutive deprotection of the silyl group and acetylation afforded the more polar diacetate (±)-**34** (38% in two steps) and the less polar diacetate (±)-**35** (37% in two steps). The more polar diacetate (±)-**34** was subjected to consecutive deprotection of the *p*-methoxyphenyl group with CAN and K_2CO_3 treatment to afford triol (±)-**36** in 76% yield. Ozonolysis of (±)-**36** followed by reductive treatment with Me_2S afforded a 1 : 1 diastereomeric mixture of (±)-**5** (66%). Spectral data (^{1}H- and ^{13}C-NMR) of the synthetic (±)-**5** were identical with those of the reported (±)-**5**.[17] The less polar diacetate (±)-**35** was subjected to consecutive deprotection of the *p*-methoxyphenyl group with CAN and K_2CO_3 treatment to afford triol (±)-**37** in 78% yield. Ozonolysis of (±)-**37** followed by reductive treatment with Me_2S afforded *ca.* 80% β-anomer of (±)-**6** (81%) with the reminder being a mixture of the α-anomer and the furanose anomers. Spectral data (^{1}H- and ^{13}C-NMR) of the synthetic (±)-**6** were identical with those of the reported (±)-**6**.[17] Consequently, the stereochemistry of the more polar (±)-**34** was determined to be 4,5-*anti*- and 5,6-*syn*, and that of the



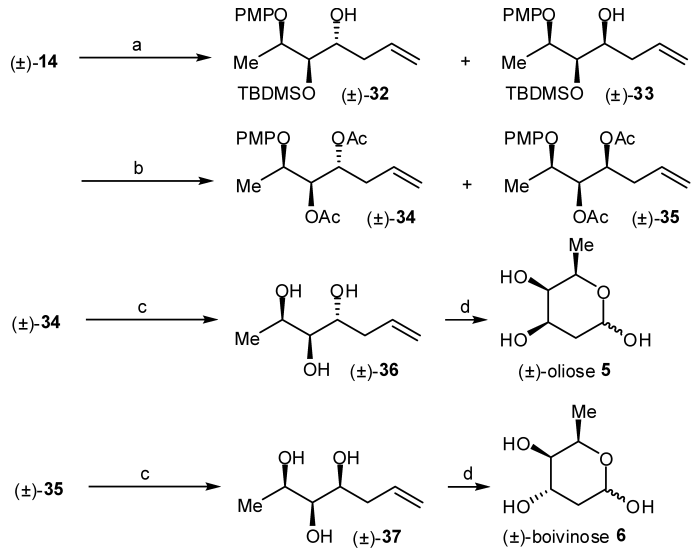
Reagents: a; LDA / CH_3COOBu^t b; 1) $LiAlH_4$ 2) n-$Bu_4N^+F^-$ 3) Ac_2O / pyridine
c; 1) CAN / MeCN / H_2O 2) K_2CO_3 / THF

Chart 4



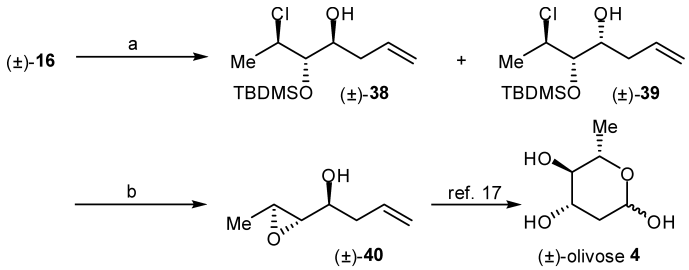
Reagents: a; In / allyl bromide / THF / H_2O b; 1) n-$Bu_4N^+F^-$ 2) Ac_2O / pyridine
c; 1) CAN / MeCN / H_2O 2) K_2CO_3 / THF d; 1) O_3 2) Me_2S

Chart 5



Reagents: a; In / allyl bromide / THF / H_2O b; 1) n-$Bu_4N^+F^-$ 2) Ac_2O / pyridine
c; 1) CAN / MeCN / H_2O 2) K_2CO_3 / THF d; 1) O_3 2) Me_2S

Chart 6



Reagents: a; In / allyl bromide / THF / H_2O b; 1) Ethylvinylether / PPTS 2) n-$Bu_4N^+F^-$
3) K_2CO_3 4) AcOH / THF / H_2O

Chart 7

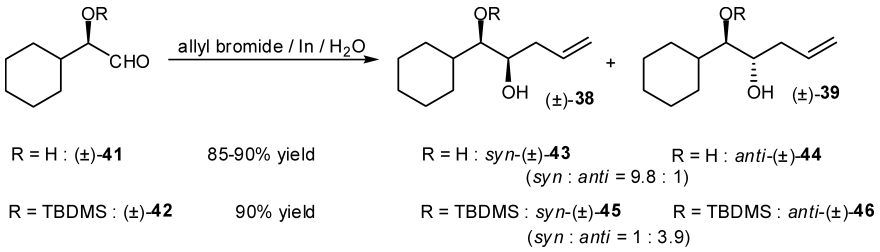


Chart 8

less polar (±)-**35** was determined to be 4,5-*syn*- and 5,6-*syn*. In the nucleophilic addition to 2,3-*syn*-disubstituted butanal derivative (±)-**14**, no stereoselective reaction occurred and the reason for this is discussed later in the text.

Formal Synthesis of (±)-Olivose (4) The reaction of (±)-**16** with allyl bromide in the presence of In gave an inseparable 8 : 1 diastereomeric mixture of (±)-**38** and (±)-**39** (93% yield) as shown in Chart 7. Protection of the secondary alcohol group of this mixture as a tetrahydropyranyl group followed by consecutive desilylation, K_2CO_3 treatment and acidification with AcOH gave epoxy alcohol (±)-**40** in 17% yield (four steps). Spectral data (^{1}H- and ^{13}C-NMR) of the synthetic (±)-**40** were identical with those of the reported (±)-**40**.[17] The synthesis of (±)-**4** from (±)-**40** was already achieved.[17] Consequently, the stereochemistry of the major component (±)-**38** was determined to be 4,5-*anti*- and 5,6-*anti*. The stereoselective formation of (±)-**38** from (±)-**16** is explained later in the text.

Disscussion

The reaction of α-hydroxy aldehyde (±)-**41** with allyl bromide in the presence of In in water was reported to give 1,2-*syn* adduct (±)-**43** and 1,2-*anti* adduct (±)-**44** in a ratio of 9.8 : 1, while that of α-protected aldehyde (±)-**42** with allyl bromide in the presence of In in water was reported to afford 1,2-*syn* adduct (±)-**45** and 1,2-*anti* adduct (±)-**46** in a ratio

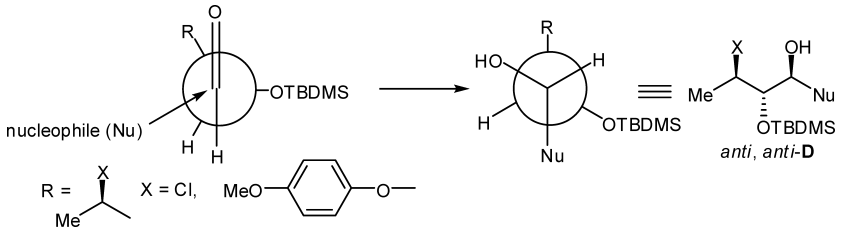


Fig. 1. Felkin–Anh Model for the Preparation of *anti*, *anti*-**D**

of 1 : 3.9 as shown in Chart 8. The *syn*-selectivity could be explained by chelation controll and the *anti*-selectivity could be interpreted as being non-chelation-controlled.[18)]

The C(4)–C(5)-*anti*-stereoselective addition against *anti*-**B** aldehydes (±)-**10** and (±)-**16** could be explained by Paquette and Mitzel[18)] who showed that 1,2-addition of the allylindium reagents to α-oxygenated aldehydes gave the non-chelation-controlled product, corresponding to the 1,2-*anti* product by the Felkin–Anh transition state model as shown in Fig. 1. No stereoselection was observed in the reaction of *syn*-**B** aldehydes (±)-**14** with allyl bromide in the presence of In in water. This fact is not sufficiently explained at the present stage, but is presumed to be due the *syn*- and *anti*-structures of the starting 1,2-disubstituted aldehyde.

Conclusion

The reaction of 2,3-*anti*-disubstituted butanal derivatives *anti*-**B** derived from *trans*-(2,3)-epoxy butanoate (**1**) with carbon nucleophile [α-furyl anion, acetate anion, and indium (In)-assisted allyl anion] gave selectively the *anti*-, *anti*-adduct **D**. This *anti*-stereoselection could be explained by the Felkin–Anh transition state model. Thus obtained *anti*-, *anti*-adducts (±)-**17** and (±)-**38** were formally converted to natural products, (±)-asperlin (**2**) and (±)-olivose (**4**), respectively. The major *anti*-, *anti*-adduct (±)-**26** was converted to (±)-digitoxose (**3**), while the minor *anti*-, *syn*-adduct (±)-**27** was also converted to (±)-olivose (**4**). Alternately, the reaction of 2,3-*syn*-disubstituted butanal derivatives *syn*-**B** derived from *trans*-(2,3)-epoxy butanoate (**1**) with a carbon nucleophile (In-assisted allyl anion) afforded a *ca.* 1 : 1 mixture of the *syn*-, *anti*-adduct **E** [(±)-**32** or (±)-**34**] and the *syn*-, *syn*-adduct **F** [(±)-**33** or (±)-**35**]. After separation of this mixture, (±)-**34** and (±)-**35** were converted to (±)-oliose (**5**) and (±)-boivinose (**6**), respectively.

Experimental

^{1}H- and ^{13}C-NMR spectra were recorded on JEOL AL 400 spectrometer in $CDCl_3$. High-resolution mass spectra (HR-MS) and the fast atom bombardment mass spectra (FAB-MS) were obtained with a JEOL JMS-600H spectrometer. High-resolution FAB-MS were obtained with a JEOL JMS-SX-102A or JMS-T100LP. IR spectra were recorded with a JASCO FT/IR-300 spectrometer. All evaporations were performed under reduced pressure. For column chromatography, silica gel (Kieselgel 60) was employed.

(±)-2,3-*anti*-2-^{t}Butyldimethylsiloxy-3-*p*-methoxyphenoxybutanal (10) i) To a solution of (±)-**7** (3.13 g, 42.9 mmol) in *N*,*N*-dimethylformamide (DMF) (120 ml) were added imidazole (5.83 g, 86 mmol) and *tert*-butyldimethylsilyl chloride (TBDMSCl; 12.9 g, 86 mmol) and the reaction mixture was stirred for 12 h at rt. The reaction mixture was diluted with brine and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and evaporated to give a crude oil, which was chromatographed on silica gel (250 g, *n*-hexane : AcOEt=40 : 1) to give (±)-**3** (13.3 g, 88%) as a colorless oil. (±)-**8**: IR (neat): 1759 cm^{-1}; ^{1}H-NMR δ: 0.05 (3H, s), 0.06 (3H, s), 0.92 (9H, s), 1.28 (3H, d, J=6.2 Hz), 3.73 (3H, s), 3.76 (3H, s), 4.41 (1H, d, J=4.4 Hz), 4.57 (1H, dq, J=4.4, 6.2 Hz), 6.80—6.87 (4H, m). ^{13}C-NMR δ: −5.16, −5.14, 14.8, 18.3, 25.6 (3C), 52.0, 55.6, 74.3, 75.9, 114.6 (2C), 117.1 (2C), 151.2, 154.1, 172.4. HR-MS (electron impact ionization (EI)): Calcd for $C_{18}H_{30}O_5Si$ (M^+): 354.1863, Found: 354.1867. ii) To a solution of (±)-**8** (5.08 g, 14 mmol) in dry toluene (60 ml) were added 1 M solution of diisobutylaluminum hydride (Dibal-H) in toluene (34 ml, 34 mmol) under ice cooling and the reaction mixture was stirred for 1 h at the same temperature. The reaction mixture was diluted with H_2O and filtered off with the aid of celite. The filtrate was extracted with AcOEt. The organic layer was dried over $MgSO_4$ and evaporated to give a crude oil, which was chromatographed on silica gel (120 g, *n*-hexane : AcOEt=10 : 1) to give (±)-**9** (3.6 g, 77%) as a colorless oil. (±)-**9**: IR (neat): 3447 cm^{-1}; ^{1}H-NMR δ: 0.12 (3H, s), 0.14 (3H, s), 0.92 (9H, s), 1.26 (3H, d, J=6.4 Hz), 3.66 (1H, dd, J=4.2, 11.2 Hz), 3.74 (1H, dd, J=4.2, 11.2 Hz), 3.76 (3H, s), 3.82 (1H, dt, J=4.2, 5.8 Hz), 4.30 (1H, dq, J=5.8, 6.4 Hz), 6.79—6.87 (4H, m). ^{13}C-NMR δ: −4.55, −4.53, 15.8, 18.1, 25.8 (3C), 55.6, 63.9, 75.1, 75.4, 114.6 (2C), 117.3 (2C), 151.6, 154.0. HR-MS (EI): Calcd for $C_{17}H_{30}O_4Si$ (M^+): 326.1913, Found: 326.1943. iii) To a solution of (±)-**9** (1.48 g, 4.5 mmol) in CH_2Cl_2 (30 ml) was added pyridinium chlorochromate (PCC; 1.95 g, 9 mmol) at rt and the reaction mixture was stirred for 15 h at the same temperature. The reaction mixture was filtered off with the aid of celite. The filtrate was concentrated to give a residue, which was chromatographed on silica gel (50 g, *n*-hexane : AcOEt=50 : 1) to give (±)-**10** (1.11 g, 75%) as a colorless oil. (±)-**10**; IR (neat): 1736 cm^{-1}; ^{1}H-NMR δ: 0.07 (3H, s), 0.11 (3H, s), 0.94 (9H, s), 1.28 (3H, d, J=6.4 Hz), 3.76 (3H, s), 4.23 (1H, dd, J=1.4, 3.6 Hz), 4.53 (1H, dq, J=3.6, 6.4 Hz), 6.80—6.86 (4H, m), 9.69 (1H, d, J=1.4 Hz). ^{13}C-NMR δ: −4.86, −4.76, 15.1, 18.2, 25.7 (3C), 55.6, 75.5, 79.5, 114.7 (2C), 117.1 (2C), 151.1, 154.2, 203.5. HR-MS (EI): Calcd for $C_{17}H_{28}O_4Si$ (M^+): 324.1757, Found: 324.1783.

(±)-2,3-*syn*-2-^{t}Butyldimethylsiloxy-3-*p*-methoxyphenoxybutanal (14) i) To a solution of (±)-**7** (6.0 g, 25 mmol) in tetrahydrofuran (THF) (80 ml) were added benzoic acid (5.49 g, 45 mmol) and triphenylphosphine (11.76 g, 45 mmol), and diisopropylazodicarboxylate (40% in toluene, 9.45 g, 36 mmol) was added dropwise under argon atmosphere at −78 °C. The reaction mixture was stirred for 1 h at the same temperature. The reaction mixture was condensed and the residue was diluted with H_2O, extracted with AcOEt. The organic layer was dried over $MgSO_4$ and evaporated to give a crude residue, which was filtered off with the aid of celite to afford filtrate. The filtrate was evaporated to give a crude product. To a solution of above crude mixture in MeOH (130 ml) was added K_2CO_3 (6.9 g, 48 mmol) and the reaction mixture was stirred for 1 h at the same temperature. The reaction mixture was condensed and the residue was diluted with H_2O, extracted with AcOEt. The organic layer was washed with 1 M aqueous NaOH (100 ml) and brine. The organic layer was dried over $MgSO_4$ and evaporated to give a crude residue, which was chromatographed on silica gel (120 g, *n*-hexane : AcOEt=5 : 1) to give (±)-**11** (3.48 g, 58%) as a colorless oil. (±)-**11**: IR (neat): 3479, 1737 cm^{-1}; ^{1}H-NMR δ: 1.39 (3H, d, J=6.4 Hz), 3.07 (1H, d, J=8.0 Hz), 3.73 (3H, s), 3.76 (3H, s), 4.20 (1H, dd, J=2.4, 8.0 Hz), 4.60 (1H, dq, J=2.4, 6.4 Hz), 6.79—6.85 (4H, m). ^{13}C-NMR δ: 15.7, 52.5, 55.6, 73.8, 76.4, 114.5 (2C), 118.2 (2C), 151.3, 154.6, 173.0. HR-MS (EI): Calcd for $C_{12}H_{16}O_5$ (M^+): 240.0998, Found: 240.0996. ii) To a solution of (±)-**11** (2.68 g, 11 mmol) in DMF (30 ml) were added imidazole (1.52 g, 22 mmol) and *tert*-butyldimethylsilyl chloride (TBDMSCl; 3.36 g, 22 mmol) and the reaction mixture was stirred for 12 h at rt. The reaction mixture was worked up in the same way as (±)-**8** to give (±)-**12** (3.63 g, 92%) as a colorless oil. (±)-**12**: IR (neat): 1754 cm^{-1}; ^{1}H-NMR δ: 0.05 (3H, s), 0.12 (3H, s), 0.91 (9H, s), 1.27 (3H, d, J=6.2 Hz), 3.72 (3H, s), 3.76 (3H, s), 4.30 (1H, d, J=6.0 Hz), 4.75 (1H, dq, J=6.0, 6.2 Hz), 6.78—6.90 (4H, m). ^{13}C-NMR δ: −5.2, −5.0, 15.7, 18.4, 25.7 (3C), 51.8, 55.6, 75.6, 77.4, 114.5 (2C), 118.3 (2C), 152.0, 154.4, 172.0. HR-MS (EI): Calcd for $C_{18}H_{30}O_5Si$ (M^+): 354.1863, Found: 354.1864. iii) To a solution of (±)-**7** (3.44 g, 10 mmol) in

dry toluene (50 ml) were added 1 M solution of diisobutylaluminum hydride (Dibal-H) in toluene (22 ml, 22 mmol) under ice cooling and the reaction mixture was stirred for 1 h at the same temperature. The reaction mixture was worked up in the same way as (±)-**9** to give (±)-**13** (2.78 g, 88%) as a colorless oil. (±)-**13**: IR (neat): 3458 cm^{-1}; ^{1}H-NMR δ: 0.06 (3H, s), 0.12 (3H, s), 0.90 (9H, s), 1.23 (3H, d, J=6.4 Hz), 2.06 (1H, dd, J=5.3, 7.2 Hz), 3.66—3.69 (1H, m), 3.74—3.80 (1H, m), 3.76 (3H, s), 3.86—3.90 (1H, m), 4.32 (1H, quintet, J=6.4 Hz), 6.80—6.85 (4H, m). ^{13}C-NMR δ: −4.81, −4.47, 14.8, 18.1, 25.8 (3C), 55.7, 63.4, 74.5, 76.4, 114.6 (2C), 117.3 (2C), 151.6, 154.0. HR-MS (EI): Calcd for $C_{17}H_{30}O_4Si$ (M^+): 326.1913, Found: 326.1917. iv) To a solution of (±)-**13** (2.55 g, 8 mmol) in CH_2Cl_2 (30 ml) was added pyridinium chlorochromate (PCC; 3.37 g, 17 mmol) at rt and the reaction mixture was stirred for 12 h at the same temperature. The reaction mixture was worked up in the same way as (±)-**10** to give (±)-**14** (2.00 g, 79%) as a colorless oil. (±)-**14**; IR (neat): 1737 cm^{-1}; ^{1}H-NMR δ: 0.08 (3H, s), 0.11 (3H, s), 0.94 (9H, s), 1.31 (3H, d, J=6.4 Hz), 3.76 (3H, s), 4.13 (1H, dd, J=0.8, 4.8 Hz), 4.48 (1H, dq, J=4.8, 6.4 Hz), 6.80—6.89 (4H, m), 9.75 (1H, d, J=0.8 Hz). ^{13}C-NMR δ: −5.02, −4.68, 15.5, 18.3, 25.7 (3C), 55.6, 76.7, 79.6, 114.6 (2C), 118.1 (2C), 151.3, 154.5, 202.9. HR-MS (EI): Calcd for $C_{17}H_{28}O_4Si$ (M^+): 324.1757, Found: 324.1761.

(±)-(1,2-*anti*, 2,3-*anti*)-2-^{t}Butyldimethylsiloxy-1-(2-furyl)-3-*p*-methoxyphenoxybutanol (17) and (±)-(1,2-*syn*, 2,3-*anti*)-2-^{t}Butyldimethylsiloxy-1-(2-furyl)-3-*p*-methoxyphenoxybutanol (18) To a solution of furan (1.73 g, 25 mmol) in THF (30 ml) was added 1.5 M solution of *n*-butyllithium in pentane (17 ml, 25 mmol) under argon atmosphere at −78 °C and the reaction mixture was stirred for 1.5 h at the same temperature. A solution of (±)-**10** (3.32 g, 10 mmol) in THF (5 ml) was added to the above mixture and the whole was stirred for 40 min at rt. The reaction mixture was diluted with saturated NH_4Cl solution and extracted with AcOEt. The organic layer was washed with brine and dried over $MgSO_4$. Evaporation of the organic solvent gave a residue, which was chromatographed on silica gel (50 g, *n*-hexane : AcOEt=20 : 1) to give (±)-**18** (0.35 g, 17%) and (±)-**17** (1.61 g, 77%) as a colorless oil in elution order. (±)-**17**: IR (neat): 3451 cm^{-1}; ^{1}H-NMR δ: −0.15 (3H, s), 0.11 (3H, s), 0.83 (9H, s), 1.28 (3H, d, J=6.4 Hz), 2.22 (1H, d, J=4.9 Hz), 3.76 (3H, s), 4.27 (1H, dd, J=2.9, 6.8 Hz), 4.53 (1H, dq, J=2.9, 6.4 Hz), 4.68 (1H, dd, J=4.9, 6.8 Hz), 6.31 (1H, d, J=3.2 Hz), 6.34 (1H, dd, J=1.9, 3.2 Hz), 6.78 (2H, d, J=9.3 Hz), 6.81 (2H, d, J=9.3 Hz), 7.37 (1H, d, J=1.9 Hz). ^{13}C-NMR δ: −5.34, −4.28, 14.0, 18.2, 25.8 (3C), 55.7, 69.8, 74.5, 75.6, 108.2, 110.5, 114.7 (2C), 116.6 (2C), 141.9, 151.6, 153.7, 154.0. HR-MS (EI): Calcd for $C_{21}H_{32}O_5Si$ (M^+): 392.2019, Found: 392.2017. (±)-**18**: IR (neat): 3520 cm^{-1}; ^{1}H-NMR δ: −0.12 (3H, s), 0.13 (3H, s), 0.91 (9H, s), 1.27 (3H, d, J=5.4 Hz), 2.99 (1H, d, J=5.8 Hz), 3.76 (3H, s), 4.20—4.24 (2H, m), 4.74 (1H, dd, J=5.8, 6.8 Hz), 6.33 (1H, d, J=3.2 Hz), 6.36 (1H, dd, J=1.5, 3.2 Hz), 6.74 (2H, d, J=9.3 Hz), 6.79 (2H, d, J=9.3 Hz), 7.40 (1H, d, J=1.5 Hz). ^{13}C-NMR δ: −5.31, −4.10, 14.9, 18.3, 26.0 (3C), 55.7, 68.8, 75.2, 76.3, 107.6, 110.5, 114.7 (2C), 117.0 (2C), 141.9, 151.3, 154.0, 154.2. HR-MS (EI): Calcd for $C_{21}H_{32}O_5Si$ (M^+): 392.2019, Found: 392.2020.

(±)-(1,2-*anti*, 2,3-*trans*)-1-(2-Furyl)-2,3-epoxybutanol (22) i) To a solution of (±)-**17** (0.865 g, 2.2 mmol) in pyridine (15 ml) were added benzoyl chloride (0.46 g, 3.3 mmol) and 4-dimethylaminopyridine (DMAP; 35 mg g, 0.3 mmol) and the reaction mixture was stirred for 3 h at rt. The reaction mixture was diluted with H_2O and extracted with AcOEt. The organic layer was washed with 2 M HCl and brine. The organic layer was dried over $MgSO_4$ and evaporated to give a crude oil, which was chromatographed on silica gel (50 g, *n*-hexane : AcOEt=35 : 1) to give (±)-**19** (1.09 g, 84%) as a colorless oil. (±)-**19**: IR (neat): 1721 cm^{-1}; ^{1}H-NMR δ: −0.16 (3H, s), 0.12 (3H, s), 0.81 (9H, s), 1.30 (3H, d, J=6.2 Hz), 3.77 (3H, s), 4.51 (1H, dq, J=2.8, 6.2 Hz), 4.66 (1H, dd, J=2.8, 7.6 Hz), 6.07 (1H, d, J=7.6 Hz), 6.34 (1H, dd, J=1.6, 3.4 Hz), 6.47 (1H, dd, J=0.8, 3.4 Hz), 6.81 (4H, br s). 7.38 (1H, dd, J=0.8, 1.6 Hz), 7.42—7.46 (2H, m), 7.55—7.59 (1H, m), 8.04—8.07 (2H, m). ^{13}C-NMR δ: −5.48, −4.27, 13.5, 18.2, 25.8 (3C), 55.7, 70.0, 73.9, 74.4, 110.5, 110.9, 114.7 (2C), 116.6 (2C), 127.78 (2C), 129.83 (2C), 133.2 (2C), 133.2, 142.3, 150.5, 151.6, 153.8, 165.1. HR-MS (EI): Calcd for $C_{28}H_{36}O_6Si$ (M^+): 496.2281, Found: 496.2216. ii) To a solution of (±)-**19** (116 mg, 0.23 mmol) in MeCN (4 ml) was added a solution of ceric ammonium nitrate (CAN; 236 mg, 0.43 mmol) in H_2O (1 ml) at rt and the reaction mixture was stirred for 0.5 h at the same temperature. The reaction mixture was diluted with H_2O and extracted with AcOEt. The organic layer was washed with brine and dried over $MgSO_4$. Evaporation of the organic solvent gave a residue, which was chromatographed on silica gel (10 g, *n*-hexane : AcOEt=20 : 1) to give (±)-**20** (52 mg, 57%) as a colorless oil. (±)-**20**: IR (neat): 3725, 1726 cm^{-1}; ^{1}H-NMR δ: −0.16 (3H, s), 0.09 (3H, s), 0.84 (9H, s), 1.24 (3H, d, J=6.4 Hz), 1.81 (1H, br s), 3.92 (1H, dq, J=3.5, 6.4 Hz), 4.38 (1H, q, J=3.5, 7.0 Hz), 6.10 (1H, d, J=7.0 Hz), 6.34 (1H, dd, J=2.0, 3.2 Hz), 6.49 (1H, d, J=3.2 Hz), 7.39 (1H, dd, J=0.8, 2.0 Hz), 7.41—7.45 (2H, m), 7.53—7.58 (1H, m), 8.02—8.05 (2H, m). ^{13}C-NMR δ: −5.29, −4.54, 17.5, 18.1, 25.8 (3C), 68.8, 69.8, 75.8, 110.5, 110.6, 128.4 (2C), 129.8 (3C), 133.2, 142.3, 150.6, 165.2. HR-MS (CI+): Calcd for $C_{21}H_{30}O_5Si$ (M^+): 390.1863, Found: 390.1872. iii) To a mixture of (±)-**20** (145 mg, 0.37 mmol) and Et_3N (0.74 ml) and DMAP (408 mg, 3.33 ml) in CH_2Cl_2 (20 ml) was added tosyl chloride (566 mg, 2.96 mmol) at rt and the reaction mixture was stirred for 14 h at the same temperature. The reaction mixture was diluted with H_2O and extracted with CH_2Cl_2. The organic layer was washed with brine and dried over $MgSO_4$. Evaporation of the organic solvent gave a residue, which was chromatographed on silica gel (15 g, *n*-hexane : AcOEt=20 : 1) to give (±)-**21** (174 mg, 86%) as a colorless oil. (±)-**21**: IR (neat): 1725 cm^{-1}; ^{1}H-NMR δ: −0.23 (3H, s), 0.10 (3H, s), 0.75 (9H, s), 1.23 (3H, d, J=6.4 Hz), 2.42 (3H, s), 4.65 (1H, dd, J=2.0, 8.8 Hz), 4.38 (1H, dq, J=2.0, 6.4 Hz), 5.79 (1H, d, J=8.8 Hz), 6.32 (1H, dd, J=1.6, 3.2 Hz), 6.49 (1H, dd, J=0.8, 3.2 Hz), 7.26 (2H, d, J=8.4 Hz), 7.37 (1H, dd, J=0.8, 1.6 Hz), 7.44—7.48 (2H, m), 7.58—7.62 (1H, m), 7.74 (2H, d, J=8.4 Hz), 7.99—8.02 (2H, m). ^{13}C-NMR δ: −5.82, −4.51, 13.5, 18.1, 21.6, 25.6 (3C), 69.1, 73.8, 79.3, 110.6, 111.4, 127.8 (2C), 128.5 (2C), 129.4, 129.7 (2C), 129.8 (2C), 130.2, 133.4, 142.6, 144.6, 149.6, 164.8. HR-MS (FAB): Calcd for $C_{28}H_{37}O_7SSi$ (M^++1): 545.2029, Found: 545.2072. iv) To a solution of (±)-**21** (205 mg, 0.38 mmol) in THF (6 ml) was added a 1.0 M solution of tetrabutylammonium fluoride (TBAF) in THF (3 ml) and the reaction mixture was stirred for 3 h at rt. To the above mixture was added K_2CO_3 (105 mg, 0.75 mmol) and the reaction mixture was stirred for 6 h at rt. The reaction mixture was diluted with H_2O and extracted with $CHCl_3$. The organic layer was washed with brine and dried over $MgSO_4$. Evaporation of the organic solvent gave a residue, which was chromatographed on silica gel (10 g, *n*-hexane : AcOEt=4 : 1) to give (±)-**22** (36 mg, 61%) as a colorless oil. (±)-**22**: IR (neat): 3401 cm^{-1}; ^{1}H-NMR δ: 1.38 (3H, d, J=5.2 Hz), 2.34 (1H, br s), 3.05 (1H, dd, J=2.4, 3.6 Hz), 3.25 (1H, dq, J=2.4, 5.2 Hz), 4.87 (1H, d, J=3.6 Hz), 6.35—6.38 (2H, m), 7.42 (1H, dd, J=0.8, 1.8 Hz). ^{13}C-NMR δ: 17.1, 51.7, 59.8, 65.2, 107.7, 110.2, 142.5, 152.4. HR-MS (FAB): Calcd for $C_8H_{11}O_3$ (M^++1): 155.0708, Found: 155.0706.

(±)-1,5-Dideoxyhexitol (25) i) *n*-Butyllithium (1.6 M in hexane, 3.8 ml, 6 mmol) was added to a stirred solution of diisopropylamine (605 mg, 6 mmol) in THF (30 ml) at −78 °C under an argon atmosphere and the reaction mixture was stirred for 30 min at the same temperature. *tert*-Butyl acetate (600 mg, 5.1 mmol) was added to the resulting lithium diisopropylamide (LDA)-THF and the reaction mixture was stirred for 0.5 h at the same temperature. To the above reaction mixture was added a solution of (±)-**10** (1.4 g, 4.3 mmol) in THF (10 ml) and the reaction mixture was stirred for 1 h at the same temperature. The reaction mixture was diluted with H_2O and extracted with AcOEt. The organic layer was washed with brine and dried over $MgSO_4$. Evaporation of the organic solvent gave a residue, which was chromatographed on silica gel (55 g, *n*-hexane : AcOEt=40 : 1) to give (±)-**23** (1.58 g, 83%) as a colorless oil. (±)-**23**: IR (neat): 3504, 1724 cm^{-1}; ^{1}H-NMR δ: 0.06 (3H, s), 0.16 (3H, s), 0.92 (9H, s), 1.25 (3H, d, J=6.4 Hz), 1.46 (9H, s), 2.04 (1H, s), 2.43 (1H, dd, J=8.0, 16.8 Hz), 2.65 (1H, dd, J=2.8, 16.8 Hz), 3.39 (1H, d, J=4.4 Hz), 3.72 (3H, s), 3.84—3.92 (1H, m), 4.62 (1H, dq, J=2.6, 6.4 Hz), 6.80—6.86 (4H, m). ^{13}C-NMR δ: −4.7, −3.9, 13.6, 18.3, 26.1 (3C), 28.1 (3C), 38.3, 55.7, 69.4, 74.0, 76.2, 81.5, 114.6 (2C), 116.5 (2C), 151.6, 153.6, 172.8. HR-MS (EI): Calcd for $C_{23}H_{40}O_6Si$ (M^+): 440.2588, Found: 440.2594. ii) $LiAlH_4$ (120 mg, 3.1 mmol) was added to a stirred solution of (±)-**23** (277 mg, 0.63 mmol) in THF (5 ml) at −78 °C and the reaction mixture was stirred for 1 h at the same temperature. The reaction mixture was diluted with H_2O and filtered off with the aid of celite. The filtrate was extracted with AcOEt. The organic layer was dried over $MgSO_4$ and evaporated to give a crude oil. To a solution of the above crude mixture in THF (10 ml) was added a 1.0 M solution of TBAF in THF (1 ml) and the reaction mixture was stirred for 2 h at rt. Condensation of the reaction mixture gave a crude product. To a solution of the above mixture in pyridine (3 ml) were added a catalytic amount of DMAP and Ac_2O (470 mg, 4.6 mmol) and the reaction mixture was stirred for 15 h at rt. The reaction mixture was diluted with H_2O and extracted with AcOEt. The organic layer was washed with 1 M HCl solution and brine. The organic layer was dried over $MgSO_4$ and evaporated to afford a residue, which was chromatographed on silica gel (20 g, *n*-hexane : AcOEt=4 : 1) to give (±)-**24** (187 mg, 78%) as a colorless oil. (±)-**24**: IR (neat): 1736 cm^{-1}; ^{1}H-NMR δ: 1.29 (3H, d, J=6.4 Hz), 1.94—2.12 (2H, m), 1.99 (3H, s), 2.05 (3H, s), 2.10 (3H, s), 3.76 (3H, s), 4.00—4.07 (1H, m), 4.11—4.17 (1H, m), 4.35 (1H, dq, J=6.0, 6.4 Hz), 5.22 (1H, dd, J=3.4,

6.4 Hz), 5.37 (1H, dt, J=3.4, 10.0 Hz), 6.81—6.86 (4H, m). ^{13}C-NMR δ: 16.2, 20.7, 20.8, 20.9, 28.5, 55.6, 60.5, 69.2, 73.6, 75.0, 114.7 (2C), 117.5 (2C), 151.0, 154.4, 169.9, 170.1, 170.9. HR-MS (EI): Calcd for $C_{19}H_{26}O_8$ (M^+): 382.1624, Found: 382.1628. iii) To a solution of (±)-**24** (187 mg, 0.49 mmol) in MeCN (5 ml) and H_2O (1 ml) was added CAN (548 mg, 1 mmol) at rt and the reaction mixture was stirred for 2 h at the same temperature. The reaction mixture was diluted with H_2O and extracted with AcOEt. The organic layer was washed with brine and dried over $MgSO_4$. Evaporation of the organic solvent gave a residue. To the above residue in MeOH (15 ml) was added K_2CO_3 (273 mg, 2 mmol) and the reaction mixture was stirred for 1 h at rt. The reaction mixture was filtered off and the filtrate was evaporated to afford a precipitate which was chromatographed on silica gel (10 g, *n*-hexane : AcOEt=1 : 1) to give (±)-**25** (70 mg, 95%) as a colorless precipitate. (±)-**25**: IR (neat): 3332 cm^{-1}; ^{1}H-NMR (D_2O) δ: 1.21 (3H, d, J=6.0 Hz), 1.62—1.72 (1H, m), 1.91—1.99 (1H, m), 3.47 (1H, t, J=6.0 Hz), 3.72—3.83 (3H, m), 3.97 (1H, quintet, J=6.0 Hz). ^{13}C-NMR (D_2O) δ: 17.4, 34.6, 59.3, 68.2, 69.5, 78.2. HR-MS (FAB): Calcd for $C_6H_{15}O_4$ (M^++1): 151.0970, Found: 151.0964.

(2,3-*anti*, 3,4-*anti*)-3-^{t}Butyldimethylsilyloxy-4-hydroxy-2-*p*-methoxyphenoxy-6-heptene (26) and (2,3-*anti*, 3,4-*syn*)-3-^{t}Butyldimethylsilyloxy-4-hydroxy-2-*p*-methoxyphenoxy-6-heptene (27) To a mixture of (±)-**10** (1.547 g, 4.7 mmol) in THF (30 ml)/H_2O (30 ml) were added In powder (3.2 g, 27.9 mmol) and allyl bromide (1.7 g, 14.1 mmol) at 0 °C and the reaction mixture was stirred for 12 h at rt. The reaction mixture was diluted with H_2O and extracted with AcOEt. The organic layer was washed with brine and dried over $MgSO_4$. Evaporation of the organic solvent gave a residue, which was chromatographed on silica gel (150 g, *n*-hexane : AcOEt=40 : 1) to give (±)-**27** (0.187 g, 11%) and (±)-**26** (1.499 g, 86%) as a colorless oil in elution order. (±)-**26**: IR (neat): 3477 cm^{-1}; ^{1}H-NMR δ: 0.07 (3H, s), 0.16 (3H, s), 0.93 (9H, s),1.27 (3H, d, J=6.2 Hz), 1.98 (1H, br s), 2.13—2.21 (1H, m), 2.48—2.54 (1H, m), 3.62—3.68 (1H, m), 3.76 (3H, s), 3.80 (1H, dd, J=3.2, 4.0 Hz), 4.56 (1H, dq, J=3.2, 6.2 Hz), 5.14—5.20 (2H, m), 5.80—5.90 (1H, m), 6.80—6.87 (4H, m). ^{13}C-NMR δ: −4.7, −3.9, 14.3, 18.4, 26.0 (3C), 37.9, 55.7, 71.8, 74.2, 76.7, 114.7 (2C), 116.6 (2C), 118.5, 134.8, 151.6, 153.6. HR-MS (EI): Calcd for $C_{20}H_{34}O_8Si$ (M^+): 366.2226, Found: 366.2224. (±)-**27**: IR (neat): 3547 cm^{-1}; ^{1}H-NMR δ: 0.12 (3H, s), 0.17 (3H, s), 0.94 (9H, s), 1.26 (3H, d, J=6.2 Hz), 2.22—2.36 (2H, m), 2.62 (1H, d, J=7.2 Hz), 3.66—3.67 (1H, m), 3.76 (3H, s), 3.82 (1H, dd, J=3.6, 4.4 Hz), 4.31 (1H, dq, J=4.4, 6.2 Hz), 5.09—5.15 (2H, m), 5.84—5.94 (1H, m), 6.77—6.86 (4H, m). ^{13}C-NMR δ: −4.6, −3.8, 15.0, 18.3, 26.0 (3C), 38.7, 55.6, 71.7, 76.20, 76.25, 114.7 (2C), 117.0 (2C), 117.2, 135.0, 151.2, 154.0. HR-MS (EI): Calcd for $C_{20}H_{34}O_8Si$ (M^+): 366.2226, Found: 366.2227.

(±)-Digitoxose (3) i) To a solution of (±)-**26** (1.97 g, 5.4 mmol) in THF (20 ml) was added a 1.0 M solution of TBAF in THF (10.7 ml) and the reaction mixture was stirred for 1 h at rt. The reaction mixture was diluted with H_2O and extracted with AcOEt. The organic layer was washed with brine. The organic layer was dried over $MgSO_4$ and evaporated to afford a residue. To a solution of the above residue in pyridine (10 ml) were added a catalytic amount of DMAP and Ac_2O (1.64 g, 16 mmol) and the reaction mixture was stirred for 15 h at rt. The reaction mixture was diluted with H_2O and extracted with AcOEt. The organic layer was washed with 1 M HCl solution and brine. The organic layer was dried over $MgSO_4$ and evaporated to afford a residue, which was chromatographed on silica gel (120 g, *n*-hexane : AcOEt=40 : 1) to give (±)-**28** (1.34 g, 74%) as a colorless oil. (±)-**28**: IR (neat): 1743 cm^{-1}; ^{1}H-NMR δ: 1.30 (3H, d, J=6.2 Hz), 2.03 (3H, s), 2.10 (3H, s), 2.32—2.40 (1H, m), 2.43—2.50 (1H, m), 3.76 (3H, s), 4.40 (1H, dq, J=6.0, 6.2 Hz), 5.02—5.08 (2H, m), 5.21—5.30 (2H, m), 5.66—5.77 (1H, m), 6.80—6.86 (4H, m). ^{13}C-NMR δ: 16.0, 20.92, 20.98, 34.5, 55.6, 71.4, 73.7, 74.6, 114.7 (2C), 117.6 (2C), 117.8, 133.4, 151.2, 154.4, 169.9, 170.1. HR-MS (EI): Calcd for $C_{18}H_{24}O_6$ (M^+): 336.1573, Found: 336.1574. ii) To a solution of (±)-**28** (634 mg, 1.88 mmol) in MeCN (5 ml) and H_2O (2 ml) was added CAN (2.07 g, 3.77 mmol) at rt and the reaction mixture was stirred for 2 h at the same temperature. The reaction mixture was diluted with H_2O and extracted with AcOEt. The organic layer was washed with brine and dried over $MgSO_4$. Evaporation of the organic solvent gave a residue. To the above residue in MeOH (15 ml) was added K_2CO_3 (1.04 g, 7.5 mmol) and the reaction mixture was stirred for 1 h at rt. The reaction mixture was filtered off and the filtrate was evaporated to afford a precipitate which was chromatographed on silica gel (20 g, *n*-hexane : AcOEt=1 : 1) to give (±)-**29** (202 mg, 73%) as a colorless oil. (±)-**29**: IR (neat): 3357 cm^{-1}; ^{1}H-NMR δ: 1.25 (3H, d, J=6.2 Hz), 2.23 (1H, dt, J=6.4, 8.8 Hz), 2.54—2.60 (1H, m), 2.69 (3H, br s), 3.44 (1H, dd, J=5.4, 6.2 Hz), 3.70 (1H, dt, J=3.6, 7.2 Hz), 3.97 (1H, quintet, J=6.2 Hz), 5.17—5.22 (2H, m), 5.83—5.93 (1H, m). ^{13}C-NMR δ: 18.3, 37.9, 69.3, 71.9, 76.5, 118.8, 134.4. HR-MS (FAB): Calcd for $C_7H_{15}O_3$ (M^++1): 147.1021, Found: 147.1022. iii) Ozone was passed through a solution of (±)-**29** (275 mg, 1.88 mmol) in MeOH (20 ml) for 0.5 h at −20 °C then Me_2S (1 ml) was added to the ozonolyzed product. The reaction mixture was stirred for 1 h at rt and evaporated to give a precipitate which was chromatographed on silica gel (20 g, $CHCl_3$: MeOH=10 : 1) to give a 3.9 : 1 diastereomeric mixture of (±)-digitoxose (**3**) (202 mg, 73%) as a colorless solide. (±)-**3**: HR-MS (FAB): Calcd for $C_6H_{13}O_4$ (M^++1): 149.0814, Found: 149.0816; ^{1}H-NMR (β-anomer, major, D_2O) δ: 1.04 (3H, d, J=6.0 Hz), 1.49—1.55 (1H, m), 1.85 (1H, ddd, J=2.4, 3.6, 14.4 Hz), 3.12 (1H, dd, J=3.2, 10.0 Hz), 3.61—3.69 (1H, m), 3.92—3.96 (1H, m), 4.91 (1H, dd, J=2.0, 10.0 Hz). ^{13}C-NMR (D_2O) δ: 18.1, 39.4, 68.1, 70.1, 73.0, 92.1. ^{1}H-NMR (α-anomer, minor, D_2O) δ: 0.99 (3H, d, J=6.8 Hz), 1.67—1.71 (1H, m), 1.88—1.90 (1H, m), 3.21 (1H, dd, J=3.1, 8.8 Hz), 3.61—3.68 (1H, m), 3.90—3.96 (1H, m), 4.97 (1H, t, J=2.8 Hz). ^{13}C-NMR (D_2O) δ: 18.0, 39.0, 65.8, 70.7, 72.5, 91.5.

(±)-Olivose (4) i) To a solution of (±)-**27** (660 mg, 1.8 mmol) in THF (10 ml) was added a 1.0 M solution of TBAF in THF (4 ml) and the reaction mixture was stirred for 1 h at rt. The reaction mixture was worked up in the same way as (±)-**28** to afford a residue. To a solution of the above residue in pyridine (10 ml) were added a catalytic amount of DMAP and Ac_2O (550 mg, 5.3 mmol) and the reaction mixture was stirred for 15 h at rt. The reaction mixture was worked up in the same way as (±)-**28** to give (±)-**30** (460 mg, 76%) as a colorless oil. (±)-**30**: IR (neat): 1744 cm^{-1}; ^{1}H-NMR δ: 1.26 (3H, d, J=6.4 Hz), 1.94 (3H, s), 2.15 (3H, s), 2.32 (2H, t, J=7.0 Hz), 3.75 (3H, s), 4.31 (1H, quintet, J=6.4 Hz), 5.06—5.11 (2H, m), 5.18—5.20 (1H, m), 5.32—5.36 (1H, m), 5.70—5.80 (1H, m), 6.77—6.84 (4H, m). ^{13}C-NMR δ: 16.1, 20.78, 20.83, 35.6, 55.6, 70.7 73.3, 74.5, 114.6 (2C), 117.6 (2C), 118.4, 132.6, 151.2, 154.4, 170.0, 170.1. HR-MS (FAB): Calcd for $C_{18}H_{25}O_6$ (M^++1): 337.1652, Found: 337.1634. ii) To a solution of (±)-**30** (383 mg, 1.13 mmol) in MeCN (4 ml) and H_2O (1 ml) was added CAN (1.24 g, 2.26 mmol) at rt and the reaction mixture was stirred for 2 h at the same temperature. The reaction mixture was worked up in the same way as (±)-**29** to give a residue. To the above residue in MeOH (5 ml) was added K_2CO_3 (620 mg, 4.5 mmol) and the reaction mixture was stirred for 1 h at rt. The reaction mixture was worked up in the same way as (±)-**29** to give (±)-**31** (120 mg, 72%) as a colorless oil. (±)-**27**: IR (neat): 3357 cm^{-1}; ^{1}H-NMR δ: 1.22 (3H, d, J=6.8 Hz), 2.29—2.23 (2H, m), 3.32 (1H, dd, J=2.4, 4.0 Hz), 3.48 (3H, br s), 3.87—3.94 (2H, m), 5.09—5.16 (2H, m), 5.77—5.87 (1H, m). ^{13}C-NMR δ: 18.8, 38.1, 69.9, 70.0, 75.1, 118.8, 134.3. HR-MS (FAB): Calcd for $C_7H_{15}O_3$ (M^++1): 147.1021, Found: 147.1030. iii) Ozone was passed through a solution of (±)-**31** (275 mg, 1.88 mmol) in MeOH (30 ml) for 0.5 h at −20 °C then Me_2S (1 ml) was added to the ozonolyzed product. The reaction mixture was stirred for 1 h at rt. The reaction mixture was worked up in the same way as (±)-**3** to give a 4 : 3 diastereomeric mixture of (±)-olivose (**4**) (202 mg, 73%) as a colorless solid. (±)-**4**: HR-MS (FAB): Calcd for $C_6H_{13}O_4$ (M^++1): 149.0814, Found: 149.0796; ^{1}H-NMR (β-anomer, major, D_2O) δ: 1.04 (3H, d, J=6.2 Hz), 1.25 (1H, dt, J=10.0, 12.0 Hz), 2.01 (1H, ddd, J=2.0, 5.2, 12.0 Hz), 2.81 (1H, t, J=10.0 Hz), 3.17 (1H, dt, J=6.2, 9.0 Hz), 3.42 (1H, ddd, J=5.2, 9.0, 12.0 Hz), 4.66 (1H, dd, J=2.0, 10.0 Hz). ^{13}C-NMR (D_2O) δ: 17.7, 40.5, 68.5, 68.6, 77.0, 93.9. ^{1}H-NMR (α-anomer, minor, D_2O) δ: 1.02 (3H, d, J=6.2 Hz), 1.46 (1H, ddd, J=3.6, 12.0, 13.2 Hz), 1.88 (1H, ddd, J=1.0, 5.2, 13.2 Hz), 2.86 (1H, t, J=9.2 Hz), 3.58—3.67 (2H, m), 5.07 (1H, d, J=3.6 Hz). ^{13}C-NMR (D_2O) δ: 17.7, 38.3, 70.9, 72.6, 77.6, 91.9.

(2,3-*syn*, 3,4-*anti*)-3,4-Diacetoxy-2-*p*-methoxyphenoxy-6-heptene (34) and (2,3-*syn*, 3,4-*syn*)-3,4-Diacetoxy-2-*p*-methoxy-phenoxy-6-heptene (35) i) To a mixture of (±)-**14** (193 mg, 0.59 mmol) in THF (3 ml)/H_2O (3 ml) were added In powder (300 mg, 2.6 mmol) and allyl bromide (170 mg, 1.4 mmol) at 0 °C and the reaction mixture was stirred for 12 h at rt. The reaction mixture was worked up in the same way as (±)-**26** and (±)-**27** to give a *ca.* 1 : 1 mixture (218 mg, 99%) of (±)-**32** and (±)-**33** as a colorless oil. HR-MS (EI): Calcd for $C_{20}H_{34}O_8Si$ (M^+): 366.2226, Found: 366.2223. ii) To a solution of the above mixture (218 mg, 0.59 mmol) in THF (2 ml) was added a 1.0 M solution of TBAF in THF (1.5 ml) and the reaction mixture was stirred for 1 h at rt. The reaction mixture was worked up in the same way as (±)-**28** to afford a residue. To a solution of the above residue in pyridine (4 ml) were added a catalytic amount of DMAP and Ac_2O (242 mg, 2.3 mmol) and the reaction mixture was stirred for 15 h at rt. The reaction mixture was worked up in the same way as (±)-**28** to give (±)-**35** (less polar, 74 mg, 37%) and (±)-**34** (more polar, 76 mg, 38%) as a colorless oil. (±)-**34**: IR (neat): 1742 cm^{-1}; ^{1}H-NMR δ: 1.27 (3H, d, J=6.4 Hz), 1.90 (3H, s), 2.11 (3H, s), 2.32—2.39 (1H, m), 2.46—2.52 (1H, m), 3.76 (3H, s), 4.40 (1H, dq, J=4.0, 6.4 Hz), 5.04—5.10 (2H, m), 5.19—5.24 (2H, m),

5.70—5.80 (1H, m), 6.79—6.90 (4H, m). ^{13}C-NMR δ: 16.1, 20.8, 20.9, 34.6, 55.7, 71.0, 73.8, 75.1, 114.7 (2C), 117.5 (2C), 118.0, 133.1, 151.9, 154.3, 169.9, 170.3. HR-MS (EI): Calcd for $C_{18}H_{24}O_6$ (M^+): 336.1573, Found: 336.1581. (±)-**35**: IR (neat): 1742 cm^{-1}; ^{1}H-NMR δ: 1.23 (3H, d, J=6.2 Hz), 2.03 (6H, s), 2.18—2.40 (2H, m), 3.73 (3H, s), 4.33 (1H, quintet, J=6.2 Hz), 5.02—5.08 (2H, m), 5.18 (1H, dd, J=4.8, 6.2 Hz), 5.27 (1H, dt, J=4.8, 7.2 Hz), 5.66—5.74 (1H, m), 6.77—6.84 (4H, m). ^{13}C-NMR δ: 16.0, 20.7, 20.9, 35.6, 55.6, 71.2, 73.8, 75.2, 114.6 (2C), 117.2 (2C), 118.5, 132.5, 151.7, 154.2, 170.2, 170.4. HR-MS (EI): Calcd for $C_{18}H_{24}O_6$ (M^+): 336.1573, Found: 336.1572.

(±)-Oliose (5) i) To a solution of (±)-**34** (54 mg, 0.16 mmol) in MeCN (4 ml) and H_2O (1 ml) was added CAN (170 g, 0.31 mmol) at rt and the reaction mixture was stirred for 2 h at the same temperature. The reaction mixture was worked in the same way as (±)-**29** to give a residue. To the above residue in MeOH (3 ml) was added K_2CO_3 (80 mg, 0.58 mmol) and the reaction mixture was stirred for 1 h at rt. The reaction mixture was worked up in the same way as (±)-**29** to give (±)-**36** (18 mg, 76%) as a colorless oil. (±)-**36**: IR (neat): 3357 cm^{-1}; ^{1}H-NMR δ: 1.22 (3H, d, J=6.4 Hz), 2.23—2.38 (2H, m), 3.00 (3H, br s), 3.29 (1H, dd, J=2.9, 4.4 Hz), 3.77 (1H, dt, J=4.4, 8.4 Hz), 4.05 (1H, dq, J=2.9, 6.4 Hz), 5.14—5.19 (2H, m), 5.77—5.87 (1H, m). ^{13}C-NMR δ: 19.5, 36.6, 66.8, 72.8, 75.9, 118.3, 134.4. HR-MS (FAB): Calcd for $C_7H_{15}O_3$ (M^++1): 147.1021, Found: 147.0985. ii) Ozone was passed through a solution of (±)-**36** (46 mg, 0.31 mmol) in MeOH (4 ml) for 0.5 h at −20 °C then Me_2S (1 ml) was added to the ozonolyzed product. The reaction mixture was stirred for 1 h at rt. The reaction mixture was worked up in the same way as (±)-**3** to give a 1 : 1 diastereomeric mixture of (±)-oliose (**5**) (31 mg, 66%) as a colorless solid. (±)-**5**: HR-MS (FAB): Calcd for $C_6H_{13}O_4$ (M^++1): 149.0814, Found: 149.0861; ^{1}H-NMR (β-anomer, D_2O) δ: 1.02 (3H, d, J=6.8 Hz), 1.39 (1H, dt, J=10.0, 12.0 Hz), 1.60—1.63 (1H, m), 3.32 (1H, br s), 3.44 (1H, br q, J=0.8, 6.6 Hz), 3.64 (1H, ddd, J=3.2, 4.8, 12.4 Hz), 4.58 (1H, dd, J=2.4, 10.0 Hz). ^{13}C-NMR (D_2O) δ: 16.8, 35.3, 68.8, 70.1, 71.5, 94.3. ^{1}H-NMR (α-anomer, D_2O) δ: 0.98 (3H, d, J=6.4 Hz), 1.53—1.58 (1H, m), 1.73—1.79 (1H, m), 3.46 (1H, br s), 3.86 (1H, ddd, J=2.8, 5.2, 11.6 Hz), 3.91 (1H, br q, J=6.4 Hz), 5.12 (1H, br s). ^{13}C-NMR (D_2O) δ: 16.6, 32.3, 65.5, 67.2, 71.2, 92.1.

(±)-Boivinose (6) i) To a solution of (±)-**35** (47 mg, 0.14 mmol) in MeCN (4 ml) and H_2O (1 ml) was added CAN (150 mg, 0.27 mmol) at rt and the reaction mixture was stirred for 2 h at the same temperature. The reaction mixture was worked in the same way as (±)-**29** to give a residue. To the above residue in MeOH (3 ml) was added K_2CO_3 (80 mg, 0.58 mmol) and the reaction mixture was stirred for 1 h at rt. The reaction mixture was worked up in the same way as (±)-**29** to give (±)-**37** (16 mg, 78%) as a colorless oil. (±)-**37**: IR (neat): 3357 cm^{-1}; ^{1}H-NMR δ: 1.14 (3H, d, J=6.4 Hz), 2.27 (2H, t, J=6.6 Hz), 2.96 (3H, br s), 3.14 (1H, dd, J=2.4, 3.6 Hz), 3.65 (1H, dt, J=2.4, 6.6 Hz), 3.82 (1H, dq, J=3.6, 6.4 Hz), 5.02—5.08 (2H, m), 5.67—5.77 (1H, m). ^{13}C-NMR δ: 19.8, 38.7, 69.8, 72.6, 75.4, 118.5, 134.2. HR-MS (FAB): Calcd for $C_7H_{15}O_3$ (M^++1): 147.1021, Found: 147.1039. ii) Ozone was passed through a solution of (±)-**37** (40 mg, 0.28 mmol) in MeOH (4 ml) for 0.5 h at −20 °C then Me_2S (1 ml) was added to the ozonolyzed product. The reaction mixture was stirred for 1 h at rt. The reaction mixture was worked up in the same way as (±)-**3** to give (±)-boivinose (**6**) (33 mg, 81%) as a colorless solid. (±)-**6**: HR-MS (FAB): Calcd for $C_6H_{13}O_4$ (M^++1): 149.0814, Found: 149.0807; ^{1}H-NMR (β-anomer, D_2O) δ: 1.00 (3H, d, J=6.8 Hz), 1.47 (1H, dt, J=3.1, 13.2 Hz), 1.58 (1H, ddd, J=3.3, 9.8, 12.9 Hz), 3.03—3.05 (1H, m), 3.61—3.65 (1H, m), 3.68 (1H, br q, J=6.2 Hz), 4.78 (1H, dd, J=4.5, 7.4 Hz). ^{13}C-NMR (D_2O) δ: 16.7, 34.7, 69.4, 69.9 (2C), 92.7.

Formal Synthesis of (±)-Olivose (4) i) To a mixture of (±)-**16** (286 mg, 1.2 mmol) in THF (3 ml)/H_2O (3 ml) were added In powder (550 mg, 4.8 mmol) and allyl bromide (300 mg, 2.48 mmol) at 0 °C and the reaction mixture was stirred for 12 h at rt. The reaction mixture was worked up in the same way as (±)-**26** and (±)-**27** to give a *ca.* 8 : 1 mixture (336 mg, 93%) of (±)-**38** and (±)-**39** as a colorless oil. (±)-**38** (major): IR (neat): 3460 cm^{-1}; ^{1}H-NMR δ: 0.13 (3H, s), 0.18 (3H, s), 0.93 (9H, s), 1.51 (3H, d, J=6.8 Hz), 1.93 (1H, d, J=3.6 Hz), 2.15—2.23 (1H, m), 2.39—2.45 (1H, m), 3.71—3.76 (1H, m), 3.79 (1H, dd, J=3.8, 5.2 Hz), 4.26 (1H, dq, J=3.8, 6.8 Hz), 5.10—5.21 (2H, m), 5.79—5.89 (1H, m). ^{13}C-NMR δ: −4.2, −4.0, 18.4, 20.0, 26.0 (3C), 37.2, 58.1, 71.9, 79.1, 118.7, 134.4. HR-MS (FAB): Calcd for $C_{13}H_{28}O_2ClSi$ (M^++1): 279.1547, Found: 279.1571. ii) To a solution of the above 8 : 1 mixture (336 mg, 1.2 mmol) in CH_2Cl_2 (3 ml) were added ethyl vinyl ether (87 mg, 1.2 mmol) and a catalytic amount of pyridinum *p*-toluenesufonate (PPTS) at rt and the reaction mixture was stirred for 3 h at the same temperature. The reaction mixture was diluted with H_2O and extracted with AcOEt. The organic layer was washed with brine and dried over $MgSO_4$. Evaporation of the organic solvent gave a crude tetrahydropyramyl (THP) ether. To a solution of THP ether in THF (5 ml) was added 1 M solution of tetrabutylammonium fluoride (TBAF) in THF (2.4 ml, 2.4 mmol) at rt and the reaction mixture was stirred for 2 h at the same temperature. The reaction mixture was evaporated to give a residue. A mixture of the above residue in MeOH (5 ml) and K_2CO_3 (166 mg, 1.2 mmol) was stirred for 1 h at rt and the reaction mixture was diluted with H_2O and extracted with AcOEt. The organic layer was washed with brine and dried over $MgSO_4$. Evaporation of the organic solvent gave a crude oil. A solution of the crude oil in THF (2.5 ml)/H_2O (2.5 ml) and AcOH (2 ml) was stirred for 5 h at rt. The reaction mixture was diluted with saturated $NaHCO_3$ solution and extracted with AcOEt. The organic layer was washed with brine and dried over $MgSO_4$. Evaporation of the organic solvent gave a residue, which was chromatographed on silica gel (10 g, *n*-hexane : AcOEt=10 : 1) to give (±)-**40** (27 mg, 17% in 4 steps) as a colorless oil. (±)-**40**: IR (neat): 3448 cm^{-1}; ^{1}H-NMR δ: 1.30 (3H, d, J=5.2 Hz), 1.97 (1H, dd, J=2.2 Hz), 2.24—2.32 (1H, m), 2.36—2.42 (1H, m), 2.72 (1H, dd, J=2.2, 4.0 Hz), 3.05 (1H, dq, J=2.2, 5.2 Hz), 3.77 (1H, dt, J=4.0, 6.4 Hz), 5.10—5.17 (2H, m), 5.79—5.89 (1H, m). ^{13}C-NMR δ: 17.2, 38.1, 51.5, 61.3, 68.3, 118.2, 133.6. HR-MS (FAB): Calcd for $C_7H_{13}O_2$ (M^++1): 129.0916, Found: 129.0921.

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