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, ($\pm$)-10 and ($\pm$)-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 ($\pm$)-17 and ($\pm$)-38 were formally converted to natural products, ($\pm$)-asperlin (**2**) and ($\pm$)-olivose (**4**), respectively. The major *anti*-, *anti*-adduct ($\pm$)-26 was converted to ($\pm$)-digitoxose (**3**), while the minor *anti*-, *syn*-adduct ($\pm$)-27 was also converted to ($\pm$)-olivose (**4**). The reaction of ($\pm$)-10 with *tert*-butyl acetate anion gave predominantly afforded the *anti*-, *anti*-adduct ($\pm$)-23, which was converted to ($\pm$)-1,5-dideoxyhexitol (**25**). Alternately, the reaction of 2,3-*syn*-2-*tert*-butyldimethylsiloxy-3-*p*-methoxyphenoxy butanal derivative [*syn*-B, ($\pm$)-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** [($\pm$)-32 or ($\pm$)-34] and *syn*-, *syn*-adduct **F** [($\pm$)-33 or ($\pm$)-35]. After separation of this mixture, ($\pm$)-34 and ($\pm$)-35 were separately converted to ($\pm$)-oliose (**5**) and ($\pm$)-boivinoose (**6**), respectively.

Key words ($\pm$)-asperlin; ($\pm$)-digitoxose; ($\pm$)-olivose; ($\pm$)-oliose; ($\pm$)-boivinoose; 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 anti-tumour and antibacterial activity, and rare deoxysugar such as D-digitoxose (**3**), D-olivose (**4**), D-oliose (**5**) and D-boivinoose (**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 ($\pm$)-2,3-Disubstituted Butanal Derivative (*anti*-B and *syn*-B) The starting ($\pm$)-2,3-*anti*-2-hydroxy-3-*p*-methoxyphenoxybutanal (**7**) was previously obtained by the $\text{BF}_3 \cdot \text{Et}_2\text{O}$ assisted reaction of ($\pm$)-**1** and *p*-methoxyphenol.²⁾ Silylation of ($\pm$)-**7** with *tert*-butyldimethylsilyl chloride (TBDMSCl) gave the corresponding silyl ether ($\pm$)-**8** (88%), which was reduced with diisobutylaluminum hydride (Dibal-H) to afford alcohol ($\pm$)-**9** in 77% yield. Pyridinium chlorochromate (PCC) oxidation of ($\pm$)-**9** gave the desired aldehyde ($\pm$)-**10** (75%) as shown in Chart 2. Alternately, the reaction of ($\pm$)-**7** with benzoic acid in the presence of triphenylphosphine (Ph_3P) and diisopropylazodicarboxylate gave ($\pm$)-2,3-*syn*-2-benzoxo-3-*p*-methoxyphenoxybutanoate, which was subjected to hydrolysis to afford ($\pm$)-2,3-*syn*-2-hydroxy-3-*p*-methoxyphenoxybutanoate **11** (58% yield). Thus obtained ($\pm$)-**11** was converted to 2,3-*syn*-disubstituted butanal derivative ($\pm$)-**14** in a similar manner as the synthesis of ($\pm$)-**10** [($\pm$)-**12**: 92%, ($\pm$)-**13**: 88%, and ($\pm$)-**14**: 79%]. ($\pm$)-3-Chloro-2-*tert*-butyldimethylsilyloxybutanal (**16**) was obtained by the reported procedure from ($\pm$)-**1**.⁵⁾

Formal Synthesis of ($\pm$)-Asperlin (2**)** (+)-Asperlin (**2**), isolated from *Aspergillus nidulans* and *Aspergillus caespitosus*, has been shown to exhibit antitumour and antibac-

terial 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 ($\pm$)-asperlin (**2**) from ($\pm$)-**10** is shown in Chart 3. The reaction of ($\pm$)-**10** with α -furyl anion gave major product ($\pm$)-**17** (77% yield) and minor product ($\pm$)-**18** (17% yield). To confirm the stereochemistry of ($\pm$)-**17**, it was converted to the known synthetic intermediate, epoxy-alcohol ($\pm$)-**22**,^{12,13)} for the synthesis of ($\pm$)-**2**. Protection of the secondary alcohol group of ($\pm$)-**17** as a benzoyl group followed by deprotection of the *p*-methoxyphenyl group with ceric ammonium nitrate (CAN) afforded ($\pm$)-**20** (57%). Tosylation of ($\pm$)-**20** gave the corresponding tosylate ($\pm$)-**21** (86%), which was subjected to consecutive desilylation and K_2CO_3 treatment to afford epoxide ($\pm$)-**22** in 61% yield. Spectral data (^1H - and ^{13}C -NMR) of the synthetic ($\pm$)-**22** were identical with those of the reported ($\pm$)-**22**.¹²⁾ The synthesis of ($\pm$)-asperlin (**2**) from ($\pm$)-**22** was already achieved by Honda *et al.*¹²⁾ Consequently, the stereochemistry of ($\pm$)-**17** was determined to be 1,2-*anti*- and 2,3-*anti*-structures, and that of minor component ($\pm$)-**18** was determined to be 1,2-*syn*- and 2,3-*anti*-. The stereoselective formation of ($\pm$)-**17** from ($\pm$)-**10** is explained

Reagents: a; TBDMSCl / imidazole / DMF b; Dibal-H c; PCC

d; 1) diisopropylazodicarboxylate / Ph_3P / PhCOOH / THF 2) K_2CO_3 / MeOH

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 LiAlH₄ followed by consecutive desilylation and acetylation gave triacetate (±)-24 in 78% yield, which was subjected to consecutive desilylation and K₂CO₃ treatment to afford tetraol (±)-25 in 95% yield. Spectral data (¹H- and ¹³C-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 K₂CO₃ treatment to afford triol (±)-29 in 73% yield. Ozonolysis of (±)-29 followed by reductive treatment with dimethyl sulfide (Me₂S) afforded a 3.9:1 diastereomeric mixture (β-isomer: α-isomer=3.9:1) of (±)-3 (73%). Spectral data (¹H- and ¹³C-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 K₂CO₃ treatment to afford triol (±)-31 in 73% yield. Ozonolysis of (±)-31 followed by reductive treatment with Me₂S afforded a 4:3 diastereomeric mixture (β-isomer: α-isomer=4:3) of (±)-olivose (4). Spectral data (¹H- and ¹³C-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 (±)-Olivose (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 K₂CO₃ treatment to afford triol (±)-36 in 76% yield. Ozonolysis of (±)-36 followed by reductive treatment with Me₂S afforded a 1:1 diastereomeric mixture of (±)-5 (66%). Spectral data (¹H- and ¹³C-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 K₂CO₃ treatment to afford triol (±)-37 in 78% yield. Ozonolysis of (±)-37 followed by reductive treatment with Me₂S afforded *ca.* 80% β-anomer of (±)-6 (81%) with the remainder being a mixture of the α-anomer and the furanose anomers. Spectral data (¹H- and ¹³C-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

Chart 4

Chart 5

Chart 6

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, K₂CO₃ treatment and acidification with AcOH gave epoxy alcohol (±)-40 in 17% yield (four steps). Spectral data (¹H- and ¹³C-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.

Discussion

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 control 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 ($\pm$)-**10** and ($\pm$)-**16** could be explained by Paquette and Mitzel¹⁸⁾ who showed that 1,2-addition of the allyl-indium 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 ($\pm$)-**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 ($\pm$)-**17** and ($\pm$)-**38** were formally converted to natural products, ($\pm$)-asperlin (**2**) and ($\pm$)-olivose (**4**), respectively. The major *anti*-, *anti*-adduct ($\pm$)-**26** was converted to ($\pm$)-digitoxose (**3**), while the minor *anti*-, *syn*-adduct ($\pm$)-**27** was also converted to ($\pm$)-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** [($\pm$)-**32** or ($\pm$)-**34**] and the *syn*-, *syn*-adduct **F** [($\pm$)-**33** or ($\pm$)-**35**]. After separation of this mixture, ($\pm$)-**34** and ($\pm$)-**35** were converted to ($\pm$)-oliose (**5**) and ($\pm$)-boivoinose (**6**), respectively.

Experimental

¹H- and ¹³C-NMR spectra were recorded on JEOL AL 400 spectrometer in CDCl₃. 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.

($\pm$)-2,3-*anti*-2'-Butyldimethylsiloxy-3-*p*-methoxyphenoxybutanal (**10**) i) To a solution of ($\pm$)-**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 (TBDMS-Cl; 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 MgSO₄ and evaporated to give a crude oil, which was chromatographed on silica gel (250 g, *n*-hexane : AcOEt = 40 : 1) to give ($\pm$)-**3** (13.3 g, 88%) as a colorless oil. ($\pm$)-**8**: IR (neat): 1759 cm⁻¹; ¹H-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). ¹³C-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 C₁₈H₃₀O₅Si (M⁺): 354.1863, Found: 354.1867. ii) To a solution of ($\pm$)-**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 H₂O and filtered off with the aid of celite. The filtrate was extracted with AcOEt. The organic layer was dried over MgSO₄ and evaporated to give a crude oil, which was chromatographed on silica gel (120 g, *n*-hexane : AcOEt = 10 : 1) to give ($\pm$)-**9** (3.6 g, 77%) as a colorless oil. ($\pm$)-**9**: IR (neat): 3447 cm⁻¹; ¹H-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). ¹³C-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 C₁₇H₃₀O₄Si (M⁺): 326.1913, Found: 326.1943. iii) To a solution of ($\pm$)-**9** (1.48 g, 4.5 mmol) in CH₂Cl₂ (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 ($\pm$)-**10** (1.11 g, 75%) as a colorless oil. ($\pm$)-**10**: IR (neat): 1736 cm⁻¹; ¹H-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). ¹³C-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 C₁₇H₂₈O₄Si (M⁺): 324.1757, Found: 324.1783.

($\pm$)-2,3-*syn*-2'-Butyldimethylsiloxy-3-*p*-methoxyphenoxybutanal (**14**) i) To a solution of ($\pm$)-**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 H₂O, extracted with AcOEt. The organic layer was dried over MgSO₄ 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 K₂CO₃ (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 H₂O, extracted with AcOEt. The organic layer was washed with 1 M aqueous NaOH (100 ml) and brine. The organic layer was dried over MgSO₄ and evaporated to give a crude residue, which was chromatographed on silica gel (120 g, *n*-hexane : AcOEt = 5 : 1) to give ($\pm$)-**11** (3.48 g, 58%) as a colorless oil. ($\pm$)-**11**: IR (neat): 3479, 1737 cm⁻¹; ¹H-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). ¹³C-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 C₁₂H₁₆O₅ (M⁺): 240.0998, Found: 240.0996. ii) To a solution of ($\pm$)-**11** (2.68 g, 11 mmol) in DMF (30 ml) were added imidazole (1.52 g, 22 mmol) and *tert*-butyldimethylsilyl chloride (TBDMS-Cl; 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 ($\pm$)-**8** to give ($\pm$)-**12** (3.63 g, 92%) as a colorless oil. ($\pm$)-**12**: IR (neat): 1754 cm⁻¹; ¹H-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). ¹³C-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 C₁₈H₃₀O₅Si (M⁺): 354.1863, Found: 354.1864. iii) To a solution of ($\pm$)-**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 ($\pm$)-**9** to give ($\pm$)-**13** (2.78 g, 88%) as a colorless oil. ($\pm$)-**13**: IR (neat): 3458 cm^{-1} ; $^1\text{H-NMR}$ 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). $^{13}\text{C-NMR}$ 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 $\text{C}_{17}\text{H}_{30}\text{O}_4\text{Si}$ (M^+): 326.1913, Found: 326.1917. iv) To a solution of ($\pm$)-**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 ($\pm$)-**10** to give ($\pm$)-**14** (2.00 g, 79%) as a colorless oil. ($\pm$)-**14**: IR (neat): 1737 cm^{-1} ; $^1\text{H-NMR}$ 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). $^{13}\text{C-NMR}$ 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 $\text{C}_{17}\text{H}_{28}\text{O}_4\text{Si}$ (M^+): 324.1757, Found: 324.1761.

($\pm$)-**1**,**2**-anti, **2**,**3**-anti-2-Butyldimethylsiloxy-1-(2-furyl)-3-*p*-methoxyphenoxybutanol (**17**) and ($\pm$)-**1**,**2**-syn, **2**,**3**-anti-2-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 ($\pm$)-**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 ($\pm$)-**18** (0.35 g, 17%) and ($\pm$)-**17** (1.61 g, 77%) as a colorless oil in elution order. ($\pm$)-**17**: IR (neat): 3451 cm^{-1} ; $^1\text{H-NMR}$ 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). $^{13}\text{C-NMR}$ 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 $\text{C}_{21}\text{H}_{32}\text{O}_5\text{Si}$ (M^+): 392.2019, Found: 392.2017. ($\pm$)-**18**: IR (neat): 3520 cm^{-1} ; $^1\text{H-NMR}$ 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). $^{13}\text{C-NMR}$ 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 $\text{C}_{21}\text{H}_{32}\text{O}_5\text{Si}$ (M^+): 392.2019, Found: 392.2020.

($\pm$)-**1**,**2**-anti, **2**,**3**-trans-1-(2-Furyl)-2,3-epoxybutanol (**22**) i) To a solution of ($\pm$)-**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, 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 ($\pm$)-**19** (1.09 g, 84%) as a colorless oil. ($\pm$)-**19**: IR (neat): 1721 cm^{-1} ; $^1\text{H-NMR}$ 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, brs), 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). $^{13}\text{C-NMR}$ δ : -5.48, -4.27, 13.5, 18.2, 25.8 (3C), 55.7, 70.0, 73.9, 74.4, 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 $\text{C}_{28}\text{H}_{36}\text{O}_6\text{Si}$ (M^+): 496.2281, Found: 496.2216. ii) To a solution of ($\pm$)-**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 ($\pm$)-**20** (52 mg, 57%) as a colorless oil. ($\pm$)-**20**: IR (neat): 3725, 1726 cm^{-1} ; $^1\text{H-NMR}$ δ : -0.16 (3H, s), 0.09 (3H, s), 0.84 (9H, s), 1.24 (3H, d, $J=6.4$ Hz), 1.81 (1H, brs), 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). $^{13}\text{C-NMR}$ 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 $\text{C}_{21}\text{H}_{30}\text{O}_5\text{Si}$ (M^+): 390.1863, Found: 390.1872. iii) To a mixture of ($\pm$)-**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 ($\pm$)-**21** (174 mg, 86%) as a colorless oil. ($\pm$)-**21**: IR (neat): 1725 cm^{-1} ; $^1\text{H-NMR}$ 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). $^{13}\text{C-NMR}$ 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 $\text{C}_{28}\text{H}_{37}\text{O}_7\text{SSi}$ (M^++1): 545.2029, Found: 545.2072. iv) To a solution of ($\pm$)-**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 ($\pm$)-**22** (36 mg, 61%) as a colorless oil. ($\pm$)-**22**: IR (neat): 3401 cm^{-1} ; $^1\text{H-NMR}$ δ : 1.38 (3H, d, $J=5.2$ Hz), 2.34 (1H, brs), 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). $^{13}\text{C-NMR}$ δ : 17.1, 51.7, 59.8, 65.2, 107.7, 110.2, 142.5, 152.4. HR-MS (FAB): Calcd for $\text{C}_8\text{H}_{11}\text{O}_3$ (M^++1): 155.0708, Found: 155.0706.

($\pm$)-**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 ($\pm$)-**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 ($\pm$)-**23** (1.58 g, 83%) as a colorless oil. ($\pm$)-**23**: IR (neat): 3504, 1724 cm^{-1} ; $^1\text{H-NMR}$ 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). $^{13}\text{C-NMR}$ 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 $\text{C}_{23}\text{H}_{40}\text{O}_6\text{Si}$ (M^+): 440.2588, Found: 440.2594. ii) LiAlH_4 (120 mg, 3.1 mmol) was added to a stirred solution of ($\pm$)-**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 ($\pm$)-**24** (187 mg, 78%) as a colorless oil. ($\pm$)-**24**: IR (neat): 1736 cm^{-1} ; $^1\text{H-NMR}$ 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 $\text{C}_{19}\text{H}_{26}\text{O}_8$ (M^+): 382.1624, Found: 382.1628. iii) To a solution of ($\pm$)-**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 ($\pm$)-**25** (70 mg, 95%) as a colorless precipitate. ($\pm$)-**25**: IR (neat): 3332 cm^{-1} ; ^1H -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 $\text{C}_6\text{H}_{15}\text{O}_4$ (M^++1): 151.0970, Found: 151.0964.

(2,3-anti,3,4-anti)-3,4-Butyldimethylsilyloxy-4-hydroxy-2-*p*-methoxyphenoxy-6-heptene (26) and (2,3-anti,3,4-syn)-3,4-Butyldimethylsilyloxy-4-hydroxy-2-*p*-methoxyphenoxy-6-heptene (27) To a mixture of ($\pm$)-**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 ($\pm$)-**27** (0.187 g, 11%) and ($\pm$)-**26** (1.499 g, 86%) as a colorless oil in elution order. ($\pm$)-**26**: IR (neat): 3477 cm^{-1} ; ^1H -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, brs), 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 $\text{C}_{20}\text{H}_{34}\text{O}_8\text{Si}$ (M^+): 366.2226, Found: 366.2224. ($\pm$)-**27**: IR (neat): 3547 cm^{-1} ; ^1H -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 $\text{C}_{20}\text{H}_{34}\text{O}_8\text{Si}$ (M^+): 366.2226, Found: 366.2227.

($\pm$)-Digitoxose (3) i) To a solution of ($\pm$)-**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 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 ($\pm$)-**28** (1.34 g, 74%) as a colorless oil. ($\pm$)-**28**: IR (neat): 1743 cm^{-1} ; ^1H -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 $\text{C}_{18}\text{H}_{24}\text{O}_6$ (M^+): 336.1573, Found: 336.1574. ii) To a solution of ($\pm$)-**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 ($\pm$)-**29** (202 mg, 73%) as a colorless oil. ($\pm$)-**29**: IR (neat): 3357 cm^{-1} ; ^1H -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, brs), 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 $\text{C}_7\text{H}_{15}\text{O}_3$ (M^++1): 147.1021, Found: 147.1022. iii) Ozone was passed through a solution of ($\pm$)-**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 ($\pm$)-digitoxose (**3**) (202 mg, 73%) as a colorless solid. ($\pm$)-**3**: HR-MS (FAB): Calcd for $\text{C}_6\text{H}_{13}\text{O}_4$ (M^++1): 149.0814, Found: 149.0816; ^1H -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. ^1H -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.

($\pm$)-Olivose (4) i) To a solution of ($\pm$)-**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 ($\pm$)-**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 ($\pm$)-**28** to give ($\pm$)-**30** (460 mg, 76%) as a colorless oil. ($\pm$)-**30**: IR (neat): 1744 cm^{-1} ; ^1H -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 $\text{C}_{18}\text{H}_{25}\text{O}_6$ (M^++1): 337.1652, Found: 337.1634. ii) To a solution of ($\pm$)-**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 ($\pm$)-**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 ($\pm$)-**29** to give ($\pm$)-**31** (120 mg, 72%) as a colorless oil. ($\pm$)-**31**: IR (neat): 3357 cm^{-1} ; ^1H -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, brs), 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 $\text{C}_7\text{H}_{15}\text{O}_3$ (M^++1): 147.1021, Found: 147.1030. iii) Ozone was passed through a solution of ($\pm$)-**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 ($\pm$)-**3** to give a 4:3 diastereomeric mixture of ($\pm$)-olivose (**4**) (202 mg, 73%) as a colorless solid. ($\pm$)-**4**: HR-MS (FAB): Calcd for $\text{C}_6\text{H}_{13}\text{O}_4$ (M^++1): 149.0814, Found: 149.0796; ^1H -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. ^1H -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*-methoxyphenoxy-6-heptene (35)

i) To a mixture of ($\pm$)-**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 ($\pm$)-**26** and ($\pm$)-**27** to give a ca. 1:1 mixture (218 mg, 99%) of ($\pm$)-**32** and ($\pm$)-**33** as a colorless oil. HR-MS (EI): Calcd for $\text{C}_{20}\text{H}_{34}\text{O}_8\text{Si}$ (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 ($\pm$)-**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 ($\pm$)-**28** to give ($\pm$)-**35** (less polar, 74 mg, 37%) and ($\pm$)-**34** (more polar, 76 mg, 38%) as a colorless oil. ($\pm$)-**34**: IR (neat): 1742 cm^{-1} ; ^1H -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 $\text{C}_{18}\text{H}_{24}\text{O}_6$ (M^+): 336.1573, Found: 336.1581. ($\pm$)-**35**: IR (neat): 1742 cm^{-1} ; ^1H -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 $\text{C}_{18}\text{H}_{24}\text{O}_6$ (M^+): 336.1573, Found: 336.1572.

($\pm$)-**Olioise (5)** i) To a solution of ($\pm$)-**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 ($\pm$)-**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 ($\pm$)-**29** to give ($\pm$)-**36** (18 mg, 76%) as a colorless oil. ($\pm$)-**36**: IR (neat): 3357 cm^{-1} ; ^1H -NMR δ : 1.22 (3H, d, $J=6.4$ Hz), 2.23—2.38 (2H, m), 3.00 (3H, brs), 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 $\text{C}_7\text{H}_{15}\text{O}_3$ (M^+): 147.1021, Found: 147.0985. ii) Ozone was passed through a solution of ($\pm$)-**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 ($\pm$)-**3** to give a 1 : 1 diastereomeric mixture of ($\pm$)-olioise (**5**) (31 mg, 66%) as a colorless solid. ($\pm$)-**5**: HR-MS (FAB): Calcd for $\text{C}_6\text{H}_{13}\text{O}_4$ (M^+): 149.0814, Found: 149.0861; ^1H -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, brs), 3.44 (1H, brq, $J=0.8, 6.6$ 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. ^1H -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, brs), 3.86 (1H, ddd, $J=2.8, 5.2, 11.6$ Hz), 3.91 (1H, brq, $J=6.4$ Hz), 5.12 (1H, brs). ^{13}C -NMR (D_2O) δ : 16.6, 32.3, 65.5, 67.2, 71.2, 92.1.

($\pm$)-**Boivinose (6)** i) To a solution of ($\pm$)-**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 ($\pm$)-**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 ($\pm$)-**29** to give ($\pm$)-**37** (16 mg, 78%) as a colorless oil. ($\pm$)-**37**: IR (neat): 3357 cm^{-1} ; ^1H -NMR δ : 1.14 (3H, d, $J=6.4$ Hz), 2.27 (2H, t, $J=6.6$ Hz), 2.96 (3H, brs), 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 $\text{C}_7\text{H}_{15}\text{O}_3$ (M^+): 147.1021, Found: 147.1039. ii) Ozone was passed through a solution of ($\pm$)-**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 ($\pm$)-**3** to give ($\pm$)-boivinose (**6**) (33 mg, 81%) as a colorless solid. ($\pm$)-**6**: HR-MS (FAB): Calcd for $\text{C}_6\text{H}_{13}\text{O}_4$ (M^+): 149.0814, Found: 149.0807; ^1H -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, brq, $J=6.2$ 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 ($\pm$)-Olivose (4) i) To a mixture of ($\pm$)-**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 ($\pm$)-**26** and ($\pm$)-**27** to give a ca. 8 : 1 mixture (336 mg, 93%) of ($\pm$)-**38** and ($\pm$)-**39** as a colorless oil. ($\pm$)-**38** (major): IR (neat): 3460 cm^{-1} ; ^1H -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 $\text{C}_{13}\text{H}_{28}\text{O}_2\text{ClSi}$ (M^+): 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 pyridinium *p*-toluenesulfonate (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 ($\pm$)-**40** (27 mg, 17% in 4 steps) as a colorless oil. ($\pm$)-**40**: IR (neat): 3448 cm^{-1} ; ^1H -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 $\text{C}_7\text{H}_{13}\text{O}_2$ (M^+): 129.0916, Found: 129.0921.

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