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-butyldimethylsiloxyc-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-butyldimethylsiloxyc-3-p-methoxylphenylx 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
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 BF₃·Et₂O assisted reaction of (±)-1 and p-methoxyphenol. Silylation of (±)-7 with tert-butyldimethylsilyl chloride (TBDMSCI) 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 (Ph₃P) 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-butyldimethylsiloxybutanal (16) was obtained by the reported procedure from (±)-1.1

**Formal Synthesis of (±)-Asperlin (2) (+)-Asperlin (2), isolated from Aspergillus nidulans and Aspergillus caespitosus, 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 K₂CO₃ treatment to afford epoxide (±)-22 in 61% yield. Spectral data (¹H- and ¹³C-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...
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). Reduction of (±)-23 with LiAlH₄ followed by consecutive desilylation and acetylation gave triacetate (±)-26 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. 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. The reaction of (±)-10 with allyl bromide in the presence of In gave major product (±)-11006 with 86% yield and minor product (±)-11007 (11% yield) as shown in Chart 5. To confirm the stereochemistry of (±)-11006, it was converted to (±)-digitoxose (3). Deprotection of the silyl group of (±)-11006 followed by acetylation afforded diacetate (±)-11008 (74%), which was subjected to consecutive deprotection of the p-methoxyphenyl group with CAN and K₂CO₃ treatment to afford triol (±)-11009 in 73% yield. Ozonolysis of (±)-12 of 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. Consequently, the stereochemistry of (±)-11010 was determined to be 4,5-anti- and 5,6-syn-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 (±)-26 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 (±)-27 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. 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 (±)-38 followed by reductive treatment with Me₂S afforded ca. 80% β-anomer of (±)-6 (81%) with the reminder 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. Consequently, the stereochemistry of the more polar (±)-34 was determined to be 4,5-anti- and 5,6-syn, and that of the
less polar \((\pm)-35\) was determined to be \(4,5\text{-syn}\) and \(5,6\text{-syn}\). In the nucleophilic addition to \(2,3\text{-syn}\)-disubstituted butanal derivative \((\pm)-14\), no stereoselective reaction occurred and the reason for this is discussed later in the text.

**Formal Synthesis of \((\pm)-\text{Olivose} (4)\)**

The reaction of \((\pm)-16\) with allyl bromide in the presence of In gave an inseparable \(8:1\) diastereomeric mixture of \((\pm)-38\) and \((\pm)-39\) (93% yield) as shown in Chart 7. Protection of the secondary alcohol group of this mixture as a tetrahydropyranyl group followed by consecutive desilylation, \(\text{K}_2\text{CO}_3\) treatment and acidification with \(\text{AcOH}\) gave epoxy alcohol \((\pm)-40\) in 17% yield (four steps). Spectral data (\(^1\text{H-}\) and \(^{13}\text{C-NMR}\)) of the synthetic \((\pm)-40\) were identical with those of the reported \((\pm)-40\). The synthesis of \((\pm)-4\) from \((\pm)-40\) was already achieved. Consequently, the stereochemistry of the major component \((\pm)-38\) was determined to be \(4,5\text{-anti}\) and \(5,6\text{-anti}\). The stereoselective formation of \((\pm)-38\) from \((\pm)-16\) is explained later in the text.

**Discussion**

The reaction of \(\alpha\)-hydroxy aldehyde \((\pm)-41\) with allyl bromide in the presence of In in water was reported to give \(1,2\text{-syn}\) adduct \((\pm)-43\) and \(1,2\text{-anti}\) adduct \((\pm)-44\) in a ratio of \(9.8:1\), while that of \(\alpha\)-protected aldehyde \((\pm)-42\) with allyl bromide in the presence of In in water was reported to afford \(1,2\text{-syn}\) adduct \((\pm)-45\) and \(1,2\text{-anti}\) adduct \((\pm)-46\) in a ratio...
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 (±)-10 and (±)-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. Thus obtained adduct (±)-adduct 1 and (±)-adduct 3 were converted to (±)-oliose (5) and (±)-bovinose (6), respectively.

**Experimental**

1H- and 13C-NMR spectra were recorded on JEOL AL 400 spectrometer in CDC13. 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 spectra were obtained with a JEOL JMS-SX-102A or JMS-T100LP. IR spectra were recorded with a JASCO FT/IR-SX-102A or JMS-T100LP. All evaporations were performed under reduced pressure. For column chromatography, silica gel (Kieselgel 60) was employed.

(±)-2,3-anti-2′-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 disopropylazodicarboxylate (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. The filtrate was extracted with AcOEt. 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 = 10 : 1) to give (±)-9 (3.66 g, 45%), as a colorless oil. (±)-9: IR (neat): 1736 cm−1; 1H-NMR δ: 0.07 (3H, s), 0.31 (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, d, 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, 152.4, 203.5. HR-MS (EI): Calcd for C17H28O5Si (M+): 326.1913. Found: 326.1943.

ii) To a solution of (±)-10 (3.48 g, 45 mmol) in CHCl3 (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 (±)-11 (11.11 g, 75%) as a colorless oil. (±)-11: IR (neat): 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 = 1.4, 5.8 Hz), 6.79—6.85 (4H, m), 9.61 (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, 152.4, 203.5. HR-MS (EI): Calcd for C17H28O5Si (M+): 324.1757. Found: 324.1783.

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

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, acetylene anion, and indium (In)-assisted allyl anion] gave selectively the indium reagents to

- To a solution of (±)-10 and (±)-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. Thus obtained adduct (±)-adduct 1 and (±)-adduct 3 were converted to (±)-oliose (5) and (±)-bovinose (6), 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 butenal derivatives syn-B derived from trans-(2,3)-epoxy butanoate (1) with a carbon nucleophile (In-assisted allyl anion) afforded a cca i. 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 (±)-bovinose (6), respectively.

Experimental

1H- and 13C-NMR spectra were recorded on JOEL AL 400 spectrometer in CDC13. 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 spectra 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.
dry toluene (50 ml) was added 1 m solution of disiocubutylalumimium 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 (±)-10 to give (±)-11 (2.78 g, 88%) as a colorless oil. (±)-13: IR (neat): 3451 cm⁻¹; ¹H-NMR δ: 0.15 (3H, s), 0.11 (3H, s), 0.83 (9H, s), 1.28 (3H, d, J = JH,F = 6.4 Hz), 2.22 (1H, d, J = JH,F = 4.4 Hz), 3.76 (3H, d, J = JH,F = 2.9, 6.4 Hz), 4.68 (1H, dq, J = JH,F = 4.9, 6.8 Hz), 6.31 (1H, d, J = JH,F = 3.4 Hz), 6.34 (1H, d, J = JH,F = 3.2 Hz), 6.78 (2H, d, J = JH,F = 9.3 Hz), 8.81 (2H, d, J = JH,F = 9.3 Hz), 7.37 (1H, d, J = JH,F = 1.9 Hz). ¹C-NMR δ: 5.34, -5.4, 14.8, 120.2, 151.1, 151.2, 151.3, 154.2, 155.1, 155.4, 156.2 HR-MS (EI): Calculated for C₇H₁₆O₃Si: M⁻⁺: 163.0882. Found: 163.0878. (±)-1,2-anti, 2,3-anti-2-Butyldimethylsilylo-1-(2-furyl)-3-p-methoxyphenylbutanol (17) and (±)-1,2-syn,2,3-syn-2-Butyldimethylsilylo-1-(2-furyl)-3-p-methoxyphenylbutanol (18) To a solution of furan (25 ml, 0.23 mmol) in THF (30 ml) was added 1.0 M solution of lithium 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 NH₄Cl solution and extracted with AcOEt. The organic layer was washed with brine and dried over MgSO₄. Evaporation of the organic solvent gave a residue, which was chromatographed on silica gel (50 g, n-hexane:AcOEt=20:1) to give (±)-11 (0.35 mm, 17%) and (±)-17 (1.6 mm, 77%) as a colorless oil in elution order. (±)-17: IR (neat): 3451 cm⁻¹; ¹H-NMR δ: 0.15 (3H, s), 0.11 (3H, s), 0.83 (9H, s), 1.28 (3H, d, J = JH,F = 6.4 Hz), 2.22 (1H, d, J = JH,F = 4.4 Hz), 3.76 (3H, d, J = JH,F = 2.9, 6.4 Hz), 4.68 (1H, dq, J = JH,F = 4.9, 6.8 Hz), 6.31 (1H, d, J = JH,F = 3.4 Hz), 6.34 (1H, d, J = JH,F = 3.2 Hz), 6.78 (2H, d, J = JH,F = 9.3 Hz), 8.81 (2H, d, J = JH,F = 9.3 Hz), 7.37 (1H, d, J = JH,F = 1.9 Hz). ¹C-NMR δ: 5.34, -5.4, 14.8, 120.2, 151.1, 151.2, 151.3, 154.2, 155.1, 155.4, 156.2 HR-MS (EI): Calculated for C₁₇H₂₈O₄Si: M⁻⁺: 360.1005. Found: 360.1002. (±)-2,3-anti-2,3-trans-2-Butyldimethylsilylo-1-(2-furyl)-3-p-methoxyphenylbutanol (22) 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; 40 mg, 0.33 mmol) to give a crude oil, which was chromatographed on silica gel (10 g, n-hexane:AcOEt=1:1) to give (±)-22 (2.35 mm, 66%) as a colorless oil. (±)-22: IR (neat): 3401 cm⁻¹; ¹H-NMR δ: 1.38 (3H, d, J = JH,F = 6.8 Hz), 1.95 (3H, s), 2.34 (1H, br, s), 3.05 (1H, d, J = JH,F = 3.4, 3.6 Hz), 3.25 (1H, dq, J = JH,F = 2.4, 5.2 Hz), 4.87 (1H, d, J = JH,F = 3.6 Hz), 5.36, -6.38 (2H, m), 7.42 (1H, dd, J = JH,F = 0.8, 1.8 Hz). ¹C-NMR δ: 17.1, 51.7, 59.8, 65.2, 107.7, 110.2, 142.5, 152.4. HR-MS (EI): Calculated for C₁₇H₂₈O₄Si: M⁻⁺: 360.1005. Found: 360.1002. (±)-1,5-Dideoxyhexitol (25) i) n-Butyl lithium (1.6 m in hexane, 3.8 ml, 6 mmol) was added to a stirred solution of disopropylamine (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 diisopropylamid (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 (±)-19 (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 H₂O and extracted with AcOEt. The organic layer was washed with H₂O and dried over MgSO₄. Evaporation of the organic solvent gave a residue, which was chromatographed on silica gel (10 g, n-hexane:AcOEt=1:1) to give (±)-23 (1.58 g, 83%) as a colorless oil. (±)-23: IR (neat): 3504, 1724 cm⁻¹; ¹H-NMR δ: 0.06 (3H, s), 0.16 (3H, s), 0.92 (9H, s), 1.25 (3H, d, J = JH,F = 6.4 Hz), 1.46 (9H, s), 2.04 (1H, s), 2.43 (1H, dd, J = JH,F = 8.0, 16.8 Hz), 2.65 (1H, dd, J = JH,F = 2.8, 16.3 Hz), 3.39 (1H, dd, J = JH,F = 4.1, 3.72 (3H, s), 3.84, 3.92 (1H, s), 4.62 (1H, dq, J = JH,F = 2.6, 6.4 Hz), 6.80, -6.86 (4H, m). ¹C-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), 151.6, 153.6, 157.8, 172.8. HR-MS (EI): Calculated for C₁₇H₂₈O₄Si: M⁻⁺: 440.2588. Found: 440.2594. (±)-23: IR (neat): 1736 cm⁻¹; ¹H-NMR δ: 1.29 (3H, d, J = JH,F = 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 = JH,F = 6.0, 6.4 Hz), 5.22 (1H, dd, J = 3.4, 5.6 Hz).
6.4 Hz), 5.37 (1H, dt, J = 3.4, 10.0 Hz), 6.81—6.86 (4H, m). 13C-NMR δ: 15.4, 16.2, 17.0, 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 C14H10O4 (M⁺): 238.0468. Found: 238.0463.

ii) To a solution of (±)-28 (217 mg, 0.59 mmol) in MeCN (5 ml) and H2O (1 ml) was added CaCO3 (135 mg, 1.3 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, CHCl3/MeOH = 1:1) to give (±)-29 (275 mg, 81%) as a colorless solid. (±)-29 (275 mg, 81%) was recrystallized from MeOH (20 ml) for 0.5 h at −20°C then Me2S (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, CHCl3/MeOH = 1:1) to give a 3.9:1 diastereomeric mixture of (±)-digoxitose (3) (202 mg, 73%) as a colorless solid. (±)-3: HR-MS (FAB): Calcd for C14H10O4 (M⁺): 238.0468. Found: 238.0463.

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1H-NMR ( orderby lambda): 149.0814, Found: 149.0861; 1H-NMR (beta-ano mer, D,O): 1.02 (3H, d, J=6.8 Hz), 1.39 (1H, dh, 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, dh, J=3.2, 4.8, 12.4 Hz), 4.58 (1H, dh, J=2.4, 10.0 Hz). 13C-NMR (D,O): 16.8, 35.3, 68.8, 70.1, 71.5, 94.3. 1H-NMR (alpha-ano mer, D,O): 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, dh, J=2.8, 5.2, 11.6Hz), 3.91 (1H, brq, J=6.4 Hz), 5.12 (1H, brs).

13C-NMR (D,O): 16.6, 32.3, 65.5, 67.2, 71.2, 92.1.

(37) IR (neat): 3357 cm^-1; 1H-NMR: 1.14 (3H, d, J=6.4 Hz), 2.27 (2H, t, J=6.6 Hz), 2.96 (3H, br.s), 3.14 (1H, dh, J=2.4, 3.6 Hz), 3.65 (1H, dh, 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), 11.85, 134.2. HR-MS (FAB): Calculated for C14H16O3 (M^+): 244.1183, Found: 244.1178.

1H-NMR (alpha-ano mer, D,O): 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, dh, J=2.8, 5.2, 11.6 Hz), 3.91 (1H, brq, J=6.4 Hz), 5.12 (1H, brs).

13C-NMR (D,O): 16.6, 32.3, 65.5, 67.2, 71.2, 92.1.

(37) IR (neat): 3357 cm^-1; 1H-NMR: 1.14 (3H, d, J=6.4 Hz), 2.27 (2H, t, J=6.6 Hz), 2.96 (3H, br.s), 3.14 (1H, dh, J=2.4, 3.6 Hz), 3.65 (1H, dh, 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), 11.85, 134.2. HR-MS (FAB): Calculated for C14H16O3 (M^+): 244.1183, Found: 244.1178.

1H-NMR (alpha-ano mer, D,O): 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, dh, J=2.8, 5.2, 11.6 Hz), 3.91 (1H, brq, J=6.4 Hz), 5.12 (1H, brs).

13C-NMR (D,O): 16.6, 32.3, 65.5, 67.2, 71.2, 92.1.

(37) IR (neat): 3357 cm^-1; 1H-NMR: 1.14 (3H, d, J=6.4 Hz), 2.27 (2H, t, J=6.6 Hz), 2.96 (3H, br.s), 3.14 (1H, dh, J=2.4, 3.6 Hz), 3.65 (1H, dh, 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), 11.85, 134.2. HR-MS (FAB): Calculated for C14H16O3 (M^+): 244.1183, Found: 244.1178.

1H-NMR (alpha-ano mer, D,O): 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, dh, J=2.8, 5.2, 11.6 Hz), 3.91 (1H, brq, J=6.4 Hz), 5.12 (1H, brs).

13C-NMR (D,O): 16.6, 32.3, 65.5, 67.2, 71.2, 92.1.