Supporting Information

Total Synthesis of (–)-Xyloketal A

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1. General Experimental Details

All non-aqueous reactions were performed under an atmosphere of dry nitrogen in oven- or flame-dried glassware. The reaction temperatures stated were those of the external bath. Diethyl ether (ether) was dried over sodium/benzophenone ketyl and distilled under an atmosphere of dry nitrogen immediately prior to use. Dichloromethane was dried over calcium hydride and distilled under an atmosphere of dry nitrogen immediately prior to use. All other solvents and reagents were purified by standard techniques or used as supplied.¹ Silica gel column chromatography ("flash chromatography") was carried out using Merck silica gel 60 (230 to 400 mesh).² Melting points (M.p.) were measured on a Gallenkamp capillary melting point apparatus and are uncorrected. Specific optical rotations ($[\alpha]_D$) were measured using a Perkin-Elmer 341 digital polarimeter. All proton and carbon nuclear magnetic resonance spectra (^1H and ^{13}C NMR, respectively) were recorded on 400 MHz (operating frequencies: ^1H , 400.13 MHz; ^{13}C , 100.61 MHz) or 500 MHz (operating frequencies: ^1H , 499.77 MHz; ^{13}C , 125.68 MHz) FT spectrometers at ambient temperature. The chemical shifts (δ) for all compounds are listed in parts per million downfield from tetramethylsilane using the NMR solvent as an internal reference. The reference values used for deuterated chloroform (CDCl_3) were 7.26 and 77.00 ppm for ^1H and ^{13}C NMR spectra, respectively. The reference values used for deuterated benzene (C_6D_6) were 7.15 and 128.02 ppm, respectively. Infrared spectra (IR) were recorded as evaporated films (ef) using a Perkin Elmer 599B IR spectrophotometer. Low-resolution mass spectra (MS) were recorded on a Varian 4000 GC/MS/MS spectrometer. The mode of ionization

(1) Armarego, W. L. F.; Perrin, D. D. *Purification of Laboratory Chemicals*, 4th ed.; Butterworth-Heinemann: Oxford, 1997.

(2) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

used was chemical ionization (CI) with methanol as the ionization gas. Microanalyses (Anal.) were performed on a Carlo Erba Model 1106 CHN analyzer.

2. Experimental Procedures and Product Characterization Data

(2'*R*,4*S*)-4-Benzyl-3-[2'-methylpent-4'-ynoyl]oxazolidin-2-one (**6**)

In order to effect a highly diastereoselective alkylation reaction of the oxazolidinone **5** with propargyl bromide, a series of experiments were performed.³ In the first instance, the oxazolidinone **5** was deprotonated with lithium diisopropylamide (LDA, 1.1 equiv) in tetrahydrofuran at -78 °C and the resultant enolate was subsequently reacted with propargyl bromide (1.5 equiv) at 0 °C for 2 h.⁴ This afforded the desired alkylated product **6** in moderate yield (49%) as a mixture of two diastereoisomers (7:1). It was attempted to improve the yield and diastereoselectivity of this process by repeating the above reaction and allowing it to warm

(3) The corresponding auxiliary, (4*S*)-4-benzyloxazolidin-2-one, was prepared in two steps from (*S*)-phenylalanine, see: (a) Dickman, D. A.; Meyers, A. I.; Smith, G. A.; Gawley, R. E. *Org. Syn.* **1985**, 63, 136. (b) Gage, J. R.; Evans, D. A. *Org. Syn.* **1990**, 68, 77. (4*S*)-4-Benzyl-3-propionyloxazolidin-2-one **5** was prepared from this auxiliary according to a literature procedure, see: (c) Gage, J. R.; Evans, D. A. *Org. Syn.* **1990**, 68, 83. Of note, this chiral auxiliary was selected because it is known to be a particularly effective chiral-director and in that derivatives of this compound are often crystalline. Thus, and in principle, the desired alkylated product could be purified by recrystallization. In addition, it was known that it would be possible to visualize the auxiliary and diastereomeric adducts by thin-layer chromatography with a UV lamp.

(4) Evans, D. A.; Ennis, M. D.; Mathre, D. J. *J. Am. Chem. Soc.* **1982**, 104, 1737.

slowly from – 78 to – 20 °C over 20 h. In this case, the alkylated oxazolidinone **6** was isolated in 55% yield as a mixture of diastereoisomers (6:1). The use of an increased amount of LDA (1.5 equiv) and propargyl bromide (4 equiv) also did not significantly increase the yield and diastereoselectivity of the reaction.⁵ However, it was subsequently found that use of hexamethylphosphoramide (HMPA) as an additive in this reaction led to an increase in both the yield and diastereoselectivity of the process.^{6,7} Accordingly, deprotonation of the oxazolidinone **5** in a mixture of tetrahydrofuran and HMPA (~10%) with LDA (1.5 equiv) on subsequent reaction with propargyl bromide (4 equiv) at – 78 °C for 20 h afforded the oxazolidinone **6** in good yield (77%) and as a single diastereoisomer. The details of these experiments are listed below.

Method A:⁴ To a solution of *N,N*-diisopropylamine (2.7 mL, 19 mmol) in tetrahydrofuran (15 mL) at 0 °C was added *n*-butyllithium (7.6 mL, 2.5 M in hexanes, 19 mmol, 1.1 equiv). The reaction mixture was stirred for 30 min and then cooled to – 78 °C. A solution of (4*S*)-4-benzyl-3-propionyloxazolidin-2-one **5**³ (3.98 g, 17.1 mmol, 1 equiv) in tetrahydrofuran (5 mL) was added and the resultant mixture was stirred for 30 min. Propargyl bromide (2.9 mL, 80 wt. % in toluene, 26 mmol, 1.5 equiv) was then added dropwise. The reaction mixture was

(5) The use of titanium tetrachloride and *N,N,N*-diisopropylethylamine to deprotonate the oxazolidinone **5**, employing propargyl chloride as well as propargyl bromide as alkylating agents, was unsuccessful. For related procedures, see: Evans, D. A.; Urpi, F.; Somers, T. C.; Clark, J. S.; Bilodeau, M. T. *J. Am. Chem. Soc.* **1990**, *112*, 8215.

(6) For related reports on the use of HMPA in alkylation reactions of derivatives of oxazolidinones, see: (a) Fadel, A. *Tetrahedron: Asymmetry* **1994**, *5*, 531. (b) Versteeg, M.; Bezuidenhout, B. C. B.; Ferreira, D.; Swart, K. J. *J. Chem. Soc., Chem. Commun.* **1995**, 1317. (c) Versteeg, M.; Bezuidenhout, B. C. B.; Ferreira, D. *Tetrahedron* **1999**, *55*, 3365.

(7) It was observed (by thin-layer chromatography) that the alkylation reaction of the enolate of the oxazolidinone **5** occurred between – 40 and – 50 °C in tetrahydrofuran. In contrast, this reaction proceeded smoothly at – 78 °C in tetrahydrofuran in the presence of HMPA.

then stirred at $-78\text{ }^{\circ}\text{C}$ for 30 min and subsequently at $0\text{ }^{\circ}\text{C}$ for 2 h. A saturated aqueous solution of ammonium chloride (10 mL) and water (10 mL) were then added. The resultant mixture was extracted with ether ($3 \times 30\text{ mL}$) and the combined organic extracts were washed with water ($3 \times 30\text{ mL}$), dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. Purification of the resultant oil by flash chromatography using hexanes:ether (2:1) as the eluant afforded the *title compound 6* (2.27 g, 49%) as a brown solid and as a mixture of two diastereoisomers (7:1).⁸

Method B: To a solution of *N,N*-diisopropylamine (1.4 mL, 10 mmol) in tetrahydrofuran (10 mL) at $0\text{ }^{\circ}\text{C}$ was added *n*-butyllithium (3.8 mL, 2.5 M in hexanes, 9.5 mmol, 1.1 equiv). The reaction mixture was stirred for 30 min and then cooled to $-78\text{ }^{\circ}\text{C}$. A solution of (4*S*)-4-benzyl-3-propionyloxazolidin-2-one **5**³ (2.00 g, 8.58 mmol, 1 equiv) in tetrahydrofuran (3 mL) was added and the resultant mixture was stirred for 30 min. Propargyl bromide (1.5 mL, 80 wt. % in toluene, 13 mmol, 1.5 equiv) was then added dropwise and the reaction mixture was allowed to warm from -78 to $-20\text{ }^{\circ}\text{C}$ over 20 h. A saturated aqueous solution of ammonium chloride (5 mL) and water (5 mL) were then added. The resultant mixture was extracted with ether ($3 \times 20\text{ mL}$) and the combined organic extracts were washed with water ($3 \times 20\text{ mL}$), dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. Purification of the resultant oil by flash chromatography using hexanes:ethyl acetate (3:1) as the eluant afforded the *title compound 6* (1.27 g, 55%) as a yellow solid and as a mixture of two diastereoisomers (6:1).⁸

Method C: To a solution of *N,N*-diisopropylamine (1.4 mL, 10 mmol) in tetrahydrofuran (10 mL) at $0\text{ }^{\circ}\text{C}$ was added *n*-butyllithium (3.8 mL, 2.5 M in hexanes, 9.5 mmol, 1.1 equiv). The reaction mixture was stirred for 30 min and then cooled to $-78\text{ }^{\circ}\text{C}$. A solution of (4*S*)-4-benzyl-

(8) In the crude ^1H NMR spectrum (400 MHz, CDCl_3), a doublet that corresponded to the methyl group of the minor diastereoisomer was observed at δ 1.43 ppm.

3-propionyloxazolidin-2-one **5**³ (2.00 g, 8.58 mmol, 1 equiv) in tetrahydrofuran (3 mL) was added and the resultant mixture was stirred for 30 min. Propargyl bromide (3.8 mL, 80 wt. % in toluene, 34 mmol, 4 equiv) was then added dropwise and the reaction mixture was allowed to warm from – 78 to 0 °C over 23 h. A saturated aqueous solution of ammonium chloride (5 mL) and water (5 mL) were then added. The resultant mixture was extracted with ether (3 × 20 mL) and the combined organic extracts were washed with water (3 × 20 mL), dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. Purification of the resultant oil by flash chromatography using hexanes:ethyl acetate (3:1) as the eluant afforded the *title compound 6* (1.24 g, 53%) as a yellow solid and as a mixture of two diastereoisomers (6:1).⁸

Method D: To a solution of *N,N*-diisopropylamine (1.9 mL, 14 mmol) in tetrahydrofuran (10 mL) at 0 °C was added *n*-butyllithium (5.0 mL, 2.5 M in hexanes, 13 mmol, 1.5 equiv). The reaction mixture was stirred for 30 min and then cooled to – 78 °C. A solution of (4*S*)-4-benzyl-3-propionyloxazolidin-2-one **5**³ (2.00 g, 8.58 mmol, 1 equiv) in tetrahydrofuran (3 mL) was added and the resultant mixture was stirred for 30 min. Propargyl bromide (3.8 mL, 80 wt. % in toluene, 34 mmol, 4 equiv) was then added dropwise and the reaction mixture was allowed to warm from – 78 to 0 °C over 23 h. A saturated aqueous solution of ammonium chloride (5 mL) and water (5 mL) were then added. The resultant mixture was extracted with ether (3 × 20 mL) and the combined organic extracts were washed with water (3 × 20 mL), dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. Purification of the resultant oil by flash chromatography using hexanes:ethyl acetate (3:1) as the eluant afforded the *title compound 6* (1.27 g, 55%) as a yellow solid and as a mixture of two diastereoisomers (6:1).⁸

Method E:⁶ To a solution of *N,N*-diisopropylamine (31 mL, 220 mmol) in tetrahydrofuran (170 mL) at 0 °C was added *n*-butyllithium (81 mL, 2.5 M in hexanes, 200

mmol). The reaction mixture was stirred for 30 min and then cooled to $-78\text{ }^{\circ}\text{C}$. Hexamethylphosphoramide (HMPA, 25 mL) and a solution of (4*S*)-4-benzyl-3-propionyl-oxazolidin-2-one **5**³ (32.5 g, 139 mmol) in tetrahydrofuran (50 mL) were added. The resultant mixture was stirred for 30 min and then propargyl bromide (62 mL, 80 wt. % in toluene, 560 mmol) was added dropwise. The reaction mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 20 h and then a saturated aqueous solution of ammonium chloride (80 mL) and water (80 mL) were added. The resultant mixture was extracted with ether ($3 \times 200\text{ mL}$) and the combined organic extracts were washed with water ($6 \times 15\text{ mL}$), dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. Purification of the resultant oil by flash chromatography using hexanes:ethyl acetate (2:1) as the eluant afforded the *title compound* **6** (29.1 g, 77%) as a brown solid and as a single diastereoisomer. This material was recrystallized from ether:hexanes (2:1) to afford the *title compound* **6** as a cream colored solid. $R_f = 0.34$, hexanes:ethyl acetate (2:1); **M.p.** 52-54 $^{\circ}\text{C}$, ether:hexanes; $[\alpha]_D^{20} = +56.2$ (c 1.18, chloroform); **¹H NMR** (400 MHz, CDCl_3) δ 1.29 (d, $J = 6.8\text{ Hz}$, 3H, *Me*), 2.03 (apparent t, $J = 2.7\text{ Hz}$, 1H, *CCH*), 2.49 (ddd, $J = 16.8, 6.6, 2.7\text{ Hz}$, 1H, *CHHCC*), 2.61 (ddd, $J = 16.8, 6.7, 2.7\text{ Hz}$, 1H, *CHHCC*), 2.78 (dd, $J = 13.4, 9.5\text{ Hz}$, 1H, *CHHPh*), 3.31 (dd, $J = 13.4, 3.2\text{ Hz}$, 1H, *CHHPh*), 3.95 (m, 1H, *CHMe*), 4.20 (m, 2H, *CH₂O*), 4.70 (m, 1H, *CHN*), 7.30 (m, 5H, *Ph*); **¹³C NMR** (101 MHz, CDCl_3) δ 16.4, 22.4, 37.1, 37.7, 55.1, 66.0, 70.0, 81.2, 127.2, 128.8, 129.3, 135.1, 152.9, 174.9; **IR** (ef) 3288, 3029, 2987, 2977, 2917, 1779, 1698, 1389, 1350, 1244, 1209 cm^{-1} ; **MS** (CI) m/z (rel. intensity) 272 ($M + H$, 100), 217 (22), 135 (14), 39 (27); **Anal.** Calcd. for $\text{C}_{16}\text{H}_{17}\text{NO}_3$: C, 70.83; H, 6.32; N, 5.16. Found: C, 70.80; H, 6.46; N, 5.33.

(2*R*)-2-Methylpent-4-yn-1-ol (7)^{9,10}

To a suspension of lithium aluminum hydride (11.3 g, 298 mmol) in tetrahydrofuran (300 mL) at 0 °C was added a solution of the oxazolidinone **6** (26.8 g, 99.0 mmol) in tetrahydrofuran (65 mL) and the resultant suspension was stirred for 45 min. Water (11 mL), an aqueous solution of sodium hydroxide (2 M, 11 mL), and an additional quantity of water (34 mL) were then added. The resultant mixture was filtered and the filter-cake was washed with ether (3 × 150 mL). The filtrate was concentrated *in vacuo* and the resultant oil was purified by Kugelrohr distillation to afford the *title compound* **7** (7.1 g, 73%) as a colorless oil. $R_f = 0.47$, ethyl acetate:hexanes (2:1); **B.p.** 67-72 °C, ~12 mm Hg (lit.⁹ 61-66 °C, ~10 mm Hg); $[\alpha]_D^{20} = +11.4$ (*c* 1.10, chloroform) [lit.⁹ +10.9 (*c* 1.10, chloroform)]. All other spectroscopic data were identical to that reported earlier.⁹

(9) For an alternative synthesis (employing a resolution procedure) and proof of absolute stereochemistry of the chiral nonracemic alcohol **7**, see: Pettigrew, J. D.; Freeman, R. P.; Wilson, P. D. *Can. J. Chem.* **2004**, 82, 1640.

(10) For a related procedure, see: Ref. 4.

(4*R*)-2,4-Dimethyl-4,5-dihydrofuran (8**)**⁹

The alcohol **7** (7.11 g, 72.6 mmol) and sodium amide (400 mg, 10.3 mmol) were heated (without solvent) at reflux for 4 h. Direct distillation of the reaction mixture at atmospheric pressure afforded the corresponding *exo*-cyclic dihydrofuran and a small amount of the *endo*-cyclic dihydrofuran **8** as a colorless oil. This material was then heated at reflux for 18 h to afford the *title compound* **8** (5.30 g, 74%) as a pale yellow oil.¹¹ *R_f* = 0.22, ethyl acetate:hexanes (2:1); [*α*]_D²⁰ = −128 (*c* 1.29, chloroform).¹² All other spectroscopic data were identical to that reported earlier.⁹

(11) The final product was contaminated with a small amount of the corresponding *exo*-cyclic dihydrofuran (<7%).

(12) The sign and magnitude of the specific optical rotation of the dihydrofuran (4*R*)-**8** and its enantiomer were previously reported incorrectly, see: Ref. 9. The value for the dihydrofuran (4*R*)-**8** should have been reported as: [*α*]_D²⁴ = −118 (*c* 0.82, chloroform).

(4*R*)-3-Trichloroacetyl-2,4-dimethyl-4,5-dihydrofuran (9) and (4'*R*)-1,1,1-trichloro-3-[4'-methyl-4,5-dihydrofuran-2'*E*-ylidene]propane-2-one (10)^{13,14}

Method A: To a solution of the dihydrofuran **8** (699 mg, 7.13 mmol) and pyridine (0.87 mL, 11 mmol) in dichloromethane (5 mL) at room temperature was added trichloroacetyl chloride (1.2 mL, 11 mmol) dropwise. The reaction mixture was stirred for 30 min and then a saturated aqueous solution of sodium bicarbonate (10 mL) was added. The resultant mixture was diluted with dichloromethane (20 mL), was washed with water (2×10 mL), dried over anhydrous sodium sulfate, and concentrated *in vacuo*. Purification of the resultant oil by flash chromatography using hexanes:ether (19:1) as the eluant afforded the *title compound* **9** (788 mg, 45%) as a pale yellow oil followed by the *title compound* **10** (790 mg, 46%) as a pale yellow solid.

Method B: To a solution of the dihydrofuran **8** (4.58 g, 46.7 mmol) and pyridine (5.6 mL, 70 mmol) in dichloromethane (90 mL) at $-78\text{ }^\circ\text{C}$ was added a solution of trichloroacetyl chloride (7.8 mL, 70 mmol) in dichloromethane (10 mL). The reaction mixture was allowed to warm to room temperature over 21 h and then a saturated aqueous solution of sodium

(13) This synthetic transformation was based on known procedures, see: (a) Hojo, M.; Masuda, R.; Sakaguchi, S.; Takagawa, M. *Synthesis* **1986**, 1016. (b) Colla, A.; Martins, M. A. P.; Clar, G.; Krimmer, S.; Fischer, P. *Synthesis* **1991**, 483.

(14) Of note, the formation of isomeric reaction products was also observed when a commercially available model compound, 2-methyl-4,5-dihydrofuran, was used as a reaction substrate in preliminary studies.

bicarbonate (50 mL) was added. The organic layer was washed with water (2 × 50 mL), dried over anhydrous sodium sulfate, and concentrated *in vacuo*. Purification of the resultant oil by flash chromatography using dichloromethane:ether (19:1) as the eluant afforded the *title compound 9* (10.5 g, 93%) as a pale yellow oil.

Title compound 9: $R_f = 0.41$, hexanes:ether (9:1); $[\alpha]_D^{20} = +44.1$ (c 1.20, chloroform); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 1.28 (d, $J = 6.4$ Hz, 3H, *Me*-4), 2.29 (s, 3H, *Me*-2), 3.57 (m, 1H, *CHMe*), 4.21 (dd, $J = 8.9, 2.3$ Hz, 1H, *OCHH*), 4.48 (apparent t, $J = 8.5$ Hz, 1H, *OCHH*); $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 16.2, 21.2, 37.6, 79.4, 108.6, 111.6, 176.7, 178.3; **IR** (ef) 2972, 2929, 2896, 1801, 1687, 1558, 1387, 1374, 1322, 1248, 1182 cm^{-1} ; **MS** (CI) m/z (rel. intensity) 249 [M ($3 \times ^{37}\text{Cl}$) + H, 3], 247 [M (^{35}Cl + $2 \times ^{37}\text{Cl}$) + H, 31], 245 [M ($2 \times ^{35}\text{Cl}$ + ^{37}Cl) + H, 100], 243 [M ($3 \times ^{35}\text{Cl}$) + H, 86], 180 (17), 125 (33), 83 (7) 39 (34); **Anal.** Calcd. for $\text{C}_8\text{H}_9\text{Cl}_3\text{O}_2$: C, 39.46; H, 3.73. Found: C, 38.09; H, 3.40.¹⁵

Title compound 10: $R_f = 0.15$, hexanes:ether (19:1); **M.p.** 39-40 °C, hexanes:ether; $[\alpha]_D^{20} = +51.5$ (c 1.41, chloroform); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 1.15 (d, $J = 6.8$ Hz, 3H, *Me*), 2.62 (m, 1H, *CHMe*), 2.86 (ddd, $J = 19.0, 6.8, 1.5$ Hz, 1H, *CHHCHMe*), 3.43 (ddd, $J = 19.0, 8.1, 1.4$ Hz, 1H, *CHHCHMe*), 3.95 (dd, $J = 8.8, 6.7$ Hz, 1H, *CHHO*), 4.45 (dd, $J = 8.8, 6.7$ Hz, 1H,

(15) The trichloroketone **9** could be converted to the corresponding carboxylic acid [LiOH (3 equiv), tetrahydrofuran:water (1:1), room temperature, 15 min, 88%] which was isolated by flash chromatography [ethyl acetate:hexanes (2:1)] as an analytically pure yellow wax. $R_f = 0.50$ ethylacetate:hexanes (2:1); **M.p.** 35-36 °C, ethyl acetate:hexanes; $[\alpha]_D^{20} = +46.0$ (c 1.12, chloroform); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 1.21 (d, $J = 6.7$ Hz, 3H, *Me*-4), 2.21 (d, $J = 1.1$ Hz, 3H, *Me*-2), 3.25 (m, 1H, *CHMe*), 4.02 (dd, $J = 9.1, 5.2$ Hz, 1H, *OCHH*), 4.49 (apparent t, $J = 9.3$ Hz, 1H, *OCHH*); $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 14.6, 19.9, 36.6, 78.2, 107.4, 171.2, 171.9; **IR** (ef) 3434 (broad), 2963, 2903, 2643, 2588, 1671, 1619, 1441, 1387, 1331, 1229 cm^{-1} ; **MS** (CI) m/z (rel. intensity) 143 ($\text{M} + \text{H}$, 100); **Anal.** Calcd. for $\text{C}_7\text{H}_{10}\text{O}_3$: C, 59.14; H, 7.09. Found: C, 59.41; H, 7.23. For a related procedure, see: Zanatta, N.; Cortellini, M. de F. M.; Carpes, M. J. S.; Bonacorso, H. G.; Martins, M. A. P. *J. Heterocyclic Chem.* **1997**, *34*, 509. Of note, this carboxylic acid could not be reduced cleanly with lithium aluminum hydride.

CHHO), 6.30 (apparent t, $J = 1.5$ Hz, 1H, CHCOCCl_3); ^{13}C NMR (101 MHz, CDCl_3) δ 17.5, 31.4, 40.0, 79.2, 90.3, 97.6, 181.0, 184.3; IR (ef) 2967, 2906, 1694, 1600, 1391, 1365, 1237, 1102 cm^{-1} ; MS (CI) m/z (rel. intensity) 249 [M ($3 \times ^{37}\text{Cl}$) + H, 3], 247 [M ($1 \times ^{35}\text{Cl} + 2 \times ^{37}\text{Cl}$) + H, 31], 245 [M ($2 \times ^{35}\text{Cl} + 1 \times ^{37}\text{Cl}$) + H, 100], 243 [M ($3 \times ^{35}\text{Cl}$) + H, 84], 210 (414), 180 (6), 125 (6), 39 (14); Anal. Calcd. for $\text{C}_8\text{H}_9\text{Cl}_3\text{O}_2$: C, 39.46; H, 3.73. Found: C, 39.26; H, 3.85.

(4R)-Methyl-2,4-dimethyl-4,5-dihydrofuran-3-carboxylate (11)^{16,17}

To a solution of the trichloroketone **9** (10.1 g, 41.6 mmol) in methanol (250 mL) was added sodium bicarbonate (1.33 g, 15.8 mmol) and the resultant mixture was heated at reflux for 1 h. The reaction mixture was then allowed to cool to room temperature and water (650 mL) was added. The resultant mixture was extracted with ether (9×80 mL) and the combined organic extracts were washed with water (2×75 mL), dried over anhydrous magnesium sulfate, and concentrated *in vacuo* to afford the *title compound* **11** (6.34 g, 98%) as a yellow oil. Attempted purification of this material by flash column chromatography using hexanes:ether (9:1) as the eluant resulted in partial loss of material and did not significantly increase the purity of the reaction product. $R_f = 0.32$, hexanes:ether (9:1); $[\alpha]_D^{20} = +27.2$ (c 1.10, chloroform); ^1H

(16) For a related procedure, see: de Buyck, L.; de Pooter, H.; Schamp, N. *Bull. Soc. Chim. Belg.* **1988**, 97, 371.

(17) A direct one-step procedure for the synthesis of dihydrofuran esters from the corresponding dihydrofurans has been reported, see: Stetter, H.; Lorenz, G. *Chem. Ber.* **1985**, 118, 1115. However, in our hands, a complex mixture of reaction products was obtained when the dihydrofuran **8** was employed as a reaction substrate.

NMR (400 MHz, CDCl₃) δ 1.14 (d, J = 6.7 Hz, 3H, *Me*-4), 2.14 (s, 3H, *Me*-2), 3.18 (m, 1H, *CHMe*), 3.67 (s, 3H, CO₂*Me*), 3.95 (dd, J = 8.9, 5.1 Hz, 1H, O*CHH*), 4.41 (apparent t, J = 9.0 Hz, 1H, O*CHH*); **¹³C NMR** (101 MHz, CDCl₃) δ 14.2, 19.9, 36.8, 50.5, 77.7, 107.6, 166.5, 168.6; **IR** (ef) 2955, 1800, 1700, 1648, 1436, 1387, 1340, 1185 cm⁻¹; **MS** (CI) m/z (rel. intensity) 157 (*M* + *H*, 100), 125 (7), 39 (12).¹⁸

(-)-Xyloketal A (1)^{19,20}

Method A: A solution of the methyl ester **11** (783 mg, 5.02 mmol) in ether (10 mL) was added to a suspension of lithium aluminum hydride (289 mg, 7.62 mmol) in ether (15 mL) at 0 °C. The resultant mixture was allowed to warm to room temperature over 20 min and then was cooled to 0 °C. Water (0.3 mL), an aqueous solution of sodium hydroxide (2 M, 0.3 mL) and an

(18) The relatively unstable methyl ester **11** is a volatile compound and so satisfactory elemental analysis could not be recorded. However, satisfactory elemental analysis was recorded for the corresponding carboxylic acid, see: Ref. 15.

(19) We have previously established, in simplified model systems, that this novel triple electrophilic aromatic substitution reaction and bicyclic acetal formation process can be promoted with a variety of acidic reagents in the presence of anhydrous magnesium sulfate. The optimized procedure involved the use of one equivalent of boron trifluoride diethyl etherate at 0 °C, see: Pettigrew, J. D.; Wilson, P. D. *J. Org. Chem.* **2006**, 71, 1620.

(20) Lin, Y.; Wu, X.; Feng, S.; Jiang, G.; Luo, J.; Zhou, S.; Vrijmoed, L. L. P.; Jones, E. B. G.; Krohn, K.; Steingröver, K.; Zsila, F. *J. Org. Chem.* **2001**, 66, 6252.

additional quantity of water (0.9 mL) were then added. The resultant mixture was filtered, the filter-cake was washed with ether (3×15 mL), and the combined filtrates were concentrated *in vacuo* to afford the unstable alcohol **3** as a pale yellow oil. This material was immediately diluted with ether (10 mL - total volume) and a portion of the resultant solution (4.0 mL, 2.0 mmol, 6 equiv) was added to a suspension of phloroglucinol **2** (42 mg, 0.33 mmol, 1 equiv) and anhydrous magnesium sulfate (0.30 g) in ether (3 mL) at 0 °C. Boron trifluoride diethyl etherate (42 μ L, 0.33 mmol, 1 equiv) was then added and the resultant mixture was stirred for 20 min. The reaction mixture was then filtered and the filter-cake was washed with ether (3×10 mL). The combined filtrates were washed with water (2×10 mL), dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. Purification by flash chromatography using dichloromethane:ether (19:1) as the eluant afforded the *title compound* **1** and 2,6-*epi*-**1** (128 mg, 85%) as a colorless oil and as a mixture of two diastereoisomers (5:2).

Method B: A solution of the alcohol **3** [(4.0 mL, 2.0 mmol, 6 equiv) prepared from the corresponding methyl ester **11** (783 mg, 5.02 mmol) and following dilution with ether (10 mL - total volume)] was added to a suspension of phloroglucinol **2** (42 mg, 0.33 mmol, 1 equiv) and anhydrous magnesium sulfate (0.30 g) in ether (3 mL) at – 78 °C. Boron trifluoride diethyl etherate (42 μ L, 0.33 mmol, 1 equiv) was then added and the resultant mixture was stirred for 20 min. The reaction mixture was then filtered and the filter-cake was washed with ether (3×10 mL). The combined filtrates were washed with water (2×10 mL), dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. Purification by flash chromatography using dichloromethane:ether (19:1) as the eluant afforded the *title compound* **1** and 2,6-*epi*-**1** (119 mg, 79%) as a colorless oil and as a mixture of two diastereoisomers (4:1).

Method C: A solution of the alcohol **3** [(2.0 mL, 1.0 mmol, 4 equiv) prepared from the corresponding methyl ester **11** (783 mg, 5.02 mmol) and following dilution with ether (10 mL - total volume)] was added to a suspension of phloroglucinol **2** (32 mg, 0.25 mmol, 1 equiv) and anhydrous magnesium sulfate (0.25 g) in ether (2 mL) at 0 °C. Boron trifluoride diethyl etherate (32 μ L, 0.25 mmol, 1 equiv) was then added and the resultant mixture was stirred for 2 h. The reaction mixture was then filtered and the filter-cake was washed with ether (3 $\times$ 10 mL). The combined filtrates were washed with water (2 $\times$ 10 mL), dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. Purification by flash chromatography using dichloromethane:ether (19:1) as the eluant afforded the *title compound 1* and 2,6-*epi-1* (16 mg, 14%) as a colorless oil and as a mixture of two diastereoisomers (5:2).

Crystallization of the *title compound 1* and 2,6-*epi-1* from petroleum ether, on slow evaporation of the solvent, afforded the analytically pure *title compound 1* as white shards and as a single diastereoisomer. **R_f** = 0.45, dichloromethane:ether (19:1); **M.p.** 158-160 °C, petroleum ether (lit.²⁰ 164-166 °C); **[α]_D²⁰** = – 6.3 (*c* 0.43, chloroform) [lit.²⁰ **[α]_D²⁰** = – 4.88 (*c* 0.205, chloroform)]; **¹H NMR** (500 MHz, CDCl₃) δ 1.05 (d, *J* = 6.6 Hz, 9H, *Me*-11), 1.49 (s, 9H, *Me*-10), 1.88 (dd, *J* = 10.9, 6.4 Hz, 3H, *H*-6), 2.13 (m, 3H, *H*-5), 2.64 (dd, *J* = 17.6, 6.8 Hz, 3H, *H*-7), 2.85 (apparent d, *J* = 17.6 Hz, 3H, *H*-7'), 3.53 (apparent t, *J* = 8.4 Hz, 3H, *H*-4), 4.16 (apparent t, *J* = 8.4 Hz, 3H, *H*-4'); **¹³C NMR** (126 MHz, CDCl₃) δ 16.0, 18.9, 22.9, 35.5, 47.5, 74.0, 98.9, 107.3, 149.7; **IR** (ef) 2955, 2934, 2876, 1615, 1455, 1378, 1205, 1115, 1008 cm⁻¹; **MS** (CI) *m/z* (rel. intensity) 457 (M + H, 34), 401 (M, 15), 359 (100), 111 (33), 43 (33); **Anal.** Calcd. for C₂₇H₃₆O₆: C, 71.03; H, 7.95. Found: C, 71.10; H, 8.11.

3. ^1H and ^{13}C NMR Spectra

^1H NMR spectrum (400 MHz, CDCl_3) of (2'*R*,4*S*)-4-benzyl-3-[2'-methylpent-4'-ynyl]oxazolidin-2-one **6**.

^{13}C NMR spectrum (101 MHz, CDCl_3) of (2'*R*,4*S*)-4-benzyl-3-[2'-methylpent-4'-ynoyl]oxazolidin-2-one **6**.

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¹H NMR spectrum (400 MHz, CDCl₃) of (4*R*)-3-trichloroacetyl-2,4-dimethyl-4,5-dihydrofuran **9**.

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^{13}C NMR spectrum (101 MHz, CDCl_3) of (4'*R*)-1,1,1-trichloro-3-[4'-methylidihydrofuran-2'*E*-ylidene]propane-2-one **10**.

11

11

^{13}C NMR spectrum (101 MHz, CDCl_3) of (4*R*)-methyl-2,4-dimethyl-4,5-dihydrofuran-3-carboxylate **11**.

^1H NMR spectrum (400 MHz, CDCl_3) of (-)-xyloketal A **1** (crude reaction mixture).

^1H NMR spectrum (400 MHz, CDCl_3) of (-)-xyloketal A **1** (purified by flash chromatography).

^1H NMR spectrum (500 MHz, CDCl_3) of (-)-xyloketal A **1** (recrystallized).