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A Practical Asymmetric Synthesis of A Pseudomonic Acid Precursor from D-Arabinose or D-Xylose

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A PRACTICAL ASYMMETRIC SYNTHESIS OF A PSEUDOMONIC ACID PRECURSOR FROM D-ARABINOSE OR D-XYLOSE

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Abstract- The asymmetric synthesis of multi-gram quantities of a pseudomonic acid precursor is described. Improvements on the literature synthesis of diacetyl arabinal from arabinose are also reported.

The antibiotic properties of the pseudomonic acids, such as pseudomonic acid A (**1**), have caused this class of molecules to be of great interest in recent years.[1] Many non-natural analogs of pseudomonic acids have been prepared by semisynthesis[1] from the natural products and several notable total syntheses have been reported.[1,2] However, the availability of a more structurally diverse array of analogs for biological testing has been limited by the lack of practical access to multi-gram quantities of optically pure synthetic intermediates possessing the core ring of the pseudomonic acids. We now report a simple asymmetric preparation of a pseudomonic acid precursor (**3**) from D-arabinose or D-xylose. The synthesis also includes significant improvements to the standard preparation of diacetyl arabinal from arabinose. Scheme 1 shows the retrosynthesis of pseudomonic acid

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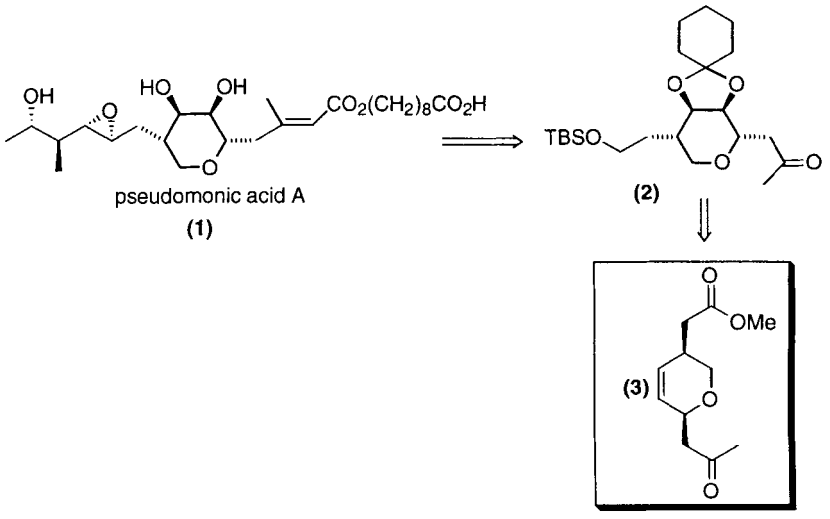
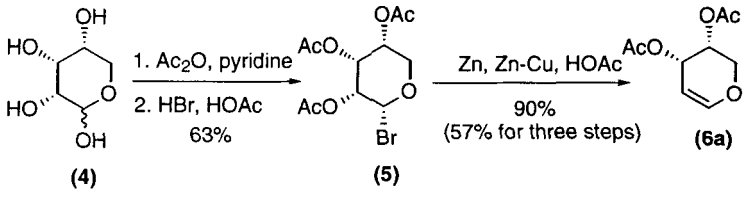
A beginning with precursor (**3**) and going on to known pseudomonic acid intermediate (**2**).[2a-d] The new asymmetric synthesis of (**3**) allows for facile synthesis of the existing pseudomonic acids and new derivatives.



Scheme 1

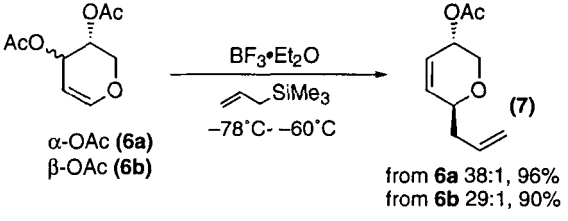
Our original strategy was based on work done previously by Curran and Suh.[2e] However, their procedure to prepare (**3**) based on a mono-Claisen rearrangement of diacetyl arabinal was found to be unsatisfactory when scaled up to multi-gram quantities. The strategy that was found to be successful was allylation of diacetyl arabinal under Lewis acidic conditions and palladium catalyzed addition of sodium dimethyl malonate followed by adjustment of the functional groups.

The literature procedure for formation of diacetyl arabinal from arabinose calls for acetylation of arabinose (**4**) and bromination in a single step to provide (**5**).[3] This procedure gave poor yields (<25%) when scaled up to 1.0 mol. We were able to improve upon the yields of diacetyl arabinal by first peracetylating the arabinose in a separate step as shown in Scheme 2. Subsequent bromide (**5**) formation with HBr/HOAc followed by Zn reduction to form diacetyl D-arabinal (**6a**) went very smoothly from the peracetylated intermediate. When starting with 250 g of D-arabinose, the yield for diacetyl D-arabinal formation was increased from 23% to 57% by using this new procedure.



Scheme 2

Danishefsky has reported the highly specific allylations of various glucals under Lewis acidic conditions.[4a] More recently, Sabol has shown precedent for highly specific allylations of diacetyl D-xylal under similar Lewis acidic conditions.[4b] Because of the similarities between xylal and arabinal and because we had quantities of arabinal available, we decided to attempt a synthesis of **3** by first allylating diacetyl D-arabinal (**6a**) in a manner similar to that of Sabol and Danishefsky.



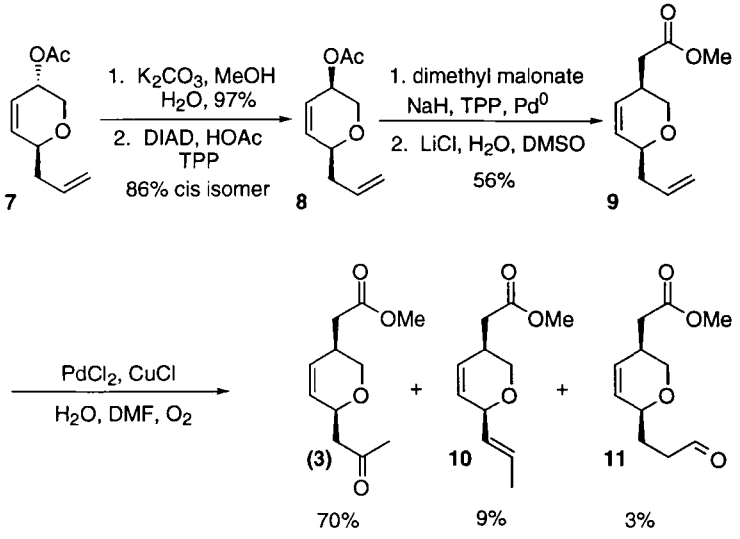
Scheme 3

Allylation of diacetyl D-arabinal (**6a**) under optimized conditions, as shown in Scheme 3, gave the acetate (**7**) in 96% yield as a 38:1 mixture of trans/cis isomers.[5] Because D-xylose is somewhat less expensive than D-arabinose, we also used this as a starting material. Allylation of diacetyl D-xylal (**6b**)[6] under similar conditions[5] gave a 29:1 mixture of trans/cis isomers in 90% yield. Under different conditions ($TiCl_4$, –20°C), Sabol reported a 14:1 ratio of isomers and a 73% yield for the allylation of (**6b**).[4b] These results suggest an S_N1-like mechanism for this allylation.

Hydrolysis of the acetate (**7**) with K_2CO_3 gave the corresponding allylic alcohol. Subsequent Mitsonobu reaction[7] with DIAD and HOAc gave the cis acetate **8** in 86% yield. Palladium(0) catalyzed addition of sodium dimethyl malonate[8] followed by decarboxylation under Krapcho conditions[9] gave the ester **9** in 56% yield. Wacker oxidation[10] of the terminal olefin gave, after silica gel

chromatography, the desired ketone (**3**), the isomerized olefin **10**, and the aldehyde **11** in yields of 70%, 9%, and 3% respectively.

The overall yield of ketone (**3**) was 34% from diacetyl D-arabinal and 19% from D-arabinose. The availability of multi-gram quantities of optically pure **3** provides access to fully synthetic analogs of pseudomonic acids.



Scheme 4

Experimental

General: All reactions were performed under an atmosphere of nitrogen or argon. Acetic anhydride was distilled from quinoline, methylene chloride and BF_3•Et_2O were distilled from CaH, and THF was distilled from sodium/benzophenone.

1α-Bromo-2,3,4-triacetyl-D-arabinose Pyranoside (5). D-Arabinose (250 g, 1.67 mol, Aldrich) (**4**) was suspended in anhydrous pyridine (265 mL, 3.33 mol) in a 2 L flask equipped with a mechanical stirrer. The mixture was cooled to 0 °C and acetic anhydride (200 mL, 2.5 mol) was added. This suspension was warmed to 25°C and stirred for 12 h. Additional acetic anhydride (700 mL, 5.85 mol) and anhydrous pyridine (530 mL, 6.68 mol) were then introduced. Continuous stirring at 25°C for 12 h afforded a clear light brown colored solution. Removal of the excess acetic anhydride and pyridine was

accomplished by repetitive azeotropic evaporation with toluene. After subjecting the residue to high vacuum, a thick syrup-like clear oil formed. This material was used in the following reaction directly.

The crude peracetylated D-arabinose (300 g, 0.943 mol) was dissolved in a mixture of HBr (500 mL, 1.89 mol, 30 wt% in acetic acid) and acetic anhydride (20 mL). The solution was stirred at 25°C until the starting material was completely consumed (45 min). The reaction was then diluted with an equal volume of CH_2Cl_2 and poured into ice-water (2 L). The mixture was extracted with CH_2Cl_2 (2 x 1 L). The combined organic phases were washed with water (2 x 1 L), and with brine (1 L) and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure until solid particles began to form. Diethyl ether (500 mL) was added to precipitate white crystals, which were collected and air dried briefly. The mother liquor was cooled to –20°C to yield a second crop of crystals. Total yield of (**5**) was 200 g (0.592 mol, 63%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.67 (1H, d, J = 3.8 Hz), 5.37 (1H, m), 5.06 (1H, m), 4.18 (1H, d, J = 13.3 Hz), 3.91 (1 H, dd, J = 13.3, 1.7 Hz), 2.13 (3H, s), 2.09 (3H, s), 2.01 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.96 (2 C overlapping), 169.71, 89.59, 67.82, 67.70, 67.46, 64.61, 20.77, 20.68, 20.58.

Acetic Acid (3S*,4R*)-3-Acetoxy-3,4-dihydro-2H-pyran-4-yl Ester (6a). Pyranosyl bromide (**5**) (250 g, 0.74 mol) and zinc dust containing 5% Zn–Cu couple (500 g) were each divided into 5 equal portions. Portions of (**5**) and zinc mixture were added to a mechanically stirred solution of 70% acetic acid (1 L) kept between –10 and –5°C at 15 min intervals. After the last portions of reagents were added, stirring was continued until (**5**) was consumed (30 min). The reaction mixture was filtered and the zinc pellet was rapidly washed with CH_2Cl_2 (500 mL). The zinc was then immediately quenched with cold water. The filtrate was extracted with CH_2Cl_2 (3 x 500 mL). The combined organic layers were then washed with water (3 x 500 mL), with saturated $NaHCO_3$ (500 mL), with brine (500 mL), and dried over anhydrous Na_2SO_4. Removal of the solvent under reduced pressure afforded crude (**6a**). Purification by silica gel chromatography eluting with 10% ethyl acetate in hexane afforded 133 g (0.665 mol, 90%) of (**6a**) as a clear oil. Attempts to distill (**6a**) resulted in significant lowering of yields. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.48 (1H, d, J = 6.0 Hz), 5.42 (1H, dd, J = 4.5 Hz), 5.16 (1H, dt, J = 11.0, 4.3 Hz), 4.83 (1H, dd, J = 5.8 Hz), 3.98 (2H, m), 2.06 (3H, s), 2.05 (3H, s).

Acetic Acid (3R*,6S*)-6-Allyl-3,6-dihydro-2H-pyran-3-yl Ester (7).[4,5] Diacetyl D-arabinal (**6a**) (39.4 g, 197 mmol) was dissolved in CH_2Cl_2 (600 mL) and then cooled to –78°C. BF_3•Et_2O (48.5 mL, 394 mmol) was then added over five min, followed by addition of allyl trimethylsilane (46.7 mL, 256 mmol). The reaction was kept at –78°C for 1 h and then slowly warmed to –60°C. When no more starting material was observable by GC and TLC, the mixture was diluted with H_2O (300 mL) and extracted with Et_2O (3 x 300 mL). The combined organic phases were washed with saturated $NaHCO_3$ (300 mL), with brine (200 mL) and dried over anhydrous $MgSO_4$. Solvent evaporation gave 34.4 g (96%) of the crude allylated product (**7**) as a 38:1 mixture of trans to cis isomers. The crude product (**7**) was used without further purification. IR (thin film): 1740, 1374, 1237 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.90 (1H, dt, J = 10.4, 1.4 Hz), 5.81 (2H, m), 5.23 (1H, m), 5.11 (2H, m), 4.17 (1H, m), 4.11 (1H, dd, J = 11.4, 5.0 Hz), 3.52 (1H, dd, J = 11.5, 6.7 Hz), 2.31 (2H, m), 2.06 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.73, 133.68, 133.25, 124.26, 117.64, 72.86, 64.87, 64.71, 38.44, 20.81.

Synthesis of (3R*,6S*)-6-Allyl-3,6-dihydro-2H-pyran-3-ol and subsequent Mitsonobu reaction to form Acetic Acid (3S*,6S*)-6-Allyl-3,6-dihydro-2H-pyran-3-yl Ester (8).[7] The crude acetate (**7**) (34.4 g, 189 mmol) was dissolved in MeOH (250 mL) and water (150 mL) followed by addition of K_2CO_3 (5.4 g, 38.5 mmol). After 1 h, the reaction was diluted with brine (1000 mL) and extracted with chloroform (8 x 200 mL). The combined organic phases were washed with brine (200 mL) and dried over anhydrous $MgSO_4$. Solvent evaporation gave 25.3 g (96%) of the crude alcohol as a clear oil. The alcohol was used without purification. IR (thin film): 3384, 1266, 1088 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.82 (3H, m), 5.10 (2H, m), 4.14 (2H, m), 4.04 (1H, dd, J = 10.1, 4.7 Hz), 3.41 (1H, dd, J = 11.1, 6.9 Hz), 2.28 (2H, m), 2.05 (1H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 133.71, 130.89, 128.56, 117.28, 72.99, 68.39, 62.18, 38.67.

The crude alcohol (25.3 g, 180.7 mmol), Ph_3P (52.08 g, 198.8 mmol) and glacial acetic acid (11.4 mL, 198.9 mmol) were dissolved in THF (650 mL) and the solution cooled to –42°C. DIAD (39.14 mL, 198.8 mmol) was then added over a 1 h period. After addition was complete, the reaction was kept at –42°C for 1 h and was then warmed to 25°C and stirred for 1 h followed by quenching with water

(400 mL). The mixture was extracted with ethyl acetate (4 x 400 mL). The combined organic phases were washed once with brine (200 mL) and dried over anhydrous $MgSO_4$. Solvent removal under reduced pressure gave a white slurry that was diluted with 10% ethyl acetate/hexane (500 mL) and filtered. Solvent removal under reduced pressure yielded the crude acetate **8** as a yellow oil. Purification by silica gel chromatography eluting with hexanes/ethyl acetate (8:1) afforded 28.3 g (86.1%) of the cis isomer **8**. IR (thin film): 1732, 1372, 1239 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.00 (1H, d, J = 10.4 Hz), 5.86 (2H, m), 5.12 (2H, m), 4.99 (1H, m), 4.05 (1H, d, J = 12.8 Hz), 3.75 (1H, dd, J = 12.9, 2.8 Hz), 2.08 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.20, 135.20, 133.48, 122.08, 117.11, 72.96, 67.36, 64.19, 38.70, 20.70; MS 141, 132, 81, 43; Exact mass cald for $C_7H_9O_3$ 141.0552; found 141.0561.

(3S*,6S*)-(6-Allyl-3,6-dihydro-2H-pyran-3-yl)-acetic Acid Methyl Ester (9).[8,9] The cis allyl acetate **8** (27.21 g, 149.5 mmol) was dissolved in THF (50 mL). Ph_3P (3.92 g, 14.95 mmol) and $(Ph_3P)_4Pd$ (0.430 g, 0.38 mmol) were then added. In a separate flask, NaH (60% in mineral oil, 6.73 g, 224 mmol) was added to THF (650 mL) followed by slow addition of dimethylmalonate (23.9 mL, 209 mmol). After 15 min, the stirring of the sodium dimethyl malonate solution was stopped and the residual solid allowed to settle for 10 minutes. The supernatant liquid was then cannulated to the 1L flask containing the cis allyl acetate **8** and Pd^0, care was taken not to transfer any particulate matter from the bottom of the flask. After transfer was complete, the solution was heated to 70°C. After 8 h, an additional 50 mmol of malonate anion was prepared and transfered to the reaction as above. After four additional hours, the reaction was complete by GC with only the desired diester and the decarboxylated analog **9** present. The reaction was poured into cold water (800 mL) and extracted with ether (4 x 300 mL). The combined organics were washed once with brine (200 mL) and dried over anhydrous $MgSO_4$. Solvent evaporation gave the crude diester as an orange oil, which was not purified before decarboxylation. Due to excess Ph_3P present in the crude product, an accurate yield for this step could not be calculated.

The crude diester (150 mmol based on acetate before malonate addition) was dissolved in dimethyl sulfoxide (350 mL). LiCl (12.6 g, 300 mmol) and H_2O (2.7 mL, 150 mmol) were then added and the solution heated to reflux. The reaction was complete after 1.5 h and was then cooled to 25°C. The cooled solution was

poured into cold water (1 L) and extracted with ether (5 x 300 mL). The combined organic phases were washed with water (2 x 400 mL), once with brine (200 mL) and dried over anhydrous $MgSO_4$. Solvent evaporation yielded the crude ester **9** as a yellow oil. Purification by silica gel chromatography eluting with hexanes/ethyl acetate (9:1) gave 16.51 g (56.3% from **8**) of the ester **9** as a pale yellow oil. IR (thin film): 1736, 1437, 1358, 1267 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.80 (2H, m), 5.67 (1H, d, J = 10.3 Hz), 5.10 (2H, m), 4.12 (1H, m), 3.76 (2H, m), 3.67 (3H, s), 2.48 (3H, m), 2.28 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.27, 133.94, 130.12, 127.60, 116.76, 73.41, 66.94, 51.06, 39.21, 36.95, 30.90; MS 196, 165, 155, 95; exact mass calcd for $C_8H_{11}O_3$ 155.0708; found 155.0697; $[\alpha]_D^{25} = -56.30$ in MeOH (c = 0.011).

(3S*,6S*)-[6-(2-Oxo-propyl)-3,6-dihydro-2H-pyran-3-yl]-acetic Acid Methyl Ester (3), (3S*,6S*)-(6-Propenyl-3,6-dihydro-2H-pyran-3-yl)-acetic Acid Methyl Ester (10), and (3S*,6S*)-[6-(3-Oxo-propyl)-3,6-dihydro-2H-pyran-3-yl]-acetic Acid Methyl Ester (11).[10,11] $PdCl_2$ (0.132 g, 0.45 mmol) and CuCl (1.77 g, 17.9 mmol) were added to DMF (44 mL) and H_2O (22 mL) and the mixture was cooled to 0°C. Oxygen was then bubbled through the solution for 2 h. The reaction turned a green color after 15 min and then turned dark brown after the 2 h period. The solution was then warmed to 25°C and the ester **9** (14.4 g, 76.53 mmol) was added in DMF (6 mL). After 14 h there was still starting olefin left by GC and additional $PdCl_2$ (0.5 mmol) was added. After 37 h the reaction was complete by GC and the solution was poured into 1N HCl (500 mL). Brine (300 mL) was added and the solution extracted with ether (6 x 200 mL). The combined organics were washed once with brine (200 mL) and dried over anhydrous $MgSO_4$. Solvent evaporation gave the crude mixture of (**3**), **10**, and **11** as an orange oil. Purification by silica gel chromatography using gradient elution with ethyl acetate/hexanes (10%, 15%, 20%, 25%) gave 3.0 g (10%) of the isomerized olefin **10**, 11.0 g (70%) of the ketone (**3**), and 1.0 g (3%) of the aldehyde **11**.

Ketone (**3**): IR (thin film): 1736, 1439, 1360, 1167 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.83 (1H, m), 5.65 (1H, d, J = 10.5 Hz), 4.52 (1H, dt, J = 7.6, 2.0 Hz), 3.72 (2H, m), 3.67 (3H, s), 2.69 (1H, dd, J = 16.0, 8.1 Hz), 2.49 (2H, dd, J = 17.7, 5.0 Hz), 2.18 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.72, 171.92, 129.50, 127.82, 70.11, 66.52, 50.93, 48.05, 36.69, 30.58, 30.09; MS

212, 195, 138, 95, 82; exact mass calcd for $C_8H_{10}O_2$ 138.0681; found 138.0688; $[\alpha]_D^{25} = -32.10°$ in MeOH (c = 0.011).

Internal olefin **10**: IR (thin film): 1736, 1437, 1169 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.72 (3H, m), 5.46 (1H, dd, *J* = 7.1, 1.6 Hz), 4.48 (1H, d, *J* = 6.9 Hz), 3.75 (2H, m), 3.67 (3H, s), 2.44 (3H, m), 1.70 (3H, d, *J* = 5.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.73, 130.09, 129.92, 129.05, 127.63, 74.77, 66.45, 51.53, 37.08, 31.09, 17.73.

Aldehyde **11**: IR (thin film): 1732, 1435, 1257, 1167 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.77 (1H, t, *J* = 1.6 Hz), 5.85 (1H, dd, *J* = 9.8, 2.1 Hz), 5.60 (1H, d, *J* = 9.8 Hz), 4.12 (1H. m), 3.72 (2H, m), 3.67 (3H, s), 2.53 (2H, dt, *J* = 6.1, 1.0 Hz), 2.45 (3H, m), 1.95 (1H, m), 1.75 (1H, virtual sextet, *J* = 7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.91, 172.31, 129.99, 128.34, 72.73, 66.81, 51.22, 39.02, 36.95, 30.87, 26.89.

References and Notes

1. (a) Forrest, A. K.; O'Hanlon, P. J.; Walker, G. *J. Chem. Soc. Perkin Trans.* **1994**, *21*, 2657; *Tetrahedron* **1994**, *36*, 10739; (b) Yanagisawa, T.; Lee, J. T.; Wu, H. C.; Kawakami, M. *J. Biol. Chem.* **1994**, *39*, 24304; (c) Clayton, J. P.; Oliver, R. S.; Rogers, N. H.; King, T. J. *J. Chem. Soc. Perkin Trans.* **1979**, 838; O'Hanlon, P. J.; Rogers, N. H. *J. Chem. Soc. Perkin Trans.* **1983**, 2655; (d) Schonenberger, B.; Summermatter, W.; Ganter, C. *Helv. Chem. Acta.* **1982**, *65*, 2333; (e) Bates, H. A.; Farina, J.; Tong M. *J. Org. Chem.* **1986**, *51*, 2637. (f) For a recent review of pseudomonic acid syntheses see Class, Y. J.; DeShong, P. *Chem. Rev.* **1995** in press.

2. (a) Jackson, R. F. W.; Raphael, R. A.; Stibbard, J. H. A.; Tidbury, R. C. *J. Chem. Soc. Perkin Trans.* **1984**, 2159; (b) Kozikowski, A. P.; Schmiesing, R. J.; Sorgi, K. L. *J. Am. Chem. Soc.* **1980**, *102*, 6577; *Tetrahedron Lett.* **1981**, 2059; (c) Snider, B. B; Rodini, R. J.; Karras, M.; Kirk, T. C.; Deutsch, E. A.; Cordova, R.; Price, R. T. *Tetrahedron* **1981**, *37*, 3927; Snider, B. B.; Rodini, D. J.; Kirk, T. C.; Cordova, R. *J. Am. Chem. Soc.* **1982**, *104*, 555; Snider, B. B.; Phillips, G. B. *J. Am. Chem. Soc.* **1982**, *104*, 1113.; Snider, B. B.; Phillips, G. B.; Cordova, R. *J. Org. Chem.* **1983**, *48*, 3003; (d) Fleet, G.W.J.; Spensley, C. R. C. *Tetrahedron Lett.* **1982**, 109; Fleet G. W. J.; Gough, M. J. *Tetrahedron Lett.* **1982**, 4509; Fleet, G. W. J.; Gough, M. J.; Shing, T. K. M.

Tetrahedron Lett. **1983**, 3661.; (e) Curran, D. P., Suh, Y.-G. *Carbohydr. Res.* **1987**, 161.

3. Humuller, F. *Methods Carbohydr. Res.* **1962**, 83.

4. (a) Danishefsky, S.; Kerwin, J. F. *J. Org. Chem.* **1982**, *47*, 3803; (b) Sabol, J. S.; Cregge, R. J. *Tetrahedron Lett.* **1989**, *30*, 6271.

5. When allylating arabinal on large scale (> 1 mol), or allylating xylal on any scale, we found that slow addition of $BF_3 \cdot Et_2O$ to the allyl silane and arabinal at –78°C gave more reliable results.

6. Xylal can be synthesized by the same route (Scheme 2) as arabinal with similar results.

7. Farina, V. *Tetrahedron Lett.* **1989**, *30*, 6645.

8. Trost, B. M.; Verhoeven, T. R. *J. Am. Chem. Soc.* **1980**, *102*, 4730.

9. Krapcho, A. P. *Synthesis* **1982**, 805.

10. Tsuji, J.; Shimaza, I.; Yamamoto, K. *Tetrahedron Lett.* **1976**, 2975. Tsuji, J. *Synthesis* **1984**, 369.

11. Compounds **10** and **11** were further purified by HPLC but neither compound could be isolated in completely pure form.

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