Preparation of Organometallic Complexed Sugars: Hetero Diels−Alder Reactivity of Tricarbonyl(formyltrimethylenemethane)-iron

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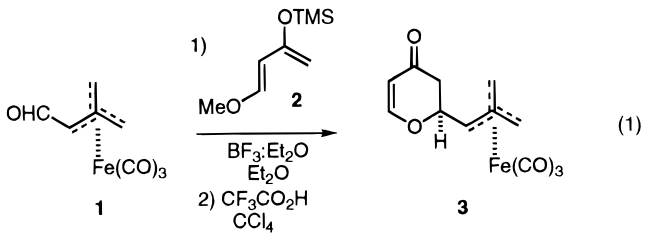
There has been considerable recent interest in the preparation of biologically important molecules which are "tagged" with a metal carbonyl group. Such compounds have been examined for use in carbonyl metallo immunoassays (CMIA) using FT-IR spectroscopy.[1] While the majority of these "tagged" molecules are within the steroidal family, the preparation of organometallic nucleotides,[2] leukotrienes,[3] and carbohydrates[4] have also been reported. σ-Bonded manganese and iron carbonyl complexes of carbohydrates have been prepared by displacement of 1-glucosyl halides or 6-deoxy-6-haloglucosides. Due to the lability of the metal−carbon σ bond, the majority of these metallo-sugar complexes are reported to be unstable. As part of our broader interest in developing methodology for the application of (TMM)$Fe(CO)_3$ complexes [(TMM) = trimethylenemethane] in organic synthesis,[5] we have investigated the hetero Diels−Alder reaction[6] of tricarbonyl(formyl-TMM)iron (**1**)[7] and further elaboration into 4,6-dideoxypyranoside derivatives.

The reaction of racemic **1** with 1-methoxy-3-[(trimethylsilyl)oxy]-1,3-butadiene (**2**), in the presence of $BF_3{\cdot}Et_2O$, followed by treatment with trifluoroacetic acid gave the dihydropyrone complex **3** as a *single* diastereomer (52%, eq 1).[8] Since cyclocondensation of **1** with **2** in the presence of $BF_3{\cdot}Et_2O$ occurred in a diastereospecific fashion, the use of other Lewis acid catalysts was not attempted. The relative stereochemistry of **3** was assigned as indicated on the basis of single crystal X-ray diffraction analysis.[9] Dihydropyrone **3** arises via attack of **2**, in the *s-trans* conformer, on the face of the aldehyde which is opposite to the sterically bulky $Fe(CO)_3$ group. This present diastereoselectivity is consistent with that observed for addition of nucleophiles to **1**.[7,10] This high selectivity for this cyclocondensation (>25:1) is superior to that observed for the cyclocondensation of (dienal)-$Fe(CO)_3$ complexes (**4**) with **2** (<4:1).[11] The aldehyde complexes **1** and **4** may each exist in an equilibrium between their two conformers, *s-trans* and *s-cis* (Figure 1). In the case of **1**, the *s-trans* conformer is more stable than the *s-cis* conformer due to the severe steric interactions between the carbonyl oxygen and the neighboring methylene group, while for **4** the *s-trans* and *s-cis* conformers are closer in energy.[12]



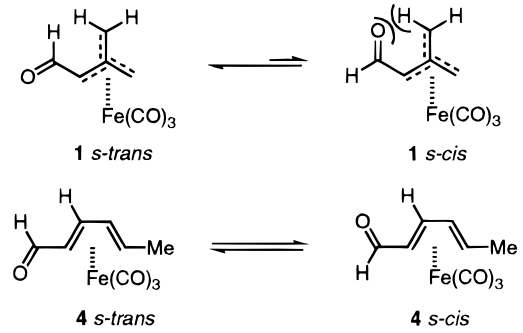
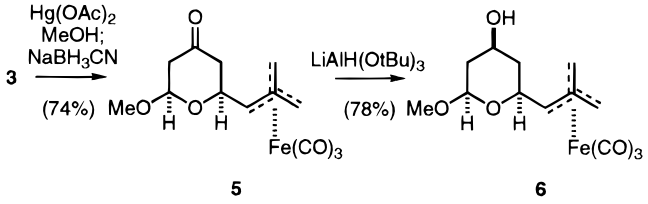


Figure 1.

Scheme 1



Reaction of **3** with mercuric acetate in methanol, followed by treatment with $NaBH_3CN$ gave the methoxy ketone **5** (74%, Scheme 1). Compound **5** was assigned the β-stereochemistry on the basis of ^{1}H NMR signal for the anomeric proton (δ 4.49, dd, J = 2.8, 8.9 Hz). Reduction of **5** with $LiAlH(OtBu)_3$ gave alcohol **6** (78%, Scheme 1). Reduction of β-pyranoside ketones under these conditions is expected to afford predominantly the equatorial alcohol.[13] The product was assigned the stereochemistry as shown on the basis of its ^{1}H NMR spectral data. In particular, the signals for the H1 (δ

(1) (a) Jaouen, G.; Vessières. A.; Top, S.; Ismail, A. A.; Butler, I. S. *J. Am. Chem. Soc.* **1985**, *107*, 4778−80. (b) Jaouen, G.; Vessières. A. *Pure Appl. Chem.* **1985**, *57*, 1865−74.

(2) (a) Dalla Riva Toma, J. M.; Bergstrom, D. E. *J. Org. Chem.* **1994**, *59*, 2418−22. (b) Bergstrom, D. E.; Schmaltz, T. *Nucleosides Nucleotides* **1989**, *8*, 1057−9. (c) Bergstrom, D. E.; Beal, P.; Lind, R. *Nucleosides Nucleotides* **1989**, *8*, 1061−3.

(3) (a) Pinsard, P.; Lellouche, J.-P.; Beaucourt, J.-P.; Grée, R. *Tetrahedron Lett.* **1990**, *31*, 1141−4. (b) Franck-Neumann, M.; Colson, J.-P. *Synlett* **1991**, 891−4.

(4) (a) DeShong, P.; Slough, G. A.; Elango, V.; Trainor, G. L. *J. Am. Chem. Soc.* **1985**, *107*, 7788−90. (b) DeShong, P.; Slough, G. A.; Elango, V. *Carbohydrate Res.* **1987**, *171*, 342−5. (c) Trainor, G. L. *J. Organomet. Chem.* **1985**, *282*, C43−5. (d) Trainor, G. L.; Smart, B. E. *J. Org. Chem.* **1983**, *48*, 2447−8. (e) Baer, H. R.; Hanna, H. R. *Carbohydrate Res.* **1982**, *102*, 169−83. (f) Adams, M. J.; Hall, L. D. *Can. J. Chem.* **1980**, *58*, 1188−97.

(5) (a) Donaldson, W. A.; Hossain, M. A.; Cushnie, C. D. *J. Org. Chem.* **1995**, *60*, 1611−8. (b) Donaldson, W. A.; Hossain, M. A. *Tetrahedron Lett.* **1992**, *33*, 4107−10. (c) Donaldson, W. A.; Hossain, M. A. *Tetrahedron Lett.* **1991**, *32*, 7047−50.

(6) (a) Danishefsky, S.; Kerwin, J. F., Jr.; Kobayshi, S. *J. Am. Chem. Soc.* **1982**, *104*, 358−60. (b) Daniskefsky, S. J. *Aldrichimica Acta* **1986**, *19*, 59−69. Boger, D. L.; Weinreb, S. M. *Hetero Diels-Alder Methodology in Organic Synthesis*; Academic Press: New York, 1987.

(7) Bonazza, B. R.; Lillya, C. P.; Magyar, E. S.; Scholes, G. *J. Am. Chem. Soc.* **1979**, *101*, 4100−6.

(8) All compounds described are racemic mixtures of enantiomers. Only one enantiomer has been diagrammed for clarity.

(9) Young, V. G., Jr.; Kleindl, P. J.; Donaldson, W. A. *Bull. Chim. Soc. Belg.*, submitted for publication.

(10) Franck-Neumann, M.; Martina, D.; Heitz, M.-P. *Tetrahedron Lett.* **1989**, *30*, 6679−82.

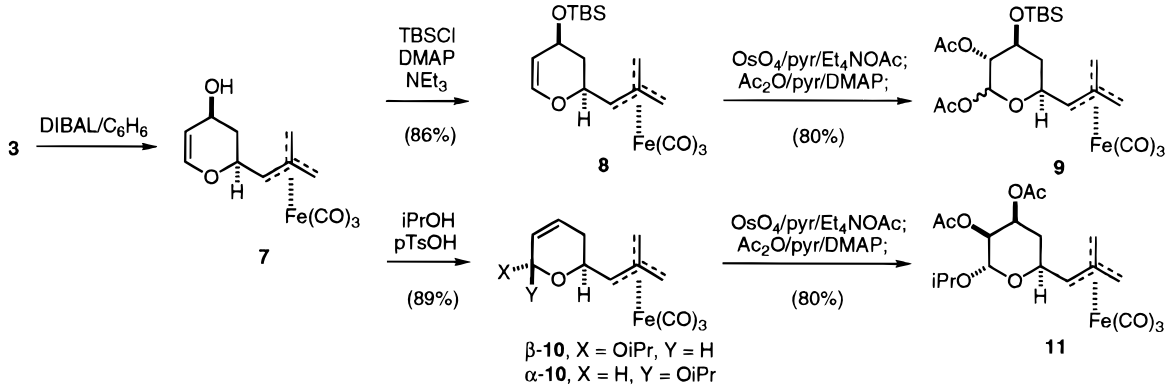
(11) (a) Donaldson, W. A.; Tao, C.; Bennett, D. W.; Grubisha, D. S. *J. Org. Chem.* **1991**, *56*, 4563−6. (b) Tao, C.; Donaldson, W. A. *J. Org. Chem.* **1993**, *58*, 2134−43.

(12) (a) Brookhart, M.; Harris, D. L. *J. Organomet. Chem.* **1972**, *42*, 441−6. (b) Howell, J. A. S.; Walton, G.; Tirvengadum, M.-C.; Squibb, A. D.; Palin, M. G. *J. Organomet. Chem.* **1991**, *401*, 91−123.

(13) Danishefsky, S.; Langer, M. *J. Org. Chem.* **1985**, *50*, 3672−4.

S0022-3263(97)00234-X CCC: $14.00

Scheme 2



4.21, dd, J = 1.8, 9.6 Hz) and for H3 (δ 3.83, br m, HW = 26 Hz) are consistent with a tetrahydropyran bearing all equatorial substituents.

Reduction of **3** gave the pseudo glycal **7** (86%) which was protected as the TBS ether **8** (86%, Scheme 2). Osmylation of **8**, followed by acylation gave the 4,6-dideoxy-glucopyranose TMM complex **9** as a separable mixture of α- and β-anomers (2:1, 80%, Scheme 2).[14] The stereochemistry of the products was assigned on the basis of their ^{1}H NMR spectral data. In particular, the signals for $H2_{ax}$ and $H3_{ax}$ of **9**-α appear at δ 4.80 (dd, J_{1-2ax} = 3.7, $J_{2ax-3ax}$ = 9.5 Hz) and 4.03 (dt, $J_{3ax-4eq}$ = 4.5, $J_{3ax-4ax}$ = 9.4 Hz), respectively, while for **9**-β the signal for $H2_{ax}$ appears at δ 4.83 (t, $J_{1-2ax} = J_{2ax-3ax}$ = 8.8 Hz). Ferrier rearrangement[15] of **7** (iPrOH/pTsOH) gave the unsaturated acetal **10** as a mixture of anomers (4.5:1, 89%, Scheme 2) from which the α-anomer could be cleanly separated by chromatography. Osmylation of **10**, followed by in acylation gave the 4,6-dideoxy-mannopyranose TMM complex **11** (81%, Scheme 2). The stereochemical assignment for **11** was based on its ^{1}H NMR spectral data.

All of the $(TMM)Fe(CO)_3$ complexes **3**, **5**−**11** exhibit five signals in their ^{1}H NMR spectra at ca. δ 2.9 (dd, J = 2.2, 9−10 Hz), 2.6−2.45 (d, J = ca. 4.4 Hz), 2.15 (d, J = 2.2 Hz), 1.9−1.8 (s), and 1.8−1.7 (d, J = 4.4 Hz) corresponding to the TMM protons. The carbohydrate derivatives **6**, **9**, and **11** all exhibit characteristic metal carbonyl stretching frequencies of ca. 2060 and 1990 cm^{-1} which could be useful for CMIA. Since the precursor **1** can be obtained in optically active form via classical resolution[10,16] or by enzyme-mediated kinetic resolution,[17] it should be possible to obtain these carbohydrate−TMM complexes in optically active form. Furthermore, since stability of the metal carbonyl complexes under biological conditions is important for CMIA, it should noted that $(TMM)Fe(CO)_3$ complexes appear to be more robust than the corresponding $(diene)Fe(CO)_3$ counterparts under a variety of reaction conditions including oxidations.[18]

Experimental Section

General Data. Unless otherwise noted, reactions were carried out in flame-dried glassware under an atmosphere of nitrogen. Spectrograde solvents were used without purification with the exception of tetrahydrofuran and diethyl ether which were distilled from the potassium and sodium benzophenone ketyls, respectively; methanol which was distilled from magnesium turnings; and CH_2Cl_2 which was distilled from P_2O_5. 1-Methoxy-3-[(trimethylsilyl)oxy]-1,3-butadiene (90%) was purchased from Aldrich Chemical Co. and used without further purification. Column chromatography was performed on silica gel grade 62, 60−200 mesh, 150 Å (Aldrich). Elemental analyses were obtained from Midwest Microlabs, LTD, Indianapolis, and high resolution mass spectral determinations were made at the Washington University Resource for Biomedical and Bio-organic Mass Spectrometry. Melting points were determined for samples in open capillaries and are uncorrected, and ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ solution at 300 MHz and 75 MHz, respectively.

Cyclocondensation of 1. To a solution of aldehyde **1**[7] (3.34 g, 15.0 mmol) and 1-methoxy-3-[(trimethylsilyl)oxy]-1,3-butadiene (**2**) (3.23 mL, 15.0 mmol) in ether (25 mL) at −78 °C was added dropwise over a period of 10 min $BF_3{\cdot}Et_2O$ (1.9 mL, 15 mmol). The mixture was stirred for 3.5 h, and then saturated aqueous $NaHCO_3$ was added. The mixture was allowed to warm to rt and separated, and the aqueous layer was extracted with ether. The combined organic layers were washed with brine and dried ($MgSO_4$), and the solvent was evaporated to afford a reddish brown crystalline mass. This residue was dissolved in CCl_4 (25 mL), trifluoroacetic acid (7 drops) was added, and the mixture was stirred for 5 h at rt. Saturated aqueous $NaHCO_3$ was added, the layers were separated, and the aqueous layer was extracted with ether. The combined organic layers were washed with brine and dried ($MgSO_4$), and the solvent was evaporated. The residue was purified by chromatography (SiO_2, hexanes−ethyl acetate (10:1 to 2:1 gradient)) to give **3** as a yellow solid (2.24 g, 52%). **3**: mp 107−110 °C; IR ($CHCl_3$, cm^{-1}) 2052, 2012, 1690, 1618; ^{1}H NMR ($CDCl_3$) δ 7.35 (dd, J = 0.6, 6.0 Hz, 1H), 5.42 (dd, J = 1.1, 6.0 Hz, 1H), 3.91 (ddd, J = 3.7, 10.0, 13.7 Hz, 1H), 2.92 (dd, J = 2.4, 10.0 Hz, 1H), 2.78 (dd, J = 13.4, 16.6 Hz, 1H), 2.58 (ddd, J = 1.2, 3.4, 16.6 Hz, 1H), 2.46 (dd, J = 1.0, 4.2 Hz, 1H), 2.21 (dd, J = 1.5, 1.9 Hz, 1H), 1.92 (s, 1H), 1.84 (d, J = 4.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 211.8, 211.3, 191.4, 163.3, 107.2, 103.8, 77.9, 74.7, 52.3, 51.8, 45.5. Anal. Calcd for $C_{12}H_{10}O_5Fe$: C, 49.69; H, 3.47. Found: C, 49.49; H, 3.48.

***β*-Methyl Glucoside 5.** To a solution of dihydropyrone **3** (188 mg, 0.649 mmol) in dry methanol (7 mL) was added $Hg(OAc)_2$ (226 mg, 0.798 mmol). The reaction mixture was stirred at rt for 24 h, diluted with methanol (2 mL), and cooled to −78 °C. To the cooled solution was added a solution of $NaBH_3CN$ (18.9 mg, 0.301 mmol) in methanol (2 mL). The reaction mixture was stirred for 2.5 h, diluted with ethyl acetate, and filtered, and the solvent was evaporated. The residue was purified by chromatography (SiO_2, hexanes−ethyl acetate (20:1 to 2:1 gradient)) to give **5** as a yellow syrup which solidified in the refrigerator (155 mg, 74%). **5**: mp ≈ 35 °C; IR ($CHCl_3$, cm^{-1}) 2062, 1996, 1724, 1130; ^{1}H NMR ($CDCl_3$) δ 4.49 (dd, J = 2.8, 8.9 Hz, 1H), 3.54 (s, 3H), 3.15 (dt, J = 3.6, 10.0 Hz, 1H), 2.93 (dd, J = 2.3, 9.4 Hz, 1H), 2.63 (ddd, J = 1.6, 2.8, 14.9 Hz, 1H), 2.58−2.35 (m, 4H), 2.18 (dd, J = 1.1, 2.3 Hz, 1H), 1.88 (s, 1H), 1.81 (d, J = 4.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 211.2, 211.0, 210.9, 204.6, 103.3, 101.6, 78.2, 70.9, 57.3, 53.1, 52.3, 50.9, 48.0. Anal.

(14) Similar methodology was used for the preparation of (±)-chalcose from acetaldehyde: Danishefsky, S.; Kerwin, J. F., Jr. *J. Org. Chem.* **1982**, *47*, 1597−8.

(15) Ferrier, J. P. *J. Chem. Soc.* **1964**, 5443−9.

(16) Franck-Neumann, M.; Stöber, P.; Passmore, G. *Tetrahedron: Asymmetry* **1996**, *7*, 3193−3202.

(17) Lee, K. M.; Martina, D.; Park, C. V.; Biellmann, J.-F. *Bull. Kor. Chem. Soc.* **1990**, *11*, 412−3.

(18) (a) Franck-Neumann, M.; Kastler, A. *Synlett* **1995**, 61−3. (b) Donaldson, W. A.; Cushnie, C. D.; Guo, S.; Kramer, M. J. *Transition Met. Chem.*, submitted for publication.

Calcd for $C_{13}H_{14}O_6Fe$: C, 48.48; H, 4.38. Found: C, 49.28; H, 4.68.

Reduction of *β*-Methyl Glucoside 5. To a solution of **5** (89 mg, 0.28 mmol) in dry THF (20 mL) was added dropwise via syringe a solution of $LiAlH(OtBu)_3$ (83 mg, 0.33 mmol) in dry THF (10 mL). The reaction mixture was stirred at rt for 1.5 h, at which time TLC analysis indicated completion. Water (10 mL) was added dropwise, the mixture was extracted with ether, the combined extracts were washed with brine and dried ($MgSO_4$), and the solvent was evaporated. The residue was purified by chromatography (SiO_2, hexanes−ethyl acetate (5:1 to 4:1 gradient)) to give **6** as a yellow oil which solidified in the refrigerator (71 mg, 78%). **6**: mp 55−59 °C; IR ($CHCl_3$, cm^{-1}) 3435, 2060, 1989; ^1H NMR ($CDCl_3$) δ 4.21 (dd, J = 1.8, 9.6 Hz, 1H), 3.83 (br m, HW = 26 Hz, 1H), 3.49 (s, 3H), 2.98 (dd, J = 1.5, 9.3 Hz, 1H), 2.92 (br q, J = 10.7 Hz, 1H), 2.42 (d, J = 4.6 Hz, 1H), 2.17 (m and s, 2H), 2.06 (br d, J = 12 Hz, 1H), 1.83 (s, 1H), 1.76 (d, J = 4.4 Hz, 1H), 1.5−1.2 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 210.9, 210.8, 210.6, 102.7, 101.0, 79.0, 70.7, 66.6, 56.7, 52.4, 51.5, 44.4, 40.4; EI-HRMS m/z 208.0183 (calcd for $C_9H_{12}O_2Fe$ (M - 3CO and MeOH) m/z 208.0187).

Reduction of Dihydropyrone 3. To a solution of dihydropyrone **3** (0.71 g, 2.4 mmol) in C_6H_6 (35 mL) at 0 °C was added dropwise via syringe a solution of DIBAL (1.0 M in toluene, 4.9 mL, 4.9 mmol). The reaction mixture was stirred at rt for 40 min, diluted with MeOH (5 mL), and poured into saturated aqueous Na_2SO_4. The precipitate which formed was removed by filtration and the solid washed with ethyl acetate. The filtrate was extracted with ethyl acetate, the combined extracts were dried ($MgSO_4$), and the solvent was evaporated. The residue was purified by chromatography (SiO_2, hexanes−ethyl acetate (10:1 to 1:1 gradient)) to give **7** as a yellow oil (0.616 g, 86%). **7**: IR ($CHCl_3$, cm^{-1}) 3433, 2050, 1998; ^1H NMR ($CDCl_3$) δ 6.36 (br d, J = 5.8 Hz, 1H), 4.74 (dt, J = 6.1, 2.0 Hz, 1H), 4.45 (br t, 1H), 3.50 (s and m, 2H), 2.95 (dd, J = 2.4, 10.0 Hz, 1H), 2.46 (d, J = 4.4 Hz, 1H), 2.32 (br dd, J = 6.6, 13.3 Hz, 1H), 2.15 (dd, J = 1.0, 2.4 Hz, 1H), 1.9−1.8 (m, 1H), 1.83 (s, 1H), 1.75 (d, J = 4.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 210.9, 210.8, 209.9, 145.1, 105.2, 103.2, 78.1, 73.1, 62.5, 52.2, 51.2, 41.8; EI-HRMS m/z 264.0092 (calcd for $C_{11}H_{12}O_4Fe$ (M − CO) m/z 264.0085).

***tert*-Butyldimethylsilyl Ether 8.** To a solution of **7** (0.161 g, 0.551 mmol) in CH_2Cl_2 (10 mL) were added NEt_3 (0.6 mL, 4 mmol), *tert*-butyldimethylsilyl chloride (0.129 g, 0.829 mmol), and DMAP (6 mg). The reaction mixture was stirred for 11 h, and additional *tert*-butyldimethylsilyl chloride (0.134 g, 0.887 mmol) was added. The reaction mixture was stirred for an additional 25 h and then treated with saturated aqueous $NaHCO_3$. The layers were separated, and the aqueous layer was extracted with ether. The combined organic layers were dried ($MgSO_4$) and concentrated. The residue was purified by chromatography (SiO_2, hexanes−ethyl acetate (10:1 to 2:1 gradient)) to give **8** as a yellow oil (0.192 g, 86%). **8**: IR ($CHCl_3$, cm^{-1}) 2054, 2000, 1641, 1119, 1074; ^1H NMR ($CDCl_3$) δ 6.30 (dd, J = 0.9, 6.3 Hz, 1H), 4.65 (td, J = 1.9, 6.3 Hz, 1H), 4.44 (m, 1H), 3.49 (dt, J = 2.4, 10.0 Hz, 1H), 3.02 (dd, J = 2.3, 9.9 Hz, 1H), 2.45 (d, J = 4.2 Hz, 1H), 2.17−2.11 (m, 2H), 1.92 (ddd, J = 8.5, 10.7, 13.8 Hz, 1H), 1.81 (s, 1H), 1.73 (d, J = 4.4 Hz, 1H), 0.90 (s, 9H), 0.08 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 211.1, 210.9, 210.0, 144.4, 105.8, 103.1, 78.7, 72.9, 63.0, 52.1, 51.2, 41.9, 31.6, 25.8, 22.6, 18.1, −4.6.

1,2-Di-*O*-acetyl-3-*O*-(*tert*-butyldimethylsilyl)-4,6-dideoxy-6-TMM-glucopyranose (9). To a solution of **8** (0.50 g, 0.123 mmol) in acetone (10 mL) was added Et_4NOAc (0.011 g, 0.042 mmol). After 30 min, the solution was cooled to 0 °C, and a solution of OsO_4 (1 mL, 0.196 M, 0.196 mmol) in pyridine was added dropwise over a 5 min period, followed by tBuOOH (0.03 mL, 0.30 mmol). After 3 h, the reaction mixture was quenched with saturated aqueous $NaHSO_3$ (7 mL), warmed to rt, and stirred for 3 h. The mixture was diluted with ethyl acetate and filtered through a filter aid. The filtrate was washed with 1 N HCl, saturated aqueous $NaHCO_3$, and brine, dried ($MgSO_4$), and concentrated. The residue was dissolved in CH_2Cl_2 (10 mL), and pyridine (1.2 mL), acetic anhydride (1.4 mL), and DMAP (6 mg) were added. The reaction mixture was stirred for 47 h, diluted with water, and extracted with ether. The ether extracts were washed with 1 N HCl and saturated aqueous $NaHCO_3$, dried ($MgSO_4$), and concentrated. The residue was purified by chromatography (SiO_2, hexanes−ethyl acetate (10:1)) to give α-**9** as a pale yellow solid (35 mg, 54%) followed by *β*-**9** as a pale yellow solid (17 mg, 26%).

α-**9**: mp 122−127 °C; IR (cm^{-1}): 2063, 1994, 1736, 1250; ^1H NMR ($CDCl_3$) δ 6.30 (d, J = 3.7 Hz, 1H), 4.80 (dd, J = 3.7, 9.5 Hz, 1H), 4.03 (dt, J = 4.5, 9.4 Hz, 1H), 3.45 (m, 1H), 2.78 (dd, J = 2.6, 9.6 Hz, 1H), 2.41 (d, J = 4.5 Hz, 1H), 2.15 (br s, 1H), 2.10 (m, 1H), 2.05 (s, 6H), 1.90 (m, 1H), 1.81 (s, 1H), 1.73 (d, J = 4.5 Hz, 1H), 0.86 (s, 9H), 0.10 (s, 3H), 0.06 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 210.2, 103.1, 90.1, 73.4, 69.0, 65.7, 52.2, 51.2, 43.8, 25.5, 20.7, −4.5, −4.8.

β-**9**: mp 127−128 °C; IR ($CDCl_3$) 2063, 1996, 1749, 1242, 1055 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.51 (d, J = 8.3 Hz, 1H), 4.83 (t, J = 8.8 Hz, 1H), 3.82 (m, 2H), 3.20 (t, J = 8.7 Hz, 1H), 2.81 (dd, J = 2.2, 9.0 Hz, 1H), 2.45 (d, J = 3.4 Hz, 1H), 2.35 (m, 1H), 2.03 (m and s, 7H), 1.80 (s, 1H), 1.72 (d, J = 4.5 Hz, 1H), 0.86 (s, 9H), 0.08 (s, 3H), 0.04 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 209.5, 169.5, 169.1, 103.3, 92.0, 74.2, 71.2, 69.9, 53.4, 50.9, 43.6, 31.6, 25.5, 22.7, 20.9, 17.8, 14.1; EI-HRMS m/z 440.1312 (calcd for $C_{22}H_{32}O_4SiFe$ (M − 3CO) m/z 440.1318).

Ferrier Rearrangement of 7. To a solution of **7** (276 mg, 0.945 mmol) in isopropyl alcohol (20 mL) at 23 °C under N_2 was added *p*-toluenesulfonic acid (14 mg). The reaction mixture was stirred for 24 h, poured into saturated aqueous $NaHCO_3$, and extracted with ether. The combined organic layers were dried ($MgSO_4$), and the solvent was evaporated to give a yellow oil (281 mg, 89%) which was determined by ^1H NMR spectroscopy to be a mixture of anomers, α-**10** and *β*-**10** (4.5:1 ratio). Separation by column chromatography gave pure α-**10** followed by a mixture of α-**10** and *β*-**10** (1:1).

α-**10**: IR ($CHCl_3$, cm^{-1}) 2052, 1988; ^1H NMR ($CDCl_3$) δ 5.94 (complex m, 1H), 5.64 (ddt, J = 1.5, 10.2, 4.1 Hz, 1H), 5.08 (br s, 1H), 4.03 (sept, J = 6.1 Hz, 1H), 3.81 (ddd, J = 4.2, 8.0, 10.0 Hz, 1H), 2.87 (dd, J = 2.7, 7.8 Hz, 1H), 2.58 (d, J = 4.4 Hz, 1H), 2.15 (m, 3H), 1.77 (s, 1H), 1.70 (d, J = 4.4 Hz, 1H), 1.17 (d, J = 5.6 Hz, 3H), 1.15 (d, J = 5.6 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 211.3, 211.2, 210.3, 127.5, 126.1, 102.4, 91.6, 80.7, 68.8, 65.8, 53.2, 51.0, 34.6, 23.3, 21.2; EI-HRMS m/z 306.0540 (calcd for $C_{14}H_{18}O_4Fe$ (M − CO) m/z 306.0554).

β-**10** ^1H NMR ($CDCl_3$, partial) δ 5.12 (br s), 3.24 (dt, J = 3.4, 9.8 Hz, 1H), 3.02 (dd, J = 2.4, 9.8 Hz, 1H), 2.44 (d, J = 4.4 Hz, 1H), 1.81 (s, 1H), 1.74 (d, J = 4.4 Hz, 1H).

Isopropyl 2,3-Di-*O*-acetyl-4,6-dideoxy-6-TMM-mannopyranoside (11). To a solution of α-**10** (0.50 g, 0.150 mmol) in acetone was added Et_4NOAc (0.013 g, 0.050 mmol). After 30 min, the solution was cooled to 0 °C, and a solution of OsO_4 (1 mL, 0.196 M, 0.196 mmol) in pyridine was added dropwise over a 5 min period, followed by tBuOOH (0.03 mL, 0.30 mmol). After 3 h, the reaction mixture was quenched with saturated aqueous $NaHSO_3$ (7 mL), warmed to rt, and stirred overnight. The mixture was diluted with ethyl acetate and filtered through a filter aid. The filtrate was washed with brine, followed by 10% aqueous HCl, and finally saturated aqueous $NaHCO_3$, dried, and concentrated. The residue was dissolved in CH_2Cl_2 (10 mL), and pyridine (1.2 mL), acetic anhydride (1.4 mL), and DMAP (6 mg) were added. The reaction mixture was stirred for 20 h, diluted with water, and extracted with ether. The ether extracts were washed with 1 N HCl (2 × 5 mL) and saturated aqueous $NaHCO_3$, dried, and concentrated to give **11** as a yellow solid (0.055 g, 81%). **11**: mp 94−96 °C; IR ($CHCl_3$, cm^{-1}) 2058, 1994, 1726, 1371; ^1H NMR ($CDCl_3$) δ 5.24 (ddd, J = 3.2, 6.0, 11.0 Hz, 1H), 4.89 (t, J = 2.3 Hz, 1H), 4.85 (d, J = 1.7 Hz, 1H), 3.87 (hept, J = 6.1 Hz, 1H), 3.69 (dt, J = 5.9, 8.5 Hz, 1H), 2.84 (dd, 2.4, 8.5 Hz, 1H), 2.55 (d, J = 4.2 Hz, 1H), 2.11 and 2.00 (2 x s, 6H), 1.97−1.89 (m, 3H), 1.78 (s, 1H), 1.69 (d, J = 4.4 Hz, 1H), 1.07 (d, J = 6.1 Hz, 6H); ^{13}C NMR ($CDCl_3$) δ 212.6, 212.5, 211.9, 171.7, 171.4, 103.4, 96.3, 80.0, 69.8, 69.0, 67.4, 66.8, 53.4, 51.7, 36.1, 29.9, 23.2, 21.2, 21.1; EI-HRMS m/z 368.0913 (calcd for $C_{16}H_{24}O_6Fe$ (M − 3CO) m/z 368.0922).

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Supporting Information Available: Copies of the ^{1}H and/or ^{13}C NMR spectra of **6**−**11** (8 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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