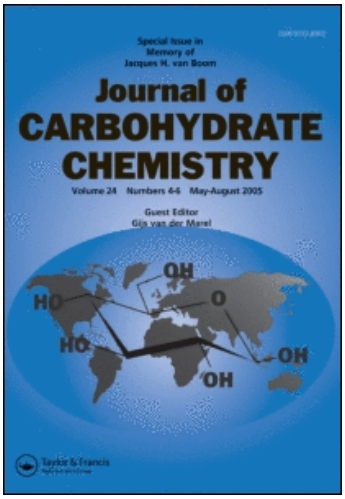

Journal of Carbohydrate Chemistry

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

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L. V. Dunkerton[a]; K. T. Brady[a]; F. Mohamed[a]; B. P. McKillican[a]
[a] Department of Chemistry and Biochemistry, Southern Illinois University at Carbondale, Carbondale, IL

To cite this Article Dunkerton, L. V. , Brady, K. T. , Mohamed, F. and McKillican, B. P.(1988) 'Palladium Promoted Allylic Rearrangement Route to 6-Substitutbd 2-O-Acetyl-Hex-3-Enopyranosides', Journal of Carbohydrate Chemistry, 7: 1, 49 — 65

To link to this Article: DOI: 10.1080/07328308808058903

URL: http://dx.doi.org/10.1080/07328308808058903

J. CARBOHYDRATE CHEMISTRY, 7(1), 49-65 (1988)

PALLADIUM PROMOTED ALLYLIC REARRANGEMENT ROUTE TO 6-SUBSTITUTED 2-O-ACETYL-HEX-3-ENOPYRANOSIDES

L. V. Dunkerton*[1], K. T. Brady[2,3], F. Mohamed[2], and B. P. McKillican[1]

Department of Chemistry and Biochemistry
Southern Illinois University at Carbondale
Carbondale, IL 62901

Received August 6, 1987 - Final Form January 11, 1988

ABSTRACT

Readily available 6-substituted 3,4-di-O-acetyl-1,2-glycals have been converted to their 2-O-acetyl-3,4-dideoxy-hex-3-enopyranosides by a stereoselective alkoxypalladation followed by addition of sodium cyanoborohydride which effected a stereoselective and regioselective allylic rearrangement with chirality transfer. Using this reaction methyl 2,6-di-O-acetyl-3,4-dideoxy-α-D-erythro-hex-3-enopyranoside (13), ethyl 2,6-di-O-acetyl-3,4-dideoxy-α-D-erythro-hex-3-enopyranoside (15), β-(trimethylsilyl) ethyl 2,6-di-O-acetyl-3,4,-dideoxy-α-D-erythro-hex-3-enopyranoside (17), methyl 2-O-acetyl-3,4-dideoxy-α-D-erythro-hex-3-enopyranoside (19), methyl 2-O-acetyl-6-azido-3,4,6-trideoxy-α-D-erythro-hex-3-enopyranoside (21), methyl 2-O-acetyl-6-O-methyl-3,4,-dideoxy-α-D-erythro-hex-3-enopyranoside (20), methyl 2,6-di-O-acetyl-3,4,-dideoxy-α-D-threo-hex-3-enopyranoside (22), methyl 4-O-acetyl-6-cyano-2,3,6-trideoxy-α-D-erythro-hex-2-enopyranoside (24), methyl 4-O-acetyl-2,3-dideoxy-α-D-glycero-pent-2-enopyranoside (25), and methyl-4-O-acetyl-2,3,6-trideoxy-α-L-erythro-hex-2-enopyranoside (26) were synthesized in excellent yield from their corresponding 1,2-glycals. In this reaction it was found that both sodium cyanoborohydride and a coordinating group at C-6 were necessary to effect the regioselective allylic rearrangement. These rearrangements can be rationalized on the basis that following transalkoxypalladation the resulting 2,3-palladium π complex is reduced to a Pd(0) complex by sodium cyanoborohydride which then undergoes allylic rearrangement assisted by coordination of the group at C-6 to control the regioselectivity.

INTRODUCTION

An ongoing program to effect, regio-, and stereoselective functionalization of carbohydrates using palladium reagents led to the investigation of palladium promoted allylic rearrangements of pyranoside glycals. Numerous examples have been recently reported in which palladium(II) salts and palladium (0) complexes have been used to catalyze [3,3] and [1,3] sigmatropic rearrangements.[4-6] Important mechanistic and synthetic features of Pd(II) catalyzed [3,3] sigmatropic rearrangements in synthesis include chirality transfer and regioselectivity based on thermodynamic preferences or relief of steric compression.[7-14] In contrast, Pd(0) allylic rearrangements are often accompanied by nonspecific inversion[10] or acetate scrambling[7], and give mixtures of [3,3] and [1,3] products.[6, 13, 14] Pd(0) catatalyzed allylic rearrangements are suggested to occur by oxidative addition followed by nucleophilic attack on the π-allyl intermediate in which regioselectivity is not expected or required but often observed. Not only are different products formed due to the oxidation state of a palladium catalyst, but also due to ligands. An example is a [3,3] sigamtropic rearrangement affected by $Pd(dppe)_2$ whereas $Pd(PPh_3)_4$ gave a mixture of [3,3] and [1,3] products, the selectivity of the former being attributed to steric effects.[6] For synthetic purposes high regio- and stereoselectivity is desired and the choice of catalyst can be suggested based on these literature precedents. Frequently when either Pd(II) or Pd(0) catalyst can be used, the former reacts much faster.[6]

The use of palladium assisted nucleophilic additions to alkenes has also been developed to be a highly stereo and regioselective synthetic method. Compared to electrophilic assisted addition to alkenes catalyzed by Lewis acids or mercury complexes, palladium is highly stereoselective, including trans addition of alcohols. More recently the stereochemical control of addition of various nucleophiles to alkenes by Bäckvall and coworkers has shown that altering the ligand environment can also be used to change the stereoselectivity of a given nucleophile, thus increasing the synthetic potential of this reaction.[15] The combination of stereoselective alkoxypalladation catalyzed by Pd(II) salts and the stereoselectivity of allylic rearrangements has been combined in our effort resulting in an efficient two-step one-pot

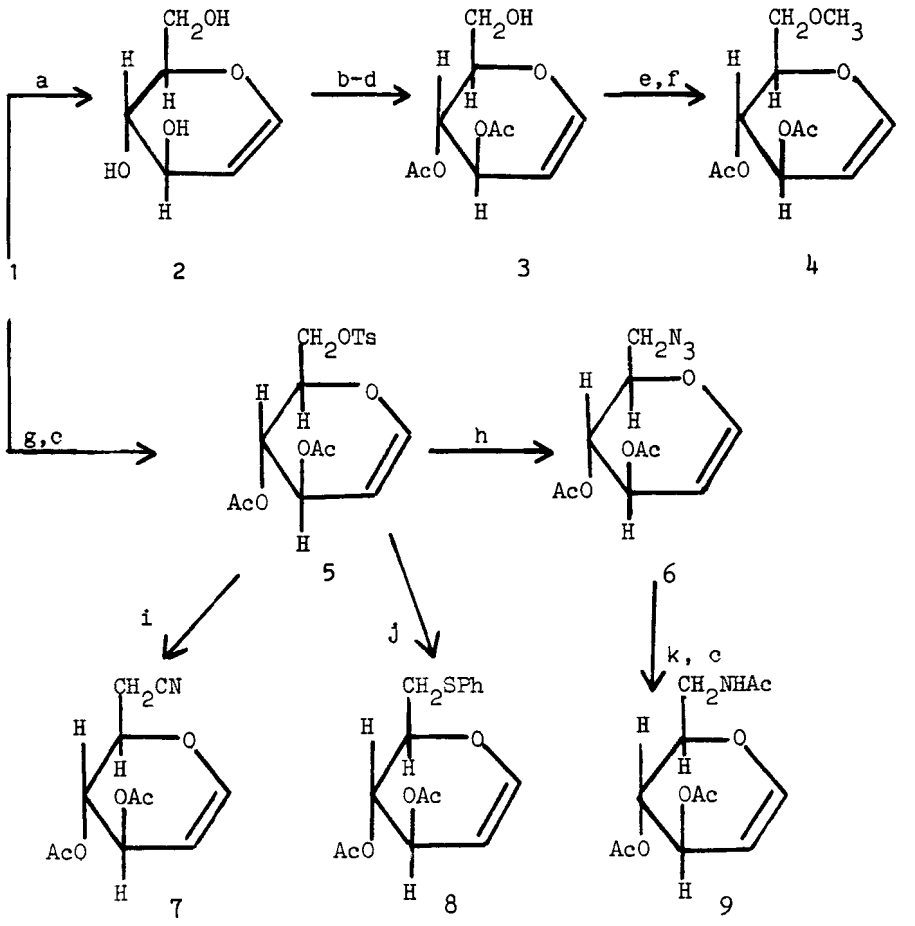
conversion of readily available glycals to their respective 3,4-dideoxy-hex-2-enopyranosides consisting of a stereoselective alkoxypalladation followed by allylic rearrangment of the resulting palladium complex after reduction.

RESULTS AND DISCUSSION

Several readily available glycals were used in this study. 3,4,6-Tri-O-acetyl-D-glucal and 3,4-di-O-acetyl-L-rhamnal were commercially available, while 3,4-di-O-acetyl-D-xylal and 3,4,6-tri-O-acetyl-D-galactal were prepared using literature procedures. Various 6-substituted 3,4-di-O-acetyl-glycals were prepared from 1 using standard methods as shown in Scheme 1.[16,17]

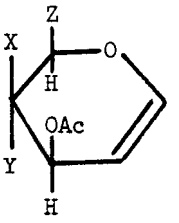
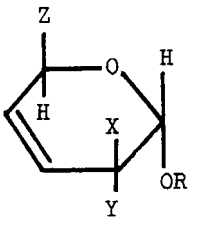
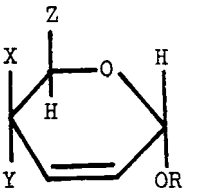
The alkoxypalladation-rearrangement of 3,4,6-tri-O-acetyl-D-glucal (1) was accomplished with the primary alcohols methanol, ethanol, and β-trimethylsilylethanol using the alcohols as a solvent. To a solution of 1 in the alcohol was added 0.5 equivalents of $PdCl_2$ and the mixture stirred 3.5 h under argon at room temperature during which trans methoxypalladation occurred stereoselectively. After cooling the suspension to -5°C, one equivalent of sodium cyanoborohydride was added and the mixture allowed to stir at -5°C for 1 h followed by workup. The results of these rearrangements are shown in Table 1. The major product from each reaction was identified spectroscopically as the product of allylic rearrangement and the minor product was that of trans methoxypalladation. If the reaction was subjected to workup without addition of sodium cyanoborohydride, only trans methoxypalladation products were isolated. From 1, the rearrangement proceeded in approximately 60-85% depending upon the alcohol. To examine the effect of the C-6 group on the extent of the allylic rearrangement, each of the C-6 substituted 3,4-di-O-acetyl-D-glucals was subjected to methoxypalladation-rearrangement using the same reaction conditions. The results as shown in Table 1 show that the best rearrangement ratios were achieved with the C-6 groups of hydroxyl, methoxy and azido, while the acetate group rearranged approximately 85%, the nitrile group underwent methoxypalladation without allylic rearrangement, and the S-phenyl and N-acetate groups prevented both methoxypalladation and rearrangement. The effect of the

SCHEME I

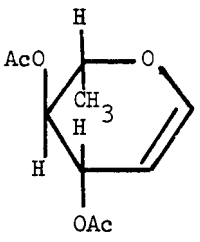


(a) NaOMe, MeOH[18]; (b) t-$BuMe_2SiCl$, imidazole, DMF; (c) Ac_2O, pyr; (d) n-Bu_4NF, THF; (e) NaH, THF; (f) CH_3I; (g) TsCl, pyr, CH_2Cl_2[19]; (h) NaN_3, DMSO; (i) NaCN, n-Bu_4NBr, CH_3CN, DMF[20]; (j) PhSNa, ether; (k) $LiAlH_4$, ether.

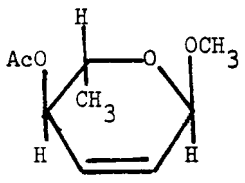
TABLE 1. Alkoxypalladation-Rearrangement Results

Reactant  Products  

COMPOUND	X	Y	Z	R	RATIO (3,4):(2,3)
1	H	OAc	CH_2OAc	CH_3	13:14 = 85:15
1	H	OAc	CH_2OAc	CH_2CH_3	15:16 = 85:15
1	H	OAc	CH_2OAc	$(CH_2)_2SiMe_3$	17:18 = 85:15
3	H	OAc	CH_2OH	CH_3	19 100% (3,4) only
4	H	OAc	CH_2OCH_3	CH_3	20 100% (3,4) only
6	H	OAc	CH_2N_3	CH_3	21 100% (3,4) only
7	OAc	H	CH_2OAc	CH_3	22:23 = 85:15
8	H	OAc	CH_2CN	CH_3	24 100% (2,3) only
9	H	OAc	CH_2SPh	CH_3	no reaction
10	H	OAc	CH_2NHAc	CH_3	no reaction
11	H	OAc	H	CH_3	25 100% (2,3) only



12



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group at C-4 did not appear to change the rearrangement ratio because 3,4,6-tri-O-acetyl-D-galactal (7) rearranged with chirality transfer in the same 85% ratio observed for 1. Glycals without coordinating groups at C-6 including 3,4-di-O-acetyl-D-xylal (11) and 3,4-di-O-acetyl-L-rhamnal (12) only underwent methoxypalladation without allylic rearrangement.

The structures of the major 3,4-dideoxy-hex-3-enopyranosides 13-22 were established from ^{1}H NMR, ^{13}C NMR, and mass spectral data. The most convincing evidence was the identity of the ^{1}H NMR data and ^{13}C NMR data for 13 and 22 to that reported by Zamojski and coworkers.[21] Since it was most important to distinguish rearranged products from their corresponding hex-2-enopyranosides, several of the hex-2-enopyranosides were prepared by either methoxypalladation or BF_3·etherate addition of methanol to the corresponding glycals.[22] The NMR spectra of hex-3-enopyranosides compared to that of hex-2-enopyranosides shows both H-1 and C-1 further upfield in the former and H-5 further upfield in the latter. Comparative spectral data for the other hex-3-enopyranosides to the already reported compounds 13 and 22 was also in accord with these trends.

These rearrangements can be rationalized on the basis that in the presence of $PdCl_2$, methanol underwent trans methoxypalladation stereoselectively adding methanol to the α face to give an intermediate Pd π-complex which is then reduced to a palladium(0) complex after the addition of sodium cyanoborohydride. The resulting Pd(0) complex effects acetate rearrangement with chirality transfer and migration of palladium to stabilize the 3,4 double bond. The role of the coordinating group at C-6 may be to effect ligand exchange during the reduction and result in the regioselectivity of the allylic rearrangement being controlled by the greater stability of the 3,4 palladium π-complex compared to that of the 2,3 palladium complex formed after methoxypalladation. Lack of a coordinating group inhibits rearrangement after methoxypalladation. Apparently the strongly coordinating C-6 S-phenyl or N-acetyl inhibited methoxypalladation. These results show that this two step sequence provides a very direct synthesis of 6-substituted 3,4-dideoxy-hex-3-enopyranosides from the readily available 1,2-glycals with appropriate choice of a coordinating group at C-6 to effect high

regioselectivity in the rearrangement. The use of this reaction in the preparation of chiral synthons for asymmetric synthesis should prove valuable.

EXPERIMENTAL

General Procedures. NMR spectra were recorded for solutions in $CDCl_3$ using either Varian T-60, Varian XL-100, Varian XL-200, Nicolet-200, or Bruker WM-500 spectrometers. ^1H NMR spectra are reported referenced to internal Me_4Si at 60, 100, 200, or 500 MHz with coupling constants reported in hertz. ^{13}C NMR spectra were recorded at 25.2 MHz, 50.3 MHz, 125.7 MHz referenced to $CDCl_3$ (77.00). Multiplicities from off resonance decoupling experiments are in agreement with the assignments. Mass spectra were obtained using either a Hewlett-Packard 5985 or Finnegan 4000 low resolution or a Kratos MS-80 medium resolution mass spectrometer in either low resolution electron impact (EI) or chemical ionization (CI, CH_4) mode. High resolution mass spectra were obtained using either a VG 7070 spectrometer (HREI) or a Kratos MS-52 (HRCI) with appropriate peak matching. IR spectra were recorded on a Perkin Elmer 281 or a Nicolet FTIR spectrometer. Optical rotations were measured using a Perkin Elmer 241 polarimeter. TLC and column chromatography were performed on silica gel GF_{254} (230-400 mesh, Merck) or using Baker silica gel (60-200 mesh). Most solvents were distilled shortly before use from an appropriate drying agent. Ether and tetrahydrofuran were distilled from sodium benzophenone ketil. Benzene and N,N-dimethylformamide were distilled from calcium hydride. Methanol used was spectrophotometric grade (99.9%, Aldrich Chemical Company) stored over 3A molecular sieves under argon. All air sensitive reactions were performed under an atmosphere of argon.

Preparation of 6-Substituted-3,4-di-O-Acetyl Glycals. 3,4,6-Tri-O- acetyl-D-glucal (1) and 3,4-di-O-acetyl-L-rhamnal (12) were purchased from Pfansteihl Laboratories and used directly. 3,4-Di-O-acetyl-6-O-p-toluenesulfonyl-D-glucal was prepared by the method of Brimacombe[19]. 3,4-Di-O-acetyl-D-xylal (11) was prepared according to Weygand,[17] and 3,4,6-tri-O-acetyl- D-galactal (7) by the method of Rosenthal and Read[16].

3,4,-Di-O-acetyl-6-O-t-butyldimethylsilyl-D-glucal (27). A solution of D-glucal (2) (1.8g, 12.4 mmol) in DMF (30 mL) was cooled to 0 °C. To this solution was added imidazole (1.95 g, 2.3 eq) and tert-butyldimethylsilyl chloride (2.06 g, 1.1 eq). The mixture was allowed to warm to room temperature and stirring was continued for 24 h. The DMF was removed at room temperature in vacuo (0.001 mm Hg). Without purification the crude syrup was dissolved in pyridine (25 mL), cooled to 0 °C and treated with acetic anhydride (25 mL). The solution was allowed to warm to room temperature and left standing for two days at room temperature. Removal of the solvents in vacuo gave a syrup which was taken up in Et_2O and successively washed with saturated sodium bicarbonate solution, water and brine. The organic layer was dried over anhydrous magnesium sulfate and the solvent removed in vacuo to give crude 27 (3.67g, 86% yield from 2). For preparation of 3 crude 27 was used without further purification. Flash chromatography (silica gel, 10% EtOAc/pentane) afforded pure 27, which crystallized as colorless needles upon standing at -5 °C. Data for 27: R_f = 0.81 (7:3 toluene/EtOAc); ^{1}H NMR (60 MHz, $CDCl_3$) δ 6.5-6.3 (m, H-1), 5.5-5.2 (m, H-3), 5.2-5.0 (m, H-4), 5.0-4.6 (m, H-2), 4.4-4.3 (m, H-5), 4.3-3.7 (m, J=6 Hz, H-2, H-6, H-6'), 2.1 (s, OAc), 0.9 (s, t-C_4H_9), 0.1, 0.07 (s, $Si(CH_3)_2$); IR (Neat) 2960, 2940, 2900 and 2870, 1750, 1650, 1380, 1250, 1110, 1080, 1050, 850 and 785 cm^{-1}; $[\alpha]_D^{25}$ -3.13° (c 0.245, $CHCl_3$).

3,4-Di-O-Acetyl-D-Glucal (3). A solution of 27 (2.0 g, 5.70 mmol) in THF (20 mL) was cooled to 0 °C under argon. To this solution was added tetrabutylammonium fluoride (12.5 mL, 1M in THF, Aldrich Chemical Co.) over 15 min. The reaction mixture was warmed to room temperature and stirred for an additional 1.5 h. Solvent removal and flash chromatography (silica gel, 15% EtOAc/pentane) afforded pure 3 (1.11 g, 85%). Data for 3: R_f = 0.48 (7:3 toluene/EtOAc); ^{1}H NMR ($CDCl_3$) δ 6.41-6.33 (dd, J=6 Hz, 2 Hz, H-1), 5.27-5.21 (dd, J=6 Hz, 3 Hz, H-3), 4.73-4.64 (dd, J=6 Hz, 3 Hz, H-2), 4.43-4.39 (m, H-4, H-5), 4.06-3.70 (m, H-6, H-6'), 3.2 (brs. OH) and 2.11 (s, OAc); ^{13}C NMR ($CDCl_3$) δ170.27, 169.68 (C=O), 144.59 (C-1), 98.81 (C-2), 76.14 (C-5), 72.36 (C-4), 66.84 (C-3), 62.57 (C-6) and 21.59, 21.25 (CH_3); IR (Neat) 3430, 2940 and 2900, 1740, 1655, 1380, 1250, 1230, 1105, 1060 and 1040 cm^{-1}; $[\alpha]_D^{25}$ -3.62° (c 0.327, $CHCl_3$).

3,4-di-O-Acetyl-6-O-methyl-D-glucal (4). Sodium hydride (43.6 mg, 1.82 mmol) was added to a solution of 3,4-di-O-acetyl-D-glucal (3) (380 mg, 1.65 mmol) in THF (10mL) at 5°C and stirred for 5 min then warmed to room temperature. Methyl iodide (684 mg, 4.82 mmol) which had been filtered through basic alumina was added via syringe and stirring was continued for 16 h. The reaction mixture was concentrated then triturated with ether (30 mL). The organic layer was extracted with saturated NaCl (2x10mL) then dried over $MgSO_4$. Filtration and concentration afforded an oil which was flash chromatographed (silica gel, 20% EtOAc/hexane) to give 4 as an oil (170 mg, 42.2%). Data for 4: R_f = 0.50 (30% EtOAc/hexane); ^1H NMR ($CDCl_3$) δ 6.43-6.40 (dd, J=6.1 Hz, 1.1 Hz, H-1), 5.35-5.32 (ddd, J=3.2 Hz, 1.1 Hz, H-3), 4.83-4.78 (dd, J=6.1 Hz, 3.2 Hz, H-2), 4.45-4.11 (m, H-4, H-5, H-6,6'), 3.50 (s, OCH_3), 2.12-2.09 (OAc); ^{13}C NMR ($CDCl_3$) δ 170.64, 170.39 (OAc), 145.34 (C-1), 99.05 (C-2), 75.06 (C-3), 74.75 (C-4), 69.37 (C-5), 62.31 (C-6), 59.11 (OCH_3), 21.19, 20.82 (OAc).

3,4-Di-O-Acetyl-6-cyano-6-deoxy-D-glucal (7). Using the procedure recently reported by Nakahara, Beppu and Ogawa,[20] a solution of 3,4-di-O-acetyl-6-O-p-toluenesulfonyl-D-glucal (5) (0.324 g, 0.842 mmol), powdered sodium cyanide (0.109 g, 2.6 eq) and tetrabutylammonium bromide (0.545 g, 2.0 eq) in acetonitrile (3 mL) and DMF (3 mL) was refluxed at 83°C (bath temperature) for 24 h. After cooling, the solution was poured onto ice water (50 mL) and extracted with Et_2O (3 x 50 mL). The combined organic layers were washed with water then brine and dried over magnesium sulfate. Concentration afforded a red-orange oil (0.120 g, 60%). Purification by flash chromatography (silica gel, 10% EtOAc/pentane) gave pure 7 (40%). Data for 7: R_f = 0.61 (7:3 toluene/EtOAc); ^1H NMR ($CDCl_3$) 6.50-6.46 (dd, J=6.1 Hz, 1.2 Hz, H-1), 5.38-5.32 (ddd, J=5.8 Hz, 3.1 Hz, 1.2 Hz, H-3), 5.28-5.20 (dd, J=7.1 Hz, 5.8 Hz, H-4), 4.88-4.83 (dd, J=6.1 Hz, 3.1 Hz, H-2), 4.47-4.36 (dd, J=7.1 Hz, 5.1 Hz, 5.1 Hz, H-5), 4.30-4.36 (dd, J=11.8 Hz, 5.1 Hz, 5.1 Hz, H-6, 6') and 2.08, 2.06 (s, OAc); ^{13}C NMR ($CDCl_3$) δ 170.60, 170.39 (OAc), 169.56 (C≡N), 145.59 (C-1), 98.96 (C-2), 73.90(C-5), 67.39 (C-3), 67.12 (C-4), 61.34 (C-6), 21.00, 20.279 (OAc); IR ($CHCl_3$) 2900, 2240, 1740, 1670, 1395, 1250, 1115 and 1050 cm^{-1}; MS (CI - CH_4) m/z 268 ($M^+ + C_2H_5$, 1.9%), 240 (MH^+, 1.1%), 214 (10%), 213 (MH^+ - HCN, 9.0%), 171 (MN^+ -HCN -CH_2CO, 9.0%), 153 (M^+ -HCN

-HOAc, 99.5%), 111 (MH^+ -HCN -HOAc -CH_2CO, 16.9%); $[\alpha]_D^{25}$ -5.85° (c 0.0728, $CHCl_3$).

3,4-Di-O-acetyl-6-azido-6-deoxy-D-glucal (6). A solution of 5 (2.51 g, 6.54 mmol) and sodium azide (0.724 g, 1.7 eq) in DMSO (50 mL) was heated at 110°C (bath temperature) for 4 h under a calcium sulfate drying tube. After cooling, the reaction mixture was poured onto ice water (200 mL) and extracted with Et_2O (5 x 50 mL). The combined ether layers were washed with water and brine and dried over magnesium sulfate. Concentration in vacuo (bath temperature 40°C) afforded a yellow oil (1.25 g, 78%) which was chromatographed (silica gel, 10% EtOAc/pentane) to give pure 6. Data for 6: R_f = 0.73 (7:3 toluene/EtOAc); ^1H NMR ($CDCl_3$) δ 6.46-6.40 (dd, J=6 Hz, 1.5 Hz, H-1), 5.32-5.06 (m, H-3, H-4), 4.88-4.78 (dd, J=6 Hz, 3.5 Hz, H-2), 4.19-4.15 (m, H-5), 3.65-3.33 (m, H-6, H-6') and 2.07, 2.04 (s, OAc); lit.[24] ^1H NMR ($CDCl_3$) δ 6.51 (d, J=6.5 Hz, H-1), 5.47-5.03 (m, H-3, H-4), 5.02-4.76 (dd, J=6.5 Hz, 3 Hz, H-2);, 4.43-4.04 (q, H-5), 3.66-3.38 (m, H-6, H-6') and 1.7 (s, OAc); ^{13}C NMR ($CDCl_3$) δ 169.04, 168.31 (OAc), 144.43 (C-1), 98.70 (C-2), 74.72 (C-5), 67.99 (C-4), 66.93 (C-3), 50.31 (C-6) and 21.54, 21.34 (CH_3); IR (Neat) 2940, 2110, 1760, 1660, 1450, 1375, 1240, 1160 and 1050; MS (CI-CH_4) m/z 284 ($M^+ + C_2H_5$, 6.9%), 256 (MH^+, 2.9%), 213 (MH^+ -Ac, 13.3%), 196 (MH^+ -HOAc, 18.4%), 168 (MH^+ -N_2 -HOAc, 100%), 153 (MH^+ -HOAc -Ac, 5.1%), 126 (20.8%) and 108 (MH^+ -2HOAc - N_2, 7.2%); $[\alpha]_D^{25}$ +0.180° (c 0.111, $CHCl_3$); lit.[24] $[\alpha]_D$ -6° (c 1.89).

3,4-di-O-Acetyl-6-deoxy-6-S-phenyl-D-glucal (9). NaH (3.43 mg, 0.145 mmol) was added to a solution of thiophenol (14.3 mg, 0.130 mmol) in anhydrous ether (10mL) and stirred at room temperature for 15 min. 3,4-di-O-Acetyl-6-O-p-toluenesulfonyl-D-glucal (50 mg, 0.130 mmol) was added and the solution refluxed for 6h . After cooling, the solution was poured into H_2O (20 mL) and extracted with ether (40 mL then, 2 x 20 mL) and the extracts dried over $MgSO_4$. Filtration and evaporation of solvents afforded an oil which was flash chromatographed (silica gel, 20% EtOAc/hexanes) to afford pure 9 as an oil (24.8 mg, 62.3%). Data for 9: R_f = 0.70 (30% EtOAc/hexane); ^1H NMR ($CDCl_3$) δ 7.50-7.10 (m, SPh) 6.43-6.40 (dd, J=6.1 Hz, 1.1 Hz, H-1), 5.36-5.29 (ddd, J=6.1 Hz, 5.5 Hz, 1.5 Hz, H-3), 5.29-5.21 (H-5), 4.90-4.82 (m, H-2, H-4), 4.27-4.16 (m, H-6,6'), 2.12, 2.09 (OAc); ^{13}C NMR ($CDCl_3$) δ

170.25, 169.66 (OAc), 145.61 (C-1), 130.28, 129.09, 129.04, 126.81 (SPh), 98.43 (C-2), 74.22 (C-3), 69.16 (C-4), 66.29 (C-5), 34.33 (C-6), 21.07, 20.91 (OAc).

6-N-Acetyl-3,4-Di-O-acetyl-6-deoxy-D-glucal (10). A solution of 6 (6.79 g, 26.6 mmol) in anhydrous ether (50 mL) was added via syringe dropwise over 1 h to a boiling suspension of lithium aluminium hydride (7.10 g, 7.0 eq) in ether (200 mL). Refluxing was continued for an additional 1 h after addition was complete. After cooling, the reaction was quenched by the slow addition of MeOH (200 mL). The resulting suspension was filtered under suction and the precipitated salts were washed with dichloromethane. Concentration in vacuo afforded a tan powder which was continuously extracted with boiling EtOAc (Soxhlet apparatus, 8 h). Removal of the solvent in vacuo gave the partially purified 6-amino-6-deoxy-D-glucal which was directly acetylated in a solution of pyridine (40 mL) and acetic anhydride (40 mL) for 2 days at room temperature. Concentration in vacuo afforded a yellow oil (4.33 g, 60% from 6) which was chromatographed (silica gel, 15% EtOAc/pentane to give pure **10**. Data for **10**: R_f = 0.59 (7:3 toluene/EtOAc); ^{1}H NMR ($CDCl_3$) δ 6.44-6.38 (dd, J=6 Hz, 1 Hz, H-1), 5.35-5.17 (m, H-3, H-4), 4.85-4.76 (dd, J=6 Hz, 3, H-2), 4.41-4.08 (m, H-5, H-6, H-6'), 2.08, 2.06, 2.03 (s, NAc, OAc); ^{13}C NMR ($CDCl_3$) δ 169.43, 169.28, 168.46 (OAc), 144.81 (C-1), 98.71 (C-2), 73.95 (C-5), 67.51 (C-4), 67.27 (C-3), 61.54 (C-6) and 21.62, 21.43 (OAc); IR (Neat) 3500, 2950, 1750, 1655, 1380, 1230 and 1050 cm^{-1}; $[\alpha]_D^{25}$ -5.45 (c 0.180, $CHCl_3$).

Alkoxypalladation Rearrangement of 3,4,6-tri-O-acetyl-D-glucal (1). A solution of 3,4,6-tri-O-acetyl-D-glucal (1) (0.0741 g, 0.272 mmol) and $PdCl_2$ (0.0243 g, 0.50 eq) in the alcohol (1.8 mL) was stirred for 3.5 h under argon at room temperature. After cooling this suspension to -5 °C, sodium cyanoborohydride (0.0172 g, 1.1 eq) was added to the mixture. The reaction temperature was maintained at -5 °C for one after which the reaction mixture was filtered through a pad of pre-cooled Filter Aid and the solids were washed with cold ethyl acetate. Concentration at room temperature in vacuo afforded products.

Using methanol as the reaction solvent afforded a mixture of 13 and 14 (53 mg, 80%, 13:14 = 85:15 on the basis of ^{1}H NMR). Data for 13 (from the mixture): R_f = 0.60 (7:3 toluene/EtOAc); ^{1}H NMR

(500 MHz, $CDCl_3$) δ 5.96-5.90 (ddd, J=15.5 Hz, 6.5 Hz, 1.2 Hz, H-4), 5.78-5.72 (ddd, J=15.5 Hz, 4.5 Hz, 1.2 Hz, H-3), 5.39-5.36 (dd, J=5.8 Hz, 4.5 Hz, H-2), 4.85-4.84 (d, J=4.5 Hz, H-1), 4.5-4.3 (m, H-5), 4.3-4.0 (m, H-6, H-6'), 3.30 (s, OCH_3) and 2.10, 2.09 (s, OAc); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.09, 169.81 (OAc), 131.54 (C-4), 128.30 (C-3), 101.41 (C-1), 73.81 (C-5), 71.13 (C-2), 64.75 (C-6), 52.64(OCH_3), 21.00, 20.78 (OAc); IR ($CHCl_3$) 1720, 1040, 1225; MS (CI-CH_4) 245 (MH^+, 1%) 213 (MH^+ - CH_3OH, 80%), 185 (MH^+ - AcOH, 11%), 153 (MH^+ - AcOH - CH_3OH, 100%), 143 (12%), 125 (25%), 111 (93%), 83 (7%); MS (HREI) calc. for $C_{11}H_{16}O_6$ 244.0947, found 244.0954; $[\alpha]_D^{25}$ +9.60° (c 0.134, $CHCl_3$).

15. Using ethanol as the reaction solvent afforded a mixture of **15** and **16** (50%, **15:16** = 85:15). Data **15**: R_f = 0.63 (7:3 toluene/EtOAc); ^1H NMR ($CDCl_3$) δ 5.83-5.74 (m, H-3, H-4), 5.36-5.20 (m, H-2), 5.00-4.84 (m, H-1), 4.31-3.97 (m, H-5, H-6, H-6'), 3.69-3.37 (m, CH_2), 2.07 (s, OAc), 1.26-1.12 (t, CH_3); ^{13}C NMR ($CDCl_3$) δ 169.78 (OAc), 131.69 (C-4), 126.80 (C-3), 99.67 (C-1), 73.90 (C-5), 71.18 (C-2), 64.87 (C-6), 60.54 (CH_2), 21.71 (OAc), 14.99 (CH_3); ^{13}C NMR ($CDCl_3$) δ 128.25 (C-3), 127.28 (C-2), 93.99 (C-1), 60.54 (CH_2), 16.01 (CH_3); MS (CI -CH_4) m/z 214 (11.2%), 213 (MH^+ -$HOCH_2CH_3$, 100%), 171 (MH^+ - $HOCH_2CH_3$ - CH_2CO, 5.4%), 154 (9.1%), 153 (MH^+ -$HOCH_2CH_3$ -HOAc, 96.8%), 139 (7.6%), 111 (36.1%); MS (HREI) calc. for $C_{10}H_{13}O_5$ (M^+-OCH_2CH_3) 213.0790, found 213.0755; $C_8H_9O_3$ (M^+ -HOAc -OCH_2CH_3) 153.0552, found 153.0546; $[\alpha]_D^{25}$ +11.75 (c 0.281, $CHCl_3$).

17. Using β-(trimethylsilyl) ethanol as the reaction solvent gave a mixture of **17** and **18** (613 mg, 75%). Data for **17** (from the mixture): R_f = 0.76 (7:3 toluene/EtOAc); ^1H NMR ($CDCl_3$) δ 5.79-5.61 (m, H-3, H-4), 5.28-5.01 (m, H-2), 4.91-4.85 (m, H-1), 4.29-3.76 (m, H-5, H-6, H-6'), 3.69-3.53 (brt, O-CH_2), 1.99, 1.97 (s, OAc) 0.97-0.81 (brt, CH_2-Si) and 0.00 (s, $Si(CH_3)_3$); ^{13}C NMR ($CDCl_3$) δ 169.05 (OAc) 130.97 (C-4), 127.59 (C-3), 99.51 (C-1), 73.87 (C-5), 71.35 (C-2), 64.95 (C-6), 60.22 (O-CH_2-C), 22.88 (OAc), 19.05 (C-CH_2-Si), -0.407 ($Si(CH_3)_3$); MS (CI -CH_4) m/z 214 (11%), 213 (MH^+ -$HOCH_2CH_2Si(CH_3)_3$, 99.1%), 171 (MH^+ -$HOCH_2CH_2Si(CH_3)_3$-CH_2CO, 11.1%), 154 (9.5%), 153 (MH^+ -$OCH_2CH_2Si(CH_3)_3$ -HOAc, 100%) and 139 (7.4%); IR ($CHCl_3$) 2960, 2900, 1750, 1730, 1650, 1380, 1270, 1050, 1040, 870, and 845; $[\alpha]_D^{25}$ +2.495 (c 0.310).

Methoxypalladation Rearrangement of 6-Substituted Glycals. Following the alkoxypalladation rearrangement procedure, a solution of

each glycal (0.05 mmol-0.5 mmol) and $PdCl_2$ (0.50 eq) in methanol (0.5 mL) was stirred for 3.5 h at room temperature. Subsequent reaction at -5 °C for 1 h with $NaBH_3CN$ (1-1.4 eq) followed by cold workup afforded products listed below.

From 3,4-di-O-acetyl-D-glucal (3) was obtained methyl 2-O-acetyl-3,4-dideoxy-α-D-erythro-hex-3-enopyranoside (**19**) (23 mg, 61%). Data for **19**: R_f = 0.35 (7:3 toluene/EtOAc); ^1H NMR ($CDCl_3$) δ 6.29 (brs, H-3, H-4), 4.97-4.78 (m, H-2), 4.36-4.30 (d, J=5.5 Hz, H-1), 4.36-4.24 (m, H-5), 3.87-3.60 (m, H-6, H-6'), 3.30, 3.29 (s, OMe) 2.35 (brs, OH), and 2.09, 2.06 (s, OAc); IR ($CHCl_3$) 3440, 2960, 2930, 1740, 1605, 1500, 1460, 1450, 1430, 1380, 1250, 1210, 1150, 1110, 1040, 1010 and 930 cm^{-1}; MS (CI-CH_4) m/z 203 (MH^+, 1.0%), 153 (39%), 112 (7.8%), 111 (MH^+ -HOAc -$HOCH_3$, 100%); MS (HREI) calc. for $C_7H_{11}O_4$ (M^+ -CH_3CO) 159.0657, found 159.0654; calc. for $C_7H_{10}O_3$ (M^+ - HOAc) 142.0630, found 142.0631; $[\alpha]_D^{25}$ +3.237° (c 0.0748, $CHCl_3$).

From 3,4-di-P-acetyl-6-O-methly-D-glucal (4) was obtained methyl-2-O-acetyl-6-O-methyl-3,4,-dideoxy-α-D-erythro-hex-3-enopyranoside (**20**) (84 mg, 100%). Data for **20**: ^1H NMR ($CDCl_3$) δ 6.36-6.07 (m, H-3, H-4), 5.94-5.76 (m, H-2), 4.89 (brs, H-1), 4.72-4.66 (m, H-5), 4.45-4.13 (m, H-6, H-6'), 3.71, 3.5 (s, OCH_3), 2.12 (s, OAc); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 171.20 (OAc) 129.88 (C-4), 126.57 (C-3), 95.49 (C-1), 73.48 (C-6), 69.57 (C-2) 62.54 (C-5), 56.11 (OCH_3), 29.70 (OAc); MS (CI-CH_4) m/z 215 (MH^+ 6.1%), 201 (16%), 187 (27%), 173 (17%), 171 (13%), 159 (31%), 155 (12%), 153 (13%), 151 (5%), 147 (9%), 145 (55%), 143 (94%), 141 (32%), 140 (16%).

From 3,4,-di-O-acetyl-6-azido-6-deoxy-D-glucal (6) was obtained methyl 2-O-acetyl-6-azido-3,4,6-trideoxy-α-D-erythro-hex-3-enopyranoside (**21**) (104 mg, 80%) along with recovered **6** (23 mg, 20%). Data for **21** (from the mixture): R_f = 0.75 (7:3 toluene/EtOAc); ^1H NMR ($CDCl_3$) δ 5.85-5.71 (m, H-3, H-4), 5.33-5.23 (dd, J=5 Hz, 5 Hz, H-2), 4.79-4.76 (d, J=3 Hz, H-2), 3.46-3.36 (m, H-5, H-6, H-6'), 3.27 (s, OMe) and 2.07 (s, OAc); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.20 (OAc), 131.19 (C-4), 127.61 (C-3), 98.94 (C-1), 74.69 (C-5), 67.89 (C-2), 52.71 (OCH_3), 49.99 (C-6), 20.95 (OAc); MS (CI - CH_4) m/z 228 (MH^+, 1.7%), 200 (MH^+ -N_2, 22.2%), 185 MH^+-HN_3, 12.8%), 170 (MH^+ -N_2 -OCH_3, 11.2%), 169 (MH^+ -N_2 -$HOCH_3$, 9.8%), 168 (MH^+ - HOAc, 97.8%), 153 (MH^+ -$HOCH_3$ -OAc, 9.9%), 141 (MH^+ -N_2 -OAc, 9.1%), 140 (MH^+ -N_2 -HOAc, 43.4%), 136 (MH^+ -HOAc-$HOCH_3$, 26.4%), 126 (MH^+ -N_2 -$HOCH_3$ -CH_2CO, 100%), 125 (MH^+ -N_2 -$HOCH_3$ -CH_3CO, 19.3%), 110 (MH^+ -N_2

-OAc $-OCH_3$, 11.4%), 108 ($MH^+ - N_2$ -HOAc $-HOCH_3$, 15.2%); MS (HRCI) calc. for $C_9H_{14}NO_4$ ($MH^+ - N_2$) 200.0950, found 220.0927; MS (HREI) calc. for $C_9H_{13}O_4$ ($M^+ - N_3$) 185.0814, found 185.0693; MS (HRCI) calc. for $MH^+ - N_2$ $C_9H_{14}NO_4$ 200.0923, found 200.0927; $[\alpha]_D^{25}$ -5.57° (c 0.0151, $CHCl_3$)

From 3,4,6-tri-O-acetyl-D-galactal (7) was obtained methyl-2,6-di-O-acetyl-3,4-dideoxy-α-D-threo-hex-3-enopyranoside (22) (32 mg, 56%), along with 23 (7%) and unreacted 7 (7%). Data for 22 (from the mixture): R_f = 0.6; ^1H NMR ($CDCl_3$) δ 3.30 (s, 3H, OCH_3), 4.83 (d, J=3 Hz, H-1), 5.02 (m, H-2), 5.78 (d, J=8.5 Hz, H-3), 5.82 (brs, H-4), 4.23 (m, H-5), 4.15 (brs, 2H, H-6,6'), 2.09 (s, OAc); ^{13}C NMR (20 MHz, $CDCl_3$) δ 170 (OAc); 131.2 (C-4), 128.5 (C-3), 101.3 (C-1), 73.5 (C-5), 70.8 (C-6), 64.9 (C-2), 52.5 (OCH_3), 20.7; IR ($CHCl_3$) 1720, 1225, 1040, cm^{-1}; MS (CI-CH_4) 245 (MH^+, 10%), 213 (MH^+-CH_3OH, 51%), 185 (MH^+-AcOH, 8%), 171 (4%), 153 (213-AcOH, 5%), 143 (1%), 125 (2%), MS HREI calc. for $C_{11}H_{16}O_6$: 244.0954, found 244.0947.

From 3,4-di-O-acetyl-6-cyano-6-deoxy-D-glucal (8) was obtained methyl 4-O-acetyl-6-cyano-2,3,6-trideoxy-α-D-erythro-hex-2-enopyranoside (24) (7 mg, 80%) along with unreacted 8 (2 mg, 20%). Data for 24 (from the mixture): R_f = 0.66 (7:3 toluene/EtOAc); ^1H NMR ($CDCl_3$) δ 5.84-5.70 (m, H-3, H-4), 5.37-5.17 (m, H-2), 4.96-4.73 (m, H-1), 4.35-3.84 (m, H-5, H-6, H-6'), 3.27 (s, OCH_3) and 2.08 (s, OAc); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.70 (OAc), 130.33 (C-4), 128.32 (C-3), 98.00 (C-1), 72.48 (C-5), 65.79 (C-2), 35.82 (C-6), 52.62 (OCH_3), 20.59 (OAc); IR ($CHCl_3$) 2960, 2920, 2860 and 2830, 1740, 1655, 1650, 1370, 1240 and 1050 cm^{-1}; MS (CI-CH_4) m/z 213 (MH^+, 100%), 185 (MH^+ -HCN, 9.6%), 180 (MH^+ $-HOCH_3$, 13%), 153 (MH^+ - OAc, 26.3%), 152 (MH^+ -HOAc, 10.3%), 143 (MH^+ -HCN $-CH_2CO$, 8.6%), and 111 (MH^+ -HCN $-HOCH_3$ $-CH_2CO$, 6.4%); MS (HREI) calc. for $C_{10}H_{13}O_4$ (M^+-CN) 185.0814, found 185.0814, calc. for $C_8H_9O_3$ (M^+ -HCN $-OCH_3$) 153.0552, found 153.0603; $[\alpha]_D^{25}$ +1.13° (c 0.032, $CHCl_3$).

From 3,4-di-O-acetyl-D-xylal (11) was obtained methyl-4-O-acetyl-2,3-dideoxy-α-D-glycero-pent-2-enopyranoside (25) (115 mg, 50%) along with recovered 11 (115 mg, 50%). The product 25 was identical to an authentic sample prepared using $BF_3 \cdot Et_2O$ in methanol on the basis of its TLC and ^1H NMR data. Data for 25: R_f = 0.64 (7:3 toluene/EtOAc); ^1H NMR (500 MHz, $CDCl_3$) δ 6.09-6.05 (ddd, J=10 Hz, 5 Hz, 1.2 Hz, H-3), 6.04-6.01 (ddd, J=10 Hz, 2.9 Hz, 0.5 Hz, H-2),

4.89-4.84 (ddd, J=2.9 Hz, 1.2 Hz, 1 Hz, H-1), 4.15-4.09 (ddddd, J=12.5 Hz, 3 Hz, 1 Hz, 0.5 Hz, H-4), 3.90-3.75 (m, H-5, H-5'), 3.43 (s, OCH_3) and 2.09 (s, OAc); $[\alpha]_D^{25}$ +7.85 (c 0.267, $CHCl_3$).

From 3,4-di-O-acetyl-L-rhamnal (12) was obtained methyl 4-O-acetyl-2,3,6-trideoxy-α-L-erythro-hex-2-enopyranoside (26) (440 mg, 100%) which was identical to that prepared using $BF_3 \cdot Et_2O$ in methanol. Data for 26: R_f = 0.73 (7:3 toluene/EtOAc); ^1H NMR (500 MHz, $CDCl_3$) δ 5.81-5.76 (brd, J=10 Hz, H-3), 5.75-5.72 (ddd, J=10 Hz, 2.5 Hz, 1.7 Hz, H-2), 5.00-4.95 (dddd, J=10 Hz, 3 Hz, 1.7 Hz, 1.2 Hz, H-4), 4.79 (brs, H-1), 3.90-3.85 (dq, J=10 Hz, 6 Hz, H-5), 3.37 (s, OCH_3), 2.02 (s, OAc) and 1.17-1.16 (d, J=6 Hz, H-6); ^{13}C NMR ($CDCl_3$) δ 170.2 (OAc), 129.5 (C-3), 127.4 (C-2) 95.2 (C-1), 70.8 (C-4), 64.7 (C-5), 55.6 (OCH_3), 21.0 (OAc) and 17.9 (C-6); MS (CI-CH_4) m/z 215 (M^+ + C_2H_5, 30.7%), 187 (MH^+, 10.5%), 173 (31%), 156 (9%), 155 (MH^+ -$HOCH_3$, 100%), 127 (MH^+ -HOAc, 52.8%) and 55 (MH^+ -$HOCH_3$ -HOAc, 28.8%); $[\alpha]_D^{25}$ -27.7° (c 0.216, $CHCl_3$).

ACKNOWLEDGEMENT

Support for this research from the National Cancer Institute (CA 21162), the American Cancer Society, and Southern Illinois University is gratefully acknowledged. A generous loan of palladium chloride was provided from Engelhard Industries. Several spectroscopic facilities, their funding agencies, and staff personnel are acknowledged as follows: Southern California Regional Nuclear Magnetic Resident Spectrometry Facility at the California Instutute of Technology (NSF), Dr. William Croasman; Purdue University Biomagnetic Resonances Laboratory (NIH), Dr. W. M. Westler; Southern Illinois University at Carbondale NMR Facility; Midwest Center for Mass Spectrometry, Department of Chemistry, University of Nebraska (NSF), Dr. Ken Tomar; Mass Spectrometry Laboratory, University of Illinois, School of Chemical Sciences (NIH GM 27029), Dr. J. C. Cook, Jr.; Mass Spectrometry Laboratory, Department of Psychiatry, Washington University School of Medicine (NIH), Dr. D. M. Bier, M.D. and Richard Burger; Mass Spectrometry Laboroatory, Coal Research Center, Southern Illinois University at Carbondale (DOE), Ken Walsh; and Mass Spectrometry Laboratory, University of Southern California (NSF).

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