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Synthesis of Pyranose Glycals via Tungsten and Molybdenum Pentacarbonyl-Induced Alkynol Cyclizations‡

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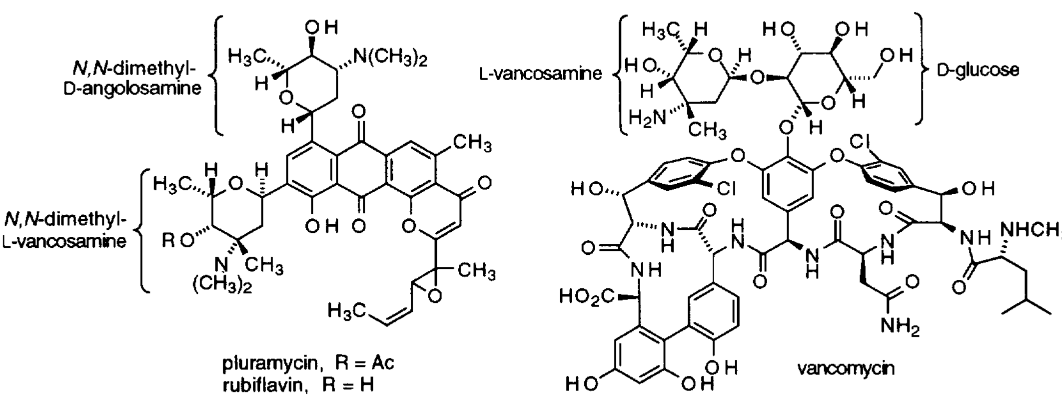
Abstract: The tungsten pentacarbonyl-induced cyclization of an acyclic alkynol substrate bearing protected oxygen and nitrogen functional groups provides the cyclic tungsten oxacarbene, which is readily converted into a pyranose glycal structurally related to the carbohydrate moieties of the pluramycin and vancomycin families of antitumor antibiotics. In addition a molybdenum-catalyzed cycloisomerization procedure provides an alternative route to this pyranose glycal.

The nature of carbohydrate substituents found in the structures of many pharmacologically important organic compounds often play critical roles in the molecular recognition between antibiotic agents and the desired biological targets, with medical implications regarding *in vivo* toxicity as well as drug potency. In many cases these carbohydrates are deoxygenated at a number of centers, and may even bear unusual amine or alkyl substituents.[1] For instance, the observed sequence selectivity for DNA strand cleavage exhibited by the pluramycin family of *C*-arylglycoside antitumor natural products (Scheme 1) is explained by cooperativity of hydrogen bond interactions between the protonated *N*, *N*-dimethylamino groups of each aminosugar with pyrimidine carbonyls on the DNA strands.[2] In the vancomycin-type antibiotics, the presence of the aminosugar moieties apparently facilitates dimerization of two vancomycin units which is cooperative with binding of the peptide target of bacterial cell walls.[3]

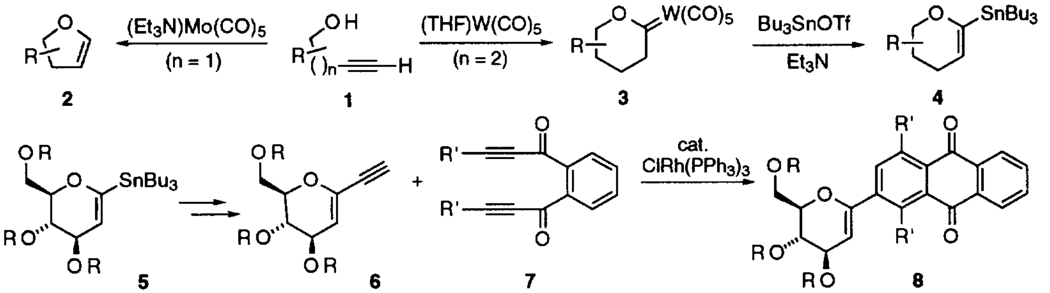
Scheme 1. Representative aminoglycoside antibiotics



‡ Dedicated to Prof. Samuel J. Danishefsky in honor of his receiving the 1996 Wolf Prize in Chemistry.

Our laboratory has been engaged in the development of new methodology for the synthesis of bioactive carbohydrates from non-carbohydrate precursors. Several years ago we discovered that triethylamine-molybdenum pentacarbonyl catalyzed the cycloisomerization of homopropargylic alcohols **1** (n = 1) to furanoid glycals **2** (Scheme 2),[4] and we have since reported applications to the efficient synthesis of several nucleoside glycoconjugates, including the anti-AIDS drug d4T as well as several nucleoside analogs based on the puromycin aminonucleosides.[5] More recently we have observed that tungsten pentacarbonyl induces cyclization of alkynyl alcohols **1** (n = 2) to six-membered ring tungsten oxacarbenes **3**, which can be subsequently converted to α-stannyl dihydropyrans **4**.[6] In a related vein we have found that 1-alkynyl-1,2-D-glucal derivatives **6** (prepared from the parent D-glucal) undergo rhodium-catalyzed alkyne cyclotrimerization with *ortho*-bis-propynoylarenes **7** to give *C*-anthracyclinone glycosides **8**.[7]

Scheme 2.

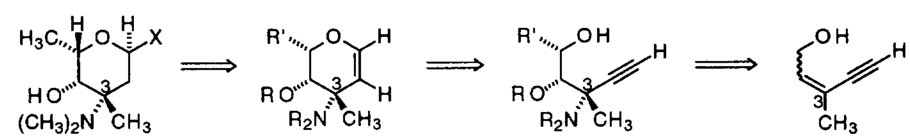


Herein we describe the compatibility of nitrogen and oxygen substituents in the tungsten-mediated alkynol cyclization reaction, and demonstrate that a six-membered tungsten oxacarbene product can be formed and converted into a pyranose glycal analogous to vancosamine carbohydrates of the pluramycin and vancomycin glycoconjugates. In addition we present the first example of single-step molybdenum-catalyzed alkynol cycloisomerization to a pyranose glycal.

RESULTS AND DISCUSSION

The synthesis plan for the preparation of an aminosugar compound corresponding to vancosamine features the vancosamine glycal **10** as the initial target (Scheme 3).[8] We perceived that this glycal might serve as an effective glycosyl donor for preparation of *O*- and/or *C*-glycoside structures, and that the glycal might be synthesized from the acyclic isomeric alkynyl alcohol **11**. A further simplification in the retrosynthesis plan featured stereoselective addition of carbon (R'), oxygen, and nitrogen substituents of **11** from the acyclic achiral enynol **12** (each of the *E* and *Z*-alkene isomers is commercially available).

Scheme 3. Retrosynthesis plan



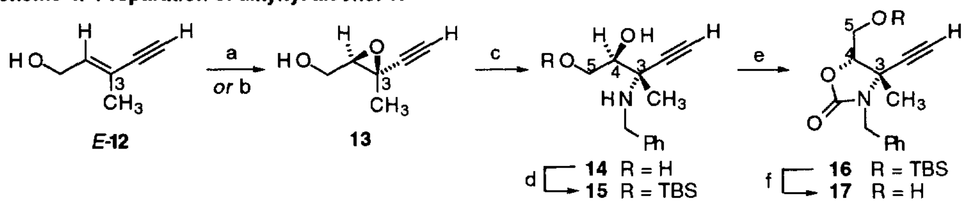
N,N-dimethyl-L-vancosamine (**9**) (X = aglycone) **10** **11** **12**

Preparation of alkynyl alcohol substrates:

Epoxidation of the *E*-enynol **12** could be achieved with *m*-chloroperoxybenzoic acid to give *rac*-**13**, or with the titanium/tartrate-catalyzed asymmetric epoxidation[9] to provide (-)-**13** (Scheme 4). Initial experiments exploring titanium-induced nucleophilic opening[10] with diethylamine or azide resulted in a mixture of products resulting from the desired addition of amine at the hindered propargylic position (C-3) of epoxide **13** accompanied by the allylic alcohol resulting from base-induced epoxide opening by deprotonation at the methyl group. Although the literature reports on the titanium-assisted addition of primary amines to epoxyalcohols suggested that overalkylation would be a problem,[10a] we found that epoxide **13** reacted cleanly with benzylamine when the amine was used as solvent. In order to achieve high *anti*-stereospecificity for benzylamine addition, it is essential that tartrate impurities from the preceding asymmetric epoxidation step are completely removed from the epoxide substrates.

Reaction of the aminodiol **14** with triphosgene gave the undesired six-membered ring carbamate from reaction of the C5-alcohol and C3-amine, but selective protection of the primary C5 alcohol as the silyl ether **15** permitted subsequent protection of the secondary C4 alcohol and amine functional groups as the cyclic carbamate **16**. Treatment of **16** with tetra-*n*-butylammonium fluoride afforded the primary alkynol substrate **17**.[11]

Scheme 4. Preparation of alkynyl alcohol 17

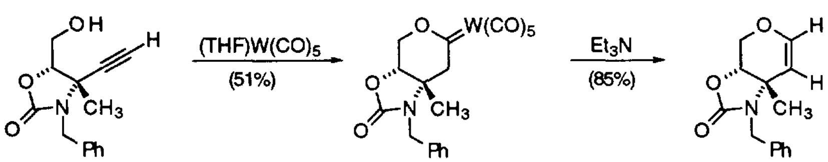


Reagents and Conditions: (a) *m*-CPBA, CH_2Cl_2 / Na_2HPO_4 buffer (64% yield, *rac*-**13a**). (b) 10 mol% $Ti(O\text{-}i\text{-}Pr)_4$, 14 mol% D-DIPT, $PhCMe_2OOH$, CH_2Cl_2 (70% yield, 78% ee). (c) $PhCH_2NH_2$ (excess), $Ti(O\text{-}i\text{-}Pr)_4$, 20°C (72% yield). (d) TBDMSCl, imidazole, DMF (90% yield). (e) triphosgene, aq. K_2CO_3, toluene (99% yield). (f) TBAF, THF (96% yield)

Tungsten and molybdenum carbonyl-induced cyclizations of alkynyl alcohols:

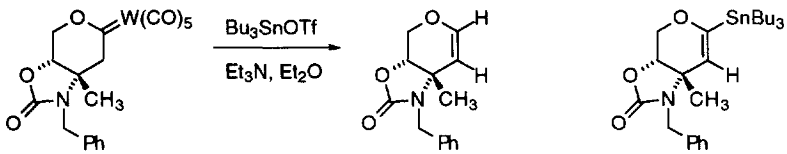
The cyclization of the alkynyl alcohol substrate **17** with (tetrahydrofuran)tungsten pentacarbonyl afforded the tungsten oxacarbene **18** in satisfactory yield (Scheme 5). The conversion of the metal carbene **18** into the organic pyranose glycal **19** proceeded cleanly and in high yield under mildly basic conditions. Surprisingly, we observed that the carbene **18** was also effectively converted into the glycal **19** during an eight-hour NMR run while standing in $CDCl_3$ solvent which undoubtably contained traces of DCl. In general carbene **18** appears to be less stable than other tungsten dihydropyranylidene carbenes previously prepared in our laboratory.[6]

Scheme 5. Tungsten carbonyl-induced cyclization of 17



The six-membered ring tungsten oxacarbene product **18** also exhibits anomalous behavior in a number of its functionalization reactions. Although we have shown that a wide variety of cyclic and acyclic group VI metal carbenes can be efficiently converted into α-stannyl enol ethers upon reaction with triethylamine and tri-*n*-butyltin triflate,[6,12] the more highly functionalized carbene **18** only gives the glycal **19** under our standard stannylation conditions (Scheme 6).

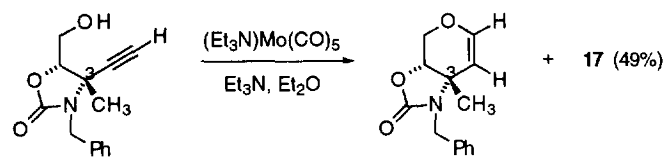
Scheme 6. Unsuccessful formation of α-stannylglycal 20



18 **19** (86%) **20** (not observed)

Given the facile formation of the glycal **19** from the corresponding tungsten carbene **18**, we decided to explore the single-step conversion of alkynol **17** into the glycal **19**.[4,5] Although we were previously unsuccessful in forming six-membered ring products from a variety of simple 1-alkyn-5-ols with molybdenum or chromium carbonyl reagents,[6] we found that the slow cyclization of the alkynol substrate **17** was promoted by (triethylamine)molybdenum pentacarbonyl to give the cycloisomeric pyranose glycal **19** in 35% isolated yield (68% based on recovered alkynol **17**, Scheme 7). The *cis*-ring fusion of the cyclic carbamate and/or the vicinal disubstitution at C3 apparently facilitates the cyclization of this specific substrate.

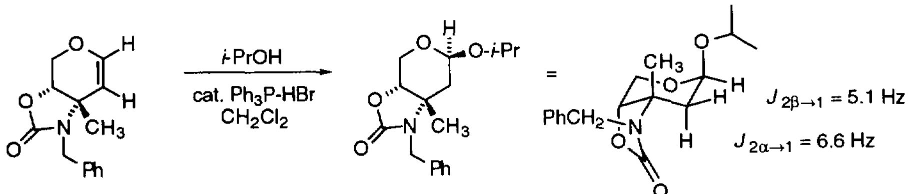
Scheme 7. Molybdenum carbonyl-induced cycloisomerization of 17



17 **19** (35%)

We have briefly explored the acid-catalyzed glycosylation of the pyranose glycal **19**. Triphenylphosphine-hydrogen bromide catalyzed[13] addition of isopropanol gives one major glycoside product, which we have assigned as the β-anomer **21** based on ^1H NMR coupling constants (Scheme 8). Further studies on the glycosylation of this and more complex pyranose glycals are in progress.

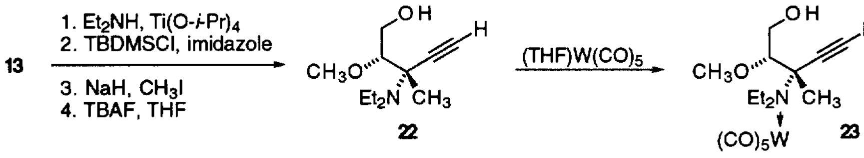
Scheme 8. Stereoselective preparation of isopropyl pyranoside **21**



19 **21**

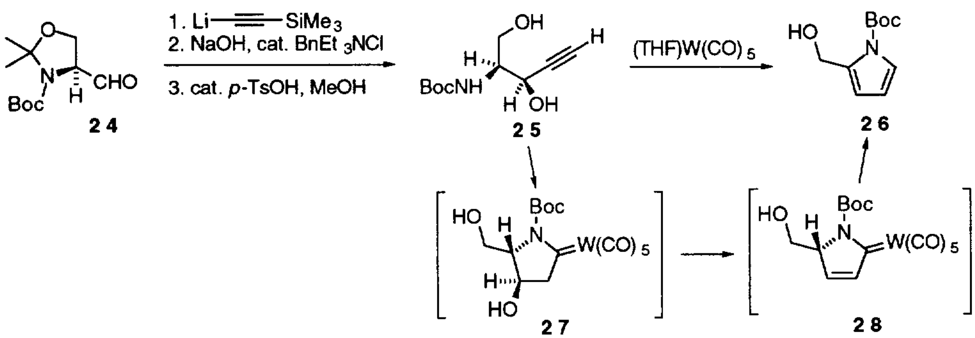
We encountered a number of enlightening observations in the course of this research. Our first explorations of tungsten pentacarbonyl-induced cyclizations of 4-pentyn-1-ol indicated that tungsten pentacarbonyl formed a strong complex with triethylamine which was subsequently inert to reaction with the alkynol substrate.[6] Attempts to cyclize the tertiary amine-containing alkynol substrate **22** indicated that reaction with the tetrahydrofuran complex of tungsten pentacarbonyl failed to undergo a clean cyclization, but instead gave the coordinated tungsten amine complex **23** (Scheme 9). Therefore, a carbamate protective group for the nitrogen substituent was chosen in the preparation of alkynol **17**.

Scheme 9.



In further exploring functional group compatibility of the alkynol cyclization reaction, we unexpectedly found that the C4 nitrogen-containing substrate **25** gave the pyrrole derivative **26** upon reaction with (THF)W$(CO)_5$ (Scheme 10).[14] In this case the secondary carbamate nitrogen is five atoms away from the central carbon atom of the tungsten vinylidene intermediate leading to a putative carbene intermediate **27**. The aromatic pyrrole ring of **26** may arise from elimination of the C3-hydroxyl group from **27**; vinylogous deprotonation of **28** and reprotonation at the tungsten-carbon bond then affords the organic pyrrole **26**.

Scheme 10. "Asymmetric synthesis" of pyrrole derivative 26



CONCLUSIONS

The application of tungsten carbonyl-mediated alkynol cyclizations to the preparation of highly functionalized pyranose glycals represents a significant advance in our program on the synthesis of carbohydrates from non-carbohydrate precursors, and holds promise for a new entry into the synthesis of bioactive *O*- and *C*-glycoconjugates. The inadvertent discovery of the novel azacyclization synthesis of pyrroles (Scheme 10, **25** → **26**) indicates that cyclic enamines might be produced upon reaction of simpler aminoalkyne substrates with appropriate organometallic catalysts.

EXPERIMENTAL SECTION

(2*R*, 3*R*)-3-Ethynyl-2-hydroxymethyl-3-methyloxirane (13): ***E*-12** (2.88 g, 30 mmol, dried over 3Å MS), D-(-)-diisopropyl tartrate (1.0 g, 4.3 mmol), and CH_2Cl_2 (50 mL) were added to powdered 3Å molecular sieves (2.0 g, flame dried). The mixture was chilled to -20°C, Ti(O-*i*-Pr)$_4$ (0.9 mL, 3.05 mmol) was added and stirred for 30 min at -20°C. Cumene hydroperoxide (7.37 g, 38.7 mmol, dried over 3Å MS) was added dropwise over 25 min. The mixture was stoppered and transferred to a freezer (-25°C) for 3 h. The mixture was then chilled to -30°C and $P(OMe)_3$ (2.3 mL, 19.5 mmol) was added dropwise over 10 min. Citric acid (576 mg, 3 mmol, dissolved in acetone / Et_2O (1 / 1, 50 mL)) was added, the mixture was stirred for 45 min, and then allowed to warm to 20°C. The mixture was filtered through Celite, and the solvents were evaporated. The residue was purified by flash chromatography on silica gel using pentane / ether (3 / 1) to yield a light yellow oil (3.20 g) as a mixture of epoxide and diisopropyl tartrate (epoxide / tartrate = 5.8 / 1 by ^1H NMR). Homogenous epoxide **13** (2.4 g, 70%) was obtained by Kugelrohr distillation (100°C - 110°C, 2 mmHg). $[\alpha]^{24}_D$ = -8.4° ($CHCl_3$, c = 4.8), (lit. for (2*S*, 3*S*) enantiomer[15] $[\alpha]^{25}_D$ = +11.36° ($CHCl_3$, c = 4.4)); IR (CH_2Cl_2) 3288, 2980, 2118, 1384, 1031 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.52 (3H, s), 2.31 (1H, s), 3.35 (1H, dd, *J* = 4.5, 6.2 Hz), 3.67 (1H, dd, *J* = 6.2, 12.4 Hz), 3.82 (1H, dd, *J* = 4.5, 12.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.1, 50.7, 60.0, 63.6, 70.6, 83.3; MS (EI) 111, 82, 81, 69, 53, 52, 43; HRMS: Calcd. for $C_6H_7O_2$ (M-1): 111.0446, Found 111.0447. Mosher ester analysis reveals ee = 78%.

(3*S*, 4*S*)-3-Benzylamino-3-methyl-1-pentyne-4,5 diol (14): Ti(O-*i*-Pr)$_4$ (0.9 mL, 3.0 mmol) was added dropwise into a solution of oxirane **13** (218 mg, 1.95 mmol) in benzylamine (10 mL) at 20 °C. After 2 h, the reaction mixture was distilled (80°C, 1 mmHg, bath temp 110°C). The residue was diluted with ethyl acetate (20 mL) followed by additon of 10% NaOH brine solution (7 mL). After 5 h, the mixture was filtered through a pad of Celite. The filtrate was dried over Na_2SO_4 overnight and concentrated *in vacuo*. The residue was purified by flash chromatography on silica using pentane / ethyl acetate (1 / 1) as eluant to yield aminodiol **14** as a light yellow oil (309 mg, 72 %) which solidified upon standing: mp = 65.0 - 66.0°C; $[\alpha]^{23}_D$ = -12.2° ($CHCl_3$, c = 0.82); IR (CH_2Cl_2) 3301, 2937, 2363, 2338, 1646, 1454, 1055 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.48 (3H, s), 2.52 (1H, s), 3.63 (1H, t, *J* = 4.6 Hz), 3.77-3.84 (2H, m), 3.95-4.00 (2H, m), 7.24-7.37 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.8, 47.5, 56.7, 63.3, 73.7, 75.8, 84.5, 126.9, 128.3, 139.5; MS (EI) 220, 204, 188, 158, 159, 106, 91, 65; HRMS Calcd for $C_{13}H_{18}NO_2$ (M+1): 220.1377, Found 220.1342.

(3*S*, 4*S*)-3-Benzylamino-3-methyl-1-pentyne-4,5 diol, 5-*t*-butyldimethylsilyl ether (15): Diol **14** (446 mg, 2.0 mmol) was dissolved in DMF (15 mL) at 0 °C. *t*-Butyldimethylsilyl chloride (330 mg, 2.2 mmol) and imidazole (300 mg, 4.4 mmol) was added sequentially. The reaction mixture was kept at 0°C for 2 h and then stirred at 20°C for 8 h. The reaction mixture was diluted with ether (150 mL) and washed with water (3 × 10 ml). The organic layer was dried over Na_2SO_4 and evaporated *in vacuo*. The residue was purified by flash chromatography on silica gel using pentane / ethyl acetate (10 / 1) to yield silyl ether **15** as a colorless oil (600 mg, 90 %) which solidified upon standing: mp = 53.0 - 53.5°C; $[\alpha]^{23}_D$ = -12.0° ($CHCl_3$, c = 7.2); IR (CH_2Cl_2) 3276, 3227, 3150, 1455, 1250 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.04 (6H, d, *J* = 3.3 Hz), 0.81 (9H, s), 1.43 (3H, s), 2.46 (1H, s), 3.54 (1H, app t, *J* = 4.4 Hz), 3.77 (1H, d, *J* = 12.0 Hz), 3.83 (1H, dd, *J* = 3.3, 10.4 Hz), 3.94 (1H, d, *J* = 12.0 Hz), 4.02 (1H, dd, *J* = 5.4, 10.4 Hz), 7.21-7.37 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ -5.6, 18.1, 23.7, 25.7, 47.6, 56.6, 64.5, 73.0, 76.2, 85.5, 126.8, 128.3, 140.3; MS (EI) 333, 318, 302, 276, 188, 158, 91; HRMS Calcd for $C_{19}H_{31}NO_2Si$: 333.2124, Found 333.2122. Elemental Analysis: calcd 68.42% C, 9.37% H, 4.20% N; found 68.38% C, 9.02% H, 4.20% N.

Cyclic carbamate (16): Aminoalcohol **15** (400 mg, 1.2 mmol) was dissolved in toluene (10 mL) and was chilled to 0°C. K_2CO_3 (220 mg dissolved in H_2O, 5 mL) was added followed by triphosgene (140 mg, 0.47 mmol). The reaction was allowed to warm to 20°C and stirred overnight. The biphasic reaction mixture was then separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and removed *in vacuo*. The residue was purified by flash chromatography on silica using pentane / ethyl acetate (10 / 1) to yield carbamate **16** as a colorless oil (426 mg, 99%): $[\alpha]^{23}_D$ = +20.4° ($CHCl_3$, c = 4.7); IR (CH_2Cl_2) 3273, 2926, 2857, 1761, 1387, 1097 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.09 (6H, s), 0.89 (9H, s), 1.36 (3H, s), 2.57 (1H, s), 3.99 (2H, d, J = 5.9 Hz), 4.16 (1H, t, J = 5.9 Hz), 4.22 (1H, d, J = 15.8 Hz), 4.80 (1H, d, J = 15.8 Hz), 7.27-7.37 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ -5.8, 17.7, 26.3, 26.8, 46.0, 59.2, 61.9, 76.4, 78.8, 81.2, 127.0, 127.4, 128.0, 137.2, 156.8; MS (EI) 360, 359, 344, 314, 302, 211, 169, 139, 91; HRMS Calcd for $C_{20}H_{30}NO_3Si$ (M+1): 360.1995, Found 360.1988. Elemental Analysis: calcd 66.81% C, 8.13% H, 3.90% N; found 66.59% C, 7.79% H, 3.90% N.

Alkynol (17): Tetrabutylammonium fluoride (1M in THF) (1.2 mL, 1.2 mmol) was added dropwise to **16** (415 mg, 1.16 mmol) dissolved in THF (5 mL) at 0°C. After 45 min at 0°C, the reaction mixture was diluted with ethyl acetate (100 mL), washed with water and brine, and dried over Na_2SO_4. Solvents were removed *in vacuo*, and the residue was purified by flash chromatography on silica using pentane / ethyl acetate (2 / 1 gradient to pure ethyl acetate) to yield alkynol **17** as a colorless oil (273 mg, 96%): $[\alpha]^{24}_D$ = +36.1° ($CHCl_3$, c = 3.3); IR (CH_2Cl_2) 3436, 3296, 2361, 1753, 1399 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.34 (3H, s), 2.63 (1H, s), 3.49 (1H, br s), 3.91-4.01 (2H, m), 4.20-4.25 (2H, m), 4.72 (1H, J = 16 Hz), 7.22-7.33 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.2, 45.3, 58.6, 61.8, 77.0, 78.8, 82.1, 127.5, 127.8, 128.4, 137.2, 157.2; MS (EI) 246, 245, 230, 150, 106, 91; HRMS Calcd for $C_{14}H_{15}NO_3$: 245.1052, Found 245.1044.

Tungsten oxacarbene (18): $W(CO)_6$ (540 mg, 1.53 mmol) was placed in a 100 mL airfree reaction tube (Pyrex) fitted with a reflux condenser and purged with N_2 for 1h. THF (40 mL) was added by syringe and the solid dissolved with stirring. The reaction mixture was then irradiated (350 nm, Rayonet photoreactor) for 3 h under N_2 with stirring. The reaction vessel was removed from the light source and allowed to cool to 20°C before the alkynol **17** (133 mg, 0.54 mmol) was added via cannula with a minimal amount of THF. The reaction mixture was then stirred at 20°C for 48 h. The solvent was removed *in vacuo* at 10°C and the residue was purified by flash chromatography on silica using pentane / ethyl acetate (10 / 1 to 1 / 1) to yield carbene **18** as brick red crystals (157 mg, 51%). mp = 163.0 - 164.0°C; ^1H NMR (300 MHz, $CDCl_3$) δ 1.12 (3H, s), 2.35 (1H, d, J = 15.0 Hz), 4.10 (1H, d, J = 15.0 Hz), 4.22 (1H, d, J = 15.0 Hz), 4.37-4.50 (2H, m), 4.82 (1H, d, J = 15.0 Hz), 4.88 (1H, dd, J = 3.8, 13.5 Hz), 7.25-7.45 (5H, m).

Pyranose glycal (19): Preparation from tungsten carbene **18**: Freshly distilled Et_3N (1 mL) was added to carbene **18** (157 mg, 0.27 mmol) solution in THF / Et_2O (5 mL / 10mL) at 20°C. After 1 h, the volatiles were removed *in vacuo* and the residue was purified by flash chromatography on silica using pentane / ethyl acetate (10 / 1 followed by 1 / 1) to yield glycal **19** as a white solid (56 mg, 85 %): mp = 107.0 - 108.0°C; $[\alpha]^{23}_D$ = +60.4° ($CHCl_3$, c = 0.81); IR (CH_2Cl_2) 3063, 2974, 1745, 1645, 1396 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.28 (3H, s), 3.89 (1H, dd, J = 2.1, 12.6 Hz), 4.24 (2H, dd, J = 3.7, 12.6 Hz), 4.26 (1H, d, J = 15.6 Hz), 4.51 (1H, d, J = 15.6 Hz), 4.68 (1H, d, J = 6.4 Hz), 6.39 (1H, d, J = 6.4 Hz), 7.23-7.34 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.5, 44.5, 55.0, 62.6, 77.0, 102.5, 127.5, 127.8, 128.5, 137.6, 144.9, 156.9; MS (EI) 246, 245, 231, 230, 96, 95, 91, 71; HRMS Calcd for $C_{14}H_{15}NO_3$: 245.1052, Found 245.1048.

Preparation from alkynyl alcohol **17**: $Mo(CO)_6$ (70 mg, 0.26 mmol) was placed in a 18 × 150 mm borosilicate test tube. Freshly distilled Et_3N (3 mL) and Et_2O (7 mL) were added and the contents dissolved by stirring. The reaction mixture was then photolyzed (350 nm, Rayonet photoreactor) for 20 min under N_2. The reaction vessel was removed from the light source, and alkynol **17** (130 mg, 0.53 mmol) was added via cannula with Et_2O (7 mL). The reaction mixture was then stirred for 86 h at 20°C. The solvents were removed *in vacuo* and the residue was purified by flash chromatography on silica gel using pentane / ethyl acetate (10 / 1 gradient to 2 / 1) to yield the glycal **19** (45 mg, 35%) and recovered alkynol **17** (64 mg, 49%).

Isopropyl pyranoside (21): Glycal **19** (49 mg, 0.2 mmol), isopropanol (36 mg, 0.6 mmol), triphenylphosphine hydrogen bromide (34 mg, 0.1 mmol) and CH_2Cl_2 (5 mL) were stirred together at 20°C. After 36 h, the mixture was diluted with CH_2Cl_2 (40 mL), washed with satd aq $NaHCO_3$ (2×5 mL) and brine (5 mL). The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel using pentane / ethyl acetate (2 / 1) to yield pyranoside **21** as a colorless oil (30 mg, 49%): $[\alpha]^{23}_D$ = +7.2° ($CHCl_3$, c = 0.53); IR (CH_2Cl_2) 2971, 2932, 1736, 1405, 1112 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.88 (3H, d, J = 6.3 Hz), 1.09 (3H, d, J = 6.3 Hz), 1.33 (3H, s), 1.46 (1H, dd, J = 6.6, 15.1 Hz), 1.88 (1H, dd, J = 5.1, 15.1 Hz), 3.67-3.78 (2H, m), 3.87 (1H, dd, J = 2.3, 13.5 Hz), 4.09 (1H, t, J = 1.8 Hz), 4.19 (1H, d, J = 15.4 Hz), 4.27 (1H, dd, J = 5.4, 6.4 Hz), 4.58 (1H, d, J = 15.4 Hz), 7.25-7.40 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.1, 23.3, 25.7, 35.6, 44.2, 57.2, 59.2, 68.5, 77.7, 93.0, 127.8, 128.2, 128.6, 137.9, 157.8; MS (EI) 305, 262, 246, 189, 172, 150, 91; HRMS Calcd for $C_{17}H_{23}NO_4$: 305.1627, Found 305.1631.

***N*-(*t*-butoxycarbonyl)-2-pyrrolemethanol (26):** Colorless oil. IR (CH_2Cl_2) 3552, 3431, 2983, 1750, 1345, 1125 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.63 (9H, s), 3.62 (1H, t, J = 7.5 Hz), 4.65 (2H, d, J = 7.5 Hz), 6.10 (1H, m), 6.18 (1H, m), 7.17 (1H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.0, 57.5, 84.4, 110.4, 113.9, 122.0, 134.5, 150.2; MS (EI) 197, 141, 124, 97, 80, 57, 41; HRMS Calcd for $C_{10}H_{15}O_3N$: 197.1052, Found 197.1041.

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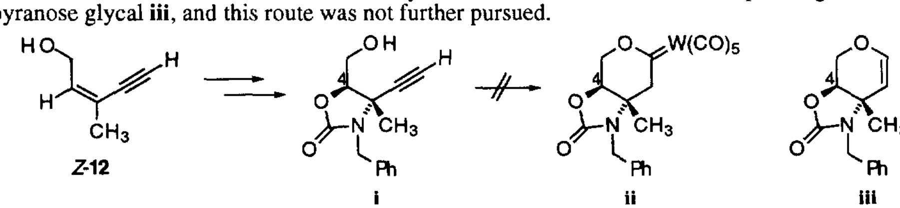
11. A similar sequence of reactions was used to convert **Z-12** into alkynol **i** (the C4-diastereomer of **17**). However, substrate **i** could not be cleanly converted into either the corresponding carbene **ii** or the pyranose glycal **iii**, and this route was not further pursued.



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