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Palladium-Catalyzed Reduction of a Propargylic Acetate Derived from a Sugar with SmI_2. Some Unexpected Results

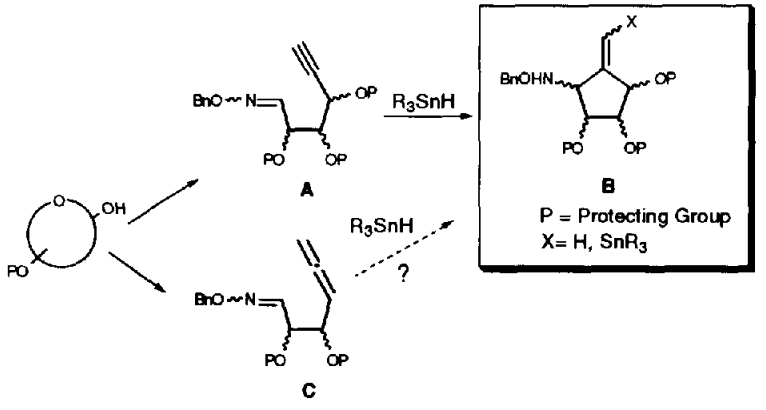
José Marco-Contelles,* Christine Destabel and José Luis Chiara

Instituto de Química Orgánica General, Juan de la Cierva, 3. 28006-Madrid, Spain

Abstract: We describe here the unexpected result that we have observed in the palladium-catalyzed reduction of the propargylic acetate **3** derived from a sugar with samarium diiodide. In addition to traces of the expected allene derived product **4**, we have obtained mostly α-elimination leading to enynes **5** in moderate yield.

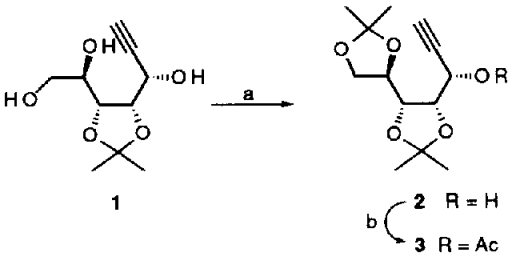
Free radical inter- and intramolecular carbon-carbon bond forming reactions are of paramount importance in organic synthesis.[1] In recent years, complex and densely functionalized carbocycles have been efficiently prepared from chiral, radical precursors.[2] As part of our ongoing research in this area,[3] we have recently reported a new and highly stereospecific method for the asymmetric synthesis of aminocyclopentitols[4] *via* the free radical cycloisomerization of enantiomerically pure, polyoxygenated alkyne-tethered oxime ethers derived from sugars.[5,6]

Our approach is shown in Scheme 1. The essential aspects of this strategy included the transformation of an aldose to afford the chiral radical precursor **A**. This product, upon attack by the appropriate tin hydride reagent, provided the vinyl radical species leading to the aminocyclopentitol **B**. In order to broaden the scope of this methodology we desired the related allene radical precursors of type **C**,[7] as shown in Scheme 1. A simple strategy for the synthesis of these intermediates was the palladium-catalyzed reduction of propargylic acetates of type **A** with SmI_2. An examination of the literature for this transformation revealed that this process gives, in selected conditions, good yields and high stereocontrolled ratios of the allene product.[8]

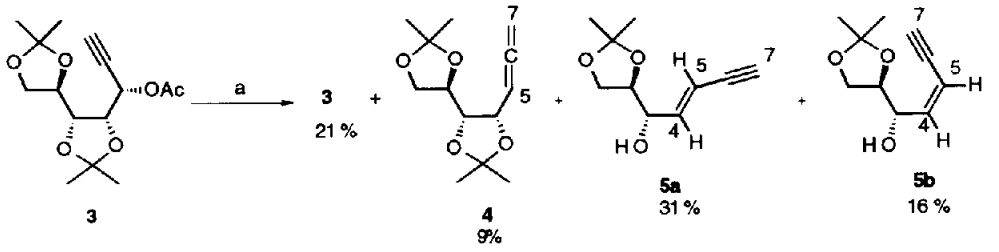


Scheme 1

An advanced intermediate for this purpose should be compound **4** (Scheme 3). This product could be prepared from acetate **3** (Scheme 2) following Inanaga's methodology.[8] This sugar could be also derived from 2,3-*O*-isopropylidene-D-ribose[9] following standard manipulations: ethynylmagnesium bromide addition to give product **1**,[10] followed by acetal formation and acetylation (Scheme 2). This provided the desired product **3** in good yield and in diastereomerically pure form. However, in the conditions reported by Inanaga,[8] using *t*-butanol as solvent, a very poor yield of the desired allene **4** product was obtained; the rest of the resulting material being recovered product **3** and a mixture of enynes **5**, in the yields and ratio shown in the Scheme 3. Compounds **4** and **5** were too unstable to give a correct microanalysis, but the ^{1}H NMR analysis of these samples gave coherent data with the proposed structures. In fact, the less polar fraction isolated during the flash chromatography was an inseparable mixture of two compounds in 14:1 ratio; the structure of the minor product could not be established; this mixture of compounds showed in the ^{1}H NMR spectrum the expected signals for the allene moiety [5.30 ppm (dd, J= 6.5 and 6.9 Hz, HC5) and 4.88 ppm (dd, J=2 and 6.6 Hz, 2 HC7)] corresponding to major product **4**. Compound **5a** showed in the ^{1}H NMR spectrum typical vicinal coupling constants ($J_{4,5}$= 16 Hz) for a double bond with *E* stereochemistry and a typical acetylenic signal at 2.91 ppm (d, J= 2.3 Hz), while the *Z* isomer showed signals for H4 and H5 with $J_{4,5}$= 11 Hz, and H7 at 3.18 ppm (d, J= 2 Hz).



Scheme 2 Reagents. a: DMP, PPTS, acetone (100 %); b: Ac_2O, pyridine (92%)



Scheme 3 Reagents. a: SmI_2 / cat. $Pd(PPh_3)_4$ / *t*- BuOH / THF

The formation of products **5** was surprising, but a detailed survey of the substrates used by Inanaga in his seminal reports,[8] has shown that *none of the substrates studied had an alkoxy substituent at the homopropargylic position*. Assuming the proposed mechanism for this transformation,[8] the carbanionic species in the propargylic position to the triple bond should be prone to eliminate the vicinal substituent or isomerize to the allenic carbanion that gives the allene upon protonation. When possible, as in this case, the α-

elimination is preferred. To our knowledge this is the first time that such an α-elimination has been reported in this important reaction and constitutes a serious drawback for this method to be used in polyfunctionalized intermediates such as **3**. Although the resulting enyne product has been obtained in moderate yield, the protocol is very simple and efficiently leads to this interesting and difficult to prepare enyne structural moiety.

Experimental Part

General Methods. Reactions were monitored by TLC using precoated silica gel aluminium plates containing a fluorescent indicator (Merck, 5539). Detection was done by UV (254 nm) followed by charring with sulfuric-acetic acid spray, 1% aqueous potassium permanganate solution or 0.5% phosphomolybdic acid in 95% EtOH. Anhydrous $MgSO_4$ was used to dry organic solutions during workups and the removal of solvents was carried out under vacuum with a rotary evaporator. Flash column chromatography was performed using Kieselgel 60 (230-400 mesh, Merck) and hexane-ethyl acetate mixtures as eluent. Optical rotations were determined with a Perkin-Elmer 257 instrument. ^1H and ^{13}C NMR spectra were recorded with a Varian VXR-300S spectrometer, using tetramethylsilane as internal standard.

1,2-Dideoxy-4,5:6,7-di-*O*-isopropylidene-D-allo-hept-1-ynitol 2. Dimethoxypropane (1.80 mL, 14.69 mmol) was added to 1,2-dideoxy-4,5-*O*-isopropylidene-D-allo-hept-1-ynitol **1**[10] (1.03 g, 4.76 mmol) and PPTS (0.06 g) in acetone (45 mL). The reaction mixture was stirred at r. t. for 4 h, saturated sodium bicarbonate solution (2 mL) was added and the solvent removed under reduced pressure. The residue was diluted in dichloromethane (60 mL) and poured into saturated sodium bicarbonate solution (30 mL), then extracted with dichloromethane (3 x 20 mL), dried over magnesium sulphate and concentrated under reduced pressure to give the protected heptynitol **2** (1.22 g, 100%) as an oil; R_f = 0.51 (30% ethyl acetate/hexane); $[\alpha]_D^{25}$ - 1.7 (*c* 1.52, $CHCl_3$); IR ν_{max} (liq. film) 3460, 3280, 2990, 2940, 2130, 1385, 1375, 1250, 1220, 1160, 1065, 850 cm^{-1}; ^1H NMR (200 MHz; $CDCl_3$) δ 1.37 (6 H, s, 2 x CH_3), 1.43 (3 H, s, CH_3), 1.44 (3 H, s, CH_3), 2.53 (1 H, d, *J* = 2.2 Hz, C(1)H), 3.73 (1 H, d, *J* = 5.1 Hz, OH), 3.97-4.34 (5 H, m, C(4)H, C(5)H, C(6)H, C(7)H_2), 4.65 (1 H, ddd, *J* = 2.2, 5.1, 7.7 Hz, C(3)H); ^{13}C NMR (50.32 MHz; $CDCl_3$) δ 110.25, 109.34 (OC), 82.04 (C-2), 79.73 (CH), 77.73 (CH), 73.76 (C-1), 72.71 (CH), 67 85 (C-7), 60.88 (CH), 27.50 (CH_3), 26.40 (CH_3), 25.15 (2 x CH_3). Anal. Calcd. for $C_{13}H_{20}O_5$: C, 60.92; H, 7.87. Found: C, 60.89; H, 7.77.

3-*O*-Acetyl-1,2-dideoxy-4,5:6,7-di-*O*-isopropylidene-D-allo-hept-1-ynitol 3. The protected heptynitol **2** (0.45 g, 1.76 mmol) was stirred with pyridine (5 mL) and acetic anhydride (5 mL) at rt for 3 h, and the solvent removed under reduced pressure. The crude product (0.54 g) was purified by flash column chromatography. Elution with ethyl acetate/hexane (10/90 and 20/80) gave the acetylated product **3** (0.48 g, 92 %) as an oil; R_f = 0.44 (20% ethyl acetate/hexane); $[\alpha]_D^{25}$ -5.7 (*c* 1.81, $CHCl_3$); IR ν_{max} (liq. film) 3280, 2990, 2940, 2130, 1750, 1385, 1375, 1230, 1160, 1065, 980, 850 cm^{-1}; ^1H NMR (200 MHz; $CDCl_3$) δ 1.31 (3 H, s, CH_3), 1.36 (3 H, s, CH_3), 1.38 (3 H, s, CH_3), 1.51 (3 H, s, CH_3), 2.10 (3 H, s, C(O)CH_3), 2.51 (1 H, d, *J* = 2.2 Hz, C(1)H),3.88 (1 H, dd, *J* = 5.3, 8.7 Hz, C(7)H_A), 4.08 (1 H, dd, *J* = 6.4, 9.5 Hz, C(5)H), 4.12 (1 H, dd, *J* = 5.9, 8.7 Hz, C(7)H_B), 4.34 (1 H, dt, *J* = 9.5, 5.7 Hz, C(6)H), 4.35 (1 H, dd, *J* = 4.5, 6.4 Hz, C(4)H), 5.67 (1 H, dd, *J* = 2.2, 4.5 Hz, C(3)H). Anal. Calcd. for $C_{15}H_{22}O_6$: C, 60.39; H, 7.43. Found: C, 60.15; H, 7.54.

Reduction of compound 3: Samarium diiodide solution[11] (0.1 M in THF, 8 mL, 0.80 mmol) was added dropwise to a stirred solution of 1,2-dideoxy-3-*O*-acetyl-4,5:6,7-di-*O*-isopropylidene-D-allo-hept-1-ynitol **3**

(0.095 g, 0.32 mmol), tetrakis(triphenylphosphine)palladium(0) (0.020 g, 0.02 mmol) and *t*-butanol (0.034 mL, 0.35 mmol) in dry THF (3.2 mL) under argon. The reaction mixture was stirred at 40°C for 3 h, then filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography. Elution with ethyl acetate/hexane (20/80 and 30/70) gave **(2*R*, 3*S*, 4*S*)-1,2:3,4-di-*O*-isopropylidendioxy-hept-5,6-diene 4** (0.007 g, 9% yield; impurified with traces of a compound of unknown structure) as an oil; R_f = 0.75 (25% ethyl acetate/hexane); $[\alpha]_D^{25}$ -3.7 (*c* 0.2, $CHCl_3$); ^1H NMR (200 MHz; $CDCl_3$) δ (major compound) 1.35 (3 H, s, CH_3), 1.36 (3 H, s, CH_3), 1.42 (3 H, s, CH_3), 1.48 (3 H, s, CH_3), 4.12 (4 H, m, 4 x CH), 4.74 (1 H, m, CH), 4.88 (1 H, dd, *J* = 2.0, 6.6 Hz, 2xCH), 5.30 (1 H, dd, *J*= 6.5 and 6.9 Hz, CH); recovered starting material **3** (0.020 g, 21%); **(*E*) (2*R*, 3*S*)-3-hydroxy-1,2-*O*-isopropylidendioxy-hept-4-en-6-yne 5a** (0.015 g, 26%) as an oil; R_f = 0.40 (25 % ethyl acetate/hexane); $[\alpha]_D^{25}$ -8.7 (*c* 0.4, $CHCl_3$); ^1H NMR (200 MHz; $CDCl_3$) δ 1.36 (3 H, s, CH_3), 1.45 (3 H, s, CH_3), 2.22 (1 H, d, *J* = 3.0 Hz, OH), 2.91 (1 H, d, *J* = 2.3 Hz, C(7)H), 3.86 (1 H, dd, *J* = 6.5, 8.4 Hz, C(1)H_A), 3.95 (1 H, dd, *J* = 6.5, 8.4 Hz, C(1)H_B), 4.12 (1 H, dt, *J* = 4.4, 6.4 Hz, C(2)H), 4.34 (1 H, m, C(3)H), 5.84 (1 H, dt, *J* = 16.0, 2.0 Hz, C(5)H), 6.20 (1 H, dd, *J*= 4.9, 16.0 Hz, C(4)H); and a mixture of enyne **5a** and **(*Z*) (2*R*, 3*S*)-3-hydroxy-1,2-*O*-isopropylidendioxy-hept-4-en-6-yne 5b** (0.012 g, 21% with **5a**:**5b** in a 1:3.5 ratio) as an oil; data for **5b**: R_f = 0.33 (25% ethyl acetate/hexane); $[\alpha]_D^{25}$ -10 (*c* 0.6, $CHCl_3$); ^1H NMR (200 MHz; $CDCl_3$) δ 1.36 (3 H, s, CH_3), 1.45 (3 H, s, CH_3), 2.30 (1 H, d, *J* = 3.0 Hz, OH), 3.18 (1 H, d, *J* = 2 Hz, C(7)H), 3.86 (1 H, dd, *J* = 6.5, 8 Hz, C(1)H_A), 3.95 (1 H, dd, *J* = 6.5, 8 Hz, C(1)H_B), 4.22 (1 H, dt, *J* = 4, 6 Hz, C(2)H), 4.80 (1 H, m, C(3)H), 5.68 (1 H, ddd, *J* = 11, 2, 3 Hz, C(5)H), 5.98 (1 H, dd, *J* = 7, 11 Hz, C(4)H). Compounds **4** and **5a,b** were too unstable to give a correct microanalysis and they decompose slowly at room temperature

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References and Notes

1. Giese, B. *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds*, Pergamon Press, New York, **1986**.
2. RajanBabu, T. V. *Acc. Chem. Res.* **1991**, *24*, 139-145.
3. Marco-Contelles, J.; Bernabé, M.; Ayala, D.; Sánchez, B. *J. Org. Chem.* **1994**, *59*, 1234-1235.
4. a) Kiguchi, T.; Tajiri, K.; Ninomiya, I.; Naito, T.; Hiramatsu, H. *Tetrahedron Lett.* **1995**, *36*, 253-256; b) Marco-Contelles, J.; Bernabé, M. *Tetrahedron Lett.* **1994**, *35*, 6361-6364; d) Maycock, C. D.; Barros, M. T.; Santos, A. G.; Godinho, L. S. *Tetrahedron Lett.* **1993**, *34*, 7985-7988.
5. Marco-Contelles, J.; Destabel, C.; Chiara, J. L.; Bernabé, M. *Tetrahedron: Asymmetry* **1995**, *6*, 1547.
6. Enholm, E.J.; Burroff, J. A.; Jaramillo, L. M. *Tetrahedron Lett.* **1990**, *31*, 3727-3730.
7. Hatem, J.; Henriet-Bernard, C.; Grimaldi, J.; Maurin, R. *Tetrahedron Lett.* **1992**, *33*, 1057.
8. Tabuchi, T.; Inanaga, J.; Yamaguchi, M. *Tetrahedron Lett.* **1986**, *27*, 5237-5240.
9. Mandal, S. B.; Achari, B. *Synth. Commun.* **1993**, *23*, 1239-1244.
10. Buchanan, J. G.; Dunn, A. D.; Edgar, A. R. *Carbohydr. Res.* **1974**, C5-C7.
11. Girard, P.; Namy, J. L.; Kagan , H. B. *J. Am. Chem. Soc.* **1980**, *102*, 2693-2698.

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