

From D-galactose to enantiopure 3-azabicyclo[3.3.0]octen-7-one derivatives *via* Pauson–Khand reaction

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Dedicated to Professor José Elguero on his 70th birthday
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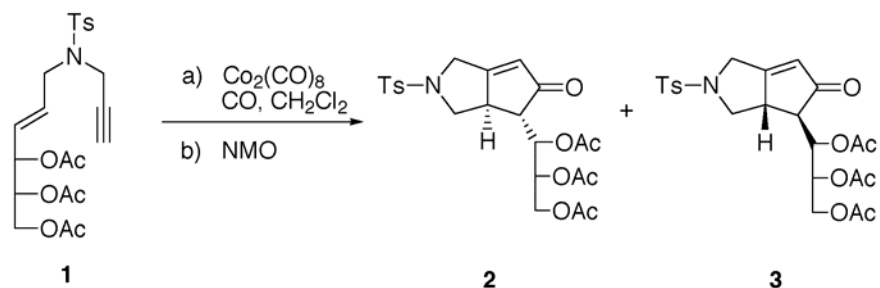
Abstract

The 8-substituted-3-azabicyclo[3.3.0]octen-2-one-7-derivatives **18** and **19** have been obtained in enantiomerically pure form from D-galactose in acceptable chemical yield (30%, nine steps) and moderate diastereomeric ratio (**18:19** = 2.5:1) *via* intramolecular Pauson–Khand (PK) reaction of the appropriate enyne.

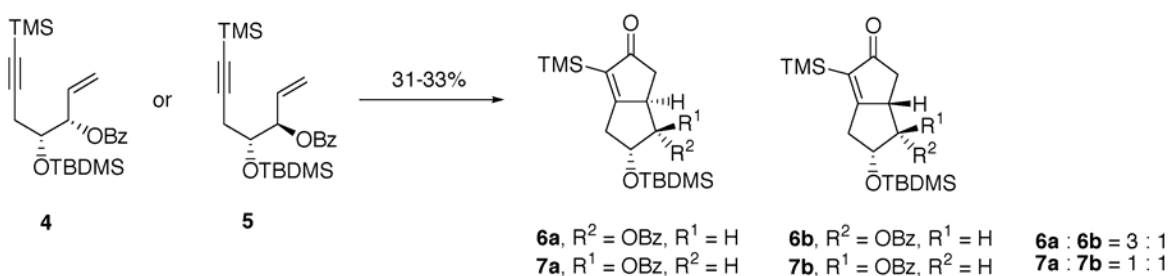
Keywords: Intramolecular Pauson–Khand reaction, cyclopentenones, carbohydrates

Introduction

The cobalt-mediated carbonylative co-cyclization of an alkene and an alkyne, the Pauson–Khand, (PK), reaction is a flexible method for the synthesis of cyclopentenones.¹ The enantioselective version of this reaction using a chiral inductor covalently bonded to the alkene or the alkyne moiety had led in some cases to useful results.² By the use of carbohydrates as sources of chirality, these compounds have been considered as chiral substrates in the intramolecular PK reaction.³ However, the introduction as chiral auxiliaries in these reactions has not been reported previously. Our group has recently reported the first case,⁴ using compound **1** derived from D-glucal, obtaining approximately 1:1 mixtures of the diastereomers **2** and **3** (Scheme 1). In order to improve the diastereoselectivity of this reaction we heeded a report by Mulzer *et al.*⁵ who observed that compounds **4** and **5**, when treated with dicobalt-octacarbonyl with subsequent thermal decomposition, gave mixtures of diastereomers **6** and **7** in 3:1 and 1:1 ratios, respectively. Thus, the diastereoselectivity of these reactions depends upon the relative stereochemistry of the benzoyl protecting group in **4** and **5** (Scheme 2).



Scheme 1. Intramolecular PK reaction of (2*E*)-4,5,6-tri-*O*-acetyl-1,2,3-trideoxy-1-(*N*-propargyltosylamine)-*D*-erythro-hex-2-enose (**1**).

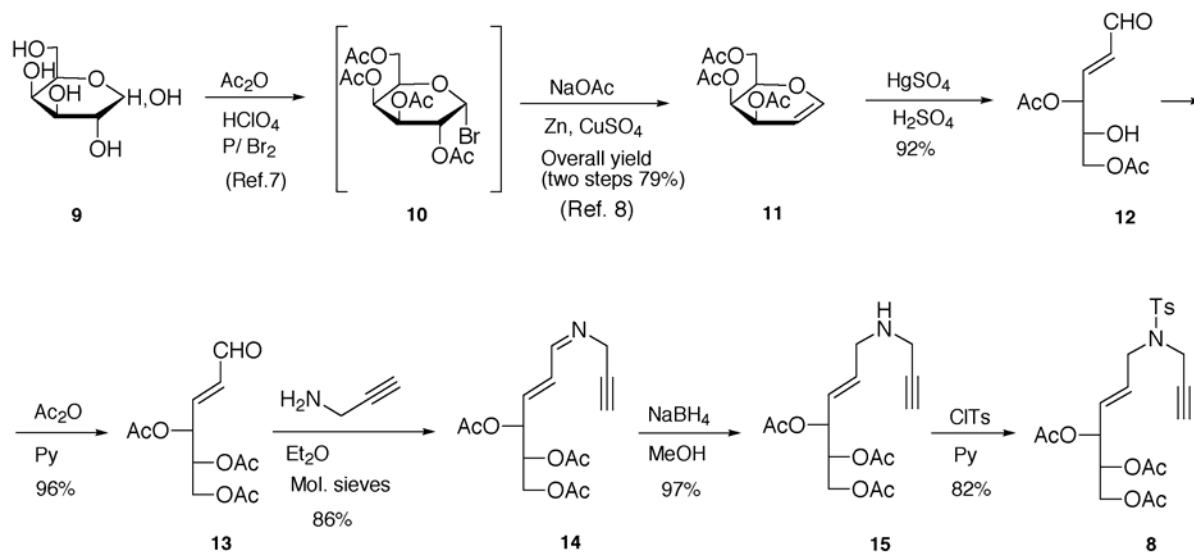


Scheme 2. PK cyclizations of chiral substrates **4** and **5**.

With this precedent in mind we speculated that the inversion of the stereochemistry of the stereogenic center at the allylic position of the sugar chain could improve the diastereomeric ratio for the resulting cyclopentenones. We now report our results in this field.

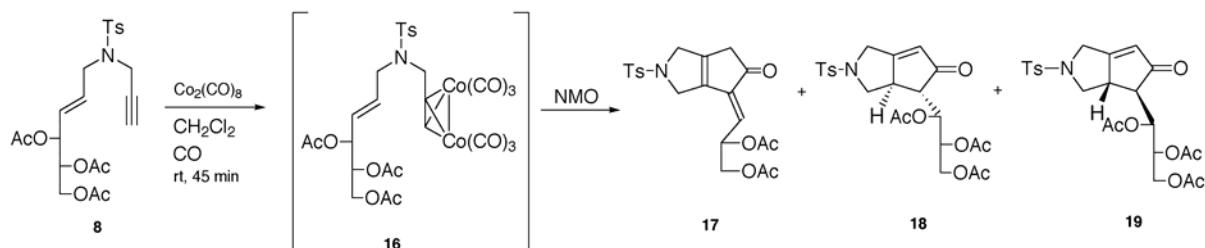
Results and Discussion

The aza-enyne **8** having the *D*-galacto configuration at the sugar chain was used as starting material (Scheme 3). This compound was obtained from tetra-*O*-acetyl-*D*-galactal **11** through a synthetic sequence involving the ring opening to give the aldehyde **13**, formation of the propargyl imine **14**, reduction, and protection of the resulting amine with tosyl chloride. On the other hand, tetra-*O*-acetyl-*D*-galactal **11** was synthesized from *D*-galactose **9** in two steps without isolation of the intermediate bromide **10**.⁶⁻⁸



Scheme 3. Synthesis of aza-enyne **8** from D-galactose.

Having compound **8** in hand, its reaction with $\text{Co}_2(\text{CO})_8$ during 15 min in CH_2Cl_2 at RT (18–20 °C) under CO atmosphere led to complete formation of the complex **16** (Scheme 4, R_F 0.39 hexane–ethyl acetate 2:1) which by reaction with N-methylmorpholine N-oxide (NMO) for 1h at RT in CH_2Cl_2 afforded a mixture of compound **17** (5%) and cyclopentenones **18** and **19** (61% isolated overall yield) in a ratio **18:19** = 2.5:1. From this crude reaction mixture, compound **17** (R_F 0.76, hexane–ethyl acetate 1:2) was isolated. On the other hand, fractional crystallization (hexane–ethyl acetate, 1:1) of the mixture **18:19** allowed the isolation of pure **18** [mp 147 °C, $[\alpha]_D -123^\circ$ (c 0.5, CHCl_3)].



Scheme 4. Intramolecular Pauson–Khand reaction of the chiral enyne **8**.

The structural determination of compounds **18** and **19** was achieved on the following basis. The X-ray analysis of compound **3**⁴ shows that, in the solid state, the conformation of this compound is that in which the tosyl group is located under the bicyclic ring (Figure 1). The ¹H-NMR spectrum also indicates that the solution-conformations of **3** and **2** might be similar. Thus, the upfield-shifted peaks for hydrogens H-3_a and H-4 show that both protons lie in the shielding region of the aryl group (Figure 1).⁹ Under these conditions the signal for hydrogen H-3_a is

shifted to low-field in the diastereomer having the sugar chain in the α -position compared to the diastereomer with the sugar chain in the β -position. Similarly, the H-4 signal is shifted upfield in the diastereomer with the sugar chain in the α -position. Assuming that the same conformational trend should be expected for compounds **18** and **19** we deduced that the major compound **18** must have an α -sited chain whereas compound **19** must show the opposite configuration.

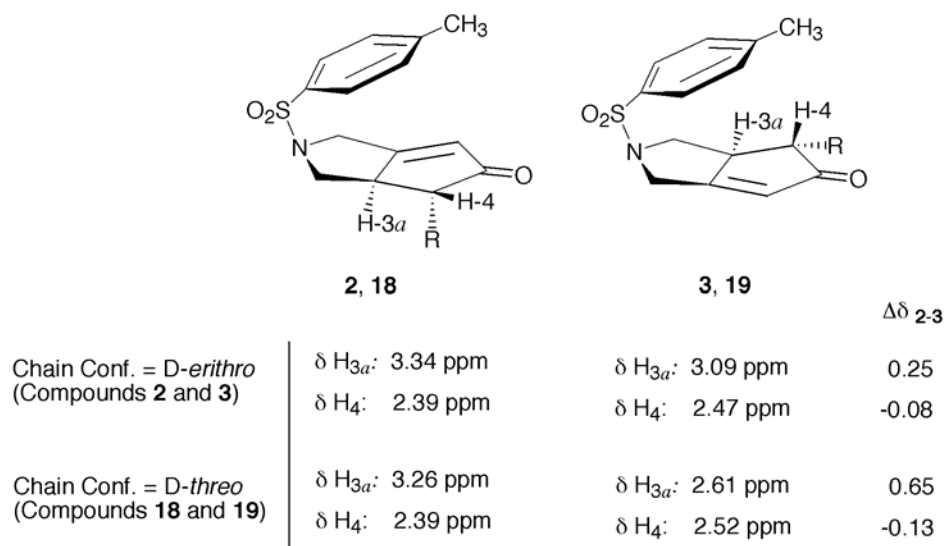
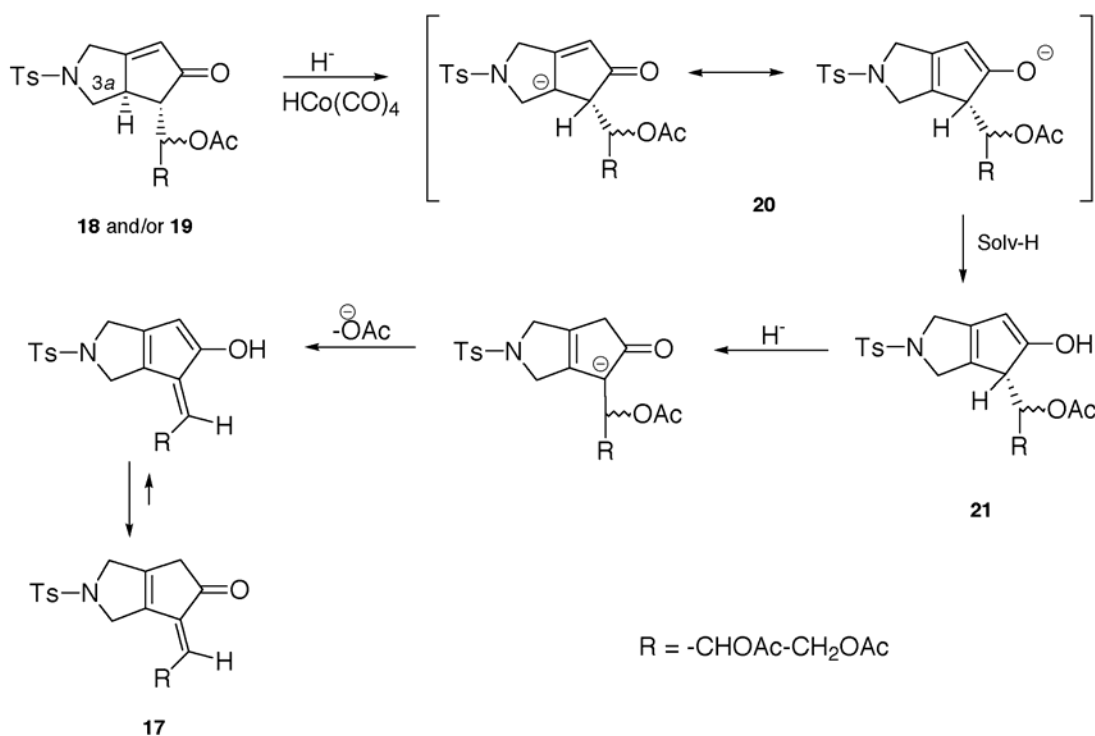


Figure 1. Conformations and chemical shifts for compounds **2**, **3**, **18** and **19**.

Compound **17** arises from the formal hydrogenolytic cleavage of Pauson–Khand adducts with concomitant double bond migration. This type of products from Pauson–Khand adducts are often obtained and, in some cases, this reaction has been synthetically useful.¹⁰ It should be noted that compound **17** was also obtained by reaction of compound **3** with pyridine at 60 °C (27% isolated yield).⁴ On this basis we propose the reaction path given in Scheme 5 for the formation of compound **17**.



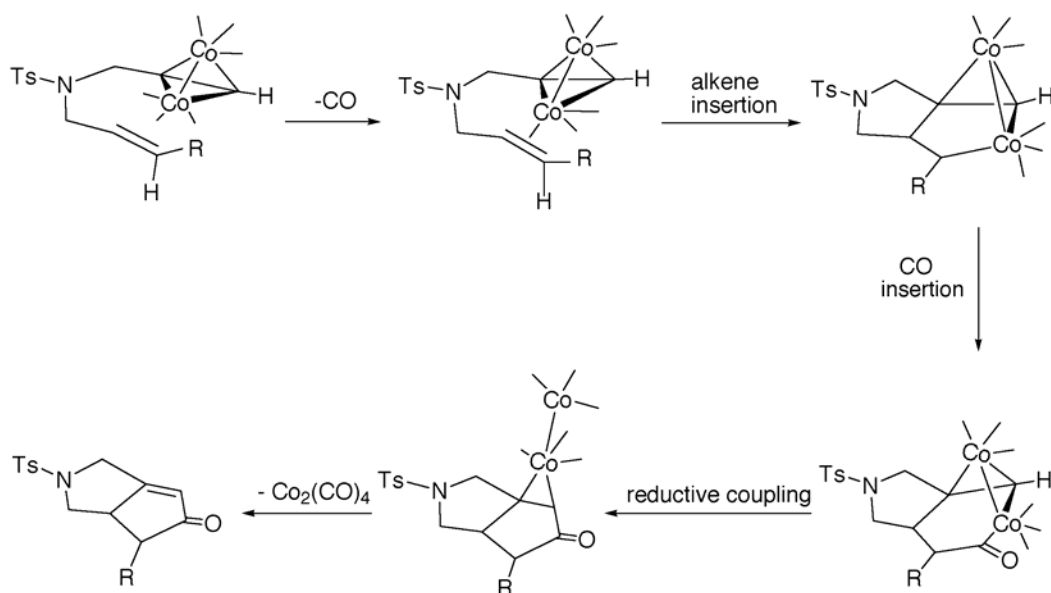
Scheme 5. Reaction path for the formation of **17**.

In this case, a hydride ion generated from the species $\text{HCo}(\text{CO})_4$ ¹¹ abstracts the acidic proton H-3a from the resulting cyclopentanone, yielding the extended enolate ion **20**. Protonation (probably by traces of water present in the NMO) affords **21**, which can again generate a conjugate carbanion after abstraction of proton H-4. Finally, the protonation during the work-up yields compound **17**.

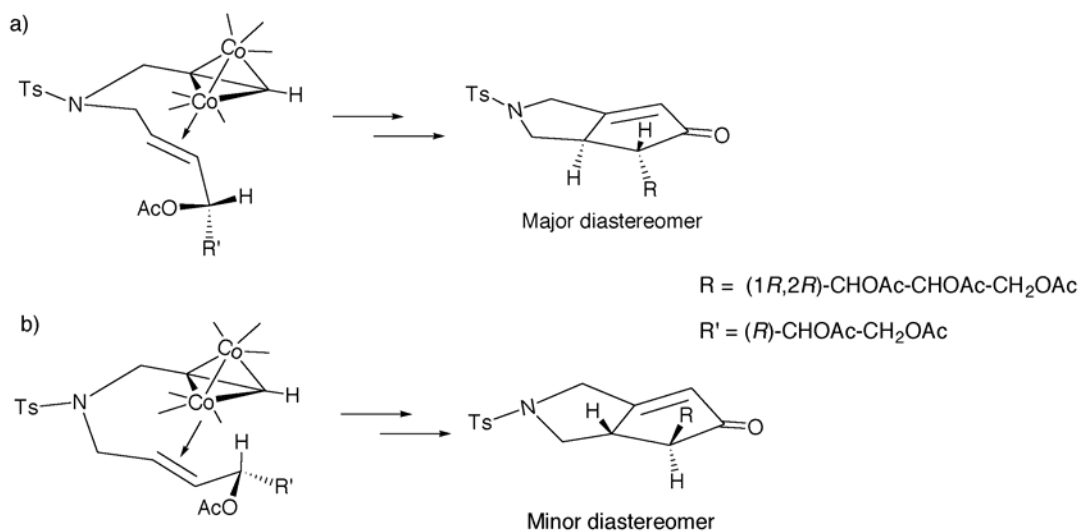
Considering the generally accepted mechanism for the intramolecular PK cycloaddition¹² made explicit for our cases, the observed diastereomeric ratio should depend on the steric demand in the insertion step of the alkene, thereby yielding the corresponding couple of diastereomers (Scheme 6).

Two approaches are possible for the alkene insertion step (Scheme 7) giving the two diastereomeric bicyclopentenones. In the approach (a) there are no important steric interactions between the sugar chain and the cobalt-alkyne complex moiety whereas in (b) the steric interference between the remote $\text{Co}(\text{CO})_3$ moiety and R' appears to be evident. Considering the distance between R' and the $\text{Co}(\text{CO})_3$ group, this steric interaction induces only a relatively small diastereomeric ratio (2.5:1). In the case of the related compounds **2** and **3** derived from D-glucal this interaction occurs between a sterically less demanding acetoxy group and the remote $\text{Co}(\text{CO})_3$ moiety, and no diastereoselectivity was observed at all.⁴ In summary, in this report we have shown that the inversion of the configuration at the allylic position of the sugar chain produces a significant change of the stereochemical outcome in the intramolecular PK reaction.

Although a tentative model has been proposed, additional work is necessary to clarify the precise origin of this change in diastereoselectivity.



Scheme 6. Mechanism proposed for the Pauson–Khand cycloaddition (CO ligands are omitted).



Scheme 7. Formation of major and minor diastereomers from different conformers of the dicobalt-hexacarbonyl–ene-yne complexes.

Experimental Section

General Procedures. IPK reactions were carried out under argon atmosphere. Anhydrous CH_2Cl_2 was distilled from sodium hydride immediately prior to use. Melting points were determined with a capillary apparatus and are uncorrected. Optical rotations were measured at $25 \pm 2^\circ\text{C}$ with a Perkin-Elmer 241 polarimeter. Analytical and preparative TLC were performed on Merck 60 GF₂₅₄ silica gel with monitoring by UV light at 254 and 360 nm or by exposure to iodine vapor. Flash chromatography¹ was performed on Merck 60 silica gel (230–400 mesh). Specific rotations $[\alpha]_D^{20}$ were determined using a Perkin Elmer Polarimeter 141. IR spectra were recorded on a Perkin-Elmer 399 or a Midac FT-IR spectrometer. Solid samples were run as KBr disks and liquids as thin films on NaCl plates. Details are reported as $\nu_{\text{max.}}/\text{cm}^{-1}$. ¹H- and ¹³C-NMR spectra were obtained on a Bruker AM 400 instrument at 400 and 100 MHz, respectively, or on a Bruker AC 200 instrument at 200 and 500 MHz, respectively, in CDCl_3 (Me_4Si as internal standard) unless otherwise specified. Elemental analyses were carried out using a Leco 932 analyzer at the Universidad de Extremadura. Mass spectra (HRMS/ CI^+) were recorded on a VG Autospec spectrometer; only significant fragment ions are reported.

(2E)-4,6-Di-O-acetyl-2,3-dideoxy-aldehydo-D-threo-hex-2-enose (12). Mercuric sulfate (0.30 g, 0.57 mmol) was added to a stirred solution of **11** (6.20 g, 26.9 mmol) in 1,4-dioxane (32 ml) and 5M sulfuric acid (120 ml), and stirring was continued for 3 h; an excess of barium carbonate was added (0.39 g, 2.03 mmol), the suspension was shaken and filtered, and the filtrate was evaporated, giving a clear oil (5.69 g, 92%); IR (film) 3460 m, 1741 s, 1690 s, 1231 s cm^{-1} . ¹H-NMR (400 MHz) δ 9.60 (d, $J_{1,2}$ 7.6 Hz, H-1), 6.84 (dd, $J_{3,4}$ 4.4 Hz, $J_{3,2}$ 15.6 Hz, H-3), 6.29 (ddd, $J_{2,4}$ 1.3 Hz, H-2), 5.64 (m, H-4), 4.22 (dd, $J = 3.6$ Hz, $J = 10.4$ Hz, H-5), 4.11 (m, H-6, 2H), 2.18 (s, 3H, OAc), 2.11 (s, 3H, OAc); ¹³C-NMR (100 MHz) δ 192.3 (C-1), 170.8, 169.3 (2 O-CO-CH₃), 149.2 (C-3), 132.8 (C-2), 72.0 (C-4), 70.1 (C-5), 64.3 (C-6), 20.4 (2 O-CO-CH₃).

(2E)-4,5,6-Tri-O-acetyl-2,3-dideoxy-aldehydo-D-threo-hex-2-enose (13). A solution of the diacetate **12** (5.82 g, 21.4 mmol) in acetic anhydride (25 ml) and pyridine (25 ml) was kept for 4 h, poured onto a slurry of ice and dilute HCl (280 ml), and extracted three times with CHCl_3 ; the extracts were combined, successively washed with aqueous NaHCO_3 solution and water, dried, and evaporated to an oil (5.63 g, 97%); $[\alpha]_D +59.2$ (c 0.5 CHCl_3); IR (film) 1750 s, 1690 m, 1220 s cm^{-1} . ¹H-NMR (400 MHz) δ 9.59 (d, $J_{1,2}$ 7.6 Hz, H-1), 6.24 (ddd, $J_{2,3}$ 15.8, $J_{2,4}$ 1.5 Hz, H-2), 6.73 (dd, $J_{3,4}$ 4.6 Hz, H-3), 5.77 (m, $J_{4,5}$ 6.1 Hz, H-4), 5.35 (m, $J_{5,6}$ 5.6 Hz, H-5), 4.35 (dd, $J_{6,6'}$ 12.0 Hz, H-6), 4.00 (dd, H-6'), 2.17 (s, 3H, OAc), 2.09 (s, 3H, OAc), 2.06 (s, 3H, OAc); ¹³C-NMR (100 MHz) δ 192.2 (C-1), 170.3, 169.7, 169.3 (3 O-CO-CH₃), 133.2 (C-2), 148.5 (C-3), 70.2, 70.1 (C-4, C-5), 61.6 (C-6), 20.6, 20.5, (3 O-CO-CH₃); HRMS Calcd for $\text{C}_{12}\text{H}_{16}\text{O}_7 + \text{H}$: 273.0974; Found 273.0983; m/z (rel. int.) 213 (M+H–AcOH, 14), 153 (M+H–2AcOH, 21).

(2E)-Tri-O-acetyl-2,3-dideoxy-aldehydo-D-threo-hex-2-enose propargylimine (14). To a stirred solution of **13** (3.52 g, 12.86 mmol) in dry ethyl ether (25 mL) at 0 °C was added propargylamine (0.81 mL, 11.9 mmol) and molecular sieve (Merck 4 Å). After stirring for 1.5 h

at RT, filtration and concentration yielded **14** as an oil (3.01 g, 86%); $[\alpha]_D +24.4$ (*c* 0.5, CHCl₃); IR (film) 3280 m, 1755 s, 1660 m, 1220 s cm⁻¹; ¹H-NMR (400 MHz) δ 8.12 (dd, *J*_{1,2} 8.8 Hz, *J*_{1,1'} 1.6 Hz, H-1), 6.40 (ddd, *J*_{2,3} 15.8 Hz, *J*_{2,4} 1.1 Hz, H-2), 6.18 (dd, *J*_{3,4} 5.5 Hz, H-3), 5.66 (ddd, *J*_{4,5} 5.3 Hz, H-4), 5.30 (m, H-5), 4.34 (dd, *J*_{6,6'} 12.0 Hz, *J*_{5,6} 4.1 Hz, H-6), 4.07 (dd, *J*_{5,6'} 6.5 Hz, H-6'), 4.46 (t, 2H, H-1'), 2.45 (t, *J*_{1',3'} 2.3 Hz, H-3'), 2.13 (s, 3H, OAc), 2.09 (s, 3H, OAc), 2.06 (s, 3H, OAc); ¹³C-NMR (100 MHz) δ 170.4, 169.7, 169.2 (3 O-CO-CH₃), 161.9 (C-1), 136.7 (C-3), 132.5 (C-2), 78.2 (C-3'), 75.6 (C-2'), 70.6, 70.5 (C-4, C-5), 61.7 (C-6), 46.7 (C-1'), 20.5, 20.4 (3 O-CO-CH₃); HRMS Calcd for C₁₅H₁₉NO₆ + H: 310.1290; Found 310.1307; *m/z* (rel. int.) 310 (M+H, 11), 273 (59), 212 (41), 170 (100), 153 (99).

(2E)-4,5,6-Tri-O-acetyl-1,2,3-trideoxy-1-propargylamine-D-threo-hex-2-enose (15). To a stirred solution of imine **14** (5.9 g, 19.07 mmol) in MeOH (32 mL) at 0°C, sodium borohydride (0.72 g, 19.07 mmol) was added. The mixture was stirred for 15 min at RT, filtered, and the filtrate diluted with CH₂Cl₂ (130 mL), then washed successively with sat. aq. NaHCO₃ (2 x 100 mL) and water (2 x 100 mL), dried with MgSO₄ and concentrated yielding **15** as an oil (5.7 g, 97%); $[\alpha]_D +9.0$ (*c* 0.5, CHCl₃); IR (film) 3280 m, 1745 s, 1660 d, 1225 s cm⁻¹; ¹H-NMR (400 MHz) δ 5.87 (dt, *J*_{1,2} 5.8 Hz, *J*_{2,3} 15.2 Hz, H-2), 5.60 (ddt, *J*_{3,4} 6.4 Hz, *J*_{1,3} 1.2 Hz, H-3), 5.47 (t, *J*_{4,5} 6.5 Hz, H-4), 5.20 (m, H-5), 4.31 (dd, *J*_{6,6'} 12.1 Hz, H-6), 4.05 (dd, H-6'), 3.38 (d, *J*_{1',3'} 2.4 Hz, H-1'a, H-1'b), 3.31 (dd, H-1a, H-1b), 2.22 (t, H-3'), 2.08 (s, 3H, OAc), 2.06 (s, 3H, OAc), 2.05 (s, 3H, OAc); ¹³C-NMR (100 MHz) δ 170.4, 170.0, 169.6 (3 O-CO-CH₃), 133.8 (C-2), 125.3 (C-3), 81.6 (C-3'), 71.8 (C-2'), 71.6 (C-5), 71.2 (C-4), 62.1 (C-6), 49.1 (C-1), 37.2 (C-1'), 20.8, 20.7, 20.6 (3 O-CO-CH₃); HRMS Calcd for C₁₅H₂₁NO₆ + H: 312.1447; Found 312.1463; *m/z* (rel. int.) 312 (M+H, 100), 252 (M+H-AcOH, 49), 192 (M+H-2AcOH, 37).

(2E)-4,5,6-Tri-O-acetyl-1,2,3-trideoxy-1-(N-propargyltosylamino)-D-threo-hex-2-enose (8). A stirred solution of **15** (2.29 g, 7.37 mmol) in pyridine (14 mL) at 0 °C was treated with tosyl chloride (4.20 g, 22.1 mmol). The mixture was kept 48 h at 4 °C and then poured into water/ice (140 mL), and extracted with Et₂O (3x70 mL). The combined organic layers were rinsed successively with 2*N* aq. HCl (3x70 mL), a saturated solution of NaHCO₃ (3x70 mL) and brine (3x70 mL), dried over MgSO₄ and filtered. Evaporation of the solvent (reduced pressure) afforded **8** as an oil which was purified by flash chromatography (hexane–ethyl acetate 2:1) (1.87 g, 82%); $[\alpha]_D +8.6$ (*c* 0.5, CHCl₃); IR (film) 3280 m, 1745 s, 1210 s, 1160 s cm⁻¹; ¹H-NMR (400 MHz) δ 7.72 (d, H-2", H-6"), 7.30 (d, H-3", H-5"), 5.70 (dt, *J*_{1a,2} 5.6 Hz, *J*_{2,3} 15.2 Hz, H-2), 5.65 (dd, *J*_{3,4} 5.8 Hz, H-3), 5.46 (t, *J*_{4,5} 5.6 Hz, H-4), 5.21 (ddd, *J*_{5,6} 4.1 Hz, *J*_{5,6'} 6.4 Hz, H-5), 4.30 (dd, *J*_{6,6'} 11.9, Hz, H-6), 4.04 (bt, *J*_{1'a,3'} = *J*_{1'b,3'} 2.5 Hz, H-1'a, H-1'b), 4.01 (dd, H-6'), 3.82 (d, *J*_{1b,2} 4.0 Hz, 2H-1), 2.43 (s, 3H, CH₃-Ar), 2.09 (s, 3H, OAc), 2.08 (s, 3H, OAc), 2.05 (s, 3H, OAc), 2.02 (t, H-3'); ¹³C-NMR (100 MHz) δ 170.4, 169.9, 169.5 (3 O-CO-CH₃), 143.6 (C-3", C-5"), 135.6 (C-1"), 129.5 (C-4"), 129.1 (C-2), 128.9 (C-3), 127.6 (C-2", C-6"), 76.2 (C-2'), 73.9 (C-3'), 71.2 (C-4), 71.0 (C-5), 61.9 (C-6), 47.5 (C-1), 35.9 (C-1'), 21.4 (CH₃-Ar), 20.8, 20.7, 20.6 (3 O-CO-CH₃); HRMS Calcd for C₂₂H₂₇NO₈-OAc: 406.1324; Found 406.1324; *m/z* (rel. int.)

406 (M–AcOH, 63), 346 (M–2AcOH, 13), 310 (M–Ts, 47), 286 (M–3AcOH, 9), 250 (M–Ts–AcOH, 23).

4-(2',3'-Diacetoxypropyliden)-2-tosyl-2,3,4,6-tetrahydro-1H-cyclopenta-[c]-pyrrole-5-one (17), (3aR,4S)-4-(tri-O-acetyl-D-threo-triol-1-yl)-2-tosyl-2,3,3a,4-tetrahydro-1H-cyclopenta-[c]-pyrrole-5-one (18) and (3aS,4R)-4-(tri-O-acetyl-D-threo-triol-1-yl)-2-tosyl-2,3,3a,4-tetrahydro-1H-cyclopenta-[c]-pyrrole-5-one (19). A solution of aza-enyne **8** (449 mg, 0.96 mmol) in freshly distilled CH₂Cl₂ (5.5 ml) was treated with Co₂(CO)₈ (405 mg, 1.05 mmol) under CO atmosphere and the mixture was stirred for 45 min. Then NMO (665 mg, 5.78 mmol) was added portionwise over a 15-min period, cooling the reaction at 0 °C before each addition and allowing it to reach RT before the next one. The mixture was stirred for 1 h at RT, diluted with CH₂Cl₂ (50 ml), washed successively with 2M HCl (2 x 50 ml), sat. NaHCO₃ (2 x 50 ml), and water (2 x 50 ml), dried (MgSO₄) and concentrated *in vacuo*. The reaction mixture was eluted through a short column (1 cm long) of SiO₂ (hexane/ethyl acetate 3:1 → ethyl acetate) to afford an initial fraction (R_F 0.80) (hexane–ethyl acetate 1:2) of the intermediate dicobalt-hexacarbonyl complex **16** (103 mg), a second fraction (R_F 0.76) of the cyclopentenone **17** (18.8 mg, 4%) and a third fraction of a mixture (R_F 0.46) of **18** and **19** (2.5:1, 247 mg, 61%) which was resolved by fractional crystallization (hexane/ethyl acetate 1:1).

18: mp 147 °C; [α]_D –123 (c 0.5 CHCl₃); IR (KBr) 1735 s, 1700 s, 1640 m, 1600 w, 1340 s, 1220 s, 1155 s cm⁻¹; ¹H-NMR (400 MHz) TM 7.74 (d, H-2", H-6"), 7.36 (d, H-3", H-5"), 5.99 (bs, H-6), 5.60 (t, J_{1',4'} = J_{1',2'}, 4.2 Hz, H-1'), 5.36 (m, H-2'), 4.36 (bd, J_{1a,1b} 16.9 Hz, H-1b), 4.26 (dd, J_{2',3'b} 4.8 Hz, J_{3'a,3'b} 11.8 Hz, H-3'b), 4.01 (bd, J_{1a,1b} 16.9 Hz, H-1a), 3.99 (m, 2H, H-3b, H-3'a), 3.26 (m, H-3a), 2.67 (dd, J_{3a,3a} = J_{3a,3b} 10.2 Hz, H-3a), 2.45 (s, 3H, CH₃-Ar), 2.39 (t, J_{1',4'} = J_{3a,4} 3.2 Hz, H-4), 2.11 (s, 3H, OAc), 2.06 (s, 3H, OAc), 2.02 (s, 3H, OAc); ¹³C-NMR (100 MHz) TM 203.9 (C-5), 177.5 (C-6a), 170.4, 169.8, 169.1 (3 O-CO-CH₃), 144.3 (C-1"), 133.2 (C-4"), 130.0 (C-3", C-5"), 127.4 (C-2", C-6"), 124.9 (C-6), 71.1 (C-2'), 68.2 (C-1'), 61.8 (C-3'), 53.0 (C-4), 52.0 (C-3), 47.5 (C-1), 45.9 (C-3a), 21.5 (CH₃-Ar), 20.8, 20.6, 20.4 (3 O-CO-CH₃). Anal. Calcd for C₂₃H₂₇NO₉S; C, 55.97; H, 5.51; N, 2.83; S, 6.49. Found C, 55.76; H, 5.54; N, 2.95; S, 6.30. HRMS calcd for C₂₃H₂₇NO₉S + H: 494.1484, found: 494.1477; *m/z* (rel. int.) 434 (M+H–AcOH, 23), 374 (M+H–2AcOH, 71), 314 (M+H–3AcOH, 42), 218 (M–2AcOH–Ts, 11), 158 (M–3AcOH–Ts, 17).

Acknowledgements

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References and Notes

1. For selected recent reviews, see: (a) Sugihara, M.; Yamaguchi, M.; Nishizawa, M. *Chem. Eur. J.* **2001**, *7*, 1589. (b) Hanson, B.E. *Comments on Inorg. Chem.* **2002**, *23*, 289. (c) Rivero, M.R.; Adrio, J.; Carretero, J.C. *Eur. J. Org. Chem.* **2002**, 2881. (d) Pericás, M.A.; Basells, J.; Castro, J.; Marchueta, J.; Moyano, A.; Riera, A.; Vázquez, J.; Verdaguer, X. *Pure Appl. Chem.* **2002**, *74*, 167. (e) Gibson, S.E.; Stevanazzi, A. *Angew. Chem., Int. Ed.* **2003**, *42*, 1800. (f) Blanco-Urgoiti, J.; Anorbe, L.; Pérez-Serrano, L.; Domínguez, G.; Pérez-Castells, J. *Chem. Soc. Rev.* **2004**, *33*, 32. (g) Boñaga, L.V.R.; Krafft, M.E. *Tetrahedron* **2004**, *60*, 9795.
2. For a concise and complete review, see: Ingate, S.T.; Marco-Contelles, J. *Org. Prep. Proc. Int.* **1998**, *30*, 121.
3. See ref. 2, p.133, and Marco-Contelles, J.; de Opazo, E. *J. Carbohydr. Chem.* **2002**, *21*, 201 and references therein.
4. Areces, P.; Durán, M.A.; Plumet, J.; Hursthouse, M.B.; Light, M.E. *J. Org. Chem.* **2002**, *67*, 3506.
5. Mulzer, J.; Graske, K.D.; Kirste, B. *Ann.* **1988**, 891.
6. Although compound **11** is commercially available (Aldrich, 5 g, 118.8 €), this product can be obtained on the multi-gram scale (21.4 g) according to the described procedure at the price of 5 g ~0.50 €.
7. (a) Levene, P.A.; Tipson, R.S. *J. Biol. Chem.* **1931**, *93*, 631. (b) Helferich, E.N.; Mulcahy, E.N.; Ziegler, H. *Ber.* **1954**, *87*, 233.
8. González, F.; Lesage, S.; Perlin, A. *Carbohydr. Res.* **1975**, *42*, 267.
9. Similar observations have been previously reported in related compounds. See: Yoo, S.; Lee, S. *J. Org. Chem.* **1999**, *59*, 6968.
10. (a) Kerr, W.J.; McLaughlin, M.; Pauson, P.L.; Robertson, S.M. *Chem. Commun.* **1999**, 2171. (b) Arjona, O.; Csaky, A.G.; Murcia, C.; Plumet, J. *J. Org. Chem.* **1999**, *64*, 7338.
11. Several processes of isomerization of cyclopentenones obtained in PK reactions have been described (See ref. 1g). Experimental evidence indicates that those reactions were catalyzed by the hydride $\text{HCo}(\text{CO})_4$ generated by reduction of $\text{Co}_2(\text{CO})_8$ in the reaction media. See, for example, Davies, S.G. In *Organotransition Metal Chemistry: Applications to Organic Synthesis*, Pergamon Press: Oxford, 1982; p 367.
12. See refs. 1f and 1g and references cited therein.