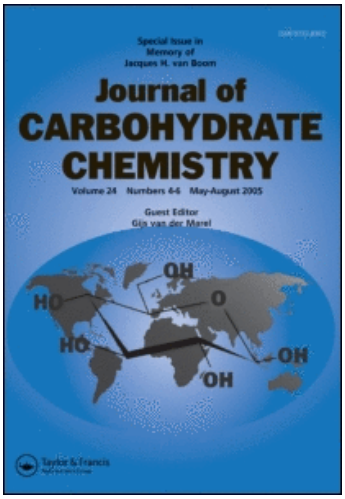


Journal of Carbohydrate Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

Stereochemistry of the Palladium(II) Promoted Carbocyclization of Hex-5-Enopyranosides

Pál László[ab]; Anne Dudon[a]
[a] Research Group for Antibiotics of the Hungarian Academy of Sciences, Debrecen, Hungary [b] 2nd Department of Medicine, University School of Medicine, Debrecen, Hungary

To cite this Article László, Pál and Dudon, Anne(1992) 'Stereochemistry of the Palladium(II) Promoted Carbocyclization of Hex-5-Enopyranosides', Journal of Carbohydrate Chemistry, 11: 5, 587 — 593
To link to this Article: DOI: 10.1080/07328309208016150
URL: http://dx.doi.org/10.1080/07328309208016150

J. CARBOHYDRATE CHEMISTRY, 11(5), 587-593 (1992)

STEREOCHEMISTRY OF THE PALLADIUM(II) PROMOTED CARBOCYCLIZATION OF HEX-5-ENOPYRANOSIDES

Pál László*[a)] and Anne Dudon

Research Group for Antibiotics of the Hungarian Academy of Sciences,
P.O.Box 70, H-4010 Debrecen, Hungary

Received January 30, 1991 - Final Form March 13, 1992

ABSTRACT

Palladium(II) promoted carbocyclization of hex-5-enopyranosides proceeds with high stereoselectivity, but accompanying elimination is observed when the substituent is an ester on C-3.

INTRODUCTION

Interest in the synthesis of chiral carbocyclic compounds has been increased due to the identification of novel aminocyclitol antibiotics and pseudo-sugar derivatives. Since the discovery of the Ferrier-II reaction[1] many substituted 5-hydroxycyclohexanones have been prepared from hex-5-enopyranosides and converted into functionalized deoxyinososes.

In 1988, a palladium(II) salt was used by Adam[2] for analogous ring transformations. The starting materials were 3-*O*-benzyl hex-5-enopyran-

---

a) Present address: 2nd Department of Medicine,
University School of Medicine, P.O.Box 20, H-4012 Debrecen, Hungary

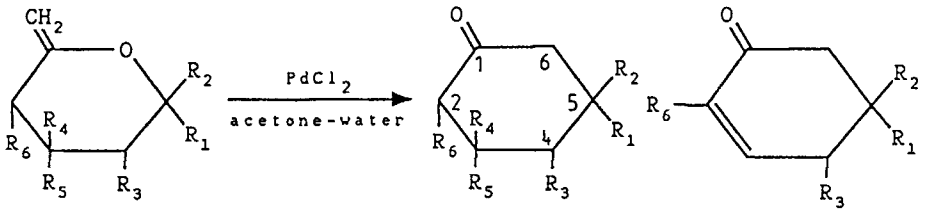
osides, which in some cases[3-7] gave isomeric mixtures under the Ferrier conditions, but only a single product was isolated from the Pd(II)-mediated carbocyclization. Later, isomeric hydroxycyclohexanones (ratio 6 : 4) were obtained by Barton et al[6] from the same starting material when similar conditions were employed. The presence of sulfuric acid (5 mM) in the reaction mixture would not cause the isomerization of the product, because similar ring transformations were performed with Ferrier(II) reaction in the presence of acetic acid[8,9] or sulfuric acid.[10,11] We were interested in determining whether the palladium(II) catalyzed carbocyclization was stereoselective.

RESULT AND DISCUSSION

The starting materials (**1a-c**) were synthesized from D-glucosamine and D-glucose, respectively, in several steps. *O*-acetyl and *O*-benzoyl were the substituents at C-3, which had turned out to play an important role in the stereochemistry of the newly developed asymmetric centre[12] at C-5.

First, methyl 3,4-di-*O*-acetyl-2-benzoylamino-2,6-dideoxy-α-D-*xylo*-hex-5-enopyranoside (**1a**) was submitted to the Pd(II) promoted carbocyclization, and besides the expected (2*S*,3*R*,4*S*,5*S*)-2,3-diacetoxy-4-benzoylamino-5-hydroxycyclohexanone (**2a**),[13] identified from ^{1}H NMR data, mp and optical rotation, the unsaturated (4*R*,5*S*)-2-acetoxy-4-benzoylamino-5-hydroxycyclohex-2-enone (**3a**) was isolated as the major product (ratio 1 : 5). Methyl 2,3,4-tri-*O*-benzoyl-6-deoxy-α-D-*xylo*-hex-5-enopyranoside (**1b**) was converted by the same method exclusively into (2*S*,3*R*,4*S*,5*S*)-2,3,4-tribenzoyloxy-5-hydroxycyclohexanone (**2b**).[8] The transformation of methyl 3,4-di-*O*-benzoyl-2,6-dideoxy-α-D-*erythro*-hex-5-enopyranoside (**1c**),[14] gave two products (ratio 1.4 : 1; according to ^{1}H NMR) and the minor compound was decomposed on column chromatography into the major product (5*S*)-2-benzoyloxy-5-hydroxycyclohex-2-enone (**3c**).[15] In this case the elimination process was more favoured[11,15] because of the *trans* relationship of BzO-3 and H-4. The elimination of the *equatorial* AcO-3 and the H-4, being in a *cis* relationship, upon transformation of **1a**, is a unique result in the application of the Ferrier-II reaction. At the

SCHEME 1.



1 2 3

1a R_2=R_5=H; R_1=OMe
R_3=NHBz; R_4=R_6=OAc
1b R_2=R_5=H; R_1=OMe
R_3=R_4=R_6=OBz
1c R_2=R_3=R_4=H; R_1=OMe
R_5=R_6=OBz

a. R_1=OH; R_2=R_5=H
R_3=NHBz; R_4=R_6=OAc
b. R_1=OH; R_2=R_5=H
R_3=R_4=R_6=OBz
c. R_2=OH; R_1=R_3=R_4=H
R_5=R_6=OBz

same time, no similar elimination was observed in the case of the per-benzoylated α-D-*xylo*-hex-5-enopyranoside **1b** (with analogous configuration), which might be explained by the weaker leaving group character of the BzO group compared to that of the AcO group.

We have observed that the Pd(II)-mediated ring transformation, similarly to the Ferrier(II) reaction, proceeds with high stereoselectivity;[12] the newly generated hydroxyl group at C-5 is *trans* to the lone pair-bearing substituent at C-3. The first step of the ring transformation is the addition of palladium(II) salt to the double bond. If this step contains a π-(allyl)-palladium intermediate, it could cause an isomerization or a rearrangement of allylic substituent[16,17] at C-4. The generated hydrochloric acid, splits the glycosidic bond as well as the hemiacetal ring and after dehydration a 1,5-dioxo compound is formed. In our method of carbocyclization reactions (see general procedure) the addition of diluted (5 mM) sulfuric acid is omitted, because the generated hydrochloric acid proved to be enough for splitting the glycosidic bond and opening the hemiacetal ring. According to Japanese authors,[18] additional acid is not necessary for the Ferrier(II) reac-

tion, when catalytic amounts of various mercury(II) salts were used. Simultaneously the palladium may coordinate to the lone pair-bearing substituent at C-3, which weakens the bond between C-3 and the substituent. This six-membered cyclopalladium intermediate, which type is known in the literature,[19,20] directs the attack of the C-6 nucleophile towards C-1, ensuring the selectivity of the ring-closure and causing elimination of the loosened substituent at C-3. The conversion is stereoselective even if it is accompanied with elimination of the substituent at C-3. This observation shows that the ring closure procedure and the elimination are occurring simultaneously. This conception is in good accordance with the reported mechanism of the Ferrier(II) reaction.[9,12,13]

EXPERIMENTAL

General Methods. Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. Optical rotations were measured with a Perkin-Elmer 241 polarimeter. IR spectra were recorded with a Perkin-Elmer 283 B instrument. ^{1}H and ^{13}C NMR spectra (200 and 50.3 MHz), respectively, were obtained with a Bruker WP 200 SY spectrometer with Me_4Si as internal standard. Mass spectra were recorded with a VG-7035 instrument. TLC and column chromatography were performed on Kieselgel 60 F_{254} (Merck) and Silica Gel 60 (Merck) adsorbent.

General procedure: To a solution of the starting material in acetone - water (2:1) was added $PdCl_2$ (20-25 mol%). The stirred mixture was refluxed for 3-4 h, diluted with acetone - water (2:1) and $NaHCO_3$ as well as $NaHSO_3$ were added in excess. The precipitated Pd was removed by filtration and washed with acetone. Most of the acetone was then distilled off under reduced pressure, the residue was extracted several times with chloroform (or ethyl acetate in the case of **3a**) and the combined extracts were washed with water, dried (Na_2SO_4) and concentrated. The products were purified by recrystallization (ethanol) or by means of column chromatography.

(2*S*,3*R*,4*S*,5*S*)-2,3-Diacetoxy-4-benzoylamino-5-hydroxycyclohexanone (2a). To a stirred solution of **1a** (113 mg, 0.31 mM) in acetone - water 2:1 (15 mL) was added $PdCl_2$ (12 mg, 0.067 mM) and the reaction was per-

formed according to the general procedure. The reaction mixture was extracted with chloroform to give 14 mg (12.8%) of **2a**: mp 200-202 °C; $[\alpha]_D$ +20.32° (*c* 0.7, pyridine). Lit.[13] mp 205 °C; $[\alpha]_D$ +24° (*c* 1.0, pyridine).

(4*R*,5*S*)-2-Acetoxy-4-benzoylamino-5-hydroxycyclohex-2-enone (3a). 146.5 mg (0.403 mM) of **1a** and 14.8 mg (0.081 mM) of $PdCl_2$ in acetone-water 2:1 (15 mL) were reacted as above, but the mixture was extracted with ethyl acetate. 70.5 mg (60.5%) of **3a** was isolated after recrystallization from ethanol: mp 188-190 °C (decomp); $[\alpha]_D$ -115° (*c* 1.6 pyridine); IR (KBr) 3380 (OH, NH), 1780 and 1710 (C=O), and 1650 and 1530 cm^{-1} (amide); ^1H NMR (DMSO-d_6) δ 2.18 (s, 3H, AcO), 2.68 (dd, 1H, $J_{5,6'}$ = 5.0 Hz, $J_{6,6'}$ = 16.0 Hz, H-6a), 2.91 (dd, 1H, $J_{5,6}$ = 3.0 Hz, $J_{6,6'}$ = 16.0 Hz H-6e), 4.33 (m, 1H, H-5), 5.24 (dt, 1H, $J_{3,4}$ =$J_{4,5}$ = 3.0 Hz, $J_{4,NH}$ = 8.0 Hz, H-4), 5.48 (d, 1H, OH), 6.46 (dd, 1H, $J_{3,4}$ = 3.0 Hz, $J_{3,5}$ = 1.5 Hz, H-3), 7.4-8.0 (m, 5H, aromatic), and 8.59 (d, 1H, $J_{4,NH}$ = 8.0 Hz, NH); MS m/z: 289 (M^+).

Anal. Calcd for $C_{15}H_{15}NO_5$: C, 62.25; H, 5.24; N, 4.84. Found: C, 61.05; H, 5.24; N, 4.62.

(2*S*,3*R*,4*S*,5*S*)-2,3,4-Tribenzoyloxy-5-hydroxycyclohexanone (2b). A mixture of 265 mg (0.54 mM) of **1b** and 23.5 mg (0.13 mM) of $PdCl_2$ in acetone-water 2:1 (15 mL) was refluxed and worked up according to the general procedure. After recrystallization 152 mg (59%) of **2b** was isolated: mp 199-201 °C; $[\alpha]_D$ -3.52° (*c* 0.91, chloroform). Lit[8] mp 196-197 °C; $[\alpha]_D$ -4° (chloroform). IR (KBr) 3410 (OH), and 1720-1705 (C=O); ^1H NMR (acetone-d_6) δ 2.77 (dd, 1H, $J_{5,6'}$ = 3.8 Hz, $J_{6,6'}$ = 15.0 Hz, H-6a), 3.29 (dd, 1H, $J_{5,6}$ = 2.5 Hz, $J_{6,6'}$ = 15.0 Hz, H-6e), 4.66 (q, 1H, J_{av} = 3.0 Hz, H-5), 5.31 (dd, 1H, OH), 5.98 (dd, 1H, $J_{3,4}$ = 10.0 Hz, $J_{4,5}$ = 2.5 Hz, H-4), 6.10 (d, 1H, $J_{2,3}$ = 10.0 Hz, H-2), 6.41 (t, 1H, $J_{2,3}$ = $J_{3,4}$ = 10.0 Hz, H-3), and 7.3-8.0 (m, 5H, aromatic); MS m/z: 334 $(M-C_7H_6O_2-H_2O)^+$, and 230 $(M-2xC_7H_6O_2)^+$.

Anal. Calcd for $C_{27}H_{22}O_8$: C, 68.35; H, 4.67. Found: C, 65.82; H, 4.42.

(5*S*)-2-Benzoyloxy-5-hydroxycyclohex-2-enone (3c). 140 mg (0.38 mM) of **1c** was dissolved in acetone - water 2:1 (45 mL) and 15 mg (0.085 mM) of $PdCl_2$ was added. The mixture was refluxed and then worked up giving two products. After column chromatography only 48.5 mg (55%) **3c** was isolated: mp 117-119 °C; $[\alpha]_D$ +20.00° (*c* 0.94, chloroform). Lit[15] mp

124-125 °C; $[\alpha]_D$ +27.8° (chloroform). IR (KBr) 3440 (OH), 1730 and 1680 (C=O), and 1650 (C=C); ^{1}H NMR (acetone-d_6) δ 2.56-3.0 (m, 4H, $J_{3,4}$ = 4.5 Hz, $J_{3,4'}$ = 4.0 Hz, $J_{4,5}$ = 4.5 Hz, $J_{4',5}$ = 6.5 Hz, $J_{5,6}$ = 4.0 Hz, $J_{5,6'}$ 8.4 Hz, $J_{4,4'}$ = 18.0 Hz, $J_{6,6'}$ = 16.0 Hz, H-4,4',6,6'), 4.38 (d, 1H, OH), 4.38 (m, 1H, $J_{4,5} = J_{5,6}$ = 4.0 Hz, $J_{4',5}$ = 6.5 Hz, $J_{5,6'}$ = 8.4 Hz, H-5), 6.76 (t, 1H, $J_{3,4} = J_{3,4'}$ = 4.0 Hz, H-3), and 7.5 -8.1 (m, 5H, aromatic); MS m/z: 232 (M^+).

Anal. Calcd for $C_{13}H_{12}O_4$: C, 67.23; H, 5.21. Found: C, 65.21; H, 5.02.

REFERENCES

1. R. J. Ferrier, *J. Chem. Soc. Perkin. Trans. I.*, 1455 (1979).

2. S. Adam, *Tetrahedron Lett.*, **29**, 6589 (1988).

3. D. Semeria, M. Philippe, J.-M. Delaumeny, A.-M. Sepulchre, and S. D. Gero, *Synthesis*, 710 (1983).

4. R. R. Schmidt, and A. Köhn, *Angew. Chem.*, **99**, 490 (1987).

5. A. Köhn, and R. R. Schmidt, *Liebigs Ann. Chem.*, 1045 (1987).

6. D. H. R. Barton, J. Camara, P. Dalko, S. D. Gero, B. Quiclet-Sire, and P. StÜtz, *J. Org. Chem.*, **54**, 3764 (1989).

7. D. H. R. Barton, S. Augy-Dorey, J. Camara, P. Dalko, J.-M. Delaumeny, S. D. Gero, B. Quiclet-Sire, and P. StÜtz, *Tetrahedron*, **46**, 215 (1990).

8. R. Blattner, R. J. Ferrier, and S. R. Haines, *J. Chem. Soc. Chem. Commun.*, 944 (1980).

9. R. Blattner, R. J. Ferrier, and S. R. Haines, *J. Chem. Soc. Perkin Trans. I.*, 2413 (1985).

10. A. S. Machado, A. Olesker, S. Castillon, and G. Lukacs, *J. Chem. Soc. Chem. Commun.*, 330 (1985).

11. A. S. Machado, A. Olesker, and G. Lukacs, *Carbohydr. Res.*, **135**, 231 (1985).

12. P. László, I. F. Pelyvás, F. Sztaricskai, L. Szilágyi, and Á. Somogyi, *Carbohydr. Res.*, **175**, 227 (1988).

13. M. Mádi-Puskás, I. Pelyvás, and R. Bognár, *J. Carbohydr. Chem.*, **4**, 323 (1985).

14. T.-M. Cheung, D. Horton, and W. Weckerle, *Carbohydr. Res.*, **58**, 139 (1977).

15. I. Pelyvás, F. Sztaricskai, and R. Bognár, *J. Chem. Soc. Chem. Commun.*, 104 (1984).

16. P. A. Chaloner, *Handbook of Coordination Catalysis in Organic Chemistry*, Butterworths: London, 1986, Chapter 5. p 403.

17. M. M. L. Crilley, B. T. Golding, and C. Pierpoint, *J. Chem. Soc. Perkin Trans. I.*, 2061 (1988).

18. N. Chida, M. Ohtsuka, K. Ogura, and S. Ogawa, *Bull. Chem. Soc. Jpn.* **64**, 2118 (1991).

19. S. J. Tremont, and H. U. Rahman, *J. Am. Chem. Soc.*, **106**, 5759 (1984).

20. C. Moberg, L. Sutin, and A. Heumann, *Acta Chem. Scand.*, **45**, 77 (1991).