Carbohydrate Research 432 (2016) 9–16

Contents lists available at ScienceDirect

Carbohydrate Research

journal homepage: www.elsevier.com/locate/carres

A one-pot synthesis of 1,6,9,13-tetraoxadispiro(4.2.4.2)tetradecane by hydrodeoxygenation of xylose using a palladium catalyst[☆]

Michael A. Jackson [a, *], Judith A. Blackburn [a], Neil P.J. Price [a], Karl E. Vermillion [b], Steven C. Peterson [c], Gregory M. Ferrence [d]

[a] *United States Department of Agriculture, Agricultural Research Service, National Center for Agricultural Utilization Research, Renewable Products Technology Research, 815 N. University, St. Peoria, IL 61604, United States*
[b] *United States Department of Agriculture, Agricultural Research Service, National Center for Agricultural Utilization Research, Functional Foods Research, 815 N. University, St. Peoria, IL 61604, United States*
[c] *United States Department of Agriculture, Agricultural Research Service, National Center for Agricultural Utilization Research, Plant Polymer Research, 1815 N. University, St. Peoria, IL 61604, United States*
[d] *Department of Chemistry, Illinois State University, Normal, IL 61790, United States*

ARTICLE INFO

Article history:
Received 26 May 2016
Accepted 9 June 2016
Available online 14 June 2016

Keywords:
Xylose
Arabinose
Pd/silica-alumina
Polymorph
1,6,9,13-tetraoxadispiro(4.2.4.2)tetradecane
11β-hydroxysteroid dehydrogenase 1

ABSTRACT

In an effort to expand the number of biobased chemicals available from sugars, xylose has been converted to 1,6,9,13-tetraoxadispiro(4.2.4.2)tetradecane in a one-pot reaction using palladium supported on silica-alumina as the catalyst. The title compound is produced in 35–40% yield under 7 MPa H_2 pressure at 733 K using 3–10 wt%Pd on silica-alumina catalyst. It is isolated using a combination of liquid-liquid extractions and flash chromatography. This dimer can be converted to its monomer, 2-hydroxy-(2-hydroxymethyl)tetrahydrofuran, which ring opens under acid conditions to 1,5-dihydroxy-2-pentanone. This diol can then be esterified with vinylacetate in phosphate buffer to produce 1,5-bis(acetyloxy)-2-pentanone which is an inhibitor of mammalian 11β-hydroxysteroid dehydrogenase 1. ^1H and ^{13}C nmr spectra of each of these species are reported. The single crystal X-ray structure of the title compound is also reported. These data were collected in a temperature range of 100 K–273 K and show a solid state phase change from triclinic to monoclinic between 175 K and 220 K without a conformational change.

1. Introduction

Xylose is a readily available pentose usually isolated from the hemicellulose of wood, typically, beech and birch. Much of the commercial use of xylose is in its hydrogenation to xylitol [1,2]. In 2013 xylitol had a global market value of US$670 million [3] that is expected to grow to US$1 billion by 2020. The hydrogenation is performed using Raney nickel in a batch slurry reactor where the catalyst effectively hydrogenates the carbonyl group of xylose. However, the utilization of xylose in a biobased chemicals program requires xylose to be converted to a wide spectrum of chemicals. Extensive research exists into the dehydration of xylose to make furfural which can then be a building block used in many industries [4–12]. The hydrogenation of furfural yields biofuel components [13–18] and diol monomers [19–22] for polymer synthesis. Other specialty products have been prepared from the pentoses. van der Klis et al. have reported on the decarbonylation of xylose and arabinose over Ru/C to give the tetritols erythritol and threitol at 25% yield [23].

We present here another specialty product from xylose, 1,6,9,13-tetraoxadispiro(4.2.4.2)tetradecane, (**1**), which was originally described simultaneously by Hurd [24] and Swadesh [25] in 1949. Hurd was attempting to resolve discrepancies previously reported on the thermal degradation of sugars. He used 2,3-dihydroxytetrahydropyran as a model compound for studying the degradation of glucose but failed to find the expected anhydroglucose analog. Instead, **1** was found in about 20% yield. Swadesh, while at Quaker Oats, was identifying the byproducts resulting from the Raney nickel hydrogenation of furfuryl alcohol

---

[☆] Mention of trade names or commercial products in this publication is solely for the purpose of providing specific information and does not imply recommendation or endorsement by the U.S. Department of Agriculture. USDA is an equal opportunity provider and employer.

[*] Corresponding author.
E-mail address: michael.jackson@ars.usda.gov (M.A. Jackson).

http://dx.doi.org/10.1016/j.carres.2016.06.003
0008-6215/Published by Elsevier Ltd.

where tetrahydrofurfurylalcohol is the main product. One of the byproducts, described as high-boiling, was isolated as a colorless crystal melting at 103 °C. Following discussions between Swadesh and Hurd, it was concluded that each group was studying the same compound, namely **1**. After a fifty year absence from the literature, the structure of **1** was determined by Gaede et al. [26] This group used a Pd/C catalyst for the hydrogenation of furfuryl alcohol and recovered **1** at a yield of less than 5%. They found the product deposited in the condenser while attempting a distillation. Each of these groups also noted the monomeric, ring-opened form of the compound, 1,5-dihydroxy-2-pentanone. More recently, Zhang, et al. [27] isolated **1** and several derivatives including the mono- and diacetylated derivatives of 1,5,-dihydroxy-2-pentanone from the fruiting spores of the basidiomycete *Catathalesma imperial*. The compounds were isolated by ethyl acetate extraction and purified by column chromatography in quantities ranging from 2 to 110 mg/kg of fungal fruiting tissue. Three of these isolated compounds in open chain form, though not the cyclic species, were found to be inhibitors of both human and mouse 11β-hydroxysteroid dehydrogenases. These enzymes are seen as targets for treating hypertension, type II diabetes, and metabolic syndrome [28]. This report offers some expectation for the utility of **1**, either as the tricyclic or its open chain form.

We rediscovered the title compound while screening catalysts for the hydrodeoxygenation of biomass hydrolysates. The hydrolysates were prepared by passing hot, compressed water over ball-milled switchgrass. These screening reactions were performed on these murky suspensions at 433 K and 7 MPa hydrogen pressure and resulted in solutions containing products from both lignin and sugar components of biomass. Analysis of these solutions by gas chromatography/mass spectrometry and HSQC NMR led to the tentative identification of **1**. The structure of **1** suggested that it originated with xylose and/or arabinose that were hydrolyzed from hemicellulose. Therefore, these pentoses were hydrogenated under the conditions of our screening reactions to see if **1** could be synthesized in high yields and to see if it could serve as biobased platform chemical. The results of these studies are presented here.

2. Results and discussion

2.1. Catalyst selection and characterization

From our screening reactions it was apparent that palladium was the active metal with the greatest tendency to produce **1** from xylose and it performed best when supported on silica-alumina (SA). Other supports that were examined included commercial 5% $Pd/CaCO_3$, 5%Pd/C, and 5%Pd/Al_2O_3. Of these, only the 5%Pd/Al_2O_3 gave **1** in yields near that obtained with Pd/SA. 5%Pd/C gave **1** at <5% and xylitol and tetrahydrofurfuryl alcohol (THFA) at selectivities of 35% and 41%, respectively. 5%$Pd/CaCO_3$ produced mostly the hydrogenolysis products acetol, 3-hydroxy-2-butanone, and acetic acid and **1** at only 6%. Palladium was also impregnated onto other supports. 5%$Pd/AlPO_4$ was prepared to examine the role support acidity might play. This catalyst did produce **1** at 12% selectivity (and THFA at 38%) but it was visibly degraded after one use. Palladium was loaded onto H-Beta zeolite, another acidic support, which gave **1** at 20% yield along with THFA and acetol. Following these results, we focused on the Pd/SA catalysts for the synthesis of **1**.

A series of Pd/SA catalysts with Pd loadings ranging from 3% to 10% were prepared by wet impregnation using $PdCl_2$ dissolved in aqueous ammonium hydroxide. The surface properties of fresh and used 5Pd/SA catalysts calcined at 673–973 K are shown in Table 1 and the N_2 isotherms of the catalyst calcined at 973 K are shown in Fig. 1. It can be seen in the table that addition of the palladium to the support causes a decrease in surface area and small changes in pore diameter and volume. Calcination at 973 K causes a greater loss in surface area compared to the lower temperatures. PdO crystallite size is also affected by calcination temperature with the higher temperatures giving larger crystallites. Metal oxide supports are known to be susceptible to degradation in hot water and this can be seen in both the table and in the shape of the N_2 isotherms. The loss in surface area and expansion of the pores reveals the change in the support structure. Fig. 1 shows the hysteresis loop of the fresh catalyst is a Type H2 typical of metal oxide gels and indicative of complex, interconnected pore structure. After use, the pore structure appears to collapse into fewer but larger pores resulting in a hysteresis loop that takes on the appearance of Type H1. This reorganization also affects the PdO crystallite size as the X-ray diffraction results from the fresh and used catalysts indicate that the crystallites are smaller after the catalysts have been used. The energy dispersive X-ray spectroscopic analysis of Pd and Al also indicate that the Pd migrates to the surface as a result of both calcination temperature and use. Overall, this means that the calcination temperature becomes irrelevant after the catalysts are exposed to hot water. (See the SI for the XRD and EDS spectra in Figs. S1 and S3).

Fig. S2 displays the temperature programmed hydrogenation of the catalysts after being calcined at temperatures of 673 K, 773 K, and 973 K. The negative peak, an area where hydrogen is being evolved from the catalyst, is indicative of the β-hydride capacity of the reduced Pd^0 on the surface of the catalyst. The TPR trace of the catalyst calcined at 673 K shows a smaller negative peak at 358 K and a large hydrogen absorption peak near 573 K. The peak around 573 K results from better dispersed Pd on the surface. At higher calcination temperatures, the β-hydride peak increases in size and the dispersed Pd is reduced in relative amounts.

2.2. Hydrodeoxygenation of D-(+)-xylose

The title compound is a colorless solid with a literature melting point of 376 K; at high purity, it sublimes; it has a fragrance variously described as like that of hazelnut or bourbon. The hydrodeoxygenation (HDO) of xylose to **1** and the successive conversion of this to the ring-opened species 1,5-dihydroxy-2-pentanone (**3**) and on to the acetylated derivative (**4**) are shown in Fig. 2. The yield-limiting step in the reaction series is the reaction of xylose with a yield of **1** typically at 35–40%. Fig. 3 displays the product selectivity at high conversion of xylose. The identified side products of this reaction result from as many as four competing pathways that need to be inhibited to increase the yield of **1**. These include hydrogenolysis in which carbon-carbon bonds are broken giving hydroxypropanone and 1-hydroxy-2-butanone. The second pathway is the HDO of xylose in which carbon-oxygen bonds are broken resulting in the formation of water and the C5 products 1-hydroxy-2-pentanone, cyclopentanone, and THFA. The third pathway is the hydrogenation of the carbonyl group to give xylitol. A fourth pathway is the dehydration of xylose to furfural, which is a well known route to platform chemicals from biomass [4–7,9,29]. But furfural is only detected at very low levels during the HDO reaction. Although furfural could be seen as the logical precursor to **1** if it was hydrogenated to furfuryl alcohol, the starting material in the previous reports for the synthesis of **1**. In fact, the hydrogenation of furfuryl alcohol over Pd/SA does not give **1**. Furfural could also be proposed as the precursor to both THFA [13] and the cyclopentanone [30,31]. The hydrogenation of furfural proceeds only slightly under these reaction conditions over Pd/SA so the THFA likely forms from the HDO pathway. Furfural is not formed if the catalyst is more active toward the reactions involving hydrogen than toward dehydration. That is, palladium catalysts activate hydrogen and produce the reduced organic species. Other