METAL-ASSISTED REACTIONS. PART 20.1 CATALYTIC TRANSFER HYDROGENOLYSIS OF PHENOLIC C-O BONDS

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After conversion of phenols into O-pseudosaccharyl ethers (2) catalytic transfer hydrogenolysis with Pd/C catalyst and sodium phosphinate as hydrogen donor gave arenes (ArH) in good yield. As an example of the application of this reaction in synthesis, cestrone was converted into cestratrienone in a high yielding, one step reaction.

In earlier work,² catalytic transfer hydrogenolysis³ of C-O bonds in readily prepared heteroaromatic ethers of phenols to give arenes was described. Principally, the heteroaromatic group (R) in phenolic ethers (ArOR) was 5-phenyltetrazolyl. Whilst these ethers afford arenes (ArH) rapidly and in high yield, the reaction suffers economically from the relatively high cost of the 5-phenyltetrazolyl group which makes it unattractive on a large scale. Replacement of the 5-phenyltetrazolyl by the cheap, readily available pseudosaccharyl group gives easily prepared, crystalline phenolic ethers (2; reaction 1) which are easily hydrogenolysed.



In a typical experiment, cestrone (9.18 mmoles) was reacted with 3-chloro-1,2benzisothiazole-1,1-dioxide4 (pseudosaccharyl chloride; 1; 9.18 mmoles; reaction 1) in the presence of triethylamine (10 mmoles) in refluxing toluene to give the corresponding 3-O-pseudosaccharyl ether of cestrone (cestra-1,3,5(10)-trien-3-ol-17-one; 2, Ar = oestronyl) in quantitative yield. Crystalization from toluene gave colourless crystals, m.p. 162ºC. The pseudosaccharyl ether (2; 0.92 mmole) in benzene (150 ml) was hydrogenolysed by refluxing it with sodium phosphinate (sodium hypophosphite; 0.03 mol) as hydrogen donor in water (50 ml) for fifteen minutes in the presence of palladium-on-charcoal catalyst (10%; 1g). The reaction mixture was worked up by extraction with ether and washing the ether extracts with water to remove the saccharin (3) so produced. Evaporation of solvent gave cestra-1,3,5(10)-trien-17-ones, m.p. 134-135°C; [a]22 +168° (dioxane); (96% yield). Other examples are given in the Table. All pseudosaccharyl ethers gave satisfactory C.H.N analyses and the expected infrared, ¹H-nur and mass spectra; melting points are reported in the Table. Product arenes were identified by gas chromatography, gas chromatography-mass spectrometry and, in many instances by isolation of the arene and its identification by m.p. and ill-nmr.

Yields of arenes from this hydrogenolysis are generally high although, as with 5-phenyltetrazolyl ethers² there are some anomalies. Thus, where the phenolic ether contains an aldehyde substituent, the Pd catalyst appears to be poisoned but conversion of the aldehyde into a cyclic acetal with ethylene glycol allows hydrogenolysis to proceed. Chlorine substituents in the phenolic ethers may be hydrogenolysed and nitro substituents are reduced to amino.

Ar-O-R (2) Þ Ar =	Melting point (°C)	Reaction time (min)	Yield of Arene ^c ArH (%)
1-Naphthy]	201-202	15	90 *
2-Naphthy1	260-261	17	94 *
3-Cyanopheny1	200-202	60	56
4-Acetylphenyl	244-245	185	80
4-Nitrophenyl	246-247	15	100 d
4-Aldehydophenyl	252-254	185	· 16
4-Ketal•	204-206	15	44 •
4-Methoxypheny1	185-186	180	98
4-Chloro-2-methylphenyl	184-185	180	99 f
4-Carbometoxypheny1	216-217	45	98
3.5-Dimethylphenyl	202-203	150	100
4-Fluorophenyl	158-159	420	63 •
3-Trifuoromethylphenyl	119-120	420	80 9

TABLE. Melting Points of 3-O-Arylpseudosaccharyl Ethers and Yields of Arenes Resulting from their Hydrogenolysis^a

- Typical reaction conditions are given on the text. For ethers wich do not contain a carbonyl group, only one third of the quoted weight of catalyst was used.
- b R = 3-(1,2-benzisothiazole-1,1-dioxide).

• Quoted yields are based on gas chromatographic results, using an internal standard and in some cases on isolation of arene (*).

- d The product was aniline.
- 3-(4-Aldehydophenyl)-1,2-benzisothiazole-1,1-dioxide was converted into its cyclic ketal with 1,2-ethanediol. With extended reaction time the ketalbenzene was hydrolysed to benzaldehyde.
- f The product was toluene.
- 9 Toluene was used as solvent.

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- ⁵ E. Caspi, E Cullen and P.K. Grover, <u>J. Chem. Soc.</u>, 1963, 212
- ⁵ The specific rotation given in reference 5, $[a]_{5}^{24}$, is +400° (dioxane). However, the specific rotation for cestrone, $[a]_{5}^{25}$, is +161° (dioxane), close to the value found here after removal of -OH from position 3, well away from the optically active centres. This suggests the value given in reference 5 may be erroneous.

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