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p-Nitrophenyl Group for Anomeric Protection of Oligosaccharides, Selective Oxidative Cleavage via *p*-Acetamidophenyl Glycosides

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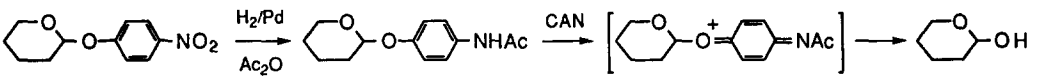
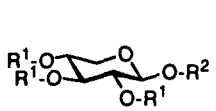
Abstract: Versatile use of the *p*-nitrophenyl group for anomeric protection of carbohydrates is described. It can be readily removed via conversion into a *p*-acetamidophenyl group followed by ammonium cerium(IV) nitrate oxidation. Copyright © 1996 Published by Elsevier Science Ltd

p-Nitrophenyl glycosides are frequently used as donors for enzymatic transglycosidation because of their high reactivity.[1a-c] In some instances, *p*-nitrophenyl glycosides are also used as versatile glycosyl acceptors for glycosidase-catalyzed glycosidation:[1d-g] progress of the enzymatic reaction and purification can be readily monitored by use of the strong UV absorption of the *p*-nitrophenyl function of the products. However, lack of methods for the selective cleavage of this group under mild conditions has hindered its practical use as a protecting group. We previously reported a new use of the *p*-nitrobenzyl (*p*-nitrophenylmethyl, NPM) group for protection of hydroxyl functions.[2] The NPM group can be removed selectively *via* reduction followed by either direct anodic oxidation of the resulting *p*-aminobenzyl derivative or oxidation with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) after *N*-acetylation. Since the *p*-methoxyphenyl group is removable by ammonium cerium(IV) nitrate [$(NH_4)_2Ce(NO_3)_6$] (CAN) oxidation,[3] we anticipated that the *p*-nitrophenyl function could also be removed similarly via conversion of the electron-withdrawing nitro group into an acetamido group followed by CAN oxidation.

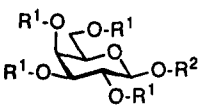


This idea was examined with peracetylated *p*-nitrophenyl β-D-xyloside (**1**), β-D-galactoside (**2**), β-D-galactosyl(1→4)β-D-xyloside (**3**)[4] and α-D-glucoside (**4**) as substrates. Conversion of the nitro group of **1**, **2**, and **3** into an acetamido group was carried out by catalytic hydrogenation using palladium black (H_2: 7 kg/cm^2) in THF-acetic anhydride or in acetic anhydride to give the corresponding acetamidophenyl glycosides, **5**, **6**, and **7**, quantitatively. Reduction of the nitro group of **4** was also readily effected by Zn-Cu/AcOH. Subsequent addition of Ac_2O to the reaction mixture gave **8**. The cleavage reaction of the *p*-acetamidophenyl group was then investigated. The reaction was carried out at 0 °C for 20 min in CH_3CN/H_2O (10:1) by using 5 eq. of CAN in a manner similar to cleavage of the *p*-methoxyphenyl group[3] to give the desired products with free 1-OH groups in satisfactory yields.[5] Xylose derivative **9**, Gal-Xyl derivative **11**, and glucose derivative **12** were obtained in 99, 81, and 97% yields, respectively, after direct purification by silica-gel preparative TLC or silica-gel column chromatography. The deprotected galactose derivative **10** was acetylated in order to

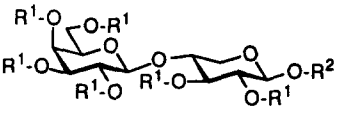
separate a concomitant oxidized product of the *p*-acetamidophenyl moiety; purification with silica-gel preparative TLC gave **13** in 85% yield from **2**.



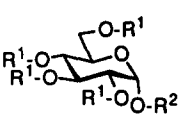
1: R^1=Ac, R^2=$C_6H_4NO_2$
5: R^1=Ac, R^2=C_6H_4NHAc
9: R^1=Ac, R^2=H
(99% from **1**)



2: R^1=Ac, R^2=$C_6H_4NO_2$
6: R^1=Ac, R^2=C_6H_4NHAc
10: R^1=Ac, R^2=H
13: R^1= R^2=Ac
(85% from **2**)



3: R^1=Ac, R^2=$C_6H_4NO_2$
7: R^1=Ac, R^2=C_6H_4NHAc
11: R^1=Ac, R^2=H
(81% from **3**)



4: R^1=Ac, R^2=$C_6H_4NO_2$
8: R^1=Ac, R^2=C_6H_4NHAc
12: R^1=Ac, R^2=H
(97% from **4**)

In conclusion, the *p*-nitrophenyl group proved to be applicable to protection of the anomeric positions of carbohydrates. The starting *p*-nitrophenyl glycosides are readily prepared by direct glycosidation of *p*-nitrophenol with acetylated glycosyl bromides. Some *p*-nitrophenyl glycosides are even commercially available. *p*-Nitrophenyl glycosides of oligosaccharide prepared, for example, by enzymatic glycosidation can be readily purified by HPLC and then applied to subsequent chemical glycosidation reactions for synthesis of more complex oligosaccharides and glycoconjugates.

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References and Notes

1. (a) Nilsson, K. G. I. *Carbohydr. Res.* **1989**, *188*, 9-17. (b) Look, G. C.; Wong, C.-H. *Tetrahedron Lett.* **1992**, *33*, 4253-4256. (c) Binder, W. H.; Kählig, H.; Schmid, W. *Tetrahedron* **1994**, *50*, 10407-10418. (d) López, R.; Fernández-Mayoralas, A. *Tetrahedron Lett.* **1992**, *33*, 5449-5452. (e) López, R.; Fernández-Mayoralas, A. *J. Org. Chem.* **1994**, *59*, 737-745. (f) Usui, T.; Murata, T.; Yabuuchi, Y.; Ogawa, K. *Carbohydr. Res.* **1993**, *250*, 57-66. (g) Matahira, Y.; Ohno, K.; Kawaguchi, M.; Kawagishi, H.; Usui, T. *J. Carbohydr. Chem.* **1995**, *14*, 213-225.
2. Fukase, K.; Tanaka, H.; Torii, S.; Kusumoto, K. *Tetrahedron Lett.* **1990**, *31*, 389-392.
3. (a) Fukuyama, T.; Laird, A. A.; Hotchkiss, L. M. *Tetrahedron Lett.* **1985**, *26*, 6291-6292. (b) Petitou, M.; Duchaussoy, P.; Choay, J. *Tetrahedron Lett.* **1988**, *29*, 1389-1390.
4. *p*-Nitrophenyl β-D-galactosyl(1→4)β-D-xyloside was prepared by β-galactosidase-catalyzed trans-glycosidation of *p*-nitrophenyl β-D-xyloside with *p*-nitrophenyl β-D-galactoside.[1d]
5. The direct oxidative cleavage of a *p*-aminophenyl glycoside with CAN also proceeded satisfactorily. However, isolation of the product from the many by-products formed by oxidation of the *p*-aminophenyl moiety was then very difficult.

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