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Hypervalent Iodine System for Debenzylation of Sugars

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Abstract: A simple and mild system using 4,4′-bis-(dichloroiodo)-biphenyl in combination with tetraethylammonium bromide (TEAB) at room temperature has been developed for selective debenzylation of sugars. Acetates, benzoate, and sensitive glycosidic linkages are unaffected.

Keywords: 4,4′-bis-(dichloroiodo)-biphenyl, debenzylation, sugars, tetraethylammonium bromide

INTRODUCTION

Benzyl ethers are widely used as protecting groups for carbohydrate compounds because of their stability toward a wide variety of reaction conditions. Although numerous methods are available for their removal,[1–5] problems associated with reagent incompatibility, slow debenzylation rate, low yield, and selectivity in the presence of multiple functionalities. Our group has been working extensively on development of novel methodologies under mild reaction conditions using hypervalent iodine reagents.[6] It was observed that 4,4′-bis-(dichloroiodo)-biphenyl is very good reagent for the iodochlorination of alkenes.[7] We observed that the 4,4′-bis-(dichloroiodo)-biphenyl in the presence of tetraethylammonium bromide (TEAB) was a highly efficient system for selective debenzylation at room temperature. In the absence of TEAB, debenzylation did not take place.

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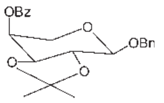
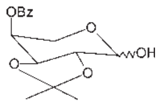
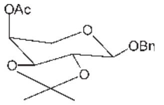
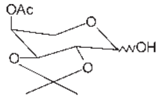
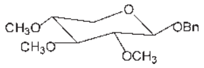
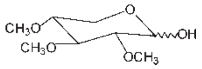
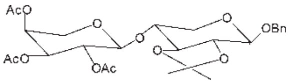
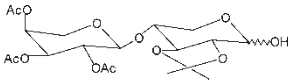
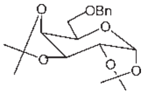
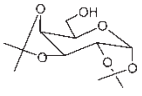
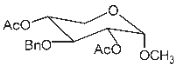
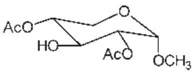
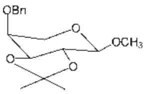
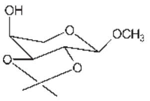
For the initial study, benzyl 4-O-benzoyl 2,3-O-isopropylidene-α-L-arabinopyranoside was chosen as a substrate, and the reaction with 4,4′-bis-(dichloroiodo)-biphenyl in the presence of TEAB was performed. It was observed that the starting material was consumed within 25 min as indicated by thin-layer chromatography (TLC) analysis, and the reaction mixture became clear. After usual workup, the debenzylated derivative (entry 1) and 4,4′-diiodobiphenyl were recovered after silica-gel chromatography.

Encouraged by this result, varieties of protected carbohydrates were subjected to a similar reaction, the results of which are presented in Table 1. Notably acetates, benzoate, and sensitive glycosidic linkages are unaffected by the reaction conditions.

Table 1. Debenzylation using 4,4′-bis-(dichloroiodo)-biphenyl and TEAB

Entry	Compound	Product[a]	Time (min)	Yield[b] (%)
1			35	90
2			30	90
3			25	89
4			30	91
5			35	90
6			30	87
7			35	90

[a] All products were characterized by ^{13}C NMR, ^{1}H NMR, IR, and optical rotation and compared with reported data.

[b] Isolated yields after purification.

GENERAL EXPERIMENTAL PROCEDURE

Benzyl 4-O-benzoyl 2,3-O-isopropylidene-α-L-arabinopyranoside (3.40 g, 10 mmol) was added to a stirred suspension of 4,4′-bis-(dichloroiodo)-biphenyl (1.7 g, 30 mmol) and TEAB (2.5 g, 12 mmol) in dry chloroform (10 ml) at room temperature. The reaction was monitored by TLC. After 25 min, the reaction mixture was quenched with water (25 ml); the organic layer was separated and washed with water (2 × 25 ml), 10% sodium bicarbonate (2 × 15 ml), 10% aqueous sodium bisulfite solution (2 × 15 ml), and finally water (2 × 10 ml). The chloroform layer was separated, dried over sodium sulfate, and concentrated, and the resultant residue was purified by silica-gel column chromatography (10% EtOAc–hexane) to afforded an αβ mixture (1:1), that is, 4-O-benzoyl 2,3-O-isopropylidene-αβ-L-arabinopyranose (2.40 g, 90%). Mp = 58°C; $[\alpha]_{20}^{D} = -32$ (c = 1, CH_2Cl_2); IR (KBr, cm^{-1}) = 1725 (C=O, ester), 3460 (OH, hydroxyl); ^1H NMR (δ ppm, 500 MHz, $CDCl_3$, αβ mixture 1:1): 7.712 (S, 10H), 5.58 (dt, *J* = 9.7 & 5.8 Hz, 1H, H-4), 5.54–5.52 (m,1H, H-4), 5.50 (t, *J* = 9.6 Hz, 1H, H-3), 5.37 (br, d, *J* = 3.2 Hz, 1H, H-1), 5.23 (t, *J* = 9.6 Hz, 1H, H-3), 4.74 (d, *J* = 8.1 Hz, 1H, H-1), 4.05 (dd, *J* = 9.56 & 7.93 Hz, 1H, H-2), 4.09–4.11 (m, 1H, H-2), 3.97–3.71 (m, 4H, H-5), 1.47 (s, 6H) & 1.42 (s, 6H); ^{13}C NMR (δ ppm): 165.786 (C=O), 133.184, 136.740, 129.711, 129.629, 128.062, 127.825 (aromatic), 111.023 (isopropyl carbon), 102.46 (C_1), 70.85 (C_2), 70.38 (C_3), 69.90 (C_5), 69.14 (C_4), 26.587 & 26.309 (2 × CH_3); Found: C, 61.0; H, 6.1; O, 32.5 %; calc. for $C_{15}H_{18}O_6$: C, 61.2; H, 6.16; O, 32.61%.

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