Tetrahedron Letters 54 (2013) 865–870

Contents lists available at SciVerse ScienceDirect

Tetrahedron Letters

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

Use of iodine for efficient and chemoselective glycosylation with glycosyl *ortho*-alkynylbenzoates as donor in presence of thioglycosides

Samrat Dutta, Swarbhanu Sarkar, Shyam Ji Gupta, Asish Kumar Sen *

Chemistry Division, CSIR-Indian Institute of Chemical Biology, 4 Raja S. C. Mullick Road, Jadavpur, Kolkata 700032, India

ARTICLE INFO

Article history:
Received 23 June 2012
Revised 22 November 2012
Accepted 24 November 2012
Available online 1 December 2012

Keywords:
Glycosylation
ortho-Alkynylbenzoates
Iodine
Chemoselective
One-pot

ABSTRACT

A novel and high yielding glycosylation protocol with glycosyl *ortho*-alkynylbenzoates as donors and iodine as promoter is described. The donors are stable and can be chemoselectively activated in the presence of thioethyl and thiophenyl glycosides. The application of this methodology in one-pot consecutive glycosylation reaction is described.

Oligosaccharides and glycoconjugates play an important role in numerous biological processes[1] such as cell–cell interaction,[2] inflammation,[3] signal transduction[4] and many others.[5] Easy and rapid access to pure oligosaccharides and glycoconjugates is, therefore, a prerequisite for further investigation of the precise role of carbohydrates in biology. Thus, the need for development of new and efficient glycosylation protocols has received the attention of organic chemists for many years.[6]

Glycosylation reaction, central to the problem of oligosaccharide and glycoconjugate syntheses, entails a reaction between a glycosyl donor, a protected monosaccharide with a leaving group at the anomeric position, and a glycosyl acceptor, usually carrying one or more free hydroxyl groups. One of the many challenges that carbohydrate chemists face is to attain high yields and complete diastereoselectivity in glycosylation reactions.[7] The development of various glycosylation techniques since the discovery of Koenigs–Knorr reaction,[8] has addressed these problems and allowed for the syntheses of complex oligosaccharides and glycoconjugates. The different glycosyl donors employed in these techniques are glycosyl halides, thioglycosides, trichloroacetimidates, sulfoxides, thioimidates, phosphate/phosphite derivatives, glycals, 1-acyl, 1-carbonate, 4-pentenyl glycosides, 1-hydroxy sugars and orthoesters.[9] Most of these donors require promoters which are toxic, carcinogenic or light and moisture sensitive. Therefore, convenient to use, non-toxic promoters are in high demand.

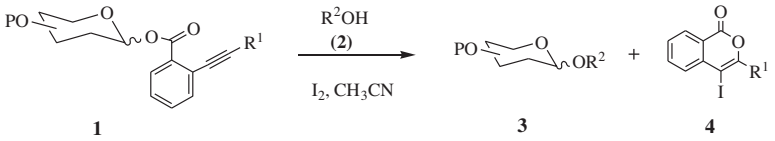
Studies on C–C triple bond activation by metals, to promote glycosylation have introduced new classes of stable and easily synthesized glycosyl donors such as ω-alkynoic acids, propargyl glycosides and glycosyl *o*-alkynylbenzoate.[10,11] These exploit the alkynophilic character of Hg(II),[10a] Au(III)[10b,10c] and Au(I).[11] Although Hg(II) and Au(III) salts are proved to be potent promoters for these donors, the application is limited to armed donors only. $AuPPh_3OTf$ complex, generated from $AuPPh_3Cl$ and AgOTf, was used for the activation of both armed and disarmed donors. Unfortunately, use of metal Lewis acid catalyst results in the disposal of enormous amounts of harmful waste. Recent researches in metal-free organic reactions led us to look for an alternative environmentally benign and cost effective promoter.

Recent reports revealed that iodolactonization of *o*-(1-Alkynyl)benzoates produces substituted 4-iodoisocoumarins.[12] This prompted us to apply the iodocyclization on glycosyl-*o*-(1-Alkynyl)benzoates (**1**); initiated by iodine it stimulates a tandem glycosylation with alcohols (**2**), to produce glycoside (**3**) and 4-iodoisocoumarin (**4**) (Scheme 1). Iodine used to promote this reaction is inexpensive, convenient to use, environmentally benign and non-toxic. The mild reaction condition can be applied to a one-pot chemoselective consecutive glycosylation reaction. It is worthwhile to mention that the use of iodonium ion for remote activation of *n*-pentenyl glycosides and glycosyl halides is well known.[13,14]

o-(1-Alkynyl)benzoic acids **5** were prepared as reported earlier.[12b,12c] Glycosyl *o*-(1-Alkynyl)benzoates **1** were prepared by EDCI coupling of the corresponding lactols **6** with **5** in high yield (entries 1–10, Table 1). In the gluco- and galacto-configurations

* Corresponding author. Tel.: +91 33 24995720; fax: +91 33 24735197.
E-mail address: aksen@iicb.res.in (A.K. Sen).

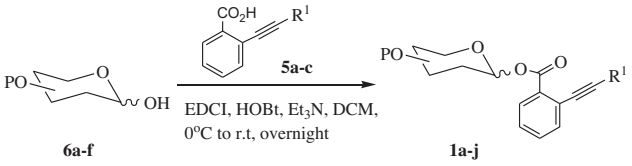
0040-4039/$ - see front matter © 2012 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tetlet.2012.11.101

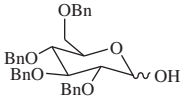
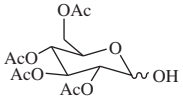
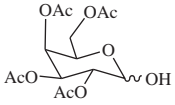
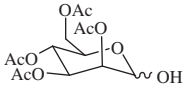
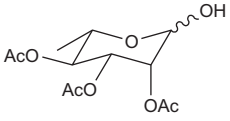
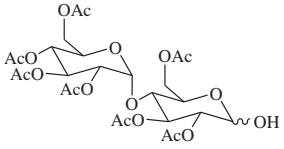


Scheme 1. Glycosylation with glycosyl *o*-(1-alkynyl)benzoate donors.

the 1,3-diaxial interaction of the bulky *ortho*-alkynylbenzoate (in the α-face) with axial H-atoms may be responsible for the formation of β-product exclusively. In the case of manno-configuration (Table 1, entry 4) two types of interactions are possible; (i) effect of 1,3-diaxial interaction in α-configuration favours β-product and (ii) steric interaction between equatorial *ortho*-alkynylbenzoate and the axial C-2 acetyl group in β-configuration, favours formation of α-product. These two interactions are probably more

Table 1
Preparation of glycosyl *o*-(1-alkynyl)benzoates[a]



Entry	*o*-(1-Alkynyl)benzoic acid **5a–c**	Lactol **6a–f**	Ester **1a–j**[b]	Yield[c] (%) (α:β)[d]
1	**5a**: $R^1 = C_6H_5$	 **6a**	**1a**	94 (0:1)
2	**5a**: $R^1 = C_6H_5$	 **6b**	**1b**	95 (0:1)
3	**5a**: $R^1 = C_6H_5$	 **6c**	**1c**	96 (0:1)
4	**5a**: $R^1 = C_6H_5$	 **6d**	**1d**	94 (5:4)
5	**5a**: $R^1 = C_6H_5$	 **6e**	**1e**	93 (1:4.8)
6	**5a**: $R^1 = C_6H_5$	 **6f**	**1f**	89 (0:1)
7	**5b**: R^1 = *p*-OMePh	**6b**	**1g**	94 (0:1)
8	**5b**: R^1 = *p*-OMePh	**6c**	**1h**	93 (0:1)
9	**5c**: R^1 = cyclopropyl	**6b**	**1i**	91 (0:1)
10	**5c**: R^1 = cyclopropyl	**6c**	**1j**	90 (0:1)

[a] All reactions were performed with lactols **3** (1 equiv), *o*-(1-alkynyl)benzoic acids **1** (1.1 equiv), EDCI (1.1 equiv), triethylamine (1.1 equiv) and HOBt (1.1 equiv) in 3 mL DCM.
[b] All the products were characterized by NMR and mass spectroscopy.
[c] Yield refers to products isolated by column chromatography.
[d] All α:β ratios are determined by ^{1}H NMR spectroscopy.