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Preliminary Communications

Iodonium Ion-Mediated Glycosidations of Phenyl Selenoglycosides

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Abstract: Fully benzylated or benzoylated phenyl selenoglycosides can be activated by the promoters iodonium di-*sym*-collidine perchlorate (IDCP) or *N*-iodosuccinimide and catalytic triflic acid (NIS/TfOH *cat.*). The potential of the iodonium ion-mediated glycosidations of phenyl selenoglycosides is illustrated in the chemoselective synthesis of 1,2-*cis*-or 1,2-*trans*-linked disaccharides.

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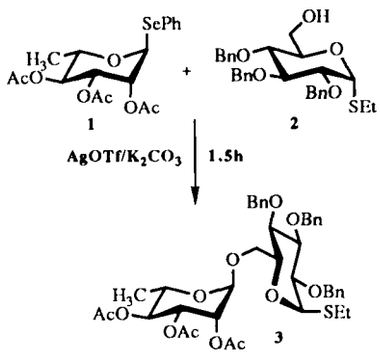
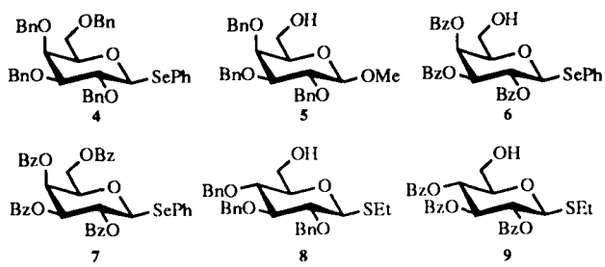
Recently, Pinto *et al.*[1] reported *inter alia* that phenyl 2,3,4-tri-*O*-acetyl-1-seleno-α-L-rhamnopyranoside (**1**) could be condensed (Scheme 1) selectively under the agency of silver triflate[2] with ethyl 2,3,4-tri-*O*-benzyl-1-thio-α-D-glucopyranoside (**2**) giving disaccharide **3** in 80% yield. It occurred to us that the importance of this interesting phenomenon had not been fully recognised. Thus, the subtle difference in reactivity earlier observed in closely related iodonium ion-mediated glycosidations of "armed" or "disarmed" thioglycosides[3] was neither discussed nor exploited by Pinto *et al.*.

Scheme 1



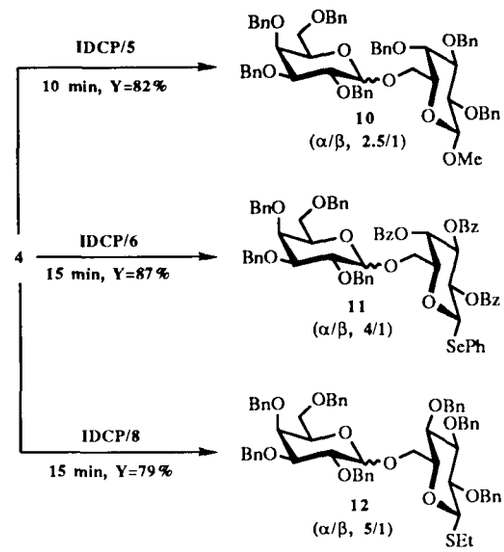
We here report that iodonium ions generated from *N*-iodosuccinimide and catalytic triflic acid (NIS/TfOH *cat*)[3b] or iodonium di-*sym*-collidine perchlorate (IDCP)[3c] are effective agents to probe in depth the glycosylating properties of phenyl selenoglycosides.

In order to evaluate in more detail the use of phenyl selenoglycosides as donors or acceptors in glycosidations, we prepared two differently fully protected phenyl 1-seleno-β-D-galactopyranoside donors[4] (*i.e.* benzylated **4** and benzoylated **7**) and four partially protected glycosyl acceptors (*i.e.* **5**, **6**[4], **8** and **9**), three of which contain either a phenyl seleno (*i.e.* **6**) or an ethyl thio group (*i.e.* **8** and **9**) at the anomeric centre.



The glycosylating capacity of the fully benzylated phenyl selenoglycoside **4** in the presence of IDCP is outlined in Scheme 2. Thus, first of all, it was established that IDCP (2 equiv.)-assisted glycosylation of acceptor **5** (0.25 *mmol*) with donor **4** (0.3 *mmol*) in 1,2-*dichloroethane* (DCE)/ether (6 mL, 1/5, v/v) proceeded rapidly at 20°C to furnish dimer **10**[5] as a mixture of anomers[6]. Interestingly,

Scheme 2

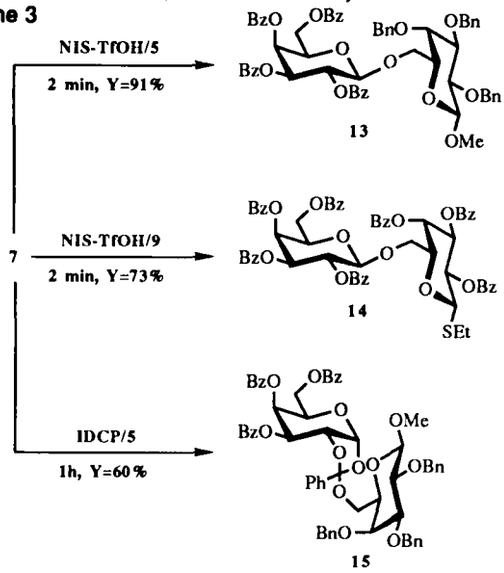


condensation of **4** with the partially benzoylated phenyl selenoglycoside **6**, under the same reaction conditions as mentioned for **10**, led to the isolation of disaccharide **11**[5] (α/β mixture) in an excellent yield, indicating that the glycosidation is a highly chemoselective process. In a similar fashion, glycosylation of the partially benzylated ethyl thioglycoside **8** with donor **4** yielded dimer **12**[5]. The

latter example illustrates that the weak thiophilic promoter IDCP displays a higher affinity towards the anomeric phenyl seleno group.

The high reactivity of phenyl selenoglycosides is exemplified further by the formation of the 1,2-orthoester **15** in Scheme 3. Thus, fully benzoylated phenyl selenoglycoside **7** could be coupled in the presence of IDCP with acceptor **5** to give the orthoester derivative **15**[5] (exo/endo mixture, 1/1) in a reasonable yield. In this respect, it is of interest to note that a fully benzoylated ethyl thioglycoside cannot be activated with IDCP[3c]. On the other hand, it was to be expected that the more powerful promoter NIS/TfOH would enhance significantly the glycosidation rate of **7**. Indeed, condensation of donor **7** (0.3 mmol) with acceptor **5** (0.25 mmol) in DCE/ether (5 mL, 1/1, v/v) in the presence of NIS (1 equiv.) and catalytic TfOH (0.1 equiv.) was a rapid, high-yielding and stereospecific process resulting in the exclusive isolation of the 1,2-*trans* linked dimer **13**[5]. Further, the preferred formation of the expected 1,2-*trans* linked disaccharide **14**[5] in the NIS/TfOH-assisted glycosylation of **9** with **7** designates that selenoglycoside donor **7** can also be activated (*cf.* formation of dimer **12** in Scheme 2) with an acceptable degree of selectivity over the thioglycoside acceptor **9**. Finally, it was of interest to find out whether **7** could be coupled selectively with the partially benzylated acceptor **8** (*cf.* glycosylation of **8** with **4** in Scheme 2). However, addition of NIS/TfOH *cat.* to a mixture of **7** and **8** led to the rapid (2 min) formation of 1,6-anhydro-2,3,4-tri-*O*-benzyl-β-D-glucopyranose (65% yield), denoting that the competitive intramolecular cyclisation of **8** proceeds in a higher rate than the glycosidation. The latter finding is in sharp contrast with the AgOTf-mediated glycosylation (Scheme 1) of **2** with the fully acetylated phenyl selenoglycoside **1**.

Scheme 3



In summary, the results described in this paper clearly show *inter alia* that: (a) iodonium ions are effective promoters for selenoglycosides; (b) a fully benzylated selenoglycoside (*i.e.* "armed" **4**) can be condensed chemoselectively with a partially benzoylated selenoglycoside (*i.e.* "disarmed" **6**) or a partially benzylated ethyl thioglycoside (*i.e.* **8**); (c) a benzoylated selenoglycoside (*i.e* **7**) can be activated selectively over a partially benzoylated ethyl thioglycoside (*i.e.* **9**) and is more reactive with respect to the promoter IDCP than the corresponding ethyl thio counterparts. The latter aspect is demonstrated by the activation of the selenoglycoside **7** with the weak promoter IDCP (see formation of **15** in Scheme 3). In comparison, a similar mild activation could only be effected in the case of a more reactive fully acetylated sugar 1,2-thio-orthoester donor[7]. In conclusion, it may not be excluded that our results together with those of Pinto *et al.* may be a stimulus in applying phenyl selenoglycosides as glycosyl donors or acceptors.

References and notes

1. *S. Mehta, B.M Pinto*, Tetrahedron Lett., **32**, 4425, 1991.
2. Phenyl selenoglycosides could also be activated (see ref 1) by the promoters methyl or phenylselenyl triflate, $CuBr_2$-Bu_4NBr-AgOTf and tris(4-bromophenyl)ammonium hexachloro antimonate originally devised for the activation of thioglycosides.
3. (a) *D.R. Mootoo, B. Fraser-Reid*, J. Am. Chem. Soc., **110**, 2662, 1988. (b) *G. H. Veeneman, S.H. van Leeuwen, J.H. van Boom*, Tetrahedron Lett., **31**, 1331, 1990. (c) *G.H. Veeneman, J.H. van Boom*, Tetrahedron Lett., **31**, 275, 1990. (d) *H.M. Zuurmond, S.C. van der Laan, G.A. van der Marel, J.H. van Boom*, Carbohydrate Res., **215**, C1-C-3, 1991.
4. Compound **4**, **6** and **7** were prepared as follows. First, phenyl 1-seleno-β-D-galactopyranoside was synthesized by reaction of the corresponding fully acetylated β-acetate with phenylselenol (1.2 equiv.) and BF_3·OEt_2 (3.5 equiv.) and subsequent Zemplén deacetylation (90% overall yield). Treatment of the resulting phenyl seleno-β-D-galactopyranoside with either benzyl bromide (4.8 equiv.) and sodium hydride (5.2 equiv.) in *N,N*-dimethylformamide or benzoyl chloride (4.8 equiv.) in pyridine afforded the respective glycosyl donors **4** (75%) and **7** (83%). On the other hand, glycosyl acceptor **6** was obtained by regioselective silylation of phenyl 1-seleno-β-D-galactopyranoside with *tert*-butyldimethylsilyl chloride (1.2 equiv.) in pyridine followed by benzoylation (BzCl/pyridine) and subsequent acidic hydrolysis of the TBDMS-group (53% overall yield).
5. Relevant ^{13}C-NMR data (δ values): **10**;(α-anomer); 56.8 (OCH_3), 67.2, 68.6 (C-6, C-6'), 72.6, 72.3, 72.9, 73.4, 74.3, 74.6, 75.0 (CH_2Ph), 98.2 (C-1', $J_{C\text{-}1',H\text{-}1'}$ 170 Hz), 104.7 (C-1). **11**;(α-anomer); 66.9, 68.9 (C-6, C-6'), 72.9, 73.1, 74.5 (3x CH_2Ph), 80.3 (C-1), 98.4 (C-1', $J_{C\text{-}1',H\text{-}1'}$ 170 Hz), 164.9, 165.1 (3x PhCOO). **12**;(α-anomer); 15.2 (SCH_2CH_3), 24.7 (SCH_2CH_3), 66.8, 68.8 (C-6, C-6'), 72.3, 72.9, 73.2, 74.7, 74.9, 75.4 (7x CH_2Ph), 86.4 (C-1), 97.8 (C-1', $J_{C\text{-}1',H\text{-}1'}$ 170 Hz). **13**; 56.5 (OCH_3), 61.7, 68.6 (C-6', C-6), 72.8, 74.3, 74.8 (3x CH_2Ph), 101.4 (C-1'), 104.6 (C-1), 165.0, 165.3, 165.8 (3x PhCOO). **14**; 14.6 (SCH_2CH_3), 23.7 (SCH_2CH_3), 61.8, 68.4 (C-6',C-6); 83.1 (C-1), 101.4 (C-1'), 165.4, 165.1 (7x PhCOO). **15**;(exo isomer); 56.9 (OCH_3); 62.2 , 62.7 (C-6, C-6'), 72.9, 74.4, 75.0 (3x CH_2Ph), 98.2 (C-1'), 104.8 (C-1), 120.1 (C_q).
6. α/β-Ratios were determined by ^{13}C-NMR spectroscopy.
7. *H.M. Zuurmond, G.A. van der Marel, J.H. van Boom*, Recl. Trav. Chim. Pays-Bas, **109**, 437 (1990)