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The Sequential Double Aryl C-Glycosidation: Introduction of a Second Sugar Unit onto Mono Aryl C-Glycosides using SnCl4/AgOTfa.

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Abstract:

The promoter combination ($SnCl_4$/AgOTfa) was successfully applied to introduce a second sugar unit onto mono aryl C-glycosides. A systematic survey of this sequential double aryl C-glycosidation is described.

Keywords: Carbohydrate mimetics; Coupling reagents; Friedel-Crafts reactions; Glycosidation.

In the course of our studies seeking a new synthetic method of aryl C-glycosides, it was disclosed[1] that a powerful promoter combination ($SnCl_4$/AgOTfa) enabled a diverse range of sugar acetate substrates to react with various aromatics via a Friedel-Crafts-type addition.

Regarding aryl C-glycosides as glycomimics of biologically important glycoepitopes, introduction of the second sugar unit onto mono aryl C-glycosides can be contended to be an expansion of their structural diversity and thus has important implications in building combinatorial libraries for glycomimic designs[2].

In this communication, we wish to report that the same promoter combination ($SnCl_4$/AgOTfa) was also successfully applied to sequential double aryl C-glycosidation, affording a new class of compounds bearing two sugar units on an aromatic ring.

The selected results are summarized in the table.

In the case of mono aryl C-glycosides having relatively active aromatic nuclei such as 2,6-dimethoxynaphthalene or 1,4-dimethoxybenzene, it was shown that peracetates of various sugars (entry 1,3,4,5), as well as a benzyl-protected sugar (entry 2), were successfully introduced onto the aromatics in good yield and in a highly β-selective manner.

The introduction of the first sugar onto an aromatic ring usually reduces its activity sufficiently to make further glycosidation of that ring unlikely. Therefore, in the case of biphenyl or diphenylmethane C-glycosides (entry 6,7), the second sugar can only be introduced onto the non-glycosylated phenyl ring, as shown by our data.

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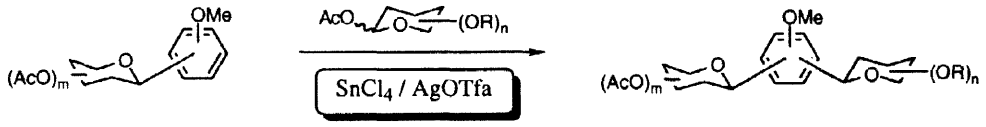
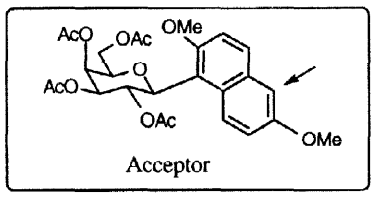
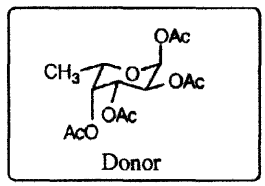
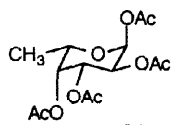
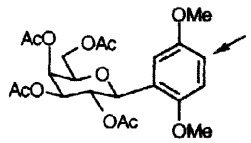
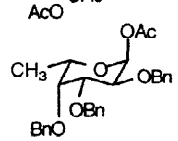
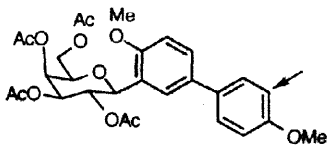
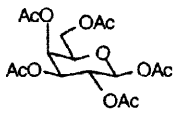
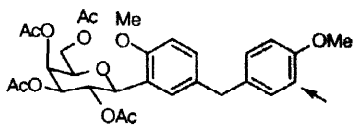
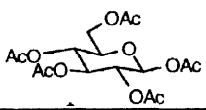
Table: Double Aryl C-Glycosidation with Various Donors and Acceptors[a)]







entry	Donor	Yield % [b)]	entry	Acceptor	Yield % [b)]
1.		90	5.		66
2.		49	6.		66
3.		94	7.		74
4.		48			

The reaction was carried out in CH_2Cl_2 at 0°C - R.T. using the following equivalency:
Accptor / Donor / $SnCl_4$ / AgOTfa = 1 / 1.5 / 1.5 / 1.5
a) The arrow in this table indicates where acceptor undergoes glycosylation. b) Only β-anomer was obtained.

We anticipate that this double aryl C-glycosidation provides a new approach to exploring a novel and biologically interesting class of glycomimics.

Typical procedure for the preparation of entry 1 in the table.

To a mixture of 2,6-dimethoxy-1-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)naphthalene (254mg, 0.49mmol), L-fucose tetraacetate (249mg, 0.75mmol) and AgOTfa (191mg, 0.75mmol) in CH_2Cl_2 (3ml) at 0°C was added a 1M $SnCl_4$ CH_2Cl_2 solution (0.75ml, 0.75mmol) under N_2 gas atmosphere. After the reaction mixture was stirred for 4h at 0°C and 18h at r.t, $NaHCO_3$ aqueous solution was added and stirred for 20 min. The inorganic material was filtered off over a Celite^R pad, and the filtrate was extracted several times with CH_2Cl_2. The combined CH_2Cl_2 solution was washed with brine and dried over anhydrous $MgSO_4$, then concentrated under reduced pressure. The remainder was purified by column chromatography on silica gel (hexane / EtOAc = 1/1) to afford 2,6-dimethoxy-1-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-5-(2,3,4-tri-*O*-acetyl-β-L-fucopyranosyl)naphthalene (348mg, 0.44mmol).

References

[1] Kuribayashi T, Ohkawa N, Satoh S. Tetrahedron Lett. preceding paper in this issue. Representative aryl C-glycosidation methods are described in this reference.

[2] Parker KA, Koh Y. J. Am. Chem. Soc. 1994;116:11149-11150.