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Preliminary communication

Trimethylsilyl trifluoromethanesulfonate as an effective catalyst for glycoside synthesis

TOMOYA OGAWA*, KAZUO BEPPU, and SATORU NAKABAYASHI**
The Institute of Physical and Chemical Research, Wako-shi, Saitama, 351 (Japan)

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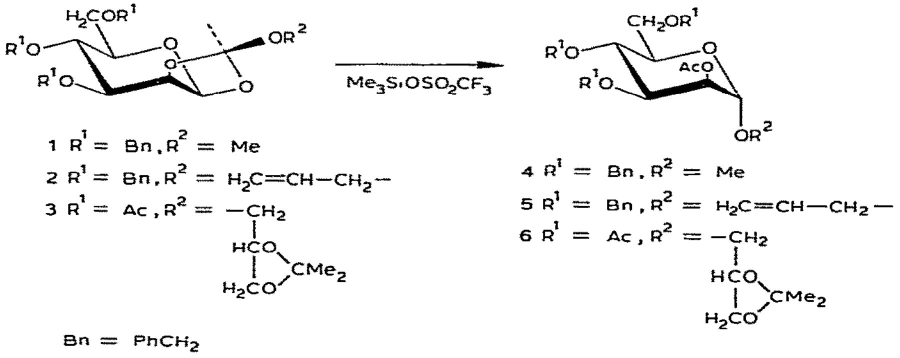
Lewis acids have been employed as efficient catalysts for the activation of the C–O bond at the anomeric carbon atom in the synthesis of 1,2-*trans*-glycosides. Typical examples are (*i*) $HgBr_2$ for the rearrangement of orthoesters[1], (*ii*) BF_3–ether and $SnCl_4$ with 1,2-*trans*-diacyl esters[2] or glycals[3], and (*iii*) $FeCl_3$ with oxazolines[4]. Recently, trimethylsilyl trifluoromethanesulfonate was successfully used as a catalyst for the synthesis of ribonucleosides[5] and for the activation of dialkoxymethanes into highly reactive electrophiles[6].

We here report efficient formation of 1,2-*trans*-glycosidic linkages by employing $Me_3SiOSO_2CF_3$ as the catalyst.

(a) Rearrangement of an orthoester.–$HgBr_2$-Catalyzed rearrangement of orthoester **1** was reported[7] to proceed at 140°, giving rise to a 71% yield of a mixture of methyl α-D-mannopyranoside (**4**) and its β anomer in the ratio of 67:4. Employing a catalytic amount of $Me_3SiOSO_2CF_3$ in the presence of powdered molecular sieve 4 A, the same reaction proceeded readily in $Cl(CH_2)_2Cl$ at 15–20°, to afford the α anomer **4** in 76% yield***, and no β anomer of **4** could be detected in t.l.c. In the same way, mild



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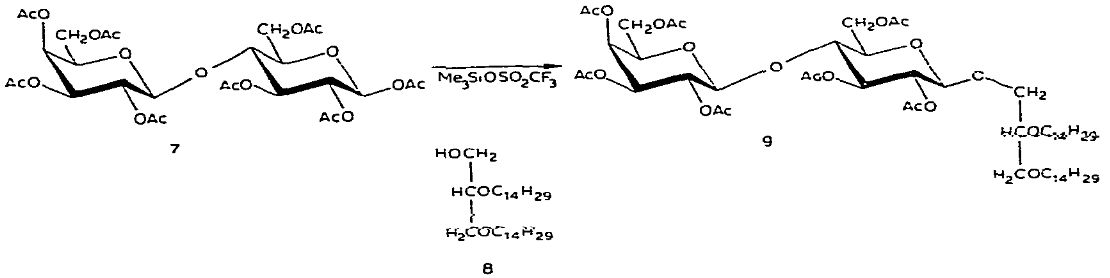
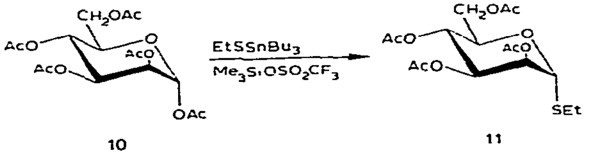
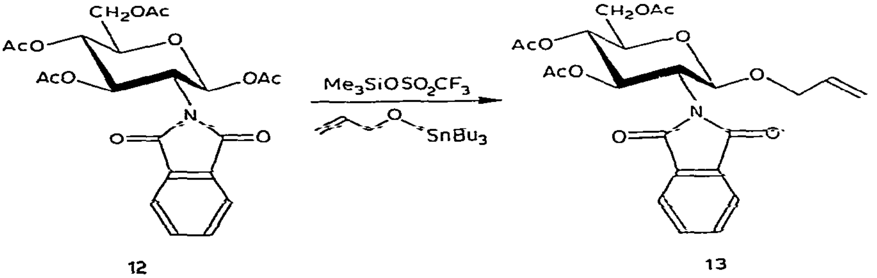
*To whom enquiries should be addressed.
**Present address: The Research Laboratory, Meiji Seika Kaisha Ltd., Morooka-cho, Kohoku-ku, Yokohama, 222, Japan.
***All reactions described in this communication were performed under argon.



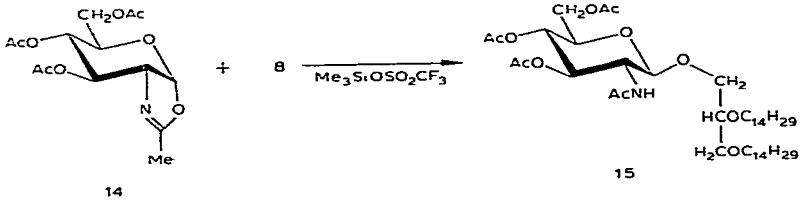


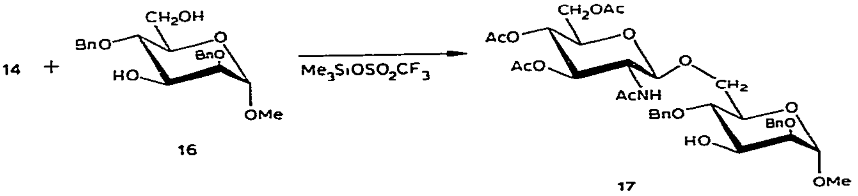
transformation of the orthoester 2 into the α-D-mannopyranoside 5 was achieved in 81% yield; $[\alpha]_D$ +30.5° ($CHCl_3$)[†]; R_F 0.54 (10:1 toluene–EtOAc); δ_H ($CDCl_3$): 2.13 (s, Ac). Similarly, orthoester 3 was readily converted into α-D-mannopyranoside 6 in 60% yield[††]; m.p. 66–68°, $[\alpha]_D$ +47.2° ($CHCl_3$); δ_H ($CDCl_3$): 5.00 (d, J 3 Hz, H-1), and 1.46 and 1.40 (2 s, Me_2C).

*(b) Reaction with a 1,2-*trans*-diacetate.*— Treatment of an equimolar mixture of octa-*O*-acetyl-β lactose (7) and alcohol 8 in $Cl(CH_2)_2Cl$ with an equivalent amount of $Me_3SiOSO_2CF_3$ in the presence of powdered molecular sieve 4 A for 3 h at 20° afforded the β-glycoside 9 (as a single spot in t.l.c.) which was isolated in 70% yield; $[\alpha]_D$ −7.85° ($CHCl_3$); δ_H ($CDCl_3$): 2.14 (s, Ac), 2.11 (s, Ac), 2.05 (s, Ac), 2.03 (s, 2 Ac), 2.02 (s, Ac), and 1.96 (s, Ac). Alkyl trialkyltin sulfide[8] and trialkyltin alkoxide[9] also proved to be suitable glycosyl acceptors for this transformation. Thus, an equimolar mixture of pentaacetate 10, ethyl tributylstannyl sulfide, and $Me_3SiOSO_2CF_3$ in $Cl(CH_2)_2Cl$ was heated for 20 h at 50° to give crystalline 1-thioglycoside 11 in 76% yield; m.p. 105–107°, $[\alpha]_D$ +90.9° ($CHCl_3$). Furthermore, an equimolar mixture of β-acetate[10] 12, tributyltin allyloxide, and $Me_3SiOSO_2CF_3$ in $Cl(CH_2)_2Cl$ was stirred for 17 h at 15–20°, to give a 72% yield of crystalline allyl β-glycoside[4] 13; m.p. 108–109°, $[\alpha]_D$ +36.0°; δ_H ($CDCl_3$): 2.16 (s, Ac), 2.08 (s, Ac), and 1.90 (s, Ac).



[†] All compounds having $[\alpha]_D$ recorded gave satisfactory data in elemental analyses.
[††] Yields are not optimized.





(c) An oxazoline. — Oxazoline **14** was also readily transformed into a β-glycoside by using $Me_3SiOSO_2CF_3$ under mild conditions. A mixture of oxazoline **14** and **8** was treated with $Me_3SiOSO_2CF_3$ in the presence of 1,1,3,3-tetramethylurea at 60°, to give the β-glycoside **15** in 70% yield; m.p. 81–82°, $[\alpha]_D$ −11.4° ($CHCl_3$); δ_H ($CDCl_3$): 5.74 (d, J 8 Hz, NH), 4.62 (d, J 8 Hz, H-1), 2.08 (s, Ac), 2.00 (s, 2 Ac), and 1.92 (s, Ac). Similar treatment of a mixture of **14** and diol **16** at 50–60° afforded a 78% yield of disaccharide **17**; m.p. 174–175°, $[\alpha]_D$ +7.7° ($CHCl_3$); R_F 0.45 (20:80:1 toluene—EtOAc—MeOH); δ_H ($CDCl_3$): 5.32 (t, J 9 Hz, H-3′), 5.02 (t, J 9 Hz, H-4′), 3.32 (s, OMe), 2.01 (s, Ac), 2.00 (s, 2 Ac), and 1.80 (s, Ac); δ_C ($CDCl_3$): 100.8 (C-1′; $^1J_{CH}$ 162.4 Hz), 97.9 (C-1, $^1J_{CH}$ 167.2 Hz), and 68.7 (C-6).

In conclusion, employing $Me_3SiOSO_2CF_3$ as an efficient Lewis acid in the presence of acid captors, such as powdered molecular sieve 4 A, 1,1,3,3-tetramethylurea, and tributylstannyl derivatives of glycosyl acceptors, a practical synthetic approach to 1,2-*trans*-glycosides, from the viewpoint of large-scale preparation, has been developed.

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