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Scandium(III) Perchlorate ($Sc(ClO_4)_3$). A Novel Catalyst in the α-C- and N-Glycosylation Reactions

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Abstract: *In the presence of a catalytic amount of scandium(III) perchlorate ($Sc(ClO_4)_3$), 1-O-acetyl-2,3,5-tri-O-benzyl-β-D-ribofuranose reacted with trimethylsilylated nucleophiles to afford the corresponding α-D-ribofuranosides in high yields with good selectivities. The catalyst could be recovered after the reactions were completed and could be reused.*

Development of stereoselective glycosylation reactions is one of the most important tasks in carbohydrate chemistry.[1] In this report, we disclose a novel catalyst, scandium(III) perchlorate ($Sc(ClO_4)_3$), which is effective in α-selective C- and N-glycosylation reactions.[2]

$Sc(ClO_4)_3$ was prepared from Sc_2O_3 and a 70% aqueous perchloric acid.[3] In the presence of 3-5 mol% $Sc(ClO_4)_3$, 1-O-acetyl-2,3,5-tri-O-benzyl-β-D-ribofuranose (**1**) reacted with 1-phenyl-1-trimethylsiloxyethene in Et_2O at room temperature to afford the corresponding α-C-ribofuranoside in a high yield. The silyl enol ether of pinacoline and allyltrimethylsilane also worked well. When **1** was treated with trimethylsilyl cyanide under the same reaction conditions, the corresponding α-glycosyl cyanide was obtained in a high yield with a good stereoselectivity. Trimethylsilyl azide was also an excellent nucleophile in this reaction, and α-ribofuranosyl azide was obtained in a high yield. The results are summarized in Table 1. It is noted that the catalyst was recovered after the reactions were completed and could be reused (see the following experimental section).

A typical experimental procedure is described for the reaction of **1** with trimethylsilyl azide; to $Sc(ClO_4)_3$ (3-5 mol%) in Et_2O (3.0 ml) was added **1** (1.2 mmol) in Et_2O (9.0 ml) and trimethylsilyl azide (1.8 mmol) in Et_2O (6.0 ml) successively at 0 °C. The mixture was stirred for 4.5 h at this temperature. Water was then added and the aqueous and organic layers were separated. The aqueous layer was extracted with dichloromethane and the combined organic layer was dried and concentrated. The crude N-glycoside thus obtained was chromatographed on silica gel to give 2,3,5-tri-O-benzyl-D-ribofuranosyl azide (96 %, α/β = 85/15). $Sc(ClO_4)_3$ could be almost quantitatively recovered from the aqueous layer and could be reused (2nd use; 97%, α/β = 83/17).

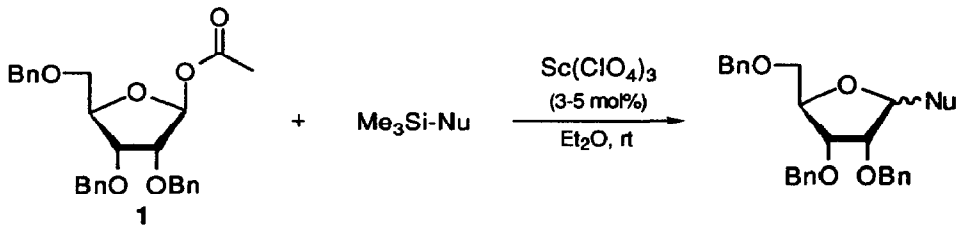
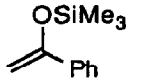
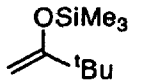
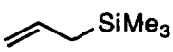


Table 1. Scandium(III) Perchlorate Catalyzed α-C- and N-Glycosylation Reactions

Me_3SiNu (eq.)	Yield / %	α / β
 (1.5)	84	94/ 6
 (2.0)	94	98/ 2
 (2.0)	80	>99/ 1
Me_3SiCN (1.5)	89	81/19
Me_3SiN_3 (1.5)	96	85/15 [a,b]

a) 2nd use; 97% yield, α/β = 83/17 (see the experimental section).
b) The reaction was carried out at 0 °C.

Thus, $Sc(ClO_4)_3$ was shown to be an excellent catalyst in α-selective C- and N-glycosylation reactions. It is noteworthy that the reactions proceed in high yields with high selectivities under extremely mild conditions by simple procedures, and that the catalyst can be easily recovered after the reaction is completed and can be reused.

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References and Notes

1) Harmange, J-C.; Figadere, B. *Tetrahedron Asym.* **1993**, *4*, 1711, and references cited therein.
2) Recently, we found that scandium trifluoromethanesulfonate ($Sc(OTf)_3$) was an excellent catalyst in aldol, Michael, and Diels-Alder reactions. Kobayashi, S.; Hachiya, I.; Araki, M.; Ishitani, H. *Tetrahedron Lett.* **1993**, *34*, 3755; Kobayashi, S.; Hachiya, I.; Araki, M.; Ishitani, H. *Synlett* **1993**, 472. In the present glycosylation reactions, $Sc(ClO_4)_3$ is superior to $Sc(OTf)_3$.
3) Scandium oxide (18 mmol) was mixed with 70% $HClO_4$ (6.17 ml) and water (1.85 ml), and the suspension was heated at 100 °C for 2 h. After unreacted oxide was removed by filtration, the filtrate was concentrated under reduced pressure and was dried *in vacuo* (100 °C/0.5 mmHg for 40 h). See, Petru, F.; Kutek, F. Z. *Chem.* **1963**, *3*, 473; *Chem. Abstr.* **1964**, *60*, 7660h.

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