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A Direct Single Ring Cleavage of Isosorbide and Isomannide with Iodotrimethylsilane

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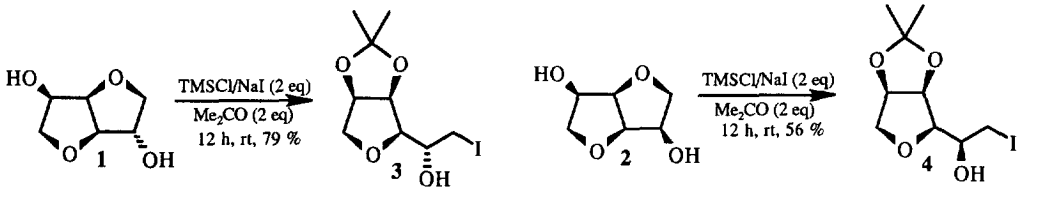
Abstract : *Treatment of isosorbide and isomannide with iodotrimethylsilane in acetonitrile in the presence of acetone induces the cleavage of only one of the two rings and provides chiral trisubstituted tetrahydrofurans.* © 1997 Published by Elsevier Science Ltd. All rights reserved.

Isosorbide and isomannide are important by-products of the starch industry, obtained by dehydration of D-sorbitol and D-mannitol respectively. They are available in large quantities and, because of this, they constitute attractive chiral synthons of low cost. Isosorbide, as isomannide, possesses a two fused tetrahydrofuran ring structure, but, contrary to isomannide, isosorbide has two sterically and electronically different hydroxy groups. This difference is commonly used to perform the selective protection or transformation of one of the two hydroxy groups[1]. Only two examples deal with the selective ring opening of these derivatives. The alkyllithium promoted eliminative ring fission of halides derived from isomannide and isosorbide, leading to functionalized 2,5-dihydrofurans[2], has been reported. Recently, a trisubstituted tetrahydrofuran was obtained by basic treatment of the *endo* carbamate of the isosorbide *exo* methylether[3].

In this communication, we report the first synthesis of optically active functionalized tetrahydrofurans by means of a selective ring cleavage of isosorbide and isomannide, *without any prior transformation* .

Scheme 1



We have previously described the ring opening of tetrahydrofurfurylic alcohols[4] and 2-alkyl-3-hydroxytetrahydrofurans[5] with iodotrimethylsilane in acetone, leading to iododiols protected as their acetonide derivatives. When isosorbide **1** was treated with two equivalents of iodotrimethylsilane (obtained *in situ* from chlorotrimethylsilane and sodium iodide) in acetone, the corresponding iodoacetonide **3** was obtained in 58% isolated yield. On the other hand, when the same reaction was performed with isomannide **2**, a mixture of several unidentified products was obtained. Fortunately, we found that better yields can be

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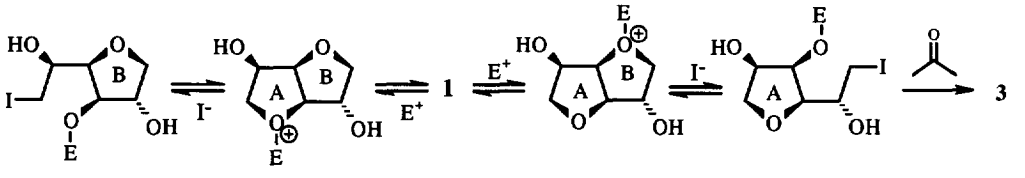
obtained when acetonitrile, containing *only two equivalents of acetone* ,was used as the solvent instead of pure acetone. Under these conditions, the iodoacetonide **4** was isolated in 56% yield from isomannide **2** and the yield of derivative **3** resulting from isosorbide **1** was improved from 58% to 79% [6] (scheme 1).

Obviously, the reaction with isomannide **2** leads to a single compound whichever ring was opened. It is noteworthy that the ring opening of isosorbide **1** was regioselective although, in this case, the cleavage of one or the other of the two cycles could provide two different stereoisomers. This regioselectivity is probably due to acetonide formation, which requires the two oxygen atoms to be *cis*. The mechanism we suggest to explain the regioselectivity is illustrated in scheme 2 for isosorbide. The cleavage of the C-O bond proceeds via the nucleophilic attack of the carbon by an iodide ion after complexation of the oxygen atom with H^+ or "Me_3Si^+". Although one of the two rings A and B could be opened, only the ring B cleavage could give rise to an acetonide. Assuming the reversibility of the reaction, we think that the acetonide formation allows displacement of the equilibria towards the product **3**.

Scheme 2



E = H or Me_3Si

To conclude, we have shown that it is possible to form optically active trisubstituted tetrahydrofurans in a one step reaction, starting from commercial compounds. These tetrahydrofurans differ only in the configuration of the carbon α to the cycle and could be used as synthetic intermediates .

References and notes

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6. Typical procedure : At room temperature, under nitrogen, a solution of freshly distilled chlorotrimethylsilane (0.9 mL, 6.9 mmol) in dry acetonitrile (2.5 mL) was added dropwise to a mixture of sodium iodide (1.03 g, 6.9 mmol) and isosorbide **1** or isomannide **2** (0.5 g, 3.42 mmol) dissolved in dry acetonitrile (11 mL). Then, dry acetone (0.5 mL, 6.9 mmol) was added. After stirring, for 12 hours, K_2CO_3 (0.2 g) and methanol (10 mL) were successively added to the reaction mixture ; then the residue from evaporation of the solvent was purified by silica gel column chromatography (Petroleum ether/ Et_2O : 80/20).
   - **Compound 3** : (0.85 g , 79%) : mp 72° C. $[\alpha]^{22}_D$ -66.6 (c = 1.0, CH_2Cl_2). IR (CH_2Cl_2) : 3600; 3500; 2940; 2860; 1430; 1380; 1280; 1220; 1170; 1100; 1070; 1040; 980; 930; 900; 860; 840 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz) δ (ppm) : 1.32 (s, 3H); 1.48 (s, 3H); 3.02 (d, 1H, J = 4.9 Hz, OH); 3.4-3.6 (m, 4H); 3.95 (dddd, 1H, J = 5.2, 5.2, 5.2, 4.9 Hz); 4.17 (d, 1H, J = 10.8 Hz); 4.72 (dd, 1H, J = 6.2, 3.6 Hz); 4.82 (dd, 1H, J = 6.2, 3.6 Hz). ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) : 9.4 (t); 24.5 (q); 25.9 (q); 69.1 (d); 72.5 (t); 80.0 (d); 81.2 (d); 84.7 (d); 112.4 (s). MS m/z (%) : 299 (M^+-15, 17); 187 (M^+-127, 3); 171 (15); 144 (30); 127 (3); 86 (26); 69 (59); 59 (51); 57 (51); 55 (23); 44 (24); 43 (100).
   - **Compound 4** : oil (0.60 g, 56%) : $[\alpha]^{22}_D$ -41,4 (c = 1.0, CH_2Cl_2). IR (neat) : 3440, 2940, 1800, 1540, 1500, 1470, 1390, 1360, 1300, 1260, 1200, 1160, 1140, 1080, 1060, 1000, 990, 940, 900, 840. cm^{-1}.^1H NMR ($CDCl_3$, 200 MHz) δ (ppm) : 1.35 (s, 3H); 1.49 (s, 3H); 2.73 (d, 1H, J = 5.6 Hz, OH); 3.3-3.6 (m, 4H); 3.7-3.9 (m, 1H); 4.04 (d, 1H, J = 10.8 Hz); 4.79 (s, 2H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) : 12.7; 24.7; 26.0; 68.8; 72.9; 80.4; 81.0; 84.0; 112.5. MS m/z (%) : 315 (M^++1, 2); 299 (M^+-15, 34); 239 (6); 187 (M^+-127, 1); 171 (14); 145 (3); 144 (34); 143 (4); 126 (10); 111 (4); 86 (24); 85 (14); 83 (4); 71 (4); 70 (3); 69 (38); 68 (6); 59 (36); 58 (8); 57 (27); 56 (3); 55 (11); 53 (3); 45 (6); 44 (26); 43 (100).

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