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A FACILE SYNTHESIS OF 2,3,4,6-TETRA-O-BENZYL-D-GLUCOPYRANOSYLIDENE ACETALS USING TRIMETHYLSILYL TRIFLUOROMETHANESULFONATE CATALYST

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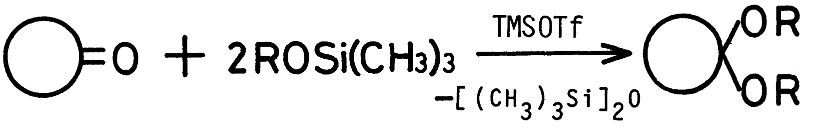
The application of acetalization of aldehydes and ketones by alkoxysilanes in the presence of trimethylsilyl trifluoromethanesulfonate catalyst to lactones and di-O-trimethylsilyl-α-diols gave readily the corresponding spiro cyclic ortho esters.

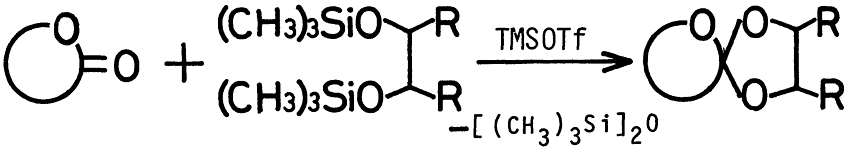
The antibiotics of orthosomycin family,1) i.e. everninomicins, flambamycin, curamycin, avilamycins, destomycins, hygromycin B, the antibiotics A-396-I and SS-56C etc., include a unique spiro cyclic ortho ester linkage of a glyconic lactone to an α-diol function of an aldose in their molecules. For the synthetic purpose of these antibiotics, it was shown that the reaction of 2,3,4,6-tetra-O-benzyl-D-glucono-1,5-lactone (1) with epoxides and direct dehydration of (1) with α-diols gave the corresponding glucopyranosylidene acetals of α-diols and monosaccharides.2) However, the application of these methods to α-diols composed of two secondary hydroxyl groups gave poor results, and therefore, was not suitable for the synthesis of the above natural products.

Recently, Noyori et al. reported that the reaction of carbonyl compounds and a stoichiometric amount of alkoxysilanes in dichloromethane in the presence of trimethylsilyl trifluoromethanesulfonate (TMSOTf) catalyst proceeded smoothly at temperatures as low as -78°C to give acetals in high yields (eqn. I).3) This report describes the application of the above method to lactones and di-O-trimethylsilyl-α-diols gave the corresponding spiro cyclic ortho esters (eqn. II).

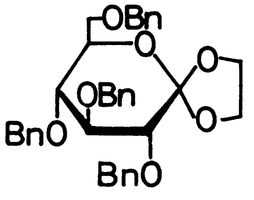
To a stirred dichloromethane solution (3 ml) of (1) (561 mg, 1.04 mmol) and di-O-trimethylsilylethanediol [prepared from 208 mg(3.35 mmol) of ethyleneglycol] was added TMSOTf(22 mg, 0.1 mmol) at -10°C under a nitrogen atmosphere. The mixture was stirred at room temperature for 2 h, quenched by addition of dry pyridine (0.2



—(I)



—(II)



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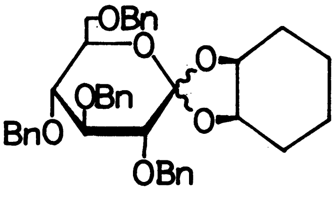
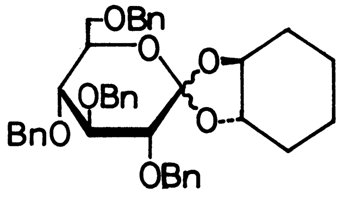
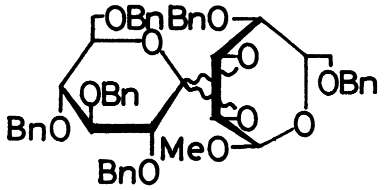


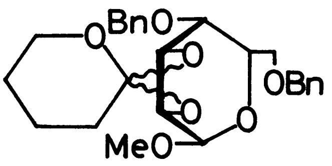
3a,b



4a,b



5a,b



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ml), poured into saturated sodium bicarbonate solution (10 ml), and extracted with ether. The usual work up of the extract gave 1,2-O-(2,3,4,6-tetra-O-benzyl-D-glucopyranosilidene)ethanediol (2)[2] in 91.2% (77%) yield. Similar reaction of (1) and trimethylsilylated cis-cyclohexanediol, and separation of the product on a flash column (hexane-ether 5:2) gave two isomers of the corresponding spiro cyclic ortho esters (3a and 3b)[2] in 30.4% (28%) and 59.3% (45%) yields, respectively. In a similar manner, two isomers from trans-cyclohexanediol (4a and 4b)[2] were obtained in 30.6% (21.9%) and 33.3% (21.0%) yields, respectively. Thus the new method gave the products in higher yields than that of the direct dehydration method shown in parenthesis.

Moreover, application of the new method to (1) and trimethylsilylated methyl 4,6-di-O-benzyl-α-D-mannopyranoside and separation of the products gave two isomers of 2,3-O-(2,3,4,6-tetra-O-benzylidene-D-glucopyranosylidene)-4,6-di-O-benzyl-α-D-mannopyranoside, 5a [mp 61-62°C; $[\alpha]_D$ +28.1°(c 1.06, $CHCl_3$); ortho ester ^{13}C, 119.0 ppm] and 5b [sirup, $[\alpha]_D$ +10.3°(c 0.2, $CHCl_3$); ortho ester ^{13}C, 120.4 ppm] in 44.8% and 26.6% yields, respectively. These compounds could not be obtained by the previous methods. Furthermore, reaction of the above mannose derivative and δ-valerolactone also gave one isomer of the corresponding ortho esters [6: mp 40-41.5°C; $[\alpha]_D$ +44.0°(c 0.35, $CHCl_3$); ortho ester ^{13}C, 118.5 ppm] in 40.2% yield.

In general, the acetalization of lactones reqiures a higher reaction temperature(over -30°C) than that of ketones. The catalyst can also be used as the silylation reagent, but, the use of much amount of the reagent causes the decomposition of the products. For example, reaction of (1) and methyl 4,6-O-benzyl-α-D-mannopyranoside in the presence of equimolar TMSOTf gave 5a and 5b in 28.5% yield in the ratio of 3:4. The yields shown above might be not the highest one, but, it is obvious that the present method is superior to the previous methods. All new compounds gave consistent NMR and IR characteristics and correct elemental analysis.

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