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Unexpected Outcome in the Reaction of Sugar Lactones with Iodotrimethylsilane

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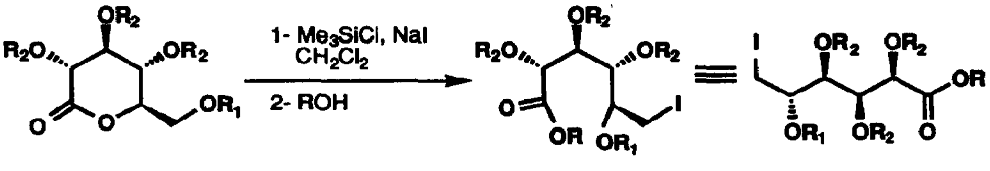
Abstract: The reaction of iodotrimethylsilane with sugar lactones protected by ester groups leads to primary iodides of the same configuration.

Iodotrimethylsilane can be used for the cleavage of various protective groups including ethers, esters, carbamates and ketals[1]. It has also proved useful for the synthesis of iodides[2] and the conversion of lactones to the corresponding ω-iodoesters.

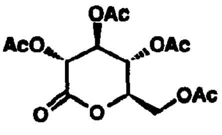
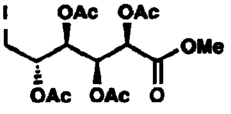
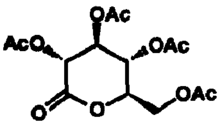
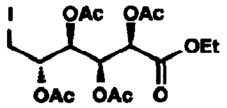
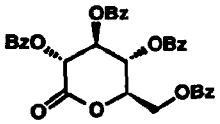
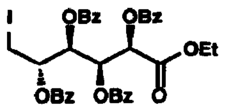
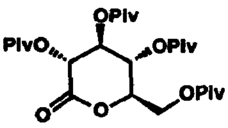
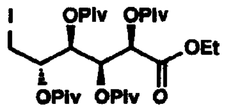
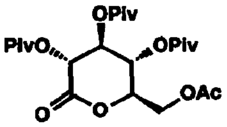
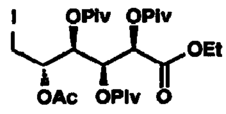
We found unexpectedly that the reaction of δ-gluconolactone tetraacetate **1** ($R_1 = R_2 =$ Ac) with excess iodotrimethylsilane (obtained *in situ* from chlorotrimethylsilane and sodium iodide) in CH_2Cl_2, followed by the addition of methanol or ethanol led to the formation of primary iodides **5** and **6**, respectively (Table 1). Treatment of **5** by sodium acetate in HMPA[3], afforded the known methyl 2,3,4,5,6-penta-*O*-acetyl-D-gluconate[4,5], as an evidence for the configuration of the reaction product[6]. Other esters derived from δ-gluconolactone (tetrabenzoate **2**, tetrapivaloate **3**, mixed ester **4**) afforded, in moderate to good yields, the corresponding iodides.



R = Me, Et
R_1 ; R_2 = Ac, Bz, Piv

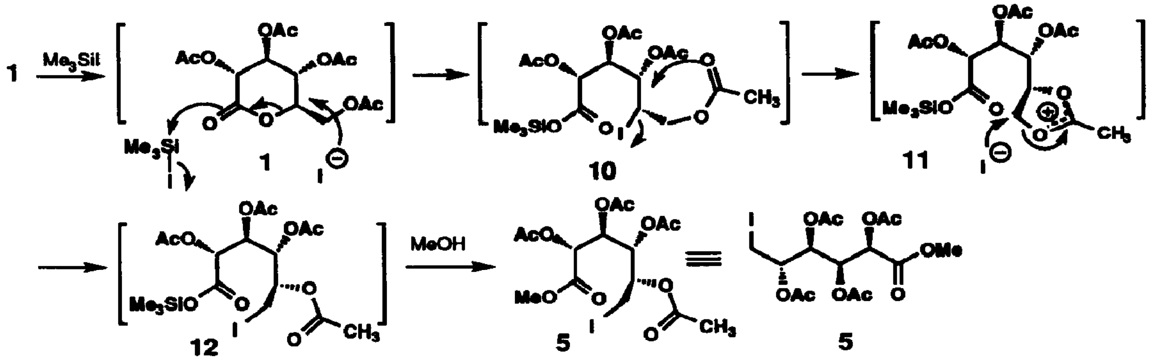
Scheme 1

Table 1 Formation of 6-iodo derivatives from sugar lactones

Lactone	Iodide	Yield %*
 1	 5	55
 1	 6	70
 2	 7	60
 3	 8	55
 4	 9	60

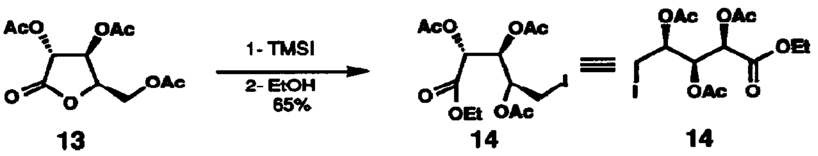
* isolated yields

The mechanism we suggest to explain the outcome of this reaction is described in scheme 2: the lactone **1** is opened by an iodide anion, with inversion of configuration at C-5. The formation of acetoxonium ion **11** then occurs from secondary iodide **10**, with a second inversion at C-5; **11** is opened regioselectively by an iodide ion, leading to primary iodide **12**, which is then quenched by alcohol addition. A similar mechanism has been proposed to explain the outcome of the reaction of iodotrimethylsilane with tetrahydrofurfurylic acetates[7,8].



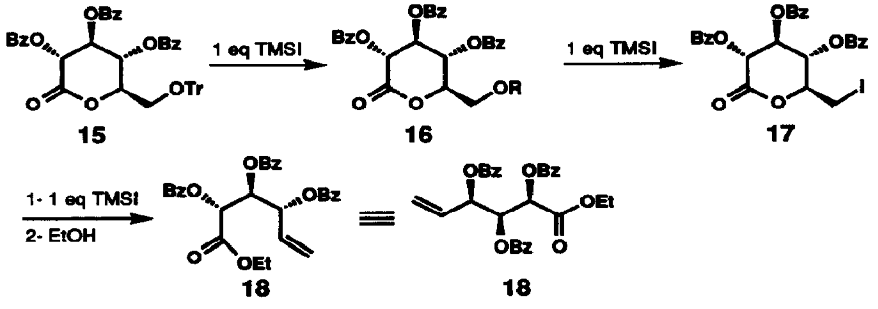
Scheme 2

Under the same conditions, furanolactone 13[9] derived from D-xylose was converted in 65% yield to primary iodide 14 (Scheme 3).



Scheme 3

Interestingly, δ-gluconolactone derivative 15, bearing a triphenylmethyl ether as protective group on the primary hydroxyl moiety, afforded the alkene derivative 18 in 60% yield by addition of an excess of TMSI[10] whereas the addition of 1 or 2 eq led to 16 (R= $SiMe_3$ or R= H after hydrolysis) or 17 in 75 and 70% yields respectively.



Scheme 4

In conclusion, we report a new application of iodotrimethylsilane for the preparation of primary iodides and alkene derivatives from sugar lactones.

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Typical procedure: To a 0°C stirred solution of lactone **1** (150mg, 0. 43 mmole) in 2ml of CH_2Cl_2, is added dropwise chlorotrimethylsilane (0.087ml, 0.63 mmole) and sodium iodide (97,4 mg, 0.63mmole). The mixture is stirred overnight at room temperature and then quenched with methanol or ethanol. After 30 min the reaction is diluted with CH_2Cl_2 and washed successively with brine (10ml) and water (2 x 10ml). The combined organic layers are dried over Na_2SO_4, filtrated and concentrated under vacuum. The crude product is purified by silicagel column chromatography (ethyl acetate / hexane 20 : 80).

References and Notes

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