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First example of the activation of polymethylhydrosiloxane with molecular iodine: a facile synthesis of 3,6-dihydropyran derivatives

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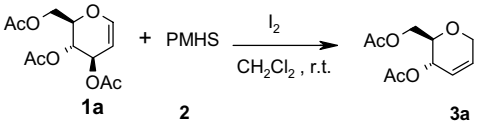
Abstract—Glycals react rapidly with polymethylhydrosiloxane (PMHS) in the presence of a catalytic amount of molecular iodine under mild conditions to afford the corresponding 3,6-dihydropyran derivatives in excellent yields. Et_3SiH/I_2 was also found to be effective for this conversion.

Naturally occurring carbohydrates have been extensively used as chiral pool starting materials in the synthesis of biologically active natural products.[1] The ready availability of a wide range of carbohydrates in nature, each having several chiral centres, coupled with their well-defined stereochemistry, make them useful intermediates in organic synthesis.[1a,2] Glycals are known to undergo acid-catalyzed allylic rearrangement with various nucleophiles to afford pseudoglycals or 2,3-unsaturated glycosides.[3,4] Pseudoglycals are versatile chiral building blocks for the synthesis of glycoconjugates and polyether antibiotics.[5] Typically, boron trifluoride, titanium tetrachloride and indium trichloride are employed as catalysts in the allylic transposition of glycals with triethylsilane.[6] However, many of these reagents are corrosive, moisture sensitive and are required in stoichiometric amounts. Therefore, the development of simple and inexpensive reagents, which are more efficient and provide convenient procedures with improved yields, are necessary. Owing to its unique catalytic properties, iodine has been extensively used for a plethora of organic transformations including glycosidation reactions.[7]

In continuation of our interest in the catalytic applications of molecular iodine for various organic transformations,[8–10] we describe herein the use of molecular iodine as the catalyst for the activation of polymethylhydrosiloxane (PMHS), which is an inexpensive and soluble hydrogen source, for the reduction of glucal acetates via Ferrier rearrangement. Initially, we attempted the allylic transposition of 3,4,6-tri-*O*-acetyl-D-glucal **1** with PMHS **2** using 2.5 mol % of molecular iodine as the catalyst. The reaction went to completion within 3.0 h and the product **3a** was obtained in 92% yield (Scheme 1).[11]

Encouraged by this result we turned our attention to various other glycals. D-Glucal derivatives 3,4,6-tri-*O*-methyl, 3,4,6-tri-*O*-allyl and 3,4,6-tri-*O*-benzyl-D-glucals were all converted into their corresponding 3,6-dihydro-2*H*-2-pyrans using this procedure (Table 1 entries b–d). Other glycals such as 3,4,6-tri-*O*-acetyl-D-galactal, 3,4-di-*O*-acetyl-L-rhamnal, 3,4-di-*O*-acetyl-D-xylal and 3,4-di-*O*-acetyl-D-arabinal also afforded the respective dihydropyran derivatives in high yields under similar conditions (Table 1 entries e–h). Hexa-*O*-acetyl-D-lactal, derived from the disaccharide, α-D-lactose, gave the corresponding 3,6-dihydro-2*H*-2-pyran derivative in 87% yield (Table 1, entry i, Scheme 2).

Similarly, hexa-*O*-acetyl-D-maltal derived from the disaccharide, α-D-maltose, also reacted smoothly with PMHS to afford the corresponding pyran derivative in



Scheme 1.

Keywords: Glycals; Molecular iodine; PMHS; Dihydropyrans.
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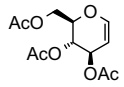
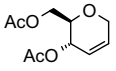
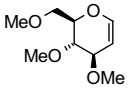
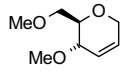
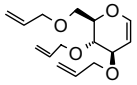
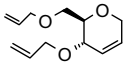
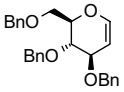
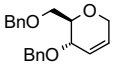
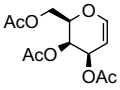
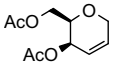
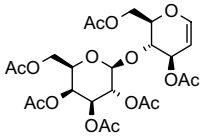
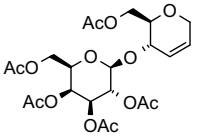
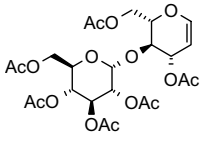
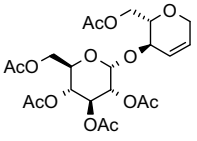
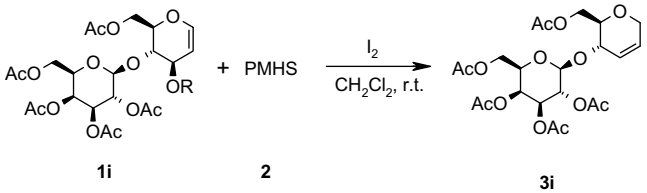
Table 1. PMHS/I_2-promoted synthesis of 3,6-dihydropyrans from glycals

Entry	Glycals **1**	Dihydropyrans **3**[a]	Time (h)	Yield (%)[b]
a			3.0	92 (71)[c]
b			3.5	86
c			3.0	82
d			4.0	90
e			3.5	87 (96)[c]
f			3.0	85 (72)[c]
g			2.5	86 (79)[c]
h			3.0	82
i			4.0	87
j			5.0	85

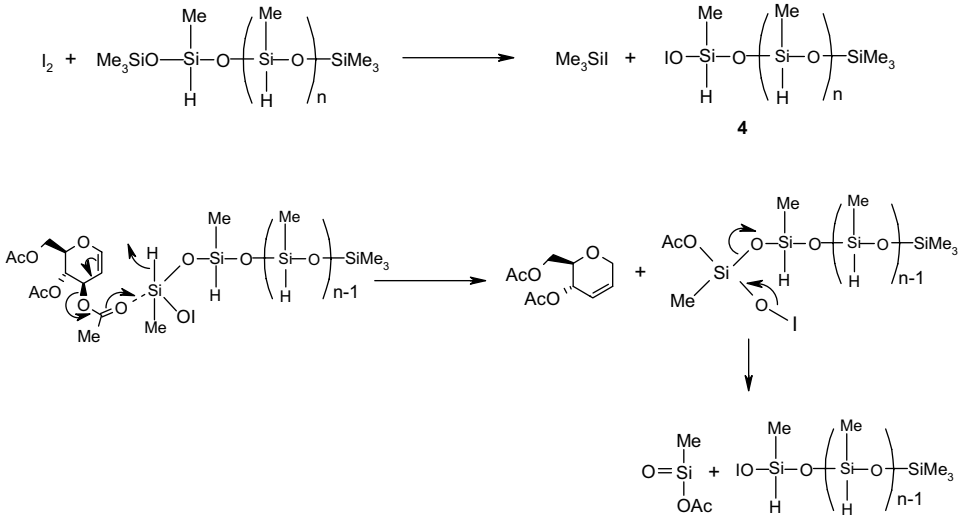
[a] All products were characterized by IR, ^1H, ^{13}C NMR and mass spectroscopy.
[b] Isolated and unoptimized yields.
[c] Yields reported in parentheses are literature yields for known compounds prepared via silane/$InCl_3$ reduction.[6b]

85% yield (Table 1 entry j). All products were characterized by ^1H, ^{13}C NMR and IR spectroscopy and also by comparison with authentic compounds.[4,6,11] There are several advantages in the use of iodine as the catalyst for this transformation, which include high yields of products, cleaner reaction profiles and easy availability of the catalyst at low cost. In addition, the reaction conditions are amenable for scaling up the reaction. Among the various catalysts such as scandium triflate, ytterbium triflate, cerium triflate, indium triflate and indium chloride employed for this conversion, molecular iodine was found to be the most effective catalyst in terms of yields and reaction rates. However, the combination of triethylsilane and 5 mol % of molecular iodine (Et_3SiH/I_2) was found to be equally effective for this conversion. It is noteworthy that the products were obtained in low to moderate yields (45–60%) along with deacetylated glycals when TMSI was employed as the catalyst for this reaction. The scope and generality of this process is illustrated with respect to various glycals and the results are presented in Table 1.



Scheme 2.

A feasible mechanism is depicted in Scheme 3. Iodine reacts initially with PMHS to produce trimethylsilyl iodide and the unstable reducing reagent **4**, which reduces the glucals.[12]



Scheme 3.

In summary, we have described the novel use of molecular iodine for the activation of polymethylhydrosiloxane and the reaction to produce 3,6-dihydropyrans from glycals under extremely mild conditions. This new reagent combination (PMHS/I_2) provides a simple and general method for the preparation of highly functionalized 3,6-dihydropyrans from glycals.

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11. *Experimental procedure*: Iodine (2.5 mol %) was added to a mixture of 3,4,6-tri-*O*-acetyl-D-glucal **1a** (2 mmol) and polymethylhydrosiloxane (6 mmol) in dichloromethane (10 mL) the reaction and stirred at room temperature for 3 h. After complete conversion, as indicated by TLC, the reaction mixture was diluted with water (10 mL) and extracted with dichloromethane (2 × 15 mL). The organic layers were dried over anhydrous Na_2SO_4 and purified by column chromatography on silica gel (Merck, 100–200 mesh, ethyl acetate–hexane, 1:9) to afford pure dihydropyran **3a**: liquid, $[\alpha]_D^{27}$ +84.2 (*c* 1.25, $CHCl_3$), IR (KBr): υ 3025, 2934, 1773, 1631, 1490, 1427, 1370, 1316, 1197, 1078, 1043, 922, 872, 769 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 2.09 (s, 6H), 3.60–3.68 (m, 1H), 4.10–4.25 (m, 4H), 5.24 (br d, J = 8.5 Hz, 1H), 5.75 (dd, J = 10.5, 1.5 Hz, 1H), 5.95 (dd, J = 10.5, 1.5 Hz, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 20.5, 21.1, 63.0, 64.5, 65.1, 73.6, 124.0, 129.3, 170.0, 170.6. EIMS: *m/z* (%): 214 (M^+, 12), 155 (100), 145 (13), 112 (56), 95 (92). Compound **3g**: liquid, $[\alpha]_D^{27}$ +67.0 (*c* 1.0, $CHCl_3$), IR (KBr): υ 2925, 2168, 1261, 1219, 1054, 850, 772 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 2.10 (s, 3H), 3.75–3.90 (m, 2H), 4.05–4.10 (m, 1H), 4.20–4.25 (m, 1H), 5.05–5.09 (m, 1H), 5.85–5.95 (dd, J = 10.3, 1.7 Hz, 1H), 6.10 (dd, J = 10.3, 1.7 Hz, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 21.0, 64.8, 64.9, 67.6, 122.4, 129.5, 170.6. EIMS: *m/z* (%): 143 (M^++1, 10), 116 (8), 101 (8), 93 (8), 83 (100), 73 (10), 57 (15), 43 (82). Compound **3j**: liquid, $[\alpha]_D^{27}$ +155.0 (*c* 0.5, $CHCl_3$), IR(KBr): υ 2996, 2355, 1765, 1633, 1439,

1376, 1195, 1078, 1015, 923, 863, 775 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 2.05–2.15 (m, 15H), 3.65–3.73 (m, 1H), 3.80–3.90 (m, 1H), 4.15–4.23 (m, 10H), 5.19–5.28 (m, 1H), 5.75 (dd, J = 10.1, 1.6 Hz, 1H), 5.90 (dd, J = 10.1, 1.6 Hz, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 20.4, 20.5, 20.6, 20.7, 20.8, 63.3, 63.9, 65.4, 66.2, 68.8, 70.3, 71.1, 76.2, 76.5, 88.5, 124.4, 129.2, 170.0, 170.4, 170.6, 170.7, 170.8. EIMS: m/z (%): 503 (M^++1, 10), 447 (10), 281 (20), 239 (35), 196 (30), 154 (50), 83 (60), 69 (70), 55 (100), 43 (90).

12. This mechanism is based on the observations that PMHS on treatment with iodine produced Me_3SiI and hydroiodic acid. However, Me_3SiI or HI or Me_3SiI–HI when treated with the glucal acetate in the presence of PMHS did not give the desired product.