Novel Reagent System for converting a Hydroxy-group into an Iodo-group in Carbohydrates with Inversion of Configuration

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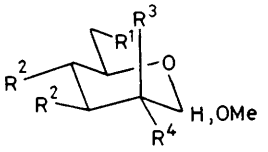
Summary Efficient conversions of primary and secondary hydroxy-groups into iodo-groups, with inversion, in carbohydrates are described using either triphenylphosphine, iodine, and imidazole or triphenylphosphine and 2,4,5-tri-iodoimidazole in toluene at elevated temperature.

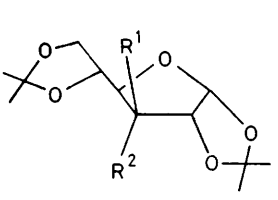
REPLACEMENT of a hydroxy-group by an iodo-group is an important transformation in carbohydrate chemistry.[1] Deoxyiodo sugars are of biological interest,[1] one example being their use in *X*-ray urology,[2] and they are useful intermediates in the synthesis of deoxy sugars.[3] Many reagents have been developed for this transformation; several of these are phosphorus-based, *e.g.* methyltriphenoxyphosphonium iodide and iodotriphenoxyphosphonium iodide.[4] The use of this type of reagent in carbohydrate synthesis has been explored.[5] Triphenylphosphine–*N*-iodosuccinimide[6] and triphenylphosphine–tetraiodomethane[7] are useful for the selective replacement of primary hydroxy-groups by iodo-groups in the presence of unprotected secondary hydroxy-groups. Synthesis of deoxyiodo sugars *via* displacement of trifluoromethanesulphonates by iodide ion has been described.[8]



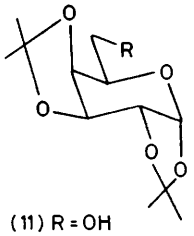
(**1**) $R^1 = R^2 = CH_2Ph$, $R^3 = OH$, $R^4 = H$, α-OMe
(**2**) $R^1 = R^2 = CH_2Ph$, $R^3 = H$, $R^4 = I$, α-OMe
(**3**) $R^1 = R^2 = CH_2Ph$, $R^3 = H$, $R^4 = OH$, β-OMe
(**4**) $R^1 = R^2 = CH_2Ph$, $R^3 = I$, $R^4 = H$, β-OMe
(**5**) $R^1 = R^2 = R^4 = OH$, $R^3 = H$, α-OMe
(**6**) $R^1 = I$, $R^2 = R^4 = OAc$, $R^3 = H$, α-OMe
(**7**) $R^1 = R^2 = R^3 = OH$, $R^4 = H$, α-OMe
(**8**) $R^1 = I$, $R^2 = R^3 = OAc$, $R^4 = H$, α-OMe

We report here two similar reagent systems capable of transforming primary as well as secondary hydroxy-groups into iodo groups: reagent (A), triphenylphosphine, iodine, and imidazole; reagent (B), triphenylphosphine and 2,4,5-tri-iodoimidazole. The reactions are carried out in toluene at elevated temperature, and proceed with inversion of configuration.

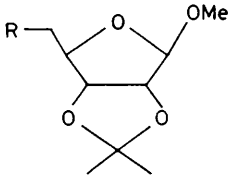
The reaction is heterogeneous. The carbohydrate component does not have to be soluble in toluene. Reaction conditions and results are shown in the Table. The products are worked up by procedures similar to those in the synthesis of dideoxyhexenopyranosides.[9] The yields of iodo compounds, including secondary iodides, are high. Reagent B is somewhat more efficient than reagent A in converting secondary hydroxy-groups into iodides. The



(**9**) $R^1 = OH$, $R^2 = H$
(**10**) $R^1 = H$, $R^2 = I$



(**11**) R = OH
(**12**) R = I



(**13**) R = OH
(**14**) R = I

TABLE. Conversion of hydroxy to iodo groups.[a]

Starting materials	Product	$Ph_3P:I_2$: imidazole: ROH (Reagent A)	Ph_3P: tri-iodo imidazole: ROH (Reagent B)	Time/h (A)	Time/h (B)	% Isolated yield (A)	% Isolated yield (B)
Methyl 3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (**1**)	Methyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-iodo-α-D-glucopyranoside (**2**)[b]	4:3:4:1	4:2:1	16	16	67	82
Methyl 3,4,6-tri-*O*-benzyl-β-D-glucopyranoside (**3**)	Methyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-iodo-β-D-mannopyranoside (**4**)[c]	3:2·5:4:1	3:1·5:1	6	3	75	87
Methyl α-D-glucopyranoside (**5**)	Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-iodo-α-D-glucopyranoside (**6**)[d,e]	1·5:1·4:3:1	1·5:0·75:1	2·5[f]	2·5	80	76
Methyl α-D-mannopyranoside (**7**)	Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-iodo-α-D-mannopyranoside (**8**)[d,g]	1·5:1·4:3:1	—	5[f]	—	70	—
1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranose (**9**)	1,2:5,6-Di-*O*-isopropylidene-3-deoxy-3-iodo-α-D-allofuranose (**10**)[h]	3:2:3:1	2·5:1·25:1	16	16	60	78
1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranose (**11**)	1,2:3,4-Di-*O*-isopropylidene-6-deoxy-6-iodo-α-D-galactopyranose (**12**)[i]	3:2:3:1	1·5:0·75:1	4	4	94	94
Methyl 2,3-*O*-isopropylidene-β-D-ribofuranoside (**13**)	Methyl 2,3-*O*-isopropylidene-5-deoxy-5-iodo-β-D-ribofuranoside (**14**)[j]	2·5:2:2·5:1	1·5:0·75:1	2·5	2·5	92	97

[a] In toluene at 120 °C (oil bath temp.). [b] M.p. 67—68 °C, $[\alpha]_D^{22} + 102°$ ($CHCl_3$). [c] $[\alpha]_D^{22} + 5°$ ($CHCl_3$). [d] After replacement of the 6-hydroxy-group by iodine, the product was acetylated with acetic anhydride and pyridine. [e] B. Helferich and E. Himmen, *Ber.*, 1928, **61**, 1825. [f] At 70 °C. [g] J. Lehman and A. A. Benson, *J. Amer. Chem. Soc.*, 1964, **76**, 4472. [h] Ref. 8. [i] O. Th. Schmidt, *Methods Carbohydrate Chem.*, 1962, **1**, 191. [j] H. M. Kissman and B. R. Baker, *J. Amer. Chem. Soc.*, 1967, **79**, 5534.

isopropylidene rearrangement previously demonstrated in the iodination of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose[5] does not take place. The easy introduction, in high yields, of iodine in the 2-position of hexopyranosides, by substitution of hydroxy by iodine is particularly noteworthy, since this has not been described previously.

Satisfactory elemental analyses as well as ^{13}C and ^{1}H n.m.r. spectra in agreement with postulated structures were obtained for the new compounds. Physical constants for known products were in agreement with literature values.

Mechanistic studies have not been conducted, but a plausible intermediate in both reaction systems is Ph_3P^+–OR I^- in which the sugar unit R would suffer nucleophilic displacement with inversion. This intermediate may be produced by several different mechanisms, probably involving phosphonium–imidazole intermediates. These need not be the same for the two reagent systems. Similar systems to those described here are useful for converting vicinal diols into the corresponding olefins.[9]

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