Phosphonium salts of diacetoxyiodine(I) anions, new reagents for the iodoacetoxylation of alkenes

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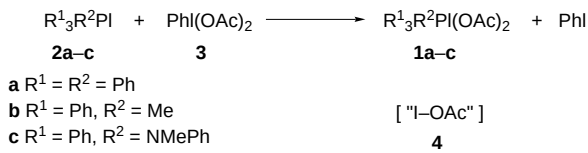
Novel phosphonium salts of diacetoxyiodine(I) anions 1 add to alkenes like tri-*O*-benzyl galactal 8 affording 1-acetoxy-2-iodopyranoses 12a,b which can efficiently be employed in the synthesis of 2-deoxyglycoside 14.

Stereo- and regio-selective 1,2-additions to alkenic double bonds are one of the most important transformations in organic synthesis.[1] Among this class of reactions, acetoxyiodinations are only rarely used. The α-iodo acetates which are created *via* this transformation can serve as starting materials for the preparation of allyl acetates or α-iodo alcohols with subsequent formation of oxiranes.[2] Current reagent systems in use for the acetoxyiodination of alkenes involve KIO_3 in glacial AcOH at 60 °C,[3] or various heavy metal salts[4] derived from silver(I), thallium(I), copper(II), mercury(II) or bismuth(III), all in the presence of I_2. AcOH and *N*-iodosuccinimide at 60 °C can also be used to form α-iodo acetates from the corresponding alkenes.[5] Due to the harsh reaction conditions employed and environmental problems involved with heavy metals, these methods have not found wide acceptance in reactions with multifunctional alkenes or in natural product synthesis.

Here we describe the preparation of a new class of reagents, the phosphonium salts of diacetoxyiodine(I) **1**,[6] which can be regarded as an acetyl hypoiodite **4** equivalent. Compound **4** has never been isolated, but has been postulated as an intermediate in the Hunsdiecker and Simonini reactions[7] and in the thermal decomposition of diacyliodobenzenes.[8] As is demonstrated, diacetoxyiodine(I) species **1** are ideally suited for promoting acetoxyiodination of alkenes under very mild conditions. Scheme 1 shows that these reagents are conveniently prepared from the corresponding phosphonium iodides **2a** and **2b** and diacetoxyiodobenzene **3** ($CHCl_3$, room temp., 2 h). After addition of Et_2O, the tetraphenylphosphonium salt **1a** precipitates as a light brown amorphous material [mp 145 °C (decomp.)], whereas the methyltriphenylphosphonium salt **1b** separates from the organic layer as a dark brown oil.†

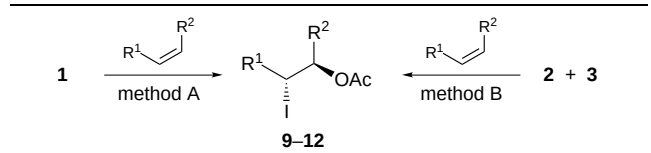
Diacyliodine(I) compounds like **1a** promote acetoxyiodination of alkenes such as cyclohexene **5** or indene **6** in a highly *anti* selective manner (Table 1). α-Iodo acetates **9**[9] and **10** are isolated in good yield. Regiocontrol is determined by the relative stability of the two possible intermediate cations. Acetoxyiodination may further be simplified by *in situ* generation of **1** from **2**,‡ including formation of **1c** from Murahashi's reagent **2c**, in various solvents followed by addition of the alkene. Under these conditions carbohydrate derived enol ethers such as **7** and **8** quantitatively afford 1-acetoxy-2-iodopyranoses **11a**,**b** and **12a**,**b**, respectively, under very mild conditions. Usually, a preference for α-glycosyl acetates is observed. Due to the reduced solubility of

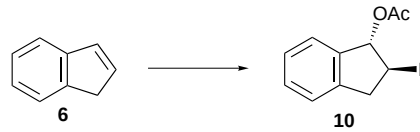
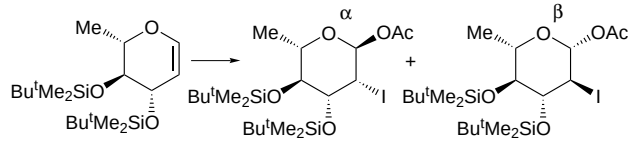
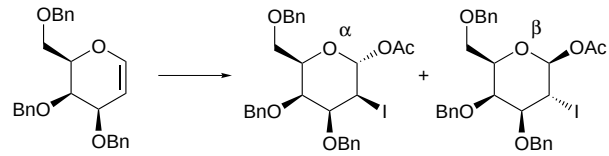


Scheme 1

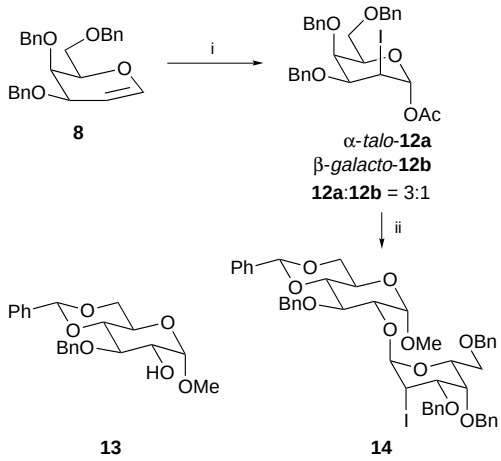
1a and **2a** in toluene, acetoxyiodination of **7** proceeds sluggishly. This obstacle may be circumvented by accellerating the reaction with catalytic $Me_3SiOSO_2CF_3$. Under these conditions the rare 2-deoxy β-anomer **11b** is formed in substantial amounts. The reaction exclusively furnishes 1,2-*trans* adducts, which can be rationalized by assuming a *trans*-diaxial addition of iodonium cation and acetoxy group to the electron-rich enol ether double bond.§

Table 1 Results of some acetoxyiodinations



Method[a]	1	Solvent	*t*/h	Ratio[b]	Yield (%)[c]
					
	5			9	
A	**1a**	CH_2Cl_2	36	—	61
					
	6			10	
A	**1a**	CH_2Cl_2	12	—	69
					
	7			11a[d]	11b[d]
A	**1a**	CH_2Cl_2	16	1.8 : 1	59
B	**1a**	MeCN	16	2.1 : 1	73
B[e]	**1a**	PhMe	72	1.1 : 1	69
B	**1b**	CH_2Cl_2	24	2.2 : 1	68
B	**1c**	CH_2Cl_2	24	2.7 : 1	72
					
	8			12a	12b
B	**1b**	MeCN	72	3.5 : 1	67
B	**1b**	PhMe	72	3.5 : 1	74[f]

[a] Method A: Preformed **1a**. Method B: **1a**–**c** generated *in situ*. All reactions carried out at room temp. [b] Determined from ^1H NMR spectra of crude product. [c] Yield of isolated product after column chromatography. [d] See footnote §. [e] Added $Me_3SiOSO_2CF_3$. [f] Crude product was contaminated with **8** (10%).



Scheme 2 *Reagents and conditions*: i, **2b**, **3**, CH_2Cl_2, 78%; ii, **12a**, **13**, $Me_3SiOSO_2CF_3$, CH_2Cl_2, −78 °C, 89%

These glycosyl acetates are ideal precursors for the construction of 2-deoxy glycosides, which occur as structural moieties of many bioactive natural products.[10] In glycosidations the 1-acetoxy group has glycosyl donor properties, while the 2-iodo substituent serves as a stereocontrol element in the glycosidation step which can be removed reductively at a later stage. In fact, acetoxyiodination of glycal **8** in CH_2Cl_2 yields glycosyl acetate **12** (α:β = 3.1:1, 78%) (Scheme 2). Separation by column chromatography gave pure α-*talo*-**12** which, after Lewis acid-promoted activation, was glycosidated in the presence of methyl glycoside **13** to afford α(1-2) disaccharide **14** as the only product in excellent yield.

In summary, phosphonium salts of diacetoxyiodine(I) represent a new class of reagents for the facile acetoxyiodination of alkenes. Starting from glycals, 1-acetoxy-2-iodo pyranoses are generated which can efficiently be employed in the synthesis of 2-deoxy glycosides.

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Footnotes and References

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† The ^{31}P NMR chemical shifts ($CDCl_3$) measured for **1a** and **1b** were identical with those for the starting iodides **2a** and **2b**. From this it can be concluded that compounds **1** are composed of an ion pair similar to phosphonium iodides **2**.

‡ *Experimental procedure*: A mixture of $PhI(OAc)_2$ **3** (0.966 g, 3.0 mmol) and Ph_3MePI **2b** (1.114 g, 3.0 mmol) in CH_2Cl_2 (15 ml) was stirred for 15 min at rom temp. until the solution turned dark red. Glycal **8** (416 mg, 1.0 mmol) was added and stirring was continued for 72 h. The solution was washed twice with aqueous $NaHSO_3$ and the aqueous phase was extracted four times with CH_2Cl_2. The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Column chromatography using light petroleum–EtOAc (4:1) gave two fractions (**12a**:**12b** = 3:1; 470 mg, 78%).

First fraction: β-**12b**; colourless crystals, mp 101 °C; $[\alpha]_D^{20}$ +52.2 (*c* 1.02, $CHCl_3$); δ_H (C_6D_6) 7.42–7.20 (m, 15 H, arom. H), 6.13 (d, 1 H, $J_{1,2}$ 9.6, 1-H), 4.84, 4.50, 4.37, 4.31, 4.26, 4.17 (6d, 6 H, *J* 11.2 and 12.0, CH_2Ph), 4.68 (dd, 1 H, $J_{2,1}$ 9.6, $J_{2,3}$ 11.2, 2-H), 3.78 (br t, 1 H, $J_{5,6} = J_{5,6'}$ = 8.0, 5-H), 3.71 (d, 1 H, $J_{4,3}$ 1.6, 4-H), 3.56 (m, 2 H, 6-H, 6′-H), 3.27 (dd, 1 H, $J_{3,2}$ 11.2, $J_{3,4}$ 1.6, 3-H), 2.10 (s, 3 H, OAc); δ_C ($CDCl_3$) 169.0, 138.0–136.9 and 128.5–127.7, 94.8 (C-1), 83.2, 74.6, 72.5 (C-3, C-4, C-5), 74.7, 73.5, 72.8 (OCH_2Ph), 67.6 (C-6), 30.5 (C-2), 20.8.

Second fraction: α-**12a**; colourless oil, $[\alpha]_D^{19}$ −7.6 (*c* 0.99, $CHCl_3$); δ_H ($CDCl_3$) 7.50–7.25 (m, 15 H, arom. H), 6.57 (d, 1 H, $J_{1,2}$ 2.4, 1-H), 5.08, 4.80, 4.58, 4.53, 4.50, 4.40 (6d, 6 H, *J* 12.0, CH_2Ph), 4.31 (ddd, 1 H, $J_{2,3}$ 4.4, $J_{2,1}$ 2.4, $J_{2,4}$ 0.8, 2-H), 4.19 (dt, 1 H, $J_{5,6} = J_{5,6'}$ = 6.0, $J_{5,4}$ 2.4, 5-H), 4.00 (dd, 1 H, $J_{4,3} = J_{4,5}$ = 2.4, 4-H), 3.70 (m, 2 H, 6-H, 6′-H), 3.49 (dd, 1 H, $J_{3,4}$ 2.4, $J_{3,2}$ 4.4, 3-H), 2.03 (s, 3 H, OAc); δ_C ($CDCl_3$) 168.5, 138.3–137.2 and 128.4–127.4, 95.2 (C-1), 73.5, 73.4, 70.9, 73.4, 73.3, 72.9 (C-3, C- 4, C-5), 68.4 (C-6), 22.4 (C-2), 20.9.

§ The ^1H NMR spectra of the crude products revealed traces of the α-*gluco* isomer, in particular when the reaction was run in toluene for a prolonged time.

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