Regioselective Acylation of Methyl α-D-Glucopyranoside and Methyl α-D-Mannopyranoside by means of Bis(2-oxooxazolidin-3-yl)phosphinic Chloride (BOP-Cl)

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A new synthetic procedure is presented which allows the regioselective acylation of methyl α-D-glucopyranoside and methyl α-D-mannopyranoside at the primary hydroxy group by means of bis(2-oxooxazolidin-3-yl)phosphinic chloride (BOP-Cl) and aromatic or aliphatic carboxylic acids. 2,6-*O*- and 3,6-*O*-diacylated derivatives have been obtained as side-products from gluco- and manno-pyranosides, respectively. Both yields and regioselectivity are comparable to those obtained in the lipase-catalysed derivatizations.

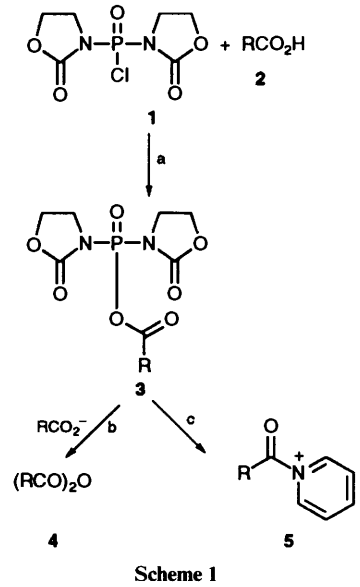
The selective derivatization of only one out of multiple hydroxy functions of similar reactivity in carbohydrate molecules is a challenging problem in organic synthesis. A good degree of regioselectivity has been achieved in the protection of the 6-OH group of methyl glucopyranosides with the acid-labile trityl group.[1] The functionalization of unprotected sugars with base-labile groups, such as benzoyl, *via* the classic acylation procedure with acyl chloride in pyridine, affords mixtures of polysubstituted derivatives.[2] Selective protection of gluco-pyranosides at the primary hydroxy group with fatty acid chains has been recently achieved by means of *N*-acyl-thiazolidine-2-thiones. The reported isolated yields (60–88%) refer, however, to the acylating agent, the sugar substrate being used in a three-fold molar excess.[3]

The problems encountered in the chemical modification of sugar molecules has, therefore, favoured the exploitation of enzyme-catalysed reactions which have shown a high degree of regioselectivity in the transesterification process between suitably activated esters and polyhydroxylated substrates.[4–8] Glucose and mannose, in the presence of a three-fold molar excess of trichloroethyl carboxylates and porcine pancreatic lipase, afforded acylated derivatives in 38–62% yield.[4] In similar experiments ethyl D-glucopyranoside was converted into 6-*O*-acylated derivatives in 44–79% isolated yield after reaction, for several days, in melted fatty acids in the presence of immobilized lipase.[8]

There is still a need, therefore, in carbohydrate chemistry for very simple chemical methods for the selective functionalization of pyranosides. Bis(2-oxooxazolidin-3-yl)phosphinic chloride (BOP-Cl, **1**, Scheme 1),[9] widely employed as a condensing agent in organic synthesis,[10–15] has shown a high degree of regioselectivity in the functionalization of deoxyribonucleosides with aroyl groups.[15] The capability of this condensing agent was, therefore, exploited in the acylation of methyl α-D-glucopyranoside (**6**, Scheme 2) and methyl α-D-mannopyranoside (**9**, Scheme 3).

Results and Discussion

The solubility properties of carbohydrates have always favoured the use of pyridine as solvent either in their chemical or enzymatic transformation into acyl derivatives. In the same solvent, BOP-Cl **1** enabled the regioselective formation of 5'-acyl derivatives of deoxyribonucleosides from aromatic carboxylic acids.[15] It has been already observed[16] that the formation of the ester bond with this synthetic scheme occurs preferentially through the mixed anhydride **3**, a transient intermediate obtained by interaction of the condensing agent with the carboxylate nucleophile (path a, Scheme 1). Nevertheless, the formation of reactive symmetrical carboxylic anhydrides **4** (path b, Scheme 1) and of acylpyridinium

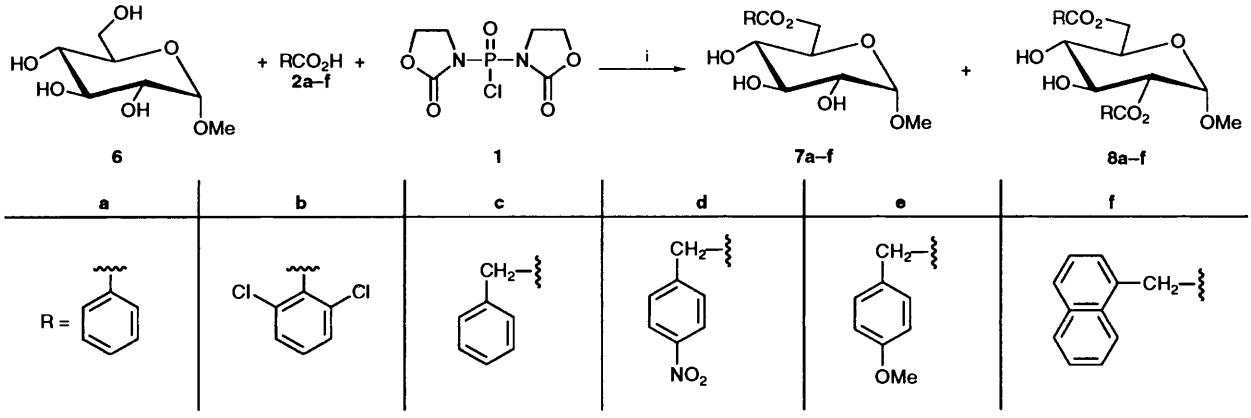


Scheme 1

derivatives **5** (path c, Scheme 1) cannot be, *a priori*, excluded. Stable compounds of type structure **5** have, in fact, been isolated in the reaction of compound **1** with some aliphatic amines.[17]

When methyl α-D-glucopyranoside **6** is allowed to react with carboxylic acids **2a–f** in the presence of BOP-Cl **1**, the two main isolated products correspond to the 6-*O*-acyl (**7a–f**) and 2,6-di-*O*-acyl derivatives (**8a–f**) reported in Scheme 2.

Short-column flash chromatography allowed the isolation of the monosubstituted (**7a–f**) and disubstituted (**8a–f**) compounds in 47–65 and 10–22% isolated yield, respectively (Table). TLC analysis of the crude material showed, also, the presence of traces of other derivatives, which have not been isolated and characterized. The pyranose substrates undergo, therefore, a preferred acylation at the primary hydroxy moiety, as clearly shown by the observed regioselectivity, which was in the range 73–86% (Table).



Scheme 2 *Reagents and conditions:* i, pyridine, room temp., 1.5–3 h.

Table 1 Acylation of methyl α-D-glucopyranoside **6** with RCOOH and BOP-Cl

	Isolated yields (%)			
RCO_2H	**7**	**8**	Regioselectivity (%)	Reaction times (*t*/h)
2a	58	16	78	2.5
2b	65	12	84	2.0
2c	50	15	77	2.5
2d	60	10	86	1.5
2e	47	16	75	3.0
2f	59	22	73	2.5

The data reported in the Table show that higher yields and better regioselectivity are obtained when a more electrophilic carboxy group is used (*cf.* **2a** with **2b** and **2c** with **2d** and **2e**, Table). Moreover, the shorter the reaction times the higher are both yields and regioselectivities. TLC monitoring of the reaction, in all the reported cases, shows that the 6-*O*-substituted derivatives **7a–f** are those initially formed, followed by the diacylated compounds **8a–f**. The relative yields of compounds **7** and **8** suggest that, apart from the preferential functionalization of the primary hydroxy group, a high degree of regioselectivity is also in operation in the derivatization of the secondary hydroxy moieties. In fact, the 2,6-*O*-diacylated compounds were the only side-products formed in substantial amounts. These data allow us to rule out the presence, in the reaction medium, of intermediates **5** (Scheme 1). When compound **6** was treated with benzoyl chloride in pyridine, under experimental conditions which should favour the formation of 1-acylpyridine **5**, a mixture of polysubstituted glycopyranosides was obtained.[2] It is, therefore, reasonable to assume that the mixed anhydride **3**, isolated in some cases,[16] is the active acylating agent. The preferred derivatization of the primary hydroxy group can be accounted for by considering the steric hindrance experienced by the acylating agent **3** when approaching the reaction site, in agreement with previous observations.[15] The data reported in the Table, however, seem to indicate that with less reactive intermediates **3**, *i.e.* that formed with *p*-methoxyphenylacetate, some symmetrical anhydride intermediates **4** (Scheme 1) might be formed, whose further reaction with the pyranoside causes a lower degree of regioselectivity.

The structure of the compounds **7a–f** and **8a–f** has been confirmed by ^1H NMR and fast-atom-bombardment mass spectrometry (FABMS). In particular, the monoacylated glucopyranosides **7a–f** showed a downfield shift for the 6-H_2 protons of 0.7 and 1.0 ppm, relative to compound **6**, for the aromatic (**7a, b**) and aliphatic (**7c–f**) substrates, respectively. Moreover the acylation of the primary hydroxy function enabled us to differentiate between the two protons at position 6 of the sugar (see Experimental section) as a consequence of the different population of *trans/gauche* conformers along the C(5)–C(6) bond, due to the chirality of the C-5 carbon of defined configuration.

FAB spectral data were in agreement with the structure of products **7a–f**. In the case of the *p*-nitrophenylacetyl derivative **7d** better analytical data were obtained in the negative ionization mode. Under this condition, both the radical $(M)^-$ and the quasimolecular anion $(M - H)^-$ were formed, thus allowing full characterization of the analyte. The electron-capture process leading to the radical molecular anion has been widely documented for species possessing low lying LUMOs which can capture low-energy electrons formed in the sputtering process.[18]

Further evidence for the structure of compounds **7** was obtained by ^{13}C NMR experiments. The spectra of methyl α-D-glucopyranoside **6** (Fig. 1A) and of the 6-*O*-(2,6-dichlorobenzoyl) derivative **7b** (Fig. 1B) provide clear-cut evidence of the derivatization of the primary carbon of the sugar whose ^{13}C resonance signal showed an upfield shift of 4.69 ppm. The ^{13}C resonances were assigned on the basis of chemical shift theory and through a comparison of the broad-band decoupled and proton-coupled *J* modulation sequences enabling the differentiation of methyl, methylene, methine and quaternary carbon atoms. ^1H NMR measurements and decoupling experiments

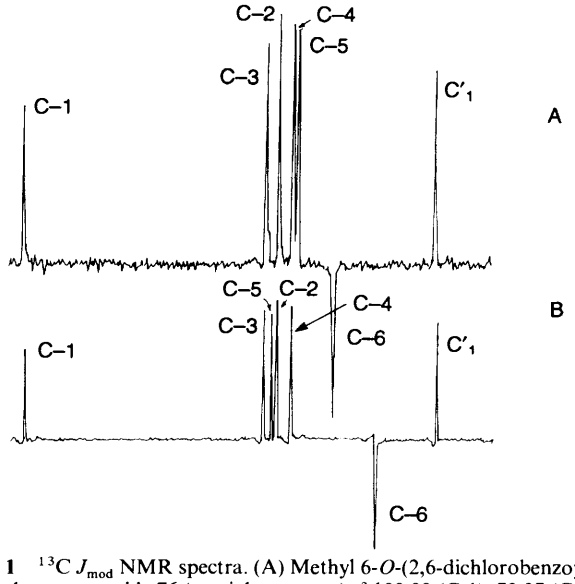
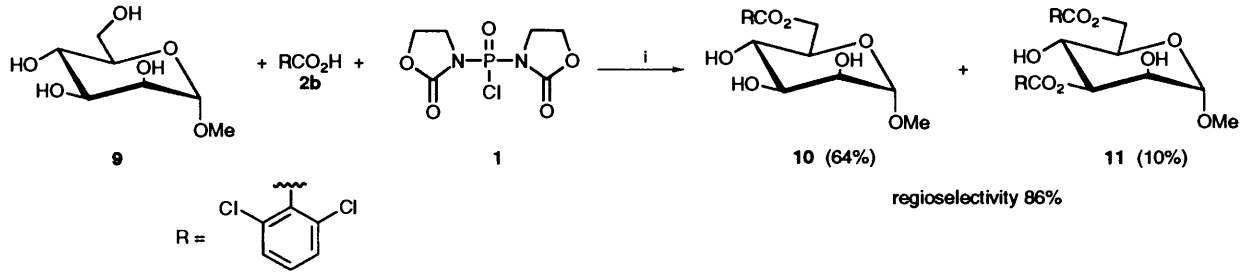


Fig. 1 ^{13}C J_{mod} NMR spectra. (A) Methyl 6-*O*-(2,6-dichlorobenzoyl)-α-D-glucopyranoside **7b** (partial spectrum): δ 100.00 (C-1), 73.37 (C-3), 71.96 (C-2), 70.43 (C-4), 69.90 (C-5), 65.84 (C-6), 54.81 (C'_1); (B) Methyl α-D-glucopyranoside **6**: δ 99.78 (C-1), 73.56 (C-3), 72.66 (C-5), 72.11 (C-2), 70.51 (C-4), 61.15 (C-6), 54.51 (C'_1).



Scheme 3 *Reagents and conditions:* i, pyridine, room temp., 2 h.

allowed, also, a complete characterization of the disubstituted derivatives **8a–f**. The C-2 proton is, in fact, easily correlated with the anomeric one, thus allowing the determination of the second acylation site. FAB positive and negative spectra gave the expected quasimolecular ions.

The results above shows a reactivity order for the hydroxy moieties of substrate **6** which is in agreement with earlier findings,[2] *i.e.*, besides the primary hydroxy function, the equatorial 2-OH is the more reactive secondary group among those present in the sugar molecule. This observation points out that in the acylation processes assisted by BOP-Cl, the intermediate **3** can selectively approach the reaction sites of the sugar substrate without altering the reactivity order observed with simple acylating agents. This observation is supported by the data obtained in the acylation, under the same experimental conditions, of methyl α-D-mannopyranoside **9**, where the equatorial 3-OH group is expected to be the more reactive among all the secondary hydroxy moieties.[2]

The reaction of compound **9** with 2,6-dichlorobenzoic acid **2b** afforded 64 and 10% isolated yields of the 6-*O*-(**10**) and 3,6-di-*O*-(**11**) acyl derivatives, respectively (Scheme 3). The structure of compounds **10** and **11** was ascertained by ^{1}H NMR and FABMS. In particular, the presence of the acyl group at C-3 of compound **11** was confirmed by extensive decoupling experiments. Irradiation of the doublet of doublets at δ 3.99 (assigned to the C-2 proton) induced a modification of the resonances at δ 5.18, corresponding to a C-3 proton, which appears as a doublet. The *J* value, 8.75 Hz, is consistent with a *trans*-diaxial relationship between the C-3 and the C-4 protons. Accordingly, the doublet at δ 4.61 corresponding to the anomeric proton becomes a singlet. The irradiation of the multiplet at δ 3.84 (attributed to the protons in position 4 and 5) simplifies the system at δ 5.18 again into a doublet; the *J* value of 3.1 Hz) is that expected for the coupling constant of the protons in the position 2 (equatorial) and 3 (axial). In the same experiment the simplification of the resonance system for the protons in position 6 allows the evaluation of geminal constant, *J* 11.80 Hz, to occur. The acylation of the mannopyranoside, therefore, showed again a high degree of regioselectivity either in the formation of monosubstituted derivatives or in the obtention of diacylated compounds.

Experimental

General Methods and Materials.—Bis(2-oxooxazolidin-3-yl)phosphinic chloride (BOP-Cl, **1**) was prepared as previously reported.[9] Pyridine was distilled from calcium hydride and stored under nitrogen. Silica gel-precoated plates were used for TLC, and Kieselgel 60 H without gypsum was used for short-column chromatography. NMR spectra were measured at 300 MHz with tetramethylsilane as internal standard and hexadeuteriodimethyl sulfoxide as solvent. *J* Values are given in Hz. FAB Mass spectra were obtained on a B-E type sector instrument, from a 2 mm^3 of glycerol solution of sample by using the M-SCAN steerable gun operated with a neutral xenon beam of 9.5 keV and a neutral current of 10 μA.

Acylation of Pyranosides **6** *and* **9** *with BOP-Cl* **1**: *General Procedure.*—A solution of the pyranoside **6** or **9** (2.5 mmol) and a carboxylic acids **2a–f** (3.0 mmol) in dry pyridine (40 cm^3) was evaporated twice to half volume to allow azeotropic removal of traces of water. BOP-Cl (**1**) (1.527 g, 6.25 mmol) was then added and the mixture was stirred at room temperature for 1–3 h (Table), until a nearly complete conversion of the pyranoside was achieved [TLC, chloroform–methanol (90:10, v/v)]. Saturated aq. sodium hydrogen carbonate (20 cm^3) was then added and the mixture was extracted with chloroform (4 × 20 cm^3). The organic layers, evaporated to dryness (the pyridine present was removed by azeotropic distillation with toluene), afforded oily residues, which were purified by short-column chromatography [chloroform–methanol (99.75:2.5, v/v)] to give the pyranosides **7a–f**, **8a–f**, **10** and **11**.

Methyl 6-O-*benzoyl*-α-D-*glucopyranoside* **7a**. (58%) Oil (Found: C, 56.5; H, 6.1. $C_{14}H_{18}O_7$ requires C, 56.37; H, 6.08%); δ_H 3.25 (2 H, m, 3- and 4-H), 3.32 (3 H, s, OMe), 3.45 (1 H, m, 2-H), 3.69 (1 H, m, 5-H), 4.35 (1 H, dd, *J* 6.0 and 9.4, 6-H), 4.58 (1 H, dd, *J* 2, 1-H), 4.71 (1 H, dd, *J* 3.2 and 9.4, 6-H), 5.25 (3 H, br, 2-, 3- and 4-OH), 7.50–7.96 (5 H, m, ArH); FABMS (+) *m/z* 299 (20%, M + H)$^+$, 267 (27) and 105 (100).

Methyl 2,6-*di*-O-*benzoyl*-α-D-*glucopyranoside* **8a**. (16%) M.p. 151–152 °C (Found: C, 62.65; H, 5.5. $C_{21}H_{22}O_8$ requires C, 62.68; H, 5.51%); δ_H 3.31 (3 H, s, OMe), 3.42 (1 H, m, 4-H), 3.83 2 H, m, 3- and 5-H), 4.42 (1 H, dd, *J* 5.5 and 9.6, 6-H), 4.63 (1 H, dd, *J* 1.7 and 9.6, 6-H), 4.77 (1 H, dd, *J* 2.8 and 9.2, 2-H), 4.82 (1 H, d, *J* 2.8, 1-H), 5.42 (1 H, br, 3-OH), 5.53 (1 H, br, 4-OH), 7.51–7.95 (6 H, m, ArH) and 7.98–8.09 (4 H, m, ArH); FABMS (+) *m/z* 403 (4%, M + H)$^+$, 371 (19) and 105 (100).

Methyl 6-O-(2,6-*dichlorobenzoyl*)-α-D-*glucopyranoside* **7b**. (65%) M.p. 85–87 °C (Found: C, 45.9; H, 4.4. $C_{14}H_{16}Cl_2O_7$ requires C, 45.80; H, 4.39%); δ_H 3.22 (2 H, m, 3- and 4-H), 3.30 (3 H, s, OMe), 3.47 (1 H, m, 2-H), 3.69 (1 H, m, 5-H), 4.38 (1 H, dd, *J* 6.23 and 10.91, 6-H), 4.55 (1 H, d, *J* 2.70, 1-H), 4.68 (1 H, dd, *J* 2.20 and 10.91, 6-H), 4.88 (1 H, d, *J* 6.26, 2-OH), 4.98 (1 H, d, *J* 5.32, 3-OH), 5.27 (1 H, d, *J* 5.63, 4-OH) and 7.66 (3 H, m, ArH); FABMS (+) *m/z* 367 (7%, M + H)$^+$, 335 (23) and 173 (100).

Methyl 2,6-*bis*-O-(2,6-*dichlorobenzoyl*)-α-D-*glucopyranoside* **8b**. (12%) M.p. 188–191 °C (Found: C, 46.5; H, 3.4. $C_{21}H_{18}Cl_4O_8$ requires C, 46.69; H, 3.36%); δ_H 3.29 (3 H, s, OMe), 3.37 (1 H, m, 4-H), 3.71 (2 H, m, 3- and 5-H), 4.38 (1 H, m, *J* 6.26 and 10.80, 6-H), 4.75 (2 H, m, 2- and 6-H), 4.79 (1 H, d, *J* 2.65, 1-H), 5.45 (1 H, d, *J* 6.41, 3-OH), 5.65 (1 H, d, *J* 6.0, 4-OH) and 7.61 (6 H, m, ArH); FABMS (+) *m/z* 539 (1%, M + H)$^+$, 507 (5) and 173 (100).

Methyl 6-O-(*phenylacetyl*)-α-D-*glucopyranoside* **7c**. (50%) M.p. 137–139 °C (Found: C, 57.6; H, 6.4. $C_{15}H_{20}O_7$ requires C, 57.69; H, 6.45%); δ_H 3.27 (2 H, m, 3- and 4-H), 3.31 (3 H, s, OMe), 3.50 (1 H, m, 2-H), 3.65 (1 H, m, 5-H), 3.71 (2 H, s, CH_2CO), 4.05

(1 H, dd, *J* 5.97 and 10.12, 6-H), 4.38 (1 H, dd, *J* 2.20 and 10.12, 6-H), 4.51 (1 H, d, *J* 2.60, 1-H), 4.71 (1 H, d, 2-OH), 4.79 (1 H, d, 3-OH), 5.08 (1 H, d, 4-OH) and 7.19–7.38 (5 H, m, ArH); FABMS (+) *m/z* 313 (19%, M + H)$^+$, 281 (34) and 91 (100).

Methyl 2,6-*bis*-O-(*phenylacetyl*)-α-D-*glucopyranoside* **8c**. (15%) M.p. 152–154 °C (Found: C, 64.15; H, 6.1. $C_{23}H_{26}O_8$ requires C, 64.18; H, 6.09%); δ_H 3.15 (3 H, s, OMe), 3.20 (1 H, m, 4-H), 3.55 (4 H, s, CH_2CO), 3.62 (2 H, m, 3- and 5-H), 4.09 (1 H, dd, *J* 5.40 and 8.70, 6-H), 4.38 (1 H, dd, *J* 1.60 and 8.70, 6-H), 4.52 (1 H, dd, *J* 2.20 and 8.60, 2-H), 4.70 (1 H, d, *J* 2.60, 1-H), 5.40 (2 H, br, 3- and 4-OH) and 7.15–7.48 (10 H), m, ArH); FABMS (−) *m/z* 429 (13%, M − H)$^-$, 193 (13) and 135 (100).

Methyl 6-O-(p-*nitrophenylacetyl*)-α-D-*glucopyranoside* **7d**. (60%) M.p. 125–127 °C (Found: C, 50.5; H, 5.4; N, 3.85. $C_{15}H_{19}NO_9$ requires C, 50.42, H, 5.36; N, 3.92%); δ_H 3.07 (1 H, m, 3-H), 3.20 (3 H, s, OMe), 3.30 (1 H, m, 4-H), 3.38 (1 H, m, 2-H), 3.54 (1 H, m, 5-H), 3.82 (2 H, s, CH_2CO), 4.09 (1 H, dd, *J* 5.20 and 9.10, 6-H), 4.38 (1 H, dd, *J* 2.0 and 9.10, 6-H), 4.53 (1 H, d, *J* 2.60, 1-H), 4.70 (1 H, br, 2-OH), 4.85 (1 H, br, 3-OH), 5.12 (1 H, br, 4-OH), 7.53–7.65 (2 H, m, Ar) and 8.18–8.27 (2 H, m, ArH); FABMS (−) *m/z* 357 (100%, M$^-$ − 356 (89, M − H$^-$) and 136 (67).

Methyl 2,6-*bis*-O-(p-*nitrophenylacetyl*)-α-D-*glucopyranoside* **8d**. (10%) M.p. 163–165 °C (Found: C, 53.1; H, 4.6; N, 5.2. $C_{23}H_{24}N_2O_{12}$ requires C, 53.08; 4.65; N, 5.38%); δ_H 3.19 (3 H, s, OMe), 3.29 (1 H, m, 4-H), 3.61 (2 H, m, 3- and 5-H), 3.93 (4 H, s, CH_2CO), 4.12 (1 H, dd, *J* 5.50 and 9.40, 6-H), 4.40 (1 H, dd, *J* 1.7 and 9.4, 6-H), 4.52 (1 H, dd, *J* 3.4 and 8.7, 2-H), 4.72 (1 H, d, *J* 2.7, 1-H), 5.28 (1 H, d, 3-OH), 5.42 (1 H, d, 4-OH), 7.48–7.65 (4 H, m, ArH) and 8.12–8.28 (4 H, m, ArH); FABMS (−) *m/z* 520 (65%, M$^-$), 519 (100, M − H) and 502 (57).

Methyl 6-O-(p-*methoxyphenylacetyl*)-α-D-*glucopyranoside* **7e**. (47%) Oil (Found: C, 56.25; H, 6.43. $C_{16}H_{22}O_8$ requires C, 56.13; H, 6.48%); δ_H 3.05 (1 H, m, 3-H), 3.18 (3 H, s, OMe), 3.32 (1 H, m, 4-H), 3.42 (1 H, m, 2-H), 3.51 (1 H, m, 5-H), 3.61 (2 H, s, CH_2CO), 3.72 (3 H, s, ArO*Me*), 4.02 (1 H, dd, *J* 5.7 and 8.5, 6-H), 4.34 (1 H, dd, *J* 1.8 and 8.5, 6-H), 4.51 (1 H, d, *J* 3.3, 1-H), 4.78 (1 H, br, 2-OH), 5.19 (2 H, br, 3- and 4-OH), 6.85–7.05 (2 H, m, ArH) and 7.12–7.25 (2 H, m, ArH); FABMS (+) *m/z* 343 (13%, M + H)$^+$, 311 (25) and 121 (100).

Methyl 2,6-*bis*-O-(p-*methoxyphenylacetyl*)-α-D-*glucopyranoside* **8e**. (16%) M.p. 101–103 °C (Found: C, 61.1; H, 6.2. $C_{25}H_{30}O_{10}$ requires C, 62.97; H, 6.12%); δ_H 3.18 (3 H, s, OMe), 3.30 (1 H, m, 4-H), 3.60 (2 H, m, 3- and 5-H), 3.72 (6 H, s, ArOMe), 3.75 (4 H, s, CH_2CO), 4.09 (1 H, dd, *J* 5.4 and 9.3, 6-H), 4.37 (1 H, dd, *J* 1.6 and 9.3, 6-H), 4.49 (1 H, dd, *J* 3.0 and 8.4, 2-H), 4.69 (1 H, d, *J* 2.7, 1-H), 5.31 (2 H, br, 3- and 4-OH), 6.82–6.95 (4 H, m, ArH) and 7.11–7.28 (4 H, m, ArH); FABMS (−) *m/z* 489 (39%, M − H)$^-$, 474 (4) and 165 (100).

Methyl 6-O-(α-*naphthylacetyl*)-α-D-*glucopyranoside* **7f**. (59%) M.p. 118–120 °C (Found: C, 63.05; H, 6.1. $C_{19}H_{22}O_{17}$ requires C, 62.97; H, 6.12%); δ_H 3.04 (1 H, m, 3-H), 3.08 (3 H, s, OMe), 3.23 (1 H, m, 4-H), 3.40 (1 H, m, 2-H), 3.49 (1 H, m, 5-H), 4.08 (1 H, dd, *J* 5.3 and 8.7, 6-H), 4.14 (2 H, s, CH_2CO), 4.37 (1 H, dd, *J* 1.7 and 8.7, 6-H), 4.48 (1 H, d, *J* 2.8, 1-H), 4.72 (1 H, d, 2-OH), 4.80 (1 H, br, 3-OH), 5.08 (1 H, br, 4-H), 7.42–7.61 (4 H, m, ArH) and 8.10–8.82 (3 H, m, ArH); FABMS (+) *m/z* 363 (2%, M + H)$^+$, 331 (13) and 141 (100).

Methyl 2,6-*bis*-O-(α-*naphthylacetyl*)-α-D-*glucopyranoside* **8f**. (22%) M.p. 134–137 °C (Found: C, 70.3; H, 5.7. $C_{31}H_{30}O_8$ requires C, 70.18; H, 5.70%); δ_H 3.09 (3 H, s, OMe), 3.26 (1 H, m, 4-H), 3.43 (1 H, m, 5-H), 3.69 (1 H, m, 3-H), 4.04 (4 H, s, CH_2CO), 4.28 (1 H, dd, *J* 4.7 and 7.8, 6-H), 4.42 (1 H, dd, *J* 1.6 and 7.8, 6-H), 4.52 (1 H, dd, *J* 2.7 and 6.7, 2-H), 4.67 (1 H, d, *J* 3.0, 1-H), 5.32 (2 H, br, 3- and 4-OH), 7.39–7.64 (8 H, m, ArH) and 7.80–8.07 (6 H, m, ArH); FABMS (+) *m/z* 351 (1%, M + H)$^+$, 499 (4) and 141 (100).

Methyl 6-O-(2,6-*dichlorobenzoyl*)-α-D-*mannopyranoside* **10**. (64%) M.p. 153–155 °C (Found: C, 45.7; H, 19.1. $C_{14}H_{16}Cl_2O_7$ requires C, 45.80; H, 4.39%); δ_H 3.23 (3 H, s, OMe), 3.49 (2 H, m, 3- and 4-H), 3.61 (2 H, m, 2- and 5-H), 4.39 (1 H, dd, *J* 4.3 and 8.7, 6-H), 4.53 (1 H, d, *J* 1.4, 1-H), 4.69 (1 H, dd, *J* 1.5 and 8.7, 6-H), 4.75 (1 H, d, 2-OH), 4.89 (1 H, d, 3-OH), 5.09 (1 H, d, 4-OH) and 7.50–7.68 (3 H, m, ArH); FABMS (+) *m/z* 367 (10%, M + H) 335 (25) and 173 (100).

Methyl 3,6-*bis*-O-(2,6-*dichlorobenzoyl*)-α-D-*mannopyranoside* **11**. (10%) M.p. 192–194 °C (Found: C, 46.8; H, 3.3. $C_{21}H_{18}Cl_4O_8$ requires C, 46.69; H, 3.36%); δ_H 3.31 (3 H, s, OMe), 3.84 (2 H, m, 4- and 5-H), 3.99 (1 H, dd, *J* 2.0 and 3.1, 2-H), 4.49 (1 H, dd, *J* 6.2 and 11.8, 6-H), 4.61 (1 H, d, *J* 2.3, 1-H), 4.75 (1 H, dd, *J* 1.2 and 11.8, 6-H), 5.18 (1 H, dd, *J* 3.1 and 8.7, 3-H), 5.28 (1 H, d, 2-OH), 5.45 (1 H, d, 4-OH) and 7.47–7.68 (6-H, m, ArH); FABMS (+) *m/z* 539 (2%, M + H)$^+$, 507 (6), 173 (6) and 105 (100).

Conclusions—The protection of the examined substrates with base-labile groups can be carried out with a high degree of regioselectivity by means of synthetic protocols which make use of the versatile BOP-Cl condensing agent, now commercially available. The isolated yield of the product thus obtained is comparable to that obtained in lipase-catalysed reaction; moreover, the adopted procedure is very simple and the conversion of the substrate takes place in a few hours at room temperature.

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