Mode of alkylation of alcohols with *O*-cyclopropylmethyl trichloroacetimidate and *O*-cyclobutyl trichloroacetimidate

Ibrahim A. I. Ali,[a] Xiangming Zhu,[a] El Sayed H. El Ashry,[b] and Richard R. Schmidt[a,c]

[a]Fachbereich Chemie, Universität Konstanz, Fach 725, D – 78457 Konstanz, Germany;
[b]Department of Chemistry, Faculty of Science, University of Alexandria, Alexandria, Egypt
[c]Chemistry Department, Faculty of Science, King Abdulaziz University, Jeddah 21589, Saudi Arabia
E-mails: Richard.Schmidt@uni-konstanz.de, eelashry@link.net, eelashry60@hotmail.com

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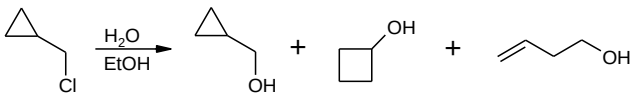
Abstract

Acid promoted alkylation of hydroxy group containing acceptors **3-14** with *O*-cyclopropylmethyl and *O*-cyclobutyl trichloroacetimidates **1** and **2**, respectively, afforded ethers with cyclopropylmethyl, cyclobutyl, and homoallyl residues as a result of the rearrangement of the cation intermediates. The dependence of product formation on acceptor structure is discussed.

Introduction

A considerable amount of work has been devoted to cyclopropyl group participation in the cyclopropylmethyl cation system.[1] Thus the rate of solvolysis of primary cyclopropylmethyl systems is enhanced because of participation by the σ bonds of the ring in the bisected conformation.[1-4] A similar participation of C-C σ bonds has been also discussed for the ion formed from the solvolysis of cyclobutyl substrates which often leads to the same products as they result from the corresponding cyclopropylmethyl substrates. The products from such solvolyses often include almost equal amounts of the cyclopropylmethyl (**Cpm**) and the respective cyclobutyl (**Cb**) derivatives in addition to minor amounts (5%) of the homoallyl (**Ha**) compound[1,5] (Scheme 1).

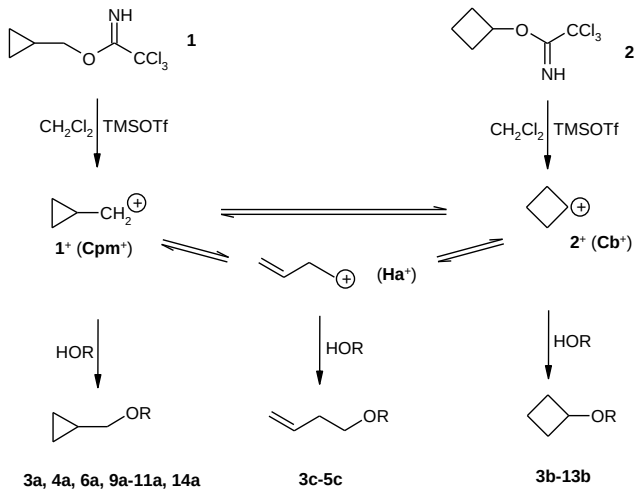


Scheme 1. Solvolysis of cyclopropylmethyl chloride.

Product formation is rationalized by assuming a type of classical (as shown in Scheme 2) or nonclassical cyclopropylmethyl-cyclobutyl-homoallyl cation as the reactive intermediate.[1-5] Such rearrangements have been also achieved with high stereoselectivity.[6-8] Factors such as the nucleophilicity of the medium play a major role in this respect. With the above aspects in mind and in continuation of our work on glycoside bond formation utilizing *O*-glycosyl trichloroacetimidates as alkylating agents,[9] this paper describes the formation of *O*-cyclopropylmethyl trichloroacetimidate **1** and *O*-cyclobutyl trichloroacetimidate **2** and their behaviour as alkylating agents particularly of hydroxy groups of varying nucleophilicities under acid catalysis. The results should also provide further information on the mode of action of other trichloroacetimidate derived alkylation reactions.[10-12]

Results and Discussion

The *O*-cyclopropylmethyl trichloroacetimidate (**1**) was readily obtained in 92% yield by reaction of cyclopropylmethanol with trichloroacetonitrile in the presence of DBU as a catalyst. **1** can be stored at room temperature without decomposition; its structure was confirmed by the ^{1}H NMR data [δ 0.3-1.2 (m), cyclopropyl, 4.13 (d), CH_2, 8.23 (s), NH]. **2** was obtained by the same procedure [δ 1.5-2.5 (m), 3 CH_2; 5.08 (q), CH; 8.16 (s), NH].



Scheme 2. TMSOTf Promoted reaction of **1** and **2** with hydroxy groups. For structures **3-14**, see Table 1.

Reaction of **1** with dibenzyl phosphoric acid (**3**) led exclusively to the cyclopropylmethyl derivative **3a** (Table 1, entry 1) whereas reaction of **2** with **3** under the same conditions furnished a mixture of all three possible products (**3a**, **3b**, **3c**, ratio 4:3:2, entry 2). Also **1** and diphenyl phosphoric acid (**4**) gave a mixture of all three possible products (**4a**, **4b**, **4c**, ratio 4:2:1, entry 3)

and *p*-toluenesulfonic acid (**5**) led to a 2:1 mixture of **5b** and **5c** (entry 4). Therefore, for the reaction of **1** with acceptor **3** transition state **3a**$^{\neq}$ (Figure 1, S_N2-type reaction) is proposed, thus avoiding rearrangement, whereas with more acidic acceptor **4** and particularly with **5** fast generation of cation intermediates **1**$^+$ (**Cpm**$^+$), **2**$^+$ (**Cb**$^+$) and **Ha**$^+$ (Scheme 2, S_N1-type reaction) is favoured.

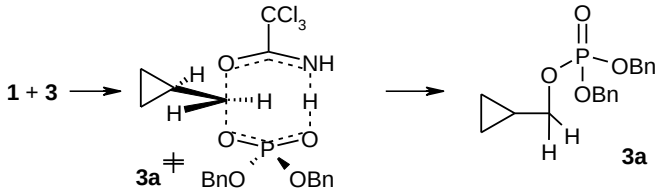
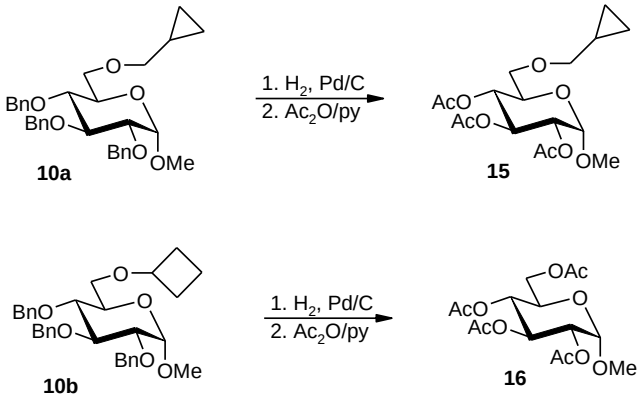


Figure 1. Reaction of **1** and **3** and proposed transition state for the reaction.

Reaction of 3,5-dinitrobenzyl alcohol (**6**) with **1** and **2** in the presence of TMSOTf (0.6 equivalents) led to 1:1 mixtures of **Cpm** derivative **6a** and **Cb** derivative **6b** (entries 5, 6). However, the less acidic **7** and benzyl alcohol (**8**) gave only **Cb** products (**7b**, **8b**, entries 7-9).[13] Cholesterol (**9**) and the 6-*O*- and 4-*O*-unprotected glucose derivatives **10** and **11** gave similar results as **6** (entries 10-13), whereas due to steric hindrance low reactive alcohols **12** and **13** afforded only **Cb** derivatives (**12b**, **13b**, entries 14, 15). The importance of the nucleophilicity of the acceptor was also demonstrated for the reaction with thiophenol (**14**) and **1** which gave exclusively the **Cpm** derivative **14a** (entry 16).[14] Therefore, in all these cases carbocation intermediates **Cpm**$^+$ and **Cb**$^+$ seem to be the decisive reaction partners which are trapped by typical alcohol acceptors in a close to 1:1 fashion whereas with increasing steric demand the **Cb** derivative is formed. The preference for the formation of **Cb** derivatives with **7** and **8** requires further studies. The equilibration between **Cpm**$^+$, **Cb**$^+$, and **Ha**$^+$ (Scheme 2) or formation of some kind of nonclassical carbocation intermediate[1] is very fast because lowering the reaction temperature to -40 °C (reaction of **1** + **10**) or varying the reaction time before adding the acceptor had practically no effect on the result.

The **Cpm** and the **Cb** ethers can be readily identified by ^{1}H NMR spectroscopy where the former group appears as a multiplet at δ 0.26-1.10 and the latter as a multiplet at δ 1.4-2.4. These data are in accordance with those reported.[15] The interest in the **Cpm** group and the 1-methyl CPM group as acid sensitive *O*-protecting groups[16,17] led us to investigate the hydrogenolysis of the **Cpm** and **Cb** group because this reaction is affected by the ring strain. In accordance with this effect, hydrogenolysis of **10a** and then *O*-acetylation under standard conditions led to **Cpm** protected derivative **15** whereas hydrogenolysis of **10b** led to removal of the **Cb** group and of the benzyl groups affording after *O*-acetylation **16** (Scheme 3).



Scheme 3. Hydrogenolysis of **10a** and **10b**.

In conclusion, the **Cpm** and **Cb** trichloroacetimidates are excellent alkylating agents under acid catalysis. Equilibration between the generated carbocation intermediates is fast,[1] therefore product formation depends essentially on the nucleophilicity and the steric demand of the acceptors. In addition, the cyclobutyl group seems to be an interesting alternative to the benzyl group for hydroxy group protection.

Table 1. Reaction of Trichloroacetimidates **1** and **2** with Acceptors **3**-**14**[a]

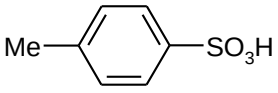
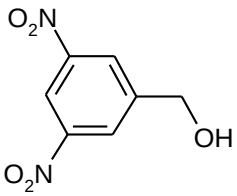
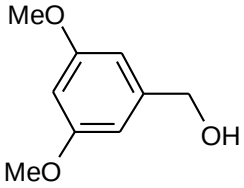
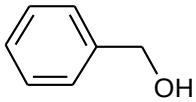
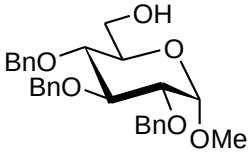
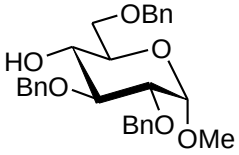
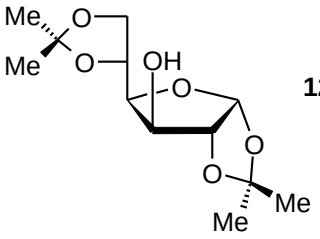
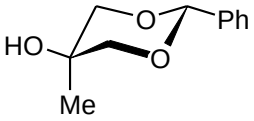
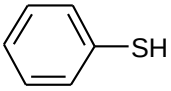
Entry	Trichloro-acetimidate	Acceptors: ROH' and R–SH	Products ROR' (Yields in%) R' = **Cpm**	R' = **Cb**	Total isolated R' = **Ha**	yield [%]
1	**1**	$(BnO)_2P(=O)-OH$ **3**	**3a** (79)	-	-	79
2	**2**	**3**	**3a** (33)	**3b** (23)	**3c** (16)	72
3	**1**	$(PhO)_2P(=O)-OH$ **4**	**4a** (51)	**4b** (25)	**4c** (13)	89
4	**1**	 **5**	-	**5b** (57)	**5c** (28)	85
5	**1**	 **6**	**6a** (42)	**6b** (47)	-	89
6	**2**	**6**	**6a** (43)	**6b** (45)	-	88

Table 1. Continued

Entry	Trichloro-acetimidate	Acceptors: ROH' and R–SH		Products ROR' (Yields in%) R' = **Cpm**	R' = **Cb**	Total isolated R' = **Ha**	yield [%]
7	**1**		**7**	-	**7b** (67)	-	67
8	**1**		**8**	-	**8b** (85)	-	85
9	**2**	**8**		-	**8b** (73)	-	73
10	**1**	Cholesterol **9**		**9a** (32)	**9b** (52)	-	84
11	**1**		**10**	**10a** (35)	**10b** (42)	-	77
12	**2**	**10**		**10a** (35)	**10b** (42)	-	77
13	**1**		**11**	**11a** (33)	**11b** (49)	-	82
14	**1**		**12**	-	**12b** (37)	-	37
15	**1**		**13**	-	**13b** (70)	-	70
16	**1**		**14**	**14a** (91)	-	-	91

[a] For abbreviations and experimental procedures see text.

Experimental Section

General. Solvents were purified in the usual way. TLC was performed on plastic plates coated with silica gel 60 F_{254} (E. Merck, layer thickness = 0.2 mm). Detection was achieved by treatment with a solution of ammonium molybdate (20 g) and cerium(IV) sulfate (0.4 g) in 10% H_2SO_4 (400 mL) or with 15% H_2SO_4 and heating at 150 °C. Flash chromatography was carried out on silica gel (Baker, 30-60 μm). Medium-pressure liquid chromatography (MPLC): LiChroprep Si 60 (Merck; particle size 15-25 μm) and detection was carried out with a differential refractometer. Optical rotations were determined at 20 °C with a Perkin-Elmer 241/MC polarimeter (1-dm cell). NMR spectra were recorded with Bruker AC 250 and 600 DRX instruments using tetramethylsilane as the internal standard. The ^{1}H NMR spectral assignments were based on chemical shift correlation (DQF COSY) and rotating frame nuclear Overhauser effect spectroscopy (ROESY). The ^{13}C NMR spectral assignments were based on carbon-proton shift-correlation heteronuclear multiple quantum coherence (HMQC). MS spectra were recorded with a MALDI-Kompakt (Kratos) spectrometer; matrix: 2,5-dihydroxybenzoic acid (DHB). Microanalyses were performed at the Microanalysis unit at the Fachbereich Chemie, Universität Konstanz.

***O*-Cyclopropylmethyl trichloroacetimidate (1).** A solution of hydroxymethylcyclopropane (1.8 g, 25.3 mmol) in dry dichloromethane (20 mL) and trichloroacetonitrile (25 mL, 250 mmol) was cooled in an ice-bath and then DBU 0.35 mL, 2.5 mmol) was added. The reaction mixture was stirred for 30 min and then evaporated under reduced pressure without heating. The product was purified by column chromatography on silica gel (3% Et_3N in toluene); yield: 5.0 g, 92%, slightly yellow oil. R_f = 0.83 (3% Et_3N in toluene). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.38 (m, 2 H, CH_2), 0.64 (m, 1 H, CH_2), 1.32 (m, 1 H, CH), 4.13 (d, *J* = 7.1 Hz, 2 H, CH_2), 8.23 (brs, 1 H, NH).

***O*-Cyclobutyl trichloroacetimidate (2)** was obtained as described for **1**. Purification of the crude material by column chromatography on silica gel (3% Et_3N in toluene) afforded **2** (4.7 g, 87%) as colourless oil. R_f = 0.90 (3% Et_3N in toluene). ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.61 (m, 1 H, CH), 1.80 (m, 1 H, CH), 2.15 (m, 2 H, CH_2), 2.40 (m, 2 H, CH_2), 5.12 (m, 1 H, CH), 8.21 (brs, 1 H, NH).

A. General procedure for the reaction of (1) or (2) with acids (3-5)

A solution of **1** or **2** (0.8 g, 1.4 mmol) and acid (1.4 mmol) in dry dichloromethane (20 mL) was stirred for 0.5-3.0 h. The reaction mixture was quenched with solid sodium bicarbonate, filtered and concentrated. The crude residue was purified by column chromatography (petroleum ether/ethyl acetate = PE/EA). For details, see Table 1.

B. General procedure for the reaction of (1) or (2) with acceptors (6-14). A solution of **1** or **2** (0.3 g, 1.4 mmol) and acceptor (1.4 mmol) were dissolved in dry dichloromethane (10 mL) at

room temperature. TMSOTf (0.15 mL, 0.83 mmol) was added and the reaction mixture stirred for 0.5-3.0 h. The reaction mixture was quenched by addition of solid sodium bicarbonate, then diluted with dichloromethane, filtered and concentrated. The crude product was purified by column chromatography. For details, see Table 1.

Reaction of (1) with (3). Procedure **A** afforded 0.3 g (49%) dibenzyl cyclopropyl-methylphosphate (**3a**)[18] as colourless oil. R_f = 0.45 (PE/EA, 5:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.24 (m, 2 H, CH_2), 0.53 (m, 2 H, CH_2), 1.16 (m, 1 H, CH), 3.81 (t, *J* = 7.3 Hz, 2 H, CH_2), 5.00 (brd, 4 H, 2 CH_2), 7.21-7.49 (m, 10 H, Ar-H). EI-MS: m/z 332.0. $C_{18}H_{21}O_4P$ (332.3), calcd. C 65.05, H 6.37; found C 64.81, H 6.45.

The reaction of **2** with **3** following procedure **A** afforded a mixture of **3a**, **3b**, **3c**; see Table 1, entry 2.

Reaction of (1) with (4). Procedure **A** afforded a mixture of **4a**, **4b** and **4c** (ratio 4:2:1, 0.37 g, 89%). R_f = 0.42 (PE/EA, 5:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.35 (m, 2 H, cyclopropyl-CH_2), 0.67 (m, 2 H, cyclopropyl-CH_2), 1.22 (m, 1 H, cyclopropyl-CH), 1.55 (m, 2 H, cyclobutyl-CH_2), 1.82 (m, 2 H, cyclobutyl-CH_2), 2.35 (m, 6 H, cyclobutyl-CH_2, allyl-2 CH_2), 4.15 (m, 2 H, cyclopropyl-CH_2), 4.35 (m, 1 H, cyclobutyl-CH), 5.00 (m, 2 H, allyl-CH_2), 7.19-7.51 (m, 10 H, Ar-H). EI-MS: *m/z* 304.0. $C_{16}H_{17}O_4P$ (332.3), calcd. C 63.15, H 5.63; found C 63.10, H 5.46.

Reaction of (1) with (5). Procedure **A** afforded a mixture of **5b** and **5c** (ratio 2:1, 0.37 g, 85%). R_f = 0.58 (PE/EA, 5:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.41 (m, 2 H, cyclobutyl-CH_2), 1.65 (m, 2 H, cyclobutyl-CH_2), 2.11 (m, 4 H, cyclobutyl-CH_2, allyl-CH_2), 2.42 (s, 3 H, CH_3), 4,00 (m, 2 H, allyl-CH_2), 4.70 (m, 1 H, cyclobutyl-CH_2), 5.00 (m, 2 H, allyl-CH_2), 5.55 (m, 1 H, allyl-CH), 7.20-7.81 (m, 4 H, Ar-H). MS: *m/z* 226.0. $C_{16}H_{17}O_4P$ (226.3), calcd. C 58.38, H 6.23; found C 58.18, H 6.44.

Reaction of (1) with (6). Procedure **B** afforded a mixture of **6a** and **6b** in about a 1:1 ratio that was separated. **6a**: colourless oil (0.15 g, 42%). R_f = 0.58 (PE/EA, 6:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.28 (m, 2 H, CH_2), 0.63 (m, 2 H, CH_2), 1.15 (m, 1 H, CH), 3.45 (d, *J* = 6.9 Hz, 2 H, CH_2), 4.72 (s, 2 H, CH_2), 8.55 (m, 2 H, Ar-H), 8.96 (dd, *J* = 2.1 Hz, 1 H, Ar-H). ^{13}C NMR (62.8 MHz, $CDCl_3$) δ 3.1 (2 CH_2), 10.4 (CH), 70.2 (CH_2), 76.1 (CH_2), 117.7, 127.0, 143.7, 148.6. EI-MS: *m/z* 252.0. $C_{11}H_{12}N_2O_5$ (252.2). **6b**: colourless oil (0.16 g, 47%). R_f = 0.62 (PE/EA, 6:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ 1,55 (m, 1 H, CH), 1.70 (m, 1 H, CH), 2.05 (m, 2 H, CH_2), 2.30 (m, 2 H, CH_2), 4.10 (m, 1 H, CH), 4.60 (s, 2 H, CH_2), 8.50-9.00 (m, 3 H, Ar-H). ^{13}C NMR (62.8 MHz, $CDCl_3$) δ 12.4 (CH_2), 30.2 (2 CH_2), 67.5 (CH_2), 73.8 (CH), 117.7, 127.1, 143.6, 148.5 (C-Ar). EI-MS: *m/z* 252.0. $C_{11}H_{12}N_2O_5$ (252.2).

Reaction of 2 with 6 following procedure **B** afforded a similar result; see Table 1, entry 6.

Reaction of (1) with (7). Procedure **B** afforded **7b** as colourless oil (0.20 g, 67%). R_f = 0.48 (PE/EA, 5:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.45-2.46 (m, 6 H, 3 CH_2), 3.78 (s, 6 H, 2 OCH_3), 4.00 (m, 1 H, CH), 4.35 (s, 2 H, CH_2), 6.13-6.50 (m, 3 H, Ar-H). EI-MS: *m/z* 222.0. $C_{13}H_{18}O_3$ (222.3), calcd. C 70.24, H 8.16; found C 70.25, H 8.42.

Reaction of (1) with (8). Procedure **B** afforded **8b** as colourless oil (0.38 g, 85%). R_f = 0.41 (PE/EA, 6:1). The analytical data are identical with the published values.[13]

Reaction of 2 with 8 following procedure **B** afforded a similar result; see Table 1, entry 9.

Reaction of (1) with (9). Procedure **B** afforded a mixture of **9a** and **9b** that was separated. **9a**: colourless oil (0.20 g, 32%). R_f = 0.76 (PE/EA, 10:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.18 (m, 2 H, CH_2), 0.52 (m, 2 H, CH_2), 0.65-2.28 (m, 43 H, cholesteryl, CH), 3.41 (d, *J* = 7.0 Hz, 1 H, CH_2), 3.50 (m, 1 H, CH), 5.32 (m, 1 H, CH), EI-MS: *m/z* 442.0. $C_{31}H_{52}O$ (442.8), calcd. C 84.09, H 12.29; found C 84.12, H 12.40. **9b**: colourless oil (0.32 g, 52%). R_f = 0.82 (PE/EA, 10:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.66-2.50 (m, 49 H, cholesteryl, 3 CH_2), 3.50 (m, 1 H, CH), 4.20 (m, 1 H, CH), 5.33 (m, 1 H, CH), EI-MS: *m/z* 442.0. $C_{31}H_{52}O$ (442.8), calcd. C 84.09, H 12.29; found C 83.87, H 11.95.

Reaction of (1) with (10). Procedure **B** afforded a mixture of **10a** and **10b** that was separated. **10a**: colourless oil (0.50 g, 35%). R_f = 0.61 (PE/EA, 5:1), $[\alpha]_D$ = 35.3 (c 1.0, CH_2Cl_2). ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.18 (m, 2 H, CH_2), 0.51 (m, 2 H, CH_2), 1.06 (m, 1 H, CH), 3.20 (dd, *J* = 7.1 Hz, 1 H, CH), 3.39 (s, 3 H, OCH_2), 3.41 (m, 1 H, CH), 3.56 (dd, $J_{2,1}$ = 3.5, $J_{2,3}$ = 9.3 Hz, 1 H, 2-H), 3.67 (m, 2 H, 4-H, 6-H), 4.00 (dd, $J_{3,2}$ = 9.3, $J_{4,3}$ = 9.6 Hz, 1 H, 3-H), 4.60 (m, 1 H, C*H*Ph), 4.63 (d, *J* = 3.5 Hz, 1 H, 1-H), 4.66 (d, J_{gem} = 12.6 Hz, 1 H, C*H*Ph), 4.82 (d, J_{gem} = 12.6 Hz, 1 H, C*H*Ph), 4.84 (d, J_{gem} = 10.9 Hz, 1 H, C*H*Ph), 4.89 (d, J_{gem} = 10.9 Hz, 1 H, C*H*Ph), 4.98 (m, J_{gem} = 10.9 Hz, 1 H, C*H*Ph), 7.15-7.38 (m, 15 H, Ar-H). ^{13}C NMR (150.8 MHz, $CDCl_3$) δ 2.9, 3.1, (2 CH_2),10.4 (CH), 55.1 (OCH_3), 66.0 (CH_2), 68.4 (CH_2), 68.6 (C-6), 69.8 (CH_2), 70.0 (C-5), 77.6 (C-4), 79.2 (C-2), 82.1 (C-3), 98.1 (C-1), 127.5, 127.6, 127.7, 127.8, 127.9, 128.1, 128.3, 128.4, 138.2, 138.4, 138.8 (C-Ar). MS (FAB, positive mode, M+NaI): 518.0. $C_{32}H_{38}O_6$ (518.6), calcd. C 74.10, H 7.38, found C 73.80, H 7.35. **10b**: colourless oil (0.6 g, 42%). R_f = 0.64 (PE/EA, 5:1); $[\alpha]_D$ = 85.4 (c 0.5, CH_2Cl_2). ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.46 (m, 1 H, CH), 1.64 (m, 1 H, CH), 1.92 (m, 2 H, CH_2), 2.15 (m, 2 H, CH_2), 3.36 (s, 3 H, OCH_3), 3.48 (m, 1 H, 6-H), 3.54 (dd, $J_{2,1}$ = 3.6, $J_{2,3}$ = 9.3 Hz, 1 H, 2-H), 3.57 (m, 1 H, 6'-H), 3.62 (dd, $J_{4,3}$ = 9.3, $J_{4,5}$ = 9.6 Hz, 1 H, 4-H), 3.70 (m, 1 H, 5-H), 3.88 (m, 1 H, CH), 3.98 (dd, $J_{3,2}$ = 9.3, $J_{3,4}$ = 9.3 Hz, 1 H, 3-H), 4.59 (d, $J_{2,1}$ = 3.6 Hz, 1 H, 1-H), 4.62 (d, J_{gem} = 10.8 Hz, 1 H, C*H*Ph), 4.64 (d, J_{gem} = 12.3 Hz, 1 H, C*H*Ph), 4.78 (d, J_{gem} = 12.3 Hz, 1 H, C*H*Ph), 4.82 (d, J_{gem} = 10.8 Hz, 1 H, C*H*Ph), 4.88 (d, J_{gem} = 10.8 Hz, 1 H, C*H*Ph), 4.99 (d, J_{gem} = 10.8 Hz, 1 H, C*H*Ph), 7.27-7.35 (m, 15 H, Ar-H). ^{13}C NMR (150.8 MHz, $CDCl_3$) δ 12.3 (CH_2), 30.0, 30.3 (2 CH_2), 55.1 (OCH_3), 65.9 (C-6), 69.2 (CH_2), 69.7 (CH_2), 69.8 (C-5), 73.5 (CH), 75.6 (CH_2), 77.6 (C-4), 79.7 (C-2), 82.1 (C-3), 98.1 (C-1), 116.4, 127.4, 127.6, 127.7, 127.8, 127.9, 128.1, 128.3, 138.1, 138.4, 138.8 (C-Ar). MS (FAB, positive mode, M+NaI): 518.0. $C_{32}H_{38}O_6$ (518.6), calcd. C 74.10, H 7.38; found C 73.72, H 7.54.

Reaction of 2 with 10 following procedure **B** afforded the same result; see Table 1, entry 12.

Reaction of (1) with (11). Procedure **B** afforded a mixture of **11a** and **11b** that was separated. **11a**: colourless oil (0.50 g, 33%). R_f = 0.53 (PE/EA, 5:1). $[\alpha]_D$ = 9.3 (c 1.0, CH_2Cl_2). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.15 (m, 2 H, CH_2), 0.37 (m, 2 H, CH_2), 1.05 (m, 1 H, CH), 3.21 (m, 1 H, 6-H), 3.35 (s, 3 H, OCH_3), 3.60 (m, 3 H, 6'-H, 2-H, 5-H), 3.72 (m, 3 H, 4-H, CH_2), 3.90 (dd, $J_{3,2}$ $J_{3,4}$ = 9.6 Hz, 1 H, 3-H), 4.56 (m, 1 H, C*H*Ph), 4.65 (m, 2 H, C*H*Ph), 4.71 (m, 1 H, C*H*Ph), 4.74 (d, $J_{1,2}$ = 2.7 Hz, 1 H, 1-H), 4.86 (m, 2 H, 2 C*H*Ph), 7.19-7.41 (m, 15 H, Ar-H). MS (FAB, positive mode, M+NaI): 518.0. $C_{32}H_{38}O_6$ (518.6), calcd. C 74.10, H 7.38, found C 73.98, H 7.52.

11b. colourless oil (0.67 g, 49%). R_f = 0.58 (PE/EA, 5:1), $[\alpha]_D$ = 53.6 (c 2.0, CH_2Cl_2). ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.40 (m, 1 H, CH), 1.65 (m, 1 H, CH), 1.90 (m, 2 H, CH_2), 2.18 (m, 2 H, CH_2), 3.37 (s, 3 H, OCH_3), 3.55 (m, 2 H, 6-H, 6'-H), 3.60-3.80 (m, 3 H, 2-H, 5-H, 4-H), 3.86 (m, 1 H, CH), 4.00 (dd, $J_{3,2}$ $J_{3,4}$ = 9.7 Hz, 1 H, 3-H), 4.62 (d, $J_{2,1}$ = 3.8 Hz, 1 H, 1-H), 4.65-4.88 (m, 2 H, 2 C*H*Ph), 4.77 (d, J_{gem} = 12.1 Hz, 1 H, C*H*Ph), 4.84 (m, 3 H, 3 C*H*Ph), 7.25-7.40 (m, 15 H, Ar-H). MS (FAB, positive mode, M+NaI): 518.0. $C_{32}H_{38}O_6$ (518.6), calcd. C 74.10, H 7.38; found C 74.46, H 7.05.

Reaction of (1) with (12). Procedure **B** afforded **12b** as colourless oil (0.31 g, 73%). R_f = 0.53 (PE/EA, 5:1). $[\alpha]_D$ = –11.5 (c 1.0, CH_2Cl_2). ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.29, 1.34, 1.42, 1.47 (4 s, 12 H, 4 CH_2), 1.52-1.90 (m, 4 H, 2 CH_2), 2.25 (m, 2 H, CH_2), 3.96 (m, 2 H, 6-H, 4-H), 4.15 (m, 2 H, 6'-H, 5-H), 4.30 (m, 2 H, 3-H, CH), 4.51 (d, $J_{2,1}$ = 3.6 Hz, 1 H, 2-H), 5.92 (d, $J_{1,2}$ = 3.6 Hz, 1 H, 1-H). MALDI (positive mode, Matrix: DHB): *m/z* 337.6 $(M+Na)^+$, 353.7 $(M+K)^+$. $C_{16}H_{26}O_6$ (314.4), calcd. C 61.13, H 8.33; found C 61.51, H 8.02.

Reaction of (1) with (13). Procedure **B** afforded **13b** as colourless oil (0.25 g, 70%). R_f = 0.64 (PE/EA, 5:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.76 (s, 3 H, CH_3), 1.40 (m, 1 H, CH), 1.60 (m, 1 H, CH), 1.82 (m, 2 H, CH_2), 2.28 (m, 2 H, CH_2), 3.64 (d, J_{gem} = 11.8 Hz, 2 H, 2 CH), 4.05 (d, J_{gem} = 11.8 Hz, 2 H, 2 CH), 4.17 (m, 1 H, CH), 5.39 (s, 1 H, CH), 7.30-7.52 (m, 5 H, Ar-H). EI-MS: *m/z* 262.35. $C_{16}H_{22}O_3$ (262.3), calcd. C 73.25, H 8.45; found C 73.00, H 8.14.

Reaction of (1) with (14). Procedure **B** afforded **14a** as colourless oil (0.40 g, 91%). R_f = 0.75 (PE/EA, 6:1). The analytical data are identical with the published values.[14]

Methyl 2,3,4-Tri-*O*-acetyl-6-*O*-cyclopropylmethyl-α-D-glucopyranoside (15). 10a (0.1 g, 0.2 mmol) was dissolved in dry methanol (10 mL) and stirred in the presence of palladium on carbon (0.05 g) under a hydrogen atmosphere for 12 h. The catalyst was filtered off and washed with methanol. The solvent was removed under reduced pressure and the crude product reacted with acetic anhydride (2 mL) and pyridine (2 mL). The reaction mixture was stirred for 15 h at room temperature and then concentrated and purified by flash chromatography on silica gel (PE/EA, 2:1) to afford **15** (0.06 g, 80%) as colourless oil. R_f = 0.32 (PE/EA, 3:1), $[\alpha]_D$ = 70.8 (c 2.0, CH_2Cl_2). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.15 (m, 2 H, CH_2), (m, 2 H, CH_2), 0.45 (m, 2 H, CH_2), 1.00 (m, 1 H, CH), 1.96, 1.98, 2.00 (3 s, 9 H, 3 AcO), 3.20 (m, 2 H, CH_2), 3.36 (s, 3 H, OCH_3), 3.53 (m, 2 H, 6-H, 6'-H), 3.88 (m, 1 H, 5-H), 4.87 (d, $J_{2,1}$ = 3.6 Hz, 1 H, 1-H), 4.94 (dd, $J_{2,1}$ = 3.6, $J_{2,3}$ = 9.7 Hz, 1 H, 2-H), 5.12 (dd, $J_{4,3}$ = 9.6, $J_{4,5}$ = 9.7 Hz, 1 H, 4-H), 5.41 (dd, $J_{3,2}$ = 9.7, $J_{3,4}$ = 9.6 Hz, 1 H, 3-H). MALDI (positive mode, Matrix: DHB) *m/z* 397.0 $(M+Na)^+$, 413.0 $(M+K)^+$. $C_{17}H_{26}O_9$ (374.4), calcd. C 54.53, H 7.00; found C 54.90, H 6.80.

Methyl 2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranoside (16). As described for **15** from **10b** known **16**[19] was obtained in quantitative yield.

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