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2-(Prenyloxymethyl)benzoyl (POMB) group: a new temporary protecting group removable by intramolecular cyclization

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Abstract—2-(Prenyloxymethyl)benzoates can be prepared from alcohols and readily available 2-(prenyloxymethyl)benzoic acid by standard acylation techniques or by Mitsunobu reaction with inversion of configuration. The POMB group can be cleaved first by oxidative removal of the prenyl group with DDQ followed by lactonization with expulsion of the alcohol catalyzed by $Yb(OTf)_3$. These reaction conditions are compatible with the presence of a large number of common protecting groups.
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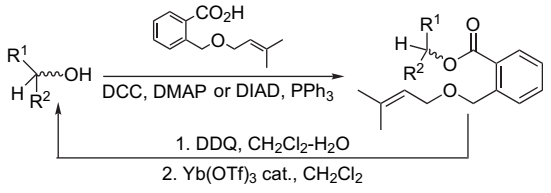
1. Introduction

The hydroxy group is one of the most present functional groups in natural products. Because it is nucleophilic, acidic, and easily oxidized in a multifunctional molecule it needs to be temporarily protected from unwanted reactions. Although over 150 hydroxy protecting groups have been reported, few have found wide applications.[1] Novel hydroxy protection and new cleavage techniques for existing protecting groups are thus required as molecular targets increase in complexity and new fields such as supported-oligosaccharide synthesis emerge.[2] Among the new principle developed for the deprotection of alcohols is the assisted cleavage. These classes of protecting groups contain an inside auxiliary group that initially exists in a chemically stable form and can be converted to a reactive nucleophile facilitating the deprotection via an intramolecular reaction.[3] Ester protecting groups designed in this way can be used to liberate hydroxy groups under mild conditions that usually do not affect common esters such as acetates or benzoates.[4] Among esters, which have been designed according to this principle, are these four *O*-substituted 2-(hydroxymethyl)benzoyl groups: 2-(isopropyl or methylthiomethoxymethyl)benzoyl (respectively, PTMT[5] and MTMT[6]), 2-(chloroacetoxymethyl)benzoyl (CAMB)[7] and 2-[4-(methoxytrityl)thiooxymethyl]benzoyl (MOB).[8] The deblocking process of these protecting groups involves the unmasking of the hydroxy auxiliary function ($Hg(ClO_4)_2$, base, THF–H_2O for the PTMT and MTMT groups; thiourea at 50 °C for 24–48 h for the CAMB group; iodine in pyridine–H_2O for the MOB group) followed by base-catalyzed lactonization with formation of the deblocked alcohol and phthalide.[5–8] The main drawbacks of these 2-substituted benzoates are: (1) for PTMT and MTMT groups, the high cost and toxicity of the Hg(II) salt used for the deprotection and for the MTMT group, the MTM deprotection step for some substrates is very sluggish;[5] (2) for the CAMB group, the deprotection of the chloroacetoxy group using thiourea is rather slow necessitating prolonged heating, which may cause side reactions[9] or uncompleted deprotection;[7] (3) commercial unavailability of 4-MeOTrSCl used for the preparation of MOBOH.[8]

In relation with an ongoing project aimed to develop the uses of the prenyl group in the protection of alcohol and amine functions,[10,11] we have reported on a preliminary account of a new protecting group namely 2-(prenyloxymethyl)-benzoyl (POMB) group selectively removable under mild conditions.[12] We now describe, in full detail, the preparation and the chemistry of POMB esters and the use of POMBOH as an *O*-nucleophile in the Mitsunobu reaction of secondary alcohols (Scheme 1).



Scheme 1.

Keywords: DDQ; Mitsunobu reaction; Prenyl ethers; Protecting groups; Ytterbium triflate.
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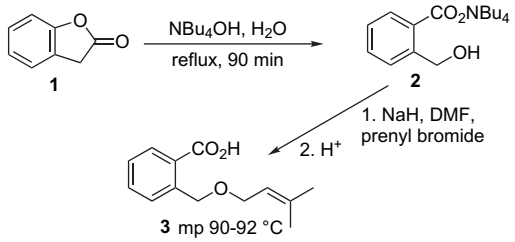
2. Results and discussion

2.1. Introduction of the 2-(prenyloxymethyl)benzoyl hydroxy protecting group

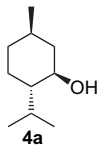
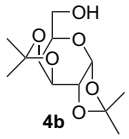
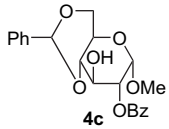
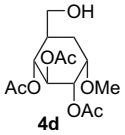
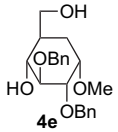
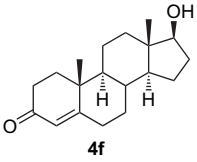
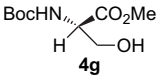
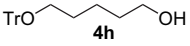
Our study commenced by the synthesis of the protecting agent 2-(prenyloxymethyl)benzoic acid (POMBOH) **3**. According to the procedure developed for the preparation of MTMOH,[6] the cheap and commercially available phthalide **1** was saponified by tetra-*N*-butylammonium hydroxide and the resulting oily salt **2**, successively treated by NaH and prenyl bromide in solution in DMF, gave crystalline POMBOH **3** in 65% yield (Scheme 2).



Scheme 2.

Diversely functionalized alcohols were esterified with 2-(prenyloxymethyl)benzoic acid at room temperature, in the presence of dicyclohexylcarbodiimide (DCC) and 4-dimethylaminopyridine (DMAP),[13] to yield esters **5a**–**5h** in excellent yields (Table 1). We next examined the efficacy of POMBOH as a partner in the Mitsunobu reaction on secondary alcohols of different steric and electronic environments. As seen in Table 2, POMBOH is a good substrate for the Mitsunobu reaction and exclusive formation of inverted esters is observed in excellent yields, even esters derived from sterically congested alcohols such as menthol (entry 3) or testosterone (entry 2). Comparison of our results with those of the literature data indicated that 2-(prenyloxymethyl)benzoic acid is notably more efficient as a oxygen nucleophile in the Mitsunobu reaction than benzoic acid (27% yield vs 85% yield in neomenthol ester (entry 3) under the same experimental conditions).[14]

Table 1. Esterification with POMBOH, DCC, and DMAP[a]

Entry	Substrate	Product	Yield (%)
1	 4a	**5a**	94
2	 4b	**5b**	92
3	 4c	**5c**	93
4	 4d	**5d**	92
5	 4e	**5e**	97
6	 4f	**5f**	90
7	 4g	**5g**	95
8	 4h	**5h**	94

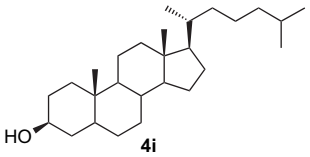
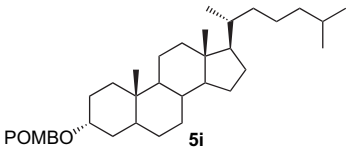
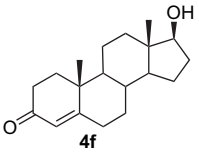
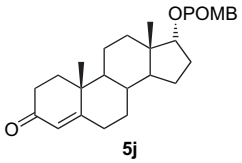
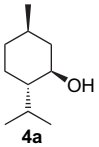
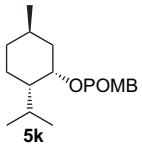
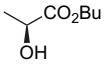
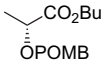
For entry 5, 2-fold of each reagent was added.
[a] Reaction conditions: ROH and POMBOH (1.2 equiv) in CH_2Cl_2 at 0 °C then DCC (1.3 equiv) and DMAP (0.2 equiv) at 0 °C to rt overnight.

2.2. Cleavage of the *O*-2-(prenyloxymethyl)benzoyl protecting group

We next studied the POMB removal using menthyl POMB ester **5a** as a model substrate (Table 3). Firstly, we tested the reaction conditions (I_2 or DDQ in CH_2Cl_2–H_2O) that we developed for the cleavage of prenyl ethers.[10] Thus, in the presence of 1.5 equiv of iodine, menthol was obtained in only 52% yield (Table 3, entry 1). HI formed during the deprenylation step induced very likely the lactonization.[10c] Exposure of **5a** to 1.5 equiv of DDQ led cleanly to the formation of the deprenylated compound **6**, accompanied by 3-methylbut-2-enal (entry 2, Table 3). The known acidity of DDQ in wet solvents is too weak to catalyze the cleavage of the ester of **6** via γ-lactonization.[15] Recently, Sharma and co-workers described a mild method of O-deprenylation using a catalytic amount of $Yb(OTf)_3$ (5 mol %) in nitromethane.[16] In the presence of 20 mol % of $Yb(OTf)_3 \cdot xH_2O$ in nitromethane, the ester **5a** was uncompletely deprenylated to give a mixture of **4a** and **6** along with two unidentified by-products (entry 3). Fortunately, in dichloromethane, $Yb(OTf)_3$ (20 mol %) promoted the removal of the POMB group of **4a** and lactone formation to afford menthol in 69% yield (entry 4). In our knowledge, it is the first example of a lactonization induced by $Yb(OTf)_3$. In order to check the efficiency of $Yb(OTf)_3$ as a catalyst for lactonization, the hydroxy ester **6** was stirred in dichloromethane in its presence (10 mol %). After 3 h, TLC showed the disappearance of the starting material and the exclusive formation of menthol and phthalide. Flash chromatography of the mixture gave menthol in 96% yield. $Sc(OTf)_3$ (10 mol %) was much less effective giving a small amount of **6** along with the starting material (entry 5).

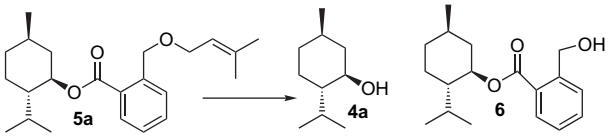
Having in hands a satisfactory two-step protocol (DDQ/$Yb(OTf)_3$) for the cleavage of the POMB group, we examined the generality of this method on diversely functionalized substrates and the results are listed in Table 4. A number of protecting groups such as acetyl, chloroacetyl,

Table 2. Mitsunobu inversion of secondary alcohols using POMBOH

Entry	Substrate	Time (h)	Temperature	Product	Yield (%)
1	 **4i**	1	rt	 **5i**	91
2	 **4f**	1	65 °C	 **5j**	85
3	 **4a**	2	rt	 **5k**	85
4	 **4l**	24	rt	 **5l**	87

benzoyl, benzyl, Boc, Fmoc, isopropylidene, levulinoyl groups are unaffected in the reaction conditions. Conversely, the benzylidene group was partially cleaved at the lactonization stage by $Yb(OTf)_3$ (entry 3). In addition of compound **4d**, methyl 2,3,6-tri-*O*-acetyl-α-D-glucopyranoside (8%) was also obtained resulting from the known propensity of the 4-*O*-acetyl to migrate in O-6 position in acid medium (entry 4).[17] As seen in Table 4 (entries 12–14), cleavage of axial POMB esters was quite sluggish, at the lactonization step, giving the desired alcohol in moderate to low yield along with elimination and/or rearrangement products.[18] Thus, treatment of the corresponding deprenylated product of epitestosterone POMBenzoate **5j** (entry 13) with 10 mol % of $Yb(OTf)_3$ for 24 h gave epitestosterone in 30% yield and a mixture of two rearranged products **8** and **9** (30%) in a ratio 7:3 (Fig. 1). The structure of **8** and **9** was established by 2D-NMR experiments. Compounds **8** and **9** arose from the migration of the angular methyl group in C-13 position, favorably disposed in antiperiplanar position to the POMB ester, followed by hydride elimination.[18c]

Table 3. Study of the removal of the POMB group for **5a**



Entry	Reagent (equiv)	Solvent(s)	Time (h)	**4a** (%)	**6** (%)
1	I_2 (1.5)	CH_2Cl_2	1.5	52	—
2	DDQ (1.5)	CH_2Cl_2–H_2O	6	—	94
3	$Yb(OTf)_3$ (0.2)	CH_3NO_2	48	—	—[a]
4	$Yb(OTf)_3$ (0.2)	CH_2Cl_2	24	69[b]	—
5	$Sc(OTf)_3$ (0.1)	CH_2Cl_2	24	—	30[c]

[a] Formation of a mixture of **4a** and **6** and less-polar by-products.
[b] Unidentified by-products formed.
[c] Unreacted starting material of 40% was isolated.

Neomenthol POMBenzoate **5k**, with the axially ester hindered by the adjacent isopropyl moiety on the same face, was very reluctant to our two-step procedure cleavage for the POMB group (entry 14). Indeed, exposure of the corresponding deprenylated compound of **5k**, obtained in only 60% yield, to 20 mol % of $Yb(OTf)_3$ for 7 days provided the desired neomenthol **4s** in only 10% yield.

3. Conclusion

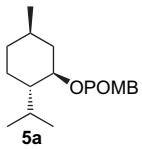
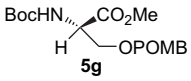
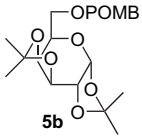
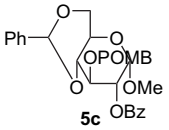
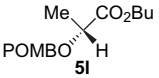
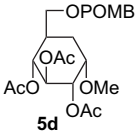
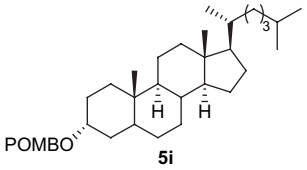
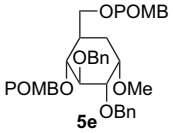
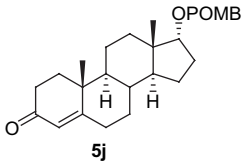
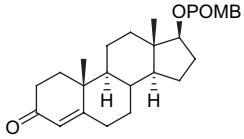
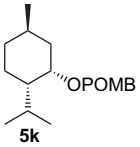
In summary, we have developed a new protecting group for alcohols: POMB group, which can be installed in high yields using 2-(prenyloxymethyl)benzoic acid, available in multigram quantities from phthalide. We have also shown that this acid is a valuable oxygen nucleophile in the Mitsunobu reaction even with sterically encumbered secondary alcohols. The reaction conditions for the removal of POMB group authorize the presence of a large number of functionalities but are to be improved for the cleavage of axial POMB esters.

4. Experimental section

4.1. General procedures

^1H NMR spectra were recorded in $CDCl_3$ (δ_H=7.25) at ambient probe temperature on a Bruker AC 200 (200 MHz) spectrometer. Data are presented as follows: chemical shift (in parts per million on the δ scale relative to δ_{TMS}=0), multiplicity (s=singlet, d=doublet, t=triplet, q=quadruplet, m=multiplet, br=broad), integration, coupling constant, and interpretation. ^{13}C NMR spectra were recorded at ambient probe temperature on a Bruker AC 200 (50.3 MHz) in $CDCl_3$, used as reference (δ_C=77.0). IR spectra were recorded on a Perkin–Elmer 298 spectrophotometer. Optical rotations were measured on a Perkin–Elmer 141 polarimeter

Table 4. Removal of POMB esters with DDQ/Yb(OTf)$_3$

Entry	Substrate	Product	Yield (%)	Entry	Substrate	Product	Yield (%)
1	 **5a**	**4a**	92[a,b]	7	 **5g**	**4g**	85
2	 **5b**	**4b**	86	8 9 10	 R=ClAc **5m** R=Lev **5n** R=Fmoc **5o**	**4m** **4n** **4o**	90 88 91
3	 **5c**	**4c**	60	11	 **5l**	**4p**	79
4	 **5d**	**4d**	79	12	 **5i**	**4q**	52
5	 **5e**	**4e**	75	13	 **5j**	**4r**	30
6	 **5f**	**4f**	90	14	 **5k**	**4s**	10

[a] For primary esters, 2 mol % of Yb(OTf)$_3$ was added and 10 mol % for secondary ones, except for substrates **5i** and **5k** for which 20 mol % were necessary.
[b] Reaction time: 6 h for deprenylation of all substrates, and 3 h for the lactonization step except for **5f** (7 h), **5i** (48 h), **5j** (24 h), and **5k** (7 days).
[c] Compound **7** (R=H) was prepared from **5h** in 90% yield.

at the sodium D line (598 nm). Melting points were determined on a Büchi 530 apparatus and are uncorrected. Combustion analyses were performed by 'Service de Microanalyse', CNRS, Solaize. Reagents and solvents were purified by standard means. Ether and tetrahydrofuran were distilled from sodium wire/benzophenone and stored under a nitrogen atmosphere. Dichloromethane, pyridine, and triethylamine were distilled from calcium hydride. Methanol was distilled from magnesium metal. All other chemicals were used as received.

4.2. 2-(Prenyloxymethyl)benzoic acid 3

A mixture of phthalide (4 g, 0.0298 mol) and tetra-*N*-butylammonium hydroxide in water (40% w/v, 20 mL, 0.031 mol) was heated at reflux for 90 min. The clear solution was cooled down, extracted with CH_2Cl_2 (3×40 mL), and the combined organic phases were washed with water (10 mL). The organic phase was dried (Na_2SO_4) and concentrated. The oily residue was dried under high vacuum at room temperature. To a solution of the ammonium salt (11.73 g) in DMF (40 mL), cooled to 0 °C, was added by portions NaH (60% dispersion in mineral oil, 3.6 g, 3 equiv). The reaction mixture was allowed to warm up to room temperature and stirred for 1 h. The reaction mixture was cooled (0 °C) and prenyl bromide (4.2 mL, 1.2 equiv) was added dropwise. The mixture was stirred at room temperature for 4 h, cooled (0 °C), and MeOH was carefully added followed by H_2O (140 mL). The solution was extracted with ether (3×40 mL). To the well-stirred aqueous phase, cooled to 0 °C, was added dropwise 2 N HCl solution until pH 2 and the resulting suspension was extracted with ether (2× 125 mL). The combined organic phases were dried (Na_2SO_4) and concentrated. Crystallization of the residue in hexane gave **3** (4.3 g, 65% yield) as colorless crystals, mp 90–92 °C. IR (KBr): 1680 cm^{-1}. ^{1}H NMR: 1.70 (s, 3H, Me), 1.78 (s, 3H, Me), 4.13 (d, 2H, J=6.95 Hz, CH_2–CH=C), 4.91 (s, 2H, CH_2Ar), 5.46 (br t, 1H, J=7 Hz, CH=CMe$_2$),

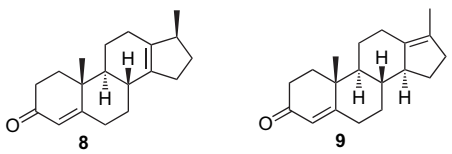

8 **9**

Figure 1.

7.4 (t, 1H, *J*=7.9 Hz, Ar), 7.58 (t, 1H, *J*=7.8 Hz, Ar), 7.68 (d, 1H, *J*=8 Hz, Ar), 8.09 (d, 1H, *J*=7.8 Hz, Ar), 9.7 (br s, 1H, CO_2H). ^{13}C NMR: 18.1, 25.9, 67.4, 70.2, 120.8, 127.6, 127.7, 128.21, 131.7, 133.2, 137.7, 141.3, 172.2. Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32; O, 21.79. Found: C, 70.64; H, 7.17; O, 21.99.

4.3. General procedure for the esterification of alcohols 4a–4h

To a cooled (0 °C) solution of alcohol (1 mmol) and 2-(prenyloxymethyl)benzoic acid **3** (0.264 g, 1.2 equiv) in CH_2Cl_2 (4 mL) were successively added DCC (0.268 g, 1.3 equiv) and DMAP (0.018 g, 0.15 equiv). After stirring the mixture overnight at room temperature, the precipitate of urea was filtered and the filtrate was evaporated. The residue was purified by flash chromatography on silica gel.

4.3.1. (1*R*,2*S*,5*R*)-Menthyl 2-(prenyloxymethyl)benzoate 5a. Ether–petroleum ether (1:9), 94% yield, oil, $[\alpha]_D^{20}$ −61 (*c* 1.7, $CHCl_3$). IR (film): 1710, 1600, 1570 cm^{-1}. ^{1}H NMR: 0.81 (d, 3H, *J*=6.9 Hz, Me), 0.92 (d, 3H, *J*=7 Hz, Me), 0.95 (d, 3H, *J*=6.4 Hz, Me), 0.96–1.2 (m, 3H), 1.5–1.62 (m, 4H), 1.69 (s, 3H, Me), 1.77 (s, 3H, Me), 1.9–2.1 (m, 2H), 4.1 (d, 2H, *J*=6.84 Hz, CH_2–CH=C), 4.91 (s, 2H, Ar), 4.93 (td, 1H, *J*=4.2 and 10.4 Hz, CHOCO), 5.45 (br t, 1H, *J*=6.9 Hz, CH=CMe_2), 7.33 (t, 1H, *J*=7.8 Hz, Ar), 7.52 (br t, 1H, *J*=7.8 Hz, Ar), 7.7 (d, 1H, *J*=7.7 Hz, Ar), 7.92 (br d, 1H, *J*=7.8 Hz, Ar). ^{13}C NMR: 16.3, 18.1, 20.9, 22.1, 20.9, 23.5, 25.9, 26.4, 31.6, 34.4, 41.1, 47.3, 67.4, 69.9, 74.8, 121.3, 126.8, 127.6, 130.2, 132.1, 136.8, 141.2, 166.8. Anal. Calcd for $C_{23}H_{34}O_3$: C, 77.05; H, 9.56; O, 13.39. Found: C, 77.02; H, 9.72; O, 13.26.

4.3.2. 6-*O*-[2-(Prenyloxymethyl)benzoyl]-1,2,3,4-di-*O*-isopropylidene-α-D-galactopyranose 5b. Ether–petroleum ether (1:4), 92% yield, oil, $[\alpha]_D^{20}$ −45.5 (*c* 1.9, $CHCl_3$). IR (film): 1715, 1670, 1600, 1570 cm^{-1}. ^{1}H NMR: 1.31 (s, 3H, Me), 1.33 (s, 3H, Me), 1.46 (s, 3H, Me), 1.66 (s, 3H, Me), 1.49 (s, 3H, Me), 1.74 (s, 3H, Me), 4.05 (d, 2H, *J*=6.8 Hz, CH_2–CH=C), 4.16 (m, 1H, H-5), 4.3 (dd, 1H, *J*=1.8 and 7.85 Hz, H-4), 4.33 (dd, 1H, *J*=2.4 and 5 Hz, H-2), 4.38 (dd, 1H, *J*=7.3 and 11.5 Hz, H-6a), 4.49 (dd, 1H, *J*=5 and 11.5 Hz, H-6b), 4.63 (dd, 1H, *J*=2.4 and 7.85 Hz, H-3), 4.9 (s, 2H, CH_2Ar), 5.41 (br t, 1H, *J*=6.8, C*H*=CMe_2), 5.55 (d, 1H, *J*=5 Hz, H-1), 7.29 (t, 1H, *J*=7.7 Hz, Ar), 7.49 (td, 1H, *J*=1.2 and 7.7 Hz, Ar), 7.66 (d, 1H, *J*=7.7 Hz, Ar), 7.93 (dd, 1H, *J*=1.2 and 7.7 Hz, Ar). ^{13}C NMR: 18.1, 24.5, 25.0, 25.8, 26.0, 26.1, 64.0, 66.1, 67.3, 70.0, 70.5, 70.8, 71.2, 96.4, 108.8, 109.7, 121.3, 126.8, 127.5, 128.1, 130.6, 132.3, 136.8, 141.3, 167.0. Anal. Calcd for $C_{25}H_{34}O_8$: C, 64.92; H, 7.41; O, 27.27. Found: C, 65.17; H, 7.39; O, 27.44.

4.3.3. Methyl 2-*O*-benzoyl-3-*O*-[2-(prenyloxymethyl)-benzoyl]-4,6-*O*-benzylidene-α-D-glucopyranoside 5c. Ether–petroleum ether (1:2), 93% yield, glass, $[\alpha]_D^{20}$ +72 (*c* 0.7, $CHCl_3$). IR (neat): 1720, 1600, 1580 cm^{-1}. ^{1}H NMR: 1.63 (s, 3H, Me), 1.75 (s, 3H, Me), 3.46 (s, 3H, OMe), 3.83–3.96 (m, 4H, 2H-6, CH_2–CH=), 4.11 (td, 1H, *J*=4.5 and 9.7 Hz, H-5), 4.4 (dd, 1H, *J*=4.5 and 10.1 Hz, H-4), 4.76 (d, 1H, *J*=14.9 Hz, CHaAr), 4.85 (d, 1H, *J*=14.9 Hz, CHbAr), 5.2 (d, 1H, *J*=3.7 Hz, H-1), 5.27 (dd, 1H, *J*=3.7 and 9.7 Hz, H-2), 5.36 (br t, 1H, *J*=6.8 Hz, C*H*=CMe_2), 5.61 (s, 1H, C*H*Ph), 6.06 (t, 1H, *J*=9.65 Hz, H-3), 7.20–7.68 (m, 12H, Ar), 7.8 (dd, 1H, *J*=1 and 7.8 Hz, Ar), 8.07 (d, 1H, *J*=7.8 Hz, Ar). ^{13}C NMR: 18.1, 25.8, 55.6, 62.6, 67.3, 69.0, 69.5, 69.7, 72.6, 79.5, 97.3, 101.7, 121.2, 126.2 (3C), 126.7, 127.2, 127.8, 128.3 (2C), 128.5 (2C), 129.2, 130.1 (3C), 132.4, 133.5, 136.8, 137.0, 141.3, 166.0, 166.2. Anal. Calcd for $C_{34}H_{36}O_9$: C, 69.37; H, 6.16; O, 24.46. Found: C, 69.05; H, 6.22; O, 24.63.

4.3.4. Methyl 2,3,4-tri-*O*-acetyl-6-*O*-[2-(prenyloxymethyl)benzoyl]-α-D-glucopyranoside 5d. Ether–petroleum ether (3:1), 92% yield, $[\alpha]_D^{20}$ +104 (*c* 0.9, $CHCl_3$). IR (neat): 1750, 1720, 1670, 1600, 1580 cm^{-1}. ^{1}H NMR: 1.67 (s, 3H, Me), 1.76 (s, 3H, Me), 2.0 (s, 3H, Me), 2.02 (s, 3H, Me), 2.07 (s, 3H, Me), 3.42 (s, 3H, OMe), 4.07 (d, 2H, *J*=6.7 Hz, CH_2–CH=), 4.14 (m, 1H, H-5), 4.34 (dd, 1H, *J*=4.5 and 12.1 Hz, H-6a), 4.42 (dd, 1H, *J*=3.1 and 12.1 Hz, H-6b), 4.9 (s, 2H, CH_2Ar), 4.91 (dd, 1H, *J*=3.7 and 9.6 Hz, H-2), 4.96 (d, 1H, *J*=3.7 Hz, H-1), 5.14 (t, 1H, *J*=9.8 Hz, H-4), 5.42 (br t, 1H, *J*=6.8 Hz, CH=CMe_2), 5.51 (t, 1H, *J*=9.6 Hz, H-3), 7.33 (t, 1H, *J*=7.8 Hz, Ar), 7.53 (td, 1H, *J*=1.3 and 7.7 Hz, Ar), 7.69 (d, 1H, *J*=7.2 Hz, Ar), 7.97 (dd, 1H, *J*=1.2 and 7.8 Hz, Ar). ^{13}C NMR: 18.1, 20.7 (3C), 25.8, 55.5, 62.6, 67.2, 67.3, 69.0, 69.9, 70.2, 70.9, 96.8, 121.2, 126.9, 127.5, 127.6, 130.5, 132.6, 137.0, 141.7, 166.5, 169.6, 170.1, 170.2. Anal. Calcd for $C_{26}H_{34}O_{11}$: C, 59.76; H, 6.56; O, 33.68. Found: C, 59.96; H, 6.55; O, 33.46.

4.3.5. Methyl 2,3-di-*O*-benzyl-4,6-di-*O*-[2-(prenyloxymethyl)benzoyl]-α-D-glucopyranoside 5e. Dichloromethane, 97% yield, glass, $[\alpha]_D^{20}$ +14.6 (*c* 0.7, $CHCl_3$). IR (neat): 1720, 1670, 1600, 1570 cm^{-1}. ^{1}H NMR: 1.66 (s, 6H, 2Me), 1.74 (s, 6H, 2Me), 3.47 (s, 3H, OMe), 3.7 (dd, 1H, *J*=3.5 and 9.6 Hz, H-2), 4.02–4.2 (m, 6H, 2CH_2–CH=C, H-3, H-5), 4.33 (dd, 1H, *J*=5 and 12 Hz, H-6a), 4.47 (dd, 1H, *J*=2.4 and 12 Hz, H-6b), 4.62–4.71 (m, 3H, CH_2Ph, H-1), 4.82–4.91 (m, 6H, 2CH_2Ar, CH_2Ph), 5.36 (t, 1H, *J*=9.8 Hz, H-4), 5.38–5.46 (m, 2H, 2CH=CMe_2), 7.3–7.76 (m, 16H, Ar), 7.88 (d, 1H, *J*=7.8 Hz, Ar), 7.98 (d, 1H, *J*=7.7 Hz, Ar). ^{13}C NMR: 18.1 (2C), 25.8 (2C), 63.2, 67.3, 67.4, 67.7, 69.9 (2C), 70.5, 73.7, 75.6, 79.1, 79.8, 98.3, 121.2 (2C), 126.7, 126.8, 126.9, 127.4, 127.5, 127.6 (2C), 128.0 (2C), 128.2 (6C), 128.3 (2C), 128.6 (2C), 130.4, 130.6, 132.8, 137.0, 137.9, 138.0, 141.6, 142.3, 165.3, 166.5. Anal. Calcd for $C_{47}H_{54}O_{10}$: C, 72.47; H, 6.99; O, 20.54. Found: C, 72.62; H, 7.0; O, 20.28.

4.3.6. Testosterone 2-(prenyloxymethyl)benzoate 5f. Ether–petroleum ether (3:2), 90% yield, white solid, mp 77–79 °C (hexane), $[\alpha]_D^{20}$ +113.3 (*c* 1.8, $CHCl_3$). IR (KBr): 1720, 1670, 1613, 1600, 1580 cm^{-1}. ^{1}H NMR: 0.96–2.07 (m, 26H), 2.27–2.44 (m, 5H), 4.08 (d, 2H, *J*=6.8 Hz, CH_2–CH=), 4.85 (t, 1H, *J*=8.7 Hz, CHOPOMB), 4.9 (s, 2H, CH_2Ph), 5.43 (br t, 1H, *J*=6.7 Hz, CH=CMe_2), 5.74 (s, 1H, COCH=C), 7.31 (t, 1H, *J*=7.7 Hz, Ar), 7.52 (t, 1H, *J*=7.6 Hz, Ar), 7.7 (d, 1H, *J*=7.8 Hz, Ar), 7.93 (d, 1H, *J*=7.6 Hz). ^{13}C NMR: 12.5, 17.5, 18.1, 20.6, 23.6, 25.9, 27.7, 31.5, 32.8, 34.0, 35.5, 35.7, 36.9, 38.7, 42.8, 50.3, 53.8, 67.3, 70.0, 83.2, 121.2, 124.0, 126.8, 127.6, 128.6, 130.4, 132.2, 137.0, 141.2, 167.1, 170.9, 199.5. Anal. Calcd for $C_{32}H_{42}O_4$: C, 78.33; H, 8.63; O, 13.04. Found: C, 78.07; H, 8.58; O, 13.06.

4.3.7. (*S*)-2-*tert*-Butyloxycarbonylamino-3-[2-(prenyloxymethyl)benzoyloxy]propionic acid methyl ester 5g. Ether–petroleum ether (1:2), 95% yield, white solid, mp 63–64 °C, $[\alpha]_D^{20}$ +11.2 (*c* 1.2, $CHCl_3$). IR (KBr): 1748, 1732, 1720, 1600, 1570 cm^{-1}. ^1H NMR: 1.45 (s, 9H, *t*-Bu), 1.65 (s, 3H, Me), 1.75 (s, 3H, Me), 3.78 (s, 3H, OMe), 4.05 (d, 2H, *J*=6.85 Hz, C*H*$_2$–CH=C), 4.6 (d, 2H, *J*=3.4 Hz, CH_2OCO), 4.67 (m, 1H, C*H*CO_2Me), 4.76 (d, 1H, *J*=14.4 Hz, CHaAr), 4.91 (d, 1H, *J*=14.2 Hz, CHbAr), 5.41 (br t, 1H, *J*=6.85 Hz, CH=CMe_2), 5.74 (d, 1H, *J*=7.95 Hz, NH), 7.33 (td, 1H, *J*=1.2 and 7.9 Hz, Ar), 7.52 (td, 1H, *J*=1.2 and 7.8 Hz, Ar), 7.61 (d, 1H, *J*=7.3 Hz, Ar), 7.88 (d, 1H, *J*=7.4 Hz, Ar). ^{13}C NMR: 18.1, 27.7, 28.3 (3C), 52.8, 53.0, 65.0, 65.9, 69.9, 80.3, 121.1, 127.2, 127.8, 128.3, 130.8, 132.6, 137.0, 141.1, 155.4, 166.7, 170.5. Anal. Calcd for $C_{22}H_{31}O_7$: C, 62.69; H, 7.41; N, 3.32; O, 26.57. Found: C, 62.63; H, 7.53; N, 3.37; O, 26.47.

4.3.8. [5-(Triphenylmethyloxy)-1-pentyl] 2-(prenyloxymethyl)benzoate 5h. Ether–petroleum ether (1:8), 94% yield, oil. IR (film): 1705, 1670, 1600, 1570 cm^{-1}. ^1H NMR: 1.21–1.64 (m, 2H, CH_2), 1.70 (s, 3H, Me), 1.71–1.79 (m, 7H, 2CH_2, Me), 3.13 (t, 2H, *J*=6.1 Hz, C*H*$_2$OTr), 4.11 (d, 2H, *J*=6.85 Hz, C*H*$_2$–CH=C), 4.31 (t, 2H, *J*=6.4 Hz, CH_2OPOMB), 4.9 (s, 2H, CH_2Ar), 5.47 (br t, 1H, *J*=6.85 Hz, CH=CMe_2), 7.20–7.58 (m, 17H, Ar), 7.72 (d, 1H, *J*=7.8 Hz, Ar), 7.96 (dd, 1H, *J*=1.1 and 7.7 Hz, Ar). ^{13}C NMR: 18.1, 22.7, 25.9, 28.7, 29.8, 63.3, 64.9, 67.4, 70.0, 86.4, 121.3, 126.8 (3C), 127.7 (7C), 128.5, 128.7 (7C), 130.4, 132.2, 137.0, 141.2, 144.5 (3C), 167.2. Anal. Calcd for $C_{37}H_{40}O_4$: C, 80.99; H, 7.35; O, 11.66. Found: C, 80.72; H, 7.47; O, 11.30.

4.4. General procedure for the Mitsunobu reaction

To a solution of the secondary alcohol (1 mmol), triphenylphosphine (1.05 g, 4 mmol), and 2-(prenyloxymethyl)benzoic acid **3** (0.88 g, 4 mmol) in dry THF (6 mL), cooled to 0 °C, was added dropwise diisopropyl azodicarboxylate (DIAD) (0.75 mL, 3.9 mmol). The reaction mixture was allowed to warm up to room temperature and stirred for the reaction time and at the temperature indicated in Table 2. The mixture was evaporated to dryness and the residue was purified by flash chromatography on silica gel.

4.4.1. 3-α-Cholestanol 2-(prenyloxymethyl)benzoate 5i. Ether–petroleum ether (5:95), 91% yield, oil, $[\alpha]_D^{20}$ +19.1 (*c* 1.6, $CHCl_3$). IR (film): 1720, 1600, 1580 cm^{-1}. ^1H NMR: 0.65 (s, 3H, Me), 0.75–2.05 (m, 49H), 4.11 (d, 2H, *J*=6.7 Hz, C*H*$_2$–CH=C), 4.94 (s, 2H, C*H*$_2$Oprenyl), 5.28 (br s, 1H, CHOPOMB), 5.45 (br t, 1H, *J*=6.7 Hz, CH=CMe_2), 7.35 (t, 1H, *J*=7.5 Hz, Ar), 7.53 (dt, 1H, *J*=1.2 and 7.6 Hz, Ar), 7.72 (d, 1H, *J*=7.7 Hz, Ar), 7.97 (dd, 1H, *J*=1.2 and 7.7 Hz, Ar). ^{13}C NMR: 11.5, 12.1, 18.2, 18.7, 20.9, 22.6, 22.8, 23.9, 24.2, 25.8, 26.3, 28.1, 28.3, 32.0, 33.1, 33.4, 35.5, 35.8 (2C), 35.9, 36.2, 39.5, 40.1, 40.6, 42.6, 54.5, 56.4, 56.6, 67.5, 70.2, 71.0, 121.3, 126.8, 127.5, 129.1, 130.5, 132.1, 136.8, 141.1, 166.6. Anal. Calcd for $C_{40}H_{62}O_3$: C, 81.3; H, 10.58; O, 8.12. Found: C, 81.39; H, 10.46; O, 7.95.

4.4.2. 17-Epitestosterone 2-(prenyloxymethyl)benzoate 5j. Petroleum ether–ethyl acetate (4:1), 85% yield, oil, $[\alpha]_D^{20}$ +18.4 (*c* 1.2, $CHCl_3$). IR (film): 1705, 1670, 1610 cm^{-1}. ^1H NMR: 0.88 (s, 3H, Me), 1.2 (s, 3H, Me), 1.16–1.89 (m, 14H), 1.67 (s, 3H, Me), 1.76 (s, 3H, Me), 2.3–2.44 (m, 5H), 4.08 (d, 2H, *J*=6.8 Hz, C*H*$_2$–CH=C), 4.89 (s, 2H, CH_2O), 5.05 (d, 1H, *J*=6 Hz, CHOPOMB), 5.43 (br t, 1H, *J*=6.7 Hz, CH=CMe_2), 5.74 (br s, 1H, COCH=C), 7.33 (t, 1H, *J*=7.7 Hz, Ar), 7.52 (t, 1H, *J*=7.6 Hz, Ar), 7.69 (d, 1H, *J*=7.3 Hz, Ar), 7.89 (dd, 1H, *J*=1.2 and 7.7 Hz, Ar). ^{13}C NMR: 16.7, 17.5, 18.1, 20.5, 24.8, 25.8, 30.1, 31.9, 32.3, 32.9, 34.0, 35.7, 35.9, 38.7, 44.9, 50.0, 53.7, 67.4, 70.0, 82.3, 121.2, 123.9, 126.8, 127.7, 128.7, 130.1, 132.2, 136.8, 141.2, 166.6, 171.0, 199.4. Anal. Calcd for $C_{32}H_{42}O_4$: C, 78.33; H, 8.63; O, 13.04. Found: C, 77.91; H, 8.73; O, 13.34.

4.4.3. Neomenthyl 2-(prenyloxymethyl)benzoate 5k. Petroleum ether–ether (95:5), 85% yield, oil, $[\alpha]_D^{20}$ +25.8 (*c* 2.4, $CHCl_3$). ^1H NMR: 0.78 (d, 3H, *J*=6.4 Hz, Me), 0.84 (d, 3H, *J*=6.7 Hz, Me), 0.92 (d, 3H, *J*=6.6 Hz, Me), 0.92–1.2 (m, 2H), 1.48 (s, 3H, Me), 1.60 (s, 3H, Me), 1.44–1.70 (m, 6H), 2.15 (dq, 1H, *J*=2.5 and 14 Hz), 4.09 (d, 2H, *J*=6.6 Hz, C*H*$_2$–CH=C), 5.21 (s, 2H, C*H*$_2$Ar), 5.54 (br t, 1H, *J*=6.7 Hz, CH=CMe_2), 5.60 (br s, 1H, CHOPOMB), 7.06 (t, 1H, *J*=7.7 Hz, Ar), 7.25 (t, 1H, *J*=7.7 Hz, Ar), 7.97 (d, 1H, *J*=7.6 Hz, Ar), 8.16 (d, 1H, *J*=7.7 Hz, Ar). ^{13}C NMR: 18.1, 20.9, 21.1, 22.3, 25.6, 25.8, 26.9, 29.4, 34.9, 39.3, 47.2, 67.4, 70.0, 71.7, 121.3, 126.7, 127.5, 128.8, 130.4, 132.1, 136.8, 141.4, 166.4. Anal. Calcd for $C_{23}H_{34}O_3$: C, 77.05; H, 9.56; O, 13.39. Found: C, 77.11; H, 9.58; O, 13.29.

4.4.4. (*R*)-2-[2-(Prenyloxymethyl)benzoyloxy]propanoic acid butyl ester 5l. Ether–petroleum ether (1:9), 87% yield, oil, $[\alpha]_D^{20}$ +4.35 (*c* 1.2, $CHCl_3$). IR (film): 1745, 1715, 1670, 1595, 1570 cm^{-1}. ^1H NMR: 0.93 (t, 3H, *J*=7.2 Hz, Me), 1.38 (sextuplet, 2H, *J*=7.2 Hz, C*H*$_2$–Me), 1.58–1.64 (m, 5H, CH_2, Me), 1.68 (s, 3H, Me), 1.76 (s, 3H, Me), 4.13 (d, 2H, *J*=6.74 Hz, C*H*$_2$–CH=CMe_2), 4.19 (t, 2H, *J*=6.8 Hz, CO_2CH_2), 4.9 (s, 2H, C*H*$_2$Ar), 5.30 (q, 1H, *J*=7.1 Hz, C*H*CO_2Bu), 5.44 (br t, 1H, *J*=6.7 Hz, CH=CMe_2), 7.34 (t, 1H, *J*=7.4 Hz, Ar), 7.55 (t, 1H, CHCO_2Bu), 7.64 (d, 1H, *J*=7.8 Hz, Ar), 8.03 (d, 1H, *J*=7.7 Hz, Ar). ^{13}C NMR: 13.7, 17.1, 18.1, 19.0, 25.8, 30.6, 65.2, 67.3, 69.2, 69.8, 121.0, 126.8, 127.4, 127.5, 130.7, 132.6, 136.9, 141.6, 166.4, 170.9. Anal. Calcd for $C_{20}H_{28}O_5$: C, 68.94; H, 8.10; O, 22.96. Found: C, 69.10; H, 8.19; O, 22.72.

4.5. Preparation of other functionalized substrates bearing the POMB group

4.5.1. 2-(Prenyloxymethyl)benzoic acid 5-hydroxypentyl ester 7. A solution of compound **5h** (1.2 g, 2.2 mmol) in 90% acetic acid was stirred at room temperature for 7 h. After evaporation in vacuo, the residue was purified by flash chromatography on silica gel (ether–petroleum ether, 2:1) to give the desired ester **7** in 90% yield, obtained as an oil. IR (film): 3410, 1714, 1600, 1579 cm^{-1}. ^1H NMR: 1.42–1.63 (m, 2H, CH_2), 1.67 (s, 3H, Me), 1.75–1.86 (m, 8H, 2CH_2, Me, OH), 3.65 (t, 2H, *J*=6.1 Hz, C*H*$_2$OH), 4.07 (d, 2H, *J*=6.85 Hz, C*H*$_2$–CH=C), 4.3 (t, 2H, *J*=6.5 Hz, CH_2OPOMB), 4.9 (s, 2H, C*H*$_2$Ar), 5.42 (br t, 1H, *J*=6.8 Hz, CH=CMe_2), 7.31 (t, 1H, *J*=7.7 Hz, Ar), 7.51 (td, 1H, *J*=1.1 and 7.6 Hz, Ar), 7.67 (d, 1H, *J*=7.7 Hz, Ar),

7.92 (dd, 1H, J=1.1 and 7.8 Hz, Ar). ^{13}C NMR: 18.1, 22.4, 25.8, 28.6, 32.3, 62.6, 64.9, 67.3, 70.0, 121.1, 126.9, 127.7, 128.5, 130.4, 132.2, 137.0, 141.1, 167.3. Anal. Calcd for $C_{18}H_{26}O_4$: C, 70.56; H, 8.55; O, 20.89. Found: C, 70.83; H, 8.54; O, 20.63.

4.5.2. 1,5-Pentanediol chloroacetyl 2-(prenyloxymethyl)-benzoyl ester 5m. To a solution of compound **7** (0.3 g, 0.98 mmol) in CH_2Cl_2 (5 mL) were successively added Et_3N (0.4 mL, 3 equiv), DMAP (0.015 g, 0.12 equiv), and chloroacetic anhydride (0.25 g, 1.5 equiv). The solution was stirred for 30 min at room temperature, diluted with ether, and successively washed with water, 2 N HCl solution, and again with water. The organic phase was dried (Na_2SO_4) and evaporated. Purification of the residue on silica gel (ether–petroleum ether, 1:2) gave the diester **5m** (0.342 g, 91% yield) as a liquid. IR (film): 1750, 1710, 1670, 1600, 1570 cm^{-1}. ^{1}H NMR: 1.48–1.60 (m, 2H, CH_2), 1.68 (s, 3H, Me), 1.72–1.88 (m, 7H, $2CH_2$, Me), 4.05 (m, 2H, CH_2Cl), 4.07 (d, 2H, J=6.8 Hz, CH_2–CH=C), 4.22 (t, 2H, J=6.4 Hz, CH_2OClAc), 4.3 (t, 2H, J=6.4 Hz, CH_2OPOMB), 4.9 (s, 2H, CH_2Ph), 5.43 (br t, 1H, J=6.85 Hz, CH=CMe_2), 7.32 (td, 1H, J=1.2 and 7.8 Hz, Ar), 7.52 (td, 1H, J=1.3 and 7.6 Hz, Ar), 7.68 (d, 1H, J=7.7 Hz, Ar), 7.92 (dd, 1H, J=1.2 and 7.8 Hz). ^{13}C NMR: 18.1, 22.5, 25.8, 28.1, 28.3, 40.9, 64.5, 66.0, 67.3, 70.0, 121.2, 126.9, 127.7, 128.4, 130.3, 132.3, 137.0, 141.2, 167.2, 167.3. Anal. Calcd for $C_{20}H_{27}ClO_5$: C, 62.74; H, 7.11; Cl, 9.26; O, 20.89. Found: C, 62.99; H, 7.18; Cl, 9.24; O, 20.59.

4.5.3. 1,5-Pentanediol 4-oxopentanoyl 2-(prenyloxymethyl)benzoyl ester 5n. To a cooled (0 °C) solution of compound **7** (0.24 g, 0.78 mmol) in CH_2Cl_2 (4 mL) containing levulinic acid (0.11 g, 1.2 equiv) were added dicyclohexylcarbodiimide (0.21 g, 1.3 equiv) and 4-dimethylaminopyridine (0.02 g, 0.2 equiv). After stirring overnight at room temperature, dicyclohexylurea was filtered and the filtrate was evaporated. Flash chromatography of the residue on silica gel (ether–petroleum ether, 1:1) afforded **5n** as a liquid (0.302 g, 96% yield). IR (film): 1720, 1600, 1570 cm^{-1}. ^{1}H NMR: 1.47–1.63 (m, 2H, CH_2), 1.67 (s, 3H, Me), 1.68–1.86 (m, 7H, $2CH_2$, Me), 2.17 (s, 3H, Me), 2.55 (t, 2H, J=6.2 Hz, CH_2CO), 2.73 (t, 2H, J=6.2 Hz, CH_2CH_2CO), 4.07 (d, 2H, J=6.7 Hz, CH_2–CH=C), 4.09 (t, 2H, J=6.5 Hz, CH_2OLev), 4.28 (t, 2H, J=6.5 Hz, CH_2OPOMB), 4.9 (s, 2H, CH_2Ph), 5.42 (br t, 1H, J=6.8 Hz, CH=CMe_2), 7.31 (t, 1H, J=7.7 Hz, Ar), 7.51 (dt, 1H, J=1.2 and 7.7 Hz, Ar), 7.67 (d, 1H, 7.7 Hz, Ar), 7.91 (dd, 1H, J=1.1 and 7.7 Hz, Ar). ^{13}C NMR: 18.1, 22.6, 25.8, 28.0, 28.3, 28.4, 29.7, 38.0, 64.4, 64.7, 67.3, 69.9, 121.2, 126.8, 127.7, 128.4, 130.3, 132.2, 137.0, 141.2, 167.2, 172.8, 206.6. Anal. Calcd for $C_{23}H_{32}O_6$: C, 68.29; H, 7.97; O, 23.73. Found: C, 68.47; H, 7.96; O, 23.56.

4.5.4. 9*H*-Fluoren-9-yl-methyl 5-[2-(prenyloxymethyl)-benzoyloxy]pentyl carbonate 5o. To a solution of compound **7** (0.27 g, 0.9 mmol) in a mixture of CH_2Cl_2–pyridine (4:1, 5 mL) was added 9-fluorenylmethyl chloroformate (0.28 g, 1.2 equiv). The solution was stirred for 1 h at room temperature, diluted with ether, washed with water, 2 N HCl solution, and again with water. The organic phase was dried (Na_2SO_4) and evaporated. Flash chromatography of the residue (ether–petroleum ether, 1:3) gave **5o** (0.432 g, 96% yield) as a viscous oil. IR (film): 1735, 1710, 1670, 1595, 1570 cm^{-1}. ^{1}H NMR: 1.2–1.65 (m, 2H, CH_2), 1.7 (s, 3H, Me), 1.78–1.91 (m, $2CH_2$, Me), 4.11 (d, 2H, J=6.8 Hz, CH_2–CH=C), 4.23 (t, 2H, J=6.4 Hz, CH–CH_2OCO), 4.29 (t, 1H, J=7.4 Hz, CH–CH_2OCO), 4.34 (t, 2H, J=6.3 Hz, CH_2OPMOB), 4.43 (d, 2H, J=7.2 Hz, CH_2OCOO), 4.93 (s, 2H, CH_2Ph), 5.46 (br t, 1H, J=6.8 Hz, CH=CMe_2), 7.29–7.80 (m, 11H, Ar), 7.96 (dd, 1H, J=1.2 and 7.7 Hz, Ar). ^{13}C NMR: 18.1, 22.5, 25.9, 28.4 (2C), 46.8, 64.7, 67.4, 68.0, 69.8, 70.0, 120.1 (2C), 121.2, 125.2 (2C), 126.9, 127.2 (3C), 127.4, 127.9, 128.4 (2C), 130.4, 132.3, 137.0, 141.2, 141.3, 143.5 (2C), 155.3, 167.2. Anal. Calcd for $C_{33}H_{36}O_5$: C, 74.98; H, 6.86; O, 18.16. Found: C, 74.77; H, 6.86; O, 18.38.

4.6. General procedure for the cleavage of the POMB group

To a solution of the POMB ester (1 mmol) in CH_2Cl_2–H_2O (9:1, 10 mL) was added dichlorodicyanoquinone (DDQ) (0.34 g, 1.5 equiv). After stirring for 6 h at room temperature, TLC revealed the absence of the starting material and the presence of two more polar compounds than the POMB ester: its corresponding 2-(hydroxymethyl)benzoate and 3,3-dimethyl acrolein. Sodium bicarbonate powder was added and stirring was continued for 10 min. The yellow phase was separated from the gum, which was washed twice with CH_2Cl_2. The combined organic phases were concentrated to a volume of about 10 mL and passed through a pad of silica gel (15 g) and eluted with a mixture of petroleum ether–ether (1:3). After evaporation of solvents, the residue was dissolved in CH_2Cl_2 (6 mL) and $Yb(OTf)_3\cdot xH_2O$ (2–20 mol % depending on the substrate) was added. After stirring at room temperature for a reaction time indicated in Table 4, saturated $NaHCO_3$ was added and stirring was continued for 5 min. After concentration, the residue was purified by flash chromatography on silica gel.

4.6.1. (1*R*,2*S*,5*R*)-Menthol 4a. Petroleum ether–ether (2:1), 92% yield, solid, mp 42–44 °C, $[\alpha]_D^{20}$ −51 (c 2.8, EtOH) (lit.[19] mp 41–43 °C, $[\alpha]_D$ −50 (10% alcoholic solution)). NMR data were in accordance with those of an authentic sample.

4.6.2. 1,2,3,4-Di-*O*-isopropylidene-α-D-galactopyranose 4b. Ether–petroleum ether (3:1), 86% yield, oil, $[\alpha]_D^{19}$ −57 (c 1.2, $CHCl_3$) (lit.[20] $[\alpha]_D$ −55 (c 3.5, $CHCl_3$)). Its spectroscopic data were in accordance with those of an authentic sample.

4.6.3. Methyl 4,6-*O*-benzylidene-2-*O*-benzoyl-α-D-glucopyranoside 4c. Ether–petroleum ether (1:1), 60% yield, solid, mp 167–169 °C, $[\alpha]_D^{20}$ +106 (c 0.8, $CHCl_3$) (lit.[21] mp 169–170 °C, $[\alpha]_D^{21}$ +107 (c 1.3, $CHCl_3$)). Spectroscopic data were in agreement with those of an authentic sample.

4.6.4. Methyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranoside 4d. Elution with ether gave first methyl 2,3,6-tri-*O*-acetyl-α-D-glucopyranoside (9% yield), syrup, $[\alpha]_D^{20}$ +99 (c 3.5, $CHCl_3$) (lit.[18c] $[\alpha]_D^{20}$ +100.8). NMR data were identical with those described in the literature.[17c] Further elution gave the desired compound **4d** (79% yield) that was obtained as a white solid, mp 103–105 °C, $[\alpha]_D^{20}$ +139.6 (c 1.6, $CHCl_3$) (lit.[18b] mp 103–104 °C, $[\alpha]_D^{28}$ +125 (c 0.72, $CHCl_3$). Its

spectroscopic data were in accordance with those described in the literature.[17b]

4.6.5. Methyl di-*O*-benzyl-α-D-glucopyranoside 4e. Ether, 75% yield, solid, mp 75–76 °C, $[\alpha]_D^{20}$ +16.1 (*c* 0.4, $CHCl_3$) (lit.[22] mp 77.5 °C, $[\alpha]_D^{27}$ +16.3 (*c* 1.01, $CHCl_3$)). Its spectroscopic data were in agreement with those of an authentic sample.

4.6.6. Testosterone 4f. Ether–petroleum ether (4:1), 90% yield, solid, mp 152–153 °C, $[\alpha]_D^{20}$ +110.7 (*c* 0.9, $CHCl_3$) (lit.[19] mp 155 °C, $[\alpha]_D^{24}$ +109 (*c* 4, EtOH). NMR data were in agreement with a sample from commercial source.

4.6.7. *N*-(*tert*-Butoxycarbonyl)-L-serine methyl ester 4g. Ether–petroleum ether (3:1), 85% yield, oil, $[\alpha]_D^{20}$ −18.6 (*c* 5, MeOH) (lit.[23] $[\alpha]_D$ −19 (*c* 4, MeOH)). Spectroscopic data were in accordance with those described in the literature.[23]

4.6.8. Chloroacetic acid 5-hydroxypentyl ester 4m. Ether–petroleum ether (4:1), 90% yield, colorless liquid. IR (film): 3350, 1740 cm^{-1}. ^1H NMR: 1.37–1.72 (m, 6H, $3CH_2$), 1.93 (br s, 1H, OH), 3.62 (t, 2H, *J*=6.2 Hz, C*H*$_2$OH), 4.04 (s, 2H, CH_2Cl), 4.18 (t, 2H, *J*=6.5 Hz, CH_2OClAc). ^{13}C NMR: 22.1, 28.3, 32.1, 41.0, 62.5, 66.2, 167.5. Anal. Calcd for $C_7H_{13}ClO_3$: C, 46.55; H, 7.25; Cl, 19.63; O, 26.57. Found: C, 46.49; H, 7.40; Cl, 19.44; O, 26.69.

4.6.9. 4-Oxo-pentanoic acid 5-hydroxypentyl ester 4n. Ether, 88% yield, oil. IR (film): 3400, 1720 (br) cm^{-1}. ^1H NMR: 1.34–1.49 (m, 2H, CH_2), 1.52–1.66 (m, 4H, $2CH_2$), 2.16 (br s, 4H, Me, OH), 2.52 (t, 2H, *J*=6.4 Hz, CH_2CO), 2.72 (t, 2H, *J*=6.4 Hz, C*H*$_2$CH$_2$CO), 3.60 (t, 2H, *J*=6.2 Hz, C*H*$_2$OH), 4.05 (t, 2H, *J*=6.4 Hz, CH_2OLev). ^{13}C NMR: 22.8, 28.0, 28.4, 29.9, 32.2, 38.0, 62.5, 64.3, 172.9, 207.0. Anal. Calcd for $C_{10}H_{18}O_4$: C, 59.39; H, 8.97; O, 31.64. Found: C, 59.28; H, 8.90; O, 31.82.

4.6.10. Carbonic acid 9*H*-fluoren-9-ylmethyl 5-hydroxypentyl ester 4o. Ether–petroleum ether (5:1), 91% yield, solid, mp 68–69 °C (hexane). IR (film): 3535, 1730 cm^{-1}. ^1H NMR: 1.43–1.82 (m, 7H, $3CH_2$, OH), 3.66 (t, 2H, *J*=6.3 Hz, C*H*$_2$OH), 4.21 (t, 2H, *J*=6.6 Hz, CH_2OFmoc), 4.29 (t, 1H, *J*=7.4 Hz, C*H*–CH_2OCOO), 4.43 (d, 2H, *J*=7.4 Hz, CH–*CH*$_2$OCOO), 7.35 (t, 2H, *J*=7.5 Hz, Ar), 7.44 (t, 2H, *J*=7.4 Hz, Ar), 7.65 (d, 2H, *J*=7.5 Hz, Ar), 7.8 (d, 2H, *J*=7.5 Hz, Ar). ^{13}C NMR: 22.1, 28.5, 32.3, 46.8, 62.6, 68.2, 69.8, 120.1 (2C), 125.2 (2C), 127.2 (2C), 127.9 (2C), 141.3 (2C), 143.5 (2C), 155.4. Anal. Calcd for $C_{20}H_{22}O_4$: C, 73.60; H, 6.79; O, 19.61. Found: C, 73.30; H, 6.86; O, 19.84.

4.6.11. (*R*)-Lactic acid butyl ester 4p. Ether–petroleum ether (1:1), 79% yield, liquid, $[\alpha]_D^{20}$ +6.35 (*c* 2.2, $CHCl_3$) ((*S*)-commercially available enantiomer: $[\alpha]_D^{20}$ −6.33 (*c* 2.1, $CHCl_3$)). Spectroscopic data were identical with those of its enantiomer obtained from commercial source.

4.6.12. 3α-Cholestanol 4q. Elution with petroleum ether–ether (9:1) gave a mixture of 2- and 3-cholestene (17% yield). Further elution with petroleum ether–ether (2:1) provided the desired epicholestanol **4q** (52% yield) as a solid, mp 184–185 °C, $[\alpha]_D^{20}$ +24.3 (*c* 1, $CHCl_3$) (lit.[24] mp 183–184 °C, $[\alpha]_D^{25}$ +25).

4.6.13. 17-Epitestosterone 4r. Elution with ether–petroleum ether (1:2) gave an unseparable mixture of **8** and **9** (30% yield, ratio 7:3). ^{13}C NMR, compound **8**: 17.0, 19.5, 22.7, 24.2, 31.1, 31.3, 32.1, 33.4, 33.93, 35.6, 36.6, 38.6, 41.4, 51.8, 124.3, 136.4, 138.8, 171.1, 199.6; compound **9**: 13.5, 18.0, 25.4, 25.8, 28.1, 32.3, 32.9, 33.99, 35.7, 37.2, 38.8, 45.3, 52.2, 53.1, 123.8, 128.5, 135.3, 171.6, 199.6. Further elution with ether–petroleum ether (3:1) gave epitestosterone **4r** (30% yield), solid, mp 215–217 °C, $[\alpha]_D^{20}$ +87 (*c* 0.8, $CHCl_3$) (lit.[18a] mp 216–218 °C, $[\alpha]_D$ +86 ($CHCl_3$)).

4.6.14. (1*S*,2*S*,5*R*)-Neomenthol 4s. Petroleum ether–ether (3:1), 10% yield, oil, $[\alpha]_D^{20}$ +20.5 (*c* 9, EtOH). Its physical data were in accordance with those of a commercial sample.

4.7. (1*R*,2*S*,5*R*)-Menthol 2-(hydroxymethyl)benzoate 6

To a solution of menthol POMB ester (0.25 g) in a mixture of CH_2Cl_2–H_2O (9:1, 9 mL) was added DDQ (0.237 g, 1.5 equiv). After stirring at room temperature for 6 h, the precipitate was filtered and the filtrate was diluted with ether, washed with $NaHCO_3$ solution and then with water. The organic phase was dried (Na_2SO_4) and evaporated. Chromatography of the residue on silica gel (petroleum ether–CH_2Cl_2, 1:2) afforded the deprenylated compound **6** (0.19 g, 94%) as an oil. $[\alpha]_D^{20}$ −74.6 (*c* 2.8, $CHCl_3$). IR (film): 3450, 1710, 1690, 1600, 1580 cm^{-1}. ^1H NMR: 0.8 (d, 3H, *J*=6.9 Hz, Me), 0.93 (d, 3H, *J*=7 Hz, Me), 0.94 (d, 3H, *J*=6.4 Hz, Me), 1.0–1.17 (m, 3H), 1.49–1.64 (m, 2H), 1.71–1.78 (m, 2H), 1.89–2.08 (m, 1H), 2.09–2.16 (m, 1H), 4.09 (t, 1H, *J*=7.2 Hz, OH), 4.78 (d, 2H, *J*=6.9 Hz, C*H*$_2$OH), 4.96 (td, 1H, *J*=4.4 and 10.8 Hz, CHOCO), 7.32–7.55 (m, 3H, Ar), 7.99 (dd, 1H, *J*=1 and 7.7 Hz, Ar). ^{13}C NMR: 16.4, 20.9, 22.1, 23.5, 26.5, 31.5, 34.3, 41.0, 47.3, 64.8, 75.5, 127.8, 129.7, 130.3, 130.9, 132.8, 143.0, 167.6. Anal. Calcd for $C_{18}H_{26}O_3$: C, 74.45; H, 9.02; O, 16.53. Found: C, 74.49; H, 9.22; O, 16.32.

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