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A convenient approach for the deprotection and scavenging of the PMB group using $POCl_3$†

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A convenient and high yielding approach for the deprotection and scavenging of the *p*-methoxybenzyl (PMB) group in PMB ethers and PMB esters was developed using $POCl_3$ as the reagent. 4-Methoxybenzyl chloride, a starting material used for the preparation of PMB ethers and esters was regenerated in the deprotection step. This mild and selective procedure tolerates several acid sensitive functional groups.

Introduction

Protective groups are used extensively in organic synthesis for the construction of highly functionalized natural products and synthetic organic molecules.[1] Hydroxyl and carboxylic acid groups are ubiquitous among different classes of organic molecules. The *p*-methoxybenzyl group (PMB) is one of the widely used hydroxyl protecting groups which can show orthogonality against other hydroxyl protecting groups including other benzyl ethers.[2] The success of a protecting group mainly depends on the mild, specific, cost effective and non toxic reagents and short and simple reaction conditions for protection as well as deprotection. Although the PMB group can be introduced selectively and removed under mild conditions, the isolation of alcohol involves rigorous purification steps to remove the side products arising out of the detached PMB group. Usually, the PMB group in the absence of a scavenger, undergoes self condensation to produce dimers and polymeric products.[3] However in order to avoid the formation of complex mixture of products, scavengers of the PMB group were used and the alklyated and poly alkylated products of the trapping agent was obtained.

DDQ[4a] was the first reagent used for the oxidative cleavage of PMB ethers. Later, several modified procedures were developed to minimize the quantity of DDQ by making use of co-oxidants such as $HClO_4$, HIO_4, HNO_3, $FeCl_3$, and $Mn(OAc)_3$.[5] Alternatively CAN[4b] was also used for the oxidative deprotection. Side products such as 4-anisaldehyde and dichlorodicyanohydroquinone were obtained and oxidation of allylic groups took place. Reductive cleavage of PMB ethers with $NaCNBH_3$–$BF_3{\cdot}Et_2O$[6] gave rise to the side product, 4-methylanisole, and this method is not suitable for the compounds with reducible and acid sensitive functional groups. When chlorosulfonyl isocyanate–NaOH[7] was used for the cleavage of PMB ethers, *N*-chlorosulfonyl-*N*-benzylcarbamate was generated and cleaved by base hydrolysis to get the alcohol. Acidic reagents such as $MgBr_2{\cdot}Et_2O$–Me_2S,[8a] $SnCl_2{\cdot}2H_2O$-EtSH,[8b] TMSI-TPP,[8c] $AlCl_3$–$Me_2NC_6H_5$,[8d] $SnCl_4$-benzenethiol[8e] $CeCl_3{\cdot}7H_2O$–NaI,[9a] $Ce(OTf)_3$,[9b] $ZrCl_4$,[9c] TfOH-*N*-methyl-*p*-toluenesulfonamide or sulfonamide-functionalized (''safety-catch'') resins,[10] TfOH-1,3-dimethoxybenzene,[11] 10% TFA in CH_2Cl_2,[12] and clay supported ammonium nitrate ''clayan'' in dry media[13] were also employed for the cleavage. Just recently, a combination of Ag(I)SbF_6 (5 mol%) and 1,3,5-trimethoxybenzene (0.5 equiv.)[14] was reported as a useful reagent for the deprotection. The literature background shows that except a few,[4b,9b–c,12,14] most of the reagents were used in stoichiometric quantity and in combination with a PMB cation scavenger. Whether it is a single reagent or a combination of reagents, the main drawback associated with the existing methods for PMB group deprotection is the formation of the side products, for example *N*-chlorosulfonyl-*N*-benzylcarbamate,[7] bis(4-methoxyphenyl)-methane[9b] alkylated or poly alkylated products[14] of trapping agents, and acetals,[14] are some of the side products formed. Moreover, acid sensitive groups get affected easily. For example use of $Ce(OTf)_3$[9b] leads to a complex mixture of products with alcohols carrying double or triple bonds and the use of AcOH as the solvent gives rise to acetates instead of alcohols.[15]

$POCl_3$ is a readily available, inexpensive Lewis acid widely used in organic synthesis for chlorination and the Vilsmeier reaction. Based on the fact that the PMB cation is formed during most of the PMB deprotection conditions, it was envisaged to trap it by the chloride ion in the presence of a Lewis acid. This may in turn avoid the formation of polymeric products and simplify the work up procedure. This interesting

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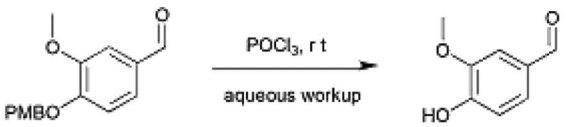
† Electronic supplementary information (ESI) available: Copies of ^1H and ^{13}C spectra for all compounds. See DOI: 10.1039/c3ra42113a

Table 1 Optimization of reaction condition for PMB deprotection using $POCl_3$



1 2

Sl. No	Solvent	$POCl_3$ (equiv.)	Time (min.)	Isolated Yield (%)
1	Neat	10	10	91
2	Toluene	0.5	30	82
3	DCM	0.5	25	85
4	THF	0.5	25	83
5	DCE	1.5	15	92
6	DCE	0.5	15	92
7	DCE	0.35	120	90

proposition impelled us to look at $POCl_3$ as a PMB unmasking reagent. Herein we present our results.

Results and discussion

Compound **1** was identified as a model for the study of $POCl_3$ mediated PMB group deprotection. Interestingly, when compound **1** was treated with excess of $POCl_3$ (10 equiv.) unmasking of the PMB group took place readily at r.t. to provide phenol **2** in just 10 min (Table 1, entry 1). Encouraged by this result, different reaction parameters were examined to arrive at the optimum conditions for the deprotection and the results are summarized in Table 1.

To minimise the quantity of $POCl_3$, the reaction was carried out at r.t., in different solvents such as DCM, THF and 1,2-dichloroethane (DCE) (Table 1, entries 2–4) with varying amount of $POCl_3$. The best result was obtained with DCE (Table 1, entry 5) and sub-stoichiometric quantity of $POCl_3$ (0.5 equiv.). The reaction time and yield did not change when the quantity was decreased from 1.5 equiv. to 0.5 equiv. However, the reaction was very slow (120 min.) when the quantity of the reagent was reduced to 0.35 equiv. Thus, the optimized conditions for further study was found to be $POCl_3$ (0.5 equiv.) in DCE at r.t. The versatility of $POCl_3$ (0.5 equiv.) as a PMB deprotection reagent was tested using various aryl ethers under standardised reaction conditions (Table 2, entries 1–9).

All the substrates underwent a clean reaction in less than 30 min to give corresponding phenols in excellent yield. This method was found to be compatible with sensitive functional groups such as *N*-bis-ethoxycarbonylvinyl (BECV),[16] aldehyde, ketone, ester, and ether. The electronic and steric factors of the benzene ring had no significant influence on the kinetics of the reaction and in general the reactions were complete within 30 min.

Encouraged by these results, we next examined the compatibility of $POCl_3$ (0.5 equiv.) against aliphatic PMB ethers (Table 3, entry 1–16).

Even though the reactivity of aliphatic PMB ethers was substantially slower compared to aryl PMB ethers, all the reactions were complete with just 0.5 equiv. of $POCl_3$. More interestingly, in contrary to our belief that $POCl_3$ may cleave some of the acid sensitive functional groups such as Ac, Bz, prenyl, allyl, TBS, and pivaloyl (Table 3, entries 1–9), high selectivity was observed under the present reaction condition and the products were obtained in high yield. The closely related benzyl group did not undergo deprotection (Table 3, entry 6).

In the cases of compound **17** and **18** (Table 3, entries 8 & 9) the reaction was not complete and the desired product was isolated only in 60% and 65% yield respectively. Efforts to take the reaction to completion by extending the duration resulted in lower yields and the purification was complicated. We presumed that the acid sensitive trityl and THP group are likely affected and the use of a PMB cation scavenger might solve the problem. Some of the known cation scavengers such as triethylsilane,[18] 1,3-dimethoxybenzene,[11] alkanethiol,[17] anisole, pentamethylbenzene,[19] and benzenesulphonamide[10] were examined for the reaction of compound **17** with $POCl_3$ (Table 4).

Even though thiophenol produced a clean reaction, the foul smell associated with it prompted us to look for cheap and commercially available odour less 1-dodecanethiol.[17] In the presence of 1-dodecanethiol (3 equiv.), the deprotected product **17a** was obtained in a short time (35 min.) and in high yield (91%). The dodecyl(4-methoxyphenyl)sulfane was obtained as one of the products.

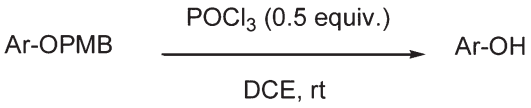
Similarly, compounds **16**, **17**, **18**, and **25** containing acid sensitive groups such as TBS, Tr, THP and acetonide underwent smooth deprotection to give corresponding products in marginally improved yield (Table 3, entries 7–9 & 16). Interestingly, the more acid sensitive acetonide group remained intact. With chiral secondary alcohols **19** and **20**, no epimerization occurred (Table 3, entries 10 & 11). Unlike other Lewis acids,[9b] no major side products were formed for PMB ethers **23** and **24** containing allylic and acetylene functional groups (Table 3, entries 14 & 15).

In contrast to the PMB ethers, there are few methods known for the deprotection of PMB esters, among which only few are milder.[9c,14] Thus we examined $POCl_3$ (0.5 equiv.) as a reagent for the deprotection of esters and it was found to be an efficient reagent for the cleavage of PMB esters **26–30**. As exemplified in Table 5, all the products were obtained in very good yield at r t. In case of compound **30** the presence of the acid sensitive N-Boc protecting group posed no threat (Table 5, entry 5).

Mechanism

In order to investigate the mechanism, 1-(ethoxymethyl)-4-methoxybenzene (4-OMe-C_6H_4OEt, **31**) was taken as the model compound. It was envisaged that studying this substrate will enable traceless removal of the alcohol component (EtOH) and

Table 2 Deprotection of aryl PMB ethers by $POCl_3$[a]



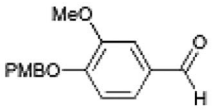
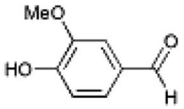
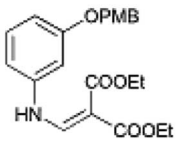
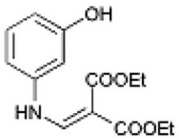
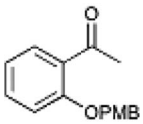
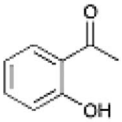
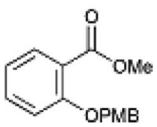
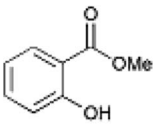
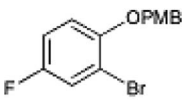
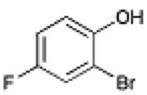
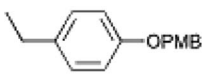
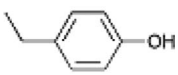
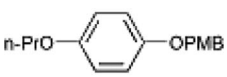
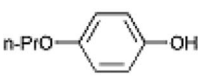
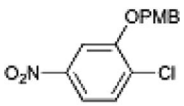
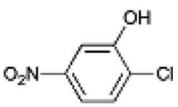
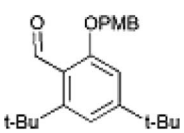
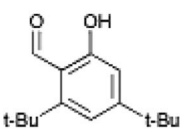
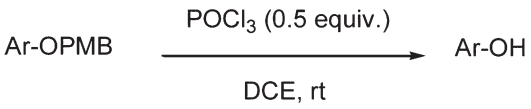
Entry	Starting material	Product	Time (min.)	Yield (%)[b]
1	 **1**	 **1a**	10	95
2	 **2**	 **2a**	25	94
3	 **3**	 3a	30	90
4	 **4**	 **4a**	30	94
5	 **5**	 **5a**	25	92
6	 **6**	 **6a**	20	95
7	 **7**	 **7a**	20	92
8	 **8**	 **8a**	25	94
9	 **9**	 **9a**	20	90

Table 2 (*Continued*)



Entry	Starting material	Product	Time (min.)	Yield (%)[b]

[a] Reaction conditions: PMB ether (1 mmol), $POCl_3$ (0.5 mmol), DCE (5 mL), r t. [b] Isolated yield.

allow better understanding about the products formed from the PMB component. Upon treatment with $POCl_3$ (0.5 equiv.), compound **31** underwent complete deprotection in 60 min. ^1H NMR and GCMS analysis of the crude product obtained from the organic layer, after water work up, revealed that PMB chloride was formed as the major product along with a very minor quantity of bis(4-methoxyphenyl)-methane.[9b] PMB chloride is an unstable compound and it is well known to undergo Fridel–Crafts type polymerisation in the presence of acids,[20] hence the formation of a very minor quantity of bis(4-methoxyphenyl)-methane was justified.

A suitable mechanism is proposed based on these observations, as shown in Scheme 1. Complex **II** formed between the PMB ether (**I**) and $POCl_3$ should undergo elimination of the PMB cation **IV** which in turn should lead to the formation of PMB chloride, by chloride attack, and the intermediate **III**. The existence of PMB cation **IV** was also confirmed by the formation of dodecyl(4-methoxybenzyl)sulfane.[21] Since the reaction goes to completion with 0.5 equiv. of $POCl_3$, the intermediate **III** is expected to undergo reaction with another molecule of PMB ether to form PMB chloride and intermediate **V** which could liberate the free alcohol upon reaction with water. To the best of our knowledge, there was no previous example of using a single reagent for deprotection and scavenging of PMB cation. Thus this work forms first such an example. Unlike the other methods where 4-methoxybenzyl group was trapped using an external scavenger under the present method and $POCl_3$ itself acted as deprotecting agent as well as trapping agent. Interestingly, the 4-methoxybenzyl chloride was the starting material used for the preparation of PMB ether and esters, thus one of the starting materials could be regenerated under the present method.

Conclusion

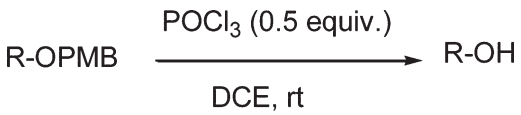
In conclusion, we have successfully developed $POCl_3$ (0.5 equiv.) as a new reagent for highly selective deprotection of PMB group in aromatic, aliphatic, carbohydrate, steroid, terpenoid PMB ethers as well as aromatic, aliphatic and amino acid esters. As detailed above, $POCl_3$ effectively worked as a single reagent for the deprotection as well as scavenging of the PMB cation. PMB chloride, which was used as the starting material for the preparation of ethers and esters was regenerated during deprotection and can be reused. $POCl_3$ is selective against various acid and base sensitive functional groups such as aldehyde, ketone, alkene, ether, BECV, Bz, prenyl, THP, trityl, allyl, TBS, Bn, pivaloyl, Boc. This study accounts for some of the important characteristics of a successful deprotection method such as use of sub-stoichiometric quantity of cheap and readily available non metallic reagent, mild but speedy completion of the reaction at r.t., high selectivity and yield and easy isolation of the product by simple workup. All these characteristics make this one of the simplest and versatile method known for the deprotection of PMB ethers and esters.

Experimental section

General remarks

All commercially available reagents were used without further purification. Solvents used in reactions were distilled over appropriate drying agents prior to use. Solvents used for extraction and purification were distilled prior to use. Reactions that required inert atmosphere and moisture control were carried out in a nitrogen atmosphere employing oven-dried glassware. Thin-layer chromatography (TLC) was performed using TLC silica gel 60 F254. Compounds were visualized with UV light (λ = 254 nm) and by immersion in KMnO4 solution, followed by heating. Products were purified by flash chromatography on silica gel (60–120 or 230–400 mesh). Melting points were obtained on a melting point apparatus with open capillary tubes and are uncorrected. ^1H (13C) NMR spectra were recorded at 300 (75) and 400 (100) MHz using $CDCl_3$ or DMSO-d_6 as the solvent. The ^1H and ^{13}C chemical shifts were referenced to residual solvent signals at δ H/C 7.26/77.0 ($CDCl_3$) and 2.5/39.5 (DMSO-d_6) relative to TMS as internal standard. Splitting patterns are designated as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and br (broad). The elemental analyses were carried out using varioMICRO instruments. The Optical Rotation was determined with a digital Polarimeter and reported as follows: $[\alpha]_D^{25}$ (*c*: g/100 mL, in solvent).

Table 3 Deprotection of aliphatic PMB ethers by $POCl_3$[a]



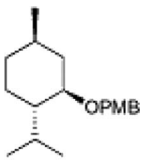
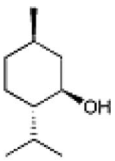
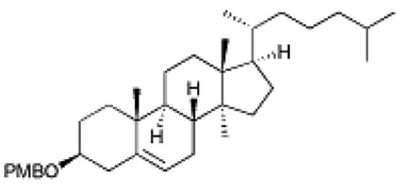
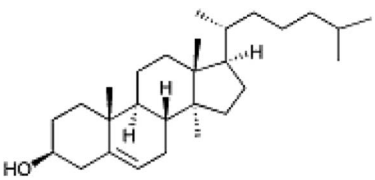
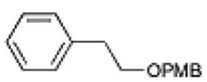
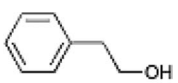
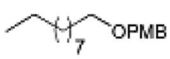
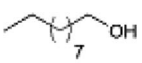
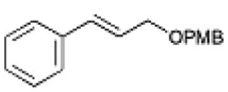
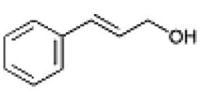
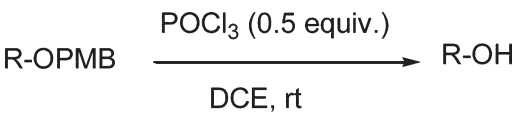
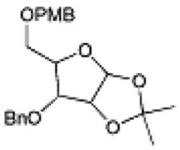
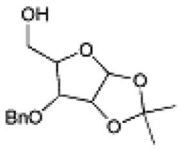
Entry	Starting material	Product	Time (min.)	Yield (%)[b]
				
1	*R* = Ac **10**	*R* = Ac **10a**	60	94
2	*R* = Bz **11**	*R* = Bz **11a**	55	90
3	*R* = Prenyl **12**	*R* = Prenyl **12a**	60	93
4	*R* = Allyl **13**	*R* = Allyl **13a**	50	91
5	*R* = Pivaloyl **14**	*R* = Pivaloyl **14a**	60	90
6	*R* = Bn **15**	*R* = Bn **15a**	50 (35)[c]	83 (91)[c]
7	*R* = TBS **16**	*R* = TBS **16a**	55 (50)[c]	83 (88)[c]
8	*R* = Tr **17**	*R* = Tr **17a**	60 (50)[c]	60 (80)[c]
9	*R* = THP **18**	*R* = THP **18a**	60 (50)[c]	65 (81)[c]
10	 **19**	 **19a**	60	80
11	 **20**	 **20a**	65	82
12	 **21**	 **21a**	55	81
13	 **22**	 **22a**	60	90
14	 **23**	 **23a**	50	90
15	 **24**	 **24a**	50	80

Table 3 (*Continued*)



Entry	Starting material	Product	Time (min.)	Yield (%)[b]
16	 **25**	 **25a**	55 (50)[c]	75 (83)[c]

[a] Reaction conditions: PMB ether (1 mmol), $POCl_3$ (0.5 mmol), DCE (5 mL) at r.t. [b] Isolated yield. [c] In the presence of 3 equiv. of 1-dodecanethiol.

General procedure for the preparation of the PMB ethers (general method A)

To a solution of appropriate phenol (1 equiv.) in dry DMF (10 times w/v), cesium carbonate (1.5 equiv.) and 4-methoxybenzylchloride (1.1 equiv.) were added and heated at 80 °C for a specific time. After cooling to room temperature, the mixture was quenched in ice water and extracted into ethyl acetate (3 × 10 mL). Combined ethyl acetate extracts were washed with brine solution (2 × 10 mL), dried (Na_2SO_4), concentrated under reduced pressure and the residue was purified by column chromatography (silica gel, EtOAc : Hexane) to afford the corresponding PMB ethers.

General procedure for the preparation of the PMB ethers (general method B)

To a solution of the alcohol (1 equiv.) in dry toluene (10 times w/v), 4-methoxybenzyl trichloroacetimidate (1.5 equiv.) and $La(OTf)_3$ (0.1 equiv.) was added and heated at 80 °C for a specific time. After cooling to room temperature, the solvent was removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, EtOAc : Hexane) to yield the corresponding PMB ether.

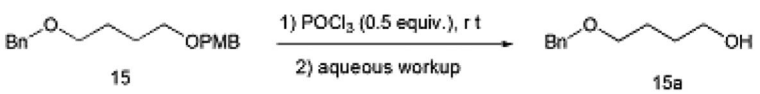
General procedure for the preparation of the PMB esters (general method C)

To a solution of the acid (1 equiv.) in dry DMF (10 times w/v), potassium carbonate (1.5 equiv.) and 4-methoxybenzylchloride (1.2 equiv.) was added and the reaction mixture was stirred at room temperature for a specific time. The mixture was quenched in ice water and extracted into ethyl acetate (3 × 10 mL). Combined ethyl acetate extract was washed with brine solution (2 × 10 mL), dried (Na_2SO_4), concentrated under reduced pressure and the residue was purified by column chromatography (silica gel, EtOAc : Hexane) to afford corresponding PMB ester.

General procedure for the deprotection of the PMB ethers and ester by $POCl_3$ (general method D)

To a solution of the PMB ether or ester (1 equiv.) in dichloroethane (5 mL), $POCl_3$ (0.5 equiv.) was added and stirred at room temperature. After completion of the reaction, it was quenched in ice water and the organic layer was separated and the aqueous layer was extracted with dichloroethane (2 × 5 mL). Combined organic layer was washed with brine solution, dried (Na_2SO_4), concentrated under reduced pressure and the residue was purified by column chromato-

Table 4 Effect of scavengers on PMB deprotection using $POCl_3$[a]

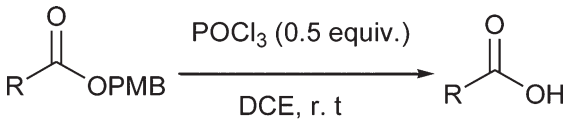


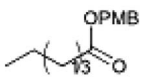
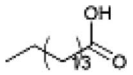
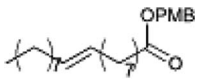
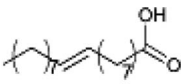
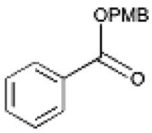
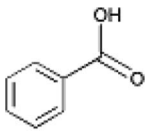
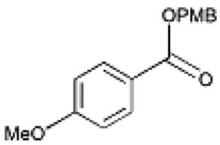
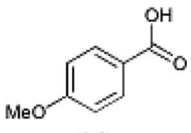
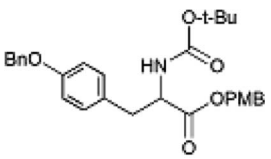
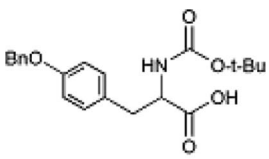
15 15a

Entry	Reagents	Time (min)	Yield[b] (%)
1	Triethylsilane	70	72
2	Thiophenol	40	85
3	Pentamethylbenzene	90	60
4	1,4-Dimethoxybenzene	70	70
5	Benzenesulphonamide	120	40
6	1-Dodecanethiol	35	91

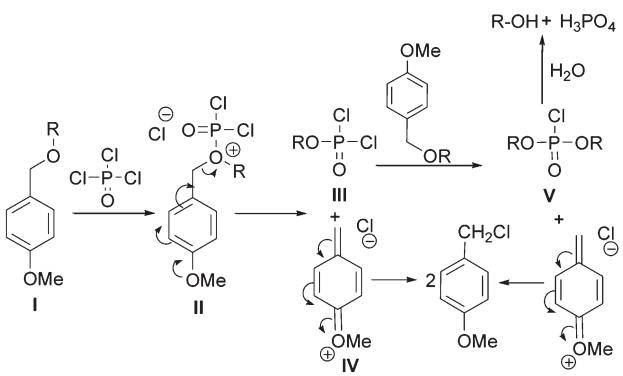
[a] Reaction conditions: PMB ether (1 mmol), $POCl_3$ (0.5 mmol), DCE (5 mL), r.t. [b] Isolated yield.

Table 5 Deprotection of PMB esters by $POCl_3$[a]



Entry	Starting material	Product	Time (min.)	Yield (%)[b]
1	 **26**	 **26a**	60	92
2	 **27**	 **27a**	50	88
3	 **28**	 **28a**	60	90
4	 **29**	 **30**	60	88
5	 **30**	 **30a**	55	82

[a] Reaction conditions: PMB ether (1 mmol), $POCl_3$ (0.5 mmol), DCE (5 mL), r.t. [b] Isolated yield.



Scheme 1 Mechanism of deprotection by $POCl_3$.

graphy (silica gel, EtOAc : Hexane) to afford the corresponding alcohol.

General procedure for the deprotection of the PMB ethers by $POCl_3$ in the presence of 1-dodecanethiol (general method E)

To a solution of the PMB ether (1 equiv.) in dichloroethane (5 mL), $POCl_3$ (0.5 equiv.) and 1-dodecanthiol (3 equiv.) were added and stirred at room temperature. After completion of the reaction, it was quenched in ice water and the organic layer was separated extracted with dichloroethane (2 × 5 mL). The combined organic layer was washed with brine solution, dried (Na_2SO_4), concentrated under reduced pressure and the residue was purified by column chromatography (silica gel, EtOAc : Hexane) to afford the corresponding alcohol.

3-Methoxy-4-((4-methoxybenzyl)oxy)benzaldehyde (1)

The reaction was carried out according to the general method A using vanillin **1a** (304 mg, 2 mmol), Cs_2CO_3 (977.4 mg, 3

mmol), 4-methoxybenzylchloride (521.6 mg, 2.2 mmol) and DMF (3 mL) for 1 h to get compound **1** (488 mg, 90%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.81 (s, 3 H), 3.93 (s, 3 H), 5.17 (s, 2 H), 6.91 (d, J = 8.4 Hz, 2 H), 7.01 (d, J = 8.4 Hz, 1 H), 7.36–7.42 (m, 4 H), 9.84 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.3, 56.0, 70.7, 109.4, 112.4, 114.1, 126.6, 128.0, 129.1, 130.2, 150.1, 153.7, 159.6, 190.9. Spectral data for the compound **1** was in agreement with the values reported in the literature.[22]

Diethyl 2-(((3-((4-methoxybenzyl)oxy)phenyl)amino)methylene) malonate (2)

The title compound was prepared by following literature procedure.[16] To solution of 3-aminophenol (0.500 g, 4.5 mol) in ethanol (2.5 mL), diethyl ethoxymethylenemalonate (0.9906 g, 4.5 mol) was added at room temperature. The mixture was stirred at room temperature for 15 min. After completion of the reaction, ethanol was evaporated under reduced pressure to get **2a** as a white solid (1.2 g, 99%). m.p.: 105 °C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.30–1.40 (m, 6 H), 4.22–4.31 (m, 4 H), 6.60–6.67 (m, 2 H), 7.15–7.19 (m, 1 H), 7.36 (d, J = 6.4 Hz, 1H), 8.49 (d, J = 14 Hz, 1H), 9.06 (d, J = 16 Hz, 1H), 10.87 (d, J = 13.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.0, 25.1, 26.7, 29.1, 30.2, 55.3, 62.3, 62.7, 64.3, 70.1, 72.7, 76.8, 77.1, 77.4, 113.8, 129.4, 130.7, 159.2, 171.3. Anal. calcd. for $C_{14}H_{17}NO_5$: C, 60.21; H, 6.14; N, 5.02; Found: C, 60.25; H, 6.16; N, 5.08.

The reaction was carried out according to general method A using diethyl 2-(((3-hydroxyphenyl)amino)methylene)malonate **2a** (558 mg, 2 mmol), Cs_2CO_3 (977.4 mg, 3 mmol), 4-methoxybenzylchloride (521.6 mg, 2.2 mmol) and DMF (5.6 mL) for 1 h to get compound **2** (558 mg, 70%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.35 (t, J = 22 Hz, 6 H), 3.82 (s, 3 H), 4.28 (q, J = 32.4 Hz, 4 H), 4.99 (s, 2 H), 6.74–6.75 (m, 2 H), 6.93 (d, J = 8.8 Hz, 2 H), 7.26–7.26 (m, 2 H), 7.35 (d, J = 8.8 Hz, 2 H), 8.49 (d, J = 13.6 Hz, 1 H), 10.95 (d, J = 13.6 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.3, 14.5, 55.3, 60.1, 60.4, 70.0, 93.7, 104.1, 109.8, 111.1, 114.1, 128.5, 129.3, 130.7, 140.5, 151.8, 159.6, 160.1, 165.7, 169.0.

1-(2-((4-Methoxybenzyl)oxy)phenyl)ethanone (3)

The reaction was carried out according to general method A using 2-hydroxy acetophenone **3a** (272 mg, 2 mmol), Cs_2CO_3 (977.4 mg, 3 mmol), 4-methoxybenzylchloride (521.6 mg, 2.2 mmol) and DMF (2.8 mL) for 1 h to get **3** (440 mg, 86%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.58 (s, 3 H), 3.84 (s, 3 H), 5.10 (s, 2 H), 6.94 (d, J = 1.9 Hz, 2 H), 7.00–7.02 (m, 2 H), 7.38 (d, J = 8.6 Hz, 2 H), 7.44–7.44 (m, 1 H), 7.76 (dd, J = 1.8, 7.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.0, 159.6, 158.1, 133.5, 130.4, 129.3, 128.7, 128.2, 120.8, 114.1, 112.8, 70.4, 55.3, 32.1. Spectral data for the compound **3** was in agreement with the values reported in the literature.[23]

Methyl 2-((4-methoxybenzyl)oxy)benzoate (4)

The reaction was carried out according to general method A using methyl salicylate **4a** (304 mg, 2 mmol), Cs_2CO_3 (977.4 mg, 3 mmol), 4-methoxybenzylchloride (521.6 mg, 2.2 mmol) and DMF (3 mL) for 6 h to get **6** (424 mg, 78%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.83 (s, 3 H), 3.90 (s, 3 H), 6.91 (s, 2 H), 6.92 (d, J = 9.5 Hz, 2 H), 6.98–7.04 (m, 2 H), 7.41–7.47 (m, 3 H), 7.81–7.84 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 51.9, 55.2, 70.6, 113.9, 114.1, 120.5, 120.8, 128.4, 128.7, 131.6, 133.3, 158.1, 159.2, 166.8. Spectral data for the compound **4** was in agreement with the values reported in the literature.[24]

2-Bromo-4-fluoro-1-((4-methoxybenzyl)oxy)benzene (5)

The reaction was carried out according to general method A using 2-bromo-4-fluorophenol **5a** (382 mg, 1 mmol), Cs_2CO_3 (977.4 mg, 3 mmol), 4-methoxybenzylchloride (521.6 mg, 2.2 mmol) and DMF (3.8 mL) for 2 h to get compound **5** (504 mg, 81%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.83 (s, 3 H), 5.05 (s, 2 H), 6.91–6.92 (m, 4 H), 7.30–7.31 (m, 1 H), 7.38 (d, J = 8.2 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.2, 71.5, 112.9, 113.9, 114.7, 120.2, 120.5, 128.3, 128.8, 151.5, 158.3, 159.4. Anal. Calcd. for $C_{14}H_{12}BrFO_2$ (310): C, 54.04; H, 3.89; Found C, 68.94; H, 3.90.

1-Ethyl-4-((4-methoxybenzyl)oxy)benzene (6)

The reaction was carried out according to general method A using 4-ethyl phenol **6a** (244 mg, 2 mmol), Cs_2CO_3 (977.4 mg, 3 mmol), 4-methoxybenzylchloride (521.6 mg, 2.2 mmol) and DMF (2.4 mL) for 2 h to get compound **6** (378 mg, 78%) as a white solid. m.p: 77 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.24 (t, J = 10.1 Hz, 3 H), 2.62 (q, J = 10.1 Hz, 2 H), 3.84 (s, 3 H), 4.99 (s, 2 H), 6.91–6.92 (m, 4 H), 7.14 (d, J = 11.5 Hz, 2 H), 7.39 (d, J = 11.6 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.8, 27.9, 55.2, 69.8, 113.9, 114.7, 128.6, 129.1, 129.2, 136.5, 156.9, 159.3. Anal. Calcd. for $C_{16}H_{18}O_2$ (242): C, 79.31; H, 7.49; Found C, 79.29; H, 7.48.

1-Methoxy-4-((4-propoxyphenoxy)methyl)benzene (7)

The reaction was carried out according to general method A using 4-propoxy phenol **7a** (304 mg, 2 mmol), Cs_2CO_3 (977.4 mg, 3 mmol), 4-methoxybenzylchloride (521.6 mg, 2.2 mmol) and DMF (3 mL) for 2 h to get compound **7** (456 mg, 84%) as a white solid. m.p: 103 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.03 (t, J = 7.4 Hz, 3 H), 1.79 (q, J = 6.9 Hz, 2 H), 3.79 (s, 3 H), 3.88 (t, J = 6.6 Hz, 2 H), 4.94 (s, 2 H), 6.82–6.83 (m, 6 H), 7.36 (d, J = 8.6 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 10.5, 22.6, 55.2, 70.1 70.4, 113.9, 115.3, 115.8, 129.1, 129.3, 152.8, 153.4, 159.3. Anal. Calcd. for $C_{17}H_{20}O_3$ (272): C, 74.97; H, 7.40; Found C, 74.98, H, 7.42.

1-Chloro-2-((4-methoxybenzyl)oxy)-4-nitrobenzene (8)

The reaction was carried out according to general method A using 2-chloro-5-nitrophenol **8a** (346 mg, 2 mmol), Cs_2CO_3 (977.4 mg, 3 mmol), 4-methoxybenzylchloride (521.6 mg, 2.2 mmol) and DMF (3.5 mL) for 1 h to get compound **8** (509 mg, 87%) as a pale brown solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.83 (s, 3 H), 5.19 (s, 2 H), 6.95 (d, J = 8.2 Hz, 2 H), 7.41 (m,2 H), 7.53 (d, J = 8.4 Hz, 1 H), 7.81 (dd, J = 8.4 Hz, 1 H), 7.86 (d, J = 8.6 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.2, 71.2, 108.4, 114.1, 116.3, 127.0, 129.1, 130.4, 130.6, 147.1, 154.5, 159.8. Spectral data for the compound **8** was in agreement with the values reported in the literature.[25]

3,5-Di-*tert*-butyl-2-((4-methoxybenzyl)oxy)benzaldehyde (9)

The reaction was carried out according to general method A using 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde **9a** (468 mg, 2

mmol), Cs_2CO_3 (977.4 mg, 3 mmol), 4-methoxybenzylchloride (521.6 mg, 2.2 mmol) and DMF (4.7 mL) for 6 h to get compound **9** (502 mg, 71%) as a white solid. m.p.: 110 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.35 (s, 9 H), 1.47 (s, 9 H), 3.85 (s, 3 H), 4.97 (s, 2 H), 6.97 (d, J = 8.1 Hz, 2 H), 7.44 (d, J = 8.1 Hz, 2 H), 7.67 (s, 1 H), 7.76 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.9, 31.3, 34.7, 35.3, 55.2, 80.3, 113.9, 123.9, 128.6, 128.9, 129.3, 130.9, 143.0, 146.5, 159.5, 159.7, 190.2. Anal. Calcd. for $C_{23}H_{30}O_3$ (354): C, 77.93; H, 8.53; Found C, 77.90, H, 8.51.

4-((4-Methoxybenzyl)oxy)butyl acetate (10)

To a mixture of 1,4-butanediol (10 mL, 113 mmol) and 4-methoxybenzyl chloride (15.3 mL, 113 mmol) solid KOH (6.3 g, 113 mmol) was added at 0 °C. The mixture was stirred vigorously for 1 h at 0 °C and then warmed to room temperature and stirred for 6 h. The reaction mixture was quenched with ice water and extracted into ether (3 × 100 mL). Combined ether extract was washed with water (2 × 5 mL) brine (5 mL), dried (Na_2SO_4), concentrated *in vacuo* and the residue was purified by column chromatography (silica gel, EtOAc : Hexane, 3 : 7) to afford 4-(4-methoxybenzyloxy)butan-1-ol as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.54 (m, 4 H), 3.36 (t, J = 6 Hz, 2 H), 3.45 (t, J = 5.8 Hz, 2 H), 3.61 (b s, 1 H), 3.64 (s, 3 H), 4.32 (s, 2 H), 6.76 (d, J = 8.5 Hz, 2 H), 7.15 (d, J = 8.8 Hz, 2 H).

To a solution of 4-(4-methoxybenzyloxy)butan-1-ol (420 mg, 2 mmol) in dichloromethane (10 mL), acetic anhydride (0.48 mL, 5 mmol) and pyridine (0.5 mL, 6 mmol) was added. The reaction was stirred for 2 h and then quenched with saturated aq. $NaHCO_3$ solution. The organic layer was washed with water (2 × 5 mL) brine (5 mL), dried (Na_2SO_4) and evaporated *in vacuo*. The crude residue was purified by flash chromatography (silica gel, EtOAc : Hexane, 2 : 8) to afford **10** (452 mg, 90%) as a colorless oil. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.68–1.71 (m, 4 H), 2.03 (s, 3 H), 3.46 (t, J = 6 Hz, 2 H), 3.80 (s, 3 H), 4.07 (t, J = 6 Hz, 2 H), 4.42 (s, 2 H), 6.88 (d, J = 8.8 Hz, 2 H), 7.25 (d, J = 8.8 Hz, 2 H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 20.9, 25.5, 29.7, 55.3, 64.3, 69.4, 72.6, 113.8, 130.6, 159.2, 171.2. Spectral data for the compound **10** was in agreement with the values reported in the literature.[26]

4-((4-Methoxybenzyl)oxy)butyl benzoate (11)

To a solution of 4-(4-methoxybenzyloxy)butan-1-ol (420 mg, 2 mmol) in dichloromethane (10 mL) benzoyl chloride (0.25 mL, 2.2 mmol) and pyridine (0.5 mL, 6 mmol) was added at 0 °C and warmed to room temperature. The reaction mixture was stirred for 2 h and then quenched with a saturated aqueous solution of $NaHCO_3$. The organic layer was washed with water (2 × 5 mL), brine (5 mL), dried (Na_2SO_4) and evaporated *in vacuo*. The crude residue was purified by flash chromatography (silica gel, EtOAc : Hexane) to afford **11** (534 mg, 85%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.73–1.78 (m, 2 H), 1.82–1.87 (m, 2 H), 3.49 (t, J = 6 Hz, 2 H), 3.76 (s, 3 H), 4.32 (t, J = 6 Hz, 2 H), 6.86 (d, J = 8.4 Hz, 2 H), 7.25 (d, J = 8.4 Hz, 2 H), 7.38–7.40 (m, 2 H), 7.54–7.58 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.7, 26.5, 55.2, 64.8, 69.5, 72.6, 113.8, 128.4, 128.4, 129.2, 129.6, 130.5, 130.6, 132.8, 159.2, 166.6. Spectral data for the compound **11** was in agreement with the values reported in the literature.[26]

1-Methoxy-4-((4-((3-methylbut-2-en-1-yl)oxy)butoxy)methyl)benzene (12)

To a suspension of NaH (52.8 mg, 2.2 mmol) in dry THF (2 mL) 4-(4-methoxybenzyloxy)butan-1-ol (420 mg, 2 mmol) was added at 0 °C. After stirring for 20 min, prenylbromide (0.25 mL, 2.2 mmol) was added. The mixture was stirred for 2 h at room temperature and quenched with ice. After extraction with ethyl acetate (3 × 5 mL) the combined organic layer was washed with brine (5 mL), dried (Na_2SO_4) and evaporated *in vacuo*. The crude residue was purified by flash chromatography (silica gel, EtOAc : Hexane, 2 : 8) to afford **12** (432 mg, 78%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.65 (s, 6 H), 1.67–1.73 (m, 4 H), 3.41–3.45 (m, 4 H), 3.78 (s, 3 H), 3.93 (d, J = 6.8 Hz, 2 H), 4.42 (s, 2 H), 5.34 (t, J = 1.2 Hz, 1 H), 6.86 (d, J = 8.4 Hz, 2 H), 7.25 (d, J = 8.40 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.9, 25.8, 26.5, 55.2, 67.2, 69.9, 72.5, 113.7, 121.4, 129.2, 130.8, 136.6, 159.1; Anal. Calcd. for $C_{17}H_{26}O_3$: C, 73.34; H, 9.41; O, 17.24 Found: C, 73.36; H, 9.40; GCMS: Actual 278; Found 278.

1-((4-(Allyloxy)butoxy)methyl)-4-methoxybenzene (13)

To a suspension of NaH (52.8 mg, 2.2 mmol) in dry THF (2 mL) a solution of 4-(4-methoxybenzyloxy)butan-1-ol (420 mg, 2 mmol) in THF was added at 0 °C. After stirring for 20 min, allyl bromide (0.2 mL, 2.4 mmol) was added. The reaction was stirred for 2 h at room temperature and quenched with ice. After extraction with ethyl acetate (2 × 5 mL), the combined organic layers were washed with brine (5 mL), dried (Na_2SO_4) and evaporated *in vacuo*. The crude residue was purified by flash chromatography (silica gel, EtOAc : Hexane, 2 : 8) to afford **13** (410 mg, 82%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.65–1.69 (m, 4 H), 3.42–3.79 (m, 4 H), 3.79 (s, 3 H), 3.95 (d, J = 8.4 Hz, 2 H), 4.43 (s, 2 H), 5.15 (d, J = 10.4 Hz, 1 H), 5.25 (d, J = 17.2 Hz, 1 H), 5.92 (d J = 10.4 Hz, 2 H), 6.87 (d, J = 8.8 Hz, 2 H), 7.25 (d, J = 8.8 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.5, 26.5, 55.3, 69.8, 70.1, 71.8, 72.5, 113.8, 116.6, 129.2, 130.7, 135.0, 159.1; Anal. Calcd. for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86; O, 19.17; Found: C, 71.95; H, 8.85; GCMS: Actual 250; Found 250.

tert-Butyl(4-((4-methoxybenzyl)oxy)butoxy)dimethylsilane (14)

A mixture of 4-(4-methoxybenzyloxy)butan-1-ol (420 mg, 2 mmol), imidazole (163.2 mg, 2.4 mmol) and TBSCl (331.6 mg, 2.2 mmol) in dichloromethane (10 mL) was stirred at room temperature for 20 h. The reaction mixture was washed with water (2 × 5 mL), brine (5 mL), dried (Na_2SO_4) and evaporated *in vacuo*. The crude residue was purified by flash chromatography (silica gel, EtOAc : Hexane, 2 : 8) to afford **14** (452 mg, 77%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.03 (s, 6 H), 0.85 (s, 9 H), 1.54-1.62 (m, 4 H), 3.42 (t, J = 6 Hz, 2 H), 3.58 (t, J = 6 Hz, 2 H), 3.75 (s, 3 H), 4.39 (s, 2 H), 6.83 (d, J = 8.8 Hz, 2 H), 7.22 (d, J = 8.80 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 18.3, 25.9, 29.6, 55.2, 62.9, 63.2, 70.0, 72.5, 113.8, 129.2, 130.8, 159.1. Spectral data for the compound **14** was in agreement with the values reported in the literature.[11]

1-((4-(Benzyloxy)butoxy)methyl)-4-methoxybenzene (15)

To a suspension of NaH (52.8 mg, 2.2 mmol) in dry THF (2 mL) a solution of 4-(4-methoxybenzyloxy)butan-1-ol (420 mg, 2

mmol) in THF was added at 0 °C. After stirring for 20 min, benzyl bromide (0.26 mL, 2.2 mmol) was added, stirred at room temperature for 2 h and quenched with ice. After extraction with ethyl acetate (3 × 5 mL), the combined organic layers were washed with water (2 × 5 mL) brine (5 mL), dried (Na_2SO_4) and evaporated *in vacuo*. The crude residue was purified by flash chromatography (silica gel, EtOAc : Hexane, 2 : 8) to afford **15** (410 mg, 82%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.69–1.71 (m, 4 H), 3.46–3.49 (m, 4 H), 3.79 (s, 3 H), 4.42 (s, 2 H), 4.49 (s, 2 H), 6.87 (d, J = 8 Hz, 2 H), 7.25 (d, J = 8 Hz, 2 H), 7.27–7.33 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.5, 55.3, 69.8, 70.2, 72.5, 72.9, 113.8, 127.5, 127.6, 128.4, 129.2, 130.8, 138.6, 159.1. Spectral data for the compound **15** was in agreement with the values reported in the literature.[11]

4-((4-Methoxybenzyl)oxy)butyl pivalate (16)

To a solution of 4-(4-methoxybenzyloxy)butan-1-ol (420 mg, 2 mmol) in dichloromethane (10 mL) pivaloyl chloride (0.26 mL, 2.2 mmol) and pyridine (0.5 mL, 6 mmol) was added at 0 °C and stirred for 2 h at room temperature. The mixture was water (2 × 5 mL) brine (5 mL), dried (Na_2SO_4) and evaporated *in vacuo*. The crude residue was purified by flash chromatography (silica gel, EtOAc : Hexane, 2 : 8) to afford **16** (534 mg, 85%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.19 (s, 9 H), 1.65–1.74 (m, 4 H), 3.46 (t, J = 6 Hz, 2 H), 3.78 (s, 3 H), 4.06 (t, J = 6.4 Hz, 2H), 4.43 (s, 2 H), 6.87 (d, J = 8.4 Hz, 2 H), 7.25 (d, J = 8.4 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.5, 26.3, 27.2, 38.7, 55.2, 64.2, 69.5, 72.6, 113.8, 129.2, 130.6, 159.2, 178.5; Anal. calcd. for $C_{17}H_{26}O_4$: C, 69.36; H, 8.90; O, 21.74; Found; C, 69.38, H, 5.57. GCMS: Actual; 294, Found 294.

1-Methoxy-4-{[4-(trityloxy)butoxy]methyl}benzene (17)

To a stirred solution of 1-(4-methoxybenzyloxy)-4-butanol (500 mg, 2.38 mmol) in dichloromethane (20 mL) triethylamine (480 mg, 4.76 mmol), trityl chloride (660 mg, 2.38 mmol) was added at 0 °C and stirred at room temperature for 2 h. The reaction mixture was diluted with water and extracted with ethyl acetate (20 mL). Organic layer was washed with water (2 × 5 mL) brine (5 mL), dried (Na_2SO_4), concentrated under reduced pressure and purified the residue by column chromatography (silica gel, EtOAc : Hexane, 2 : 8) to give **17** (900 mg, 85%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.7–1.73 (m, 4 H), 3.08 (t, J = 5.9 Hz, 2 H), 3.44 (t, J = 6.1 Hz, 2 H), 3.82 (s, 3 H), 4.42 (s, 2 H), 6.88 (d, J = 8.3 Hz, 2 H), 7.24 (d, J = 8.3 Hz, 2 H), 7.29–7.24 (m, 9 H), 7.42–7.37 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.7, 29.7, 29.9, 62.8, 63.4, 86.4, 126.7, 126.8, 127.6, 127.7, 128.6, 144.2, 144.4. Spectral data for the compound **17** was in agreement with the values reported in the literature.[27]

2-(4-((4-Methoxybenzyl)oxy)butoxy)tetrahydro-2*H*-pyran (18)

To a solution of 1-(4-methoxybenzyloxy)-4-butanol (420 mg, 2 mmol) in dichloromethane were added 2,3-dihydropyran (252 mg, 3 mmol) and camphorsulfonic acid (42 mg). The reaction was stirred for 16 h. Organic layer was separated, washed with brine (10 mL), dried (Na_2SO_4), concentrated under reduced pressure and purified the residue by column chromatography (silica gel, EtOAc : Hexane, 1 : 9) to give **18** (441 mg, 75%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.42–1.90 (m, 10 H), 3.34–3.57 (m, 4 H), 3.67–3.93 (m, 5 H), 4.44 (s, 2 H), 4.56–4.59 (m, 1 H), 6.88 (d, J = 8.2 Hz, 2 H), 7.27 (d, J = 8.2 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 19.6, 25.5, 26.6, 26.8, 30.7, 55.3, 62.2, 67.3, 70.0, 72.5, 98.8, 113.6, 129.2, 130.7, 159.1. Spectral data for the compound **18** was in agreement with the values reported in the literature.[26]

1-((1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl)oxy)methyl)-4-methoxybenzene (19)

The reaction was carried out according to general method B using (1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexanol **19a** (312 mg, 2 mmol), 4-methoxybenzyl trichloroacetimidate (847 g, 3 mmol), $La(OTf)_3$ (117.2 mg, 0.2 mmol) and toluene (3 mL) for 2 h to get **19** (441 mg, 80%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.73 (d, J = 7.0 Hz, 3 H),0.85–1.06 (m, 9 H), 1.30–1.35 (m, 2 H), 1.61–1.68 (m, 2 H), 2.17–2.33 (m, 2 H), 3.11–3.19 (m, 1 H), 3.81 (s, 3 H), 4.34 (d, J = 11.1 Hz, 1 H), 4.59 (d, J = 11.1 Hz, 1 H), 6.88 (d, J = 8.7 Hz, 2 H), 7.27 (d, J = 8.7 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.0, 20.9, 22.3, 23.2, 25.42, 31.5, 34.5, 40.3, 48.2, 55.2, 70.0, 78.3, 113.6, 129.3, 131.2, 159.0. Spectral data for the compound **19** was in agreement with the values reported in the literature.[11]

1-((Cholesteryloxy)methyl)-4-methoxybenzene (20)

The reaction was carried out according to general method B using cholesterol **20a** (772 mg, 2 mmol), 4-methoxybenzyl trichloroacetimidate (847 g, 3 mmol), $La(OTf)_3$ (117.2 mg, 0.2 mmol) and toluene (7.7 mL) for 2 h to get **20** (690 mg, 68%) as a white solid. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 0.69 (s, 3 H), 0.88 (d, J = 6.4 Hz, 6 H), 0.92 (d, J = 6.5 Hz, 3 H), 0.96–1.58 (m, 25 H), 1.85–2.03 (m, 5 H), 2.23–2.29 (m, 1 H), 2.38–2.42 (m, 1 H), 3.23–3.27 (m, 1 H), 4.51 (s, 3 H), 5.35 (s, 2 H), 6.88 (d, J = 8 Hz, 2 H), 7.28 (d, J = 8 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.9, 18.7, 19.4, 21.1, 22.6, 23.8, 24.2, 27.9, 28.2, 28.4, 31.8, 31.9, 35.7, 36.1, 36.8, 37.2, 39.1, 39.5, 39.7, 42.3, 50.1, 55.2, 56.1, 56.7, 69.5, 78.2, 113.7, 121.4, 129.1, 131.1, 141.0, 159.0. Spectral data for the compound **20** was in agreement with the values reported in the literature.[11]

1-Methoxy-4-(phenethoxymethyl)benzene (21)

The reaction was carried out according to general method B using 2-phenylethanol **21a** (244 mg, 2 mmol), 4-methoxybenzyl trichloroacetimidate (847 g, 3 mmol), $La(OTf)_3$ (117.2 mg, 0.2 mmol) and toluene (2.4 mL) for 1 h to get **21** (445 mg, 92%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.93 (t, J = 7.3 Hz, 2 H), 3.67 (t, J = 7.3 Hz, 2 H), 3.80 (s, 3 H), 4.47 (s, 2 H), 6.87 (d, J = 8.7 Hz, 2 H), 7.21–7.22 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 36.4, 55.3, 70.9, 72.6, 113.8, 126.2, 128.3, 128.9, 129.3, 129.7, 130.5, 139.0, 159.1. Spectral data for the compound **21** was in agreement with the values reported in the literature.[11]

1-((Decyloxy)methyl)-4-methoxybenzene (22)

The reaction was carried out according to general method B using 1-decanol **22a** (260 mg, 2 mmol), 4-methoxybenzyl trichloroacetimidate (847 g, 3 mmol), $La(OTf)_3$ (117.2 mg, 0.2 mmol) and toluene (3.2 mL) for 1 h to get **22** (425 mg, 85%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, J = 6.8 Hz, 3 H), 1.25–1.34 (m, 14 H), 1.57–1.61 (m, 2 H), 3.43 (t, J = 6.8 Hz,

2 H), 3.78 (s, 3 H), 4.42 (s, 2 H), 6.86 (d, J = 8.4 Hz, 2 H), 7.25 (d, J = 8.4 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.1, 22.7, 29.2, 29.3, 29.4, 29.5, 32., 55.2, 70.3, 72.5, 113.7, 129.2, 130.8, 159.1. Spectral data for the compound **22** was in agreement with the values reported in the literature.[11]

1-((Cinnamyloxy)methyl)-4-methoxybenzene (23)

The reaction was carried out according to general method B using cinnamyl alcohol **23a** (268 mg, 2 mmol), 4-methoxybenzyl trichloroacetimidate (847 g, 3 mmol), $La(OTf)_3$ (117.2 mg, 0.2 mmol) and toluene (2.7 mL) for 1 h to get **23** (447 mg, 88%) as a colorless oil. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 3.81 (s, 3 H), 4.17 (dd, J = 1.2, 6 Hz, 2 H), 4.51 (s, 2 H), 6.28–6.35 (m, 1 H), 6.62 (d, J = 16 Hz, 1 H), 6.89 (d, J = 8.4 Hz, 2 H), 7.25–7.26 (m, 1 H), 7.29–7.33 (m, 2 H), 7.39 (d, J = 8.4 Hz, 2 H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 55.3, 70.5, 71.9, 113.9, 126.2, 126.5, 127.6, 128.5, 129.5, 130.4, 132.5, 136.8, 159.3. Spectral data for the compound **23** was in agreement with the values reported in the literature.[11]

1-((Hex-5-yn-1-yloxy)methyl)-4-methoxybenzene (24)

The reaction was carried out according to general method B using hex-5-yn-1-ol **24a** (196 mg, 2 mmol), 4-methoxybenzyl trichloroacetimidate (847 g, 3 mmol), $La(OTf)_3$ (117.2 mg, 0.2 mmol) and toluene (2 mL) for 1 h to get **24** (331 mg, 76%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.65–1.66 (m, 2 H), 1.71–1.72 (m, 2 H), 1.96–1.96 (m, 1 H), 2.21–2.22 (m, 2 H), 3.49 (t, J = 6.3 Hz, 2 H), 3.83 (s, 3 H), 4.45 (s, 2 H), 6.90 (d, J = 8.5 Hz, 2 H), 7.29 (d, J = 8.4 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 18.1, 25.2, 28.7, 55.2, 68.3, 69.3, 72.5, 84.3, 113.7, 129.1, 130.6, 159.0; Anal. calcd. for $C_{14}H_{18}O_2$; C, 77.03; H, 8.31; O, 14.66; Found; C, 77.04, H, 8.33; GCMS: Actual; 218, Found 218.

6-benzyloxy-5-(((4-methoxybenzyl)oxy)methyl)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]-dioxole (25)

To a suspension of NaH (200 mg, 4.6 mmol) in dry THF (15 mL) diacetonegalactose (600 mg, 2.3 mmol) was added in portions over a period of 30 min at 0 °C. After 30 min, 4-methoxybenzyl bromide (460 mg, 2.3 mmol) was added and stirred for 17 h at room temperature. The reaction mixture was quenched with ice and extracted with ethyl acetate (2 × 5 mL). The combined organic layers were washed with water (2 × 5 mL), brine (5 mL), dried (Na_2SO_4) and evaporated *in vacuo*. The crude residue was purified by flash chromatography (silicagel, EtOAc : Hexane, 3 : 7) to afford the mono substituted product (622 mg, 70%) as a colorless oil.

To a suspension of NaH (0.2 g, 4.6 mmol) in dry THF (15 mL) the product (0.6 g, 1.84 mmol) from the above mentioned procedure was added in portions over a period of 30 min at 0 °C. After 30 min, benzyl bromide (0.46 g, 2.3 mmol) was added and stirred for 4 h at room temperature. The reaction mixture was quenched with ice and extracted with ethyl acetate. The combined organic layers were washed with water (2 × 5 mL), brine (5 mL), dried (Na_2SO_4) and evaporated *in vacuo*. The crude residue was purified by flash chromatography (silica gel, EtOAc : Hexane, 2 : 8) to afford **25** (605 mg, 88%) as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.32 (s, 3 H), 1.49 (s, 3 H), 3.73–33.75 (m, 2 H), 3.80 (s, 3 H), 3.96 (d, J = 6.8 Hz, 1 H), 4.37–4.64 (m, 6 H), 5.93 (d, J = 4.8 Hz, 1 H), 6.87 (d, J = 8 Hz, 2 H), 7.19–7.34 (m, 7 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.3, 26.8, 55.3, 67.6, 72.0, 73.5, 77.0, 79.3, 81.8, 82.5, 105.1, 111.7, 113.8, 127.6, 127.9, 129.3, 129.5, 129.6, 138.1, 159.4. Spectral data for the compound **25** was in agreement with the values reported in the literature.[9c]

4-Methoxybenzyl palmitate (26)

The reaction was carried out according to general method C, using palmitic acid **26a** (512 mg, 2 mmol), K_2CO_3 (414 mg, 3 mmol), 4-methoxybenzylchloride (374.4 mg, 2.4 mmol) and DMF (5.1 mL) for 3 h to get **26** (638 mg, 85%) as a colorless oil. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 0.89 (t, J = 6.8 Hz, 3 H), 1.26 (m, 24 H), 1.62–1.64 (m, 2 H), 2.31 (t, J = 6.8 Hz, 2 H), 3.80 (s, 3 H), 5.04 (s, 2 H), 6.88 (d, J = 8.8 Hz, 2 H), 7.29 (d, J = 8.8 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1, 22.7, 24.9, 29.1, 29.3, 29.4, 29.5, 29.6, 29.7, 29.7, 31.94, 34.4, 55.2, 65.9, 113.9, 128.3, 130.0, 159.6, 173.8. Spectral data for the compound **26** was in agreement with the values reported in the literature.[28]

4-Methoxybenzyl oleate (27)

The reaction was carried out according to general method C using oleic acid **27a** (564 mg, 2 mmol), K_2CO_3 (414 mg, 3 mmol), 4-methoxybenzylchloride (374.4 mg, 2.4 mmol) and DMF (5.6 mL) for 3 h to get **27** (658 mg, 82%) as a colorless oil. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 0.88 (t, J = 6.8 Hz, 3 H), 1.27–1.28 (m, 22 H), 1.60–1.61 (m, 2 H), 2.00–2.02 (m, 4 H), 2.30 (t, J = 7.6 Hz, 2 H), 3.76 (s, 3 H), 5.03 (s, 2 H), 5.32–5.35 (m, 2 H), 6.86 (d, J = 8.4 Hz, 2 H), 7.26 (d, J = 8.4 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1, 22.7, 25.0, 25.7, 27.2, 29.1, 29.3, 29.5, 29.6, 29.8, 31.6, 32.0, 34.3, 55.1, 55.2, 65.8, 113.9, 128.0, 128.34, 129.7, 130.0, 159.6, 173.5. Spectral data for the compound **27** was in agreement with the values reported in the literature.[29]

4-Methoxybenzyl benzoate (28)

The reaction was carried out according to general method C, benzoic acid **28a** (244 mg, 2 mmol), K_2CO_3 (414 mg, 3 mmol), 4-methoxybenzylchloride (374.4 mg, 2.4 mmol) and DMF (2.4 mL) for 5 h to get **28** (446 mg, 92%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.83 (s, 3 H), 5.31 (s, 2 H), 6.93 (d, J = 8.2 Hz, 2 H), 7.40–7.42 (m, 5 H), 8.07 (t, J = 0.8 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.2, 66.5, 113.8, 128.1, 128.2, 129.6, 129.9, 130.2, 132.8, 159.6, 166.4. Spectral data for the compound **28** was in agreement with the values reported in the literature.[27]

4-Methoxybenzyl 4-methoxybenzoate (29)

The reaction was carried out according to general method C, 4-methoxybenzoic acid **29a** (304 mg, 2 mmol), K_2CO_3 (414 mg, 3 mmol), 4-methoxybenzylchloride (374.4 mg, 2.4 mmol) and DMF (3 mL) for 5 h gave **29** (490 mg, 90%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.79 (s, 3 H), 3.83 (s, 3 H), 5.28 (s, 2 H), 6.90–6.93 (m, 4 H), 7.39 (d, J = 8.5 Hz, 2 H), 8.02 (d, J = 8.8 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.2, 55.3, 66.2, 113.5, 113.9, 122.6, 128.4, 128.2, 129.3, 129.9, 129.9, 131.6, 159.5, 163.3, 166.2. Spectral data for the compound **29** was in agreement with the values reported in the literature.[30]

(4-Methoxybenzyl 3-(4-(benzyloxy)phenyl)-2-((*tert*-butoxycarbonyl)amino)propanoate) (30)

The reaction was carried out according to general method C, 3-(4-(benzyloxy)phenyl)-2-((tertbutoxycarbonyl)amino)propanoic acid **30a** (742 mg, 2 mmol), K_2CO_3 (207 mg, 1.5 mmol), 4-methoxybenzylchloride (187.2 mg, 1.2 mmol) for 2 h gave **30** (785 mg, 80%) as a white solid. m.p.: 72.2 °C–74.3 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.30 (s, 9 H), 2.78–2.81 (m, 2 H), 3.73 (s, 3 H), 4.07–4.09 (m, 1 H), 4.98 (s, 2 H), 5.04 (s, 2 H), 6.87–6.89 (m, 4 H), 7.11 (d, J = 11.1 Hz, 2 H), 7.21 (d, J = 11.32 Hz, 2 H), 7.11 (d, J = 11.1 Hz, 2 H), 7.28–7.43 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.4, 36.0, 55.5, 56.1, 66.2, 69.6, 78.7, 114.2, 114.9, 128.0, 128.2, 128.9, 130.0, 130.2, 130.6, 137.6, 155.8, 157.5, 159.6, 172.5. Anal. Calcd. for $C_{29}H_{33}NO_6$ (491): C, 70.86; H, 6.77; N, 2.85 Found C, 70.89; H, 6.79; N, 2.87.

Deprotection of PMB ethers and esters

Vanillin (1a)

According to General Method D, 3-methoxy-4-((4-methoxybenzyl)oxy)benzaldehyde **1** (272 mg, 1 mmol), $POCl_3$ (76.6 mg, 0.5 mmol) gave compound **1a** (136 mg, 90%) as a white solid. Spectral data for the compound **1a** was in agreement with the commercially available sample.

Diethyl 2-(((3-hydroxyphenyl)amino)methylene)malonate (2a)

According to general method D, diethyl 2-(((3-((4-methoxybenzyl)oxy)phenyl)amino)methylene)malonate **2** (400 mg, 1 mmol) and $POCl_3$ (76.6 mg, 0.5 mmol) gave **2a** (262 mg, 94%) as a white solid. Spectral data for the compound **2a**[16] was in agreement with the starting material **2**.

2-Hydroxy acetophenone (3a)

According to general method D, 1-(2-((4-methoxybenzyl)oxy)-phenyl)ethanone **3** (256 mg, 1 mmol) and $POCl_3$ (76.6 mg, 0.5 mmol) gave **3a** (122 mg, 90%) as a white solid. Spectral data for the compound **3a** was in agreement with the commercially available sample.

Methyl salicylate (4a)

According to general method D, methyl 2-((4-methoxybenzyl)oxy)benzoate **4** (272 mg, 1 mmol) and $POCl_3$ (76.6 mg, 0.5 mmol) gave **4a** (140 mg, 90%) as a colorless oil. Spectral data for the compound **4a** was in agreement with the commercially available sample.

2-Bromo-4-fluorophenol (5a)

According to general method D, 2-bromo-4-fluoro-1-((4-methoxybenzyl)oxy)benzene **5** (311 mg, 1 mmol) and $POCl_3$ (76.6 mg, 0.5 mmol) gave **5a** (112 mg, 92%) as a white solid. Spectral data for the compound **5a** was in agreement with the commercially available sample.

4-Ethylphenol (6a)

According to general method D, 1-ethyl-4-((4-methoxybenzyl)oxy)benzene **6** (242 mg, 1 mmol) and $POCl_3$ (76.6 mg, 0.5 mmol) gave **6a** (116 mg, 95%) as an off-white solid. Spectral data for the compound **6a** was in agreement with the commercially available sample.

4-Propoxyphenol (7a)

According to general method D,1-methoxy-4-((4-propoxyphenoxy)methyl)benzene **7** (272 mg, 1 mmol) and $POCl_3$ (76.6 mg, 0.5 mmol) gave **7a** (140 mg, 92%) as a pale brown solid. Spectral data for the compound **7a** was in agreement with the commercially available sample.

2-Chloro-5-nitrophenol (8a)

According to general method D, 1-chloro-2-((4-methoxybenzyl)oxy)-4-nitrobenzene **8** (292 mg, 1 mmol) and $POCl_3$ (76.6 mg, 0.5 mmol) gave **8a** (162 mg, 94%) as a pale brown solid. Spectral data for the compound **8a** was in agreement with the commercially available sample.

3,5-di-*tert*-Butyl-2-hydroxybenzaldehyde (9a)

According to general method D, 3,5-Di-*tert*-butyl-2-((4-methoxybenzyl)oxy)benzaldehyde **9** (354 mg, 1 mmol) and $POCl_3$ (76.6 mg, 0.5 mmol) gave **9a** (210 mg, 90%) as a yellow solid. Spectral data for the compound **9a** was in agreement with the commercially available sample.

4-Hydroxybutyl acetate (10a)

According to general method D, 4-((4-methoxybenzyl)oxy)butyl acetate **10** (252 mg, 1 mmol) and $POCl_3$ (76.6 mg, 0.5 mmol) gave **10a** (124 mg, 94%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.68–1.71 (m, 4 H), 2.03 (s, 3 H), 3.46 (t, J = 6 Hz, 2 H), 3.80 (s, 3 H), 4.07 (t, J = 6 Hz, 2 H), 4.42 (s, 2 H), 6.88 (d, J = 8.8 Hz, 2 H), 7.25 (d, J = 8.8 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.9, 25.5, 29.7, 55.3, 64.3, 69.4, 72.6, 113.8, 130.6, 159.2, 171.2. Spectral data for the compound **10a** was in agreement with the values reported in the literature.[31]

4-Hydroxybutyl benzoate (11a)

According to general method D, 4-((4-methoxybenzyl)oxy)butyl acetate **11** (314 mg, 1 mmol) and $POCl_3$ (76.6 mg, 0.5 mmol) gave **11a** (174 mg, 90%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.74–1.76 (m, 2 H), 1.86–1.90 (m, 2 H), 3.73 (t, J = 6.4 Hz, 2 H), 4.37 (t, J = 6.4 Hz, 2 H), 7.44–7.46 (m, 2 H), 7.56–7.59 (m, 1 H), 8.03–8.05 (m, 2 H). Spectral data for the compound **11** was in agreement with the values reported in the literature.[32]

4-((3-Methylbut-2-en-1-yl)oxy)butan-1-ol (12a)

According to general method D, 1-methoxy-4-((4-((3-methylbut-2-en-1-yl)oxy)butoxy)methyl)benzene **12** (278 mg, 1 mmol) and $POCl_3$ (76.6 mg, 0.5 mmol) gave **12a** (184 mg, 93%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.67 (s, 3 H), 1.67–1.69 (m, 4 H), 1.75 (s, 3 H), 3.46 (t, J = 6 Hz, 2 H), 3.64 (t, J = 6 Hz, 2 H), 3.97 (t, J = 6 Hz, 2 H), 5.33–5.36 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 18.0, 25.8, 27.0, 30.5, 62.8, 67.4, 70.2, 120.8, 137.2. Spectral data for the compound **12** was in agreement with the values reported in the literature.[33]

4-(Allyloxy)butan-1-ol (13a)

According to general method D, 1-((4-(allyloxy)butoxy)methyl)-4-methoxybenzene **13** (250 mg, 1 mmol) and $POCl_3$ (76.6 mg,

0.5 mmol) gave **13a** (118 mg, 91%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.65–1.72 (m, 4 H), 3.48 (t, J = 6 Hz, 2 H), 3.65 (d, J = 6 Hz, 2 H), 3.99 (d, J = 6 Hz, 2 H), 5.19 (d, J = 11 Hz, 1 H), 5.28 (d, J = 18 Hz, 1 H), 5.86–5.96 (m, 1 H). Spectral data for the compound **13a** was in agreement with the values reported in the literature.[34]

4-((*tert*-Butyldimethylsilyl)oxy)butan-1-ol (14a)

According to general method D, *tert*-butyl(4-((4-methoxybenzyl)oxy)butoxy)dimethylsilane **14** (324 mg, 1 mmol) and $POCl_3$ (76.6 mg, 0.5 mmol) gave **14a** (168 mg, 83%) as a colorless oil. Spectral data for the compound **14a** was in agreement with the values reported in the literature.[35]

According to general method E, *tert*-butyl(4-((4-methoxybenzyl)oxy)butoxy)dimethylsilane **14** (162 mg, 0.5 mmol), $POCl_3$ (38.3 mg, 0.25 mmol) and 1-dodecanethiol (303.6 mg, 1.5 mmol) gave **14a** (90 mg, 88%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.65 (s, 6 H), 0.84 (s, 9 H), 1.55–1.56 (m, 4 H), 3.54–3.61 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ −5.4, 18.2, 25.8, 29.6, 62.3, 63.2. Spectral data for the compound **14a** was in agreement with the values reported in the literature.[35]

4-(Benzyloxy)butan-1-ol (15a)

According to general method D, 1-((4-(benzyloxy)butoxy)methyl)-4-methoxybenzene **15** (150 mg, 0.5 mmol) and $POCl_3$ (38.3 mg, 0.25 mmol) gave **15a** (75 mg, 83%) as a colorless oil. Spectral data for the compound **15a** was in agreement with the values reported in the literature.[36]

According to general method E, 1-((4-(benzyloxy)butoxy)methyl)-4-methoxybenzene **15** (150 mg, 0.5 mmol) $POCl_3$ (38.3 mg, 0.25 mmol) and 1-dodecanethiol (303.6 mg, 1.5 mmol) gave **15a** (82 mg, 91%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.68–1.72 (m, 4 H), 3.52 (t, J = 6 Hz, 2 H), 3.65 (d, J = 6 Hz, 2 H), 4.52 (s, 2 H), 7.33–7.35 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.7, 30.1, 62.7, 70.3, 73.0, 127.7, 127.7, 128.4, 138.2. Spectral data for the compound **17a** was in agreement with the values reported in the literature.[36]

4-Hydroxybutyl pivalate (16a)

According to general method D, 4-((4-methoxybenzyl)oxy)butyl pivalate **16** (294 mg, 1 mmol) and $POCl_3$ (76.6 mg, 0.5 mmol) gave **16a** (90 mg, 90%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.20 (s, 9 H), 1.62–1.75 (m, 4 H), 3.67 (t, J = 6 Hz, 2 H), 4.09 (t, J = 6 Hz, 2 H), 4.43 (s, 2 H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 25.1, 27.1, 29.0, 38.7, 62.1, 64.2, 178.8. Spectral data for the compound **16a** was in agreement with the values reported in the literature.[37]

4-(Trityloxy)butan-1-ol (17a)

According to general method D, 1-methoxy-4-{[4-(trityloxy)butoxy]methyl}benzene **17** (226 mg, 0.5 mmol) and $POCl_3$ (38.3 mg, 0.25 mmol) gave **17a** (99 mg, 60%) as a colorless oil. Spectral data for the compound **17a** was in agreement with the values reported in the literature.[9c]

According to general method E, 1-methoxy-4-{[4-(trityloxy)butoxy]methyl}benzene **17** (226 mg, 0.5 mmol) $POCl_3$ (38.3 mg, 0.25 mmol) and 1-dodecanethiol (303.6 mg, 1.5 mmol) gave **17a** (133 mg, 80%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.68–1.72 (m, 4 H), 3.13 (t, J = 5.8 Hz, 2 H), 3.64 (t, J = 5.8 Hz, 2 H), 7.21–7.34 (m, 10 H), 7.43–7.47 (m, 5 H). Spectral data for the compound **17a** was in agreement with the values reported in the literature.[9c]

4-((Tetrahydro-2*H*-pyran-2-yl)oxy)butan-1-ol (18a)

According to general method D, 2-(4-((4-methoxybenzyl)oxy)-butoxy)tetrahydro-2*H*-pyran **18** (147 mg, 0.5 mmol) and $POCl_3$ (38.3 mg, 0.25 mmol) gave **18a** (56 mg, 65%) as a colorless oil.

According to general method E, 2-(4-((4-methoxybenzyl)oxy)butoxy)tetrahydro-2*H*-pyran **18** (147 mg, 0.5 mmol), $POCl_3$ (38.3 mg, 0.25 mmol) and 1-dodecanethiol (303.6 mg, 1.5 mmol) gave **18a** (71 mg, 81%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.38–1.54 (m, 4 H), 1.71–1.78 (m, 5 H), 1.83 (m, 1 H), 3.41–3.56 (m, 2 H), 3.68 (t, J = 6 Hz, 2 H), 3.73–3.91 (m, 2 H), 4.62 (t, J = 4 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 19.5, 25.3, 26.5, 29.8, 30.6, 62.2, 62.6, 67.4, 98.8. Spectral data for the compound **18a** was in agreement with the values reported in the literature.[14,38]

(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexanol (19a)

According to general method D, 1-((((1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl)oxy)methyl)-4-methoxybenzene **19** (276 mg, 1 mmol) and $POCl_3$ (76.6 mg, 0.5 mmol) gave **19a** (124 mg, 83%) as a white solid. Spectral data for the compound **19a** was in agreement with the commercially available sample.

Cholestrol (20a)

According to general method D, 1-((Cholesteryloxy)methyl)-4-methoxybenzene **20** (506 mg, 1 mmol) and $POCl_3$ (76.6 mg, 0.5 mmol) gave **20a** (632 mg, 82%) as a white solid. Spectral data for the compound **20a** was in agreement with the commercially available sample.

2-Phenylethanol (21a)

According to general method D, 1-methoxy-4-(phenethoxymethyl)benzene **21** (242 mg, 1 mmol) and $POCl_3$ (76.6 mg, 0.5 mmol) gave **21a** (98 mg, 81%) as a colorless oil. Spectral data for the compound **21a** was in agreement with the commercially available sample.

Cinnamyl alcohol (22a)

According to general method D, 1-((cinnamyloxy)methyl)-4-methoxybenzene **22** (254 mg, 1 mmol) and $POCl_3$ (76.6 mg, 0.5 mmol) gave **22a** (116 mg, 90%) as a colorless oil. Spectral data for the compound **22a** was in agreement with the commercially available sample.

1-Decanol (23a)

According to general method D, 1-((Decyloxy)methyl)-4-methoxybenzene **23** (205 mg, 1 mmol) and $POCl_3$ (76.6 mg, 0.5 mmol) gave **23a** (112 mg, 90%) as a colorless oil. Spectral data for the compound **23a** was in agreement with the commercially available sample.

Hex-5-yn-1-ol (24a)

According to general method D, 1-((hex-5-yn-1-yloxy)methyl)-4-methoxybenzene **24** (218 mg, 1 mmol) and $POCl_3$ (76.6 mg, 0.5 mmol) gave **24a** (88 mg, 90%) as a colorless oil. Spectral data

for the compound **24a** was in agreement with the commercially available sample.

(6-(Benzyloxy)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-5-yl)methanol (25a)

According to general method D, 6-(benzyloxy)-5-(((4-methoxybenzyl)oxy)methyl)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxole **25** (200 mg, 0.5 mmol) and $POCl_3$ (38.3 mg, 0.25 mmol) gave **25a** (75 mg, 75%) as a colorless oil. Spectral data for the compound **25a** was in agreement with the values reported in the literature.[9c]

According to general method E, 6-(benzyloxy)-5-(((4-methoxybenzyl)oxy)methyl)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxole **25** (200 mg, 0.5 mmol), $POCl_3$ (38.3 mg, 0.25 mmol) and 1-dodecanethiol (303.6 mg, 1.5 mmol) gave **25a** (83 mg, 83%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.33 (s, 3 H), 1.49 (s, 3 H), 3.65 (bs, 2 H), 3.91–3.99 (m, 2 H), 4.24–4.31 (m, 1 H), 4.53 (d, J = 3.7 Hz, 1 H), 4.58 (d, J = 3.8 Hz, 1 H), 4.66 (d, J = 4.8 Hz, 1 H), 6.00 (d, J = 4.4 Hz, 1 H), 7.29–7.39 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 26.2, 26.8, 68.2, 74.1, 78.0, 85.3, 104.8, 111.6, 127.9, 128.1, 128.6, 137.1. Spectral data for the compound **25a** was in agreement with the values reported in the literature.[9c]

Palmitic acid (26a)

According to general method D, 4-methoxybenzyl palmitate **26** (376 mg, 1 mmol) and $POCl_3$ (76.6 mg, 0.5 mmol) gave **26a** (236 mg, 92%) as a colorless oil. Spectral data for the compound **26a** was in agreement with the commercially available sample.

Oleic acid (27a)

According to general method D, 4-methoxybenzyl oleate **27** (402 mg, 1 mmol) and $POCl_3$ (76.6 mg, 0.5 mmol) gave **27a** (248 mg, 88%) as a colorless oil. Spectral data for the compound **27a** was in agreement with the commercially available sample.

Benzoic acid (28a)

According to general method D, 4-methoxybenzyl benzoate **28** (242 mg, 1 mmol) and $POCl_3$ (76.6 mg, 0.5 mmol) gave **28a** (110 mg, 88%) as a white solid. Spectral data for the compound **28a** was in agreement with the commercially available sample.

4-Methoxy benzoic acid (29a)

According to general method D, 4-methoxybenzyl 4-methoxybenzoate **31** (272 mg, 1 mmol) and $POCl_3$ (76.6 mg, 0.5 mmol) gave **29a** (134 mg, 88%) as a white solid. Spectral data for the compound **29a** was in agreement with the commercially available sample.

3-(4-(Benzyloxy)phenyl)-2-((*tert*-butoxycarbonyl)amino)propanoic acid (30a)

According to general method D, (4-methoxybenzyl 3-(4-(benzyloxy)phenyl)-2-((*tert*-butoxycarbonyl)amino)propanoate) **30a** (591 mg, 1 mmol) and $POCl_3$ (76.6 mg, 0.5 mmol) gave **30a** (304 mg, 88%) as a white solid. Spectral data for the compound **30a** was in agreement with the commercially available sample.

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