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Silver(I)-Catalyzed Deprotection of *p*-Methoxybenzyl Ethers: A Mild and Chemoselective Method

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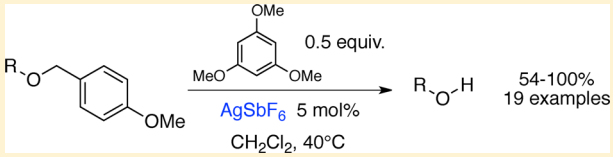
Supporting Information

ABSTRACT: The *p*-methoxybenzyl protecting group (PMB) on various alcohols and an acid was efficiently and selectively cleaved by the action of a catalytic amount of silver(I) hexafluoroantimonate combined with 0.5 equiv of 1,3,5-trimethoxybenzene in dichloromethane at 40 °C.



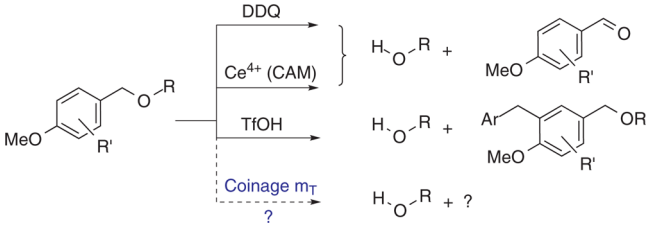
INTRODUCTION

The syntheses of complex molecules, e.g., natural products, is still a challenge despite the tremendous progress made in the last 20 years.[1] Most of these syntheses still require many protection and deprotection steps, although achieving syntheses without protecting groups is becoming another current challenge[2] within the green chemistry revolution.[3]

In response to the increasing complexity of the molecular structures synthesized, numerous protecting groups have been developed, as well as methods for their introduction and their deprotection.[4] Nevertheless, new and more selective protecting groups are still required[5] while milder and more selective conditions are actively pursued.[6]

Among protecting groups, benzyl derivatives occupy a unique position due to their deprotection conditions being orthogonal to other protecting and functional groups, and due to their broad applications, including the protection of alcohols, thiols, amines, and carboxylic acids.[7] Methoxy-substituted benzyl derivatives are even more interesting due to the very specific oxidative conditions[8] used to deprotect them and are thus widely used. So far, dichlorodicyanoquinone (DDQ) is the reagent of choice, usually applied in dichloromethane in the presence of water (Scheme 1, top).[9] However, this reagent must be used at least in stoichiometric amount and leads to side products, anisaldehyde and acidic hydroquinone.

Scheme 1. Known Deprotection of Methoxybenzyl Ethers (R′ = H or OMe) and a Proposed Coinage Metal-Catalyzed Deprotection



There is thus a need to replace this reagent with a milder, greener, catalytic method. Acting by two successive single electron transfers (SET), DDQ could be replaced by species also prone to SET but in a more selective way. Interestingly, a version catalytic in DDQ has been developed using Fe^{3+} or Mn^{3+} as an electron relay.[10] Various conditions based on cerium(III/IV) salts have also been reported;[11] however, only cerium(IV) ammonium nitrate (CAN) seems to be regularly used (Scheme 1, middle). Cerium(III) versions proceed with variable amounts of catalyst in nitromethane at reflux and seem to be water dependent.[11d,12] Stronger Lewis acids such as $AlCl_3$, $SnCl_2$, $MgBr_2{\cdot}Et_2O$, and $ZrCl_4$ are also known to promote PMB cleavage.[13] However, these methods suffer from drawbacks such as the use of stoichiometric reagents, their association with nucleophiles, or purification problems.

A few examples of PMB deprotection by protic acid are also known.[14] Among them, a few reported the simultaneous use of sulfonamides[14c] and 1,3-dimethoxybenzene[14d] as trapping agents. Recently, Jung et al. proposed an approach using triflic acid,[14e] with or without 1,3-dimethoxybenzene as stoichiometric trapping reagent, despite some limitations notably for allylic and propargylic alcohols and the inherent problem of orthogonality with the other acidic-sensitive protecting groups (Scheme 1).

This context led us to explore the role of coinage metal salts in the selective deprotection of PMB protecting groups (Scheme 1, bottom). Coinage metals, mostly copper and silver, are well-known not only for their redox properties[15] but also for their Lewis acid character.[16] Combining both would facilitate the cleavage of redox-active protecting groups. Herein, we describe a new Ag-catalyzed mild and chemoselective method for the removal of such protecting groups.[14c]

RESULTS AND DISCUSSION

Catalyst and Condition Survey. To find the best conditions for the deprotection of methoxybenzyl ethers, the

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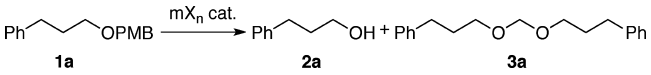
most common *p*-methoxybenzyl (PMB) derivatives were considered. We looked for a simple compound but one heavy enough for easy handling and quantification of the formed product(s). The PMB 3-phenylpropyl ether **1a** was thus selected. It was readily obtained from the commercially available alcohol **2a** by deprotonation with NaH and alkylation with the PMB iodide prepared in situ.[17]

This PMB ether was subjected to various common salts of coinage metals under various conditions (Table 1). Copper salts did not give any significant transformation, whatever their oxidation states; modifying the solvent and reaction temperature made no difference (entries 1−4). In contrast, silver salts gave interesting results that were dependent on the nature of their counterion. Silver chloride did not give any transformation, probably for solubility reasons, even in polar and coordinating solvents and at high temperatures (entries 5 and 6). More soluble in common organic solvents, silver triflate and hexafluoroantimonate gave mixtures of products, among which was the desired deprotected alcohol. At room temperature, the former gave the expected alcohol **2a** in modest yield and after a long reaction time (entry 7). Surprisingly, a major side product could be isolated and spectroscopic investigations revealed its symmetrical acetal structure **3a**. With silver hexafluoroantimonate, the same results were observed but with a higher overall yield and with a higher alcohol−acetal ratio in favor of the required alcohol (5.5:1 vs 2:1 respectively; entry 8 vs 7). Upon warming, the reaction became quantitative within a few hours, giving 68% and 15% of **2a** and **3a**, respectively (i.e., 98% of the mass balance, entry 9).

Table 1. Condition Screening for PMB Ether 1a Deprotection[a]



1a **2a** **3a**

entry	catalyst	conditions	time (h)	yield[b] **1a** (%)	yield[c] **2a** (%)	yield[b,d] **3a** (%)
1	CuCl	CH_2Cl_2, rt→rfx	4	100	–	–
2	CuCl	CH_3CN, rt→rfx	20	100	–	–
3	$CuCl_2$	CH_2Cl_2, rt→rfx	4	100	–	–
4	$CuCl_2$	CH_3CN, rt→rfx	20	100	–	–
5	AgCl	CH_2Cl_2, rt→rfx	1	100	–	–
6	AgCl	CH_3CN, rt→rfx	20	100	–	–
7	AgOTf	CH_2Cl_2, rt	20	trace	30	15
8	$AgSbF_6$	CH_2Cl_2, rt	20	trace	55	10
9	$AgSbF_6$	CH_2Cl_2, rfx	4	–	**68**	15
10	$AgSbF_6$	$Cl(CH_2)_2Cl$, rfx	1	–	67	13
11	$AgSbF_6$	$CHCl_3$, rt→rfx	6	–	39	27
12	$AgSbF_6$	PhMe, rt→rfx	20	–	deg.	deg.
13	$AgSbF_6$	THF, rt→rfx	20	97	trace	trace
14	$AgSbF_6$	CH_3CN, rt→rfx	20	100	–	–
15	$AgSbF_6$	CH_3NO_2, rt→rfx	20	100	–	–
16	AuCl	CH_2Cl_2, rt	5	–	46	13
17	PPh_3AuNTf_2	CH_2Cl_2, rt	5	49[e]	21	9
18	$AuCl_3$	CH_2Cl_2, rt	1	–	39	15

[a]Reaction conditions: *C* = 0.1 mol/L in solvent, 5 mol % catalyst. [b]Estimated yield based on the ^{1}H NMR of the crude mixture. [c]Yields of isolated pure product. [d]Reported yields were based on the stoichiometry of the reaction. [e]No evolution of the conversion was observed after 5 h of reaction.

The unexpected formation of the acetal **3a** suggested the intervention of the solvent, dichloromethane, as a possible source of the extra carbon of this acetal. Therefore, we further screened other solvents with silver hexafluoroantimonate as catalyst to improve the reaction, while minimizing the acetal formation. Dichloroethane and chloroform gave conversions similar to those of dichloromethane but with some variation in the alcohol−acetal ratio (5.1:1 and 1.4:1 vs 4.5:1, respectively (entries 10 and 11 vs 9). The fact that dichlorethane provided the same mixture of **2a** and **3a** products excluded the CH_2Cl_2 origin of the acetal carbon (entry 10). In sharp contrast, less polar as well as more polar solvents either led to rapid degradation upon warming (entry 12) or to almost no transformation (entries 13−15).

Gold chloride provided similar results but in a faster reaction and with an increase of the ratio in favor of the acetal (3.5:1 vs 5.5:1, respectively; entry 16 vs 9). The more cationic $Ph_3PAuNTf_2$ proved less effective than AuCl presumably due to degradation of the catalyst after 5 h (gold mirror formation, entry 16 vs 17). Gold trichloride did not improve the reaction yield nor the alcohol:acetal ratio (entry 18 vs 16).

Mechanistic Hypothesis and Condition Optimization. During these catalyst screening studies, we noticed in all reactions the presence of numerous side products, notably the bis(4-methoxyphenyl)methane. The latter clearly derived from the PMB part of the starting materials. These observations suggested a purely Lewis acid mechanism and another origin of the acetal extra carbon coming from the PMB motif itself.[11d]

Scheme 2. Proposed Mechanism for the Silver-Catalyzed Deprotection of PMB Ethers and the Formation of Acetal 3

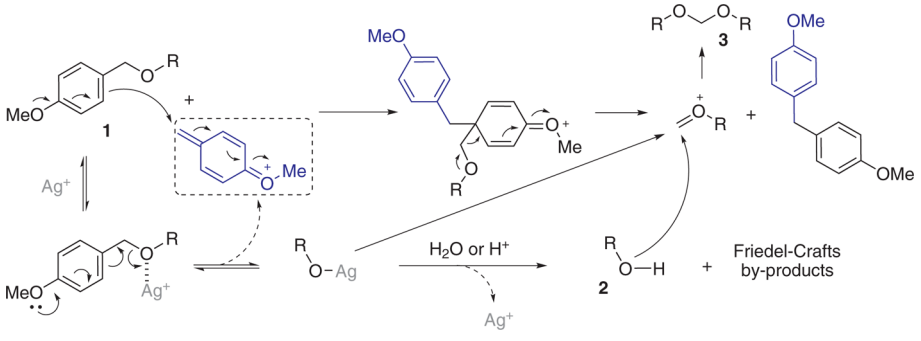


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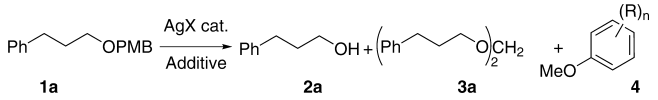
Table 2. Effect of Water and Aromatic Donors and Conditions on PMB Ether Deprotection[a]



1a 2a 3a 4

entry	catalyst	additive (equiv)	time (h)	yield **2a** (%)	yield[b] **3a** (%)	ratio[c] TMB[d]:**4a**:**4b**:**4c** (%)
1	$AgSbF_6$	–	5	68	15	
2	$AgSbF_6$	H_2O (1)	5	75	12	
3	$AgSbF_6$	H_2O (10)	20	–	–	
4	$AgSbF_6$	TMB (1)	5	100	–	27:46:26:1
5	$AgSbF_6$	TMB (0.5)	5	100	–	0:38:52:10
6	$AgNTf_2$	TMB (0.5)	7	99	–	
7	AgOTf	TMB (0.5)	24	97	–	
8	$AgBF_4$	TMB (0.5)	24	96	–	
9	$AgPF_6$	TMB (0.5)	24	32	–	
10	$AgNO_3$	TMB (0.5)	24	0	–	
11	AgCl	TMB (0.5)	24	0	–	

[a]Reaction conditions: C = 0.1 mol/L in CH_2Cl_2 at 40 °C, 5 mol % catalyst. [b]Estimated yield from the ^1H NMR of the crude mixture. [c]Ratio relative to TMB, estimated from NMR analysis. [d]TMB = 1,3,5-trimethoxybenzene.

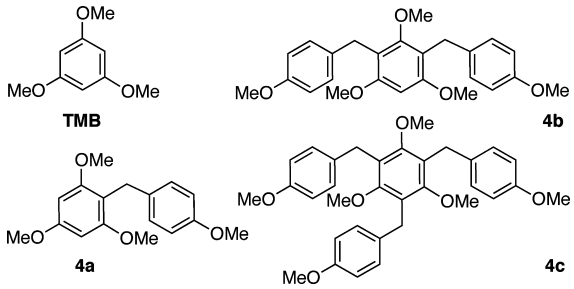
Indeed, taking into account the lack of reactivity with Cu(I) or Cu(II) and the strong Lewis acidity of AuCl and $AuCl_3$ (Table 1, entries 1–4, 16, and 18), a nonredox mechanism seemed more pertinent for the present PMB deprotection. Such a mechanism would thus produce a very reactive electrophilic methylene quinone intermediate, which could react with any nucleophile including the methoxyphenyl moiety of the starting material leading to Friedel–Crafts products (Scheme 2). Moreover, the formation of isolated byproduct could also be explained by the condensation of the protected alcohol **1** on the postulated methylene quinone. The resulting intermediate adduct would lead after rearrangement to the bis(4-methoxyphenyl)methane and the methylene oxonium of the alcohol, which could be trapped by deprotected alcohol, forming the symmetric acetal **3**. It is noteworthy that presence of a trace of water, or protons coming from the rearomatization of Friedel–Crafts adducts, could easily explain the hydrolysis of silver alcoholate.

To diminish the production of byproduct, but also to support this hypothesis, we ran the deprotection reaction in the presence of water or a better nucleophile than the methoxyphenyl group, i.e., 1,3,5-trimethoxybenzene (TMB), to trap the putative *p*-methoxybenzyl cation (Table 2).

Expecting some in situ deacetalization, the model PMB ether **1a** was thus subjected to the best conditions we had found ($AgSbF_6$ in dichloromethane at 40 °C) but in the presence of water. However, only slight improvement was achieved using 1 equiv of H_2O with a better ratio in favor of the alcohol, while an excess of water blocked the catalytic activity (entries 2 and 3 vs 1).

Switching to 1 equiv of TMB as additive, the Ag-catalyzed deprotection efficiently proceeded within mostly the same reaction time and, rewardingly, *without* the formation of acetal **3a** as expected (Table 2, entry 4 vs 1). Moreover, the purification was considerably simplified as a series of new apolar aromatic derivatives were produced along with some remaining TMB. Their isolation and characterization revealed that they resulted from addition of PMB moieties to the added TMB. Three TMB derivatives containing one, two, and three PMB units (**4a–c** in Scheme 3) were isolated, indicating that TMB was able to react up to three times. Therefore, one-third equivalent of TMB should have been sufficient, but experiments showed that half an equivalent was the best compromise. Indeed, under such conditions, the deprotection was still quantitative and TMB was fully consumed, leading to the **4a–c** mixture, in which the bis-adduct **4b** was the major one (entry 5 vs 4). It is worth noting that such results corroborated our mechanistic hypothesis (Scheme 2).

Scheme 3. Structures of the Aromatic Side Products Derived from Trimethoxybenzene (TMB) Used as a Trap during Deprotection of PMB Ethers



A rapid screening showed that under these updated conditions, silver hexafluoroantimonate was still the best catalyst. Nevertheless, the corresponding triflimide was almost as efficient, requiring a slightly longer reaction time (entry 6 vs 5). Silver triflate and tetrafluoroborate were also very efficient catalysts, but they drastically lowered the reaction rate (entries 7 and 8 vs 5). Other salts gave either only slow deprotection, such as the hexafluorophosphate (entry 7 vs 5), or no reaction, such as the nitrate and chloride (entries 8 and 9).

Scope and Limitation. Having compared the efficiency of various catalysts and established optimum conditions, we looked at the scope and limitation of this novel silver-catalyzed deprotection reaction. We thus screened a series of PMB ethers derived from representative alcohols (Table 3).

PMB ethers derived from primary aliphatic alcohols readily reacted, quantitatively yielding the corresponding alcohols after 5–7 h (entries 1 and 2). Secondary alcohols were as reactive, and no epimerization occurred with chiral alcohols (entries 3 and 4). Unexpectedly, PMB ethers derived from allylic alcohols led to complex mixtures of products from which traces (entry 5) or small amounts (entry 6) of the corresponding alcohol could be isolated. It is noteworthy that the allylic alcohols

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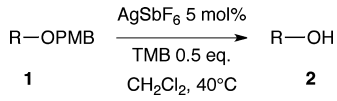
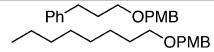
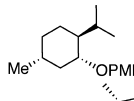
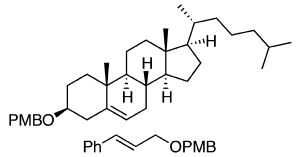
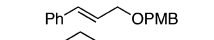
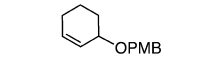
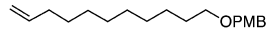
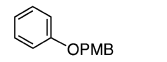
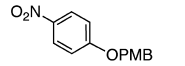
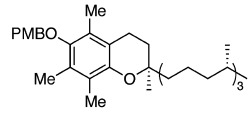
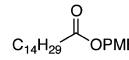
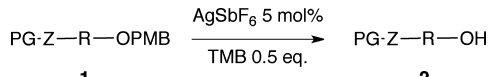
Table 3. Scope of the Ag-Catalyzed PMB Ether Deprotection

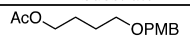
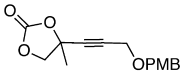
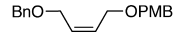
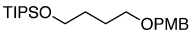
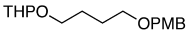
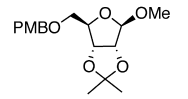
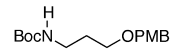
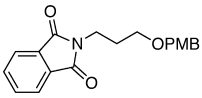
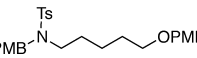


Entry	Substrate		Time (h)	Yield (%)	
1		**1a**	5	100	**2a**
2		**1b**	7	99	**2b**
3		**1c**	2.5	93	**2c**
4		**1d**	10	85	**2d**
5		**1e**	2	2[a]	**2e**
6		**1f**	20	10[a]	**2f**
7		**1g**	5	99	**2g**
8		**1h**	2	85	**2h**
9		**1i**	8	72	**2i**
10		**1j**	8	95	**2j**
11		**1k**	6	93	**2k**
12		**1l**	8	99	**2l**

[a]Decomposition occurs.

Table 4. Compatibility of the Ag-Catalyzed PMB Ether Deprotection with Other Protecting and Functional Groups



Entry	Substrate		Time (h)	Yield (%)	
1		**1m**	17	94	**2m**
2		**1n**	5	99	**2n**
3		**1o**	23	93	**2o**
4		**1p**	4	99	**2p**
5		**1q**	11	54[a]	**2q**
6		**1r**	21	58	**2r**
7		**1s**	2	75	**2s**
8		**1t**	24	-[b]	**2t**
9		**1u**	2	82	**2u**
10		**1v**	16	80[c,d]	**2v**

[a]The bis-silylated diol was isolated (16%). [b]No conversion. [c]The *N*-tosylamino alcohol was also isolated (10%). [d]Deprotected alcohol **2v** was isolated in 88% of yield after 8 h of reaction.

themselves are unstable under our conditions probably due to the formation of allyl cation. Once in a nonallylic position, an alkene function was fully compatible with the reaction conditions (entries 4 and 7). In sharp contrast to allyl ethers, PMB ethers derived from propargylic alcohols proved very reactive toward this Ag-catalyzed deprotection, and the corresponding alcohol was rapidly obtained in high yield (entry 8). Phenol PMB ethers could be deprotected without problems in good to excellent yields (entries 9–11 vs 1–3). Finally, even the 4-methoxybenzyl ester **1l** could be cleaved using our smooth conditions, affording palmitic acid in a quantitative yield (entry 12).

The tolerance of the deprotection conditions toward other protecting and functional groups was also explored (Table 4). To look at protecting group compatibility, a series of butan-1,4-diol derivatives were prepared and subjected to the Ag-catalyzed deprotection conditions. These diols were monoprotected with PMB bromide using standard conditions and then further protected with various groups.

Ester groups, including carbonate, were fully stable under the Ag-catalyzed deprotection conditions, and the PMB ether was selectively cleaved in high yields (Table 4, entries 1 and 2). Interestingly, the benzyl protecting group was also fully compatible with such conditions (entries 3 and 4). Despite the disappointing results gained with allylic PMB ethers (Table 3), the PMB and benzyl ether of *Z*-butene-1,4-diol was surprisingly readily deprotected, in a fast, clean, and quantitative reaction (entry 4).

However, silyl groups such as triisopropylsilyl (TIPS) gave rise to an unexpected side reaction. Although the PMB group was readily cleaved, a silyl transfer occurred, leading to the corresponding bis-silylated diol. The latter was isolated with 16% yield (entry 5).

Acetal cleavage has been reported in the presence of various Lewis acids, even at room temperature.[4] It was therefore gratifying that the present Ag-catalyzed deprotection proved to be compatible with acetal groups (entries 6 and 7). Simple THP-PMB-protected diol could be selectively deprotected, and the corresponding THP alcohol was isolated with a modest yield (entry 6). Interestingly, the PMB ether derived from a ribose diacetal proved even more compatible, as a good yield of the selective PMB cleavage product could be achieved (entry 7).

Protected amino alcohols gave different results depending on the nature of the protecting group on the nitrogen atom (entries 8–10). The *tert*-butyloxycarbonyl group seemed to preclude any deprotection (entry 8). Surprisingly, no *N*-Boc deprotection occurred, and the starting materials were mostly recovered, suggesting that *N*-Boc could act as a ligand toward the Ag^{I} catalyst. To check this hypothesis, the PMB ether derived from 5-phthalimidopentan-1-ol was prepared and subjected to the deprotection conditions. The reaction readily and rapidly occurred, selectively giving the expected 5-phthalimidopentan-1-ol in high yield (entry 9).

To look at some selectivity between *N*- and *O*-PMB, we prepared the *N*-tosyl,*N*-PMB,*O*-PMB derivative from 5-aminopentan-1-ol and subjected it to the Ag-catalyzed deprotection conditions. Interestingly, a high selectivity was observed in favor of the deprotection of the *O*-PMB ether, and only after a long reaction time did some *N*-PMB deprotection occur (entry 10).

These examples clearly show that the Ag-catalyzed PMB deprotections are compatible with a large variety of functional groups, including other protecting groups.

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CONCLUSION

In the present work, we have reported that silver(I) salts catalyzed the smooth deprotection of PMB ethers in the presence of an external nucleophile, i.e., trimethoxybenzene. These conditions were compatible with various functions. Moreover, the orthogonality with different protecting groups, notably the benzyl group, was demonstrated. Further studies on the application of this procedure to other methoxybenzyl ethers and their extension to the protection of acids and ketones are ongoing in our laboratory.

EXPERIMENTAL SECTION

General Information. Proton (^{1}H NMR) and carbon (^{13}C NMR) nuclear magnetic resonance spectra were recorded on 300, 400, or 500 MHz instruments. Chemical shifts are given in part per million (ppm) on the delta scale. Solvent peaks were used as reference values, with $CDCl_3$ at 7.26 ppm for ^{1}H NMR and 77.23 ppm for ^{13}C NMR. Data are presented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, m = multiplet), integration and coupling constants (J in hertz). Assignments were determined on the basis of either unambiguous chemical shifts or coupling patterns, and of COSY, HMQC, HMBC, ROESY experiments when required. Infrared spectra were recorded neat. Wavelengths of maximum absorbance (ν_{max}) are quoted in wave numbers (cm^{-1}). High resolution mass spectra (HRMS) data were recorded on a microTOF spectrometer equipped with orthogonal electrospray interface (ESI). The parent ions $[M + H]^+$, $[M + Na]^+$, or $[M + Li]^+$ are quoted. Analytical thin layer chromatography (TLC) was carried out on silica gel 60 F_{254} plates with visualization by ultraviolet light, potassium permanganate, or ceric ammonium molybdate (CAM) dip. Flash column chromatography was carried out using silica gel 60 (40−63 μm) using cyclohexane and EtOAc as eluent, and the procedure included the subsequent evaporation of solvents in vacuo. Reagents and solvents were purified using standard means. Dichloromethane (CH_2Cl_2) and acetonitrile (CH_3CN) were distilled from CaH_2 under an argon atmosphere; THF was distilled from sodium metal/benzophenone. $AgSbF_6$ (98%), AgOTf (99%), $AgBF_4$ (99%), $AgNO_3$ (99%+), and AgCl (99.9%) were purchased from STREM Chemicals. $AgNTf_2$ was prepared from commercially available $HNTf_2$ and Ag_2CO_3.[18] Alcohols, phenols, or acids **2a**−**l** were commercially available. All other chemicals were used as received. All other extractive procedures were performed using technical solvents, and all aqueous solutions used were saturated.

General Procedure 1 for the Formation of *p*-Methoxybenzyl Ethers from Alcohols. To a solution of alcohol (4 mmol) in anhydrous THF (20 mL) cooled to 0 °C was added sodium hydride (57% in mineral oil, 4.8 mmol) in several portions. The suspension was stirred for 20 min at 0 °C, and *p*-methoxybenzyl chloride and tetrabutylammonium iodide were then added. The mixture was stirred at room temperature until completion. An aqueous solution of ammonium chloride was added to the reaction mixture. The aqueous layer was extracted with ethyl acetate (3 × 30 mL). The combined organic layers were washed with water and brine, dried over anhydrous sodium sulfate, and evaporated. The crude residue was purified by flash chromatography (cyclohexane/EtOAc).

*1-(4-Methoxybenzyloxy)-3-phenylpropane (**1a**).*[19] According to general procedure 1, 3-phenylpropan-1-ol **2a** (545 mg, 4 mmol) gave **1a** (882 mg, 86%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32−7.22 (m, 4 H), 7.21−7.14 (m, 3 H), 6.90 (d, J = 8.7 Hz, 2 H), 4.45 (s, 2 H), 3.82 (s, 3 H), 3.47 (t, J = 6.4 Hz, 2 H), 2.71 (t, J = 7.7 Hz, 2 H), 2.00−1.87 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 142.1, 130.7, 129.3, 128.5, 128.3, 125.8, 113.8, 72.6, 69.2, 55.3, 32.4, 31.4.

*4-Methoxybenzyloxyoctane (**1b**).*[13e] According to general procedure 1, octan-1-ol **2b** (521 mg, 4 mmol) gave **1b** (832 mg, 83%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (d, J = 8.6 Hz, 2 H), 6.88 (d, J = 8.6 Hz, 2 H), 4.43 (s, 2 H), 3.80 (s, 3 H), 3.43 (t, J = 6.7 Hz, 2 H), 1.59 (tt, J = 6.7, 7.3 Hz, 2 H), 1.42−1.18 (m, 10 H), 0.88 (t, J = 6.8 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 130.8, 129.2, 113.7, 72.5, 70.3, 55.3, 31.7, 29.8, 29.5, 29.3, 26.2, 22.7.

*(−)-4-Methoxybenzyl Menthyl Ether (**1c**):*[14e] According to general procedure 1, (−)-menthol **2c** (625 mg, 4 mmol) gave **1c** (718 mg, 65%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (d, J = 8.7 Hz, 2 H), 6.87 (d, J = 8.7 Hz, 2 H), 4.59 (d, J = 11 Hz, 1 H), 4.33 (d, J = 11 Hz, 1 H), 3.80 (s, 3 H), 3.15 (dt, J = 10.6, 4.2, Hz, 1 H), 2.80 (dhept, J = 6.8, 2.8 Hz, 1 H), 2.22−2.13 (m, 1 H), 1.72−1.56 (m, 3 H), 1.44−1.18 (m, 2 H), 1.15−0.76 (m, 10 H), 0.70 (d, J = 7 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 131.3, 129.4, 113.7, 78.2, 70.1, 55.3, 48.3, 40.4, 34.6, 31.6, 25.5, 23.3, 22.4, 21.1, 16.1.

*Cholesteryl 4-Methoxybenzyl Ether (**1d**).*[14e] To a solution of cholesterol **2d** (600 mg, 1.55 mmol) in dry toluene (15 mL) were added 4-methoxybenzyl trichloroacetimidate (0.48 mL, 2.32 mmol) and $Sc(OTf)_3$ (38 mg, 0.077 mmol). The reaction mixture was maintained for 2 h at reflux. After cooling to room temperature, the mixture was concentrated and the residue was treated with acetone to precipitate the PMB ether **1d**. The precipitate was filtered off, washed with acetone, and dried (235 mg, 30%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (d, J = 8.6 Hz, 2 H), 6.86 (d, J = 8.6 Hz, 2 H), 5.35−5.33 (m, 2 H), 4.49 (ab, J_{ab} = 11.6 Hz, 2 H), 3.80 s, 3 H), 3.28−3.23 (m, 1 H), 2.42−2.38 (m, 1 H), 2.29−2.23 (m, 1 H), 2.04−1.79 (m, 5 H), 1.60−0.94 (m, 25 H), 0.91 (d, J = 6.5 Hz, 3 H), 0.87 (d, J = 6.6 Hz, 3 H), 0.86 (d, J = 6.5 Hz, 3 H), 0.68 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.1, 141.1, 131.3, 129.1, 121.5, 113.8, 78.3, 69.6, 56.8, 56.2, 55.3, 50.2, 42.4, 39.8, 39.5, 39.2, 37.3, 36.9, 36.2, 35.8, 32.0, 31.9, 28.5, 28.2, 28.0, 24.3, 23.8, 22.8, 22.6, 21.1, 19.4, 18.7, 11.9.

*1-(4-Methoxybenzyloxy)-3-phenylprop-2-ene (**1e**).*[20] According to general procedure 1, cinnamyl alcohol **2e** (537 mg, 4 mmol) gave **1e** (865 mg, 85%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44−7.20 (m, 7 H), 6.90 (d, J = 8.7 Hz, 2 H), 6.62 (td, J = 1.5, 15.8 Hz, 1 H), 6.33 (td, J = 6.0, 15.8 Hz, 1 H), 4.51 (s, 2 H), 4.18 (dd, J = 1.5, 6.0 Hz, 2 H), 3.61 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 136.8, 132.5, 130.4, 129.5, 128.6, 127.7, 126.5, 126.2, 113.9, 71.9, 70.5, 55.3.

*1-(4-Methoxybenzyloxy)cyclohex-2-ene (**1f**).*[21] According to general procedure 1, cyclohex-2-en-1-ol **2f** (300 mg, 3.05 mmol) gave **1f** (426 mg, 65%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29 (d, J = 8.6 Hz, 2 H), 6.88 (d, J = 8.6 Hz, 2 H), 5.94−5.70 (m, 2 H), 4.53 (d, J = 11.6 Hz, 1 H), 4.47 (d, J = 11.6 Hz, 1 H), 4.00−3.87 (m, 1 H), 3.79 (s, 3 H), 2.16−1.44 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.0, 131.1, 130.7, 129.1, 127.9, 113.7, 71.8, 69.6, 55.2, 28.4, 25.2, 19.3.

*1-(4-Methoxybenzyloxy)undec-10-ene (**1g**).*[22] According to general procedure 1, undec-10-en-1-ol **2g** (1 g, 5.87 mmol) gave **1g** as a yellow oil (1.05 g, 62%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (d, J = 8.6 Hz, 2 H), 6.88 (d, J = 8.6 Hz, 2 H), 5.88−5.75 (m, 1 H), 4.99 (dq, J = 17.1, 1.7 Hz, 1 H), 4.93 (dquint, J = 10.3, 1.1 Hz, 1 H), 4.48 (s, 2H), 3.80 (s, 3 H), 3.43 (t, J = 6.8 Hz, 2 H), 2.04 (dt, J = 7.8, 6.8 Hz, 2 H), 1.64−1.51 (m, 2 H), 1.44−1.31 (m, 4 H), 1.31−1.23 (m, 8 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 139.3, 130.1, 129.2, 114.1, 113.8, 72.5, 70.3, 55.3, 33.8, 29.8, 29.6, 29.5, 29.2, 29.0, 26.2.

*1-(4-Methoxybenzyloxy)hept-2-yne (**1h**).* According to general procedure 1, hept-2-yn-1-ol **2h** (450 mg, 4 mmol) gave **1h** (808 mg, 87%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (d, J = 8.7 Hz, 2 H), 6.87 (d, J = 8.7 Hz, 2 H), 4.51 (s, 2 H), 4.11 (t, J = 2.2 Hz, 2 H), 3.80 (s, 3 H), 2.24 (tt, J = 6.8, 2.2 Hz, 2 H), 1.57−1.35 (m, 4 H), 0.91 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.6, 130.1, 114.1, 113.8, 87.5, 76.2, 71.3, 57.7, 55.6, 31.1, 22.3, 18.8, 13.9; IR (neat) ν_{max} 2955, 2931, 2857, 2281, 2220, 1979, 1611, 1585, 1511, 1464, 1441, 1381, 1352, 1301, 1246, 1172, 1133, 1069, 1034, 941, 922, 898, 819, 757, 723, 637 cm^{-1}; HR-MS 255.1355 ($C_{15}H_{20}O_2$ + Na calcd 255.1361).

*4′-Methoxybenzyloxybenzene (**1i**).*[23] To a solution of phenol **2i** (600 mg, 6.35 mmol) in anhydrous THF were added tetrabutylammonium iodide (236 mg, 0.64 mmol, 10 mol %), potassium carbonate (2.64 g, 19.1 mmol), and *p*-methoxybenzyl chloride (0.9 mL, 6.7 mmol). The reaction mixture was heated at reflux for 20 h, cooled at room temperature, and quenched with a saturated aqueous solution of ammonium chloride. The aqueous layer was extracted with dichloro-

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methane. The organic layer was washed with brine, dried over anhydrous sodium sulfate, and evaporated. The crude residue was purified by flash chromatography to afford **1i** as a white solid (1.31 g, 97%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 (d, J = 9.0 Hz, 2 H), 7.26 (t, J = 7.2 Hz, 1 H), 7.03−6.88 (m, 6 H), 5.00 (s, 2 H), 3.82 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.8, 137.1, 129.5, 128.6, 127.9, 127.5, 120.9, 114.8, 69.9.

*4′-Methoxybenzyloxy-4-nitrobenzene (**1j**).*[11e] To a solution of 4-nitrophenol **2j** (667 mg, 4.79 mmol) in anhydrous THF were added tetrabutylammonium iodide (177 mg, 0.48 mmol, 10 mol %), potassium carbonate (1.32 g, 9.58 mmol), and *p*-methoxybenzyl chloride (0.65 mL, 4.79 mmol). The reaction mixture was heated to reflux for 4 h, cooled at room temperature, and quenched with a saturated aqueous solution of ammonium chloride. The aqueous layer was extracted with dichloromethane. The organic layer was washed with brine, dried over anhydrous sodium sulfate, and evaporated. The crude residue was purified by flash chromatography (cyclohexane/EtOAc) to afford **1j** (1.12 g, 90%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (d, J = 9.3 Hz, 2 H), 7.35 (d, J = 8.6 Hz, 2 H), 7.01 (d, J = 9.3 Hz, 2 H), 6.94 (d, J = 8.6 Hz, 2 H), 5.08 (s, 2 H), 3.82 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.8, 159.9, 141.6, 129.3, 127.5, 125.9, 114.9, 114.2, 70.6, 55.3.

*4-Methoxybenzyl (R,R,R)-α-Tocopheryl Ether (**1k**).* According to general procedure 1, (*R*,*R*,*R*)-α-tocopherol **2k** (1 g, 2.32 mmol) gave the title compound **1k** (1.2 g, 95%) as a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (d, J = 8.5 Hz, 2 H), 6.94 (d, J = 8.7 Hz, 2 H), 4.64 (s, 2 H), 3.84 (s, 3 H), 3.61 (t, J = 6.6 Hz, 2 H), 2.23 (s, 3 H), 2.18 (s, 3 H), 2.12 (s, 3 H), 1.88−1.76 (m, 2 H), 1.60−1.02 (m, 32 H), 0.90−0.86 (m, 15 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.4, 148.2, 147.9, 130.3, 129.4, 128.0, 126.0, 122.9, 117.5, 113.9, 74.8, 74.5, 55.3, 40.1, 39.4, 37.6, 37.4, 37.3, 32.8, 32.7, 31.4, 31.3, 28.0, 24.8, 24.5, 23.9, 22.7, 22.6, 21.0, 20.7, 19.8, 19.7, 12.9, 12.0, 11.8; HR-MS 573.4302 ($C_{37}H_{58}O_3$ + Na calcd 573.4284).

*4′-Methoxybenzyl Hexadecanoate (**1l**).*[24] Palmitic acid **2l** (2 g, 7 mmol) was dissolved in *N*-methyl-2-pyrrolidone (25 mL). Diisopropylamine (1.2 mL, 7 mmol), sodium iodide (3.5 mmol), and 4-methoxybenzyl chloride (0.95 mL, 7 mmol) were then added. The resulting mixture was heated to 80 °C for 1 h. The reaction was cooled down and poured into 100 mL of water. After extraction with dichloromethane, the combined organic layers were washed with water and brine and dried over $MgSO_4$. After flash chromatography (cyclohexane/EtOAc), 1.58 g (60%) of **1l** was obtained as a colorless powder. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (d, J = 8.6 Hz, 2 H), 6.88 (d, J = 8.7 Hz, 2 H), 5.04 (s, 2 H), 3.81 (s, 3 H), 2.31 (t, J = 7.4 Hz, 2 H), 1.62 (quint, J = 7.3 Hz, 2 H), 1.34−1.21 (m, 24 H), 0.88 (t, J = 6.9 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.8, 159.6, 130.0, 128.3, 113.9, 65.9, 55.3, 34.4, 31.9, 29.7, 29.7, 29.6, 29.6, 29.5, 29.4, 29.3, 29.1, 25.0, 22.7, 14.1.

*4-(4-Methoxybenzyloxy)butan-1-ol (**I**).*[25] According to general procedure 1, butan-1,4-diol (1 g, 11 mmol) gave the title compound **I** (1.28 g, 55%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, J = 8.7 Hz, 2 H), 6.88 (d, J = 8.7 Hz, 2 H), 4.45 (s, 2 H), 3.80 (s, 3 H), 3.63 (t, J = 5.9 Hz, 2 H), 3.49 (t, J = 5.9 Hz, 2 H), 2.39 (s, 1 H), 1.76−1.62 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.0, 130.0, 129.2, 113.7, 72.7, 70.0, 62.7, 55.3, 30.3, 26.8.

*4-(4-Methoxybenzyloxy)butyl Acetate (**1m**).* To a solution of **I** (315 mg, 1.5 mmol) in dichloromethane were added acetic anhydride (0.24 mL, 2.5 mmol) and pyridine (0.25 mL, 3 mmol). The reaction was stirred for 2 h and then quenched with a saturated aqueous solution of sodium hydrogencarbonate. After extraction with ethyl acetate, the combined organic layers were washed with brine and evaporated in vacuo. The crude residue was purified by flash chromatography (cyclohexane/EtOAc) to afford **1m** (360 mg, 95%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, J = 8.7 Hz, 2 H), 6.87 (d, J = 8.7 Hz, 2 H), 4.43 (s, 2 H), 4.07 (t, J = 6.5 Hz, 2 H), 3.80 (s, 3 H), 3.46 (t, J = 6.0 Hz, 2 H), 2.03 (s, 3 H), 1.80−1.59 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8, 158.7, 130.1, 128.8, 113.3, 72.2, 69.0, 63.9, 54.8, 25.8, 25.1, 20.6; IR (neat) ν_{max} 2936, 2854, 1743, 1611, 1585, 1512, 1464, 1364, 1301, 1238, 1172, 1092, 1033, 955, 818, 757, 708, 636, 606 cm^{-1}; HR-MS 275.1266 ($C_{14}H_{20}O_4$ + Na calcd 275.1259).

*4-(3-(4-Methoxybenzyloxy)prop-1-ynyl)-4-methyl-1,3-dioxolan-2-one (**1n**).* A solution of 2-methylbut-1-en-3-yne (661 mg, 10 mmol) in THF (25 mL) was cooled to −78 °C, and then a solution of *n*BuLi in hexanes (6.9 mL, 1.6 M) was added dropwise. The mixture was stirred at −78 °C for 30 min, and then *p*-formaldehyde (348 mg, 11 mmol) was added in one portion. The reaction mixture was allowed to warm at room temperature and then poured in a separatory funnel containing a saturated aqueous solution of ammonium chloride (30 mL). After extraction with diethyl ether, the combined organic layers were washed with brine, dried over anhydrous magnesium sulfate, and evaporated in vacuo. The crude residue was purified by filtration through a small pad of silica with pentane/ether (4:1) as an eluent to give 4-methylpent-4-en-2-yn-1-ol as a pale yellow oil (896 mg, 93%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.30 (s, 1 H), 5.27−5.20 (m, 1 H), 4.39 (s, 2 H), 1.91−1.87 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 126.2, 122.3, 86.8, 86.3, 51.4, 23.3.

A solution of 4-methylpent-4-en-2-yn-1-ol (890 mg, 9.3 mmol) in anhydrous THF (20 mL) was cooled to 0 °C. Sodium hydride (424 mg, 9.7 mmol, 57% suspension in mineral oil) was added in one portion. The solution was stirred at 0 °C for 20 min. Tetrabutylammonium iodide (342 mg, 0.9 mmol) and *p*-methoxybenzyl chloride (1.6 g, 10.2 mmol) were then added. The reaction was stirred at room temperature for 1 h and then heated to reflux for 30 min. The reaction was quenched with a saturated aqueous solution of ammonium chloride (25 mL). After extraction with ethyl acetate, the combined organic layers were washed with water and brine and then dried over anhydrous sodium sulfate and evaporated in vacuo. The crude residue was purified by flash chromatography (cyclohexane/EtOAc) to give 4-methoxybenzyloxy(4-methylpent-4-en-2-yne) (1.7 g, 84%) as a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 (d, J = 8.7 Hz, 2 H), 6.89 (d, J = 8.7 Hz, 2 H), 5.35 (s, 1 H), 5.30−5.22 (m, 1 H), 4.57 (s, 2 H), 4.27 (s, 2 H), 3.83 (s, 3 H), 1.91−1.89 (m, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.4, 129.8, 129.5, 122.2, 113.8, 87.6, 84.2, 71.2, 57.4, 55.3, 23.4.

To a solution of 5-(4-Methoxybenzyloxy)-2-methylpent-1-en-3-yne (1.43 g, 6.6 mmol) in a acetone/water (4/1) (20 mL) mixture was added *N*-methylmorpholine oxide (1.55 g, 13.2 mmol). The reaction mixture was cooled to 0 °C. An osmium tetroxide solution (0.83 mL, 0.08 M, 0.132 mmol, 1 mol %) was then added dropwise. The solution was stirred for 17 h, and then the reaction was quenched with a saturated aqueous solution of sodium bisulfate. The aqueous layer was saturated with sodium chloride and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous sodium sulfate, and evaporated in vacuo. The crude residue was purified by flash chromatography to give 5-(4-methoxybenzyloxy)-2-methylpent-3-yne-1,2-diol as a colorless oil (1.24 g, 75%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (d, J = 8.7 Hz, 2 H), 6.87 (d, J = 8.7 Hz, 2 H), 4.50 (s, 2 H), 4.14 (s, 2 H), 3.78 (s, 3 H), 3.62 (d, J = 11.2 Hz, 1 H), 3.59 (s, 2 H), 3.47 (d, J = 11.2 Hz, 1 H), 1.44 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) 159.8, 130.2, 129.6, 114.3, 88.6, 80.5, 71.9, 70.9, 68.9, 57.4, 55.7, 25.6.

To a solution of 5-(4-methoxybenzyloxy)-2-methylpent-3-yne-1,2-diol **2n** (411 mg, 1.86 mmol) in anhydrous dichloromethane (5 mL) was added pyridine (0.75 mL, 9.3 mmol, 5 equiv). The reaction mixture was cooled to 0 °C, and then trisphosgene (1.1 g, 3.72 mmol, 2 equiv) was added in one portion. The reaction mixture was stirred for 15, and min then a saturated aqueous solution of copper sulfate was added. The mixture was vigorously stirred for 1 h. After extraction with dichloromethane, the combined organic layers were washed with brine, dried over anhydrous sodium sulfate, and evaporated in vacuo. The crude residue was purified by flash chromatography to give **1n** (411 mg, 90%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, J = 8.7 Hz, 2 H), 6.87 (d, J = 8.7 Hz, 2 H), 4.49 (s, 2 H), 4.48 (d, J = 8.2 Hz, 1 H), 4.21 (d, J = 8.2 Hz, 1 H), 4.16 (s, 2 H), 3.79 (s, 3 H), 1.77 (s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.8, 153.7, 130.0, 129.1, 114.1, 84.8, 83.2, 75.8, 75.5, 72.0, 56.9, 55.5, 26.8; IR (neat) ν_{max} 2839, 1797, 1611, 1585, 1512, 1465, 1442, 1386, 1372, 1354, 1282,

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1236, 1174, 1146, 1086, 1060, 1031, 945, 819, 768, 711, 621 cm^{-1}; HR-MS 299.0887 ($C_{15}H_{16}O_5$ + Na calcd 299.0895).

*1-Benzyloxy-4-(4-methoxybenzyloxy)butane (**1o**).*[14e] According to general procedure 1 using benzyl chloride, **I** (315 mg, 1.5 mmol) gave **1o** (432 mg, 95%) as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ 7.31−7.15 (m, 7 H), 6.80 (d, J = 8.7 Hz, 2 H), 4.43 (s, 2 H), 4.36 (s, 2 H), 3.75 (s, 3 H), 3.49−3.34 (m, 4 H), 1.78−1.57 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 138.6, 130.7, 129.2, 128.3, 127.6, 127.5, 113.8, 72.9, 72.5, 70.2, 69.8, 55.3, 26.5.

*(Z)-1-Benzyloxy-4-(4-methoxybenzyloxy)but-2-ene (**1p**).*[11e] According to general procedure 1, (*Z*)-4-(benzyloxy)but-2-en-1-ol[26] **2p** (833 mg, 4 mmol) gave **1p** (432 mg, 65%) as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ 7.30−7.11 (m, 7 H), 6.78 (d, J = 8.7 Hz, 2 H), 5.75−5.64 (m, 2 H), 4.40 (s, 2 H), 4.33 (s, 2 H), 3.96 (dd, J = 8.6, 4.4 Hz, 4 H), 3.71 (s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.8, 137.7, 129.8, 129.4, 129.3, 129.0, 128.0, 127.4, 127.3, 113.4, 71.9, 71.5, 65.4, 65.0, 54.9.

*1-Triisopropylsilyloxy-4-(4-methoxybenzyloxy)butane (**1q**).* According to general procedure 1, 4-(triisopropylsilyloxy)butan-1-ol[27] **2q** (493 mg, 2 mmol) gave **1q** (594 mg, 81%) as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, J = 8.7 Hz, 2 H), 6.87 (d, J = 8.7 Hz, 2 H), 4.43 (s, 2 H), 3.80 (s, 3 H), 3.69 (t, J = 6.3 Hz, 2 H), 3.47 (t, J = 6.3 Hz, 2 H), 1.74−1.53 (m, 4 H), 1.14−0.97 (m, 21 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 130.8, 129.2, 113.7, 72.5, 70.1, 63.2, 55.3, 29.7, 26.3, 18.0, 12.0; IR (neat) ν_{max} 2940, 2863, 1612, 1586, 1512, 1462, 1382, 1362, 1301, 1245, 1205, 1171, 1102, 1037, 1012, 995, 918, 881, 819, 784, 722, 678, 657, 638 cm^{-1}; HR-MS 389.2480 ($C_{21}H_{38}O_3Si$ + Na calcd 389.2488).

*1-Tetrahydropyranyloxy-4-(4-methoxybenzyloxy)butane (**1r**).*[28] To a solution of **I** (315 mg, 1.5 mmol) in dichloromethane were added 2,3-dihydropyran (168 g, 2 mmol) and camphorsulfonic acid (10 mol %). The reaction was then stirred for 16 h. The mixture was partitioned between water and ethyl acetate. After extraction, the combined organic layers were washed with brine, dried over anhydrous sodium sulfate, and evaporated in vacuo. The crude residue was purified by flash chromatography (cyclohexane/EtOAc) to afford **1r** (357 mg, 81%) as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ 7.26 (d, J = 8.7 Hz, 2 H), 6.87 (d, J = 8.7 Hz, 2 H), 4.60−4.53 (m, 1 H), 4.43 (s, 2 H), 3.93−3.67 (m, 5 H), 3.57−3.34 (m, 4 H), 1.90−1.42 (m, 10 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 130.7, 129.2, 113.7, 98.8, 72.5, 69.9, 67.3, 62.2, 55.3, 30.7, 26.6, 26.5, 25.5, 19.6.

*Methyl 5-(4-Methoxybenzyloxy)-2,3-O-isopropylidene-β-D-ribofuranoside (**1s**).* According to general procedure 1, methyl 2,3-*O*-isopropylidene-β-D-ribofuranoside[29] **2s** (408 mg, 2 mmol) gave **1s** (550 mg, 85%) as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ 7.26 (d, J = 8.7 Hz, 2 H), 6.87 (d, J = 8.7 Hz, 2 H), 4.95 (s, 1 H), 4.65 (dd, J = 0.7, 6.0 Hz, 1 H), 4.55 (d, J = 6.0 Hz, 1 H), 4.47 (s, 2 H), 4.39−4.30 (m, 1 H), 3.79 (s, 3 H), 3.48 (dd, J = 6.4, 9.7 Hz, 1 H), 3.41 (dd, J = 8.1, 9.7 Hz, 1 H), 3.28 (s, 3 H), 1.47 (s, 3 H), 1.30 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 130.1, 129.3, 113.8, 112.3, 109.2, 85.1, 82.1, 72.9, 70.8, 55.2, 54.8, 26.4, 25.0; IR (neat) ν_{max} 2989, 2936, 2835, 1612, 1585, 1512, 1464, 1372, 1302, 1245, 1208, 1193, 1173, 1161, 1086, 1048, 960, 868, 848, 817, 759, 735, 703 cm^{-1}; HR-MS 347.1455 ($C_{17}H_{24}O_6$ + Na calcd 347.1471).

*tert-Butyl (3-((4-Methoxybenzyl)oxy)propyl)carbamate (**1t**).*[8] According to general procedure 1, *tert*-butyl (3-hydroxypropyl)carbamate **2t** (500 mg, 2.86 mmol) gave **1t** (758 mg, 90%) as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, J = 8.6 Hz, 2 H), 6.88 (d, J = 8.6 Hz, 2 H), 4.70−5.05 (broad s), 4.43 (s, 2 H), 3.80 (s, 3 H), 3.51 (t, J = 6.0 Hz, 2 H), 3.22 (q, J = 6.0 Hz, 2 H), 1.77 (tt, J = 6.3, 6.3 Hz, 2 H), 1.43 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) 159.2, 156.0, 130.4, 129.3, 113.8, 79.0, 72.7, 68.4, 55.3, 38.8, 29.7, 28.5.

*3-(4-Methoxybenzyloxy)-1-phthalimidopropane (**1u**).* According to general procedure 1, 3-phthalimidopropan-1-ol[30] **2u** (800 mg, 3.42 mmol) gave **1u** (350 mg, 30%) as a yellow oil. ^1H NMR (300 MHz, $CDCl_3$) δ 7.82 (dd, J = 3.2, 5.4 Hz, 2 H), 7.69 (dd, J = 3.2, 5.4 Hz, 2 H), 7.21 (d, J = 8.4 Hz, 2 H), 6.82 (d, J = 8.4 Hz, 2 H), 4.39 (s, 2 H), 3.82 (t, J = 6.1 Hz, 2 H), 3.79 (s, 3 H), 3.51 (t, J = 6.1 Hz, 2 H), 2.03−1.94 (m, 2 H); ^{13}C NMR (75 MHz, CDCl3) δ 168.4, 159.1, 133.8, 132.2, 130.4, 129.3, 123.1, 113.7, 72.7, 67.7, 55.3, 35.7, 28.7; IR (neat) ν_{max} 2858, 1697, 1635, 1606, 1509, 1395, 1371, 1241, 1176, 1143, 1036, 901, 851; HR-MS 348.1215 ($C_{19}H_{19}NO_4$ + Na calcd 348.1212).

*N-(4-Methoxybenzyl)-N-(5-(4-methoxybenzyloxy)pentyl)-4-methylbenzenesulfonamide (**1v**).* According to general procedure 1, *N*-tosyl-5-aminopentan-1-ol[31] (500 mg, 1.95 mmol) gave **1v** (280 mg, 29%) as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ 7.71 (d, J = 8.2 Hz, 2 H), 7.30 (d, J = 8.3 Hz, 2 H), 7.23 (d, J = 8.6 Hz, 2 H), 7.18 (d, J = 8.6 Hz, 2 H), 6.87 (d, J = 8.6 Hz, 2 H), 6.82 (d, J = 8.6 Hz, 2 H), 4.37 (s, 2 H), 4.24 (s, 2 H), 3.80 (s, 3 H), 3.78 (s, 3 H), 3.30 (t, J = 6.5 Hz, 2 H), 3.05 (dd, J = 7.6, 7.6 Hz, 2 H), 2.43 (s, 3 H), 1.48−1.37 (m, 2 H), 1.37−1.25 (m, 2 H), 1.24−1.10 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.6, 159.5, 143.5, 137.6, 131.0, 130.1, 130.0, 129.6, 128.8, 127.6, 114.3, 114.2, 73.0, 70.2, 55.7, 51.8, 48.2, 29.6, 28.3, 27.3, 23.7, 21.9; IR (neat) ν_{max} 2931, 2852, 1690, 1612, 1512, 1392, 1247, 1169, 1092, 1034, 820; HR-MS 520.2129 ($C_{28}H_{35}NO_5S$ + Na calcd 520.2134).

General Procedure 2 for the Cleavage of *p*-Methoxybenzyl Ethers. A mixture of *p*-methoxybenzyl ether (0.4 mmol) and 1,3,5-trimethoxybenzene (33.6 mg, 0.2 mmol) in anhydrous dichloromethane (3 mL) was added via a cannula to a solution of silver hexafluoroantimonate (6.9 mg, 20 μmol, 5 mol %) in anhydrous dichloromethane (1 mL). The reaction mixture was heated to reflux until completion and filtered through a small pad of Celite with dichloromethane as eluent. Solvents were removed in vacuum, and the crude residue was purified by flash chromatography (cyclohexane/EtOAc).

*4-(Acyloxy)butan-1-ol (**2m**).*[32] According to general procedure 2, **1m** (101 mg, 0.4 mmol) gave **2m** (71.3 mg, 94%) as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ 4.04 (t, J = 6.4 Hz, 2 H), 3.61 (t, J = 6.4 Hz, 2 H), 2.12 (s, 1 H), 1.99 (s, 3 H), 1.76−1.49 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.3, 64.3, 62.1, 29.0, 25.0, 20.9.

*4-(3-Hydroxyprop-1-yn-1-yl)-4-methyl-1,3-dioxolan-2-one (**2n**).* According to general procedure 2, **1n** (110.5 mg, 0.4 mmol) gave **2n** (62 mg, 99%) as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ 4.52 (d, J_{ab} = 8. Four Hz, 1 H), 4.27 (s, 2 H), 4.24 (d, J_{ab} = 8.4 Hz, 1 H), 2.83 (s, −OH, 1 H), 1.74 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.1, 86.8, 81.9, 76.1, 75.5, 50.4, 26.4; IR (neat) ν_{max} 3406, 2919, 1784, 1544, 1478, 1388, 1375, 1282, 1232, 1148, 1092, 1050, 1007, 949, 858, 769, 711, 611 cm^{-1}; HR-MS 179.0310 ($C_7H_8O_4$ + Na calcd 179.0320).

4-(Benzyloxy)butan-1-ol[33] *(**2o**).* According to general procedure 2, **1o** (120.2 mg, 4 mmol) gave **2k** (67 mg, 93%) as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ 7.31−7.18 (m, 5 H), 4.42 (s, 2 H), 3.53 (t, J = 5.9 Hz, 2 H), 3.42 (t, J = 5.9 Hz, 3 H), 1.70−1.48 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.6, 128.8, 128.2, 128.1, 73.5, 70.8, 63.1, 30.5, 27.1.

*(Z)-4-(Benzyloxy)but-2-en-1-ol (**2p**).*[26] According to general procedure 2, **1p** (119.3 mg, 0.4 mmol) gave **2p** (71.3 mg, 100%) as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ 7.39−7.26 (m, 5 H), 5.87−5.78 (m, 1 H), 5.78−5.68 (m, 1 H), 4.53 (s, 2 H), 4.16 (d, J = 6.2 Hz, 2 H), 4.09 (d, J = 6.2 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 132.4, 128.5, 128.2, 127.9, 127.8, 72.5, 65.7, 58.7.

*4-(Triisopropylsilyloxy)butan-1-ol (**2q**).*[27] According to general procedure 2, **1q** (134.6 mg, 0.4 mmol) gave **2q** (53.2 mg, 54%) as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ 3.75 (t, J = 5.5 Hz, 2 H), 3.66 (t, J = 5.5 Hz, 2 H), 1.77−1.57 (m, 4 H), 1.20−0.96 (m, 21 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 63.2, 62.4, 30.0, 29.7, 17.6, 11.5.

*4-(Tetrahydropyranyloxy)butan-1-ol (**2r**).*[34] According to general procedure 2, **1r** (117.8 mg, 0.4 mmol) gave **2r** (53.2 mg, 54%) as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ 4.56 (t, J = 3.5 Hz, 1 H), 3.82 (m, 1 H), 3,74 (dt, J = 9.8, 5.8 Hz, 1 H), 3.60 (m, 2 H), 3.47 (m, 1 H), 3.38 (dt, J = 9.8, 5.6 Hz, 1 H), 2.78 (s, −OH, 1 H), 1.77 (m, 1 H), 1.61−1.67 (m, 5 H), 1.38−1.54 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 98.7, 67.4, 62.3, 62.1, 30.5, 29.8, 26.3 25.3, 19.4.

*Methyl 2,3-O-Isopropylidene-β-D-ribofuranoside (**2s**).*[29] According to general procedure 2, **1s** (150 mg, 0.46 mmol) gave **2s** (70 mg, 75%) as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ 4.97 (s, 1 H), 4.83 (d, J = 6.0 Hz, 1 H), 4.59 (d, J = 6.0 Hz, 1 H), 4.43 (t, J = 2.8 Hz, 1 H), 3.76−3.53 (m, 2 H), 3.43 (s, 3 H), 3.31−3.12 (m, 1 H), 1.48 (s, 3

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H), 1.32 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 125.8, 112.1, 110.0, 88.8, 86.2, 81.9, 64.4, 55.9, 26.7, 25.0.

*3-Phthalimidopropan-1-ol (**2u**).*[30] According to general procedure 2, **1u** (130 mg, 0.4 mmol) gave **2u** (76 mg, 82%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (dd, J = 5.4, 3.2 Hz, 2 H), 7.73 (dd, J = 5.4, 3.2 Hz, 2 H), 3.86 (t, J = 6.4 Hz, 2 H), 3.62 (q, J = 6.1 Hz, 2 H), 2.47 (t, J = 6.6 Hz, 1 H), 1.88 (quint, J = 6.1 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.0, 134.1, 132.0, 123.4, 59.0, 34.2, 31.4.

*N-(5-Hydroxypentyl)-N-(4-methoxybenzyl)-4-methylbenzenesulfonamide (**2v**).* According to general procedure 2, **1v** (50 mg, 0.1 mmol) gave **2v** (30 mg, 80%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (d, J = 8.2 Hz, 2 H), 7.31 (d, J = 8.2 Hz, 2 H), 7.18 (d, J = 8.6 Hz, 2 H), 6.83 (d, J = 8.6 Hz, 2 H), 4.24 (s, 2 H), 3.80 (s, 3 H), 3.51 (t, J = 6.5 Hz, 2 H), 3.06 (t, J = 7.5 Hz, 2 H), 2.44 (s, 3 H), 1.44–1.30 (m, 4 H), 1.21–1.13 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) 159.3, 143.1, 137.1, 129.7, 129.6, 128.5, 127.2, 114.0, 62.6, 55.3, 51.6, 47.8, 32.1, 27.9, 22.8, 21.5. IR (neat) ν_{max} 3295, 2933, 1611, 1511, 1454, 1328, 1245, 1153, 1089, 1031, 813, 745, 655, 547; HR-MS 400.1539 ($C_{20}H_{27}NSO_4$ + Na calcd 400.1558).

*Bis(3-phenylpropoxy)methane (**3a**):*[35] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30–7.14 (m, 10 H), 4.69 (s, 2 H), 3.56 (t, J = 6.4 Hz, 4 H), 3.69 (dd, J = 7.6, 7.6 Hz, 4 H), 1.94–1.84 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.9, 128.5, 128.4, 125.8, 95.4, 67.2, 32.5, 31.4.

*1,3,5-Trimethoxy-2-(4-methoxybenzyl)benzene (**4a**):*[36] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.15 (d, J = 8.7 Hz, 2 H), 6.76 (d, J = 8.7 Hz, 2 H), 6.15 (s, 2 H); 3.87 (s, 2 H), 3.80 (s, 3 H), 3.79 (s, 6 H), 3.75 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.8, 159.0, 157.6, 134.7, 129.5, 113.6, 111.0, 90.9, 55.9, 55.5, 55.4, 27.6.

*1,3,5-Trimethoxy-2,4-bis(4-methoxybenzyl)benzene (**4b**).* White solid; mp 102–103 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.11 (d, J = 8.5 Hz, 2 H), 6.76 (d, J = 8.5 Hz, 2 H), 6.35 (s, 1 H), 3.92 (s, 4 H), 3.78 (s, 6 H), 3.75 (s, 6 H), 3.47 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) 158.3, 157.5, 157.4, 134.2, 129.1, 115.3, 113.5, 92.1, 61.9, 55.8, 55.2, 28.4; IR (neat) ν_{max} 3000, 2939, 2834, 1597, 1507, 1463, 1238, 1199, 1169, 1092, 1033, 799, 558, 526; HR-MS 431.1821 ($C_{25}H_{28}O_5$ + Na calcd 431.1834).

*1,3,5-Trimethoxy-2,4,6-tris(4-methoxybenzyl)benzene (**4c**):*[37] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.11 (d, J = 8.8 Hz, 6 H), 6.80 (d, J = 8.7 Hz, 6 H), 3.99 (s, 6 H), 3.77 (s, 9 H), 3.50 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.6, 157.1, 133.6, 129.0, 124.3, 113.6, 61.6, 55.2, 29.4.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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