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Article

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Highly Discriminative and Chemoselective Deprotection/Transformations of Acetals with the Combination of Trialkylsilyl Triflate/2,4,6-Collidine

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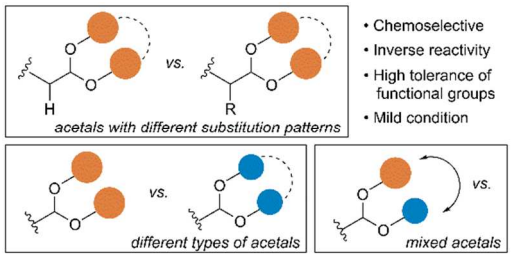


ABSTRACT: Acetals are the most useful protecting groups for carbonyl functional groups. In addition to the role of protection, they can also be used as synthons of carbonyl functions. Previously, we have developed a chemoselective deprotection and nucleophilic substitution of acetals from aldehydes in the presence of ketals. This article describes the highly discriminative and chemoselective transformations of acetals bearing different substitution patterns, different types of acetals, as well as mixed acetals. These reactions can achieve the transformations which can't be attained by conventional methods, and their results strongly suggest the combination of R_3SiOTf/2,4,6-collidine to promote such unprecedented phenomena.

INTRODUCTION

Acetals including ketals are the most useful protecting groups for carbonyl functions, and are widely used in synthetic organic chemistry.[1)] Moreover, acetals are the synthetic equivalent of carbonyl functions. This then gave the impetus for the development of several protection methods that are used nowadays. Generally, deprotection of acetals proceeds via the formation of oxocarbenium ion A (Figure 1, eq. 1). Lewis acid treatment of an acetal then gives the same oxocarbenium ion **A**, which spontaneously reacts with a nucleophile in the reaction mixture (Figure 1, eq. 2, Trimethylsilyl enol ether is shown as a nucleophile.). The extent of deprotection depends on the rate of formation of the oxocarbenium ion **A**. On the other hand, ketals are deprotected more readily than acetals because of the faster formation of the oxocarbenium ion due to the additional electron-donating alkyl groups.[2)] The same principle can also be applied to acetals containing various functionalities.[3)] Since the rate-determining step of acetal deprotection is the formation step of the oxocarbenium ions via the C–O cleavage of the acetal, factors affecting this step will influence the rate of deprotection. For example, it has been reported that acetals containing electron-donating alkyl group at the at the α-position undergo faster deprotection compared to unsubstituted ones.[2)] Moreover, when comparing different acetals bulkier alkoxy acetals are deprotected more readily than smaller alkoxy ones or cyclic acetals[3b, c, 4)] (Figure 1, eq. 3). Since the previous notions have been the standard beliefs in organic chemistry and a methodology with the inverse reactivity of acetal deprotection has not been reported until now, development of such methodology is both conceptually new and synthetically useful.

Previously, we reported a novel method of deprotection and nucleophilic substitution of acetals using the combination of trialkylsilyl triflate (R_3SiOTf) and pyridines (Figure 1, eq. 4 and 5).[5] While it is interesting that the reaction proceeds under weakly basic conditions, its usefulness has been validated by the recent wide applications of the method to total synthesis of natural products or bioactive compounds.[6] It is noteworthy that this method can be used to deprotect an acetal in the presence of a ketal, as ketals had been known to be deprotected much faster than acetals until then.[2] To the best of our best knowledge, this is the only method that allows the deprotection of acetals in the presence of ketals. In 2006, we reported the detailed study of the above chemistry including mechanistic considerations via a pyridinium-type salt intermediate **B** which is an acidic species that reacts with many nucleophiles including H_2O.[7]

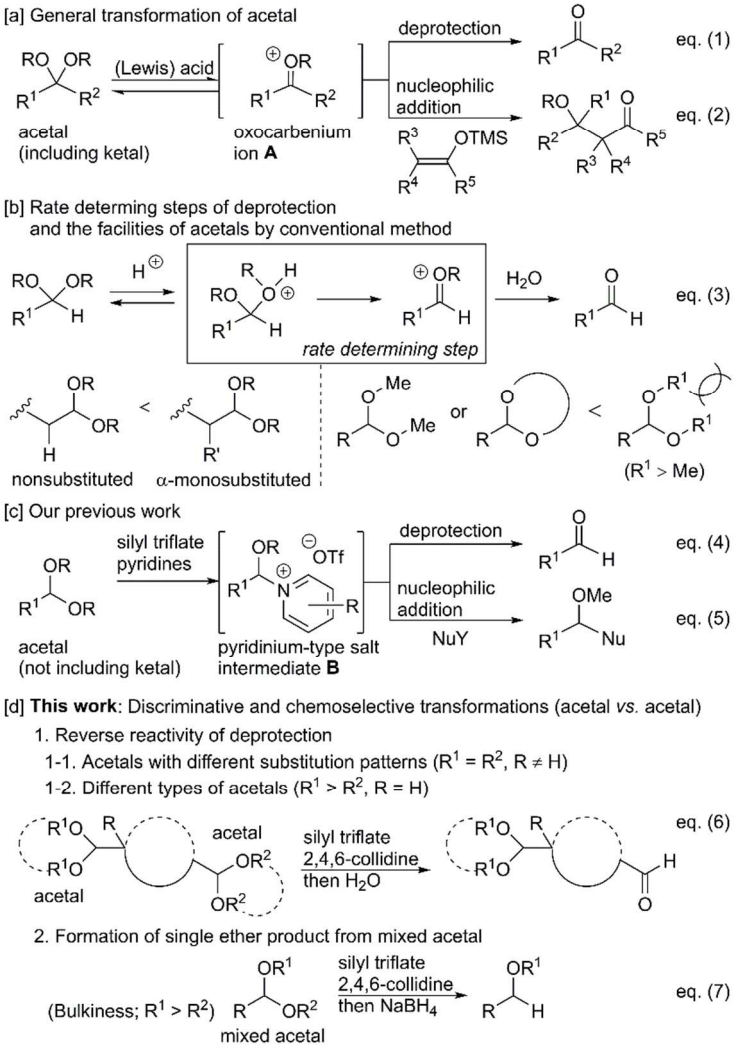


Figure 1. Reactivity of acetal via oxocarbenium ion and our reported work.

In this article, we developed highly discriminative and chemoselective transformations of acetals such as: 1) Reverse reactivity of deprotection [(1-1) deprotection of acetals with different substitution patterns, and (1-2) deprotection of different types of acetals (Figure 1, eq. 6)] and 2) Formation of single ether product from mixed acetal (Figure 1, eq. 7). We believe that these unprecedented reactions will add value to the field of acetal chemistry.

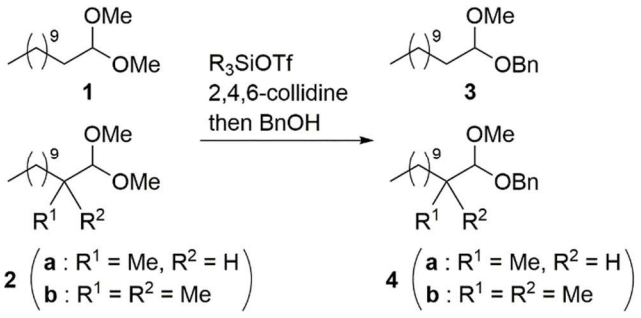
RESULTS AND DISCUSSION

1. Reverse Reactivity of Deprotection

1-1. Acetals with Different Substitution Patterns. The nucleophilic substitution of a 1:1 mixture of dimethyl acetal **1** and dimethyl acetals with methyl group(s) at the α-position (**2a** or **2b**) with benzyl alcohol (BnOH) was selected as the model reaction to confirm the reactivity of acetals with different substitution patterns. Initially, we examined dimethyl acetal **1** with α-monomethylated dimethyl acetal **2a**. Treatment of the mixture with trimethylsilyl triflate (TMSOTf) and 2,4,6-collidine followed by addition of BnOH produced mixed acetal **3** in 49% yield and mixed acetal **4a** in 24% yield

(Table 1, entry 1). The use of triethylsilyl triflate (TESOTf) and 2,4,6-collidine produced mixed acetal **3** in 40% yield and mixed acetal **4a** in a much lower 7% yield (entry 2). We then examined dimethyl acetal **1** with α-dimethylated dimethyl acetal **2b**. The use of TMSOTf and 2,4,6-collidine selectively produced mixed acetal **3** in 37% yield with no detection of mixed acetal **4b** at all (entry 3). Finally, the use of TESOTf instead of TMSOTf resulted in the exclusive formation of mixed acetal **3** in 99% yield from **1** with no formation of **4b** from **2b** (entry 4). This highlights the importance of the bulkiness of R group in the R_3SiOTf/2,4,6-collidine complex for the discrimination of the steric environments in the substrates.

Table 1. Evaluation of the selective deprotection of acetals with different substitution patterns.[a]

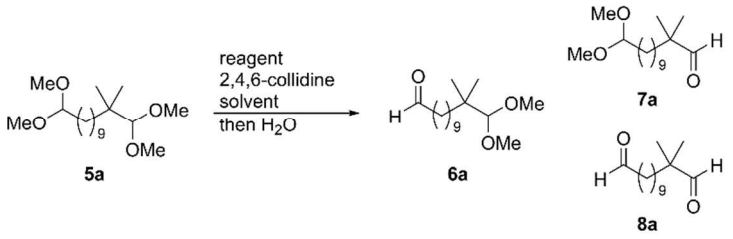


entry	R^1	R^2	R_3SiOTf	**3** (%)[b,c]	**4** (%)[b,d]
1	Me	H	TMSOTf	49	24
2	Me	H	TESOTf	40	7
3	Me	Me	TMSOTf	37	N.D.[e]
4	Me	Me	TESOTf	99	N.D.[e]

[a]Reaction conditions. R_3SiOTf (1.5 equiv) and 2,4,6-collidine (2.25 equiv) in CH_2Cl_2 at 0 °C for 1 h then BnOH (2.0 equiv). [b]Determined by ^1H NMR analysis of unpurified reaction mixture. [c]SM **1** was also recovered. [d]SM **2** was also recovered. [e]Not detected.

The superiority of the combination of TESOTf/2,4,6-collidine was confirmed by the selective deprotection of acetals with different substitution patterns using **5a** as a model substrate, which contains both an α-unsubstituted dimethyl acetal unit and an α-dimethylated one (Table 2). The reactions were allowed to stand until the disappearance of **5a**. The use of TMSOTf/2,4,6-collidine in CH_2Cl_2 afforded the desired deprotected product **6a** in 44% yield, along with the other mono-deprotected product **7a** and bis-deprotected product **8a** (entry 1). Changing the solvent to THF, CH_3CN or toluene did not improve the yield and selectivity for **6a** (entries 2–4). However, to our delight, the use of TESOTf/2,4,6-collidine in CH_2Cl_2 greatly increased the selectivity for **6a**, forming low amounts of **8a** and no **7a** at all (entry 5). Also, lowering the reaction temperature to −30 °C further improved the yield of **6a** to 94% (entry 6). Lastly, the use of other conventional methods that utilize a Lewis acid such as TMSCl or a Brønsted acid such as *p*-TsOH only gave negligible amounts of **6a** with no selectivity. Thus, our methodology using TESOTf/2,4,6-collidine combination induces an effective chemoselective deprotection of α-unsubstituted acetals in the presence of α-disubstituted acetals.

Table 2. Study of reaction conditions.[a]

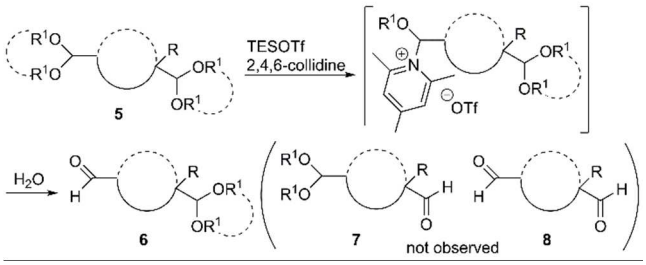


entry	reagent	solvent	temp. (°C)	**6a** : **7a** : **8a**[b]	**6a** (%)[c]
1	TMSOTf	CH_2Cl_2	0	49 : 2 : 49	44
2	TMSOTf	THF	0	48 : 0 : 52	42
3	TMSOTf	CH_3CN	0	38 : 0 : 62	35
4	TMSOTf	toluene	0	39 : 12 : 49	38
5	TESOTf	CH_2Cl_2	0	93 : 0 : 7	87
6	TESOTf	CH_2Cl_2	-30	95 : 0 : 5	94
7[d]	TMSI	CH_2Cl_2	0	0 : 14 : 86	0
8[d]	*p*-TsOH	acetone /H_2O	r.t.	14 : 23 : 63	10

[a]Reaction conditions. R_3SiOTf (2.0 equiv) and 2,4,6-collidine (3.0 equiv) in solvent then H_2O. [b]The ratio was determined by ^1H NMR analysis of the unpurified reaction mixture. [c]Isolated yield. [d]Without 2,4,6-collidine.

We then explored the substrate scope for the chemoselective deprotection of α-unsubstituted acetals in the presence of α-substituted or aromatic acetals (Table 3). In the cases of cyclic acetals such as 1,3-dioxolane-type **5b** and 1,3-dioxane-type **5c**, acetals with no substitution at the α-position were selectively deprotected to afford products **6b** and **6c** respectively in excellent yields under our reaction conditions (entries 1 and 2). When the α-position was substituted with an isopropyl group instead, the deprotection proceeded similarly to selectively give product **6d** in 87% yield (entry 3). In all cases, mono-deprotected products **7** and bis-deprotected products **8** were not produced. Furthermore, our method proved to be useful for the selective deprotection of an aliphatic acetal in the presence of an aromatic acetal, affording a good yield of the deprotected aliphatic aldehyde **6e** (entry 4). This pattern of selectivity is the complete opposite from that of the conventional method.[3d)]

Table 3. Substrate scope for the chemoselective deprotection of α-unsubstituted acetals.[a]

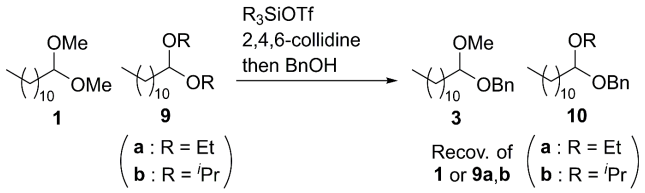


entry	substrate	result[b]
1[c]	**5b**	**6b** (92%)
2[d]	**5c**	**6c** (90%)
3	**5d**	**6d** (87%)
4	**5e**	**6e** (68%)

[a]Reaction conditions. TESOTf (2.0 equiv) and 2,4,6-collidine (3.0 equiv) in CH_2Cl_2 at −30 °C then H_2O. [b]Isolated yield. [c]TESOTf (4.0 equiv) and 2,4,6-collidine (6.0 equiv) were used at −30 °C to 0 °C. [d]TMSOTf (4.0 equiv) and 2,4,6-collidine (6.0 equiv) were used at 0 °C.

1-2. Different Types of Acetals. The remarkable reversal of the reactivity of deprotection of acetals by our method is made more concrete in the reaction of different types of acetals. First, we investigated the reactivity of different types of acetals via nucleophilic substitution using a 1:1 mixture of dimethyl acetal **1** and diethyl acetal **9a** or diisopropyl acetal **9b** (Table 4).[8)] The use of TMSOTf and 2,4,6-collidine to a mixture of **1** and **9a** followed by BnOH produced mixed acetal **3** from dimethyl acetal **1** in 82% yield along with 31% of mixed acetal **10a** from diethyl acetal **9a** accompanied with the recovered **1** (17%) and **9a** (63%) (entry 1). The use of TESOTf and 2,4,6-collidine gave similar results (entry 2), while the reaction of TMSOTf and 2,4,6-collidine with a mixture of **1** and **9b** did not result in improved selectivity either (entry 3). Pleasingly, it was found that the use of TESOTf instead of TMSOTf resulted in exclusive reactivity for dimethyl acetal **1**, producing mixed acetal **3** in quantitative yield with no formation of mixed acetal **10b** from diisopropyl acetal **9b** (entry 4).

Table 4. Evaluation of the selective deprotection of different types of acetals.[a]



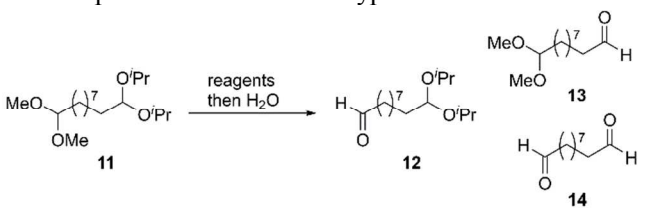
entry	R_3SiOTf	R	**3** (%)[b]	**10** (%)[b]	**1** (%)[b]	**9** (%)[b]
1	TMSOTf	Et	82	31	17	63
2	TESOTf	Et	92	33	0	61
3	TMSOTf	^{i}Pr	75	49	13	31
4	TESOTf	^{i}Pr	quant.	0	0	quant.

[a]Reaction conditions. R_3SiOTf (1.5 equiv) and 2,4,6-collidine (2.25 equiv) in CH_2Cl_2 at 0 °C for 1 h then BnOH (2.0 equiv) for 2 h. [b]Isolated yield.

Next, we examined the deprotection of acetal **11** containing both a dimethyl and diisopropyl acetal unit. The diisopropyl acetal unit of acetal **11** is quite labile under acidic conditions. [9] In fact, purification of **11** by SiO_2 flash column chromatography sometimes gave α-alkanoyl dimethyl acetal **13** and less amount of dialdehyde **14** (see Table 5) as a result of the slightly long stay of **11** in the column.

Even though the diisopropyl acetal unit is unstable under acidic conditions, our method didn't affect it and α-alkanoyl diisopropyl acetal **12** was obtained selectively. The results of our method as well as conventional ones are shown in Table 5. The use of TESOTf and 2,4,6-collidine affected the deprotection of the dimethyl acetal unit with complete selectivity to give **12** in 77% yield, leaving the diisopropyl acetal unit intact (entry 1). In contrast, the use of conventional methods using TMSI or *p*-TsOH did not result to the formation of **12** but instead resulted to small amounts of diisopropyl acetal-deprotected product **13** and high yields of **14** (entries 2 and 3).

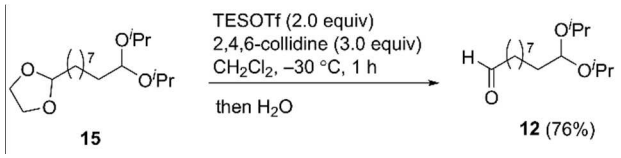
Table 5. Selective deprotection of different types of acetals in the same molecule.



entry	reagents	**12** : **13** : **14**[a]	**12** (%)[b]
1[c]	TESOTf/ 2,4,6-collidine	100 : 0 : 0	77
2[d]	*p*-TsOH	0 : 15 : 85	0
3[e]	TMSI	0 : 5 : 95	0

[a]Determined by ^{1}H NMR analysis of unpurified reaction mixtures. [b]Isolated yield. [c]TESOTf (2.0 equiv) and 2,4,6-collidine (3.0 equiv) in CH_2Cl_2 at −30 °C for 1 h then H_2O at r.t. [d]*p*-TsOH (1.0 equiv) in acetone/H_2O (1:1) at r.t. for 2 h. [e]TMSI (1.0 equiv) in CH_2Cl_2 at 0 °C for 10 min.

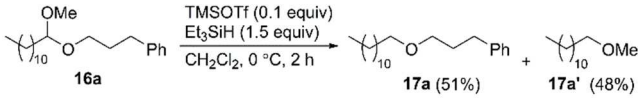
The usefulness of our method was further exemplified in the deprotection of acetal **15** which contains both a cyclic acetal unit and a diisopropyl acetal one (Scheme 1). Treatment of **15** with TESOTf and 2,4,6-collidine showed complete selectivity and gave a **12** in 76% yield, leaving the diisopropyl acetal unit intact. These results support that our methodology provides excellent chemoselectivity for the deprotection of acetals, which complements the conventional methods.



Scheme 1. Deprotection of acetal **15**.

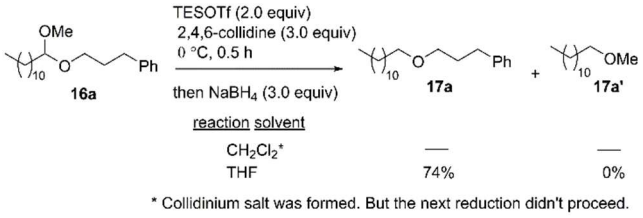
2. Formation of Single Ether Product from Mixed Acetal. Finally, we applied our method for the transformation of mixed acetals to ethers. Alkyl ether moieties are found in many pharmaceutical and bioactive compounds because they are often chemically and metabolically stable.[10] Several methods, including the representative Williamson ether synthesis, are available for ether synthesis.[11] However, many of these methods involve harsh conditions, limited substrate scopes or complicated operation procedures. Most methods of ether synthesis from acetals that have been reported to date only work on symmetrical acetals. In 2009 and 2011, Bode *et al.* reported the nucleophilic substitution of unsymmetrical acetals, methoxymethyl (MOM) ethers and their derivatives.[12] However, these nucleophiles are limited to *sp*- and sp^2-carbon nucleophiles and do not include sp^3-ones such as alkyl groups. We have recently developed a mild and versatile method for the synthesis of alkyl ethers from MOM ethers and mixed acetals.[13] The reaction proceeds by nucleophilic substitution reaction of the collidinium salts, which are derived from acetals by treatment with R_3SiOTf and 2,4,6-collidine, with Gillman reagent.

In this section, we present an alternative method, namely reductive alkyl ether synthesis from acetals. The conventional method uses a combination of TMSOTf and Et_3SiH to convert acetals into ethers and is particularly useful for symmetric acetals.[14] However, this methodology gives poor results in the reactions of mixed acetals. In fact, the mixed acetal **16a** afforded the mixture of two ether compounds **17a** and **17a'** equally in 51% and 48% respectively (Scheme 2).



Scheme 2. Reduction of mixed acetal **16a** with TMSOTf-Et_3SiH.

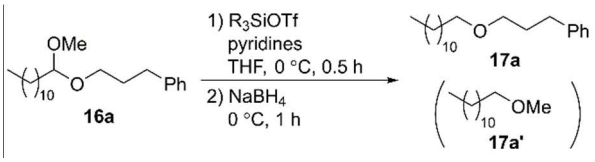
We used $NaBH_4$ as a hydride source due to its easy handling and examined the reductive alkyl ether synthesis using mixed acetal **16a**. When CH_2Cl_2 was used as the reaction solvent, the $NaBH_4$-reduction did not work even though the collidinium salt was formed by treatment of **16a** with TESOTf and 2,4,6-collidine. However, when THF was used in place of CH_2Cl_2, the desired **17a** was obtained in 74% and wit no formation of **17a'** (Scheme 3).



Scheme 3. Reductive alkyl ether synthesis form mixed acetal **16a**.

We then reexamined the reactions of several silyl triflates and pyridines in THF using **16a** (Table 6). Entry 1 shows the same results in Scheme 3. The use of TMSOTf in place of TESOTf slightly increased the yield of **17a** (entry 2), whereas *tert*-butyldimethylsilyl trifluoromethanesulfonate (TBSOTf) was completely ineffective (entry 3). Next, we examined pyridines, 2,6-lutidine, 2-methoxypyridine, and 2,2'-bipyridyl using TMSOTf (entries 4-6). Although they afforded the desired ether **17a** in high to moderate yields, 2,4,6-collidine still gave the most promising result (entry 2). The reaction conditions in entry 2 was then further optimized by forming the collidinium salt at −30 °C (entry 7) to avoid any decomposition of the rather unstable collidinium salt intermediate that occurred gradually at 0 °C. In all cases, ether **17a** (and not **17a'**) was obtained as the exclusive product. This selectivity is likely due to the bulkiness around the silicon atom. Finally, we chose TMSOTf and 2,4,6-collidine at −30 °C as the optimal conditions (entry 7) for further studies of the reduction of mixed acetals.[15)]

Table 6. Optimization for the reductive alkyl ether synthesis from mixed acetal **16a**.[a]

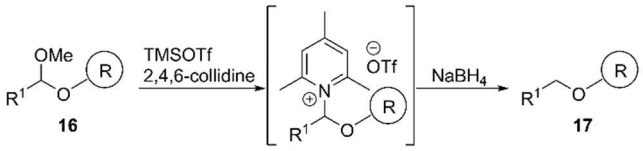


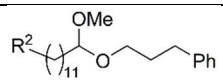
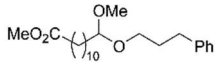
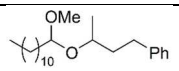
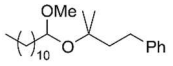
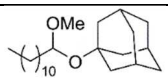
entry	R_3SiOTf	pyridines	**17a** (%)[b]
1	TESOTf	2,4,6-collidine	74
2	TMSOTf	2,4,6-collidine	80
3	TBSOTf	2,4,6-collidine	-[c]
4	TMSOTf	2,6-lutidine	77
5	TMSOTf	2-methoxypyridine	73
6	TMSOTf	2,2'-bipyridyl	51
7[d]	TMSOTf	2,4,6-collidine	91

[a]Reaction conditions: R_3SiOTf (2.0 equiv) and pyridines (3.0 equiv) in THF at 0 °C for 0.5 h then $NaBH_4$ (3.0 equiv) at 0 °C for 1 h. [b]Isolated yield. [c]Salt intermediate was not formed. [d]Reaction was performed at −30 °C to 0 °C.

Using the optimized conditions, we investigated the substrate scope of this selective reduction of mixed acetals using **16b**–**16k** (Table 7). As a result, good to excellent yields were obtained in the presence of many functional groups, such as acetoxy (OAc), benzoyloxy (OBz), *tert*-butyldimethylsilyloxy (OTBS), trityloxy (OTr), and halogens (entries 1–6). Pleasingly, both base labile substrates **16b**, **16c**, and **16h** (entries 1, 2, and 7), which are typically sensitive in conventional etherification, as well as acid labile substrates **16d** and **16e** (entries 3 and 4) were tolerated under this reaction conditions. Furthermore, this method could be applied to the sterically crowded substrates **16i**–**16k**, where 2-methoxypyridine was used in place of 2,4,6-collidine (entries 8–10). These results show that our method is useful for accessing various types of alkyl ethers.

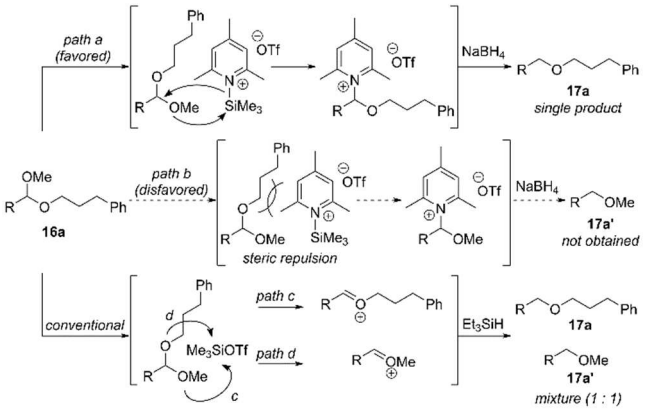
Table 7. Substrate scope of the mixed acetal for the reductive alkyl ether synthesis.[a]



entry	**16**	**17** (%)[b]
1	 **16b** (R^2 = OAc)	89
2	**16c** (R^2 = OBz)	83
3	**16d** (R^2 = OTBS)	86
4	**16e** (R^2 = OTr)	92
5	**16f** (R^2 = Cl)	73
6	**16g** (R^2 = Br)	61
7	 **16h**	90
8[c]	 **16i**	65
9[c]	 **16j**	70
10[c]	 **16k**	76

[a]Reaction conditions; procedure A: TMSOTf (4.0 equiv) and 2,4,6-collidine (6.0 equiv) (for entries 1-4) or procedure B: TMSOTf (2.0 equiv) and 2,4,6-collidine (3.0 equiv) (for entries 5-10) in THF at -30 °C then $NaBH_4$ (3.0 equiv) at -30 °C to 0 °C. [b]Isolated yield. [c]2-Methoxypyridine was used instead of 2,4,6-collidine.

Based on the above experimental results, we proposed a possible reaction mechanism (Scheme 4; **16a** is shown as an example of substrate). TMSOTf in the presence of 2,4,6-collidine *in situ* generates a Lewis acid/base complex.[16, 17] This complex recognizes the steric environment around the oxygen atoms and preferentially activates the smaller alkoxyl group in the mixed acetal to avoid steric hindrance (path a in Scheme 4). Subsequent hydride reduction of the resultant salt intermediate produces the corresponding alkyl ether **17a**. In this reaction, the other ether product **17a'** was not obtained, suggesting that the larger alkoxyl group in the mixed acetal is not activated by the complex because of unfavorable steric repulsion (path b). As a result, reduction of the mixed acetal proceeds with highly discriminative control and chemoselectivity. However, the conventional use of TMSOTf gives no selectivity because both alkoxyl groups are activated by TMSOTf (paths c and d).



Scheme 4. Proposed mechanism.

CONCLUSION

In this article, we developed highly discriminative and chemoselective transformations of acetals using the combination of R_3SiOTf/2,4,6-collidine. It is noteworthy that the deprotections illustrated here are the first examples of discriminative and chemoselective deprotections between acetals (acetal *vs.* acetal), where such selectivity has been unprecedented with conventional methods. Furthermore, formation of a single ether product from a mixed acetal is noteworthy because conventional reaction conditions that use Et_3SiH-TMSOTf produce two different ethers from a mixed acetal. We anticipate that the R_3SiOTf/2,4,6-collidine complex recognizes the steric environments in the substrate to effect deprotection or nucleophilic substitution quite selectively. We expect that these reactions will widen the scope of synthetic utility of acetal functions.

EXPERIMENTAL SECTION

General. All reagents were purchased from commercial sources and used without further purification, unless otherwise noted. Reactions were performed under a nitrogen atmosphere using purchased anhydrous solvent. All reactions were monitored by thin-layer chromatography using Merck SiO_2 gel 60 F254. The products were purified by column chromatography over SiO_2 Kieselgel 60 (70-230 mesh ASTM) purchased from Merck or SiO_2 60N (40-50 μm, spherical neutral) purchased from Kanto Chemical. ^{1}H NMR and ^{13}C NMR spectra were recorded at 25 ^{o}C on a JEOL JNM-AL300 (at 300 MHz and 75 MHz, respectively), a JEOL JNM-ECS 400 (at 400 MHz and 100 MHz, respectively) or a JEOL JNM-LA 500 (at 500 MHz and 125 MHz, respectively), and the chemical shifts are reported relative to internal TMS (^{1}H, δ = 0.00) and $CDCl_3$ (^{13}C, δ = 77.0). Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ ppm) (integration, multiplicity, coupling constant (Hz)). Multiplicity and qualifier abbreviations are as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. High-resolution mass spectra (MALDI-TOF) were performed by the Elemental Analysis Section of Graduate School of Pharmaceutical Science in Osaka University.

The substrates **1**[18], **3**[19], **4a**[19], **4b**[19], **9a**[20], **9b**[20], **10a**[19], **10b**[19] and **17a'**[21] are known compounds.

Synthesis of Substrates and Experimental Details for Table 1, 2, 3, 5 and Scheme 1.

*1,1-Dimethoxy-2-methyldodecane (**2a**).* To a solution of 2-methyldodecanal (1.21 g, 6.10 mmol) in MeOH (20 mL)/CH_2Cl_2 (20 mL) were added 10-camphorsulfonic acid (CSA) (141.7 mg, 0.610 mmol) and MS3A (0.50 g) at r.t. After stirring for overnight, the reaction mixture was quenched with sat. $NaHCO_3$ aq., and the mixture was extracted with CH_2Cl_2. The extract was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash SiO_2 column chromatography to afford **2a** (1.36 g, 5.55 mmol, 91%). Colorless oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 4.02 (d, 1H, J = 6.9 Hz), 3.35 (s, 6H), 1.74-1.71 (m, 1H), 1.10-1.48 (m, 18H), 0.88 (m, 6H).; ^{13}C NMR ($CDCl_3$, 125 MHz): δ 109.0, 54.0, 53.9, 35.7, 31.9, 31.7, 29.9, 29.6, 29.3, 26.9, 22.7, 14.3, 14.1.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{15}H_{32}O_2Na$ 267.2295, found 267.2295.

*1,1-Dimethoxy-2,2-dimethyldodecane (**2b**). (Step 1)* To a solution of methyl 2,2-dimethyldodecanoate (3.25 g, 13.4 mmol) in THF (134 mL) was added dropwise diisobutylaluminum hydride (DIBAL-H) (1 M in THF, 40.2 mL, 40.2

mmol) at -78 °C. After stirring for overnight at r.t., the reaction mixture was quenched with H_2O at 0 °C, and the mixture was extracted with EtOAc. The extract was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash SiO_2 column chromatography (*n*-hexane/EtOAc = 4/1) to afford the corresponding alcohol (2.58 g, 12.1 mmol, 90%). *(Step 2)* Then, to a solution of the alcohol (0.50 g, 2.3 mmol) in DMSO (1.2 ml) was added 2-iodoxybenzoic acid (IBX) (0.98 g, 3.5 mmol) at r.t. After stirring for 2 h, the reaction mixture was diluted with EtOAc, filtered through Celite pad, and washed with H_2O and brine. The extract was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was used in the next reaction without further purifications. *(Step 3)* To a solution of the residue in MeOH (2.3 mL)/CH_2Cl_2 (2.3 mL) were added *p*-TsOH (43.8 mg, 0.23 mmol) and MS3A (0.23 g). After stirring for overnight, the reaction mixture was quenched with sat. $NaHCO_3$ aq., and the mixture was extracted with CH_2Cl_2. The extract was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash SiO_2 column chromatography to afford **2b** (232.2 mg, 5.76 mmol, 43% in 2 steps). Eluent: *n*-hexane/EtOAc = 30/1. Colorless oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.83 (s, 1H), 3.50 (s, 6H), 1.26 (bs, 18H), 0.88 (s, 6H), 0.88 (t, 3H, *J* = 6.9 Hz).; ^{13}C NMR ($CDCl_3$, 125 MHz): δ 114.1, 58.5, 39.3, 37.8, 31.9, 30.7, 29.7, 29.6, 29.3, 23.6, 22.7, 21.9, 14.1.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{16}H_{34}O_2Na$ 281.2451, found 281.2457.

*2,2-Dimethyldodecanedial (**8a**). (Step 1)* To a solution of methyl 12-((*tert*-butyldimethylsilyl)oxy)-2,2-dimethyldodecanoate (1.91 g, 5.13 mmol) in THF (14 mL) was added dropwise DIBAL-H (1 M in THF, 12.1 mL, 12.1 mmol) at -78 °C. After stirring for 1 h, the reaction mixture was quenched with H_2O at 0 °C, and the mixture was extracted with EtOAc. The extract was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was used in the next reaction without further purifications. *(Step 2)* To a solution of the residue in THF (26 mL) was added tetra-*n*-butylammonium fluoride (TBAF) (1 M in THF, 10.3 mL, 10.3 mmol) at r.t. After stirring for overnight, the reaction mixture was concentrated under reduced pressure. The residue was purified by flash SiO_2 column chromatography (*n*-hexane/EtOAc = 1/1) to afford the corresponding alcohol (1.07 g, 4.62 mmol, 90% in 2 steps). *(Step 3)* To a solution of oxalyl chloride (7.1 ml, 83.9 mmol) in CH_2Cl_2 (30 mL) was added dropwise a solution of DMSO (7.1 mL) in CH_2Cl_2 (33 mL) at -78 °C. After stirring for 15 min, a solution of the above alcohol (3.85 g, 16.7 mmol) in CH_2Cl_2 (21 mL) was added to the reaction mixture by cannula. After stirring for 15 min, Et_3N (23.5 mL, 16.7 mmol) was added to the reaction mixture. After stirring for 10 min, the reaction mixture was warmed to r.t., then quenched with H_2O at 0 °C. The mixture was extracted with CH_2Cl_2. The extract was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash SiO_2 column chromatography to afford **8a** (2.59 g, 11.4 mmol, 68%). Eluent: *n*-hexane/EtOAc = 15/1. Colorless oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.77 (t, 1H, *J* = 1.8 Hz), 9.45 (s, 1H), 2.42 (td, 2H, *J* = 7.4, 1.8 Hz), 1.67-1.58 (m, 2H), 1.47-1.41 (m, 2H), 1.26 (bs, 12H), 1.04 (s, 6H).; ^{13}C NMR ($CDCl_3$, 125 MHz): δ 206.6, 202.9, 45.8, 43.8, 37.3, 29.30, 29.25, 29.1, 24.2, 22.0, 21.2.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{14}H_{26}O_2Na$ 249.1825, found 249.1823.

*2-Isopropyldodecanedial (**8d**).* To a solution of Celite (1.0 g) and pyridinium chlorochromate (PCC) (544.7 mg, 2.53 mmol) in CH_2Cl_2 was added a solution of 2-isopropyldodecane-1,12-diol (154.4 mg, 0.631 mmol) in CH_2Cl_2 (6.3 mL). After stirring for 3.5 h, the reaction mixture was filtered through a Celite pad. The filtrate was then concentrated to afford **8d** without further purification. Colorless oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.77 (t, 1H, *J* = 1.8 Hz), 9.60 (d, 1H, *J* = 3.4 Hz), 2.42 (td, 2H, *J* = 7.3, 1.8 Hz), 2.04-1.95 (m, 2H), 1.47-1.43 (m, 4H), 1.29-1.18 (m, 12H), 0.961 (d, 3H, *J* = 6.9 Hz), 0.957 (d, 3H, *J* = 6.9 Hz).; ^{13}C NMR ($CDCl_3$, 125 MHz): δ 206.1, 202.9, 58.7, 43.9, 29.7, 29.31, 29.27, 29.1, 28.3, 27.6, 26.1, 22.0, 20.3, 19.8.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{15}H_{28}O_2Na$ 263.1982, found 263.1982.

*1,1,12,12-Tetramethoxy-2,2-dimethyldodecane (**5a**).* To a solution of 2,2-dimethyldodecanedial (**8a**) (1.00 g, 4.40 mmol) in MeOH (8.8 mL) were added *p*-TsOH·H_2O (836 mg, 4.40 mmol) and MS3A (0.88 g). After stirring for 8 h, the reaction mixture was quenched with sat. $NaHCO_3$ aq., and the mixture was extracted with CH_2Cl_2. The extract was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash SiO_2 column chromatography to afford **5a** (504.3 mg, 1.54 mmol, 35%). Eluent: CH_2Cl_2/EtOAc = 40/1. Colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 4.36 (t, 1H, *J* = 5.7 Hz), 3.82 (s, 1H), 3.50 (s, 6H), 3.31 (s, 6H), 1.59 (m, 2H), 1.28-1.24 (m, 16H), 0.86 (s, 6H).; ^{13}C NMR ($CDCl_3$, 125 MHz): δ 114.0, 104.5, 58.5, 52.6, 39.2, 37.8, 32.5, 30.6, 29.63, 29.55, 29.46, 24.6, 23.6, 21.9.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{18}H_{38}O_4Na$ 341.2662, found 341.2667.

*2,2'-(10-Methylundecane-1,10-diyl)bis(1,3-dioxolane) (**5b**).* To a solution of **5a** (197.3 mg, 0.619 mmol) in ethyleneglycol (0.17 mL, 3.04 mmol) was added *p*-TsOH·H_2O (10.7 mg, 0.06 mmol) at 50 °C. After the disappearance of **5a** (monitored by TLC), the reaction mixture was quenched with sat. $NaHCO_3$ aq., and the mixture was extracted with CH_2Cl_2. The extract was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford **5b** (185.1 mg, 0.588 mmol, 95%). Colorless oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 4.84 (t, 1H, *J* = 5.0 Hz), 4.54 (s, 1H), 4.00-3.82 (m, 8H), 1.69-1.62 (m, 2H), 1.43-1.36 (m, 16H), 0.88 (s, 6H).; ^{13}C NMR ($CDCl_3$, 125 MHz): δ 110.0,

104.7, 65.2, 64.8, 37.7, 37.0, 33.9, 30.6, 29.6, 29.5, 24.1, 23.5, 21.3.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{18}H_{34}O_4Na$: 337.2349, found 337.2351.

*2,2'-(10-Methylundecane-1,10-diyl)bis(1,3-dioxane) (**5c**).* To a solution of **5a** (175.6 mg, 0.55 mmol) in 1,3-propanediol (0.20 ml, 2.75 mmol) was added *p*-TsOH·H_2O (10.7 mg, 0.06 mmol) at 50 °C. After the disappearance of **5a** (monitored by TLC), the reaction mixture was quenched with sat. $NaHCO_3$ aq., and the mixture was extracted with CH_2Cl_2. The extract was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford **5c** (171.0 mg, 0.500 mmol, 91%). Colorless oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 4.51 (t, 1H, *J* = 5.0 Hz), 4.13 (s, 1H), 4.13-4.08 (m, 4H), 3.80-3.68 (m, 4H), 2.13-1.98 (m, 2H), 1.61-1.55 (m, 2H), 1.36-1.23 (m, 18H), 0.86 (s, 6H).; ^{13}C NMR ($CDCl_3$, 125 MHz): δ 107.6, 102.5, 67.1, 66.9, 37.8, 37.4, 35.3, 30.6, 29.65, 29.55, 29.53, 29.49, 26.0, 25.9, 24.0, 23.5, 22.0.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{20}H_{38}O_4Na$ 365.2662, found 365.2662.

*11-(Dimethoxymethyl)-1,1-dimethoxy-12-methyltridecane (**5d**).* To a solution of **8d** in MeOH (0.65 ml) and CH_2Cl_2 (0.65 ml) were added *p*-TsOH·H_2O (120.2 mg, 0.63 mmol) and MS3A (0.3 g) at r.t. After stirring for 11 h, the reaction mixture was quenched with K_2CO_3 and sat. $NaHCO_3$ aq. and extracted with CH_2Cl_2. The extract was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash SiO_2 column chromatography to afford **5d** (84.3 mg, 0.253 mmol, 40% in 2 steps). Eluent: CH_2Cl_2/EtOAc = 40/1. Colorless oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 4.36 (t, *J* = 6.0 Hz, 1H), 4.18 (d, *J* = 6.0 Hz, 1H), 3.35 (s, 3H), 3.33 (s, 3H), 3.31 (s, 6H), 1.90-1.86 (m, 1H), 1.60-1.56 (m, 2H), 1.46-1.43 (m, 1H), 1.30-1.21 (m, 16H), 0.90 (d, 3H, *J* = 7.1 Hz), 0.87 (d, 3H, *J* = 7.1 Hz).; ^{13}C NMR ($CDCl_3$, 125 MHz): δ 107.8, 104.5, 54.4, 53.7, 52.5, 45.7, 32.5, 30.2, 29.55, 29.46, 29.3, 27.4, 26.0, 24.6, 20.5, 18.8.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{19}H_{40}O_4Na$ 355.2819, found 355.2819.

*1-(10,10-Dimethoxydecyl)-4-(dimethoxymethyl)benzene (**5e**).* To a solution of 4-bromobenzaldehyde dimethylacetal (295.3 mg, 1.28 mmol) in Et_2O (1.5 mL) was added dropwise *n*-BuLi (1.2 mL, 1.92 mmol) at -78 °C. After stirring for 30 min, 10-bromo-1,1-dimethoxydecane in Et_2O (1.0 mL) was added. Then the reaction mixture was warmed to reflux. After stirring for 12 h, the reaction mixture was cooled to r.t., then the mixture was quenched with sat. $NaHCO_3$ aq., and extracted with EtOAc. The extract was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash SiO_2 column chromatography to afford **5e** (111.7 mg, 0.320 mmol, 25%). Eluent: *n*-hexane/EtOAc = 40/1. Colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.34 (d, 2H, *J* = 8.1 Hz), 7.17 (d, 2H, *J* = 8.1 Hz), 5.36 (s, 1H), 4.36 (t, 1H, *J* = 5.7 Hz), 3.33 (s, 6H), 3.31 (s, 6H), 2.60 (t, 2H, *J* = 7.7 Hz), 1.58 (m, 2H), 1.28 (bs, 14H).; ^{13}C NMR ($CDCl_3$, 125 MHz): δ 143.2, 135.3, 128.2, 126.5, 104.5, 103.3, 52.7, 52.6, 35.7, 32.5, 31.4, 29.5, 29.4, 29.2, 24.6.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{21}H_{36}O_4Na$ 375.2506, found 375.2504.

*1,1-Diisopropoxy-10,10-dimethoxydecane (**11**). (Step 1)* To a solution of 6,6-dimethoxyhex-1-ene (0.33 g, 2.31 mmol) in isopropanol (0.9 ml, 11.5 mmol) was added *p*-TsOH (43.9 mg, 0.23 mmol) at 50 °C. After the disappearance of starting material (monitored by TLC), the reaction mixture was quenched with sat. $NaHCO_3$ aq., and the mixture was extracted with CH_2Cl_2. The extract was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was used in the next step without further purification. *(Step 2)* To a solution of the residue and 6,6-dimethoxyhex-1-ene (1.00 g, 6.93 mmol) in CH_2Cl_2 (92 mL) was added Grubbs 2nd catalyst (392 mg, 0.462 mmol, 20 mol%) at reflux. After stirring for overnight, the reaction mixture was concentrated under reduced pressure. Then 10% Pd/C (29.2 mg) was added to the residue in MeOH (3.0 mL), and air was replaced to H_2 gas (balloon). After stirring for 3 h, the reaction mixture was filtrated with Celite pad, and concentrated under reduced pressure. The residue was purified by flash SiO_2 column chromatography to afford **11** (243 mg, 0.83 mmol, 36%). Eluent: *n*-hexane/EtOAc = 40/1. Colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 4.36 (t, 1H, *J* = 5.9 Hz), 4.18 (t, 1H, *J* = 5.9 Hz), 3.34 (heptet, 2H, *J* = 6.2 Hz), 3.31 (s, 6H), 1.62-1.55 (m, 4H), 1.28 (m, 12H), 1.19 (d, 6H, *J* = 6.0 Hz), 1.14 (d, 6H, *J* = 6.0 Hz).; ^{13}C NMR ($CDCl_3$, 125 MHz): δ 104.5, 100.3, 67.4, 52.5, 35.4, 32.4, 29.5, 29.43, 29.39, 29.36, 24.83, 24.81, 24.5, 23.4, 22.6.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{19}H_{40}O_4Na$ 355.2819, found 355.2819.

*2-(9,9-Diisopropoxynonyl)-1,3-dioxolane (**15**). (Step 1)* To a solution of 2-(pent-4-en-1-yl)-1,3-dioxolane (0.33 g, 2.31 mmol) in isopropanol (0.9 ml, 11.5 mmol) was added *p*-TsOH·H_2O (43.9 mg, 0.23 mmol) at 50 °C. After the disappearance of starting material (monitored by TLC), the reaction mixture was quenched with sat. $NaHCO_3$ aq., and the mixture was extracted with CH_2Cl_2. The extract was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue used the next step without further purification. *(Step 1)* To a solution of the above residue and 2-(pent-4-en-1-yl)-1,3-dioxolane (1.00 g, 6.93 mmol) in CH_2Cl_2 (92 mL) was added Grubbs 2nd catalyst (392 mg, 0.462 mmol, 20 mol%) at reflux. After stirring for overnight, the reaction mixture was concentrated under reduced pressure. Then 10% Pd/C (29.2 mg) was added to the residue in MeOH (3.0 mL), replaced air to H_2 gas (balloon). After stirring for 3 h, the reaction mixture was filtrated with Celite pad, and concentrated under reduced pressure. The residue was purified by flash SiO_2 column chromatography to afford **15** (200 mg, 0.63 mmol, 27%). Eluent: *n*-hexane/EtOAc =

40/1. Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.83 (t, 1H, J = 4.6 Hz), 4.52 (t, 1H, J = 5.5 Hz), 3.96 (q, 2H, J = 4.6 Hz), 3.97-3.70 (m, 6H), 1.66-1.51 (m, 4H), 1.39-1.21 (m, 12H), 1.17 (d, 3H, J = 6.0 Hz), 1.16 (d, 3H, J = 6.0 Hz), 1.12 (d, 3H, J = 6.0 Hz), 1.11 (d, 3H, J = 6.0 Hz).; ^{13}C NMR ($CDCl_3$, 76 MHz): δ 104.6, 100.3, 67.4, 64.8, 35.4, 33.9, 29.5, 29.5, 29.4, 24.8, 24.0, 23.4, 22.6.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{18}H_{36}O_4Na$ 339.2505, found 339.2505.

Experimental Details of Table 1. To a solution of the 1 to 1 mixture of dimethyl acetal **1** (1.0 equiv) and **2** (1.0 equiv) in CH_2Cl_2 were added dropwise 2,4,6-collidine (2.25 equiv) and TMSOTf (1.5 equiv) at 0 °C. After stirring for 1 h, BnOH (2.0 equiv) was added to the reaction mixture at 0 °C. After disappearance of the polar component, the reaction mixture was quenched with sat. $NaHCO_3$ aq., and the mixture was extracted with CH_2Cl_2. The extract was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash SiO_2 column chromatography to give the fractions which contain the mixed acetal **3** (with or without mixed acetal **4**). The fraction was measured by ^{1}H NMR to determine the ratio of products.

Experimental Details of Table 2. (entries 1-5) To a solution of **5a** (1.0 equiv) in solvent were added 2,4,6-collidine (3.0 equiv) and R_3SiOTf (TMSOTf or TESOTf) (2.0 equiv) at 0 °C. After checking the disappearance of **5a** and the formation of the polar compound on TLC, H_2O was added to the reaction mixture, and the resulting mixture was allowed to warm to r.t. After disappearance of the polar component, the reaction mixture was quenched with sat. $NaHCO_3$ aq., and the mixture was extracted with CH_2Cl_2. The extract was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was measured by ^{1}H NMR to determine the ratio of products and purified by flash SiO_2 column chromatography to give **6a**.

(entry 6) To a solution of **5a** (75.7 mg, 0.238 mmol) in CH_2Cl_2 (2.4 mL) were added 2,4,6-collidine (94 μL, 0.713 mmol) and TESOTf (107 μL, 0.475 mmol) at -30 °C. After checking the disappearance of starting material and the formation of the polar compound on TLC, H_2O (0.24 mL) was added to the reaction mixture at r.t. After disappearance of the polar component, the reaction mixture was quenched with sat. $NaHCO_3$ aq., and the mixture was extracted with CH_2Cl_2. The extract was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was measured by ^{1}H NMR to determine the ratio of products and purified by flash SiO_2 column chromatography to give **6a** (60.9 mg, 0.223 mmol, 94%). Eluent: 1% Et_3N in CH_2Cl_2.

(entry 7) To a solution of **5a** (66.7 mg, 0.209 mmol) in CH_2Cl_2 (2.1 mL) was added TMSI (30 μL) at 0 °C. After stirring for 15 min, the reaction mixture was quenched with sat. $NaHCO_3$ aq., and the mixture was extracted with CH_2Cl_2. The extract was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was measured by ^{1}H NMR to determine the ratio of products and purified by flash SiO_2 column chromatography to give **7a** (8.0 mg, 0.029 mmol, 14%) and **8a** (40.7 mg, 0.179 mmol, 86%). Eluent: 1% Et_3N in CH_2Cl_2.

(entry 8) To a solution of **5a** (102 mg, 0.319 mmol) in acetone (3.2 mL) and H_2O (3.2 mL) was added *p*-TsOH·H_2O (60.7 mg, 0.319 mmol) at r.t. After stirring for 1 h, the reaction mixture was added H_2O, and the mixture was extracted with CH_2Cl_2. The extract was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was measured by ^{1}H NMR to determine the ratio of products and purified by flash SiO_2 column chromatography to give **6a** (8.7 mg, 0.032 mmol, 10%), **7a** (14.8mg, 0.054 mmol, 17%) and **8a** (33.2 mg, 0.147 mmol, 46%). Eluent: 1% Et_3N in CH_2Cl_2.

*12,12-Dimethoxy-11,11-dimethyldodecanal (**6a**)*. Colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.77 (t, 1H, J = 1.9 Hz), 3.82 (s, 1H), 3.50 (s, 6H), 2.42 (td, 2H, J = 7.4, 1.9 Hz), 1.62-1.59 (m, 2H), 1.28-1.24 (m, 14H), 0.86 (s, 6H).; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 203.1, 114.0, 58.5, 43.9, 39.2, 37.7, 30.6, 29.6, 29.4, 29.3, 29.1, 23.5, 22.0, 21.9.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{16}H_{32}O_3Na$ 295.2244, found 295.2242.

*12,12-Dimethoxy-2,2-dimethyldodecanal (**7a**)*. Colorless oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.45 (s, 1H), 4.36 (t, 1H, J = 5.8 Hz), 3.31 (s, 6H), 1.58 (m, 2H), 1.47-1.41 (m, 2H), 1.35-1.22 (m, 14H), 1.04 (s, 6H).; ^{13}C NMR ($CDCl_3$, 125 MHz): δ 206.6, 104.5, 52.6, 45.8, 37.3, 32.4, 30.2, 29.5, 29.41, 29.39, 24.5, 24.2, 21.3.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{16}H_{32}O_3Na$ 295.2244, found 295.2246.

Experimental Details of Table 3. To a solution of **5** (1.0 equiv) in CH_2Cl_2 were added 2,4,6-collidine (3.0 equiv) and TESOTf (2.0 equiv) at −30 °C. After checking the disappearance of **5** and the formation of the polar compound on TLC, H_2O was added to the reaction mixture at r.t. After disappearance of the polar component, the reaction mixture was quenched with sat. $NaHCO_3$ aq., and the mixture was extracted with CH_2Cl_2. The extract was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash SiO_2 column chromatography to afford **6**.

*11-(1,3-Dioxolan-2-yl)-11-methyldodecanal (**6b**)*. According to the general procedure, **5b** (49.7 mg, 0.158 mmol), 2,4,6-collidine (126 μL, 0.948 mmol), TESOTf (114 μL, 0.632 mmol) and H_2O (0.16 mL) gave **6b** (39.4 mg, 0.146 mmol, 92%). Eluent: CH_2Cl_2/EtOAc = 40/1. Colorless oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.77 (t, 1H, *J* = 1.9 Hz), 4.55 (s, 1H), 3.95-3.83 (m, 4H), 2.42 (td, 2H, *J* = 7.4, 1.9 Hz), 1.64-1.57 (m, 2H), 1.27 (m, 14H), 0.88 (s, 6H).; ^{13}C NMR ($CDCl_3$, 125 MHz): δ 203.0, 110.0, 65.2, 43.9, 37.7, 37.0, 30.6, 29.5, 29.4, 29.3, 29.1, 23.5, 22.1, 21.3.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{16}H_{30}O_3Na$ 293.2087, found 293.2090.

*11-(1,3-Dioxan-2-yl)-11-methyldodecanal (**6c**)*. According to the general procedure, **5c** (47.8 mg, 0.140 mmol), 2,4,6-collidine (110 μL, 0.840 mmol), TESOTf (101 μL, 0.560 mmol) and H_2O (0.14 mL) gave **6c** (35.6 mg, 0.126 mmol, 90%). Eluent: CH_2Cl_2/EtOAc = 40/1. Colorless oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.77 (t, 1H, *J* = 1.8 Hz), 4.13 (s, 1H), 4.13-4.09 (m, 2H), 3.75-3.69 (m, 2H), 2.42 (td, 2H, *J* = 7.3, 1.8 Hz), 2.08-1.99 (m, 1H), 1.64-1.58 (m, 1H), 1.32-1.23 (m, 16H), 0.86 (s, 6H).; ^{13}C NMR ($CDCl_3$, 125 MHz): δ 203.1, 107.6, 67.1, 43.9, 37.7, 37.4, 30.5, 29.6, 29.4, 29.3, 29.1, 26.0, 23.5, 22.1, 22.0.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{17}H_{32}O_3Na$ 307.2244, found 307.2240.

*11-(Dimethoxymethyl)-12-methyltridecanal (**6d**)*. According to the general procedure, **5d** (41.8 mg, 0.126 mmol), 2,4,6-collidine (50 μL, 0.251 mmol), TESOTf (57 μL, 0.316 mmol), and H_2O (0.13 mL) gave **6d** (31.3 mg, 0.109 mmol, 87%). Eluent: CH_2Cl_2/EtOAc = 50/1. Colorless oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.76 (t, 1H, *J* = 1.9 Hz), 4.18 (d, 1H, *J* = 6.0 Hz), 4.18 (s, 1/2H), 3.35 (s, 3H), 3.33 (s, 3H), 2.42 (td, 2H, *J* = 7.4, 1.9 Hz), 1.90-1.87 (m, 1H), 1.64-1.60 (m, 2H), 1.46-1.44 (m, 1H), 1.37-1.21 (m, 14H), 0.90 (d, 3H, *J* = 7.0 Hz), 0.87 (d, 3H, *J* = 7.0 Hz).; ^{13}C NMR ($CDCl_3$, 125 MHz): δ 203.0, 107.8, 54.4, 53.8, 45.7, 43.9, 30.2, 29.5, 29.4, 29.32, 29.26, 29.1, 27.4, 26.0, 22.1, 20.5, 18.8.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{17}H_{34}O_3Na$ 309.2400, found 309.2396.

*10-(4-(Dimethoxymethyl)phenyl)decanal (**6e**)*. According to the general procedure, **5e** (22.5 mg, 0.0638 mmol), 2,4,6-collidine (25 μL, 0.191 mmol), TESOTf (29 μL, 0.128 mmol), and H_2O (65 μL) gave **6c** (13.3 mg, 0.0434 mmol, 68%). Eluent: CH_2Cl_2/EtOAc = 100/1. Colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.76 (t, 1H, *J* = 1.9 Hz), 7.35 (d, 2H, *J* = 8.1 Hz), 7.18 (d, 2H, *J* = 8.1 Hz), 5.36 (s, 1H), 3.33 (s, 6H), 2.60 (t, 2H, *J* = 7.5 Hz), 2.42 (td, 2H, *J* = 7.5 Hz, 1.9 Hz), 1.64-1.57 (m, 2H), 1.28-1.25 (m, 12H).; ^{13}C NMR ($CDCl_3$, 125 MHz): δ 192.0, 150.5, 134.4, 129.9, 129.1, 104.5, 52.6, 36.2, 32.5, 31.0, 29.47, 29.44, 29.42, 29.38, 29.2, 24.5.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{19}H_{30}O_3Na$ 329.2087, found 329.2088.

Experimental Details of Table 4. To a solution of the 1 to 1 mixture of dimethyl acetal **1** (1.0 equiv) and **9** (1.0 equiv) in CH_2Cl_2 were added dropwise 2,4,6-collidine (2.25 equiv) and R_3SiOTf (TMSOTf or TESOTf) (1.5 equiv) at 0 °C. After stirring for 1 h, BnOH (2.0 equiv) was added to the reaction mixture at 0 °C. After disappearance of the polar component, the reaction mixture was quenched with sat. $NaHCO_3$ aq., and the mixture was extracted with CH_2Cl_2. The extract was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash SiO_2 column chromatography to give the fractions which contain the mixed acetal **3** (with or without mixed acetal **10**). The fraction was measured by ^{1}H NMR to determine the ratio of products.

Experimental Details of Table 5. (entry 1) To a solution of **11** (30.2 mg, 0.09 mmol) in CH_2Cl_2 (0.9 mL) were added 2,4,6-collidine (37 μL, 0.28 mmol) and TESOTf (43 μL, 0.19 mmol) at -30 °C. After checking the disappearance of **11** and the formation of the polar compound on TLC, H_2O was added to the reaction mixture and the resulting solution was allowed to warm to r.t. After disappearance of the polar component, the reaction mixture was quenched with sat. $NaHCO_3$ aq., and the mixture was extracted with CH_2Cl_2. The extract was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash SiO_2 column chromatography to afford **12** (243 mg, 0.069 mmol, 77%). Eluent: CH_2Cl_2/EtOAc = 40/1.

(entry 2) To a solution of **11** (29.3 mg, 0.0920 mmol) in acetone (0.9 mL) and H_2O (0.9 mL) was added *p*-TsOH (15.8 mg, 0.0920 mmol) at r.t. After stirring for 1 h, the reaction mixture was quenched with sat. $NaHCO_3$ aq., and the mixture was extracted with CH_2Cl_2. The extract was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was measured by ^{1}H NMR to observe the component ratio, **12** (0%), **13** (15%) and **14** (86%).

(entry 3) To a solution of **11** (15.5 mg, 0.0487 mmol) in CH_2Cl_2 (0.5 mL) was added TMSI (7 μL, 0.0493 mmol) at r.t. After stirring for 15 min, the reaction mixture was quenched with sat. $NaHCO_3$ aq., and the mixture was extracted with CH_2Cl_2. The extract was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was measured by ^{1}H NMR to observe the component ratio, **12** (0%), **13** (5%) and **14** (95%).

*10,10-Diisopropoxydecanal (**12**).* Colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.76 (t, 1H, *J* = 1.9 Hz), 4.53 (t, 3H), 3.90-3.82 (m, 2H), 2.42 (td, 2H, *J* = 7.4, 1.9 Hz), 1.65-1.53 (m, 4H), 1.29 (bs, 10H), 1.19 (d, 6H, *J* = 6.3 Hz), 1.14 (d, 6H, *J* = 5.7 Hz).;^{13}C NMR ($CDCl_3$, 125 MHz): δ 203.0, 100.3, 67.5, 43.9, 35.4, 29.7, 29.44, 29.37, 29.3, 29.1, 24.8, 23.5, 22.6, 22.0.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{16}H_{32}O_3Na$ 295.2244, found 295.2242.

Experimental Details of Scheme 1. To a solution of **15** (94.9 mg, 0.3 mmol) in CH_2Cl_2 (1.5 mL) were added 2,4,6-collidine (119 μL, 0.9 mmol) and TESOTf (135 μL, 0.6 mmol) at -30 °C. After checking the disappearance of **15** and the formation of the polar compound on TLC, H_2O (0.3 mL) was added to the reaction mixture which was allowed to warm to r.t. After disappearance of the polar component, the reaction mixture was quenched with sat. $NaHCO_3$ aq., and the mixture was extracted with CH_2Cl_2. The extract was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was measured by ^{1}H NMR to observe the component ratio. The residue was purified by flash SiO_2 column chromatography to afford **12** (49.0 mg, 0.23 mmol, 76%). Eluent: *n*-hexane/ EtOAc = 15/1.

Synthesis of Substrates and Experimental Details for Scheme 2, 3, and Table 6, 7.

General Procedure for the Preparation of Mixed Acetals. To a solution of dimethyl acetal (1.0 equiv) in CH_2Cl_2 (0.1 M) were added dropwise 2,4,6-collidine (3.0 equiv) and TMSOTf (2.0 equiv) at 0 °C. After checking the disappearance of starting material and the formation of the polar compound on TLC, alcohol (3.0 equiv) was added to the reaction mixture at the same temperature. After disappearance of the polar component, the reaction mixture was quenched with sat. $NaHCO_3$ aq., and the mixture was extracted with CH_2Cl_2. The extract was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash SiO_2 column chromatography to afford the desired mixed acetal.

*3-((1-Methoxydodecyl)oxy)propylbenzene (**16a**).* According to the general procedure, 1,1-dimethoxydodecane (2.0 g, 8.68 mmol), 2,4,6-collidine (3.4 mL, 26.0 mmol), TMSOTf (3.1 mL, 17.4 mmol), and 3-phenylpropan-1-ol (3.5 ml, 26.0 mmol) gave **16a** (2.63 g, 7.90 mmol, 91%). Eluent: 1% Et_3N in *n*-hexane/benzene = 3/2 to 2/3. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30-7.17 (5H, m), 4.43 (1H, t, *J* = 5.8 Hz), 3.61 (1H, dt, *J* = 9.6, 6.4 Hz), 3.43 (1H, dt, *J* = 9.6, 6.4 Hz), 3.32 (3H, s), 2.71 (2H, t, *J* = 7.8 Hz), 1.94-1.87 (2H, m), 1.63-1.58 (2H, m), 1.37-1.24 (18H, m), 0.88 (3H, t, *J* = 6.9 MHz).; ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.0, 128.4, 128.3, 125.8, 104.0, 64.9, 52.5, 33.0, 32.5, 31.9, 31.5, 29.7, 29.62, 29.57, 29.5, 29.3, 24.7, 22.7, 14.1.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{22}H_{38}O_2Na$ 357.2770, found 357.2764.

*12-Methoxy-12-(3-phenylpropoxy)dodecyl acetate (**16b**).* According to the general procedure, 12,12-dimethoxydodecyl acetate (310 mg, 1.07 mmol), 2,4,6-collidine (424 μL, 3.22 mmol), TMSOTf (388 μL, 2.15 mmol), and 3-phenylpropan-1-ol (438 μL, 3.22 mmol) gave **16b** (300 mg, 0.856 mmol, 80%). Eluent: *n*-hexane/benzene = 7/1. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30-7.17 (5H, m), 4.41 (1H, t, *J* = 5.5 Hz), 4.05 (2H, t, *J* = 6.9 Hz), 3.61 (1H, dt, *J* = 9.4, 6.4 Hz), 3.43 (1H, dt, *J* = 9.4, 6.4 Hz), 3.32 (3H, s), 2.71 (2H, t, *J* = 7.8 Hz), 2.05 (3H, s), 1.95-1.90 (2H, m), 1.64-1.58 (4H, m), 1.31-1.28 (16H, m).; ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.3, 142.0, 128.4, 128.3, 125.8, 104.0, 65.0, 64.7, 52.6, 52.5, 33.0, 32.5, 31.5, 29.54, 29.52, 29.48, 29.45, 29.36, 29.25, 28.6, 25.9, 22.1, 21.0.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{24}H_{40}O_4Na$ 415.2824, found 415.2819.

*12-Methoxy-12-(3-phenylpropoxy)dodecyl benzoate (**16c**).* According to the general procedure, 12,12-dimethoxydodecyl benzoate (60.1 mg, 0.171 mmol), 2,4,6-collidine (135 μl, 0.514 mmol), TMSOTf (124 μL, 0.342 mmol), and 3-phenylpropan-1-ol (70 μL, 0.514 mmol) gave **16c** (64.3 mg, 0.142 mmol, 83%). Eluent: 1% Et_3N in *n*-hexane/EtOAc = 10/1 to 8/1. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06-8.04 (2H, m), 7.58-7.54 (1H, m), 7.47-7.43 (2H, m), 7.31-7.20 (5H, m), 4.42 (1H, t, *J* = 5.5 Hz), 4.32 (2H, t, *J* = 6.9 Hz), 3.61 (1H, dt, *J* = 9.6, 6.0 Hz), 3.45 (1H, dt, *J* = 9.6, 6.4 Hz), 3.32 (3H, s), 2.72 (2H, t, *J* = 7.8 Hz), 1.93-1.90 (2H, m), 1.79-1.75 (2H, m), 1.60-1.57 (2H, m), 1.44-1.29 (16H, m).; ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.7, 142.0, 132.8, 130.5, 129.5, 128.4, 128.3, 125.8, 104.0, 65.1, 64.9, 52.6, 33.0, 32.5, 31.5, 29.6, 29.3, 28.7, 26.0, 24.7.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{29}H_{42}O_4Na$ 477.2981, found 477.2975.

*tert-Butyl((12-methoxy-12-(3-phenylpropoxy)dodecyl)oxy)dimethylsilane (**16d**).* According to the general procedure, *tert*-butyl((12,12-dimethoxydodecyl)oxy)dimethylsilane (100 mg, 0.277 mmol), 2,4,6-collidine (110 μL, 0.831 mmol), TMSOTf (100 μL, 0.555 mmol), and 3-phenylpropan-1-ol (113 μl, 0.831 mmol) gave **16d** (132 mg, 0.277 mmol, quant.). Eluent: 1% Et_3N in *n*-hexane/benzene = 1/1. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31-7.20 (5H, m), 4.42 (1H, t, *J* = 5.5 Hz), 3.63-3.58 (3H, m), 3.44 (1H, dt, *J* = 9.6, 6.4 Hz), 3.32 (3H, s), 2.72 (2H, t, *J* = 7.8 Hz), 1.95-1.90 (2H, m), 1.64-1.50 (4H, m)., 1.37-1.25 (16H, m), 0.90 (9H, s), 0.04 (6H, s).; ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.0, 128.4, 128.3,

125.8, 64.9, 63.3, 52.5, 33.0, 32.9, 32.5, 31.5, 29.62, 29.58, 29.56, 29.5, 29.4, 26.0, 25.8, 24.7, 18.4.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{28}H_{52}O_3NaSi$ 487.3583, found 487.3578.

*((12-Methoxy-12-(3-phenylpropoxy)dodecyl)oxy)methanetriyltribenzene (**16e**)*. According to the general procedure, (((12,12-dimethoxydodecyl)oxy)methanetriyl)tribenzene (400 mg, 0.819 mmol), 2,4,6-collidine (324 µL, 2.48 mmol), TMSOTf (296 µL, 1.64 mmol), and 3-phenylpropan-1-ol (338 µL, 2.48 mmol) gave **16e** (454 mg, 0.762 mmol, 93%). Eluent: 1% Et_3N in *n*-hexane/benzene = 1/2. Colorless oil; ^1H NMR (300 MHz, $CDCl_3$): δ 7.46-7.16 (20H, m), 4.42 (1H, t, *J* = 5.8 Hz), 3.62-3.57 (1H, m), 3.47-3.39 (1H, m), 3.32 (3H, s), 3.02 (2H, t, *J* = 6.8 Hz), 2.71 (2H, t, *J* = 7.9 Hz), 1.95-1.88 (2H, m), 1.64-1.58 (4H, m), 1.33-1.24 (16H, m).; ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.5, 142.0, 128.7, 128.4, 128.3, 127.7, 126.8, 125.8, 104.0, 86.2, 64.9, 63.7, 52.5, 33.0, 32.5, 31.5, 30.1, 29.58, 29.53, 29.51, 26.3, 24.7.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{41}H_{52}O_3Na$ 615.3814, found 615.3809.

*3-((12-Chloro-1-methoxydodecyl)oxy)propylbenzene (**16f**)*. According to the general procedure, 12-chloro-1,1-dimethoxydodecane (122 mg, 0.461 mmol), 2,4,6-collidine (182 µL, 1.38 mmol), TMSOTf (166 µL, 0.92 mmol), and 3-phenylpropan-1-ol (188 µL, 1.38 mmol) gave **16f** (74.2 mg, 0.203 mmol, 44%). Eluent: 1% Et_3N in *n*-hexane/benzene = 3/2. Colorless oil; ^1H NMR (300 MHz, $CDCl_3$): δ 7.31-7.19 (5H, m), 4.43 (1H, t, *J* = 5.8 Hz), 3.62 (1H, dt, *J* = 9.3, 6.5 Hz), 3.52 (2H, t, *J* = 6.9 Hz), 3.44 (1H, dt, *J* = 9.3, 6.5 Hz), 3.32 (3H, s), 2.72 (2H, t, *J* = 7.9 Hz), 1.95-1.86 (2H, m), 1.77 (2H, quin, *J* = 6.9 Hz), 1.62-1.55 (2H, m), 1.45-1.27 (16H, m).; ^{13}C NMR (100 MHz, $CDCl_3$): δ 128.42, 128.39, 128.3, 125.8, 104.0, 64.9, 52.5, 45.2, 33.0, 32.6, 32.5, 31.5, 29.52, 29.50, 29.47, 29.43, 28.9, 26.9, 24.7.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{22}H_{37}ClO_2Na$ 391.2380, found 391.2374.

*3-((12-Bromo-1-methoxydodecyl)oxy)propylbenzene (**16g**)*. According to the general procedure, 12-bromo-1,1-dimethoxydodecane (353 mg, 1.14 mmol), 2,4,6-collidine (451 µL, 3.42 mmol), TMSOTf (412 µL, 2.28 mmol), and 3-phenylpropan-1-ol (465 µL, 3.42 mmol) gave **16g** (470 mg, 1.14 mmol, quant.). Eluent: 1% Et_3N in *n*-hexane/EtOAc = 15/1. Colorless oil; ^1H NMR (500 MHz, $CDCl_3$): δ 7.31-7.18 (5H, m), 4.43 (1H, t, *J* = 5.8 Hz), 3.62 (1H, dt, *J* = 9.8, 6.3 Hz), 3.47-3.40 (3H, m), 3.32 (3H, s), 2.59 (2H, t, *J* = 7.5 Hz), 1.82-1.70 (4H, m), 1.51-1.45 (2H, m), 1.31-1.16 (16H, m).; ^{13}C NMR (125 MHz, $CDCl_3$): δ 142.0, 128.4, 128.3, 125.8, 104.0, 64.9, 52.5, 34.1, 33.0, 32.8. 32.5, 31.5, 29.51, 29.49, 29.47, 29.41, 28.8, 28.2, 24.7.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{22}H_{37}O_2NaBr$ 435.1875, found 435.1869.

*Methyl 12-methoxy-12-(3-phenylpropoxy)dodecanoate (**16h**)*. According to the general procedure, methyl 12,12-dimethoxydodecanoate (310 mg, 1.13 mmol), 2,4,6-collidine (446 µL, 3.39 mmol), TMSOTf (408 µL, 2.26 mmol), and 3-phenylpropan-1-ol (461 µL, 3.39 mmol) gave **16h** (290 mg, 0.768 mmol, 68%). Eluent: 1% Et_3N in *n*-hexane/EtOAc = 10/1 to 2/1. Colorless oil; ^1H NMR (500 MHz, $CDCl_3$): δ 7.31-7.08 (5H, m), 4.29 (1H, t, *J* = 5.8 Hz), 3.67 (3H, s), 3.61 (1H, dt, *J* = 9.5, 6.3 Hz), 3.44 (1H, dt, *J* = 9.5, 6.3 Hz), 3.32 (3H, s), 2.72 (2H, t, *J* = 7.7 Hz), 2.31 (2H, d, *J* = 7.4 Hz), 1.94-1.89 (2H, m), 1.63-1.60 (4H, m), 1.37-1.28 (14H, m).; ^{13}C NMR (125 MHz, $CDCl_3$): δ 174.4, 142.0, 128.4, 128.3, 128.27, 125.8, 104.0, 64.9, 52.5, 51.4, 34.1, 33.0, 32.5, 32.46, 31.5, 29.5, 29.4, 29.2, 29.1, 24.9, 24.7.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{23}H_{38}O_4Na$ 401.2668, found 401.2662.

*3-((1-Methoxydodecyl)oxy)butylbenzene (**16i**)*. According to the general procedure, 1,1-dimethoxydodecane (1.04 g, 4.34 mmol), 2,4,6-collidine (1.72 mL, 13.1 mmol), TMSOTf (3.1 mL, 8.63 mmol), and 4-phenylbutan-2-ol (2.02 mL, 13.1 mmol) gave **16i** (320 mg, 0.91 mmol, 21%). Eluent: 1% Et_3N in *n*-hexane/EtOAc = 5/4 to 1/1. Colorless oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.16-7.02 (5H, m), 4.39 (1H, t, *J* = 5.5 Hz) , 3.63 (1H, qt, *J* = 6.6, 6.0 Hz), 3.17 (3H, s), 2.67-2.61 (1H, m), 2.58-2.50 (1H, m), 2.28 (2/2H, t, *J* = 7.3 Hz), 2.279 (2/2H, t, *J* = 7.3 Hz), 1.82-1.73 (1H, m), 1.67-1.59 (1H, m), 1.53-1.40 (2H, m), 1.14 (18H, m), 1.03 (3H, d, *J* = 6.0 Hz), 0.76 (3 H, t, *J* = 6.9 Hz).; ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.2, 128.3, 128.3, 125.7, 104.5, 103.2, 72.9, 52.5, 51.2, 38.6, 33.6, 32.4, 31.9, 31.7, 29.6, 29.59, 29.55, 29.52, 29.49, 29.45, 29.3, 24.8, 24.6, 22.7, 21.1, 14.1.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{23}H_{40}O_2Na$ 371.2926, found 371.2921.

*3-((1-Methoxydodecyl)oxy)-3-methylbutylbenzene (**16j**)*. According to the general procedure, 1,1-dimethoxydodecane (502 mg, 2.18 mmol), 2,4,6-collidine (0.86 mL, 6.54 mmol), TMSOTf (0.79 mL, 4.35 mmol), and 2-methyl-4-phenylbutan-2-ol (1.12 mL, 6.54 mmol) gave **16j** (640 mg, 1.85 mmol, 85%). Eluent: 1% Et_3N in *n*-hexane/EtOAc = 1/1. Colorless oil; ^1H NMR (300 MHz, $CDCl_3$): δ 7.31-7.17 (5H, m), 4.73 (1H, t, *J* = 5.8 Hz), 3.26 (3H, s), 2.74-2.66 (2H, m), 1.84-1.78 (2H, m), 1.64-1.56 (2H, m), 1.31-1.25 (24H, m), 0.89 (3H, t, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.9, 128.3, 125.6, 97.3, 75.4, 49.5, 44.4, 34.0, 31.9, 30.5, 29.7, 29.66, 29.62, 29.56, 29.3, 26.7, 26.1, 24.9, 14.1.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{24}H_{42}O_2Na$ 385.3080, found 385.3077.

*1-((1-Methoxydodecyl)oxy)adamantine (**16k**).* According to the general procedure, 1,1-dimethoxydodecane (690 mg, 2.99 mmol), 2,4,6-collidine (1.08 mL, 8.98 mmol), TMSOTf (1.18 mL, 5.99 mmol), and adamantan-1-ol (1.36 g, 8.98 mmol) gave **16k** (856 mg, 2.41 mmol, 81%). Eluent: 1% Et_3N in *n*-hexane/EtOAc = 1/4. Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.80 (1H, t, *J* = 5.5 Hz), 3.24 (3H, s), 2.15 (2H, brs), 1.81-1.80 (6H, m), 1.73-1.53 (12H, m), 1.27 (15H, m), 0.88 (3H, t, *J* = 6.8 Hz).; ^{13}C NMR (100 MHz, $CDCl_3$): δ 95.9, 72.9, 49.9, 45.3, 42.7, 36.3, 36.0, 34.4, 31.9, 30.7, 30.6, 29.65, 29.62, 29.58, 29.53, 29.4, 29.3, 24.9, 22.7, 14.1.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{23}H_{42}O_2Na$ 373.3083, found 373.3077.

Experimental Details of Scheme 2. To a solution of mixed acetal **16a** (40.8 mg, 0.122 mmol) in CH_2Cl_2 (1.2 mL) were added dropwise TMSOTf (3 μL, 0.012 mmol) and Et_3SiH (30 μL, 0.183 mmol) at 0 °C. After stirring for 2 h, checking the disappearance of **16a** on TLC, the reaction mixture was quenched with sat. $NaHCO_3$ aq., and the mixture was extracted with CH_2Cl_2. The extract was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash SiO_2 column chromatography to afford **17a** (19.1 mg, 0.0622 mmol, 51%) and **17a'** (11.3 mg, 0.0586 mmol, 48%). Eluent: *n*-hexane/benzene = 5/2.

*3-(Dodecyloxy)propylbenzene (**17a**).* Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30-7.16 (5H, m), 3.41 (2H, t, *J* = 6.4 Hz), 3.40 (2H, t, *J* = 6.9 Hz), 2.70 (2H, t, *J* = 7.8 Hz), 1.91-1.87 (2H, m), 1.62-1.56 (2H, m), 1.40-1.26 (18H, m), 0.88 (3H, t, *J* = 6.4 Hz).; ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.1, 128.5, 128.3, 125.7, 71.0, 69.9, 32.4, 31.9, 31.3, 29.8, 29.6, 29.7, 29.5, 29.3, 26.2, 22.7, 14.1.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{21}H_{36}ONa$ 327.2664, found 327.2658.

Experimental Details of Scheme 3. To a solution of mixed acetal **16a** (50.0 mg, 0.149 mmol) in solvent (0.75 mL) were added dropwise 2,4,6-collidine (59 μL, 0.448 mmol) and TESOTf (63 μL, 0.299 mmol) at 0 °C. After checking the disappearance of **16a** and the formation of the polar compound on TLC, $NaBH_4$ (17 mg, 0.448 mmol) was added to the reaction mixture at the same temperature and the mixture was allowed to warm to 0 °C. After disappearance of the polar component, the reaction mixture was quenched with sat. $NaHCO_3$ aq., and the mixture was extracted with CH_2Cl_2. The extract was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash SiO_2 column chromatography to afford **17a** (solvent = CH_2Cl_2: 0%; solvent = THF: 33.5 mg, 0.110 mmol, 74%). Eluent: *n*-hexane/benzene = 5/2.

Experimental Details of Table 7. To a solution of mixed acetal **16** (1.0 equiv) in CH_2Cl_2 were added dropwise pyridines and TMSOTf at -30 °C. After checking the disappearance of **16** and the formation of the polar compound on TLC, $NaBH_4$ (3.0 equiv) was added to the reaction mixture at the same temperature and the resulting mixture was allowed to warm to 0 °C. After disappearance of the polar component, the reaction mixture was quenched with sat. $NaHCO_3$ aq., and the mixture was extracted with CH_2Cl_2. The extract was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash SiO_2 column chromatography to afford the corresponding ether **17**. (Procedure A: pyridines (6.0 equiv), TMSOTf (4.0 equiv); Procedure B: pyridines (3.0 equiv), TMSOTf (2.0 equiv))

*12-(3-Phenylpropoxy)dodecyl acetate (**17b**).* According to the general procedure A, **16b** (58.0 mg, 0.140 mmol), 2,4,6-collidine (118 μL, 0.838 mmol), TMSOTf (108 μL, 0.558 mmol), and $NaBH_4$ (15.9 mg, 0.420 mmol) gave **17b** (47.9 mg, 0.125 mmol, 89%). Eluent: *n*-hexane/EtOAc = 8/1. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23-7.09 (5H, m), 3.98 (2H, t, *J* = 6.9 Hz), 3.35 (2H, t, *J* = 6.4 Hz), 3.32 (2H, t, *J* = 6.9 Hz), 2.62 (2H, t, *J* = 7.8 Hz), 1.97 (3H, s), 1.85-1.79 (2H, m), 1.58-1.47 (4H, m), 1.29-1.20 (16H, m).; ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2, 142.1, 128.5, 128.3, 125.7, 71.0, 70.0, 64.7, 32.3, 31.3, 29.8, 29.5, 29.5, 29.2, 28.6, 26.2, 25.9, 21.0.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{23}H_{38}O_3Na$ 385.2719, found 385.2713.

*12-(3-Phenylpropoxy)dodecyl benzoate (**17c**).* According to the general procedure A, **16c** (34.6 mg, 0.0761 mmol), 2,4,6-collidine (60 μL, 0.457 mmol), TMSOTf (55 μL, 0.304 mmol), and $NaBH_4$ (8.6 mg, 0.1522 mmol) gave **17c** (26.1 mg, 0.0632 mmol, 83%). Eluent: *n*-hexane/EtOAc = 15/1. Colorless oil; ^{1}H NMR (400MHz, $CDCl_3$): δ 8.06 (2H, d, *J* = 7.3 Hz), 7.56 (1H, t, *J* = 7.3 Hz), 7.45 (2H, t, *J* = 7.3 Hz), 7.31-7.17 (5H, m), 4.32 (2H, t, *J* = 6.9 Hz), 3.42 (2H, t, *J* = 6.4 Hz), 3.41 (2H, t, *J* = 6.4 Hz), 2.70 (2H, t, *J* = 7.6 Hz), 1.90 (2H, m), 1.77 (2H, m), 1.60-1.55 (2H, m), 1.47-1.41 (2H, m), 1.29 (14H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.69, 142.05, 132.7, 130.5, 129.5, 128.50, 128.45, 128.3, 125.7,71.0, 69.9, 65.1, 32.3, 31.3, 29.8, 29.58, 29.56, 29.50, 29.49, 29.3, 28.7, 26.2, 26.0.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{28}H_{40}O_3Na$ 447.2875, found 447.28701.

*tert-Butyldimethyl((12-(3-phenylpropoxy)dodecyl)oxy)silane (**17d**).* According to the general procedure A, **16d** (56.7 mg, 0.122 mmol), 2,4,6-collidine (96 μL, 0.732 mmol), TMSOTf (88 μL, 0.488 mmol), and $NaBH_4$ (13.8 mg, 0.366 mmol) gave **17d** (45.7 mg, 0.105 mmol, 86%). Eluent: *n*-hexane/EtOAc = 30/1. Colorless oil; ^{1}H NMR (300MHz,

$CDCl_3$): δ 7.32-7.19 (5H, m), 3.61 (2H, t, *J* = 6.9 Hz), 3.45-3.39 (4H, m), 2.71 (2H, t, *J* = 7.9 Hz), 1.93-1.88 (2H, m), 1.60-1.50 (4H, m), 1.29 (16H, m), 0.91 (9H, s), 0.06 (6H, s).; ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.1, 128.5, 128.3, 125.7, 71.0, 69.9, 63.3, 32.9, 32.4, 31.3, 29.8, 29.6, 29.5, 29.4, 26.2, 26.0, 25.8, 18.4, 5.3.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{27}H_{50}O_2NaSi$ 457.3476, found 457.3472.

*((12-(3-Phenylpropoxy)dodecyl)oxy)methanetriyltribenzene (**17e**)*. According to the general procedure A, **16e** (55.2 mg, 0.0931 mmol), 2,4,6-collidine (74 μL, 0.559 mmol), TMSOTf (67 μL, 0.372 mmol), and $NaBH_4$ (21.1 mg, 0.559 mmol) gave **17e** (49.3 mg, 0.0875 mmol, 94%). Eluent: *n*-hexane/EtOAc = 30/1. Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.39-7.08 (20H, m), 3.34 (2H, t, *J* = 6.2 Hz), 3.32 (2H, t, *J* = 6.5 Hz), 2.96 (2H, t, *J* = 6.9 Hz), 2.62 (2H, t, *J* = 7.9 Hz), 1.87-1.77 (2H, m), 1.58-1.45 (4H, m), 1.26-1.11 (18H, m).; ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.5, 128.7, 128.5, 128.3, 127.7, 126.8, 125.7, 86.2, 71.0, 69.9, 63.7, 32.4, 31.3, 30.0, 29.8, 29.6, 29.58, 29.5, 26.3, 26.2.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{40}H_{50}O_2Na$ 585.3709, found 585.3703.

*3-((12-Chlorododecyl)oxy)propylbenzene (**17f**)*. According to the general procedure B, **16f** (74.0 mg, 0.201 mmol), 2,4,6-collidine (79 μL, 0.602 mmol), TMSOTf (73 μL, 0.401 mmol), and $NaBH_4$ (22.8 mg, 0.602 mmol) gave **17f** (49.7 mg, 0.147 mmol, 73%). Eluent: *n*-hexane/benzene = 3/1. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30-7.18 (5H, m), 3.53 (2H, t, *J* = 6.8 Hz), 3.42 (2H, t, *J* = 6.0 Hz), 3.40 (2H, t, *J* = 6.4 Hz), 2.69 (2H, t, *J* = 7.8 Hz), 1.92-1.84 (2H, m), 1.80-1.73 (2H, m), 1.67-1.54 (2H, m), 1.43-1.41 (2H, m), 1.35-1.27 (14H, m).; ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.1, 128.5, 128.3, 125.7, 71.0, 69.9, 45.2, 32.6, 32.4, 31.3, 29.8, 29.6, 29.54, 29.51, 29.48, 29.45, 28.879, 28.877, 26.2.; HRMS (FAB) m/z: $[M + H]^+$ calcd for $C_{21}H_{36}OCl$ 339.2455, found 339.2455.

*3-((12-Bromododecyl)oxy)propylbenzene (**17g**)*. According to the general procedure B, **16g** (99.2 mg, 0.240 mmol), 2,4,6-collidine (95 μL, 0.720 mmol), TMSOTf (87 μL, 0.480 mmol), and $NaBH_4$ (27.2 mg, 0.720 mmol) gave **17g** (59.3 mg, 0.146 mmol, 61%). Eluent: *n*-hexane/EtOAc = 15/1. Colorless oil; ^{1}H NMR (500MHz, $CDCl_3$): δ 7.18-7.07 (5H, m), 3.31-3.27 (6H, m), 2.58 (2H, t, *J* = 7.7 Hz), 1.81-1.70 (4H, m), 1.47-1.44 (2H, m), 1.37-1.16 (16H, m).; ^{13}C NMR (125 MHz, $CDCl_3$): δ 142.1, 128.5, 128.4, 128.3, 125.7, 71.0, 69.9, 34.1, 32.8, 32.4, 31.3, 29.8, 29.57, 29.53, 29.50, 29.49, 29.42, 28.8, 28.2, 26.2.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{21}H_{35}ONaBr$ 405.1769, found 405.1764.

*Methyl 12-(3-phenylpropoxy)dodecanoate (**17h**)*. According to the general procedure A, **16h** (83.6 mg, 0.221 mmol), 2,4,6-collidine (174 μL, 1.33 mmol), TMSOTf (160 μL, 0.883 mmol), and $NaBH_4$ (25.1 mg, 0.663 mmol) gave **17h** (79.8 mg, 0.199 mmol, 90%). Eluent: *n*-hexane/EtOAc = 15/1. Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30-7.17 (5H, m), 3.67 (3H, s), 3.42 (2H, t, *J* = 6.3 Hz), 3.41 (2H, t, *J* = 6.9 Hz), 2.70 (2H, t, *J* = 7.4 Hz), 2.31 (2H, t, *J* = 7.5 Hz), 1.93-1.86 (2H, m), 1.64-1.55 (4H, m), 1.34-1.27 (14H, m). ; ^{13}C NMR (125 MHz, $CDCl_3$): δ 174.3, 142.1, 128.5, 128.3, 125.7, 71.0, 69.9, 51.4, 34.1, 32.4, 31.3, 29.8, 29.6, 29.51, 29.48, 29.41, 29.2, 29.1, 26.2, 24.9.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{22}H_{36}O_3Na$ 371.2562, found 371.2557.

*3-(Dodecyloxy)butylbenzene (**17i**)*. According to the general procedure B, **16i** (43.0 mg, 0.119 mmol), 2-methoxypyridine (37 μL, 0.356 mmol), TMSOTf (42 μL, 0.237 mmol), and $NaBH_4$ (13.0 mg, 0.356 mmol) gave **17i** (24.6 mg, 0.077 mmol, 65%). Eluent: *n*-hexane/EtOAc = 2/1. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22-7.08 (5H, m), 3.45-3.39 (1H, m), 3.32-3.21 (2H, m), 2.70-2.53 (2H, m), 1.84-1.72 (1H, m), 1.67-1.58 (1H, m), 1.53-1.46 (2H, m), 1.30-1.19 (18H, m), 1.08 (3H, d, *J* = 6.0 Hz), 0.81 (3H, t, *J* = 7.3 Hz).; ^{13}C NMR (100 MHz, CDC l_3): δ 142.5, 128.4, 128.2, 125.6, 74.4, 68.5, 38.4, 31.9, 31.8, 30.2, 29.66, 29.62, 29.5, 29.3, 26.3, 22.7, 19.7, 14.1.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{22}H_{38}ONa$ 341.2820, found 341.2815.

*3-(Dodecyloxy)-3-methylbutylbenzene (**17j**)*. According to the general procedure B, **16j** (90.0 mg, 0.248 mmol), 2-methoxypyridine (78 μL, 0.745 mmol), TMSOTf (104 μL, 0.496 mmol), and $NaBH_4$ (28.2 mg, 0.745 mmol) gave **17j** (57.7 mg, 0.174 mmol, 70%). Eluent: *n*-hexane/EtOAc = 1/1. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31-7.16 (5H, m), 3.36 (2H, t, *J* = 6.4 Hz), 2.67-2.63 (2H, m), 1.78-1.76 (2H, m), 1.57-1.53 (2H, m), 1.35-1.26 (18H, m), 1.22 (6H, s), 0.88 (3H, t, *J* = 6.9 Hz).; ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.1, 128.30, 128.29, 125.6, 73.9, 61.2, 42.1, 31.9, 30.7, 30.3, 29.7, 29.64, 29.58, 29.4, 26.4, 25.8, 22.7, 14.1.; HRMS (FAB) m/z: $[M + H]^+$ calcd for $C_{23}H_{41}O$ 333.3157, found 333.3156.

*1-(Dodecyloxy)adamantine (**17k**)*. According to the general procedure B, **16k** (90.1 mg, 0.257 mmol), 2-methoxypyridine (82 μL, 0.771 mmol), TMSOTf (93 μL, 0.514 mmol), and $NaBH_4$ (29.0 mg, 0.771 mmol) gave **17k** (62.6 mg, 0.195 mmol, 76%). Eluent: *n*-hexane/EtOAc = 4/1. Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.39 (2H, t, *J* = 6.8 Hz), 2.06 (2H, brs), 1.54-1.46 (10H, s), 1.46-1.41 (2H, m), 1.36-1.12 (21H, m), 0.89 (3H, t, *J* = 7.2 Hz).; ^{13}C NMR (125 MHz, $CDCl_3$): δ 71.6, 59.8, 41.6, 36.5, 31.9, 30.8, 30.5, 29.7, 29.63, 29.61, 29.5, 29.4, 26.3, 22.7, 14.1.; HRMS (MALDI-TOF) m/z: $[M + Na]^+$ calcd for $C_{22}H_{40}ONa$ 343.2977, found 343.2971.

ASSOCIATED CONTENT

The Supporting Information is available free of charge on the ACS Publications website at DOI:
^{1}H and ^{13}C NMR spectra of new compounds, and ^{1}H NMR study of Tables 1, 4, 5 and X-ray crystallographic data for compounds (PDF)
Crystal data for TMSOTf/2,4,6-collidine complex (CIF)
Crystal data for TMSOTf/pyridine complex (CIF)

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Notes

The authors declare no competing financial interest.

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