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# A simple and highly efficient deprotecting method for methoxymethyl and methoxyethoxymethyl ethers and methoxyethoxymethyl esters

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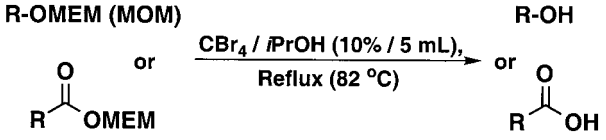
**Abstract**—A series of methoxyethoxymethyl (MEM)- and methoxymethyl (MOM)-ethers and MEM-esters were hydrolyzed to their corresponding alcohols and carboxylic acids by a catalytic amount of $CBr_4$ (10%) in *i*PrOH under refluxing reaction condition. The chemoselective hydrolysis between $R_3Si$- and MEM-protected alcohols can be achieved by using different steric bulkness solvents such as MeOH or *i*PrOH. © 2001 Elsevier Science Ltd. All rights reserved.

## 1. Introduction

In order to synthesize more complicated molecules, chemists have developed increasingly satisfactory protective groups and effective methods for the formation and cleavage of protected compounds. Selective protection and deprotection of hydroxyl and carboxyl groups is an important tool in multi-step synthesis of complex natural products.[1,2] Transformation of hydroxy group into methoxyethoxymethyl (MEM) or methoxymethyl (MOM) ethers is a commonly used protective process for alcohol.[3,4] Acidic reaction condition is the typically used hydrolyzing method for protected hydroxyl functionality. MEM- and MOM-ethers are generally hydrolyzed in protic solvent by acids such as HCl[5–7] and pyridinium *p*-toluenesulfonate,[8] or hydrolyzed by Lewis acids such as $LiBF_4$[9], $Me_2BBr$,[10] $(iPrS)_2BBr$,[11] $Ph_2BBr$,[12] catechol boron bromide,[13] $ZnBr_2$,[14] and $TiCl_4$. Recently, our laboratory reported a novel and highly selective deprotecting method for acetal/ketal,[15] tetrahydropyranyl ether[16] and trialkylsilyl ether.[17,18] The deprotection was performed with a catalytic amount of $CBr_4$ in $CH_3OH$ or $CH_3CN/H_2O$ reaction mixture under refluxing or ultrasonic conditions. These results showed that the in situ generation of HBr led to an acidic reaction condition.[19–21] We expected that this type of hydrolyzing system can be further extended to the application of deprotecting MEM- and MOM-protected alcohol and MEM-protected carboxylic acids. Therefore, we investigated this hydrolyzing method for deprotection of MEM- and MOM-ethers and MEM-esters. Herewith, we wish to report a simple and efficient hydrolyzing method for MEM- and MOM-ethers and MEM-esters (Scheme 1).

## 2. Results and discussions

Previous studies showed that acetals/ketals and tetrahydropyranyl ethers were hydrolyzed with a catalytic amount of $CBr_4$ in MeOH or $CH_3CN/H_2O$ reaction mixture under thermal or ultrasonic conditions. Therefore, we investigated methoxyethoxymethyl ether (ROMEM) and methoxymethyl ether (ROMOM) with $CBr_4$/MeOH or $CBr_4$/$CH_3CN/H_2O$ reaction system using thermal or ultrasound as energy source (Scheme 2). We first investigated the deprotection of decyl MEM-ether and decyl MOM-ether with a catalytic amount of $CBr_4$ (0.05–0.1 equiv.) in $CH_3CN/H_2O$ reaction mixture under refluxing condition. The better result was achieved when 0.1 equiv. of $CBr_4$ was introduced and the reaction mixture was refluxed after a prolonged reaction time. The MEM-ether was hydrolyzed completely after 16 h and a 97% yield was obtained, whereas MOM-ether was hydrolyzed incompletely. Interestingly, we observed that sonochemical reaction condition[15] cannot hydrolyze MEM- and MOM-ethers in $CH_3CN/H_2O$ solvent system even when a higher amount of $CBr_4$ (0.2 equiv.) was introduced. We also investigated the deprotection of ROMEM and ROMOM with $CBr_4$ in MeOH reaction system under thermal reaction condition.




**Scheme 1.**

*Keywords*: MEM-esters; MOM-ethers; deprotection.

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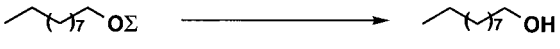
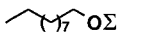
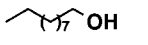
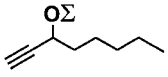
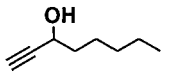
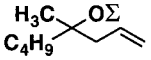
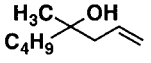
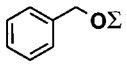
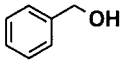
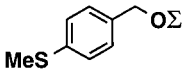
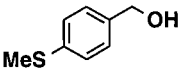
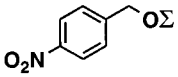
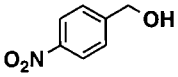
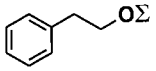
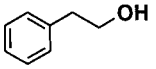
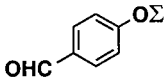
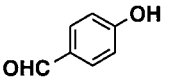
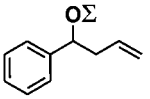
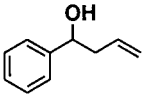
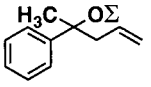
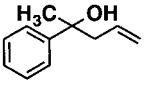


| | Σ = MOM | Σ = MEM |
|---|---|---|
| * $CBr_4/CH_3CN/H_2O$ (5%/2mL/1mL), reflux | N.R. (9h) | N.R. (22h) |
| * $CBr_4/CH_3CN/H_2O$ (10%/2mL/1mL), reflux | 8%+88%S.M. (7h) | 52% (4h)<br>92% (9h) |
| * $CBr_4/CH_3CN/H_2O$ (10%/1mL/2mL), reflux | 48%+34%S.M. (16h) | 97% (16h) |
| * $CBr_4/CH_3CN/H_2O$ (20%/1mL/2mL), ))) | N.R. (4h) | N.R. (4h) |
| * $CBr_4$ / MeOH (10%/5 mL), reflux | 94% (3h) | 90% (2h) |
| * $CBr_4$ / MeOH (15%/5 mL), reflux | 94% (2.5h) | 90% (1.5h) |
| * $CBr_4$ / *i*PrOH (10%/5 mL), reflux | 94% (2h) | 98% (1.5h) |
| * $CBr_4$ / *i*PrOH (15%/5 mL), reflux | 94% (2h) | 98% (1.5h) |

**Scheme 2.**

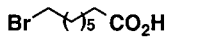
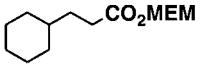
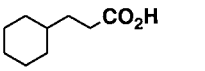
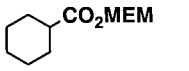
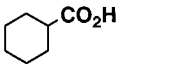
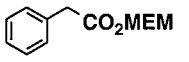
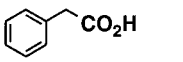
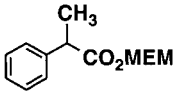
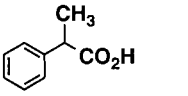
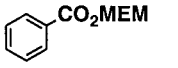
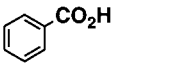
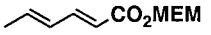
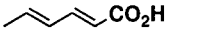
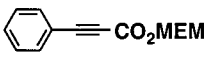
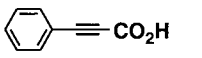
A mixture of decyl methoxyethoxymethyl ether (or decyl methoxymethyl ether), $CBr_4$ (0.1 equiv.) and $CH_3OH$ (5 mL) was refluxed for 3 h, and a 90% yield and a 94% yield of 1-decanol was produced individually. The results showed that the hydrolysis in $CH_3OH$ proceeded more efficiently and a higher yield was obtained. The higher amount of $CBr_4$ accelerated the hydrolysis but the equal yield of alcohol was afforded. A catalytic amount (10%) of $CBr_4$ is adequate enough for the deprotection reaction. Interestingly, we observed that the hydrolysis was faster, cleaner and more complete when *i*PrOH was used instead of MeOH. Therefore, a series of MEM- and MOM-ethers were investigated with $CBr_4$/*i*PrOH (10%/5 mL) reaction system under refluxing reaction condition. These MEM- and MOM-protected ethers were hydrolyzed to their corresponding alcohols and the results are shown in Table 1.

**Table 1.** Hydrolysis of MEM- and MOM-ethers

| Entry | Substrate | Product | Σ | Time (h) | Yield[a] |
|---|---|---|---|---|---|
| 1 |  |  | MOM<br>MEM | 2<br>1.5 | 94%<br>98% |
| 2 |  |  | MOM<br>MEM | 2<br>1.5 | 97%<br>97% |
| 3 |  |  | MEM | 1 | 90% |
| 4 |  |  | MOM<br>MEM | 0.7<br>1.5 | 91%<br>96% |
| 5 |  |  | MOM<br>MEM | 3<br>3 | 85%(14%)[b]<br>85%(11%)[b] |
| 6 |  |  | MOM<br>MEM | 2.5<br>3.5 | 87%<br>88% |
| 7 |  |  | MOM<br>MEM | 0.7<br>1.5 | 88%<br>93% |
| 8 |  |  | MOM<br>MEM | 1.5<br>1.5 | 97%<br>95% |
| 9 |  |  | MOM<br>MEM | 2<br>1.5 | 92%<br>97% |
| 10 |  |  | MEM | 3 | 85% |

[a] The yields were determined after chromatographic purification.
[b] The yield of isopropyl ether.

**Table 2.** Hydrolysis of MEM-esters

| Entry | Substrate | Product | Time (h) | Yield[a] |
|---|---|---|---|---|
| 1 |  |  | 1.5 | 95% |
| 2 |  |  | 1.5 | 92% |
| 3 |  |  | 1.5 | 96% |
| 4 |  |  | 2 | 93% |
| 5 |  |  | 1.5 | 92% |
| 6 |  |  | 2 | 95% |
| 7 |  |  | 2 | 93% |
| 8 |  |  | 1.5 | 91% |

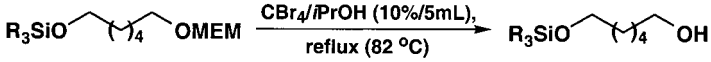
[a] The yields were determined after chromatographic purification.

Primary, secondary and tertiary MEM- and MOM-ethers (Table 1) were deprotected to their corresponding alcohols with high yields under the reaction conditions. Benzyl and phenolic MEM-ethers were deprotected to their corresponding benzyl alcohol and phenol with high yields. 4-(Methylthio)-benzyl-methoxyethoxymethyl and 4-(methylthio)-benzyl-methoxymethyl ethers (Table 1, entry 5) were converted partially into isopropyl ethers. Our observations showed that the isomerization was not occurred under this type of acidic hydrolyzing condition (Table 1, entries 3, 9, 10).

Transformation of carboxylic acid into MEM-ester ($RCO_2MEM$) is a commonly used protective method. A Beilstein on-line search suggests that there are more than a hundred MEM-protected acids and their derivatives were synthesized as intermediate material or potential therapeutic medicine in the literature. MEM-esters are usually hydrolyzed by HCl,[22,23] or hydrolyzed by Lewis acids such as $MgBr_2$,[24,25] and $ZnBr_2$.[26] Therefore, we investigated this deprotecting reaction condition for the deprotection of MEM-esters. A series of MEM-esters were prepared and were hydrolyzed under the reaction condition. These results are shown in Table 2.

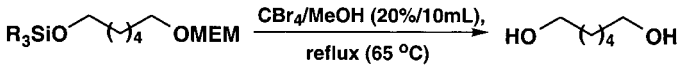
Primary and secondary alkyl-, aryl-substituted, $sp^2$- and sp-tethered MEM-esters (Table 2) were deprotected to their corresponding carboxylic acids with high yields without acidic quenching under the reaction conditions.

A simple and selective deprotection method for multifunctionalized molecule is valuable in organic synthesis. Our previous studies showed that the desilylation of trialkylsilyl ethers can be achieved with $CBr_4$/MeOH reaction mixture under refluxing condition.[17] The results showed that the desilylating reaction becomes much slower when the methanol is replaced with more steric hindered alcohol such as isopropanol. Therefore, 1-methoxyethoxymethoxyl-6-trialkylsilyloxylhexanes were synthesized and investigated under the reaction condition. 1-*tert*-Butyldiphenylsilyloxyl-6-methoxyethoxymethoxylhexane or 1-methoxyethoxymethoxyl-6-triisopropyisilyloxylhexane was refluxed under $CBr_4$/*i*PrOH reaction mixture and a 94% yield and a 92% yield of selective MEM-deprotected product 6-trialkylsilyloxylhexan-1-ol was obtained (Scheme 3). 1-*tert*-Butyldimethylsilyloxyl-6-methoxyethoxymethoxylhexane was investigated under the reaction condition and a 86% yield of bis-deprotected diol and a low yield (10%) of chemoselective deprotected product was afforded individually. *tert*-Butyldimethylsilyloxy and methoxyethoxymethoxy functionalities were hydrolyzed under the reaction condition, whereas triisopropylsilyloxy and *tert*-butyldiphenylsiloxy functionalities were stable under the reaction condition. *tert*-Butyldimethylsilyloxyl,




| $R_3Si$ | Time | Yield |
|---|---|---|
| *t*BuMe$_2$Si | 3h | 10% (86% Diol) |
| *i*Pr$_3$Si | 6h | 92% |
| *t*BuPh$_2$Si | 7h | 94% |

**Scheme 3.**




| $R_3Si$ | Time | Yield |
|---|---|---|
| $t$BuMe$_2$Si | 3h | 90% |
| $i$Pr$_3$Si | 9h | 80% |
| $t$BuPh$_2$Si | 10h | 72% |

**Scheme 4.**

triisopropylsilyloxyl, *tert*-butyldiphenylsiloxyl and methoxyethoxymethoxyl groups were hydrolyzed to their corresponding hydroxyl groups when MeOH was used instead of *i*PrOH (Scheme 4). A mixture of 1-*tert*-butyldimethylsilyloxyl-6-methoxyethoxymethoxylhexane and $CBr_4$/MeOH was refluxed for 3 h and a 90% yield of 1,6-dihydroxylhexane was obtained.

In conclusion, this reaction condition provides an efficient deprotection method for MEM- and MOM-ethers and MEM-esters. This method enables the chemoselective deprotection between trialkylsiloxyl group and methoxyethoxymethoxyl group that is manipulated by the used solvent bulkness.

## 3. Experimental

### 3.1. General

The $^1$H NMR (proton nuclear magnetic resonance) spectra were recorded at 300 MHz (Bruker-AC300P) with deuteriochloroform ($CDCl_3$, Aldrich 99.8 at.% D) as the solvent and the internal standard. The $^{13}$C NMR (carbon nuclear magnetic resonance) spectra were recorded at 75.5 MHz (Bruker-AC300P) with $CDCl_3$ as the solvent and the internal standard. Chemical shifts are reported in parts per million and resonance patterns are reported with the notations of either s (singlet), d (doublet), t (triplet), q (quartet), or m (multiplet). Coupling constants (*J*) are reported in hertz (Hz). All experiments were carried out under a nitrogen atmosphere which was dried primarily by passing through a column of sodium hydroxide (NaOH) layered with calcium sulfate ($CaSO_4$). Methanol and isopropanol were distilled from magnesium turning and recirculated prior to use. Hexane and ethyl acetate were distilled from calcium hydride. Thin-layer chromatography (TLC) analysis was performed on a plastic plate (or aluminum sheet) precoated with silica gel (Merck, 5554 Silica gel 60$F_{254}$). Visualization was accomplished by UV light or developed by spraying with a 10% phosphomolybdic acid ethanol solution. Column chromatography was performed using silica gel (Merck 230–400 mesh) and ethyl acetate/hexane mixture as the eluent. All the alcohols and carboxylic acids (Tables 1 and 2) were purchased from Aldrich, Merck and Riedel-deHaen and all were used directly without further purification. The MEM-, MOM-ethers and MEM-esters in Tables 1 and 2 were synthesized by the previously reported methods.[7,14,27,28] Hydrolysis of these ethers and esters were investigated under the typical procedure shown below and the yields were the isolated yields after chromatography.

### 3.2. Typical procedure for the MEM- and MOM-ethers hydrolysis reaction

A solution of MEM- or MOM-ether (1.0 mmol), $CBr_4$ (0.1 mmol) in anhydrous *i*PrOH (5 mL) was refluxed at 82°C. After the reaction was completed (monitored by TLC), the solution was cooled to room temperature and the organic solvent was directly removed under reduced pressure. Further purification was achieved on a flash chromatograph with silica gel and ethyl acetate/hexane.

### 3.3. Typical procedure for the MEM-ester hydrolysis reaction

A solution of MEM-ester (1.0 mmol), $CBr_4$ (0.1 mmol) in anhydrous *i*PrOH (5 mL) was refluxed at 82°C. After the reaction was completed (monitored by TLC), the solution was cooled to room temperature and the organic solvent was directly removed under reduced pressure. Further purification was achieved on a flash chromatograph with silica gel and ethyl acetate/hexane.

**3.3.1. Decyl methoxymethyl ether (Table 1, entry 1).** $^1$H NMR: $\delta$ 0.88 (3H, t, $J$=6.7 Hz), 1.12–1.41 (12H, m), 1.51–1.64 (4H, m), 3.36 (3H, s), 3.51 (2H, t, $J$=6.6 Hz), 4.62 (2H, s). $^{13}$C NMR: $\delta$ 14.0, 22.6, 26.2, 29.3, 29.4, 29.5, 29.6, 29.7, 32.0, 55.0, 67.8, 96.3.

**3.3.2. Decyl methoxyethoxymethyl ether (Table 1, entry 1).** $^1$H NMR: $\delta$ 0.87 (3H, t; $J$=6.7 Hz), 1.19–1.39 (12H, m), 1.50–1.64 (4H, m), 3.39 (3H, s), 3.51–3.57 (4H, m), 3.70 (2H, m), 4.71 (2H, s). $^{13}$C NMR: $\delta$ 14.0, 22.5, 26.1, 29.2, 29.3, 29.4, 29.6, 30.6, 31.8, 58.9, 66.5, 67.9, 71.7, 95.3.

**3.3.3. 1-Octyn-2-methoxymethyl ether (Table 1, entry 2).** $^1$H NMR: $\delta$ 0.90 (3H, t, $J$=6.8 Hz), 1.24–1.140 (4H, m), 1.41–1.59 (2H, m), 1.68–1.80 (2H, m),2.40 (1H, d, $J$= 2 Hz), 3.38 (3H, s), 4.31 (1H, td, $J$=6.8, 2.1 Hz), 4.59 (1H, d, $J$=6.9 Hz), 4.9 (1H, d, $J$=6.9 Hz). $^{13}$C NMR: $\delta$ 14.0, 22.5, 24.9, 31.5, 35.6, 55.6, 65.5, 73.3; 82.7, 94.2.

**3.3.4. 1-Octyn-2-methoxyethoxymethyl ether (Table 1, entry 2).** $^1$H NMR: $\delta$ 0.84 (3H, t, $J$=6.8 Hz), 1.25–1.39 (4H, m), 1.40–1.52 (2H, m), 1.65–1.78 (2H, m), 2.38 (1H, d, $J$=2.1 Hz), 3.38 (3H, s), 3.51–3.59 (2H, m), 3.65 (1H, m), 3.77 (1H, m), 4.35 (1H, td, $J$=6.8, 2.1 Hz), 4.70 (1H, d $J$=7.0 Hz), 5.99 (1H, d, $J$=7.0 Hz). $^{13}$C NMR: $\delta$ 13.9, 22.4, 24.7, 31.3, 35.4, 58.9, 65.5, 67.1, 71.6, 73.4, 82.6, 93.1.

**3.3.5. Benzyl-methoxymethyl ether (Table 1, entry 4).** $^1$H NMR: $\delta$ 3.42 (3H, s), 4.61 (2H, s), 4,72 (2H, s), 7.28-7.40

(5H, m). $^{13}$C NMR: δ 55.3, 69.2, 95.7, 127,7, 128.0, 128.4, 137.8.

**3.3.6. Benzyl-methoxyethoxymethyl ether (Table 1, entry 4).** $^{1}$H NMR: δ 3.40 (3H, s), 3.57 (2H, m), 3.74 (2H, m), 4.63 (2H, s), 4.81 (2H, s), 7.25–7.40 (5H, m). $^{13}$C NMR: δ 58.9, 66.9, 69.3, 71.7, 94.8, 127.6, 127.8, 128.3, 137.9.

**3.3.7. 4-(Methylthio)-benzyl-methoxymethyl ether (Table 1, entry 5).** $^{1}$H NMR: δ 2.48 (3H, s), 3.41 (3H, s), 4.56 (2H, m), 4.70 (2H, s) 7.25–7.32 (4H, m). $^{13}$C NMR: δ 16.0, 55.3, 68.7, 95.6, 126.8, 129.5, 134.8, 137.9.

**3.3.8. 4-(Methylthio)-benzyl-methoxyethoxymethyl ether (Table 1, entry 5).** $^{1}$H NMR: δ 2.43 (3H, s), 3.37 (3H, s), 3.53 (2H, m), 3.69 (2H, m), 4.54 (2H, s), 4.75 (2H, s), 7.16–7.28 (4H, m). $^{13}$C NMR: δ 15.7, 58.7, 66.7, 68.6, 71.6, 94.5, 126.4, 128.3, 134.6, 137.6.

**3.3.9. 4-Nitro-benzyl-methoxymethyl ether (Table 1, entry 6).** $^{1}$H NMR: δ 3.41 (3H, s), 4.70 (2H, s), 47.4 (2H, s), 7.53 (2H, d, *J*=8.5 Hz), 8.20 (2H, d, *J*=8.5 Hz). $^{13}$C NMR: δ 55.6, 68.0, 96.1, 123.6, 127.8, 145.6, 147.8.

**3.3.10. 4-Nitro-benzyl-methoxyethoxymethyl ether (Table 1, entry 6).** $^{1}$H NMR: δ 3.37 (3H, s), 3.56 (2H, m), 4.71 (2H, s), 4.82 (2H, s), 7.50 (2H, d, *J*=8.6 Hz), 8.18 (2H, d, *J*= 8.6 Hz). $^{13}$C NMR: δ 59.0, 67.1, 68.0, 71.6, 95.1, 123.5, 127.8, 145.6, 147.7.

**3.3.11. Phenethyl-methoxymethyl ether (Table 1, entry 7).** $^{1}$H NMR: δ 2.92 (2H, t, *J*=7.0 Hz), 3.30 (3H, s), 3.78 (2H, t, *J*=7.0 Hz), 4.62 (2H, s), 7.18–7.32 (5H, m). $^{13}$C NMR: δ 36.3, 55.1, 68.4, 96.4, 126.2, 128.3, 128.8, 138.9.

**3.3.12. Phenethyl-methoxyethoxymethyl ether (Table 1, entry 7).** $^{1}$H NMR: δ 2.90 (2H, t, *J*=7.0 Hz), 3.37 (3H, s), 3.50 (2H, m), 3.60 (2H, m), 3.80 (2H, t, *J*=7.0 Hz), 4.71 (2H, s) 7.16–7.32 (5H, m). $^{13}$C NMR: δ 36.1, 58.8, 66.5, 68.3, 71.6, 95.2, 126.0, 128.2, 128.7, 138.8.

**3.3.13. 4-methoxymethoxyl benzaldehyde (Table 1, entry 8).** $^{1}$H NMR: δ 3.50 (3H, s), 5.25 (2H, s), 7.16 (2H, m), 4.62 (2H,s) 7.83 (2H, m), 9.90(1H, s). $^{13}$C NMR: δ 56.3, 94.1, 116.3, 130.8, 131.8, 162.2, 190.8.

**3.3.14. 4-methoxyethoxymethoxyl benzaldehyde (Table 1, entry 8).** $^{1}$H NMR: δ 3.49 (3H, s, 3.63 (2H, t, *J*= 11.4 Hz), 3.94 (2H, t, *J*=11.4 Hz), 5.25 (2H, s), 7.13 (2H, m), 7.84 (2H, m), 9.90 (1H, s). $^{13}$C NMR δ 56.3, 69.1, 93.1, 94.1, 116.3, 131.0, 132.0, 162.0, 190.8.

**3.3.15. 1-Phenyl-2-(methoxy)methoxyl-4-pentene (Table 1, entry 9).** $^{1}$H NMR: δ 2.46 (1H, m), 2.59 (1H, m), 3.36 (3H, s), 4.54 (2H, s), 4.62 (1H, m), 5.01–5.14 (2H, m), 5.78 (1H, m), 7.23–7.38 (5H, m). $^{13}$C NMR: δ 42.3, 55.5, 77.7, 94.1, 117.1, 126.9, 127.6, 128.3, 134.7, 141.5.

**3.3.16. 1-Phenyl-2-(methoxyethoxy)methoxyl-4-pentene (Table 1, entry 9).** $^{1}$H NMR: δ 2.47 (1H, m), 2.58 (1H, m), 3.38 (3H, s), 3.55–3.61 (4H, m), 3.81 (1H, m), 4.58–4.72 (2H, m), 4.99–5.12 (2H, m), 5.74 (1H, m), 7.24–7.38 (5H, m). $^{13}$C NMR: δ 42.3, 59.0, 67.0, 71.7, 77.9, 93.2, 117.1, 127.0, 127.6, 128.3, 134.7, 141.5.

**3.3.17. 1-Phenyl-2-(methoxyethoxy)methoxyl-2-methyl-4-pentene (Table 1, entry 10).** $^{1}$H NMR: δ 1.59 (3H, s), 2.52 (1H, m), 2.68 (1H, m),3.37 (3H, s), 3.50–3.58 (2H, m), 3.68 (1H, m), 3.82 (1H, m), 4.69 (1H, d, *J*=11.0 Hz), 5.00 (1H, m), 5.08–5.19 (2H, m), 5.63 (1H, m), 7.20–7.48 (5H, m). $^{13}$C NMR: δ 24.0, 29.8, 48.3, 67.0, 71.7, 73.5, 119.3, 124.6, 126.0, 126.5, 128.0, 133.5, 147.5.

**3.3.18. Bromooctanoic-methoxyethoxymethyl ester (Table 2, entry 1).** $^{1}$H NMR: δ 1.29–1.46 (6H, m), 1.54–1.71 (4H, m), 1.81–1.91 (2H, m), 2.34 (2H, t, *J*=7.5 Hz), 3.39 (3H, s), 3.40 (2H, t, *J*=6.8 Hz), 3.57 (2H, m), 3.77 (2H, m), 5.32 (2H, s). $^{13}$C NMR: δ 26.1, 26.4, 30.8, 31.8, 32.0, 32.9, 37.1, 59.0, 69.3, 71.4, 89.1, 173.5.

**3.3.19. Cyclohexanylpropinic-methoxyethoxymethyl ester (Table 2, entry 2).** $^{1}$H NMR: δ 0.82–0.95 (2H, m), 1.08–1.30 (4H, m), 1.50–1.60 (3H, m), 1.52–1.76 (4H, m), 2.35 (2H, t, *J*=7.8 Hz), 3.39 (3H, s), 3.56 (2H, m), 3.76 (2H, m), 5.32 (2H, s). $^{13}$C NMR: δ 24.5, 27.8, 28.3, 28.7, 32.6, 34.1, 58.9, 69.3, 71.4, 89.1, 173.1.

**3.3.20. Cyclohexane carboxylic-methoxyethoxymethyl ester (Table 2, entry 3).** $^{1}$H NMR. δ l.20–1.38 (2H, m), 1.40–1.56 (2H, m, 1.65 (1H, m), 1.71–1.82 (2H, m), 1.88–1.98 (2H, m), 2.33 (1H, m), 3.38 (3H, s), 3.55 (2H, m), 3.77 (2H, m), 5.32 (2H, s). $^{13}$C NMR: δ 25.3, 25.6, 28.8, 43.1, 59,0, 69.2, 71.4, 89.0, 175.4.

**3.3.21. Phenylacetic-methoxyethoxymethyl ester (Table 2, entry 4).** $^{1}$H NMR: δ 3.36 (3H, s), 3.51 (2H, m), 3.66 (2H, s), 3.71 (2H, m), 5.33 (2H, s), 7.22–7.38 (5H, m). $^{13}$C NMR: δ 41.3, 58.8, 69.3, 71.3, 89.5, 127.0, 128.4, 129.1, 133.5, 171.0.

**3.3.22. (*dl*)-2-Phenylpropionic-methoxyethoxymethyl ester (Table 2, entry 5).** $^{1}$H NMR: δ 1.51 (3H, d, *J*=7.2 Hz), 3.33 (3H, s), 3.45 (2H, m), 3.63 (2H, m), 3.74 (1H, q, *J*=7.2 Hz), 5.31 (2H, m), 7.20–7.42 (5H, m). $^{13}$C NMR: δ 18.2, 45.6, 59.0, 69.2, 71.3, 89.4, 127.1, 127.S, 128.6, 140.2, 174.0.

**3.3.23. Benzoic-methoxyethoxymethyl ester (Table 2, entry 6).** $^{1}$H NMR: δ 3.39 (3H, s), 3.60 (2H, m), 3.87 (2H, m), 5.59 (2H, s), 7.45 (2H, m), 7.59 (1H, m), 8.08 (2H, m). $^{13}$C NMR: 8 59.0, 69.6, 71.(5, 90.0, 128.3, 130.0, 133.2, 166.0).

**3.3.24. 2,4-Hexadienoic-methoxyethoxymethyl ester (Table 2, entry 7).** $^{1}$H NMR. δ 1.81 (3H, d, *J*=5.3 Hz), 3.33 (3H, s), 3.52 (2H, m), 3.75 (2H, m), 5.35 (2H, s), 5.70 (1H, d, *J*=5.3 Hz), 6.10–6.25 (2H, m), 7.24 (1H, m). $^{13}$C NMR: δ 18.5, 59.0, 69.3, 71.4, 89.1, 118.3, 130.0, 140.0, 146.0, 166.4.

**3.3.25. Phenylpropiolic-methoxyethoxymethyl ester (Table 2, entry 8).** $^{1}$H NMR: δ 3.41 (3H, s), 3.60 (2H, m), 3.87 (2H, m), 5.47 (2H, s), 7.36 (2H, m), 7.45 (1H, m), 7.59 (2H, m). $^{13}$C NMR: δ 59.0, 60.2, 69.8, 71.3, 80.2, 90.5, 119.3, 128.5, 130.7, 133.0, 153.3.

**3.3.26. 1-*tert*-Butyldimethylsillyloxy-6-methoxyethoxy-methoxyl-hexane (Scheme 3).** $^{1}$H NMR: δ 0.42 (6H, s), 0.90 (9H, s), 1.32–1.39 (4H, m), 1.48–1.66 (4H, m), 3.40

(3H, s), 3.50–3.64 (6H, m), 3.66–3.72 (2H, m), 4.71 (2H, s). $^{13}$C NMR: $\delta$ 18.4, 25.7, 26.0, 29.7, 32.8, 59.0, 63.2, 66.7, 67.9, 71.8, 95.5.

**3.3.27. 1-Triisopropylsilyloxy-6-methoxyethoxymethoxyl-hexane (Scheme 3).** $^1$H NMR: $\delta$ 0.96–1.20 (21H, m), 1.25–1.42 (4H, m), 1.48–1.68 (4H, m), 3.40 (3H, s), 3.50–3.591 (4H, m), 3.62–3.72 (4H, m), 4.71 (2H, s). $^{13}$C NMR 5 12.1, 17.7, 18.0, 25.7, 26.1, 29.7, 33.0, 59.0, 63.4, 66.7, 67.9, 71.8, 95.5.

**3.3.28. 1-*tert*-Butyldiphenylsilyloxy-6-methoxyethoxy-methoxyl-hexane (Scheme 3).** $^1$H NMR: $\delta$ 1.04 (9H, s), 1.02–1.09 (2H, m), 1.32–1.39 (2H, m), 1.52–1.62 (4H, m), 3.39 (3H, s), 3.48–3.59 (4H, m), 3.61–3.72 (4H, m), 4.71 (2H, s), 7.33–7.44 (6H, m), 7.62–7.70 (4H, m). $^{13}$C NMR: $\delta$ 19.2, 25.6, 26.0, 26.9, 29.7, 32.5, 59.0, 63.9, 66.7, 67.9, 71.8, 95.5, 127.6, 129.5, 134.2, 135.6.

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