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Nucleophilic Deprotection of *p*-Methoxybenzyl Ethers Using Heterogeneous Oxovanadium Catalyst

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Nucleophilic deprotection of *p*-methoxybenzyl (PMB) [*p*-methoxyphenylmethyl (MPM)] ethers was developed using a heterogeneous oxovanadium catalyst V-MPS4 and a thiol nucleophile. The deprotection method had a wide reaction scope, including PMB ethers of primary, secondary, and tertiary alcohols bearing various functional groups. In addition, the PMB ether of an oxidation-labile natural product was successfully removed by V-MPS4 catalysis, while a common oxidative method of PMB deprotection afforded a complex mixture. The V-MPS4 catalyst was reusable up to six times without a significant loss in the product yield. The advantages of using the heterogeneous catalyst were further demonstrated by conducting the deprotection reaction in a continuous flow process, which resulted in a 2.7-fold higher catalyst turnover number and 60-fold higher turnover frequency compared to those of the corresponding batch reaction.

Key words heterogeneous catalysis, mesoporous silica, oxovanadium catalyst, *p*-methoxybenzyl ether, *p*-methoxyphenylmethyl ether, flow reaction

Introduction

Heterogeneous catalysis has inherent advantages in chemical transformations because of the ease of catalyst separation and reuse as well as its applicability to continuous flow processes.[1] Extensive application of heterogeneous catalysts in synthetic organic chemistry can contribute to resource conservation and reduce waste production, rendering the synthetic process more sustainable and economical. We previously developed a highly active heterogeneous oxovanadium catalyst, V-MPS4, in which the oxovanadium species were covalently bound to the inner surface of mesoporous silica with a 4-nm diameter[2,3] (Fig. 1a). V-MPS4 catalyzed the reversible C–O bond heterolysis of alcohols to mediate racemization, and this was combined with a lipase-catalyzed acylative kinetic resolution to realize dynamic kinetic resolution[4] (Fig. 1b). More recently, V-MPS4 was found to catalyze the direct nucleophilic substitution of alcohols with various nucleophiles *via* C–O bond cleavage[5] (Fig. 1c). During the course of our continuous research on V-MPS4 catalysis,[6–10] we realized that V-MPS4 could also catalyze the C–O bond cleavage of reactive ethers such as *p*-methoxybenzyl (PMB) [also known as *p*-methoxyphenylmethyl (MPM)] ethers. Based on this finding, we report herein the V-MPS4-catalyzed nucleophilic deprotection of PMB ethers to furnish alcohols (Fig. 1d). We also demonstrate the advantages of this heterogeneous V-MPS4 catalyst in a continuous flow process.

PMB ethers are protecting group and have been widely used to mask alcohols in multistep synthesis.[11] Typically, PMB ethers are deprotected using stoichiometric oxidants such as 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ)[12] and ceric ammonium nitrate (CAN).[13] Catalytic oxidative deprotection methods have been also reported, using inexpensive terminal oxidants.[14–18] Recently, other methods like photoredox catalysis,[19–21] electrochemical oxidation,[22,23] and Brønsted acid catalysis[24,25] have been developed for PMB deprotection. Lewis acid catalysis has been also widely explored for PMB deprotection in the presence[26–28] or absence[29,30] of nucleophiles. While these methods mainly use homogeneous catalysts, reports on PMB deprotection by heterogeneous catalysis are limited,[31] despite its significance amidst the growing demand of sustainable manufacturing of fine chemicals such as pharmaceutically relevant compounds.[32]

Results and Discussion

Initially, the reaction conditions were screened using PMB ether **1a** (Table 1). The reaction was conducted using 4 mol% of V-MPS4 in 1,2-dichloroethane at 80 °C for 24 h. Deprotection of the PMB group proceeded without a nucleophile (Nu-H) to afford the corresponding alcohol **2a** (45%), along with the recovery of **1a** (37%) (Entry 1). The PMB group was probably removed *via* the nucleophilic attack by a methoxyphenyl group in another molecule of **1a**, as shown in a previous study.[29] Further, external nucleophiles were screened to improve the yield of **2a** (Entries 2–7). While C and N nucleophiles such as 1,3,5-trimethoxybenzene (**4**) and 4-methylaniline (**5**) were not effective (Entries 2 and 3), the yield of **2a** increased dramatically in the presence of S nucleophiles (Entries 4–7). In particular, 4-*tert*-butylbenzenethiol (**8**) and 4-methoxybenzenethiol (**9**) gave the best results, affording **2a** in 90 and 92% NMR yields, respectively; however, a small amount of **1a** (less than 5%) still remained in both cases (Entries 6 and 7). Using 2 eq. of **9**, complete conversion of **1a**, along with 82% isolate yield of **2a**, was achieved (Entry 8). The yield decreased significantly at a lower temperature (Entry 9). The use of other halogenated and aromatic solvents afforded **2a** in moderate yields (Entries 10–12), while the yield decreased significantly when MeCN was used (Entry 13). Thus, 1,2-dichloroethane was chosen as the optimal solvent. Although the reaction proceeded to some extent in the absence of the V-MPS4 catalyst, the catalyst exhibited a prominent effect in accelerating the reaction as a Lewis acid (Entry 14 *vs.* 8).

With the optimal reaction conditions (Table 1, Entry 8) in hand, we next investigated the substrate scope and limita-

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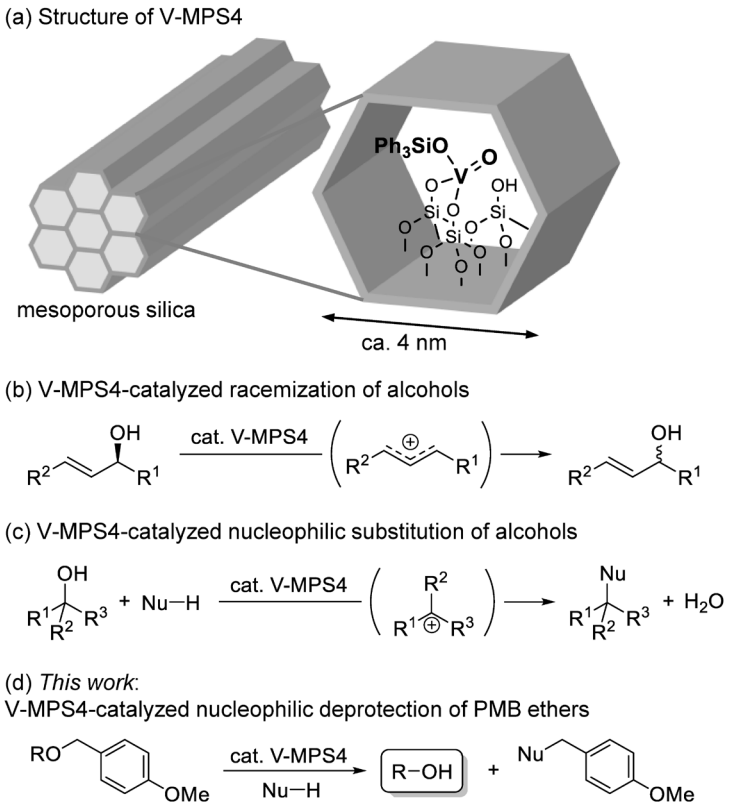
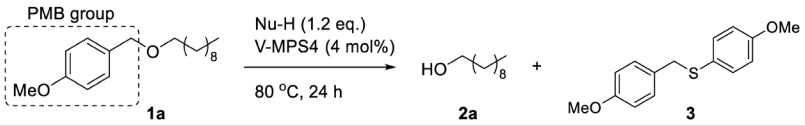


Fig. 1. V-MPS4-Catalyzed Reactions and the General Concept of This Work

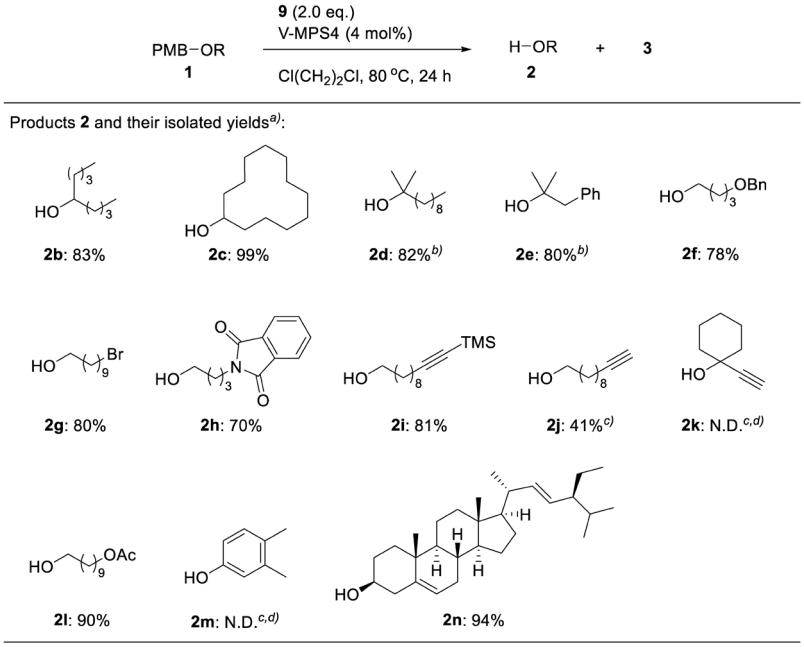
Table 1. Screening of Reaction Conditions for the V-MPS4-Catalyzed Deprotection of PMB Ether **1a**[a)]



Entry	Nu-H	Solvent	Yield [%] of **2a**[b)]
1	—	$Cl(CH_2)_2Cl$	45
2	1,3,5-$(MeO)_3$-C_6H_3 (**4**)	$Cl(CH_2)_2Cl$	44
3	4-Me-$C_6H_4NH_2$ (**5**)	$Cl(CH_2)_2Cl$	<5
4	$^{n}C_{12}H_{25}SH$ (**6**)	$Cl(CH_2)_2Cl$	83
5	2,4,6-$^{i}Pr_3$-C_6H_2SH (**7**)	$Cl(CH_2)_2Cl$	78
6	4-^{t}Bu-C_6H_4SH (**8**)	$Cl(CH_2)_2Cl$	90
7	4-MeO-C_6H_4SH (**9**)	$Cl(CH_2)_2Cl$	92
8[c,d)]	**9**	$Cl(CH_2)_2Cl$	98 (82)
9[c,d,e)]	**9**	$Cl(CH_2)_2Cl$	37
10[c,f)]	**9**	$CHCl_3$	58
11[c)]	**9**	PhCl	61
12[c)]	**9**	toluene	74
13[c)]	**9**	MeCN	14
14[c,g)]	**9**	$Cl(CH_2)_2Cl$	43

a) Unless otherwise stated, the reaction was conducted with **1a** (0.10 mmol), Nu-H (1.2 equivalent (equiv.)), and V-MPS4 (4.0 mol%) in the indicated solvent (0.10 M) at 80 °C for 24 h. *b*) Yield was determined by ^{1}H-NMR analysis of the crude reaction mixture using CH_2Br_2 as an internal standard. Isolate yield is indicated in parentheses. *c*) **9** (2.0 equiv.) was used. *d*) Reaction was conducted at the 0.2 mmol-scale. *e*) Reaction was conducted at 60 °C. *f*) Reaction was conducted at 70 °C. *g*) The reaction was conducted without V-MPS4.

tion of the V-MPS4-catalyzed PMB deprotection (Chart 1). Secondary alcohols **2b** and **2c** were obtained from the corresponding PMB ethers under the standard conditions in 83 and 99% yields, respectively. Notably, the reactions of *α*-tertiary PMB ethers were much faster than those of *α*-primary and secondary PMB ethers and were complete within 3 h to afford tertiary alcohols **2d** and **2e** in 82 and 80% yields, respectively. The higher reaction rate of the *α*-tertiary PMB ethers can be rationalized by the lower nucleophilicity of the produced *tert*-alcohols **2**. The *α*-primary and secondary PMB ethers reacted not only with thiol **9** but also with **2** to decrease the net reaction rate, while *α*-tertiary PMB ethers did not react with **2** (Supplementary Chart S1). The functional group tolerance of the reaction was evaluated using PMB ethers bearing various



a) Unless otherwise stated, the reaction was conducted with **1** (0.10 mmol), **9** (2.0 equiv.), and V-MPS4 (4.0 mol%) in 1,2-dichloroethane (0.10 M) at 80 °C for 24 h. *b*) Reaction time was 3 h. *c*) Reaction was conducted using 0.20 mmol of **1**. *d*) N.D.: not detected.

Chart 1. Substrate Scope of the Reaction

functional groups. In the presence of a benzyl (Bn) ether, the PMB group was selectively deprotected, and **2f** was obtained in 78% yield. While the unreacted PMB ether **1f** was detected, no Bn-deprotected side products were detected in the ^{1}H-NMR spectrum of the crude product mixture, indicating the predominant deprotection of the PMB ether in the presence of the Bn group. A bromo group, which is prone to nucleophilic substitution, was tolerated under the reaction conditions and **2g** was obtained in 80% yield. The phthalimide group was also compatible with this reaction, and **2h** was obtained in 70% yield. The reaction of the PMB ether bearing an alkynylsilane moiety afforded the corresponding alcohol **2i** in 81% yield, with the alkynylsilane moiety remaining unaffected. On the other hand, the PMB ether with a terminal acetylene group underwent significant decomposition, resulting in a low yield of **2j**. The reaction of the PMB ether of a propargyl alcohol gave a complex mixture, and **2k** was not detected in the crude reaction mixture, probably because of the V-MPS4-catalyzed side reactions, such as the Meyer–Schuster rearrangement, of **2k**.[6] An ester moiety such as an acetoxy group was tolerated under the reaction conditions, and PMB-deprotected **2l** was obtained in 90% yield. Reaction of the phenolic PMB ether gave a complex mixture and did not afford alcohol **2m**, probably because nucleophilic side reactions occurred at the *ortho*-positions of the phenolic hydroxy group of the generated **2m**. A steroid structure, *i.e.*, the PMB ether of stigmasterol, was also tolerated under the reaction conditions, affording **2n** in high yield.

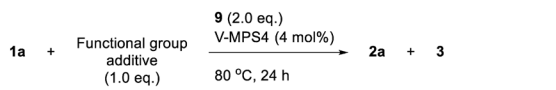
Many pharmaceutically relevant molecules contain nitrogen atoms and/or polar functional groups. Thus, we next evaluated the functional group tolerance of the developed reaction (Table 2). Thus, the reaction was conducted in the presence of a stoichiometric amount of additives bearing certain functional groups. The reactions of **1a** in the presence of aromatic nitro and cyano compounds and methanesulfonamide gave **2a** in high yields, and the additives were recovered quantitatively in all cases, suggesting that these functional groups were tolerated in this reaction (Entries 1–3). In contrast, carboxylic acid, amide, and carbamate inhibited the reaction (Entries 4–6).

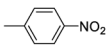
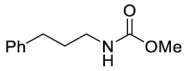
The functional group tolerance of the V-MPS4-catalyzed PMB deprotection was further examined by comparing its outcome with that of a common PMB deprotection method, *i.e.*, DDQ oxidation[12] (Table 3). The deprotection reaction of α-tocopherol PMB ether (±)-**1o** using V-MPS4 (4 mol%) afforded the corresponding alcohol **2o** in 80% yield (Entry 1), while the oxidative deprotection using a stoichiometric amount of DDQ gave a complex mixture (Entry 2). Thus, the V-MPS4-catalyzed nucleophilic PMB deprotection method is also suitable for oxidation-labile compounds.

The V-MPS4-catalyzed nucleophilic deprotection method was also applicable to some other common protective groups of alcohols, namely the tetrahydropyranyl (THP) and trityl (Tr) groups (Chart 2). In the presence of thiol **9**, the THP group in **10** was removed to give **2a** in 78% yield after 24 h, with the concomitant generation of *O*,*S*-acetal **11** [Eq. (1)]. Trityl ether **12** was also reactive under these deprotection conditions, and **2a** was obtained quantitatively along with sulfide **13** within 4 h [Eq. (2)]. Trapping the removed protective groups with the nucleophile was essential to achieve high yields since the reactions without **9** gave **2a** in low yields in both cases.

The catalytic performance of V-MPS4 was further investigated by comparing its behavior with that of other oxovanadium catalysts in the PMB deprotection reaction (Table 4). The catalyst precursor of V-MPS4, $VO(OSiPh_3)_3$,[3,5] showed a reasonably low conversion although it was homogeneously soluble in the solvent (Entry 1 *vs.* 2). The use of vanadyl sulfate hydrate ($VOSO_4 \cdot nH_2O$) afforded **2a** in 94% yield after 24 h, which is as high as that obtained using V-MPS4 (Entry 3). However, the reaction rate was higher with V-MPS4 than with $VOSO_4 \cdot nH_2O$, and the yield of **2a** using the former was twice

Table 2. V-MPS4-Catalyzed Deprotection of PMB Ether in the Presence of Functional Group Additives[a)]



Entry	Additive	Yield of **2a** [%][b)]	Recovered additive [%][b)]
1		94	>95
2	Ph–CN	>95	>95
3	Me–SO_2NH_2	94	>95
4		17	>95[c)]
5		14	>95[c)]
6		<5	>95[c)]

a) Unless otherwise stated, the reaction was conducted with **1a** (0.10 mmol), **9** (2.0 equiv.), the indicated additive (1.0 equiv.), and V-MPS4 (4.0 mol%) in 1,2-dichloroethane (0.10 M) at 80 °C for 24 h. *b*) Yield was determined by ^{1}H-NMR analysis of the crude reaction mixture using CH_2Br_2 as an internal standard. *c*) Reaction was conducted for 72 h.

Table 3. Deprotection of α-Tocopherol PMB Ether (±)-**1o**

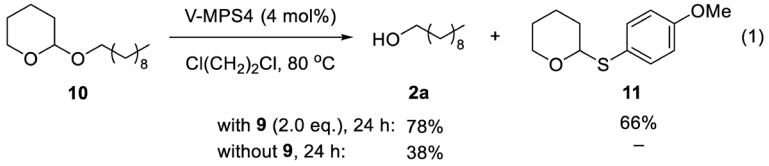
Entry	Conditions	Yield of **2o** [%][a)]
1	**9** (2.0 equiv.), V-MPS4 (4 mol%) $Cl(CH_2)_2Cl$ (0.1 M), 80 °C, 24 h	80
2	DDQ (1.2 equiv.) CH_2Cl_2-H_2O (18 : 1, 0.01 M), RT, 21 h	Decomposition

a) Isolated yield.

that obtained using $VOSO_4 \cdot nH_2O$ at the early stage of the reaction (Entry 1 *vs.* 3). The superior catalytic performance of V-MPS4 over $VOSO_4$ was further demonstrated in the deprotection of the PMB ether of **2l** (Supplementary Chart S2). The use of another vanadium (IV) species, V_2O_4, instead of the vanadium (V) species, decreased the yield of **2a** (Entry 4).

We next investigated the reusability of the V-MPS4 catalyst in the deprotection reaction of **1a** (Table 5). After 24 h of reaction, the reaction mixture was centrifuged, and the precipitated catalyst was used in the next reaction after washing and drying. The supernatant was collected to determine the yield of **2a** (detailed procedure is given in Section 4 of Supplement ary material). High yields were obtained for the first six runs. The V-MPS4 catalyst showed a turnover number (TON) of 1.3×10^2 and a turnover frequency (TOF) of 0.90 h^{-1} for all these runs (calculations of TON and TOF are provided in Supplementary materials). However, the yield decreased in the seventh run. To investigate the reason for the decreased catalytic efficiency, fresh V-MPS4 and V-MPS4 that was used eight times were observed by scanning electron microscopy (SEM), and their vanadium contents were analyzed by inductively coupled plasma-optical emission spectrometry (ICP-OES). The particle size distribution decreased from 10–60 μm for the fresh catalyst to less than 5 μm for the catalyst that was used eight times, and the vanadium content decreased from 0.25 to 0.12 mmol/g (Supplementary Fig. S1). Thus, the decrease in the catalytic efficiency by repeated use could be attributed to the gradual degradation of the catalyst particles and/or the decrease in the vanadium content due to leaching.

Finally, the present reaction was applied to a continuous flow process by packing V-MPS4 in a fixed-bed reactor[33)] (Fig. 2, Supplementary Fig. S2). We anticipated that the flow reaction would show a higher TON compared to the batch reaction, because the catalyst morphology would be maintained in a flow reaction, whereas the catalyst particles would be degraded by the vigorous stirring in a batch reaction. The reaction was conducted by flowing a solution of **1a** (0.1 M) and **9** (0.2 M) in 1,2-dichloroethane through the fixed-bed reactor, in which a homogeneous mixture of V-MPS4 and MPS4, the latter being a catalyst support for the immobilization of oxovanadium, was packed (V-MPS4/MPS4 = 1/5, 300 mg). A quantitative yield of **2a** was maintained over 7 h at 80 °C and a flow rate of 0.1 mL/min (residence time = 10 min, shaded cir-



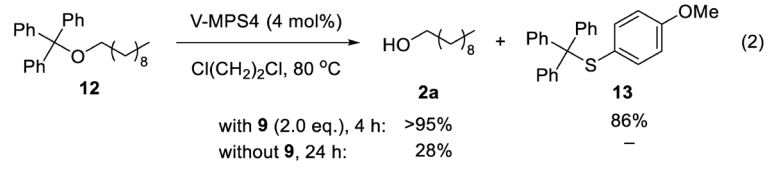


Chart 2. Removal of THP and Tr Groups Using V-MPS4 Catalyst

cles). Notably, no metal leaching was detected under this condition (Supplementary Fig. S3). The catalyst showed a TON of 3.5×10^2 and TOF of $54\,h^{-1}$, which are 2.7-fold and 60-fold higher than those obtained upon reusing the catalyst in a batch reaction (calculated based on 1–6 runs), respectively (calculations of TON and TOF are provided in Supplementary materials). The TOF further increased to $94\,h^{-1}$ upon increasing the flow rate to 0.2 mL/min (unshaded circles). The conversion decreased at a lower temperature (60 °C, triangle), similar to that observed in the batch reaction (Table 1, Entry 9). The use of MPS4 as a diluent was essential to achieve high conversions, since the conversion remained low in its absence (square).

Table 4. Comparison of Oxovanadium Catalysts in the Deprotection of **1a**[a)]

1a + **9** (2.0 eq) —catalyst (4 mol%), $Cl(CH_2)_2Cl$, 80 °C, 24 h→ **2a** + **3**

Entry	Catalyst	Yield of **2a** [%][b)]
1	V-MPS4	98 (52)[c)]
2	$VO(OSiPh_3)_3$	38
3	$VOSO_4 \cdot nH_2O$[d)]	94 (26)[c)]
4	V_2O_4	22

a) Unless otherwise stated, the reaction was conducted with **1a** (0.10 mmol), **9** (2.0 equiv.), and catalyst (4.0 mol%) in 1,2-dichloroethane (0.10 M) at 80 °C for 24 h. *b*) Yield was determined by ^{1}H-NMR analysis of the crude reaction mixture using CH_2Br_2 as an internal standard. *c*) Yield after a 3-h reaction is given in parentheses. *d*) Commercial reagent with $n = 3$–4.

Table 5. Reuse Test of the V-MPS4 Catalyst[a)]

1a + **9** (2.0 eq) —V-MPS4 (4 mol%), $Cl(CH_2)_2Cl$, 80 °C, 24 h→ **2a** + **3**

Run	1	2	3	4	5	6	7	8
Yield of **2a** [%][b)]	94	88	96	88	91	92	76	55

a) Each reaction was conducted with **1a** (0.10 mmol) and **9** (2.0 equiv.) in 1,2-dichloroethane (0.10 M) at 80 °C for 24 h. V-MPS4 (17 mg, 4.0 mol%) was used for the first run. After the reaction, the catalyst was recovered and reused for the next run. *b*) Yield was determined by ^{1}H-NMR analysis of the crude reaction mixture using CH_2Br_2 as an internal standard.

Conclusion

We developed a deprotection method of PMB ethers under mild and redox-neutral conditions. The reaction was catalyzed by a mesoporous silica-supported oxovanadium V-MPS4 catalyst in the presence of thiol nucleophiles. The product was obtained in high yield by using a small excess of thiol (Table 1, Entry 7), and full conversion was ensured by using two equivalents of the thiol (Table 1, Entry 8). The reaction exhibited a wide functional group tolerance and was applicable to PMB ethers of primary, secondary, and tertiary alcohols. The heterogeneous V-MPS4 catalyst could be reused up to six times without any significant decrease in the product yield and could also be applied to the continuous flow reaction. The TON and TOF in the flow reaction were significantly higher than those in the batch reaction, and no catalyst leaching was observed. The present flow deprotection method will contribute to the synthesis of alcohols bearing various functional groups at a productive scale. Investigations on the further applications of V-MPS4 catalysis in flow processes are currently underway in our laboratory.

Experimental

General procedure for the V-MPS4-catalyzed deprotection of the PMB group: 4-Methoxybenzenethiol (**9**) (25 μL, 0.20 mmol) was added to a mixture of PMB ether **1** (0.10 mmol), V-MPS4 (18.1 mg, 4.0 mol%), and anhydrous 1,2-dichloroethane (1.0 mL, 0.10 M) in a grass tube (φ8 × 50 mm). The glass tube was sealed with a plastic cap, and the resulting mixture was stirred at 80 °C for 24 h. After cooling to room temperature, the reaction mixture was filtered through a pad of Celite, and the filtrate was concentrated under reduced pressure. The crude residue was purified by silica gel flash chromatography (hexane/EtOAc) to give **2**. The ^{1}H- and ^{13}C-NMR spectra of alcohols **2a**, **2b**, **2c**, **2e**, **2j**, **2n**, and **2o** were identical to those of the commercial source.

*Calculation of the catalyst loading: The V-MPS4 used in this reaction contained 0.22 mmol of vanadium per gram of the catalyst (0.22 mmol/g, see the section 2 in Supplementary material for the detail). Thus, 18.1-mg portion of V-MPS4 contains 4.0 μmol of vanadium, which corresponds to 4.0 mol%

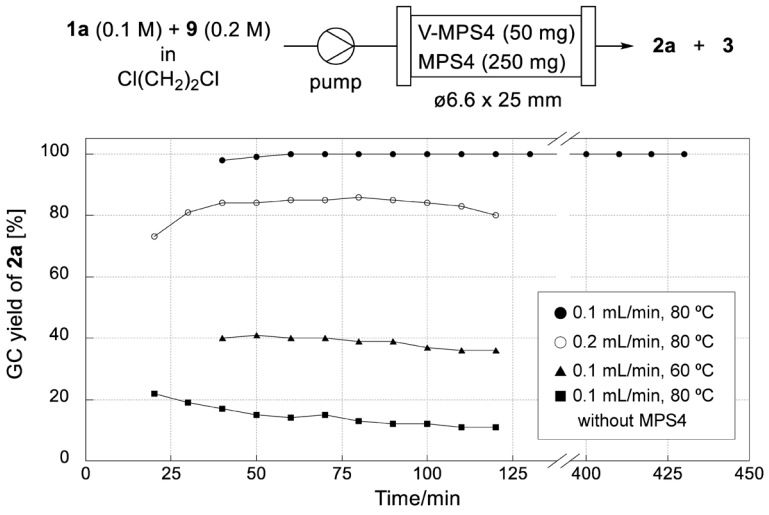


Fig. 2. Continuous Flow Reaction of the PMB Ether Deprotection Using a Fixed-Bed Reactor Containing V-MPS4; The Yield of 2a Was Determined by GC Analysis Using the Peak-Area Ratio

loading of vanadium atom to the reaction.

The NMR spectra of alcohols **2d**, **2f**, **2g**, **2h**, and **2l** were in good agreement with the reported spectra. Alcohol **2i** was fully characterized by ^{1}H- and ^{13}C-NMR spectroscopy, IR spectroscopy, and HRMS because its spectroscopic data are not reported in literature.

Decan-1-ol (2a) ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 3.64 (t, $J = 6.6$ Hz, 2H), 1.62–1.52 (m, 2H), 1.44 (s, 1H), 1.38–1.20 (m, 14H), 0.88 (t, $J = 7.2$ Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 63.1, 32.8, 31.9, 29.6, 29.5, 29.4, 29.3, 25.7, 22.7, 14.1.

Nonan-5-ol (2b) ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 3.60–3.56 (m, 1H), 1.47–1.27 (m, 13H), 0.90 (t, $J = 7.0$ Hz, 6H); ^{13}C-NMR (75 MHz, $CDCl_3$): 72.0, 37.2, 27.8, 22.8, 14.1.

Cyclododecanol (2c) ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 3.86–3.82 (m, 1H), 1.73–1.62 (m, 2H), 1.49–1.27 (m, 20H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 69.2, 32.5, 24.2, 23.8, 23.34, 23.25, 20.9.

2-Methylundecan-2-ol (2d)[34] ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.48–1.43 (m, 2H), 1.37–1.23 (m, 14H), 1.21 (s, 6H), 0.88 (t, $J = 6.9$ Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 71.1, 44.0, 31.9, 30.2, 29.64, 29.56, 29.3, 29.2, 24.4, 22.7, 14.1.

2-Methyl-1-phenylpropan-2-ol (2e) ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.34–7.20 (m, 5H), 2.77 (s, 2H), 1.23 (s, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 137.7, 130.4, 128.2, 126.5, 70.7, 49.7, 29.2.

4-(Benzyloxy)butan-1-ol (2f)[26] ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.38–7.27 (m, 5H), 4.52 (s, 2H), 3.65 (t, $J = 6.0$ Hz, 2H), 3.53 (t, $J = 5.8$ Hz, 2H), 1.76–1.64 (m, 4H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 138.1, 128.4, 127.71, 127.65, 73.1, 70.3, 62.7, 30.2, 26.7.

10-Bromodecan-1-ol (2g)[35] ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 3.63 (t, $J = 6.6$ Hz, 2H), 3.40 (t, $J = 6.9$ Hz, 2H), 1.87–1.82 (m, 2H), 1.59–1.53 (m, 2H), 1.43–1.39 (m, 2H), 1.36–1.29 (m, 11H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 63.0, 34.0, 32.88, 32.84, 29.4, 29.3 (2C), 28.7, 28.1, 25.7. Although only 9 out of 10 peaks were found in ^{13}C-NMR spectrum, the HRMS spectrum was consistent with the target molecular formula; HRMS (CI) *m/z* Calcd. for $C_{10}H_{22}BrO$ $[M + H]^+$: 237.0854, found: 237.0846.

2-(4-Hydroxybutyl)isoindoline-1,3-dione (2h)[36] ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.83 (dd, $J = 5.4$, 3.2 Hz, 2H), 7.70 (dd, $J = 5.4$, 3.2 Hz, 2H), 3.73 (t, $J = 7.2$ Hz, 2H), 3.68 (t, $J = 6.3$ Hz, 2H), 1.82–1.74 (m, 2H), 1.68 (br s, 1H), 1.66–1.57 (m, 2H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 168.5, 133.9 132.1, 123.2, 62.3, 37.7, 29.8, 25.1.

11-(Trimethylsilyl)undec-10-yn-1-ol (2i) IR (NaCl) 3368, 2929, 2856, 2175, 1249, 841; ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 3.64 (t, $J = 6.6$ Hz, 2H), 2.21 (t, $J = 7.2$ Hz, 2H), 1.61 (br s, 1H), 1.59–1.46 (m, 4H), 1.41–1.25 (m, 10H), 0.14 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 107.7, 84.3, 63.0, 32.8, 29.4, 29.3, 29.0, 28.7, 28.6, 25.7, 19.8, 0.2; HRMS (CI) *m/z* Calcd. for $C_{14}H_{29}OSi$ $[M + H]^+$: 241.1988. Found: 241.1986.

Undec-10-yn-1-ol (2j) ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 3.63 (t, $J = 6.6$ Hz, 2H), 2.18 (td, $J = 7.3$, 2.8 Hz, 2H), 1.94 (t, $J = 2.8$ Hz, 1H), 1.62–1.46 (m, 4H), 1.44–1.22 (m, 11H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 84.8, 68.0, 63.0, 32.8, 29.4, 29.3, 29.0, 28.7, 28.4, 25.7, 18.4.

9-Hydroxynonyl Acetate (2l)[37] ^{1}H-NMR (500 MHz, $CDCl_3$): 4.04 (t, $J = 6.9$ Hz, 2H), 3.63 (t, $J = 6.6$ Hz, 2H), 2.04 (s, 3H), 1.65–1.50 (m, 5H), 1.39–1.22 (m, 12H); ^{13}C-NMR (125 MHz, CDCl3) δ: 171.2, 64.6, 63.0, 32.8, 29.44, 29.37, 29.3, 29.2, 28.6, 25.8, 25.7, 21.0.

Stigmasterol (2n) ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 5.35–5.34 (m, 1H), 5.15 (dd, $J = 15.2$, 8.9 Hz, 1H), 5.01 (dd, $J = 15.2$, 8.9 Hz, 1H), 3.57–3.47 (m, 1H), 2.34–2.18 (m, 2H), 2.09–1.91 (m, 3H), 1.89–1.79 (m, 2H), 1.75–1.65 (m, 1H), 1.58–1.36 (m, 10H), 1.30–0.90 (m, 14H), 0.84 (d, $J = 6.9$ Hz, 3H), 0.82–0.76 (m, 6H), 0.70 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 140.7, 138.3, 129.2, 121.7, 71.8, 56.8, 55.9, 51.2, 50.1, 42.3, 42.2, 40.5, 39.7, 37.2, 36.5, 31.9, 31.6, 28.9, 25.4, 24.3, 21.2, 21.1, 21.0, 19.4, 19.0, 12.2, 12.0.

(±)-α-Tocopherol (2o) ^{1}H-NMR (500 MHz, $CDCl_3$): ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 4.22 (s, 1H), 2.62 (t, $J = 6.9$ Hz, 2H), 2.17 (s, 3H), 2.12 (s, 6H), 1.84–1.76 (m, 2H), 1.66–1.02 (m, 24H), 0.90–0.80 (m, 12H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 145.5, 144.5, 122.6, 121.0, 118.5, 117.3, 74.5, 39.9, 39.8, 39.4, 37.4 (multi peaks), 32.8, 32.7, 31.6, 31.5, 28.0, 24.8, 24.4, 23.8, 22.7, 22.6, 21.1, 20.8, 19.7 (multi peaks), 12.2, 11.8, 11.3.

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Supplementary Materials This article contains supplementary materials.

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