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Reaction of Tetrahydropyranyl Ethers with Triethylsilyl Trifluoromethanesulfonate–2,4,6-Collidine Combination: Speculation on the Intermediate, Efficient Deprotection, and Application to Efficient Ring-Closing Metathesis as a Tether

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Dedicated to Prof. Masakatsu Shibasaki on the occasion of his 60th birthday.

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Abstract: The reaction of tetrahydropyranyl (THP) ethers with triethylsilyl trifluoromethanesulfonate (TESOTf)–2,4,6-collidine proceeded *via* collidinium salt intermediates to give the alcohol and 4-triethylsiloxybutanal in good yields. The structure of the intermediate was confirmed by ^{1}H NMR and FAB-MS studies and by trapping it with EtOH. The reaction was applied for mild, efficient, and highly chemoselective deprotection method of THP ethers. The characteristic feature of the reaction is that the reaction conditions are weakly basic. Then, the reaction can proceed without affecting acid-labile protecting groups. Furthermore, the intermediates from alkenol–THP ether were trapped with other alkenols to give acyclic mixed acetals, which were subjected to efficient ring-closing metathesis by using the tetrahydropyranyl unit as a tether.

Keywords: 2,4,6-collidine; deprotection; mixed acetal; ring-closing metathesis; tetrahydropyranyl ethers; triethylsilyl trifluoromethanesulfonate

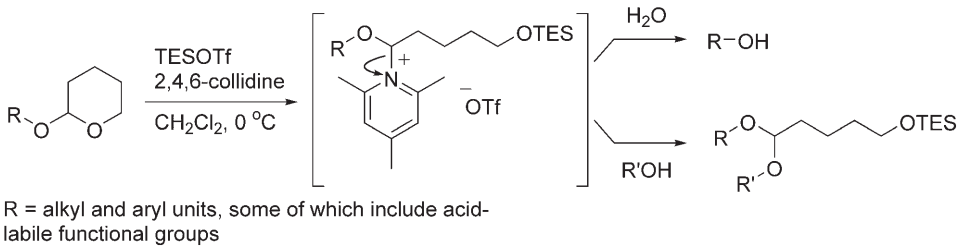
Introduction

Tetrahydropyranyl ethers (THP ethers) are used widely in synthetic organic chemistry because of their stability under basic and neutral conditions.[1] Quite recently, we have developed a mild, efficient, and highly chemoselective deprotection method for acetals by the triethylsilyl trifluoromethanesulfonate (TESOTf)–2,6-lutidine (or 2,4,6-collidine) combination. Usually, acetals are deprotected under acidic or electron-transfer conditions, and the corresponding carbonyl compounds are directly obtained. On the other hand, our method proceeds through pyridinium-type intermediates, and we succeeded in trapping them by alcohols to give mixed acetals. The reaction proceeds under weakly basic condition and many functional groups are tolerated.[2] In consideration of the reaction, we could easily suppose that the methodology would be applicable to THP ethers since they have acetal-type units. We found that treatment of THP ethers with TESOTf–2,4,6-collidine also first afforded the pyridinium-type intermediates. We then applied the reaction to the weakly basic deprotection of THP ethers under mild conditions and the formation of the mixed acetal by trapping the intermediates with alcohol (Scheme 1). Furthermore, the mixed acetal forming reaction was applied to an efficient ring closing metathesis of two different olefinic alcohols using the THP unit as a tether (Scheme 2).

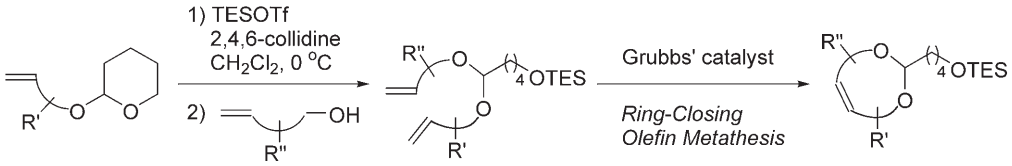
Results and Discussion

Optimization of the Reaction Conditions

First of all, the optimization of the reaction conditions was examined using decanol THP ether **1a**. The results are shown in Table 1. Although TESOTf–2,6-lutidine combination gave decanol **2a** in a fairly good yield (65%), the enol ether **4** (18%) was also formed by H_2O work-up at 0 °C for 10 min (entry 1). We then examined other bases. The use of pyridine slightly im-

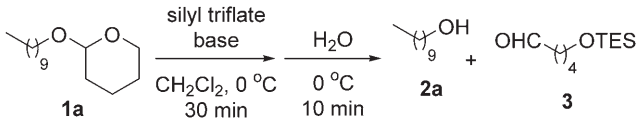


Scheme 1.



Scheme 2.

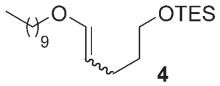
Table 1. Optimization of the reaction conditions.[a]



Entry	Silyl triflate	Base	Yield of **2a** [%]
1[b]	TESOTf	2,6-lutidine	65
2[c]	TESOTf	pyridine	72
3	TESOTf	2,4,6-collidine	97
4	TMSOTf	2,4,6-collidine	78

[a] 2.0 equivs. of silyl triflate and 3.0 equivs. of base were used.

[b] 18% of enol ether **4** was also obtained.



[c] H_2O work-up was carried out at 40 °C for 7 h.

proved the yield of **2a** (72%), although the H_2O treatment needed a long reaction time (7 h) and higher reaction temperature (40 °C) (entry 2). On the other hand, the use of 2,4,6-collidine gave better results, 97% yield of **2a** by H_2O work-up at 0 °C for 10 min (entry 3). Then we decided that 2,4,6-collidine was the base of choice. The use of TMSOTf in place of TESOTf decreased the yield (entry 4). From these results, the combination of TESOTf–2,4,6-collidine proved to be best for the deprotection of THP ethers. In every reaction, 5-triethylsilyloxypentanal **3** was formed.

^{1}H NMR Study and Speculation on the Reaction Mechanism

Figure 1 shows the ^{1}H NMR charts of 2,4,6-collidine (Chart A), the acetal **1a** (Chart B), the reaction mixture of **1a**, TESOTf, and 2,4,6-collidine (Chart C), aldehyde **3** (Chart D), and alcohol **2a** (Chart E). Each spectrum was measured in CD_2Cl_2 and the proton signal of residual, non-deuterated solvent (5.32 ppm for $CHDCl_2$) was used as an internal reference. Several characteristic features are observed from Figure 1: the newly formed peak at 6.02 ppm (dd) derived from the proton on the *N,O*-acetal carbon (Chart C), the low field shifts of the protons of 2,4,6-collidine (Chart A *vs.* Chart C), the disappearance of the acetal proton of THP ether (Chart B *vs.* Chart C), and the changes of the chemical shifts and shapes of the protons next to oxygen atoms (peaks between 3–4 ppm in Chart B *vs.* Chart C). It is noteworthy that **3** (Chart D) and **2a** (Chart E) are not present in the reaction mixture (see Chart C). From our previous work,[2b] the formation of the collidinium salt **i** in Figure 2 was supposed. In fact, FAB(+)-MS of the reaction mixture of **1a**, TESOTf, and 2,4,6-collidine showed a peak corresponding to the cationic part of collidinium salt **i** (Figure 3). On the other hand, the formation of another collidinium salt **ii** in Figure 2 was absent since H_2O work-up of the reaction mixture gave the alcohol **2a** and 5-triethylsilyloxypentanal **3** in exclusive yields and a peak for collidinium salt **ii** ($C_{13}H_{20}NO^+$; 206) was not observed at FAB(+)-MS (see Supporting Information).

From the above observations, a plausible reaction mechanism is shown in Scheme 3. The collidinium salt **i** was first formed from **1a**. Although compound **1a** has two oxygen atoms, an acyclic and a cyclic one, 1-

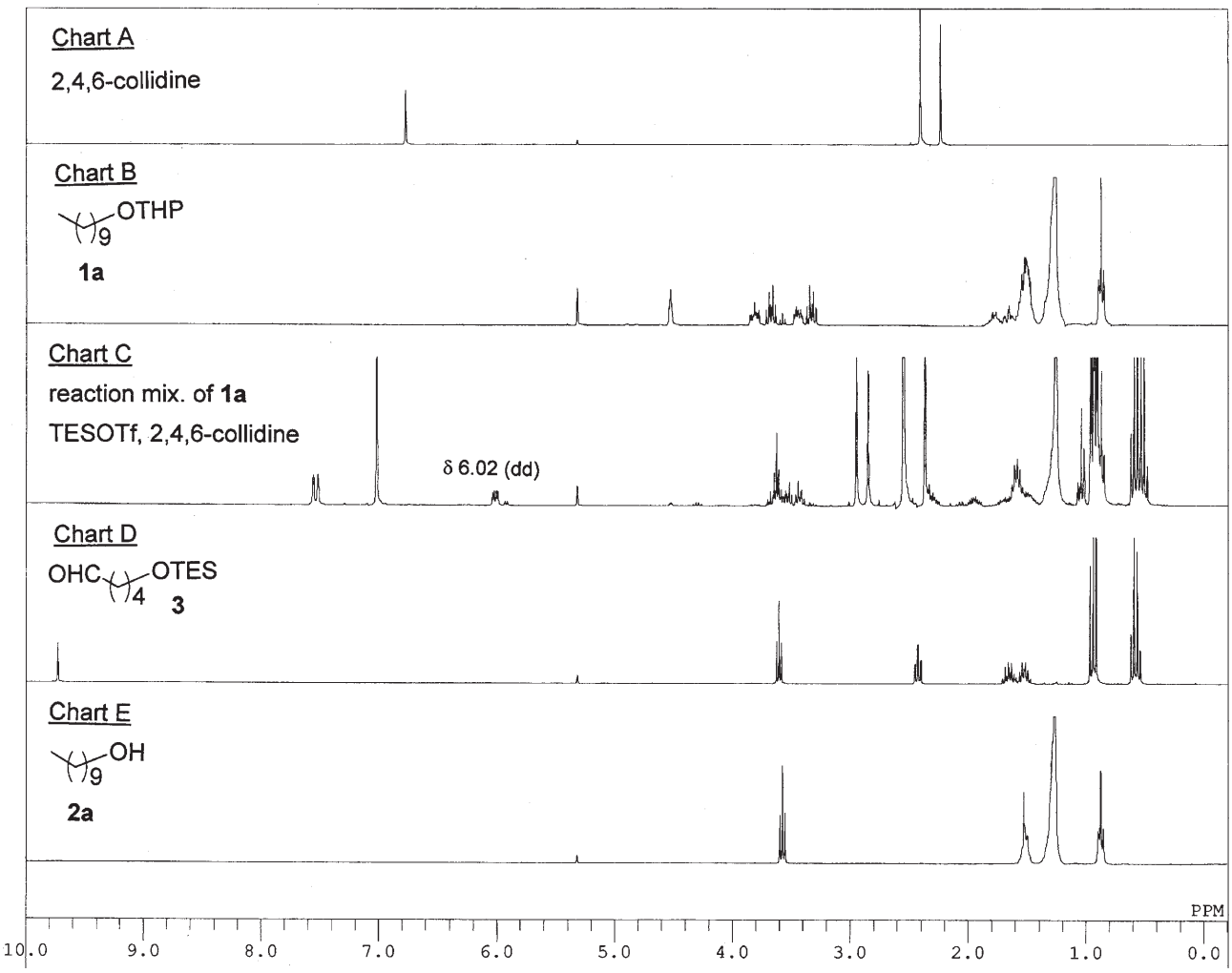


Figure 1. ^{1}H NMR charts for the reaction of **1a** with TESOTf–2,4,6-collidine in CD_2Cl_2.

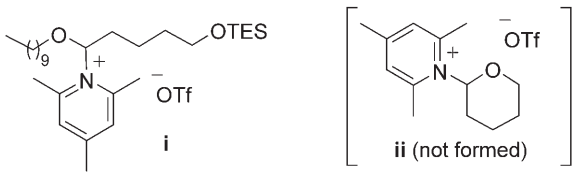


Figure 2. Possible cationic intermediates.

decanol **2a** was only obtained by the reaction between TESOTf and the cyclic oxygen atom, possibly due to steric and electronic reasons. This high discriminating ability of the two oxygen atoms under these reaction conditions was a crucial point for the success of the deprotection of the THP ethers. After H_2O work-up of the reaction mixture, hydrolysis of collidinium salt **i** occurred *via* the hemiacetal **ii**, and THP deprotected

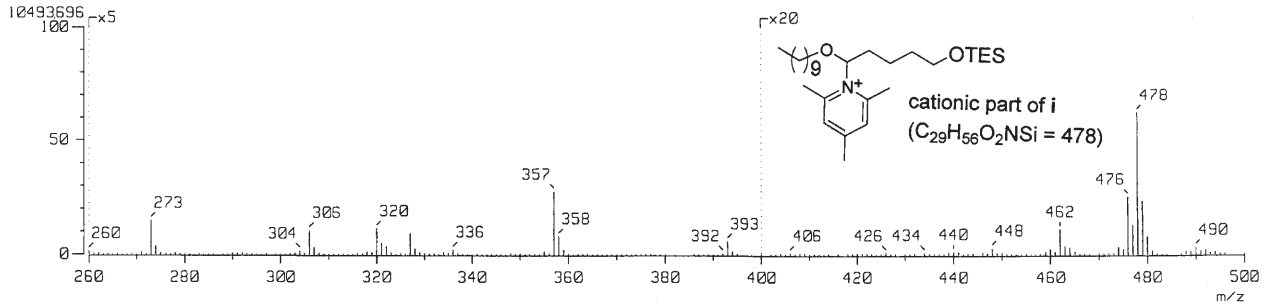
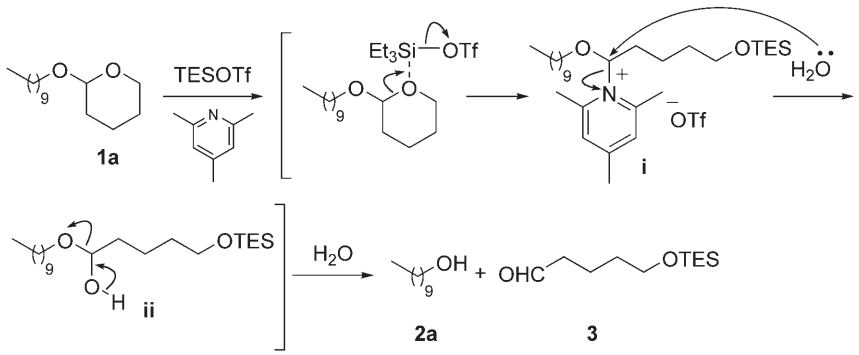


Figure 3. FAB(+)-MS ($m/z = 260$–500) of the mixture of **1a**, TESOTf, and 2,4,6-collidine.



Scheme 3. Plausible reaction mechanism.

compound **2a** and silylated aldehyde **3** were formed together.

Formation of the intermediate **i** was also confirmed by using EtOH in place of water. Thus, after disappearance of **1a** (TLC check), 1.5 equivs. of EtOH were added to the reaction mixture. We then could obtain the 4-triethylsilyloxybutanal mixed acetal **5** in good yield (83%) (Scheme 4). Compound **5** was stable and usual SiO_2 purification did not cause any problems.

Efficient Deprotection of THP Ethers

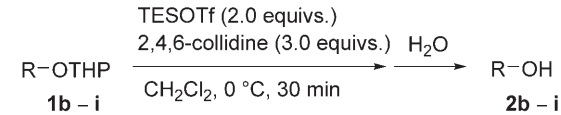
The most popular way for the deprotection of THP ethers is acid hydrolysis. However, under such conditions acid-labile functional groups are attacked and cannot survive.[1] Although very mild deprotecting conditions[3] often can allow the presence of acid-labile functional groups such as acetals, silyl ethers, trityl ethers and so on, a mild and efficient non-acidic deprotection reaction is still highly desirable.

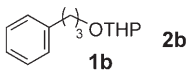
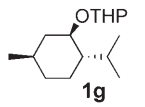
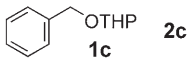
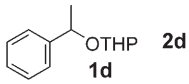
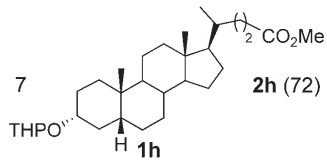
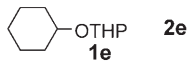
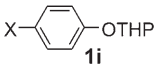
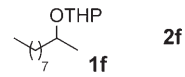
In our procedure, an excess amount of collidine is used as shown in Table 1. Then the reaction proceeds under weakly basic condition. In fact, our previous acetal hydrolysis under the same conditions did not affect acid-labile functional groups.[2] Then, the reactions using various types of THP ethers were examined.

Table 2 shows the results using various THP ethers. For aliphatic alcohols, the reaction proceeds not only for primary alcohols (entries 1 and 2), but also for secondary alcohols (entries 3–7). However, the reaction did not work for aromatic THP ethers at all, and no corresponding alcohol was obtained under these conditions (entry 8). This fact indicates that the described method has a high chemoselectivity between aliphatic and aromatic THP ethers.

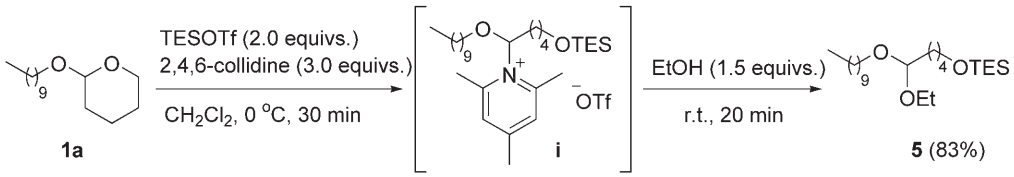
A peculiar feature of our method, the high chemoselectivity and mildness, is also shown in Table 3.

Table 2. Deprotection of various THP ethers.



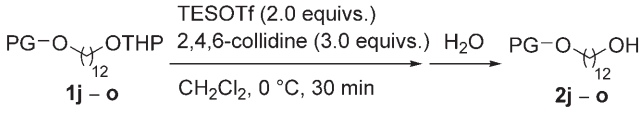
Entry	1	2 (Yield [%])	Entry	1	2 (Yield [%])
1		**2b** (94)	6		**2g** (84)
2		**2c** (90)			
3		**2d** (89)	7		**2h** (72)
4		**2e** (70)	8		NR[a]
5		**2f** (69)		X = H, OMe, CN, NO_2	

[a] No reaction.



Scheme 4. Trapping of the intermediate with EtOH.

Table 3. Deprotection of various THP ethers having another protecting group.

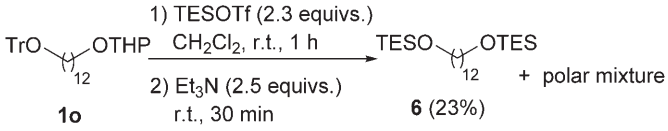


Entry	1	2 (Yield [%])	Entry	1	2 (Yield [%])
1	MeO–(CH2)12–OTHP 1j	2j (87)	4	BzO–(CH2)12–OTHP 1m	2m (90)
2	BnO–(CH2)12–OTHP 1k	2k (91)	5	TBSO–(CH2)12–OTHP 1n	2n (87)
3	AcO–(CH2)12–OTHP 1l	2l (88)	6	TrO–(CH2)12–OTHP 1o	2o (87)

Many kinds of protecting groups for the hydroxyl function, e.g., methyl ether (MeO) (entry 1), benzyl ether (BnO) (entry 2), acetate ester (AcO) (entry 3), benzoate ester (BzO) (entry 4), *tert*-butyldimethylsilyl ether (TBSO) (entry 5), and triphenylmethyl ether (TrO) (entry 6), are tolerated under these reaction conditions. It is noteworthy that the acid-labile TBS ether (TBSO) and Tr ether (TrO), especially the Tr ether, can remain intact (entries 5 and 6).

Although Oriyama et al. reported that a reagent system of trialkylsilyl trifluoromethanesulfonate (R_3SiOTf) and triethylamine (Et_3N) effects the cleavage of THP ethers followed by silylation of the resulting alcohols to give trialkylsilyl ethers,[4] this procedure (the treatment of THP ethers with TESOTf first, then addition of Et_3N) is different from ours (the treatment of THP ethers with base first, then addition of TESOTf). Thus **1o** was treated by Oriyama's method to give the bis-TES ether **6**, which may be formed by the deprotection of both Tr ether and THP ether followed by triethylsilylation of the formed alcohols (Scheme 5).

High chemoselectivity and the mildness of the method are also observed in the reaction of THP



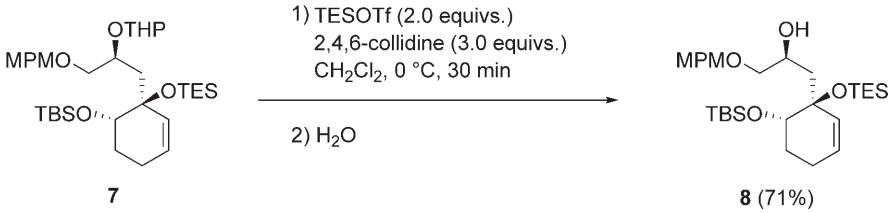
Scheme 5. Direct conversion of THP ether into TES ether.

ether **7** with many functional groups such as the TBS ether (TBSO), TES ether (TESO), MPM ether (4-methoxyphenylmethyl ether) (MPMO), olefin, and allyl TES ether units (Scheme 6). Surprisingly, the reaction of the THP ether **7** afforded the corresponding alcohol **8** in high yield with other functional groups remaining intact.

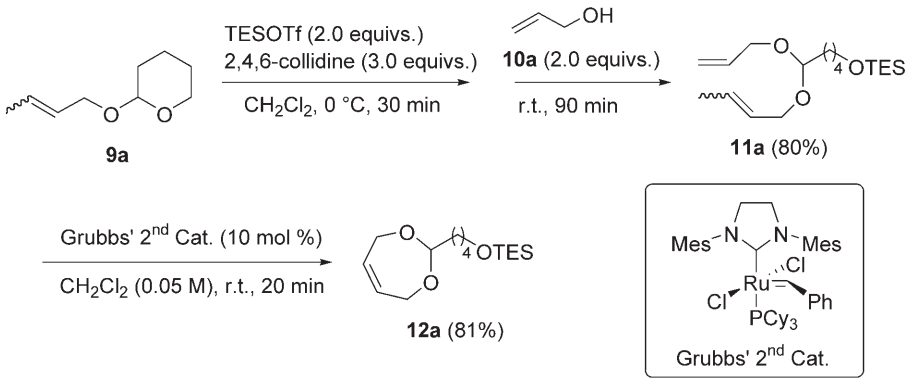
Application in Efficient Ring-Closing Metathesis as a Tether

Olefin metathesis is, undoubtedly, one of the most valuable methods in organic synthesis and is used in many synthetic studies. The reactions proceed under mild conditions in high yields.[5] However, when two very similar olefins, for example, having only one carbon difference, like allyl alcohol and butenol, are used in the reactions, intermolecular olefin metathesis would give a complex mixture of homo-coupling and hetero-coupling products. Thus, an intramolecular method for silicon-tethered ring-closing metathesis has been developed to overcome this disadvantage for the olefin metathesis of two alkenols.[6] This methodology needs first formation of a bis(alkoxy)silane by the reaction of alkenol and dichlorodiphenylsilane. Especially, for the preparation of a bis(alkoxy)silane having two different alkoxy groups, this method requires a rather complicated procedure. Recently, another efficient methodology using phosphate tethers has been reported.[7] We present here a novel tether methodology using the THP unit as a tether.

Since we could succeed in trapping the collidinium salt intermediate with alcohol in good yield (see Scheme 4), we applied the reaction for an efficient ring-closing olefin metathesis (Scheme 7). Treatment of 3-butenol THP ether **9a** with TESOTf–2,4,6-collidine followed by trapping the intermediate with allyl alcohol **10a** gave the 4-triethylsilyloxybutanal mixed



Scheme 6. Chemoselective deprotection of THP ether **7** in the presence of many functional groups.

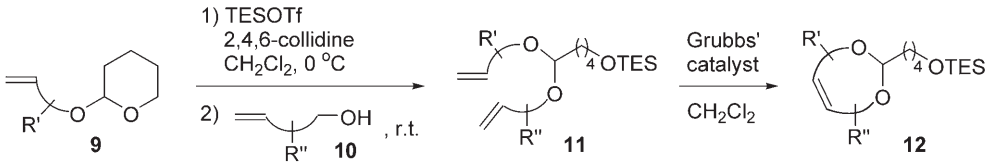


Scheme 7. Formation of mixed acetal **11a**, and efficient olefin metathesis.

acetal **11a** in 80% yield. Ring-closing metathesis of **11a** using Grubbs' 2nd generation catalyst gave medium-ring acetal **12a** in 81% yield. This type of mixed acetal would be difficult to obtain by other acetal formation methodologies since they require acidic conditions and the yield of mixed acetals would be moderate because of simultaneous symmetrical acetal formation. On the other hand, our method can give the mixed acetal **11a** in high yield because the reaction proceeds *via* the collidinium salt intermediate (see Scheme 4).

Table 4 shows the generality of this ring-closing olefin metathesis. The reactions of THP ethers **9b–d** with various alcohols, allyl alcohol **10a**, 3-buten-1-ol **10b**, and 2-buten-1-ol **10c**, gave the corresponding acyclic mixed acetals **11b–d** in good yields. Ring-closing olefin metathesis proceeded well to give medium-ring acetals **12b** and **c** in good yields. For the construction of seven-membered ring acetals **12a** and **b**, the use of Grubbs' 2nd generation catalyst in CH_2Cl_2 (0.05 M) at room temperature was the most effective method. On the other hand, the use of Grubbs' 1st

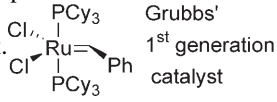
Table 4. Synthesis of medium-ring acetals by RCM.



Entry	THP Ether **9**	Alkenol **10**	Mixed Acetal **11**	Yield [%]	Cyclic Acetal **12**	Yield [%]
1	**9b**	**10a** (2.0 equivs.)	**11b**	79	**12b**	94[a]
2	**9c**	**10b** (3.0 equivs.)	**11c**	84	**12c**	81[b]
3	**9d**	**10c** (3.0 equivs.)	**11d**	89	**12c**	75[b]

[a] Grubbs' 2nd generation catalyst (10 mol%) was used (0.05 M) at room temperature.

[b] Grubbs' 1st generation catalyst (10 mol%) was used (0.01 M) under reflux.



generation catalyst in more dilute solution (0.01 M) under reflux was the best choice for the preparation of eight-membered ring acetal **12c**.

Conclusions

We have found that the reaction of THP ethers with TESOTf–2,4,6-collidine proceeds *via* collidinium salt intermediates in a chemoselective manner. The structure of the intermediate was confirmed by ^{1}H NMR and FAB-MS. The reaction was applied for a mild, an efficient, and highly chemoselective deprotection method of THP ethers. The reaction also can proceed in the presence of acid-labile protecting groups without affecting such functional groups because of the weakly basic conditions. Furthermore, the reaction was applied to an efficient ring-closing metathesis of two different alkenols using the THP unit as a tether. Hence, this article should open a new aspect of protecting chemistry using THP ethers.

Experimental Section

General Techniques

The ^{1}H and ^{13}C NMR spectra were measured on 300 MHz or 270 MHz spectrometers with tetramethylsilane as an internal standard at 20–25 °C. IR spectra were recorded by diffuse reflectance measurement of samples dispersed in KBr powder. Merck silica gel 60 was used for column chromatography.

General Procedure for Preparation of THP Ethers 1a–i and 7

According to a literature method,[9] a solution of an alcohol **2** or **8** (1 equiv.), pyridinium *p*-toluenesulfonate (PPTS) (0.1 equiv.) and 3,4-dihydro-2*H*-pyran (1.8–2 equivs.) in dry CH_2Cl_2 (0.1 M) was stirred at room temperature (except for **8**, at 35 °C). After checking for the disappearance of the alcohol on TLC, the mixture was quenched with saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The organic layer was washed with brine, dried over Na_2SO_4, filtered, and evaporated under vacuum. The residue was purified by flash SiO_2 column chromatography to give the THP ether. Alcohols **2a**–**g** are commercially available; **1a**,[10a] **1b**,[10b] **1c**,[10c] **1d**,[10d] **1e**,[10e] **1g**,[10f] and **1i**[10g] are known in the literature.

1f: Colorless oil; IR (KBr): $\nu = 1130\ cm^{-1}$; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.88$ (3H, t, $J = 6.6$ Hz), 1.10 (1.5H, d, $J = 6.1$ Hz), 1.22 (1.5H, d, $J = 6.4$ Hz), 1.20–1.88 (20H, m), 3.44–3.54 (1H, m), 3.66–3.84 (1H, m), 3.86–3.99 (1H, m), 4.64 (0.5H, t like, $J = 2.7$ Hz), 4.71 (0.5H, t, $J = 3.5$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 14.1$, 19.1, 19.7, 20.1, 21.6, 22.7, 25.46, 25.51, 25.6, 25.9, 29.25, 29.29, 29.56, 29.57, 29.71, 29.75, 31.20, 31.21, 31.9, 36.5, 37.5, 62.4, 62.8, 71.1, 73.9, 95.5, 98.6; anal. calcd. for $C_{15}H_{30}O_2$: C 74.32, H 12.47; found: C 74.39, H 12.24.

1h: Colorless oil; IR (KBr): $\nu = 1742$, 1026 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.63$ (3H, s), 0.85–2.00 (38H, m), 2.15–2.28 (1H, m), 2.29–2.42 (1H, m), 3.43–3.52 (1H, m), 3.67 (3H, s), 3.55–3.72 (1H, m), 3.88–3.97 (1H, m), 4.70–4.75 (1H, m); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 11.8$, 14.0, 18.1, 19.81, 19.84, 20.6, 23.19, 23.21, 24.0, 25.4, 26.2, 26.6, 27.0, 27.2, 28.0, 28.4, 30.79, 30.81, 31.09, 31.13, 32.5, 34.2, 34.6, 35.2, 35.4, 35.6, 39.97, 40.04, 41.9, 42.1, 42.5, 51.2, 55.8, 56.3, 62.50, 62.52, 75.6, 75.8, 96.3, 96.6, 174.4; HR-MS (FAB): $m/z = 475.3785$, calcd. for $C_{30}H_{51}O_4$ ($M^+ + H$): 475.3788.

7: Colorless oil; IR (KBr): $\nu = 1651$, 1248 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.06$ (3H, d, $J = 3.9$ Hz), 0.09 (3H, d, $J = 2.9$ Hz), 0.53–0.66 (6H, m), 0.87 (4.5H, s), 0.88 (4.5H, s), 0.93 (4.5H, t, $J = 7.9$ Hz), 0.94 (4.5H, t, $J = 7.9$ Hz), 1.41–2.22 (12H, m), 3.35–3.49 (1.5H, m), 3.50–3.59 (1H, m), 3.70–4.05 (2.5H, m), 3.80 (3H, s), 4.06–4.15 (0.5H, m), 4.19–4.29 (0.5H, m), 4.45 (1H, s), 4.50 (1H, s), 4.66–4.71 (0.5H, m), 4.89 (0.5H, t like, $J = 3.5$ Hz), 5.42–5.65 (2H, m), 6.85 (2H, d, $J = 8.5$ Hz), 7.26 (2H, t, $J = 8.5$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -4.5$, −4.1, 6.9, 7.3, 18.1, 19.8, 20.1, 23.4, 23.6, 25.5, 25.6, 25.88, 25.92, 28.3, 31.0, 31.2, 39.8, 40.9, 55.2, 62.5, 62.6, 72.4, 72.6, 72.8, 73.5, 73.6, 73.9, 75.2, 75.5, 76.0, 97.9, 98.2, 113.5, 113.6, 127.8, 128.2, 128.9, 129.1, 131.0, 131.1, 132.4, 132.7, 158.9; HR-MS (FAB): $m/z = 643.3822$, calcd. for $C_{34}H_{60}O_6Si_2Na$ ($M^+ + Na$): 643.3826.

Preparation of THP Ethers 1j–o

THP ether 1j: NaH (60% in mineral oil, 43.6 mg, 1.09 mmol) was added to a solution of 12-(tetrahydropyran-2′-yloxy)dodecan-1-ol[11] (208 mg, 0.73 mmol) in dry THF (7.3 mL) at 0 °C. After stirring for 1 h at the same temperature, MeI (68 μL, 1.09 mmol) was added and the reaction mixture was warmed to room temperature. After stirring for 4 h at the same temperature, NaH (60% in mineral oil, 43.6 mg, 1.09 mmol) and MeI (226 μL, 3.63 mmol) were added again and the reaction mixture was refluxed for 30 min. After cooling to room temperature, the mixture was quenched with H_2O and extracted with Et_2O. The organic layer was washed with brine, dried over Na_2SO_4, filtered, and evaporated under vacuum. The residue was purified by flash SiO_2 column chromatography using hexanes-AcOEt (20/1) to give **1j** as a colorless oil; yield: 207 mg (96%). IR (KBr): $\nu = 1119\ cm^{-1}$; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.27$–1.40 (16H, m), 1.43–1.65 (8H, m), 1.66–1.87 (2H, m), 3.33 (3H, s), 3.36 (2H, t, $J = 6.6$ Hz), 3.38 (1H, dt, $J = 10.0$, 6.6 Hz), 3.46–3.55 (1H, m), 3.73 (1H, dt, $J = 9.5$, 7.1 Hz), 3.83–3.93 (1H, m), 4.58 (1H, dd, $J = 3.9$, 3.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 19.7$, 25.5, 26.1, 26.2, 29.5, 29.57, 29.64, 29.8, 30.8, 58.5, 62.3, 67.7, 73.0, 98.8; HR-MS (FAB): $m/z = 323.2570$, calcd. for $C_{18}H_{36}O_3Na$ ($M^+ + Na$): 323.2562.

THP-ether 1k: NaH (60% in mineral oil, 42.9 mg, 1.07 mmol) was added to a solution of 12-(tetrahydropyran-2′-yloxy)dodecan-1-ol[11] (205 mg, 0.72 mmol) in dry DMF (7.2 mL) at 0 °C. After stirring for 1 h at the same temperature, BnBr (128 μL, 1.07 mmol) and NaI (10.8 mg, 0.072 mmol) were added and the reaction mixture was warmed to room temperature. After stirring for 4 h at the same temperature, NaH (60% in mineral oil, 42.9 mg, 1.07 mmol) and NaI (10.8 mg, 0.072 mmol) were added again to the reaction mixture, and stirred for 1 h. The mix-

ture was quenched with H_2O at 0 °C, and extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, filtered, and evaporated under vacuum. The residue was purified by flash SiO_2 column chromatography using hexanes-AcOEt (20/1) to give **1k** as a colorless oil; 208 mg (77 %). IR (KBr): $\nu = 3030\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.15–1.42$ (16 H, m), 1.44–1.84 (10 H, m), 3.37 (1 H, dt, $J = 9.8$, 6.6 Hz), 3.45 (2 H, t, $J = 6.6$ Hz), 3.42–3.54 (1 H, m), 3.73 (1 H, dt, $J = 9.5$, 6.8 Hz), 3.83–3.92 (1 H, m), 4.49 (2 H, s), 4.57 (1 H, dd, $J = 4.2$, 2.9 Hz), 7.24–7.39 (5 H, m); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 19.6$, 25.4, 26.1, 26.2, 29.4, 29.5, 29.67, 29.69, 30.7, 62.2, 67.6, 70.4, 72.7, 98.7, 127.3, 127.5, 128.2, 138.6; anal. calcd. for $C_{24}H_{40}O_3$: C 76.55, H 10.71; found: C 76.65, H 10.71.

THP ether 1l: Ac_2O (99 μL, 1.05 mmol) was added to a solution of 12-(tetrahydropyran-2′-yloxy)dodecan-1-ol[11] (200 mg, 0.70 mmol) in pyridine (169 μL, 2.10 mmol) at 0 °C. The reaction mixture was then stirred at room temperature overnight, and quenched with H_2O. The mixture was extracted with AcOEt. The organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, filtered, and evaporated under vacuum. The residue was purified by flash SiO_2 column chromatography using hexanes-AcOEt (15/1) to give **1l** as a colorless oil; yield: 222 mg (97 %). IR (KBr). $\nu = 1732\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.18–1.43$ (16 H, m), 1.46–1.92 (10 H, m), 2.05 (3 H, s), 3.38 (1 H, dt, $J = 9.5$, 6.6 Hz), 3.45–3.56 (1 H, m), 3.73 (1 H, dt, $J = 9.8$, 6.8 Hz), 3.82–3.93 (1 H, m), 4.05 (2 H, t, $J = 6.7$ Hz), 4.57 (1 H, dd, $J = 4.4$, 2.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 19.7$, 21.0, 25.5, 25.9, 26.2, 28.6, 29.2, 29.45, 29.50, 29.52, 29.7, 30.7, 62.3, 64.6, 67.6, 98.8, 171.2; anal. calcd. for $C_{19}H_{36}O_4$: C 69.47, H 11.05; found: C 69.42, H 10.79.

THP ether 1m: Et_3N (0.14 mL, 1.00 mmol) and BzCl (0.12 mL, 1.00 mmol) were added to a solution of 12-(tetrahydropyran-2′-yloxy)dodecan-1-ol[11] (192 mg, 0.67 mmol) in CH_2Cl_2 (3.3 mL) at 0 °C. The reaction mixture was then stirred at room temperature for 4 h, and quenched with H_2O. The mixture was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, filtered, and evaporated under vacuum. The residue was purified by flash SiO_2 column chromatography using hexanes-AcOEt (20/1) to give **1m** as a colorless oil; 225 mg (86 %). IR (KBr): $\nu = 1713\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.26–1.84$ (26 H, m), 3.38 (1 H, dt, $J = 9.5$, 6.6 Hz), 3.44–3.55 (1 H, m), 3.73 (1 H, dt, $J = 9.5$, 6.8 Hz), 3.83–3.92 (1 H, m), 4.31 (2 H, t, $J = 6.7$ Hz), 4.58 (1 H, t, $J = 3.6$ Hz), 7.44 (2 H, t like, $J = 7.4$ Hz), 7.56 (1 H, tt, $J = 7.4$, 1.5 Hz), 8.05 (2 H, d like, $J = 7.1$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 19.7$, 25.5, 26.0, 26.2, 28.7, 29.3, 29.47, 29.50, 29.53, 29.6, 29.7, 30.8, 62.3, 65.1, 67.7, 98.8, 128.3, 129.5, 132.8, 166.7; HR-MS: $m/z = 390.2770$, calcd. for $C_{24}H_{38}O_4$ (M^+): 390.2770.

THP-ether 1n: Imidazole (143 mg, 2.10 mmol) and TBSCl (159 mg, 1.05 mmol) were added to a solution of 12-(tetrahydropyran-2′-yloxy)dodecan-1-ol[11] (201 mg, 0.70 mmol) in DMF (1.5 mL) at room temperature. After stirring for 24 h at the same temperature, imidazole (143 mg, 2.10 mmol) and TBSCl (159 mg, 1.05 mmol) were added again to the reaction mixture. After being stirred at room temperature for 24 h, the resulting mixture was quenched with saturated aqueous $NaHCO_3$, and extracted with Et_2O. The organic layer was washed with saturated aqueous NH_4Cl and brine, dried over Na_2SO_4, filtered, and evaporated under vacuum. The residue was purified by flash SiO_2 column chromatography using hexanes-AcOEt (40/1) to give **1n** as a colorless oil; yield: 234 mg (83 %). IR (KBr): $\nu = 1076\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.05$ (6 H, s), 0.90 (9 H, s), 1.16–1.42 (16 H, m), 1.43–1.95 (10 H, m), 3.28 (1 H, dt, $J = 9.5$, 6.6 Hz), 3.45–3.54 (1 H, m), 3.60 (2 H, t, $J = 6.6$ Hz), 3.73 (1 H, dt, $J = 9.5$, 6.8 Hz), 3.82-3.94 (1 H, m), 4.57 (1 H, dd, $J = 4.4$, 2.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -5.3$, 18.4, 19.7, 25.5, 25.8, 26.0, 26.2, 29.4, 29.5, 29.58, 29.62, 29.8, 30.8, 32.9, 62.3, 63.3, 67.7, 98.8; anal. calcd. for $C_{23}H_{48}O_3Si$: C 68.94, H 12.07; found: C 69.18, H 11.96.

THP ether 1o: Pyridine (113 μL, 1.40 mmol) and TrCl (292 mg, 1.05 mmol) were added to a solution of 12-(tetrahydropyran-2′-yloxy)dodecan-1-ol[11] (200 mg, 0.70 mmol) in CH_2Cl_2 (1.4 mL) at 0 °C. The reaction mixture was then stirred at room temperature overnight, and quenched with H_2O at 0 °C. The mixture was extracted with AcOEt. The organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, filtered, and evaporated under vacuum. The residue was purified by flash SiO_2 column chromatography using hexanes-AcOEt (25/1) to give **1o** as a colorless oil; yield: 344 mg (93 %). IR (KBr): $\nu = 3022\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.12–1.43$ (16 H, m), 1.44–1.92 (10 H, m), 3.04 (2 H, t, $J = 6.6$ Hz), 3.38 (1 H, dt, $J = 9.5$, 6.6 Hz), 3.43–3.55 (1 H, m), 3.73 (1 H, dt, $J = 9.3$, 6.8 Hz), 3.81–3.93 (1 H, m), 4.57 (1 H, br s), 7.15–7.35 (9 H, m), 7.44 (6 H, d, $J = 8.1$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 19.7$, 25.5, 26.23, 26.24, 29.47, 29.49, 29.6, 29.7, 30.0, 30.8, 62.3, 63.6, 67.7, 86.2, 98.8, 126.7, 127.6, 128.7, 144.5; HR-MS (FAB): $m/z = 551.3501$, calcd. for $C_{36}H_{48}O_3Na$ ($M^+ + Na$): 551.3501.

General Procedure for Deprotection of THP Ethers by TESOTf–2,4,6-Collidine Combination

2,4,6-Collidine (3.0 equivs.) and TESOTf (2.0 equivs.) were added to a solution of a THP ether in CH_2Cl_2 (0.1 M) at 0 °C under N_2. The reaction mixture was stirred for 30 min at the same temperature. After checking for the disappearance of the THP ether on TLC, H_2O was added and the reaction mixture was stirred for 10 min. Disappearance of the polar component was ascertained by TLC analysis. The mixture was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, filtered, and evaporated under vacuum. The residue was purified by flash SiO_2 column chromatography to give the alcohol.

Alcohols **2a–g** are commercially available; alcohols **2k**,[12a] **2l**,[12b] **2n**,[12c] and **2o**[12d] are known in the literature. Their structures are very simple and their ^1H NMR spectra were provided.

Experiments in Table 1

Entry 1 (TESOTf–2,6-lutidine): According to the general procedure, treatment of **1a** (31.5 mg, 0.130 mmol) with 2,6-lutidine (45 μL, 0.390 mmol) and TESOTf (59 μL, 0.260 mmol) gave **2a** (yield: 13.5 mg, 66 %) and **4** (E/Z = 12/88, yield: 10.9 mg, 18 %) after purification by flash SiO_2 column chromatography using hexanes-AcOEt (100/1 to 2/1).

4: Colorless oil; IR (KBr): $\nu = 1663$, $1097\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.60$ (6 H, q, $J = 8.1$ Hz), 0.88 (3 H, t,

$J=6.8$ Hz), 0.96 (9H, t, $J=8.1$ Hz), 1.19–1.41 (14H, m), 1.59 (4H, quin, $J=6.8$ Hz), 1.97 (0.24H, qd, $J=7.3$, 1.0 Hz), 2.10 (1.76H, qd, $J=7.3$, 1.5 Hz), 3.61 (2H, t, $J=6.8$ Hz), 3.69 (2H, t, $J=6.6$ Hz), 4.32 (0.88H, td, $J=7.3$, 6.3 Hz), 4.75 (0.12H, dt, $J=14.8$, 7.3 Hz), 5.92 (0.88H, dt, $J=6.3$, 1.5 Hz), 6.23 (0.12H, dt, $J=12.5$, 1.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=4.4$, 6.8, 14.1, 20.3, 22.7, 25.8, 29.3, 29.4, 29.6, 29.8, 31.9, 33.0, 62.7, 72.2, 106.1, 145.2; HR-MS (FAB): $m/z=357.3183$, calcd. for $C_{21}H_{45}O_2Si$ ($M^+ + H$): 357.3189.

Entry 2 (TESOTf–pyridine): According to the general procedure, treatment of **1a** (42.3 mg, 0.175 mmol) with pyridine (42 μL, 0.524 mmol) and TESOTf (79 μL, 0.349 mmol) at 0 °C for 2 h followed by H_2O treatment (1.0 mL) at 40 °C for 7 h gave **2a** (yield: 19.8 mg, 72%) after purification by flash SiO_2 column chromatography using hexanes-AcOEt (20/1 to 5/1).

Entry 3 (TESOTf–2,4,6-collidine): According to the general procedure, treatment of **1a** (32.0 mg, 0.132 mmol) with 2,4,6-collidine (52 μL, 0.396 mmol) and TESOTf (60 μL, 0.264 mmol) gave **2a** (yield: 20.1 mg, 97%) and **3** (yield: 25.6 mg, 90%) after purification by flash SiO_2 column chromatography using hexanes-AcOEt (20/1 to 2/1).

3: Colorless oil; IR (KBr): $\nu=1720$, 1097 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=0.60$ (6H, q, $J=7.9$ Hz), 0.96 (9H, t, $J=7.9$ Hz), 1.54–1.61 (2H, m), 1.66-1.74 (2H, m), 2.46 (2H, td, $J=7.1$, 1.9 Hz), 3.63 (2H, t, $J=6.2$ Hz), 9.77 (1H, t, $J=1.9$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=4.4$, 6.7, 18.6, 32.1, 43.6, 62.3, 202.7; HR-MS (FAB): $m/z=215.1448$, calcd. for $C_{11}H_{23}O_2Si$ ($M^+ - H$): 215.1467.

Entry 4 (TMSOTf–2,4,6-collidine): According to the general procedure, treatment of **1a** (50.5 mg, 0.208 mmol) with 2,4,6-collidine (82 μL, 0.625 mmol) and TMSOTf (75 μL, 0.417 mmol) gave **2a** (yield: 25.8 mg, 78%) after purification by flash SiO_2 column chromatography using hexanes-AcOEt (10/1).

Experiments in Table 2

Entry 1: According to the general procedure, treatment of **1b** (32.8 mg, 0.149 mmol) with 2,4,6-collidine (59 μL, 0.447 mmol) and TESOTf (67 μL, 0.298 mmol) gave **2b** (yield: 19.0 mg, 94%). Eluent; hexanes-AcOEt (20/1 to 2/1).

Entry 2: According to the general procedure, treatment of **1c** (103.6 mg, 0.539 mmol) with 2,4,6-collidine (214 μL, 1.62 mmol) and TESOTf (244 μL, 1.08 mmol) gave **2c** (yield: 25.8 mg, 78%). Eluent; hexanes-AcOEt (10/1).

Entry 3: According to the general procedure, treatment of **1d** (93.6 mg, 0.454 mmol) with 2,4,6-collidine (180 μL, 1.36 mmol) and TESOTf (205 μL, 0.907 mmol) gave **2d** (yield: 50.1 mg, 90%). Eluent; hexanes-Et_2O (10/1).

Entry 4: According to the general procedure, treatment of **1e** (28.5 mg, 0.155 mmol) with 2,4,6-collidine (61 μL, 0.464 mmol) and TESOTf (70 μL, 0.309 mmol) gave **2e** (yield: 10.7 mg, 70%). Eluent; hexanes-Et_2O (25/1).

Entry 5: According to the general procedure, treatment of **1f** (34.0 mg, 0.140 mmol) with 2,4,6-collidine (56 μL, 0.421 mmol) and TESOTf (63 μL, 0.281 mmol) gave **2f** (yield: 15.4 mg, 69%). Eluent; hexanes-AcOEt (50/1 to 2/1).

Entry 6: According to the general procedure, treatment of **1g** (61.1 mg, 0.254 mmol) with 2,4,6-collidine (101 μL, 0.762 mmol) and TESOTf (115 μL, 0.508 mmol) gave **2g** (yield: 33.3 mg, 84%). Eluent; hexanes-AcOEt (7/1).

Entry 7: According to the general procedure, treatment of **1h** (75.2 mg, 0.158 mmol) with 2,4,6-collidine (63 μL, 0.475 mmol) and TESOTf (72 μL, 0.317 mmol) gave **2h** (yield: 44.5 mg, 72%). Eluent; hexanes-AcOEt (4/1). White solid; mp 130–132 °C, IR (KBr): $\nu=3325$, 1740 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=0.64$ (3H, s), 0.82–2.02 (33H, m), 2.14–2.28 (1H, m), 2.29–2.41 (1H, m), 3.66 (3H, s), 3.56–3.71 (1H, m); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=12.0$, 18.9, 20.8, 23.3, 24.2, 26.4, 27.2, 28.2, 30.5, 30.97, 31.02, 34.5, 35.32, 35.33, 35.8, 36.4, 40.1, 40.4, 42.1, 42.7, 51.5, 55.9, 56.5, 71.8, 174.8; HR-MS (FAB): $m/z=391.3189$, calcd. for $C_{25}H_{43}O_3$ ($M^+ + H$): 391.3202.

Experiments in Table 3

Entry 1: According to the general procedure, treatment of **1j** (49.7 mg, 0.165 mmol) with 2,4,6-collidine (65 μL, 0.496 mmol) and TESOTf (75 μL, 0.331 mmol) gave **2j** (yield: 31.1 mg, 87%). Eluent; hexanes-AcOEt (5/1). White solid; mp 31–32 °C; IR (KBr). $\nu=3360$, 1109 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=1.15$–1.43 (16H, m), 1.46–1.66 (5H, m), 3.33 (3H, s), 3.36 (2H, t, $J=6.6$ Hz), 3.63 (2H, t, $J=6.6$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=25.7$, 26.1, 29.4, 29.45, 29.52, 29.53, 29.55, 29.61, 32.8, 58.5, 63.0, 72.9; HR-MS: $m/z=217.2176$, calcd. for $C_{13}H_{29}O_2$ ($M^+ + H$): 217.2168.

Entry 2: According to the general procedure, treatment of **1k** (54.7 mg, 0.145 mmol) with 2,4,6-collidine (57 μL, 0.436 mmol) and TESOTf (66 μL, 0.291 mmol) gave **2k**[10a] (yield: 38.5 mg, 91%). Eluent; hexanes-AcOEt (6/1 to 5/1).

Entry 3: According to the general procedure, treatment of **1l** (35.5 mg, 0.108 mmol) with 2,4,6-collidine (43 μL, 0.324 mmol) and TESOTf (49 μL, 0.216 mmol) gave **2l**[10b] (yield: 23.2 mg, 88%). Eluent; hexanes-AcOEt (3/1).

Entry 4: According to the general procedure, treatment of **1m** (28.1 mg, 0.072 mmol) with 2,4,6-collidine (29 μL, 0.216 mmol) and TESOTf (33 μL, 0.144 mmol) gave **2m** (yield: 19.7 mg, 90%). Eluent; hexanes-AcOEt (3/1).White solid; mp 41–42 °C, IR (KBr): $n=3348$, 1713 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=1.15$–1.50 (17H, m), 1.56 (2H, quin, $J=7.6$ Hz), 1.77 (2H, quin, $J=7.6$ Hz), 3.64 (2H, t, $J=6.6$ Hz), 4.31 (2H, t, $J=6.6$ Hz), 7.41–7.47 (2H, m), 7.55 (1H, tt, $J=7.4$, 1.7 Hz), 8.03-8.07 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=25.7$, 26.0, 28.7, 29.2, 29.4, 29.47, 29.50, 29.6, 32.8, 63.1, 65.1, 128.3, 129.5, 130.5, 132.8, 166.7; anal. calcd. for $C_{19}H_{30}O_3$: C 74.47, H 9.87; found: C 74.43, H 9.92.

Entry 5: According to the general procedure, treatment of **1n** (37.8 mg, 0.094 mmol) with 2,4,6-collidine (37 μL, 0.282 mmol) and TESOTf (43 μL, 0.188 mmol) gave **2n**[10c] (yield: 26.0 mg, 87%). Eluent; hexanes-AcOEt (5/1).

Entry 6: According to the general procedure, treatment of **1o** (50.7 mg, 0.0959 mmol) with 2,4,6-collidine (38 μL, 0.288 mmol) and TESOTf (43 μL, 0.192 mmol) gave **2o**[10d] (yield: 37.1 mg, 87%). Eluent; hexanes-AcOEt (4/1).

Experiment in Scheme 5 (TESOTf then Et_3N)

According to a literature method,[4] a solution of TESOTf (72 μL, 0.32 mmol) in CH_2Cl_2 (0.46 mL) was added to a solution of **1o** (53.4 mg, 0.10 mmol) in CH_2Cl_2 (0.31 mL) at room temperature under argon. After 1 h, a solution of Et_3N (48 μL, 0.35 mmol) in CH_2Cl_2 (0.31 mL) was added, and the reaction mixture was stirred for 20 min at the same

temperature. The reaction mixture was quenched with phosphate buffer (pH 7), and extracted with CH_2Cl_2. The organic layer was washed with brine, dried over Na_2SO_4, filtered, and evaporated under vacuum. The residue was purified by flash SiO_2 column chromatography using hexanes-AcOEt (100/1) to give **6** (yield: 9.8 mg, 23%). Colorless oil; IR (KBr): $\nu = 1097\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.57$ (12H, q, $J = 8.0$ Hz), 0.97 (18H, t, $J = 8.0$ Hz), 1.22–1.38 (16H, m), 1.45–1.58 (4H, m), 3.59 (4H, t, $J = 6.7$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 4.4$, 6.8, 25.8, 29.5, 29.59, 29.63, 32.9, 63.0; anal. calcd. for $C_{24}H_{54}O_2Si_2$: C 66.90, H 12.63; found: C 67.18, H 12.49.

Experiment in Scheme 6

According to the general procedure, treatment of **7** (36.6 mg, 0.059 mmol) with 2,4,6-collidine (23 μL, 0.177 mmol) and TESOTf (27 μL, 0.118 mmol) gave **8** (yield: 22.4 mg, 71%) after purification by flash SiO_2 column chromatography using hexanes-AcOEt (10/1). Colorless oil; $[\alpha]_D^{20}$: −12.6 (*c* 1.40, $CHCl_3$); IR (KBr): $\nu = 3482$, 1612, 1514, 1463 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.11$ (3H, s), 0.14 (3H, s), 0.62 (6H, q, $J = 7.2$ Hz), 0.91 (9H, s), 0.93 (9H, t, $J = 7.2$ Hz), 1.62-1.77 (3H, m), 1.98 (1H, dd, $J =$ 14.7, 9.0 Hz), 2.07–2.13 (2H, m), 3.35–3.46 (2H, m), 3.80 (3H, s), 3.84 (1H, dd, $J = 10.8$, 4.2 Hz), 4.11–4.18 (2H, m), 4.50 (2H, s), 5.62–5.64 (2H, m), 6.86 (2H, d, $J = 8.7$ Hz), 7.26 (2H, d, $J = 8.7$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta =$ −4.6, −4.4, 6.6, 6.8, 7.0, 7.1, 18.0, 24.5, 25.7, 25.8, 28.8, 41.8, 55.1, 66.0, 72.7, 74.5, 77.7, 113.5, 127.7, 129.1, 130.6, 133.0, 158.9; HR-MS (FAB): $m/z = 559.3265$, calcd. for $C_{29}H_{52}O_5Si_2Na$ ($M^+ + Na$): 559.3251.

General Procedure for Preparation of Mixed Acetals 5 and 11a–d

2,4,6-Collidine (3.0 equivs.) and TESOTf (2.0 equivs.) were added to a solution of a THP ether, **1a** or **9a–d**, in CH_2Cl_2 (0.1 M) at 0 °C under nitrogen. The mixture was stirred at the same temperature. After checking for the disappearance of the THP ether on TLC, EtOH (1.5 equivs.) or an alkenol **10a–c** (equivalents are shown in Table 4), was added to the mixture and the resulting mixture was stirred at room temperature. Disappearance of the polar component was ascertained by TLC. The mixture was quenched with water and extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, filtered, and evaporated under vacuum. The residue was purified by flash SiO_2 column chromatography to give a mixed acetal, **5** or **11a–d**.

Mixed acetal 5: Obtained from **1a** (37.3 mg, 0.15 mmol), TESOTf (70 μL, 0.31 mmol), 2,4,6-collidine (61 μL, 0.46 mmol), and EtOH (14 μL, 0.23 mmol); yield: 51.2 mg (83%). Eluent: hexanes-AcOEt (30/1). Colorless oil; IR (KBr): $\nu = 2856$, 912, 744 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.59$ (6H, q, $J = 7.9$ Hz), 0.88 (3H, t, $J = 6.6$ Hz), 0.96 (9H, t, $J = 7.9$ Hz), 1.17-1.44 (19H, m), 1.51-1.74 (6H, m), 3.37-3.69 (6H, m), 4.47 (1H, t, $J = 5.7$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 4.4$, 6.6, 14.1, 15.3, 21.1, 22.7, 26.2, 29.3, 29.5, 29.56, 29.59, 29.9, 31.9, 32.7, 33.3, 60.9, 62.7, 65.5, 103.0; anal. calcd. for $C_{23}H_{50}O_3Si$: C 68.59, H 12.51; found: C 68.76, H 12.36.

Mixed acetal 11a: Obtained from **9a**[10a] (216 mg, 1.38 mmol), TESOTf (0.62 mL, 2.76 mmol), 2,4,6-collidine (0.55 mL, 4.14 mmol), and **10a** (0.19 mL, 2.76 mmol); yield: 355 mg (80%). Eluent: hexanes-AcOEt (20/1). Colorless oil; IR (KBr): $\nu = 2875$, 1099, 748 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.57$ (6H, q, $J = 7.9$ Hz), 0.93 (9H, t, $J = 7.9$ Hz), 1.34–1.44 (2H, m), 1.49–1.70 (7H, m), 3.58 (2H, t, $J =$ 6.4 Hz), 3.88–4.10 (4H, m), 4.56 (1H, t, $J = 5.7$ Hz), 5.14 (1H, d, $J = 9.6$ Hz), 5.26 (1H, dd, $J = 17.1$, 1.2 Hz), 5.51–5.76 (2H, m), 5.83–5.96 (1H, m); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 4.3$, 6.7, 17.7, 21.1, 32.6, 33.2, 62.6, 66.0, 66.1, 101.9, 116.5, 127.4, 129.2, 134.8; anal. calcd. for $C_{18}H_{36}O_3Si$: C 65.80, H 11.04; found: C 65.79, H 10.93.

Mixed acetal 11b: Obtained from **9b**[13] (323 mg, 1.90 mmol), TESOTf (0.86 mL, 3.80 mmol), 2,4,6-collidine (0.75 mL, 5.70 mmol), and **10a** (0.26 mL, 3.80 mmol); yield: 516 mg (79%). Eluent: hexanes-AcOEt (25/1). Colorless oil; IR (KBr): $\nu = 912$, 742 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.59$ (6H, q, $J = 7.9$ Hz), 0.85–0.98 (12H, m), 1.38–1.69 (8H, m), 3.57–3.62 (2H, m), 3.81–4.13 (3H, m), 4.55–4.62 (1H, m), 5.11–5.32 (4H, m), 5.56–5.97 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 4.4$, 6.8, 9.5, 9.8, 21.0, 21.1, 28.1, 28.5, 32.6, 33.7, 62.7, 64.7, 66.2, 79.0, 79.3, 99.9, 101.7, 115.9, 116.3, 116.5, 117.2, 134.9, 135.1, 138.8, 139.4; anal. calcd. for $C_{19}H_{38}O_3Si$: C 66.61, H 11.18; found: C 66.72, H 11.06.

Mixed acetal 11c: Obtained from **9c**[13] (149 mg, 1.05 mmol), TESOTf (0.47 mL, 2.10 mmol), 2,4,6-collidine (0.42 mL, 3.15 mmol), and **10b** (0.27 mL, 3.15 mmol); yield: 290 mg (84%). Eluent: hexanes-AcOEt (30/1). Colorless oil; IR (KBr): $\nu = 2875$, 1004, 746 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.59$ (6H, q, $J = 7.9$ Hz), 0.96 (9H, t, $J = 7.9$ Hz), 1.26–1.45 (2H, m), 1.51–1.68 (4H, m), 2.33 (2H, qt, $J = 6.6$, 1.2 Hz), 3.46-3.54 (1H, m), 3.58–3.66 (3H, m), 3.96–4.14 (2H, m), 4.55 (1H, t, $J = 5.7$ Hz), 5.02–5.19 (3H, m), 5.28 (1H, dq, $J = 17.1$, 1.7 Hz), 5.76–5.98 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 4.4$, 6.8, 21.1, 32.6, 33.1, 34.3, 62.7, 64.5, 66.3, 102.5, 116.4, 116.6, 134.8, 135.3; anal. calcd. for $C_{18}H_{36}O_3Si$: C 65.80, H 11.04; found: C 66.02, H 10.87.

Mixed acetal 11d: Obtained from **9d**[14] (104 mg, 0.67 mmol), TESOTf (0.30 mL, 1.33 mmol), 2,4,6-collidine (0.26 mL, 2.00 mmol), and **10c** (0.17 mL, 2.00 mmol); yield: 203 mg (89%). Eluent: hexanes-AcOEt (30/1). Colorless oil; IR (KBr): $\nu = 2952$, 1099, 744 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.59$ (6H, q, $J = 7.9$ Hz), 0.96 (9H, t, $J = 7.9$ Hz), 1.34–1.44 (2H, m), 1.50–1.72 (7H, m), 2.33 (2H, q, $J =$ 6.7 Hz), 3.45–3.65 (4H, m), 3.91 (1H, dd, $J = 11.5$, 6.4 Hz), 4.04 (1H, dd, $J = 11.4$, 5.7 Hz), 4.53 (1H, t, $J = 5.8$ Hz), 5.03–5.13 (2H, m), 5.52–5.90 (3H, m); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 4.4$, 6.7, 17.7, 21.1, 32.6, 33.1, 34.3, 62.7, 64.3, 66.3, 102.3, 116.2, 127.5, 129.2, 135.3; anal. calcd. for $C_{19}H_{38}O_3Si$: C 66.61, H 11.18; found: C 66.69, H 11.07.

General Procedure for Preparation of Cyclic Acetals 12a and b

Grubbs' 2nd generation catalyst (10 mol%) was added to a solution of mixed acetal **11a**, **b** in CH_2Cl_2 (0.05 M) at room temperature under argon. The mixture was stirred at the same temperature. After checking for the disappearance of the mixed acetal on TLC, the mixture was evaporated under vacuum. The residue was purified by flash SiO_2 column chromatography to give the cyclic acetal **12a**, **b**.

Cyclic acetal 12a: Obtained from **11a** (235 mg, 0.72 mmol) and Grubbs' 2nd cat. (60.7 mg, 10 mol%); yield: 165 mg (81%). Eluent: hexanes-AcOEt (30/1). Colorless oil; IR (KBr): $\nu = 912$, 742 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta =$ 0.60 (6H, q, $J = 7.8$ Hz), 0.96 (9H, t, $J = 7.8$ Hz), 1.37–1.47 (2H, m), 1.53–1.71 (4H, m), 3.61 (2H, t, $J = 6.6$ Hz), 4.16 (2H, d, $J = 15.3$ Hz), 4.40 (2H, d, $J = 15.6$ Hz), 4.76 (1H, t, $J = 5.5$ Hz), 5.73 (2H, br s); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta =$ 4.4, 6.8, 21.1, 32.6, 33.3, 62.7, 65.1, 104.4, 129.8; HR-MS (FAB): $m/z = 287.2033$, calcd. for $C_{15}H_{31}O_3Si$ ($M^+ + H$): 287.2043.

Cyclic acetal 12b: Obtained from **11b** (57.8 mg, 0.17 mmol) and Grubbs 2nd cat. (14.3 mg, 10 mol%); yield: 49.9 mg (94%). Eluent: hexanes-AcOEt (30/1). Colorless oil; IR (KBr): $\nu = 2875$, 1099, 742 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.59$ (6H, q, $J = 7.9$ Hz), 0.93–1.00 (12H, m), 1.38–1.73 (8H, m), 3.61 (2H, t, $J = 6.4$ Hz), 4.02–4.46 (3H, m), 4.76 (2/5H, t, $J = 5.7$ Hz), 4.86 (3/5H, t, $J = 5.8$ Hz), 5.56–5.74 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 4.4$, 6.8, 10.1, 10.5, 21.2, 21.5, 28.4, 28.8, 32.6, 32.7, 33.0, 33.8, 62.69, 62.73, 63.0, 67.4, 70.8, 79.2, 102.7, 104.2, 129.3, 129.6, 134.0, 134.1; HR-MS (FAB): $m/z = 315.2356$, calcd. for $C_{17}H_{35}O_3Si$ ($M^+ + H$): 315.2355.

Cyclic Acetal 12c

Grubbs' 1st generation catalyst (10 mol%) was added to a solution of mixed acetal **11c** or **11d** in CH_2Cl_2 (0.01 M) at room temperature under argon. The mixture was refluxed under argon. After checking for the disappearance of the mixed acetal on TLC, the mixture was cooled to room temperature and evaporated under vacuum. The residue was purified by flash SiO_2 column chromatography to give cyclic acetal **12c**; yield: 38.6 mg [81% from **11c** (51.9 mg, 0.16 mmol) and Grubbs' 1st cat. (13.0 mg, 10 mol%)] or 33.4 mg [75% from **11d** (57.8 mg, 0.17 mmol) and Grubbs' 1st cat. (14.3 mg, 10 mol%)]. Eluent: hexanes-AcOEt (25/1). Colorless oil; IR (KBr): $\nu = 2875$, 742 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): $\delta = 0.59$ (6H, q, $J = 7.8$ Hz), 0.96 (9H, t, $J = 7.8$ Hz), 1.34–1.45 (2H, m), 1.51–1.71 (4H, m), 2.40–2.55 (2H, m), 3.43-3.52 (1H, m), 3.60 (2H, t, $J = 6.4$ Hz), 3.86-3.94 (1H, m), 4.09 (1H, dd, $J = 15.1$, 4.3 Hz), 4.34 (1H, dd, $J = 15.1$, 5.4 Hz), 4.64 (1H, t, $J = 5.6$ Hz), 5.62–5.70 (1H, m), 5.79–5.89 (1H, m); ^{13}C NMR (68 MHz, $CDCl_3$): $\delta = 4.5$, 6.9, 21.1, 28.4, 32.7, 33.9, 62.7, 63.3, 66.4, 103.1, 127.7, 129.4; HR-MS (FAB): $m/z = 301.2191$, calcd. for $C_{16}H_{33}O_3Si$ ($M^+ + H$): 301.2199.

Supporting Information

Full scale FAB(+)-mass spectra of the mixture of **1a**, TESOTf, and 2,4,6-collidine.

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References

[1] a) T. W. Green, P. G. Wuts, *Protective Groups in Organic Synthesis*, 3rd edn., John Wiley and Sons, New York, **1999**, pp 297–329; b) J. R. Hanson, *Protecting Groups in Organic Synthesis*, 1st edn., Blackwell Science Inc., Malden, MA, **1999**, pp 37–43.

[2] a) H. Fujioka, Y. Sawama, N. Murata, T. Okitsu, O. Kubo, S. Matsuda, Y. Kita, *J. Am. Chem. Soc.* **2004**, *126*, 11800–11801; b) H. Fujioka, T. Okitsu, Y. Sawama, N. Murata, R. Li, Y. Kita, *J. Am. Chem. Soc.* **2006**, *128*, 5930–5938.

[3] For selected recent examples on deacetalization, see: a) A. Ates, A. Gautier, B. Leroy, J.-M. Plancher, Y. Quesnel, J.-C. Vanherck, I. E. Markó, *Tetrahedron* **2003**, *59*, 8989–8999; b) N. Maulide, I. E. Markó, *Synlett* **2005**, 2195–2198; c) H. Miyake, T. Tsumura, M. Sasaki, *Tetrahedron Lett.* **2004**, *45*, 7213–7215; d) A. T. Khan, S. Islam, L. H. Choudhury, S. Ghosh, *Tetrahedron Lett.* **2004**, *45*, 9617–9621; e) S. Kim, J. H. Park, *Tetrahedron Lett.* **1987**, *28*, 439–440.

[4] T. Oriyama, K. Yatabe, S. Sugawara, Y. Machiguchi, G. Koga, *Synlett* **1996**, 523–525.

[5] For recent reviews on ring-closing metathesis, see: a) A. Fürstner, *Angew. Chem. Int. Ed.* **2000**, *39*, 3012–3043; b) T. M. Trnka, R. H. Grubbs, *Acc. Chem. Res.* **2001**, *34*, 18–29; c) C. S. Poulsen, R. Madsen, *Synthesis* **2003**, 1–18; d) A. Deiters, S. F. Martin, *Chem. Rev.* **2004**, *104*, 2199–2238.

[6] P. A. Evans, J. Cui, G. P. Buffone, *Angew. Chem. Int. Ed.* **2003**, *42*, 1734–1737, and references cited therein.

[7] A. Whitehead, M. D. McReynolds, J. D. Moore, P. R. Hanson, *Org. Lett.* **2005**, *7*, 3375–3378, and references cited therein.

[8] S. A. Stanton, S. W. Felman, C. S. Parkhurst, S. A. Godleski, *J. Am. Chem. Soc.* **1983**, *105*, 1964–1969.

[9] M. Miyashita, A. Yoshikoshi, P. A. Grieco, *J. Org. Chem.* **1977**, *42*, 3772–3774.

[10] a) A. T. Khan, E. Mondal, B. M. Borah, S. Ghosh, *Eur. J. Org. Chem.* **2003**, 4113–4117; b) T. Suzuki, T. Oriyama, *Synthesis* **2001**, 555–558; c) A. S. Pilcher, D. K. Hill, S. J. Shimshock, R. E. Waltermire, P. DeShong, *J. Org. Chem.* **1992**, *57*, 2492–2494; d) S. Hoyer, P. Laszlo, *Synthesis* **1986**, 655–657; e) D. S. Brown, S. V. Ley, S. Vile, M. Thompson, *Tetrahedron* **1991**, *47*, 1329–1342; f) Y.-S. Hon, C.-F. Lee, R.-J. Chen, P.-H. Szu, *Tetrahedron* **2001**, *57*, 5991–6001; g) X = H: see Ref.[10f]; h) X = OMe, CN: A. Quedraogo, J. Lessard, *Can. J. Chem.* **1991**, *69*, 474–480; i) $X = NO_2$: H. G. Bull, K. Koehler, T. C. Pletcher, J. J. Ortiz, E. H. Cordes, *J. Am. Chem. Soc.* **1971**, *93*, 3002–3011.

[11] M. J. Cryle, N. J. Matovic, J. J. De Voss, *Org. Lett.* **2003**, *5*, 3341–3344.

[12] a) M. Shimojo, K. Matsumoto, M. Hatanaka, *Tetrahedron* **2000**, *56*, 9281–9288; b) K. V. N. S. Srinivas, I. Mahender, B. Das, *Synlett* **2003**, 2419–2421; c) M. E. Krafft, W. J. Crooks, B. Zorc, S. E. Milczanowski, *J. Org. Chem.* **1988**, *53*, 3158–3163; d) J.-H. Kang, S. Y. Kim, J. Lee, V. E. Marquez, N. E. Lewin, L. V. Pearce, P. M. Blumberg, *J. Med. Chem.* **2004**, *47*, 4000–4007.

[13] O. Tsuge, S. Kanemasa, H. Suga, *Bull. Chem. Soc. Jpn.* **1988**, *61*, 2133–2146.

[14] R. Csuk, A. Kern, *Tetrahedron* **1999**, *55*, 8409–8842.

