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Organic Chemistry Using Weakly Electrophilic Salts: Efficient Formation of *O*,*O*-Mixed, *O*,*S*- and *N*,*O*-Acetals

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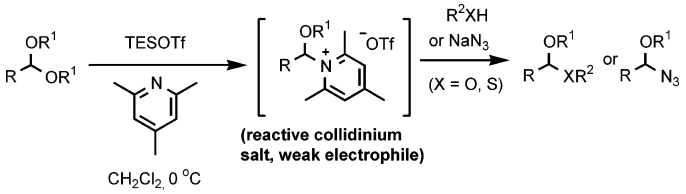


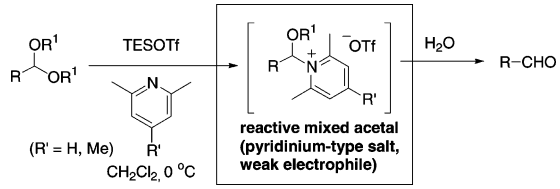
A mild and efficient method for the preparation of *O*,*O*-mixed, *O*,*S*- and *N*,*O*-acetals from symmetrical *O*,*O*-acetals has been developed. Thus, the treatment of symmetrical *O*,*O*-acetals with TESOTf and 2,4,6-collidine formed weakly electrophilic collidinium salts. The addition of nucleophiles, such as an alcohol, lithium thioxide, and sodium azide, to the salts afforded the corresponding *O*,*O*-mixed, *O*,*S*- and *N*,*O*-acetals in good yields. The reaction proceeded under weakly basic conditions. No overreaction then occurred and many acid-labile functional groups could remain intact.

Introduction

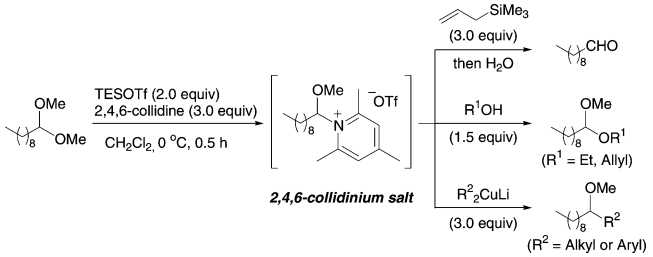
Recently, we developed a novel chemical transformation in which acetals can be chemoselectively deprotected in the presence of ketals,[1] whereas the reported procedures[2] usually deprotect ketals faster than acetals. We also found that the reaction proceeded via polar intermediates and determined them to be pyridinium-type salts[1b,c] (Scheme 1).

The properties of the collidinium salt (R′ = Me, Scheme 1) are as follows: The salt does not react with the allyltrimethylsilane, a very popular nucleophile for oxonium ions, whereas it reacts with EtOH and allyl alcohol in high yields (Scheme 2). These results suggest that the collidinium salts have a weak electrophilicity, and strong nucleophiles, such as water, alcohols, and Gilman reagents,[3] can react with these salts. Another characteristic feature is that the reaction proceeds under weakly basic conditions. On the basis of these advantages, we reported the *O*,*O*-mixed acetal formations using this method.[1b]

SCHEME 1



SCHEME 2



This unique, attractive, and interesting reaction allowed us to develop further application, in particular, the reactions of the 2,4,6-collidinium salt with various heteronucleophiles. Herein,

(1) (a) Fujioka, H.; Sawama, Y.; Murata, N.; Okitsu, T.; Kubo, O.; Matsuda, S.; Kita, Y. *J. Am. Chem. Soc.* **2004**, *126*, 11800−11801. (b) Fujioka, H.; Okitsu, T.; Sawama, Y.; Murata, N.; Li, R.; Kita, Y. *J. Am. Chem. Soc.* **2006**, *128*, 5930−5938. (c) Fujioka, H.; Okitsu, T.; Ohnaka, T.; Sawama, Y.; Kubo, O.; Okamoto, K.; Kita, Y. *Adv. Synth. Catal.* **2007**, *349*, 636−646.

(2) (a) Greene, T. W.; Wuts, P. G. *Protecting Groups in Organic Synthesis*, 3rd ed.; John Wiley and Sons: New York, 1999. (b) Hanson, J. R. *Protecting Groups in Organic Synthesis*, 1st ed.; Blackwell Science, Inc: Malden, MA, 1999. (c) Kocienski, P. J. *Protecting Groups*, 1st ed.; George Thieme Verlag: Stuttgart, 1994.

(3) Fujioka, H.; Okitsu, T.; Sawama, Y.; Ohnaka, T.; Kita, Y. *Synlett* **2006**, *18*, 3077−3080.

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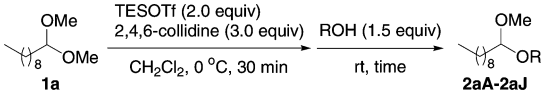
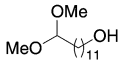
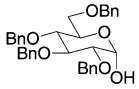
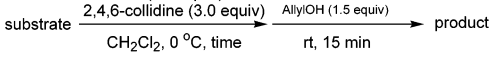
TABLE 1. Reaction of Acetal 1a with Various Alcohols

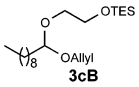
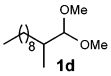
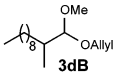
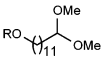
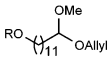


entry	alcohol	time (min)	product	yield (%)
1	EtOH	15	**2aA**	94
2	allyl alcohol	15	**2aB**	88
3	propargyl alcohol	15	**2aC**	94
4	BnOH	15	**2aD**	quant.
5	*i*PrOH	15	**2aE**	88
6	*t*BuOH	15	**2aF**	78
7	1-adamantanol	60	**2aG**	82
8		15	**2aH**	79
9		30	**2aI**	68
10		60	**2aJ**	63[a]

[a] A 5:4 diastereomeric mixture.

TABLE 2. Reaction of Acetals 1b−h with Allyl Alcohol



entry	substrate	product	time (min)	yield (%)
1[a]	 **1b**	 **3bB**	120	quant.
2	 **1c**	 **3cB**	120	77
3	 **1d**	 **3dB**	120	99
				
4	**1e** R = Me	**3eB** R = Me	30	82
5	**1f** R = Ac	**3fB** R = Ac	30	89
6	**1g** R = TBS	**3gB** R = TBS	30	81
7	**1h** R = Tr	**3hB** R = Tr	30	84

[a] TESOTf (3.0 equiv), 2,4,6-collidine (4.0 equiv), and allyl alcohol (2.5 equiv) were used.

we present the novel formation of *O*,*O*-mixed acetals, *O*,*S*-acetals, and *N*,*O*-acetals, which occurs under basic conditions and in a highly chemoselective manner.

Results and Discussion

Efficient Formation of *O*,*O*-Mixed Acetals: *O*,*O*-Mixed acetals are recognized as the synthetic equivalents of esters and are widely used in many reactions, such as the Diels−Alder reaction[4] and radical cyclization[5] for avoiding dipole repulsion. Although several studies reported the preparation of mixed acetals, most of them are limited to the methods for the transacetalization of symmetrical acetals with an alcohol in the presence of a Lewis acid catalyst.[6] Therefore, the yields of the desired mixed acetals are moderate due to the overreaction. Furthermore, previously reported acidic methods are not applicable to compounds having acid-labile functional groups.

On the other hand, our method proceeded under weakly basic conditions and is quite good for the preparation of *O*,*O*-mixed acetals, as shown in Scheme 2. We then examined the generality of the method using various alcohols (Table 1). The reaction process is as follows. After the acetal **1a** disappeared by treatment with TESOTf (2.0 equiv)/2,4,6-collidine (3.0 equiv), the alcohol (1.5 equiv) was added to the mixture. Alcohols, such as allyl alcohol, propargyl alcohol, and benzyl alcohol, which easily form cation species by the S_N1-type elimination of the hydroxyl group under acidic conditions, did not cause any problem and afforded the corresponding *O*,*O*-mixed acetals in high yields (entries 2−4). Secondary and tertiary alcohols also gave the mixed acetals in high yields (entries 5−7), although sterically hindered alcohols usually cannot react with acetals.[6i] Furthermore, the alcohols with acid-labile functional groups, such as an epoxide (entry 8), dimethyl acetal (entry 9), and a sugar unit (entry 10), gave the corresponding mixed acetals in sufficient yields. The results in Table 1 suggested that the use of sterically hindered ones (entries 7 and 10) needed a longer reaction time to consume the collidinium salt. Even acetic acid and phenol worked as nucleophiles and gave the corresponding mixed acetal-type products (71% in the case of acetic acid, 64% in the case of phenol), although they also needed longer reaction times (60 min for each reaction) to consume the collidinium salt.

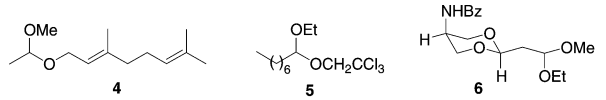
We next examined the reaction with various starting acetals and the allyl alcohol as a nucleophile. The results are shown in Table 2. Diethyl acetal (entry 1), dioxolane (entry 2), and the dimethyl acetal having a secondary carbon (entry 3) afforded the desired mixed acetals. Dimethyl acetals having various functional groups were also available for this reaction (entries 4−7). It is noteworthy that acid-labile protective groups, such as TBS (*tert*-butyldimethylsilyl) ether and trityl (triphenylmethyl) ether, are not affected under the stated conditions (entries 6 and 7). Since the previously reported methods for mixed acetal formations under acidic conditions were difficult to produce the mixed acetals with acid-labile functional groups, these results show the advantage of our method, which proceeds under weakly basic conditions.

A comparison of our method with the previously reported ones has already been reported.[1b] Summary of the results, the yields of the prepared mixed acetals **4**−**6**, is shown in Figure 1. Values of the top are the yields by our method. Those of the bottom are the yields by other methods: the mixed acetal **4** was obtained from dimethyl acetal and geraniol (H_3PO_4, HCO_2H, xylene, 140 °C);[6d] the mixed acetal **5** was obtained from diethyl acetal and 2,2,2-trichloroethanol (*p*-TsOH·H_2O,

(4) Boeckman, R. K., Jr.; Flann, C. J. *Tetrahedron Lett.* **1983**, *24*, 5035−5038.

(5) For recent examples, see: (a) Affo, W.; Ohmiya, H.; Fujioka, T.; Ikeda, Y.; Nakamura, T.; Yorimitsu, H.; Oshima, K.; Imamura, Y.; Mizuta, T.; Miyoshi, K. *J. Am. Chem. Soc.* **2006**, *128*, 8068−8077. (b) Miura, K.; Ootsuka, K.; Hosomi, A. *Synlett* **2005**, 3151−3153. (c) Yamada, R.; Obika, S.; Nishimori, N.; Yamaguchi, M.; Takemoto, Y. *Tetrahedron Lett.* **2004**, *45*, 2331−2334.

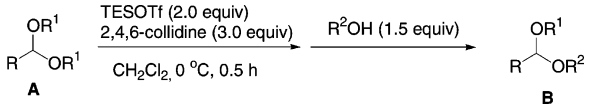
(6) For selected examples on mixed acetal formation, see: (a) Isidor, J. L.; Carlson, R. M. *J. Org. Chem.* **1973**, *38*, 554−556. (b) Boeckman, R. K., Jr.; Flann, C. J. *Tetrahedron Lett.* **1983**, *24*, 4923−4926. (c) Overman, L. E.; Thompson, A. S. *J. Am. Chem. Soc.* **1988**, *110*, 2248−2259. (d) Baeckström, P.; Li, L. *Tetrahedron* **1991**, *47*, 6521−6532. (e) Kitahara, T.; Warita, T.; Abe, M.; Seya, M.; Takagi, Y.; Mori, K. *Agric. Biol. Chem.* **1991**, *55*, 1013−1017. (f) Panda, J.; Ghosh, S. *Tetrahedron Lett.* **1999**, *40*, 6693−6694. (g) Bi, L.; Zhao, M.; Wang, C.; Peng, S. *Eur. J. Org. Chem.* **2000**, 2669−2676. (h) Nomura, M.; Shuto, S.; Matsuda, A. *Bioorg. Med. Chem.* **2003**, *11*, 2453−2461. (i) Ledneczki, I.; Molnár, A. *Synth. Commun.* **2004**, *34*, 3683−3690.



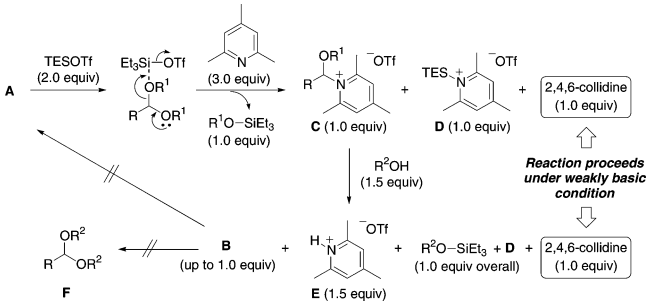
	4	5	6
by our method	87%	91%	79%
by other method	57%	81%	67%

FIGURE 1. Comparison of the yields of the mixed acetals by our method and the reported ones.

SCHEME 3



SCHEME 4



benzene, 81 °C);[6a] the mixed acetal **6** was obtained from dimethyl acetal and ethanol (concd HCl aq, $CHCl_3$, rt).[6g] In every case, our result is superior to the reported one. These facts show that our method for the mixed acetal synthesis is very mild and superior to the previous methods.

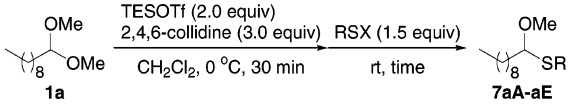
We would like to now discuss the mixed acetal formation from a mechanistic point of view.

For the mixed acetal formation, the protocol is as follows. Acetal **A** was treated with TESOTf (2.0 equiv) and 2,4,6-collidine (3.0 equiv) first. After disappearance of **A** (checked by TLC), the alcohol (R^2OH, 1.5 equiv) was added to the mixture to give the mixed acetal **B** in high yield (Scheme 3).

Our previous study shows the formation of the 2,4,6-collidinium salt intermediate **C** by the reaction of **A** with TESOTf (2.0 equiv) and 2,4,6-collidine (3.0 equiv),[1b] along with $R^1O-SiEt_3$ (1.0 equiv). TESOTf (1.0 equiv) and 2,4,6-collidine (2.0 equiv) cannot complete the preparation of **C**, probably because the amount of 2,4,6-collidine reacts with TESOTf. The formation of 1-(triethylsilyl)collidinium triflate **D** was confirmed by MS study. Anyway, more than 1.0 equiv of 2,4,6-collidine exists so that the reaction system remains weakly basic. In the next step, the addition of the alcohol (1.5 equiv) to the reaction mixture afforded the mixed acetal **B** in high yield. In this process, the collidinium triflate **E** (1.5 equiv) should be released. However, more than 1.0 equiv of 2,4,6-collidine has existed since the reaction started; therefore, the reaction system is still kept weakly basic. This is the reason why (1) acid-labile functional groups were tolerated under this conditions, and (2) the reversible reaction of mixed acetal **B** to raw material **A** or overreaction of **B** to symmetrical acetal **F** did not occur (Scheme 4). These advantages clearly overcome troublesome problems of traditional mixed acetal formations.

Efficient Formation of *O*,*S*-Acetals and *N*,*O*-Acetals: *O*,*S*-Acetals and *N*,*O*-acetals are also useful as protective groups of carbonyl functions[2a] as well as versatile units in synthetic organic chemistry.[7] They are usually prepared by transacetalization in the presence of a Lewis acid.[8,9] Their preparation methods were limited to acidic conditions, so we applied our method to the formation of the *O*,*S*- and *N*,*O*-acetals.

TABLE 3. Reaction of Acetal 1a with Various Thiols



entry	RSX	time (min)	product	yield (%)
1	EtSH	40	**7aA**	89
2	*i*PrSH	105	**7aB**	66
3[a]	*t*BuSH	60	**7aC**	54
4	BnSH	75	**7aD**	61
5	PhSH	120	**7aE**	69
6[b]	PhSLi[c]	5	**7aE**	quant

[a] 2.5 equiv of *t*BuSH was added. [b] 3.0 equiv of PhSLi was added. [c] 1.0 M in THF solution was used.

In the beginning, the formation of *O*,*S*-acetals **7aA**−**aE** was examined by the addition of various thiols to the collidinium salt intermediate (Table 3). The primary thiol gave the desired product in good yield (entry 1), whereas the secondary, tertiary, and benzyl thiols afforded the *O*,*S*-acetals in moderate yields (entries 2−4). Although the use of thiophenol also resulted in a moderate yield (entry 5), the use of its lithium salt (PhSLi) improved the yield and the reaction time (entry 6).

As a nitrogen nucleophile, we chose azidation reagents, such as NaN_3 and trimethylsilyl azide ($TMSN_3$).[10] As mentioned above about the procedure, after the disappearance of the starting **1a**, the azidation reagent was added (Table 4). However, almost no reaction occurred for both reagents (entries 1 and 3). We then examined the optimized conditions to obtain the *N*,*O*-acetal **8aA**. In the case of using sodium azide, the use of a crown ether as an additive produced the *N*,*O*-acetal in excellent yield (entry 2). On the other hand, in the case of $TMSN_3$, tetrabutylammonium difluorotriphenylsilicate (TBAT) was the best additive (entry 5). However, the yield was less than that of NaN_3. Finally, we determined that the combination of NaN_3 and 18-crown-6 was the most efficient method for the formation of the *N*,*O*-acetals (entry 2).

Since the optimized conditions for supplying the *O*,*S*- and *N*,*O*-acetals were in hand, they were applied to various acetals (Table 5). The cyclic acetal, dioxolane (entry 1), and dimethyl acetal having a secondary carbon (entry 2) gave the desired *O*,*S*-

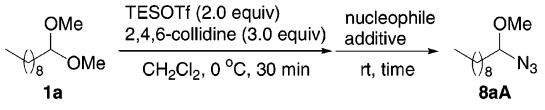
(7) For *O*,*S*-acetals, see: (a) Mandai, T.; Hara, K.; Nakajima, T.; Kawada, M.; Otera, J. *Tetrahedron Lett.* **1983**, *24*, 4993−4996. (b) Sato, T.; Okura, S.; Otera, J.; Nozaki, H. *Tetrahedron Lett.* **1987**, *28*, 6299−6302. (c) Sato, T.; Kobayashi, T.; Gojo, T.; Yoshida, E.; Otera, J.; Nozaki, H. *Chem. Lett.* **1987**, 1661−1664. (d) Sasaki, M.; Noguchi, T.; Tachibana, K. *J. Org. Chem.* **2002**, *67*, 3301−3310 and references cited therein. For *N*,*O*-acetals, see: (e) Hassner, A.; Fibriger, R.; Amarasekara, A. S. *J. Org. Chem.* **1988**, *53*, 22−27. (f) Yanai, H.; Taguchi, T. *Tetrahedron Lett.* **2005**, *46*, 8639−8643.

(8) For selected examples on *O*,*S*-acetal formation, see: Miura, T.; Masaki, Y. *Tetrahedron* **1995**, *51*, 10477−10486 and refs 2 and 7a,b.

(9) For selected examples on *N*,*O*-acetal formation, see: (a) Kirchmeyer, S.; Mertens, A.; Olah, G. A. *Synthesis* **1983**, 500−502. (b) Kim, S.; Park, J. H.; Lee, S. *Tetrahedron Lett.* **1989**, *30*, 6697−6700. (c) Kim, S.; Do, J. Y.; Kim, S. H.; Kim, D. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2357−2358.

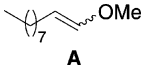
(10) *N*-Nucleophiles such as benzyl amine and aniline were also tried. Although collidinium salt from acetal **1a** was consumed, desired *N*,*O*-acetals could not be isolated probably due to their stabilities. The introduction of other *N*-nucleophiles except azide is on progress.

TABLE 4. Reaction of Acetal 1a with NaN_3 or $TMSN_3$



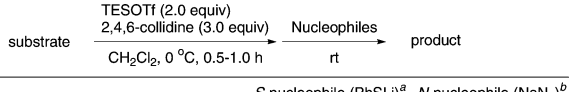
entry	nucleophile	additive[a]	time (h)	yield (%)
1	NaN_3 (3.0 equiv)	none	12	trace
2	NaN_3 (1.5 equiv)	18-crown-6	1.5	97
3	$TMSN_3$ (1.2 equiv)	none	20	0[b]
4	$TMSN_3$ (1.2 equiv)	CsF	16	39[b]
5	$TMSN_3$ (1.2 equiv)	TBAT	1.5	77

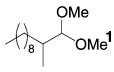
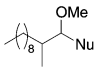
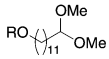
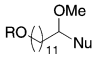
[a] Same molar additive as that of nucleophile was added. [b] 49% of enol ether **A** was obtained together in each entry.



A

TABLE 5. Reactions of Various Acetals with *S*- or *N*-Nucleophile



entry	substrate	product	*S*-nucleophile (PhSLi)[a] product	*S*-nucleophile (PhSLi)[a] yield (%)	*N*-nucleophile (NaN_3)[b] product	*N*-nucleophile (NaN_3)[b] yield (%)
1	 **1c**		**7cE**	91	**8cA**	71
2	 **1d**		**7dE**	87	**8dA**	85
3	 R = Me **1e**		**7eE**	91	**8eA**	87
4	R = Ac **1f**		**7fE**	94	**8fA**	86
5	R = TBS **1g**		**7gE**	90	**8gA**	86
6	R = Tr **1h**		**7hE**	88	**8hA**	91

[a] 1.0 M in THF solution (3.0 equiv) was added. Reaction time was 5 min in each entry. [b] NaN_3 (1.5 equiv) and 18-crown-6 (1.5 equiv) were added. Reaction time was 30 min in each entry.

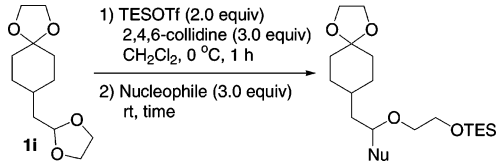
and *N*,*O*-acetals in good yields. Various functional groups, such as methyl ether, acetate ester, TBS ether, and trityl ether, were also intact under the stated conditions (entries 3−6). It is noteworthy that acid-labile protective groups, such as TBS ether and trityl ether, were not affected because the reactions proceeded under weakly basic conditions.

Chemoselectivity of the Reaction: Finally, we examined the chemoselectivity of our method. As a substrate, we chose compound **1i** that included the acetal and ketal functions in the same molecule. As shown in Table 6, in every reaction, the compounds, which are selectively reacted at the acetal, and not the ketal, were obtained in fairly good yields. No products formed by the reaction at the ketal function were observed. The reactions proceed via 2,4,6-collidinium salt intermediates as shown above, and we already have proved the chemoselective formation of the intermediates from the substrates having the acetal and ketal functions in the same molecule (for chemoselective formation of the 2,4,6-collidinium salt intermediates, see refs 1a,b and 3). Then, these results show the high chemoselectivity of our method.

Conclusion

We have developed an efficient method for preparing *O*,*O*-mixed acetals, *O*,*S*-acetals, and *N*,*O*-acetals from *O*,*O*-symmetric

TABLE 6. Chemoselectivity of the Reactions



entry	nucleophile	time (min)	product	yield (%)
1	allylOH	30	**3iB** (Nu = OAllyl)	70
2	PhSLi[a]	5	**7iE** (Nu = SPh)	72
3	NaN_3[b]	10	**8iA** (Nu = N_3)	73

[a] 1.0 M in THF solution was used. [b] 18-Crown-6 (3.0 equiv) was added as additive.

acetals in high yields. The reaction proceeds under weakly basic conditions. Therefore, no overreaction occurs, and many acid-labile functional groups can remain intact. The chemoselectivity of the reaction is very high, and only acetals can react under the stated conditions. The introduction of other nucleophiles to the collidinium salt intermediates and their applications are now in progress.

Experimental Section

General Procedure for the Synthesis of *O*,*O*-Mixed Acetals. 2,4,6-Collidine (3.0 equiv) and TESOTf (2.0 equiv) were added to a solution of an acetal in CH_2Cl_2 (0.1 M solution) at 0 °C under N_2. The mixture was stirred at the same temperature. After checking for the disappearance of an acetal on TLC, an alcohol (1.5 equiv) was added to the resulting mixture and stirred at rt. Disappearance of the polar component was ascertained by TLC. The mixture was quenched with saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, filtered, and evaporated in vacuo. The residue was purified by column chromatography using neutralized SiO_2 (purchased from Kanto Chemical) to give an *O*,*O*-mixed acetal.

Entry 3 in Table 1: 2aC (31.0 mg, 94%) was obtained from **1a** (29.6 mg, 0.146 mmol), TESOTf (66 μL, 0.293 mmol), 2,4,6-collidine (58 μL, 0.439 mmol), and propargyl alcohol (13 μL, 0.219 mmol). Eluent: hexane/Et_2O = 40/1. **2aC**: colorless oil; IR (KBr) 3310, 1117, 1049 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.86 (3H, t, J = 6.6 Hz), 1.13−1.40 (14H, m), 1.56−1.64 (2H, m), 2.38 (1H, t, J = 2.5 Hz), 3.30 (3H, s), 4.18 (2H, d, J = 2.5 Hz), 4.58 (1H, t, J = 5.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 22.7, 24.5, 29.3, 29.4, 29.49, 29.50, 31.9, 32.6, 52.4, 52.8, 73.8, 79.9, 102.7. Anal. Calcd for $C_{14}H_{26}O_2$: C, 74.29; H, 11.58. Found: C, 74.54; H, 11.55.

Entry 1 in Table 6: 3iB (40.4 mg, 70%) was obtained from **1i** (32.8 mg, 0.144 mmol), TESOTf (65 μL, 0.288 mmol), 2,4,6-collidine (57 μL, 0.432 mmol), and allyl alcohol (29 μL, 0.432 mmol). Eluent: CH_2Cl_2/AcOEt = 20/1. **3iB**: colorless oil; IR (KBr) 1647, 1107, 912 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.61 (6H, q, J = 7.9 Hz), 0.96 (9H, t, J = 7.9 Hz), 1.19−1.33 (2H, m), 1.43−1.60 (5H, m), 1.71−1.75 (4H, m), 3.50−3.65 (2H, m), 3.75 (2H, t, J = 5.3 Hz), 3.93 (4H, s), 4.01 (1H, dd, J = 5.4, 12.9 Hz), 4.12 (1H, dd, J = 5.4, 12.9 Hz), 4.70 (1H, t, J = 5.7 Hz), 5.16 (1H, d, J = 10.2 Hz), 5.28 (1H, d, J = 17.0 Hz), 5.85−5.98 (1H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 4.4, 6.7, 30.27, 30.30, 32.4, 34.37, 34.39, 39.5, 62.2, 64.16, 64.19, 66.1, 66.2 101.0, 108.9, 116.6, 134.8. Anal. Calcd for $C_{21}H_{40}O_5Si$: C, 62.96; H, 10.06. Found: C, 63.05; H, 10.00.

General Procedure for the Synthesis of *O*,*S*-Acetals. 2,4,6-Collidine (3.0 equiv) and TESOTf (2.0 equiv) were added to a solution of an acetal in CH_2Cl_2 (0.1 M solution) at 0 °C under N_2. The mixture was stirred at the same temperature. After checking

for the disappearance of an acetal on TLC, a thiol or PhSLi (1.0 M solution in THF) (1.5−3.0 equiv) was added to the resulting mixture and stirred at rt. Disappearance of the polar component was ascertained by TLC. Workup and purification were the same as that of the *O*,*O*-mixed acetal procedure to give an *O*,*S*-acetal.

Entry 6 in Table 3: 7aE[8a] (40.1 mg, quant) was obtained from **1a** (29.0 mg, 0.143 mmol), TESOTf (65 μL, 0.286 mmol), 2,4,6-collidine (57 μL, 0.429 mmol), and PhSLi (1.0 M in THF, 0.43 mL, 0.429 mmol). Eluent: hexane/AcOEt = 75/1.

Entry 2 in Table 6: 7iE (53.4 mg, 72%) was obtained from **1i** (37.5 mg, 0.164 mmol), TESOTf (74 μL, 0.328 mmol), 2,4,6-collidine (65 μL, 0.492 mmol), and PhSLi (1.0 M in THF, 0.49 mL, 0.492 mmol). Eluent: hexane/AcOEt = 15/1. **7iE**: colorless oil; IR (KBr) 1103, 912 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.61 (6H, q, J = 7.9 Hz), 0.96 (9H, t, J = 7.9 Hz), 1.14−1.31 (2H, m), 1.45−1.78 (9H, m), 3.53−3.60 (1H, m), 3.79 (2H, t, J = 5.1 Hz), 3.93 (4H, s), 3.90−4.00 (1H, m), 4.87 (1H, dd, J = 5.3, 8.0 Hz), 7.26−7.31 (3H, m), 7.47−7.50 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 4.4, 6.7, 29.6, 30.2, 33.2, 34.3, 42.2, 62.0, 64.2, 69.1, 87.5, 108.9, 127.4, 128.6, 133.2, 133.5. Anal. Calcd for $C_{24}H_{40}O_4SSi$: C, 63.67; H, 8.91; S, 7.08. Found: C, 63.89; H, 8.93; S, 6.95.

General Procedure for the Synthesis of *N*,*O*-Acetals. 2,4,6-Collidine (3.0 equiv) and TESOTf (2.0 equiv) were added to a solution of an acetal in CH_2Cl_2 (0.1 M solution) at 0 °C under N_2. The mixture was stirred at the same temperature. After checking for the disappearance of an acetal on TLC, NaN_3 (1.5 equiv) and 18-crown-6 (1.5 equiv) were added to the resulting mixture and stirred at rt. Disappearance of the polar component was ascertained by TLC. Workup and purification were the same as that of the *O*,*O*-mixed acetal procedure to give an *N*,*O*-acetal.

Entry 2 in Table 4: 8aA (36.7 mg, 97%) was obtained from **1a** (36.0 mg, 0.178 mmol), TESOTf (81 μL, 0.356 mmol), 2,4,6-collidine (71 μL, 0.534 mmol), NaN_3 (17.4 mg, 0.267 mmol), and 18-crown-6 (70.6 mg, 0.267 mmol). Eluent: hexane/Et_2O = 50/1. **8aA**: colorless oil; IR (KBr) 2106, 1103 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.88 (3H, t, J = 6.7 Hz), 1.27−1.40 (14H, m), 1.72 (2H, quint, J = 6.4 Hz), 3.47 (3H, s), 4.27 (1H, t, J = 6.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 22.7, 24.7, 29.18, 29.26, 29.45, 31.9, 34.4, 56.5, 94.3. Anal. Calcd for $C_{11}H_{23}N_3O$: C, 61.93; H, 10.87; N, 19.70. Found: C, 61.93; H, 10.77; S, 19.36.

Entry 3 in Table 6: 8iA (44.7 mg, 73%) was obtained from **1i** (36.1 mg, 0.158 mmol), TESOTf (72 μL, 0.316 mmol), 2,4,6-collidine (63 μL, 0.474 mmol), NaN_3 (30.8 mg, 0.474 mmol), and 18-crown-6 (125 mg, 0.474 mmol). Eluent: CH_2Cl_2/AcOEt = 50/1. **8iA**: colorless oil; IR (KBr) 2106, 1105, 912 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.61 (6H, q, J = 7.9 Hz), 0.96 (9H, t, J = 7.9 Hz), 1.22−1.34 (2H, m), 1.49−1.76 (9H, m), 3.56−3.65 (1H, m), 3.78−3.86 (3H, m), 3.94 (4H, s), 4.50 (1H, t, J = 6.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 4.3, 6.7, 29.9, 30.2, 32.4, 34.3, 40.6, 62.0, 64.2, 70.3, 91.4, 108.7. Anal. Calcd for $C_{18}H_{35}N_3O_4Si$: C, 56.07; H, 9.15; N, 10.90. Found: C, 56.20; H, 9.03; N, 10.75.

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Supporting Information Available: Full experimental details including the detailed spectroscopic data of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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