Short Articles

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A Novel Regioselective Desulfation Method Specific to Silyl Ester of Primary Sulfate Using Silylating Agents. Selective Preparation of Secondary Alkyl Sulfates Having a Primary Hydroxy Group

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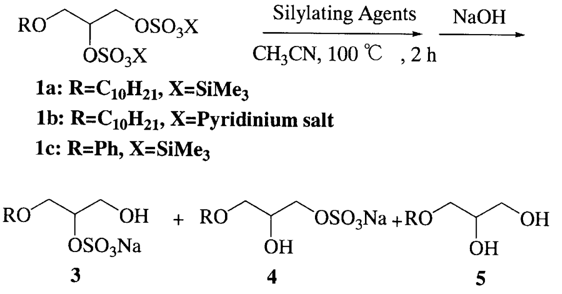
The treatment of bis(trimethylsilyl)ester of 1-*O*-decylglycerol-2,3-disulfate with trimethylsilyl-*N*-trimethylsilylacetimidate (BSA) or (dimethylamino)trimethylsilane caused regioselective desulfation to afford 1-*O*-decyl glycerol-2-sulfate selectively in good yield. Silylating agents, having nitrogen, seems to be responsible for facilitating trimethylsiloxysulfonyl cation transfer.

During the past decade, considerable attention has been given to *O*-alkyl glycerol sulfate esters as surfactants, because of their unique properties, such as high dispersibility and biodegradation.[1,2] In general, *O*-alkyl glycerol sulfate esters are prepared from alkyl glycerol by the sulfation of hydroxy groups with sulfation reagents, such as sulfur trioxide and chlorosulfuric acid.[3,4,5] Because these sulfation reagents are considerably reactive, it is difficult to obtain regioselective sulfation products from glycerol derivatives having plural hydroxy groups. Especially, secondary alkyl sulfate, having a primary hydroxy group, is difficulty to obtain.

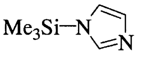
Recently, Takano and co-workers have reported that pyridinium salts of primary alkyl sulfates are easily desulfated in the presence of trimethylsilyl-*N*-trimethylsilylacetimidate (BSA) to give the corresponding trimethylsilylated alcohols, and in the case of secondary alkyl sulfates, the sulfate group is not removed under these conditions.[6,7] The results imply that the desulfation reaction would provide a useful method for the selective synthesis of secondary alkyl sulfates having primary hydroxy groups. In this context, we tried to investigate the desulfation reactions of bistrimethylsilyl esters of 1-*O*-decyl glycerol-2,3-disulfate by various silylating agents (Scheme 1, Table 1).



1a: R=$C_{10}H_{21}$, X=$SiMe_3$
1b: R=$C_{10}H_{21}$, X=Pyridinium salt
1c: R=Ph, X=$SiMe_3$

Scheme 1.

Table 1. Reaction of Glyceryl Ether Disulfates with Various Silylating Agents

Entry	Substrate	Silylating Agent		Yield/%[a)] 3	4	5
1	**1a**	BSA	**2a**	81	4	0
2	**1b**	BSA	**2a**	63	< 1	25
3	**1a**	Me_2NSiMe_3	**2b**	81	< 1	0
4	**1a**	$(Me_3SiNH)_2CO$	**2c**	29	< 1	0
5	**1a**		**2d**	32	3	0
6	**1a**	$(Me_3Si)_2NH$[b)]	**2e**	31	6	0
7	**1a**	Me_3SiCl	**2f**	6	26	0
8	**1c**	Me_3SiOTf	**2g**	0	0	0
9	**1a**	$(Me_3SiO)_2SO_2$	**2h**	0	7	0
10	**1c**	BSA	**2a**	41	< 1	0

a) Determined by measuring the relative integration (^{1}H NMR) of the quenched mixtures. b) The reaction was carried out in the presence of catalytic amount of Me_3SiCl.

The treatment of bis(trimethylsilyl) ester of 1-*O*-decyl glycerol-2,3-disulfate **1a**[8] with 2 mol amt. of trimethylsilyl-*N*-trimethylsilylacetimidate (BSA) **2a**, and the subsequent hydrolysis with NaOH afforded the corresponding 1-*O*-decyl glycerol-2-sulfate **3** in 81% yield with a high regioselectivity (Entry 1). In contrast, the reaction of dipyridinium salt of 1-*O*-decyl glycerol-2,3-disulfate **1b** with 2 mol amt. of **2a** afforded a mixture consisting of **3** (63%), 1-*O*-decyl glycerol (**5**: 25%), and small amount of 1-*O*-decyl glycerol-3-sulfate **4** (Entry 2).

Various silylating agents were also allowed to react with **1a**, as summarized in Table 1. The use of (dimethylamino)trimethylsilane **2b** equally provided the desired sulfate **3** in good yield with a high regioselectivity (Entry 3). In the case of **2c–e**, **3** was barely obtained in 30–40% yield, but the formation of **3** was favored in these cases (Entries 4–6). On the other hand, **2f** gave **4** predominantly (Entry 7), and no **3** was obtained by the use of **2g–h** (Entries 8 and 9). The high regioselectivity in the secondary sulfate formation by using **2a** is not limited to the reaction of the 1-*O*-alkyl glycerol-2,3-disulfate derivatives (**1a** and **1b**). Similar regioselectivity was observed in the 1-*O*-phenylglycerol-2,3-disulfate **1c** as well (Entry 10). It is noteworthy that only silylating agents having nitrogen gave **3** predominantly (Entries 1–6 and 10).

In order to elucidate the reaction mechanism, the following two reactions were carried out:

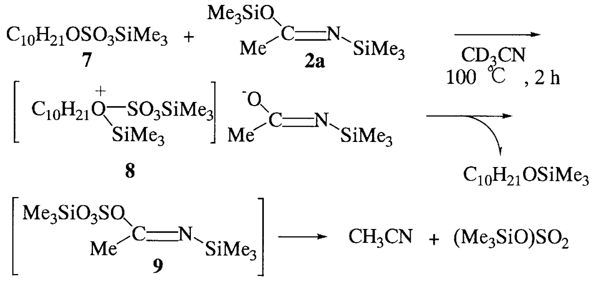
$$\underset{\mathbf{6}}{C_{10}H_{21}OSO_3SiEt_3} \xrightarrow[\substack{CH_3CN \\ 100\,^\circ C,\, 2\ h}]{\mathbf{2a}} C_{10}H_{21}OSiMe_3 \qquad (1)$$

In the first of these, decyl triethylsilyl sulfate **6** was treated with 2 mol amt. of **2a** in acetonitrile. In this case, decyl trimethylsilyl ether was obtained as the main product (63%).

The result suggests that the trimethylsilyl group in **2a** attacks the nucleophilic oxygen of **6** in the reaction process. In the second study, the desulfation reaction of decyl trimethylsilyl sulfate **7** with **2a** in acetonitrile-d_3 was monitored by ^1H and ^{29}Si NMR spectroscopies.[8] In the resulting reaction mixture, bis(trimethylsilyl)sulfate and acetonitrile were detected along with decyl trimethylsilyl ether as the main products:

$$\underset{\textbf{7}}{C_{10}H_{21}OSO_3SiMe_3} \xrightarrow[CD_3CN,\,100\,^\circ C,\,2\,h]{\textbf{2a}} C_{10}H_{21}OSiMe_3 + CH_3CN + (Me_3SiO)_2SO_2. \quad (2)$$

From these results, we postulate a possible mechanism of the desulfation reaction, illustrated in Scheme 2. As shown, since the trimethylsilyl group seems to attack the alcoholic oxygen of **7**, oxonium salt **8** would be generated. The oxonium salt should be liable to release the trimethylsiloxy sulfonyl cation, and the released cation would be trapped by the imidate anion to give **9**, which would subsequently decompose to acetonitrile and bis(trimethylsilyl)sulfate. Because the oxonium salt **8** would be the intermediate, a steric hindrance in the vicinity of the oxygen atom of **8** would cause a difference in the oxonium formation between the primary alkyl sulfate and secondary alkyl sulfate, and the difference would affect the selectivity of the reaction.



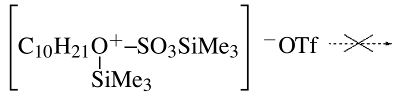
Scheme 2.

The postulated mechanism requires an electrophilic attack of the trimethylsiloxysulfonyl cation on the imidate anion to form bis(trimethylsilyl)sulfate. Evidence for this electrophilic reaction process was gained in the reaction of **7** with **2b**. In this reaction, $Me_2NSO_3SiM_3$ was obtained as a by-product along with decyl trimethylsilyl ether (Eq. 3). This result shows that an electrophilic attack of the trimethylsiloxysulfonyl cation to Me_2N^- occurred in the reaction.[9]

$$\underset{\textbf{7}}{C_{10}H_{21}OSO_3SiMe_3} + \underset{\textbf{2b}}{Me_2NSiMe_3} \xrightarrow[CD_3CN,\,100\,^\circ C,\,2\,h]{} C_{10}H_{21}OSiMe_3 + Me_2NSO_3SiMe_3. \quad (3)$$

In the case of **2g**, which did not give a secondary sulfate in the reaction with **1a**, it seems reasonable to assume that the formed oxonium salt is very stable because of the stability of OTf anion. Therefore, the transfer of the trimethylsiloxysulfonyl cation from the oxonium ion to OTf^- did not occur in the reaction (Eq. 4).

$$\underset{\textbf{7}}{C_{10}H_{21}OSO_3SiMe_3} + SiMe_3OTf \longrightarrow$$



$$\left[C_{10}H_{21}\underset{SiMe_3}{\overset{+}{O}}-SO_3SiMe_3\right]{}^{-}OTf \not\dashrightarrow \quad (4)$$

2g

In summary, we developed an efficient method for the preparation of secondary alkyl sulfates having a primary hydroxy group by the regioselective desulfation of bis(trimethylsilyl) ester of 1-*O*-decyl glycerol-2,3-disulfate. The oxomium salts might play an important role in proceeding the reaction.

Experimental

Preparation of 1a. After a mixture of 1-*O*-decyl glycerol (10.8 g, 50.0 mmol) with chloro sulfuric acid (14.0 g, 120.0 mmol) in dichloromethane (40.0 ml) was stirred at r.t. for 0.5 h , chlorotrimethylsilane (19.6 g, 180.0 mmol) was added. The solution was stirred for 0.5 h at 50 °C and then concentrated under reduced pressure to give the blown amorphous of **1a** (26.0 g) quantitatively without any impurities. **1a**: ^1H NMR($CDCl_3$) δ 0.42 (s, 18H), 0.85 (t, 3H), 1.24 (m, 14H), 1.53 (m, 2H), 3.45 (t, 2H), 3.69 (d, 2H), 4.38 (dd, 1H), 4.48 (dd, 1H), 4.83 (m, 1H).

General Procedure. A solution of **1a** (2.6 g, 5.0 mmol) and **2a** (2.03 g, 10.0 mmol) in acetonitrile (5.0 ml) was heated at 100 °C for 2 h. A NaOH solution was then added, and the solution was evaporated. The yield was determined by ^1H NMR of this residue. The residue was easily purified by ODS gel chromatography or recrystallization. **3**: ^1H NMR (D_2O) δ 0.90 (t, 3H), 1.31 (m, 14H), 1.61 (m, 2H), 3.52 (m, 2H), 3.71–3.89 (m, 3H), 3.85 (dd, 1H), 4.51 (m, 1H). **4**: ^1H NMR (D_2O) δ 0.89 (t, 3H), 1.31 (m, 14H), 1.62 (m, 2H), 3.50–3.64 (m, 4H), 3.98–4.13 (m, 3H).

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8 ^{29}Si NMR($CDCl_3$) δ 15.9 ($C_{10}H_{21}OSiMe_3$), 33.9 ($(Me_3SiO)_2SO_2$), 35.6 ($C_{10}H_{21}OSO_3SiMe_3$).

9 ^{29}Si NMR($CDCl_3$) δ 31.6 ($Me_2NOSO_3SiMe_3$).