On the Mechanism of the Cleavage Reaction of (Methylthio)methyl Ether with Triphenylmethyl Cation

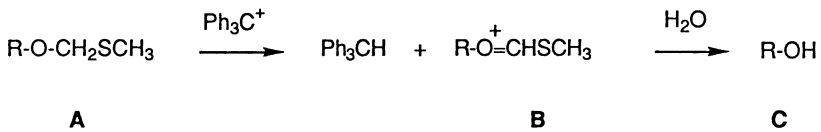
Haruki NIWA* and Yasuyoshi MIYACHI
Department of Chemistry, Faculty of Science, Nagoya University, Chikusa, Nagoya 464
(Received September 21, 1990)

Synopsis. The cleavage reaction of a (methylthio)methyl (MTM) ether with triphenylmethyl cation was not initiated by the previously proposed hydride abstraction with triphenylmethyl cation but promoted by the coordination of triphenylmethyl cation as a Lewis acid to the sulfur atom in the MTM group.

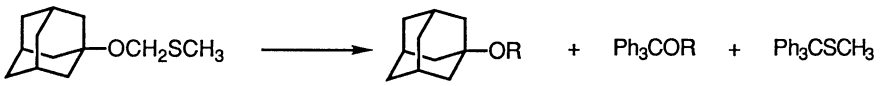
In the synthesis of polyfunctional molecules, (methylthio)methyl (MTM) ethers have been recognized as excellent protecting groups for hydroxyl functions, especially for tertiary alcohols owing to their facile formation and unique stability characteristics.[1] Although there have been reported various methods for removing the MTM protecting groups,[2] the reaction with triphenylmethyl tetrafluoroborate (Ph_3CBF_4)[2g] seems to be the most efficient and promising procedure owing to the mild reaction conditions, the simple procedure, and the wide applicability to polyfunctional molecules.[3] The mechanism of cleavage reaction of the MTM group has been thought *a priori* to be the same as proposed by Barton[4] for the oxidative cleavage of methylenedioxy (O-CH_2-O) groupings with Ph_3CBF_4: The initial step is abstraction of a hydride anion from MTM ether **A** with triphenylmethyl (trityl) cation to form intermediate **B**, which upon hydrolysis (workup) gave parent alcohol **C** (Scheme 1).[2g] However, we have found that this cleavage reaction is not initiated by hydride abstraction with trityl cation but promoted by the coordination of trityl cation to the sulfur in the MTM group.

As the substrate for the present investigation, we have chosen 1-adamantanol (tricyclo[3.3.1.$1^{3,7}$]decan-1-ol) MTM ether (**1**) prepared from 1-adamantanol (**2**) by Yamada's procedure (Ac_2O-DMSO).[2b] The reaction of **1** with 1.05 equiv of Ph_3CBF_4 in CH_2Cl_2 at room temperature for 10 min followed by quenching with aqueous $NaHCO_3$ (workup) provided 1-adamantanol (**2**) (88%) together with Ph_3COH (**6**) (77%) and Ph_3CSCH_3 (**8**) (16%) (Scheme 2). However, Ph_3CH was detected in only trace amounts (<1%). When the cleavage reaction of **1** with Ph_3CBF_4 was quenched with a large excess of methanol prior to aqueous workup, **2** was again obtained in 87% yield together with 1-adamantanol MOM ether (**3**) (11%), Ph_3COCH_3 (**7**) (84%), and Ph_3CSCH_3 (**8**) (8%). Only trace amounts (<1%) of Ph_3CH was again detected.

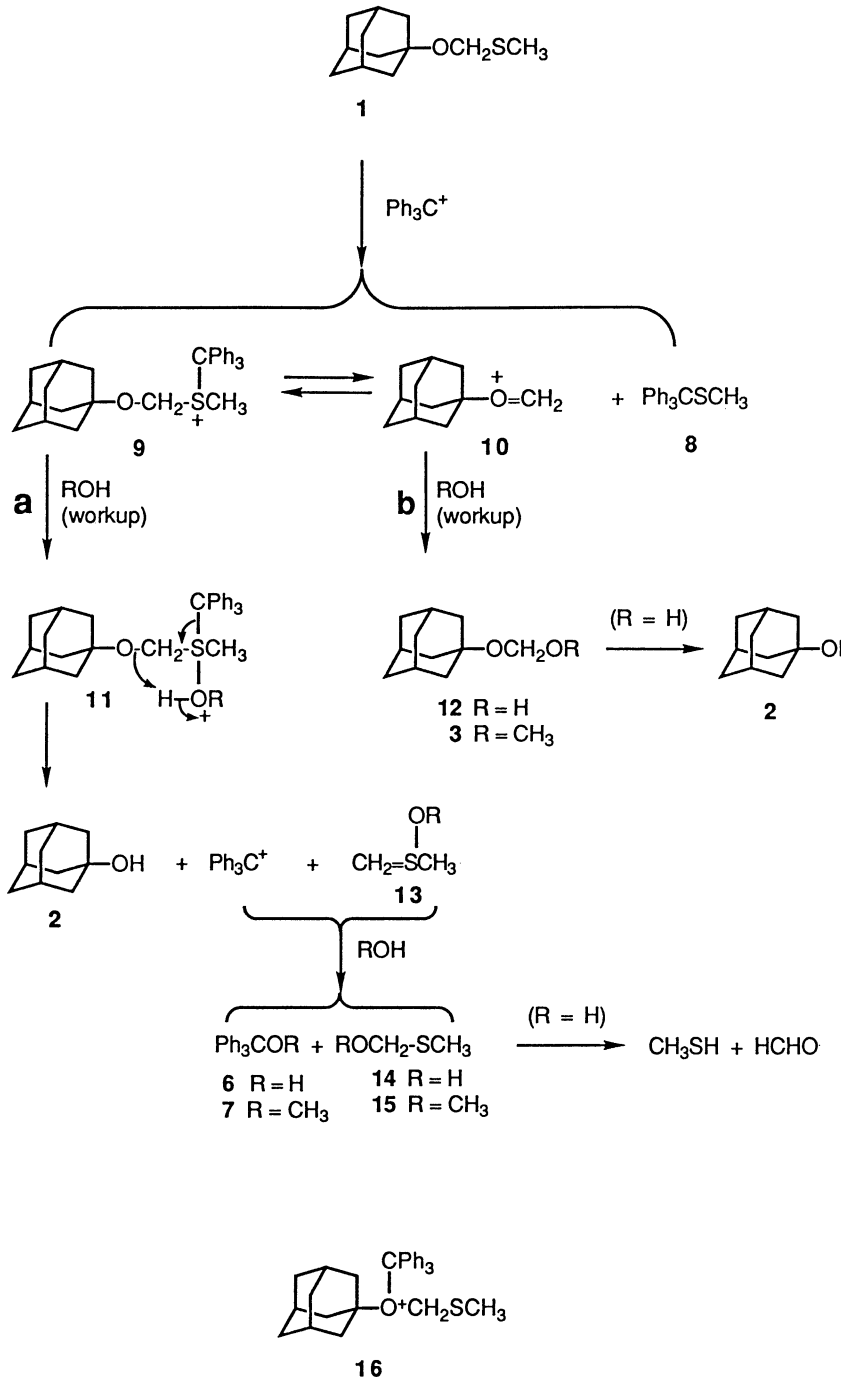
The above results clearly indicate that the cleavage of the MTM ether **1** with Ph_3CBF_4 is not initiated by hydride abstraction with trityl cation as proposed previously.[2g] Although trityl cation is well-documented[5] as a hydride ion acceptor, it has been also known to behave as a Lewis acid.[6] Therefore, the initial step in the cleavage reaction of the MTM ether **1** with Ph_3CBF_4 is supposed to be the complexation of trityl cation to the sulfur atom in the MTM group, forming the sulfonium salt **9** (Scheme 3).[6] Then, the sulfonium salt **9** comes to equilibrium with the collapsed oxonium salt **10** and Ph_3CSCH_3(**8**). During workup the sulfonium salt **9** and oxonium salt **10** may be decomposed via two competing reaction pathways [**a** and **b**]. When the reaction is quenched with H_2O (aqueous workup) (R=H) route **a** gives rise to the parent alcohol **2** and Ph_3COH (**6**) via **11**, whereas route **b** affords also **2** along with Ph_3CSCH_3 **8** through the intermediate **12** generated from **10**. On the other hand, quenching the reaction with methanol (R=CH_3) prior to aqueous workup provides the MOM ether **3** arising from the intermediate **10**, and again Ph_3CSCH_3 **8** in a ratio of ca. 1:1 through route **b**, whereas route **a** provides the parent alcohol **2** and



Scheme 1.



Scheme 2.



Scheme 3.

Ph_3COCH_3 (**7**) in a ratio of ca. 1 : 1. These experimental results suggest that the cleavage of the MTM ether **1** with Ph_3BF_4 predominantly proceeds through route **a**. The clean generation of the parent alcohol **2** without forming the corresponding trityl ether **4** precludes the intervention of the oxonium intermediate **16** during the course of the cleavage reaction. Intervention of 1-adamantyl cation is also ruled out because none of 1-adamantyl methyl ether (**5**) was formed on treatment of the reaction mixture with MeOH prior to aqueous workup. The reported results[2g,3] also indicate that the MTM groups can be removed with the complete retention concerning the configuration of the corresponding hydroxyl groups, precluding intervention of carbocation intermediates during the cleavage reactions.

Based on our understanding of the mechanism of this cleavage reaction, one would expect that Ph_3CClO_4 is also effective reagent to cleave the MTM ether **1**. Our experimental results on the reaction of **1** with Ph_3CClO_4 agree with this prediction, giving the similar result as the cleavage of **1** with Ph_3CBF_4 (see Experimental section).

In summary, the cleavage reaction of the MTM

ether **1** with Ph_3CBF_4 or Ph_3CClO_4 is found to be promoted by the coordination of trityl cation to the sulfur in the MTM group and not initiated by hydride abstraction with trityl cation.

Experimental

Infrared (IR) spectra were recorded on a JASCO Model IR-810 spectrophotometer in $CHCl_3$. Proton nuclear magnetic resonance (^1H NMR) spectra were determined on a JEOL FX-90QE (90 MHz) spectrometer in $CDCl_3$. Chemical shifts are expressed in ppm downfield from internal tetramethylsilane using the δ scale. The low (EIMS) and high resolution (HREIMS) mass spectra were measured on a JEOL-LG2000 instrument. Fuji-Davison silica gel BW-820-MH was used for column chromatography. Merck precoated silica gel 60 F_{254} plates, 0.25 mm thickness, were used for analytical thin-layer chromatography. Unless otherwise stated, materials were obtained from commercial suppliers and used without further purification. Trityl tetrafluoroborate (Ph_3CBF_4)[6] and trityl perchlorate (Ph_3CClO_4)[7] were purified by the reported procedures, respectively. Dichloromethane was freshly distilled from CaH_2. Methanol was distilled from magnesium methoxide. The organic solutions obtained by extractive workup were washed with saturated brine, dried over anhydrous sodium sulfate, and concentrated with a rotary evaporator under reduced pressure.

1-[(Methylthio)methoxy]tricyclo[3.3.1.1^{3,7}]decane (1). A mixture of tricyclo[3.3.1.1^{3,7}]decan-1-ol (**2**) (200 mg, 1.32 mmol), dimethyl sulfoxide (2.5 mL), and acetic anhydride (2.5 mL) was stirred at room temperature for 19 h and then 40 °C for 4 h.[2b] After cooling, the mixture was concentrated in vacuo and the resulting oily residue was purified by column chromatography on silica gel (1 : 1 benzene-ethyl acetate) to give **1** (141 mg, 51%) as a colorless oil: IR 1450, 1355, 1300, 1070, 1035 cm^{-1}; ^1H NMR δ=4.60 (s, 2H), 2.0—2.3 (m, 3H), 2.19 (s, 3H), 1.86 (m, 6H), 1.64 (m, 6H); EIMS *m/z* (rel intensity) 212 (M^+; 7), 182 (9), 165 (5), 152 (10), 136 (15), 135 (100), 95 (28), 79 (16). HREIMS. Found: *m/z* 212.1252. Calcd for $C_{12}H_{20}OS$: M, 212.1235.

Cleavage Reaction of 1 with Ph_3CBF_4. A. Quenching with Saturated $NaHCO_3$ Solution. To a stirred solution of **1** (93 mg, 0.44 mmol) in dichloromethane (4 mL) under nitrogen was added Ph_3CBF_4 (152 mg, 0.46 mmol) at room temperature. After being stirred for 15 min at room temperature, the reaction mixture was diluted with saturated $NaHCO_3$ solution (3 mL) and the mixture was stirred for 10 min and extracted with chloroform (3×10 mL). The combined organic layers were washed with saturated $NaHCO_3$ solution and saturated brine, dried and concentrated. The crude product was purified by column chromatography on silica gel (2 : 1 hexane-chloroform→chloroform) to provide 1-adamantanol (**2**) (59 mg, 88%), trityl alcohol (**6**) (92 mg, 77%), and methyl trityl sulfide (**8**) (22 mg, 16%). The spectral (IR , ^1H NMR, MS) properties of these compounds were identical with those of the authentic samples, respectively.

B. Quenching with MeOH Prior to Aqueous Work Up. After reaction of **1** (82 mg, 0.39 mmol) with Ph_3CBF_4 (134 mg, 0.41 mmol) in dichloromethane (4 mL) for 10 min at room temperature, the reaction mixture was diluted with MeOH (1 mL). After being stirred for 10 min at room temperature, the mixture was diluted with H_2O (5 ml) and extracted with chloroform (4×7 mL). The combined organic solutions were washed with saturated $NaHCO_3$ solution and saturated brine, dried, and concentrated. Purification of the resulting crude product by column chromatography on silica gel (2 : 1 hexane-chloroform→chloroform) afforded **2** (51 mg , 87%), 1-(methoxymethoxy)tricyclo-[3.3.1.1^{3,7}]decane (**3**) (8 mg, 11%), methyl trityl ether (**7**) (93 mg, 84%), and **8** (9 mg, 8%). **3**: A colorless oil; IR 1455, 1355, 1145, 1035, 910 cm^{-1} ^1H NMR δ=4.77 (s, 2H), 3.37 (s, 3H), 2.0—2.3 (m, 3H), 1.82 (m, 6H), 1.63 (m, 6H); EIMS *m/z* (rel intensity) 196 (M^+; 76), 166 (37), 139 (47), 135 (100), 109 (78), 107 (63), 95 (44), 79 (33). HREIMS. Found: *m/z* 196.1491. Calcd for $C_{12}H_2O_2$: M, 196.1463.

Cleavage Reaction of 1 with Ph_3CClO_4. To a stirred solution of **1** (44 mg, 0.21 mmol) in dichloromethane (2 mL) under nitrogen was added Ph_3CClO_4 (78 mg, 0.23 mmol) at room temperature. After being stirred for 30 min, the reaction mixture was diluted with saturated $NaHCO_3$ solution (3 mL). The mixture was vigorously stirred for 10 min and extracted with chloroform (4×10 mL). The combined organic solutions were washed, dried and concentrated. Purification of the crude residue by column chromatography on silica gel (2 : 1 hexane-chloroform→chloroform) provided **2** (27 mg, 85%), **6** (44 mg, 75%), and **8** (17 mg, 25%).

We are deeply indebted to Professor Kiyoyuki Yamada for the valuable discussions and the encouragement for the present research.

References

1) T. W. Greene, "Protective Groups in Organic Synthesis," Wiley-Interscience, New York (1981).

2) a) E. J. Corey and M. G. Bock, *Tetrahedron Lett.*, **1975**, 3269. b) K. Yamada, K. Kato, H. Nagase, and Y. Hirata, *Tetrahedron Lett.*, **1976**, 65. c) P. M. Pojer and S. J. Angyal, *Tetrahedron Lett.*, **1976**, 3067. P. M. Pojer and S. J. Angyal, *Aust. J. Chem.*, **31**, 1031 (1978). d) R. A. Holton and R. G. Davis, *Tetrahedron Lett.*, **1977**, 533. 4) H. Niwa and M. Kurono, *Chem. Lett.*, **1979**, 23. f) Y. Guindon, H. E. Morton, and C. Yoakim, *Tetrahedron Lett.*, **24**, 3969 (1983). Y. Guindon, C. Yoakim, and H. E. Morton, *J. Org. Chem.*, **49**, 3912 (1984). g) P. K. Chowdhury, R. P. Sharma, and J. N. Baruah, *Tetrahedron Lett.*, **24**, 4485 (1983). h) N. C. Barua, R. P. Sharma, and J. N. Baruah, *Tetrahedron Lett.*, **24**, 1189 (1983). D. N. Sarma, N. C. Barua, and R. P. Sharma, *Chem. Ind.*, **1984**, 223.

3) Recent application to the synthesis of a polyfunctional natural product: H. Niwa, Y Miyachi, Y. Uosaki, A. Kuroda, H. Ishiwata, and K. Yamada, *Tetrahedron Lett.*, **27**, 4609 (1986).

4) D. H. R. Barton, P. D. Magnus, G. Smith, G. Streckert, and D. Zurr, *J. Chem. Soc., Perkin Trans. 1*, **1972**, 542.

5) C. D. Nenitzescu, "Intermolecular Hydride Transfer Reactions Involving Carbonium Ion in Carbonium Ions," ed by G. A. Olah and P. von R. Schleyer, Wiley-Interscience, New York (1970), Vol. 2.

6) A synthetic reaction promoted by complexation of trityl cation to the sulfur in the thioacetal has been reported: M. Ohshima, M. Murakami, and T. Mukaiyama, *Chem. Lett.*, **1985**, 1871, and references cited therein.

7) H. J. Dauben, Jr., L. R. Honnen, and K. M. Harmon, *J. Org. Chem.*, **25**, 1442 (1960).