Intramolecular Oxymercuration with Mercuric Triflate

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Five- and six-membered ring cyclic ethers are efficiently prepared by *exo*-mode oxymercuration of the corresponding olefinic alcohols with $Hg(OTf)_2$. A seven-membered ring ether is prepared using $Hg(OTf)_2$ along with TMU. However, this procedure is not effective for the preparation of four- and eight-membered ring ethers.

Key words   mercuric triflate; oxymercuration; cyclic ether; *exo* cyclization

Mercuric triflate, $Hg(OTf)_2$, has been developed in this laboratory as an effective olefin cyclization agent[2,3] and employed for total syntheses of a variety of polycyclic terpenoids.[4–9] Although the oxymercuration with $Hg(OTf)_2$ is an efficient procedure for the preparation of cyclic ether during total syntheses of gelsemine,[10,11] the scope and limitation of the methodology have not been reported. To check the limitation, we examined the reaction of a less reactive substrate such as *tert*-alcohol containing monosubstituted olefin. We describe here the intramolecular oxymercuration with $Hg(OTf)_2$, which is an efficient procedure to prepare five-, six-, and seven-membered ring ethers *via exo*-mode cyclization, although, the procedure is not sufficiently effective to construct four- and eight-membered ring ethers. To prepare a seven-membered ring ether, the $Hg(OTf)_2$ itself is not useful

due to the equilibrium between the starting material and the product leading to low yield. However, $Hg(OTf)_2$ in the presence of tetramethylurea (TMU) affords a seven-membered ring ether in high yield under a kinetically controlled reaction.

A 1.2 equivalent of $Hg(OTf)_2$ is prepared *in situ* by mixing mercuric oxide yellow and triflic anhydride in acetonitrile,[3] and to this was added olefin alcohol at 0 or $-20\,°C$. After stirring at the same temperature for 5 min, the mixture was quenched by the addition of brine and $NaHCO_3$ solution. The results are summarized in Table 1. Although the reaction of **1a** with $Hg(OTf)_2$ in acetonitrile at $0\,°C$ afforded five-membered ring ether **1b** in 86% yield (entry 1), reaction at $-20\,°C$ afforded 97% yield with nearly complete *exo* selectivity (entry 2). The *exo/endo* ratio was determined by GLC analysis
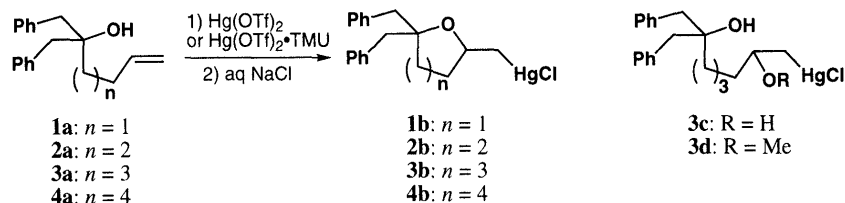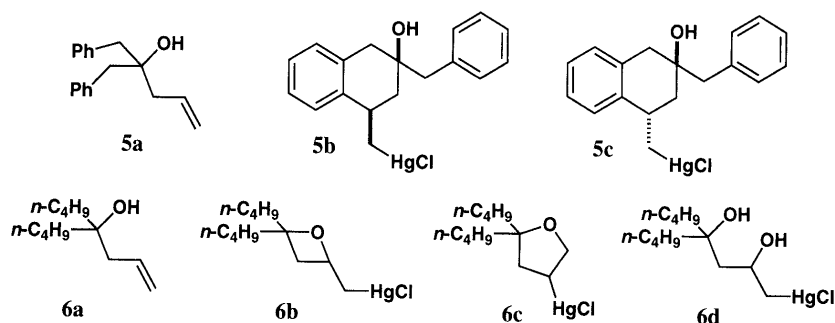
1a: $n = 1$
2a: $n = 2$
3a: $n = 3$
4a: $n = 4$

1b: $n = 1$
2b: $n = 2$
3b: $n = 3$
4b: $n = 4$

3c: R = H
3d: R = Me

Table 1. Intramolecular Oxymercuration of Olefinic Alcohols with Mercuric Salts[a]

Entry	Substrate	Reagent	Solvent	Temp. (°C)	Yield	*Exo/Endo*
1	1a	$Hg(OTf)_2$	CH_3CN	0	86	>99:1
2	1a	$Hg(OTf)_2$	CH_3CN	−20	97	>99:1
3	1a	$Hg(OTf)_2$	CH_3NO_2	0	91	>99:1
4	1a	$Hg(OTf)_2$	CH_3NO_2	−20	96	>99:1
5	1a	$Hg(OTf)_2$	CH_2Cl_2	−20	99	>99:1
6	1a	$Hg(OAc)_2$	CH_3CN	−20	33	>99:1
7	1a	$Hg(OCOCF_3)_2$	$CH3CN$	−20	90	>99:1
8	2a	$Hg(OTf)_2$	CH_3CN	0	95	>99:1
9	2a	$Hg(OTf)_2$	CH_3CN	−20	99	>99:1
10	2a	$Hg(OTf)_2$	CH_3NO_2	0	90	>99:1
11	2a	$Hg(OTf)_2 \cdot PhNMe_2$	$CH3CN$	−20	92	>99:1
12	2a	$Hg(OAc)_2$	CH_3CN	−20	2	>99:1
13	2a	$Hg(OCOCF_3)_2$	CH_3CN	−20	98	>99:1
14	3a	$Hg(OTf)_2$	CH_3CN	−20	74	>99:1
15	3a	$Hg(OTf)_2 \cdot TMU$	CH_3CN	−20	92	>99:1
16	3a	$Hg(OAc)_2$	CH_3CN	−20	0	
17	3a	$Hg(OCOCF_3)_2$	CH_3CN	−20	77	>99:1
18	3a	$Hg(OCOCF_3)_2 \cdot TMU$	CH_3CN	−20	33	>99:1
19	4a	$Hg(OTf)_2 \cdot TMU$	CH_3CN	−20	0	

a) Each reaction was carried out with 1.2 equiv. of mercuric salt for 5 min.

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of the Bu₃SnH reduction[12] products by comparing with the authentic sample. Nitromethane and dichloromethane also gave similar results (entry 4 and 5). Although mercuric acetate, $Hg(OAc)_2$, afforded poor results (entry 6), mercuric trifluoroacetate, $Hg(OCOCF_3)_2$, gave **1b** in satisfactory yield (entry 7). Both $Hg(OTf)_2$ and $Hg(OCOCF_3)_2$ afforded six-membered ring ether **2b** by the reaction with **2a** in acetonitrile in high yield with complete *exo* selectivity (entry 9 and 13). Reaction of **3a** with $Hg(OTf)_2$ afforded seven-membered ring ether **3b** in only 74% yield (entry 14) along with the starting material and hydroxymercuration product **3c**. When methanol was added to the reaction mixture before quenching, methoxymercuration product **3d** was isolated in 13% yield. Thus the existence of an equilibration between **3a** and a seven-membered ring ether related to **3b** under the reaction conditions is deduced. The equilibrium was confirmed by the exposure of seven-membered ring ether **3b** with $Hg(OTf)_2$ (0.5 equiv.) in acetonitrile at −20 °C for 5 min to give a mixture of **3a**, **3b**, and **3c** (38%, 56%, and 5% yields, respectively) after quenching with brine. A similar reverse reaction was also observed by treatment of **3b** with triflic acid (0.5 equiv.) in acetonitrile at −20 °C for 5 min, providing a mixture of **3a** and **3b** (63% and 37%, respectively). However, the reaction of **3a** in the presence of TMU (1.2 equiv.) afforded the ether **3b** in 92% yield under the ordinary concentration in acetonitrile (entry 15). The $Hg(OCOCF_3)_2$ was not sufficiently reactive in the presence of TMU to prepare a seven-membered ring ether (entry 18). No trace of eight-membered ring ether **4b** was detected by the reaction of **4a** with $Hg(OTf)_2$ even in the presence of TMU (entry 19), and starting **4a** was recovered.

When the reaction of homoallyl alcohol **5a** with $Hg(OTf)_2$ was examined in acetonitrile at −20 °C for 5 min, *exo*-mode cyclization toward the aromatic ring took place to give *cis* **5b** and *trans* **5c** in 15% and 47% yield, respectively.[13] Reaction of *n*-butyl analogue **6a** with $Hg(OTf)_2$ under the same conditions afforded four-membered ring ether **6b** and five-membered ring ether **6c** in 17 : 83 ratio, respectively (total 9% yield), along with hydroxy mercuration product **6d** in 55% yield.

References and Notes
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