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Cyclization of dienols, polyenes, and dienyne mediated by mercuric salts: course of cyclizations controlled by stability of cationic intermediates

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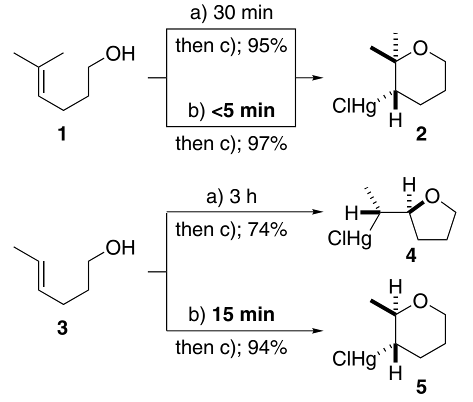
Abstract—Course of cyclization of dienols, polyenes, and dienyne mediated by mercuric salts were controlled by stability of cationic intermediates and source of mercuric salts. Reaction of (*E*)-5,9-dimethyl-4,8-decadiene-1-ol with mercuric acetate gave the intramolecular oxymercuration product, whereas one with mercuric triflate produced the olefin cyclization products.

We have demonstrated that mercuric triflate[1] mediates cyclization of isoprenoid-type polyolefins and utilized for the synthesis of a variety of polycyclic terpenoids.[2] Recently, we also reported mercuric triflate-mediated intramolecular oxymercuration of simple alkenyl alcohols.[3,4] As shown in Scheme 1, use of mercuric triflate shortened the reaction time in the Markovnikov-type cyclization of **1**. In addition, the intramolecular oxymercuration of **3** with mercuric triflate afforded **5** selectively via the 6-*endo* mode cyclization, whereas the 5-*exo* product **4** was produced with mercuric acetate.[3b,5] For substrates where both olefin cyclization and oxymercuration are possible, which process will be more favorable? To answer this question, we started to investigate reactions of 4,8-decadien-1-ol derivatives with mercuric salts.



Scheme 1. Reagents and conditions: (a) $Hg(OAc)_2$ (1.2 equiv)/MeCN, −20 °C; (b) $Hg(OTf)_2$ (1.2 equiv)/MeCN, −20 °C; (c) satd $NaHCO_3$ aq–satd NaCl aq, −20 to 0 °C.

At first reactions of (*E*)-5,9-dimethyl-4,8-decadien-1-ol (**6a**) with mercuric salts under various conditions were investigated. The results are summarized in Table 1. With mercuric acetate, the intramolecular oxymercuration proceeded slowly to produce **7** in good yield (entry 1). While addition of a small amount of trifluoromethanesulfonic acid (TfOH) shortened the reaction time (entry 2), presence of a large amount of TfOH changes the reaction course producing the olefin cyclization products **8** and **9** (entries 3 and 4). With mercuric trifluoroacetate, known to mediate the olefin cyclization,[6] the intramolecular oxymercuration was still predominant (entry 5). In contrast, mercuric triflate selectively mediated the olefin cyclization in short reaction time (entry 6). In addition, the presence of *N*,*N*,*N*′,*N*′-tetramethylurea (TMU) changed the distribution of products **8** and **9**, though the reaction rate was slowed down (entry 7). Addition of TfOH may afford equilibrium between the cyclic ether **7** and the original **6a** and also promote formation of mercuric triflate. Therefore,

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Keywords: Cyclization; Mercury and compounds.

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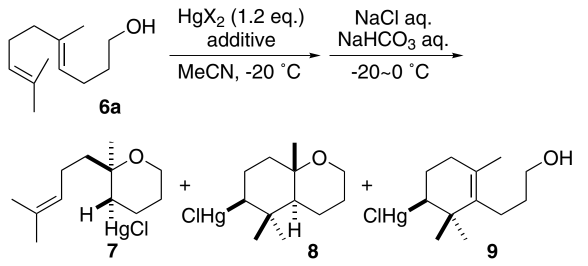
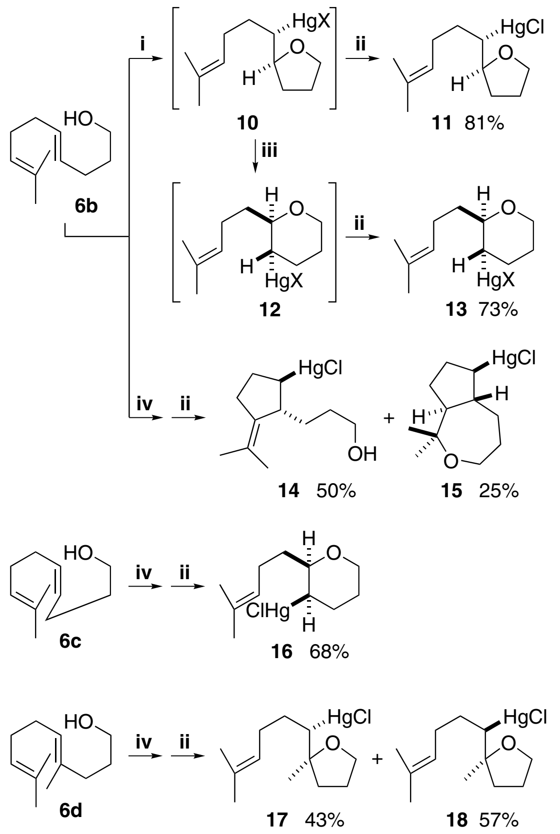
Table 1. Cyclization of **6a** mediated by various mercuric salts

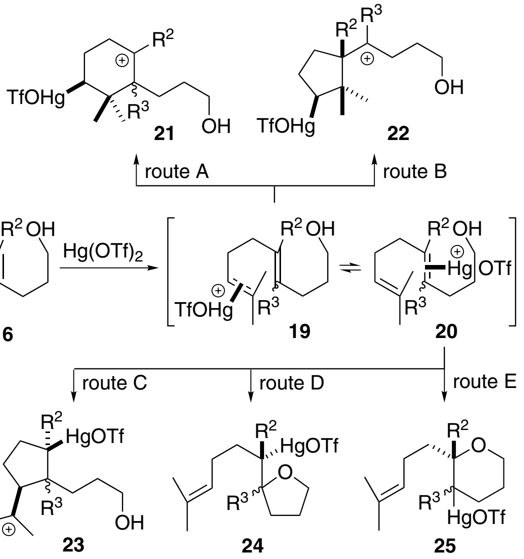


Entry	X	Additive (equiv)	Time (min)	Yield[a] (%)		
				7	8	9
1	OAc	—	1440	95		
2	OAc	TfOH (0.2)	20	91		
3	OAc	TfOH (1.2)	20	27	42	30
4	OAc	TfOH (2.4)	20	—	37	61
5	$OCOCF_3$	—	1440	71	27	—
6	OTf	—	<5	—	20	60
7	OTf	TMU (1.2)	1440	—	47	40

[a] Isolated yields.



Scheme 2. Reagents and conditions: (i) $Hg(OAc)_2$ (1.2 equiv)/MeCN, −20 °C, 1 d; (ii) $NaHCO_3$–NaCl aq, −20 to 0 °C; (iii) TfOH (0.6 equiv), −20 °C, 1.5 d; (iv) $Hg(OTf)_2$ (1.2 equiv), TMU (1.2 equiv)/MeCN, −20 °C, 1 d.

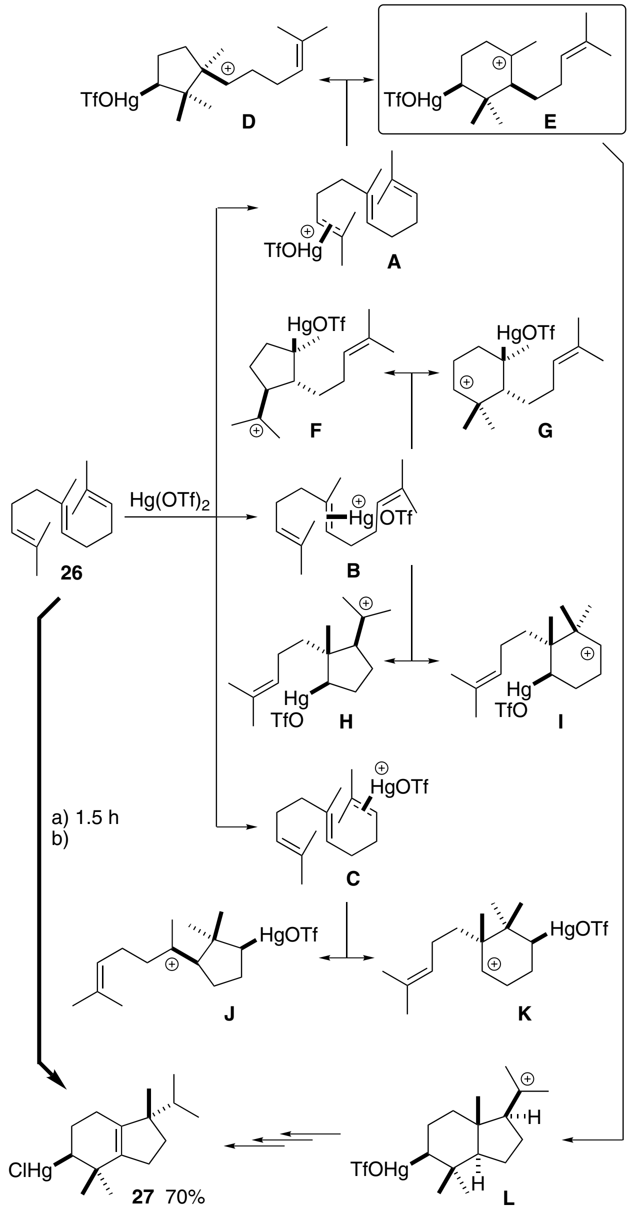


Scheme 3.

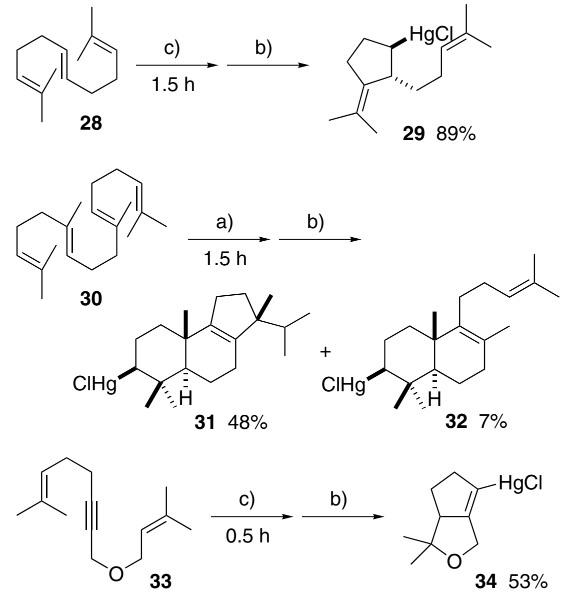
the olefin cyclization proceeded in the presence of TfOH even when mercuric acetate was used. On the other hand, addition of TMU, a weak base, prevented acid-mediated cleavage of the cyclic ether **8** and acid-mediated decomposition of **8** and **9**. Therefore, distribution of **8** and **9** was changed and yields of these products were slightly increased by the presence of TMU.

The same trend of reactivity was obtained in the reaction of **6b** with mercuric salts (Scheme 2). Mercuric acetate promoted the 5-*exo* mode oxymercuration to produce the kinetic product **11** and addition of 0.6 equiv of TfOH changed the reaction course to the 6-*endo* one as obtained previously to give the thermodynamically more stable **13**.[3b] In contrast, mercuric triflate promoted the olefin cyclization to produce the cyclopentane derivatives **14** and **15** via the 5-*endo* mode cyclization, which was disfavored process according to the Baldwin's rule.[7] When the *Z*-isomer **6c** was used as a substrate, the oxymercuration proceeded selectively to produce **16** even with mercuric triflate. The same preference of the oxymercuration over the olefin cyclization was also obtained in the cyclization of **6d**.

At quick glance, the substituent pattern of the olefins dramatically influences the reaction course. Considering reagent accessibility and electron density of the olefinic part of **6a**, the complex **19** may be produced at first and decomplexation–complexation equilibrium affords the isomer **20** (Scheme 3). Since the cyclization mediated by mercuric salts is known to obey the Markovnikov rule and produces the less strained five- or six-membered ring system, cyclization of **19** produces the cationic intermediates **21** and **22**, and **20** affords **23**–**25**. The results shown in Table 1 reveals that mercuric triflate has greater tendency to mediate olefin cyclization in preference to oxymercuration. Therefore, it is anticipated that formation of the carbocyclic compounds **21**–**23** is more prefer than that of the cyclic ethers **24** and **25** when mercuric triflate is used. In the case of **6a** (*E*-isomer; $R^2 = Me$, $R^3 = H$), the Markovnikov-type oxymerculation proceeds via **25** in the presence of mercuric acetate and trifluoroacetate, since these mercuric salts do not have enough reactivity to mediate olefin cyclization. With mercuric triflate, which is anticipated to have enough reactivity to mediate olefin cyclization, **21**–**23**



Scheme 4. Reagents and conditions: (a) $Hg(OTf)_2$ (1.2 equiv), TMU (1.2 equiv)/$MeNO_2$, −20 °C; (b) satd $NaHCO_3$–NaCl aq, −20 to 0 °C.



Scheme 5. Reagents and conditions: (a) $Hg(OTf)_2$ (1.2 equiv), TMU (1.2 equiv)/$MeNO_2$, −20 °C; (b) $NaHCO_3$–NaCl aq, −20 to 0 °C; (c) $Hg(OTf)_2$ (1.2 equiv), TMU (1.2 equiv)/CH_2Cl_2, −20 °C.

become the possible intermediates. Since **22** has less stable secondary cation and **23** has severe steric repulsion between the substituents on the five-membered ring, **21** becomes more stable intermediate than **22** and **23**, and finally **8** and **9** were produced. In the case of **6b** (*E*-isomer; $R^2 = R^3 = H$), while the kinetically controlled oxymercuration intermediate **24** is produced with less reactive mercuric acetate, the presence of TfOH affords equilibrium among **20**, **24**, and **25**, and finally the reaction is ended up with formation of the thermodynamically stable **25**.[3b] With mercuric triflate, **21** and **22** are ruled out from entries of the possible intermediates because they have less stable secondary cations. Hence, the cyclization proceeds via **23**, in which the all substituents on the five-membered ring are in *trans–trans* relationship, even the mode of cyclization was considered as unfavorable according to the Baldwin's rule.[7] On the other hand, when the reaction with mercuric triflate started from **6c** (*Z*-isomer; $R^2 = R^3 = H$), **23** becomes unstable because of the steric repulsion between the substituents on the ring, which are in the *cis–trans* relationship. Since all the possible intermediates for olefin cyclizations **21**–**23** become unstable, considering steric and electronic natures, the reaction proceeded via the intermediate **25** to produce the cyclic ether **16**. In the case of **6d** (*E*-isomer; $R^2 = H$, $R^3 = Me$), **21** is secondary cation and both **22** and **23** have severe steric repulsion between the substituents on the ring. Therefore, the Markovnikov-type oxymercuration proceeds to give **24** even with mercuric triflate. The electronic and steric stability of the cationic intermediates and the source of mercuric salts greatly affect the reaction courses.

A good and characteristic example of mercuric triflate-mediated olefin cyclization controlled by stability of the cationic intermediates is shown in Scheme 4. Triene **26** had three similar trisubstituted olefins and therefore, there is a couple of possibilities in reaction courses. Since the secondary cations are electronically less stable than the tertiary ones, formation of the intermediates **D** from the complex **A**, **G** and **I** from **B** and **K** from **C** seemed to be difficult. Among the remaining possible intermediates **E**, **F**, **H**, and **J**, **E** was the most stable considering the steric repulsion between the substituents on the rings. Thus, the cyclization of **26** proceeded smoothly and cleanly to give the bicyclic product **27** in good yield via the complex **A** and the stable cationic intermediates **E** and **L** followed by the 1,2-shift of hydrogen and methyl group.

As seen in Scheme 5, triene **28**, tetraene **30**, and dienyne **33**[8] with a number of possible courses of cyclizations, were cyclized selectively in the presence of mercuric triflate as the manner producing the electronically and sterically stable cationic intermediates.

Acknowledgements

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