INTRAMOLECULAR OXYMERCURATION OF 4-HEXEN-1-OLS: KINETIC *VS*. THERMODYNAMIC PRODUCTS REGULATED BY MERCURIC SALTS[†]

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Abstract - The rate and mode of intramolecular oxymercuration of 4-hexen-1-ol derivatives was greatly affected by mercuric salts. Mercuric acetate induced a slow reaction to give substituted tetrahydrofurans *via* 5-*exo-trans* cyclization. In contrast, 6-*endo-trans* cyclization proceeded exclusively by mercuric triflate with or without *N,N,N',N'*-tetramethylurea.

Mercuric salts mediated hydration of alkenes, so-called oxymercuration, was discovered a century ago.[1] The intramolecular reaction of alkenyl alcohol was also investigated since the beginning of the researches[2] and is now considered as one of the most convenient and promising methods to construct cyclic ethers. We have developed mercuric triflate[3] and demonstrated that it is useful not only for olefin cyclization[4] but also oxymercuration.[5,6] According to the Baldwin's rule,[7] the *exo*-mode cyclization is usually preferred over the *endo*-mode one, and therefore, cyclic ethers with smaller ring size have been produced predominantly. Now we would like to describe that the nature of mercuric salts greatly affected the rate and cyclization mode in the competition between 5-*exo*-mode and 6-*endo*-mode oxymercuration of 4-hexen-1-ol derivatives.

When the reaction of (*E*)-1,1-dibenzyl-4-hexen-1-ol (**1**) with mercuric triflate was carried out, quick reaction took place to give two diastereomers (**2**) and (**3**), while the reaction with mercuric acetate afforded **2** as a sole product (Scheme 1).[8] Since oxymercuration usually produces the *trans*-cyclization product[9] such as **2** and the *cis*-adduct is usually obtained only when strained alkenes such as norbornene

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† This paper is dedicated to Professor Shô Itô on the occasion of his 77th birthday ("Ki-Ju").

Scheme 1
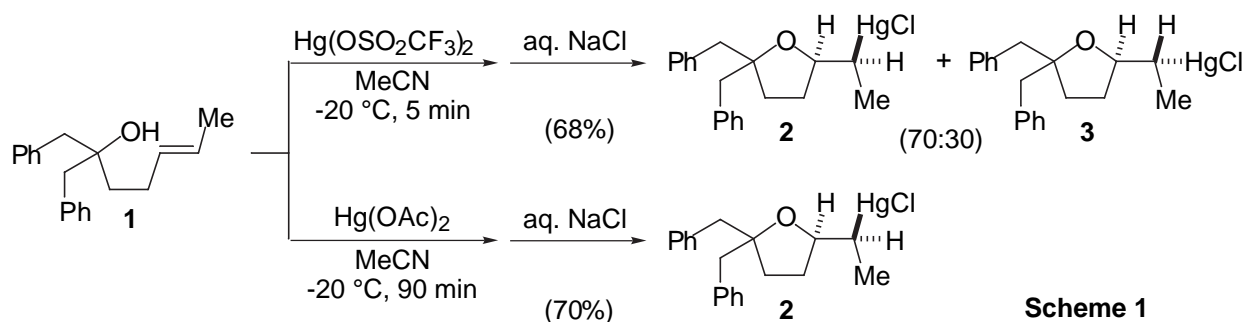
are used as substrate,[10] mercuric triflate showed somewhat different reactivity from mercuric acetate. This result prompted us to study oxymercuration of (*E*)-4-hexen-1-ol (**4**) with various mercuric salts, and the results are summarized in Table 1.
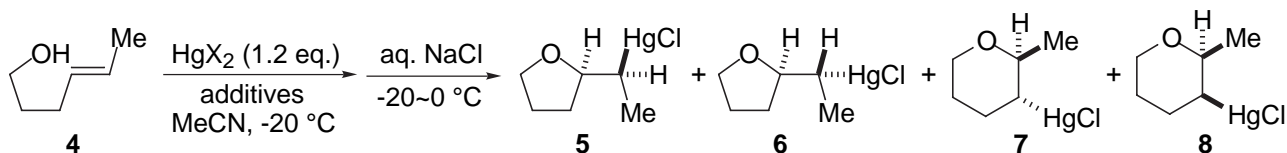

Table 1. Intramolecular oxymercuration of (*E*)-4-hexene-1-ol (**4**) with various mercuric salts.

Entry	X	Additive (eq.)	Time (min)	Total Yield (%)	Ratio of Products			
					5	**6**	**7**	**8**
1	OAc	–	180	86	92	–	8	–
2	$OCOCF_3$	–	80	86	13	–	87	–
3	OSO_2CF_3	–	5	82	–	–	88	12
4 [a]	OSO_2CF_3	–	15	94	–	–	100	–
5	OSO_2CF_3	–	1080	68 [b]	–	–	54	46
6	OSO_2CF_3	–	2040	27 [c]	–	–	51	49
9	OSO_2CF_3	CF_3SO_3H (1.2)	1440	23 [e]	–	–		
7	OSO_2CF_3	TMU [d] (1.2)	10	85	–	–	100	–
8	OSO_2CF_3	TMU [d] (2.4)	70	85	–	–	100	–
10	NO_3	–	50	84	–	–	100	–

a) The reaction was carried out at –40 °C. b) **4** was also recovered in 20% yield. c) **4** was also recovered in 54% yield. d) TMU is *N,N,N',N'*-tetramethylurea. e) **4** was also recovered in 48% yield.
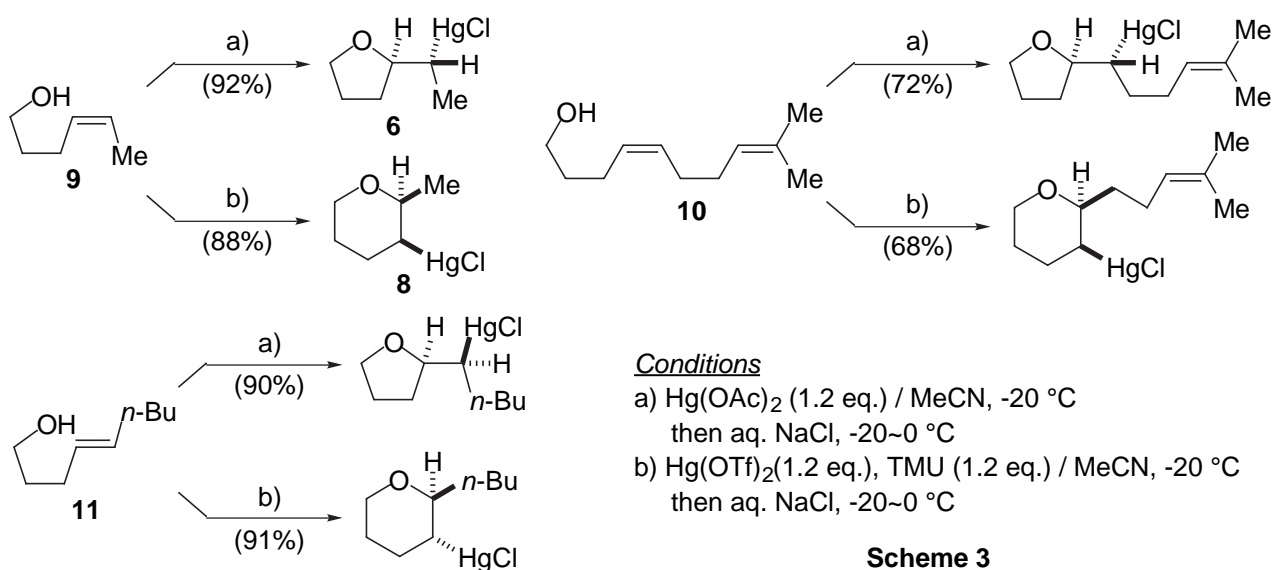
While the reaction of **4** with mercuric acetate gave 5-*exo-trans* cyclization product **5** selectively (Entry 1), mercuric trifluoroacetate afforded a mixture of **5** and 6-*endo-trans* cyclization product (**7**) (Entry 2).[8] On the other hand, the reaction with mercuric triflate was completed within a few minutes to give an 88:12 mixture of **7** and **8** at –20 °C (Entry 3) or **7** as a sole product at –40 °C (Entry 4). Although the prolonged reaction period caused increasing the formation of **8** (Entry 5), the prolonged reaction period facilitated

the reverse process returning to the starting material (**4**) (Entry 6). Since it is known that the acid treatment of β-alkoxy organomercurials afford the alkenyl alcohols,[11] the observed reverse process should be induced by the generated trifluoromethanesulfonic acid, that was the side-product of the reaction. When trifluoromethanesulfonic acid was added after the completion of the cyclization of **4** with mercuric acetate, the formation of **4**, **5'**, and **7'** was observed at the early stage, and finally **7** was solely obtained in a good yield (Scheme 2).

Scheme 2
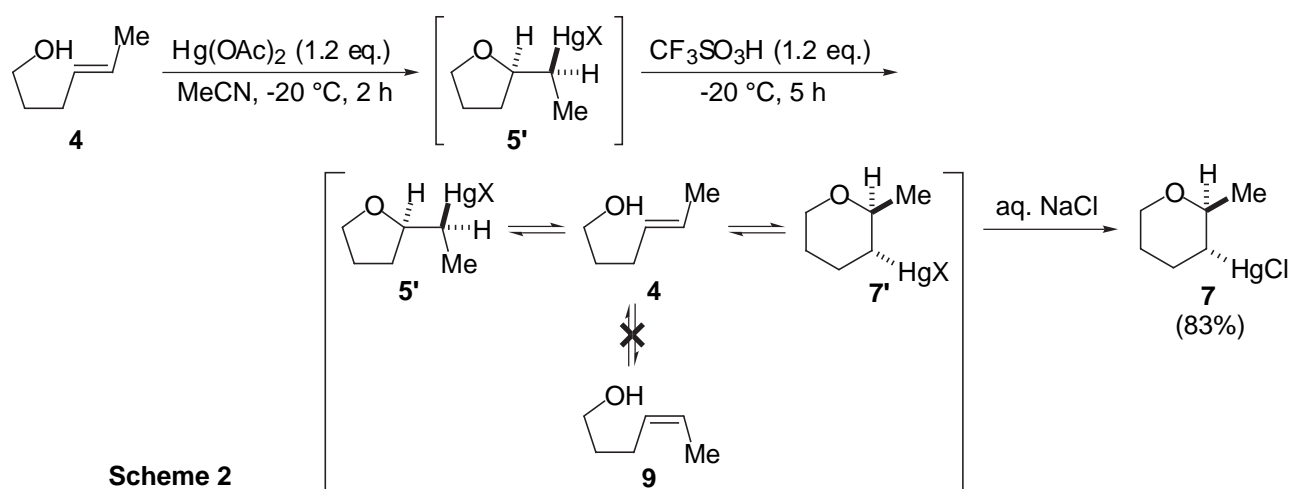
The result suggested that trifluoromethanesulfonic acid induced an equilibrium between the starting material (**4**) and the oxymercuration products (**5'**) and (**7'**), and the reaction finally ended up with the formation of thermodynamically more stable **7'**. Comparison of Entries 3-7 and Scheme 2 revealed that the acid existed in the reaction mixture influenced not only the equilibrium between **4**, **5'**, and **7'** but also the distribution of the 6-*endo*-mode cyclization products (**7**) and (**8**). Since (*Z*)-4-hexen-1-ol (**9**) was not detected at all during the reaction, **8** might be produced directly from **4** *via* the 6-*endo-cis* cyclization. Upon addition of 1.2 eq. of *N,N,N',N'*-tetramethylurea (TMU) as the acid scavenger, **7** was exclusively produced in a good yield (Entry 8), although the presence of an excess amount of TMU resulted in slowing down the rate of cyclization (Entry 9). Finally, mercuric nitrate was also effective for this reaction although the prolonged reaction period was required to complete the reaction (Entry 10). Overall, the intramolecular oxymercuration of **4** with mercuric triflate and TMU gave the thermodynamic product (**7**) *via* 6-*endo-trans* cyclization whereas the reaction with mercuric acetate led to the formation of the kinetic product (**5**) *via* 5-*exo-trans* cyclization. These two conditions can be also applied to other substrates such as **9**, **10**, and **11** (Scheme 3).[8]

Since [199]Hg has -1/2 nuclear spin value and its natural abundance is 17.0 %, the satellite peaks are observed in ^{1}H- and ^{13}C-NMR spectra of the organomercurials. Analysis of the NMR spectral data of **5**,

Scheme 3

Conditions
a) Hg(OAc)$_2$ (1.2 eq.) / MeCN, -20 °C
   then aq. NaCl, -20~0 °C
b) Hg(OTf)$_2$(1.2 eq.), TMU (1.2 eq.) / MeCN, -20 °C
   then aq. NaCl, -20~0 °C

6, **7**, **8**, and the related compounds reveals the relationship between the $^1J_{C\text{-}Hg}$ values and the structure of the organomercurials. The typical ^{13}C-NMR data of **5**, **6**, **7**, and **8** are summarized in Table 2. When the mercuric chloride is located in the side chain of the tetrahydrofuran derivatives, the $^1J_{C\text{-}Hg}$ values become over 1600 Hz. In contrast, the tentahydropyran derivatives possessing the mercury chloride moiety on the ring indicate the $^1J_{C\text{-}Hg}$ values below 1600 Hz. The values may be useful for an assignement of the oxymercuration products.
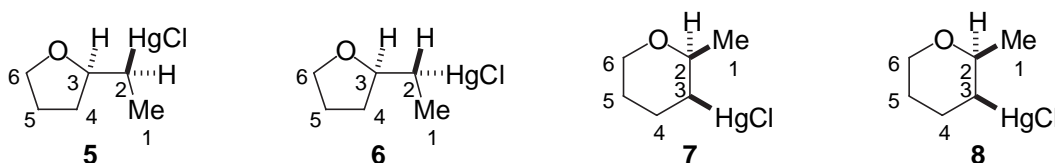

Table 2. The ^{13}C-NMR data of **5**, **6**, **7**, and **8**.

	5		6		7		8	
	ppm	$J_{C\text{-}Hg}$ (Hz)	ppm	$J_{C\text{-}Hg}$ (Hz)	ppm	$J_{C\text{-}Hg}$ (Hz)	ppm	$J_{C\text{-}Hg}$ (Hz)
C1	16.91	71.4	17.80	71.4	24.70	31.1	24.67	96.5
		($^3J_{H\text{-}Hg}$ = 276 Hz)		($^3J_{H\text{-}Hg}$ = 285 Hz)		($^4J_{H\text{-}Hg}$ = –$^{a)}$ Hz)		($^4J_{H\text{-}Hg}$ = 14.7 Hz)
C2	54.42	1623	54.90	1631	76.42	37.5	77.18	116
C3	82.99	87.9	84.12	102	58.48	1591	63.54	1570
C4	33.52	103	33.36	168	30.78	82.4	29.98	49.2
C5	25.45	–$^{a)}$	25.63	–$^{a)}$	28.24	–$^{a)}$	28.33	58.4
C6	67.62	–$^{a)}$	67.28	–$^{a)}$	67.95	–$^{a)}$	68.70	–$^{a)}$

a) The coupling constant has not been detected.

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