Ring-opening Reaction of Oxiranes, Oxetanes, and Tetrahydropyran by Mercury(II) Salts and Alkyl Halides

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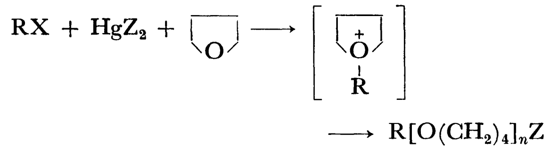
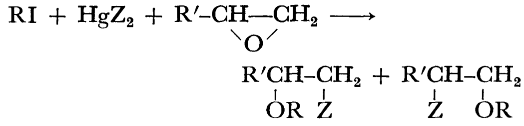
The reaction of primary and secondary alkyl halides with mercury(II) acetate in oxiranes, oxetanes, and tetrahydropyran results in ring-opening to give the corresponding alkoxyalkyl acetates. Similar reactions with mercury(II) thiocyanate in oxetanes afford alkoxyalkyl isothiocyanate and thiocyanate, $ROCH_2C(R')_2CH_2NCS$ and $ROCH_2C(R')_2CH_2SCN$, where the isomer ratios (N/S ratios) are 82—96/4—18. It is suggested that the reactions involve the initial formation of a three-, four-, or six-membered *O*-alkyloxonium ion intermediate and subsequent attack by $XHgZ_2^-$.

It has been established that primary and secondary alkyl halides react with mercury(II) thiocyanate, acetate, and chloride in tetrahydrofuran (THF) to give the THF-incorporated compounds, $R[O(CH_2)_4]_nZ$ (n=1, 2; Z=SCN, NCS, OAc, Cl). The reaction was thought to proceed through an *O*-alkyltetrahydrofuranium ion intermediate as shown in Scheme 1.[1,2] In the case of mercury(II) thiocyanate the products were the isomeric alkyl thiocyanate and isothiocyanate, the results revealing the ambident reactivity of the mercury salt.[1] It is of interest to ascertain whether similar reactions occur with three-, four-, and six-membered ring cyclic ethers and how the ambident character of thiocyanate ion is reflected in the products. The results of the reactions of several alkyl halides with several mercury(II) salts in oxiranes, oxetanes, and tetrahydropyran will be described.


(1)

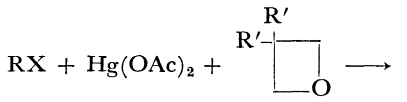
Results and Discussion



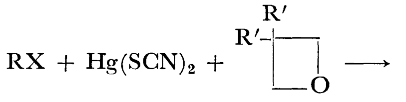
$$RI + HgZ_2 + R'CH{-}CH_2(O) \longrightarrow \underset{\mathbf{1}}{\underset{OR\ \ Z}{R'CH{-}CH_2}} + \underset{\mathbf{2}}{\underset{Z\ \ OR}{R'CH{-}CH_2}} \quad (2)$$

The reaction of alkyl iodides with mercury(II) acetate or chloride in several oxiranes afforded the isomeric ring-opening products (**1** and **2**) in a good to moderate yield (Scheme 2). In the cases of 1,2-epoxypropane (R'=Me) and 1,2-epoxybutane (R'=Et) the yields of **1** and **2** were nearly equal, while **1** was the sole product in the case of epichlorohydrine (R'=$ClCH_2$). From the reaction of cyclohexene oxide only *trans*-product was formed. Typical results are summarized in Table 1.

Treatment of alkyl halide with mercury(II) acetate in several oxetanes afforded the oxetane-incorporated compounds (**3**) as shown in Scheme 3. Such ring-opening reaction also occurred with mercury(II) thiocyanate to give the isomeric oxetane-incorporated alkoxyalkyl isothiocyanate (**4**) and thiocyanate (**5**) (Scheme 4), and the isomer ratio (N: S=82—96: 4—18) differed very much from that of the products obtained in THF solvent (N: S=*ca.* 1: 1).[1] Typical results are shown in Table 2.



$$ROCH_2C(R')_2CH_2OAc \quad (3)$$
3



$$ROCH_2C(R')_2CH_2NCS + ROCH_2C(R')_2CH_2SCN \quad (4)$$
4 **5**

The reaction in tetrahydropyran gave similar ring-opening compounds such as **6**, **7**, and **8** in low yields

TABLE 1. REACTION OF ALKYL IODIDE WITH MERCURY(II) SALT IN OXIRANE

Alkyl iodide R(5 mmol)	Mercury(II) salt (5 mmol)	Oxirane R' (10 ml)	React temp °C	React time h	Yield/%[a] of **1**+**2**	Isomer ratio **1** : **2**
Et	$Hg(OAc)_2$	Me	36	48	64	47 : 53
i-Pr	$Hg(OAc)_2$	Me	36	20	62	52 : 48
Et	$HgCl_2$	Me	36	26	19	44 : 56
Et	$Hg(OAc)_2$	Et	55—60	15	74	45 : 55
Et	$Hg(OAc)_2$	$ClCH_2$	35—40	48	50	100 : 0
Et	$Hg(OAc)_2$	$ClCH_2$	75	7	54	100 : 0
Et	$Hg(OAc)_2$	b)	70—78	5	66[c]	

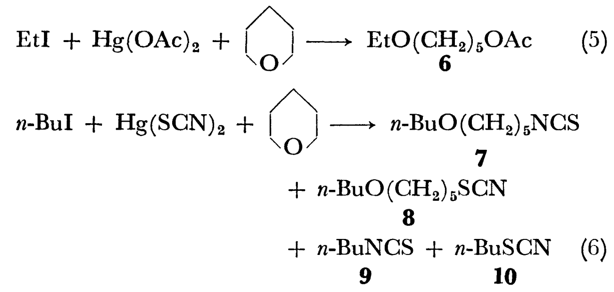
a) Determined by GLC analysis. b) Cyclohexene oxide. c) *trans*-1-Acetoxy-2-ethoxycyclohexane.

TABLE 2. REACTION OF ALKYL HALIDE WITH MERCURY(II) SALT IN OXETANE

Alkyl halide (5 mmol)	Mercury(II) salt (5 mmol)	Oxetane R′ (10 ml)	React temp/°C	React time/h	Yield/% of product and isomer ratio[a]
EtI	$Hg(OAc)_2$	H	45—48	7	**3** 51
EtI	$Hg(OAc)_2$	Me	78	5	**3** 76
i-PrI	$Hg(OAc)_2$	Me	73—77	7	**3** 53
i-PrBr	$Hg(OAc)_2$	Me	60—62	20	**3** 52
CH_2=$CHCH_2Br$	$Hg(OAc)_2$	Me	69—72	5	**3** 45
$PhCH_2Br$	$Hg(OAc)_2$	Me	67—73	5	**3** 75
EtI	$Hg(OAc)_2$	$ClCH_2$	64—69	5	**3** 70
i-PrI	$Hg(OAc)_2$	$ClCH_2$	65—70	5	**3** 66
EtI	$Hg(SCN)_2$	H	46—51	28	**4**+**5** trace
EtI	$Hg(SCN)_2$	Me	73—75	5	**4**+**5** 29 (96 : 4)
i-PrI	$Hg(SCN)_2$	Me	69—71	5	**4**+**5** 32 (96 : 4)
EtI	$Hg(SCN)_2$	$ClCH_2$	67—71	8	**4**+**5** 74 (82 : 18)
i-PrI	$Hg(SCN)_2$	$ClCH_2$	71	5	**4**+**5** 82 (85 : 15)

a) Determined by GLC analysis.

(Schemes 5 and 6). In the reaction with mercury(II) thiocyanate the main products were **9** and **10** and the yields of the tetrahydropyran-incorporated compounds (**7** and **8**) were *ca.* one-fifth of those of **9** and **10**. The



$EtI + Hg(OAc)_2 + \longrightarrow EtO(CH_2)_5OAc$ (5)

6

$n\text{-}BuI + Hg(SCN)_2 + \longrightarrow n\text{-}BuO(CH_2)_5NCS$

7

$+ n\text{-}BuO(CH_2)_5SCN$

8

$+ n\text{-}BuNCS + n\text{-}BuSCN$ (6)

9 **10**

N/S ratios of **7** and **8** was almost the same as that of the products obtained in THF solvent.

For reactions in oxiranes, the isomer ratios of **1** and **2** are consistent with the directions of ring-opening in the addition of alcohol to such oxiranes in acidic conditions,[3] where reaction proceeds through the formation of a protonated oxirane followed by either direct attack by a nucleophile or nucleophilic attack on a carbonium ion after ring-opening.[4] The basicity of oxygen of oxiranes is known to be lower than that of THF.[5] Nevertheless the presence of the *O*-alkyloxonium ion of ethylene oxide has been confirmed by ^{1}H-NMR[6] and also assumed in the case of its acid-catalyzed polymerization.[4] The following pathways are thus conceivable

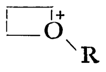
TABLE 3. BOILING POINTS AND ANALYTICAL DATA OF THE PRODUCTS

Compound	Bp °C/mmHg	Found (Calcd), % C	H	N
1+**2** (R′=Me, R=Et, Z=OAc)	59/20[a]			
1+**2** (R′=Me, R=*i*-Pr, Z=OAc)	78—83/62	59.76 (59.97)	10.20 (10.07)	
1+**2** (R′=Et, R=Et, Z=OAc)	95—97/57	59.82 (59.97)	10.32 (10.07)	
1 (R′=$ClCH_2$, R=Et, Z=OAc)	105—110/30	46.08 (46.55)	7.32 (7.25)	
trans-1-Acetoxy-2-ethoxycyclohexane	102/19[b]			
1+**2** (R′=Me, R=Et, Z=Cl)	35—40/53[c]			
3 (R′=H, R=Et)	60—70/20[d]			
3 (R′=Me, R=Et)	87—88/40	61.98 (62.04)	10.61 (10.41)	
3 (R′=Me, R=*i*-Pr)	82—83/20	63.60 (63.80)	10.64 (10.71)	
3 (R′=Me, R=CH_2=$CHCH_2$)	100—101/27	64.60 (64.49)	9.50 (9.74)	
3 (R′=Me, R=$PhCH_2$)	122—124/2	71.26 (71.16)	8.24 (8.53)	
3 (R′=$ClCH_2$, R=Et)	98—99/2	44.52 (44.46)	6.80 (6.63)	
3 (R′=$ClCH_2$, R=*i*-Pr)	104—105/2	46.84 (46.71)	7.07 (7.06)	
4+**5** (R′=Me, R=Et)	80—83/20	55.51 (55.45)	8.95 (8.73)	7.81 (8.08)
4+**5** (R′=Me, R=*i*-Pr)	95—98/17	58.01 (57.71)	9.19 (9.15)	7.55 (7.48)
4+**5** (R′=$ClCH_2$, R=Et)	112—116/2	39.59 (39.68)	5.38 (5.41)	5.50 (5.78)
4+**5** (R′=$ClCH_2$, R=*i*-Pr)	116—120/2	42.18 (43.19)	5.90 (5.90)	5.49 (5.47)
$EtOCH_2C(Me)_2CH_2Br$	85—87/60	43.01 (42.09)	7.88 (7.75)	
$EtOCH_2C(CH_2Cl)_2CH_2Br$	106—107/10	31.87 (31.85)	4.90 (4.96)	
6	55—60/6[e]			
7+**8**	105—109/2	59.60 (59.66)	9.66 (9.51)	6.71 (6.96)

a) Lit,[6] bp for **2** 77—80 °C/50 mmHg. b) Lit,[11] bp 91—92 °C/10 mmHg. c) Lit, bp for **1** 117—118 °C,[12] bp for **2** 113—115 °C.[13] d) Lit,[14] bp 174.5—175.5 °C. e) Lit,[15] bp 105 °C/14 mmHg.

(neutral or slightly acidic condition); (a) the initial formation of an *O*-alkyloxonium ion intermediate, followed by the S_N2-like attack by $XHgZ_2^-$ as has been proposed in the reaction in THF,[1] and (b) the S_N1-like reaction of the oxonium ion with $XHgZ_2^-$ (a more carbonium ion-like mechanism than (a)). Both pathways (a) and (b) occurred concurrently in the cases of 1,2-epoxypropane and 1,2-epoxybutane, while pathway (a) predominated in the case of epichlorohydrine.

The reactions in oxetanes and tetrahydropyran appear to proceed *via* an *O*-alkyloxonium ion intermediate (I, III) as in the case of the reaction in THF, since the basicity of oxygen in these cyclic ethers is known to be similar.[5] The difference of the N/S isomer ratio of the products obtained in oxetanes with that obtained in THF may reflect the stability differences between the intermediate oxonium ions. In the reaction of alkyl halides with mercury(II) thiocyanate, it was found that the N/S ratio of the isomeric products became larger as the S_N1 reactivity of the alkyl halide increased: *i.e.*, N/S=21/79 for *n*-Bu, 85/15 for *i*-Pr, and 99/1 for PhCH(Me).[7] By comparing the stability of I, II, and III, it may be seen that I is the most unstable and apt to react *via* a S_N1-like pathway, resulting in the preferred formation of alkyl isothiocyanate. The almost similar N/S ratio in the products obtained in THF and tetrahydropyran may reflect a similar stability of II and III. That the N/S ratios in the products obtained in the reactions of mercury(II) thiocyanate with 4-alkoxybutyl bromide and 5-ethoxypentyl bromide (*via* II and III respectively)[1] were almost the same supports this consideration.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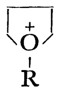
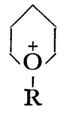

II


III

Experimental

The isomer ratios in the products were determined by GLC. The GLC analyses were conducted on a Shimadzu 4BMPF and Yanagimoto G800-T apparatus, using SE-30(1 m), DEGS (1 m), PEG-6000 (2 m), TEA (3 m), and EGSS-X (1 m) columns (carrier gas, H_2 and N_2 respectively). The ^{1}H-NMR spectra were recorded with a JEOL MH-100 (100 MHz) and a Hitachi R-24 (60 MHz) spectrometer in CCl_4, using TMS as the internal standard.

Materials. All the organic substances were used after distillation. The commercial mercury(II) salts were used without further purification. Oxetane (bp 47—48 °C),[8] 3,3-dimethyloxetane (bp 79—80 °C),[9] and 3,3-bis(chloromethyl)-oxetane (bp 80 °C/10.5 mmHg)[10] were prepared from 3-chloropropyl acetate, 2,2-dimethyl-1,3-propanediol, and 3-chloro-2,2-bis(chloromethyl)propyl acetate, respectively, by the reported methods. All compounds except **1** and **2** (R′=Me, R=Et, Z=OAc or Cl), *trans*-1-acetoxy-2-ethoxycyclohexane, **3** (R′=H, R=Et), and **6** are new and were isolated by distillation or preparartive GLC; the boiling points and analytical data of the new compounds are shown in Table 3. The ^{1}H-NMR spectra for all compounds supported each structure.

Reaction of Alkyl Halide with Mercury(II) Acetate in Oxirane or Oxetane. The following example shows a typical procedure. A suspension of $Hg(OAc)_2$(1.62 g, 5.1 mmol) and ethyl iodide (0.78 g, 5.0 mmol) in 1,2-epoxybutane (10 ml) was stirred at 55—60 °C for 15 h, and the mixture subsequently treated as described in a previous report.[1] Distillation afforded a mixture of **1** and **2** (R′=Et, R=Et, Z=OAc) which was analyzed by ^{1}H-NMR spectroscopy. The proton signals of $-CH_2OAc$ at δ 3.88—4.14 and those of $-\overset{|}{C}HOAc$ at δ 4.70—4.96 were characteristic for **1** and **2**, respectively. GLC analysis of the crude reaction mixture using triethanolamine (TEA) column (3 m) revealed the isomer ratio of **1**: **2** to be 55: 45 and that using SE-30 column (1 m) (this column did not separate the two products) with 4-ethoxybutyl acetate as the internal standard showed the combined yield of products to be 74% (3.68 mmol) based on ethyl iodide charged.

Reaction of Alkyl Iodide with Mercury(II) Thiocyanate in Oxetane. The following example shows a typical procedure. To a suspension of $Hg(SCN)_2$(1.58 g, 4.97 mmol) in 3,3-dimethyloxetane (10 ml) was added ethyl iodide (0.87 g, 5.54 mmol) at 73—75 °C and the resulting homogeneous solution stirred for 5 h. After the work-up as described above, GLC analysis of the ether extract using PEG 6000 (2 m) column with diphenyl ether as the internal standard revealed the presence of **4** and **5** (R′=Me, R=Et) (0.27 g, 1.58 mmol, 29% yield, **4**: **5**=96: 4). Analytically pure **4** and **5** were obtained by simple distillation and determined by ^{1}H-NMR spectroscopy.

Authentic samples of **4** and **5** (R′=Me, R=Et) and **4** and **5** (R′=$ClCH_2$, R=Et) for GLC analysis were prepared as follows. A mixture of ethyl iodide (4 g, 25 mmol), $HgBr_2$ (9 g, 25 mmol), and 3,3-dimethyloxetane (2.2 g, 25 mmol) in 1,2-dichloroethane (10 ml) was maintained at 70—75 °C for 4 h with stirring. After the work-up described above, distillation gave 3-ethoxy-2,2-dimethylpropyl bromide (0.8 g 4.1 mmol, 16% yield) which reacted with KSCN (25 mmol) in DMF (5 ml) at 75—80 °C for 30 h to give two products, the retention times of which were identical with those of **4** and **5** (R′=Me, R=Et) on several different columns (**4**: **5** =17: 83). A similar procedure using 3,3-bis(chloromethyl)-oxetane afforded 1-bromo-2,2-bis(chloromethyl)-3-ethoxypropane (23% isolated yield) which then reacted with KSCN to give **4** and **5** (R′=$ClCH_2$, R=Et) (**4**: **5**=1: 99).

Reaction of Alkyl Iodide with Mercury(II) Salt in Tetrahydropyran. Treatment of ethyl iodide (5 mmol) and $Hg(OAc)_2$ (5 mmol) in tetrahydropyran (10 ml) at reflux temperature for 24 h afforded **6** in 30% isolated yield. Similarly, the reaction of butyl iodide (40 mmol) with $Hg(SCN)_2$ (40 mmol) in tetrahydropyran (15 ml) at 85—90 °C for 2 h gave **7** and **8** (7% isolated yield, **7**: **8**=49: 51) and **9** and **10** (39% isolated yield, **9**: **10**=38: 62).

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