film) ν 3400, 1780, 1740 cm^{-1}] in 37% yield and **4b** [ir (liquid film) ν 3400, 1775, 1740 cm^{-1}] in 44% yield. From **4a** and **4b** the synthesis of the target PGs was carried out using essentially the same experimental conditions as described earlier by Corey, *et al.*[2] Thus **4a** or **4b** was converted into the diol by hydrolysis of the acetyl group, the two hydroxy groups were protected with dihydropyran and a catalytic amount of *p*-toluenesulfonic acid, and the lactone ring was reduced with diisobutylaluminium hydride to obtain the corresponding lactol **5a** in 100% yield from **4a** or **5b** in 97% yield from **4b**.

5a and **5b** were condensed with 4-carboxy-*n*-butylidenetriphenylphosphorane in dimethyl sulfoxide to form bis(tetrahydropyranyl) ethers (**6a** and **6b**) in 52 and 63% yield, respectively. Hydrolysis of **6a** and **6b** using AcOH–H_2O (2:1) afforded 16(*R*)-methyl-$PGF_{2\alpha}$[4] (**7a**), $[\alpha]^{21}D$ +26.7° (*c* 0.493, EtOH), in 77% yield and 16(*S*)-methyl-$PGF_{2\alpha}$[4] (**7a**), $[\alpha]^{21}D$ +45.2° (*c* 0.438, EtOH), in 75% yield.

Oxidation by chromic acid reagent and hydrolysis using AcOH–H_2O (2:1) of **6a** and **6b** afforded 16(*R*)-methyl-PGE_2[4] (**8a**), $[\alpha]^{21}D$ −56.4° (*c* 0.841, EtOH), in 56% yield and 16(*S*)-methyl-PGE_2[4] (**8b**), $[\alpha]^{21}D$ −66.9° (*c* 0.797, EtOH), in 62% yield.

Selective reduction[5] of the cis double bond of **6a** and **6b** using 5% palladium/carbon catalyst afforded **9a** and **9b** in 96 and 96% yield, respectively.

Hydrolysis of **9a** and **9b** using AcOH–H_2O (2:1) afforded 16(*R*)-methyl-$PGF_{1\alpha}$ (**10a**) in 62% yield and 16(*S*)-methyl-$PGF_{1\alpha}$ (**10b**) in 61% yield. Oxidation by chromic acid reagent and hydrolysis of **9a** and **9b** afforded 16(*R*)-methyl-PGE_1[4] (**11a**), $\alpha^{21}D$ −44.8° (*c* 0.592, EtOH), in 50% yield and 16(*S*)-methyl-PGE_1[4] (**11b**), $\alpha^{21}D$ −53.4° (*c* 0.608, EtOH), in 72% yield.

Dehydration[6] of **8a**, **8b**, **11a**, and **11b** in AcOH–H_2O (9:1) afforded respectively 16(*R*)-methyl-PGA_2 (**12a**), in 81% yield, 16(*S*)-methyl-PGA_2[4] (**12b**), $[\alpha]^{21}D$ +165.4° (*c* 0.256, EtOH), in 74% yield, 16(*R*)-methyl-PGA_1 (**13a**), in 77% yield, and 16(*S*)-methyl-PGA_1 (**13b**), in 71% yield.

In a similar manner the 16(*R*)-methyl-15-epi-PGs and 16(*S*)-methyl-15-epi-PGs were obtained from acetoxy alcohols **4'a** and **4'b**. Ir and nmr spectra of these 15-epi-PGs were essentially identical with those of 16-methyl-PGs, but R_f values of 15-epi-PGs on tlc on silica gel were slightly larger than those of the corresponding 16-methyl-PGs.

The 16(*R*)- and 16(*S*)-methyl-PGs showed much stronger PG-like biological activities than the natural PGs. For example, 16(*R*)-methyl-PGE_2 was 100–200 times more active than PGE_2 in gastric juice inhibition (rat). 16(*R*)- and 16(*S*)-methyl-15-epi-PGs also showed strong activity. It is of interest that compounds with different C-15 stereochemistry show similar bioactivity.

(3) P. A. Levene and L. A. Mikeska, *J. Biol. Chem.*, **84**, 584 (1929).

(4) Ir and nmr (at 100 MHz) spectra were in agreement with the assigned structure and will appear following these pages in the microfilm edition of this volume of the journal. Single copies may be obtained from the Business Operations Office, Books and Journals Division, American Chemical Society, 1155 Sixteenth St., N. W., Washington, D. C. 20036, by referring to code number JOC-73-1250. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche.

(5) E. J. Corey, R. Noyori, and T. K. Schaaf, *J. Amer. Chem. Soc.*, **92**, 2586 (1970).

(6) J. E. Pike, F. H. Lincoln, and W. P. Schneider, *J. Org. Chem.*, **34**, 3552 (1969).

Biological activities of these PGs will be described in a subsequent paper.

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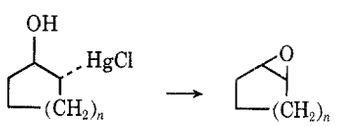
The Base-Catalyzed Decomposition of β-Hydroxyalkylmercuric Chlorides

Summary: A series of β-hydroxyalkylmercuric chlorides undergo decomposition to epoxides and ketones upon treatment with base in diglyme.

Sir: Although the addition of mercuric salts to olefins in the presence of water to give β-hydroxyalkylmercuric salts was discovered at the turn of the century, these compounds have received little consideration as synthetic intermediates.[1,2] Indeed, their best known transformation is a facile reversion to starting olefin under a variety of conditions.[1b] In view of the fact that mercury has been demonstrated to function as a leaving group in the solvolysis of alkylmercuric salts,[4] β-hydroxyalkylmercuric salts would be anticipated to undergo reactions similar to those of 1,2-halohydrins and β-hydroxy tosylates. Although early reports indicate that mercury-free products are not formed on exposure of these compounds to bases,[5] we have treated a series of β-hydroxyalkylmercuric chlorides with a variety of bases in diglyme at elevated temperature and wish to report that they undergo facile decomposition to epoxides and ketones (Table I).

In analogy to the corresponding 1,2-halohydrins,[6] *trans*-2-hydroxycyclopentylmercuric chloride (**1a**) and



1a, $n = 1$ **2a**, $n = 1$
b, $n = 2$ **b**, $n = 2$
c, $n = 3$ **c**, $n = 3$

trans-2-hydroxycyclohexylmercuric chloride (**1b**), on treatment with base, provide a convenient and high yield source of cyclopentene oxide (**2a**) and cyclohexene oxide (**2b**), respectively. The cycloheptyl derivative

(1) For reviews, see (a) N. S. Zefirov, *Russ. Chem. Rev.*, **34**, 527 (1965); (b) J. Chatt, *Chem. Rev.*, **48**, 7 (1951).

(2) Hydroxymercuration followed by demercuration with $NaBH_4$ has recently been shown to be a useful procedure for the Markovnikov hydration of olefins.[3]

(3) (a) H. C. Brown and P. Geoghegan, Jr., *J. Amer. Chem. Soc.*, **89**, 1522 (1967); (b) H. C. Brown and W. J. Hammar, *ibid.*, **89**, 1524 (1967); (c) H. C. Brown, J. H. Kawakami, and S. Ikegami, *ibid.*, **89**, 1525 (1967); (d) S. Moon and B. H. Waxman, *Chem. Commun.*, 1283 (1967).

(4) (a) F. R. Jensen and R. J. Ouellette, *J. Amer. Chem. Soc.*, **83**, 4478 (1961); (b) F. R. Jensen and R. J. Ouellette, *ibid.*, **83**, 4477 (1961).

(5) (a) K. A. Hofmann and J. Sand, *Chem. Ber.*, **33**, 1340 (1900); (b) J. Sand and K. A. Hofmann, *ibid.*, **33**, 1358 (1900); (c) W. Manchot and A. Klug, *Justus Liebigs Ann. Chem.*, **420**, 170 (1920).

(6) (a) L. Goodman, A. Benitez, and B. R. Baker, *J. Amer. Chem. Soc.*, **80**, 1680 (1958); (b) A. E. Osterberg, "Organic Syntheses," Collect. Vol I, Wiley, New York, N. Y., 1941, p 185.

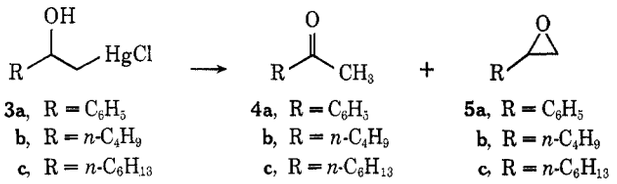
TABLE I

DECOMPOSITION OF REPRESENTATIVE β-HYDROXYALKYLMERCURIC CHLORIDES WITH VARIOUS BASES IN DIGLYME[a]

Hydroxymercurial	Base[b]	Temp, °C	Time, hr	Product yield, %[c] Epoxide	Ketone	Olefin	Mercury
1a	NaOMe	90	1	22	0	39	
			21.5	56	5		
1a	$KOCMe_3$	90	1	69	24	8	
1b	K_2CO_3[d]	120	25	33		18	23[e]
1b	NaH[f]	125	19	45		8	44[e]
1b	NaOMe[g]	120	0.75	81 (43[e])			
1b	$KOCMe_3$	117	0.75	99			88[h]
1c	NaOMe	115	0.75		<2	56	
			2.5		10	58	
			23	15	35	57	51[e]
1c	$KOCMe_3$[g]	100	19	19	70	5	
3a	$KOCMe_3$	107	6	0	31	25	
3b	NaOMe	120	2.5	0	18	39	
			23	<2	50		
3b	$KOCMe_3$	100	1.2	0	5	45	
			24.5	0	22[i]		
3c	NaOMe	120	21		40	48	

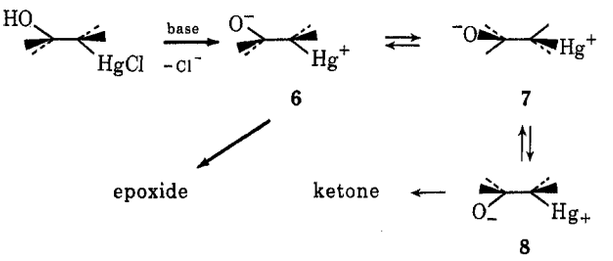
[a] The reactions were carried out under a nitrogen atmosphere. [b] A 1.1 mol ratio of base to hydroxymercurial was employed unless otherwise specified. [c] Determined by quantitative gas chromatography unless otherwise specified; structural assignments were made by comparison with authentic samples. [d] A 1.0 mol ratio of base to hydroxymercurial was employed. [e] Isolated yield. [f] A 3.1 mol ratio of base to hydroxymercurial was employed. [g] A 1.3 mol ratio of base to hydroxymercurial was employed. [h] Isolated yield after a 19-hr reaction period. [i] Based on incomplete reaction. There was a 29% recovery of **3b**.

1c,[7,8] however, affords primarily cycloheptanone, the product of a 1,2-hydride shift. The acyclic hydroxymercurials **3a**, **3b**,[7] and **3c**[7] also afforded ketone rearrangement products **4a**, **4b**, and **4c** in good yield while essentially none of the corresponding epoxides **5a**, **5b**, and **5c** were obtained. Aldehyde formation, which would result from alkyl or aryl migration, was not observed. This, therefore, provides a convenient synthetic procedure for carrying out a directed pinacol-type rearrangement under basic conditions in acyclic compounds or cycloheptyl derivatives, a transformation for which there are no satisfactory existing methods. Analogous 1,2-halohydrins, β-hydroxy tosylates, and related compounds afford epoxides under basic conditions.[9]



3a, R = C_6H_5 **4a**, R = C_6H_5 **5a**, R = C_6H_5
b, R = n-C_4H_9 **b**, R = n-C_4H_9 **b**, R = n-C_4H_9
c, R = n-C_6H_{13} **c**, R = n-C_6H_{13} **c**, R = n-C_6H_{13}

The base-catalyzed reaction of β-hydroxyalkylmercuric chlorides to give either epoxides or ketones presumably occurs through an initial proton abstraction to give a zwitterion[5a] which could adopt conformations **6**, **7**, or **8**. With the cyclopentyl and cyclohexyl derivatives **1a** and **1b**, the rigidity of the ring system permits the resulting zwitterion to exist in conformations **6** or **7** but not **8**. The trans relation of oxygen and mercury in **6** would permit displacement of mercury by oxygen and result in epoxide formation. The cycloheptyl ring system, however, is sufficiently flexible to adopt conformation **8**. The electrostatic interaction between the charged oxygen and mercury atoms would be anticipated to render this conformation more stable than **6** or **7**, where it is permitted by steric and geometric considerations.[10] In conformation **8**, the substituents on the carbon bearing oxygen approach the trans relationship to mercury necessary for the observed rearrangements.[11]



Some dehydroxymercuration was also observed in each of the reactions examined. Olefin formation was very rapid in comparison to rearrangement and epoxide formation. This side reaction could be suppressed, however, by proper selection of base. The sterically hindered base potassium *tert*-butoxide was found to be most satisfactory for this purpose.

(7) Satisfactory C and H analyses were obtained for all new compounds.

(8) The stereochemistry of **1c** is assumed on the basis of a normal trans addition to the double bond of cycloheptene.[1a]

(9) (a) A. Rosowsky in "Heterocyclic Compounds with Three- and Four-Membered Rings," part 1, A. Weissberger, Ed., Interscience, New York, N. Y., 1964, pp 1–523; (b) S. Winstein and R. B. Henderson, *Heterocycl. Compounds*, **I**, 1 (1950).

(10) Indeed, some covalent bond character would be expected between oxygen and mercury.

(11) The absence of aldehyde formation suggests that rearrangement of an intermediate epoxide is not responsible for the observed ketones.[9] This unusual type of epoxide isomerization is, however, catalyzed by dicobalt octacarbonyl.[12]

(12) J. L. Eisenmann, *J. Org. Chem.*, **27**, 2706 (1962).

(13) National Science Foundation Undergraduate Research Participant, 1972.

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