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DIASTEREOSELECTIVE DEOXYMERCURATION IN ACYCLIC SYSTEM. A REMARKABLE ASSISTANCE BY THE NEIGHBORING CARBONATE GROUP

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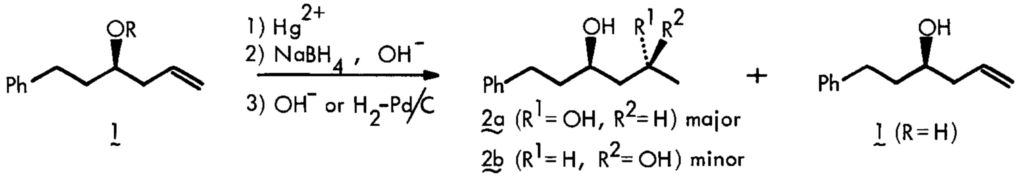
Summary: Deoxymercuration of acyclic 4-t-butoxycarbonyloxy-2-hydroxyalkylmercuric iodides was found to be much more facile for the syn isomer than for the anti isomer.

Directing effects on oxymercurations by a pre-existing chiral center or a functional group in neighborhood leading to diastereoselective oxymercurations have been well documented.[1)] Such an effect on deoxymercuration, however, seemed very small[2)] though little has been studied. We disclose herein a first example of a remarkably large effect in this context. The rate of deoxymercuration of acyclic 4-alkoxycarbonyloxy-2-hydroxyalkyl mercurials is highly dependent on the relative stereochemistry of the two asymmetric centers C_2 and C_4: the neighboring carbonate group in the syn isomer accelerates its deoxymercuration effectively, but not in the anti isomer.

In connection with our studies on developing new methods for the stereoselective functionalization of acyclic olefinic alcohols,[3)] we examined the oxymercuration [$Hg(OCOCF_3)_2$/THF or $Hg(OAc)_2$/ aq THF] of acyclic homoallylic alcohol and its O-protected derivatives (1). After reductive demercuration with alkaline $NaBH_4$,[4)] most of the derivatives [1 : R=H, CO_2t-Bu (t-BOC), $CONH_2$, COPh, $COCF_3$, $COCCl_3$, $COCHCl_2$, CH_2Ph] showed low to moderate anti selectivity (2a : 2b = 1.5 : 1 ~ 6 : 1), which has never been achieved by iodo-functionalization of 1 (R=CO_2^-, t-BOC, $CONH_2$).[3a,5)] This oxymercuration-demercuration procedure, however, suffered from the unsatisfactory yield of 2, and the diastereomer ratio fluctuated considerably in each experiment. It suggested that a deoxymercuration occurred during the reductive demercuration[4)] and that the diastereomers of the oxymercuration products had a different deoxymercuration rate.[2)]



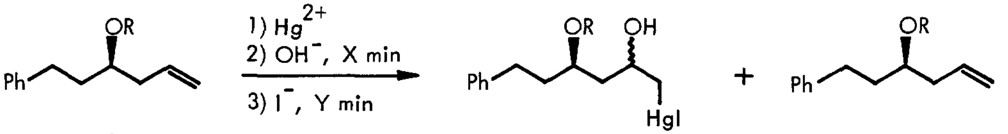
1

2a (R^1= OH, R^2= H) major
2b (R^1= H, R^2= OH) minor

1 (R=H)

Therefore, we focused our attention to find conditions to achieve the highest diastereoselectivity using 1 (R=t-BOC). After some preliminary experiments, we found that aqueous KI[6)] in alkaline media accelerated the deoxymercuration of syn oxymercurial (Table). Entries 2 and 3 in Table disclose the effect of alkali: ca. 30% of oxymercurials reverts to olefins immediately without appreciable difference

Table. Oxymercuration-deoxymercuration of 1-phenyl-5-hexen-3-ol t-butylcarbonate (1: R=t-BOC).



1
(R=t-BOC)

3a : 2α-OH (anti)
3b : 2β-OH (syn)
(R=t-BOC and R=H)

1
(R=t-BOC and R=H)

Entry[a]	aq NaOH X min	aq KI Y min	3, Isolated Yield, % R=t-BOC	R=H	Ratio 3a:3b (R=t-BOC)	1, Isolated Yield, % R=t-BOC	R=H
1	<0.1[b]	<0.1[c]	78	1	60 : 40	4	11
2	5	<0.1[c]	56	0	70 : 30	19	16
3	22	<0.1[c]	41	16	60 : 40	16	14
4	1	17	35	6	97 : 3	11	16
5	3	17	36	4	98 : 2	18	38
6	5	17	37	6	>99 : 1	11	37
7	5	0.5	46	0	74 : 26	11	18
8	5	4	36	4	98 : 2	16	31
9	5	9	36	5	>99 : 1	11	35
10	5	30	30	5	>99 : 1	10	31
11	---	<1	0	0	----	95	0

a) The standard procedure: After 1 (R=t-BOC, 0.35 mmol) was stirred at room temperature for 22 min with Hg(OCOCF$_3$)$_2$ (2.2 eq.) in dry THF (2.4 ml), the reaction mixture was cooled to 0°C, and treated successively with 2.75 M NaOH (2 ml added dropwise in 20 sec.) for X min and saturated aq. KI (4 ml added dropwise in 40 sec.) for Y min. Dilution with water and extraction with CHCl$_3$ afforded the mixture of fairly stable iodomercurials (3: R=t-BOC[7] and R=H) and the olefins (1: R=t-BOC and R=H), which were separated by SiO$_2$ chromatography. The 3a: 3b ratio (R=t-BOC) was determined by HPLC on the corresponding epoxides [(*i*) I$_2$ CHCl$_3$; (*ii*) NaOH aq. THF] respectively.[8]

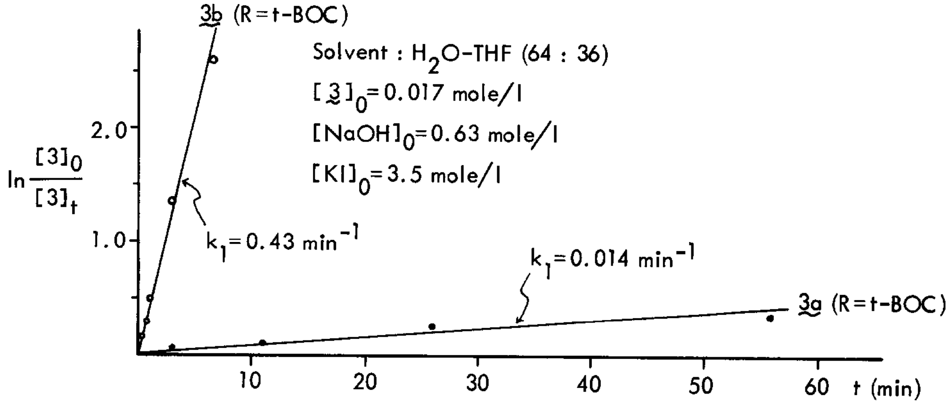
b) Aq. KI solution was added immediately after the addition of aq. NaOH completed.

c) Worked up immediately after the addition of aq. KI completed.

in rate between diastereoisomers; prolonged contact with alkali has little effect both on yield and ratio. However, when the contact with aq. KI is lengthened (Entries 4-6), the ratio changes rapidly in favor of anti isomer irrespective of the contact time with alkali (X min), at the expense of 3 (R=t-BOC). Entries 6-10 demonstrate (1) how rapid the deoxymercuration of the syn isomer is, and that (2) the process is likely associated with hydrolysis of t-BOC group. Aqueous KI in neutral media induced instantaneous and complete deoxymercuration without hydrolysis (Entry 11).

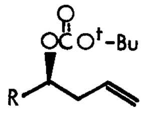
These findings suggested that the β-hydroxy mercuric iodide species 3 (R=t-BOC), rather than alkylmercuric trifluoroacetate or hydroxide, were responsible for the diastereoselective deoxymercuration. This was confirmed by the reactions of the chromatographically isolated **3a** and **3b** (R=t-BOC). Each isomer was treated with a mixture of excess KI and NaOH in aqueous THF at 0°C. The progress of the decomposition was followed by HPLC using internal standard(triphenylcarbinol). As shown in Figure, the reactions were found to be 1st-order for ca. 80% conversion and the pseudo-first-order[9)] rate constant k_1 was obtained. Apparently, the syn isomer **3b** decomposed 30 times faster than the anti isomer **3a** under the conditions.

Fig. The rate of deoxymercuration of **3a** and **3b** (R=t-BOC) with alkaline KI at 0°C.



Oxymercuration products of a variety of homoallylic t-butylcarbonates **4** (R=CH_2Ph, Ph, n-C_4H_9, i-C_3H_7, t-C_4H_9) also underwent the same diastereoselective deoxymercuration, though the reaction rate varied with the structure of substituent R to a certain extent.

In order to clarify the effect of alkali and iodide, the 1 : 1 mixture of the mercuric iodide **3a** and **3b** (R=t-BOC) was treated with KI and NaOH separately. The treatment of the mixture with KI (55 eq, 0°C, 1 h) in aqueous THF yielded the olefinic carbonate **1** (R=t-BOC) in 16% yield besides 84% of the recovered mixture, the diastereomer ratio of which remained the same, and no alcohol **1** (R=OH) was detected. Alkali (2.5 N NaOH, 18 eq, 0°C, 1 h),[10)] however, induced a faster decomposition to afford the olefinic alcohol **1** (R=H, 38%) along with the recovered **3** (49%) and the olefinic t-butylcarbonate **1** (R=t-BOC, 12%); the ratio of recovered **3a** and **3b** changed to 5.3 : 1. These experiments clearly indicate that (1) the iodide ion alone decomposes the mixture in a non-selective manner, and (2) for the syn-selective deoxymercuration alkali is needed in addition to iodide ion already present, and (3) the reaction is accompanied by the hydrolysis of the carbonate group.

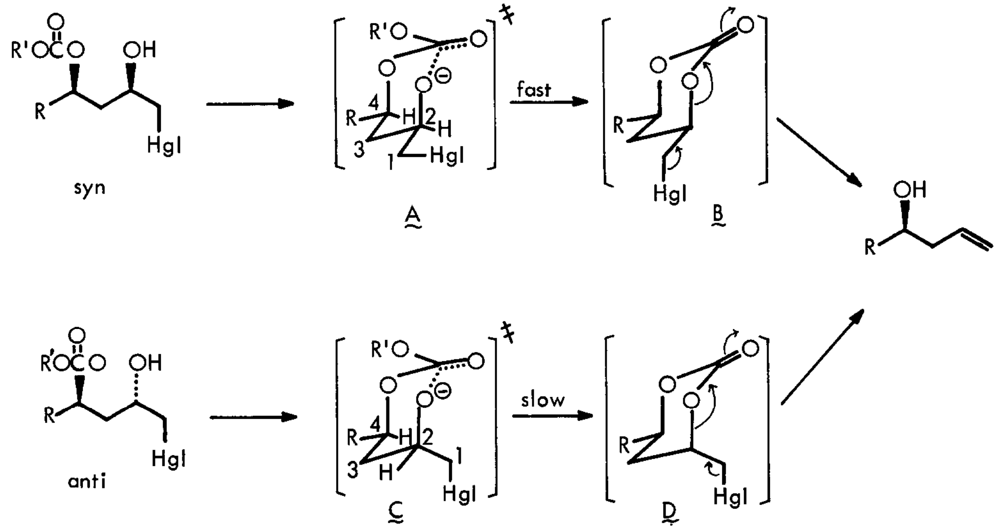


4

The enhancement of deoxymercuration of β-hydroxyalkylmercuric iodides under the alkaline conditions can be rationalized by the intramolecular participation of the carbonate group. Additional several experiments support this speculation. The oxymercuration products of the methyl carbonate **1** (R=

CO$_2$Me)[11] exhibited a similar and faster decomposition than the t-butylcarbonate, but those of acetate 1 (R=OAc)[11] as well as benzyl ether 1 (R=CH$_2$Ph) did not show any time-dependent selectivity change.

Therefore, we postulate a formation of the cyclic carbonate intermediate B through the rate-determining transition state A for the alkali-accelerating decomposition of the syn mercuric iodide; the slower decomposition of the anti isomer could be rationalized by a higher energy of its transition state C possibly due to an unfavorable gauche interaction between C$_2$-C$_1$ and C$_3$-C$_4$ bonds.



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7) Satisfactory microanalytical and spectroscopic data were obtained.

8) The ratios remained virtually the same after their conversion to the corresponding epoxides and diols (2), as long as the sequence was followed quickly.

9) When the concentrations of KI and NaOH were reduced, the reactions were retarded.

10) Under this alkaline condition, a direct hydrolysis of the t-butylcarbonate group of 1 (R=t-BOC) was not detected.

11) Milder conditions [0.5 M NaOH (2.5 eq., 5 min) and 1 M KI (6 eq., Y min)] were used because under the alkaline conditions applied to 1 (R=t-BOC) the methylcarbonate (or acetate) group of oxymercurated products was directly hydrolyzed before undergoing the diastereoselective deoxymercuration.

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