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MECHANISMS OF TRANSOXYMERCURATION REACTIONS

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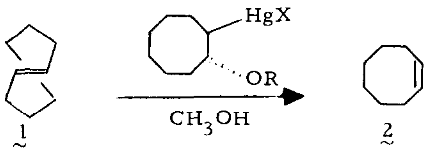
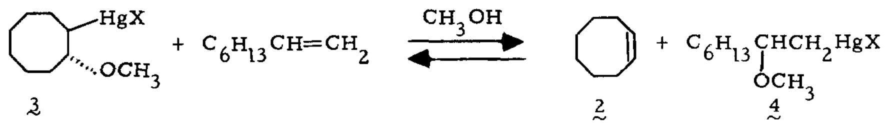
It has recently been reported[2] that addition of an equimolar amount of norbornene to the reversible cyclohexene-mercuric trifluoroacetate system liberates cyclohexene in quantitative yield. Similarily, the *exo-cis*-acetoxymercurial derived from the relatively hindered 1, 4, 7, 7-tetramethylnorbornene has also been shown to undergo an olefin exchange reaction with norbornene.[3] The olefin exchange reaction of *trans*-2-hydroxycyclohexyl mercuric acetate with 1-methylcyclohexene was also recently carried out in an unsuccessful attempt to "trap" a mercurinium ion intermediate.[4] These data were interpreted as evidence against a rate-determining transition state for oxymercuration involving a mercurinium ion intermediate. In the above cases, the results were interpreted as a reversible deoxymercuration-oxymercuration[5] sequence involving elimination of HgX_2. The recent observation[6] of mercurinium cations by nmr spectroscopy prompts us to propose a reaction pathway for olefin exchange reactions that involves deoxymercuration induced by attack of olefin on the oxymercurial. Transoxymercuration reactions, including a novel *trans-cis* olefin isomerization, as well as alkoxy and olefin exchange reactions with oxymercurials, might proceed by three general pathways as outlined in Scheme 1. We wish to report experimental evidence pertinent to evaluating the relative significance of these pathways and their dependence upon reaction conditions. Since inception of our own work, Halpern and co-workers[7] have reported a kinetic study of the exchange of oxymercurials with various unsaturated alcohols in aqueous solution.

Our initial observation of a transoxymercuration reaction was the isomerization of the strained olefin *trans*-cyclooctene (**1**) to *cis*-cyclooctene (**2**) by the action of oxymercurials in alcohol solvent (eq. 1). This irreversible process provided us with a unique opportunity to examine olefin interactions with a variety of oxymercurials. The isomerization of **1** was



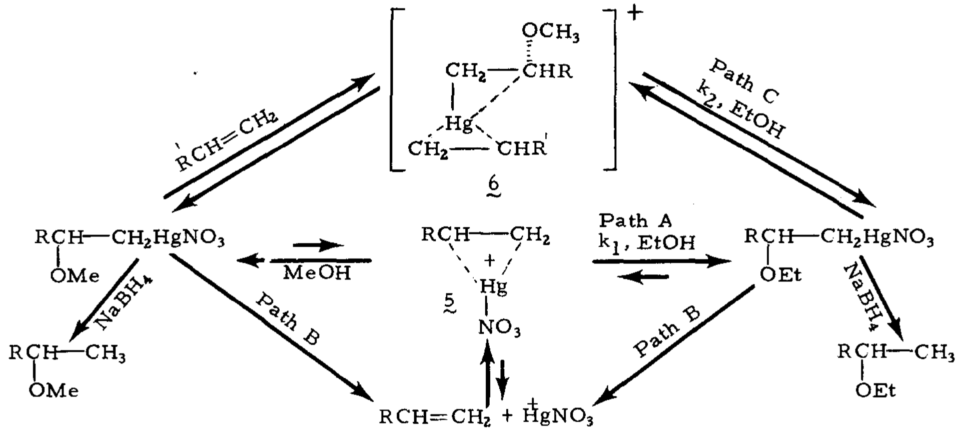
(1)

followed by gas chromatographic determination of the mixture of *cis* and *trans* olefins. The reaction exhibited psuedo-first order kinetics in methanol solvent. The rate of isomerization at 25° was found to be concentration dependent in both **1** and oxymercurial **3b** ($k_2 = 7.8 \times 10^{-2} M^{-1} sec^{-1}$). This kinetic behavior, by analogy to the oxymercuration mechanism, is consistent



a, X = ClO_4 c, X = OAc
b, X = NO_3 d, X = Cl

with a transoxymercuration mechanism involving electrophilic attack of the positively charged mercury atom of 3b on the nucleophilic olefin 1. The resulting bis-olefin-mercury cation (Scheme 1) may then eliminate 2, while the more reactive mercurinium ion of 1, regenerates the trans-oxymercurial 3b via a cis-addition of solvent alcohol. However, these data cannot distinguish between this mechanism and the formation of a transient bis-oxymercurial[7] which preceeds loss of methanol and liberation of 2. We failed to observe extensive isomerization of 1 in aprotic solvents such as THF and CH_2Cl_2 in presence of 3c or 3d. Exchange of olefin in alcohol solvent is also accompanied by exchange of the alkoxy group. Thus trans-2-acetoxycyclooctylmercuric acetate upon transoxymercuration with 1 in CH_3OH afforded the 2-methoxy compound 3c (isolated and characterized as 3d).



(Scheme 1)

The transoxymercuration reaction is a general reaction that may be catalyzed by H^+ or alkene as evidenced by the data presented in Table 1. Treatment of 3a with 1-octene in methanol results in the liberation of 91% cis-cyclooctene and the formation of a corresponding quantity of 2-methoxy-1-octylmercuric perchlorate (4) in 15 min (eq. 2). Conversely, treatment of 4a with cis-cyclooctene under identical reaction conditions liberated less than 1% of the acyclic olefin. The position of equilibrium was established by reduction with $NaBH_4$ and subsequent GC analysis of the resulting mixture of ethers and olefins.

The hydroxy and alkoxy group of oxymercurials may also be exchanged in protic solvents in the absence of added olefin. trans-2-Hydroxycyclooctylmercuric perchlorate readily affords

3a in methanol at 25° ($t_{1/2}$=35 min.). Similarily, the ethoxy group of trans-2-ethoxycyclooctylmercuric perchlorate was 94% exchanged in 1 hour in CH_3OH affording 3a. Transoxymercuration reactions occur much faster when the Hg-X bond of the oxymercurial is ionic ($X=ClO_4 > NO_3 > OAc >> Cl$). A parallel order of reactivity of mercuric salts in the oxymercuration reaction [$Hg(ClO_4)_2 > Hg(OAc)_2 >> HgCl_2$] provides support for an olefin exchange mechanism involving electrophilic addition of the oxymercurial to the carbon-carbon double bond of the exchanging olefin. The olefin exchange reaction only goes to completion when the attacking olefin catalyst is more reactive towards electrophilic mercury than the olefin being displaced. We have established the relative reactivity of olefins in the oxymercuration and olefin exchange reactions to be trans-cyclooctene~norbornene>1-octene>cyclohexene>cis-cyclooctene. A similar observation was made by Halpern.[7] However, oxymercurials derived from olefins that exhibit enhanced reactivity toward HgX_2, undergo alkoxy exchange slowly. This is best exemplified by norbornene which rapidly displaces olefins from oxymercurials, although its cis-exo-mercurial has an estimated half-life for alkoxy exchange of several months even as the ionic perchlorate.

TABLE 1

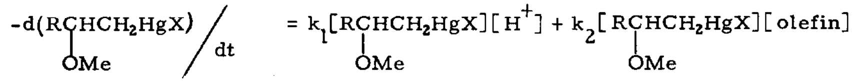
Transoxymercuration reactions in Ethanol[a]

I　　II

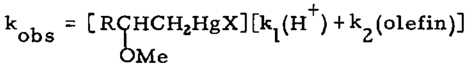
Parent Olefin	X^-	Catalyst	$k_{obs}(sec^{-1})^b$	$t_{1/2}$(hr)
Cyclohexene	ClO_4	HOAc	4×10^{-4}	0.5
	NO_3	--	3.5×10^{-5}	5.5
	NO_3	HOAc	4.3×10^{-5}	4.8
	NO_3	HNO_3	1.7×10^{-3}	0.1
	Cl	--	no reaction	
cis-Cyclooctene	NO_3	--	2.6×10^{-5}	7.4
	NO_3	HOAc	4.4×10^{-5}	4.4
Norbornene[d]	ClO_4	HOAc	very slow[e]	
	NO_3	HNO_3	2.0×10^{-7}	960.
1-Octene	ClO_4	HOAc	6.5×10^{-5}	3.0
	NO_3	--	2.2×10^{-6}	88.
	NO_3	HOAc	1.9×10^{-5}	10.
	NO_3	HNO_3	2.6×10^{-4}	0.7
	OAc	HOAc	very slow[e]	
	NO_3	1-octene	$4.2 \times 10^{-3} M^{-1} sec^{-1}$	0.4[f]

a) Reactions were at 25°C with acid and mercurial concentration = 0.1M; b) Rate constants are an average of at least two experiments that agree within 10%; c)No detectable exchange after three weeks; d) Adduct stereochemistry is cis and exo; e) 1-2% after two weeks; f) Calculated $t_{1/2}$ at 0.1M 1-octene.

Our results suggest that alkoxy exchange and olefin exchange proceed by different pathways (Scheme 1). The methoxymercurial may be in equilibrium with the mercurinium ion 5 which is kinetically indistinguishable from the equilibrium between 5 and the olefin from which it was derived. Ethanolysis of 5 effects the alkoxy exchange (Path A). Alternatively, transoxymercuration may be achieved by deoxymercuration induced by olefin arising from equilibrium with **5** (Path B) or by added olefin catalyst (Path C). This overall reaction exhibited pseudo-first order kinetic behavior since the olefin, H^+ and ROH concentrations were essentially constant for each experiment. The equilibrium constant for the oxymercuration reaction with ionic mercuric salts lies far in the side of the oxymercurial ($K_{eq} = 10^4 - 10^7$)[7] even in strongly acid solution. More importantly, transoxymercuration reactions are much more facile with ionic ligands on the oxymercurial, while deoxymercuration reactions are only observed with mercuri halides.[8] These data would tend to exclude Path B and are consistent with an alkoxy exchange reaction that proceeds largely *via* a mercurinium ion



$$-d(\text{R}\underset{\text{OMe}}{\text{C}}\text{HCH}_2\text{HgX})/dt = k_1[\text{R}\underset{\text{OMe}}{\text{C}}\text{HCH}_2\text{HgX}][H^+] + k_2[\text{R}\underset{\text{OMe}}{\text{C}}\text{HCH}_2\text{HgX}][\text{olefin}]$$



$$k_{obs} = [\text{R}\underset{\text{OMe}}{\text{C}}\text{HCH}_2\text{HgX}][k_1(H^+) + k_2(\text{olefin})]$$

intermediate in the absence of olefin catalysis (Path A). However, when the ratio of olefin catalyst to oxymercurial exceeds 0.1, k_2 is several orders of magnitude greater than k_1 and Path C is dominate.

These data provide a rational explanation for the failure of Whitham and co-workers[4] to "trap" a mercurinium ion[6] intermediate. Moreover, the failure to include Path C in the reaction scheme for reversible oxymercuration reactions explains the observed "contra-thermodynamic" kinetic preference reported by these authors since the rate constant for olefin exchange k_2, is several orders of magnitude greater than the rate of alkoxy exchange, k_1. Thus the major pathway for olefin exchange is *not* a reversible deoxymercuration sequence. We propose a mechanism involving the reversible rate determining formation of the *bis*-olefin mercury cation **6**.

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