Equilibrium Control in Oxymercuration: Attempt to "Trap" a Mercurinium Ion

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Summary In the presence of catalytic quantities of mineral acid the oxymercuration of olefins is a thermodynamically controlled process, equilibration occurring by reversible oxymercuration–deoxymercuration, and at least for the system studied, mercurinium ions are not kinetically important intermediates in oxymercuration.

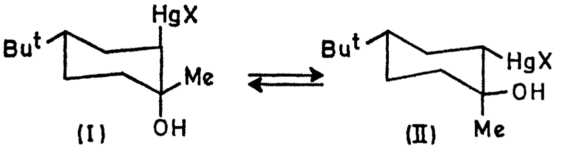
THE oxymercuration of olefins under neutral conditions is a kinetically controlled process and the stereochemistry of the adducts is determined by the stereoelectronic constraint for an antiperiplanar addition of mercuric species and solvent. Thus we find (see Table) that hydroxymercuration–reduction[1] of 4-t-butylcyclohexene gives axial alcohols almost exclusively. A more synthetically useful example is provided by 1-methyl-4-t-butylcyclohexene as substrate, where 99% of the alcohol product is the axial tertiary alcohol.

Olefin hydroxymercuration under neutral and acidic conditions

Olefin	Conditions (at 20°)	Products[a]			
		cis-4-,	*trans*-4-,	*cis*-3-,	*trans*-3-t-Butylcyclohexanol
4-t-Butylcyclohexene	50% aq. THF (1 h)	47	—[b]	—[b]	53
	3% $HClO_4$ in 50% aq THF (1 h) ..	6	43	46	5
		cis-1-,	*trans*-1-Methyl-4-t-butylcyclohexanol[c]		
1-Methyl-4-t-butylcyclohexene	50% aq. THF (30 min.)	1·2	98·8		
	0·2% H_2SO_4 in 50% aq. THF (20 h)[d]	73	27		

[a] Products are quoted as % total alcohols after $NaBH_4$ reduction.
[b] <1% Equatorial alcohols.
[c] Configurational designation refers to relation of methyl to t-butyl.
[d] Shorter reaction time gave incomplete equilibration.

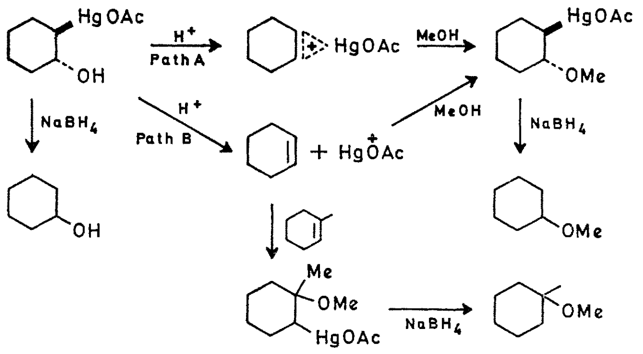
In the presence of sulphuric or perchloric acid we find that the reaction becomes subject to equilibrium control, even though the overall equilibrium is still in favour of adduct (see Table). Thus the alcohol products from 4-t-butylcyclohexene are now a mixture of epimeric 3- and 4-t-butylcyclohexanols in which the equatorial alcohols predominate. The ratio equatorial alcohols/axial alcohols (8·1) corresponds roughly to an equilibrium determined by the conformational preference for an hydroxy-group.[2]



(I) (II)

1-Methyl-4-t-butylcyclohexene gives a mixture of 4-t-butyl-1-methylcyclohexanols containing a predominance of the equatorial alcohol.†

The reversible nature of oxymercuration under acidic conditions is readily demonstrated by the rapid methanolysis of a hydroxymercurial. Thus *trans*-2-hydroxycyclohexylmercuric acetate is converted into the methoxymercurial, monitored by reduction to methoxycyclohexane, on treatment with methanol containing sulphuric acid (0·1%) in a reaction of half-life *ca.* 40 min. at 20°. The methanolysis of a hydroxymercurial offers a possibility of trapping a mercurinium ion, the often postulated[5] intermediate in oxymercuration of olefins. We have therefore carried out the acid catalysed methanolysis of *trans*-2-hydroxycyclohexyl mercuric acetate in the presence of 1-methylcyclohexene‡ (see Scheme). If the mercurinium ion represents an important kinetic and product-determining intermediate it should be captured by solvent in the early stages of reaction to give, after borohydride reduction, methoxycyclohexane (path A). Alternatively, if methanolysis involves reversible deoxymercuration–oxymercuration then at the early stages of reaction, when 1-methylcyclohexene is in considerable excess, the product, after reduction, will be 1-methoxy-1-methylcyclohexene (path B).



SCHEME

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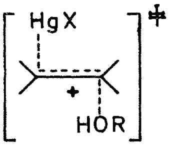
† If the ratio of the alcohols is determined by equilibration between the adducts (I) and (II) the greater stability of the latter $\Delta G^0 = -0{\cdot}5$ kcal/mole, is surprising since equilibrium between the two 1-methyl-4-t-butylcyclo-hexanols[3] favours the axial alcohol, $\Delta G^0 = -0{\cdot}2$ kcal/mole. Accepting the conformational preference for mercury as negligible,[4] we believe the observation to be evidence for a stabilising Hg · · · OH interaction in (II), $\Delta G^0 = ca.\ -0{\cdot}7$ kcal/mol.

‡ The relative reactivity of methylcyclohexene to cyclohexene under these conditions was estimated to be 1·1 by a competitive experiment.

Preliminary results on the reaction using *trans*-2-hydroxycyclohexylmercuric acetate (0·08M) at 20° in methanol containing sulphuric acid (0·1%) in the presence of 1-methylcyclohexene (0·085M) followed by borohydride reduction of samples show that after 10 min. < 1% of methoxycyclohexane is formed while 10% of 1-methoxy-1-methylcyclohexane is present. On prolonged reaction the favoured product is methoxycyclohexane, so the kinetic preference for the tertiary ether is contra-thermodynamic. We conclude, at least for the above system, that the product- and rate-determining transition state for oxymercuration (and by microscopic reversibility for deoxymercuration) is to be represented by (III) and, either mercurinium ions are not involved or they only represent a shallow 'well' in the free energy profile between reactants and the transition state (III).



(III)

An interesting contrast is provided in the chemistry of 2-acetoxycobaloximes[6] where analogous solvolyses have been shown to involve a capturable cationic intermediate.

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[5] *cf.* W. Kitching, *Organometallic Chem. Rev.*, 1968, **3**, 61; W. L. Waters and E. F. Kiefer, *J. Amer. Chem. Soc.*, 1967, **89**, 6261; R. D. Bach, *ibid.*, 1969, **91**, 1771.

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