Inorganica Chimica Acta, 27 (1978) L111–L113

Reactions of Methylmercuric Chloride with Soft Lewis Bases in Anhydrous Media

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Received February 18, 1978

The importance of methylmercury compounds as environmental problems has been well-established [1], and numerous attempts are being made to relate the toxicological actions of organomercurials to their known coordination chemistry [2, 3]. The aquomethylmercury(II) cation is a very powerful Lewis acid whose stability constants with a variety of naturally occurring oxygen-, nitrogen- and sulphur-donating ligands are very large [4–7]. Compounds containing thiol groups coordinate especially strongly and it is widely accepted that the toxicity of methylmercury compounds is to be largely attributed to their very high affinity for the SH groups of proteins [1–3], although conversion to the aquated mercury(II) complex ("inorganic" mercury), an even better Lewis acid, may also be important [2, 8].

A general reaction of organomercurials which has not, to our knowledge, been seriously considered in biological contexts is the symmetrization reaction [9], *i.e.*

$$2MeHgCl \rightleftharpoons Me_2Hg + HgCl_2 \qquad (1)$$

Normally the position of equilibrium of (1) lies well to the left. The presence of ligands which can coordinate the liberated $HgCl_2$, however, can draw the equilibrium to the right, a reaction which has been observed for a few nitrogen [9–11] and phosphorus [12] donors. It seemed possible, therefore, that certain functional groups in proteins might also induce symmetrization, a reaction which would not only generate the mercury(II) ion, but also dimethylmercury. The latter is a very weak Lewis acid which forms no known coordination compounds [5]. It is also lipid-soluble, and therefore would be expected to exhibit a mobility denied to the more electrophilic, hydrophilic methylmercury(II) and mercury(II) ions. Thus besides providing a mechanism for the formation of inorganic mercury, symmetrization could also have the insidious effect of generating dimethylmercury, which could reach parts of the body inaccessible to the other forms of mercury, but which it could it turn generate in a number of ways [9].

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In an effort to better assess the possible significance of the symmetrization reaction under various conditions, we have studied the nature of the reactions of methylmercuric chloride and nitrate with a variety of oxygen, nitrogen, sulphur and phosphorus donors in a variety of solvents. We have also initiated kinetics studies where feasible in an attempt to deduce the mechanism(s) of the symmetrization reaction.

As an analytical tool, we have used proton nuclear magnetic resonance spectroscopy to determine the nature of the products. The three equivalent protons of the methyl group give a single, sharp, easily observed line which can be used to identify even very low concentrations of methylmercury-containing species. In addition, the magnitude of the spin–spin coupling constant between the methyl protons and mercury-199 (I = ½, natural abundance 16.9%) varies greatly with the nature of the other group coordinated to the mercury, and can often be used to infer the nature of the donor atom [6, 13–15].

The results of reactions of amines with $MeHgNO_3$ in D_2O and with MeHgCl in $CDCl_3$ were somewhat disappointing. Although ethylenediamine rapidly yielded a white precipitate of a complex of mercuric chloride, as well as dimethylmercury (see also references 10, 11), other water-soluble amines formed stable complexes with the methylmercuric cation. Similar results were reported by others [6, 7, 16] while this work was in progress and, as no symmetrization was observed, it was discontinued.

Methylmercuric chloride exhibits a very high affinity for tertiary phosphines, generally reacting rapidly with displacement of chloride [12, 17, 18], *i.e.*,

$$MeHgCl + PR_3 \xrightarrow{K} [MeHgPR_3]^+ + Cl^- \qquad (2)$$

Symmetrization often follows, yielding Me_2Hg and complexes of the type $HgCl_2(PR_3)_2$, but the possible role of the cationic species is not known.

On addition of small amounts of tertiary phosphine to a solution of MeHgCl in methylene chloride, the MeHg resonance shifted upfield and J_{HgMe} decreased, the extent of change of the two parameters decreasing in the order $PEt_3 > PMe_2Ph > PMePh_2 > PPh_3$. No new resonances appeared except for those of the phosphines and, in the cases of PMe_2Ph and $PMePh_2$, the PMe resonances were shifted downfield from the free ligand positions and J_{PMe} first decreased from the value of the free ligands and then increased as the ratio $[PR_3]/[MeHgCl]$ increased from zero to unity.

For PEt_3, at least, the stability constant for the reaction with MeHgCl is expected to be very large ($\sim 10^{10}$) [19], and the n.m.r. data are consistent with rapid phosphine exchange between unreacted

TABLE I. N.m.r. Parameters of Methylmercury(II) Complexes[a].

Complex	Chemical Shifts (ppm)			Coupling Constants (Hz)				
	δ_{MeHg}[b]	δ_{MeP}[b]	δ_{P}[c]	$^{2}J_{MeHg}$	$^{2}J_{MeP}$	$^{3}J_{MePHg}$	$^{3}J_{MeHgP}$	$^{1}J_{PHg}$
MeHgCl	1.03	–	–	210	–	–	–	–
Me_2Hg	0.27	–	–	105	–	–	–	–
$[MeHgPMe_2Ph]Cl$	0.77	2.20	29.1[d]	173	11.0	38	6.0	2543[d]
$[MeHgPEt_3]Cl$	0.72	–	–	167	–	–	5.5	–
$[MeHgPMe_3]Cl$[e]	0.72	1.82	27.4	171	11.5	44	6.0	1875

[a] In CH_2Cl_2 unless otherwise stated. [b] Ppm from TMS. [c] Ppm from ext. H_3PO_4. [d] In acetone. [e] Ref. 18.

MeHgCl and $[MeHgPR_3]Cl$. On cooling solutions of MeHgCl containing less than one molar equivalent of PEt_3 or PMe_2Ph, exchange between MeHgCl and $[MeHgPR_3]Cl$ was sufficiently slowed that the two components could be observed, MeHg coalescence temperatures being ~ –50 °C, and ~ –75 °C for the PEt_3 and PMe_2Ph systems, respectively. In contrast, the coalescence temperature of the PPh_3 system is less than –75 °C, while that of the PMe_3 system appears to be well above –70 °C [18]. N.m.r. data for MeHgCl, Me_2Hg and the cationic complexes, $[MeHgPR_3]Cl$, are listed in Table I. There is some correlation between the expected donor properties of the ligand *trans* to the methyl group and both the lability of the system and J_{MeHg}. Furthermore, since the n.m.r. parameters of the complexes $[MeHgPR_3]Cl$ (Table I) are very similar, the changes in the MeHg parameters as a function of relative phosphine concentration, noted above, probably suggest that values of the formation constants, K, also decrease in the order $PEt_3 > PMe_2Ph > PMePh > PPh_3$.

The apparently peculiar variation of J_{PMe} occurs because J_{PMe} changes sign on going from the free to the coordinated phosphine [18]. In the presence of large excesses of the phosphine the room temperature MeHg spectral parameters approximate those of the cationic complexes with the exception that the MeHg-P coupling is not observed because of exchange.

On standing at room temperature, CH_2Cl_2 solutions containing MeHgCl and tertiary phosphines (1:1 molar ratio) slowly generate Me_2Hg, as indicated by the n.m.r. spectra. The Me_2Hg formed does not take part in rapid exchange reactions with any of the other components in the solutions, and its rate of formation can be measured by integrating the spectra.

Preliminary studies of the initial rates under these conditions indicated that the relative rates decreased in the order $PEt_3 > PMe_2Ph > PMePh_2 > PPh_3$, the expected order of decreasing nucleophilicity of the tertiary phosphines and consistent with the equilibrium studies discussed above. In contrast to the situation with ethylenediamine, where the equilibrium may be shifted by the low solubility of one of the products, the phosphine systems are all homogeneous; thus the observed trend is to be directly attributed to electronic effects.

Detailed kinetics studies were hampered, however, by the observation that while rates increased as the ratio $[PR_3]/[MeHgCl]$ increased to unity, they decreased above that ratio and were too slow to be measured accurately at ratios of 10:1. In contrast, the symmetrization reaction of MeHgCl in presence of 10–20 fold excesses of PMe_2Ph in DMSO-d_6 at 70 °C did proceed of reasonable rates, and a rate law of the type

$$\frac{-d[MeHgCl]}{dt} = k[MeHgCl]^2[PMe_2Ph]^{1/2} \qquad (3)$$

was obtained. Careful monitoring of the reaction using ^{1}H and ^{31}P n.m.r. spectroscopy demonstrated a preliminary equilibrium as in (2) and an overall reaction as in (1), with the $HgCl_2$ present as the complex $HgCl_2(PMe_2Ph)_2$ (δ_P = 11.8 ppm, $^{1}J_{PHg}$ = 5624 Hz, as compared with δ12.95, $^{1}J_{PHg}$ = 550 Hz for $HgCl_2(PMe_3)_2$ [18]; $^{1}J_{PHg}$ would be expected to be much larger for a 1:1 complex with PMe_2Ph [21], much smaller for a 3:1 or 4:1 complex [18]). While the second order term in MeHgCl is not unexpected [9], the half order term in tertiary phosphine defies rationalization at present and unfortunately only adds to confusion in the literature about the role of ligands as symmetrization agents [20].

Thiols, such as EtSH, $HSCH_2CH_2SH$ and BAL, exhibited little affinity for methylmercuric chloride in organic solvents. The n.m.r. spectrum of methylmercuric chloride changed very little over a wide temperature range of the addition of a thiol, although the direction of the change was that expected for partial replacement of chlorine by sulfur [7, 16]. The spectra of the thiols exhibited a more significant change at room temperature, loss of spin–spin coupling between the SH and CH protons. On cooling, however, the spectra became essentially those of the thiols in the absence of methylmercuric chloride. The spectral changes can be interpreted in terms of very slight coordination of thiol to mercury, exchange be-

tween free and coordinated thiol being rapid on the n.m.r. time scale. Coordination would be expected to increase the acidity of the SH group, and the loss of spin–spin coupling between the SH group and the rest of the thiol molecule indicates an exchange of this proton which is faster than occurs in the free ligand.

No symmetrization was observed with the thiols after standing several weeks. More surprising, however, was the apparently low affinity of MeHgCl for the thiols, which seemed to be in direct contrast with commonly accepted ideas [2, 3]. The stability constant for the reaction of the methylmercury cation with chloride ion is quite large (logK = 5.25) [4], however, and chloride ion will compete with the sulphur ligand. Treatment of the equilibrium constant data as outlined in ref. 3 (especially pp. 744–750) shows that in water the equilibrium constant for (4) will only be approximately ten:

$$MeHgCl + RSH \rightleftharpoons MeHgSR + H^+ + Cl^- \qquad (4)$$

Solvation energies in other media would be quite different and could have a large effect on the position of equilibrium, which we find to be very small in solvents of low dielectric constant. A survey of the literature on the effects of treatment of animals with methylmercurials shows that distinction is rarely made between the expected chemistry of, for instance, MeHgCl and the aquo complex, $[MeHgOH_2]^+$. Our results show that the former can be much the less reactive of the two, and indeed that it may be very unreactive when in a hydrophobic environment.

Acknowledgments

We thank Queen's University, Health and Welfare Canada and the National Research Council of Canada for support of this research.

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