Direct Detection of Mercury(II)–Thio-ether Bonding in Complexes of Methionine and *S*-Methylcysteine by ^{1}H Nuclear Magnetic Resonance

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Summary Mercury(II) bonds to the sulphur atom of methionine and *S*-methylcysteine in 1M-HNO_3; at pH 9 N,O–metal bonding is favoured in complexes between methionine and mercury(II), whereas N,S–metal bonding occurs for *S*-methylcysteine.

IT is accepted that Ag^I bonds to the thio-ether groups of methionine and *S*-methylcysteine, but Hg^{II} does not,[1–3] in spite of such bonding being well-known in other ligands.[4,5] We have obtained evidence, based on the ^{1}H n.m.r. spectra of the above ligands, that Hg^{2+} does, in fact, form stable, labile complexes in which Hg^{II}–thio-ether bonding occurs.

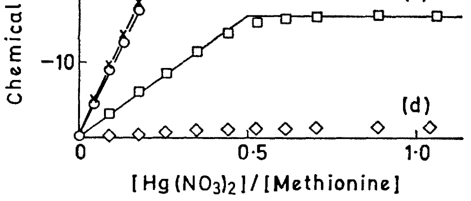


FIGURE. *Molar ratio plots for the chemical shifts of all observable protons of methionine and* $Hg(NO_3)_2$ *in 2M-nitric acid.*

The Figure shows a plot of the chemical shifts of the observable protons of methionine against the molar ratio of $Hg(NO_3)_2$ to ligand in D_2O in the presence of 1M-HNO_3. A complex of type $Hg(LH_2)_2^{4+}$ is formed, and the chemical shifts of those protons nearest the sulphur atom are preferentially displaced to low field (see Figure and Table)

Chemical shift differences between the mercury(II) complexes of methionine and S-methylcysteine and the corresponding free ligands

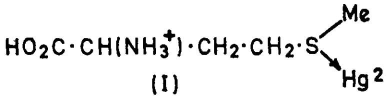
Methionine: $CH_3{\cdot}S{\cdot}CH_2{\cdot}CH_2{\cdot}CH(NH_3^+){\cdot}CO_2H = LH_2^+$ (a) (b) (c) (d)

Complex	Chemical shift differences (Hz)[a] (a)	(b)	(c)	(d)
$Hg(LH_2)_2^{4+}$	−45·8	−48·5	−16·05	−1·3
HgL_2	−3·4	−10·5	−14·8	−33·9

S-Methylcysteine: $CH_3{\cdot}S{\cdot}CH_2{\cdot}CH(NH_3^+){\cdot}CO_2H = LH_2^+$ (a) (b) (c)

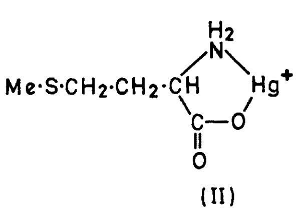
Complex	Chemical shift differences (Hz)[a] (a)	(b)	(c)
$Hg(LH_2)_2^{4+}$	−45·5	−40·2	−12·75
HgL_2	−12·5	−23·5	−35·5

[a] Difference between the chemical shift for the ligand alone, and in the form of the specified complex. A negative sign indicates a downfield shift of the peak on addition of the metal ion. The measurements were performed at 60 MHz.

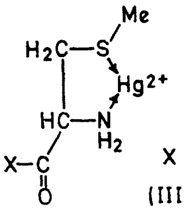


$HO_2C{\cdot}CH(NH_3^+){\cdot}CH_2{\cdot}CH_2{\cdot}S(Me) \rightarrow Hg^{2+}$

(I)



(II)



X = O⁻ or OMe

(III)

indicating that the metal bonds as in (I). *S*-Methylcysteine behaves identically.

The stability constant for the complex (I) was estimated to be $K_2 = 8{\cdot}4 \times 10^6$ l mol^{-1} $\{=[HgCl(LH_2)^{2+}]/[HgCl^+][LH_2^+]\}$ by comparison with the known value[6,7] for

$$HgCl_2 \rightleftharpoons HgCl^+ + Cl^-$$

in solution containing chloride ions where competitive complexing occurs. Data similar to those in the Figure were analysed by the method of linear plotting.[8]

On ionisation of the carboxyl and amino-groups, methionine and *S*-methylcysteine form quite different complexes with Hg^{2+}. For methionine, comparison of the spectrum with that of (I) shows the CH resonance to be displaced to low field, while the other signals move upfield. This is interpreted in terms of complex (II). This complex, (II), has been isolated in the form of bis(methioninato)mercury(II), by McAuliffe *et al.*[2] who obtained i.r. evidence for N,O–metal bonding, as indicated.

On ionisation of the amino-proton of *S*-methylcysteine, however, the chemical shifts of all three types of proton are displaced a comparable amount to low field (when allowance is made for the number of protons of each type) in the presence of Hg^{2+} (see Table) indicating a complex of type (III; $X = O^-$). *S*-Methylcysteine methyl ester (III; X = OMe) gives identical results to those of the parent acid. O–Metal bonding cannot occur for the ester, which thus affords good supporting evidence for N,S–metal bonding between mercury(II) and *S*-methylcysteine in solution. This conclusion is contrary to that of Lenz and Martell,[1] who considered that N,O–metal bonding occurred between Hg^{II} and *S*-methylcysteine on the basis of potentiometric results.

The different behaviour of methionine and *S*-methylcysteine with Hg^{2+} in alkaline solution is probably due to the ability of the latter to form a 5-membered chelate ring involving N,S–metal bonding, whereas a 6-membered ring would be required for this type of bonding in methionine.

The fact that Hg^{2+} may bond to an isolated thio-ether group is of importance in protein chemistry, as it provides an additional, and previously unknown example of a mercury(II) binding site in a protein chain.

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