trigonal-bipyramidal sites around each phosphorus. The structure of A is consistent with ^{1}H, ^{13}C, and ^{11}B NMR spectra which indicate only one environment for each respective type of nucleus. However the spectra do not absolutely rule out isomer B or a mixture of isomers since five-coordinate phosphorus compounds are often stereochemically nonrigid. Unfortunately we have not yet been able to confirm or eliminate this possibility with low-temperature NMR studies.

The ^{11}B NMR spectrum of II consists of an octet of relative intensities 1:3:1:3:3:1:3:1 which results from a quartet due to three hydrogens coupled to boron (J = 88 Hz) doubled in turn by splitting due to ^{31}P (J = 147 Hz). (The spectrum has a substantially different appearance from that of the symmetrical quintet of $(CH_3O)_3P{\cdot}BH_3$.) The assignment is confirmed by the ^{31}P spectrum which, under broad-band proton decoupling, is a symmetrical 1:1:1:1 quartet due to spin coupling with the ^{11}B nucleus (J = 149 Hz). Long-range coupling between nonadjacent phosphorus and boron atoms, if present, could not be resolved. These spectra as well as ^{1}H and ^{13}C spectra described in the Experimental Section are consistent with structures of the proposed isomers of II, assuming in the case of isomer B that a rapid exchange occurs at 35° among phosphorus coordination sites.

The high-field shift of the carbons as well as of the methyl and borane protons on formation of II from I may be an indication of increased electron density around those nuclei in II as expected for anion formation. The marked upfield shift seen in the ^{31}P spectrum probably arises from the increase in coordination number of phosphorus.[9]

Evidence indicating the presence of a phosphorus–phosphorus bond in the product comes from vibrational spectra. The characteristic stretching frequency range for P–P bonds is about 400–600 cm^{-1}.[10] For example the frequency assigned for the P–P stretch in diphosphine is 437 cm^{-1}.[11] This type of stretching vibration is expected to be ir inactive but Raman active. The Raman band at 499 cm^{-1} meets the requirements and we tentatively assign that as the P–P stretch. Other spectral assignments are made only by analogy to earlier assignments.[12-16]

Another indication sometimes used for detecting the presence of diphosphine moieties is a uv absorption near 216 nm or higher.[17] Although there are obviously many possible interferences, an aqueous solution of II gave three absorptions in this region at 275, 226, and 213 nm while I in glyme solution gave only two bands at 282 and 273 nm. Again these spectra are consistent with the presence of a P–P bond.

Although we know of no other examples of compounds with this specific type of diphosphine structure, it does not appear to violate the rules of valence. It is possible that the borane groups, in removing electron density from the phosphorus atoms, play an important role in stabilizing the dimeric anion. This may explain why no such dimers have been prepared from phosphites alone where lone-pair orbitals might interact unfavorably.

The proposed structure of II suggests that it should be possible to reoxidize the compound and recover I. When bromine and II were combined in glyme solvent, a white precipitate was formed and ^{1}H NMR of the product solution confirmed the formation of trimethyl phosphite–borane

$$Na_2[(CH_3O)_3P{\cdot}BH_3]_2 + Br_2 \rightarrow 2NaBr + 2(CH_3O)_3P{\cdot}BH_3$$

If our assessment of the structure of $Na_2[(CH_3O)_3P{\cdot}BH_3]_2$ is correct, its synthesis represents a new method for obtaining P–P linkages. We are currently investigating the reactions of other phosphine–boranes to determine whether additional examples of this type of structure can be found.

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Registry No. $Na_2[(CH_3O)_3P{\cdot}BH_3]_2$, 57325-21-0; $NaC_{10}H_8$, 3481-12-7; $(CH_3O)_3P{\cdot}BH_3$, 6867-39-6.

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Contribution from the Istituto di Chimica Generale ed
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Chloroauric Acid as Oxidant. Stereospecific Oxidation of Methionine to Methionine Sulfoxide[1]

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Gold(III) halides have been known for many years to be able to oxidize sulfides to sulfoxides, but the redox reaction has never been fully investigated, nor its potentiality widely exploited. Herrmann[2] reported many years ago that benzyl sulfide could be oxidized stoichiometrically to the corresponding sulfoxide by gold trichloride in the presence of water, the gold(III) being reduced to gold(I).[2,3] Phillips[4] reported in 1901 that gold trichloride reacted with dimethyl sulfide to give a complex of gold(I) but he did not isolate or detect dimethyl sulfoxide. Since the oxidative process is most probably consequent to the coordination of the organic sulfide to gold in a sterically controlled process, we thought that optically active products could be obtained in this way. The results obtained in the oxidation of the amino acid methionine, which contains a thioether function, by gold(III) chloride are reported in this paper.

Experimental Section

Chloroauric acid was purchased from Johnson Matthey and Co. and used without further purification. The amino acids were available from Fluka AG.; all other chemicals were reagent grade.

Optical rotation was measured with a Perkin-Elmer 141 polarimeter, and a Carlo Erba 3A27 amino acid analyzer was used to test the reaction products. The kinetics were followed spectrophotometrically with an Optica CF4R instrument equipped with a thermostated cell compartment.

Reaction of Methionine with Chloroauric Acid. In a typical experiment, the stoichiometric amount of (S)-methionine (10^{-3} mol in 10 cm^3 of water) was added under stirring to a 10-ml water solution

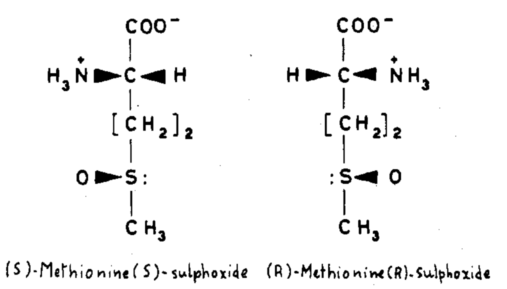

Figure 1. Absolute configurations of (*S*)-methionine (*S*)-sulfoxide and (*R*)-methionine (*R*)-sulfoxide.

of chloroauric acid (10^{-3} mol). After an initial clouding, the deep yellow solution turned clear and slowly became almost colorless. If the reaction mixture was left standing for several hours, the color turned yellow and metallic gold was deposited on the walls of the reaction vessel. The complete disappearance of the starting amino acid was verified by thin layer chromatography and with the amino acid analyzer. The methionine sulfoxide was precipitated by adding acetone–ethanol (1:1 volume ratio) to the reaction solution previously brought to pH 4. The yield was over 95% in four different experiments, mp 238°C. Found: C, 36.3; H, 6.8; N, 8.5; S, 19.3. Methionine *S*-oxide requires: C, 36.3; H, 6.7; N, 8.5; S, 19.4.

The same product (methionine *S*-oxide) was obtained when gold chloride was added in excess. In this case, the excess oxidant could be removed either by extraction with ethyl ether or by reduction with hydrazine bis(hydrochloride) and subsequent filtration.

Kinetics. The kinetics were followed by measuring the absorbance changes in the uv region of the spectrum. The chloroauric acid and the (*S*)-methionine solutions were thermostated in a water bath controlled within 0.1°C. The reaction mixture was prepared by adding a known volume of stock (*S*)-methionine solution to the solution of $[AuCl_4]^-$. All kinetic runs were carried out under pseudo-first-order conditions by the use of an excess of amino acid. In the set of runs at variable methionine concentration and constant acid, the ionic strength was determined by the concentration of perchloric acid (0.05 *M*). The set of runs at constant concentration of amino acid (6.09×10^{-3}) and variable perchloric acid was performed at $I = 0.2$ *M* by addition of lithium perchlorate. Methanol containing 5% water was used as solvent unless otherwise stated.

Results and Discussion

The reaction of an equimolar amount of (*S*)-methionine and chloroauric acid in water was complete in a few minutes and the solution initially yellow became colorless. Thin-layer chromatography and amino acid analysis showed the complete absence of the starting amino acid and the presence of the corresponding sulfoxide.

The value found of $[\alpha]^{25}{}_D$ 132 ± 1° ($c = 0.8$; 1 *N* HCl) corresponds to that of the (*S*)-methionine (*S*)-sulfoxide,[5] and clearly indicates that the oxidative process occurred stereospecifically, giving only one of the two possible diastereoisomers. No optical purity is revealed from the amino acid analyzer since, in the conditions under which it operates, partial interconversion occurs. The formation of (*R*)-methionine (*R*)-sulfoxide starting from (*R*)-methionine was established performing the same reaction on (*R*)-methionine (Figure 1).

The same results were obtained in buffered solutions at pH 2, 3, and 5 and also using an excess of gold chloride. Performing the same reaction on (50.0% S + 50.0% R)-, (54.5% S + 45.5% R)-, and (65.0% S + 35.0% R)-methionine, the $[\alpha]^{25}{}_D$ values for the three mixtures corresponded to the ratio of the two sulfoxide enantiomers (*S*)–(*S*):(*R*)–(*R*) = 1.00, 1.19, and 1.86 as would be expected if the reaction maintains its stereospecificity.

The formation of chiral sulfoxide has been reported in the oxidation of sulfides by microorganisms;[6] the product obtained was sometimes more than 90% optically pure, but the yield was usually very poor. Also, when using *tert*-butyl hypochlorite as reagent for the oxidation of sulfides to sulfoxides, stereochemical control has been found in some cases.[7] In order to gain more information on the mechanism of oxidation we have measured the reaction rate under different experimental conditions.

The kinetics were followed spectrophotometrically in acidic aqueous methanol at 25°C. The change of optical density with time at 320 nm took place in two stages. Initially the OD increased considerably, then decreased more slowly to zero. The first stage most probably corresponds to the substitution of one chloride ion by a methionine molecule with formation of the complex $[AuCl_3(\text{methionine})]$. Analogous spectral changes were observed for the reaction of the tetrachloroaurate ion and trichloroaminegold(III) complex with dialkyl sulfides.[8] In these cases, the final spectrum of the first step could be successfully compared to that of an authentic sample of $[AuCl_3(SR_2)]$ prepared independently. In the second stage of the reaction, the absorbance falls to zero, a clear indication that the gold(III) species is disappearing. Analysis of the final reaction products showed the presence of methionine oxide and gold(I) species. The first step (the substitution reaction) was too fast to be followed by conventional techniques under these conditions, and was beyond the scope of this work. We, therefore, followed only the second step, the reduction of $[AuCl_3(\text{methionine})]$ to the gold(I) species.

The reaction rate as a function of [methionine] was measured under pseudo-first-order conditions using methanol containing 5% water as solvent. Perchloric acid was also added to a 5×10^{-2} *M* concentration in order to obtain satisfactory concentration of amino acid and to maintain constant pH. The observed rate constants are reported in Table I and plotted against the concentration of amino acid in Figure 2.[16]

It is apparent that the pseudo-first-order rate constants are a function of the methionine concentration and obey the relationship

$$k_{\text{obsd}} = k[\text{methionine}]$$

This result implies that a second methionine is required in order to promote the reduction of $[AuCl_3(\text{methionine})]$ to gold(I).

A different behavior was observed in the kinetics of oxidation of $SbPh_3$ and $AsPh_3$ by $[AuCl_4]^-$ in aprotic solvents,[9] where both the reaction stoichiometry and the rate data were consistent with a path which involved a slow reduction of $[AuCl_4]^-$ to $[AuCl_2]^-$, followed by a rapid equilibrium formation of $[AuClL]$ (L = $SbPh_3$, $AsPh_3$). An alternative path in which a chloride is replaced in $[AuCl_4]^-$ giving a reactive substituted product, $[AuCl_3L]$, as an intermediate was considered unlikely because it was noted that at least for $AsPh_3$ the complex $[AuCl_3L]$ was stable in acetonitrile. In the case of PPh_3, on the other hand, it was suggested that the rate-determining step involved the formation of $[AuCl_3PPh_3]$ by the usual associative square-planar substitution path. A rapid reduction reaction involving another molecule of phosphine would then follow to give products.

The different behavior for $SbPh_3$ and $AsPh_3$ as compared with that for PPh_3 was explained on the basis that the latter is a weaker reducing agent and yet still a very powerful nucleophile toward gold(III). Thus for PPh_3, chloride substitution was favored over a redox rearrangement process, at least for the first replacement.

An analogous argument can be invoked to explain the kinetic behavior of the methionine, but in the case of the substitution of the first chloride in $[AuCl_4]^-$, the redox process is still slow and requires the substitution of a further halogen ion by a sulfide molecule. It should be noted that in this way the gold(III) substrate becomes increasingly positive and therefore also increases the tendency of the central metal to oxidize the coordinated ligand.

After coordination to the metal, the configuration about the sulfur atom is trigonal pyramidal; it follows that coordination creates chiral centers at sulfur. In principle this chirality could be determined to some extent by that of the asymmetric carbon.[10]

From what is known in the platinum complex,[11] however, this does not seem to be the case, at least in the solid state, when only one molecule of amino acid is coordinated to the metal. The situation could be different when two methionines are coordinated to the metal since the two coordinated chiral centers could now influence one another. The influence of an asymmetric coordinated ligand on the approach of a second has been recently successfully employed in the resolution of racemates.[12]

A second point of interest is to see if methionine acts as monodentate S-donor ligand or as bidentate S- and N-donor toward gold in the conditions under the experiment. Although the reaction medium was very acidic, and the amino group is therefore nearly totally protonated, the second hypothesis cannot be excluded, a priori, since the ring-closing process would be favored by the large chelate effect.[13] We have varied the acid concentration from 2×10^{-2} to 2×10^{-1} and no significant changes were observed in the reaction rate (Table II[16]).

However, when perchloric acid was not added to the reaction solution and the pH was governed only by the protic dissociation of methionine,[14] we measured a reaction rate of 0.15 sec^{-1} at a methionine concentration of 6.09×10^{-3} *M* about 65 times bigger than that found for the same amino acid concentration but at pH below 2. We do not know if the measured rate refers to the redox step or to the substitution of the first chloride in $[AuCl_4]^-$, since as the redox process becomes faster the substitution by the first methionine could become rate determining. These results indicate that in less acidic medium there is definitely a participation of the unprotonated amino group of the amino acid in the reaction process; we cannot exclude this participation even at pH below 2, although in this range it would become irrelevant from a kinetic point of view.

A further point to be discussed is whether the oxidation occurs through transfer of two chlorine atoms from gold to methionine giving a sulfur dihalide intermediate which in turn hydrolyzes to sulfoxide and hydrochloric acid, or alternatively, there is a direct attack by water at sulfur while it is still in the coordination sphere of gold. The former type of mechanism has been found in the oxidation of phosphines, arsines, and stilbines by gold(III) chloride in aprotic solvents.[9] A sulfur dihalide intermediate has been postulated in the inversion reaction of sulfoxides catalyzed by hydrogen chloride.[15] It would therefore appear improbable that optical purity could be expected with such an intermediate. On the other hand, the trigonal-bipyramidal structure of the dichloro sulfide (the sulfur atom in addition to the two organic radicals and the two chlorine atoms bears a lone pair of electrons) can have an asymmetrical structure and give an optically pure sulfoxide after hydrolysis.

The latter mechanism (participation of water to the redox process), however, appears to be a more suitable explanation of the overall picture. The oxidation of sulfides to the corresponding sulfoxides by gold trichloride takes place only in the presence of water.[2] We have also measured the reaction rate as a function of the percentage of water in the reaction mixture and we have observed an increase of reaction rate as the percent of water increases (Table III[16]).

This result is in line with our hypothesis; however, it does not provide unequivocal proof for the participation of water in the redox step, since the variation of rate could also be attributed to solvation effects and variation of the dielectric constant of the medium.

In conclusion we have found that: (1) two methionine molecules are required to promote the reduction of gold(III) to gold(I); (2) the unprotonated amino groups are involved in the reaction process at least in less acidic media; (3) the water probably takes part directly in the redox process. These data give some indications on the possible mechanism; however, they alone are not sufficient to fully explain the stereospecificity of this reaction. In our opinion the key to the solution of this problem is to gain direct information on the chirality of the sulfur atom once it is coordinated to the metal.

We believe that performing analogous experiments on other metal substrates which behave as gold(III) from a coordinative point of view but do not undergo fast reduction will enable us to better understand the stereospecificity of this reaction.

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Registry No. (*S*)-Methionine, 63-68-3; chloroauric acid, 16903-35-8; (*S*)-methionine (*S*)-sulfoxide, 23631-84-7; (*R*)-methionine (*R*)-sulfoxide, 50896-97-4; $[AuCl_3(\text{methionine})]$, 57139-09-0.

Supplementary Material Available: Tables I, II, and III (rate constant data) and Figure 2 (plot of rate constant vs. methionine concentration) (4 pages). Ordering information is given on any current masthead page.

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