A ^{1}H NMR Study of the Reaction of Gold(III) with DL-Seleno-methionine in Aqueous Solution

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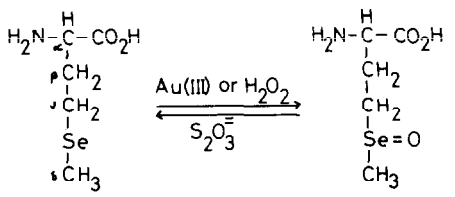
Received March 15, 1983

The major gold drugs which are available on the market for the treatment of rheumatoid arthritis are in the +1 oxidation state [1]. The gold(III) complexes are regarded as too toxic for medicinal use [2] because of their very high oxidising power. Gold(III) oxidises almost all sulphur containing amino acids in the biological system. For example, it oxidises thiol to disulphide [2], disulphide to sulphonic acid [3], and methionine to methionine sulphoxide [4, 5].

The oxidation of methionine and its derivatives with gold(III) has been studied using various techniques [4, 5]. We report here for the first time the reaction of gold(III) with DL-seleno-methionine (Se-Met) in aqueous solution by ^{1}H NMR spectroscopy.

Figure 1 shows the effect of successive additions of gold(III) to 20 m*M* Se-Met in D_2O at pH*1. pH* is not corrected for its deuterium effects, but is measured before the addition of gold(III) since it has been found that gold(III) has a corrosive effect on the Ag/AgCl combination electrode [6]. [Se-Met and $NaAuCl_4 \cdot 2H_2O$ were obtained from K and K Labs, Plainview, New York and used without any purification].

When Au(III) is added to Se-Met, two effects are quite apparent as shown in Fig. 1, (a) the methyl resonance, shown by an arrow at 3.164 ppm and γ-CH_2 multiplets at 3.74 ppm, increases in intensity. These resonances are due to the formation of DL-methionine-selenoxide (Met-Selenoxide), (b) another methyl resonance shifts to low field as the amount of $AuCl_4^-$ increases. When the oxidation of Se-Met occurs it generates Au(I) which is in a fast



DL-seleno-methionine DL-methionine-selenoxide

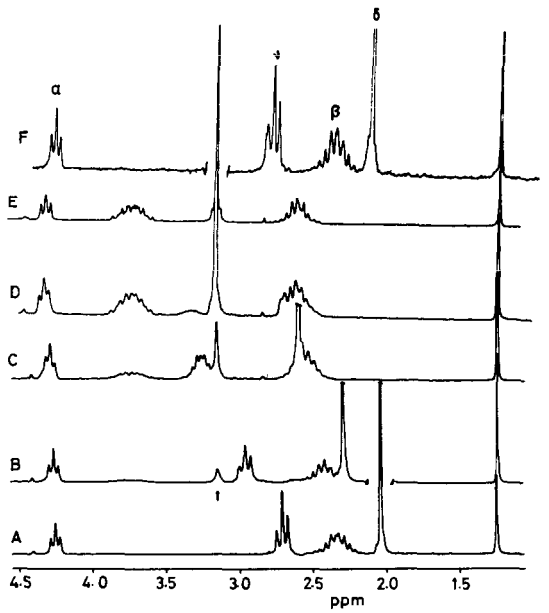


Fig. 1. 200 MHz ^{1}H NMR spectra of DL-seleno-methionine (20 m*M*) in the presence of (A) 0.0, (B) 0.1, (C) 0.2, (D) 0.4, (E) 0.5 molar equivalents of $NaAuCl_4 \cdot 2H_2O$ in aqueous solution. Spectrum F was recorded after the addition of two equivalents of $S_2O_3^{2-}$ to E reaction mixture. Chemical shifts were measured from tert-butanol (1.23 ppm downfield from 2,2-dimethyl-2-silapentane-5-sulphonate) as an internal reference.

exchange [4] with unoxidised Se-Met. The solution becomes colourless when Au(III) is added and some metallic gold can be observed on the side of the tube. The reaction is completed at a 2:1 ratio of Se-Met: Au(III). The experiment is done at low pH because Au(III) makes the solution more acidic [6] and therefore there is no control at neutral pH.

The exchange reaction of Se-Met with Au(I) will presumably be *via* Se. Goddard *et al.* [7] have determined the stability constants for selenourea and thiourea type molecules and they found that the order of affinity for a 'class b' metal like Hg(II) is $Se > S \gg O$.

When two equivalents of $S_2O_3^{2-}$ was added to a 2:1 ratio of Se-Met: Au(III) reaction mixture the methyl resonance from 3.164 ppm and γ-CH_2 multiplets were shifted toward the free position of Se-Met, [see spectra (A) and (F)].

Oxidation of Se-Met also occurs after the addition of H_2O_2. At a 1:1 ratio of Se-Met:H_2O_2, hydrogen peroxide oxidises Se-Met to Met-Selenoxide and after the addition of two equivalents of $S_2O_3^{2-}$ it reduces Met-Selenoxide to Se-Met. Similar results are obtained with $KAuBr_4$. The oxidation of Se-Met also results from the addition of *m*-chloroperbenzoic acid which is

0020-1693/83/$3.00

not very soluble in water but still oxidises some of Se-Met to Met-Selenoxide.

These observations shows that gold(III) halides not only oxidise methionine and its derivatives but also oxidise DL-selenomethionine in aqueous solutions.

The ^2J (^{77}Se, ^1H for the CH_3 group is measured for Se-Met) is 10.1 ± 0.1 Hz, which changes to 11.0 ± 0.1 Hz for Met-Selenoxide. Similar ^2J values were obtained for dimethyl selenide (^2J = 10.5 ± 0.1 Hz) which changes to 11.7 ± 0.2 Hz for dimethyl selenoxide [8].

Acknowledgements

This research was supported by the University of Petroleum and Minerals, Dhahran, Saudi Arabia (Grant # CY/METALION/54). Helpful discussion of this work with Dr. P. J. Sadler (Chemistry Department Birkbeck College, University of London) and Dr. M. S. Hussain of this university is gratefully acknowledged.

References

1 P. J. Sadler, *Structure and Bonding, 29,* 171 (1976); C. F. Shaw III, *Inorg. Perspec. Biol. Med., 2,* 287 (1979); D. H. Brown and W. E. Smith, *Chem. Soc. Rev., 9,* 217 (1980).
2 L. Libenson, *Exp. Med. Surg., 3,* 146 (1943).
3 C. F. Shaw, M. P. Cancro, P. L. Witkiewicz and J. E. Eldridge, *Inorg. Chem., 19,* 3198 (1980).
4 A. A. Isab and P. J. Sadler, *Biochim. Biophys. Acta, 494,* 322 (1979).
5 G. Natilie, E. Bordingnon and E. Catalini, *Inorg. Chem., 15,* 246 (1976).
6 A. A. Isab, *Ph.D. Thesis, University of London* (1978).
7 D. R. Goddard, B. D. London, S. O. Ajayi and M. J. Campbell, *J. Chem. Soc., A,* 506 (1969); R. D. Goddard and S. O. Ajayi, *J. Chem. Soc., A,* 2673 (1971).
8 W. McFarlane and R. J. Wood, *J. Chem. Soc. Dalton,* 1397 (1972).