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Thermolysis of Dimethylgold(III) Complexes Having a Nucleoside Ligand

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Relative ease of dissociaiton of nucleosides from dimethylgold(III) complexes, estimated from the kinetics of thermolysis of dimethylgold(III) complexes having a nucleoside ligand, $AuMe_2$(nucleoside)X, lies in the order of Cyd $<$ Guo $<$ Ado $\ll$ dThd.

Interaction of nucleosides with organotransition metal complexes has considerable attention, since it is possibly relevant to their unique antitumor activity and related reactions.1) Recently we have reported selective formation of dimethylgold(III) complexes containing a nucleoside as a stabilizing ligand by the reactions of dimethylhalogold(III) dimer with corresponding nucleosides in DMSO.2)

On the other hand, organogold(III) complexes having a tertiary phosphine ligand are known to be thermolyzed to liberate a reductive eliminaiton product, by a mechanism involving rate limiting ligand dissociation process.3) We now report the thermolysis of dimethylchloro(base)gold(III) (base = purine, pyrimidine and nucleosides) in DMSO, from which the relative ease of dissociation of various bases from the dimethylgold(III) moiety is evaluated.

Thermolysis of dimethylchloro(base)gold(III), $AuMe_2$(base)Cl, (base= Cyt, **1a**; Ade, **1b**; Cyd, **2a**; Guo, **2b**; Ado, **2c**) was performed in DMSO at 70-100 °C to give a quantitative yield of reductive elimination product, ethane. The rates of the reaction, which were followed periodically by measuring ethane evolved, were the first order in the concentration of $AuMe_2$(base)Cl. The first order rate constant k_{obsd} decreases with an increase in the concentration of free nucleoside. The plot of the reciprocal of k_{obsd} and the concentration of corresponding nucleosides gave straight lines with intercepts in the y-axis as shown in Fig. 1. These results were best interpreted by the rate limiting dissociation of the base ligand from **1** or **2**, followed by rapid reductive elimination of ethane, as reported in the thermolysis of trialkylgold(III) complexes having a tertiary phosphine ligand.

$$AuMe_2(base)Cl \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} AuMe_2Cl + base \xrightarrow[k_2]{} C_2H_6 \qquad (1)$$

$$-\frac{d[\underset{\sim}{1}]}{dt} = \frac{k_1k_2[\underset{\sim}{1}]}{k_2 + k_{-1}[L]} = k_{obsd}[\underset{\sim}{1}] \qquad (2)$$

$$\frac{1}{k_{obsd}} = \frac{1}{k_1} + \frac{k_{-1}}{k_1k_2} \qquad (3)$$

Table 1 summarizes the estimated first order dissociation rate constants k_1 for complexes **1** and **2** at 80 °C in DMSO. The k_1 values for Cyt and Ade complexes are considerably smaller than those for the corresponding nucleosides probably due to the stronger basicity of sugar free bases in comparison with nucleosides.[4)]

Table 1. Dissociation rates of bases from complexes **1** and **2** in DMSO at 80 °C

Complex	$10^4k_1/s^{-1}$
1a	1.01
1b	0.93
2a	1.49
2b	2.25
2c	4.26

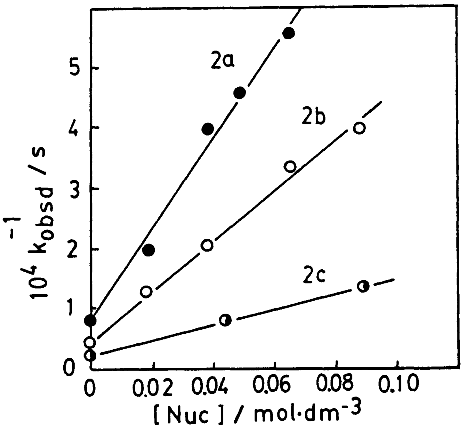

Fig. 1. Relationship between the reciprocal of k_{obsd} and the concentration of nucleosides in DMSO at 80 °C

Cyd is the most resistant toward the dissociation from dimethylgold(III) moiety among these nucleosides. Thus the k_1 value increases in the order of Cyd < Guo < Ado. Kinetic parameters of k_1 for **2b** were estimated as $\Delta G^{\ddagger}$ = 111 kJ/mol, $\Delta H^{\ddagger}$ = 123 kJ/mol and $\Delta S^{\ddagger}$ = 36 J/deg.mol at 80 °C. The positive value of $\Delta S^{\ddagger}$ is in good agreement with the dissociation process. On the other hand, dThd showed no inhibitory effect on the reductive elimination, the result being consistent with the previous NMR study,[2)] in which no interaction of dThd with dimethylgold(III) was verified. The present coordination ability of various nucleosides is in contrast to the well known specific coordination of Guo unit in DNA with a Pt-anticancer reagent.[5)]

References

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