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Dissociative Ligand Exchange in Organoplatinum(II) and -gold(III) Complexes Having a Nucleoside Ligand. Dynamic NMR as a Mechanistic Probe for Ligand Exchange Process

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Application of simple dynamic NMR technique to intermolecular ligand exchange reactions in dimethylchloro(guanosine)gold-(III) and [ethyl(1,5-cyclooctadiene)(cytidine)platinum(II)]$^+$ reveals that both reactions proceed by a dissociative mechanism.

Ligand exchange reactions are frequently encountered process in various inorganic and organometallic reactions.[1] Two types of ligand exchange mechanisms are conceivable in square planar metal complexes. An associative mechanism is generally accepted for nickel triads[2] and gold(III)[3] complexes, whereas a dissociative mechanism is also proposed in the thermolysis of alkylmetal complexes as well as in the ligand exchange reactions of sterically bulky ligand.[1,3]

$$ML_4 + L \rightleftharpoons ML_5$$
(associative exchange)

$$ML_4 \rightleftharpoons ML_3 + L$$
(dissociative exchange)

Although NMR is a convenient tool to examine the rate of exchange process between two sites, discriminaiton of the above two processes sometimes becomes a subtle problem. An application of dynamic NMR technique to such intermolecular ligand exchange processes is performed to solve the problem. We wish to report the dissociative ligand exchange in organoplatinum(II) and organogold(III) complexes having a nucleoside ligand, which is proved by the dynamic NMR. Merit to use of a well popularized personal computer for the simulation is also noted.

Interaction of nucleobases with platinum metal complexes has a considerable attention because of their powerful anticancer activity.[4] We previously reported the formation of organogold(III)[5] and -platinum(II)[6] complexes having a nucleoside ligand, in which a facile ligand exchange reaction of nucleoside is observed in the NMR spectra. We chose dimethylchloro(guanosine)gold(III), **1** and ethyl(1,5-cyclooctadiene)(cytidine)platinum(II) nitrate, **2** as probes of NMR analysis.

Figure 1 shows the observed and simulated ^{1}H NMR spectra of H8 proton in the mixture of **1** and free guanosine. The line shape of the observed spectra changes

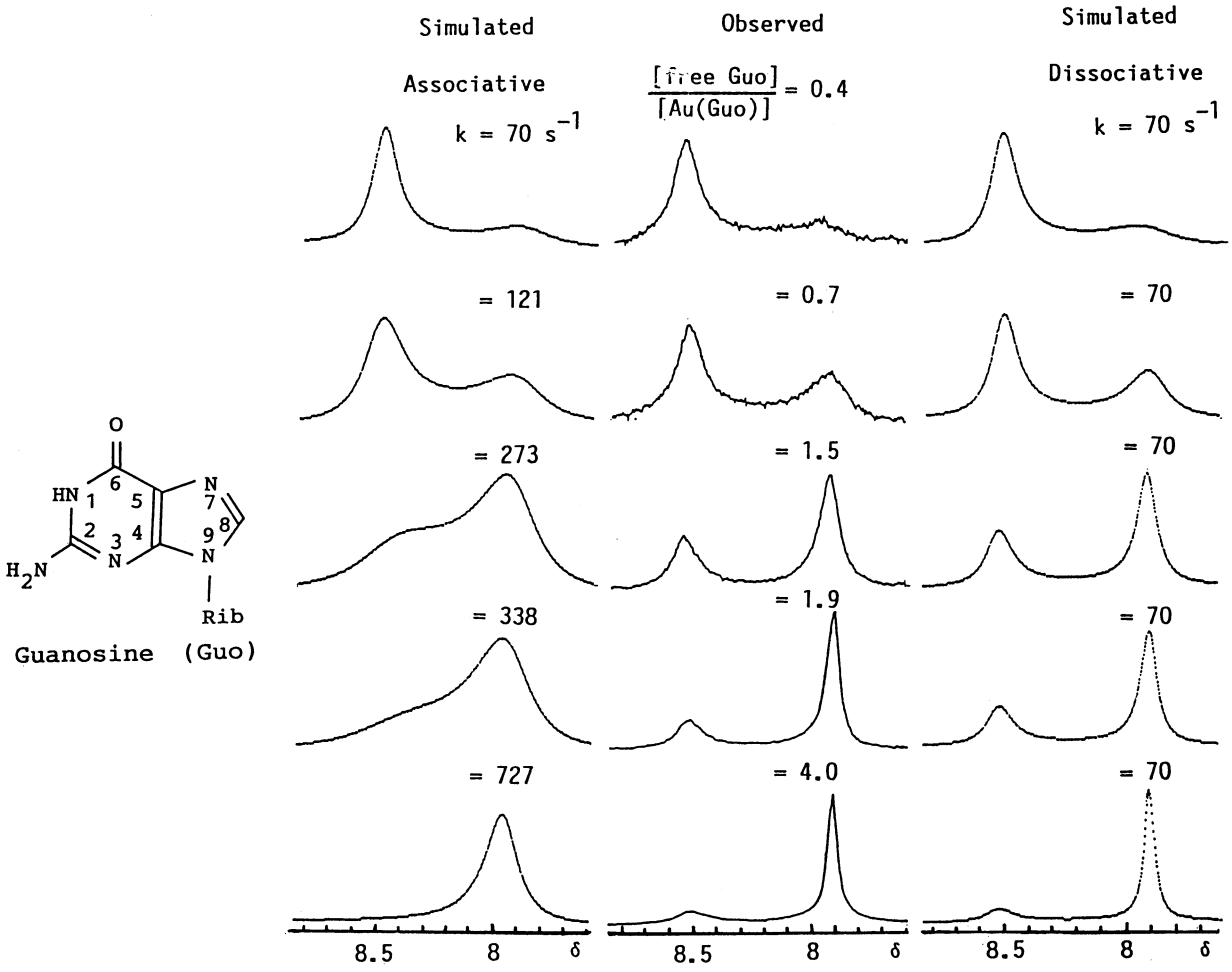

Fig. 1. Observed and simulated ^{1}H-NMR spectra of H8 of Guo in the mixture of [$AuMe_2Cl(Guo)$] and free Guo in DMSO-d_6 at 33 °C.

with increasing the concentration of free guanosine. Two types of simulated spectra are also shown in Fig. 1. In the associative mechanism, the first order rate constant k of foregoing process is assumed to increase in proportion to the concentration of added ligand. On the other hand, in the dissociative mechanism, k is invariable irrespective of the amount of added ligand. The amount of dissociated guanosine was negligible when **1** dissolved in DMSO-d_6, indicating that the equilibrium of the dissociative process lies far to the left.

$$AuMe_2Cl(Guo)_2 \overset{+Guo}{\rightleftharpoons} AuMe_2Cl(Guo) \overset{-Guo}{\rightleftharpoons} AuMe_2Cl$$

Observation of both signals due to coordinated and free guanosine in the presence of excess guanosine suggests that the formation of 5-coordinated species is also negligible and the ligand exchange process is relatively slow in the NMR time

scale under these conditions. Such assumptions are not unreasonable in many cases, where the square planar four coordinate complexes are isolable.

Comparison of the observed spectra with both simulated spectra as shown in Fig. 1 clearly demonstrated that the ligand exchange reaction proceeds by a dissociative mechanism. Such a dissociative ligand exchange is in sharp contrast to the facile associative ligand exchange in organogold(III) complexes having a tertiary phosphine as a ligand.[3] The difference suggests the much stronger coordination ability of tertiary phosphine ligands than nucleosides. In fact, no ligand displacement reaction of organogold(III) having triphenylphosphine with nucleosides such as cytidine and guanosine took place.

In contrast to the above relatively slow process, a fast exchange process was observed in the case of **2**. Thus signals due to the coordinated and free cytidine appear as coalescent peaks.

$$[PtEt(Cyd)(cod)]NO_3 \rightleftharpoons [PtEt(cod)]NO_3 + Cyd$$

Figure 2 shows the observed and simulated spectra of H5 proton in the mixture of **2** and free cytidine, in which H6 proton has been decoupled throughout the measurement because of simplification of the spectra. The observed signal once broadened and then sharpened with increasing the amount of added cytidine. The similar assumptions as described in the case of **1** are also employed for the dymnamic NMR simulation. In spite of coalescence of the signals due to coordinated and free cytidine, it can be concluded from the line shape that the dissociative mechanism is also operative here.

Kinetic parameters estimated for the dissociative ligand exchange reactions in **1** and **2** are summarized in Table 1. Small negative $\Delta S^{\ddagger}$ values are estimated in spite of the dissociative process. Although extensive solvation to the 3-coordinate intermediate might be responsible for the results, we should await further discussion on the entropy of activation, until more data are accumulated.[7]

Table 1. Kinetic Parameters for the Ligand Exchange Reactions in **1** and **2**

Complex	$\Delta H^{\ddagger}$/kJ mol^{-1}	$\Delta S^{\ddagger}$/J mol^{-1} K^{-1}	$\Delta G^{\ddagger}$/kJ mol^{-1}
1[a)]	67	-10	71
2[b)]	53	-8	55

a) In DMSO-d_6 at 80 °C. b) In D_2O at 33 °C.

Thus the simple dynamic NMR technique has been shown to discriminate whether the ligand exchange process is associative or dissociative. The method is considered to be applicable to many other ligand exchange processes.

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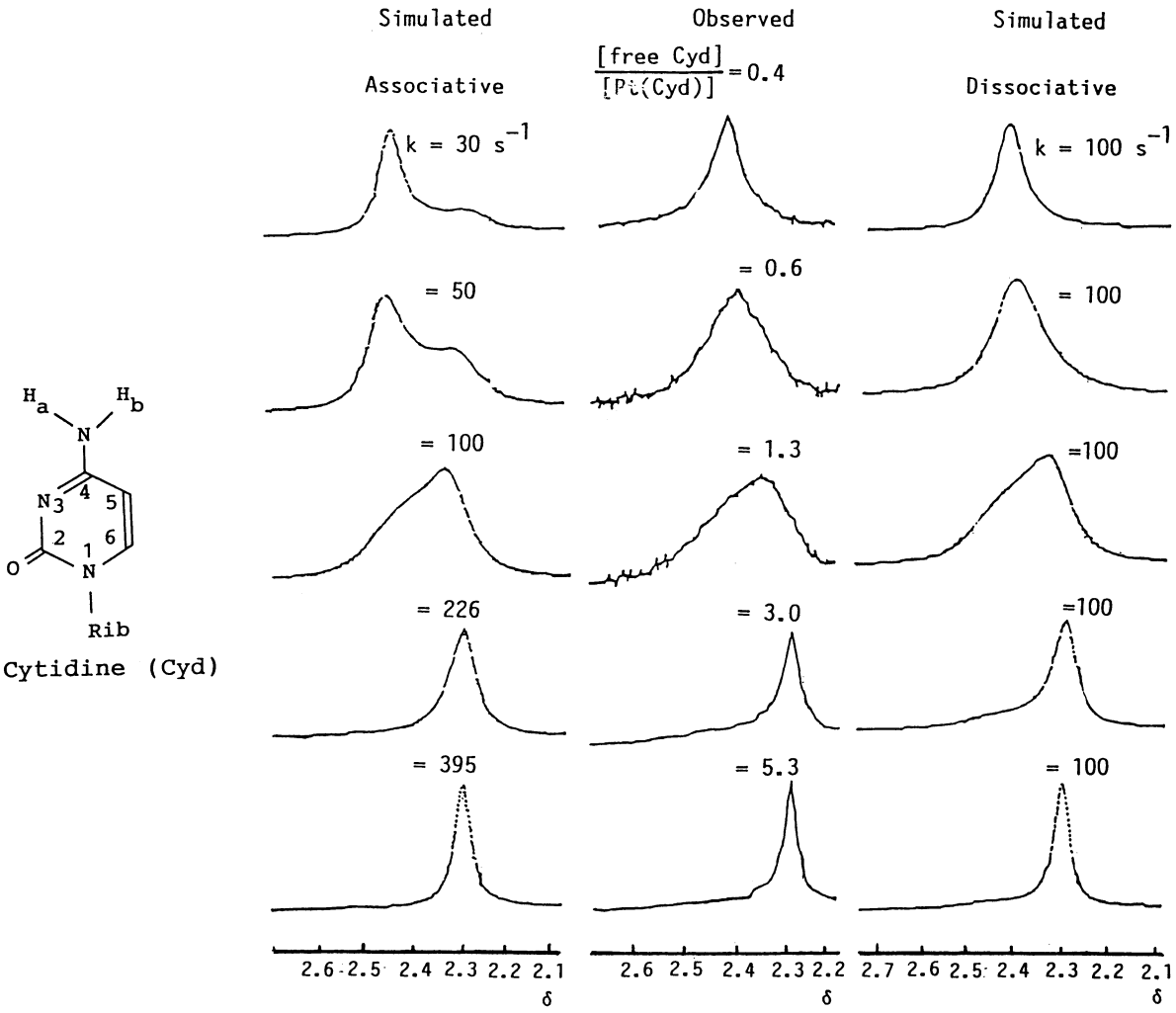

Fig. 2. Observed and simulated ^{1}H-NMR spectra of H5 of Cyd in the mixture of [PtEt(Cyd)(cod)]NO_3 and free Cyd in D_2O at 33 °C.

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