Olefin−Amino Acid Complexes of Platinum(II). 3. NOE Difference and Low-Temperature NMR Determinations of Rotamer Populations of Coordinated Olefins and the Stereoselectivity of Coordination of Prochiral Olefins

Kevin F. Morris, Luther E. Erickson,* Biliana V. Panajotova, David W. Jiang, and Fei Ding

Department of Chemistry, Grinnell College, Grinnell, Iowa 50112

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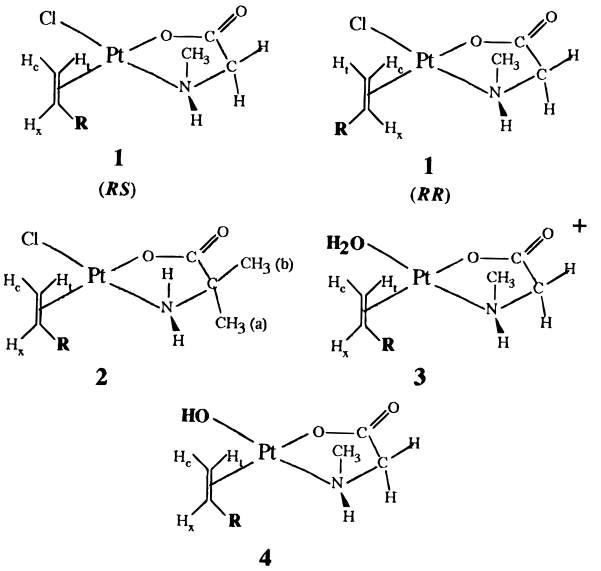
The exceptional stereoselectivity of coordination of 2-methyl-3-buten-2-ol in *cis*(*N*,*olefin*)-Pt(2-methyl-3-buten-2-ol)(sarcosine)X, **1** (X = Cl), has been attributed to stabilization of one rotamer of the H^2-coordinated olefin by intramolecular hydrogen bonding between the OH oxygen on the olefinic alcohol and the N−H proton of coordinated sarcosine. Nuclear Overhauser enhancement (NOE) difference experiments on **1** have confirmed that the preferred conformation in solution corresponds to that found in the crystalline solid. Both NOE and low-temperature NMR experiments were used to establish approximate rotamer ratios for a series of complexes as a function of olefin structure, X substituent (Cl^-, H_2O, OH^-), and solvent composition (D_2O vs CD_3OD). Olefins that show strong stereoselectivity in diastereomeric complexes containing sarcosine and proline also show a strong preference for one rotamer in complexes containing the achiral amino acid α-aminoisobutyric acid. The strong stereoselectivity and rotamer preference noted for **1** is reduced substantially by substituting H_2O for Cl^- and is almost eliminated by further deprotonation to OH^-. A similar reduction in stereoselectivity of binding and of rotamer preference is noted in going from CD_3OD to D_2O as solvent. These findings all emphasize the importance of hydrogen bonding and olefin conformation to the stereoselectivity of coordination of substituted ethylenes in these species.

Introduction

In our studies of the stereoselectivity of coordination of prochiral olefins in diastereometric olefin−amino acid complexes of Pt(II), we have established that the diastereomer ratio for mixed olefin−sarcosine complexes such as **1** is very sensitive



to olefin structure.[1,2] It was initially suggested that the stereoselectivity is closely linked to the energy stabilization of one rotamer of the *RS* diastereomer of **1** by a favorable intramolecular hydrogen-bonding interaction between the N−H proton of the coordinated sarcosine and a proton acceptor on the coordinated olefin.[1] A more recent comparison of the stereoselectivities of olefin coordination for a large number of olefins added weight to this hypothesis.[2]

Several olefin−amino acid complexes have now been examined by low-temperature NMR spectroscopy to slow the rotation about the Pt−olefin bond enough to determine the relative populations of rotamers below the coalescence temperature and to determine the complete free energy profile for rotation about the Pt−olefin bond. Details of the kinetic studies will be reported in a subsequent paper,[3] but the variation in low-temperature rotamer ratios provides clear evidence to support the postulated close connection between olefin rotamer distributions and diastereomer ratios.

The connection between the rotamer ratio observed for complexes of achiral amino acids and the diastereomer ratio observed for complexes of chiral amino acids is shown in Figure 1. If one of the rotamers of a coordinated prochiral olefin, CH_2═CHR, is favored by an attractive interaction between N−H protons of the amino acid moiety in an achiral amino acid and a proton acceptor atom of R, the corresponding rotamer of the olefin in the complex containing a chiral amino acid (D in Figure 1) would be similarly stabilized, so that the diastereomer which includes the favored rotamer would also be preferred. Complexes of α-aminoisobutyric acid (aba), **2**, were selected for studies of internal rotation alone, while complexes of both sarcosine (sar) and proline (pro) were included in the study of internal rotation in diastereomers of chiral amino acids.

In NMR experiments with complexes containing achiral amino acids, the temperature can be cooled well below coalescence and resonances for the two rotamers are clearly evident. In the case of complexes containing chiral amino acids, though, the presence of more than one diastereomer often results

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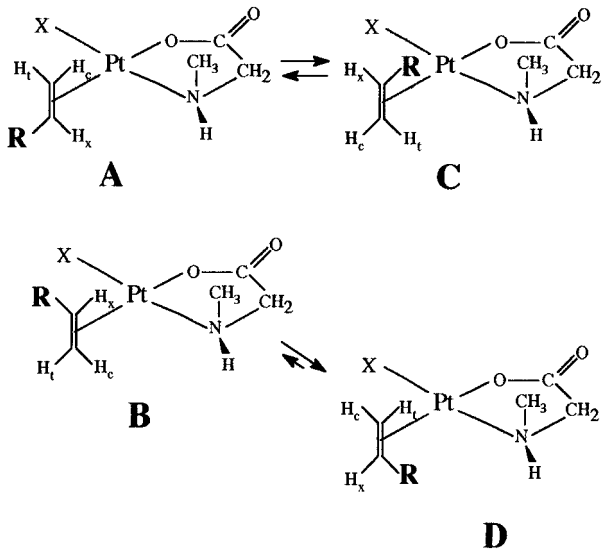

Figure 1. Structures and possible relative free energies of the four rotamers of the two diastereomers (A and C for *RR* and B and D for *RS*) of Pt(CH_2═CHR)(sar)Cl.

in crowded spectra, and at low temperature, when resonances for both rotamers of both diastereomers are evident, the spectra often become intractable. Therefore, nuclear Overhauser effect (NOE) difference spectroscopy has been employed to quantify the rotamer populations at room temperature in complexes containing chiral amino acids. NOE techniques have found wide application in the conformational analysis of solution species[4] including structural elucidation in transition metal complexes such as chiral Rh catalysts[5,6] and Cd-containing peptides.[7]

Figure 1 suggests how this experiment can be used to quantify rotamer ratios in solution. For the *RS* diastereomer, rotation about the Pt−olefin bond places either the H_t or H_x protons on the olefin in close proximity to the *N*-methyl protons of the sarcosine ring. Therefore, equal enhancements between the *N*-methyl and H_t and H_x resonances at room temperature would indicate that both rotamers are present in nearly equal concentrations, and the absence of *N*-methyl to H_x NOE indicates that one rotamer of the diastereomer is strongly preferred. Thus, the ratio (*N*-methyl to H_t NOE)/(*N*-methyl to H_x NOE) can be expected to be a sensitive indicator of the rotamer population ratio in the complexes considered here.

NOE measurements were also employed to examine solutions of several aqua, **3**, and hydroxo, **4**, complexes that were derived from corresponding chloro complexes by treatment with aqueous $AgNO_3$, followed by neutralization with carbonate. By providing a second hydrogen bond donor and/or acceptor, these species would be expected to offer comparable hydrogen-bonding opportunities to either rotamer of a coordinated olefinic alcohol, for example. Quantitative measurements of these effects have been obtained from both NOE and low-temperature population data for several species.

Experimental Section

Materials. All of the olefins and amino acids used in this study were purchased from Aldrich Chemical and used without further purification. The NMR solvents deuterium oxide (99.9 atom % D) and methyl-d_3 alcohol-*d* (99.8 atom % D) were also provided by Aldrich.

Synthesis of Pt Complexes. *cis*(*N*,*olefin*) isomers of Pt(2-methyl-3-buten-2-ol)(sar)Cl, Pt(allyl alcohol)(sar)Cl, Pt(2-methyl-3-buten-2-ol)(pro)Cl, and Pt(2-methyl-3-buten-2-ol)(aba)Cl were synthesized as described previously.[8] The 2-methyl-3-buten-2-ol (2-mb) complexes were then used as the starting material for the synthesis of the other Pt(olefin)(amino acid)Cl complexes which were prepared by facile olefin exchange. The 2-mb complex was usually first converted to the more stable Pt(ethylene)(amino acid)Cl compound[2] by bubbling ethylene gas through a methanol solution of the complex until all of the solvent had evaporated. The ethylene ligand was then exchanged for another olefin by treating the ethylene complex with either a stoichiometric amount (for the nonvolatile olefins allyl sulfonate and 3-(allyloxy)-1,2-propanediol) or a large excess (for all other olefins studied) of a second olefin in methanol. After equilibration, the solution was then rotary evaporated to dryness at least three times, thereby driving off the much more volatile ethylene ligand to effect essentially complete conversion to the desired species.

The Pt(2-mb)(amino acid)$(H_2O)^+$ complexes were synthesized by adding a stoichiometric amount of silver nitrate and the Pt(2-mb)(amino acid)Cl complex to D_2O and heating the mixture at 50 °C for 3 h. The formation of AgCl precipitate and an increased turbidity of the solution were observed as the reaction proceeded. The solution was then filtered, and the aqua product was confirmed by ^{1}H NMR spectroscopy. Such aqua complexes react, especially at high concentration and at pH values near the pK_a (∼4), to form OH-bridged dimers; but, at low or high pH, the Pt−OH_2^+ or Pt−OH species predominate. This behavior closely parallels that of analogous DMSO complexs.[9]

The hydroxy complexes were prepared by mixing a stoichiometric amount of Na_2CO_3 and the Pt(2-mb)(amino acid)$(H_2O)^+$ complex in D_2O. The solution was allowed to equilibrate at room temperature for at least 1 h, and the product was confirmed by ^{1}H NMR spectroscopy.

NMR Experiments. All NMR spectra were collected at 300.15 MHz on a Bruker AF300 spectrometer equipped with an Aspect 3000 computer. Five millimeter NMR tubes were used, and sample concentrations were ∼50 mM for all amino acid−olefin complexes except the sparingly soluble Pt(sarcosine)(allyl alcohol)Cl for which the concentration of the complex was roughly 5 mM. Typical acquisition parameters for these samples were as follows: 90° pulses, a 3000 Hz spectral width, 8K time domain data points, and a 1 s relaxation delay. The spectra were processed with the resident Aspect 3000 software or were transferred to an AST-Premium PC and processed using PC-NMR. The COSY and NOE difference experiments were performed using pulse sequences provided with the Bruker DISR90 software package.

NOE difference spectra were collected by first irradiating the peak of interest (typically the sarcosine N−CH_3 resonance) for 8 s at a decoupler power 40 dB below 0.2 W. An identical free induction decay was then collected with the decoupler frequency set off-resonance. In all experiments, 400 or more transients were collected in this manner. The on- and off-resonance FIDs were then apodized (2 Hz exponential line broadening) and subtracted, and the resulting FID was Fourier transformed to yield the difference spectrum. The percent NOE values were calculated using eq 1, where $(I - I_0)$ is the peak integral in the

$$\% \text{ NOE} = ((I - I_0)/I_0) \quad (1)$$

difference spectrum and I_0 is the integral in the spectrum collected with the decoupler frequency set off-resonance.

The temperature was controlled in all experiments with a Bruker VT-1000 control unit, which regulated the sample temperature to ±2 °C. In the NOE difference studies, the temperature was controlled at 298 K in all experiments except those with the Pt(allyl alcohol)-(sarcosine)Cl compound in which the temperature was 313 K. In the low-temperature studies the sample was cooled using the cold nitrogen gas delivery system provided with the instrument. The rotamer ratios

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Table 1. Comparative Indexes of Olefin Stereochemistry for Pt(olefin)(amino acid)X

X/cpd type	formula/solvent	diastereomer ratio[a]	Ht/H_X NOE ratio[b]	rotamer ratio for aba complex[c]
Cl; very selective	Pt(2-mb)(sar)Cl/ CD_3OD	>50	>20	>40
Cl; very selective	Pt(2-mb)(sar)/D_2O	>50	>20	
Cl; very selective	Pt(pro)(2-mb)Cl/CD_3OD	>50	>20	>40
Cl; not selective	Pt(3-buten-1-ol) (sar)Cl/CD_3OD	1.1	1.1	1.2
Cl; not selective	Pt(4-pentene-1-ol)(sar)Cl/CD_3OD	1.1	1.0	1.5
Cl; not selective	Pt(allyl sulfonate) (sar)Cl/CD_3OD	0.79	1.0	1.0
Cl; intermediate	Pt(allyl ethyl ether)(sar)Cl/CD_3OD	4.1	3.5	3.3
Cl; intermediate	Pt(allyl alcohol)(sar)Cl/CD_3OD	6.0	∼7	5.0
Cl; intermediate	Pt(3-allyloxy-1,2-propanediol)(sar)Cl/CD_3OD	8.3	>10	9.1
D_2O, aqua	Pt(2-mb)(sar)D_2O^+/CD_3OD	15.2	>20	>10
D_2O, aqua	Pt(2-mb)(sar)D_2O^+/D_2O	5.3	3	
OD, hydroxo	Pt(2-mb)(sar)OD/CD_3OD	2.1		8−9
OD, hydroxo	Pt(2-mb)(sar)OD/D_2O	0.72	1	

[a] Defined as $RS/RR = 1/K_i$ in ref 2. [b] For irradiation of sarcosine *N*-methyl protons or proline H_1 proton (Figure 7) of *RS* isomer. [c] For corresponding aba complexes at temperatures of <230 K.

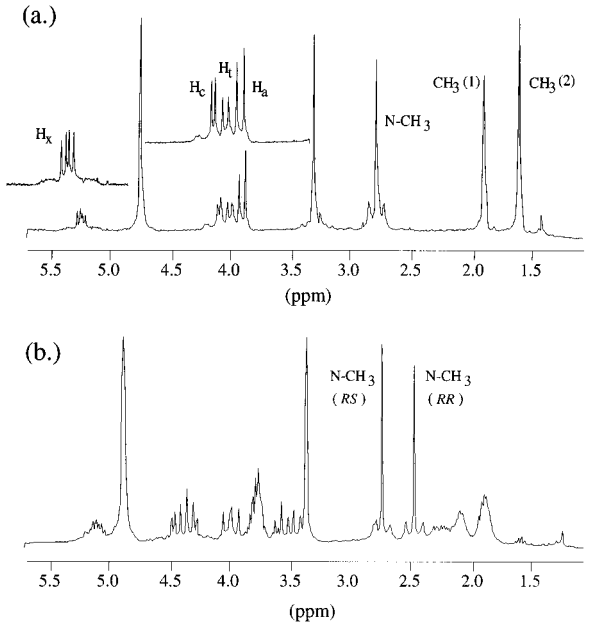

Figure 2. (a) Proton NMR spectrum of Pt(2-mb)(sar)Cl in CD_3OD showing only a single (*RS*) diastereomer; (b) proton NMR spectrum of Pt(3-buten-1-ol)(sar)Cl in CD_3OD showing equal concentrations of *RS* and *RR* diastereomers.

reported in Table 1 were all determined by integrating the peaks for the separate rotamers at sample temperatures at or below 230 K.

Results

Overview: Diastereomer Ratios, NOE Data, and Rotamer Ratios. The connection between diastereomer ratios, NOE data, and low-temperature rotamer ratios is evident in a comparison of the spectral data for four similar reference compounds: Pt-(2-mb)(sar)Cl, Pt(2-mb)(pro)Cl, Pt(3-buten-1-ol)(sar)Cl, and Pt-(3-buten-1-ol)(aba)Cl. As shown in Figure 2, the contrasting stereoselectivities of 2-mb and 3-but are most clearly revealed by the distinction between one *N*-methyl peak for the 2-mb complex at 2.8 ppm and the two nearly equal intensity *N*-methyl peaks for the corresponding 3-but species at 2.7 and 2.4 ppm. This exceptional stereoselectivity for 2-mb coordination is also shown by the single diastereomer of Pt(2-mb)(pro)Cl that is evident in Figure 3. Finally, the single species evident in the room-temperature spectrum of Pt(3-buten-1-ol)(aba)Cl (Figure 4) becomes two nearly equal concentration rotamers (Figure 5a,b) at 220 K.

The NOE enhancements that establish the stereochemistry in solution for the Pt(2-mb)(sar)Cl in methanol are displayed

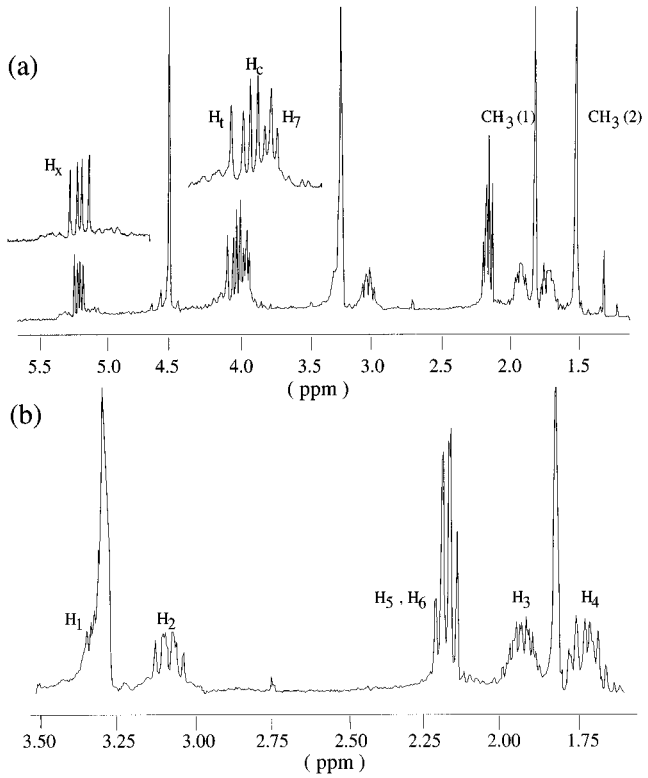

Figure 3. Proton NMR spectra of Pt(2-mb)(pro)Cl in CD_3OD showing a single isomer.

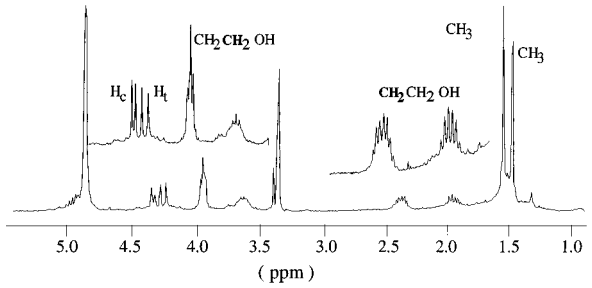

Figure 4. Proton NMR spectrum of Pt(3-buten-1-ol)(aba)Cl in CD_3-OD.

in Figure 6. The enhancements observed between the *N*-methyl protons on the sarcosine ring and the olefinic H_t proton (4.4%) and between the olefin CH_3(1) and amino acid H_a protons (3.6%) clearly demonstrate that the *RS* diastereomer is strongly preferred. The absence of a measurable *N*-methyl to H_c NOE rules out the possibility that the *RR* diastereomer could be the single isomer observed.

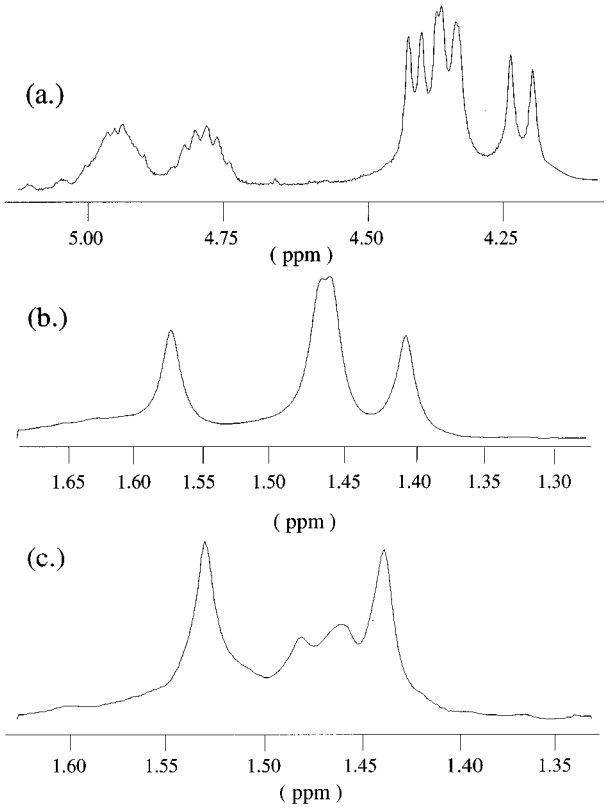

Figure 5. Proton NMR spectra of Pt(olefin)(aba)Cl in CD_3OD at 230 K showing overlapping peaks of rotamers: (a) H_x, H_c, H_t resonances of Pt(3-butene-1-ol)(aba)Cl; (b) methyl resonances of Pt(3-buten-1-ol)(aba)Cl; (c) methyl resonances of Pt(allyl ethyl ether)(aba)Cl.

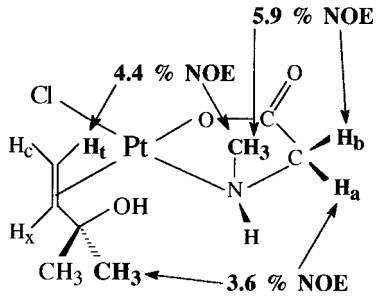

Figure 6. NOEs observed for Pt(2-mb)(sar)Cl.

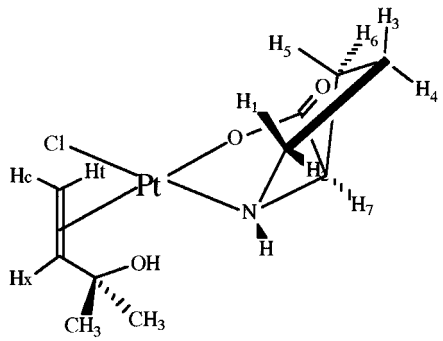

Figure 7. Structure of Pt(2-mb)(pro)Cl. Peaks for each of the numbered proline protons are assigned in the proton NMR spectrum (Figure 3).

The structure of Pt(2-mb)(pro)Cl is shown in Figure 7, and the NMR spectrum of this compound in methanol solution is shown in Figure 3. The assignments of the resonances on the proline ring as labeled in the spectrum were made using a combination of COSY and NOE difference experiments. Here, the presence of single H_x , H_t, and H_c resonances at 5.34, 4.17, and 4.10 ppm, respectively, is the clearest indicator that one

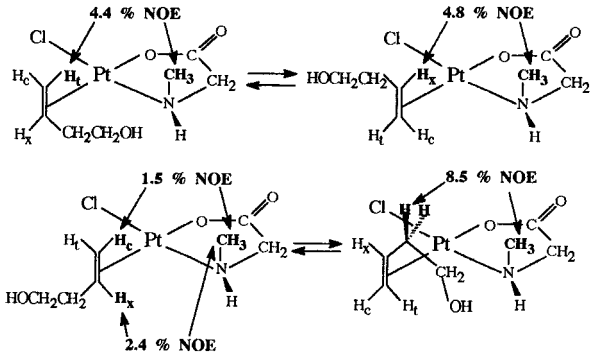

Figure 8. NOEs observed for the two diastereomers of Pt(3-buten-1-ol)(sar)Cl and the rotamer distributions implied by these values.

diastereomer is strongly preferred. Although no *N*-methyl group is present on the amino acid, an intraligand NOE enhancement was observed between a proton of the $N-CH_2$ moiety on the proline ring (labeled H_1 in Figure 7) and the H_t proton of the olefin. Again, the observation of this enhancement and the lack of any H_1 to H_c NOE rules out the possibility that the *RR* diastereomer is the favored isomer.

The ratio of the NOE enhancement observed at the olefin H_t and H_x protons when the *N*-methyl resonance of the sarcosine (or the H_1 resonance in the case of proline compounds) is irradiated is a direct measure of the rotamer populations at room temperature for the *RS* diastereomer. Ratios of these enhancements for all compounds studied are summarized in Table 1. In the Pt(2-mb)(sar)Cl complex, in which the *RS* diastereomer dominates strongly, a 4.4% NOE is observed between the *N*-methyl and the H_t protons, but no enhancement to the H_x proton was detected. Assuming that a weak NOE of 0.25% could be observed, this sets the lower limit of the H_t/H_x enhancement ratio at ~20 for this complex. Similarly, in the very stereoselective Pt(2-mb)(pro)Cl compound, no H_1 to H_x NOE was observed. Therefore, in both compounds one rotamer of the *RS* diastereomer dominates strongly.

The NOE enhancements observed for both diastereomers of the Pt(3-buten-1-ol)(sar)Cl complex are shown in Figure 8. Here, the 4.4 and 4.8% NOE from the *N*-methyl to the H_t and H_x protons, respectively, provides strong evidence that the two rotamers of the *RS* diastereomer are present in nearly equal concentrations. Analogous results were obtained for the *RS* diastereomers of the 4-penten-1-ol and allyl sulfonate complexes.

Figure 8 also shows the intraligand enhancements observed in the Pt(3-buten-1-ol)(sar)Cl complex when the *N*-methyl resonance of the *RR* diastereomer is irradiated. Enhancements were observed at both the H_c proton and the CH_2CH_2OH methylene protons of the olefin indicating that, as with the *RS* diastereomer, two rotamers are present. The ratio of the percent enhancements in this diastereomer, though, does not provide a quantitative measure of rotamer populations at room temperature because the through space distance between the methylene and the *N*-methyl protons in one rotamer is shorter than the H_c to *N*-methyl distance in the other rotamer. Therefore, the NOE observed at the methylene protons is much stronger. In addition, a 2.4% enhancement is observed at the olefin H_x proton, indicating that, in this diastereomer, the amino acid chelate ring and the coordinated olefin adopt a conformation which places the *N*-methyl protons a comparable distance from both H_c and H_x.

The room-temperature proton NMR spectrum of the Pt(3-buten-1-ol)(aba)Cl complex is shown in Figure 4. At this temperature, the two rotamers of the compound are interconverting rapidly on the NMR time scale and a single average spectrum is observed. The assignments of the methyl reso-

nances of the amino acid chelate ring to either the CH_3(a) or CH_3(b) positions as labeled in **2** were made on the basis of an NOE difference experiment. A 3.2% NOE was observed only between the downfield methyl resonance and the CH_2CH_2OH protons of the olefin, indicating that the downfield resonance must correspond to CH_3(a) position.

Figure 5a and b show the $H_x/H_c/H_t$ and methyl regions of the Pt(3-buten-1-ol)(aba)Cl spectrum, respectively, at a temperature of 230 K. In both these regions of the spectrum, resonances for two rotamers with equal concentrations are clearly evident. In Figure 5a, two sets of H_x peaks are observed at 4.78 and 4.95 ppm and two distinct sets of doublets, corresponding to the H_c and H_t resonances for each rotamer, are seen in the spectral region from 4.0 to 4.5 ppm. The methyl region from 1.4 to 1.6 ppm, though, was often found to be the most convenient portion of the spectrum for observing resonances from the two rotamers at low temperature. Figure 5b shows that each of the two nonequivalent methyl peaks observed at room temperature has separated into two distinct resonances of approximately equal intensity at 230 K. Strong overlap of two methyl singlets at 1.46 ppm is observed giving a 1:2:1 intensity pattern for the three resolved peaks.

Comparative data on the stereoselectivity of 2-mb coordination (from diastereomer area ratios), NOE ratios for olefinic protons, and low-temperature rotamer ratios (from area ratios of rotamers at 200−230 K) for sarcosine, proline, and α-aminoisobutyric acid complexes, in methanol or water solvents, are summarized in Table 1. Note that isomer ratios in Table 1 are *RS*/*RR* so that values ≫1 indicate great selectivity and preference for *RS* isomer. For compounds that exhibit extreme stereoselectivity, the values listed are approximate or limiting values rather than precise values. For compounds with very little selectivity, values are estimated to be accurate to ±10%. The data are organized into five categories, based on the extent of stereoselectivity (for chloro compounds) and the identity of the ligand at the chloro position (Cl, H_2O, or OH).

Diastereomer ratios for several olefins in Pt(olefin)(sarcosine)Cl complexes are shown in Table 1. As previously reported, stereoselectivity is evident in complexes containing olefins, such as 2-mb, 3-(allyloxy)-1,2-propanediol, allyl alcohol, and allyl ethyl ether, which have a good hydrogen bond acceptor atom (an oxygen for the complexes considered here) connected to the first carbon of the side chain of the olefin.[2] Location of the hydrogen bond acceptor further down the hydrocarbon chain as in 3-buten-1-ol and 4-penten-1-ol or attached to a sulfur atom directly bound to the allyl group, as in allyl sulfonate, eliminates the stereoselectivity altogether. The observed isomer ratios for stereoselective olefins also increase in the series 2-mb > 3-(allyloxy)-1,2-propanediol > allyl alcohol, indicating that, in addition to intraligand hydrogen bonding, steric effects of the other substituents also contribute in an important manner to the overall isomer ratios.

The low-temperature rotamer ratios reported for aba complexes in Table 1 show the same general trend as the ratios of the H_t to H_x NOE enhancements. the Pt(2-mb)(aba)Cl complex shows ∼1 order of magnitude greater rotamer preference than the corresponding allyl alcohol or allyl ethyl ether compounds. The chloro complexes also show a greater rotamer preference than the corresponding aqua complexes, again by a factor of ∼10, and finally, allyl sulfonate, 3-buten-1-ol, and 4-penten-1-ol complexes have essentially equal concentrations of the two rotamers at low temperature. These three ligands also show similar NOE enhancements to H_x and H_t and essentially no stereoselectivity of coordination in their Pt(olefin)(sar)Cl complexes.

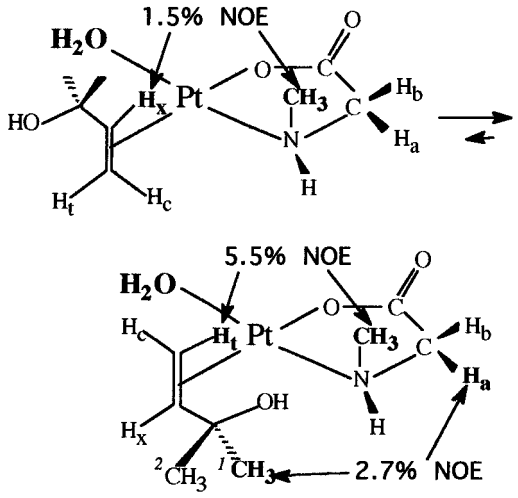

Figure 9. NOEs observed for Pt(2-mb)(sar)$(H_2O)^+$.

Effect of Substitution of Cl by D_2O or OH. The stereoselectivity of olefin coordination is also observed to change substantially when the Cl atom in the Pt(olefin)(amino acid)Cl complexes is replaced with either an aqua or hydroxy ligand. Table 1 lists the diastereomer ratios of Pt(2-mb)(sar)X (where X = Cl, H_2O, OH) complexes in D_2O solution. Any solvent effect on the stereoselectivity of 2-mb coordination in Pt(2-mb)(sar)Cl is too small to be evident, and again only the *RS* diastereomer is observed. The spectrum of the Pt(2-mb)(sar)-H_2O^+ complex, though, clearly shows that a significant amount of the *RR* diastereomer is now present. In both the *N*-methyl (2.7−3.0 ppm) and H_x regions (5.0−5.5 ppm), peaks assignable to both diastereomers are observed with a diastereomer ratio equal to 5.3. Therefore, the stereoselectivity of 2-mb coordination is decreased by ∼1 order of magnitude upon the replacement of the Cl ligand with H_2O. Likewise, conversion of the aqua complex to the hydroxo further decreases the diastereomer ratio by a factor of 7.3 (from 5.3 to 0.72) so that the *RR* diastereomer of the hydroxo species is now preferred slightly over the *RS* isomer.

The effect of chloride substitution for Pt(2-mb)(pro)Cl, most evident in well-resolved H_x quartets of D_2O solutions in the 5.0−5.5 ppm range, closely parallels the effect observed for Pt(2-mb)(sar)Cl. Again, only one diastereomer is present in the chloro complex, but the diastereomer ratio is reduced to 2.6 and 1.0 when the Cl ligand is replaced with H_2O and OH, respectively. The diastereomer ratio of the Pt(2-mb)(pro)H_2O^+ complex is also observed to be a factor of 2 less than the ratio for the corresponding sarcosine compound.

NOE data indicate a similar effect of chloride substitution on the rotamer preference of species derived from Pt(2-mb)-(sar)Cl. Figure 9 shows that in the Pt(2-mb)(sar) $(H_2O)^+$ complex both H_t and H_x NOEs were observed when the *N*-methyl of the *RS* diastereomer was irradiated. The ratio of these enhancements, 3, indicates that the D rotamer (Figure 1) is preferred. This ratio is similar to the diastereomer ratio of 5.0 observed for this compound and parallels the behavior of Pt(allyl ethyl ether)(sar)Cl (diastereomer ratio 4.1; NOE ratio 3) and Pt(allyl alcohol)(sar)Cl (diastereomer ratio 6.0; NOE ratio 7 ± 3, but low solubility reduced accuracy of determination).

Solvent Effects on Stereoselectivity of Olefin Coordination. The stereoselectivities of olefin coordination also show a marked dependence on solvent with diastereomer ratios consistently being higher in methanol solution than in D_2O. Diastereomer ratios for the chloro, aqua, and hydroxy complexes of Pt(2-mb)(sar)X and Pt(2-mb)(pro)X in these two solvents are shown in Tables 1 and 2, respectively, and the diastereomer ratios

Table 2. Effect of pH and Solvent on Diastereomer Ratios for Pt(olefin)(proline)X

X/pH (qualitative)	dominant species/solvent	*RS*/*RR* Ratio
Cl/ mid pH	Pt(2-mb)(pro)Cl/CD_3OD	>50
D_2O/pH < pK_a	Pt(2-mb)(pro)D_2O^+/D_2O	2.6
D_2O/pH < pK_a	Pt(2-mb)(pro)D_2O^+/CD_3OD	4.9
OD/pH ≫ pK_a	Pt(2-mb)(pro)OD/D_2O	1.3
OD/pH ≫ pK_a	Pt(2-mb)(pro)OD/CD_3OD	1.0

Table 3. Effect of Solvent on Diastereomer Ratios of Pt(olefin)(sarcosine)Cl for Chloro Compounds That Exhibit Intermediate Stereoselectivity

	RS/*RR* ratio	
compound	in CD_3OD	in D_2O
Pt(allyloxypropane-1,2-diol)(sar)Cl	8.3	4.0
Pt(allyl alcohol)(sar)Cl	6.0	2.6
Pt(allyl ethyl ether)(sar)Cl	4.1	1.8

Table 4. Differences in the Chemical Shifts of Sarcosine H_a and H_b Resonances in Pt(olefin)(sarcosine)X Complexes

compound/solvent	isomer	H_a-H_b chemical shift (ppm)
Pt(2-mb)(sar)Cl/CD_3OD	*RS*	0.672
Pt(2-mb)(sar)H_2O^+/CD_3OD	*RS*	0.788
Pt(2-mb)(sar)H_2O^+/D_2O	*RS*	0.817
	RR	0.295
Pt(allyl alcohol)(sar)Cl/D_2O	*RS*	0.721
	RR	0.466
Pt(3-buten-1-ol)(sar)Cl/CD_3OD	*RS*	0.463
	RR	0.515
Pt(4-penten-1-ol)(sar)Cl/CD_3OD	*RS*	0.491
	RR	0.460

observed for chloro complexes containing olefins that exhibit an intermediate degree of stereoselectivity in both D_2O and CD_3OD are given in Table 3. In each case the isomer ratio is reduced by a factor of ∼2 upon changing from methanol to D_2O as the solvent.

Sarcosine Chemical Shifts as Indicator of Stereoselectivity of Olefin Coordination. Further insight can be gained into the conformation of the amino acid chelate ring by examining the difference between the chemical shifts of the nonequivalent amino acid methylene protons (labeled H_a and H_b for the less and more shielded protons, respectively, in Figure 6) for several of the sarcosine complexes (Table 4). Here, a correlation between the difference in the chemical shifts observed for the H_a and H_b protons and the stereoselectivity of olefin coordination is observed. Pt(2-mb)(sar)Cl and the *RS* isomers of Pt(2-mb)(sar)H_2O^+ and Pt(allyl alcohol)(sar)Cl all show large differences between the chemical shifts of the H_a and H_b resonances (0.7−0.8 ppm), while this difference is much smaller for the *RR* diastereomers of these compounds and for both diastereomers of the Pt(3-buten-1-ol)(sar)Cl and Pt(4-penten-1-ol)(sar)Cl complexes. The value of 0.4 ppm observed for the 3-buten-1-ol and 4-penten-1-ol complexes suggests an average of two conformations, one with a large difference and another with a much smaller difference.

Large chemical shift differences between the H_a and H_b protons would be expected if the amino acid chelate ring adopted a rigid conformation placing the two protons in very different environments. Such a conformation would be expected to be present in complexes in which an intraligand hydrogen bond is formed between the amino acid NH and the olefin OR moieties. In contrast, with complexes where this hydrogen bond is not formed, the ring is more fluxional and the average chemical shifts of the H_a and H_b resonances are more nearly equal.

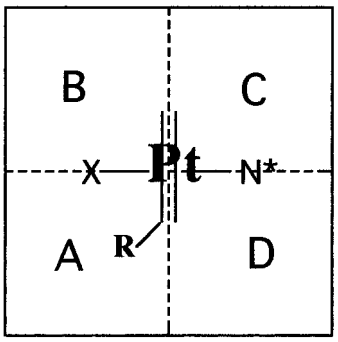

Figure 10. Quadrant labels for the four rotamers of the two diastereomers of Pt(CH_2═CHR)(sar)Cl as denoted in Figure 1.

Conclusions and Discussion

Principal Conclusions. The following conclusions can be drawn from the NMR experiments reported here:

1. For the Pt(2-mb)(sar)Cl and Pt(2-mb)(pro)Cl complexes, which exhibit exceptional stereoselectivity in both methanol and water, the *RS* diastereomer is the predominant isomer in solution as well as in the solid state.

2. For chiral Pt(olefin)(sar)X complexes, the ratio of the NOE enhancements observed at the H_t and H_x protons when the amino acid *N*-methyl resonance of the *RS* diastereomer is irradiated is a sensitive measure of the olefin rotamer ratio for that isomer.

3. Olefins that exhibit no stereoselectivity have H_t to H_x NOE enhancement ratios equal to ∼1, but olefins that exhibit some stereoselectivity give higher ratios. This suggests that the preference for the *RS* diastereomer is a result of a selective lowering of the energy (stabilization) of one of the rotamers of the *RS* diastereomer.

4. When olefin complexes containing achiral amino acids are cooled below their NMR coalescence temperatures (i.e., to <230 K), one rotamer is strongly preferred by olefins that exhibit stereoselective coordination in similar complexes containing N-chiral amino acids, but nearly equal rotamer populations are observed for olefins that show no stereoselectivity. Thus, these low-temperature NMR results correlate well with the NOE experiments.

5. Identification of the attractive interaction between the amino acid NH and olefinic R groups as an intramolecular (but inter-ligand) hydrogen bond is supported by the reduction or elimination of the stereoselectivity which is observed when the Cl atom in Pt(olefin)(amino acid)Cl complexes (amino acid = sarcosine or proline) is replaced with the hydrogen bond acceptor (or donor) ligands H_2O and OH.

6. Large differences between the chemical shifts of the H_a and H_b resonances in the *RS* diastereomers of stereoselective Pt(olefin)(sar)X complexes suggest that the amino acid chelate ring adopts a rigid conformation in these compounds. This result is again consistent with formation of an inter-ligand hydrogen bond in the strongly favored *RS* diastereomer.

Reflections on Hydrogen Bond Stabilization. The evidence reported here and the variation in stereoselectivity shown by over 30 olefins in mixed sarcosine−olefin complexes[2] provide convincing evidence that the origin of stereoselectivity in these systems is the stabilization of one rotamer of the dominant isomer by intramolecular hydrogen bonding, as depicted in Figure 1. These four rotamers, two for each diastereomer, fit the scheme suggested by Gladyz—and shown in Figure 10—for categorizing the stereochemistry of chiral metal complexes that also contain a metal bound prochiral olefin.[10] The effect of replacement of the Cl^- by H_2O and OH^- on the hydrogen-

(10) Gladyz, J., private communication, 1996.

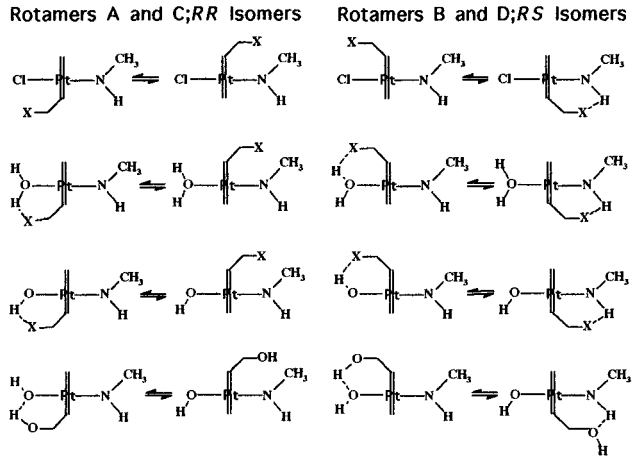

Figure 11. Rotamers of isomers of complexes between a monosubstituted prochiral olefin and an N-chiral square planar platinum(II) template showing hydrogen-bonding opportunities for chloro, aqua, and hydroxo species, including hydroxo acting as proton acceptor for olefinic alcohols. See Figure 1 for structures and Figure 10 for A−D pattern.

bonding opportunities for olefin rotamers is shown in more detail in Figure 11. The rotamers are labeled A−D according to the quadrant occupied by the olefin R group in Figure 1. For the chloro complex, only conformation D permits intramolecular hydrogen bonding, so preference is for *RS* isomers. By contrast, replacement of Cl^- by H_2O permits intramolecular hydrogen bonding for both diastereomers, though both rotamers B and D of the *RS* species allow hydrogen bond formation while only conformation A of the *RR* isomer allows intramolecular hydrogen bond formation. As a result, the diastereomer ratio is closer to 1 for the aqua complex than it is for the chloro species. Deprotonation of the aqua species to the hydroxo species produces a further decrease in stereoselectivity. Two factors might be contributing to this further decrease in selectivity. First of all, the stability of the O−H···X bond might be greater than that of the $O-H_2\cdots X$. In addition, for olefinic alcohols at least, the Pt−O−H oxygen could also be involved as a proton acceptor, so conformations A and B might be dominant rotamers for the *RR* and *RS* isomers, respectively, to yield a nearly equal ratio of the two isomers.

All of these hydrogen-bonding effects on rotamer and isomer populations are attenuated by a change from methanol to water as the solvent. Intramolecular hydrogen bonding is always in competition with intermolecular hydrogen bonding and water is a much better donor and acceptor, so this result is not surprising. One would expect to see even greater stereoselectivity and rotamer preferences in nonpolar solvents, where intramolecular hydrogen bonding does not compete with hydrogen bonding to the solvent. Unfortunately, very low solubility of these complexes in nonpolar aprotic solvents make such measurements impractical.

Barriers to Internal Rotation. The free energy barriers to internal rotation in these complexes do not vary greatly. For the aba complexes, separate rotamers are often detectable (in proton spectra at 300 MHz) substantially above 200 K, while a single weighted average spectrum—albeit considerably broadened by exchange—is observed above 280 K. Attempts to separate the contribution of the energy and entropy to the free energy of activation will be described in a subsequent report.[3]

Reactions of Coordinated Olefins. The factors that influence stereoselectivity of coordination have important implications for catalytic applications for chiral syntheses. We have not investigated the reactions of these coordinated olefins thoroughly, but we have noted that most of them undergo slow decomposition in solution at room temperature, and we have attempted to identify the products of some of those reactions. The coordinated esters allyl acetate and vinyl acetate undergo solvolysis in methanol,[11] and methyl vinyl ketone reacts quite rapidly in methanol to produce a complex mixture of products, so reliable equilibrium constants for displacement of 2-mb and for isomerization were not determined for the latter two. The proline complex, with the stereochemistry controlled by the chirality of the chiral α-carbon is a potential chiral auxiliary for prochiral olefins,[12] but the synthesis of the cis(N,olefin) complex is not very efficient, and the trans(N,olefin) complex shows no stereoselectivity for olefin coordination. Nevertheless, if an efficient reaction of platinum coordinated olefin can proceed without destruction of the Pt−proline template, the reagent might have some utility as a chiral auxiliary for stereoselective modification of prochiral olefins.

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