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Several Novel N-Donor Tridentate Ligands Formed in Chemical Studies of New *fac*-Re(CO)₃ Complexes Relevant to *fac*-^{99m}Tc(CO)₃ Radiopharmaceuticals. Attack of a Terminal Amine on Coordinated Acetonitrile

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Synopsis

A novel ligand was discovered in which acetonitrile appears to have inserted between the two protons and the nitrogen of a primary amine. A proposed pathway for this process involves a putative seven-membered chelate ring (formed by attack of a primary amine on coordinated acetonitrile) that undergoes proton transfer and rearrangement. The pathway is supported by the structure of a related compound that has a methyl group in place of one of the protons.

To evaluate syntheses of *fac*-[Re(CO)₃L]⁺ complexes in organic solvents, we treated *fac*-[Re(CO)₃(CH₃CN)₃]PF₆/BF₄ in acetonitrile with triamine ligands (L). When L had two primary or two tertiary terminal amine groups, the expected *fac*-[Re(CO)₃L]⁺ complexes formed. In contrast, *N,N*-dimethyldiethylenetriamine (*N,N*-Me₂dien) formed an unusual compound, *fac*-[Re(CO)₃(DAE)]BF₄ {DAE = (*Z*)-*N'*-(2-(2-(dimethylamino)ethylamino)ethyl)acetimidamide = (Me₂NCH₂CH₂)NH(CH₂CH₂N=C(NH₂)Me)}. DAE is formed by addition of acetonitrile to the *N,N*-Me₂dien terminal primary amine, converting this sp³ nitrogen to an sp² nitrogen with a double bond to the original acetonitrile sp carbon. The three N's bound to Re derive from *N,N*-Me₂dien. The pathway to *fac*-[Re(CO)₃(DAE)]BF₄ is suggested by a second unusual compound, *fac*-[Re(CO)₃(MAE)]PF₆ {MAE = *N*-methyl-*N*-(2-(methyl-(2-(methylamino)ethyl)amino)ethyl)acetimidamide = MeN(H)-CH₂CH₂-N(Me)-CH₂CH₂-N(Me)-C(Me)=NH}, isolated after treating *fac*-[Re(CO)₃(CH₃CN)₃]PF₆ with *N,N',N''*-trimethyldiethylenetriamine (*N,N',N''*-Me₃dien). MAE chelates via a terminal and a central sp³ N from *N,N',N''*-Me₃dien and via one sp² NH in a C(Me)=NH group. This group is derived

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Supporting Information Available: Crystallographic data for [Re(CO)₃(MAE)]PF₆, [Re(CO)₃(MAEH)F]PF₆, [Re(CO)₃(EAE)]BF₄, and [Re(CO)₃(DAE)]BF₄ in CIF format, a scheme based on X-ray structures for formation of [Re(CO)₃(DAE)]⁺, a figure with seven-membered chelate ring pucker, ¹H-¹H COSY NMR spectra of [Re(CO)₃(MAE)]PF₆ and [Re(CO)₃(DAE)]BF₄ in DMSO-*d*₆, ROESY NMR spectra of [Re(CO)₃(DAE)]BF₄ in DMSO-*d*₆ and in acetonitrile-*d*₃, and ¹H NMR spectra of [Re(CO)₃(DAE)]BF₄ in acetonitrile-*d*₃ at different temperatures. This material is available free of charge via the internet at <http://pubs.acs.org>.

from acetonitrile by addition of the other N,N',N'' -Me₃dien terminal amine to the nitrile carbon. This addition creates an endocyclic NMe group within a seven-membered chelate ring. The structure and other properties of fac -[Re(CO)₃(MAE)]PF₆ allow us to propose a reaction scheme for the formation of the unprecedented DAE ligand. The new compounds advance our understanding of the spectral and structural properties of Re analogues of ^{99m}Tc radiopharmaceuticals.

Introduction

Radiopharmaceuticals containing the fac -{^{99m}Tc^I(CO)₃}⁺ core hold promise for the development of new clinically useful imaging agents, fac -[^{99m}Tc^I(CO)₃L]ⁿ (L is a facially coordinated tridentate ligand).^{1,2} The development of ^{99m}Tc radiopharmaceutical agents benefits from an understanding of the features of fac -[Re^I(CO)₃L]ⁿ analogues. Also, ¹⁸⁶Re and ¹⁸⁸Re are among the most promising radionuclides for therapeutic applications.³ Many ligands having the ability to chelate facially with three donors such as N or a combination of N and O donors form stable and kinetically inert complexes with the fac -{M^I(CO)₃}⁺ core (M = ^{99m}Tc, Re).^{3–5} Although N donor groups are superior to the carboxylate O donor group in enhancing the ability of L to form fac -[^{99m}Tc^I(CO)₃L]ⁿ complexes,⁶ carboxylate groups generally have superior biological properties as radiopharmaceutical renal imaging agents.^{1,7} fac -[^{99m}Tc^I(CO)₃(NTA)]^{2–} (NTAH₃ = nitrilotriacetic acid) was recently reported to have pharmacodynamic renal clearance properties in rats good enough to merit testing in humans.⁸ This radiopharmaceutical is based on an aminopolycarboxylate ligand that can realistically form only one isomer. However, renal imaging agents with other target ligands, which usually have more N donors (such as polyamino-polycarboxylic acid ligands), form isomers under the normal aqueous conditions in which they are made.^{7,9} The presence of isomers complicates biomedical imaging.

While much of our work has centered on examining preparations of fac -[M(CO)₃L]ⁿ (M = Re or ^{99m}Tc) complexes in water,^{1,7,8,10–14} for a number of reasons we wished to explore preparative chemistry in non-aqueous solvents. First, understanding the non-aqueous chemistry might allow us to prepare renal agents with only one or mainly one isomer. Second, isostructural technetium (radioactive imaging) and rhenium (fluorescence microscopic imaging) compounds allow correlation of images from in vivo and in vitro studies, respectively.^{4,15,16} However, the ligands needed to prepare fluorescent compounds are often only sparingly soluble in aqueous media. Third, for some L, the preparation of fac -[M(CO)₃L]ⁿ (M = Re or ^{99m}Tc) complexes in water was not successful. Reasoning that reactions in organic solvents might be followed more easily in real time by NMR spectroscopy, we decided to evaluate fac -[Re(CO)₃(CH₃CN)₃]⁺ as a soluble precursor for synthesizing fac -[Re(CO)₃L]ⁿ compounds in organic solvents. We began our work with relatively simple tridentate amine ligands because complexes of several of these ligands had already been prepared in water.

Treatment of fac -[Re(CO)₃(CH₃CN)₃]⁺ with various tridentate amine ligands has produced several novel compounds, which most likely arise from reaction of the coordinated nitrile with ligand terminal amines. The reactivity of coordinated nitriles is an important, well-studied topic, and the reader is referred to several excellent recent reviews and articles for background information.^{17–20}

An important goal is to interpret how structure affects the NMR spectra of the fac -[Re^I(CO)₃L]ⁿ complexes. Previous work having this goal benefited from the study of the interaction of the chloride anion with the protons of the Re–NH groups of fac -[Re(CO)₃L]ⁿ complexes.¹⁰ The topic of metal complexes as anion receptors is currently under intense study.^{21–23} Thus, we utilize here the same approach to evaluate the interaction of Cl[–] with some of the new fac -[Re(CO)₃L]ⁿ complexes because these complexes have unusual NH groups. When

discussing specific compounds, we generally do not use the *fac*-designation because all the new compounds have this geometry.

Experimental Section

Materials

Re(CO)₁₀, diethylenetriamine (dien), *N,N',N''*-trimethyldiethylenetriamine (*N,N',N''*-Me₃dien), *N,N,N',N'',N'''*-pentamethyldiethylenetriamine (*N,N,N',N'',N'''*-Me₅dien), tetraethylammonium chloride, AgPF₆ and AgBF₄ from Aldrich, *N,N*-dimethyldiethylenetriamine (*N,N*-Me₂dien) from Ames Laboratories, *N,N',N''*-triethyldiethylenetriamine (*N,N',N''*-Et₃dien) from City Chemical LLC, and *N'*-methyldiethylenetriamine (*N'*-Medien) from TCI America were used as received. Re(CO)₅Br, and [Re(CO)₃(CH₃CN)₃]⁺ salts were synthesized by using slight modifications of known methods.^{24–26} [Re(CO)₃(dien)]PF₆ was prepared as previously reported.¹⁰

NMR Measurements

¹H NMR spectra were recorded on a Bruker 400 MHz spectrometer. Peak positions are relative to TMS or solvent residual peak, with TMS as reference. All NMR data were processed with TopSpin and Mestre-C software.

X-ray Data Collection and Structure Determination

Colorless single crystals were placed in a cooled nitrogen gas stream at 90 K on a Nonius Kappa CCD diffractometer fitted with an Oxford Cryostream cooler with graphite-monochromated Mo K α (0.71073 Å) radiation. Data reduction included absorption corrections by the multi-scan method, with HKL SCALEPACK.²⁷ All X-ray structures were determined by direct methods and difference Fourier techniques and were refined by full-matrix least squares by using SHELXL97.²⁸ All non-hydrogen atoms were refined anisotropically. All H atoms were visible in difference maps, but were placed in idealized positions, except for some on N, which were refined when their positions were not unambiguously predictable. A torsional parameter was refined for each methyl group. The anion in [Re(CO)₃(EAE)]BF₄ also exhibits both orientational and substitutional disorder. The F atoms of the BF₄[–] occupy two sets of sites, and a site of apparent ~5% occupancy by Br[–] lies near the B position. Crystal data and refinement details are presented in Table 1.

[Re(CO)₃(DAE)]BF₄ (DAE = (*Z*)-*N'*-(2-(2-(dimethylamino)ethylamino)ethyl)acetimidamide)

N,N-Me₂dien (15 μ L, 0.10 mmol) was added to a solution of [Re(CO)₃(CH₃CN)₃]BF₄ (48 mg, 0.10 mmol) in 6 mL of acetonitrile, and the reaction mixture was heated at reflux for 24 h. The volume was reduced to ~2 mL, and diethyl ether was added until a fine precipitate was just visible. The reaction mixture was allowed to stand at room temperature; colorless crystals were observed in 2–3 days (15 mg, 28% yield). ¹H NMR signals (ppm) in DMSO-*d*₆: 7.99 (s, 1H, NH), 7.28 (s, 1H, NH), 7.10 (s, 1H, NH), 3.19 (m, 4H, CH₂), 3.03 (s, 3H, CH₃), 2.97 (m, 2H, CH₂), 2.63 (m, 2H, CH₂), 2.44 (s, 3H, CH₃), 2.31 (s, 3H, CH₃). The product was characterized by single-crystal X-ray diffraction.

[Re(CO)₃(MAE)]PF₆ (MAE = *N*-methyl-*N'*-(2-(methyl-(2-(methylamino)ethyl)amino)ethyl)acetimidamide)

A 10% excess of *N,N',N''*-Me₃dien (16 μ L, 0.11 mmol) was added to a solution of [Re(CO)₃(CH₃CN)₃]PF₆ (54 mg, 0.10 mmol) in 10 mL of acetonitrile. The reaction mixture was heated at reflux for 24 h. A white powder was collected, which later gave X-ray quality crystals upon slow evaporation of a methanol solution (29 mg, 48% yield). ¹H NMR signals (ppm) in DMSO-*d*₆: 7.17 (s, 1H, NH), 4.50 (s, 1H, NH), 4.22 (m, 1H, CH₂), 3.20 (m, 1H, CH₂), 3.10

(s, 3H, CH₃), 3.03 (m, 2H, CH₂), 2.98 (s, 3H, CH₃), 2.91 (d, 3H, N1CH₃), 2.80 (m, 2H, CH₂), 2.60 (m, 2H, CH₂), 2.14 (s, 3H, CH₃). The above complex can be prepared more readily and reliably by the following procedure: *N,N',N''*-Me₃dien (14 μL, 0.10 mmol) was added to a solution of [Re(CO)₃(CH₃CN)₃]PF₆ (54 mg, 0.10 mmol) in 8 mL of acetonitrile, and the reaction mixture was heated at reflux for 16 h, whereupon a very small amount of a fine precipitate was visible. The reaction mixture was transferred to a vial and allowed to evaporate to dryness at room temperature. The residue was dissolved in methanol, an excess of diethyl ether was added, and the mixture was left at room temperature. The white precipitate that had aggregated into clumps after 2 days was scraped from the walls of the vial, placed on a filter, and washed with diethyl ether. The NMR spectrum of this precipitate was identical to that of the crystals described above. The BF₄[−] salt could also be obtained by using a similar procedure, which yielded a white precipitate having an NMR spectrum identical to that of the PF₆[−] crystals; however, the precipitate could not be crystallized.

[Re(CO)₃(MAEH)F]PF₆

Crystallization of the precipitate obtained during one of the syntheses of [Re(CO)₃(MAE)]PF₆ produced two types of crystals. One type, which was more abundant, was that just described for [Re(CO)₃(MAE)]PF₆, as confirmed by measurement of the unit cell dimensions. The less abundant type of crystals (needle-like), characterized by single-crystal X-ray diffraction, contained [Re(CO)₃(MAEH)F]PF₆. ¹H NMR signals (ppm) of the mixture in DMSO-*d*₆ attributable to [Re(CO)₃(MAEH)F]PF₆: 6.93 (s, N4H), 6.19 (s, N1H), 3.03 (s, CH₃), 2.99 (s, CH₃), 2.56 (d, N1CH₃), 2.23 (s, C12H₃).

[Re(CO)₃(EAE)]BF₄ (EAE = *N*-ethyl-*N*-(2-(ethyl-(2-(ethylamino)ethyl)amino)ethyl)acetimidamide)

A 10% excess of *N,N',N''*-Et₃dien (20 μL, 0.11 mmol) was added to a solution of [Re(CO)₃(CH₃CN)₃]BF₄ (48 mg, 0.10 mmol) in 6 mL of acetonitrile, and the reaction mixture was heated at reflux for 16 h. The volume was reduced to ~2 mL, and diethyl ether (10–15 mL) was added, whereupon a fine precipitate formed. After about 30 min the precipitate was collected on a filter and washed with diethyl ether (24 mg, 40% yield). (When the precipitate was too fine to filter, crystals could be obtained by letting the mixture stand covered and undisturbed for 1 day.) Crystals suitable for single-crystal X-ray diffraction grew upon slow evaporation of a solution of the compound in methanol. ¹H NMR signals (ppm) in DMSO-*d*₆: 7.03 (s, 1H, NH), 4.40 (s, 1H, NH), 4.15 (m, 1H, CH₂), 3.42 (m, 2H, CH₂), 3.20 (m, 2H, CH₂), 3.08 (m, 5H, CH₂), 2.80 (m, 2H, CH₂), 2.62 (m, 2H, CH₂), 2.18 (s, 3H, CH₃), 1.23 (t, 3H, CH₃), 1.14 (overlapping triplets, 6H, CH₃). The PF₆[−] salt could also be obtained by using a similar procedure, which yielded a white precipitate having an NMR spectrum identical to that of [Re(CO)₃(EAE)]BF₄.

Cl[−] Titrations

Aliquots of a NEt₄Cl stock solution containing 5 mM of the desired *fac*-[Re(CO)₃(L)]⁺ complex in DMSO-*d*₆ or acetonitrile-*d*₃ was added to 600 μL of a 5 mM solution of the complex, giving 1 to 140–150 mM Cl[−]. The solution was monitored by ¹H NMR spectroscopy upon each addition.

Addition of Base to [Re(CO)₃(MAE)]PF₆ and [Re(CO)₃(EAE)]BF₄

A 5 mM solution of [Re(CO)₃(MAE)]PF₆ crystals in DMSO-*d*₆ (600 μL) was treated with aqueous sodium hydroxide (0.1 M, 10 μL), and the solution was monitored by ¹H NMR spectroscopy. Similar experiments were conducted with a dilute NaOH solution (0.033 M, 10 μL) and with [Re(CO)₃(EAE)]BF₄ (0.1 M, 10 μL).

Results and Discussion

Synthetic Results

New $[\text{Re}(\text{CO})_3\text{L}]^n$ products prepared from $[\text{Re}(\text{CO})_3(\text{CH}_3\text{CN})_3]\text{PF}_6/\text{BF}_4$ in acetonitrile are shown in Scheme 1. In water starting with $[\text{Re}(\text{CO})_3(\text{H}_2\text{O})_3]^+$, the ligands in Scheme 1 coordinate unchanged in a tridentate fashion to form normal $[\text{Re}(\text{CO})_3\text{L}]^n$ products.¹⁰ Because dien and $N,N,N',N'',N'''\text{-Me}_5\text{dien}$ gave the same normal $[\text{Re}(\text{CO})_3\text{L}]^n$ products in acetonitrile starting with $[\text{Re}(\text{CO})_3(\text{CH}_3\text{CN})_3]\text{PF}_6/\text{BF}_4$ (details not given) or in water starting with $[\text{Re}(\text{CO})_3(\text{H}_2\text{O})_3]^+$,¹⁰ the formation of different products in acetonitrile than in water for $N,N\text{-Me}_2\text{dien}$, $N,N',N''\text{-Me}_3\text{dien}$, and $N,N',N''\text{-Et}_3\text{dien}$ is attributable to the presence in these ligands of both steric bulk and NH groups. The reaction pathways in acetonitrile leading to the compounds in Scheme 1 are best discussed after we describe the structures of the new $[\text{Re}(\text{CO})_3\text{L}]^n$ complexes.

Structural Results

All complexes reported here exhibit a pseudo octahedral structure, with the three carbonyl ligands occupying one face and having typical Re–CO bond distances.¹⁰ The remaining three coordination sites are occupied by three nitrogen atoms of novel ligands in $[\text{Re}(\text{CO})_3(\text{DAE})]\text{BF}_4$ (Figure 1), $[\text{Re}(\text{CO})_3(\text{MAE})]\text{PF}_6$ (Figure 2a), and $[\text{Re}(\text{CO})_3(\text{EAE})]\text{BF}_4$ (Figure 2c). However, in $[\text{Re}(\text{CO})_3(\text{MAEH})\text{F}]\text{PF}_6$, two coordination sites are occupied by nitrogens and the third by fluoride (Figure 2b). Crystal data and details of the structural refinement for all these complexes are summarized in Table 1. The atom numbering systems in the ORTEP figures are used to describe the solid-state data. All complexes in Table 2 have a five-membered chelate ring with comparable N1–Re–N2 angles.

The molecular structure of $[\text{Re}(\text{CO})_3(\text{DAE})]\text{BF}_4$ (Figure 1) reveals that the bound tridentate DAE ligand is an addition product between $N,N\text{-Me}_2\text{dien}$ and acetonitrile. None of the Re-bound N's are derived from acetonitrile. One of the two five-membered chelate rings anchored by the central N (N2) is terminated by N3, the original $N,N\text{-Me}_2\text{dien}$ primary amine N. The relatively short N3–C10 bond (1.293(6) Å; C10 is the original nitrile C) indicates double-bond character and an sp^2 N. The other chelate ring is terminated by N1, the original $N,N\text{-Me}_2\text{dien}$ tertiary amine N.

In $[\text{Re}(\text{CO})_3(\text{MAE})]\text{PF}_6$ (Figure 2a), one terminal amine N of the $N,N',N''\text{-Me}_3\text{dien}$ ligand has now become an endocyclic nitrogen (N3) having three bonds to C and no NH bonds. This N has characteristics of an sp^2 N and is part of a seven-membered chelate ring terminated by N4 (the original nitrile N) and anchored by N2, the original $N,N',N''\text{-Me}_3\text{dien}$ central N. N2 anchors the other chelate ring, and thus an uncommon five-membered/seven-membered chelate ring combination is created.

The bond lengths and angles centered on N3, N4 and C11 show that these are sp^2 hybridized (relatively planar, bond angles near 120°) and that the N4–C11–N3 grouping exhibits electron delocalization. The N4–C11 (1.318(3) Å) and N3–C11 (1.344(3) Å) bonds show double-bond character. $[\text{Re}(\text{CO})_3(\text{EAE})]\text{BF}_4$ (Figure 2c) has a structure very similar to that of $[\text{Re}(\text{CO})_3(\text{MAE})]\text{PF}_6$, differing only in having ethyl groups instead of methyl groups at N1, N2, and N3.

Compared to $[\text{Re}(\text{CO})_3(\text{MAE})]\text{PF}_6$, the molecular structure of $[\text{Re}(\text{CO})_3(\text{MAEH})\text{F}]\text{PF}_6$ (Figure 2b) has the striking feature that N4 (derived from acetonitrile) is no longer part of an NH group bound to Re; the N4H has been protonated to become a dangling NH_2 group, as found in $[\text{Re}(\text{CO})_3(\text{DAE})]\text{BF}_4$. This NH_2 group forms a hydrogen bond to F, which is directly bound to Re.

Other complexes are known to have a seven-membered chelate ring similar to the type found in the MAE and EAE complexes.^{29–32} One example is *cis*-[Pt(NH=CPhNBu'^tCH₂CH₂NHBu'^t)Cl₂]; Natile and co-workers³⁰ described this pseudo square planar Pt^{II} compound as the final product of the addition of *N,N'*-Bu'^t₂ethylenediamine to coordinated benzonitrile. The obvious difference in geometry between six-coordinate Re^I tricarbonyl complexes versus four-coordinate Pt^{II} complexes might suggest that useful comparisons are not possible because octahedral complexes are usually subject to greater interligand steric interactions. However, Re^I tricarbonyl complexes are sterically undemanding because of the small size of the CO ligands and the relatively long bonds made by Re^I. Bond distances involving Re^I are longer than those involving Pt^{II}.^{11,25,33,34} N–M–N bite angles for chelate rings in related Pt^{II} and Re^I compounds are more acute in Re^I compounds.^{11,35} We believe this is true because the chelate rings normally adopt a preferred conformation or pucker; this conformation fixes the N-to-N non-bonded distance. However, the angles in the Pt^{II} and the Re^I seven-membered chelate rings being compared here have similar values, 89.0(7) and 90.47(7)°, in contrast to the normal situation. Also in contrast to the normal situation, the non-bonded distance between these N atoms is much smaller in the Pt complex (2.79(2) Å) than in the Re complex (3.178(3) Å). The seven-membered chelate ring may be inherently strained and, unlike in other cases, the longer Re–N bond distances seem to allow the ring to reduce strain, explaining the unusually long N-to-N non-bonded distance, the large N–Re^I–N bite angle, and the low chelate ring pucker in Re^I vs. Pt^{II} (Figure S1, Supporting Information). This strain aids in the transformation of the seven-membered chelate ring to a five-membered chelate ring as discussed next.

Implications for the Reaction Pathway Forming [Re(CO)₃(DAE)]BF₄ from the Structures of [Re(CO)₃(MAE)]PF₆ and [Re(CO)₃(MAEH)F]PF₆

We believe that a complex of the [Re(CO)₃(MAE)]⁺ type initially formed as an intermediate, which then rearranged to give [Re(CO)₃(DAE)]⁺ (Scheme 2). We propose that the early phase of the reaction between *N,N*-Me₂dien and [Re(CO)₃(CH₃CN)₃]BF₄ includes an attack of a terminal amine on the sp carbon of a coordinated acetonitrile. This attack leads to formation of a seven-membered ring (as found in [Re(CO)₃(MAE)]PF₆); this ring then rearranges to give the [Re(CO)₃(DAE)]BF₄ product. The key reason that the rearrangement is possible relates to the fact that the putative [Re(CO)₃(MAE)]⁺ type intermediate on the pathway to the [Re(CO)₃(DAE)]BF₄ product would have an endocyclic NH (N3H) rather than an N3Me group in the seven-membered ring of [Re(CO)₃(MAE)]PF₆ (Scheme 3). The stable [Re(CO)₃(MAE)]⁺ and [Re(CO)₃(EAE)]⁺ compounds share with the stable Pt complex, *cis*-[Pt(NH=CPhNBu'^tCH₂CH₂NHBu'^t)Cl₂],³⁰ the feature that the endocyclic non-coordinated nitrogen does not have a bound proton. All bonds to N3 in [Re(CO)₃(MAE)]PF₆ are to carbon. The N3 atom in this ring has no lone pair available to coordinate to Re. However, the similarly situated N3 of the postulated seven-membered ring of the intermediate on the pathway to [Re(CO)₃(DAE)]BF₄ has one bound proton; this N3H could release its proton as it generates the lone pair needed to form the Re–N3 bond. This proton can serve as the proton needed to convert the dissociating N4H to a NH₂ group (Scheme 2); this process could be stepwise or concerted. In the Supporting Information, we illustrate some of these points using a scheme based on the X-ray structures.

The large angle within the chelate ring involving N4 (Re–N4–C11 ~ 139°) of [Re(CO)₃(MAE)]PF₆ provides evidence that strain may predispose N4 to dissociate. The molecular structure of [Re(CO)₃(MAEH)F]PF₆ (Figure 2b) may provide some evidence as to the tendency of N4H to dissociate and be protonated to form an NH₂ group. Although the process involves a proton from the HF formed *in situ* from the PF₆[–] anion or present as an impurity in the AgPF₆ reagent, [Re(CO)₃(MAEH)F]PF₆ may be considered to resemble a species that could be present in the rearrangement pathway discussed in the preceding paragraph if the process is not concerted.

NMR Spectroscopy

All complexes reported were characterized by NMR spectroscopy in DMSO- d_6 and acetonitrile- d_3 . On the basis of the molecular structure of $[\text{Re}(\text{CO})_3(\text{MAE})]\text{PF}_6$, two different types of NH groups are present, as illustrated in Figure 3. For *fac*- $[\text{Re}(\text{CO})_3\text{L}]^n$ complexes,^{7, 10} N1H is referred to as an *exo*-NH proton, as it points away from the carbonyl groups (versus an *endo*-NH proton pointing toward the carbonyl groups). The N4H is not classified in this way because N4 is sp^2 hybridized. Two ^1H NMR peaks of $[\text{Re}(\text{CO})_3(\text{MAE})]\text{PF}_6$ in DMSO- d_6 decreased in size when D_2O was added, indicating that these are NH signals. The broad NH signal at 4.50 ppm (Table 3), assigned to the *exo*-N1H from the COSY cross-peak to the N1CH₃ doublet at 2.91 ppm (Figure S2, Supporting Information), falls within the range observed for *exo*-NH's.¹⁰ Of the four methyl peaks for $[\text{Re}(\text{CO})_3(\text{MAE})]\text{PF}_6$, only N1CH₃ could be a doublet. The sharp NH peak at 7.17 ppm, which must be from N4H, has a COSY cross-peak to a singlet at 2.14 ppm; this must be the C12H₃ signal.

Additional confirmation for the C12H₃ signal assignment comes from the presence of a similar methyl singlet at 2.18 ppm in the spectrum of $[\text{Re}(\text{CO})_3(\text{EAE})]\text{BF}_4$, which can have only the C12H₃ signal as a singlet because the other three methyl groups are in the ethyl groups. Many signals such as a multiplet at ~4.2 ppm (assigned by COSY to one of the protons of the C7H₂ methylene group bonded to the delocalized N3–C11–N4 amidine group) and the NH signals have similar shifts for both $[\text{Re}(\text{CO})_3(\text{MAE})]\text{PF}_6$ and $[\text{Re}(\text{CO})_3(\text{EAE})]\text{BF}_4$ (Table 3). For both, the NH signals are more upfield in acetonitrile versus DMSO, a finding attributable to the weaker interaction of acetonitrile with the NH groups.

For $[\text{Re}(\text{CO})_3(\text{DAE})]\text{BF}_4$ (Figure 1), 2D NMR experiments were used to assign the signals in DMSO- d_6 (Figures S3 and S4, Supporting Information), and NH signals were identified by addition of D_2O (Table 3). The N1CH₃ signals were assigned from an NOE cross-peak at 3.03 and 2.44 ppm. The peak of the central NH (N2H, 7.10 ppm) was identified by COSY and NOE correlations with two multiplets, at 3.19 and 2.97 ppm, from the N2-CH₂ groups. The COSY cross-peak between the relatively sharp NH peak at 7.28 ppm (Figure 4) and the CCH₃ signal at 2.31 ppm (Figure S4, Supporting Information) assigns these to N4Ha and the methyl group derived from acetonitrile. (See Figure 5 for the designations of the N4Ha and N4Hb protons.) This assignment was confirmed by the relatively stronger NOE cross-peak from the CCH₃ peak to the N4Hb signal (7.99 ppm) than to the N4Ha signal.

In general, the NH signals of the new compounds were sharp at 25 °C. In contrast, for $[\text{Re}(\text{CO})_3(\text{DAE})]\text{BF}_4$ the NH₂ peaks were sharp in DMSO- d_6 but broad in acetonitrile- d_3 (Figure 4), a solvent that interacts weakly with NH groups. We reasoned that the NH₂ group may rotate at room temperature, but that DMSO may restrict this rotation by H-bonding to the NH₂ protons. Indeed, all three NH signals were sharp in acetonitrile- d_3 at –5 °C. Increasing the temperature resulted in considerable broadening of the NH₂ signals (Figure S5, Supporting Information). The peak width of the central NH (N2H) was hardly affected. The behavior of the NH₂ signals above 25 °C was complicated, suggesting that a dynamic process in addition to rotation about the C–N bond occurs at elevated temperatures. Therefore, we performed a ROESY experiment at –5 °C in acetonitrile- d_3 . The spectrum contained a negative cross-peak between NH signals at 6.58 and 6.02 ppm (Figure S6, Supporting Information). The magnitude was larger than a negative N4Ha–N4Hb exchange cross-peak in a ROESY spectrum recorded in DMSO- d_6 at room temperature (Figure S3, Supporting Information). Thus, the rate of rotation of the N4H₂ group is faster in acetonitrile- d_3 at –5 °C than in DMSO- d_6 at 25 °C.

NH to ND Exchange

After addition of D_2O (100 μL) to DMSO- d_6 solutions (5 mM, 600 μL), the two NH₂ protons of $[\text{Re}(\text{CO})_3(\text{DAE})]\text{BF}_4$ underwent immediate H to D exchange, whereas the central N2H had

an exchange half-life of ~5 min. A similar experiment for $[\text{Re}(\text{CO})_3(\text{MAE})]\text{PF}_6$ showed that the *exo*-NH in the terminal $\text{NH}(\text{CH}_3)$ group had a half-life of ~30 min, and N4H had a half-life of 24 h. The N4H exchange half-life of $[\text{Re}(\text{CO})_3(\text{EAE})]\text{BF}_4$ (24 h) was the same as that of $[\text{Re}(\text{CO})_3(\text{MAE})]\text{PF}_6$. However, the half-life of the exchange of the *exo*-N1H of $[\text{Re}(\text{CO})_3(\text{EAE})]\text{BF}_4$ was longer (~1 h) than that of $[\text{Re}(\text{CO})_3(\text{MAE})]\text{PF}_6$, undoubtedly because of the better electron donation of Et vs. Me. These results indicate that the Re-bound sp^2 N of the seven-membered ring is relatively electron rich and therefore could protonate and dissociate.

Under similar experimental conditions, the exchange half-lives of the $[\text{Re}(\text{CO})_3(\text{dien})]\text{PF}_6$ complex were found to be ~1 h, 2 h, and 12 h for the central, *exo*-NH and *endo*-NH protons, respectively.

Interaction of NH Protons with the Cl^- Anion

When Cl^- was added to 5 mM solutions of *fac*- $[\text{Re}(\text{CO})_3\text{L}]^+$ complexes, downfield shift changes, $\Delta\delta$, were observed.¹⁰ The $\Delta\delta$ of the relatively upfield $[\text{Re}(\text{CO})_3(\text{MAE})]\text{PF}_6$ *exo*-N1H signal reached a plateau of ~1.3 ppm at 100 mM Cl^- in $\text{DMSO}-d_6$ (Figure 6). This behavior is in agreement with the finding that the *exo*-NH group typically shifts downfield by ~1 ppm in $\text{DMSO}-d_6$ on addition of Cl^- to *fac*- $[\text{Re}(\text{CO})_3\text{L}]^+$ complexes having $\text{L} = \text{dien}$ or simple dien-related derivatives.¹⁰ Because H-bonding to solvent causes downfield shifts, the relatively upfield shift of *exo*-NH signals was attributed to steric hindrance to solvation of the *exo*-NH groups of $[\text{Re}(\text{CO})_3(\text{dien})]\text{PF}_6$ by virtue of their being located in the pocket (as illustrated for $[\text{Re}(\text{CO})_3(\text{MAE})]\text{PF}_6$ in Figure 3 above). This $\Delta\delta$ behavior was explained by suggesting that the Cl^- anion, owing to its small size, can enter the sterically hindered pocket and form H-bonds to the two *exo*-NH's. These *exo*-NH's are close enough (~2.5 Å) to interact simultaneously with the chloride ion; this two-proton interaction was more favorable than when only one *exo*-NH was present in the complex.¹⁰ A similar explanation accounts for the $\Delta\delta$ of the *exo*-NH signal of $[\text{Re}(\text{CO})_3(\text{MAE})]\text{PF}_6$. The plot in Figure 6 is very close to that for the *exo*-NH of $[\text{Re}(\text{CO})_3(\text{dien})]\text{PF}_6$.¹⁰ The $\Delta\delta$ of the N4H signal of $[\text{Re}(\text{CO})_3(\text{MAE})]\text{PF}_6$ exactly paralleled that of the *exo*-NH, but $\Delta\delta$ was only ~0.6 ppm. These results are consistent with synergistic interaction with chloride of both NH protons, which are separated by ~2.5 Å (Figure 3).

In acetonitrile- d_3 , on addition of Cl^- the relatively upfield $[\text{Re}(\text{CO})_3(\text{MAE})]\text{PF}_6$ *exo*-N1H signal (at 3.39 ppm, Table 3) shifted downfield ($\Delta\delta \sim 3.3$ ppm). The N4H signal (at 6.41 ppm) shifted downfield only ~1.8 ppm. The maximum shift change was observed at a much lower concentration of Cl^- in acetonitrile- d_3 (20 mM, Figure 7) than in $\text{DMSO}-d_6$ (~100 mM), consistent with the weaker H-bonding of the acetonitrile solvent. The plots for $\Delta\delta$ for both signals are parallel for the reason given in the preceding paragraph, namely both protons interact with chloride ion.

When Cl^- was added to a solution of $[\text{Re}(\text{CO})_3(\text{DAE})]\text{BF}_4$ in acetonitrile- d_3 , the three NH signals shifted downfield in parallel ($\Delta\delta$ plateau values at ~110 mM $\text{Cl}^- = \sim 1.5$, ~0.8, and ~2 ppm for N4Ha, N4Hb, and the central NH, respectively, Figure 8). A $\Delta\delta$ of 2 ppm is large for a central NH signal, as the maximum change in shift for the central NH of related N donor $\text{L}'\text{s}$ in *fac*- $[\text{Re}(\text{CO})_3\text{L}]^n$ complexes is ≤ 1 ppm and occurs at higher Cl^- concentration (unpublished results).¹⁰ The NH_2 group of $[\text{Re}(\text{CO})_3(\text{DAE})]\text{BF}_4$ is not close enough to the central NH to interact synergistically with Cl^- . In other cases in which the central NH group was present, the complex had *exo*-NH groups that could cooperatively bind the Cl^- anion.¹⁰ Thus, Cl^- interacted preferentially at this site. The resulting H-bonded ion pair would have zero overall charge, decreasing the interaction of a second Cl^- with the central NH of the complex, which is now a neutral ion pair. However, the competing NH_2 site of $[\text{Re}(\text{CO})_3(\text{DAE})]\text{BF}_4$ is far from the positive metal center (Figure 5), and this group interacts relatively weakly with Cl^- . Thus, the

interaction of Cl^- with the central NH may be more favorable than in previous cases.¹⁰ Nevertheless, this interaction is relatively weak because a fairly high Cl^- concentration is needed for $\Delta\delta$ of the central NH signal of $[\text{Re}(\text{CO})_3(\text{DAE})]\text{BF}_4$ to plateau (Figure 8).

Isomerization of $[\text{Re}(\text{CO})_3(\text{MAE})]\text{PF}_6$

One important issue relevant to radiopharmaceuticals is the stereochemistry of coordinated secondary amines, which have two configurations that can interconvert via base catalysis.^{7, 10} We assessed isomerization at N1 of $[\text{Re}(\text{CO})_3(\text{MAE})]\text{PF}_6$, resulting from addition of aqueous NaOH to a $\text{DMSO}-d_6$ solution. An initial NMR spectrum (Figure 9, top) recorded before addition of OH^- confirmed that the complex was isomerically pure. After addition of OH^- (1.7 mM), a new set of signals observable in the first recorded spectrum (5 min) grew within 20 min to its final intensity (13% new signals vs. 87% initial signals). The new product has a sharp and a broad NH signal (Figure 9, bottom) and a methyl doublet (not shown). The broad signal and an associated methyl doublet allow us to establish that the new signals come from the isomer of $[\text{Re}(\text{CO})_3(\text{MAE})]\text{PF}_6$ having the inverted N1 configuration (*endo* NH, the H points toward the carbonyls). Upon addition of D_2O to this base-isomerized sample, the N1CH_3 doublet for both isomers immediately became singlets. The new *endo*-NH signal is more downfield (6.19 ppm) than the *exo*-NH signal (4.50 ppm), and the new *exo*- N1CH_3 signal (2.56 ppm) is more upfield than the *endo*- N1CH_3 signal (2.91 ppm). The more downfield NH signal correlates with the more upfield CH_3 signal. These shift values and correlations agree well with data for *chiral* $[\text{Re}(\text{CO})_3(\text{N,N',N''-Me}_3\text{dien})]\text{PF}_6$ (ppm: *endo*-N1H, 6.39, *exo*- N1CH_3 doublet 2.66; and *exo*-N1H 5.15, *endo*- N1CH_3 doublet 2.94).¹⁰ The sharp signal (6.90 ppm, Figure 9) upfield of the initial N4H signal (7.18 ppm) was assigned to the N4H of this new *endo*-N1H/*exo*- N1CH_3 isomer.

To confirm that OH^- is acting as a catalyst and does not coordinate directly to Re, a 1.7 mM NaOH and a 0.54 mM NaOH solution were prepared from the same stock solution of $[\text{Re}(\text{CO})_3(\text{MAE})]\text{PF}_6$. If hydroxide adds to Re and is not acting as a catalyst, decreasing the hydroxide concentration to 0.54 mM would not only decrease the rate of reaction but would also decrease the percentage of the new product. When the solutions were monitored by NMR spectroscopy, the 1.7 mM NaOH sample reached equilibrium in 20 min as before, whereas the 0.54 mM NaOH sample required more time (1–2 h) to reach equilibrium, as expected. In both solutions, the new product abundance was the same (13%). Thus, hydroxide is not coordinating but is acting as a catalyst.

In the identical 1.7 mM NaOH study, but with $[\text{Re}(\text{CO})_3(\text{EAE})]\text{BF}_4$, the new minor set of signals appeared and reached its maximum intensity in 40 min (12% minor isomer, 88% major isomer). The new *endo*-NH signal appears more downfield (5.78 ppm) than the *exo*-NH signal (4.40 ppm) of the original isomer. The new N4H signal appeared upfield (6.77 ppm) of the initial N4H signal (7.03 ppm). The faster rate of isomerization of $[\text{Re}(\text{CO})_3(\text{MAE})]\text{PF}_6$ versus $[\text{Re}(\text{CO})_3(\text{EAE})]\text{BF}_4$ is attributable to the slightly greater N1H acidity of $[\text{Re}(\text{CO})_3(\text{MAE})]\text{PF}_6$, as suggested by its shorter NH to ND exchange half-life than that of $[\text{Re}(\text{CO})_3(\text{EAE})]\text{BF}_4$.

When Cl^- was added to a base-isomerized sample of $[\text{Re}(\text{CO})_3(\text{MAE})]\text{PF}_6$, the N1H signal of the minor *endo*-N1H/*exo*- N1CH_3 isomer shifted only minimally downfield ($\Delta\delta \sim 0.28$ ppm at 150 mM Cl^-), while the N4H signal was not shifted. The NH signals of the starting major *exo*-N1H/*endo*- N1CH_3 isomer shifted as described previously. This observation highlights a new application of Cl^- addition as an aid in identifying which isomer of a *fac*- $[\text{Re}(\text{CO})_3\text{L}]^n$ complex has an *endo*-NH/*exo*-alkyl and which has an *exo*-NH/*endo*-alkyl terminal amine. The small $\Delta\delta$ for the N4H signal further indicates that this proton is not very acidic. The isomerization at N1 should have no effect on the electronic character of N4. This result and the relatively long half-life for H to D exchange indicate a lower acidity for the N4H. This

lower acidity in turn means that N4 is relatively electron rich, and thus N4 is poised to accept a proton during the reaction pathway to $[\text{Re}(\text{CO})_3(\text{DAE})]\text{BF}_4$ (Scheme 2).

Conclusions

As shown by Natile et al.³⁰ for a stable Pt^{II} compound with a closely related seven-membered ring, we conclude that the Re^{I} seven-membered chelate rings in $[\text{Re}(\text{CO})_3(\text{MAE})]\text{PF}_6$ and $[\text{Re}(\text{CO})_3(\text{EAE})]\text{BF}_4$ products shown in Scheme 1 arise from intramolecular attack by a terminal amine on a coordinated acetonitrile. The novel DAE ligand in $[\text{Re}(\text{CO})_3(\text{DAE})]\text{BF}_4$ provides an interesting and highly unusual variation having an sp^2 N donor derived from an sp^3 primary amine. Complexed DAE has a five-membered chelate ring and a dangling NH_2 group. DAE is formed via a series of steps, and the likely pathway has two proton transfer steps and a Re–N bond disruption step, Scheme 2. The stable Pt^{II} and Re^{I} complexes with seven-membered chelate rings cannot convert to a complex with the DAE-type ligand (Scheme 3), because the endocyclic nitrogen bears an alkyl or aryl group rather than the proton needed for the second proton transfer step forming the dangling NH_2 group in DAE, as shown in Scheme 2. Thus, the seven-membered chelate ring of the MAE-type ligand serves as a model for one likely intermediate in the formation of the DAE ligand. Two types of evidence suggest that the sp^2 NH donor bound to Re in this MAE-type ring is poised to undergo dissociation and protonation. First, $[\text{Re}(\text{CO})_3(\text{MAE})]\text{PF}_6$ has a large Re–N4–C11 angle, indicating strain and favoring Re–N bond breaking. Second, N4H is relatively non-acidic (revealed by slow H to D exchange and by weak interaction with chloride ion of the N4H of the minor *endo*-N1H/*exo*-N1CH₃ isomer of $[\text{Re}(\text{CO})_3(\text{MAE})]\text{PF}_6$), indicating an electron-rich N ready to accept a second proton.

Our studies on chloride interaction complement reports of the use in anion receptors³⁶ of transition-metal fragments to serve as scaffolds onto which H-bonding donor groups can be connected.²³ Chloride and other anions interact with the pyrazole NH's of *fac*- $[\text{Re}^{\text{I}}(\text{CO})_3(\text{generic pyrazole})_3]^+$ cations.²² This work is related to our present findings on chloride interactions with six-coordinate Re^{I} tricarbonyl complexes. However, we expand the field of the interaction of anions with NH groups in metal complexes by showing that such interactions provide a useful approach for both interpreting NMR data and for elucidating the structure of isomers; such information is useful for probing properties of Re analogues of $^{99\text{m}}\text{Tc}$ radiopharmaceuticals.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Lipowska M, He H, Malveaux E, Xu X, Marzilli LG, Taylor AT. J. Nucl. Med 2006;47:1032–1040. [PubMed: 16741314]
2. Alberto R, Schibli R, Schubiger AP, Abram U, Pietzsch HJ, Johannsen B. J. Am. Chem. Soc 1999;121:6076–6077.
3. Desbouis D, Struthers H, Spiwok V, Küster T, Schibli R. J. Med. Chem 2008;51:6689–6698. [PubMed: 18837546]
4. Wei L, Babich J, Zubieta J. Inorg. Chim. Acta 2005;358:3691–3700.
5. Schibli R, Schubiger AP. Eur. J. Nucl. Med. Mol. Imaging 2002;29:1529–1542. [PubMed: 12397472]

6. Rattat D, Eraets K, Cleynhens B, Knight H, Fonge H, Verbruggen A. *Tetrahedron Lett* 2004;45:2531–2534.
7. Lipowska M, Cini R, Tamasi G, Xu X, Taylor AT, Marzilli LG. *Inorg. Chem* 2004;43:7774–7783. [PubMed: 15554642]
8. Lipowska M, Marzilli LG, Taylor AT. *J. Nucl. Med* 2009;50:454–460. [PubMed: 19223406]
9. Lipowska M, He H, Xu X, Taylor AT, Marzilli PA, Marzilli LG. Manuscript in Preparation.
10. Christoforou AM, Marzilli PA, Fronczek FR, Marzilli LG. *Inorg. Chem* 2007;46:11173–11182. [PubMed: 18044880]
11. Christoforou AM, Fronczek FR, Marzilli PA, Marzilli LG. *Inorg. Chem* 2007;46:6942–6949. [PubMed: 17655222]
12. He HY, Lipowska M, Christoforou AM, Marzilli LG, Taylor AT. *Nucl. Med. Biol* 2007;34:709–716. [PubMed: 17707812]
13. He H, Lipowska M, Xu X, Taylor AT, Marzilli LG. *Inorg. Chem* 2007;46:3385–3394. [PubMed: 17375908]
14. He H, Lipowska M, Xu X, Taylor AT, Carlone M, Marzilli LG. *Inorg. Chem* 2005;44:5437–5446. [PubMed: 16022542]
15. Bartholomä M, Valliant J, Maresca KP, Babich J, Zubieta J. *Chem. Commun. (Cambridge, U.K.)* 2009;5:493–512.
16. Banerjee SR, Babich J, Zubieta J. *Inorg. Chem. Commun* 2004:481–484.
17. Michelin RA, Mozzon M, Bertani R. *Coord. Chem. Rev* 1996;147:299–338.
18. Kukushkin VY, Pombeiro AJL. *Chem. Rev* 2002;102:1771–1802. [PubMed: 11996549]
19. Natile G, Intini FP, Bertani R, Michelin RA, Mozzon M, Sbovata SM, Venzo A, Seraglia R. *J. Organomet. Chem* 2005;690:2121–2127.
20. Cornacchia D, Pellicani R, Intini FP, Pacifico C, Natile G. *Inorg. Chem.* 2009 DOI: 10.1021/ic9011372.
21. Pérez J, Riera L. *Chem. Soc. Rev* 2008;37:2658–2667. [PubMed: 19020679]
22. Nieto S, Pérez J, Riera L, Miguel D, Golen JA, Rheingold AL. *Inorg. Chem* 2007;46:3407–3418. [PubMed: 17367132]
23. Nieto S, Pérez J, Riera L, Riera V, Miguel D. *Chem.-Eur.J* 2006;12:2244–2251.
24. Schmidt SP, Trogler WC, Basolo F. *Inorg. Synth* 1990;28:160–165.
25. Perera T, Fronczek FR, Marzilli PA, Marzilli LG. Manuscript in Preparation.
26. Edwards DA, Marshalsea J. *J. Organomet. Chem* 1977;131:73–91.
27. Otwinowski, Z.; Minor, W. *Macromolecular Crystallography, part A*. Vol. Vol. 276. New York: New York Academic Press; 1997.
28. Sheldrick, GM. *SHELXL97, Program for Crystal Structure Solution and Refinement*. Gottingen, Germany: University of Gottingen; 1997.
29. Maresca L, Natile G, Intini FP, Gasparrini F, Tiripicchio A, Camellini MT. *J. Am. Chem. Soc* 1986;108:1180–1185.
30. Tiripicchio A, Camellini MT, Maresca L, Natile G. *Acta Crystallogr., Sect. C* 1990;C46:549–551.
31. Kukushkin YN, Kiseleva NP, Zangrando E, Kukushkin VY. *Inorg. Chim. Acta* 1999;285:203–207.
32. Syamala A, Chakravarty AR. *Inorg. Chem* 1991;30:4699–4704.
33. Britten JF, Lock CJL, Pratt WMC. *Acta Crystallogr., Sect. B* 1982;38:2148–2155.
34. Maheshwari V, Carlone M, Fronczek FR, Marzilli LG. *Acta Crystallogr., Sect. B* 2007;B63:603–611. [PubMed: 17641431]
35. Perera T, Marzilli PA, Fronczek FR, Marzilli LG. Manuscript in Preparation.
36. Beer PD. *Chem. Commun. (Cambridge, U.K.)* 1996:689–696.

Figure 1. ORTEP plot of the cation in $[\text{Re}(\text{CO})_3(\text{DAE})]\text{BF}_4$. Thermal ellipsoids are drawn with 50% probability.

Figure 2. ORTEP plots of the cations in (a) $[\text{Re}(\text{CO})_3(\text{MAE})]\text{PF}_6$, (b) $[\text{Re}(\text{CO})_3(\text{MAEH})\text{F}]\text{PF}_6$, and (c) $[\text{Re}(\text{CO})_3(\text{EAE})]\text{BF}_4$. Thermal ellipsoids are drawn with 50% probability.

Figure 3.

Designation of the *exo*-NH proton (pointing away from the carbonyl groups and toward the hydrophobic pocket of the ligand) of $[\text{Re}(\text{CO})_3(\text{MAE})]\text{PF}_6$ and $[\text{Re}(\text{CO})_3(\text{EAE})]\text{BF}_4$. N4H is not classified as either *endo* or *exo*.

Figure 4.

^1H NMR spectrum showing NH signals of $[\text{Re}(\text{CO})_3(\text{DAE})]\text{BF}_4$ in $\text{DMSO-}d_6$ at $25\text{ }^\circ\text{C}$ (top), in $\text{acetonitrile-}d_3$ at $25\text{ }^\circ\text{C}$ (middle), and in $\text{acetonitrile-}d_3$ at $-5\text{ }^\circ\text{C}$ (bottom).

Figure 5. Designation of the N4Ha and N4Hb protons of [Re(CO)₃(DAE)]BF₄, indicating the proximity of N4Hb to the methyl group and the rotation of the NH₂ group.

Figure 6. Change in chemical shift ($\Delta\delta$, ppm) of the NH signals of $[Re(CO)_3(MAE)]PF_6$ (5 mM) caused by added Cl^- in $DMSO-d_6$ at 25 °C.

Figure 7. Change in chemical shift ($\Delta\delta$, ppm) of the NH signals of $[Re(CO)_3(MAE)]PF_6$ (5 mM) caused by added Cl^- in acetonitrile- d_3 at 25 °C.

Figure 8. Change in chemical shift ($\Delta\delta$, ppm) of the NH signals of $[\text{Re}(\text{CO})_3(\text{DAE})]\text{BF}_4$ (5 mM) caused by added Cl^- in acetonitrile- d_3 at 25 °C.

Figure 9.

^1H NMR spectra of $[\text{Re}(\text{CO})_3(\text{MAE})]\text{PF}_6$ (5 mM) in $\text{DMSO-}d_6$ at 25 °C before (top) and 20 min after (bottom) addition of OH^- (1.7 mM). The multiplet at ~4.2 ppm arises from one of the C7H_2 protons.

Scheme 1.

Products obtained in the syntheses using acetonitrile as a solvent. The compound numbers correspond to the structures in Figure 1 and Figure 2. Adventitious HF from the decomposition of PF₆⁻ transformed some of **2a** to **2b**.

Scheme 2.

The likely pathway for DAE ligand formation from *N,N*-Me₂dien and acetonitrile (green). Stars indicate the location of the lone pair on the nitrogens known to be used or likely to be used in Re coordination at each stage of the process. The *fac*-{Re(CO)₃}⁺ fragment is not shown.

Scheme 3.

The likely pathway for MAE ligand formation from N,N',N'' -Me₃dien and acetonitrile (green). Stars indicate the location of the lone pair on the nitrogens known to be used or likely to be used in Re coordination at each stage of the process. The fac -{Re(CO)₃}⁺ fragment is not shown. Only one proton can be transferred (in the second step). The hypothetical step which would be needed to form the DAE analogue does not occur because the methyl group can not transfer.

Table 1

Crystal Data and Structure Refinement for [Re(CO)₃(DAE)]BF₄ (**1**), [Re(CO)₃(MAE)]PF₆ (**2**), [Re(CO)₃(MAEH)F]PF₆ (**3**), and [Re(CO)₃(EAE)]BF₄ (**4**)

	1	2	3	4
empirical formula	C ₁₁ H ₂₀ N ₄ O ₃ Re·BF ₄	C ₁₂ H ₂₂ N ₄ O ₃ Re·PF ₆	C ₁₂ H ₂₃ FN ₄ O ₃ Re·PF ₆	C ₁₅ H ₂₈ N ₄ O ₃ Re·(BF ₄) _{0.95} ·Br _{0.05}
fw	529.32	601.51	621.51	586.98
crystal system	monoclinic	monoclinic	monoclinic	triclinic
space group	<i>Cc</i>	<i>C2/c</i>	<i>P2₁/n</i>	<i>P1</i>
unit cell dimensions				
<i>a</i> (Å)	12.521(2)	30.442(4)	7.4371(10)	8.4928(15)
<i>b</i> (Å)	9.4781(15)	10.7593(14)	18.446(3)	10.491(2)
<i>c</i> (Å)	14.730(2)	11.8166(12)	14.738(3)	12.073(3)
α (deg)	90	90	90	76.289(8)
β (deg)	106.172(8)	97.335(7)	96.900(12)	79.818(10)
γ (deg)	90	90	90	87.570(11)
<i>V</i> (Å ³)	1678.9(4)	3838.7(8)	2007.2(6)	1028.6(4)
<i>T</i> (K)	90.0(5)	90.0(5)	90.0(5)	90.0(5)
<i>Z</i>	4	8	4	2
ρ_{calc} (g/m ³)	2.094	2.082	2.057	1.895
abs coeff (mm ⁻¹)	7.30	6.49	6.22	6.06
$2\theta_{\text{max}}$ (°)	67.4	69.8	60.0	63.8
<i>R</i> indices ^a	0.026	0.026	0.047	0.033
wR2 = [<i>I</i> > 2σ(<i>I</i>)] <i>b</i>	0.069	0.054	0.079	0.072
data/param	5921/222	7926/257	5840/258	7050/257

$$^a R = (\Sigma \|F_o\| - \|F_c\|) / \Sigma \|F_o\|;$$

$$^b wR2 = [\Sigma [w(F_o^2 - F_c^2)^2] / \Sigma [w(F_o^2)^2]]^{1/2}, \text{ in which } w = 1/[\sigma^2(F_o^2) + (dP)^2 + (eP)] \text{ and } P = (F_o^2 + 2F_c^2)/3$$

d = 0.0368, 0.0192, 0.0151, and 0.0305 and *e* = 5, 5.2495, 4.1664, and 1.826 for [Re(CO)₃(DAE)]BF₄, [Re(CO)₃(MAE)]PF₆, [Re(CO)₃(MAEH)F]PF₆, and [Re(CO)₃(EAE)]BF₄, respectively.

Table 2

Selected Bond Distances (Å) and Angles (deg) for [Re(CO)₃(DAE)]BF₄ (**1**),^a[Re(CO)₃(MAE)]PF₆ (**2**), [Re(CO)₃(MAEH)F]PF₆ (**3**), and [Re(CO)₃(EAE)]BF₄ (**4**)

	1	2	3	4
bond distances				
Re–N1	2.272(4)	2.235(2)	2.228(5)	2.241(3)
Re–N2	2.216(4)	2.2695(19)	2.274(4)	2.273(3)
Re–Nx	2.242(4) ^b	2.206(2) ^c		2.201(3) ^c
N3–C10	1.293(6)	1.463(3)	1.465(7)	1.473(5)
N4–C10	1.350(6)			
N4–C11		1.318(3)	1.321(7)	1.304(5)
N3–C11		1.344(3)	1.305(7)	1.346(5)
bond angles				
N1–Re–N2	78.33(14)	79.30(7)	79.56(17)	79.59(12)
N1–Re–Nx	88.96(13) ^b	80.10(7) ^c		80.13(13) ^c
N2–Re–Nx	75.97(14) ^b	90.47(7) ^c		87.56(12) ^c
Re–N4–C11		138.74(16)		141.2(3)
N3–Cx–N4	123.8(4) ^d	120.6(2) ^e	121.5(5) ^e	122.1(4) ^e
C3–Re–C1	88.5(2)	89.4(10)	88.4(2)	87.89(17)
C3–Re–N1	92.33(16)	92.86(9)	94.3(2)	93.98(15)
C1–Re–Nx	89.41(18) ^b	98.05(8) ^c		98.12(15) ^c
N4–C11–N3–C7		23.4(4)	4.1(8)	15.9(6)

^aThe N3–C10 bond distance of **1** should be compared with the N3–C11 bond distance of complexes **2–4**.

^bN_x = N3.

^cN_x = N4.

^dC_x = C10.

^eC_x = C11.

Table 3

^1H NMR Chemical Shifts (ppm) of $[\text{Re}(\text{CO})_3(\text{DAE})]\text{BF}_4$ (**1**), $[\text{Re}(\text{CO})_3(\text{MAE})]\text{PF}_6$ (**2**), and $[\text{Re}(\text{CO})_3(\text{EAE})]\text{BF}_4$ (**4**) in $\text{DMSO}-d_6$ at 25 °C and Selected NH Shifts in Acetonitrile- d_3 ^a

	1	2	4
<i>exo</i> -N1H		4.50 (3.39)	4.40 (3.22)
N2H	7.10 (5.53)		
N4H/N4Ha	7.28 (6.02)	7.17 (6.41)	7.03 (6.28)
N4Hb	7.99 (6.48)		
CH_3CN -derived CH_3	2.31	2.14	2.18
$\text{C}7\text{H}_2$	3.19	4.22, 3.20	4.15, 3.42

^a Assignments of the NH signals were verified by COSY spectra in $\text{DMSO}-d_6$. NH shifts in acetonitrile- d_3 are enclosed in parentheses.