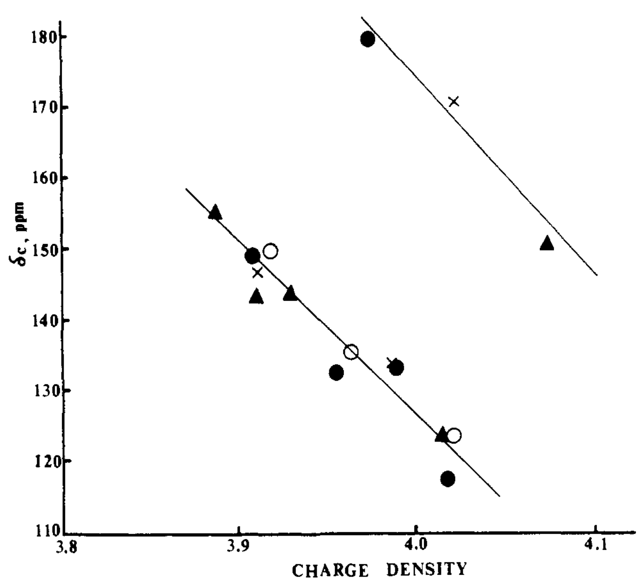

Figure 2. Observed ^{13}C shieldings for uncoordinated pyridine (○), complexes **1b** (●), **2b** (▲), and **3b** (×) vs. the calculated charge densities, the upper straight line referring to the quaternary carbons bonded to palladium and the lower one to the other ring carbons.

ciated with the H, C, N, P, and Cl atoms, while those of Pd were estimated using the experimental data[12] ½($I_\mu + A_\mu$), 4d, 8.33, 5s, 4.135, and 5p, 1.835 eV, and $-\beta_\mu^\circ$, 4d, 20.00, 5s, 8.47, 5p, 3.76 eV, where I, A, and β° stand for the valence state ionization potential, electron affinity, and bonding parameter, respectively, and μ is the subscript associated with each atomic orbital.

The ^{13}C NMR chemical shift is known to be correlated with the charge density on a given carbon atom in a molecule.[13] As is seen in Figure 2, the plot of observed ^{13}C shieldings for pyridine carbons against the calculated charge densities gave two straight lines, one for the carbon atoms bonded to palladium and the other for other carbons inclusive of those in uncoordinated pyridine. The specific behavior of the quaternary carbons might be caused by the contribution of dσ orbital to the Pd-C bond.

From the standpoint of valence-bond theory, the back-donation from palladium might be largest in the case of **1b**, since the carbon atom adjacent to nitrogen in uncoordinated pyridine has the lowest charge density and hence the highest electron acceptability as evidenced by the ^{13}C chemical shielding (Figure 1).

Compounds **2a**, **3a**, and PdCl[C$_5$H$_3$(6-Cl)-C^2](PPh$_3$)$_2$, which was obtained as a mononuclear complex from the reaction between Pd(PPh$_3$)$_4$ and 2,6-dichloropyridine, react with carbon monoxide in THF at room temperature to afford the acyl complexes in high yields, which in turn readily react with methanol in the absence of base to yield methyl nicotinate, methyl isonicotinate, and methyl 6-chloropicolinate, respectively. On the contrary, the triethylphosphine complexes **1b**, **2b**, and **3b** as well as the dinuclear complex **1a** are not carbonylated under the same conditions. Catalysis of **1a** for the cross-coupling reaction between 2-chloropyridine and methylmagnesium bromide and other reactions of the pyridylpalladium(II) complexes will be reported elsewhere.

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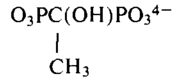
Structural Characterization of a ^{99}Tc–Diphosphonate Complex. Implications for the Chemistry of ^{99m}Tc Skeletal Imaging Agents

Sir:

Diagnostic nuclear medicine involves the investigation, development, production, and use of radiopharmaceuticals, i.e., γ-ray-emitting isotopes in specific chemical forms designed to concentrate in specific organs of the body. Subsequent scanning of the organs with a γ-ray camera provides valuable diagnostic and prognostic data by an essentially noninvasive technique.[1-3] ^{99m}Tc has been the isotope of choice for diagnostic nuclear medicine because of its optimal nuclear properties, its diverse chemistry, and its general availability.[4-8] Several X-ray structural determinations of technetium complexes have recently appeared,[4,9-12] but none have involved ligands that form the basis of clinically useful ^{99m}Tc radiopharmaceuticals. This communication reports the structural characterization of a ^{99m}Tc complex with methylenediphosphonate (MDP), the simplest member of the class of diphosphonate ligands which is used in the preparation of efficacious ^{99m}Tc skeletal imaging agents and ^{99m}Tc myocardial infarct imaging agents.[1-5,7,13-15] The constitutions of the clinically used diphosphonates MDP and HEDP (1-hydroxyethylidenediphosphonate) are shown below along with that of the

$O_3POPO_3{}^{4-}$
PYP

$O_3PCH_2PO_3{}^{4-}$
MDP



$O_3PC(OH)PO_3{}^{4-}$ with CH_3 on C
HEDP

related ligand pyrophosphate (PYP). While it is generally assumed that ^{99m}Tc complexes of these three ligands are avid bone seekers because the coordinated phosphonate or phosphate ligand still has considerable affinity for calcium, the chemistry of these systems is very complex and no coherent theory explaining their in vivo mechanism(s) of action has yet been developed. In large part this situation obtains because, until now, there has been no firm information as to the possible mode(s) of bonding and interaction between diphosphonate ligands and technetium. In this communication we report on the preparation and structure of a ^{99}Tc–MDP complex.

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Table I. Summary of Crystal Data[a]

molecular formula[b]	$\{[Li(H_2O)_3][Tc(OH)(MDP)]\cdot{}^1/_3H_2O\}_n$
formula weight, amu	$n \times 354.98$
obsd density, g cm^{-3}	2.12 (2)
cald density, g cm^{-3}	2.11
space group	$R\bar{3}$, No. 148, hexagonal setting
Z	18
unit cell constants, Å	$a = 21.771$ (8), $c = 12.208$ (3)
unit cell volume, Å^3	5011.3
data collection specifics	Cu Kα radiation, $\lambda = 1.5418$ Å $\theta/2\theta$ technique, $2\theta_{max} = 112°$ 1108 reflections with $I > 2\sigma(I)$

[a] Estimated standard deviations of the last significant figure are given in parentheses. [b] MDP = methylenediphosphonate.

Table II. Selected Bond Parameters[a]

	Tc Distances		
Tc-O(1)	2.000 (14)	Tc-O(3)	1.983 (14)
Tc-O(6)	2.036 (16)	Tc-O(5)	2.029 (12)
Tc-OH	1.968 (15)	Tc-OH′	1.917 (12)
	Diphosphonate Distances		
P(1)-O(1)	1.534 (15)	P(2)-O(4)	1.502 (18)
P(1)-O(2)	1.460 (16)	P(2)-O(5)	1.552 (14)
P(1)-O(3)	1.551 (14)	P(2)-O(6)	1.552 (15)
P(1)-C	1.83 (2)	P(2)-C	1.78 (2)
	Diphosphonate Angles		
O(1)-P(1)-O(2)	114.4 (9)	O(4)-P(2)-O(5)	108.9 (9)
O(1)-P(1)-O(3)	110.1 (8)	O(4)-P(2)-O(6)	109.9 (9)
O(1)-P(1)-C	106.7 (9)	O(4)-P(2)-C	111.9 (10)
O(2)-P(1)-O(3)	111.1 (9)	O(5)-P(2)-O(6)	111.1 (8)
O(2)-P(1)-C	110.4 (10)	O(5)-P(2)-C	106.6 (10)
O(3)-P(1)-C	103.4 (9)	O(6)-P(2)-C	108.4 (10)
P(1)-C-P(2)	110.7 (12)		

[a] Distances are in angstroms, angles are in degrees, and atom identifications are as shown in Figures 1 and 2. Estimated standard deviations of the last significant figure(s) are given in parentheses.

In a typical preparation 0.2 mmol of $(NH_4)_2TcBr_6$ is dissolved in ~10 mL of *N*,*N*-dimethylformamide and a ninefold molar excess of H_4MDP is added to the stirred solution. Within a few minutes the solution changes from an orange-red to a brown-gold color, and it is then heated at 80 °C with stirring for ~20 min. After dilution with ~300 mL of aqueous chloroacetate buffer solution, the pH is adjusted to 3.2. This solution is loaded onto a column (1.25-cm-i.d. × 5.0 cm) of anion-exchange resin (Bio-Rad, AG MP-1, 100-200 mesh, chloride form) and the column rinsed with 0.05 M aqueous chloroacetate buffer at pH 3.2. At this stage the brown product is sorbed at the top of the column; passage of 0.5 M $LiClO_4$ through the column removes most of this material by what appears to be a displacement phenomenon. Upon standing for several weeks, small brown crystals of quality suitable for the X-ray diffraction experiment appear in the acidified eluant solution. A well-formed, but rather small (0.08 × 0.08 × 0.05 mm), crystal was subjected to X-ray diffraction analysis and the structure was solved using standard Patterson and least-squares analysis. Table I lists data pertinent to this experiment. Full-matrix least-squares refinement using statistical weights and varying (1) the overall scale factor, (2) all independent positional parameters, (3) the lithium atom isotropic temperature factors, and (4) anisotropic temperature factors for all remaining atoms, converged at $R = 0.077$ (0.067 weighted). The final difference map shows no features other than a random background below 1.2 e/Å^3 and no indications of disorder. Portions of the structure are shown in Figures 1 and 2, while selected bond parameters are listed in Table II.

The solid state structure of the Tc-MDP complex consists of infinite polymeric chains. Each MDP ligand bridges two symmetry related technetium atoms (Figure 1), and each technetium atom is bound to two symmetry related MDP ligands (Figure 2)—the MDP/Tc ratio within the polymer is therefore 1:1. The polymeric repeat unit is completed by an oxygen atom (presumably in the form of an hydroxyl ion) that bridges two symmetry-related technetium atoms (Figure 1) and by an hydrated lithium cation which neutralizes the charge associated with each repeat unit. In addition, there is a single oxygen atom (presumably in the form of a disordered water molecule) on the threefold axis of the space group. The molecular formula of the polymeric Tc-MDP complex may thus be represented as $\{[Li(H_2O)_3][Tc^{IV}(OH)(MDP)]\cdot{}^1/_3H_2O\}_n$ where the indicated protonation states of the bridging and noncoordinated oxygen atoms are chemically reasonable and consistent with an assumed Tc(IV) oxidation state, but are not definitively established by the X-ray diffraction data. Alternate, equivalently reasonable, representations may be constructed about other technetium oxidation states and other degrees of protonation of the bridging and noncoordinated oxygen atoms, e.g. $\{[Li(H_2O)_3][Tc^{IV}(O)MDP)]\cdot{}^1/_3H_3O\}_n$ or $\{[Li(H_2O)_3][Tc^{V}(O)(MDP)]\cdot{}^1/_3H_2O\}_n$.

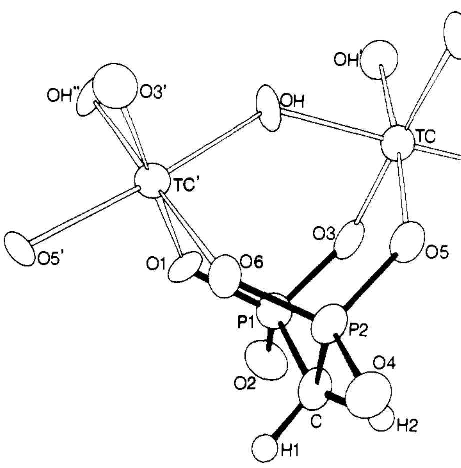

Figure 1. Perspective view of a portion of the $\{[Li(H_2O)_3][Tc(OH)(MDP)]\cdot{}^1/_3H_2O\}_n$ structure showing one MDP ligand bridging two technetium centers.

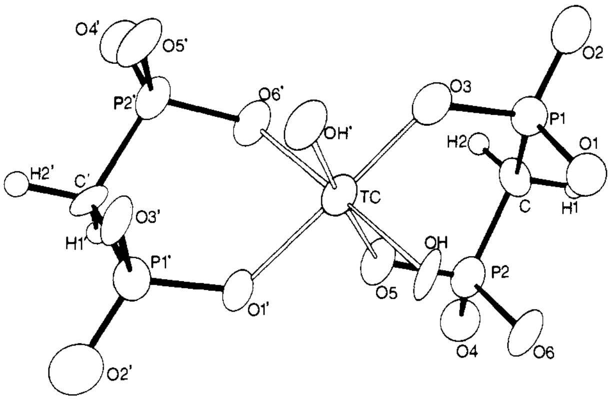

Figure 2. Perspective view of a portion of the $\{[Li(H_2O)_3][Tc(OH)(MDP)]\cdot{}^1/_3H_2O\}_n$ structure showing one Tc center bridging two MDP ligands.

Each technetium center has approximately octahedral coordination geometry, the two bridging oxygen atoms occupying cis coordination sites. The bridging oxygen to technetium bond distance (1.94 (2) Å average) is generally in line with observed Tc-O single bond lengths (2.00-2.03 Å),[12] Tc=O double bond lengths being considerably shorter (1.65-1.70 Å).[12] Bond lengths and bond angles within the MDP ligand are generally as expected from structural studies on the free acid H_4MDP[16] and on related diphosphonate salts.[17-19] One of the most important structural features of the diphosphonate ligands is the orientation of the $-PO_3$ groups with respect to the P-C-P plane. The "W" configuration, wherein the atoms O(2)-P(1)-C-P(2)-O(4) form a planar "W", has been previously described[17,19] and can easily be seen in Figure 1. This configuration allows the ligand to be doubly bidentate with O(1) and O(6) on one side of the "W" coordinating to one metal center and O(3) and O(5) on the other side of the "W" coordinating to another metal center.

The salient structural characteristic of the Tc-MDP complex is its polymeric nature, and it seems likely that polymeric metal-diphosphonate complexes play a central role in the chemistry of technetium-diphosphonate skeletal imaging agents. The propensity of diphosphonates to form polymeric complexes presumably arises from the ability of these ligands to function minimally as doubly bidentate bridges, as for example in Figure 1 where MDP bridges two technetium centers. If the diphosphonate ligand contains a suitable functional group on the central carbon atom (e.g., the hydroxyl group of HEDP) then the diphosphonate can function as a mixed bidentate-tridentate bridge. It has been postulated[17] that the additional hydroxyl group in ligands such as HEDP (relative to MDP which has no hydroxyl group on the central carbon atom) allows this ligand to bind to bone or hydroxyapatite in a tridentate fashion and therefore enhances the sorption of metal-HEDP complexes onto the surface of bone. The relative affinities of metal-HEDP and metal-MDP complexes for calcium(II), hydroxyapatite, and bone are currently under investigation in these laboratories.

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Shape-Selective Fischer–Tropsch Synthesis Catalyzed by Zeolite-Entrapped Cobalt Clusters

Sir:

Catalyst selectivity is the central problem in Fischer–Tropsch (F–T) synthesis of fuels and petrochemical substitutes from $CO + H_2$.[1] Standard F–T catalysts include supported metals (e.g., Co on silica) typically used at 200–400 °C and 10–200 atm and exhibiting product distributions in the C_1–C_{30} range. Metal clusters are potentially valuable as selective F–T catalysts, having unique structures with neighboring metal centers, but only catalysts of very low activity have been reported.[2] A cobalt complex supported on a polymer was found to be catalytically active for F–T synthesis at 200 °C, but, although it apparently contained unique, stabilized mononuclear metal species, it was unselective, giving products in the C_3–C_{20} range.[3] We have inferred that metal clusters having unique structures and stabilized on a support[4] might provide the sought-for combination of activity and selectivity. Our goal was to extend the class of F–T catalysts to metals supported in zeolites[5]—molecular sieves offering both the prospect of stable encapsulation[6] of metal clusters within the molecular-scale cages and the prospect of shape-selective catalysis.[7,8]

The results summarized here show that zeolite-encapsulated cobalt clusters are the first shape-selective F–T catalysts, also offering the advantages of high activity and stability under conditions of potential commercial significance. The catalysts were prepared by reduction of Co^{2+} ions exchanged into A- and Y-type zeolites.[9]

CoA zeolite has been reported to be a propylene hydroformylation catalyst,[10] but its lack of shape selectivity, indicated by the *n*- to isobutyraldehyde product distribution, suggests that destruction of the alumino-silicate structure occurred, which, we infer, might have resulted from high-temperature reduction of Co^{2+} ions by reactant H_2 inside the zeolite pores during catalysis.[11] Therefore, to prevent "decationization"[5] followed by destruction of the zeolite, we used metal vapors instead of hydrogen as the reducing agent.[12] The products of Cd-vapor reduction of CoA (designated Co^0-CdA) and of CoY (designated Co^0-CdY) were shown by X-ray diffraction to have maintained their zeolitic framework structures.

Results of catalytic reaction experiments with $CO + H_2$ in an isothermal flow reactor are summarized in Table I. *The striking result is that Co^0-CdA catalyzed CO-H_2 conversion at 151 °C and ~6 atm, selectively giving propylene as the only detectable hydrocarbon product* (expt 2). The catalytic activity initially increased for 2–3 h on stream, after which there was no change for 17.5 h, the full period of the experiment. The steady-state conversion was ~1%, and the reaction rate was ~0.4 CO molecules converted/(Co atom h). The initial induction period is suggested to be an indication of the gradual formation of the catalytically active species inside the zeolite cages. The infrared spectrum of the catalyst removed from the reactor after the experiment shows a cobalt carbonyl complex (or a mixture of complexes) (Figure 1); this spectrum suggests the presence of Co clusters with terminal but no bridging carbonyls.[13]

We infer from these results that, at 151 °C, Co^0-CdA acted as a shape-selective F–T catalyst, the active species being cobalt carbonyls (presumably clusters) encapsulated in the ~11-Å pores. The selectivity indicated by the lack of hydrocarbon products other than propylene suggests that nearly uniform cobalt carbonyls were responsible for the catalysis. The Cd ions[14] introduced into the zeolite as a result of the reduction of Co might have played a role in the catalysis.

At a higher reaction temperature, the same catalyst produced propane–propylene mixtures of varying proportions, depending on the CO:H_2 ratio of the reactant stream, and

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