large Mn_x complexes that exhibit intramolecular, ferromagnetic interactions and $S_T \neq 0$ ground states and then modify them so that there are bridges between two Mn ions, one from each of two neighboring Mn_x complexes in the solid state. For example, there has been a recent report[35] of the preparation of polymeric forms of $[Fe_4S_4(SR)_4]^{2-}$ clusters that were prepared by employing difunctional thiolate ligands. If Mn_x complexes with $S_T \neq 0$ ground states can be "cross-linked" in the solid state with ferromagnetic exchange propagating bridges, then long-range ferromagnetic ordering would be possible.

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Registry No. **1**, 109862-72-8; **2**, 120204-09-3; **3**, 120204-11-7; $(Et_3NH)_2[Mn(biphen)_2(biphenH)]$, 116275-78-6; $(Et_3NH)_2[Mn(Br_4biphen)_2(O_2CPh)]$, 120172-76-1; $Mn_6O_2(O_2CPh)_{10}(py)_2(MeCN)_2$, 120204-08-2.

Supplementary Material Available: Tables of fractional coordinates and thermal parameters, anisotropic thermal parameters of manganese ions, all bond lengths and angles for complexes **2** and **3**, and observed vs calculated susceptibility data and the distribution of spin states for **2** (32 pages); listings of calculated and observed structure factors for complexes **2** and **3** (32 pages). Ordering information is given on any current masthead page. Complete MSC structure reports for complexes **2** (No. 87 204) and **3** (No. 87 200) are available upon request from the Indiana University Chemistry Library.

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Contribution from the Department of Chemistry, Wake Forest University, Winston-Salem, North Carolina 27109, and Department of Radiology, Bowman Gray School of Medicine, Winston-Salem, North Carolina 27103

Synthesis, Characterization, and Aqueous Proton Relaxation Enhancement of a Manganese(II) Heptaaza Macrocyclic Complex Having Pendant Arms

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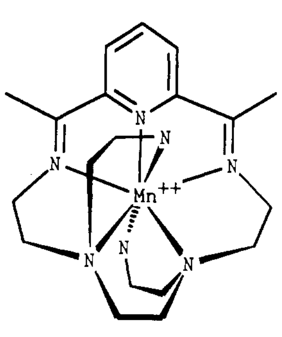
The complex $Mn(NH_2Et)_2[15]pydieneN_5^{2+}$ has been prepared by template condensation of diacetylpyridine and penten in the presence of Mn^{2+} in ethanol ($(NH_2Et)_2[15]pydieneN_5$ is 2,13-dimethyl-6,9-bis(2-aminoethyl)-3,6,9,12,18-pentaazabicyclo[12.3.1]octadeca-1(18),2,12,14,16-pentaene and penten is *N,N,N',N'*-tetrakis(2-aminoethyl)ethylenediamine). The complex is isolated as $Mn(NH_2Et)_2[15]pydieneN_5(PF_6)_2$ and can be converted to the Cl^- salt for aqueous studies. The ligand is a 15-membered pentaaza macrocycle having two aminoethyl pendant arms that are branched from nitrogen atoms and that coordinate through amino groups at axial sites to give a pentagonal-bipyramidal complex. The high-spin Mn(II) complex has identical UV-visible spectra in aqueous and nonaqueous solvents. The EPR spectra are indicative of approximate axial symmetry. It is concluded that the aminoethyl groups are coordinated in solution as well as in the solid state. The aqueous proton NMR relaxation rate enhancement by the complex is 0.92 $mM^{-1}\ s^{-1}$ at 24 MHz and 25 °C. In comparison to complexes with exchanging aquo coordination sites, the relaxation enhancement is small, indicative of relaxation via an outer-sphere mechanism only.

Introduction

At present there is renewed interest in aqueous proton relaxation enhancement by paramagnetic metal complexes because of their application as contrast-enhancing agents for medical magnetic resonance imaging.[1] In particular, for a given complex, it is very desirable to be able to predict the aqueous proton relaxation enhancement over the frequency range of 0.01 to approximately 200 MHz. However, at present this is not possible because our quantitative understanding of relaxation enhancement extends only to the aquo ions. The lack of predictability for metal chelates arises from the fact that there are multiple contributions to the relaxation enhancement from the effects of inner-sphere water, outer-sphere water, and the field modulation of each through the fluctuations provided by molecular motions of solute and solvent and internal processes such as electron spin relaxation.[2] It is not possible to predict any of these components quantitatively, partially because very few complexes have been studied to date. One problem is the estimation of the fraction of the rate enhancement due to the solvating or outer-sphere water molecules. In this project the goal is to prepare a coordinatively saturated nonlabile complex having a ligand structure comparable to that of other known complexes. By comparison with analogous complexes having aquo ligands, the contributions of inner- and outer-sphere water can be estimated. To do this, we have prepared a macrocyclic complex of Mn(II) having coordinated pendant arms terminating in amine groups to ensure that the complex is coordinatively saturated by the ligand. Manganese(II) is preferred as the metal ion because it has good relaxation enhancement characteristics: long electron spin relaxation time and high magnetic moment. Related macrocyclic complexes of Mn(II) lacking the pendant arms and thus having inner-sphere water are available for comparison.

This paper describes the synthesis and characterization of the complex



$Mn(NH_2Et)_2[15]pydieneN_5^{2+}$

The complex is based on the $[15]pydieneN_5$ macrocycle,[3] which is known to coordinate to Mn in an approximately pentagonal-planar fashion[4] but has in addition two aminoethyl pendant arms

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coordinated at the axial sites. Many members of the class of macrocycle based upon the [*X*]pydieneN$_y$ system have been prepared by metal ion promoted template reactions.[5,6] For the present purpose, the manganese(II)-promoted template reaction between diacetylpyridine and penten was utilized to prepare the complex.

This complex is a new member of the growing class of macrocyclic complexes with pendant arms terminating in amine,[7-16] pyridine,[17-20] amide,[15,21-23] or nitro[24] groups that are coordinated to the metal ion. The complex was characterized by elemental analyses, magnetic moments, IR spectra, conductivity measurements, pH titrations, solid-state and solution EPR spectra, and aqueous proton NMR relaxation rate measurements.

Experimental Section

Materials. The starting materials for the preparation of the ligand were purchased from Aldrich Chemical Co. and Fisher Scientific Co. and used without further purification. NH_4PF_6 was purchased from Alfa Products. $MnCl_2 \cdot 4H_2O$ was purchased from Aldrich as the tetrahydrate and was dried under vacuum to remove most of the water of hydration.

Methods. Infrared spectra were obtained as mineral oil mulls on KBr plates with a Perkin-Elmer 1330 infrared spectrometer. A Cahn Model 7600 Faraday balance was used to determine magnetic moments with $Hg(Co(SCN)_4)$ as the standard. Diamagnetic corrections were estimated by using Pascal's constants. Conductivity measurements were obtained with an Industrial Instruments Model RCM-5B1 conductance meter and an immersion type cell with a cell constant of 1.0578 cm^{-1}. The concentrations of the Mn^{2+} complex solutions were determined by atomic absorption with a Perkin-Elmer Model 306 atomic absorption spectrophotometer and standard solutions purchased from Fisher Scientific Co. pH measurements were obtained by using a Beckman Model 4500 pH meter. Electronic absorption spectra were recorded with a Hewlett-Packard 8452A diode array spectrophotometer in the range 190–450 nm. Elemental analyses on solid samples were performed by Galbraith Laboratories, Knoxville, TN. Electron paramagnetic resonance spectra on polycrystalline samples at room temperature were obtained by using a Varian E-109 electron spin resonance spectrometer with a Varian E-102 microwave bridge at 9.1 GHz. ^{1}H NMR spectra were obtained from a Varian VXR-200 NMR spectrometer in the deuterated solvents $CDCl_3$ and D_2O. Pulsed NMR measurements were made on a 24.033-MHz Spin-Lock Ltd. coherent pulse NMR spectrometer. T_1 relaxation times were measured on aqueous solutions in the millimolar concentration range at room temperature. Nuclear magnetic relaxation dispersion (NMRD) measurements were obtained from S. H. Koenig at the IBM T. J. Watson Research Center in New York. The instrument was built in that laboratory, and a description of the instrument can be found in ref 2. NMRD data were obtained at frequencies ranging from 0.01 to 50 MHz. The Mn concentration of the NMRD solutions was analyzed by atomic absorption.

Preparations. Syntheses of Starting Materials. The syntheses of starting materials and intermediates leading to penten were optimized to greater than 90% yield for each step and, therefore, are included in detail in this report.

ClEtNHTs (*N*-(*p*-tolylsulfonyl)-2-chloroethylamine) was prepared by a modification of the procedure of Jen and Efros.[25] $ClEtNH_2 \cdot HCl$ (11.6 g, 0.1 mol) and Na_2CO_3 (10.6 g, 0.1 mol) were dissolved in distilled water (400 mL). TsCl (23.0 g, 0.12 mol) was added slowly with stirring. The reaction mixture was stirred at room temperature for about 24 h. The resulting precipitate was collected by using suction filtration, washed with distilled water, and dried in vacuo (22.9 g, 98% yield). Mp: 77–78 °C. IR (Nujol): 3280, 1920, 1600 cm^{-1}. ^{1}H NMR ($CDCl_3$): 7.9 (2 H, dd), 7.4 (2 H, dd), 5.2 (1 H, s), 3.52 (2 H, t), 3.28 (2 H, q), 2.4 (3 H, s) ppm.

Tosylaziridine was prepared by the method of Jen and Efros.[25] ClEtNHTs (23.4 g, 0.1 mol) was added to a stirred solution of NaOH (300 mL, 1.4 M) in a salt/ice bath, and stirring was continued for about 1.5 h. The precipitate was then allowed to settle for 3 h at 10 °C. The product was collected, washed with cold distilled water, and dried in vacuo (18.1 g, 92% yield). Mp: 51–52 °C. IR (Nujol): 1930, 1600 cm^{-1}. ^{1}H NMR ($CDCl_3$): 7.8 (2 H, dd), 7.3 (2 H, dd), 2.4 (3 H, s), 2.3 (4 H, s) ppm.

penten-4-Ts (*N*,*N*,*N'*,*N'*-tetrakis(tetrakis(2-((*p*-tolylsulfonyl)amino)ethyl))ethylenediamine) was prepared as described by Gauss et al.[26] Tosylaziridine (23.6 g, 0.12 mol) was dissolved in dry benzene (25 mL). A mixture of ethylenediamine (1.65 mL, 0.025 mol) and dry benzene (25 mL) was added dropwise at a rate of about 25 mL/40 min. The system was fitted with a drying tube to prevent absorption of water. It was also placed in a cool water bath to prevent the temperature from going above 25 °C. When the addition was finished, the mixture was stirred between 20 and 25 °C for about 4 h. Then it was heated to about 30 °C for the next 45 h. It was then allowed to cool. The precipitate was collected, washed with a small amount of dry benzene, and dried in vacuo (20.8 g, 98% yield). IR (Nujol): 3280, 2050, 1930, 1600 cm^{-1}. ^{1}H NMR ($CDCl_3$): 7.75 (8 H, d), 7.27 (8 H, d), 5.9 (4 H, s), 2.95 (8 H, t), 2.55 (8 H, t), 2.45 (4 H, t), 2.4 (12 H, s) ppm.

penten·6HBr (*N*,*N*,*N'*,*N'*-tetrakis(2-aminoethyl)ethylenediamine hexahydrobromide) was prepared as described by Gauss et al.[26] penten-4Ts (8.48 g, 0.1 mol) and phenol (20.0 g, 0.2 mol) were dissolved in a mixture of HBr (64 mL) and acetic acid (36 mL) in a 250-mL round-bottom flask. The flask was fitted with a reflux condenser and heated to reflux. As it was warmed, the reaction mixture became more and more red until it was a deep brick red. A dark oil formed after about 24 h. Heating was continued for another 24 h to ensure that the reaction was completed. The reaction mixture was cooled to room temperature and then placed in an ice bath. A 1:1 mixture (v/v) of ether and absolute ethanol was added slowly to the reaction mixture while it was stirred in the ice bath. The mixture was stirred in the ice bath until all the ice had melted, about 1 h. The resulting precipitate was collected, washed with the ether/absolute ethanol mixture, and dried in vacuo (7.0 g, 98% yield). IR (Nujol): 2700–2000, 1970, 1600 cm^{-1}. ^{1}H NMR (D_2O): 4.1 (8 H, s), 2.66 (8 H, m), 2.63 (2 H, d), 2.60 (2 H, d), 2.53 (8 H, d) ppm.

penten (*N*,*N*,*N'*,*N'*-tetrakis(2-aminoethyl)ethylenediamine) was prepared from the hydrobromide salt by ion-exchange chromatography. Dowex 200 resin in the basic (OH$^-$) form was regenerated by using a 1% NaOH wash, followed by washes with CO_2-free water. penten·6HBr (1.0 g, 0.1 mol) in CO_2-free water (40 mL) was loaded on the regenerated Dowex resin column (75 mL bed volume). The eluate was tested with litmus paper periodically. The column was eluted with water, and fractions testing basic were collected until the eluate became neutral again as evidenced by litmus paper. The collected fractions were evaporated to an oil under reduced pressure and then transferred to a weighed 100-mL round-bottom flask with the aid of distilled water and ethanol. The mixture was evaporated to dryness under reduced pressure and placed in a vacuum desiccator overnight. The product was a colorless oil. (0.3 g, 95% yield). IR (Nujol): 2020, 1600 cm^{-1}. ^{1}H NMR (D_2O): 4.15 (8 H, s), 2.45 (8 H, t, J = 0.3 Hz), 2.16 (8 H, t, J = 0.3 Hz), 2.05 (4 H, s) ppm.

Template Reaction Products. $Mn(NH_2Et)_2[15]pydieneN_5(PF_6)_2$ was prepared by a modification of the procedure for the preparation of $Mn([15]pydieneN_5)Cl_2$.[3] Anhydrous $MnCl_2$ (0.38 g, 3 mmol) and diacetylpyridine (DAP; 0.49 g, 3 mmol) were dissolved in absolute ethanol

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Table I. Conductivity Measurements and UV-Visible Spectra

compd[a]	Λ_M[b]	Λ_0[b]	slope[b]	λ_{max}[c]	$10^{-4}\epsilon$[c]
$Mn(R[15]pydieneN_5)(PF_6)_2$	312	193	800	214	1.79
2:1 electrolyte in CH_3CN[d]	220–300	170–220	900–1050		
$Mn(R[15]pydieneN_5)Cl_2\cdot 3H_2O$	239	140	250	214	1.84
2:1 electrolyte in H_2O[d]	225–270	75–150	200		
$Mn([15]pydieneN_5)Cl_2$	221	126	209	210	2.05
$Mn([17]pydieneN_5)Cl_2$	248	158	260	214	2.10

[a] R = $(NH_2Et)_2$. [b] Λ_M is the molar conductance for a 10^{-3} M solution, and Λ_0 is the conductance at infinite dilution, with units of Ω^{-1} cm^2 equiv^{-1}. The slope is given in units of Ω^{-1} cm^{-1}. [c] λ_{max} is given in units of nm and ϵ in units of M^{-1} cm^{-1}. [d] See ref 27 and 28.

(25 mL). penten (0.70 g, 3 mmol) was dissolved in absolute ethanol (25 mL). Both solutions were clear and colorless or slightly yellow. The penten solution was added dropwise to the $MnCl_2$/DAP solution. The reaction mixture became cloudy white initially, indicating formation of $Mn(OH)_2$. With heat and stirring, the mixture cleared and gradually became more yellow. After about a 1.5-h reflux, the reaction mixture was bright orange. NH_4PF_6 (1.08 g, 6.6 mmol) in absolute ethanol (25 mL) was added through a gravity filter. The mixture was allowed to cool and the precipitate to settle for about 1 h. The resulting precipitate was collected, washed with absolute ethanol, and dried in vacuo overnight. The product was a bright pumpkin orange powder. The crude product was recrystallized by using hot acetonitrile (5 mL) and absolute ethanol (30 mL). It was collected, washed with a small amount of absolute ethanol, and dried in vacuo (1.6 g, 75% yield). IR (Nujol): 3380, 3320, 2740, 1650, 1610, 880–820, 550 cm^{-1}. Anal. Calcd for $MnC_{19}H_{33}N_7P_2F_{12}$: C, 32.59; H, 4.71; N, 14.00. Found: C, 32.37; H, 4.86; N, 13.76.

$Mn(NH_2Et)_2[15]pydieneN_5Cl_2\cdot 3H_2O$ was prepared from recrystallized $Mn(NH_2Et)_2[15]pydieneN_5(PF_6)_2$ by a metathesis reaction. $Mn(NH_2Et)_2[15]pydieneN_5(PF_6)_2$ (2.1 g, 3 mmol) was dissolved in CH_3CN (35 mL) to give a cherry red solution. Bu_4NCl (1.8 g, 6 mmol) was dissolved in CH_3CN (25 mL) and was added dropwise to the $Mn(NH_2Et)_2[15]pydieneN_5(PF_6)_2$ solution with the use of an addition funnel. A brick red precipitate appeared as Bu_4NCl was added. The mixture was stirred for about 1 h. The product, a red-orange powder, was collected by suction filtration and dried in vacuo. The crude product was recrystallized from absolute ethanol (10 mL) and ether (50 mL). It was collected, washed with ether, and dried in vacuo (1.6 g, 97% yield). IR (Nujol): 3450, 3375, 3320, 3240, 3150, 1640, 1590 cm^{-1}. Anal. Calcd for $MnC_{19}H_{39}N_7O_3Cl_2$: C, 42.63; H, 6.59; N, 18.31. Found: C, 42.31; H, 7.15; N, 18.21.

Results and Discussion

Synthesis and Characterization. The synthesis of the PF_6^- salt of $Mn(NH_2Et)_2[15]pydieneN_5^{2+}$ was carried out via template condensation of diacetylpyridine and penten in the presence of Mn^{2+} in ethanol. The reaction was a modification of the one originally used to prepare $Mn[15]pydieneN_5$.[3] While it is theoretically possible for penten to condense in two ways, one to give a 12-membered tetraaza macrocycle and the other to give a 15-membered pentaaza macrocycle, only one product containing the $[15]pydieneN_5$ ring was observed. This is most likely due to the fact that the 12-membered ring is too small to encircle the Mn(II) ion. The product was isolated as the PF_6 salt and converted to the chloride salt to give a water-soluble form of the complex. Both compounds had elemental analyses consistent with the formulations given in the Experimental Section. The solid-state magnetic moments of 5.87 and 5.84 μ_B for the PF_6^- and Cl^- salts, respectively, are indicative of high-spin Mn(II) in each case. The conductivities of the PF_6^- salt in acetonitrile and the Cl^- salt in water (see Table I) are indicative of 2:1 electrolyte behavior in each case. The UV-visible spectra of the two compounds are identical in CH_3CN and H_2O, respectively. There are three bands near 300 nm with molar absorptivity about 5000 and two more intense bands above 200 nm with ϵ_m about 1.8×10^4. All of these bands are probably charge-transfer bands[29,30] associated with the pyridine–diimine moiety of the macrocycle since they vary little between these complexes and the related $[15]pydieneN_5$ and $[17]pydieneN_5$ complexes (Table I).

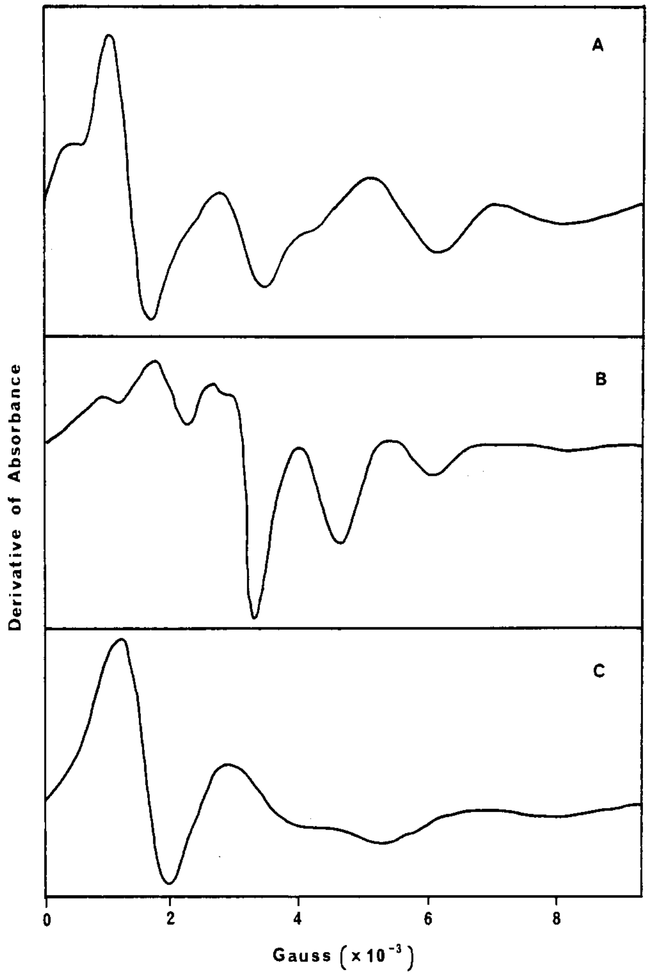
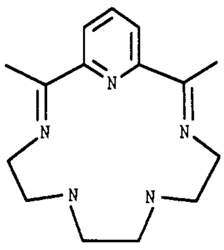
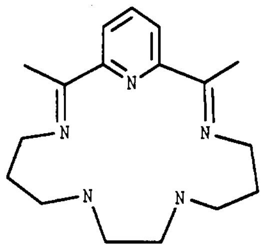


Figure 1. Room-temperature EPR spectra of (A) polycrystalline $Mn((NH_2Et)_2[15]pydieneN_5)Cl_2\cdot 3H_2O$, (B) polycrystalline $Mn([15]pydieneN_5)Cl_2\cdot 6H_2O$, and (C) polycrystalline $Mn([17]pydieneN_5)Cl_2\cdot 5H_2O$. Conditions are the same as in the footnotes of Table III.


$[15]pydieneN_5$


$[17]pydieneN_5$

It was of interest to confirm that the aminoethyl pendant arms are coordinated in aqueous solution and do not become dissociated and protonated. The chloride salt of $Mn(NH_2Et)_2[15]pydieneN_5^{2+}$ was titrated with HCl in order to see if the arms could be protonated. The pH of the initial solution was near neutrality. This indicates that the arms are coordinated since the pH would be alkaline in the presence of free amino groups. The pH decreased with each aliquot of HCl, and the accompanying change in color from light yellow to colorless indicated that the complex decomposed in acidic solution. There was no inflection point in the titration curve, indicating that the arms cannot be protonated without destroying the complex. These results along with the identity of the visible spectra in aqueous and nonaqueous solvents lead to the conclusion that the aminoethyl pendant arms are coordinated in solution under conditions where the complex is stable. Further support of this conclusion is provided by the EPR spectra.

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Table II. EPR Absorptions (G) for Chloride Salts of Three Manganese Complexes

$(NH_2Et)_2$[15]pydieneN$_5$[a]	[15]pydieneN$_5$[b]	[17]pydieneN$_5$[c]
450 sh	600 w, sh	1660 main
1400 main	1100 sh	3400
2200 sh	1900 sh	5200 sh
3100	2800 sh	7700 sh
4100 sh	3200 main	8400 sh
5600	4750 sh	
8150 sh	6200	
	8200 sh	

[a] Room temperature, polycrystalline sample (trihydrate), 9.101 GHz, 20-mW microwave power, 100-kHz modulation amplitude. [b] Same conditions as in *a*, except 9.085 GHz and hexahydrate. [c] Same conditions as in *a*, except 9.099 GHz and pentahydrate.

EPR Spectra. The EPR spectra of polycrystalline samples of Mn($(NH_2Et)_2$[15]pydieneN$_5$)Cl_2, Mn([15]pydieneN$_5$)Cl_2, and Mn([17]pydieneN$_5$)Cl_2 are shown in Figure 1. The EPR absorptions taken from the spectra are listed in Table II. Dowsing and Gibson[31,32] have shown that the zero-field parameters for high-spin Mn(II) complexes can be estimated from a comparison of the observed EPR lines with those calculated for various λ and D values. λ is the ratio of zero-field-splitting parameters E and D and varies between zero for axial or octahedral symmetry and $^1/_3$ for rhombic symmetry.[33] D is the axial zero-field-splitting parameter, and E is a measure of the asymmetry of the field along the x and y directions. Complexes with axially symmetric ligand fields have $\lambda = 0$ and D from zero to several reciprocal centimeters, depending on the nature of the axial ligands. For axial systems the major EPR line is centered near $g = 2$ (3400 G) for small values of D and at $g = 6$ (1100 G) for large values of D. As the symmetry is lowered from axial to rhombic, the major absorption splits and shifts toward $g = 4.3$ as λ increases. The high-field lines can be used to estimate D. The spectrum of Mn([15]pydieneN$_5$)Cl_2·$6H_2O$ has been interpreted previously by Van Heuvelen et al.[4] as indicative of approximate axial symmetry (λ near zero). The high-field line near 8200 G and the low-field lines at 1100 and 600 G indicate that D is about 0.1 cm^{-1}. In comparison, the EPR spectrum of Mn($(NH_2Et)_2$[15]pydieneN$_5$)Cl_2 is different from that of Mn([15]pydieneN$_5$)Cl_2·$6H_2O$ even though each compound has the same 15-membered N_5 macrocyclic ligand. The main line is shifted by 1800 G toward the $g = 6$ position, but the high-field lines extend similarly to about 8200 G. These lines are consistent with the positions in the Dowsing and Gibson diagram[31] with $\lambda = 0.03$ or less and $D = 0.2$ cm^{-1}. Thus, the spectra are indicative of approximate axial symmetry in both cases but with a larger axial zero-field splitting in the bis(ethylamino)-substituted complex. This is consistent with the larger ligand field splitting expected from amino versus aquo and chloride axial ligands. In contrast, the spectrum of Mn([17]pydieneN$_5$)Cl_2 has its main line near $g = 4.3$, indicative of rhombic symmetry. This is consistent with the larger macrocycle coordinated in a nonplanar or folded fashion and with chloride or water filling the sixth coordination site. The relaxation enhancement data to be discussed below are also consistent with one exchanging aquo ligand in the case of the 17-membered ring versus two for the 15-membered ring.

The results of EPR studies of polycrystalline samples at room temperature showed very little difference between the two complex salts of Mn$(NH_2Et)_2$[15]pydieneN$_5$, suggesting very little anion dependence in the spectrum of the complex. The frozen-solution EPR spectrum of the chloride salt at 14 K in a 50:50 glycerol/water mixture varied very little from the polycrystalline room-temperature spectrum. The major peak was still at $g = 4.8$ with medium-intensity peaks at $g = 2.1$ and $g = 1.5$. The great similarity between the polycrystalline studies at room temperature and the frozen-solution studies at about 14 K suggest that the structure is the same in the solid state and in solution. Since the zero-field-splitting parameters are indicative of axial symmetry with an axial field different from that of the related complex having the macrocycle [15]pydieneN$_5$ with axial water molecules, the results are consistent with coordinated ethylamino groups trans to each other. Also, the lack of hyperfine structure in the low-temperature spectra and in the solid state is consistent with a relatively large amount of zero-field splitting due to the crystal field.[34]

Table III. Relaxivities of Manganese Complexes at 24 MHz and 25 °C

complex	R_1, mM^{-1} s^{-1}	ref
$Mn(H_2O)_6^{2+}$	7.4	42
$Mn(EDTA)(H_2O)^{2-}$	3.0	42
$Mn(DTPA)^{3-}$	1.3	42
Mn$(NH_2Et)_2$[15]pydieneN$_5^{2+}$	0.92	this work
Mn[15]pydieneN$_5$$(H_2O)_2^{2+}$	5.83	this work
Mn[17]pydieneN$_5$$(H_2O)^{2+}$	3.35	this work

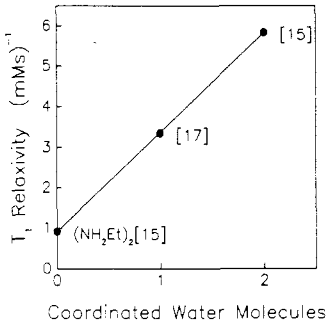

Figure 2. Plot of aqueous proton T_1 relaxivity at 24 MHz and 25 °C versus the number of exchanging coordinated water molecules for several Mn(II) complexes of [*X*]pydieneN$_5$ macrocycles.

Aqueous Proton Nuclear Relaxation. The nuclear magnetic relaxation enhancement of water protons in a solution of a paramagnetic chelate complex is primarily due to the dipolar interaction between the electron spin magnetic moment of the metal ion and the proton nuclear moment of coordinated water protons.[35] The rapid exchange of aquo ligands communicates the relaxation to the bulk solvent. In addition to inner-sphere relaxation there is a smaller effect due to the dipole–dipole interaction between the metal ion and water molecules that solvate the complex but are not coordinated to the metal ion, called the outer-sphere contribution. The total aqueous proton relaxation rate is the sum of three contributions arising from the solvent relaxation and the inner-sphere and the outer-sphere contributions. The relaxation enhancement is the sum of the last two contributions and usually cannot be separated into the two terms. In order to more quantitatively understand the inner-sphere mechanism in complexes such as Mn[15]pydieneN$_5$$(H_2O)_2^{2+}$ and Mn[17]pydieneN$_5$$(H_2O)^{2+}$, some estimate of the outer-sphere contribution is necessary. The Mn$(NH_2Et)_2$[15]pydieneN$_5^{2+}$ complex provides a good estimate of the outer-sphere contribution for this type of complex since its size, charge, and ligands are so similar to those of the other [*X*]pydieneN$_5$ complexes, but it has no inner-sphere water.

At a given frequency, the longitudinal relaxation rate enhancement per millimolar concentration of paramagnetic complex, called the T_1 relaxivity, is expressed in mM^{-1} s^{-1}. Table III gives a comparison of T_1 relaxivities for several Mn(II) complexes at 24 MHz and room temperature. In comparison to the values for all of the complexes having one or more inner-sphere water ligands, the relaxivity of Mn$(NH_2Et)_2$[15]pydieneN$_5^{2+}$ is small. Figure 2 shows a correlation plot of the T_1 relaxivity for the three [*X*]pydieneN$_5$ complexes with the assumed number of coordinated

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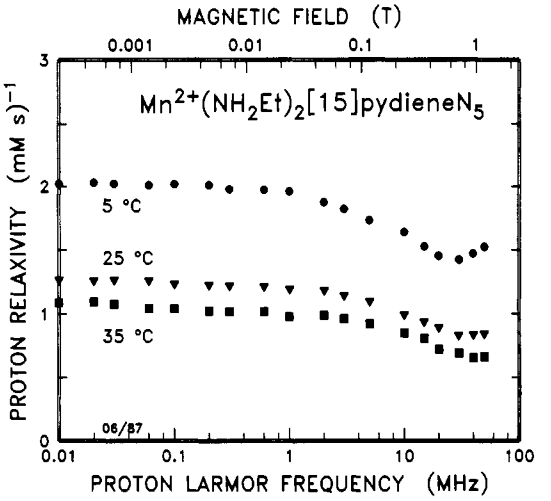

Figure 3. Nuclear magnetic relaxation dispersion profiles of proton relaxivity versus proton Larmor frequency for an aqueous solution of $Mn(NH_2Et)_2[15]pydieneN_5^{2+}$ at three different temperatures.

water molecules for each complex. The linearity of the plot may be in part fortuitous but is consistent with the same outer-sphere contribution in each case.

The theory of outer-sphere relaxation enhancement is more complicated than the Solomon–Bloembergen–Morgan theory for inner-sphere relaxation. The modulation of the dipole–dipole interaction occurs through the diffusional motions of the interacting spins and requires the assumption of a solvent model for its description. Several models with varying degrees of sophistication have been applied by Hubbard,[36] Pfeiffer,[37] Freed,[38] Albrand,[39] and others. These have been applied recently to study rate enhancement by nitroxide free radicals.[40,41] Qualitatively, over the frequency range 0.01–50 MHz, the theory predicts a smaller and broader dispersion than that of the SBM theory for inner-sphere relaxation. The broad and shallow nuclear magnetic relaxation dispersion (NMRD) profile observed for $Mn(NH_2Et)_2[15]pydieneN_5^{2+}$ (Figure 3) is consistent qualitatively with the outer-sphere model. The temperature dependence of the NMRD profile qualitatively reflects the changes in the diffusion coefficients and correlation times of water and the complex with temperature. The 5 °C curve reveals a dependence on the electron spin relaxation time as evidenced by the slight increase in relaxation rate seen above 20 MHz.[35] This implies that the purely diffusion-controlled model is inadequate to treat this complex since it assumes that solvating water molecules spend too little time near the metal center to be influenced by electron spin relaxation.

Figure 4 shows a comparison of NMRD profiles for $Mn(DTPA)^{3-}$ and two other Mn(II) complexes with coordinatively saturating polyamino polycarboxylate chelating ligands and $Mn(NH_2Et)_2[15]pydieneN_5^{2+}$. It is significant that all three of the complexes of DTPA, NOTA, and DOTA, which are anionic, have the same profile while that of the cationic $(NH_2Et)_2[15]$-pydieneN_5 complex is very different. At the low-field limit, the relaxivity is close to half that observed for the anionic complexes.

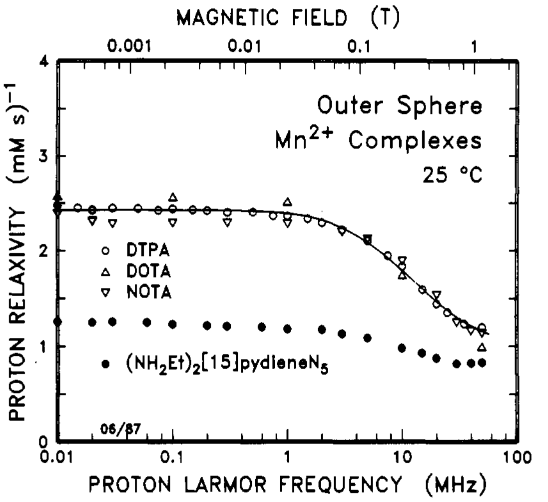

Figure 4. Comparison of NMRD profiles of four Mn(II) complexes having coordinatively saturating chelating ligands. DTPA, DOTA, and NOTA are respectively diethylenetriaminepentaacetate, 1,4,7,10-tetraazacyclododecanetetraacetate, and 1,4,7-triazacyclononanetriacetate.

Qualitatively, this difference can be explained in terms of the difference in solvation of comparably sized anionic versus cationic chelates and the effect on the average distance of closest approach of water protons to the paramagnetic center. The curve drawn through the DTPA, NOTA, and DOTA curves results from a least-squares comparison of the data with a theory of outer-sphere relaxation[2] that involves the following parameters: a, the distance of closest approach of solvating water protons (approximately 3.5 Å); D, the relative diffusion constant (approximately 2.8×10^{-5} cm^2 s^{-1}); τ_{S_0}, the low-field limiting value of the electron spin relaxation time (approximately 200 ps); τ_v, the correlation time for modulation of the zero-field splitting by solvent collisions (about 40 ps). With the exception of a, all of these parameters are expected to be similar for the cationic manganese complex. The fact that the cationic complex will be solvated with the oxygen end of the water dipole closest to the metal center will cause a to be about 1 Å larger in its case. At the low-field limit[42,43] the dependence of the relaxivity on a is proportional to $(1/a)^3$; thus, the predicted ratio of relaxivities is $(3.5/4.5)^3$ or 0.47 in agreement with the observed values.

Conclusion. The complex $Mn(NH_2Et)_2[15]pydieneN_5^{2+}$ has been prepared and characterized. The aminoethyl pendant arms are coordinated in the solid state and in aqueous and nonaqueous solution. The EPR spectra indicate approximate axial symmetry consistent with a pentagonal-bipyramidal coordination geometry. The aqueous proton magnetic relaxation enhancement by the complex is also consistent with a coordinatively saturated cationic complex.

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Registry No. $Mn(NH_2Et)_2[15]pydieneN_5(PF_6)_2$, 120022-68-6; ClEtNHTs, 6331-00-6; $ClEtNH_2$, 689-98-5; $Mn(NH_2Et)_2[15]pydieneN_5Cl_2 \cdot 3H_2O$, 120022-69-7; $Mn([15]pydieneN_5)Cl_2$, 27577-84-0; $Mn([17]pydieneN_5)Cl_2$, 63280-54-6; $Mn[15]pydieneN_5(H_2O)_2^{2+}$, 63280-48-8; $Mn[17]pydieneN_5(H_2O)^{2+}$, 120022-70-0; diacetylpyridine, 1129-30-2; penten, 4097-90-9; tosyl aziridine, 3634-89-7; penten-4Ts, 103635-08-1; ethylenediamine, 107-15-3; penten-6HBr, 119999-75-6.

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