Experimental Section

Fab HA5-19A4 was prepared by digestion of IgG HA5-19A4 with papain according to a standard protocol (Pierce No. 44885). The IgG was obtained from a standard hybridoma protocol described in the supporting information of Hasserodt and colleagues.[6] For sequence determination the total RNA from 1×10^7 hybridoma cells was prepared with Tri Reagent according to the manufacturer's protocol (Molecular Research Center, Inc., Cincinnati, OH). Reverse transcription and PCR amplification of the light-chain and Fd-fragment sequences were performed as described.[14] The primer 5′-GAYGTNCARCTCGAGGAGTCAGGACCT-3′ was used to amplify the 5′ end of the Fd-fragment sequence. Light-chain and Fd-fragment sequences were digested with *Sac*I/*Xba*I and *Xho*I/*Spe*I, respectively, and ligated into the phagemid vector pComb3H.[15] After electrotransformation into XL1-Blue *E. coli* cells, clones were randomly selected for protein expression induced with isopropyl-β-D-thiogalactopyranoside.[16] Fab specific to HA5-BSA antigen was detected by enzyme-linked immunosorbent assay (ELISA) by using goat anti-mouse $F(ab')_2$ (Pierce) conjugated to alkaline phosphatase as a secondary antibody. Plasmid DNA from ELISA-positive clones was sequenced to determine the light-chain and Fd-fragment sequences.

Crystals of the HA5-19A4 Fab–**5** complex were obtained by equilibrating 5 μL of protein solution (11.4 mg mL^{-1} Fab, 10 mM $CdCl_2$, 10 mM **5**, 50 mM Tris (pH 7.0)) with 5 μL of precipitant buffer (30% polyethylene glycol ($M_r = 6000$), 100 mM 2-[4-(2-hydroxyethyl)-1-piperazinyl]ethanesulphonic acid (HEPES; pH 7.9)) in a hanging drop suspended over a 1 mL reservoir of precipitant buffer at room temperature. Small rectangular plates appeared within three days. These crystals diffracted X-rays with a resolution of 2.7 Å (93.5% complete, $R_{merge} = 0.088$). Crystal dimensions 0.6 mm × 0.1 mm × 0.05 mm, space group $C2$, $a = 101.3$, $b = 70.3$, $c = 69.6$ Å, $\beta = 114.2°$, one molecule in the asymmetric unit. The structure was solved by molecular replacement by using the atomic coordinates[17] of Fab D2.3 to construct a polyalanine probe for rotation and translation function calculations with AmoRe.[18] Refinement and rebuilding of the model were performed with X-PLOR[19] and O;[20] refinement converged smoothly to a final crystallographic R factor of 0.165 ($R_{free} = 0.257$). Two Cd^{2+} binding sites were identified: one between Glu^{L187} and Glu^{L213}, and a second between Asp^{H173} and Glu^{L81} of symmetry-related molecules in the crystal lattice. The final model has excellent stereochemistry with rms deviations from ideal bond lengths and angles of 0.011 Å and 1.7°, respectively. The Ramachandran plot shows that 318, 49, and 3 residues adopt the most favored, additionally allowed, and generously allowed backbone conformations, respectively; only 4 residues adopt disallowed backbone conformations, and these are found in poorly characterized loop regions. Atomic coordinates of the Fab-**5** complex have been deposited in the Brookhaven Protein Data Bank (http://www2.ebi.ac.uk/pdb) with accession code 1CF8.

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A Polycationic Metallodendrimer with 24 $[Fe(\eta^5\text{-}C_5Me_5)(\eta^6\text{-}N\text{-Alkylaniline})]^+$ Termini That Recognizes Chloride and Bromide Anions

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Dendrimers[1] are the first well-defined, monodisperse synthetic macromolecules that should be able to achieve various supramolecular functions.[2–7] Several applications as, for example, antennas,[3] boxes,[4] and catalysts[5] have already

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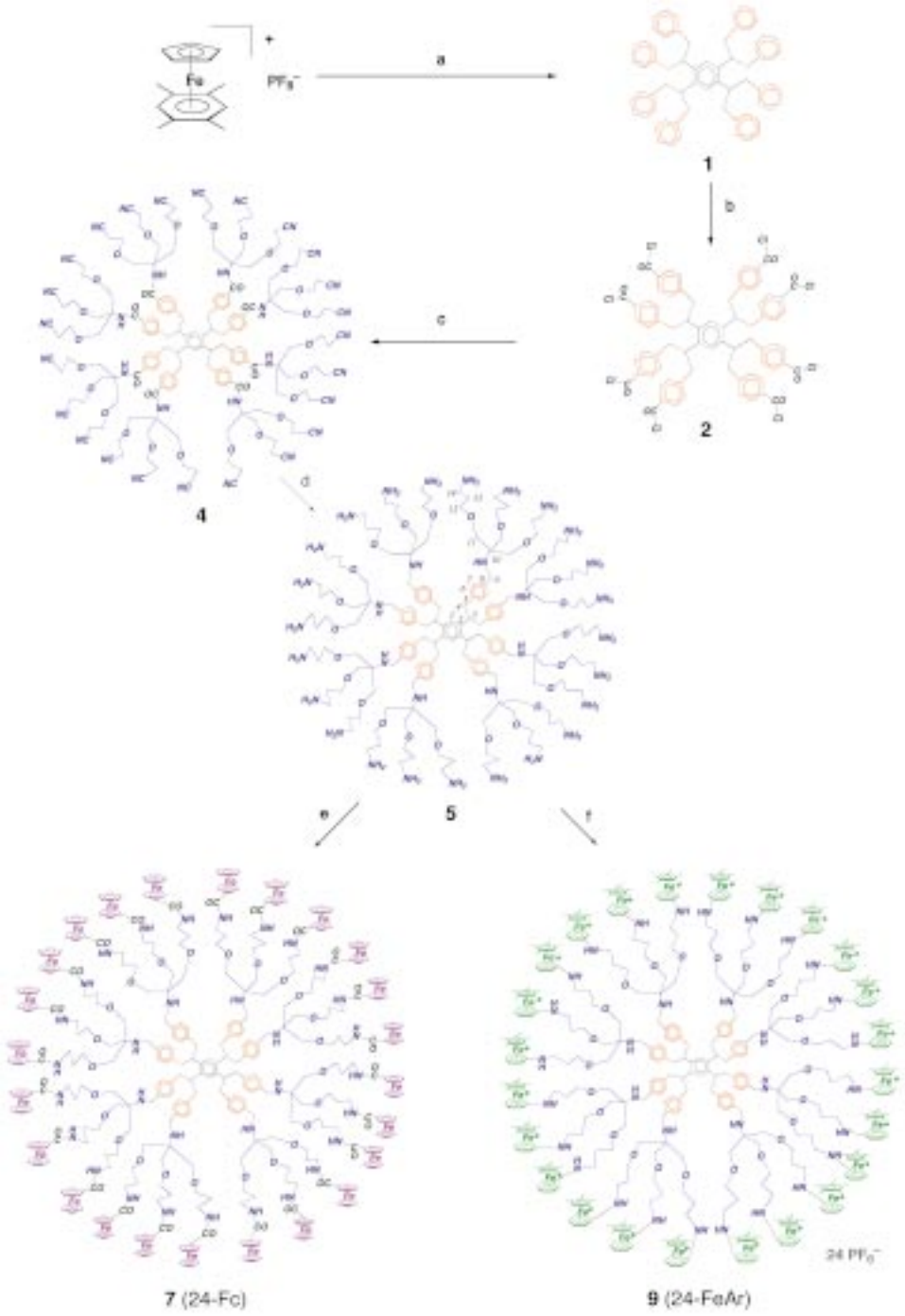
been highlighted. Molecular recognition, including that of anions, is a function directly related to supramolecular chemistry,[2] and has been studied using *endo* receptors.[6–19] For instance, Lehn has recently reported hosts which are specific for chloride,[19] and anion recognition is becoming more and more important for biological and environmental purposes.[10] The design and investigation of new types of receptors is thus timely, especially in view of the multiple properties of dendrimers.[1] Reports on anion sensing by Tomalia could find useful extensions in drug transport and gene therapy.[20, 21] Indeed, dendrimers resemble viruses in view of the fractality of their surfaces and can consequently be considered as *exo* receptors.

The recognition of oxo anions by 9- and 18-amidoferrocene dendrimers was recently determined with electrochemistry,[22] and other polyferrocene dendrimers were shown to be promising biosensors.[24, 25] The recognition abilities of such polyamidoferrocene dendrimers could not be observed by NMR spectroscopy, except for $H_2PO_4^-$, because the neutral diamagnetic 18-electron form does not usually interact efficiently with anions. Recently, Beer et al. have shown with NMR spectroscopy that some neutral ferrocenoyl receptors can recognize anions.[10c] Electrochemistry was the method of choice for studying oxo anions because the anodically generated cationic ferricinium form strongly interacts electrostatically with the anions; this interaction operates in synergy with $X^- \cdots HN$ bonding. Halides could not be recognized with these polyferrocene dendrimers, however, as they interact only weakly with the ferrocene moieties, even the cationic amidoferricinium forms.[22]

We report here the synthesis of a new polycationic metallodendrimer, and present ^1H NMR results for its use as an *exo* receptor for the selective recognition of chloride and bromide anions. We also compare the remarkable recognition ability of this metallodendrimer, which is polycationic in its 18-electron form, to that of a polyamidoferrocene dendrimer of comparable topology, whose metal moieties are neutral in their 18-electron forms.

To improve the selectivity in the recognition of various anions, we have chosen new, large cationic metal–sandwich termini with bulky C_5Me_5 ligands and a new type of core. The construction of the dendritic core is based on a regiospecific chlorocarbonylation in the *para* position of the octabenzyl core **1** (68% yield of **2**), which is easily available by $CpFe^+$-induced octabenzylation of 1,2,4,5-tetramethylbenzene (durene; Scheme 1).[26] Reaction of fresh samples of Newkome's tripodal amine $NH_2C(CH_2OCH_2CH_2CN)_3$ (**3**)[27] with **2** at 20 °C in CH_2Cl_2 with NEt_3 gave the 24-nitrile dendrimer **4**



Scheme 1. a) $PhCH_2Br$, KOH, DME, 2 d, RT; b) $(COCl)_2$, $AlCl_3$, CH_2Cl_2, 15 °C, 1 h; c) $NH_2C(CH_2OCH_2CH_2CN)_3$, NEt_3, CH_2Cl_2, 3 d, RT; d) $BH_3 \cdot Me_2S$, THF, RT, 1 d; e) $[FeCp(C_5H_4COCl)]$ (**6**), CH_2Cl_2, 4 d; f) $[FeCp^*(\eta_6\text{-}C_6H_5F)][PF_6]$ (**8**), CH_2Cl_2, RT, 15 d.

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(61 % yield after chromatographic purification on neutral alumina with dichloromethane as eluent). This dendrimer was characterized by its molecular peak (*m*/*z* 3328.57 [*M*+Na$^+$]) in the MALDI-TOF mass spectrum (MALDI-TOF = matrix-assisted laser desorption/ionization time-of-flight).

Reduction of the 24 nitrile and 8 carbonyl groups of **4** with $BH_3 \cdot SMe_2$ (THF, 20 °C) followed by methanolysis gave the 24-amino dendrimer **5** (90 % yield) as a white, hygroscopic, water-soluble powder. Nucleophilic substitution of chloride by amine was known for [Fe(η^5-C_5H_5)($\eta^6C_6H_5Cl$)]$^+$,[28] but initial attempts with this substrate showed that the sandwich termini were relatively fragile. The use of Cp* (Cp* = η^5-C_5Me_5) as ligand considerably increases the stability of the sandwich complexes. However, the analogous nucleophilic substitution reactions were unknown for the Cp* compounds, which were clearly going to be less reactive because of the decreased positive charge on the arene ligand. Reaction of the 24-amine dendrimer with a twofold excess of [FeCp*(η^6-C_6H_5F)][PF_6] (**8**)[29] in CH_2Cl_2 in the presence of NEt_3 gave the robust 24-[FeCp*(η^6-arene)]$^+$ dendrimer **9** as an orange powder in 30 % yield after chromatography on alumina with methanol as eluent. To compare the recognition ability of **9** with those of a mononuclear compound and of a tripod having structures resembling that of the dendrimer, we also synthesized the mononuclear compound **10** and the trinuclear species **11** (Figure 1; these compounds also gave satisfactory analytical and spectroscopic data).

Titration of **9**[30, 31] and cationic complexes **10** and **11** with nBu_4N^+ salts of Cl^-, Br^-, $H_2PO_4^-$, and HSO_4^- was monitored by the variation of the ^{1}H NMR chemical shift δ_{NH} of the exocyclic amine proton in [D_6]DMSO. The results are in contrast to those obtained with amidoferrocene dendrimers such as **7** (synthesized by the reaction of **5** with ferrocenylcarbonyl chloride and NEt_3 in CH_2Cl_2) and others[22] (Figure 1 and Table 1).

The changes in δ_{NH} and the apparent association constant K_{app} upon addition of Cl^- to **9** are larger than those obtained upon addition of the other anions; a sharp transition is observed for eight equivalents of Cl^- per dendrimer, which corresponds to one Cl^- ion per tripodal dendrimer branch (Figure 1 a). There is a distinction between the relatively sharp transition with Cl^- and the smooth transition with Br^-. Moreover, the magnitude of the variation of δ_{NH} (Figure 1 a) and K_{app} for Cl^- (Table 1) is much larger with dendrimer **9** than with the tripodal compound **11**; thus, the dendritic effect is strong. In fact, in the case of **10** and **11**, no clear equivalence point can be obtained. The dendritic effect can be measured by the low-field shift in the NMR spectrum and the increase in K_{app}, when a given anion is added to the solution of the dendrimer, obtained in switching from **11** to **9** (tripodal **11** has the same structure as the tripods of dendrimer **9**). Molecular models show that in **9** the tripod branches are forced by the bulkly groups at the periphery to approach one another more closely than in **11**. The channels defined by the large organoiron groups become narrow because of the steric compression at the dendrimer periphery, so that Cl^- presumably fits well in the tripodal semicavities of the dendritic periphery of **9**.

Upon addition of Br^- to **9**, the change of the ^{1}H NMR shift smoothly reaches a plateau after approximatively one equivalent of Br^- per dendrimer branch. A large dendritic effect is also found, the ^{1}H NMR shifts and apparent association constants K_{app} increasing as the number of branches is raised (1-FeAr → 3-FeAr → 24-FeAr, Figure 1 b and Table 1). As for Cl^-, in the titration of complexes **10** and **11** with Br^- there is no sharp equivalence point, which is in contrast to what was found for **9**. The affinity of **9** for Br^- is weaker than for Cl^- because the NH···X^- hydrogen bond is also weaker (a well-known trend[2]) due to a reduced electrostatic attraction.[7] In

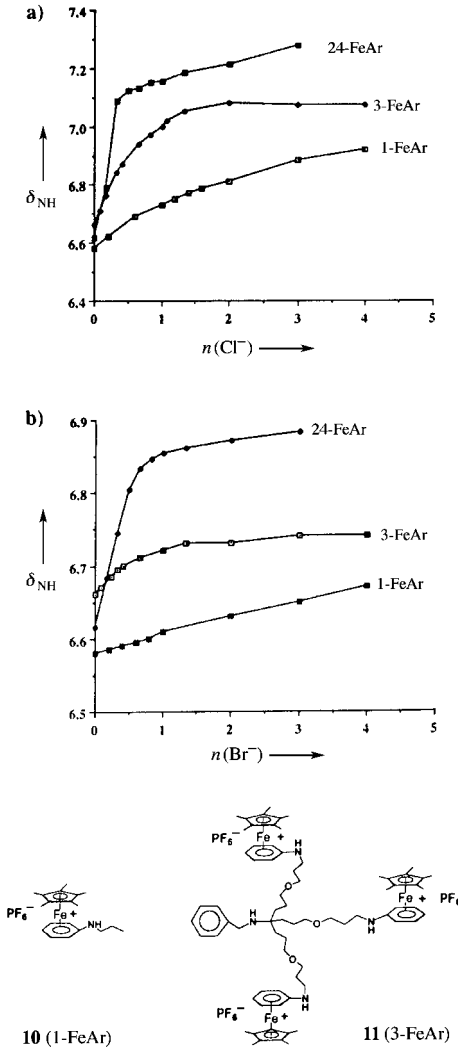

Figure 1. Variation of δ_{NH} for the exocyclic amine proton measured by ^{1}H NMR spectroscopy upon addition of nBu_4NCl (a) and nBu_4Br (b), given in number of equivalents *n* per branch, to **10** (1-FeAr), **11** (3-FeAr), and **9** (24-FeAr).

Table 1. Apparent association constants K_{app} [dm^{3}mol^{-1}], determined from the variation of the δ_{NH} signal in [D_6]DMSO at 20 °C with the EQ-NMR program[31] (the uncertainty is 10 %). Small values of the order of 10 obtained with Cl^- and Br^- for the monometallic complex **10** have no physical meaning, but signify that no equivalence point is reached for one equivalent of anion per FeAr branch (this emphasizes the dendritic effect). Also note the negative dendritic effect for HSO_4^- upon comparison of the values obtained for **9** and **11**.

	10 (1-FeAr)	**11** (3-FeAr)	**9** (24-FeAr)
Cl^-	10	118	1221
Br^-	2	129	431
HSO_4^-	14	461	6

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the case of Br^-, the recognition is simply accounted for by a 1:1 hydrogen-bonding interaction between the anion and the dendrimer branch. On the other hand, it is probable that for Cl^- each anion interacts through hydrogen bonding with the three dendrimer arms of each tripodal dendrimer branch.

The addition of $[n\mathrm{Bu_4N}][\mathrm{H_2PO_4}]$ to **9** provoked the precipitation of the corresponding salt of the dendrimer, which was not the case for the other anions. With HSO_4^-, δ_{NH} changed continuously even beyond one equivalent per branch without reaching a break point. This indicated that there is no specificity of the dendrimer for this anion. On the other hand, the tripodal compound **11** is selective; equivalence is reached at one equivalent of HSO_4^- per branch, and the apparent association constant ($K_{app} = 461$) is two orders of magnitude larger than for **10** ($K_{app} = 14$) and **9** ($K_{app} = 6$). This means that the semicavities defined by the eight tripodal branches at the dendrimer surface cannot open to encapsulate HSO_4^- anions, unlike the situation with the more flexible **11**. This lack of selective recognition contrasts with the favorable dendritic effect found for oxo anions with ferrocene dendrimers such as **7** and other neutral and less bulky dendrimers.[22]

The new polycationic metallodendrimer **9**, designed with large cationic termini, shows large dendritic effects for recognition of Cl^- and Br^- according to ^{1}H NMR spectroscopy. These halides could not be recognized by neutral polyferrocene dendrimers such as **7** (no change in the NMR shift δ_{NH} upon addition of the anion), which has a topology comparable to that of **9**, and other structures that have already been reported.[22–25] Likewise, electrochemistry was a workable sensing technique in the case of amidoferrocene dendrimers, but only little effects are found for the polycationic dendrimer **9**. These striking differences of behavior between neutral and cationic dendrimers with the same topology demonstrate the essential role of the positive charge for efficient interaction with anions and for the recognition ability observed by ^{1}H NMR spectroscopy. For instance, a polycationic dendrimer such as **9** must have a much larger hydrodynamic radius than the compact, neutral 24-amido-ferrocene dendrimer **7**. Besides the ferrocene groups, we believe that another important factor is the number of hydrogen bonds. Whereas the amido group is a chelating zwitterion that is potentially able to form two hydrogen bonds with chelating anions such as $H_2PO_4^-$, this feature is not available with **9** because only one anchoring nitrogen atom can enter into hydrogen bonding with the single-atom halogen anion.

In summary, the recognition of choride and bromide, as determined by the NMR shifts of δ_{NH} for **10**, is due to the synergy between the single $X^- \cdots HN$ hydrogen bond per branch, the electrostatic attraction, and the shape selectivity brought about by the peripheral cavities formed by the dendrimer branches and tripods.

Experimental Section

For the numbering of the atoms, see the formula of **5** (Scheme 1). Descriptions of the syntheses as well as spectroscopic data and elemental analyses for compounds **2**–**11** can be found in the supporting information.

9: A mixture of **5** (0.12 g, 0.0365 mmol), NEt_3 (1.22 mL, 8.76 mmol), and **8** (0.76 g, 1.75 mmol) in CH_2Cl_2 (10 mL) was stirred for 15 d at ambient temperature. After removal of the solvent under vacuum, CH_2Cl_2 (50 mL) was added. The organic phase was washed with a 1M solution of KPF_6 (3×20 mL) and then water (2×20 mL), dried over Na_2SO_4, and filtered. The solvent was removed under vacuum. After chromatography on alumina (activity II–III) with methanol as eluent, **9** was obtained as a yellow-brown powdery solid (0.143 g, 30% yield). Elemental analysis calcd for $C_{562}H_{774}O_{24}N_{32}Fe_{24}P_{24}F_{144}$: H 5.92, C 51.21, N 3.4; found: H 6.12, C 51.80, N 3.89; cyclic voltammetry (scan rate 0.3 Vs^{-1}, Pt, DMF, 20°C, 0.1M Bu_4NPF_6): a single reversible cathodic 24-electron wave at $E_{1/2} = -1.88$ V vs. SCE with ferrocene as internal reference.

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A New Route to Organic Intercalates Consisting of Vanadium Pentoxide and Pyridines: $(4\text{-}H_2N\text{-}C_5H_5NH)V_2O_5$**

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Layered intercalation compounds have attracted increased research attention due to their applications in such diverse areas as rechargeable batteries, heterogeneous catalysis, and ion exchange.[1] Interest is particularly high in the insertion of organic molecules into layered hosts for the purpose of synthesizing organic – inorganic composite materials with well-defined stoichiometries and organized structures.[2–7] Such materials may possess hybrid properties that have a synergism of the properties shown by the host and the guest.[3, 8] Pyridine and its derivatives are the class of organic Lewis bases that has been most investigated for intercalation in a variety of layered hosts including transition metal dichalcogenides,[4] metal phosphorus trisulfides,[9] metal oxides,[10, 11] and metal phosphates.[12, 13]

The conventional synthetic scheme for intercalating such molecules into layered hosts entails a direct reaction of the guest with the host lattice.[1e] Such heterogeneous reactions usually afford products with insufficient crystallinity. As a result, definitive structural information with regard to the arrangement of the organic molecules in the interlamellar space is difficult to obtain. Contradicting structural models have sometimes been proposed for the same host – guest system based on X-ray powder diffraction results.[14] Recently, hydrothermal techniques have been demonstrated to facilitate the synthesis and single-crystal growth of organic-based intercalation compounds.[15] For example, α- and β-$(enH_2)_{0.5}V_2O_5$ (en = ethylenediamine)[16] as well as $(DABCOH_2)V_6O_{14}$ (DABCO = 1,4-diazabicyclo[2.2.2]octane)[17] have been synthesized by the hydrothermal technique and structurally characterized by X-ray single-crystal analysis.

We have been interested in synthesizing novel microporous – mesoporous composite materials using layered compounds containing intercalated small molecules (e.g. pyridines, alkylamines, and alkalimetal ions) as starting materials in liquid crystal templating reactions. Here we describe the hydrothermal synthesis and X-ray structure of $(4\text{-}H_2N\text{-}C_5H_5NH)V_2O_5$ (**1**), the first pyridine intercalation compound to be characterized by single-crystal X-ray analysis. This study has not only provided insight into the molecular orientation of the pyridine ring with respect to the host layer, but has also shed light on the formation mechanisms of the pyridine intercalate under hydrothermal conditions.

The structure of **1** was determined by X-ray single-crystal analysis.[18] Compound **1** crystallizes in the monoclinic system with an asymmetric unit containing two V, five O, five C, two N, and seven H atoms in general positions. Both V atoms have square-pyramidal coordination with double-bonded O atoms occupying the axial positions. The structure can best be described as a two-dimensional intercalation compound of the organic $(4\text{-}H_2N\text{-}C_5H_5NH)^+$ cations into the anionic $[V_2O_5]^-$ layers (Figure 1). Each $[V_2O_5]^-$ layer is formed parallel to the [001] plane consisting of distorted VO_5 square pyramids linked by edge- and corner-sharing O atoms. Figure 2 gives a projection of a $[V_2O_5]^-$ layer in **1**, and the bonding modes of the V and O atoms in the layer. The square pyramids share two edges of their base with neighboring square pyramids to form double ribbons along the [100] direction in such a way that the axial vertices alternatively point up and down. The ribbons are then connected with one another along the same direction through corner sharing. Because all the ribbons within a layer adopt the same orientation, the vertices of neighboring ribbons point in opposite directions across the corner-shared O atoms. Overall, the orientation of the square pyramids alternates up and down along the [001] direction. The O atoms are engaged in terminal (O2 and O4), doubly

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