Table I. Phase Transfer of Picrate Salts at 25 °C[a]

cation	complexing agent	salt transferred, %
Li^+	18-crown-6	63
	poly-**6**[b]	37
K^+	18-crown-6	74
	dibenzo-18-crown-6	11
	poly-**6**[b]	53
	poly-**7**[c]	0
	poly-**3**(threo)[d]	58
	poly-**3**(erythro)[d]	0
	poly-**4**(threo)[d]	9
Ba^{2+}	poly-**6**[b]	67
methylene blue$^+$ [e]	18-crown-6	2
	poly-**6**[b]	83

[a] [Salt] in water = 0.025 g/L; [complexing agent] in $CHCl_3$ = 2.5 g/L. [b] Sample contained 77% of **6** units recurring in long segments. (Remainder consisted largely of segments of oxirane units.) [c] Sample contained 65% of **7** units recurring in long segments. [d] Samples were the indicated structures (i.e., >90%). [e] Dye extractions were performed by using equal solution volumes of methylene blue (0.1 mg in water) and complexing agent (140 mg in $CHCl_3$).

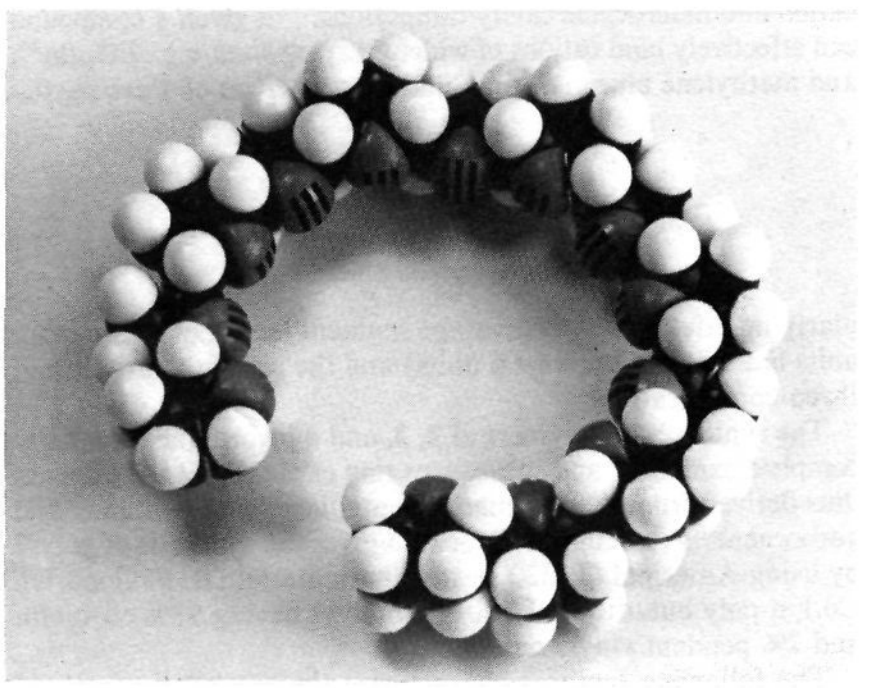
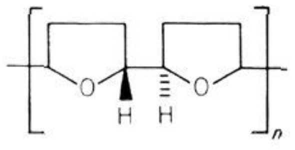


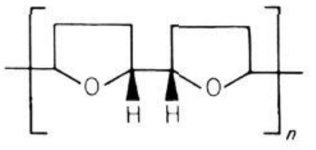
Figure 1. Segment of poly-**6** (*cis*-**2**-units).

the trans precursors were found to be completely ineffective (Table I).

Oxirane formation involves cis addition but can occur from either face of the four coplanar carbons in which the double bond is centered. Base-catalyzed oxirane ring opening occurs with inversion of configuration.[7] Application of these stereochemical generalizations provides two important conclusions regarding the nature of the chiral centers in poly-**1** structures. (1) The cyclic ether units formed from either *cis*- or *trans*-alkenes can have either meso- or *dl*-like configurations. (2) All *cis*-alkenes lead only to ring junctures having threo configuration, while all *trans*-alkenes produce only ring junctures of erythro configuration. Poly-**2** structures having these ring juncture configurations are shown.



threo configuration, **6**



erythro configuration, **7**

CPK molecular models were used to construct long segments of **6** and **7**. Examination of these showed the **6** chains, regardless of cis or trans configuration of inidividual rings, can readily assume flexible, coiled conformations in which the steric crowding of methylene hydrogens of the THF ring strongly favor the inward orientation of oxygen atoms, an arrangement similar to that of a crown ether (Figure 1).[8] Unlike the crowns, however, **6** can form helical conformers in which the principal degrees of freedom involve variations in pitch and cavity size. It is possible that **6** binds cations of widely varying sizes so effectively because it is capable of adapting its conformation to optimize its multidentate coordination with a given cation.

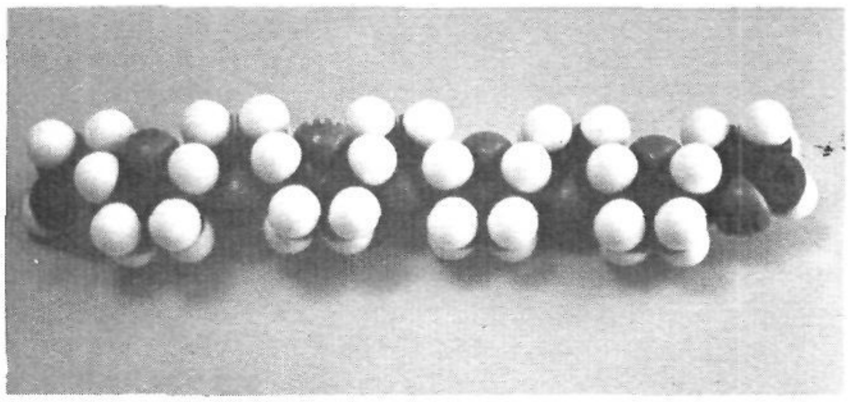


Figure 2. Segment of poly-**7** (*cis*-**2**-units).

In contrast, models of **7** showed that steric crowding of methine hydrogens tends to favor an extended chain conformation in which the oxygen atoms alternate direction along a linear chain (Figure 2). Possible conformers of **7** seem to present no reasonable geometry for multidentate coordination of oxygens with any cation. Only minor effects on the chain flexibilities of **6** and **7** resulted from varying the ratio of *cis*- to *trans*-THF units.

We are now studying the solution properties of these materials to gain more information on the effect of complex formation on polymer conformation.

Acknowledgment. We are grateful to A. R. Katritzky and R. A. Newmark for their considerable help in understanding the chemistry of these new compounds.

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Further Characterization of the Oxidation and Spin States of Iron in the Nitrogen-Bridged Metalloporphyrin μ-Nitrido-bis[(5,10,15,20-tetraphenylporphinato)iron]

Sir:

The nitrogen-bridged metalloporphyrin $(TPPFe)_2N$ is the only known *μ-nitrido complex bridging two first-row transition-metal* ions.[1-3] Consequently, considerable efforts have been directed toward determining the structure of the complex and the physical properties of the two metal centers. These include Mössbauer and EPR spectroscopy,[2] X-ray crystallography,[4] electrochemical studies,[5] and X-ray photoelectron spectroscopy.[6] These studies have resulted in conflicting views on the oxidation and spin states of the two iron atoms in the complex. It was originally proposed on the basis of Mössbauer studies[2] that the two iron atoms are

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[1] Abbreviations used: μ-nitrido-bis[(5,10,15,20-tetraphenylporphinato)iron], $(TPPFe)_2N$; μ-oxo-bis[(5,10,15,20-tetraphenylporphinato)iron], $(TPPFe)_2O$; electron paramagnetic resonance, EPR.

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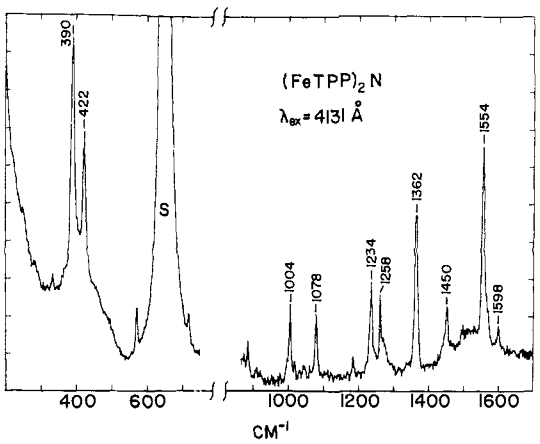

Figure 1. Resonance Raman spectrum of $(TPPFe)_2N$ in CS_2 (concentration 0.03 mg/mL). The spectrum was recorded in 2-cm^{-1} steps with a counting time of 2 s per point; spectral resolution 2.5 cm^{-1}; incident laser power 160 mW. The gain in the low-frequency region of the spectrum is twice that in the high-frequency region. The peak labeled "S" is due to the solvent.

Table I. Comparison of the Frequencies[a] of the Raman Bands of $(TPPFe)_2N$ and $(TPPFe)_2O$ Observed with 4131-Å Excitation

$(TPPFe)_2N$	$(TPPFe)_2O$	$(TPPFe)_2N$	$(TPPFe)_2O$
390	360	1258	1264
422	388	1362	1360
1004	1002	1450	1448
1078	1078	1554	1552
1234	1232	1598	1596

[a] Frequencies in cm^{-1}.

high spin with a formal oxidation state of either Fe(III$^1/_2$) or rapidly exchanging Fe(III)/Fe(IV). X-ray crystallographic investigations[4] have shown that $(TPPFe)_2N$ has structural features similar to both high- and low-spin metalloporphyrins. More recently, X-ray photoelectron studies[6] have shown that the two iron atoms are equivalent on the time scale of this experiment (10^{-15} s) and have binding energies slightly less than other iron(III) porphyrins. It was concluded that the two iron atoms in $(TPPFe)_2N$ are best described as low-spin Fe(III).

We report in this communication the first resonance Raman spectrum of $(TPPFe)_2N$ and compare it with that of the analogous oxygen-bridged metalloporphyrin dimer $(TPPFe)_2O$.[7] Resonance Raman spectroscopy has been shown to be a sensitive probe of the oxidation and spin states of the iron atom in porphyrins,[8-11] and it was anticipated that this study would aid in determining these properties of the iron atoms in $(TPPFe)_2N$. We conclude on the basis of our resonance Raman data that the iron atoms in $(TPPFe)_2N$ are best characterized as high-spin Fe(III). A more complete resonance Raman study will be reported later. We also report the EPR spectrum of $(TPPFe)_2N$ obtained at 10 and 50 K in a CS_2 glass. A previous EPR study[2] of $(TPPFe)_2N$ conducted on a solid sample at 93 K failed to reveal any nuclear hyperfine splittings on the observed signals. Under the conditions of our experiments, however, the EPR signal observed at $g = 2.15$ exhibits well-resolved ^{14}N nuclear hyperfine splittings. These results indicate that the unpaired electron in the complex is localized in an orbital which has substantial nitrido character.

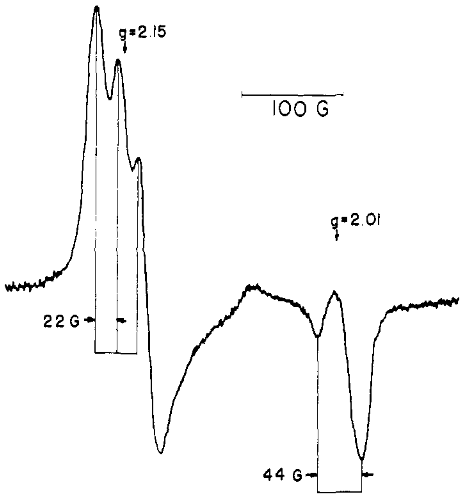

Figure 2. EPR spectrum of $(TPPFe)_2N$ in a CS_2 glass at 50 K (concentration 0.1 mg/mL). Modulation amplitude 4 G; Microwave power 5 mW.

The resonance Raman spectrum of $(TPPFe)_2N$ obtained with excitation in the Soret region (4131 Å) is shown in Figure 1. The frequencies of the most intense Raman bands observed for $(TPPFe)_2N$ are compared in Table I with those observed for $(TPPFe)_2O$ at the same excitation wavelength. It can be seen that the frequencies of the Raman bands observed for the two molecules are virtually indentical above 500 cm^{-1}. These frequencies are also in good agreement with those reported previously for $(TPPFe)_2O$ with 4579-Å excitation.[12,13] The resonance Raman spectra of the two molecules are also identical at frequencies less than 500 cm^{-1}, except that the spectrum of $(TPPFe)_2O$ exhibits a strong band at 360 cm^{-1} which is not observed in the spectrum of $(TPPFe)_2N$. Similarly, there is an intense band in the spectrum of $(TPPFe)_2N$ at 422 cm^{-1} which is not observed in the spectrum of $(TPPFe)_2O$. The band observed at 360 cm^{-1} in the resonance Raman spectrum of $(TPPFe)_2O$ has been assigned by Burke et al.[13] as the symmetric Fe–O–Fe stretching vibration. We assign the band observed at 422 cm^{-1} in the spectrum of $(TPPFe)_2N$ as the symmetric Fe–N–Fe stretching mode. The increase in the frequency of the symmetric iron–ligand–iron stretching mode observed upon replacement of the oxygen bridge with nitrogen is consistent with the increase in the frequency of the asymmetric iron–ligand–iron stretching vibration observed in the infrared[2] and reflects the increased π-bonding capabilities of the nitrido ligand relative to the oxo ligand.

The frequencies of certain skeletal vibrations in iron porphyrins are quite sensitive to changes in the π-electron distribution in the porphyrin macrocycle which occur upon changes in the spin and oxidation states of the iron atom.[8-11] In particular, the band observed at 1362 cm^{-1} is quite sensitive to the oxidation state of the iron atom, while certain bands observed in the spectral region 1450–1650 cm^{-1} are sensitive to the spin state. The vibrational frequencies of these bands typically shift by 10–40 cm^{-1} with changes in the spin and oxidation states of the iron atom. The virtually identical vibrational frequencies for the porphyrin skeletal vibrations of $(TPPFe)_2N$ and $(TPPFe)_2O$ indicate that the π-electron distribution in the porphyrin rings of the two complexes is quite similar. Since the two iron atoms in $(TPPFe)_2O$ are formally high-spin Fe(III),[14] this observation strongly suggests that the two iron atoms in $(TPPFe)_2N$ are also best described as high-spin Fe(III). This characterization of the spin states of the iron atoms in $(TPPFe)_2N$ is in agreement with that determined

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(7) The $(TPPFe)_2N$ complex was prepared and purified as described in ref 2. The identity of the molecule was confirmed by UV-vis and infrared spectroscopy. The $(TPPFe)_2O$ complex was used as received from Man-Win Chemical Co. (Washington, DC). The resonance Raman spectra of $(TPPFe)_2N$ and $(TPPFe)_2O$ were obtained in a CS_2 solution by using the rotating-cell technique. The excitation source was the 4131-Å line of a Coherent Radiation CR-2000K krypton ion laser. The EPR spectra were recorded on a Varian E-line Century Series X-band EPR spectrometer equipped with an Air Products Helitrans low-temperature system.

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from Mössbauer studies[2] but differs from that determined from X-ray photoelectron experiments,[6] which suggest that the two iron atoms are low-spin Fe(III).

The X-band EPR spectra of $(\mathrm{TPPFe})_2\mathrm{N}$ recorded at 50 K in a CS_2 glass is shown in Figure 2. The spectrum recorded at 10 K (not shown) showed slightly broader bands, but the salient features remained the same. The spectrum exhibits a signal at $g = 2.15$ which is split into a triplet with a spacing of 22 G. This fine structure is assigned as $^{14}\mathrm{N}$ ($I = 1$) nuclear hyperfine splitting which arises from interaction of the unpaired electron with the nucleus of the bridging nitrogen. The EPR signal observed at $g = 2.01$ is split into a doublet with a separation of 44 G. This splitting could arise from a number of different sources, including nuclear hyperfine interaction or additional magnetic species. The g values which we observe for the EPR signals of $(\mathrm{TPPFe})_2\mathrm{N}$ are identical with those reported by Summerville and Cohen.[2] However, in the previous EPR study, *no* nuclear hyperfine splittings were resolved. The origin of the difference between the EPR spectra reported here and those reported previously is not clear. However, a likely possibility is that in the earilier study, which was conducted on a solid sample, the nitrogen hyperfine interactions were rendered unobservable by broadening due to the increased dipolar interactions between the molecules in the solid. In any case, the observation of the large $^{14}\mathrm{N}$ hyperfine interaction clearly indicates that the unpaired electron in $(\mathrm{TPPFe})_2\mathrm{N}$ is localized in an orbital which has substantial nitrido character.

The resonance Raman and EPR results for $(\mathrm{TPPFe})_2\mathrm{N}$ reported here should aid in better characterizing the electronic structure of the iron atoms in the complex. Additional resonance Raman studies at different excitation wavelengths will further elucidate the properties of the metal centers in the complex. It is also apparent that high-field EPR studies will be useful in order to better determine the origin of the splittings of the EPR signals observed near $g = 2.01$.

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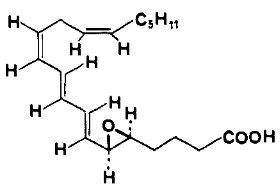
Leukotriene B. Total Synthesis and Assignment of Stereochemistry

Sir:

Arachidonic acid is transformed by incubation with polymorphonuclear leukocytes in low yield into a 5-(*S*),12-(*R*)-dihydroxy-6,8,10,14-eicosatetraenoic acid of undetermined stereochemistry with regard to the Δ^6, Δ^8, and Δ^{10} double bonds.[1] This substance was devoid of smooth muscle stimulating activity in the conventional guinea pig ileum assay and its biological role was initially unclear. More recently this compound, now termed leukotriene B (or LTB), has been shown to arise enzymically from the same progenitors, 5-(*S*)-hydroperoxy-6-*trans*-8,11,14-*cis*-eicosatetraenoic acid (5-HPETE) and 5-(*S*)-*trans*-5,6-oxido-7,9-*trans*-11,14-*cis*-eicosatetraenoic acid (leukotriene A),[2,3] which give rise to the slow reacting substances (leukotrienes C, D, and E).[4] Furthermore leukotriene B has been shown to be chemotactic for macrophages and neutrophils at concentrations of ~1 ng/mL[5] and as a result powerfully inflammatory. The detection of LTB in the synovia of patients with rheumatoid arthritis[5b] coupled with its chemotactic potency (greater than any other known lipid chemotactic factor) implies a major role for this substance in the underlying mechanisms of inflammatory and allergic states.[6]

The rarity of native LTB (available in only microgram amounts hitherto), the lack of a detailed structural assignment, and the obvious need for analytical methodology and radiolabeled LTB have prompted the synthetic studies described in this and the following communication. These studies have now led to the complete elucidation of the structure and the capability to prepare readily gram amounts of LTB by a stereoselective and effective process.

Acid-catalyzed hydrolysis of leukotriene A (LTA) (**1**), studied in these laboratories with pure synthetic LTA,[3] leads to two diastereomeric 5,6-dihydroxy-7,9,11,14-eicosatetraenoic acids (rapidly cleaved by aqueous periodate) and two diastereomeric 5,12-dihydroxy-6,8,10,14-eicosatetraenoic acids (unreactive to aqueous periodate, UV$_{\max}$ 268 nm), *neither of which* corresponds by reversed phase high performance liquid chromatography (RP-HPLC) to LTB; this is in accord with previous findings using uncharacterized in situ LTA generated from polymorphonuclear leukocytes.[7-9]



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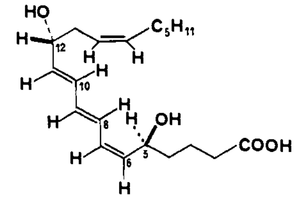

2

The diastereomeric 5,12-diols from LTA are clearly 6,8,10-*trans*-trienes on the basis of their mode of formation (carbonium ion formation and neutralization to give the kinetically more favored all-trans triene system), UV absorption,[1,7a] and comparison with totally synthetic reference compounds (vide infra). In LTB the most probable 6,8,10-triene geometry involves two trans and one cis double bond as previously pointed out.[1,7a] Our analysis of the transition states for cation formation leading to the three isomers of this type suggested that the most favored energetically should be that affording the 6-*cis*,8-*trans*,10-*trans*-triene (**2**) and the least favored should be that which leads to the 6-trans,8-trans,10-cis isomer (**3**) with the 6-trans,8-cis,10-trans geometry (**4**) intermediate. (Formation of **3** involves severe repulsion between HC(9) and $\mathrm{H_2C}(13)$ groups; formation of **4** involves less steric repulsion (principally between HC(7) and HC(10) groups); formation of **2** entails relatively little steric repulsion.) On this basis we favored structure **2** for LTB, a surmise shown to be correct by its total synthesis (and that of the isomers **3** and **4** as well[10]).

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(9) Small amounts of other products arise from acid-catalyzed hydrolysis of LTA, but no LTB could be detected by RP-HPLC analysis.

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