16. This synthetic sample was shown to be identical with the material from nature by comparison of their physical data and biological potencies in stimulation of carbon clearance, stimulation of delayed-type hypersensitivity reaction and antibody production, mitogenic effect on mouse spleen lymphocytes, protective effect against bacterial infections, etc.,[24] thereby confirming the structure of **1**.

This synthesis of **1** is unique in the two pivotal steps: the asymmetric hydrolysis (**4** → **5**) by the microorganism-originated aminopeptidase and the selective carbobenzyloxylation (**5** → **6**) via the novel copper chelate amino protection. In particular, the feature of the latter reaction may provide significant implications in the amino acid and peptide chemistry fields. Moreover, this synthetic route to **1** is capable of providing the amounts necessary for detailed biological tests, instead of having to resort to a tedious isolation process from the natural source, and may also be followed for the preparation of analogous compounds.[25]

Acknowledgment. We are indebted to Y. Miyazaki and T. Nakamura for their technical assistance during the course of this work.

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(23) ^{1}H NMR spectrum (100 MHz, D_2O), amino acid analysis, and elemental analysis data of **1** were as follows: δ 1.2–2.5 (m, 10 H), 1.40 (d, J = 7 Hz, 3 H), 1.46 (d, J = 7 Hz, 3 H), 3.88 (t, J = 6 Hz, 1 H), 4.02 (s, 2 H); Ala 1.00, Glu 1.01, Gly 0.97, *meso*-2,2′-diaminopimelic acid 1.06. Anal. Calcd. for $C_{20}H_{33}O_{11}N_5 \cdot 2H_2O$: C, 43.24; H, 6.71; N, 12.61; H_2O, 6.71. Found: C, 43.47; H, 6.57; N, 12.57; H_2O, 6.37.

(24) The biological data of **1** will be reported by Nishida et al. elsewhere.

(25) We also synthesized some stereoisomers of **1** for ascertainment of the chiral and geometric centers in **1** and for a structure–activity relationship study. These will be reported in forthcoming full papers.

Direct Evidence for Solvent Coordination in Migratory CO Insertion

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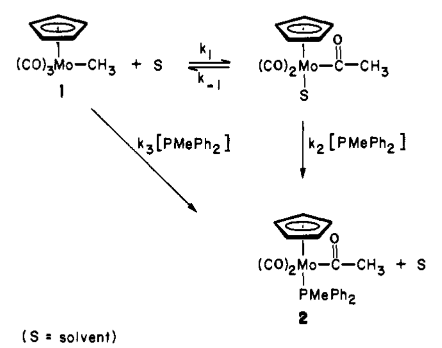
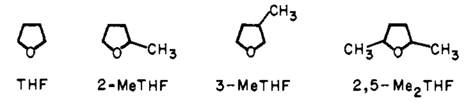
Migratory CO insertion, perhaps the most thoroughly studied process in organotransition metal chemistry,[1] is subject to solvent effects which in some cases are quite large. In early work on the carbonylation of pentacarbonylmethylmanganese(I), Calderazzo and Cotton[2] observed enhanced rates in polar, donating solvents which they attributed to variations in dielectric constant. Since that time, other systems have been found to exhibit similar behavior.[1] The stereochemistry of CO migratory insertion also is affected markedly by changes in solvent. As Flood and his coworkers have pointed out recently,[3] two conflicting explanations have been postulated for these effects: (a) generalized stabilization of the migratory insertion transition state by solvation and (b) direct attack of solvent at the metal center. Neither experimental work nor semi-empirical theory[4-6] has provided a convincing means of distinguishing between these two models.

Scheme I





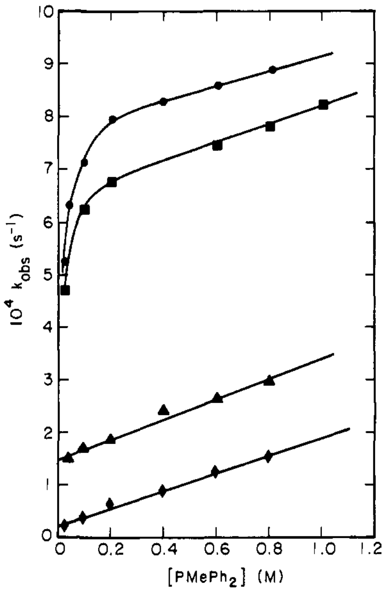


Figure 1. Dependence of the pseudo-first-order rate constant k_{obsd}, for conversion of **1** to **2** in excess $PMePh_2$, upon phosphine concentration in the following solvents: (●) THF; (■) 3-MeTHF; (▲) 2-MeTHF; (♦) 2,5-Me_2THF.

Complicating interpretation of rate data are changes in kinetic order encountered when alkylcarbonyl complexes are treated with nucleophiles in various solvents. Butler, Basolo, and Pearson found that the rate of reaction of $CpMo(CO)_3CH_3$ (**1**, Cp = η^5-C_5H_5) is a linear function of triphenylphosphine concentration in benzene but is independent of the amount of phosphine present in tetrahydrofuran (THF).[7] In chloroform, both of these types of behavior are exhibited simultaneously by the ethyl analogue of **1**.[8] Pentacarbonylmethylmanganese(I) reacts according to either first or second order or saturation kinetics, depending upon the nucleophile and solvent used.[9]

The cyclopentadienyltricarbonyl(alkyl)molybdenum insertion has been the object of intense study and displays large medium effects. In this paper we report the application of a technique to this system which distinguishes between the two solvent-involvement models mentioned above. We believe our results offer the first truly compelling support for the original hypothesis of Mawby, Basolo, and Pearson:[9,10] in this case *the effect of solvent*

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(1) For leading references, see: (a) Collman, J. P.; Hegedus, L. S. "Principles and Applications of Organotransition Metal Chemistry"; University Science Books: Mill Valley, CA, 1980; pp 260–288. (b) Kuhlman, E. J.; Alexander, J. J. *Coord. Chem. Rev.* **1980**, *33*, 195–225.

(2) Calderazzo, F.; Cotton, F. A. *Inorg. Chem.* **1962**, *1*, 30–36.

(3) Flood, T. C.; Jensen, J. E.; Statler, J. A. *J. Am. Chem. Soc.* **1981**, *103*, 4410–4414.

(4) Berke, H.; Hoffmann, R. *J. Am. Chem. Soc.* **1978**, *100*, 7224–7236.

(5) Saddia, D.; Freund, H. J.; Hohlneicher, G. *J. Organomet. Chem.* **1980**, *186*, 63–75.

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(7) Butler, I. S.; Basolo, F.; Pearson, R. G. *Inorg. Chem.* **1967**, *6*, 2074–2079.

(8) Craig, P. J.; Green, M. *J. Chem. Soc. A* **1968**, 1978–1981.

(9) Mawby, R. J.; Basolo, F.; Pearson, R. G. *J. Am. Chem. Soc.* **1964**, *86*, 3994–3999.

(10) Cotton, J. D.; Crisp, G. T.; Daly, V. A. *Inorg. Chim. Acta* **1981**, *47*, 165–169.

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Table I. Rate Constants[a, b] for the Reaction of $Cp(CO)_3Mo(CH_3)$ (1) with $PMePh_2$ at 59.9 ± 0.01 °C

solvent	10^4k_1, s^{-1}	k_1/k_2, M	10^4k_3, M^{-1} s^{-1}
THF	7.78 ± 0.07	0.0104 ± 0.0004	1.73 ± 0.08
3-MeTHF	6.46 ± 0.05	0.00821 ± 0.00045	1.86 ± 0.08
2-MeTHF	1.48 ± 0.05		1.95 ± 0.12
2,5-Me_2THF	0.23 ± 0.03		1.67 ± 0.07

[a] Defined as shown in Scheme I; values obtained as described in ref 16. [b] Variances indicated in table are standard deviations of the derived rate constants. Standard deviation in measured values of k_{obsd} is ±1%; reproducibility is ±5% or better.

can be explained only in the context of direct attack of donor solvents at the metal center as the alkyl migration is occurring. In other words, these migrations are "solvent catalyzed".

Separation of donor and polarity effects in solvent-influenced reactions is hindered by the relatively high nucleophilicity which often is exhibited by polar solvents. In order to avoid this difficulty, we have confined our studies to a series of methyl-substituted tetrahydrofurans (Scheme I), which would be expected to vary widely in donicity[11] but not in dielectric constant.[12]

In reaction 1 the specific reaction under examination is shown,

$$\underset{\mathbf{1}}{CpMo(CO)_3CH_3} + PPh_2Me \rightarrow \underset{\mathbf{2}}{CpMo(PPh_2Me)(CO)_2C({=}O)CH_3} \quad (1)$$

chosen because of our interest in it as a model for related processes[13] involving the reaction of metal hydrides with **1** and because of its similarity to reactions studied by others.[7,8,10] When **1** is allowed to react with varying (but at least five-fold molar excess) concentrations[14] of diphenylmethylphosphine in THF at 60 °C, production of $CpMo(CO)_2(PMePh_2)COCH_3$[15] (**2**) is seen to occur concomitant with first-order disappearance of starting material.[16] A plot of observed rate constant vs. nucleophile concentration for this reaction (Figure 1) indicates superimposed saturation and second-order kinetics (eq 2). The same rate law and similar rate

$$k_{obsd} = \frac{k_1k_2[PMePh_2]}{k_{-1} + k_2[PMePh_2]} + k_3[PMePh_2] \quad (2)$$

constants are obtained in 3-methyltetrahydrofuran (Figure 1, Table I), supporting the idea that the electronic effect of the added methyl group is small.[12]

Simpler behavior is seen in 2-MeTHF, namely, parallel first- and second-order paths (Figure 1). The value of the second-order rate constant k_3 is essentially unchanged from that in THF, whereas k_1 (defined by the nonzero intercept in Figure 1) is significantly diminished (Table I). An even greater decrease in k_1, with no change in k_3, is observed on using a 2,5-dimethyltetrahydrofuran[17] (2,5-Me_2THF) medium. The simplest explanation for the linearity here is that in both 2-substituted solvents the rate law is still that given in eq 2, but k_2/k_{-1} has become sufficiently large to prevent the saturation route from entering a second-order regime at low phosphine concentrations.

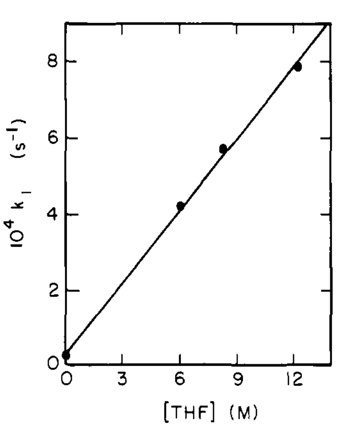

Figure 2. Dependence upon [THF] of k_1 for reaction of **1** with $PMePh_2$, determined in studies using 0.01 M **1** and varying excess concentrations of phosphine in THF/2,5-Me_2THF mixtures.

Given the similarity in dielectric constants of methyl-substituted THF's, the only rational explanation for the effect of α-methyl substitution on k_1 is steric hindrance to direct coordination of THF to molybdenum in the transition state for migratory insertion. One consequence of this conclusion may be probed: the rate of the solvent-assisted pathway should be first order in the concentration of solvent itself (that is, k_1 is actually the product of a second-order rate constant k_1' and the solvent concentration). The near equality in the dielectric constants of THF and 2,5-Me_2THF has allowed us to test this prediction. In Figure 2 are plotted the k_1 values obtained from studies of the reaction of 0.01 M **1** with varying concentrations of $PMePh_2$ in THF/2,5-Me_2THF mixtures. As these data demonstrate, k_1 is a linear function of [THF] over the entire mole fraction range (0–1.0), with $k_1' = 6.21 \times 10^{-5}$ M^{-1} s^{-1}.

It should be noted that the k_2 step also must involve direct phosphine attack; i.e., it is an S_N2 displacement of solvent by phosphine. A dissociative mechanism for this step would proceed through a coordinatively unsaturated acyl (or perhaps η^2-acyl) complex. It is difficult to see why such an intermediate would not also be accessible directly from **1**; our results show that it is not.

The results described here are understandable only in terms of direct coordinative solvent assistance to migratory CO insertion. This hypothesis provides a satisfying explanation for the large solvent effects which have been observed on the rate of this reaction in several different complexes.[18] Our conclusions may not apply to systems such as $CpFe(CO)_2R$ in which solvent effects are small. Amusingly, in the iron system a solvent-coordinated acyl complex actually is formed in dimethyl sulfoxide,[19] but Nicholas, Raghu, and Rosenblum have suggested that this complex is not on the path from alkyl to phosphine-substituted acyl.[19,20] It is perhaps important to realize, therefore, that direct observation of such an "intermediate" is not always compelling evidence for its involvement in a reaction mechanism. In any event, in cases similar to the molybdenum system where large solvent effects on rates are observed, we hope that α-substituted THF's will be useful in

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(11) Reichardt, C. "Solvent Effects in Organic Chemistry"; Verlag Chemie: New York, 1979.

(12) The visible absorption maximum of indigo, a positive solvatochromatic dye, in all of these solvents is 601 ± 1 nm (compared with 588 nm in chloroform and 620 nm in Me_2SO[11]), indicating that they have comparable polarities.

(13) Jones, W. D.; Bergman, R. G. *J. Am. Chem. Soc.* **1979**, *101*, 5447–5449.

(14) A typical concentration range was from 0.023 to 1.00 M.

(15) Data for **2**: IR (THF) 1938 s, 1851 vs, 1627 m cm^{-1}; ^1H NMR (benzene-d_6) δ 7.47–6.89 (m, 10 H), 4.57 (d, J = 1.9 Hz, 5 H), 2.90 (s, 3 H), 1.75 (d, J = 8 Hz, 3 H). Anal. Calcd for $C_{22}H_{21}MoO_3P$: C, 57.40; H, 4.60. Found: C, 57.23; H, 4.62.

(16) Rates were measured by following the magnitude of the symmetric CO stretch of **1** (ca. 2020 cm^{-1}) by infrared spectroscopy. Values of k_1, k_{-1}/k_2, and k_3 (Table I) were obtained by fitting the data to curves defined by eq 2, as shown in Figure 1.

(17) Obtained from Aldrich Co. as an approximately 1:1 mixture of the cis and trans isomers.

(18) A referee has suggested further study of these insertion reactions in a series of solvents having similar nucleophilicities but different polarities. We agree that this would constitute a useful set of experiments, but we are not confident that dielectric constant can be varied systematically without also varying donicity. Merely ascertaining that the coordinating abilities of different solvents toward molybdenum are the same might be difficult, as apparent nucleophilicity often varies with changes in substrate in an unpredictable way (see, for example: Pearson, R. G.; Sobel, H.; Songstad, J. *J. Am. Chem. Soc.* **1968**, *90*, 319–326). However, we do not claim to have shown that solvent polarity plays no role in migratory insertion reactions. Our data require only the *positive* conclusion that coordinative solvent assistance is involved. The examination of a possibly superimposed solvent polarity effect must await the design of more ingenious experiments.

(19) Nicholas, K.; Raghu, S.; Rosenblum, M. *J. Organomet. Chem.* **1974**, *78*, 133–137.

(20) For an alternative point of view, see: Cotton, J. D.; Crisp, G. T.; Latif, L. *Inorg. Chim. Acta* **1981**, *47*, 171–176.

separating polarity and direct coordination properties of etheral solvents.

Acknowledgment. This work was supported by the Director, Office of Energy Research, Office of Basic Energy Sciences, Chemical Science Division of the U.S. Department of Energy, under Contract W-7405-ENG-48.

Binuclear Ruthenium(II) Porphyrins: Reinvestigation of Their Preparation, Characterization, and Interactions with Molecular Oxygen

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Ruthenium porphyrins have recently shown some promise in understanding the reactions of iron hemes with molecular oxygen.[1] Although reports of ruthenium porphyrins first appeared 10 years ago,[2] surprisingly little is known about their properties and reactivity.[3] In view of the rich chemistry exhibited by closely related iron porphyrins,[4] we have begun a general investigation of the properties of ruthenium–porphyrin complexes.

In 1975 Whitten and co-workers[5] reported an interesting binuclear ruthenium(II)–porphyrin complex and suggested that a metal–metal bond exists between the two ruthenium centers constraining the two porphyrin macrocycles in a cofacial orientation. In our own studies[6] we have found that the complexes originally characterized by Whitten were μ-oxido-bridged dimers formed from the oxidation of the metal–metal bonded dimers by molecular oxygen. Here we report the results of our investigations into this area.

Dipyridine complexes of several ruthenium porphyrins, Ru(P)py$_2$ (P = OEP, **1**; TPP, **2**; TTP, **3**),[7] were synthesized by literature methods.[8] Vacuum pyrolysis (10^{-5} torr, 190–210 °C, 5 h) of polycrystalline samples of **1** caused the red solid to turn dark green. The ^{1}H NMR spectrum (Figure 1A)[9] of the product, dissolved in benzene-d_6 with the careful exclusion of oxygen or other potential ligands,[10] is indicative of a single *paramagnetic* OEP complex, **4**.

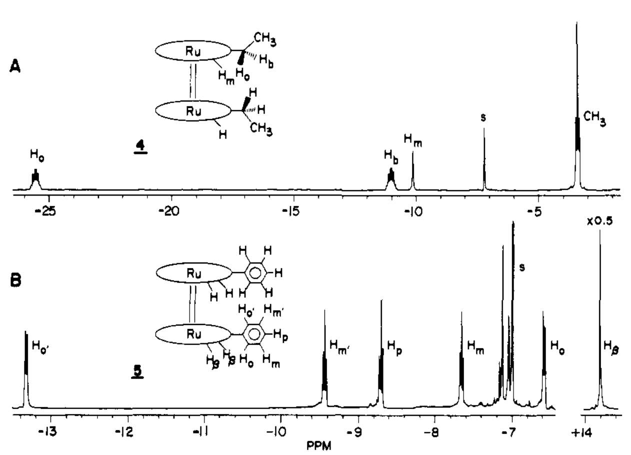

Figure 1. (A) ^{1}H NMR[11] (100 MHz) of **4** in oxygen-free benzene-d_6 (s = residual solvent protons) at 30 °C. Ethyl group (AMX$_3$ system) coupling constants: $^2J_{H_a-H_b} = 14.7$ Hz, $^3J_{H_a-CH_3} = {}^3J_{H_b-CH_3} = 7.0$ Hz. (B) ^{1}H NMR (360 MHz) of **5** in oxygen-free toluene-d_8 (s = residual solvent protons) at 25 °C. Absorptions for the phenyl protons were assigned on the basis of observed splitting patterns, decoupling, and comparison with the spectrum of the analogous TTP complex, **6**. The relative assignments between pairs of protons o, o′ and m, m′ are tentative.[17]

Assignment of the resonances is greatly facilitated by the observation of all proton spin–spin splittings.[11] Decoupling irradiation of the methyl triplet causes the two downfield multiplets (-11.1 and -25.6 ppm) to collapse into a pair of doublets exhibiting a 14.7-Hz geminal coupling constant. The two multiplets can thus be assigned to the diastereotopic methylene protons.[12] The porphyrin meso proton appears as a sharp singlet, exhibiting only a small (<1 ppm) paramagnetically induced shift.

Compound **2** was pyrolyzed by using a similar procedure[13] to give an air-sensitive complex, **5**, whose proton NMR spectrum is shown in Figure 1B. The phenyl proton resonances are completely resolved due to paramagnetic shifts both up- and downfield from the estimated diamagnetic positions. The β-pyrrolic protons experience a large upfield shift to +14.2 ppm.[14]

Elemental analyses of **4** and **5** are consistent with the molecular formulas (RuOEP)$_n$ and (RuTPP)$_n$, respectively.[15] Addition of 2 equiv of pyridine per ruthenium atom to benzene solutions of

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[1] (a) Farrell, N.; Dolphin, D. H.; James, B. R. *J. Am. Chem. Soc.* **1978**, *100*, 324. (b) James, B. R.; Addison, A. W.; Cairns, M.; Dolphin, D. H.; Farrell, N.; Paulson, D.; Walker, S. In "Fundamental Research in Homogeneous Catalysis"; Tsutsui, M., Ed.; Plenum Press: New York, 1979; Vol. 3, p 751.

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[3] (a) Eaton, S. S.; Eaton, G. R.; Holm, R. H. *J. Organomet. Chem.* **1972**, *39*, 179. (b) Bonnet, J. J.; Eaton, S. S.; Eaton, G. R.; Holm, R. H.; Ibers, J. A. *J. Am. Chem. Soc.* **1973**, *95*, 2141. (c) Brown, G. M.; Hopf, F. R.; Meyer, T. J.; Whitten, D. G. *Ibid.* **1975**, *97*, 5385. (d) Masuda, H.; Taga, T.; Osaki, K.; Sugimoto, H.; Mori, M.; Ogoshi, H. *Ibid.* **1981**, *103*, 2199.

[4] (a) James, B. R. In "The Porphyrins"; Dolphin, D. H., Ed.; Academic Press: New York, 1979; Vol. 5, Chapter 6. (b) Collman, J. P. *Acc. Chem. Res.* **1977**, *10*, 265. (c) Jones, R. D.; Summerville, D. A.; Basolo, F. *Chem. Rev.* **1979**, *79*, 139.

[5] (a) Hopf, F. R.; O'Brien, T.; Scheidt, W.; Whitten, D. G. *J. Am. Chem. Soc.* **1975**, *97*, 277. (b) Sovocool, G. W.; Hopf, F. R.; Whitten, D. G. *Ibid.* **1972**, *94*, 4350.

[6] Collman, J. P.; Collins, T. J.; Barnes, C. E.; Brothers, P. J.; Gallucci, J.; Ibers, J. A., manuscript in preparation.

[7] Abbreviations used: RuP = ruthenium porphyrin in general; RuOEP = ruthenium octaethylporphyrin; RuTPP = ruthenium *meso*-tetraphenylporphyrin; RuTTP = ruthenium *meso*-tetra-*p*-tolylporphyrin; py = pyridine; H$_m$ = meso proton of OEP ligand. L = coordinated axial ligand.

[8] Antipas, A.; Buckler, J.; Gouterman, M.; Smith, P. *J. Am. Chem. Soc.* **1978**, *100*, 3015.

[9] The paramagnetic convention is used in the discussions of all NMR spectra. Signals downfield from Me$_4$Si are referred to as negative and those upfield are positive.

[10] All manupulations of these air-sensitive compounds were performed in an inert atmosphere box or directly on a vacuum line. NMR solvents were vacuum distilled from benzophenone ketyl.

[11] Electron relaxation times in these binuclear complexes are estimated to be 10^{-13} s. La Mar, G. N.; Walker (Jenson), F. A. In "The Porphyrins"; Dolphin, D. H., Ed.; Academic Press: New York, 1978; Vol. 4, p 61. Swift, T. J. In "NMR of Paramagnetic Molecules: Principles and Applications"; La Mar, G. N., Horrocks, W. D., Jr., Holm, R. J., Eds; Academic Press: New York, 1973; p 53.

[12] (a) La Mar, G. N.; Eaton, G. R.; Holm, R. H.; Walker, F. A. *J. Am. Chem. Soc.* **1973**, *95*, 63. (b) Busby, C.; Dolphin, D. H. *J. Magn. Reson.* **1976**, *23*, 211. (c) The tremendous chemical-shift difference between the diastereotopic protons originates from differential π-spin density transfer from the porphyrin system to each of the protons. Similar effects have been observed for ferric porphyrin systems. See: Walker, F. A.; La Mar, G. N. *Ann. N.Y. Acad. Sci.* **1973**, *206*, 328. La Mar, G. N.; Walker, F. A. *J. Am. Chem. Soc.* **1973**, *95*, 1782.

[13] The pyrolysis of **2** requires completely *noncrystalline* solid samples. A convenient method of preparing such amorphous samples is to freeze benzene solutions of the ruthenium porphyrin and sublime the solvent away under vacuum at room temperature.

[14] Comparison of the shifts for **4** and **5** indicates large π-spin density in the pyrrole rings and little to none at the meso positions. Such a pattern of contact shifts is consistent with a spin transfer via $3e(\pi)P \rightarrow Ru(d_{xz}d_{yz})$ charge transfer. A detailed analysis of the NMR spectra and magnetic properties of these complexes is in progress.

[15] (RUOEP)$_{n=1}$ = $C_{36}H_{44}N_4Ru$. Anal. Calcd: C, 68.10; H, 6.99; N, 8.84. Found: C, 67.90; H, 7.00; N, 8.75. (RuTPP)$_{n=1}$ = $C_{45}H_{28}N_4Ru$. Anal. Calcd: C, 74.10; H, 3.89; N, 7.72. Found: C, 74.59; H, 3.90; N, 7.63.

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