Experimental Section

Complexes **1** and **5** were prepared according to literature procedures[2,5]. Catalytic runs were performed as described in reference [2]. GC analyses of ethane/ethene mixtures were performed with a 2-m Carboxen-1004 micropacked column. Ethylidene dipropionate analyses were perfomed with a 2-m Silicone column. $C_2H_5COOD/(C_2H_5CO)_2O$ mixtures were prepared by adding D_2O to propionic anhydride and refluxing the solution for a short time. A sample of partially deuterated ethylidene dipropionate, as formed in the catalytic reaction in $C_2H_5COOD/(C_2H_5CO)_2O$, was obtained by neutralization at pH 8 with $NaHCO_3$, extraction with Et_2O, solvent evaporation, and distillation of the residue under vacuum: ^{2}H NMR (300 MHz, THF): $\delta = 6.7$ (br), 1.4 ppm (br).

3: Complex **5** (1.60 g, 3.25 mmol) was dissolved in $C_2H_5COOH/(C_2H_5CO)_2O$ (50 mL, 10% anhydride) and stirred under ethene (25 atm) at 130 °C. After 2 h, the gases were discharged and solvents removed by distillation (55 °C, 0.1 mmHg). The oily residue was treated first with toluene (10 mL) and then with hexane (200 mL). The first aliquot of precipitate was discarded by filtration and crystals of **3** (0.47 g, 0.6 mmol, 37% yield) were obtained by cooling the mother liquor at −20 °C. IR (nujol mull): $\tilde{\nu}_{CO} = 2064$(vs), 1994(vs), 1633(s) cm^{-1}. IR ($C_2H_5COOH/(C_2H_5CO)_2O$ solution): $\tilde{\nu}_{CO} = 2059$(s), 1984(vs), 1600(s) cm^{-1}. ^{1}H NMR (CD_3COOD): $\delta = 6.41$ (q), 6.35 (q), 6.16 ppm (q); $\delta = 6.16$ ppm (1H, q) upon addition of C_2H_5COOCs (0.8 M). ^{1}H NMR ([D$_8$]THF): $\delta = 6.45$ (1H, q), 2.64 (2H, q), 1.81 (3H,d), 1.20 ppm (3H, t).

Complex **3** (0.1 M in C_2H_5COOD) was maintained at 90 °C for 3 h. Aliquots of 1 mL, taken at 30 min intervals, were evaporated to dryness and examined by ^{1}H NMR spectroscopy in [D$_8$]THF. The spectra showed the gradual decrease of both the quartet ($\delta = 6.45$ ppm) and doublet ($\delta = 1.81$ ppm) signals of **3**.

Single-crystal X-ray diffraction was carried out with a Bruker P4 diffractometer using $Mo_{K\alpha}$ graphite-monochromated radiation ($\lambda = 0.71073$ Å), the sample being sealed in a glass capillary under an argon atmosphere. The crystal used for the measurement was a rather large colorless prism with approximate dimensions $0.50 \times 0.34 \times 0.21$ mm^3. Cell parameters were calculated on the setting angles of 40 strong reflections with $5.0° \le \theta \le 12.6°$. Crystal data: $C_{16}H_{18}F_6O_{14}Ru_2S_2$, $M_r = 814.56$, $T = 293(2)$ K, monoclinic, space group $P2_1/n$ (No. 14), $a = 11.298(1)$, $b = 10.525(1)$, $c = 12.788(1)$ Å, $\beta = 112.26(1)°$, $V = 1407.3(2)$ Å^3, $Z = 2$, $\rho_{cald} = 1.922$ g cm^{-3}, $\mu(Mo_{K\alpha}) = 1.322$ mm^{-3}, $F(000) = 800$. The intensities of 3238 reflections with $2.0° \le \theta \le 25°$ were collected. After merging the equivalent reflections and after corrections for Lorentz, polarization, and absorption effects with an empirical method,[7a] an internal R value of 0.0131 was obtained.

The structure was solved by standard direct and Fourier methods and refined by full-matrix least-squares procedures. The hydrogen atoms were placed in calculated positions and allowed to ride on the connected carbon atoms. In the final refinement cycle anisotropic thermal parameters were used for all heavy atoms, giving a conventional R factor (F_o) of 0.0347, calculated for 181 parameters on 2100 observed reflections [$I > 2\sigma(I)$], and a wR_2 value of 0.0436 for all 2489 data. The residual peaks in the final difference Fourier map range between 0.80 and −0.72 e Å^{-3}. The calculations were carried out using SHELX97[7b] contained in the WINGX[7c] suite.

CCDC-191095 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).

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Selective Measurements of a Nitroxide–Nitroxide Separation of 5 nm and a Nitroxide–Copper Separation of 2.5 nm in a Terpyridine-Based Copper(II) Complex by Pulse EPR Spectroscopy**

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Coordination by transition metals is one of the main design principles of supramolecular chemistry.[1] The structures of such supramolecular assemblies are often elucidated by NMR spectroscopy and X-ray diffraction analysis. The latter method fails for the structural determination of noncrystalline assemblies. For paramagnetic transition metals, structural determination is further complicated by the failure of NMR methods from fast paramagnetic relaxation. In particular, the characterization of long-range arrangements over several nanometers has proved to be a significant barrier towards the further development of supramolecular structural design. On the other hand, it has been shown in the past few years that modern pulse EPR techniques[2] are capable of measuring separations up to at least 5 nm between organic radicals in disordered systems with high precision.[3] The application of such techniques to transition metals with considerable anisotropy of the g and/or hyperfine tensors, such as Cu^{II}, Co^{II}, V^{IV}, Mo^{V}, or Fe^{III} is more complicated, since only a small fraction of the EPR spectrum of these species can be excited by the pulses. Indeed, attempts to measure Mo···Fe separations in the Mo^{V}/Fe^{III} state of sulfite oxidase did not result in appreciable dipolar modulations[4] and, except for a preliminary conference report on the measurement of a Cu···Cu separation in azurin,[5] no applications to transition metals have been reported to date. An estimate of the separation of a transition metal and a nitroxide spin label can also be obtained from relaxation measurements. However, this approach is restricted to separations shorter than 3 nm and to systems where the

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longitudinal relaxation of the transition metal ion is much faster than that of the nitroxide spin label.[6] Herein we show that the separation of a Cu^{II} ion and a nitroxide group can be measured using the double electron electron resonance (DEER) experiment with pump excitation, both in the nitroxide and the copper spectrum. The latter result indicates that measurement of the separation of two copper centers will also be feasible. Furthermore, we demonstrate that in a spin system consisting of two nitroxide radicals and a Cu^{II} ion, the nitroxide–nitroxide and nitroxide–copper separations can be independently determined by appropriate spectral selection. Such experiments are of interest not only for artificial supramolecular assemblies but also for biological macromolecules such as metalloproteins, where nitroxide spin labels can be attached by site-directed spin labeling,[7] and for membrane proteins, where artificial metal ion binding sites can be designed.[8]

To verify the reliability of our approach to measuring copper–nitroxide separations, we have designed a model system, copper complex **1**, with well-defined, predictable separations between the paramagnetic sites (Figure 1). The ligand **2** consists of a terpyridine unit[9] to guarantee a well-defined coordination geometry for the Cu^{II} center, a phenylene-ethynylene-based rigid spacer, and 1-oxyl-2,2,5,5-tetramethylpyrroline-3-yl as the nitroxide label, attached through an ester moiety. The latter choice was made based on our previous experience with shape-persistent biradicals[3c,10] to ensure low exchange coupling and restricted conformational flexibility.

To predict the separations between the paramagnetic centers we overlaid a force-field structure (MMFF94) of ligand **2** and a density functional theory (DFT) structure of the bis(4′-ethynyl-2,2′:6′,2″-terpyridine)copper(II) complex. In the force-field simulation we replaced the N–O group by a keto group to avoid difficulties with force-field parametrization[11] and assumed that the center of spin density corresponds to the center of the C=O bond. For the theoretical separation between this center and the N'_{tpy} atom, we find a value of 2.26 nm. Based on an earlier comparison of such a force-field computation with DFT computations for a nitroxide biradical,[12] we estimate that this value may be too large by approximately 0.04 nm. The DFT computation predicts a N'_{tpy}–Cu bond length of 0.204 nm, which compares to 0.197–0.201 nm observed in the X-ray crystal structures of several related copper complexes with terpyridine and a 4′-substituted terpyridine group.[13] Furthermore, the N′–Cu and C≡C bonds have been found to be colinear. Hence, we expect a copper–nitroxide separation of 2.43 nm and a nitroxide–nitroxide separation of approximately 4.86 nm (Figure 1).

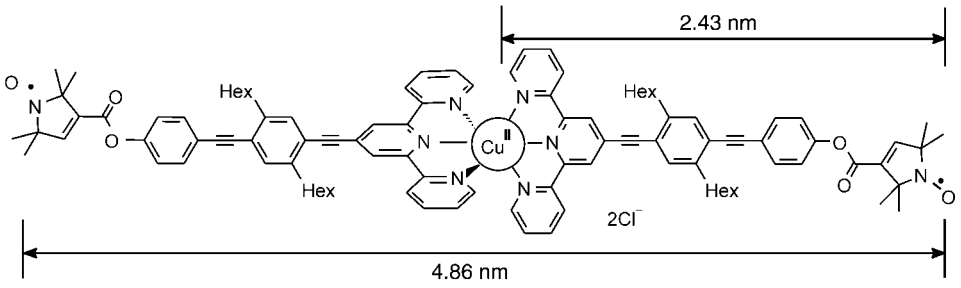

Figure 1. Rigid, doubly labeled copper(II) complex **1** with the calculated copper–nitroxide and nitroxide–nitroxide separations. The copper(II) center is hexacoordinated by two spin-labeled terpyridyl ligands **2**.

The EPR spectra of the copper ion and the nitroxide moieties (Figure 2) overlap only moderately, so that the two different paramagnetic species can be excited selectively by microwave pulses with a length of 32 ns (excitation bandwidth

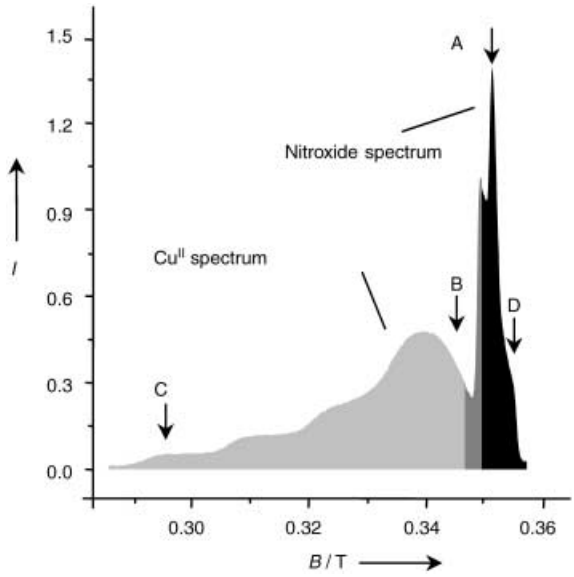

Figure 2. Excitation positions within the echo-detected EPR absorption spectra of the copper ion and the nitroxide radical.

of approximately 30 MHz or 1 mT). The maximum depth of the dipolar oscillations corresponding to the nitroxide–copper separation is obtained by applying the pump pulse at the maximum of the nitroxide spectrum (pump field A) and the observer pulses at a frequency that is larger by 200 or 1465 MHz and, thus, well outside the nitroxide spectrum (observer fields B and C, respectively).

Although we expected a significant extent of orientation selection in the copper spectrum, we obtained satisfying fits for the DEER time-domain data with our fit program[12] that neglects such orientation selection (Figure 3a, b). This is because the data is dominated by the singularity of the Pake pattern which results from orientations that are perpendicular to the spin–spin vector. Such orientations contribute at both observer fields B and C, which indicates that the spin–spin vector is perpendicular to the g_z principal axis ($g_z = 2.258$) of the Cu^{II} g tensor. Accordingly, the outer shoulders of the dipolar spectra that correspond to orientations along the spin–spin vector can only be observed at position B (Figure 4, arrows), that is, along the g_x or g_y axes. The relative enhancement of the narrow singularity at observer position B also gives rise to slow modulations in the time–domain data that are not fitted by the expressions neglecting orientation selection (Figure 3b). The separation values obtained from the preliminary fits (Table 1) are in good agreement with those expected theoretically.[14]

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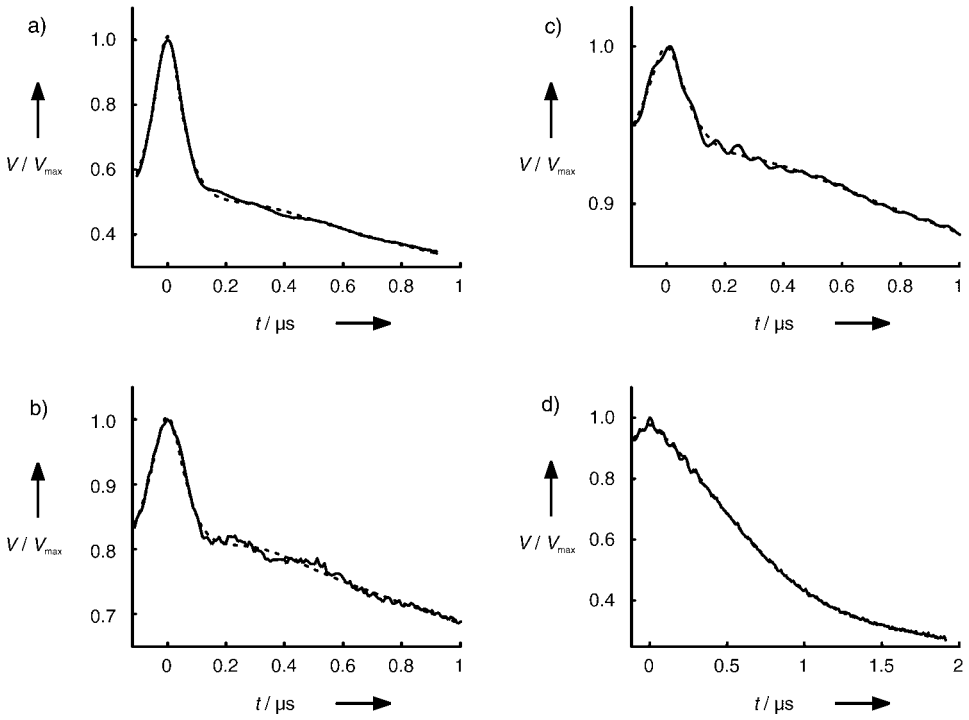

Figure 3. DEER time–domain data for several choices of pump and observer field (compare Figure 2). The dashed lines represent fits based on equation 13 in Ref. [12], with $G(r)$ given by a single Gaussian peak. Measurement times are given in parentheses. a) Pump A, observer B, separation 2.43 nm (1.5 h); b) Pump A, observer C, separation 2.46 nm (12 h); c) Pump B, observer A, separation 2.38 nm (12 h); d) Pump A, observer D, separation 5.20 nm (3.5 h).

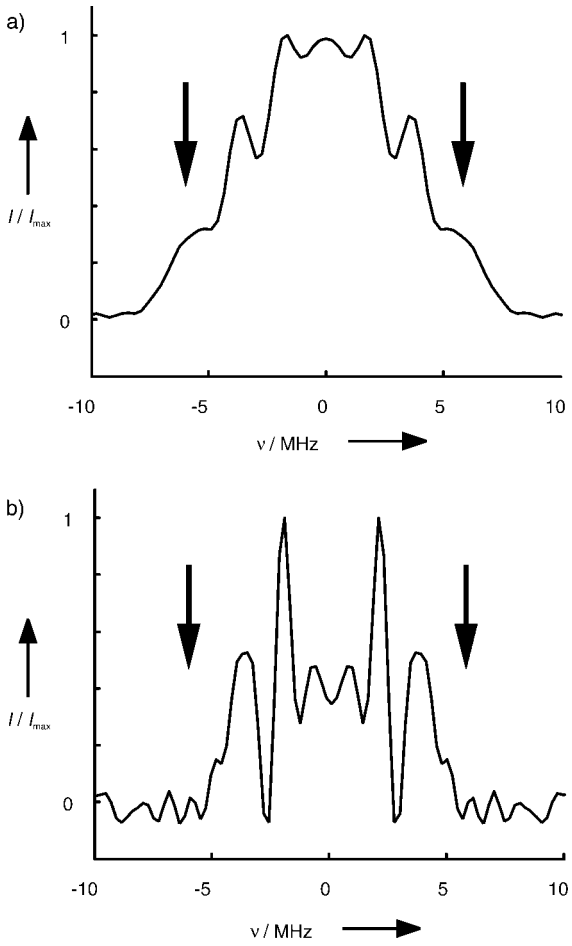

Figure 4. The effect of orientation selection on the dipolar spectra obtained by Fourier transformation of baseline-corrected DEER time–domain data. Arrows mark the dipolar frequency corresponding to the direction of the copper–nitroxide vector. a) Pump A, observer B. b) Pump A, observer C.

Table 1. Comparison of experimental and theoretical copper–nitroxide and nitroxide–nitroxide separations.

Pump field	Observer field	r_{exp} [nm]	r_{th} [nm]
A	B	2.43	Cu–NO: 2.43
A	C	2.46	Cu–NO: 2.43
B	A	2.38	Cu–NO: 2.43
A	D	5.20	NO–NO: 4.86

For the inverse experiment with the pump field B in the copper spectrum and the observer field A in the nitroxide spectrum, we obtained a much lower modulation depth (Figure 3c), which is expected as the fraction of pumped spins is smaller. In addition, nuclear modulations resulting from nearby protons are more prominent. Nevertheless, we again obtained a satisfying fit and a separation that is close to the expected value (Table 1). These results indicate that the DEER experiment can also be performed for pairs of paramagnetic centers which both feature considerable anisotropy of the g and/or hyperfine tensors. A control experiment with both the pump and observer field in the copper spectrum yielded a purely exponential decay that corresponds to the homogeneous distribution of the complexes (1 mmol L^{-1}) in the glassy frozen solution (data not shown).

By choosing both the pump field (A) and the observer field (D) within the nitroxide spectrum, we selectively observed dipolar modulation from the nitroxide–nitroxide pair, superimposed again by initial weak proton modulation (Figure 3d). In this case, the agreement between the predicted separation (4.83 nm) and the observed separation (5.20 nm) is not as good as for the nitroxide–copper separation. This is because a maximum dipolar evolution time of only 2 µs could be achieved, which is too short for the precise measurement of such long separations. Nevertheless, the precision is sufficient

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to confirm the expected linear structure of the complex. Such selective measurements of intergroup separations of several nanometers should thus open up a new route for the structural determination of noncrystalline supramolecular assemblies.

Experimental Section

Synthesis and full characterization of ligand **2** is described in the Supporting Information.

EPR measurements: Four-pulse DEER time–domain signals were obtained with the sequence $(\pi/2)_{\nu 1}$–τ_1–$(\pi)_{\nu 1}$–t–$(\pi)_{\nu 2}$–$\tau_1+\tau_2$–t–$(\pi)_{\nu 1}$–τ_2–echo at a temperature of 15 K on a Bruker E 580 X-Band spectrometer. A Bruker Flexline split-ring resonator ER 4118X-MS3 was used with overcoupling to $Q \approx 100$. Pump pulses were generated by feeding the output of an HP8350B sweep oscillator to one microwave-pulse-forming unit of the spectrometer. All pulse lengths were 32 ns, the dwell time was 8 ns, and the fixed interpulse delays were $\tau_1 = 400$ ns and $\tau_2 = 1200$ ns (Figure 3a–c) or $\tau_2 = 2000$ ns (Figure 3d). Details are discussed in the Supporting Information.

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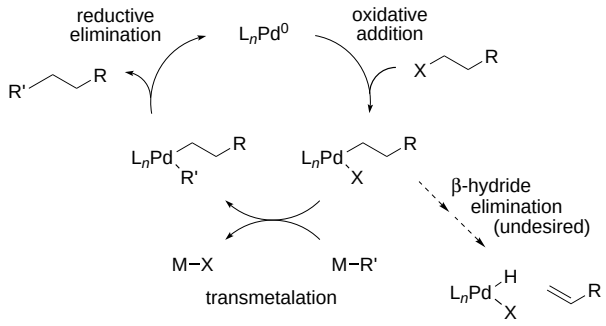
[14] A quantitative analysis of the orientation selection requires additional information on the experimental coordination geometry and the orientation of the copper *g* and hyperfine tensors with respect to the coordination polyhedron. This analysis is now underway.

Suzuki Cross-Couplings of Alkyl Tosylates that Possess β Hydrogen Atoms: Synthetic and Mechanistic Studies**

Matthew R. Netherton and Gregory C. Fu*

During the past few decades, remarkable progress has been reported in the development of mild and efficient nickel- and palladium-catalyzed protocols for carbon–carbon bond-forming reactions of electrophiles that contain $C(sp^2)$-X bonds (e.g., aryl and vinyl halides and sulfonates).[1] In contrast, general methods to cross-couple unactivated electrophiles that contain $C(sp^3)$-X bonds, especially when β hydrogen atoms are present in the molecule, are scarce, presumably because of slow oxidative addition and/or facile β-hydride elimination (Scheme 1).[2] In the case of alkyl halides, some advances have been described, specifically, examples of Suzuki cross-couplings of alkyl iodides, bromides, and chlorides,[3] Negishi reactions of alkyl iodides and bromides,[4] and Kumada couplings of alkyl bromides and a chloride.[5]



Scheme 1. Generalized mechanism for palladium-catalyzed cross-coupling reactions.

In contrast, to the best of our knowledge, at the time that we initiated our program in this area, there were no reports of palladium- or nickel-catalyzed cross-couplings of alkyl sulfonates. In the interim, however, Kambe and co-workers have described nickel-catalyzed Kumada couplings of two unfunctionalized alkyl tosylates.[5] In this communication, we establish that Pd/P*t*Bu$_2$Me can achieve Suzuki reactions of a range of functionalized alkyl sulfonates [Eq. (1); 9-BBN = 9-borabicyclo[3.3.1]nonane], and we report preliminary mechanistic studies of this new catalyst system.

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