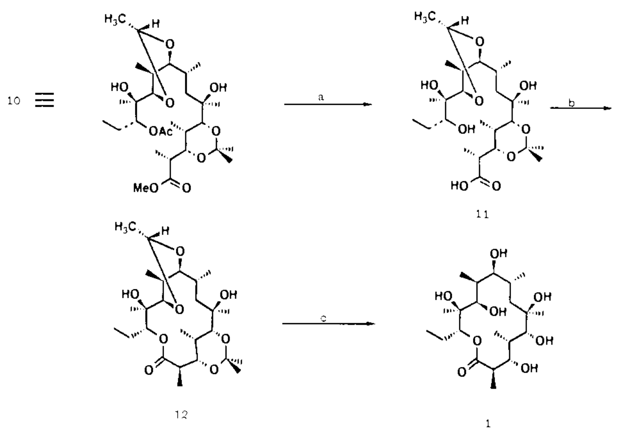
Scheme III[a]



[a] (a) KOH, aqueous MeOH; (b) see text; (c) HCl, aqueous MeOH, 50 °C.

tection of the five-membered acetal was now required to set the stage for the final cyclization. This was accomplished by selective ozonolysis of the methyl ester **9** with ozone,[16,17] which gave the monoacetate **10** in 75% yield. Subsequent hydrolysis gave the seco acid **11** in quantitative yield.

The simple protection and deprotection sequence described here greatly simplified the selective protection problems which had to be solved in the construction of **11**. Cyclization of seco acid **11** was achieved by using the conditions recently reported by Keck (Scheme III).[7] Seco acid **11** was added to a refluxing chloroform solution of dicyclohexylcarbodiimide, 4-(dimethylamino)pyridine, and its trifluoroacetate salt, via a syringe pump, to give macrocyclic lactone **12**, which was isolated in 64% yield. It was shown to be identical with an authentic sample, prepared from natural erythromycin A,[18] by ^{1}H NMR, IR, MS, TLC in two different solvent systems, and optical rotation ($[\alpha]^{25}_{265}$ +54° (c 0.2, methanol). Treatment of macrocyclic lactone **12** with acidic methanol removed (56%) the protecting groups to give (9*S*)-dihydroerythronolide A, identical with an authentic sample[1] by ^{1}H NMR, IR, and TLC.

The synthesis we have just described leads in 26 steps and 1.3% overall yield[19] from optically pure ethyl (4*R*)-4-hydroxy-2-hexynoate to (9*S*)-dihydroerythronolide A. Since the latter has previously been converted to erythromycin A,[3] this work also constitutes a formal total synthesis of antibiotic.

Acknowledgment. We thank the National Institutes of Health and the National Science Foundation for their financial support of this work.

Supplementary Material Available: Experimental details for the synthesis of (+)-(9*S*)-dihydroerythronolide A (23 pages). Ordering information is given on any current masthead page.

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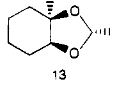
(16) Deslongchamps, P.; Atlani, P.; Frehel, D.; Malaval, A.; Moreau, C. *Can. J. Chem.* **1974**, *52*, 3651. Deslongchamps, P.; Moreau, C. *Can. J. Chem.* **1971**, *49*, 2465.

(17) (a) The ozonolysis reactions were run in a Rubin apparatus by adding a large excess of ozone-saturated dichloromethane to a −78 °C solution of the acetal and quenching with excess dimethyl sulfide after the alloted time. (b) Rubin, M. *J. Chem. Educ.* **1964**, *41*, 388. Under these conditions, the five-membered acetal **13** showed 90% oxidation after 3 min but acetal **14** showed only 5% oxidation after 15 min.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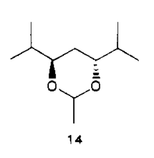
14

(18) The preparation of **12** from naturally derived **1** (ref 1) is described in the supplementary material.

(19) Previous syntheses have led to ~0.01 to 0.04% overall yields.

The First Magic Angle Spinning NMR Spectrum of a Captive Intermediate: Direct Observation of a Singlet Ground State Biradical, 3,4-Dimethylenefuran

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Received August 11, 1986

Immobilization in matrices or rigid glasses, in combination with modern spectroscopic methods, has become an invaluable technique for the study of reactive intermediates. This has been particularly useful in the study of paramagnetic species such as radicals and triplet carbenes, as they can be readily observed by ESR spectroscopy in rigid glasses.[1-3] On the other hand, characterization of singlet ground state intermediates under these conditions has been difficult. Most investigations have relied on solution-phase chemical trapping, structurally nonspecific time-resolved optical spectroscopy, and negative results from ESR.[4,5] The study of important reactive intermediates such as singlet carbenes,[5] biradicals,[4] and silylenes[6] has been impeded by this lack of suitable spectroscopic tools.

This paper reports on the first solid-state ^{13}C NMR study of a *captive intermediate*, i.e., an intermediate whose persistence requires matrix isolation. The species is 3,4-dimethylenefuran (**1**), a π-conjugated non-Kekulé biradical which has been tentatively assigned a singlet ground state on the basis of previous experimental[4] and computational[12] criteria. Given the strong correlation between ^{13}C chemical shifts and structure, matrix-isolation ^{13}C NMR studies of ESR-silent intermediates such as **1** should be especially informative. The feasibility of matrix-isolation NMR has been previously demonstrated in a variety of circumstances.[7-10] The most promising technique is the combination of cross polarization with magic angle spinning (CP/MAS) as it avoids the problems with overlap of powder patterns encountered in static measurements.[8,9] Yannoni, Reisenauer, and Maier[10] have shown that ^{13}C CP/MAS NMR can be used to follow photochemistry at low temperatures in rigid glasses. While these preliminary experiments have been encouraging, no solid-state NMR studies have yet been reported on a captive intermediate due to the difficulties encountered in combining CP/MAS with matrix-isolation conditions. As Yannoni and co-workers[10] point out, their particular methodology is not applicable to most matrix problems. The species to be studied, including the precursor, must be sufficiently stable to permit exposure of the matrix to the atmosphere as their samples are not sealed, and irradiation is difficult as light can only enter the top of the sample cell. This also makes it difficult to use any matrices that must be deposited onto a cold surface as when gas-phase pyrolysis of precursors is used.

In order to make matrix-isolation NMR more generally applicable, CP/MAS hardware was specifically designed in this work

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(1) Perutz, R. N. *Chem. Rev.* **1985**, *85*, 77-128.

(2) McGlynn, S. P.; Azumi, T.; Kinoshita, M. *Molecular Spectroscopy of the Triplet State*; Prentice-Hall: Englewood Cliffs, NJ, 1969; pp 369-402.

(3) Weltner, W., Jr. *Magnetic Atoms and Molecules*; Van Nostrand Reinhold: New York, 1983.

(4) Stone, K. J.; Greenberg, M. M.; Goodman, J. L.; Peters, K. S.; Berson, J. A. *J. Am. Chem. Soc.* **1986**, *108*, 8088-8089.

(5) Lapin, S. C.; Schuster, G. B. *J. Am. Chem. Soc.* **1985**, *107*, 4243-4248.

(6) (a) Gaspar, P. P. *React. Intermed.* (*Plenum*) **1981**, *2*, 335-387. (b) Nefedov, O. M.; Kolesnikov, S. P.; Ioffe, A. I. *J. Organomet. Chem. Libr.* **1981**, *5*; *Organomet. Chem. Rev.*

(7) Kohl, J. E.; Semack, M. G.; White D. *J. Chem. Phys.* **1978**, *69*, 5378-5385.

(8) Zilm, K. W.; Grant, D. M. *J. Am. Chem. Soc.* **1981**, *103*, 2913-2922.

(9) Zilm, K. W.; Conlin, R. T.; Grant, D. M.; Michl, J. *J. Am. Chem. Soc.* **1978**, *100*, 8083.

(10) Yannoni, C. S.; Reisenauer, H. P.; Maier, G. *J. Am. Chem. Soc.* **1983**, *105*, 6181-6182.

(11) Gay, I. D. *J. Magn. Reson.* **1984**, *58*, 413-420.

(12) (a) Lahti, P. M.; Rossi, A. R.; Berson, J. A. *J. Am. Chem. Soc.* **1985**, *107*, 2273. (b) Lahti, P. M. Ph.D. Dissertation, Yale University, New Haven, CT. (c) Du, P.; Hrovat, D. A.; Borden, W. T. *J. Am. Chem. Soc.* **1986**, *108*, 8086-8087.

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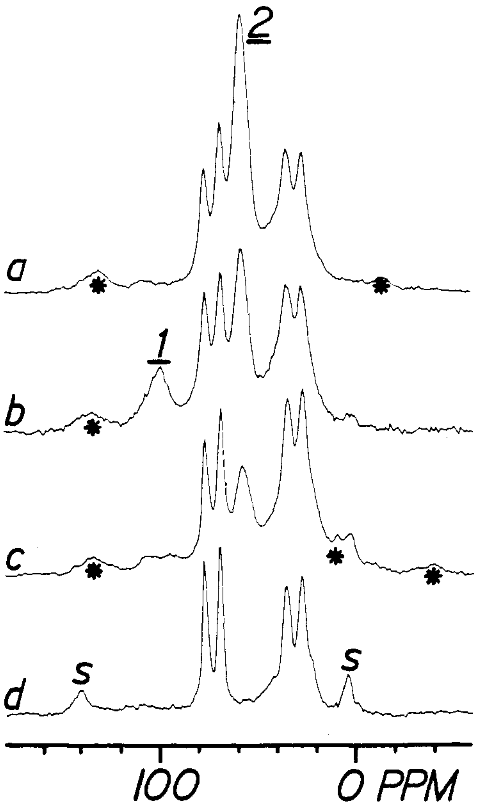
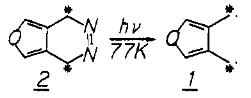


Figure 1. ^{13}C CP/MAS spectra as described in the text: (a) **2** in 2-mTHF; (b) after 7-h photolysis; (c) spectrum after melting and reglassing the sample used in (b); (d) result of photobleaching. * indicates spinning sidebands as verified by taking several spectra at various spin rates. s indicates the resonances for the secondary photoproduct. All spectra are the result of 100–300 scans, using 100-μL samples and an average measuring time of 10 min.

to accommodate the evacuated and sealed quartz sample tubes typically used in ESR. This ensures the integrity of the samples, both precursors and photoproducts, accommodates gas-phase deposition of matrices, and provides for efficient photolysis. The MAS turbine design adopted for the difficult task of spinning NMR tubes at kilohertz rates is due to Gay.[11] Low-temperature operation has been achieved by further extending the sample tube to 3.5 cm below the room temperature spinner turbine and cooling this region only. This is a significant departure from previous low-temperature MAS probe designs[10] as the sample is cooled with a separate flow of cold gas and this allows the probe to be precooled to 77 K with or without a sample in place. Samples can therefore be prepared outside of the probe and subsequently transferred from a storage Dewar to the MAS turbine through a window in the side of the NMR probe body and spun up. This operation takes only a few seconds, just as in transferring a cold sample to a precooled ESR cavity. The MAS device spins quite stably, is fairly indifferent to the balancing of the sample, and does not vary measurably from the magic angle condition over the entire temperature range. More complete details of the low-temperature MAS double-resonance probe and its operating characteristics are to be published elsewhere.

For NMR experiments, biradical di-$^{13}CH_2$ **1** was generated from dimethyl furan-3,4-dicarboxylate-*dicarboxy*-^{13}C (>98% enriched). The latter was prepared[13] by using bis-^{13}C enriched dimethyl acetylenedicarboxylate[14] and subsequently reduced to the diol with $LiAlH_4$. By use of dimethyl sulfide and *N*-chlorosuccinimide[15] the diol was converted to the dichloride which was then carried on to the azo compound[4] **2**. The ^{13}C CP/MAS spectrum of **2** in a 2-methyltetrahydrofuran (2-MTHF) glass (0.32 M, 1 mol %) at 77 K is depicted in Figure 1a showing a single line at 58 ppm[16] for the ^{13}C-enriched centers. The line widths



observed here are wider than typically encountered in CP/MAS of polycrystalline organic compounds due to the disordered nature of the 2-MTHF glass.[10] In methanol glasses the line widths for both the precursor **2** and any subsequent photoproducts are observed to be about 3 times narrower. This indicates that the width of the lines for the isolated species is primarily due to site effects. The sample in 2-MTHF was removed from the probe and transferred to another Dewar for photolysis by a 200-W high-pressure Hg arc lamp with both band-pass (300 nm < λ < 400 nm) and IR blocking filters. After 7 h the sample had acquired the deep purple color associated[4] with **1** and when returned to the NMR probe gave the spectrum in Figure 1b revealing a new resonance at 100 ppm assigned to **1**. From the relative intensity changes, the photoconversion is estimated to be about 25%. It should be noted that under similar conditions no ESR spectrum attributable to **1** has ever been observed at any temperature. When the sample was softened in a −160 °C bath, the purple color dissipated quickly, and the ^{13}C NMR spectrum of the reglassed sample no longer contained the 100 ppm peak (Figure 1c). The concomitant reduction in the peak for **2** suggests that the precursor can act as a trap for **1**. Further support for the assignment of the observed species to **1** is provided by photobleaching a sample which gave the spectrum in Figure 1b. After irradiation for 6 h at 77 K using a 450-W medium-pressure Hanovia immersion lamp with Pyrex filtering, the purple color had disappeared along with the 100 ppm peak in the CP/MAS spectrum, Figure 1d. The new lines appearing at 141 and 3 ppm are suggestive of several possibilities for the structure of the secondary photoproduct which is under active investigation. The same experiments using a concentration of 0.09 M in **2** showed total conversion to **1** with some secondary photolysis as well indicating that a filtering effect is associated with **2** at higher concentrations. Similar spectra are also observed in methanol glasses except that all lines are about 4 times narrower.

The observation of a relatively narrow line in the middle of the ^{13}C chemical shift range for the biradical centers in **1** confirms its singlet nature. It is well-known that contact shifted NMR spectra can be observed for paramagnetic molecules if the electron exchange or relaxation rates are sufficiently rapid compared to the electron–nuclear hyperfine interaction.[17,18] However, the isolation of **1** at low concentration in a rigid glass makes it unlikely that these conditions are satisfied. Even if this is disregarded, the spectrum for **1** is not compatible with any physically reasonable model having a triplet ground state. The small line width and the absence of a large contact shift would imply that in the triplet the ^{13}C hyperfine interaction A is only the of order of 30 mG. In fact A would be expected to be much larger for the biradical centers in **1**, closer to 20 G, as calculated for allyl radical.[18] Taking 5 G as a lower limit for A, a contact shift of the order of 10000 ppm would be expected if the biradical **1** had a triplet ground state. On the other hand, if the singlet is placed ~1 kcal mol^{-1} below the triplet as indicated by INDO/S-CI[12a,b] and ab initio calculations,[12b,c] the contact shift is estimated to be only 10's of ppm,

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(13) Alder, K.; Rickert, H. F. *Ber. Dtsch. Chem. Ges.* **1937**, *70*, 1354–1363.

(14) (a) Beale, J. M., personal communication. (b) Huang, S.; Beale, J. M.; Keller, P. J.; Floss, H. G. *J. Am. Chem. Soc.* **1986**, *108*, 1100–1101.

(15) Corey, E. J.; Kim, C. U.; Takeda, M. *Tetrahedron Lett.* **1972**, 4339–4342.

(16) (a) All shifts are reported relative to external Me_4Si. Errors are estimated at ±0.5 ppm. (b) δ 55.97 in toluene-d_8, ref 4.

(17) Kreilick, R. W. In *Advances in Magnetic Resonance*; Waugh, J. S., Ed.; Academic: New York, 1973; Vol. 6, pp 141–181.

(18) La Mar, G. N. In *NMR of Paramagnetic Molecules*; La Mar, G. N., Horrocks, W. DeW., Jr.; Holm, R. H., Eds.; Academic: New York, 1973; p 103.

(19) (a) Young, R. N. *Prog. Nucl. Magn. Reson. Spectrosc.* **1979**, *12*, 261–286. (b) Brownstein, S.; Bywater, S.; Worsfold, D. J. *J. Organomet. Chem.* **1980**, *199*, 1–8.

(20) Spiesecke, H.; Schneider, W. G. *Tetrahedron Lett.* **1961**, 468–472.

in line with the experimental results. The preceding analysis is of course somewhat oversimplified for a solid, as the anisotropic parts of the electron–nuclear interactions have not been considered.[21] When these effects are also included, the evidence against a triplet ground state for **1** becomes even stronger and these aspects will be discussed fully in a subsequent paper. In the absence of a contact shift the chemical shift measured here can be compared with those of other diamagnetic trivalent carbon centers. While speculative, the placement of the biradical resonance approximately halfway between the ranges observed for the terminal carbons in allylic anions and cations[19] is consistent with the approximately linear chemial shift variation with charge density exhibited by many series of compounds.[19,20]

In conclusion this work demonstrates that matrix-isolation NMR can be a very powerful tool for following the chemistry of captive intermediates such as **1** in rigid glasses. The spectra reported in this work provide the first direct confirmation that **1** is indeed a singlet ground state, and this will be a useful benchmark in future studies of biradicals with small singlet–triplet gaps. Future work will extend this technique to the direct observation of other captive intermediates such as singlet carbenes and silylenes.

Acknowledgment. We gratefully acknowledge the support of the National Science Foundation under Grants CHE-8517584 and CHE-8506590. Partial support of this work was also provided by a Grant for Newly Appointed Young Faculty in Chemistry from the Camille and Henry Dreyfus Foundation, Inc. In addition we are grateful to Prof. J. Beale for the procedure used in preparing acetylene dicarboxylic-^{13}C acid.

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(21) Chacko, V. P.; Ganapathy, S.; Bryant, R. G. *J. Am. Chem. Soc.* **1983**, *105*, 5491–5492.

Dynamics of Bond Conjugation Defects in *trans*-Polyacetylene

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Received May 12, 1986

Extensive interest and controversy have been generated by the proposal that the paramagnetic defects observed in *trans*-polyacetylene are topological solitons.[1] Solitons are unique excitations of degenerate 1-D electronic structures and are thought to play a major role in describing the photoexcited states and transport properties of these systems. Polyacetylene, the prototype conducting polymer, is the first material in which these excitations were thought to have been observed. A fundamental aspect of soliton theory as applied to polyacetylene is the high on-chain mobility of the soliton, which presumably transports spin in the pristine material and charge in the doped polymer along the polyene chain[2] at near-phonon frequencies. In this paper, we present ENDOR results on low-spin samples of *trans*-polyacetylene. Our results contradict previous interpretations of ENDOR as well as NMR and EPR experiments that were exclusively based on a model of fast 1-D soliton diffusion.

Soliton theory makes specific predictions about the structure[3] and mobility[3,4] of paramagnetic defects in *trans*-polyacetylene. In principle, the spin density profile of the immobile soliton should be directly observable from the hyperfine couplings obtained by EPR or NMR experiments. At issue for the defect structure is the quantitative form of the spin density profile;[5] that the spin is a π radical and is highly delocalized has been well established.

In practice, the intractable and disordered nature of polyacetylene has limited the observation of hyperfine interactions to the ENDOR spectrum of *cis*/*trans*-polyacetylene composites and to the trans isomer at $T < 4$ K.[6–10] Because *cis*-polyacetylene does not have a degenerate ground-state structure, this result was interpreted as evidence for highly mobile solitons in *trans*-polyacetylene and fixed, immobile solitons in the cis isomer.[10,11] During the thermal treatment that converts the cis isomer to *trans*-polyacetylene, solitons trapped on short segments of the trans isomer are liberated to diffuse freely along the polyene chain, thereby reducing the local hyperfine couplings in *trans*-polyacetylene as observed by ENDOR. This interpretation was supported by NMR proton T_1 and dynamic nuclear polarization (DNP) experiments[12] but was not consistent with ^{13}C NMR T_{1n},[13] NMR nutation,[13] and pulsed EPR experiments.[14]

Samples in which the spin density, morphology, conjugation lengths, and crystallinity are controlled are required in order to characterize unambiguously the magnetic defects in polyacetylene. *cis*-Polyacetylene prepared by the Shirakawa process[15] contains about 1 unpaired spin/30 000 carbon atoms, and the thermal isomerization step that yields the trans isomer consistently increases the spin density by 10 times. Recently, it was shown that *trans*-polyacetylene can be directly prepared giving materials with up to 10 times fewer defects[16,17] than polyacetylene obtained by the Shirakawa process. This material is identical in terms of its IR spectrum, morphology, and crystal structure, but the EPR line width of the magnetic defects was 5 times broader. Since the 10-fold increase in unpaired spin density that accompanies the conversion of *cis*-polyacetylene to the trans isomer greatly complicates the magnetic measurements and their interpretation, we decided to test the soliton model by performing ENDOR experiments on samples of low-spin *trans*-polyacetylene.

Shown in Figure 1A is the spectrum of a sample (95% trans isomer content by IR) which had been prepared as a powder. The spin density of this sample (1 spin/30 000 carbon atoms) is comparable to cis-rich samples prepared by the Shirakawa method. Remarkably, this spectrum shows that the defects in the low-spin *trans*-polyacetylene are identical not with those found in the trans Shirakawa material but rather with those in *cis*-polyacetylene.

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[‡] Bell Communications Research.

(1) Su., W. P.; Schrieffer, J. R.; Heeger, A. J. *Phys. Rev. Lett.* **1979**, *42*, 1698.

(2) For a review of recent work, see: Skotheim, T. *Handbook of Conducting Polymers*; Marcel Dekker: New York, 1986.

(3) Weinberger, B. R.; Ehrenfreund, E.; Pron, A.; Heeger, A. J.; MacDiarmid, A. G. *J. Chem. Phys.* **1979**, *72*, 4749.

(4) Maki, K. *Phys. Rev. B: Condens. Matter* **1982**, *26*, 2187.

(5) A debate exists over whether the ENDOR spectrum observed for the trapped immobile paramagnetic defect is consistent with the simple soliton model. Thomann et al.[6–8] and more recently Mehring et al.[9] have concluded that the spectrum cannot arise from the spin densities of a simple immobile soliton, while Kuroda et al.[10] concluded that the spectrum is direct evidence for soliton spin densities. This topic has recently been reviewed in great detail elsewhere.[8] Here we simply state that whether the soliton spin density profile corresponds to the ENDOR spectrum is irrelevant to our observations and conclusions presented in this paper.

(6) Thomann, H.; Dalton, L. R.; Tomkiewicz, Y.; Shiren, N. S.; Clarke, T. C. *Phys. Rev. Lett.* **1983**, *50*, 533.

(7) Thomann, H.; Dalton, L. R. *Handbook of Conducting Polymers*; Skotheim, T., Ed.; Marcel Dekker: New York, 1986; Chapter 32.

(8) Thomann, H. *Electronic Magnetic Resonance of the Solid State*; Weil, J., E.; Canadian Chemical Society: Ottowa, Ontario, 1986.

(9) Kahol, P. K.; Mehring, M. *J. Phys. C.* **1986**, *19*, 1045.

(10) Kuroda, S.; Bando, H.; Shirakawa, H. *J. Phys. Soc. Jpn.* **1985**, *54*, 3956.

(11) Heeger, A. J.; Schrieffer, J. R. *Solid State Commun.* **1983**, *48*, 207.

(12) Nechtschein, M.; Devreux, F.; Genoud, F.; Guglielmi, M.; Holczer, K. *J. Phys. Colloq.* **1983**, *44*, 209.

(13) Clarke, T. C.; Scott, J. C. *Handbook of Conducting Polymers*; Skotheim, T. Ed., Marcel Dekker: New York, 1986; Chapter 31.

(14) Shiren, N. S.; Tomkiewicz, Y.; Kazyaka, T. G.; Taranko, A. R.; Thomann, H.; Dalton, L. R.; Clarke, T. C. *Solid State Commun.* **1982**, *44*, 1157.

(15) Ito, T.; Shirakawa, H.; Ikeda, S. *J. Polym. Sci., Polym. Chem. Ed.* **1974**, *12*, 11.

(16) Baker, G. L.; Shelburne, J. A., III; Bates, F. S. *J. Am. Chem. Soc.* **1986**, *108*, 7377.

(17) The spin density is sample dependent. Typical samples had spin densities ranging from 1 spin/30 000 C atoms to 1 spin/10 000 C atoms.

0002-7863/87/1509-1569$01.50/0