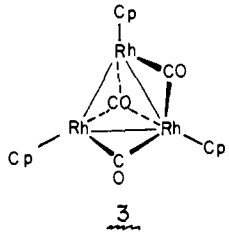
A lower limit for the isomerization rate of the 47e⁻ monocation (eq 3) is ca. 10^5.[8] Since the thermal isomerization of **1** to **2** is very slow at room temperature,[9] removing an electron from **1** speeds up its isomerization rate by at least a factor of 10^6 and probably by much more.

In an attempt to estimate $E°_1$, the formal potential of the couple $\mathbf{1}/\mathbf{1}^+$, a series of fast linear scans to negative potentials was made on solutions of **1** beginning from different initial potentials, E_{app}. This experiment varies from that of Figure 1 only in the rapidity of the potential scan, 10 V/s, which "freezes" the electrode reaction layer during the scan. The peak heights of the two reduction waves are then proportional to the steady-state concentrations of **1** and **2** at the electrode surface. Figure 2 shows that a plot of the C_{3v} isomer reduction wave height increases approximately sigmoidally as a function of E_{app}, analogous to a potentiometric curve. The midpotential of this plot, +0.25 V, is analogous to an $E_{1/2}$ value and was taken as an estimate of $E°_1$. The $E_{1/2}$ for **2**, directly measured at the rotating platinum electrode, is +0.55 V, consistent with the requirements of eq 2 and 4.[10]

The mechanism whereby **1** is isomerized to **2** so much more easily in the 47e⁻ cations than in the 48e⁻ neutral complexes may include a third isomer, **3**, with two edge-bridging and one face-



3

bridging CO groups. Analysis of the ^{13}C NMR behavior of **1**[6] suggests that **3** is an energetically accessible intermediate in the fluxionality of the C_s isomer. However, since **1** and **2** do not share a common intermediate in their fluxional rearrangements,[6,8] structure **3** cannot convert to **2** in the 48e⁻ species. We postulate that the conversion of $\mathbf{3}^+$ to $\mathbf{2}^+$ is favored in the 47e⁻ cations, perhaps facilitated by increased delocalization of positive charge over all three metals in the isomer with the face-bridging CO. Thus, we propose the following route for the anodic catalytic isomerization of **1** to **2**. Since 48e⁻ clusters with the ground-state structure **3** are known,[12] this mechanistic hypothesis will be tested.

$$\mathbf{1} \xrightarrow{-e^-} \mathbf{1}^+ \rightarrow \mathbf{3}^+ \rightarrow \mathbf{2}^+ \xrightarrow{+e^-} \mathbf{2}$$

This result shows that the structural preferences of carbonyls bound to metal clusters may be dramatically affected by the electron count (or charge) of the cluster. Since the above trirhodium clusters have been proposed as having particular relevance to CO adsorbates on metal surfaces,[13] our data suggest that the type of bonding of CO to a metal surface may be influenced or controlled by the oxidation state level of the metal.

Acknowledgment. We gratefully acknowledge the financial support of the National Science Foundation (CHE86-03728) and the donors of the Petroleum Research Fund (13900-AC3-C), administered by the American Chemical Society, and thank Prof. J. Shapley for an initial sample of **2**. The Johnson-Matthey Co. provided a generous loan of rhodium trichloride.

(7) In the terminology of Hawley and Feldberg, eq 2–4 describe an ECE process "without nuance". See: Hawley, M. D.; Feldberg, S. W. *J. Phys. Chem.* **1966**, *70*, 3459.

(8) This estimate is based on the lack of anodic waves between 0 and +0.45 V up to v = 100 V/s, and finite difference theoretical simulations of an ECE process. We thank Dr. P. H. Rieger for a copy of the simulation program.

(9) Lawson, R. J.; Shapley, J. R. *Inorg. Chem.* **1978**, *17*, 772.

(10) $E_{1/2}$ is quoted instead of $E°$ because the oxidation of **2** is electrochemically irreversible but chemically reversible. Details will be published later.

(11) Lawson, R. J.; Shapley, J. R. *J. Am. Chem. Soc.* **1976**, *98*, 7433.

(12) (a) Cotton, F. A.; Jamerson, J. D. *J. Am. Chem. Soc.* **1976**, *98*, 1273. (b) Cirjak, L. M.; Huang, J.-S.; Zhu, Z.-H.; Dahl, L. F.; *J. Am. Chem. Soc.* **1980**, *102*, 6623. (c) Bailey, W. I., Jr.; Cotton, F. A.; Jamerson, J. D.; Kolthammer, B. W. S. *Inorg. Chem.* **1982**, *21*, 3131. (d) Green, M.; Hankey, D. R.; Howard, J. A. K.; Louca, P.; Stone, F. G. A. *J. Chem. Soc., Chem. Commun.* **1983**, 757.

(13) Reference 3b, pp 129–130.

Studies of *Stemona* Alkaloids. Total Synthesis of (+)-Croomine

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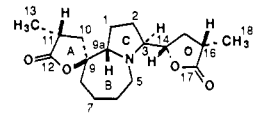
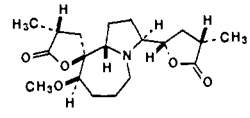
The roots and rhizomes of plants of Stemonaceae (*Stemona* and *Croomia*) produce a rich alkaloidal extract. Herbal teas have been used in Chinese folk medicine as "concocts" for pulmonary tuberculosis, bronchitis, and pertussis as well as to rid the human body of ringworm and intestinal parasites. Furthermore, extracts and dried plant materials are used throughout Eastern Asia to rid livestock of ticks and mites. Thus far, 14 highly oxygenated, polycyclic alkaloids have been determined, mostly as a result of X-ray diffraction studies.[1] Croomine[2] (**1**) and stemospironine[3]



Croomine (1)



Stemospironine (2)

(**2**) are prototypical examples of this family of compounds, all of which characteristically contain the 1-azabicyclo[5.3.0]decane nucleus. Herein we report the first synthesis within this novel class of alkaloids by communication of our recent total synthesis of (+)-croomine (**1**).

From the onset of our investigations, we had sought to develop a strategy involving preliminary construction of a branched acyclic carbon chain to be followed by timely consecutive ring closures of each heterocycle (A → B → C → D). Since the methyl substituents of croomine (C_{13} and C_{18}) could be incorporated into the carbon framework beginning with (*S*)-(+)-methyl 3-hydroxy-2-methylpropionate and (*R*)-(−)-methyl 3-hydroxy-2-methylpropionate, respectively, we sought to establish the correct relative configurations of the β-amino alcohol of C_9 and C_{9a} at an early stage. Moreover, it was imperative to utilize a surrogate amino functionality, which would withstand several oxidations throughout the route. This necessary protection was assured by our selection of azide for introduction of the nitrogen unit at C_{9a}.

The carbon framework of croomine was assembled as summarized in Scheme I.[4] Acylation of the terminal acetylene **3**[5]

(1) (a) Xu, R.-S.; Lu, Y.-J.; Chu, J.-H.; Iwashita, T.; Naoki, H.; Naya, Y.; Nakanishi, K. *Tetrahedron* **1982**, *38*, 2667. (b) Nakanishi, K.; Goto, T.; Ito, S.; Natori, S.; Nozoe, S. *Natural Products Chemistry*; Academic Press: New York, 1975; Vol. 2, pp 292–293. (c) Koyama, H.; Oda, K. *J. Chem. Soc. B* **1970**, 1330. (d) Lizuka, H.; Irie, H.; Masaki, N.; Osaki, K.; Uyeo, S. *Chem. Commun.* **1973**, 125. (e) Irie, H.; Masaki, N.; Ohno, K.; Osaki, K.; Taga, T.; Uyeo, S. *Chem. Commun.* **1970**, 1066.

(2) Noro, T.; Fukushima, S.; Ueno, A.; Litaka, Y.; Saiki, Y. *Chem. Pharm. Bull.* **1979**, *27*, 1495.

(3) Sakata, K.; Aoki, K.; Chang, C.-F.; Sakaurai, A.; Tamura, S.; Mukakoshi, S. *Agric. Biol. Chem.* **1978**, *42*, 457. We have noted that stemospironine (**2**) appears to have virtually identical physical and spectral data as subsequently reported for stemonidine.[1a] The marked similarities suggest that a direct comparison of these two alkaloids is necessary. Stemospironine (**2**) was assigned by X-ray diffraction.

(4) All yields are reported for purified samples. Each compound has been fully characterized by optical rotation, infrared, ^1H NMR, ^{13}C NMR, and high-resolution mass spectral data. Selected combustion analyses have also been obtained. Complete experimental details will be forthcoming in a full account of this work.

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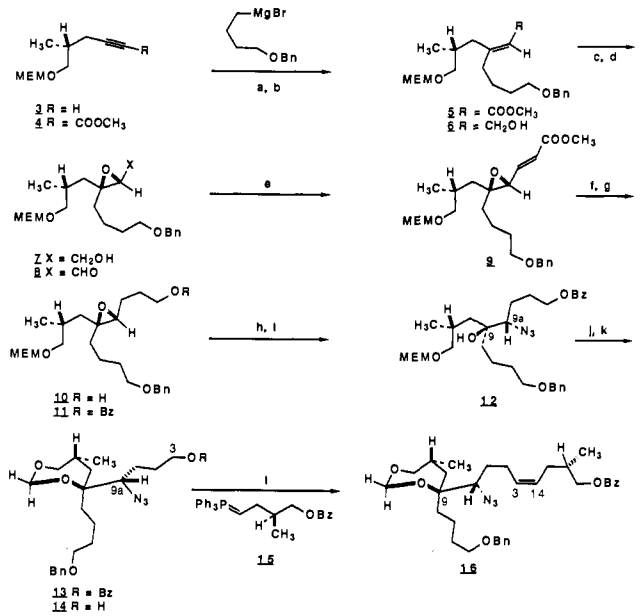
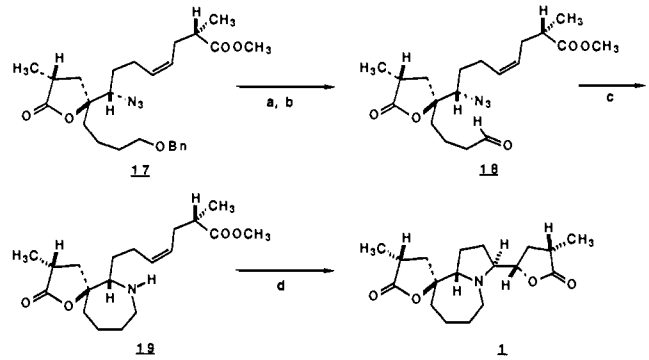
Scheme I[a]



[a] (a) *n*-BuLi; THF; −78 → 0 → 78 °C; then $ClCO_2CH_3$ (63%); (b) RMgBr; Et_2O; −78 °C; add DMS·CuBr (1 equiv); TMEDA (3.3 equiv); then add **4** (95%); (c) DIBAL, CH_2Cl_2; −78 °C (98%); (d) Ti(O-*i*-Pr)$_4$ (10 mol %); D-DIPT (12 mol %); *t*-BuOOH (3 equiv); 4-Å sieves; CH_2Cl_2 at −50 °C (83%); (e) ClCOCOCl (1.2 equiv); DMSO (2.4 equiv); CH_2Cl_2; Et_3N (2.5 equiv) at −78 → 0 °C; then add $Ph_3P{=}CHCOOCH_3$ (1.2 equiv); 0 °C → room temperature (89%); (f) $LiBH_4$ (1.2 equiv), Et_2O, MeOH (2 equiv); 0 °C (81%); (g) 5% Rh/Al_2O_3; H_2 (1 atm); THF (62%); (h) BzCl (1.1 equiv); Et_3N; CH_2Cl_2; 0 °C → room temperature (97%); (i) LiN_3 (10 equiv); DMPU; 110 °C (94%); (j) $BF_3{\cdot}Et_2O$ (1.2 equiv); CH_2Cl_2; 0 °C (81%); (k) LiOH; THF; aq MeOH (97%); (l) ClCOCOCl (1.2 equiv); DMSO (2.4 equiv); CH_2Cl_2; Et_3N (2.5 equiv) at −78 → 0 °C (91%); then ylide **15** from KO-*t*-Bu; THF at −10 °C (70–81% yields).

with methyl chloroformate at −78 °C afforded the chiral unsaturated ester **4** ($[a]^{24.1}_D$ + 16.2° (*c* 2.92, $CHCl_3$)). Formation of (4-benzyloxy)butylmagnesium bromide in anhydrous ether followed by addition into an ethereal solution of cuprous bromide–dimethyl sulfide complex (1.1 equiv) at −78 °C gave a mixed Gilman reagent, which was pretreated with tetramethylethylenediamine (TMEDA; 3.3 equiv) followed by addition of **4**. Conjugate syn addition to the acetylenic ester **4** was optimized by a controlled quench with methanol at −78 °C, providing excellent yields (95%) and high stereoselectivity (*Z*/*E* ratio is 50:1).[6] Diisobutylaluminum hydride reduction of **5** gave the trisubstituted allylic alcohol **6**, which served as a substrate for Sharpless epoxidation in the presence of powdered 4-Å molecular sieves at −50 °C. Good diastereofacial selection was observed with ratios ranging from 10:1 to 13:1 favoring the desired β-epoxide **7** in overall 83% yield from **5**.[7] Initial Sharpless oxidation studies of the *tert*-butyldiphenylsilyl analogue (replacing MEM) of **6** using (−)-DET (1–2 equiv; without molecular sieves) gave a low yield of diastereomeric α/β-oxiranes in 3:2 ratio. Oxidation of **6** with *m*-chloroperbenzoic acid (CH_2Cl_2; −40 °C) also favored the unwanted α-epoxide (α/β ratio of 5:1), demonstrating the unexpectedly strong influence of the somewhat remote homoallylic chiral center of **6**. Swern oxidation of **7** gave a sensitive α,β-epoxy aldehyde **8**, which, in large-scale applications, was not isolated.[8] Oxidations of **7** were allowed to warm to 0 °C followed by addition of solid (carbomethoxymethylene)triphenylphosphorane with continued warming to room temperature, affording excellent yields (89%) of the α,β-unsaturated ester **9** (*E*/*Z* ratios of 6:1). Reaction of **9** with lithium borohydride gave varying amounts of conjugate reduction as well as carbonyl reduction, providing an inseparable mixture of **10** and its corresponding (*E*/*Z*) allylic alcohols. Hydrogenation of the mixture with 5% rhodium on alumina completed conversion to the saturated alcohol **10**.[9]

Scheme II[a]



[a] (a) BCl_3; CH_2Cl_2; −78 → 0 °C; then MeOH at −78 °C (77%); (b) ClCOCOCl (1.2 equiv); DMSO (2.4 equiv); CH_2Cl_2; Et_3N (2.5 equiv) at −78 → 0 °C (92%); (c) Ph_3P (4.6 equiv); THF; 22 °C; then add $NaBH_4$ (1.5 equiv); MeOH (90%); (d) I_2 (1.5 equiv); CH_2Cl_2; Et_2O; 22 °C (25%).

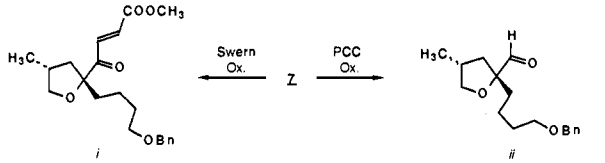
Esterification of the primary alcohol **10** gave the corresponding benzoate **11**, which was treated with lithium azide in 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (DMPU, Aldrich) at 110 °C, providing β-azido alcohol **12** ($[\alpha]^{28.4}$ −7.8° (*c* 1.96, $CHCl_3$)).[10] Varying amounts of diol (20–40%) resulting from oxirane opening and subsequent cleavage of the benzoate ester required resubmission to benzoyl chloride to net a 94% yield of the desired alcohol **12**.[11] It was essential to protect the hindered tertiary alcohol of **12** prior to attempted oxidations at the C_3 (croomine numbering) primary hydroxyl and chain elongation. This was conveniently accomplished by transforming the neighboring (β-methoxyethoxy)methyl ether into the saturated dioxepine **13** using boron trifluoride etherate (81% yield). No loss of stereochemical integrity at C_9 was observed. Saponification of **14** and Swern oxidation led to an unstable aldehyde, which was

(5) The terminal pentyne **3** was prepared from (+)-methyl 3-hydroxy-(2-(*S*)-methylpropionate by a four-step sequence: (a) MEM-Cl; Hünig's base, CH_2Cl_2, room temperature; (b) $LiAlH_4$; Et_2O at 0 °C; (c) TsCl; Et_3N; CH_2Cl_2 at 0 → room temperature; (d) lithium acetylide; THF, DMSO at 0 → 22 °C (72% yield).

(6) This conjugate addition was routinely accomplished on a 60-g scale. However, excellent stereoselectivity is only observed by slow addition of methanol via a syringe pump (10 mL/h) with stirring at −78 °C followed by dropwise addition of saturated aqueous NH_4Cl. If methanol is added via a standard dropping funnel, then *Z*/*E* ratios of 11:1 are obtained. Anderson, R. J.; Corbin, V. L.; Cotterrell, G.; Cox, G. R.; Henrick, C. A.; Schaub, F.; Siddall, J. B. *J. Am. Chem. Soc.* **1975**, *97*, 1197.

(7) Hanson, R. M.; Sharpless, K. B. *J. Org. Chem.* **1986**, *51*, 1922.

(8) Swern oxidations of **7** required freshly distilled dimethyl sulfoxide and oxalyl chloride with addition of triethylamine at −78 °C. Traces of acid provoked intramolecular opening of the oxirane by the MEM ether and continued oxidations leading to the Wittig product i. Pyridinium chlorochromate oxidations of **7** gave the tetrahydrofurancarboxaldehyde ii.



(9) These reductive operations could also be reversed. However, rhodium-catalyzed hydrogenation of **9** was slow, and allylic C–O oxirane cleavage became a troublesome side reaction (10%). Reduction of **9** using 10% Pd–$CaCO_3$ (EtOAc) rapidly provided the saturated tertiary alcohol resulting from hydrogenolysis.

(10) A number of procedures using Lewis acid additives were explored to facilitate epoxide opening under milder conditions. For example, treatment with TMS–N_3 in the presence of Et_2AlCl in methylene chloride at room temperature gave only isomerization to one (C_{9a}) diastereomeric ketone with hydrogen migration.

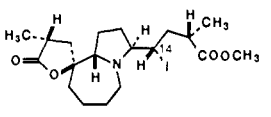
(11) The primary alcohol must be protected prior to the epoxide opening to prevent tetrahydrofuran formation. The benozate of **11** is apparently cleaved subsequent to introduction of azide and formation of the tertiary alkoxide.

immediately submitted for Wittig olefination with the chiral phosphorane **15**,[12] producing exclusively the (Z)- alkene **16**.

Our results, featuring sequential construction of the saturated heterocyclic system of croomine, are illustrated in Scheme II. Acid hydrolysis of the dioxepine acetal **16** (aqueous HBF_4; CH_3OH; 30 min, 72%) and basic saponification (LiOH; THF; CH_3OH; H_2O (3:1:1 by volume) at 22 °C; 86% yield) led to the expected triol ($[\alpha]^{26.0}_D$ +10.0° (*c* 2.17, $CHCl_3$)). Slow addition of excess Jones' reagent to a tetrahydrofuran solution of triol at 0 °C with a Celite suspension (2-propanol quench) allowed for a convenient filtration to remove chromium salts. Further concentration of solvents followed by esterification with ethereal diazomethane gave a 78% yield of the butyrolactone methyl ester **17**.

Our strategy for formation of the central perhydroazepine ring has demonstrated the utility of the Staudinger reaction as a viable approach to these complex nitrogen heterocycles.[13] Removal of the benzyl ether and subsequent oxidation gave the requisite azido aldehyde **18**. Treatment of **18** with triphenylphosphine in anhydrous tetrahydrofuran led to in situ formation of an aza ylide. Subsequent intramolecular Wittig condensation afforded a seven-membered imine, which was reduced upon addition of sodium borohydride in methanol, producing a 90% yield of the perhydroazepine **19** ($[\alpha]^{25.2}_D$ +15.0° (*c* 1.54, CH_3OH)). The Staudinger methodology was particularly noteworthy in light of the degree of functionalization in these molecules.[14]

The final cyclizations of the C and D rings of the vicinal pyrrolidino butyrolactone segment of croomine were accomplished in a single step. Our preliminary studies of iodine-induced intramolecular cyclizations of bishomoallylic *N*-alkoxy amines were found to favor formation of trans-2,5-disubstituted pyrrolidino iodides, particularly for cases of (Z)-alkenes.[15] Furthermore, Harding had previously shown that cases of pyrrolidine formation by amidomercuration proceed with 2,5-trans stereoselectivity.[16] Treatment of our secondary amine **19** with iodide (1.1 equiv), 0 → 22 °C) afforded direct conversion to (+)-croomine (**1**).[17] This double cyclization involved formation of the initial iodoamination product **20** followed by nucleophilic anchimeric assistance by the



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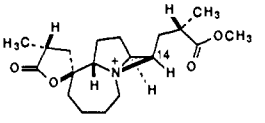

21

vicinal tertiary amine. Intramolecular capture of the intermediate aziridinium salt **21** by participation of the proximate ester resulted in net retention of carbon configuration (C_{14}). Synthetic (+)-croomine was compared with spectral data for the natural product.[18] An unambiguous assignment of our synthetic material was provided by X-ray crystallographic analysis of the corresponding methiodide salt of **1**.[19]

In conclusion, our route to (+)-croomine has demonstrated the utility of the Staudinger reaction for preparation of 1-azabicyclo[5.3.0]decanes. An iodine-induced cyclization of our bishomoallylic amine occurred with a stereocontrolled intramolecular nucleophilic capture of the intermediate aziridinium salt by the proximate methyl ester, providing a vicinal pyrrolidino butyrolactone. Further efforts toward the *Stemona* alkaloids are in progress.

Acknowledgment. We thank the National Science Foundation (Grant CHE 8618955) and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research. We also acknowledge the National Institutes of Health for partial funding of these efforts. We gratefully acknowledge the efforts of Michael Dart for large-scale preparations of many intermediates along the synthetic route.

Supplementary Material Available: Spectral data for key substances (5 pages). Ordering information is given on any current masthead page.

(12) Closely related phosphoranes have been examined. Bergelson, L. D.; Shemyakin, M. M. *Angew. Chem., Int. Engl. Ed.* **1964**, *3*, 250. Preparation of **15** will be available in the full account of this work.

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(14) Preliminary investigations of substrates leading to a primary amino group at C_{9a} had demonstrated a facile intramolecular acyl transfer to form the six-membered lactam.

(15) Williams, D. R.; Osterhout, M. H.; McGill, J. M. *Tetrahedron Lett.*, in press.

(16) Harding, K. E., Burks, S. R. *J. Org. Chem.* **1984**, *49*, 40.

(17) This reaction proceeded slowly with incomplete conversion to (+)-croomine (25% yield) and reisolation of starting amine **19** (50–60%), which was readily recycled to improve the overall production of **1**. However, increased amounts of iodine and/or longer reaction times led to numerous products. Oxidation of the pyrrolidine ring of **1** to the corresponding pyrrole is well known.[2]

(18) We gratefully acknowledge Dr. Tadataka Noro (Shizuoka College of Pharmacy, Shizuoka-shi, Japan) for comparison spectra (IR, ^1H NMR, and ^{13}C NMR) of the natural product.

(19) Structure assignment of our synthetic material was unambiguously confirmed by a single-crystal X-ray diffraction study (at −145 °C) of the monohydrate of the methiodide salt of **1** (mp 187–192 °C; acetone). All atoms were located and refined to final residuals of $R_{(F)} = 0.085$ and $R_{w(F)} = 0.075$. Complete crystallographic data are available from the Indiana University Chemistry Library. Request Molecular Structure Center Report 88128.

Synthesis of an Ambient Temperature Stable, High Spin Density Organic Solid with an Anomalously Small Interspin Coupling

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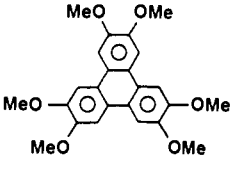
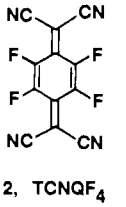
To date, ambient temperature stable organic ferromagnets still remain as challenging compounds to be synthesized.[1] There are two important prerequisites for the generation of room temperature magnets: ambient temperature stable high spin density in the bulk of the material and a significant ferromagnetic interaction between spins. Unfortunately, most organic solids are either diamagnetic or weakly paramagnetic with a low spin density. Recently, several ground-state triplet molecules, such as dicationic 2,3,6,7,10,11-hexamethoxytriphenylene[2] (**1** (HMT)), its derivatives, and oc-



1, HMT



2, $TCNQF_4$

†Present address: Physics Department, Ames Laboratory, USDOE, Iowa State University, Ames, IA 50011.

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