stirring the solution for 45 min at −78 °C with 0.11 mol of powdered Na_2CO_3 which had been flame-dried under vacuum, and the solvent was removed from the filtered solution at −35 °C under vacuum. The resulting gummy solid was extracted with 150 mL of 2:1 pentane:diethyl ether in three aliquots, and the solvent was removed under vacuum at −35 °C. The product was recrystallized from 10 mL of pentane at −80 °C to give dark red crystals.

The ^{13}C and ^1H NMR spectra[10] of the compound showed that it was $[Mo(CO)_5CPh_2]$.[11] The ^{13}C NMR spectrum was particularly informative, showing resonances which could be attributed to the alkylidene carbon, the trans carbonyl ligand, the four equivalent cis carbonyl ligands, and the carbons of the phenyl groups at frequencies very similar to those reported for the Cr and W analogues.[1f] The visible spectrum of the compound[12] is very similar to that of the W analogue, and we were able to use the extinction coefficient of the main absorption at 503 nm to determine that crude mixtures contained ca. 25% yields[13] of the product. The isolated yield[13] of the product was 15%. The molybdenum complex is considerably less stable thermally than its Cr and W analogues, with a half-life of approximately 2 h at −20 °C in toluene.[14] The complex is also air and light sensitive.

No observable reaction occurred when $[Mo(CO)_5CPh_2]$ was dissolved in isobutylene at temperatures below −10 °C, but at room temperature decomposition to $[Mo(CO)_6]$[15] and a mixture of organic products was complete in 2 h. The diphenylalkylidene moieties were recovered in three forms:[16] 40% as 1,1-diphenylethylene, 45% as 1,1,2,2-tetraphenylethane, and 15% as hexaphenylcyclopropane. The formation of 1,1-diphenylethylene indicates that a metathetical reaction is occurring analogous to that observed when $[W(CO)_5CPh_2]$ is heated in isobutylene, but the isolation of a similar quantity of 1,1,2,2-tetraphenylethane[17] would suggest that this reaction is competitive with thermal decomposition of the complex.

The complexes $[Cr(CO)_5CPh_2]$ and $[W(CO)_5CPh_2]$ were also prepared by the reaction sequence outlined in eq 2, with only minor variations in the experimental details. In the Cr case, the deamination of the intermediate metalate was carried out at −30 °C, and the solvent could be removed from the crude product at −15 °C. Pentane solutions were handled at −5 °C, and pure $[Cr(CO)_5CPh_2]$[19] was finally obtained in 53% yield. In the W case, the deamination was carried out at 0 °C, and the material could be handled in solution at 0 °C. The yield of recrystallized $[W(CO)_5CPh_2]$[20] was 27%.

The low yields of the tungsten and molybdenum complexes prompted extensive experiments to determine the optimum conditions for the tungsten reaction. Deamination with other proton acids or with Lewis acids gave poorer results, and the quantity of excess acid used in deamination did not have a significant influence on the reaction. Varying the temperature at which the initial reaction between the dianion and the imminium salt was carried out from −78 to −40 °C had no effect on the yield, nor did the use of $Li_2[W(CO)_5]$[7] or $Cs_2[W(CO)_5]$.[9]

Chromatographic investigation of the organic side products formed in the tungsten reaction resulted in the isolation of a 30% yield of Ph_2CHNMe_2[16] and traces of benzophenone. The two side reactions most likely to give rise to this amine are one-electron transfer during the reaction of the dianion with the imminium salt to give Ph_2CNMe_2·, which could abstract H· from the solvent, from the solvent, or alternatively protonation at the metal which could be followed by reductive elimination to give the amine during the deamination. Use of DCl in ether for the deamination gave a 3:1 mixture of the d_0 and d_1 Ph_2CHNMe_2, and since control experiments showed that the amine was stable to exchange under the isolation conditions, it was concluded that both side reactions were occurring but that one-electron transfer was the major competing reaction.

No direct evidence was obtained for the formation of the putative intermediate (aminomethyl)metalates during these reactions. Several attempts were made to isolate the product of the initial reaction between $Na_2[W(CO)_5]$ and $[Ph_2CNMe_2][OSO_2F]$ by using methods analogous to those which enabled Fischer and his co-workers to characterize the closely related species $[N(PPh_3)_2][W(CO)_5C(OMe)Ph_2]$,[18] but no tractable complexes were obtained. Precedent does, however, exist for nucleophilic attack by transition-metal anions on iminium salts in the reaction of $Na[Fe(\eta\text{-}C_5H_5)(CO)_2]$ with iminium salts to give species of the type $[Fe(\eta\text{-}C_5H_5)(CO)_2CR_2NR'_2]$[21] and the preparation of Fe- and Cr-aminocarbene complexes from reactions of dianionic precursors with a chloroformiminium chloride,[22] a chloroformamidinium chloride,[22] and dimethylformiminium iodide.[23]

Acknowledgment. We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, the Exxon Educational Foundation, and the National Science Foundation (Grants CHE78-25699 and CHE80-16162) for financial support.

(10) $^{13}C\{^1H\}$ NMR (ppm, CD_2Cl_2, −40 °C) 384.2 (s, CPh_2), 223.5 (s, *trans*-CO), 206.0 (s, *cis*-CO), 163.9, 131.1, 127.4, 126.0 (C_6H_5). ^1H NMR (δ, CD_2Cl_2, −40 °C) 7-8 (m, C_6H_5). These spectra showed that $Mo(CO)_6$ and pentane were trace impurities.

(11) The instability of the product precluded elemental analysis.

(12) Visible spectrum (pentane, −35 °C) 423 (sh), 503 nm (ε 10000).

(13) Based on the quantity of iminium salt used in the reaction.

(14) $t_{1/2}$ = 11 h for $[W(CO)_5CPh_2]$ in pentane at 30 °C: Fong, L.; Cooper, N. J., unpublished results.

(15) As indicated by IR spectra of the solution.

(16) Characterized by ^1H NMR and MS.

(17) This could be formed from diphenylcarbene, or a related carbenoid, by an abstraction-recombination sequence involving the solvent.[18]

(18) Kirmse, W.; Horner, L.; Hoffmann, H. *Liebigs Ann. Chem.* **1958**, *614*, 19.

(19) Identified by comparison of its ^{13}C NMR spectrum with that reported in the literature.[1f]

(20) Identified by comparison of IR, ^1H NMR, and UV/visible spectra of the solution with those of an authentic sample.[1c]

(21) Barefield, E. K.; Sepelak, D. J. *J. Am. Chem. Soc.* **1979**, *101*, 6542.

(22) Cetinkaya, B.; Lappert, M. F.; Turner, K. *J. Chem. Soc., Chem. Commun.* **1972**, 851.

(23) Fong, C. W.; Wilkinson, G. *J. Chem. Soc., Dalton Trans.* **1975**, 1100.

A Mild Procedure for the Generation of Azomethine Imines. Stereochemical Factors in the Intramolecular 1,3-Dipolar Addition of Azomethine Imines and a Synthetic Approach to Saxitoxin

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Saxitoxin (**4**), the paralytic agent of the California mussel *Mytilus californianus*,[1] has long been recognized as one of the most toxic of the nonprotein poisons known. With an LD_{50} in mice of 5-10 μg/kg, it has been suggested that a single dose of 0.2-1.0 mg would prove fatal in humans. Paradoxically, however, this identical substance is also the object of intense medical interest,[5] and as a consequence the synthesis of this molecule continues to be an intriguing and important goal.[4]

† On leave from Boehringer Ingelheim Ltd., July-Nov, 1978.

(1) For the comprehensive listing of sources for the isolation of saxitoxin, see V. E. Ghazarossian, E. J. Schantz, H. K. Schnoes, and F. M. Strong, *Biochem. Biophys. Res. Commun.*, **59**, 1219 (1974). Other noteworthy studies include the structural work of Rapoport,[2] the X-ray analysis by Clardy and Schantz,[3] and the elegant total synthesis by Kishi et al.[4]

(2) J. L. Wong, R. Oesterlin, and H. Rapoport, *J. Am. Chem. Soc.*, **93**, 7344 (1971), and references cited therein. See also J. Bordner, W. E. Thiessen, H. A. Bates, and H. Rapoport, *J. Am. Chem. Soc.*, **97**, 6008 (1975).

(3) E. J. Schantz, V. E. Ghazarossian, H. K. Schnoes, F. M. Strong, J. P. Springer, J. O. Pezzanite, and J. S. Clardy, *J. Am. Chem. Soc.*, **97**, 1238 (1975).

(4) H. Tanino, T. Nakata, T. Kaneko, and Y. Kishi, *J. Am. Chem. Soc.*, **99**, 2818 (1977).

(5) B. H. Takman, R. N. Boyes, and H. G. Vassallo in "Principles of Medicinal Chemistry", W. O. Foye, Ed., Lea and Febiger, Philadelphia, 1974, p 316. See also J. M. Ritchie and R. B. Rogart, *Rev. Physiol. Biochem. Pharmacol.*, **79**, 1 (1977); *Proc. Natl. Acad. Sci. U.S.A.*, **74**, 211 (1977).

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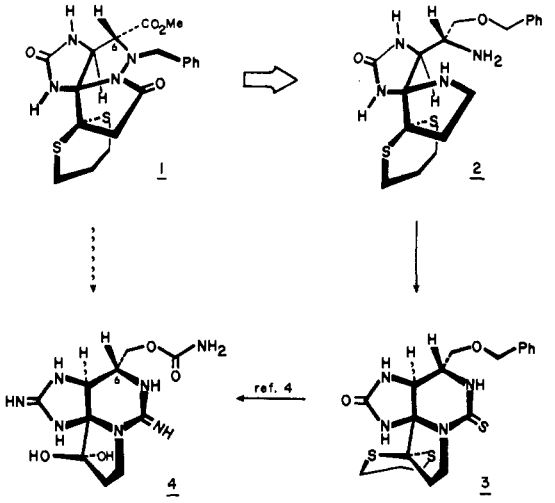
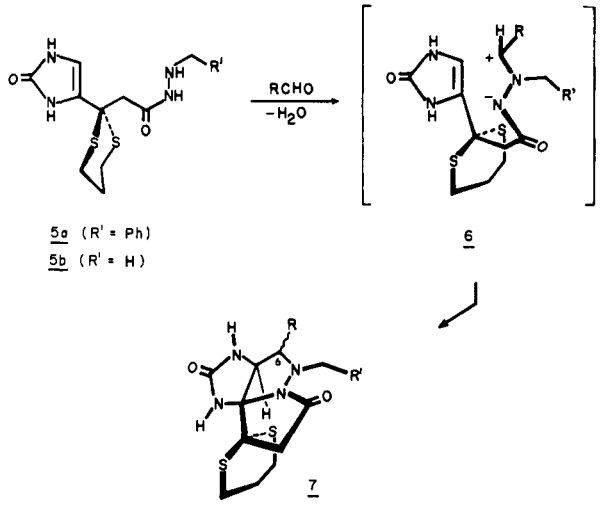
Scheme I

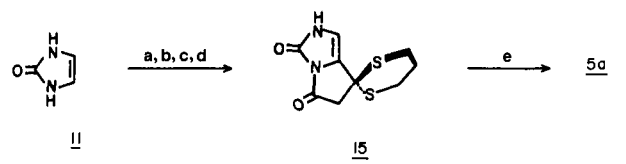


Scheme II



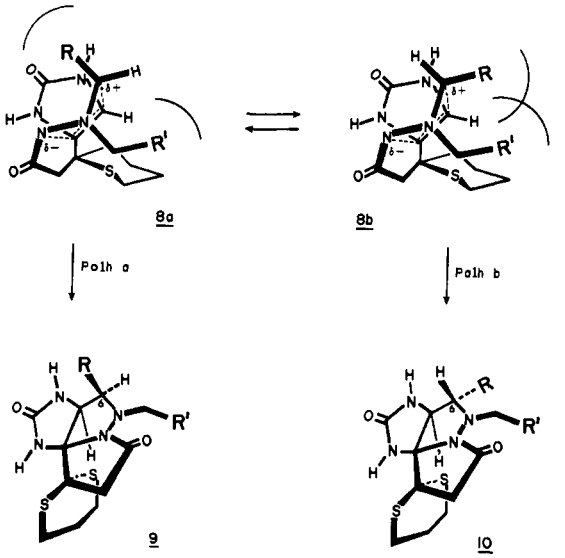
It occurred to us that an attractive route to **4** could be envisioned through the intermediacy of a fused-ring pyrazolidine derivative such as **1** (Scheme I). In particular, the geometrical and conformational restraints in this compound should allow for an extremely efficient control of stereochemical features.[6] There was ample precedence for the reductive cleavage of **1** to **2**[7] as well as the ultimate conversion of **3** to **4** (previously reported by Kishi et al.[4]). And of special interest, the possibility existed that structures of type **1** might be derived through the generation and trapping of azomethine imines such as **6**, in close analogy to the noteworthy studies of Oppolzer et al. (Scheme II).[8] With regard to this latter point, however, we were surprised to find that the stereochemical outcome of such dipolar additions has apparently not been determined.[8d] In order to study this question we have

Scheme III[a]



[a] (a) $ClCOCH_2CO_2Et$, $SnCl_4$, CH_3NO_2, 60%; (b) $HS(CH_2)_3SH$, BF_3Et_2O, 74%; (c) KOH, H_2O, 80%; (d) TFAA, PhH, 92%; (e) $PhCH_2NHNH_2$, THF, 74%.

Scheme IV



developed a highly efficient route to the requisite hydrazides **5a** (**5b**) which may be conveniently carried out on multigram scales with no chromatographic separations (Scheme III).

We note in passing the central role of the bicyclic imide **15** to the successful preparation of **5a**. It has been our experience that monoalkylhydrazides cannot be obtained in pure form by the action of alkylhydrazines on simple carboxylic acid esters. This failure derives from the usual problem of selectivity encountered in the acylation of monosubstituted hydrazines[9] as well as the forcing conditions required for reactions of this type. By way of contrast, however, the highly electrophilic **15** reacted smoothly at ambient temperature and the desired isomer **5a** separated cleanly from the reaction mixture.[10] In this case, we presume, the nucleophilic trajectory of benzylhydrazine *must* pass in close proximity to the spirocyclic dithiane ring,[11] leading, in turn, to considerable steric crowding and to a more favorable outcome in the regiochemical course of reaction.

We were less successful in our initial attempts at generating dipolar species of type **6** (cf. Scheme II). Under the usual conditions (RCHO, refluxing xylene, continuous removal of water),[8] for example, we could find no evidence for the desired reaction between **5a** and benzaldehyde, obtaining in every case a quantitative return of starting materials. Furthermore, this outcome was unaffected by a variety of modifications in the experimental parameters,[12] and we have found a similar lack of reactivity with other aldehydes which have previously been employed with marked success in simpler model systems.[8] We can now report, however, on an exceedingly mild method for the generation of azomethine imines **6** which appears to be entirely general in nature and leads to excellent yields of adducts of type **9** (Scheme IV). Thus, for

(6) With a cis ring juncture assured, the "unnatural" configuration of **1** would not only require that a sterically demanding group be oriented on a highly concave surface, but it would also lead to strongly eclipsing interactions at positions 3 and 4 of the pyrazolidine ring. With an epimerizable group at C-6 the thermodynamically most favored configuration would clearly be as indicated.[8a]

(7) (a) "Pyrazoles, Pyrazolines, Pyrazolidines, Indazoles, and Condensed Rings", R. H. Wiley, Ed., Interscience Publishers, New York, 1967; (b) P. Laur, Ph.D. Thesis, University of Munich, 1962; (c) H. Stetter and H. Spangerberger, *Chem. Ber.*, **91**, 1982 (1958); H. Stetter and K. Findeisen, *ibid.*, **98**, 3228 (1965); (d) H. Feuer and F. Brown, Jr., *J. Org. Chem.*, **35**, 1468 (1970); (e) D. S. Kemp, M. D. Sidell, and T. J. Shortridge, *J. Org. Chem.*, **44**, 4473 (1979); (f) H. H. Wasserman, R. P. Robinson, and H. Matsuyama, *Tetrahedron Lett.*, 3493 (1980).

(8) (a) W. Oppolzer, *Tetrahedron Lett.*, 2199 (1970); (b) *ibid.*, 3091 (1970); (c) *ibid.*, 1707 (1972); (d) W. Oppolzer, *Angew. Chem., Int. Ed. Engl.*, **16**, 10 (1977).

(9) R. L. Hinman and D. Fulton, *J. Am. Chem. Soc.*, **80**, 1895 (1958).

(10) Satisfactory elemental analyses and spectral data were obtained for all new compounds reported. All yields refer to isolated and purified materials.

(11) J. E. Baldwin, *J. Chem. Soc., Chem. Commun.*, 738 (1976).

(12) Including, for example, the utilization of a variety of water scavengers and a thorough exploration of the catalytic role of both Lewis and protic acids.

example, a mixture of 1.82 g (5.0 mmol) of hydrazide **5a** and 1.14 g (1.25 equiv) of benzaldehyde diethyl acetal was heated at 80 °C, with vigorous stirring, in 50 mL of freshly distilled DMF containing a catalytic amount of TsOH.[13] Solution (bright yellow) was generally obtained within 1 h, and after a total of 5 h the reaction was concentrated and the residue crystallized (*n*-PrOH) to give 1.88 g (83%) of adduct **9a** (Scheme IV, R, R′ = phenyl).[14] Similarly prepared were the following (R′ = phenyl): (compound, R, % yield): **9b**, *p*-methoxyphenyl, 90%; **9c**, *p*-methylphenyl, 91%; **9d**, *p*-nitrophenyl, 52%; **9e**, 2-furyl, 68%; **9f**, 2-thienyl, 80%; **9g**, H, 64%. It is interesting to note that in no case could we detect a measurable quantity of adduct having the α-configuration at C-6.[15]

The extraordinary selectivity of these reactions is easily rationalized on the basis of severe nonbonded interactions in transition state **8b** (cf. Scheme IV). In agreement with this hypothesis, with R′ = H (**5b**),[16] up to 5% of the epimeric material **10** could be observed in the crude reaction mixtures. Of greater importance, however, the stereochemical consequences of kinetic control could be readily reversed upon equilibration. Thus, for example, with R = CO_2Me (R′ = phenyl), our preliminary results indicate that the α configuration is favored to the extent of at least 98:2 at thermodynamic equilibrium.[8a] This latter material, we believe, has all of the functionality requisite for its eventual conversion to **4**, and studies are currently under way with the goal of achieving this transformation.

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Supplementary Material Available: Fractional coordinates, temperature factors, bond distances, bond angles, crystallographic details, and ORTEP drawing of **9a** (7 pages). Ordering information is given on any current masthead page.

(13) All of these reactions are highly dependent upon the nature of the solvent, proceeding only moderately well in acetonitrile and not at all in glyme or less polar solvents [cf. P. K. Kadaba, *Synthesis*, 71 (1973)]. Furthermore, they fail completely in the absence of TsOH. TsOH, we believe, serves only in the capacity of bringing about an initial ionization of the aldehyde acetal, which is subsequently trapped by the strongly basic nitrogen of hydrazide **5a**. In accordance with this hypothesis, the relative rates for these conversions varied in a manner fully consistent with the ability of R to stabilize a developing cationic center (i.e., **9b, 9e > 9a, 9c, 9f > 9g > 9d**). Aliphatic acetals either fail to react under these conditions or they give much lower yields of adducts (17% with phenylacetaldehyde diethyl acetal).

(14) The stereochemistry of this adduct was conclusively demonstrated by X-ray analysis.[15] Physical properties of adduct **9a**: mp 258–259 °C; IR 1710 cm^{-1}, five-membered ring lactam; NMR ($CDCl_3$) δ 2.02 (2 H, m), 2.82 (1 H, d, J = 17.4 Hz), 2.88 (4 H, m), 2.94 (1 H, d, J = 17.4 Hz), 3.98 (1 H, d, J = 14.1 Hz), 4.33 (1 H, d, J = 5.1 Hz), 4.58 (1 H, s), 4.88 (1 H, d, J = 14.1 Hz), 4.99 (1 H, d, J = 5.1 Hz), 5.90 (1 H, s), 7.23–7.44 (10 H, m).

(15) We are grateful to Drs. James Springer and Karst Hoogsteen, of the Merck Sharp and Dohme Research Laboratories, for carrying out an X-ray analysis on adduct **9a**.

(16) This modest, but reproducible, enhancement is undoubtedly a reflection of decreased steric crowding in transition state **8b**. **5b** was prepared by the reaction of 1-*tert*-butoxycarbonyl-1-methylhydrazine with **15** followed by TFA catalyzed decarboxylation (cf. K. A. Jensen, U. Anthoni, B. Kägi, C. Larsen, and C. T. Pedersen, *Acta Chem. Scand.*, **22**, 1 (1968).

First Manganese(III) Spin Crossover and First d^4 Crossover. Comment on Cytochrome Oxidase

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Although the phenomenon of spin-state crossover has been observed in d^{5-8} transition-metal complexes and is theoretically possible in d^4 systems, it has not previously been observed in d^4 systems. Nearly all known manganese(III) complexes are high spin (^5E in O_h). The only known low-spin manganese(III) compound is $[Mn(CN)_6]^{3-}$.[1,2] For example, the dithiocarbamate ligands can induce intermediate- and low-spin behavior in iron(III),[3] but manganese(III) is the only case with a theoretical choice of spin states for which all the tris(dithiocarbamate) complexes are high spin.[4] The observation that pyrrole, and especially pyrrole bound up in the ligand TRP [tris[1-(2-azolyl)-2-azabuten-4-yl]amine] (**1**), induces a very strong ligand field[5] prompted us to make a study of [Mn(TRP)]. This choice is justified by the spin-state crossover found to occur in [Mn(TRP)]. The magnetic moment and susceptibility alter dramatically in the 40–50 K region (Figure 1). The moment falls from 4.9 to 3.2 μ_B, corresponding to a change from four to two unpaired electrons. This is a nominally $^5E_g \rightleftarrows {}^3T_{1g}$ spin-state crossover, in O_h symmetry. Above the crossover point the moment is temperature invariant, as expected in ^5E, and below 40 K the behavior is compatible with the temperature dependence characteristic of a $^3T_1$ ground state split by spin–orbit coupling and distortion from O_h symmetry.

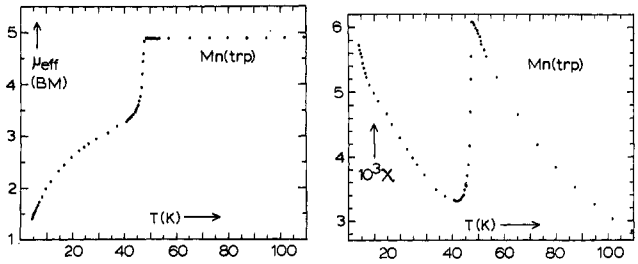

Figure 1. (Left) Magnetic moments and (right) susceptibilities of [Mn(TRP)] at various temperatures.

The crystal structure was determined to shed further light on the manganese environment.[6] Table I gives the resulting atomic parameters, Tables II and III give the bond lengths and angles, and Figure 2 shows the molecular structure. For comparison, bonding data for the related, low-spin [Fe(TRP)] complex are given. The experimental details are as given elsewhere.[5] The metal atom lies on a crystallographic threefold axis so that the three CH_2–CH_2–N–CH–C_4H_4N arms of the ligand are structurally identical. The coordination is distorted about the threefold axis from octahedral toward trigonal-prismatic symmetry, with a twist angle of ϕ = 50.8° defined by projections of the two equilateral NNN ligand triangles (Figure 2). Values of 60° and 0° for ϕ are conditions for octahedral and trigonal-prismatic geometries, respectively. The trigonal distortion splits the $^3T_1$ state in [Mn(TRP)] into a $^3A_1$ and ^3E. If the crystal-field splitting is about 25 000 cm^{-1}, the low-temperature magnetic data correspond to a $^3T_1$ splitting of about 150 cm^{-1} and spin–orbit coupling of about −180 cm^{-1}, though these values are not unique.[7]

The observed ϕ value compares with less trigonally distorted [Fe(TRP)] with a twist angle of 54.6°.[5] The difference in twist angles between the iron and manganese complexes is as expected from the shorter metal–ligand bond lengths in the iron complex if the ligand "bite" remains approximately constant. The difference in metal–ligand bond lengths between the two complexes arises from two factors: (1) mainly their different spin states, high spin in manganese(III) (at room temperature) and low spin

(1) Charles, I. D.; Frank, M. J. *J. Inorg. Nucl. Chem.* **1970**, *32*, 555.
(2) Cooke, A. H.; Duffies, H. J. *Proc. Phys. Soc. London, Sect. A* **1955**, *A68*, 32.
(3) Ewald, A. H.; Martin, R. L.; Sinn, E.; White, A. H. *Inorg. Chem.* **1969**, *8*, 1837.
(4) Golding, R. M.; Healy, P.; Newman, P.; Sinn, E.; Tennant, W. C.; White, A. H. *J. Chem. Phys.* **1970**, *52*, 3105.
(5) Sim, P. G.; Sinn, E. *Inorg. Chem.* **1978**, *17*, 1288.
(6) Crystal data [Mn(TRP)]: $MnN_7C_{21}H_{24}$, mol wt 429, space group $I\bar{4}3d$, a = 20.309 (6) Å, V = 8377 Å^3, Z = 16, μ(Mo Kα) = 6.85 cm^{-1}; θ–2θ data collected in the range 1° < 2θ < 48° produced 663 independent reflections, of which 169 were nonsystematically absent; R = 5.9% for 494 reflections.
(7) A detailed treatment of the magnetism will be presented elsewhere.

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