strength is relevant, irrespective of the flip angle of the individual rf pulses. In addition, neither matching of the effective fields at the two spins nor exact transverse polarization is required.

On the other hand, coherent transfer through J-coupling is only effective when the chemical shift evolution is efficiently suppressed during the mixing period. This can be achieved by refocusing with a series of 180° pulses or in an even more sophisticated way with highly compensated composite π pulses, such as MLEV-17.[7] However, refocusing is not operative for pulses with small flip angles.

Further investigations concerning this useful effect are in progress. After finishing the experimental investigation we learned that equivalent observations have been made by Redwine and Wüthrich.[8]

Acknowledgment. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. C.G. was funded by a personal grant of the Fonds der Chemischen Industrie.

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(8) Redwine, O. D.; Wüthrich, K., personal communication.

From Carbohydrates to Optically Active Carbocycles I: Stereochemical Control in Sugar Hex-5-enyl Radical Cyclization

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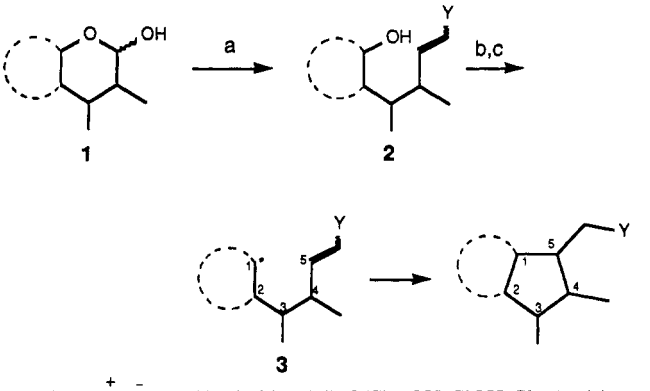
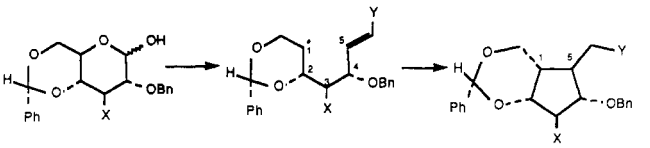
Recently, there has been growing synthetic interest in the use of free radical reactions to prepare five-membered ring compounds by cyclization of hex-5-enyl radicals.[1] Reaction conditions necessary for successful applications of this radical chain process have been delineated[2] based on the kinetic parameters for the prototypes of the primary steps, i.e., the generation, rearrangement, and subsequent trapping and regeneration of the radicals. The stereochemistry of products from variously substituted hex-5-enyl radicals also has been studied[3,4] and the process has been elegantly exploited in the syntheses of complex cyclopentanoid natural products.[5] However, for C-1 substituted hex-5-enyl and analogous cyclic radicals,[4] the stereoselectivity is generally not very high with regard to the newly formed 1,5-bond, although 1,5-cis products often predominate.[4c] In this paper, we wish to report an *unprecedented and exclusive 1,5-trans cyclization mode*[4e] that we discovered while developing a general synthetic strategy to transform readily available pyranose sugars to highly oxygenated

Scheme I[a]



[a] (a) $Ph_3\overset{+}{P}-\overset{-}{C}HY$; (b) $(imidazolyl)_2C(S)$, CH_2ClCH_2Cl, Δ; (c) Bu_3SnH, AIBN, $PhCH_3$, Δ.

Scheme II



4 X=OBn

5a X=OBn Y=H
5b X=OBn Y=OMe

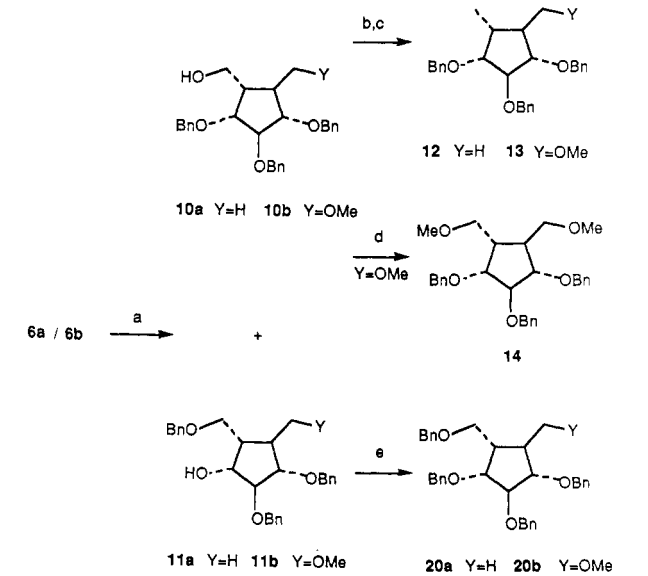
6a X=OBn Y=H
6b X=OBn Y=OMe

7 X=H

8 X=H Y=OMe

9 X=H Y=OMe

Scheme III[a]



[a] (a) LAH, $AlCl_3$; (b) NBS, Ph_3P; (c) Bu_3SnH; (d) NaH, MeI; (e) NaH, BnBr.

(1) For reviews, see: (a) Julia, M. *Pure Appl. Chem.* **1974**, *40*, 553. (b) Beckwith, A. L. J. *Tetrahedron* **1981**, *37*, 3073. (c) Beckwith, A. L. J.; Ingold, K. U. In *Rearrangements in Ground and Excited States*; de Mayo, P., Ed.; Academic Press: New York, 1980; Vol. 1. (d) Stork, G. In *Current Trends in Organic Synthesis*; Nozaki, H., Ed.; Pergamon Press: Oxford, 1983. (e) Hart, D. J. *Science (Washington, D.C.)* **1984**, *223*, 883. (f) Giese, B. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 553. (g) See also: *Selectivity and Synthetic Applications of Radical Reactions*; Tetrahedron: Symposia-in-print No. 22; Giese, B., Ed.; Pergamon Press: Oxford, 1985; Vol. 41.

(2) (a) Chatgilialoglu, C.; Ingold, K. U.; Scaiano, J. C. *J. Am. Chem. Soc.* **1981**, *103*, 7739. (b) For a compilation of other relevant references, see also: Park, S.-U., Chung, S.-K.; Newcomb, M. *J. Am. Chem. Soc.* **1986**, *108*, 240.

(3) (a) Beckwith, A. L. J.; Blair, I.; Phillipou, G. *J. Am. Chem. Soc.* **1974**, *96*, 1613. (b) Beckwith, A. L. J.; Easton, C. J.; Serelis, A. K. *J. Chem. Soc., Chem. Commun.*, **1980**, 482 and references cited therein. (c) Beckwith, A. L. J.; Easton, C. J.; Lawrence, T.; Serelis, A. K. *Aust. J. Chem.* **1983**, *36*, 545. (d) For a theoretical study, see: Beckwith, A. L. J.; Schiesser, C. H. *Tetrahedron* **1985**, *41*, 3925. See ref 14 in this paper.

(4) (a) Beckwith, A. L. J.; Phillipou, G.; Serelis, A. K. *Tetrahedron Lett.* **1981**, *22*, 2811. (b) Wolff, S.; Agosta, W. C. *J. Chem. Res. Synop.* **1981**, 78. (c) For cyclization of 2-(but-3-enyl)cyclopentyl and cyclohexyl radicals the 1,5-cis/trans ratio is reported to be 8.3 and 3.5, respectively.[4a,b] It must be emphasized that Beckwith has recognized the relative importance of C-1 vs. C-4 substituent in these cyclizations. See ref 3c. (d) For a conformationally rigid system, see: Corey, E. J.; Pyne, S. G. *Tetrahedron Lett.* **1983**, *24*, 2821. (e) For a case of trans-selective (trans to cis ratio, 2/1) cyclization with an exceptionally bulky C-1 substituent, see: Bradney, M. A. M.; Forbes, A. D.; Wood, J. *J. Chem. Soc., Perkin Trans. 2* **1973**, 1655. (f) RajanBabu, T. V., unpublished results.

(5) (a) Burnett, D. A.; Choi, J-K.; Hart, D. J.; Tsai, Y.-M. *J. Am. Chem. Soc.* **1984**, *106*, 8201, see also ref 10b. (b) Curran, D. P.; Chen, M.-H. *Tetrahedron Lett.* **1985**, *26*, 4991. (c) Curran, D. P.; Rakiewicz, D. M. In ref 1g, p 3943. (d) Corey, E. J.; Shimoji, K.; Shih, C. *J. Am. Chem. Soc.* **1984**, *106*, 6425. (e) Reference 1d. (f) See also: Clive, D. L. J.; Beaulieu, P. L. *J. Chem. Soc., Chem. Commun.* **1983**, 307. Wujek, D. G.; Porter, N. A. In ref 1g, p 3973.

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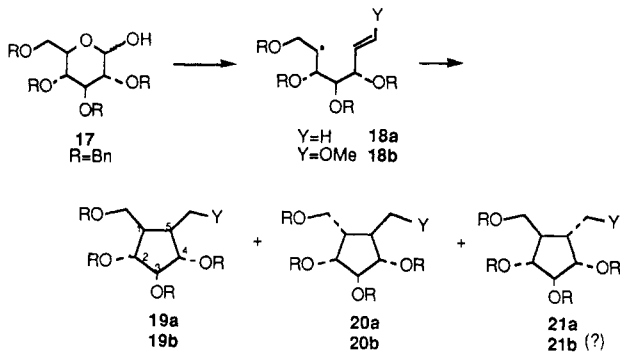
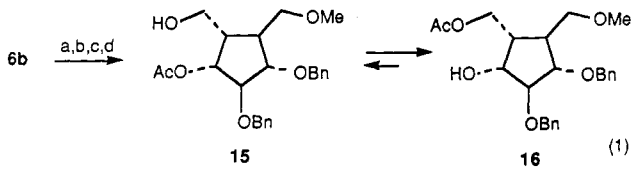
Scheme IV



cyclopentanoid molecules,[6] as illustrated in Scheme I.

We find that the Wittig product derived from 4,6-*O*-benzylidene-2,3-di-*O*-benzyl-D-glucopyranose (**4**)[7] is readily converted via the Barton procedure[8] to the radical **5**. The radical **5a** readily cyclizes to give a single product **6a** (50% based on **4**). Vinyl ether radicals **5b** and **8** (*E* and *Z* isomers) derived from **4** and **7**[9] also undergo the exclusive trans cyclization to give **6b** and **9**, respectively.[10] Structure assignments of **6a** and **6b** rest on, in addition to NOE experiments, the chemical transformations described in Scheme III.[11] The absence of a plane of symmetry in **12** and **14** revealed in the ^1H and ^{13}C spectra unequivocally establishes the 1,5-trans relationship in **6a** and **6b**. The 1,2-cis relationship in **6b** is evidenced by the facile migration of the acetyl group in **15**[12] as shown in eq 1.

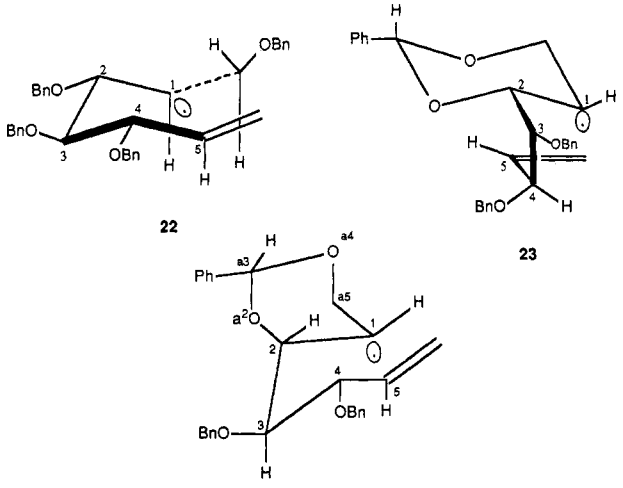


(1)

a. H_3O^+ b. TrCl, Py c. Ac_2O, Py d. H^+

In sharp contrast, the acyclic radical **18a** derived from tetra-*O*-benzyl-D-glucopyranose **17** cyclizes to give a mixture of **19a**, **20a**, and **21a** in a ratio of 74:14:12 (55% based on **17**). Similarly, both *Z*- and *E*-vinyl ethers **18b** produce a mixture of **19b** and **20b** in a ratio of 75:23. Except for a minor (~2%) product (**21b** in Scheme IV), the product structures have been unequivocally determined either by chemical correlation with one of the compounds described above or by a combination of selected NOE experiments and comparison of ^{13}C NMR chemical shifts.[13]

The stereochemistry of cyclization of the acyclic radical **18** can be rationalized by invoking a chairlike transition state[3] **22**, in which



all the substituents are in the equatorial positions, thus leading to the 1,5-cis products **19**. The exclusive 1,5-trans stereochemistry in the products from the 1,3-dioxane radicals is totally unexpected, since related carbocyclic[4a-d] and other[4f] radicals are known to give predominantly 1,5-cis products. If one assumes that the dioxane ring maintains the chair conformation at the transition state and that the bulky phenyl and the butenyl groups occupy the equatorial sites, the 1,5-trans relationship in the products can only be rationalized by invoking the boatlike cyclization transition state depicted by the structure **23** in which the axial radical center attacks the pseudoequatorial butenyl side chain. Although the boatlike transition state has been shown to be energetically accessible in hex-5-enyl radical cyclizations by recent theoretical calculations,[14] Beckwith[4a] earlier proposed that 2-(but-3-enyl)-cyclohexyl radicals cyclize via transition states in which a pseudoequatorial radical center attacks the axial butenyl group. Such a conformation is deemed impossible in the present system, because the axial butenyl chain will force the phenyl group also into an unfavorable axial orientation.

Another intriguing possibility arises if one assumes that the dioxane radicals exist in a flexible boat form. In the $B_{a2,a5}$ boat conformation, the bulky phenyl and butenyl groups occupy the pseudoequatorial positions, the lone-pair repulsion between the ring oxygen atoms is minimized, and the flag-pole repulsion that destabilizes the cyclohexane boat form also is absent. The observed 1,5-trans products then arise from the chairlike transition state, **24**, in which the pseudoequatorial radical center attacks the butenyl group in a pseudoequatorial position. Furthermore, the benzyloxy groups on the butenyl sidechain occupy the favorable equatorial sites[15] in the chairlike transition-state structure. We should note that the six-membered radical containing one ring oxygen atom, i.e, glucopyranosyl radical, has been reported to have a boat conformation[16a] and that, unlike the chair radical in **23**, the boat radical in **24** contains a favorable β-σ_{CO}•–SOMO interaction.[16,17]

(6) First example of a free radical route to cycloalkanes from carbohydrates involved the use of unsaturated halo sugars: Wilcox, C. S.; Thomasco, L. M. *J. Org. Chem.* **1985**, *50*, 546. Wilcox, C. S.; Gaudino, J. J. *J. Am. Chem. Soc.* **1986**, *108*, 3102. See also: Tsang, R.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1986**, *108*, 2116.

(7) Liptak, A.; Imre, J.; Harangi, J.; Nanasi, P. *Carbohydr. Res.* **1983**, *116*, 217.

(8) (a) Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1574. (b) See also: Robins, M. J.; Wilson, J. S.; Hansske, F. *J. Am. Chem. Soc.* **1983**, *105*, 4059.

(9) Prepared from 3-deoxyglucose in five steps: (a) Allyl alcohol, H^+; (b) $PhCHBr_2$, py, Δ; (c) $PhCH_2Br$, NaH, DMF; (d) $Ir(COD)(PPh_2Me)_2^+PF_6^-$, H_2; (e) $HgCl_2$, HgO, H_2O. For a related 2-deoxy derivative, see: Reed, L. A., III; Ito, Y.; Masamune, S.; Sharpless, K. B. *J. Am. Chem. Soc.* **1982**, *104*, 6468.

(10) (a) For the only other examples of intramolecular radical additions to enol ethers, see: Ladlow, M.; Pattenden, G. *Tetrahedron Lett.* **1984**, *25*, 4317; ref 2b. (b) *E* or *Z* geometry and the electronic nature of the olefin appear to have little effect on the stereochemistry of hex-5-enyl radical cyclization: Hart, D. J.; Tsai, Y.-M. *J. Am. Chem. Soc.* **1984**, *106*, 8209. See also ref 2b.

(11) Compound **9** has been converted into a triol via hydrogenolysis (Pd/C, H_2, H^+) and subsequently to a known series of prostaglandin intermediates[12a] including Corey lactone: RajanBabu, T. V., unpublished results.

(12) For relative effects of cis vs. trans stereochemistry on similar acetyl migrations, see: (a) Jones, G.; Raphael, R. A.; Wright, S. *J. Chem. Soc., Perkin Trans. 1* **1974**, 1676. (b) Doria, G.; Gaio, P.; Gandolfi, C. *Tetrahedron Lett.* **1972**, 4307.

(13) For example, irradiation of CH_3 of **19a** shows strong NOE's on signals corresponding to H_4, H_2, and CH_2OBn. In the ^{13}C NMR, the chemical shifts of CH_3, C_5, and C_1 are at δ 13.41, 37.03, and 44.42, respectively, and are considerably shifted upfield compared to those in **20a** and **21a**. In **21a** irradiation of H_5 causes enhancement of H_4 signal and vice versa. Also ^{13}C and ^1H NMR and difference NOE spectra of **21a** are similar to those of **13** prepared from **10b**.

(14) Houk, K. N.; Spellmeyer, D. C., unpublished results.

(15) The conformation of the allyl ether segment (C_3–C_6) in both **23** and **24** is the one that has been proposed to be most favorable. See: (a) Karabatsos, G. J.; Fenglio, D. J. *Top. Stereochem.* **1970**, *5*, 167. (b) Cha, J. K.; Christ, W. J.; Kishi, Y. *Tetrahedron* **1984**, *40*, 2247. (c) For a theoretical treatment of staggered models, see: Paddon-Row, M. N.; Rondan, N. G.; Houk, K. N. *J. Am. Chem. Soc.* **1982**, *104*, 7162.

(16) (a) Dupuis, J.; Giese, B.; Ruegge, D.; Fischer, H.; Korth, H.-G.; Sustmann, R. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 896. (b) Reference 1f. (c) Korth, H.-G.; Sustmann, R.; Dupuis, J.; Giese, B. *J. Chem. Soc., Perkin Trans 2* **1986**, 1453.

We are currently extending the methodology to the synthesis of prostaglandin and brefeldin intermediates. Experimental and theoretical studies are also in progress to explore the characteristics and synthetic potentials of boat forms of the dioxane and related ring systems.

(17) For additional examples of the importance of β-σ_{CO}*-SOMO interactions in the control of the reactivity and stereochemistry, see: (a) Barton, D. H. R.; Hartwig, W.; Motherwell, W. B. *J. Chem. Soc., Chem. Commun.* **1982**, 447. (b) Baumberger, F.; Vasella, A. *Helv. Chim. Acta* **1983**, *66*, 2210. (c) Giese, B.; Dupuis, J. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 622. (d) Ireland, R. E.; Norbeck, D. W.; Mandel, G. S.; Mandel, N. S. *J. Am. Chem. Soc.* **1985**, *107*, 3285. (e) Adlington, R. M.; Baldwin, J. E.; Basak, A.; Kozyrod, R. P. *J. Chem. Soc., Chem. Commun.* **1983**, 944. (f) Recent ESR studies suggest that deoxypyranosan-2-yl, 3-yl, and 4-yl radicals retain the $^4C_1$ conformation of their precursors: Korth, H.-G.; Sustmann, R.; Groninger, K. S.; Witzel, T.; Giese, B. *J. Chem. Soc., Perkin Trans 2* **1986**, 1461.

Detection of High-Valent Intermediates in the Chlorine(I) Oxidation of (Porphinato)manganese(III) Complexes

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Recent years have seen a growing fascination with transition-metal complexes that effect efficient oxygen transfer from an oxo ligand source to organic substrates such as alkanes and alkenes. The hypochlorite system set forth by Meunier and co-workers[1] is intriguing for its economic implications as well as those of general structure–reactivity relationships. This system is biphasic in nature with an aqueous phase containing hypochlorite ion (OCl^-) in the form of commercial bleach and an organic phase consisting of the (tetraphenylporphinato)manganese(III) catalyst (Mn(TPP)X; X = Cl^-, Br^-, or OAc^-) and an alkene substrate in CH_2Cl_2. A phase-transfer catalyst is employed to shuttle OCl^- from the aqueous to the organic phase where it oxidizes Mn(TPP)X to produce a putative high-valent, oxomanganese intermediate (such high-valent oxo complexes are known for Cr(IV) and Cr(V) and have been suggested for analogous Fe(IV) and Mn(V) derivatives).[2] This oxomanganese intermediate in turn oxidizes the alkene to an epoxide. Montanari and co-workers[3] have recently shown that the functionality of such a system does not require that the aqueous phase be at the pH of commercial bleach (i.e , pH 12.8). In fact, it was demonstrated that if the pH is lowered to approximately 9.5, the system turns over more rapidly, even in the absence of the phase-transfer catalyst. This suggests that a neutral chlorine(I) compound is crossing the phase boundary and serves to generate the high-oxidation-state manganese complex. It has been postulated that this neutral chlorine(I) species is HOCl.[3]

In the gas phase, HOCl is in equilibrium with its anhydride, chlorine monoxide (Cl_2O), and water. Relatively large concentrations of Cl_2O can be produced in organic solution (i.e., on the order of 1.5 M in CCl_4).[4,5] It is thus conceivable that Cl_2O is present and acts as the oxidant in the organic phase of the manganese porphyrin catalytic system. Accordingly, we have employed Cl_2O in CCl_4 solution as an oxidant for Mn(TPP)Cl.

(1) (a) Meunier, B.; Guilmet, E.; De Carvalho, M.; Poilblanc, R. *J. Am. Chem. Soc.* **1984**, *106*, 6668. (b) Bortolini, O.; Ricci, M.; Meunier, B. *Nouv. J. Chim.* **1986**, *10*, 39.

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(3) Montanari, F.; Penso, M.; Quici, S.; Vigano, P. *J. Org. Chem.* **1985**, *50*, 4888.

(4) Cady, G. H. *Inorganic Synthesis*; Moeller, T., Ed.; McGraw-Hill: New York, 1957; Vol. V.

(5) (a) Yost, D. M.; Felt, R. C. *J. Am. Chem. Soc.* **1934**, *56*, 68. (b) Secoy, C. H.; Cady, G. H. *J. Am. Chem. Soc.* **1941**, *63*, 2504.

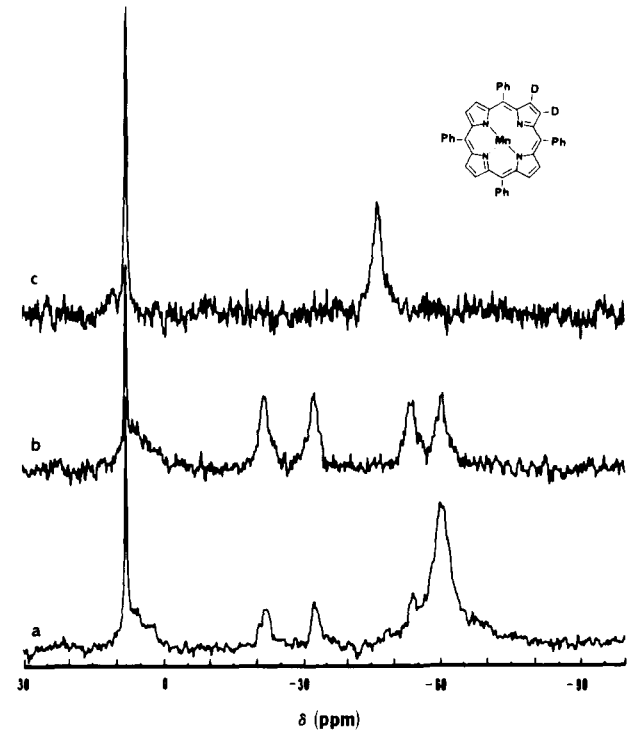

Figure 1. 55-MHz ^2H NMR acquired at −80 °C, $CHClF_2$ solvent. The sharp signal at 7.44 ppm is due to natural abundance $CDClF_2$. (a) Mn(TPP-d_8)Cl treated with Cl_2O at −165 °C and warmed to −80 °C. (b) Sample further warmed to −60 °C and cooled back to −80 °C. (c) Mn(TPP-d_8)X regenerated by addition of cyclohexene to the sample.

Oxidations were carried out at temperatures ranging from −165 to −78 °C in the absence of a substrate in an effort to generate the high-oxidation-state manganese intermediate at concentrations suitable for examination by ^2H NMR spectroscopy. Inasmuch as the low gyromagnetic ratio of the deuterium nucleus results in much narrower NMR lines (relative to proton line widths) for paramagnetic molecules, we have employed (tetraphenylporphinato)manganese(III) deuteriated at the β-pyrrole positions [Mn(TPP-d_8)Cl].[6]

Upon treatment of Mn(TPP-d_8)Cl at low temperature in CH_2Cl_2 or $CHClF_2$ with a CCl_4 solution of Cl_2O or HOCl, a red-brown color is immediately observed. This solution was subsequently examined by low-temperature NMR spectroscopy. The deuterium NMR spectra in Figure 1 (acquired at 55 MHz) indicate the presence of two high-valent species that can be produced concurrently or exclusively. Mixing Mn(TPP-d_8)Cl and Cl_2O in $CHClF_2$ at −165 °C followed by careful warming to −78 °C affords an oxidized (porphinato)manganese complex with a single β-pyrrole NMR signal at −60 ppm. When the solution is warmed to −60 °C in the presence of excess Cl_2O, the first product is quantitatively converted to a second product with no further color change. This second species consistently exhibits four upfield β-pyrrole deuteron NMR peaks of equal area over a range of temperatures, thus suggesting formation of a species that has lost the 4-fold symmetry of the Mn(TPP)X molecule. Conversion of the symmetric to the asymmetric product is irreversible upon cooling the solution back to −80 °C. Through the addition of Cl_2O as a CCl_4 solution to Mn(TPP-d_8)Cl at −78 °C a mixture of the symmetric and asymmetric products is obtained. Although treatment of the product mixture with a limited amount of cyclohexene at −78 °C shows preferential reduction of the symmetric species, both components of the mixture react with cyclohexene to regenerate the Mn(TPP-d_8)X complex with little degradation of the porphyrin. Titration of Mn(TPP-d_8)Cl with Cl_2O indicates that approximately a 2:1 mole ratio (Cl_2O:Mn) is required for formation of the asymmetric species.

(6) Shirazi, A.; Goff, H. M. *J. Am. Chem. Soc.* **1982**, *104*, 6318.

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