Chart II

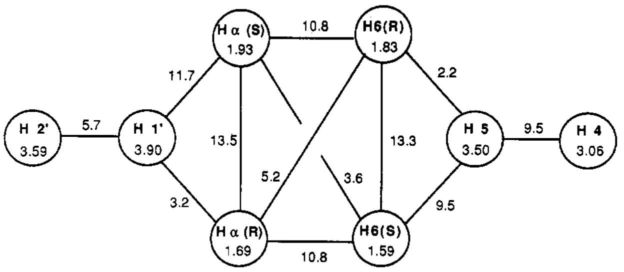
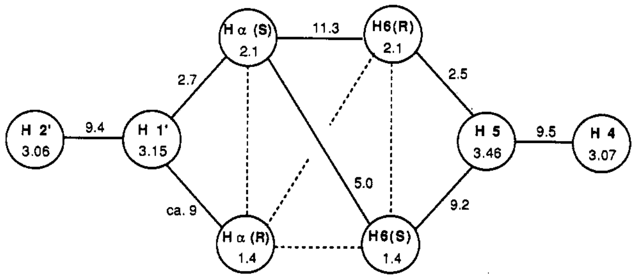


Chart III



spin-spin coupling constants observed (Chart III[9]) demonstrate that **2** exists predominantly in the predicted conformation **2A**. From a modified Karplus equation,[13] the spin-spin coupling constants listed in Table I yield ϕ -35°, ψ -60°, and ω -35°.[14]

The C-disaccharides are, like the corresponding parent disaccharides, not conformationally rigid. Nonetheless, the weighted average of available conformers corresponds extremely well to the one predicted. Comparison of the preferred conformation observed for carbon analogues of 1,6-disaccharides with that of corresponding parent disaccharides is constrained since only limited experimental data is available on the solution conformation of parent substances at this time.[17] We are currently engaged in some experimental work to compare the solution conformations between these two classes of compounds.

Acknowledgment. Financial supports from the National Institutes of Health (NS 12108) and the National Science Foundation (CHE 86-10505) are gratefully acknowledged.

Registry No. **1**, 110352-40-4; **1**-d_2, 110316-60-4; **2**, 89160-13-4; **3**, 499-40-1; **4**, 554-91-6; **5**, 110316-55-7; **6**, 110316-56-8; **7**, 110316-57-9; **8**, 110316-58-0; **8**-d_2, 110316-59-1.

Supplementary Material Available: The complete tables listing chemical shifts and spin-spin coupling constants of **1** and **2** and the summary for the assignment of absolute configuration of **8**-d_2 (3 pages). Ordering information is given on any current masthead page.

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(15) Rouzaud, D.; Sinay, P. *J. Chem. Soc., Chem. Commun.* **1983**, 1353.

(16) The details of this study will be published in a full account.

(17) For the conformational analysis of 1,6-disaccharides in solution, for example, see: (a) Ohrui, H.; Nishida, Y.; Watanabe, M.; Hori, H.; Meguro, H. *Tetrahedron Lett.* **1985**, *26*, 3251. (b) Lemieux, R. U.; Wong, T. C.; Thogersen, H. *Can. J. Chem.* **1982**, *60*, 81. (c) Bock, K.; Vignon, M. *Nouv. J. Chim.* **1982**, *6*, 301. (d) Melberg, S.; Rasmussen, K. *Carbohydr. Res.* **1980**, *78*, 215. (e) Gagnaire, D. Y.; Nardin, R.; Taravel, F. R.; Vignon, M. R. *Nouv. J. Chim.* **1977**, *1*, 423.

(18) (a) Omura, K.; Swern, D. *Tetrahedron* **1978**, *34*, 1651. (b) Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480.

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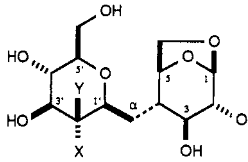
Preferred Conformation of C-Glycosides. 3. Preferred Conformation of Carbon Analogues of 1,4-Disaccharides

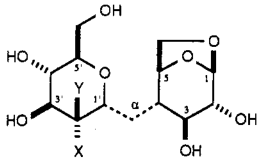
Summary: Through the studies on the carbon analogues of 1,4-disaccharides, a simple but effective method is developed to analyze the conformational preference of disaccharides and related compounds.

Sir: In the preceding papers, we have demonstrated that simple C-glycosides as well as the carbon analogues of 1,6-disaccharides exist predominantly in the predicted conformation.[1] In this paper, we would like to extend this study to the carbon analogues of 1,4-disaccharides. On the basis of the results reported in one of the preceding papers,[1a] the conformational preference around the C1′–Cα bond is predicted to be such that the Cα–C4 bond is antiperiplanar to the C1′–C2′ bond. With respect to the Cα–C4 bond, we have considered the steric interactions around this bond to analyze the problem.

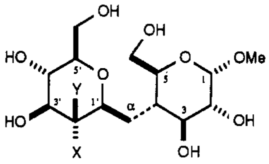
The eight carbon analogues **1–8** of 1,4-disaccharides[2] were subjected to NMR studies in CD_3OD-D_2O (9:1) (Table I[3]). The values of spin-spin coupling constants[3] clearly demonstrate that both pyranose rings adopt a chair conformation in all the cases. The assignment of the *pro-R* and *pro-S* protons at the Cα position was unambiguously made through the synthesis of the corresponding specifically monodeuteriated glycosides with known absolute configuration.[4]



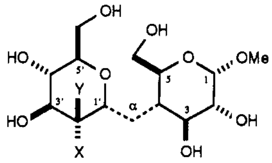
1: X = OH, Y = H
2: X = H, Y = OH



3: X = OH, Y = H
4: X = H, Y = OH



5: X = OH, Y = H
6: X = H, Y = OH



7: X = OH, Y = H
8: X = H, Y = OH

No ambiguity remains in specifying the preferred conformation of the carbon analogues **1–4** of 1,4-disaccharides belonging to the 1,6-anhydrogluco series. Namely, the spin-spin coupling constants between the C1′ and Cα protons clearly confirm that the C-glycosidic bond adopts preferentially the predicted conformation. Similarly, the spin-spin coupling constants between the C4 and Cα protons establish the preferred conformation around this bond. This conformational preference is straightforwardly explained in terms of steric interactions, which is conveniently recognized by using a diamond lattice. Among the three ideal staggered conformers A–C available for **1** and **2**, conformer C is considered to be least favored be-

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(1) (a) Wu, T.-C.; Goekjian, P. G.; Kishi, Y. *J. Org. Chem.* preceding paper in this issue. (b) Goekjian, P. G.; Wu, T.-C.; Kang, H.-Y.; Kishi, Y. *J. Org. Chem.*, second preceding paper in this issue.

(2) Babirad, S. A.; Wang, Y.; Kishi, Y. *J. Org. Chem.* **1987**, *52*, 1370.

(3) The complete tables listing chemical shifts and spin-spin coupling constants are included in the supplementary material.

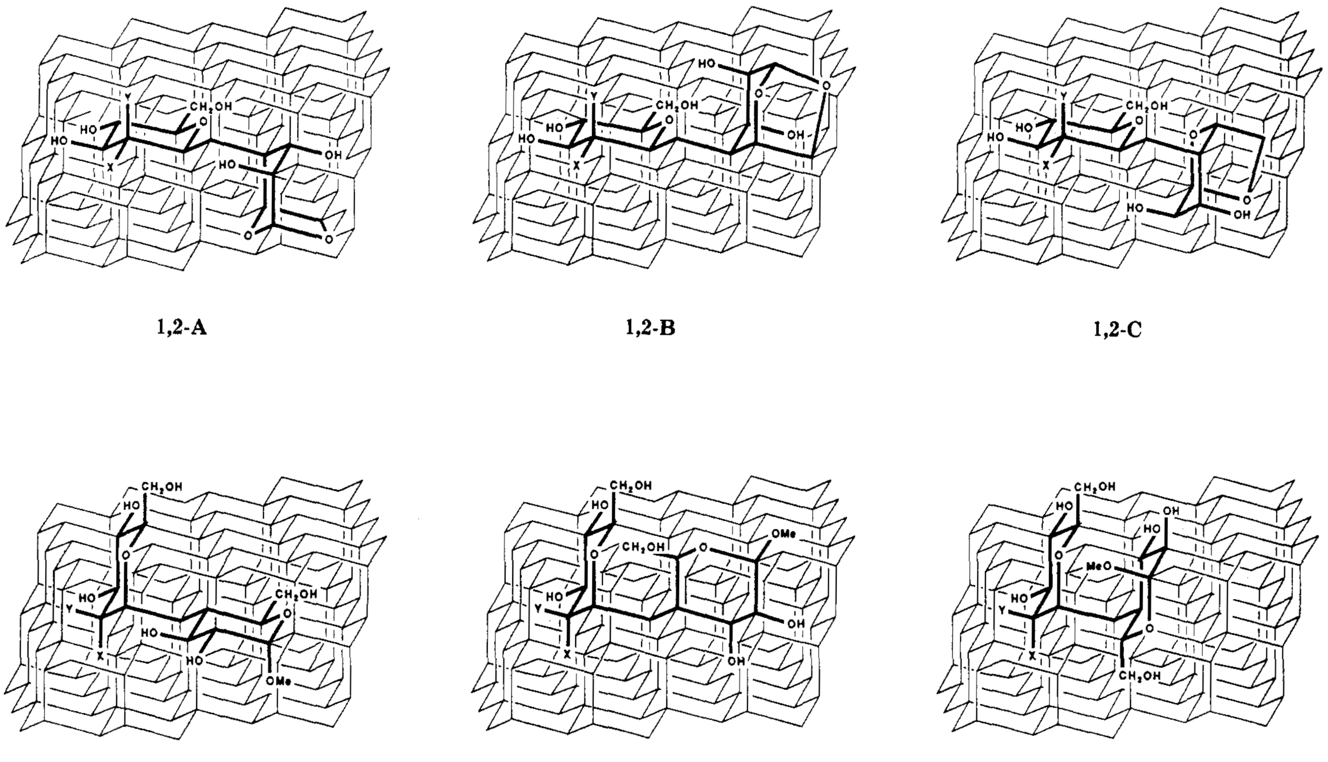
(4) The synthetic scheme of specifically monodeuterated substances is included in the supplementary material.

0022-3263/87/1952-4825$01.50/0

Table I.[3] ^{1}H NMR Data (in ppm) of Glycosides 1–8[a]

compd	C4	Cα(*pro-S*)	Cα(*pro-R*)	C1′
1	1.88 (dd, 9.9, 4.5)	2.26 (ddd, 14.4, 9.9, 2.4)	1.66 (ddd, 14.4, 9.9, 4.5)	3.30 (9.9, 8.7, 2.4)
2	1.81 (dd, 9.3, 5.4)[c]	1.83 (ddd, *b*, 9.3, 3.2)	2.05 (ddd, *b*, 10.0, 5.4)[c]	3.61 (dd, 10.0,[c] 3.2)
3	1.78 (dd, 8.4, 6)	1.99 (ddd, *b*, 10.1, 6)	2.01 (ddd, *b*, 8.4, 4.2)	4.09 (ddd, 10.1, 5.6, 4.2)
4	1.79 (dd, 9.0, 4.6)	2.06 (ddd, 14.0, 11.2, 4.6)	1.85 (ddd, 14.0, 9.0, 3.1)	4.04 (ddd, 11.2, 3.2, 3.1)
5	1.72 (dddd, 10.9, 10.3, 4.7, 3.5)	2.08 (ddd, 15.3, 4.7, 1.7)	1.59 (ddd, 15.3, 9.2, 3.5)	3.28 (ddd, 9.2, 9.2, 1.7)
6	1.67 (dddd, 10.2, 10.1, 5.2, 3.8)	1.75 (ddd, 15.1, 3.8, 3.8)	1.86 (ddd, 15.1, 9.1, 5.2)	3.63 (dd, 9.1, 3.8)
7	1.82 (dddd, 10.6, 8.8, 5.5, 2.9)	1.92 (ddd, 15.0, 10.3, 2.9)	1.75 (ddd, 15.0, 5.5, 3.1)	4.23 (ddd, 10.3, 5.6, 3.1)
8	1.73 (dddd, 11.3, 10.8, 5.3, 3.3)	1.82 (ddd, 14.4, 9.0, 3.3)	1.67 (ddd, 14.4, 5.3, 4.6)	4.11 (ddd, 9.0, 4.6, 3.7)

[a] The spectra were recorded on a Bruker AM-500 (500 MHz) spectrometer. The chemical shifts are relative to the signal of CHD_2OD (3.30 ppm). The spin–spin coupling constants (in Hz) given in parentheses were obtained by first-order analysis. [b] Because of a higher order spin system, this spin–spin coupling constant could not be obtained by first-order analysis. [c] Because of higher order spin–spin coupling patterns, these couplings were determined from the Cα(*S*)-deuteriated compound.



1,2-A 1,2-B 1,2-C

7,8-A 7,8-B 7,8-C

Figure 1.

cause of the steric interactions due to the Cα–C1′ bond surrounded by the C4–C3 and C4–C5 bonds (Figure 1). Conformer B is sterically destabilized because of the 1,3-diaxial-like interactions between the C1′–O bond and the C4–C3.[5] Thus, conformer A is anticipated to be the most favored. Indeed, the observed NMR data support this conclusion. The preferred conformation of **3** and **4** can be analyzed in the same manner.[6]

From the spin–spin coupling constants between the C1′ and Cα protons, it is evident that the C-glycosidic bond adopts preferentially the predicted conformation in the methyl glycosides **5**–**8** as well. However, the analysis of the conformational preference around the C4–Cα bond is somewhat more complicated. With the hydrolytic cleavage of the C1–O6 bond of the 1,6-anhydroglucose moiety, the pyranose ring flips from one chair conformation into the alternative one—note $J_{2,3}$, $J_{3,4}$, and $J_{4,5}$.[3] As a result, none of the three ideal staggered conformers A–C available for **7** and **8** is free from steric congestion. Among them, conformer C seems to suffer from the most severe steric interactions since the Cα–C1′ bond is surrounded by the C4–C3 and C4–C5 bonds. 1,3-Diaxial-like interactions are obvious in both conformers A and B. However, inspection of the drawing on a diamond lattice may suggest that conformer A is slightly less sterically crowded than conformer B; there is one 1,3-diaxial-like interaction in conformer A (C1′–Cα/C3–OH), whereas there are two 1,3-diaxial-like interactions in conformer B (C1–Cα/C5–C6 and C1′–O/C4–C5). The spin–spin coupling constants observed for the C4 and Cα protons indicate that the C4–Cα bond does not exist predominantly in either of the ideal staggered conformers A or B but exists as a mixture of the conformers A and B, weighted toward the former, or in a conformer slightly deviated from A.[7,8] The pre-

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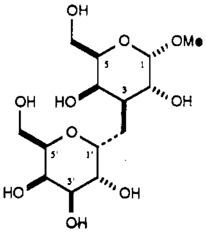
[5] The importance of this type of 1,3-diaxial-like interactions for the conformational preference of carbohydrates was first recognized by Horton and co-workers. For example, see: El Khadem, H. S.; Horton, D. *J. Org. Chem.* **1968**, *33*, 734.

[6] The conformational analysis of these substances based on a diamond lattice is included in the supplementary material.

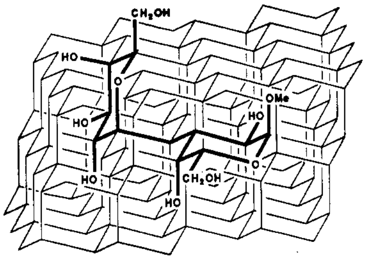
[7] Applying a modified Karplus equation (Haasnoot, C. A. G.; de Leeuw, F. A. A. M.; Altona, C. *Tetrahedron* **1980**, *36*, 2783), the following torsional angles (ϕ and ψ, respectively) were obtained: **1**, 50° and 80°; **2**, 50° and 85°; **3**, −80° and −90°; **4**, −70° and −85°; **5**, 40° and 5°; **6**, 85° and −5°; **7**, −80° and −10°; **8**, −90° and −5°. For the definition of ϕ and ψ, see ref 17e in ref 1b.

ferred conformation of **5** and **6** can also be analyzed in the same manner.[6] The conformational behavior of **5**–**8** seems to agree well with that of the corresponding parent disaccharides.[9]

It is noteworthy that the conformation preference around the C-glycosidic bond is so overwhelming that a structural deviation from the ideal staggered conformer to avoid the steric interactions takes place in rotating primarily the nonglycosidic C4–Cα bond rather than the glycosidic C1′–Cα bond. The recognition of this phenomenon allows to predict the conformational behavior of di-C-saccharides and higher C-saccharides and their parent substances. For example, the carbon analogue **9** of 3-*O*-α-D-galactopyranosyl-*D*-galactopyranose, a structural unit of human blood group determinants,[10] possesses one unique conformer **9A**, which meets with all the criteria to exist predominantly in one conformer. Indeed, we have recently succeeded in the synthesis of **9** and demonstrated that the NMR data confirm this prediction.[11]



9



9A

Acknowledgment. Financial support from the National Institutes of Health (NS 12108) and the National Science Foundation (CHE 86-10505) are gratefully acknowledged.

Registry No. **1**, 110316-61-5; **2**, 110352-41-5; **3**, 110352-42-6; **4**, 110352-43-7; **5**, 107032-98-4; **6**, 106929-15-1; **7**, 106974-31-6; **8**, 106974-29-2; i, 110316-62-6; ii, 110316-63-7; iii, 110352-44-8; iv, 110316-64-8; v, 110316-65-9.

Supplementary Material Available: The complete tables listing chemical shifts and spin–spin coupling constants, the synthesis of monodeuteriated substances, and the conformational analysis of **3**–**6** based on a diamond lattice (4 pages). Ordering information is given on any current masthead page.

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(8) We observed small temperature effects; for instance, $J_{4,\alpha(pro\text{-}R)}$ and $J_{4,\alpha(pro\text{-}S)}$ of **5** were 3.7 and 4.7 Hz at 40 °C, 3.5 and 4.7 Hz at 25 °C, 3.1 and 4.9 Hz at 0 °C, 2.9 and 5.1 Hz at −20 °C, and 2.8 and 5.2 Hz at −40 °C. We are currently engaged in NOE experiments to gain more information.

(9) For the conformational analysis of cellobiose and maltose in solution, for example, see: (a) Shashkov, A. S.; Lipkind, G. M.; Kochetkov, N. K. *Carbohydr. Res.* **1986**, *147*, 175 and references cited therein. (b) Nardin, R.; Saint-Germain, J.; Vincendon, M.; Taravel, F.; Vignon, M. *Nouv. J. Chim.* **1984**, *8*, 305 and references cited therein. (c) Lemieux, R. U.; Bock, K.; Delbaere, L. T. J.; Koto, S.; Rao, V. S. *Can. J. Chem.* **1980**, *58*, 631 and references cited therein. (d) St. Jacques, M.; Sundararajan, P. R.; Taylor, K. J.; Marchessault, R. H. *J. Am. Chem. Soc.* **1976**, *98*, 4386 and references cited therein.

(10) There are a number of excellent review articles on this subject. For example, see: Lemieux, R. U. *Chem. Soc. Rev.* **1978**, *7*, 423. *Frontiers of Chemistry*; Laidler, K. J. Ed.; Pergamon: New York; 1982; p 1 and references cited therein.

(11) The spin–spin coupling constants observed for **9** are $J_{1',\alpha(pro\text{-}S)}$ = 12.1 Hz, $J_{1',\alpha(pro\text{-}R)}$ = 3.1 Hz, $J_{3,\alpha(pro\text{-}S)}$ = 3.3 Hz, $J_{3,\alpha(pro\text{-}R)}$ = 11.1 Hz, and $J_{\alpha,\alpha}$ = 14.3 Hz: Goekjian, P. G.; Kang, H.-Y.; Kishi, Y., unpublished results.

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Reaction of the Dianion of (η^6:η^6-Biphenyl)bis(tricarbonylchromium)with Electrophiles. A Highly Regioselective Route from Biphenyl to 2-Alkylbiphenyls and 5-Alkyl-5-phenyl-1,3-cyclohexadienes

Summary: The dianion formed by reduction of (η^6:η^6-biphenyl)[$Cr(CO)_3$]$_2$ reacts with electrophiles such as H_2O, D_2O and methyl or primary alkyl halides in a highly stereoselective and regioselective manner to form an intermediate with one ring coordinated to a $Cr(CO)_3$ group as a η^5-cyclohexadienyl anion, substituted in the 1-position by the electrophile, and the other ring η^6 coordinated to the second $Cr(CO)_3$ group. Appropiate workup of the alkylated intermediates yields either 2-alkylbiphenyls or (5-alkyl-η^6-5-phenyl-1,3-cyclohexadiene)chromium tricarbonyls in essentially quantitative yields.

Sir: Two-electron reduction of conjugated arenes complexed by two $Cr(CO)_3$ groups produces stable dianions.[1,2] (η^6:η^6-Biphenyl)[$Cr(CO)_3$]$_2$ (**1**, Scheme I) has been reduced chemically to generate a dianion which is sufficiently stable to isolate and store in an argon drybox.[2] ^{13}C and ^1H NMR spectrometric data of the dilithium salt of the dianion are consistent with a (η^5:η^5-biphenyl)[$Cr(CO)_3$]$_2$ structure (**2** in Scheme I).[3,4] In this paper we wish to report the intermediates and products of the reaction of (η^5:η^5-biphenyl)[$Cr(CO)_3$]$_2$ dianion (**2**) with H_2O, D_2O, and methyl or 1-alkyl iodides and bromides.

In a typical reaction, **2** is placed in dry, argon-saturated THF or DMF-d_7.[5] One equivalent of the electrophile (E in Scheme I) is injected into the reaction vessel and stirred at ambient temperature. D_2O or H_2O causes a nearly instantaneous color change from the dark brown of the dianion to a yellow orange solution. Alkyl halides react more slowly to give similar color changes over the course of several minutes. NMR data for products obtained from the reaction of **2** with the electrophiles listed are consistent with structure **3** in which one ring is a $Cr(CO)_3$-coordinated η^5-cyclohexadienyl anion substituted by the electrophile in the 1-position and the other arene ring is neutral and η^6 coordinated to the other $Cr(CO)_3$ group. ^{13}C and ^1H NMR data of some of the products formed by reaction of **2** with electrophiles are shown in Tables I and II, respectively. NMR shift assignments are made by comparison with isoelectronic (η^5-cyclohexadienyl)metal–carbonyl complexes for which ^{13}C NMR[2,6–10] and ^1H NMR [2,6,7,11–15]

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(1) Milligan, S. N.; Rieke, R. D. *Organometallics* **1983**, *2*, 171.

(2) Rieke, R. D.; Milligan, S. N.; Schulte, L. D. *Organometallics* **1987**, *6*, 699 and references therein. Note: The isolated (η^5:η^5-biphenyl)[$Cr(CO)_3$]$_2$ dianion (**2**) has been found to be pyrophoric.

(3) Deviation of saturated carbon 1 from the plane formed by carbons 2–6 is well known for a variety of η^5-cyclohexadienyl rings.[7,13] The angle of deformation is on the order of 38° to 45° in complexes for which X-ray data is available. A MO explanation of the deformation has been presented in a theoretical discussion of η^5-cyclohexadienyl rings.[7] The angle of deformation in **2**, with its unsaturated carbon 1, is unknown at present.

(4) Hoffmann, R.; Hofmann, P. *J. Am. Chem. Soc.* **1976**, *98*, 598.

(5) The (η^5:η^5-biphenyl)[$Cr(CO)_3$]$_2$ dianion (**2**) is not sufficiently soluble in THF for optimum NMR examinations. DMF-d_7 was found to be an excellent solvent for NMR work. THF was used for the reactions for which yield data is described.

(6) Henry, W. P.; Rieke, R. D. *J. Am. Chem. Soc.* **1983**, *105*, 6314–6316.

(7) Paquette, L. A.; Daniels, R. G.; Gleiter, R. *Organometallics* **1984**, *3*, 560 and references therein.

(8) Whitesides, T. H.; Budnik, R. A. *Inorg. Chem.* **1976**, *15*, 874–879 and references therein.

(9) Dobish, P. A.; Greshem, D. G.; Kowalski, D. J.; Lillya, C. P.; Magyar, E. S. *Inorg. Chem.* **1978**, *17*, 1775.

(10) Pearson, A. J. *J. Chem. Soc., Perkin Trans. 1* **1977**, 2069.

(11) Semmelhack, M. F.; Hall, H. T.; Farina, R.; Yoshifuji, M.; Clark, G.; Bargar, T.; Hirotsu, J.; Clardy, J. *J. Am. Chem. Soc.* **1979**, *101*, 3535 and references therein.

(12) Connelly, N. G.; Kelly, R. L. *J. Chem Soc., Dalton Trans.* **1974**, 2334.