illustrated in eq 6 is operative was demonstrated by irradiating **7-*O-d***. NMR and mass spectral analysis of the resulting **8** showed that the deuterium was located almost entirely, if not exclusively, at C-2 of **8** (eq 6). Thus the a priori possible nucleophilic addition mechanism[13] for formation of **8** is ruled out as a major process.

The evidence that carbene formation does occur in certain 3-alkyl-1,1-diphenylpropenes is conclusive. It is, therefore, highly likely that the carbene mechanism for net 1,3-hydrogen migration in **2** is the one operative,[14] and that carbene formation from 3-alkyl-1,1-diphenylpropenes may well be a general process. The mechanisms of previously observed 1,3-hydrogen migrations[1a] deserve further scrutiny.

Acknowledgment. We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

References and Notes

(1) (a) G. W. Griffin, A. F. Marcantonio, H. Kristinsson, R. C. Petterson, and C. S. Irving, *Tetrahedron Lett.*, 2951 (1965); (b) H. Kristinsson and G. W. Griffin, *J. Am. Chem. Soc.*, **88**, 378 (1966); (c) S. S. Hixson and T. P. Cutler, *ibid.*, **95**, 3031, 3032 (1973); (d) S. S. Hixson, submitted for publication; (e) N. K. Hamer and A. J. Willis, *J. Chem. Soc., Chem. Commun.*, 458 (1973), *J. Chem. Soc., Perkin Trans. 2*, 88 (1974); (f) E. C. Sanford and G. S. Hammond, *J. Am. Chem. Soc.*, **92**, 3497 (1970); (g) R. C. Cookson et al., *Chem. Commun.*, 107, 108, 385 (1971); *Q. Rev., Chem. Soc.*, **22**, 423 (1968); *Tetrahedron*, **24**, 3955 (1968); *Chem. Commun.*, 823 (1967).

(2) Vycor-filtered light from a 450-W medium-pressure mercury arc was used. Progress of the reaction was monitored closely by gas chromatography.

(3) Griffin[1a] has suggested two consecutive 1,2-hydrogen shifts as a likely mechanism for the conversion of 1,1-diphenylpropene to 3,3-diphenylpropene.

(4) We assume a normal isotope effect would be operative in the migration.

(5) This is the preferred stereochemistry in the analogous 1,2-migration of vinyl substituents (the di-π-methane rearrangement). See H. E. Zimmerman, J. D. Robbins, R. D. McKelvey, C. J. Samuel, and L. R. Sousa, *J. Am. Chem. Soc.*, **96**, 4630 (1974), and references therein.

(6) S. J. Cristol and C. S. Ilenda, Abstracts of the 167th National Meeting of the American Chemical Society, Los Angeles, Calif., April 1974, ORGN 113.

(7) T. R. Fields and P. J. Kropp, *J. Am. Chem. Soc.*, **96**, 7559 (1974).

(8) S. S. Hixson, *J. Am. Chem. Soc.* **97**, 1981 (1975).

(9) The insertion of carbenes into the O–H bond of alcohols has been frequenctly observed, both with methylene itself and with more stabilized carbenes.[10] Intramolecular OH insertion of a carbene has also been noted.[11]

(10) W. Kirmse, "Carbene Chemistry", Academic Press, New York, N.Y., 1971, p 423 ff.

(11) A. C. Day and M. C. Whiting, *J. Chem. Soc. C*, 1719 (1966).

(12) (a) NMR ($CDCl_3$) δ 0.59 (s, 3), 1.03 (s, 3), 1.66–2.10 (m, 2), 3.62–3.93 (m, 2), 4.13 (AB quartet, 2, J = 10 Hz), 7.14–7.55 (m, 10); mass spectrum (80 eV) m/e 266 (M^+, 0.5%), 264 (0.5), 167 (7.6), 165 (5.5), 152 (2.7), 99 (100). (b) Small amounts of other unidentified products as well as polymeric material were also formed.

(13) See, e.g., S. S. Hixson, *Tetrahedron Lett.*, 4211 (1972).

(14) A minor amount of another pathway, either a 1,3-hydrogen shift or two consecutive 1,2-hydrogen shifts, must also be followed.

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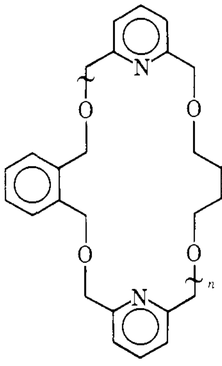
Chemistry of Heterocyclic Compounds. 20. Multidentate Chelating Agents. Pyridine Macrocyclic Ether Synthesis

Sir:

In view of the current interest in the design and construction of specific metal ion ligands,[1] we wish to report convenient direct nucleophilic displacement by alkoxide of pyridine 2,6-dihalides to prepare several new pyridine-containing macrocyclic ethers in which the oxygen is attached *directly* to the hetero ring. Recently, we described the facile preparation of 22-, 33-, 44-, and 55-membered macrocyclic azaethers (**1**) that contained the 2,6-pyridino moiety;[2] however, in this series the pyridine rings were isolated from the ether linkage by a $-CH_2-$ group. Further examples of this latter type of pyridine-containing multiheteromacrocycle have been described by Vögtle and Weber[3] and Cram et al.[4] (**2a**[5] and **2b**, respectively).



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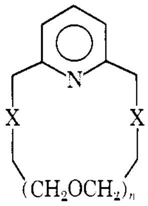


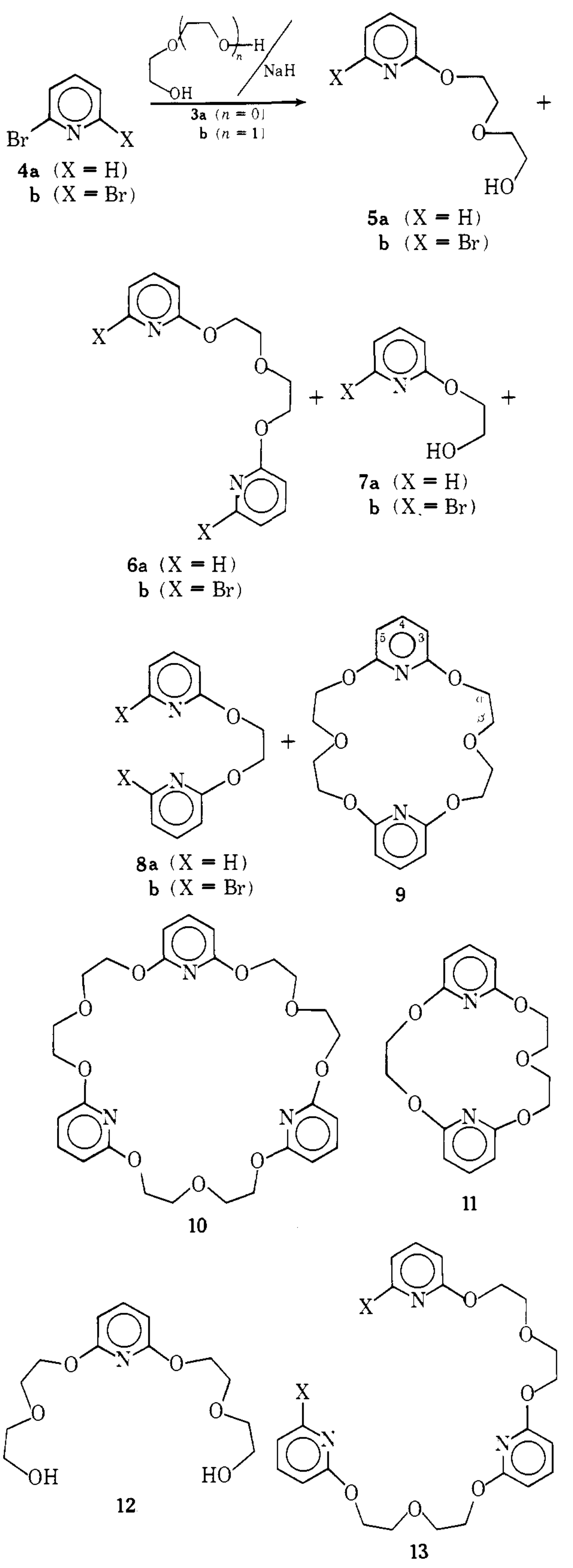
2a (X = S)
2b (X = O)

During our ketalization studies of substituted di(2-pyridyl) ketones[6] as well as attempted synthesis of different pyridylacetylenes,[7] several minor products were isolated that had resulted from nucleophilic displacement of a 2-pyridyl substituent. In practice, application of this substitution reaction has resulted in a convenient selective 2-pyridone synthesis[8] as well as the herein reported new route to heteromacrocyclic ethers.

Treatment of diethylene glycol (**3b**) with sodium hydride in anhydrous diethylene glycol diethyl ether (DEE) smoothly generated diethylene glycol dianion in near quantitative yield. 2-Bromopyridine (**4a**) was added and the mixture warmed to 140° for 24 hr. After removal of solvent and unreacted starting materials, the major products were the monoether **5a**[9] and diether **6a** isolated in 27 and 35% yields, respectively, along with traces (<3%) of **7a** and **8a.** These latter trace products and ethylene oxide resulted from thermal fragmentation of polyethylene glycols under reaction conditions; both fragmentation and oligomerization are precedented reactions of ethylene glycols.[10] Side reactions are minimized by maintaining the reaction temperatures below 150°. Substantiation of the oligomerization process was demonstrated when **4a** was subjected to ethylene glycol dianion under identical conditions: the major products were 2-(2-pyridinoxy)ethanol (**7a**) and 1,2-di(2-pyridinoxy)ethane (**8a**), along with traces of **5a** and **6a.**

When 2,6-dibromopyridine (**4b**) was subjected to dianion **3b** in DEE at 140°, the desired cyclized ethers **9** (mp 111–112°; 18%; NMR ($CDCl_3$) δ 3.86 (t, β-CH_2O, J = 5 Hz), 4.48 (t, α-CH_2O, J = 5 Hz), 6.23 (d, 3,5-PyrH, J = 8 Hz), 7.45 (t, 4-PyrH, J = 8 Hz)), **10** (mp 120.5–121.5°; 3%; identical NMR), and **11** (mp 94.5–95.5°; 5%; NMR ($CDCl_3$) δ 3.81 (dd, β-CH_2-O, J = 6 Hz), 4.50 (dd, α-CH_2O, J = 6 Hz), 4.64 (s, OCH_2CH_2O), 6.38 (dd, 3,5-PyrH, J = 8.8 Hz), 7.48 (t, 4-PyrH, J = 8 Hz)) were isolated along with several intermediates **5b** (ca. 25%), **6b, 8b, 12,** and **13.**[11] The structure of unsymmetrical ether **11** was substantiated by successful cyclization of 1,2-di(6-bromo-2-pyridinoxy)ethane (**8b**) with dianion **3b;** however, **6b** could not be cyclized with dianion **3a** under diverse reaction conditions. An identical mixture of heteromacrocyclic ethers (**9, 10,** and **11**) were obtained when ether **5b** in DEE was treated with 1 equiv of sodium hydride, then the reaction mixture heated to 140°.

When triethylene glycol (**3c**) is utilized in this synthesis with 2,6-dibromopyridine (**4b**), the 1:1 cyclic ether **14a** was isolated. Pure **14a** was obtained by preparative thick layer



4a (X = H)
b (X = Br)

5a (X = H)
b (X = Br)

6a (X = H)
b (X = Br)

7a (X = H)
b (X = Br)

8a (X = H)
b (X = Br)

9

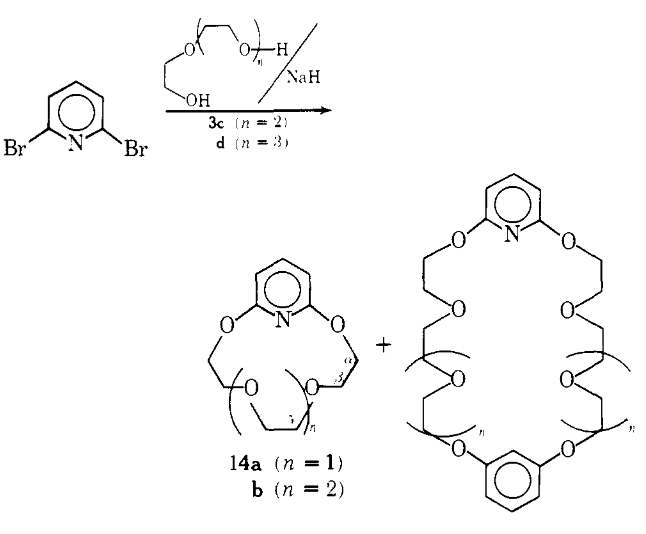
10

11

12

13

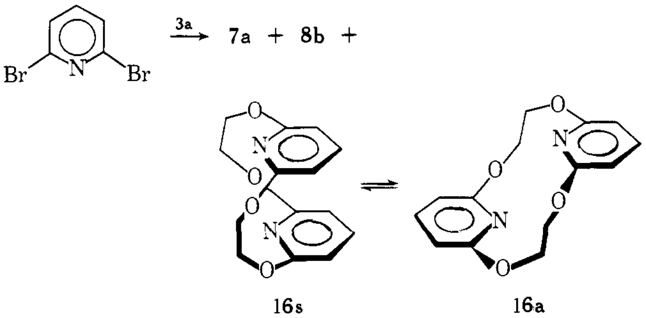
chromatography: mp 83-84°; 16%; NMR ($CDCl_3$) δ 3.70 (s, γ-CH_2O), 3.82 (t, β-CH_2O, J = 6 Hz), 4.58 (t, α-CH_2O, J = 6 Hz), 6.47 (d, 3,5-PyrH, J = 8 Hz), 7.47 (t, 4-PyrH, J = 8 Hz). Also isolated in trace amounts (2%) was the 2:2 macrocycle **15a:** mp 117-120°; identical NMR to **14.** Other key intermediates were isolated and characterized. Tetraethylene glycol **3d** also afforded predominantly an analogous 1:1 cyclic ether **14b:** mp 76-78°; 4.2%; NMR ($CDCl_3$) δ 3.62 (m, γ, δ-CH_2O), 3.92 (t, β-CH_2O, J = 6 Hz), 4.62 (t, α-CH_2O, J = 6 Hz), 6.28 (d, 3,5-PyrH, J = 8 Hz), 7.46 (t, 4-PyrH, J = 8 Hz).



14a (n = 1)
b (n = 2)

15a (n = 1)
b (n = 2)

Reaction of 2,6-dibromopyridine (**4b**) with **3a** afforded macrocycle **16** (mp 215-216°; 16%; NMR δ 4.66 (bs {38°}, -CH_2O-), 6.30 (d {38°}, 3,5-PyrH, J = 8 Hz), 7.50 (t, 4-PyrH, J = 8 Hz)). Variable temperature NMR spectrum of **16** at 100 MHz exhibits a broad singlet for the bridged methylene protons at 40°. This singlet coalesces at 15° and affords two multiplets (δ 3.57 and 4.94) at −50°. Similarly, the 3,5-ring hydrogens are transformed from a sharp doublet to two doublets at −50°. Based on these data, the energy barrier to syn-anti isomer interconversion (**16a** $\rightleftarrows$ **16s**) is calculated to be $\Delta G_c^{\ddagger}$ = 13.5 ± 0.3 kcal/mol. The pronounced conformational mobility of **16** at ambient temperature is strikingly similar to related smaller metacyclophane systems.[12,13]



16s **16a**

Further work is in progress on the synthesis and complexation of these and related multiheteromacrocyclic systems.

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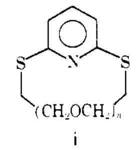
References and Notes

(1) (a) D. St. C. Black and A. J. Hartshore, *Coord. Chem. Rev.*, **9**, 219 (1973), and references cited therein; (b) B. Dietrich, J. M. Lehn, and J. P. Sauvage, *Chem. Unserer Zeit*, 7, 120 (1973); (c) J. M. Lehn, *Struct. Bonding (Berlin)*, **16**, 1 (1973); (e) C. J. Pedersen and H. K. Frensdorff, *Angew. Chem., Int. Ed. Engl.*, **11**, 16 (1972).
(2) G. R. Newkome and J. M. Robinson, *J. Chem. Soc., Chem. Commun.*, 831 (1973).
(3) F. Vögtle and E. Weber, *Angew. Chem., Int. Ed. Engl.*, **13**, 149 (1974).

(4) M. Newcomb, G. W. Gokel, and D. J. Cram, *J. Am. Chem. Soc.*, **96**, 6810 (1974); J. M. Timko, R. C. Helgeson, M. Newcomb, G. W. Gokel, and D. J. Cram, *ibid.*, **96**, 7097 (1974).

(5) This structure was incorrectly presented as i in *Chem. Abstr.*, **80**, 1461245 (1974).



i

(6) G. R. Newkome, J. D. Sauer, and G. L. McClure, *Tetrahedron Lett.*, 1599 (1973).

(7) G. L. McClure, to be submitted for publication.

(8) G. R. Newkome, J. Broussard, S. K. Staires, and J. D. Sauer, *Synthesis*, **10**, 691 (1974).

(9) All new compounds had satisfactory elemental analyses.

(10) E. Staude and F. Patat in "The Chemistry of the Ether Linkage", S. Patai, Ed., Interscience Publishers, 1967, pp 46–49; R. E. Lubowicz and P. Reich, *Chem. Eng. Prog.*, **67**, 59 (1971).

(11) In this preliminary study all products were isolated utilizing thick layer chromatography; Brinkmann silica gel PF, 2 mm thickness, eluting with cyclohexane–ethyl acetate (10:1). Several elutions were necessary to effect maximum separation.

(12) T. Sato, S. Akabori, M. Kainosho, and K. Hata, *Bull. Chem. Soc. Jpn.*, **39**, 856 (1966); J. R. Fletcher and I. O. Sutherland, *Chem. Commun.*, 1504 (1969); I. Gault, B. J. Price, and I. O. Sutherland, *ibid.*, 540 (1967); J. F. Haley, Jr., and P. M. Keehn, *Tetrahedron Lett.*, 4017, 4021 (1973); S. M. Rosenfeld and P. M. Keehn, *J. Chem. Soc., Chem. Commun.*, 119 (1974).

(13) F. Vögtle, *Justus Liebigs Ann. Chem.*, **728**, 17 (1969); F. Vögtle and L. Schunder, *Chem. Ber.*, **102**, 2677 (1969); F. Vögtle and P. Neumann, *Tetrahedron.*, **26**, 5299 (1970).

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An Electron Spin Resonance Study of the 1-Norbornyl Radical

Sir:

The 1-norbornyl radical offers an opportunity to study the vicinal and long-range proton hyperfine interactions in a radical with a pyramidal radical center and of unusually rigid structure. In this communication we report an ESR study of this radical.

Figure 1A shows the ESR spectrum of the 1-norbornyl radical observed during photolysis[1] of a cyclopropane solution[2] of bis(norbornane-1-carbonyl) peroxide[3] at −121°. To improve the signal-to-noise ratio of the spectrum, the low field wing of the spectrum (underlined part a of Figure 1A) was computer averaged using signals from eight samples.[6] The improved low field wing of the spectrum is shown in Figure 1B. The absorptions are analyzed as five sets of 1:2:1 triplets (9.81, 2.35, 1.23, 0.49, and 0.36 G) further split into a 1:1 doublet of 2.45 G. Figure 1C shows the low field wing of the simulated spectrum with the parameters given above. The assignment of the 2.45 G doublet to H_4 is straightforward.

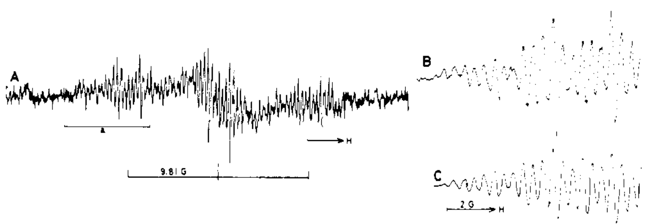


Figure 1. (A) ESR spectrum of the 1-norbornyl radical in cyclopropane solution at −121°; (B) accumulated spectrum of part a of the spectrum in A; (C) low-field wing of the simulated spectrum.

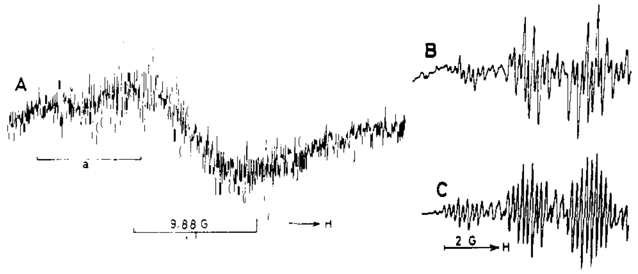
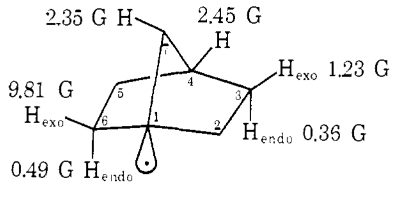


Figure 2. (A) ESR spectrum of the *exo,cis*-2,3-dideuterio-1-norbornyl radical at −122°; (B) computer averaged spectrum of part a of the spectrum in A; (C) low-field wing of the simulated spectrum.

Table I. INDO Hyperfine Coupling Constants (G) for the 1-Norbornyl Radical

Z, Å	H_{2exo}	H_{2endo}	H_{3exo}	H_{3endo}	H_4	H_7
0.0	7.67	0.19	0.31	0.17	2.46	1.23
0.1	9.67	0.30	0.73	0.12	3.64	1.36
0.2	11.91	0.47	1,44	0.10	5.68	1.44
0.3	14.42	0.67	2.64	0.12	8.99	1.43
Obsd	9.81	0.49	1.23	0.36	2.45	2.35

For assignments of the hyperfine splitting constants (hfsc) of the triplets, the *exo,cis*-2,3-dideuterio-1-norbornyl radical[7] was examined at −122°. Figure 2A shows a whole spectrum of the deuterated radical. Figure 2B shows the low field wing of the spectrum (underlined part a of Figure 2A) obtained by computer averaging of signals from 22 samples. The spectra were analyzed as three sets of doublets (9.88, 1.23, and 2.53 G) of three sets of 1:2:1 triplets (2.38, 0.53, and 0.34 G) further slit into two sets of 1:1:1 triplets (1.50 and 0.17 G). A comparison of these parameters with those of the 1-norbornyl radical shows that the hfsc's of 9.81 and 1.23 G belong to H_{2exo} and H_{3exo}, and that the hfsc's of 2.35, 0.49, and 0.36 G are due to H_7, H_{2endo}, and H_{3endo}. An inspection of a stereomodel suggests the assignment of the 9.81 G triplet to H_{2exo} and H_{6exo}. The proton hfsc's of the radical were calculated by an unrestricted Hartree-Fock method with INDO approximations[8] and are listed in Table I. INDO calculations were performed with the structure in which H_1 was simply taken off from the parent molecule[9] and also with structures in which C_1 was displaced Z Å (Z = 0.1, 0.2, and 0.3) inward along the C_1–H_1 bond axis in the parent hydrocarbon. From a comparison between the calculated and observed hfsc's, the experimental hfsc's are assigned as shown below.



In Figure 3 the β-proton hfsc's of the 1-norbornyl radical are plotted against values of $\cos^2 \theta$, where θ are the dihedral angles between the axis of the odd electron orbital on C_1 and the C_β–H_β bonds (approximated by the dihedral angles between the C_1–H_1 bond axis and the corresponding C–H bonds in norbornane[9]). The three experimental values of $a_\beta{}^H$ fit fairly well the line $a(H_\beta) = B\rho \cos^2 \theta$, where B = 16 G and ρ = 0.892 (INDO spin density on C_1 of the radical with Z = 0.1). This suggests that the $\cos^2 \theta$ relation for the β-proton hfsc's holds for the pyramidal 1-norbornyl radical although the coefficient B is about a quarter of the corre-