Synthesis and Conformational Studies of [7](2,6)Pyridinophanes

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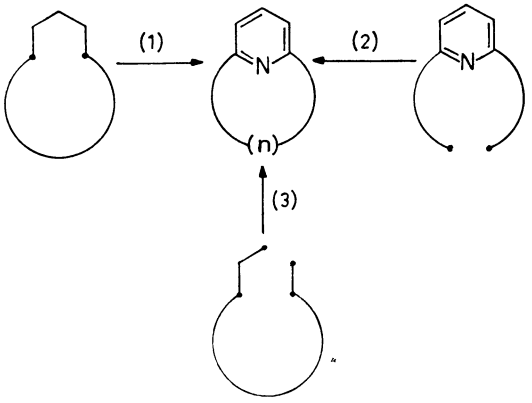
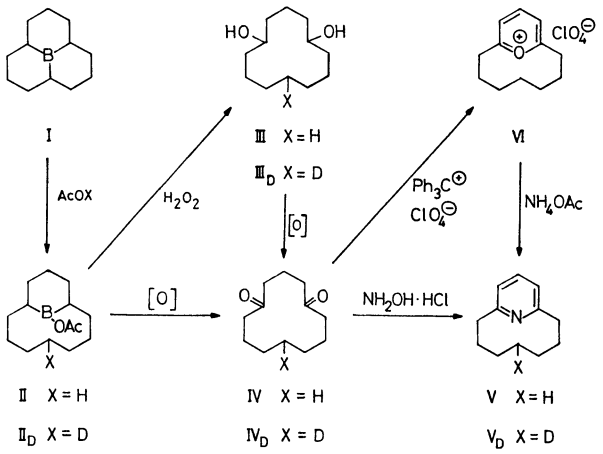
[7](2,6)Pyridinophane (V) and the 4-deuterio derivative (V_D) are prepared from cyclododecane-1,5-diones (IV and IV_D). Lithiation at the α-position of V and the subsequent derivation give 1-methoxycarbonyl- (VIII), 1-hydroxy- (IX), 1-oxo- (X), and 1,1-dimethoxy[7](2,6)pyridinophane (XI). A bathochromic shift in UV spectra is observed and ascribed to the nonplanarity of the pyridine ring. The protons on the C_4 of these heterophanes experience strong shielding due to the magnetic anisotropy of the respective pyridine rings. The shielding of the C_4 protons is more pronounced at low temperatures; this can be explained by assuming an extreme conformation such as XII. The temperature dependence of the NMR spectra is examined, and the energy barriers ($\Delta G_c^{\ddagger}$) for the conformational changes (XII⇄XII') are estimated to be 9.0 for V and 9.6 kcal/mol for XI. [7](2,6)Pyrylophanium perchlorate (VI) is prepared, in which a similar shielding effect of the pyrylium ring is observed.

The chemistry of uniquely strained meta- and paracyclophanes has been the subject of extensive research.[1] Particularly, their conformational changes have been investigated by means of temperature-variable NMR spectrometry.[2] The heteroaromatic analogs (heterophanes[3]) have recently attracted much attention, since two natural products, muscopyridine[4] and metacycloprodigiosin,[5] were characterized as the derivatives of [10](2,6)pyridinophane and [9](2,4)pyrrolophane respectively. In continuation of our studies of [8]-[6] and [9]heterophanes,[7] the present paper will describe [7](2,6)pyridinophanes with the shortest 2,6-polymethylene bridge ever reported.[8]



Scheme 1

Synthesis of [7](2,6)Pyridinophanes. Scheme 1 shows three possible ways of constructing [*n*](2,6)pyridinophanes: (1) the aromatization of 1,5-bifunctional cyclic compounds,[4,9] (2) the cyclization of 2,6-disubstituted pyridines,[10] and (3) pyridine-ring synthesis accompanying simultaneous bridge formation.[11,12] We have chosen the first approach and have utilized cyclododecane-1,5-dione (IV) as a precursor (see Scheme 2).



Scheme 2

The treatment of 9*b*-boraperhydrophenalene (I) with an equimolar amount of acetic acid and the subsequent Brown oxidation gave IV in a 30% yield.[13] The 1,5-diketone IV was also obtained by the oxidation of the corresponding diol III, which was in turn prepared by the oxidation of a partially-acetolyzed product II with alkaline hydrogen peroxide.

The heating of an alcoholic solution of IV and hydroxylamine hydrochloride gave [7](2,6)pyridinophane (V) in a 44% yield.[14] 4-Deuterated pyridinophane (V_D) was synthesized in a similar method.

1) a) R. W. Griffin, Jr., *Chem. Rev.*, **63**, 45 (1963); b) B. H. Smith, "Bridged Aromatic Compounds," Academic Press, New York (1964); c) T. Sato, *Kagaku no Ryoiki*, **23**, 672, 765 (1969); d) H. J. Reith and D. J. Cram, *J. Amer. Chem. Soc.*, **91**, 3505 (1969).

2) a) F. Vögtle, *Chem. Ber.*, **102**, 3077 (1969); b) F.A.L. Anet and M. A Brown, *J. Amer. Chem. Soc.*, **91**, 2389 (1969); c) D. H. Hefelfinger and D. J. Cram, *ibid.*, **92**, 1073 (1970).

3) For the nomenclature of this kind of compounds, see F. Vögtle and P. Neumann, *Tetrahedron Lett.*, **1969**, 5329.

4) K. Biemann, G. Büchi, and B. H. Walker, *J. Amer. Chem. Soc.*, **79**, 5558 (1957).

5) a) H. H. Wasserman, G. C. Rodgers, and D. D. Keith, *ibid.*, **91**, 1263 (1969); b) H. H. Wasserman, D. D. Keith, and J. Nadelson, *ibid.*, **91**, 1264 (1969).

6) H. Nozaki, T. Koyama, and T. Mori, *Tetrahedron*, **25**, 5357 (1969).

7) S. Fujita, T. Kawaguti, and H. Nozaki, This Bulletin, **43**, 2596 (1970).

8) A preliminary account of a portion of this work has appeared: H. Nozaki, S. Fujita, and T. Mori, *ibid.*, **42**, 1163 (1969).

9) A. T. Balaban, *Tetrahedron Lett.*, **1968**, 4643.

10) F. Vögtle, *Tetrahedron*, **25**, 3231 (1969).

11) A. T. Balaban, M. Gavat, and C. D. Nenitzescu, *ibid.*, **18**, 1079 (1962).

12) H. Gerlach and E. Huber, *Helv. Chim. Acta*, **51**, 2027 (1968).

13) The 1,5-diketone IV was previously prepared by fermentation technique. See G. S. Fonken, M. E. Herr, H. Murray, and L. M. Reineke, *J. Amer. Chem. Soc.*, **89**, 672 (1967).

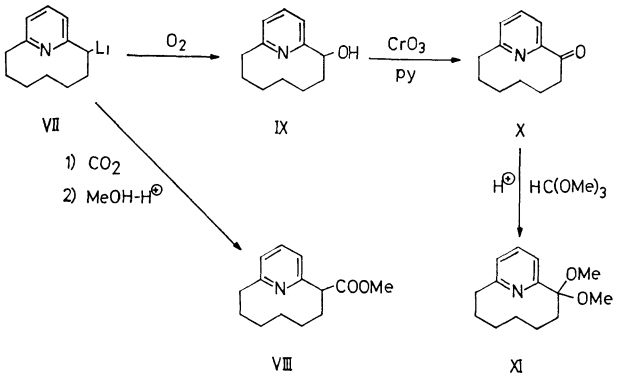
14) Treatment of 9-acetoxycyclododecane-1,5-dione with hydroxylamine hydrochloride gave no pyridinophane derivative. See S. Fujita and H. Nozaki, This Bulletin, **43**, 2995 (1970).

The treatment of I with acetic acid-*d*, oxidation with alkaline hydrogen peroxide, and final oxidation afforded cyclododecane-1,5-dione-9*d* (IV_D), the subsequent cyclization of which gave [7](2,6)-pyridinophane-4*d* (V_D). The C–D stretching absorption of V_D appeared at 2140 cm^{-1}.

The dehydration and hydride abstraction[15] of IV with trityl perchlorate gave [7](2,6)pyrylophanium perchlorate (VI). The treatment of the pyrylium salt VI with ammonium acetate yielded the pyridinophane V, which was identical with the sample prepared directly from IV.

The addition of *n*-butyllithium to a solution of V gave an orange-red solution of 1-lithio[7](2,6)pyridinophane (VII), which then afforded methyl [7](2,6)pyridinophane-1-carboxylate (VIII) upon quenching with carbon dioxide and subsequent esterification. The 1-lithio compound VII reacted with oxygen to form the corresponding alcohol, IX. The Cornforth oxidation of IX gave [7](2,6)-pyridinophan-1-one (X). The treatment of X with methyl orthoformate afforded the corresponding dimethyl acetal (XI).

The heating of V with hydrogen peroxide in acetic acid resulted in the recovery of the starting pyridinophane under conditions sufficient for [10](2,6)pyridinophane to afford the corresponding *N*-oxide in a fair yield.[4] This is due to a steric hindrance introduced by the shorter heptamethylene chain.



Scheme 3

UV and NMR Spectra of [7](2,6)Pyridinophanes and [7](2,6)-Pyrylophanium Perchlorate. The ultraviolet spectra of the [7](2,6)pyridinophanes are summarized in Table 1, together with those of the decamethylene homologs. Bathochromic shifts were observed upon a comparison of the UV bands (^1L_b bands) of [7]pyridinophanes with those of [10]-homologs. This effect can be explained by assuming a nonplanar pyridine ring bridged by the heptamethylene group.[1b]

Table 1. UV spectra of [*n*](2,6)pyridinophanes[a]

α-Substituent	[7](2,6)-Pyridinophane λ_{max}nm (log ε)	[10](2,6)-Pyridinophane[b] λ_{max}nm (log ε)
None	211.5 (3.87)	213 (3.82)
	272 (3.49)	267 (3.62)
–OH	211.5 (3.86)	212 (3.77)
	271 (3.53)	266 (3.54)
=O	236 (3.85)	236 (3.81)
	279 (3.56)	276 (3.66)

a) Ethanol was used as the solvent.
b) Reported in Ref. 4.

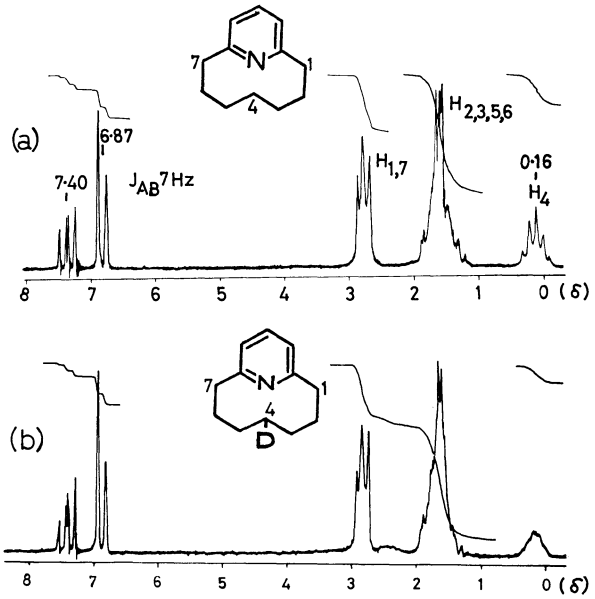


Fig. 1. NMR Spectra of V (a) and V_D (b) (in $CDCl_3$ at 24°C, 60 MHz. TMS as an internal standard).

The NMR spectra of V and V_D are shown in Fig. 1. The aromatic NMR signal of V showed a typical AB_2 pattern, one which resembled the splitting pattern of 2,6-lutidine very closely. The absorptions due to the heptamethylene protons of V were composed of three groups of multiplets (intensity: 4:8:2). In particular, two protons (a quintet at δ 0.16) of the heptamethylene chain were unexpectedly shielded in comparison with usual methylene group linking tetrahedral carbons. The signal at the high field can be ascribed to the C_4 protons, since the 4-monodeuterio-substituted derivative (V_D) showed the corresponding one proton peak which was broadened by a *geminal* H–D coupling. An inspection of the molecular models of V shows that H_a on C_4 is forced close to the π-cloud of the pyridine ring in an extreme conformation, XII. The apparently less crowded conformation, XIII, may be less favored, as the four C–C bonds linking C_2 through C_6 are all in an eclipsed conformation in XIII. The shielding effect in V is ascribed to the magnetic anisotropy of the pyridine ring.[16] Since the peak due to C_1 and C_7 (centered at δ 2.84) and that

15) M. Siemiatycki, *Bull. Soc., Chim. Fr.*, **1961**, 538.

16) The magnetic effect may consist of the diamagnetic ring current of the pyridine ring and/or the anisotropy of the nitrogen atom (Ref. 17). 2,6-Dithia[7]metacyclophane (XVI), in which such magnetic anisotropy of nitrogen atom was absent, was reported to exhibit the signal of C_4 protons at δ 0.45 (in dichloromethane-d_2). See Ref. 18.

17) a) V. M. S. Gil and J. N. Murrell, *Trans. Faraday Soc.*, **60**, 248 (1964); b) K. Sisido, K. Tani, and H. Nozaki, *Tetrahedron*, **19**, 1323 (1963); c) E. V. Donckt, R. H. Martin, and F. Greerts-Evrard, *ibid.*, **20**, 1495 (1964); d) F. Bohlmann, D. Schumann, and C. Arndt, *Tetrahedron Lett.*, **1965**, 2705; e) F. Bohlmann, D. Schumann, and H. Schulz, *ibid.*, **1965**, 173.

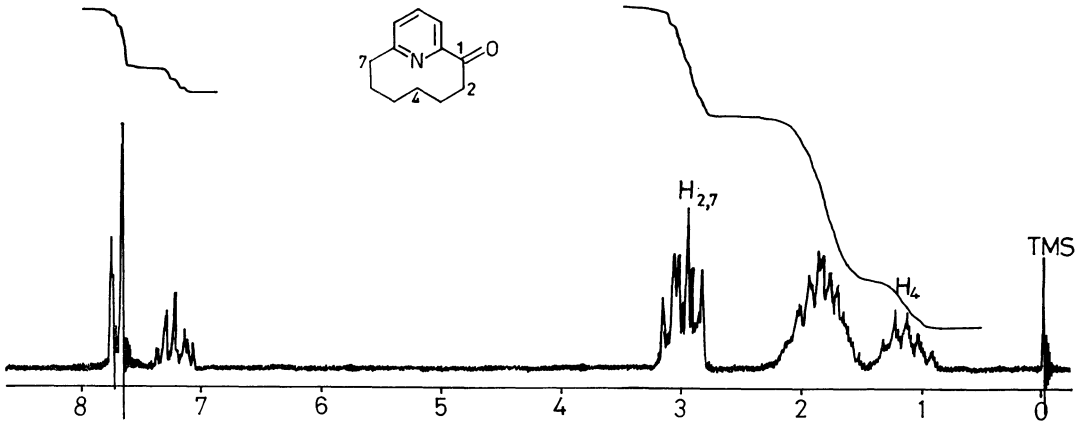


Fig. 2. NMR spectrum of X (in $CDCl_3$ at 24°C, 60 MHz).

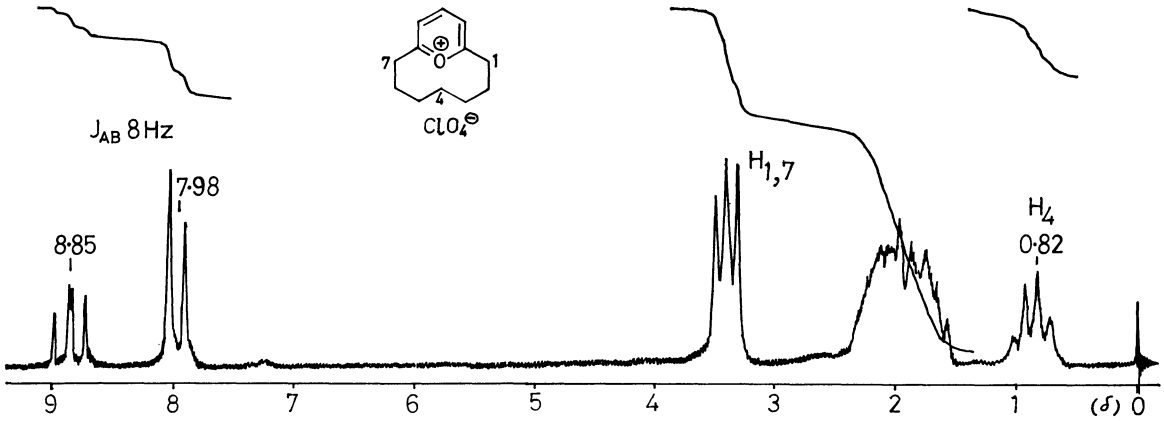


Fig. 3. NMR spectrum of VI (in CF_3COOH at 24°C, 60 MHz).

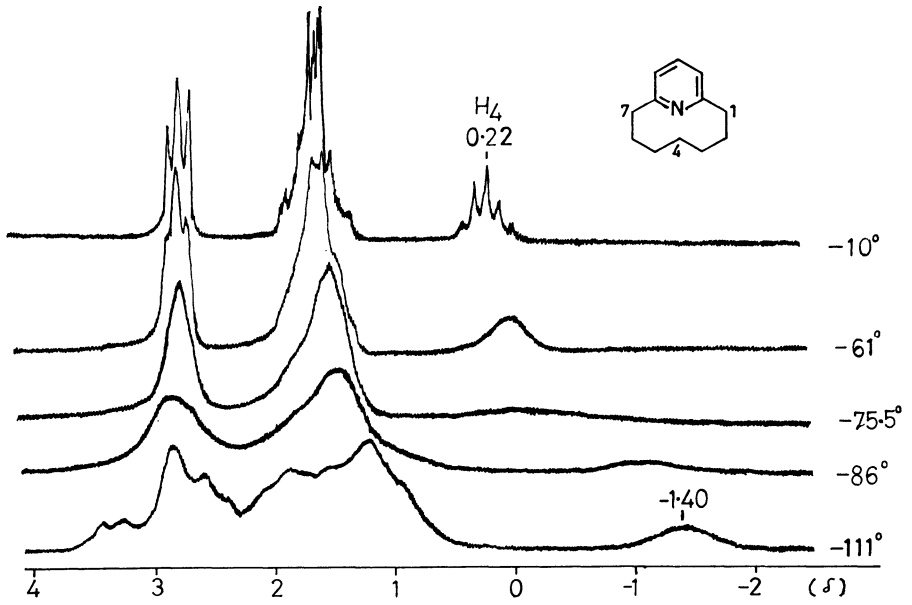
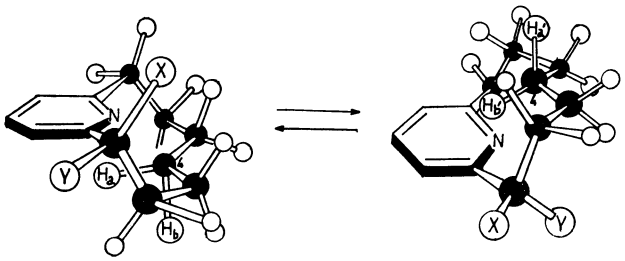


Fig. 4. Dynamic NMR spectra of the heptamethylene chain of V (in $CFCl_3$ at 60 MHz, TMS as an internal standard).

of the C_4 protons can be approximately regarded as a triplet and a quintet respectively, the heptamethylene chain of V possibly flips up and down (XII⇄XII') and its protons show average NMR signals at room temperature (*vide infra*).

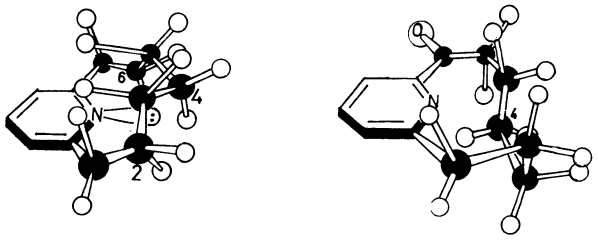
The incorporation of a trigonal α-carbon in X resulted in a drastic reduction of the diamagnetic shielding effect as compared with the cases of V, IX, and XI. The conjugation of the pyridine ring of X with the α-carbonyl group should favor a conformer such as XIV, in which C_4 protons are forced out of the center of the pyridine-ring field.

The NMR spectrum of VI (Fig. 3) showed an AB_2-type signal of pyrylium-ring protons. The C_4 methylene of VI was also shielded, appearing at δ 0.82. This is the first example of the diamagnetic shielding effect of a pyrylium ring.



XII XII'

a : X=Y=H
b : X=Y=OMe
c : X=H, Y=COOMe
d : X=H, Y=OH



XIII XIV

Conformational Changes of [7](2,6)Pyridinophanes. The temperature dependence of the NMR spectrum of V is shown in Fig. 4. The signal of the C_4 protons of V broadened at −75.5°C and reappeared at δ −1.40; this is consistent with the extreme conformation, XIIa. The low-field counterpart of the signal is possibly concealed behind the multiplets of the other methylenes.

The C_4 protons of the 1,1-dimethoxy derivative (XI) are also shielded by the magnetic anisotropy of the pyridine ring. Fig. 5 shows the temperature dependence of the NMR spectrum of XI. The signal of the C_4 protons of XI broadened at −62.5°C, and then that of methoxy methyl broadened at −77.0°C. The signals at δ 3.21 and δ 2.98 may be assigned to the *pseudo*-equatorial and *pseudo*-axial methoxy groups of XIIb respectively.

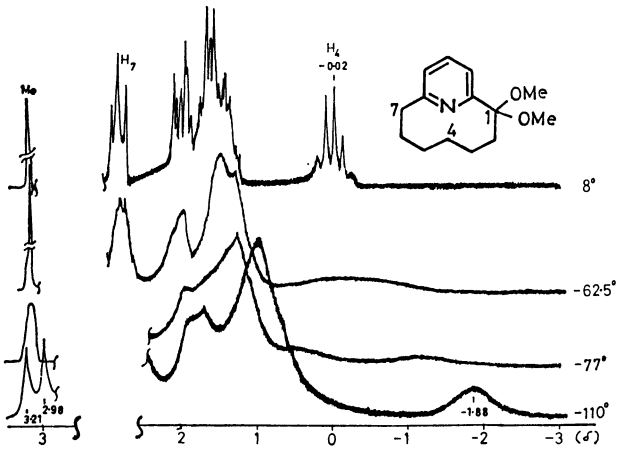


Fig. 5. Dynamic NMR spectra of the heptamethylene chain and methoxy of XI (in $CFCl_3$ at 60 MHz, TMS as an interanl standard).

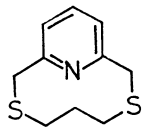
The estimated energy barriers for the conformational changes (XII⇄XII') of V and XI are shown in Table 2. The ΔG_c^* value reported for 2,6-dithia[7](2,6)pyridinophanes (XV)[10] is smaller than that of our [7](2,6)pyridinophanes. Moreover, even 2,6-dithia[7]metacyclophane (XVI)[18] has a ΔG_c^* value comparable to those of V and XI. The flexibility introduced by S–substitution may be ascribed to the fact that C–S bonds are longer than C–C bonds and C–S–C bending requires much less energy than does C–C–C bending.

Table 2. Energy barriers of the flipping of V and XI[a]

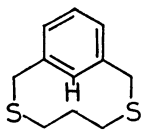
Compd.	Signal	T_c °C	$\Delta\nu$ Hz	k_c[b] sec^{-1}	ΔG_c^*[c] kcal/mol
V	C_4-protons	−75.5	194[d,e]	432	9.0
XI	C_4-protons	−62.5	223[d,f]	495	9.6
	MeO	−77.0	13.8[f]	30.6	10.0

a) The dynamic NMR spectra were determined on a JEOL-C-60-H spectrometer at 60 MHz, using $CFCl_3$ as the solvent and tetramethylsilane (TMS) as the internal standard. See Figs. 4 and 5.
b) $k_c=\pi\Delta\nu/\sqrt{2}$ (Ref. 19)
c) $\Delta G_c^*=2.303RT_c$ (10.319−log k_c+log T_c) (Ref. 19)
d) As the signal of the low-field counterpart of the C_4 protons was hidden behind those of other methylenes, $\Delta\nu$ was estimated by the equation, $\Delta\nu=2(\nu_{high}-\nu_{average})$, where ν_{high} was the chemical shift of the high field counterpart at a low temperature and where $\nu_{average}$ was the average chemical shift at room temperature. This approximation may be rough. The discussions in the text may thus be of limited, qualitative meaning. (The authors are grateful to one of the referees for his helpful criticism on this point.)
e) Determined at −111°C.
f) Determined at −110°C.

The two conformers of 1-monosubstituted pyridinophanes (XII and XII') are nonequivalent: the (Y) substituent occupies the *pseudo*-equatorial position in XII and the *pseudo*-axial position in XII'. The NMR spectrum of the 1-hydroxy derivative IX (Fig. 6) showed the multiplet of the two C_4 protons at δ 0.2—δ −0.3. This fact suggests that the conformational change (XIId⇄XIId') is as fast as the NMR time scale at room temperature. On the other hand, even at room temperature, the flipping (XIIc⇄XIIc') of the heptamethylene chain of VIII may be slow enough



XV
ΔG_c^* <10.2 kcal/mol
T_c<−60°C



XVI
ΔG_c^* 10.2 kcal/mol
T_c−50°C

18) R. H. Mitchell and V. Boekelheide, *ibid.*, **1969**, 2013.
19) a) G. Binsch, in "*Topics in Stereochemistry.*" ed. by E. L. Eliel and N. L. Allinger, Vol. 3, Interscience Publishers, New York (1968) pp. 97—192; b) I. C. Calder and P. J. Garratt, *J. Chem. Soc., B*, **1967**, 660; c) A. Allerhand, H. S. Gutowsky, J. Jonas, and R. A. Meinzer, *J. Amer. Chem. Soc.*, **88**, 3185 (1966).

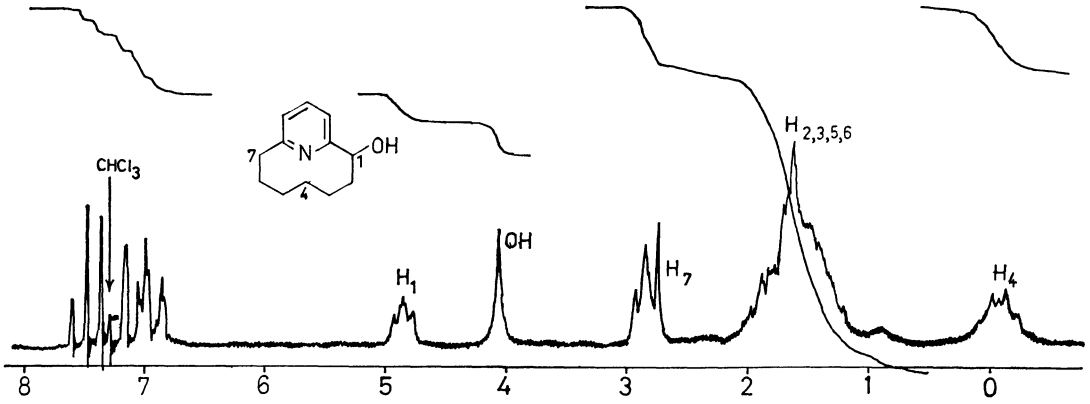


Fig. 6. NMR spectrum of IX (in $CDCl_3$ at 24°C, 60 MHz. TMS as an internal standard).

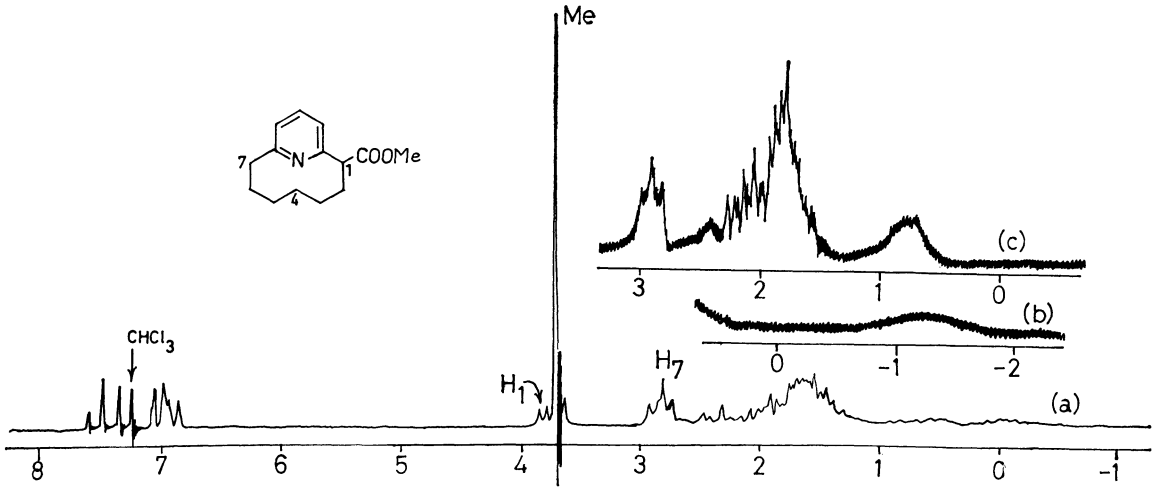


Fig. 7. NMR spectrum of VIII at 60 MHz: (a) in $CDCl_3$ at 24°C; (b) in $CDCl_3$ at −77°C; (c) in hexachlorobutadine at 140°C. TMS as an internal standard.

to induce the observed coalescence of the C_4 proton signal (Fig. 7). The signal of the two C_4 protons appeared at δ 0.70 at 140°C, corresponding to rapid exchange.

Experimental

All the melting points are uncorrected. The NMR spectra were determined on a JEOL C-60-H spectrometer at 60 MHz with deuteriochloroform, fluorotrichloromethane, and/or hexachlorobutadiene as the solvents. The mass spectra were obtained on a Hitachi RMU-6L spectrometer.

9b-Boraperhydrophenalene (I). A previous method of preparation[20] was modified as follows. A mixture of cyclododeca-1*t*,5*t*,9*c*-triene (42.0 g, 0.26 mol), the trimethylamine-borane complex[21] (19.0 g, 0.26 mol), tetrahydrofuran (THF) (50 m*l*), and cumene (110 m*l*) was added, under a nitrogen atmosphere over a 3-hr period, to cumene maintained at 135—150°C. After concentration *in vacuo*, the oily residue was distilled to give I (33.3 g, 73%); bp 122—128°C/16 mmHg.[20]

Cyclododecane-1,5-dione (IV). *(a) The Brown Oxidation of II*: A solution of I (22.2 g, 0.13 mol) and acetic acid (7.61 g, 0.13 mol) in benzene (150 m*l*) was refluxed at 100—110°C for 3 hr. After the evaporation of the solvent under a nitrogen atmosphere, the oily residue was dissolved in dry ether (120 m*l*) and a chromic acid solution (a mixture of sodium dichromate dihydrate (75.6 g), sulfuric acid (56.6 m*l*), and water 380 m*l*)) was added over a 1-hr period. The reaction mixture was extracted with ether, washed, and dried over sodium sulfate. Concentration and column chromatography on silica gel (ether-benzene 1:9) gave the diketone IV (7.47 g, 30%); mp 66.5—67.5°C (*n*-hexane, lit,[13] mp 64—65°C).

(b) The Jones Oxidation of III: The diol III (20.0 g, quantitative) was obtained from I (17.6 g, 0.10 mol) according to the method in Ref. 20a. A mixture of chromium (VI) oxide (11.2 g), sulfuric acid (9.6 m*l*), and water (30 m*l*) was added at 0°C to a solution of III (20.0 g, 0.10 mol) in acetone (700 m*l*). After filtration, 2-propanol (10 m*l*) and sodium hydrogen carbonate were added to the filtrate. The solid was filtered off, and the filtrate was concentrated and extracted with ether. Concentration and recrystallization then afforded IV (12.3 g, 63%).

[7](2,6)Pyridinophane (V). A mixture of IV (3.19 g, 16 mmol), hydroxylamine hydrochloride (2.84 g, 41 mmol), and absolute ethanol (40 m*l*) was heated at 150—175°C in a 100-m*l* autoclave for 15 hr. The reaction mixture was made strongly basic with concentrated sodium hydroxide, and, the ethanol was removed *in vacuo*. The residue was steam distilled. The distillate was extracted with ether and dried over sodium sulfate. Subsequent concentration and

20) a) G. W. Rotermund and R. Köster, *Ann. Chem.*, **686**, 153 (1965); b) H. C. Brown and W. C. Dickason, *J. Amer. Chem. Soc.*, **91**, 1226 (1969); c) N. N. Greenwood and J. H. Morris, *J. Chem. Soc.*, **1960**, 2922.

21) J. Bonham and R. S. Drago, *Inorg. Synth.*, **9**, 8 (1967).

distillation gave the pyridinophane V (1.26 g, 44%), bp 70—73°C/3 mmHg. IR (neat): 3060 2920, 2840, 1588, 1575, 1458, 1317, 1156, 788, 772, 745, and 723 cm^{-1}. The NMR and UV spectra are found in Fig. 1a and in Table 1 respectively. MS *m/e* (relative abundance): 175 (28), 147 (100), 146 (25), 123 (metastable peak for *m/e* 175→147), 121 (21), and 106 (22).

Found: C, 82.5; H, 9.9; N, 7.7%. Calcd for $C_{12}H_{17}N$: C, 82.2; H, 9.8; N, 8.0%.

[7](2,6)Pyrylophanium Perchlorate (VI). A mixture of IV (1.03 g, 5.3 mmol), trityl perchlorate (1.91 g, 5.6 mmol), and acetic acid (13 m*l*) was heated at 110—120°C for 10 min. After cooling, the reaction mixture was treated with dry ether (50 m*l*); the crystals thus precipitated (VI) (0.94 g, 65%) were collected by filtration. Mp 150°C (dec.). IR (Nujol): 3060, 1627, 1550, 1498, 1088 (broad), 868, and 798 cm^{-1}. The NMR of VI is shown in Fig. 3.

Found: C, 52.6; H, 6.0; Cl, 12.6%. Calcd for $C_{12}H_{17}ClO_5$: C, 52.1; H, 6.2; Cl, 12.8%.

[7](2,6)Pyridinophane (V) from VI. The pyrylium salt (VI) (0.31 g, 1.1 mmol) was added to a solution of ammonium acetate (0.56 g, 7.2 mmol) in acetic acid (10 m*l*). The mixture was then heated at 110°C for 5 min. After cooling, the reaction mixture was diluted with water (30 m*l*), neutralized with sodium carbonate, and extracted with ether. Drying (sodium sulfate) and concentration, followed by column chromatography on silica gel (benzene as an eluent), gave V (0.13 g, 66%); this was identical with the sample described above.

*Cyclododecane-1,5-dione-9*d (IV_D). A solution of I (7.76 g, 44 mmol) and acetic acid-*d* (2.71 g, 44 mmol) in benzene (50 m*l*) was heated at reflux for 2.5 hr and then cooled. To the mixture we then added, successively, methanolic potash (10 g potassium hydroxide in 100 m*l* methanol) and 30% aq. hydrogen peroxide (15 m*l*). After the evaporation of the solvent, the diol, III_D (6.05 g), was collected by filtration. The filtrate was extracted with ether and dried over sodium sulfate. Concentration afforded an additional crop of crystals (3.06 g). The total yield was 9.11 g (quantitative).

The oxidation of III_D (5.26 g, 26 mmol) gave cyclododecane-1,5-dione-9*d* (IV_D) (3.72 g, 72%); mp 58.5—59.0°C (*n*-hexane). IR (Nujol): 2150, 1715, 1216, 1186, 1134, 1120, 1046, 1008, 982, 891, 876, 853, 793, 780, 757, and 702 cm^{-1}. The D content as determined by MS: d_0, 8.3%; d_1, 90.6%; d_2, 1.1%.

*[7](2,6)Pyridinophane-4*d (V_D). A mixture of IV_D (1.45 g, 7.4 mmol), hydroxylamine hydrochloride (1.28 g, 18 mmol), and absolute ethanol (30 m*l*) was heated at 160—170°C in an autoclave. Work-up gave V_D as a colorless oil (0.54 g, 42%), bp 103°C (bath temperature)/7 mmHg. IR (neat): 3060, 2140, 1588, 1576, 1457, 1152, 996, 847, 780, 772, and 745 cm^{-1}. The D content as determined by NMR: 0.87 d_1/molecule. The NMR of V_D is found in Fig. Ib.

Attempted Synthesis of the N-*Oxide of V.* A mixture of V (0.15 g, 0.86 mmol), 30% aq. hydrogen peroxide (0.13 g) and acetic acid (2.0 m*l*) was heated at 80°C during 3 days. An additional 0.2 m*l* of peroxide was added in two portions during this time. The usual work-up resulted in the recovery of the starting pyridinophane.

Methyl [7](2,6)Pyridinophane-1-carboxylate (VIII). To THF (10 m*l*) there was added, at room temperature, a solution (5.0 m*l*) of *n*-butyllithium (0.74 N, 3.7 mmol) in *n*-hexane, and subsequently a solution of V (0.52 g, 3.0 mmol) in THF (10 m*l*). After sitrring under a nitrogen atmosphere for 35 min, the orange-red solution was poured onto dry ice and the solvent was evaporated to give lithium [7](2,6)-pyridinophane-1-carboxylate (0.97 g). A solution of the lithium salt in methanol (35 m*l*) was then saturated with dry hydrogen chloride and allowed to stand at room temperature for 2 days. The evaporation residue was dissolved in chloroform (15 m*l*), neutralized with aq. sodium carbonate, and dried over sodium sulfate. Concentration and dry column chromatography on silica gel (benzene as an eluent) afforded VIII as a colorless liquid (0.36 g, 52%), bp 84°C (bath temperature)/0.03 mmHg. IR (neat): 3060, 2930, 2850, 1738, 1588, 1576, 1457, 1233, 1190, 1150, 1066, 1017, 784, 778, 750, 726, and 710 cm^{-1}. MS *m/e* (relative abundance): 233 (34), 218 (100), 205 (57), 174 (53), 173 (23), 172 (35), 147 (25), 146 (46), 145 (31), 144 (43), 133 (77), 132 (33), and 119 (34). The NMR spectrum of VIII is shown in Fig. 7.

Found: C, 72.2; H, 8.1; N, 6.1%. Calcd for $C_{14}H_{19}NO_2$: C, 72.1; H, 8.2; N, 6.0%.

[7](2,6)Pyridinophan-1-ol (IX). To THF (10 m*l*) we added, successively, a solution (8.0 m*l*) of *n*-butyllithium (0.74 N) in *n*-hexane and a solution of V (0.54 g, 3.1 mmol) in THF (10 m*l*). After stirring under a nitrogen atmosphere for 35 min, the orange-red solution was cooled to −75°C and oxygen was passed through the solution for 1.5 hr. The reaction mixture was then treated with aq. ammonium chloride (5 m*l*), extracted with ether, and dried over potassium carbonate. Concentration and dry-column chromatography on silica gel (benzene and ether as eluents) afforded IX as white crystals (0.38 g, 65%); bp 95°C (bath temperature)/0.1 mmHg; mp 53.5—54.0°C (*n*-hexane). IR (KBr disk): 3250, 3060 (shoulder), 1596, 1576, 1467, 1293, 1264, 1087, 1072, 1050, 1000, 880, 853, 797, 786, 750, 723, and 700 cm^{-1}. MS *m/e* (relative abundance): 191 (100), 174 (22), 172 (23), 163 (51), 144 (36), 134 (76), 121 (41), 93 (27), 77 (26), and 65 (26). The NMR spectrum is found in Fig. 6, and the UV data, in Table 1.

Found: C, 75.4; H, 8.9; N, 7.3%. Calcd for $C_{12}H_{17}NO$: C, 75.4; H, 9.0; N, 7.3%.

[7](2,6)Pyridinophan-1-one (X). To cooled pyridine (10 m*l*) we added a solution of chromium(VI) oxide (1.00 g) in water (1 m*l*) and a solution of IX (0.31 g, 1.6 mmol) in pyridine (10 m*l*). The mixture was then allowed to stand overnight at room temperature, poured into water (200 m*l*), and extracted with ether. The combined extracts were thoroughly washed with water and dried over sodium sulfate. Subsequent concentration and dry-column chromatography on silica gel (benzene as an eluent) yielded the ketone X (0.17 g, 55%); mp 33.5—34.5°C (*n*-hexane). IR (KBr disk): 3060, 1693, 1585, 1455, 1446, 1345, 1310, 1263, 1247, 1216, 1141, 1061, 1029, 1017, 1001, 929, 851, 799, 760, 752, 730 cm^{-1}. MS *m/e* (relative abundance): 189 (47), 161 (13), 133 (100), 132 (26), 91 (19), and 89 (19). The NMR is shown in Fig. 2, and the UV data, in Table 1.

Found: C, 76.1; H, 7.9; N, 7.2%. Calcd for $C_{12}H_{15}NO$: C, 76.2; H, 8.0; N, 7.4%.

1,1-Dimethoxy[7](2,6)pyridinophane (XI). A mixture of X (0.15 g, 0.80 mmol), *p*-toluenesulfonic acid (0.24 g), methyl orthoformate (1.29 g), and methanol (30 m*l*) was heated under reflux for 2 hr and then neutralized after cooling with methanolic sodium hydroxide (1 g of sodium hydroxide in 5 m*l* of methanol). After the evaporation of the solvent, the residue was diluted with water (30 m*l*), extracted with ether, and dried over sodium carbonate. Subsequent concentration and distillation gave XI as a colorless liquid (0.16 g, 86%); 85°C (bath temperature)/0.06 mmHg. IR (neat): 3060, 1590, 1579, 1127, 1099, 1083, 1050, 810, 790, 757, 750, 728 cm^{-1}. MS *m/e* (relative abundance): 235 (1), 220 (38), 204 (15), 203 (19), 188 (100), 160 (32). The

NMR spectrum is shown in Fig. 5.

Found: C, 71.3; H, 9.0; N, 5.9%. Calcd. for $C_{14}H_{21}NO_2$: C, 71.5; H, 9.0; N, 6.0%.

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