BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 46, 1579—1580 (1973)

2,2-Dimethyl[7](2,6)pyridinophane and the Flipping of Its Heptamethylene Chain

Shinsaku Fujita, Kazuo Imamura, and Hitosi Nozaki
Department of Industrial Chemistry, Kyoto University, Sakyo-ku, Kyoto 606

(Received October 20, 1972)

The NMR spectra of heterophanes give useful information on the stereochemistry of the polymethylene chains incorporated.[1–8] The present report will deal with two 2,2-dimethyl derivatives of [7](2,6)pyridinophane (I).

The methylation of [7](2,6)pyridinophan-1-one (II) with potassium *t*-butoxide and methyl iodide gave 2,2-dimethyl[7](2,6)pyridinophan-1-one (III), the Huang Minlon reduction of which then afforded 2,2-dimethyl-[7](2,6)pyridinophane (IV).

At room temperature, the NMR spectrum of IV (Fig. 1) showed the singlet signal of 1-methylene at δ 2.58 and the singlet signal of *gem*-dimethyl at δ 0.84. The two-proton multiplet centered at δ 0.01 was assigned to the C-4 protons by analogy with [7]-(2,6)pyridinophane (I) itself.[5] In the most reasonable crown-type conformation (V) for IV, one proton (H_x) on C-4 was forced into the π-cloud and should be subject to anisotropic shielding due to the pyridine ring. At low temperatures (−87.5 °C and −111 °C), the two methyl groups, finding themselves in different environments, showed two broad singlets, at δ 1.04 and δ 0.56 respectively (Fig. 1). The AB spin system of 1-methylene showed an average singlet peak at room temperature, but a typical AB quartet at low temperatures. The C-4 protons were also found to exhibit a one-proton signal at δ −1.44.

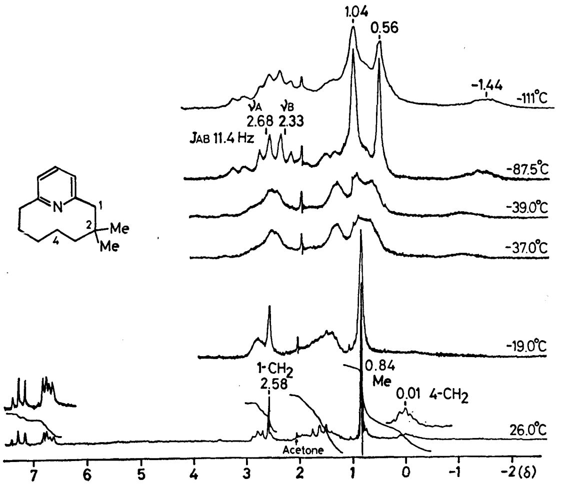
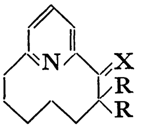
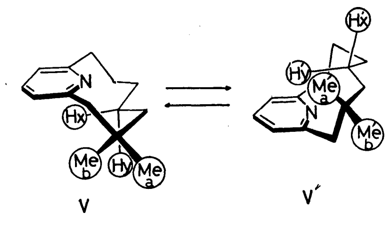


Fig. 1. The Dynamic NMR Spectra of IV (60 MHz in CFCl$_3$, TMS Internal Standard)

These facts indicated that the conformation of IV was frozen to the extreme conformer (V) at low temperatures. The estimated energy barriers ($\Delta G_c^{\neq}$) for the conformational change ($V \rightleftarrows V'$) are shown in Table 1, as well as the coalescence temperature (T_c). The NMR spectra of the ketone (III) was also temperature-dependent. The signal of the methyl groups appeared as a singlet (δ 1.21) at room temperature, broadened at the coalescence temperature (−61.0 °C) and then reappeared as two broad singlets (δ 1.26 and δ 1.06) at −94.0 °C). The estimated $\Delta G^{\neq}_c$ value is shown in Table 1.



I R=H, X=H$_2$
II R=H, X=O
III R=Me, X=O
IV R=Me, X=H$_2$



Experimental

2,2-Dimethyl[7](2,6)pyridinophan-1-one (III). A solution of [7](2,6)pyridinophan-1-one (II) (567 mg, 3.0 mmol)[5] in *t*-butyl alcohol (5 ml) was added to a solution (10 ml) of potassium *t*-butoxide (from 4.0 g of potassium). The mixture was heated under reflux for 1 hr. After cooling, methyl iodide (10 ml) was added in one portion, and then the mixture was heated at reflux for 19 hr. The reaction mixture was poured into water and extracted with ether. The combined ethereal extracts were dried over sodium sulfate and concentrated *in vacuo*. The concentrate was methylated once more with potassium *t*-butoxide (from 3.0 g of potassium) and methyl iodide (10 ml). The crude product was distilled, giving III as a colorless oil (441 mg, 68%); bp 77 °C/0.07 mmHg. IR (neat): 3075, 2960, 2927, 2875, 1679, 1590, 1574, 1474, 1458, 1440, 1379, 1354, 1322, 1298, 1245, 1208, 1147, 1070, 1020, 999, 911, 863, 819, 775, 752, 739, 664 cm^{-1}. MS *m/e* (relative abundance): 217 (37), 202 (11), 200 (11), 189 (20), 188 (10), 174 (16), 163 (15), 161 (10), 160 (14), 147 (10), 146 (18), 133 (12), 132 (11), 121 (12), 120 (12), 107 (30), 106 (64), 94 (10), 93 (100), 92 (10), 91 (11), 77 (11), 65 (17), 41 (26). UV $\lambda_{max}^{n\text{-hexane}}$ (log ε): 234.5 nm (3.79), 272 nm (3.50).

---

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

2) S. Fujita, T. Kawaguti, and H. Nozaki, *Tetrahedron Lett.*, **1971**, 1119.

3) H. Nozaki, T. Koyama, T. Mori and R. Noyori, *ibid.*, **1968**, 2181; *Tetrahedron*, **25**, 5357 (1969).

4) S. Fujita and H. Nozaki, *Yuki Gosei Kagaku Kyokai Shi*, **30**, 679 (1972).

5) a) S. Fujita and H. Nozaki, This Bulletin, **44**, 2827 (1971). b) H. Nozaki, S. Fujita, and T. Mori, *ibid.*, **42**, 1163 (1969).

6) S. Fujita, K. Imamura, and H. Nozaki, *ibid.*, **45**, 1881 (1972).

7) S. Fujita, S. Hirano, and H. Nozaki, *Tetrahedron Lett.*, **1972**, 403.

8) S. Fujita, Y. Hayashi, and H. Nozaki, *ibid.*, **1972**, 1645.

TABLE 1. THE ENERGY BARRIERS OF THE FLIPPING OF THE HEPTAMETHYLENE CHAINS[a]

Compound	Signal	T_c (°C)	$\Delta\nu$ (Hz)	J_{AB} (Hz)	k_c (sec^{-1})	$\Delta G^{\ddagger}_c$[b] (kcal/mol)
IV	*gem*-dimethyl	−37.0	28.8[c]	—	64.1[d]	11.8
	1-methylene	−39.0	18.1[c]	11.4[c]	45.9[e]	11.8
	C-4 protons	−19.0	174[c,f]	—	387[d]	11.9
I[g]	C-4 protons	−75.5	194[h,f]	—	432[d]	9.0
III	gem-dimethyl	−61.0	12.0[i]	—	26.7[d]	10.8

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 as the internal standard. See Fig. 1. b) $\Delta G^{\ddagger}_c = 2.303RT_c(10.319 - \log k_c + \log T_c)$ (Ref. 9).

c) Determined at −111 °C. d) $k_c = \pi\Delta\nu/\sqrt{2}$ (Ref. 9). e) $k_c = \pi\sqrt{\Delta\nu^2 + 6J_{AB}^2}/\sqrt{2}$ (Ref. 9).

f) As the signal of the low-field counterpart of the C-4 protons was concealed behind those of other methylenes, the $\Delta\nu$ value was estimated on the basis of the average chemical shift at room temperature and of the high-field shift at a low temperature.

g) Reported in Ref. 5. h) Determined at −111 °C. i) Determined at −94.0 °C.

Found: C, 77.5; H, 8.7; N, 6.2%. Calcd for $C_{14}H_{19}NO$: C, 77.4; H, 8.8; N, 6.5%.

2,2-Dimethyl[7](2,6)pyridinophane (IV). To a solution of potassium hydroxide (127 mg, 2.3 mmol) in triethylene glycol (5 ml), were added the ketone (III) (160 mg, 0.74 mmol) and hydrazine hydrate (80%, 0.5 ml). The mixture was heated under nitrogen at a reflux temperature for 2 hr. An additional portion of hydrazine hydrate (0.1 ml) was added during this period. The bath temperature was raised to 230 °C, and the excess hydrazine and water were distilled off over a 3-hr period. After the solution had been cooled, water was added to the mixture and the product was extracted with *n*-hexane. The combined extracts were dried over sodium sulfate. Concentration and distillation afforded the 2,2-dimethyl derivative (IV) (50 mg, 33%); bp 49°C/0.2 mmHg. IR (neat): 3070, 2955, 2930, 2870, 1590, 1579, 1459, 1383, 1362, 1325, 1239, 1138, 1086, 994, 862, 810, 798, 755, 747, 729, 710 cm^{-1}. MS *m/e* (relative abundance): 203 (38), 202 (17), 188 (34), 161 (13), 160 (18), 149 (15), 147 (44), 146 (18), 134 (11), 121 (23), 120 (80), 108 (10), 107 (100), 106 (19), 77 (14), 41 (18). UV $\lambda_{max}^{n\text{-hexane}}$ 214 (3.94), 269.5 (3.34).

Found: C, 82.6; H, 10.5; N, 6.8%. Calcd for $C_{14}H_{21}N$: C, 82.7; H, 10.4; N, 6.9%.

---

9) a) G. Binsch, "Topics in Stereochemistry," Vol. 3, ed. by E. L. Eliel and N. L. Allinger, Interscience Publishers, New York (1968), pp. 97—192. b) I. C. Calder and P. J. Garratt, *J. Chem. Soc., B*, **1967**, 660.