

## Lithium Complexation of Configurational Isomers of Tetra-aza Macrocycle containing 2,2'-Bipyridine. X-Ray Molecular Structure of the *trans*-Isomer of a Dibutyl Dicyano Macrocycle

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Two configurational isomers of a dicyano dibutyl tetra-azamacrocycle containing four pyridine rings were obtained. The *cis*-isomer showed a higher complexing ability toward Li<sup>+</sup> and Li<sup>+</sup>/Na<sup>+</sup> selectivity than did the *trans*-isomer. The *trans*-isomer, the structure of which was established by X-ray analysis, displayed marked spectral changes due to significant conformational changes upon complexation.

Crown ethers are known to form stable complexes with alkali and alkaline earth metal ions. Maximum stability is usually observed when the optimum macrocyclic ring size is reached for a particular metal ion. Lithium ion is known to be complexed by the 12–19-membered crown ethers, and recently Olsher reported that dibenzo-14-crown-4 is a particularly stable and selective ionophore for Li<sup>+</sup>.<sup>1</sup> We recently reported a synthesis of a new type of conjugated macrocycle (**2**), containing pyridin-2-yl-[pyridin-2(1*H*)-ylidene]acetonitrile structures, and several of its alkylated derivatives (**4**)–(**6**).<sup>2,†</sup> Exposure of dibutyl macrocycle (**6**) to lithium chloride solution resulted in the formation of lithium complex (**7**) with a concomitant and remarkable colour change due to the change of the conjugated system, where we have shown that the N<sub>4</sub>-donor macrocycle formed a stable and selective complex with lithium ion, although the co-ordination force of nitrogen toward alkali and alkaline earth metal ions is known to be much weaker than that of the oxygen of crown ethers. Dibutyl dicyano macrocycle (**5**), which is a precursor of macrocycle (**6**), has two configurational isomers (**5a**) and (**5b**). In this paper, we report the separation of the two isomers of macrocycle (**5**) and the properties of these isomers as aza-crown ether-type compounds.

Treatment of 6,6'-dibromo-2,2'-bipyridine (**1**) with  $\alpha$ -cyanoacetamide and sodium hydride in dimethylformamide (DMF) gave a mixture of dicyano macrocycle (**2**) and open-chain dibromo compound (**3**). Reaction of compound (**2**) with butyl iodide and sodium hydride in DMF gave a mixture of monoalkylated product (**4**) and the *trans* and *cis* isomers of macrocycle (**5**) as we tentatively reported previously.<sup>2</sup> The products were successfully separated by silica gel column chromatography with chloroform–diethyl ether–hexane (2:2:1, v/v/v) as eluant. Recrystallization of *trans*-isomer (**5a**) from the chloroform–ether–hexane system afforded a suitable crystal for X-ray analysis.

*Crystal Data for Isomer (5a)*.—C<sub>32</sub>H<sub>30</sub>N<sub>6</sub>, *M* = 498.63, triclinic, space group *P* $\bar{1}$ , *a* = 9.008(2), *b* = 12.503(2), *c* = 6.562(3) Å,  $\alpha$  = 91.84(3),  $\beta$  = 106.83(3),  $\gamma$  = 102.76(1)°, *V* = 686.2(4) Å<sup>3</sup>, *Z* = 1, *F*(000) = 264, *D*<sub>x</sub> = 1.207 g cm<sup>-3</sup>, (*M*<sub>o</sub>-*K*<sub>α</sub>) = 0.69 cm<sup>-1</sup>.

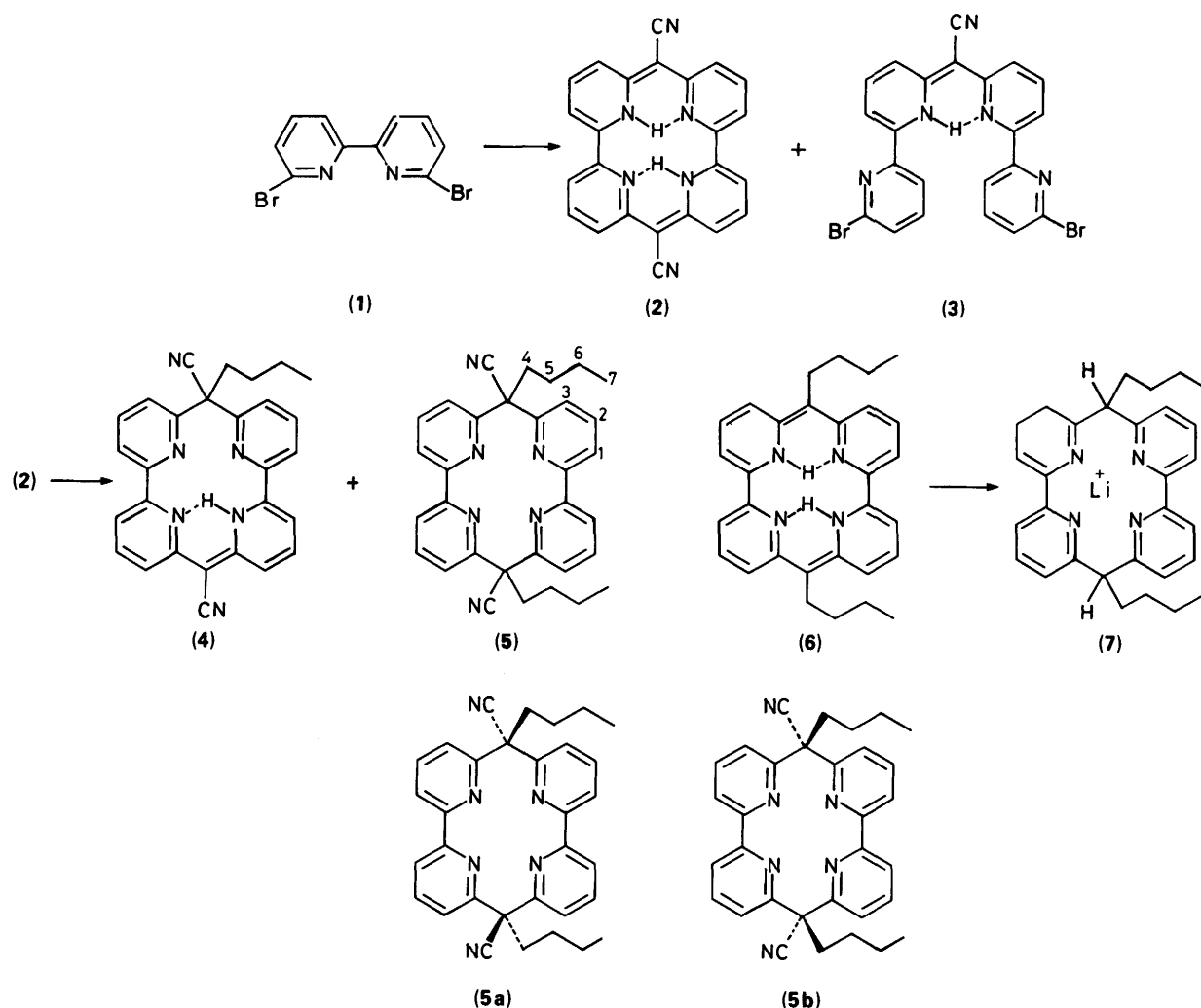
*X-Ray Structure Determination of Compound (5a)*.—A

colourless prismatic crystal of dimensions 0.2 × 0.3 × 0.7 mm, grown from the mixed solvent system chloroform–ether–hexane, was mounted on a Rigaku AFC-5 diffractometer which used graphite-monochromatized Mo-*K*<sub>α</sub> radiation ( $\lambda$  = 0.710 73 Å). Cell parameters were determined using least-squares refinement on 20 accurately centred reflections (30° < 2 $\theta$  < 37°). Intensity measurements:  $\theta$ –2 $\theta$  scan technique; scan speed 4° min<sup>-1</sup> in 2 $\theta$ ; scan width (1.0 + 0.5 tan  $\theta$ )° in  $\theta$ ; counting time of background 3.75 s. Three standard reflections, –442, 6-61, and 17-3, monitored every 100 reflections, showed an intensity variation < ±3%. In the *hkl* index range from –11, –17, 0 to 11, 17, 9 (2 $\theta$  ≤ 60°), 4 341 reflections were collected; 4 014 were unique, and 1 929 were used in the analysis [*F*<sub>0</sub> ≥ 3 $\sigma$ (*F*<sub>0</sub>)]. All the non-H atoms were obtained from direct methods (MULTAN84).<sup>3</sup> Block-diagonal least-squares refinement with anisotropic thermal parameters was used for non-H atoms, with 217 parameters. The function minimized was  $\sum w(|F_o| - k|F_c|)^2$ , where  $w = [\sigma^2(F) + 0.001|F_o| + 0.001|F_o|^2]^{-1}$ . H-atom positions were obtained from a difference map, *B* = 4.0 Å<sup>2</sup>, and fixed positional parameters were added to the final cycle. *R*, *wR*, and *S* are 0.059, 0.071, and 1.32, respectively, and ( $\Delta/\sigma$ )<sub>max</sub> = 0.79. In the final difference map,  $\Delta\rho$  excursions were 0.23 and –0.20 e Å<sup>-3</sup>. Scattering factors were taken from International Tables for X-Ray Crystallography.<sup>4</sup> Computations were performed using a Panafacom U-1200 IIA with the Rigaku RASA-5P program package system and a HITAC M-680H at the Computer Centre of the University of Tokyo with the UNICS program system (local version).<sup>5</sup>

The final positional and equivalent thermal parameters of non-H atoms are given in Table 1. Bond distances and angles are shown in Figure 1 with the crystallographic atomic numbering scheme. The conformation of molecule (**5a**) is illustrated in Figure 2 by an ORTEP drawing.†

† Newkome *et al.* have also synthesized a macrocycle containing pyridin-2-yl[pyridin-2(1*H*)-ylidene]acetonitrile units: G. R. Newkome, Y. J. Joo, and F. R. Fronczek, *J. Chem. Soc., Chem. Commun.*, 1987, 854.

‡ Supplementary data (see section 5.6.3 of Instructions for Authors, in the January issue. Lists of anisotropic thermal parameters and H-atom parameters are available on request from the Cambridge Crystallographic Data Centre.



Scheme 1.

**Table 1.** Fractional atomic co-ordinates for non-H atoms of compound (5a).

	x	y	z
N(1)	0.124 5(3)	-0.078 8(2)	-0.144 0(4)
N(2)	0.170 5(3)	0.140 0(2)	0.044 4(4)
N(3)	-0.174 8(4)	-0.415 8(2)	-0.558 6(5)
C(1)	-0.068 3(3)	-0.255 6(2)	-0.246 8(5)
C(2)	0.046 2(3)	-0.158 1(2)	-0.303 2(5)
C(3)	0.062 3(4)	-0.152 3(3)	-0.507 4(5)
C(4)	0.168 2(4)	-0.061 2(3)	-0.543 0(5)
C(5)	0.251 4(4)	0.021 5(3)	-0.379 3(6)
C(6)	0.220 9(3)	0.010 9(2)	-0.183 3(5)
C(7)	0.284 2(3)	0.102 6(2)	-0.006 3(5)
C(8)	0.445 5(4)	0.145 2(3)	0.103 1(6)
C(9)	0.486 9(4)	0.226 3(3)	0.271 4(6)
C(10)	0.369 0(4)	0.263 5(3)	0.326 7(6)
C(11)	0.213 1(3)	0.218 3(2)	0.208 5(5)
C(12)	-0.129 6(4)	-0.346 3(3)	-0.426 0(6)
C(13)	0.020 3(4)	-0.300 6(2)	-0.039 9(5)
C(14)	0.156 0(4)	-0.350 8(3)	-0.062 5(5)
C(15)	0.249 1(4)	-0.382 6(3)	0.148 3(6)
C(16)	0.379 4(4)	-0.437 8(3)	0.128 9(7)

The molecule is centrosymmetric. All the bond distances and angles are within normal values except for the C(6)–C(7) length

of 1.494(5) Å, the value of which corresponds to a bond order between 1 and 2. The pyridine ring moieties are nearly planar [maximum deviation from the least-squares planes is 0.03 Å for C(6)]. The dihedral angles between pyridine rings are 61.5° [across the C(6)–C(7) bond] and 75.0°, respectively. The torsion angle N(1)–C(6)–C(7)–N(2) is 58.9°.

It is worth noting that the two pyridine rings of each of the bipyridyl moieties of compound (5a) are twisted, with N-lone pairs pointing successively above, below, below, and above the plane of the four nitrogen atoms as illustrated in Scheme 1. It can be also seen from Figure 2 that the alkyl groups are relatively vertical and that the cyano groups are relatively horizontal to the plane.

UV absorption spectra were quite different for the two isomers (Figure 3). The  $\lambda_{\max}$ -value of the *trans*-isomer was at 266 nm, suggesting that the conformation of the *trans*-isomer in solution is similar to that in the crystal state. On the other hand the  $\lambda_{\max}$ -value of the *cis*-isomer was at 281 nm, which is at considerably higher wavelength than that of the *trans*-isomer. This may be due to the double-bond character of the 2,2'-bond in the bipyridyl moiety in contrast to the *trans*-isomer. Interestingly, the UV spectra of these isomers in methanol became quite similar when they were exposed to lithium chloride.

The experimental observation described above may show that the two pyridine rings of the bipyridine moiety of the *trans*-

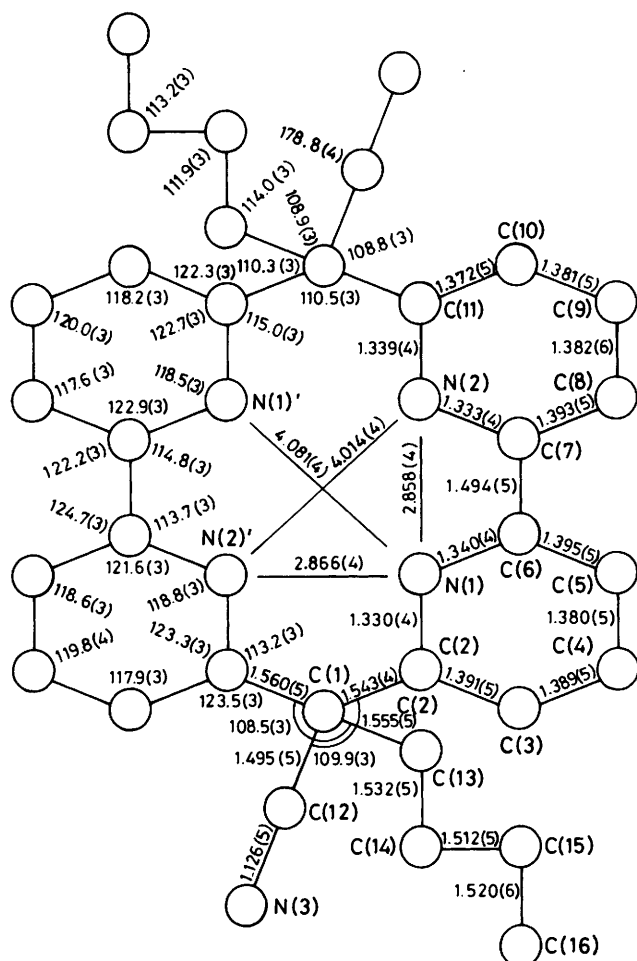


Figure 1. Atomic distances (Å) and angles (°) in molecule (5a) with the crystallographic numbering scheme.

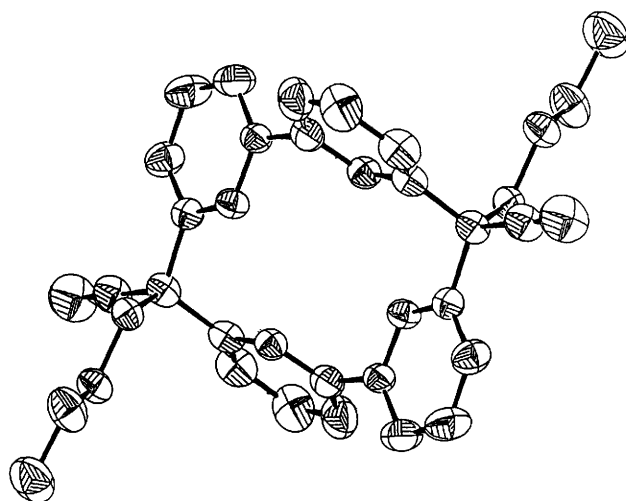


Figure 2. ORTEP drawing of molecule (5a).<sup>6</sup> H-Atoms have been omitted for clarity. Thermal ellipsoids are drawn at the 50% probability level.

isomer (5a) become coplanar by complexation with lithium ion as shown in Scheme 2.

Table 2 shows the <sup>1</sup>H NMR chemical shifts of the two isomers (5a) and (5b) and their Li complexes which can be easily obtained by shaking solutions of isomers (5) in CDCl<sub>3</sub> with

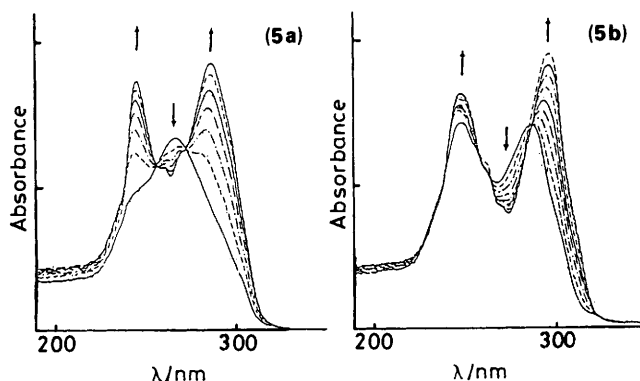


Figure 3. UV spectral changes of isomers (5a) and (5b) when coordinated with LiCl in CHCl<sub>3</sub>. Arrows indicate the direction of the changes in absorption.

solid LiCl. The  $\alpha$ -methylene protons (4-H) of the butyl groups of isomer (5b) showed a remarkable downfield shift on complexation as compared with those of isomer (5a), indicating that these protons were most influenced by the complexed ion. The temperature-dependent <sup>1</sup>H NMR spectrum of the lithium complex of isomer (5a) strongly supported the square pyramidal unsymmetrical structure shown in Scheme 2, in which the signal due to the methylene protons nearest to the macroring was split below -40 °C (Figure 4). Two different types of methylene protons were observed at low temperatures, under which conditions conformational inversion of the Li complex was sufficiently slow and the unsymmetrical square pyramidal structure was fixed. No split was observed in the case of the metal-free *trans*-isomer or the lithium complex of the *cis*-isomer even below -60 °C. Such square pyramidal geometry with a 'V'-shaped conformation of the ligand was observed by Choham *et al.* in the complex between dibenzo-14-crown-4 and LiSCN.<sup>7</sup>

The stability constants in methanol were determined by the method of Rose and Drago<sup>8</sup> from the UV spectral changes (Table 3). For both isomers, the *K*-values of the sodium complexes are smaller than those of the lithium complexes. The *cis*-isomer, in particular, showed much higher complexing ability and selectivity than did the *trans*-isomer. The lower binding ability in isomer (5a) can be ascribed in part to an apparent increase in strain during complexation, because one cyano group becomes vertical.

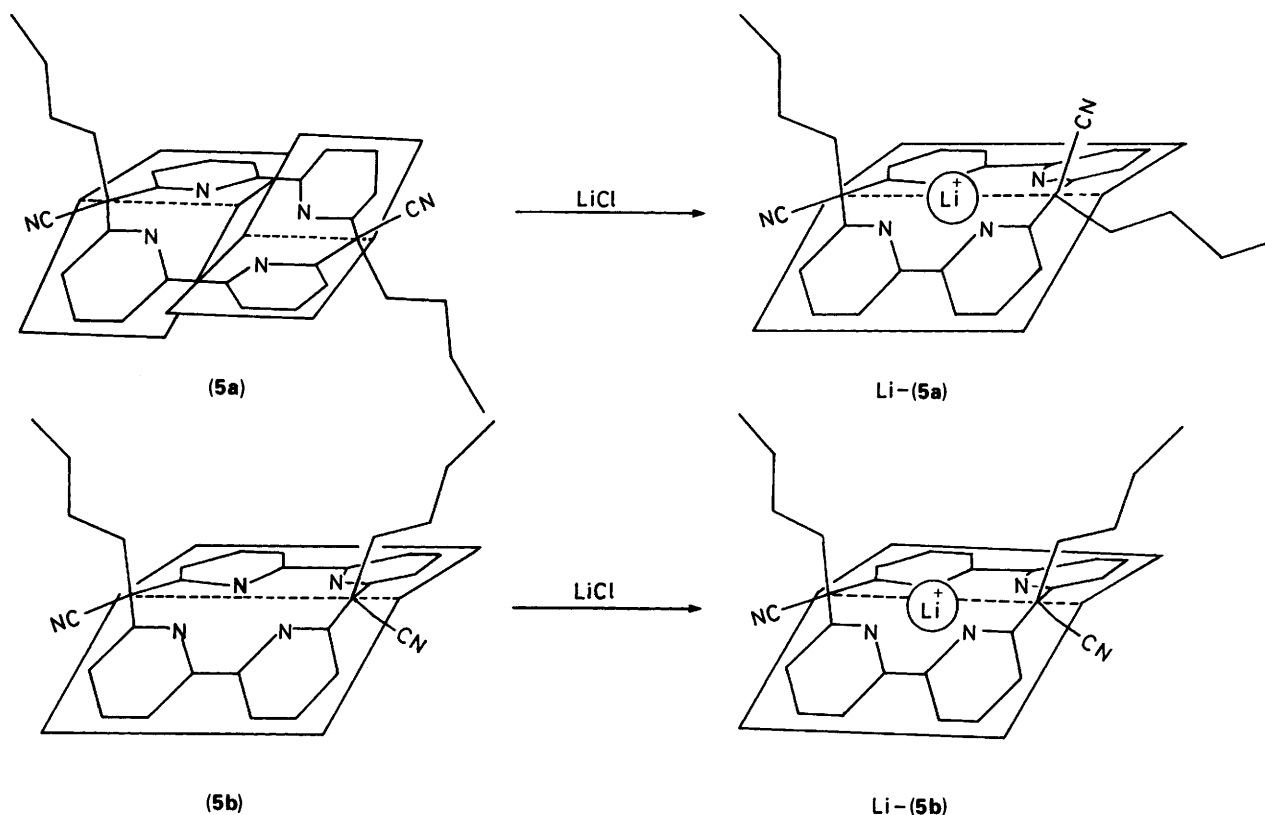
These results might help us in designing a more selective ionophore for lithium, because by changing the structure of substituents, the direction of N-lone pairs and the cavity size might be controlled.

### Experimental

IR spectra were measured for KBr discs with a JASCO IRA-1 spectrophotometer. Absorption spectra were recorded with a Shimadzu UV-240 spectrophotometer. <sup>1</sup>H NMR spectra were measured for solutions in CDCl<sub>3</sub> with a JEOL-JNM GX-400 NMR instrument with SiMe<sub>4</sub> as internal reference. The mass spectra were obtained by direct insertion into the ion source of a Hitachi RMU-7L high-resolution mass spectrometer. Light petroleum refers to the fraction boiling in the range 35–60 °C.

**6,6'-Dibromo-2,2'-bipyridine (1).**—Compound (1) was prepared by the literature method.<sup>9</sup>

**Dicyano Macrocycle (2).**—The apparatus was swept with N<sub>2</sub> during the course of the reaction. A dispersion of 60% sodium hydride in mineral oil (9.6 g) was placed in a 500 ml four-necked



Scheme 2. Schematic representation of complexation of isomers (5a) and (5b) with LiCl.

Table 2.  $^1\text{H}$  NMR shifts<sup>a</sup> of isomers (5a) and (5b), and of their Li-complexes Li-(5a) and Li-(5b).

Compd.	1-H	2-H	3-H	4-H	5-H	6-H	7-H
(5a)	7.95	7.82	7.54	2.40	1.18	0.74	
(5b)	7.76	7.70	7.63	3.05	1.36	0.85	
Li-(5a)	8.16	8.08	7.94	2.43	1.12	1.04	0.70
Li-(5b)	8.16	8.07	8.11	3.51	1.49	1.36	0.84

<sup>a</sup> In  $\text{CDCl}_3$ , relative to  $\text{SiMe}_4$ .

Table 3. Stability constants of isomers (5) in methanol at 25 °C.

	LiCl	NaCl	Li/Na
(5a)	$7.9 \times 10^3$	$1.3 \times 10^2$	61
(5b)	$2.0 \times 10^6$	$4.0 \times 10^2$	5 000

flask fitted with a reflux condenser, mechanical stirrer, pressure-compensated dropping funnel, and thermometer. After the mineral oil had been removed by washing of the dispersion with dry light petroleum ( $3 \times 50$  ml), anhydrous DMF (100 ml) was added at room temperature and the mixture was cooled to 5 °C. To the cooled dispersion was added dropwise a solution of  $\alpha$ -cyanoacetamide (10.08 g, 0.12 mol) in DMF (50 ml), whereupon hydrogen gas evolved vigorously. After the evolution of hydrogen ceased, a suspension of compound (1) (9.42 g, 0.03 mol) in DMF (100 ml) was added dropwise. The reaction temperature was raised slowly to 120 °C and was maintained at this temperature for 6 h. The mixture was cooled to 80 °C and water (25 ml) was added. The resulting red needles were collected by suction filtration, washed successively with water

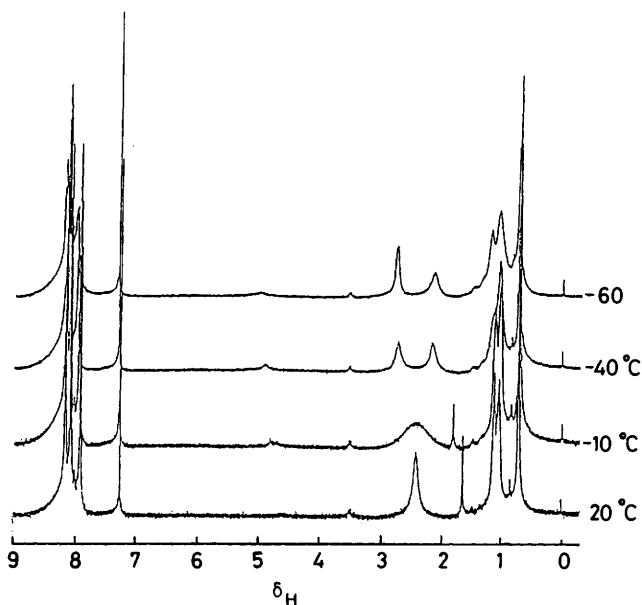


Figure 4.  $^1\text{H}$  NMR spectral change of Li-(5a) in  $\text{CDCl}_3$  (400 MHz).

and acetone, and dried to give the pure product (2) (0.832 g, 14.4%), m.p. > 360 °C;  $\nu_{\text{max}}$  2 180  $\text{cm}^{-1}$  (CN);  $m/z$  386 ( $M^+$ ) and 193 ( $M^{2+}$ ) (Found: C, 74.3; H, 3.4; N, 21.8. Calc. for  $\text{C}_{24}\text{H}_{14}\text{N}_6$ : C, 74.6; H, 3.7; N, 21.7%).

The resultant filtrate was concentrated under reduced pressure. Open-chain compound (3) was isolated from the residual solid by column chromatography (alumina; chloroform) in 60% yield: m.p. 210 °C (red needles);  $\nu_{\text{max}}$  2 189  $\text{cm}^{-1}$  (CN);  $m/z$  505, 507, and 509 ( $M^+$ );  $\delta_{\text{H}}$  16.0 (NH) (Found: C, 53.0; H, 2.8; N, 13.3.  $\text{C}_{22}\text{H}_{13}\text{Br}_2\text{N}_5$  requires C, 52.1; H, 2.6; N, 13.8%).

*Synthesis of the Monobutyl and Dibutyl Dicyano Macrocycles.*—A dispersion of 60% sodium hydride in mineral oil (0.4 g) was placed in a 20 ml, three-necked flask in an atmosphere of nitrogen. After the mineral oil had been removed by washing of the dispersion with dry light petroleum ( $\times 3$ ), anhydrous DMF (20 ml) was added at room temperature, followed by compound (2) (0.2 g,  $5.17 \times 10^{-4}$  mol), and the mixture was agitated ultrasonically for 1 h, whereupon hydrogen gas evolved and the colour of the reaction mixture turned red. Butyl iodide (2 ml) was added and the reaction temperature was raised to 110 °C and maintained at this temperature for 3 h. The mixture was poured in water and the resulting solid was collected by suction filtration, washed with water, and dried. Silica gel column chromatography with chloroform–ether–hexane (2:2:1, v/v/v) as eluant gave *trans*-dibutyl dicyano macrocycle from the first fraction, *cis*-dibutyl dicyano macrocycle from the second fraction, and monobutyl dicyano macrocycle from the third fraction.

Monobutyl dicyano macrocycle (4). Red needles (65%), m.p. 214 °C. The IR spectrum showed two nitrile absorptions, at  $2240\text{ cm}^{-1}$  (non-conjugated) and  $2180\text{ cm}^{-1}$  (conjugated).

*trans*-Dibutyl dicyano macrocycle (5a). Prisms (17%), m.p. > 360 °C;  $\nu_{\text{max}} 2240\text{ cm}^{-1}$ .

*cis*-Dibutyl dicyano macrocycle (5b). Needles (15%), m.p. > 360 °C;  $\nu_{\text{max}} 2240\text{ cm}^{-1}$ .

#### Acknowledgements

This work was supported by Grant-in-Aid for Special Project Research from the Ministry of Education.

#### References

- 1 U. Olsher, *J. Am. Chem. Soc.*, 1982, **104**, 4006.
- 2 S. Ogawa, R. Narushima, and Y. Arai, *J. Am. Chem. Soc.*, 1984, **106**, 5760.
- 3 P. Main, G. Germain, and M. M. Woolfson, 1984, MULTAN84, A System of Computer Programs for the Automatic Solution of Crystal Structures from X-Ray Diffraction Data, Univ. of York, England, and Louvain, Belgium.
- 4 International Tables for X-Ray Crystallography, Kynoch Press, Birmingham, 1974, vol. IV (present distributor Kluwer Academic Publishers, Dordrecht).
- 5 Universal Crystallographic Computation Program System, ed. T. Sakurai, The Crystallographic Society of Japan, Tokyo, Japan, 1967.
- 6 C. K. Johnson, ORTEPII. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee, 1976.
- 7 G. Choham, W. N. Lipscomb, and U. Olsher, *J. Chem. Soc., Chem. Commun.*, 1983, 208.
- 8 N. J. Rose and R. S. Drago, *J. Am. Chem. Soc.*, 1959, **81**, 6138.
- 9 J. E. Parks, B. E. Wagner, and R. H. Holm, *J. Organomet. Chem.*, 1973, **56**, 53; G. R. Newkome, A. Nayak, F. Fronczek, T. Kawato, H. C. R. Taylor, L. Meade, and W. Mattice, *J. Am. Chem. Soc.*, 1979, **101**, 4472.

Paper 9/03017D

Received 17th July 1989

Accepted 29th January 1990