Effects of Sodium Ions on the Molecular Dynamics of Bis(aza-15-crown-5)thiuram Disulphide *

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Oxidative dimerization of sodium (aza-15-crown-5) dithiocarbamate affords bis(aza-15-crown-5)-thiuram disulphide, which exhibits dramatic changes in the dynamic ^{13}C-{^1H} n.m.r. spectrum upon addition of sodium ions.

Compounds which contain both a crown ether moiety and a suitable transducer to detect ion binding are a topic of current interest, because of their potential biomedical applications. Several papers have appeared describing work in which ion binding is coupled to redox energies,[1] optical absorbances,[2] and acidities.[3] We have undertaken the syntheses of new dithiocarbamate and thiuram disulphide molecules incorporating crown ether moieties, as well as transition-metal complexes of crown ether dithiocarbamate ligands. We have begun to examine the various physicochemical changes of these new crown ether molecules as a function of binding to alkali-metal cations. Here we report dramatic changes in the molecular dynamics of bis(aza-15-crown-5)thiuram disulphide upon addition of sodium ions, as observed by dynamic n.m.r.

Experimental

Reaction of aza-15-crown-5[4] (3.20 g) with an aqueous solution of NaOH (0.58 g) and CS_2 (1.0 cm^3) at 0 °C for 6 h yielded, after work-up, a white powder of the sodium (aza-15-crown-5) dithiocarbamate (**2**) (3.17 g, 68%) (Found: C, 41.4; H, 6.5; N, 4.35; S, 19.6. $C_{11}H_{20}NaO_4S_2$ requires C, 41.6; H, 6.35; N, 4.4; S, 20.2%); $\lambda_{max.}(H_2O)$: 276(sh) (ε 5 200), 257 (5 900), and 204 nm (7 900 dm^3 mol^{-1} cm^{-1}); $\nu_{max.}$ at 1 479s cm^{-1} (C–N) (CsI pellet); ^1H n.m.r. (300 MHz, D_2O): δ 4.11 [4 H, t, *J*(HH) 6 Hz, 2 NCH_2], 3.76 [4 H, t, *J*(HH) 6 Hz, 2 $NCH_2C\mathit{H}_2$], and 3.55 (12 H, m, 6 CH_2); ^{13}C n.m.r. (62.89 MHz, D_2O): δ 211.5 (1 C, s, NCS_2), 68.4 (8 C, m, 8 CH_2), and 56.1 p.p.m. [2 C, t, *J*(CH) 140 Hz, 2 NCH_2].

Compound (**2**) is a convenient starting material for the syntheses of many electroactive transition-metal crown ether complexes,[5] for example reaction of (**2**) with $NiCl_2$ yielded the new crystalline complex nickel bis(aza-15-crown-5) dithiocarbamate, (**3**) (81%) (Found: C, 40.9; H, 6.5; N, 4.3. $C_{22}H_{40}N_2NiO_8S_4$ requires C, 40.8; H, 6.2; N, 4.3%); $\lambda_{max.}$ ($CHCl_3$): 431(sh) (ε 700), 392 (3 900), 324 (21 500), and 245 nm (23 000 dm^3 mol^{-1} cm^{-1}); $\nu_{max.}$ at 1 510s (C–N), 992s and 915m cm^{-1} (CS_2) (CsI pellet); ^1H n.m.r. (300 MHz, $CDCl_3$): δ 3.86 (8 H, m, 4 NCH_2), 3.79 (8 H, m, 4 $NCH_2C\mathit{H}_2$), and 3.64 (24 H, m, 12 CH_2); ^{13}C n.m.r. (62.89 MHz, $CDCl_3$): δ 209.9 (2 C, s, 2 NCS_2), 70.5 (16 C, m, 8 CH_2), 67.8 [4 C, t, *J*(CH) 145 Hz, 4 $NCH_2\mathit{C}H_2$], and 51.6 p.p.m. [4 C, t, *J*(CH) 140 Hz, 4 NCH_2]; *m*/*z* 647 [(*M* + H)$^+$, 100%], 648 (30), 649 (62), 650 (19), 651 (17), 652 (5), and 653 (4) (fast atom bombardment). Oxidative dimerization of (**2**) with $K_3[Fe(CN)_6]$ formed the new compound bis(aza-15-crown-5)thiuram disulphide, (**1**) (56%). The formulation of (**1**), as depicted in the Scheme is supported by both spectroscopic and microanalytical data (Found: C, 44.8; H, 6.9; N, 4.7; S, 21.4. $C_{22}H_{40}N_2O_8S_4$ requires C, 44.9; H, 6.85; N, 4.8; S, 21.8%); $\lambda_{max.}(CH_2Cl_2)$: 278(sh) (ε 7 700), 247(sh) (8 800), and 222 nm (13 700 dm^3 mol^{-1} cm^{-1}); $\nu_{max.}$ at 1 494s cm^{-1} (C–N) (CsI pellet); ^1H n.m.r. (300 MHz; $CDCl_3$): δ 4.30 (8 H, m, 4 NCH_2), 4.10 [4 H, t, *J*(HH) 6.7 Hz, 2 $NCH_2C\mathit{H}_2$], 3.89 [4 H, t, *J*(HH) 5.3 Hz, 2 $NCH_2C\mathit{H}_2$], and 3.66 (24 H, m, 12 CH_2); ^{13}C-{^1H} n.m.r. [62.89 MHz, $CDCl_3$–$(CD_3)_2CO$]: δ 193.0 (2 C, 2 NCS_2), 70.1—69.1 (12 C, 12 CH_2), 67.6 (2 C, $NCH_2\mathit{C}H_2$), 66.5 (2 C, 2 $NCH_2\mathit{C}H_2$), 58.4 (2 C, 2 NCH_2), and 54.3 p.p.m. (2 C, 2 NCH_2); *m*/*z* 589 (M^+) (fast atom bombardment).

Results and Discussion

Interestingly the ^{13}C-{^1H} spectrum of (**1**) measured at 62.89 MHz, in a $CDCl_3$–$(CD_3)_2CO$ (1:1) mixture, at 30 °C has resonances at δ 54.3 and 58.4 p.p.m., which are assigned to the methylene carbons directly bonded to the nitrogen atom. This observation may be explained by restricted rotation about the carbon–nitrogen bond, which arises due to the canonical form of (**1**), depicted as (**1b**) in the Scheme. When the spectrum of (**1**) was recorded with two equivalents of $NaBPh_4$ present at the same temperature, the resonances for the methylene carbons bound directly to nitrogen had collapsed into the baseline. This suggests that the addition of small amounts of Na^+ had sufficiently lowered the barrier to rotation about the carbon–nitrogen bond such that the spectrum was recorded very close to the coalescence temperature for this process. Careful variable-temperature ^{13}C-{^1H} n.m.r. studies support this conclusion. Figures 1 and 2 show the variable temperature ^{13}C-{^1H} n.m.r. spectra of (**1**) alone, and of (**1**) with two equivalents of $NaBPh_4$ present. The value of the energy barrier † for rotation about the C–N bond, $\Delta G^\ddagger$, is 63.5 ± 0.5 kJ mol^{-1} and is lowered to 54.5 ± 0.5 kJ mol^{-1} upon addition of two equivalents of $NaBPh_4$. In a control experiment the dynamic ^{13}C-{^1H} n.m.r. spectra of tetraethylthiuram disulphide[6] were recorded in the absence and presence of $NaBPh_4$ and no change in $\Delta G^\ddagger$ was observed. This observation implies that ion binding by the crown ether moieties in (**1**) plays an important role in lowering the energy barrier to rotation about the C–N bond. Clearly any sodium cation bound by the crown ethers and interacting with

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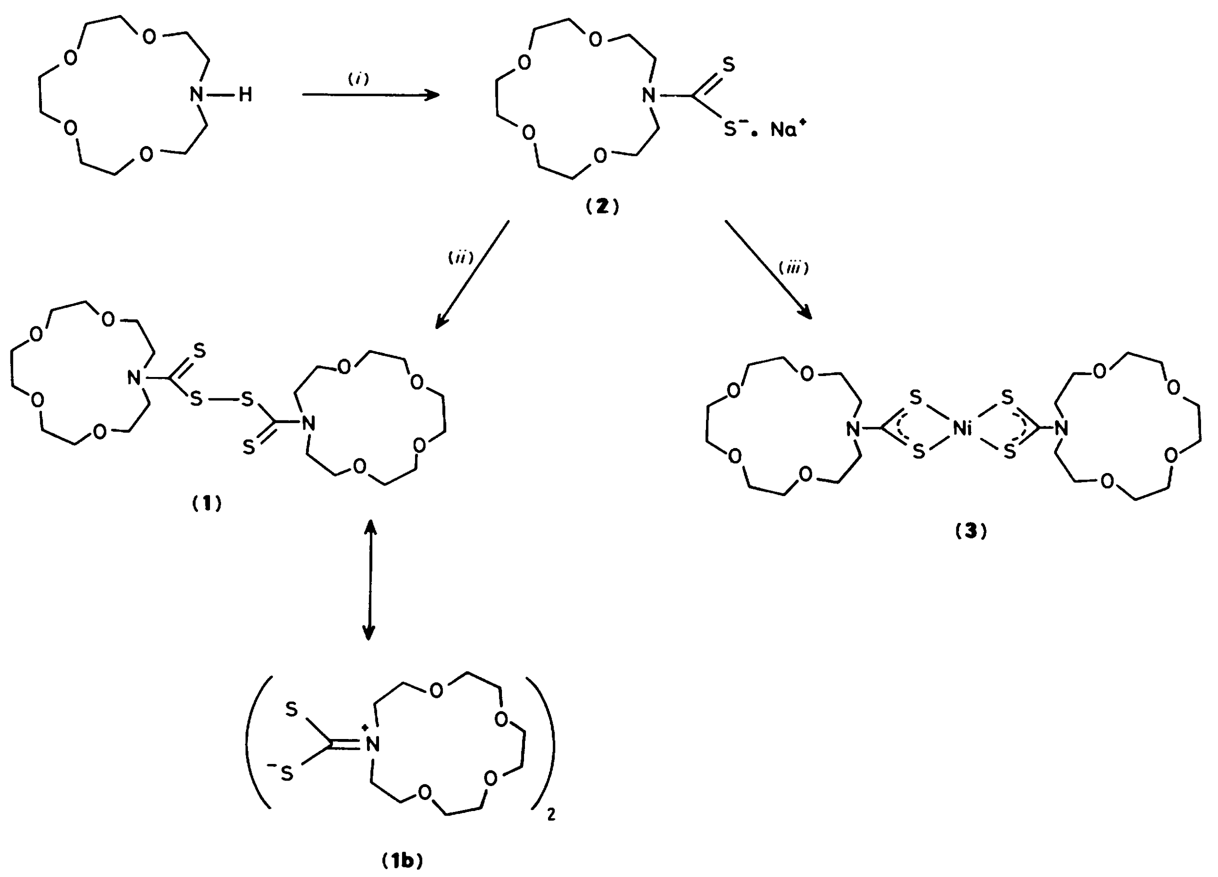
* 13,13′-(1,4-Dithioxo-2,3-dithiabutane-1,4-diyl)di(1,4,7,10-tetraoxa-13-azacyclopentadecane).

† The rate constant, *k*, at the coalescence temperature, T_c, is given by the expression $k = \pi\delta\nu/2$ for uncoupled two-site exchange (D. Kost, E. H. Carlson, and M. Raban, *Chem. Commun.*, 1971, 656). The value of $\Delta G^\ddagger$ can then be obtained from the Eyring equation (i) (H. Eyring, *Chem. Rev.*, 1935, **17**, 65), where *K* is the transmission coefficient and can be assumed to be close to or equal to unity for adiabatic reactions (J. Sandstrom, 'Dynamic N.M.R. Spectroscopy,' Academic Press, London, 1982).

$$k = \frac{Kk_B}{h} T e^{-\Delta G^\ddagger/RT} \qquad \text{(i)}$$



Scheme. (*i*) NaOH(aq), CS_2, 0 °C, 6 h; (*ii*) $K_3[Fe(CN)_6]$(aq); (*iii*) $NiCl_2$(aq)

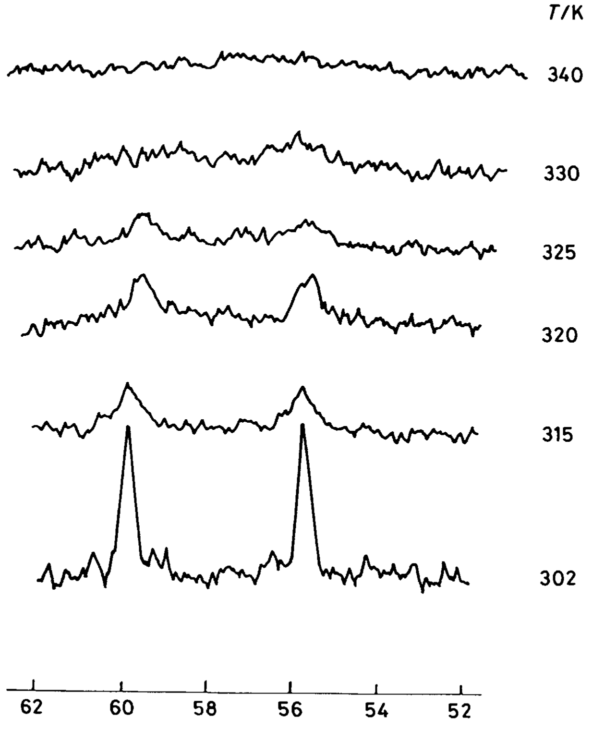


Figure 1. Variable-temperature ^{13}C-{^1H} n.m.r. spectra of (**1**) in $CDCl_3$–CD_3CN (1:1)

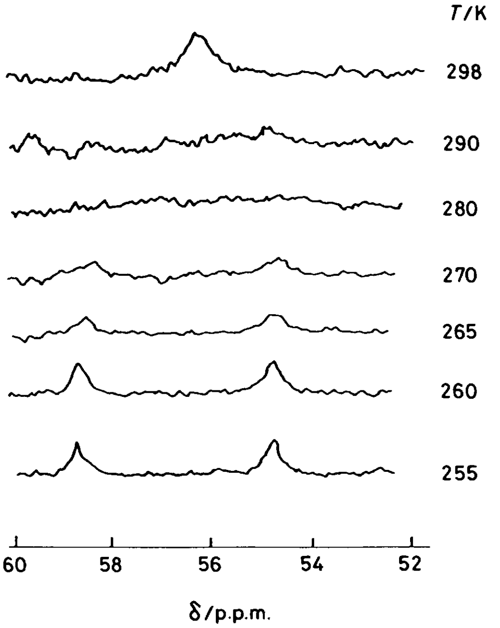


Figure 2. Variable-temperature ^{13}C-{^1H} n.m.r. spectra of (**1**) with two equivalents of $NaBPh_4$ in $CDCl_3$–CD_3CN (1:1)

the nitrogen atom reduces the electron density on nitrogen available for C–N π bonding, thereby lowering the C–N bond order and the energy barrier to rotation about the C–N bond.

When less than one equivalent of $NaBPh_4$ was added to a

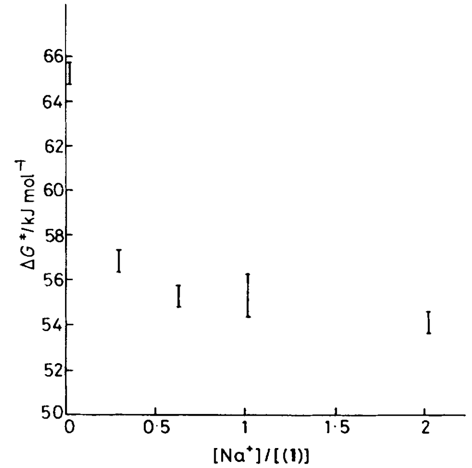


Figure 3. Plot of $\Delta G^{\ddagger}$ for C–N bond rotation in (**1**) *vs.* equivalents of $NaBPh_4$

$CDCl_3$–CD_3CN (1 : 1) solution of (**1**) the change in $\Delta G^{\ddagger}$ was correspondingly smaller, as shown in Figure 3. As expected when less than one equivalent of $NaBPh_4$ per crown ether moiety was added intermolecular exchange of Na^+ was fast on the n.m.r. time-scale. Thus, the methylene carbon atoms bonded to nitrogen for crown ether moieties with Na^+ bound and those with no Na^+ bound gave rise to an averaged signal.

A spectrum of (**1**) with one equivalent of $NaBPh_4$, and with one equivalent of benzo-15-crown-5 * also present, showed two sharp resonances for the methylene carbon atoms at 23 °C. This further underlines the importance of ion binding by the crown ether moieties in (**1**) with respect to the lowering of $\Delta G^{\ddagger}$.

We were interested to see whether the diminution of C–N bond order in (**1**) upon binding to Na^+ would manifest itself in the i.r. spectrum. Whereas the i.r. spectrum of a CsI pellet of (**1**) showed two bands in the C–N bond stretching region, one strong band at 1 493 cm^{-1}, and one of lower intensity at 1 476 cm^{-1}, the i.r. spectrum of (**1**) cocrystallized with one equivalent of $NaBPh_4$ had only one strong band at 1 477 cm^{-1}. Thus the higher intensity band assigned to C–N stretching has been shifted by 16 cm^{-1} to a lower frequency upon binding of sodium, indicating a reduction of electron density on the nitrogen available for C–N π bonding.

In conclusion, our study has demonstrated that the electronic nature of the C–N bond of crown ether thiuram disulphide (**1**) is dramatically affected by ion binding, which manifests itself in the dynamic n.m.r. behaviour of this molecule.

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* Benzo-15-crown-5 (2,3,5,6,8,9,11,12-octahydrobenzo[1,4,7,10,13]-pentaoxacyclopentadecine) has a substantially higher affinity for Na^+ than compound (1).[5]