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Nickel(II) Chelation by Three Bicyclic Tetrathioethers: Solution and Solid-State Data

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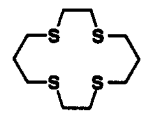
There is considerable interest in the complexation of late transition metal ions by polythioethers, but relatively little is known about the way in which changes in ligand structure affect chelation efficacy in solution.[1,2] We have previously examined simple peripheral modifications to tetrathio-14-crown-4 (**1**; first reported by Rosen and Busch[3]) and found that the *gem*-dimethyl substituents of **2** and **3** enhance Ni(II)[4] and Cu(II)[5] binding strength. We now describe the chelating affinities for Ni(II) of bicyclic polythioethers, **4–6**.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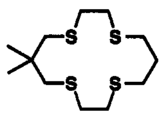
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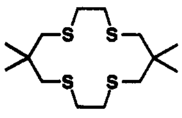
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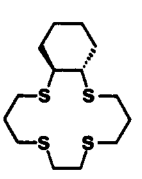
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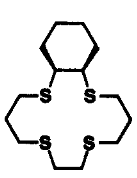
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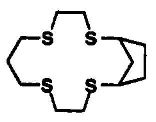
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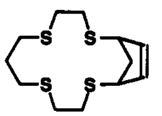
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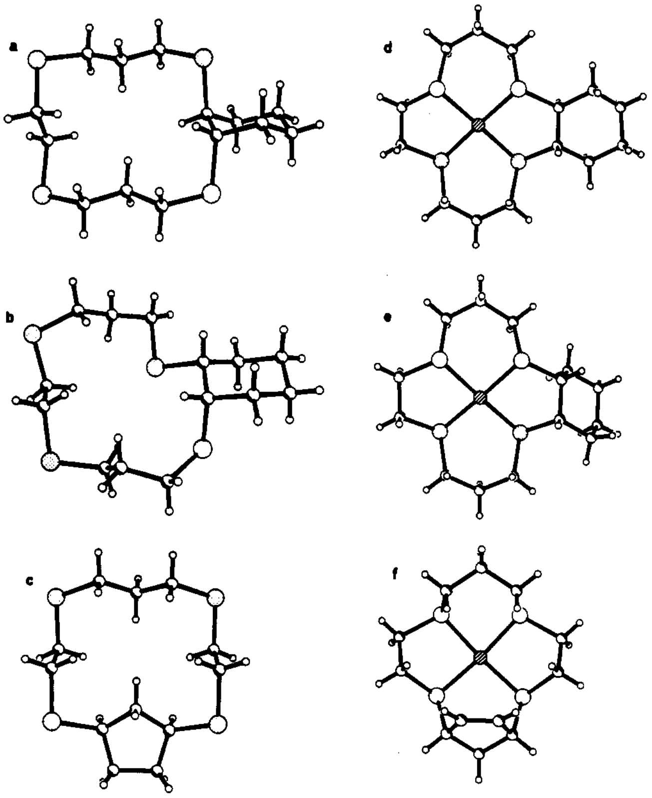

Figure 1. Ball-and-stick representation of the crystallographically observed thioether conformations: (a) **4**; (b) **5**; (c) **6**; (d) **4**-Ni(II) (ClO_4 counterions not shown); (e) **5**-Ni(II) (ClO_4 counterions not shown); (f) **7**-Ni(II) (ClO_4 counterions not shown). Disorder in the **5**-Ni(II) unit in the crystal of **5**-Ni(ClO_4)$_2$ could be modeled as an approximately 4:1 mixture of the structure shown and a minor but qualitatively similar structure.

Competition between ligands monitored by ^1H NMR was previously used to evaluate the relative Ni(II) affinities of **1–3** in CD_3NO_2 (room temperature; ClO_4 counterion).[4] Those experiments showed that **2** binds Ni(II) about 7 times more strongly than does **1** and that **3** binds about 50 times more strongly than does **1**. This method takes advantage of the *gem*-dimethyl resonances, and we have used competition experiments to examine the Ni(II) affinities of **4–6** relative to **2** or **3** in CD_3NO_2. The trans- and cis-cyclohexyl-fused isomers **4** and **5** have similar Ni(II) affinities under these conditions, with **4** binding Ni(II) 3–4 times more strongly than does **3** and with **5** binding Ni(II) about twice as strongly as **3** (i.e., **4** and **5** both have $\geq$100-fold higher Ni(II) affinities than does parent macrocycle **1**). Tetrathioether **6** has only about one-quarter of the affinity of **2** for Ni(II), implying that **6** and parent compound **1** have similar Ni(II) binding constants. (The cis 1,3-cyclopentylene unit has been reported to improve chelation, relative to a propylene unit, in the 16-crown-5-family.[6])

Figure 1 shows the conformations of metal-free **4–6** and the conformations of **4**-Ni(II), **5**-Ni(II), and **7**-Ni(II) in the solid state (ClO_4 counterions not shown). We were unable to grow suitable-quality crystals of **6**-Ni(II), but the conformational and metal-binding properties of **6** and **7** are expected to be similar. (We could not verify this assumption by structural or solution binding studies because metal-free **7** is relatively unstable.) The macrocycle conformations in the three Ni(II) complexes are similar to one another, but one difference is not readily apparent from the perspective in Figure 1: **4**-Ni(II) and **5**-Ni(II) have anti conformations (the six-membered chelate rings extend on opposite sides of the plane defined by S_4Ni, as in the Ni(II) complexes of **1–3**[4]), while **7**-Ni(II) displays a syn conformation (the six-membered chelate rings extend on the same side of the S_4Ni plane, as in **2**-Cu(II)[5]).

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Our previous comparisons among **1**–**3** suggest that the *gem*-dimethyl substituents improve binding strength by diminishing the torsional strain required for the ligand to adopt a chelating conformation.[4,5] The small carbocyclic rings of **4**–**6** are expected to rigidify the macrocyclic skeleton, relative to **1**, thus decreasing the conformational entropy cost of chelation, but the carbocyclic rings might also affect the amount of strain induced in the ligand by complex formation. The 14-membered ring conformations observed for metal-free **4** and **6** are very similar to that displayed by **1**. In each case, conversion of the metal-free conformation to the chelated conformation requires every macrocyclic C–S bond to change from gauche to anti and every macrocyclic C–C bond to change from anti to gauche. These alterations, particularly forcing the six C–C bonds gauche, are expected to cause significant torsional strain in the chelating conformation.[1c,4] This strain should, however, be diminished for **4** relative to **1**. Data from Zefirov et et. indicate that gauche and anti torsion angles about the SC–CS unit embedded in the ring fusion are very similar in energy,[7] while this difference for a simple SCH_2–CH_2S fragment appears to favor anti by roughly 2 kcal/mol.[4b] Figure 1c indicates that a parent-like 14-membered ring conformation is compatible with placement of the cis substituent at the equatorial positions of an envelope cyclopentane conformation (see ref 8 for nomenclature). Since this type of conformation is expected to be favorable for cis-1,3-disubstituted cyclopentanes,[8] it is not surprising that **6** shows no improvement relative to **1**.

The macrocyclic conformation observed for metal-free **5** seems to require less additional torsional strain than that of metal-free **4** to accommodate tetracoordination, because three of the 14-membered ring's six C–C bonds are already gauche in **5**. If this solid-state conformation approximates the minimum-energy structure of metal-free **5** in solution, then it seems puzzling that **5** is not superior to **4**. The answer to this puzzle may be contained in the structure of **5**-Ni(II). The S–C bond that is equatorial with respect to the cyclohexane ring approaches an eclipsed conformation (CH_2S–$CH(C)CH_2$ = 25.7 (10)°), implying that chelation is accompanied by the development of significant strain at this site. Thus, the advantages stemming from "built in" torsional strain about C–C bonds in **5** may be counterbalanced by unavoidable strain, involving the rigidifying substituent, in the complexed form.

In summary, both trans- and cis-fused cyclohexyl rings are effective preorganizing elements for an ethylene unit in the tetrathio-14-crown-4 skeleton. The cis 1,3-cyclopentylene fragment, however, does not appear to preorganize a propylene unit for this task. The availability of both solution and solid-state data on the complexation properties of these new bicyclic ligands is important, because previous discussions of the relationship between polythioether conformational propensities and chelation efficacy have tended to focus on crystallographic data alone.[1]

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Supplementary Material Available: Crystallographic data for the six structures shown in Figure 1, including tables of structure determination details, bond lengths and angles, atomic coordinates and thermal parameters, and selected torsion angles (50 pages). Ordering information is given on any current masthead page.

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