Synthesis and Coordination Chemistry of *C*-Substituted 1,4,7-Trithiacyclononanes

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C-Functionalised derivatives of the macrocyclic thioether ligand 1,4,7-trithiacyclononane (9S3), synthesised from 3-thiapentane-1,5-dithiol and a variety of substituted vicinal dibromides, retain the unusual coordination chemistry characteristic of the unsubstituted 9S3 ligand.

1,4,7-Trithiacyclononane (9S3) **1** is a powerful thioether ligand that is uniquely well suited to facial tridentate coordination. It forms stable complexes with many transition and main group metals, in many cases imparting unusual structural and electronic properties.[1] The possibility of exploiting these aspects of the chemistry of 9S3 by incorporating it into more complex ligand structures, for a variety of uses, by means of substitution in the carbon skeleton is an attractive one. Of immediate interest to us is the synthesis of bifunctional derivatives for the attachment of class b metallic radionuclides to substrates such as immunoglobulins.

Many of the unique properties of 9S3 complexes, including their high stability (thioethers are typically relatively weakly coordinating ligands), high coordination numbers, access to unusual oxidation states, high electron self-exchange rates, *etc.*, appear to derive at least in part from its predisposition to facial coordination as a result of the preferred endodentate conformation. Thus, the question arises as to whether introducing substituents into the ring will weaken this conformational preference to the detriment of its coordination chemistry. This communication addresses this question. We report the synthesis of some substituted 9S3 derivatives,[†] and preliminary studies of their coordination chemistry.

The new ligands **3a**–**3g** were synthesised by reaction of 3-thiapentane-1,5-dithiol with a range of substituted vicinal dibromides, *via* the template complex $[Mo(CO)_3(SCH_2CH_2SCH_2CH_2S)]^{2-}$ **2** (see Scheme 1). A solution of **2** (prepared *in situ* as a bistetramethylammonium salt by the literature method[5]) in acetonitrile was treated with the racemic dibromide to generate the trithiamacrocyclic complex. The macrocycle was displaced from the complex in dimethyl sulphoxide (DMSO) solution by addition of $[NMe_4]_2[SCH_2CH_2SCH_2CH_2S]$ and purified by silica gel chromatography. No intermediates were isolated. In all cases a major by-product was 1,4-dithiacyclohexane. The hydroxymethyl derivative **3b** was further modified by alkylation of the hydroxy group.

The coordination chemistry of **3a** with Fe^{II}, Ni^{II}, Cu^{II}, Ag^{I} and Hg^{II}, and of **3c** with Fe^{II}, has been investigated. Reaction of the metal perchlorate or tetrafluoroborate with **3a** in nitromethane or acetonitrile gave water-stable complexes of stoichiometry $M(ligand)_2{}^{n+}$, analogous to the parent (unsubstituted) 9S3 complexes.[‡] Their electronic spectra closely resemble those of the analogous 9S3 complexes.[§] The analogy

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[†] The only known examples of 9S3 derivatives are the benzo derivative[2] and a tribenzo derivative.[3] The former is known only as a ruthenium complex, formed in low yield by an obscure mechanism;[2] the latter forms a copper complex, which has been structurally characterised.[3] A recent publication describes some derivatives of the homologous ligand 10S3.[4]

[‡] All ligands and complexes gave satisfactory elemental microanalysis, and IR, ^1H NMR and mass spectra.

[§] Electronic spectroscopic data (λ_{max}/nm; MeCN solution) $[Fe(\mathbf{3a})_2][ClO_4]_2$: λ_{max} 398 and 523; $[Fe(\mathbf{3c})_2][ClO_4]_2$: 395 and 524 {*cf.* $[Fe(9S3)_2][ClO_4]_2$: 395 and 523)}; $[Ni(\mathbf{3a})_2][ClO_4]_2$: 527 and 786 {*cf.* $[Ni(9S3)_2][ClO_4]_2$: 527 and 784)}; $[Cu(\mathbf{3a})_2][BF_4]_2$: 449 ($\epsilon$ 7241 $dm^3\ mol^{-1}\ cm^{-1}$) {*cf.* $[Cu(9S3)_2][BF_4]_2$: 446 (5018)}; $[Ag(\mathbf{3a})_2][BF_4]$: no absorption; $[Hg(\mathbf{3a})_2][ClO_4]_2 \cdot 1.5\ MeNO_2$: 294 ($\epsilon$ 829) {*cf.* $[Hg(9S3)_2][ClO_4]_2 \cdot 2\ MeNO_2$: 295 (696)}.

extends to electrochemical behaviour: in acetonitrile solution at a glassy carbon electrode $[Ni(\mathbf{3a})_2]^{2+}$ shows a quasi-reversible one-electron oxidation at +0.97 V (*vs.* ferrocene/ferrocenium, Fc/Fc^+) and a quasi-reversible one-electron reduction at −1.10 V. $[Ni(9S3)_2]^{2+}$ shows similar processes at +0.97 and −1.09 V.[6]

These results show that the $Mo(CO)_3$-based template synthesis of 9S3 can be extended to *C*-functionalised derivatives and gives acceptable yields, and that elaboration of the 9S3 ring by substitution in the carbon skeleton does not markedly alter its coordination chemistry. Those complex properties (stability, stoichiometry, coordination number and electrochemical behaviour) that distinguish 9S3 from other polythioether ligands persist in the substituted derivatives. This will promote interest in the synthesis of more complex ligands, *e.g.* polynucleating ligands or bifunctional chelates incorporating the 1,4,7-trithiamacrocycle. Compounds **3b** and **3d–g** provide potential synthetic starting points for such ligands.

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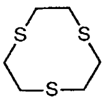

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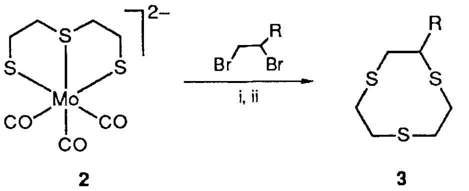
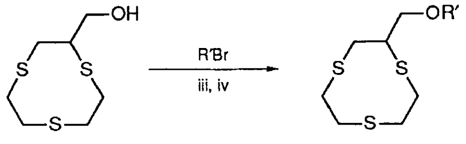


2

3

a R = Me, 25%
b R = CH_2OH, 24%
c R = CH_2OCH_2Ph, 6%
d R = $CH_2OCH_2C_6H_4$-4-Br, 20%
e R = $CH_2OCH_2C_6H_4$-4-CO_2H, 8%



3b

3

c R′ = CH_2Ph, 87%
f R′ = $CH_2C_6H_4$-4-CN, 43%
g R′ = $CH_2C_6H_4$-3-Br, 57%

Scheme 1 *Reagents and conditions*: i, dibromide in MeCN, room temp., 24 h; ii, $(NMe_4)_2(SCH_2CH_2SCH_2CH_2S)$ in DMSO, room temp., 24 h; iii, NaH in DMF, room temp., 10 min; iv, substituted benzyl bromide, DMF, room temp., 60 h

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