Tetrahedron Letters, Vol. 33, No. 21, pp. 3035-3038, 1992
Printed in Great Britain

0040-4039/92 \$5.00 + .00
Pergamon Press Ltd

SYNTHESIS OF ANNELATED BIS-CROWNETHERS.

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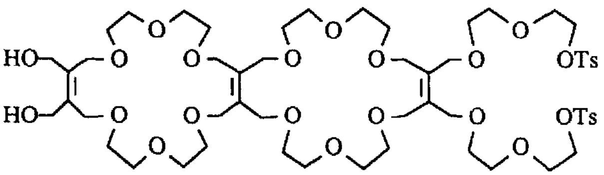
Symmetrical or unsymmetrical annelated bis-crownethers are prepared via the stepvise reaction of disodium-1,3-dithole-2-thione-4,5-dithiolate with a bis-alkylating reagent, $BrCH_2(CH_2OCH_2)_nCH_2Br$.

Since the discovery of crown-ethers[1], research on macrocyclic polyethers has become an exciting and rapidly growing area. Most studies on complexation phenomena in crown-ethers involve a single host and a single guest but molecular receptors with multiple interacting binding sites is of current interest in the chemical literature[2,3]. Walba *et al.*[4] have introduced annelated crown-ethers such as **1** for the purpose of making cylindrical macro-polycyclic hosts and molecular Möbius strips. Due to the synthetic difficulty in annelating two crown-ethers these tetrahydroxymethylene (THYME)-based systems are the only examples known so far. We assumed interesting structural features could be expected from complexes of annelated crowns and that the study of competition and inhibition between interacting binding sites could be of interest as well. Furthermore some recent papers[2b,5,11,14] descibe the synthesis of compounds where a metal ion complexed in a crown compartment induces a physical change in the near-environment. In the case of **4** and **5** this change could be a shift in redoxpotential. These results prompted us to attempt synthesis of annelated bis-crowns.

We now report a new method for the synthesis of annelated bis-crownethers e.g. **3** based on a tetrathioethene unit. Beside synthetic convenience this unit has been chosen because mixed sulfur-oxygen crowns has affinity for alkali metal ions (e.g. Na^+) as well as transition metal ions (e.g. Ag^+). The synthesis can easily be varied to form unsymmetrical bis-crowns. Direct use of the tetrathiolate[6] $[S_2C{=}CS_2]^{4-}$ is inherently risky due to the possible formation of isomers such as **2** and **3**. In order to avoid formation of **2** we



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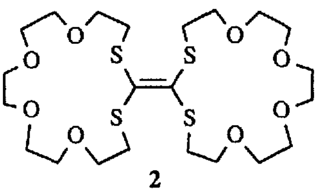

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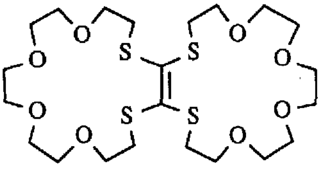

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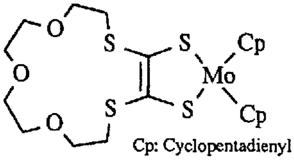
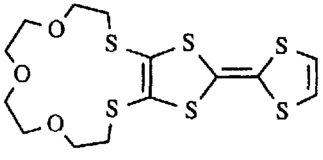


Cp: Cyclopentadienyl

4



5

have used stepwise approaches (Route A and B) to the bis-crownethers **9**, **10** and **3** (see scheme).

Route A: Reaction of the 1,3-dithiole-2-thione-4,5-dithiolate (prepared by deprotection of 4,5-bis(benzoylthio)-1,3-dithiole-2-thione **6**[7]) followed by one equivalent of the appropriate bis-alkylating reagents, $BrCH_2(CH_2OCH_2)_nCH_2Br$, in a mixture of tetrahydrofuran (THF) and ethanol (1:1) gave macrocycles **7** or **8**[8]. Ring opening of **7** or **8** and repeated alkylation with a new equivalent of a bis-alkylating reagents gave bis-crownethers **9**, **10** or **3**[9].

Route B: Reaction of 4,5-bis(benzoylthio)-1,3-dithiol-2-thione **6** with $Hg(OAc)_2$ in acetic acid gave 4,5-bis(benzoylthio)-1,3-dithiole-2-one **11**[10] (yield 80%). Deprotection of **11**, followed by alkylation resulted in macrocycle **12**[11] or **13**[12] and subsequently bis-crownethers **9**, **10** or **3**.

The bis-crownethers **9**, **10** and **3** are white crystals and the total yields of analytically pure compounds obtained *via* route B calculated from **11** are: **9** (21%), **10** (27%) and **3** (39%).

Although route B involves an extra step this method is usually advantageous due to the much slower ring opening of the 1,3-dithiole-2-thione ring compared to the corresponding 1,3-dithiole-2-one, furthermore route A results in a more complex reaction mixture. Thus thin layer cromatography (TLC) demonstrated that ring opening of the thione is about ten times slower than ring opening of the corresponding ketone.

Treatment of **3** with silver perchlorate in acetonitrile affords a silver complex in high yield (87%), elemental analyses of this complex indicates that two equivalents of silver perchlorate and one equivalent of acetonitrile per ligand molecule are incorporated in the complex[13]. Otsubo *et al.*[14] have reported the structure of TTF-crown **5** complex with TCNQ, in this molecular complex the crownether ring is uncomplexed and situated almost perpendicular to the plane of the TTF. In accordance with this result a CPK-molecular model of **3** reveals that it is possible for **3** to adopt a conformation in which both crownether groups bind to one metal ion, thus **3** can act like a "molecular jaw". A complexation study of **3** was performed using our PDMS strategy[15] (Plasma Desorption Mass Spectroscopy) which indicates that **3** has high affinity for silver ions, sodium ions and potassium ions. After mixing a sample of **3** with an equimolar amount of aqueous lithium chloride, sodium acetate and potassium acetate (fig. 1) or silver nitrate (fig. 2) a PDMS revealed the following affinity sequence: $Ag^+ > Na^+ > K^+ \gg Li^+$. Such a sequence was expected for a ligand with this cavity size and the given mixture of "hard" and "soft" donoratoms.

These new macrocyclic compounds are of interest due to their ability to form binuclear complexes and further synthetic work will report the replacement of the polyether chain with related groups.

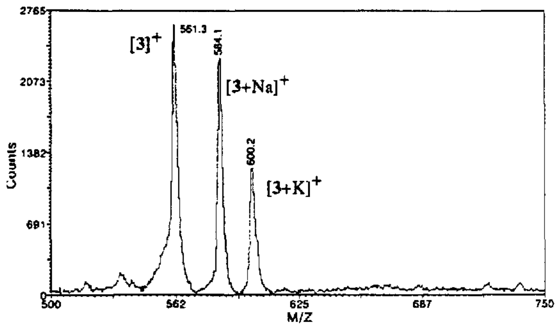


Fig.1: **3** + Li^+, Na^+, K^+.

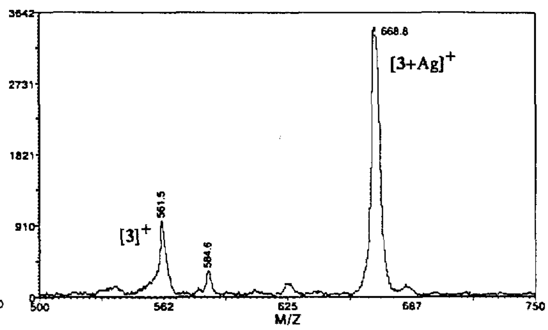


Fig. 2: **3** + Ag^+.

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9. **9**: *5,8,11,19,22-Pentaoxa-2,14,16,25-tetrathiabicyclo[13,10,0]pentacos-1(15)-ene*, m.p. 121-122°C ($CHCl_3/Et_2O$); (Found: C, 44.77; H, 6.48. $C_{16}H_{28}O_5S_4$ requires C, 44.83; H, 6.58); m/z (EI) 428 (M^+, 100%), 237 (16), 148 (10), 88 (23), 45 (43); δ_H($CDCl_3$, TMS) 3.65 (10 H, m) 3.1 (4 H, m). **10**: *5,8,11,19,22,25-Hexaoxa-2,14,16,28-tetrathiabicyclo[13,13,0]octacos-1(15)-ene*, m.p. 167°C ($CHCl_3/Et_2O$); (Found: C, 45.73; H, 6.95. $C_{18}H_{32}O_6S_4$ requires C, 45.74; H, 6.82); m/z (EI) 472 (M^+, 100%), 148 (8), 87 (12), 61 (16), 45 (31); δ_H($CDCl_3$, TMS) 3.65 (6 H, m) 3.03 (2 H, t, J=7 Hz). **3**: *5,8,11,14,22,25,28,31-Octaoxa-2,17,19,34-tetrathiabicyclo[16,16,0]tetratriacont-1(18)-ene*, m.p. 116-118°C ($CHCl_3/Et_2O$); (Found: C, 47.18; H, 7.19. $C_{22}H_{40}O_8S_4$ requires C, 47.12; H,7.19); m/z (EI) 560 (M^+, 100%), 148 (8), 88 (16), 61 (18), 45 (67); δ_H($CDCl_3$, TMS) 3.75 (8 H, m) 3.1 (2 H, t, J=6 Hz).
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11. M. L. H. Green, W. B. Heuer, G. C. Saunders, *J. Chem. Dalton Trans.*, **1990**, 3789. This paper describe the preparation of **12** and report that this compound is unstable. However in our hands crystalline **13** is perfectly stable, m.p. 82-83°C ($CHCl_3$/MeOH); (Found: C, 39.00; H, 4.72; S, 37.35. $C_{11}H_{16}O_4S_4$ requires C, 38.80; H, 4.74; S, 37.67). It is noteworthy that $Hg(OAc)_2$ oxidation of **7** (n=2) gave a fair yield of **13** in contrast to oxidation of **8** (n=3) which only gave a low yield (<5%) of **14**. The low yield of **14** is most likely due to complexation of the product with Hg_2^{2+}.
12. **14**: *5,8,11,14-Tetraoxa-2,7,19,21-tetrathiabicyclo[16,3,0]henicos-1(18)-ene-20-one*, m.p. 67--69°C ($CHCl_3/CH_3OH$); (Found: C, 40.57; H, 5.24. $C_{13}H_{20}O_5S_4$ requires C, 40.60; H, 5.24); m/z (EI) 384 (M^+, 100%), 180 (10), 146 (9), 88 (28), 45 (46); δ_H($CDCl_3$, TMS) 3.77 (2H, t, *J*=6Hz) 3.67 (6H, s) 3.07 (2H, t, *J*=6Hz).
13. (Found: C, 28.39; H, 4.28. $C_{24}H_{43}NO_{16}S_4Ag_2Cl_2$ requires C, 28.36; H, 4.26).
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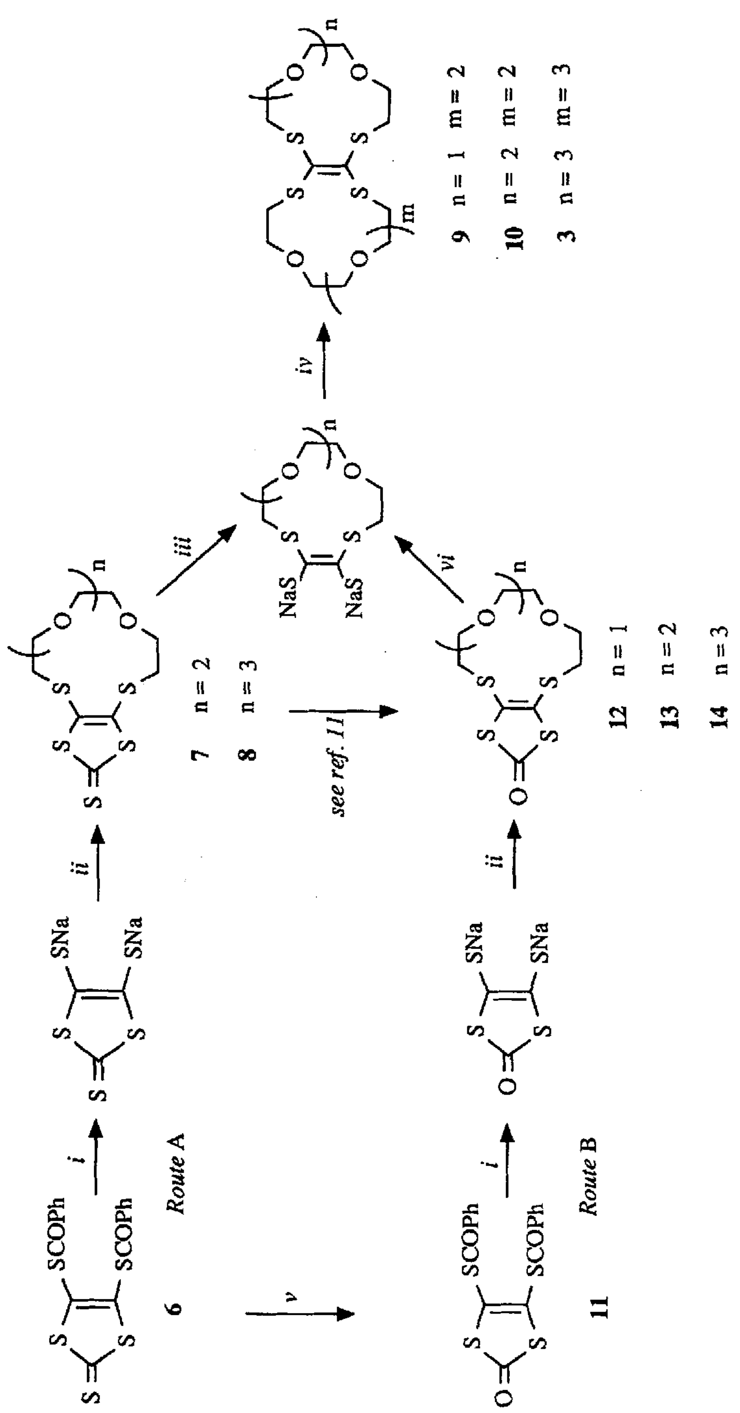
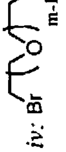


Scheme : *Reagents and conditions: i:* 2 eq NaOEt, EtOH, 15 min . *ii:* 

, THF/EtOH, 24 h. *iii:* 2 eq NaOEt, EtOH, 24 h. *iv:* 

, THF/EtOH, 24 h . *v:* Hg(OAc)$_2$, CH$_3$COOH/CHCl$_3$. *vi:* 2 eq NaOEt, EtOH, 2 h. (all reactions carried out in dry solvents under N$_2$)

(Received in UK 26 February 1992)