Pergamon

Tetrahedron Vol. 50, No. 7, pp. 2095-2098, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4020/94 $6.00+0.00

0040-4020(93)E0151-5

Synthesis of the Macrocyclic Thiocrown Ethers 1,4,7,10,13,16,19-Heptathiaheneicosane (21-S-7) and 1,4,7,10,13,16,19,22-Octathiatetraeicosane (24-S-8)

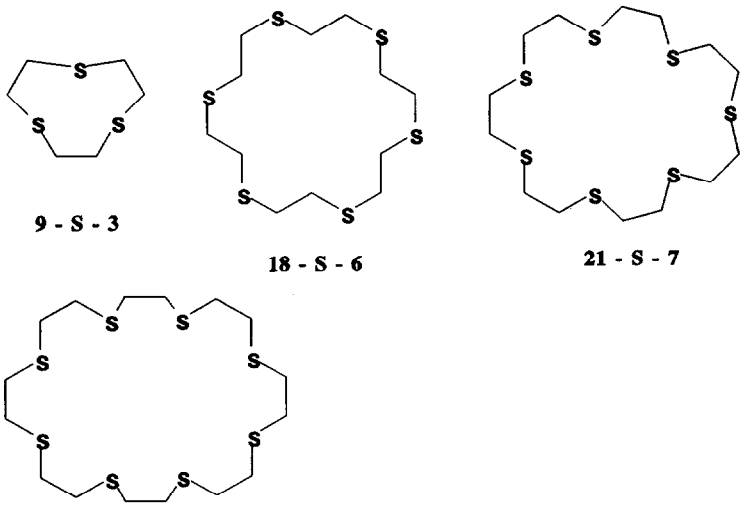
Jilles J.H. Edema, Jan Buter, Richard M. Kellogg*

Department of Chemistry, University of Groningen, Nijenborgh 4,
9747 AG Groningen, The Netherlands

Abstract: The synthesis and characterization of the two macrocyclic sulfides, 1,4,7,10,13,16,19-heptathiaheneicosane (21-S-7) and 1,4,7,10,13,16,19,22-octathiatetraeicosane (24-S-8), are described starting from different combinations of dithiols and dichlorides of differing chain lengths. Cs_2CO_3 is used for the cyclizations.

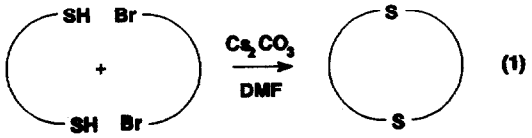
The development of efficient synthetic strategies for the preparation of macrocyclic thiocrown ethers has led to an increased interest in the coordination chemistry of these ligand systems.[1-6] Owing to the soft character of the sulfur ligating sites, thioethers are quite apt for the complexation of heavy transition metals.

Figure 1



The majority of the thiocrown ethers synthesized thus far possess sulfide ligating sites that are separated by ethylenic (-CH_2CH_2-) or propylenic (-$CH_2CH_2CH_2$-) bridges.[1,6,7] This topological arrangement gives rise to a typical inside-outside arrangement of the sulfur atoms, especially for the smaller thiocrown ethers (up to 18-S-6, which is illustrated in Fig. 1). An exception is 9-S-3, which for steric reasons is forced to have the sulfur atoms cis.[1] The all-anti conformation of the sulfur atoms may be influenced or changed for the better by increasing the ring size of the thiocrown ether.

Equation 1



(1)

A synthetic strategy for the preparation of thiocrown ethers, developed by us, is depicted schematically in eq. 1. Nucleophilic substitution of an α,γ-cesium dithiolate with a bifunctional dibromide or dichloride results in the assembly of the macrocycle.

Results

These two macrocyclic thioethers, 21-S-7 and 24-S-8, have been prepared in various ways employing different dithiols and dihalides (eq. 2 and eq. 3). The dihalides **1-4** were prepared from the corresponding alcohols by reaction with thionyl chloride following literature procedures,[7,8] and were used immediately without further purification. *CAUTION: THESE COMPOUNDS ARE POWERFUL VESICANTS!* Further purification is both risky and unneeded.

The dithiols **5-7** were prepared from the (unpurified) dihalides by substitution with $Cs(SCOCH_3)_2$ in dimethyl formamide (DMF) followed by reduction with $LiAlH_4$. The use of cesium thioacetate is a slight modification (and significant improvement) of a literature procedure.[8] It is our experience that an alternative procedure whereby the diols (instead of dichlorides) are converted to dithiols using thiourea under acidic conditions is less suitable owing to greater isolation problems.

Despite the failure to achieve complete purification of the starting materials, cyclization yields are good. The macrocycles themselves are readily purified. There is some experimental advantage to using the longer chain dihalides **3,4** rather than **1,2** owing to the fact that the former are solids that are reasonably easy to handle. The yields shown in eqs. 2 and 3 are those of isolated, pure macrocycle. Extension to other systems is possible.

Experimental

All reactions were carried out under an inert atmosphere of N_2. Solvents were dried and distilled prior to use following standard procedures. Cs_2CO_3 and $SOCl_2$ were purchased from Aldrich and were used as received. ^{1}H-NMR (200 MHz) and ^{13}C-NMR (50.3 MHz) spectra were recorded on Varian spectrometers. Exact mass spectra were taken on an AEI-MS 902 mass spectrometer at 70 eV.

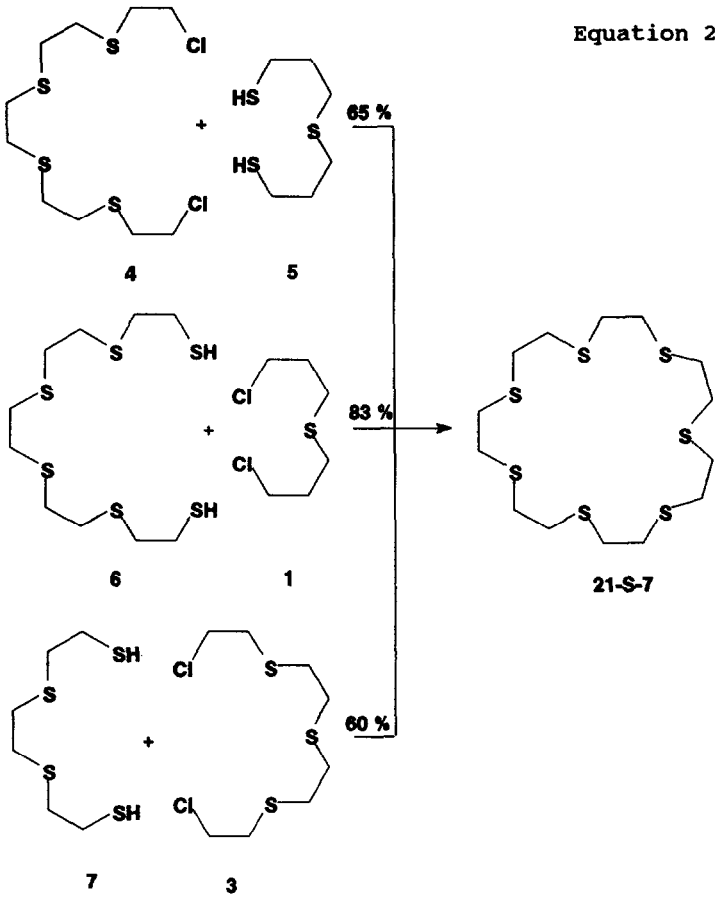
General procedures for the preparation of the thiodihalides **1-4** are derived from Cooper and coworkers,[7] de Groot and Loeb,[8] and Rosen and Busch.[9] These procedures entail the synthesis of the diol precursors of **1-4** (OH instead of Cl), conversion of these diols with $SOCl_2$ to **1-4**, and conversion of **1** to dithiol **5**, **2** to dithiol **7**, and **4** to dithiol **6** using $Cs(SCOCH_3)_2$ in DMF followed by reduction with $LiAlH_4$. None of the intermediates was purified; characterization was done on the basis of NMR spectra.

Caution! The dichlorides 1-4 are strong vesicants!

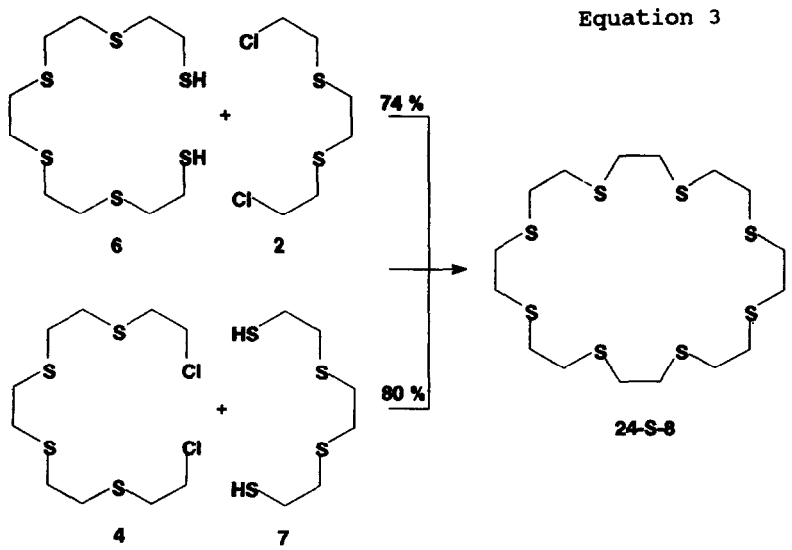
General procedure for the synthesis of dithiols from dichlorides. We describe here the use of $Cs(SCOCH_3)_2$ as nucleophile.

To 30 mmol of thiolacetic acid in 50 mL CH_3OH was added in small portions 15 mmol of Cs_2CO_3. After stirring for 30 min the reaction mixture was evaporated to dryness. The white, solid $Cs(SCOCH_3)_2$ was dissolved in 250 mL DMF and 15 mmol of the requisite dichloride was added dissolved in a little

Equation 2



Equation 3



DMF if required. The suspension obtained was stirred overnight, the DMF was evaporated and the residue was extracted with several 50 mL portions of diethyl ether. This ethereal solution was added dropwise to a 10% excess of $LiAlH_4$ in diethyl ether. After usual workup the dithiol was obtained in about 50% yield.

1,4,7,10,13,16,19-Heptathiaheneicosane (21-S-7) (typical example).

A solution of 3,6,9,12-tetrathiaundecane-1,14-dithiol **6** (5.0 mmol) and 3-thiapentane-1,5-dichloride **1** (5.0 mmol) in 75 mL DMF was added during 20 h to a warm (55-60°C), vigorously stirred suspension of 2 eqv. of Cs_2CO_3 (3.26 g, 10.0 mmol) in 350 mL of DMF. The yellow mixture was filtered and the solvent was removed in vacuo leaving a yellowish oily residue. The filter cake was extracted repeatedly with $CHCl_3$. The combined $CHCl_3$ layers were concentrated to provide a colorless oil. The combined oil fractions were chromatographed over silica gel using toluene/CH_2Cl_2 (1:3) as eluent to yield 1.74 g of a white solid (4.1 mmol, 83% yield), mp. 50.0-51.0°C, ^{1}H-NMR ($CDCl_3$): 2.80 (s, 28H), ^{13}C-NMR ($CDCl_3$):32.59 (t), HRMS $(M/z)^+$: 420.024 (calcd. 420.024 for $C_{14}H_{28}S_7$).

1,4,7,10,13,16,19,22-Octathiatetraeicosane (24-S-8) (typical example)

A solution of 3,6,9,12-tetrathiatetradecane-1,14-dithiol **6** (5.0 mmol) and 3,6-dithiaoctane-1,8-dichloride **2** (5.0 mmol) in 100 mL DMF was added over 20 h to a warm (55-60°C), vigorously stirred suspension of 2 eqv. of Cs_2CO_3 (3.26 g, 10.0 mmol) in 350 mL of DMF. After the addition was complete, the yellow mixture was filtered and the solvent was removed in vacuo leaving a waxy residue. The filter cake was extracted repeatedly with CH_2Cl_2. The combined organic layers were concentrated and evaporated to provide a colorless oil. The combined oil fractions were chromatographed over silica gel using toluene/CH_2Cl_2 (1:3) as eluent to yield 1.77 g. of a white solid (3.7 mmol, 74% yield), mp. 82.0-83.5°C, ^{1}H-NMR ($CDCl_3$): 2.77 (s, 32H), ^{13}C-NMR ($CDCl_3$) 32.14 (t), HRMS $(M/z)^+$: 480.027 (calcd. 480.026 for $C_{16}H_{32}S_8$).

References

1. (a) Rawle, S.C., Cooper, S.R. *Structur. Bonding (Berlin)* **1991**, *72*, 1; (b) Cooper, S.R. *Acc. Chem. Res.* **1988**, *21*, 141; (c) Blake, A.J., Schroeder, M. *Adv. Inorg. Chem.* **1989**, *35*,1; (d) Schroeder, M. *Pure Appl. Chem.* **1988**, *60*, 517; (e) Pedersen, C.J. *J. Org. Chem.* **1971**, *36*, 254; (f) Cooper, S.R., Rawle, S.C. *Structur. Bonding* **1990**, *72*, 1.
2. (a) de Groot, B., Loeb, S.J., Giesbrecht, G.R. *Inorg. Chem.* **1991**, *30*, 177; (b) de Groot, B., Loeb, S.J. *Inorg. Chem.* **1991**, *30*, 3103; (c) de Groot, B., Loeb, S.J. *Inorg. Chem.* **1990**, *29*, 4048; (d) de Groot, B., Loeb, S.J., Shimizu, G.K.H. *J. Chem. Soc., Chem. Commun.* **1991**, 1119.
3. (a) Setzer, W.N., Tang, Y., Grant, G.J., Vanderveer, D.G. *Inorg. Chem.* **1991**, *30*, 3652; (b) Setzer, W.N. Caccioppo, E.L., Guo, Q., Grant, G.J., Kim, D.D., Vanderveer, D.G. *Inorg. Chem.* **1990**, *29*, 2672; (c) Glass, R.S., Wilson, G.S., Setzer, W.N. *J. Am. Chem. Soc.* **1980**, *102*, 5068; (d) Blake, A.J., Pasteur, E.C., Reid, G., Schroeder, M. *Polyhedron* **1991**, 1545.
4. Buter, J., Kellogg, R.M., van Bolhuis, F. *J. Chem. Soc., Chem. Commun.* **1990**, 1119.
5. (a) Buter, J., Kellogg, R.M., van Bolhuis, F. *J. Chem. Soc. Chem. Commun.* **1991**, 910; (b) Edema, J.J.H., Stock, H.T., Buter, J., Kellogg, R.M., Smeets, W.J.J., Spek, A.L., van Bolhuis, F. *Angew. Chem.* **1993**, *105*, 448; (c) Edema, J.J.H., Stock, H.T., Buter, J., Kellogg, R.M., van Bolhuis, F., Meetsma, A., Kooijman, H., Spek, A.L. *Inorganica. Chim. Acta.* **1993**, *207*, 263.
6. (a) Buter, J., Kellogg, R.M. *J. Chem. Soc., Chem. Commun.* **1980**, 460; (b) Buter, J., Kellogg, R.M., *J. Org. Chem.* **1987**,*46*,4481; (c) Buter, J., Kellogg, R.M. *Org. Synth.* **1987**, *65*, 150; (d) Edema, J.J.H., Buter, J., Stock, H.T., Kellogg, R.M. *Tetrahedron* **1992**, *48*, 8065; (e) Edema, J.J.H., Hoogenraad, M., Kellogg, R.M., Kooijman, H., Spek, A.L. accepted for publication in *J. Org. Chem.*
7. Wolf, R.E., Hartman, J.A., Ochrymowycz, L.A., Cooper, S.R. *Inorg. Synth.* **1988**, *25*, 122.
8. de Groot, B., Loeb, S.J. *Inorg. Chem.* **1989**, *28*, 3573.
9. Rosen, W., Busch, D.H. *J. Am. Chem. Soc,* **1989**, *91*, 4694.

(*Received in UK* 1 *June* 1993; *revised* 17 *November* 1993; *accepted* 19 *November* 1993)