for 14 and 15·DMF, respectively, those 2652 and 2547 reflections with $I > 3.0\sigma(I)$ were retained for the structure analyses, and the usual Lorentz and polarization corrections were applied. Refined unit cell parameters for each crystal were derived by least-squares treatment of the diffractometer setting angles for 25 reflections ($41° < \theta < 66°$ for 14; $33° < \theta < 43°$ for 15·DMF) widely separated in reciprocal space.

The crystal structures were both solved by direct methods, assuming at the outset that the crystals were centrosymmetric. Approximate coordinates for all non-hydrogen atoms were obtained from E-maps and weighted Fourier syntheses. Hydrogen atoms were all located in difference Fourier syntheses evaluated following several rounds of full-matrix least-squares adjustment of non-hydrogen atom positional and anisotropic thermal parameters. With the inclusion of hydrogen atom positional and isotropic thermal parameters as variables in the subsequent least-squares calculations, the refinements converged at $R = 0.040$ ($R_w = 0.050$) for 14 and $R = 0.047$ ($R_w = 0.064$) for 15·DMF.

Neutral atom scattering factors used in the structure factor calculations were taken from ref 23. In the least-squares iterations, $\sum w\Delta^2$ [$w = 1/\sigma^2(|F_o|)$, $\Delta = (|F_o| - |F_c|)$] was minimized.

Acknowledgment. Part of this investigation received financial support from the World Health Organization (Special Programme of Research, Development, and Research Training in Human Reproduction). E.W., P.D.R.M., and S.R.P. are indebted to D. Verdon for the preparation of yuehchukene.

Registry No. **1a**, 17771-42-5; **1b**, 16886-00-3; **1c**, 83-34-1; **2a**, 108665-92-5; **2b**, 108665-93-6; **3a**, 102210-79-7; **3b**, 108666-00-8; **3c**, 58500-84-8; **4a**, 120-72-9; **4b**, 91-55-4; **4c**, 108665-94-7; **4d**, 16863-96-0; **4e**, 108665-95-8; **4f**, 108665-96-9; **4g**, 70390-93-1; **4h**, 108665-97-0; **4j**, 108665-98-1; **4k**, 108665-99-2; **4l**, 40899-71-6; (±)-**13**, 96624-37-2; (±)-**14**, 108675-04-3; (±)-**15**, 108666-01-9; (±)-**15**·DMF, 108739-47-5.

Supplementary Material Available: Tables of non-hydrogen atom positional and anisotropic thermal parameters, hydrogen atom positional and isotropic thermal parameters, interatomic distances and bond angles, and torsion angles for 14 and 15·DMF (16 pages). Ordering information is given on any current masthead page.

Synthesis and Structural Aspects of (2,5)-1,3,4-Thiadiazolo and (3,5)-1,3,4-Thiadiazolino Thia Crown Ethers[1]

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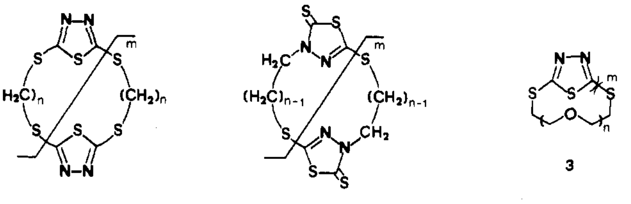
A general route to (2,5)-1,3,4-thiadiazolo thia crown ethers **3**, by the high-dilution reaction of 2,5-dimercapto-1,3,4-thiadiazole dipotassium salt **8** with oligoethylene glycol dihalides **9** in ethanol, is described. The reaction of **8** with bis[2–(2–bromoethoxy)ethyl] ether (**9c**) produced also small amounts of the 15-membered (3,5)-1,3,4-thiadiazolino thione macrocycle **10**, which possesses a ring nitrogen pointing into the complexing cavity. The structures of the macrocycles were firmly established by ^{1}H and ^{13}C NMR spectroscopy. Macrocycle **10** was further characterized by a single-crystal X-ray diffraction study.

Introduction

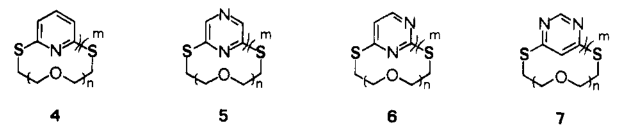
Various 1,3,4-thiadiazoles exhibit a penchant for the formation of stable complexes with heavy- and transition-metal ions,[2] some of which have industrial importance[3] or show interesting pharmacological properties.[2d] Besides, some 1,3,4-thiadiazoles have been proposed to act in the presence of appropriate metals as N,N-bridging ligands,[4] giving rise to one-dimensional polynuclear structures,[5] which may be of interest as semiconductors.[6]

Chart I



1 2 3

Chart II



4 5 6 7

In light of the general interest on the construction of synthetic macrocycles containing heterocyclic subunits,[7] as well as the limited examples of 1,3,4-thiadiazole inclusion in a macrocyclic framework,[8] we became interested

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[1] Presented at the 11th International Symposium on Macrocyclic Chemistry, Florence, Italy, Sept 1–4, 1986.

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Table I. ^{1}H and ^{13}C NMR Spectral Data of 1,3,4-Thiadiazolo Thia Crown Ethers 3 and Related Open-Chain Models 11 and 12[a–c]

				chemical shift, δ						
compd	n	m	NMR	α-CH_2	β-CH_2	γ-CH_2	δ-CH_2	C_2	C_5	others
3b	1	2	^{1}H	3.42 (t)	3.87 (t)					
			^{13}C	33.6	68.9			164.8	164.8	
3c	1	3	^{1}H	3.45 (t)	3.86 (t)					
			^{13}C	33.6	69.3			165.1	165.1	
3d	1	4	^{1}H	3.46 (t)	3.85 (t)					
			^{13}C	33.8	69.4			165.3	165.3	
3e	2	1	^{1}H	3.26 (t)	3.85 (t)	3.27 (s)				
			^{13}C	37.5	69.6	73.2		167.3	167.3	
3f	2	2	^{1}H	3.45 (t)	3.84 (t)	3.64 (s)				
			^{13}C	34.2	69.5	70.6		165.5	165.5	
3g	3	1	^{1}H	3.29 (t)	3.82 (t)	3.58 (m)	3.58 (m)			
			^{13}C	35.6	70.1	70.5	70.7	167.3	167.3	
3h	3	2	^{1}H	3.49 (t)	3.87 (t)	3.65 (s)	3.65 (s)			
			^{13}C	33.9	69.4	70.7	70.8	165.3	165.3	
11			^{1}H	3.36 (t)	3.61 (t)					3.25 (OMe)
			^{13}C	33.4	70.4			165.1	165.1	58.6
12a	1		^{1}H	3.48 (t)	3.85 (t)			166.0	163.9	2.76 (SMe)
			^{13}C	33.2	68.5					16.0
12b	2		^{1}H	3.49 (t)	3.84 (t)	3.64 (s)				2.75 (SMe)
			^{13}C	33.6	69.2	70.2		166.3	164.6	16.2
12c	3		^{1}H	3.50 (br t)	3.84 (br t)	3.65 (s)	3.65 (s)			2.76 (SMe)
			^{13}C	33.8	69.4	70.5	70.5	166.4	164.8	16.3

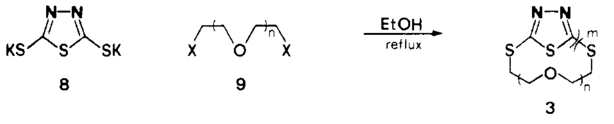
[a] All compounds were dissolved in $CDCl_3$ (10%) with Me_4Si as the internal standard. [b] ^{1}H NMR multiplicities are given in parentheses. [c] ^{1}H NMR J values of the triplets are ca. 5.5–6.0 Hz.

in the synthesis of 1,3,4-thiadiazole-containing macrocycles[9] and recently reported the synthesis and characterization of tetrathia[(n + 2).(n + 2)](2,5)-1,3,4-thiadiazolophanes **1** and of isomeric dithia[(n + 1).(n + 1)](3,5)-1,3,4-thiadiazolinophanedithiones **2**[10] (Chart I). These macrocycles resulted from the heterocyclization of 2,5-dimercapto-1,3,4-thiadiazole with 1,ω-dibromoalkanes in alkaline medium under high-dilution conditions. We herein describe the application of this procedure to the synthesis of novel (2,5)-1,3,4-thiadiazolo thia crown ethers **3** with differing ring sizes (from 13- to 40-membered) and flexibility. Numerous structurally related open-chain models have been also synthesized, in view of further studies on the complexing behavior and chemical reactivity of 1,3,4-thiadiazole acyclic vs. cyclic structures.

Results and Discussion

Over the past decade, efforts toward the synthesis of S-bridged multifunctional N-heterocyclic coronands, in which the sulfur atoms are directly connected to the heterocyclic ring, have been conducted.[7] Vögtle originally reported the preparation of (2,6)pyridino thia crown ethers **4** from 2,6-pyridinedithiol and the appropriate ethereal terminal dihalide or ditosylate,[11] while Newkome approached the synthesis of **4**,[12a] as well as (2,6)pyrazino,[12b] (2,4)pyrimidino,[12c] and (4,6)pyrimidino[12d] thia crown ethers **5**–**7**, respectively, via direct nucleophilic substitution on the N-heteroaromatic dihalide with an appropriate dimercaptide (Chart II). The latter cyclization step, however, was plagued by typical sulfur side reactions, such as polymerization, fragmentation, oxidation, and oligomerization.[12a]

Scheme I



	n	X
9a	1	I
9b	2	I
9c	3	Br

	n	m
3a	1	1
3b	1	2
3c	1	3
3d	1	4
3e	2	1
3f	2	2
3g	3	1
3h	3	2

Our earlier report[10] has shown that the heterocyclization of 2,5-dimercapto-1,3,4-thiadiazole with 1,ω-dibromoalkanes in alkaline medium offers a practical route to S-bridged (2,5)1,3,4-thiadiazolo coronands. Taking advantage of this efficient ring-closure procedure, incorporation of 1,3,4-thiadiazole subunit(s) into a thia crown ether framework was readily accomplished by coupling 2,5-dimercapto-1,3,4-thiadiazole dipotassium salt **8** with appropriate oligoethylene glycol dihalides **9** in refluxing ethanol (EtOH) under high-dilution conditions. The general reaction, shown in Scheme I, afforded coronands **3b**–**h** in reasonable yield.

The cyclic nature of **3b**–**h** has been confirmed by their NMR and mass spectra. Since ^{13}C NMR spectroscopy has been shown to provide a powerful tool for distinguishing between S- vs. N-substitution in heterocyclic thiols capable of thiol–thione tautomerism,[9c,10,13] we have extensively used

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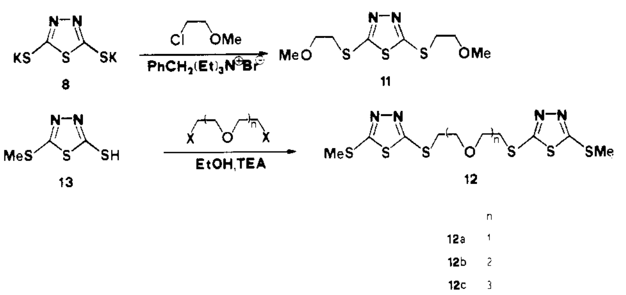
Scheme II



this technique to firmly establish the structures of the macrocycles obtained. ^{1}H and ^{13}C NMR spectral data of coronands **3b–h** are listed in Table I. The methylene C resonances in **3b–h** were easily assigned by comparison of their ^{13}C NMR spectra with those of open-chain models **11** and **12**.

Reaction of 8 with bis(2-iodoethyl) ether (**9a**) gave the 20-membered coronand **3b** as the major cyclic product (35%), along with minor amounts of the larger 30-membered coronand **3c** (6%) and 40-membered coronand **3d** (3.4%). Separation of **3b–d** was conveniently effected by careful column chromatography of the reaction mixture, using chloroform–ethyl acetate as the eluent.

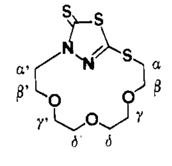
The smallest member **3a** of this series, which would possess a 10-membered ring, was not detected in the reaction mixture. Although 10-membered S-bridged coronands could be generated in the related pyridine,[11,12a] pyrazine,[12b] and pyrimidine series,[12c,d] molecular models show that 2,5-dimercapto-1,3,4-thiadiazole is unable to form unstrained 10-membered rings, probably due to the quite different geometry of its 5-membered ring and in particular to the enlargement of the angle between the two exocyclic sulfur atoms, which is close to 180°.[14]

The ^{1}H and ^{13}C NMR spectral data for **3b–d** (Table I) were virtually superimposable; however, the ring sizes were ascertained by EI or CI mass spectrometry, and the symmetrical macrocyclic structures were confirmed by their NMR patterns. The bridging methylenes are readily characterized by ^{1}H NMR in that the SCH_2CH_2O units appear as two distinct triplets, while ^{13}C NMR spectra display a single peak for the endocyclic quaternary carbons, confirming that the oxyethylene chains are symmetrically bridgehead to sulfurs.[9c,10]

The high-dilution reaction of 8 with 1,2-bis(2-iodoethoxy)ethane (**9b**) afforded the expected 13-membered coronand **3e** (34%), along with small amounts of the larger 26-membered coronand **3f** (3%). The macrocyclic structures were easily ascertained by the simple NMR pattern: all other spectral and physical data were consistent with the assignments. It is worth noting that both α- and γ-methylene protons in **3e** are shifted to higher fields as compared to those in **3f** [the most dramatic shift being observed for γ-methylenes ($\Delta\delta = 0.37$)]; conversely, the corresponding methylene carbons (together with the quaternary carbons) resonate to significantly lower fields (Table I).

Inspection of molecular models reveals that coronand **3e** can exist in several interconverting conformations, owing to the great flexibility of the bridging chain, and in any of these conformations the γ-methylene protons (and the α-methylenes to a less extent) lie always under the shielding region of the juxtaposed heterocyclic ring. These observations could account for the upfield shift of α- and γ-methylenes in **3e**, while the origin of the downfield shift experienced by the corresponding methylene carbons and by the endocyclic quaternary carbons is still unclear.

When bis[2-(2-bromoethoxy)ethyl] ether (**9c**) was reacted with **8** under standard reaction conditions, the 16-membered (2,5)-1,3,4-thiadiazolo coronand **3g** was isolated as the major cyclic product (48%), along with minor amounts of the 15-membered isomer (3,5)-1,3,4-thiadiazolino thione coronand **10** (3%), which possesses a ring nitrogen pointing into the complexing hole, and of the larger 32-membered coronand **3h** (2%). Structures **3g**, **3h**, and **10** were assigned on the basis of their NMR and mass spectra.



10

The ^{1}H NMR spectrum of **3g** displayed two triplets for α- and β-methylenes, while γ- and δ–methylenes showed up as an A_2B_2 system, centered at δ 3.58 (Table I). The α- and β-methylenes in **3h** also showed up as two distinct triplets, while γ- and δ-methylenes appeared as a singlet, as a consequence of the increased ring size and flexibility. As expected, the chemical shifts of α- and γ-methylene protons in **3g** are slightly shifted to higher fields as compared to those in **3h**, while the corresponding methylene and quaternary carbon resonances move once again to lower fields (Table I).

The ^{1}H NMR spectrum of **10** showed two distinct triplets at δ 3.26 ($J = 6.4$ Hz) and 4.53 ($J = 4.6$ Hz) for α- and α'-methylenes, a complex multiplet (two partly overlapped triplets) in the region at δ 3.85–3.99 for β- and β'-methylene protons and two singlets at δ 3.59 and 3.63 for γ,δ- and γ',δ'-methylenes. The assignments made were confirmed by spin-decoupling experiments. Irradiation of the α-methylene signal modified the pattern at δ 3.85–3.99 to a triplet centered at δ 3.94, which was assigned to the β'-methylene protons; the central line of this triplet was very intense, indicating that the expected singlet for β-methylene protons was superimposed to the triplet. Conversely, upon irradiation on the α'-methylene signal, the β-protons showed up as a broad triplet centered at δ 3.92, partly overlapped to a broad singlet, assigned to the β'-protons. Further irradiation at δ 3.93 caused the coalescence of the α- and α'-methylene patterns to two sharp singlets. Unfortunately, the assignment of the two singlets at δ 3.59 and 3.63 to the respective protons remained indefinite.

Unsymmetrical **10** was substantiated by its ^{13}C NMR spectrum, which showed eight well-resolved peaks for the magnetically nonequivalent methylene carbons, along with the expected two peaks for the endocyclic carbon atoms at 153.9 (C–S) and 186.4 (C=S) ppm.

Coronand **10** was further characterized by a single-crystal X-ray diffraction study. The thiadiazoline ring is planar, with maximum deviation of 0.005 (2) Å. Cyclization through N2 produces a conformation in which nitrogen atom N1 is directed inward, although torsion angles N1–N2–C10–C9 (−79.7°) and C1–S2–C3–C4 (79.0°) cause the entire polyether chain to be below the thiadiazoline ring. The C2=S3 bond distance is 1.657 (2) Å, the S2–C3 distance is 1.807 (2) Å, and all other C–S bonds are equal, 1.739 (1) Å. Angles at sulfur are 89.49 (8)° at S1 and 101.32 (9)° at S2. The C–O and C–C bond lengths are 1.399(2)–1.425(2) and 1.482(3)–1.496(3) Å, respectively.

Finally, open-chain **11** and **12** were synthesized as outlined in Scheme II. 2,5-Bis[(2-methoxyethyl)thio]-1,3,4-

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(14) Bats, J. W. *Acta Crystallogr., Sect. B* **1976**, *B12*, 2866.

thiadiazole (**11**) was obtained by treating **8** with a large excess of (2-chloroethyl)methyl ether in the presence of benzyltriethylammonium bromide, acting as phase-transfer catalyst.[15] Models **12a–c** were obtained in good yield as low-melting crystalline solids by condensation of 2-mercapto-5-(methylthio)-1,3,4-thiadiazole (**13**) with 0.5 equiv of the appropriate dihalide **9** in EtOH in the presence of triethylamine (TEA). ^1H and ^{13}C NMR spectral data of **11** and **12** are shown in Table I. Studies of the thermal conversion of **3g** to **10** and the complexing properties of 1,3,4-thiadiazole coronands toward transition-metal ions are under way.

Experimental Section

General Comments. Melting points were determined on a Kofler apparatus and are uncorrected. NMR spectra were recorded on a Bruker WP-80 NMR spectrometer. Chemical shifts are quoted in ppm (δ) from Me_4Si. Coupling constants (J) are reported in Hz. For ^{13}C NMR spectra a pulse length of 3 μs (90° pulse = 12 μs) and a pulse delay of 5 s were used in order to obtain satisfactory signal/noise ratio for quaternary carbons sandwiched between three heteroatoms. EI mass spectra (18 eV) were obtained by direct insertion into the ion source of an LKB 9000S instrument, while CI mass spectra (for **3c** and **3d**) were determined on a Kratos MS 50 double-focusing mass spectrometer. The mass spectral features of the thiadiazolo thia crown ethers synthesized have been discussed in detail elsewhere.[16] Elemental analyses were obtained commercially. Compound **8** was purchased from Aldrich Chemical and used without purification. Compounds **9a**,[17] **9b**,[17] **9c**,[18] and **13**[9a] were prepared by the literature procedures.

General Macrocycle Preparation. Reaction of 8 with 9a. Solutions of 2,5-dimercapto-1,3,4-thiadiazole dipotassium salt **8** (2.26 g, 10 mmol) in $EtOH-H_2O$ (4:1, 100 mL) and bis(2-iodoethyl) ether (3.26 g, 10 mmol) in EtOH (100 mL) were dropped separately but synchronously into stirred boiling EtOH (1 L). The addition took 3 h. After the reaction mixture was refluxed for 24 h, the solvent was removed in vacuo. The residue was partitioned between $CHCl_3$ and water. The organic layer was separated, dried over anhydrous Na_2SO_4, and concentrated to leave a solid, which was chromatographed (column, SiO_2), by eluting with $CHCl_3$–EtOAc (9:1), to give the following fractions.

Fraction A afforded 20⟨[OS(2,5)1,3,4-thiadiazolo,S]$_2$-coronand-8⟩[19] (**3b**), as white needles: 0.77 g, 35%; R_f 0.19; mp 153–154 °C (EtOH); MS, m/e 440 (M$^+$, 36%). Anal. Calcd for $C_{12}H_{16}N_4O_2S_6$: C, 32.71; H, 3.66; N, 12.71. Found: C, 32.48; H, 3.55; N, 12.84.

Fraction B gave 30⟨[OS(2,5)1,3,4-thiadiazolo,S]$_3$-coronand-12⟩ (**3c**), as white crystals: 0.13 g, 6%; R_f 0.17; mp 97–98 °C (dioxane); CI MS, m/e 661 (MH$^+$, 13%). Anal. Calcd for $C_{18}H_{24}N_6O_3S_9$: C, 32.71; H, 3.66; N, 12.71. Found: C, 32.28; H, 3.82; N, 12.55.

Fraction C yielded 40⟨[OS(2,5)1,3,4-thiadiazolo,S]$_4$-coronand-16⟩ (**3d**), as white scales: 75 mg, 3.4%; R_f 0.14; mp 124.5–126 °C (EtOH); CI MS, m/e 881 (MH$^+$, 5%). Anal. Calcd for $C_{24}H_{32}N_8O_4S_{12}$: C, 32.71; H, 3.66; N, 12.71. Found: C, 32.47; H, 3.58; N, 12.85.

Reaction of 8 with 9b. The general procedure was followed except for the substitution of 1,2-bis(2-iodoethoxy)ethane (10 mmol). The usual workup afforded a semisolid residue, which was chromatographed (column, SiO_2), by eluting with $CHCl_3$–EtOAc (9:1), to give the following fractions.

Fraction A afforded 13⟨O_2S(2,5)1,3,4-thiadiazolo,S-coronand-5⟩ (**3e**), as white prisms: 0.89 g, 34%; R_f 0.19; mp 132–133 °C (acetone); MS, m/e 264 (M$^+$, 27%). Anal. Calcd for $C_8H_{12}N_2O_2S_3$: C, 36.34; H, 4.57; N, 10.60. Found: C, 36.52; H, 4.44; N, 10.76.

Fraction B gave 26⟨[O_2S(2,5)1,3,4-thiadiazolo,S]$_2$-coronand-10⟩ (**3f**), as white needles: 80 mg, 3%; R_f 0.15; mp 95–96 °C (acetone); MS, m/e 528 (M$^+$, 32%). Anal. Calcd for $C_{16}H_{24}N_4O_4S_6$: C, 36.34; H, 4.57; N, 10.60. Found: C, 36.42; H, 4.51; N, 10.55.

Reaction of 8 with 9c. The general procedure was followed except for the substitution of bis[2-(2-bromoethoxy)ethyl] ether (10 mmol). The usual workup afforded a thick oily residue, which was chromatographed (column, SiO_2), by eluting with 15% AcOEt in $CHCl_3$, to give the following fractions.

Fraction A afforded 15⟨O_3(3,5)1,3,4-thiadiazolino,S-coronand-5⟩-15-thione (**10**), as white prisms: 90 mg, 3%; R_f 0.65; mp 117–118 °C (methanol); ^1H NMR δ 3.26 (t, J = 6.4 Hz, α-CH_2, 2 H), 3.59, 3.63 (s, γ-, δ-, γ'-, and δ'-CH_2, 8 H), 3.92 (t, J = 6.4 Hz, β-CH_2, 2 H), 3.94 (t, J = 4.6 Hz, β'-CH_2, 2 H), and 4.53 (t, J = 4.6 Hz, α'-CH_2, 2 H); ^{13}C NMR δ 32.7 (α-CH_2), 51.2 (α'-CH_2), 67.5 (β'-CH_2), 69.5 (β-CH_2), 69.8, 70.3, 70.4, 71.9 (γ-, δ-, γ'-, and δ'-CH_2), 153.9 (C_2), and 186.4 (C_5); MS, m/e 308 (M$^+$, 100%). Anal. Calcd for $C_{10}H_{16}N_2O_3S_3$: C, 38.94; H, 5.23; N, 9.08. Found: C, 38.76; H, 5.11; N, 8.95.

Fraction B gave the isomer 16⟨O_3S(2,5)1,3,4-thiadiazolo,S-coronand-6⟩ (**3g**), as white prisms: 1.48 g, 48%; R_f 0.27; mp 79.5–80 °C (methanol–ether); MS, m/e 308 (M$^+$, 18%). Anal. Calcd for $C_{10}H_{16}N_2O_3S_3$: C, 38.94; H, 5.23; N, 9.08. Found: C, 38.75; H, 5.18; N, 8.99.

Fraction C yielded 32⟨[O_3S(2,5)1,3,4-thiadiazolo,S]$_2$-coronand-12⟩ (**3h**), as white needles: 63 mg; 2%; R_f 0.10; mp 70–72 °C (acetone); MS, m/e 616 (M$^+$, 11%). Anal. Calcd for $C_{20}H_{32}N_4O_6S_6$: C, 38.94; H, 5.23; N, 9.08. Found: C, 39.12; H, 5.14; N, 8.85.

2,5-Bis[(2-methoxyethyl)thio]-1,3,4-thiadiazole (11). A stirred slurry of **8** (2.26 g, 10 mmol) in 2-chloroethyl methyl ether (20 mL) containing benzyltriethylammonium bromide (0.2 g) was heated on a water bath for 2 h. The NaBr formed was filtered, and the filtrate was evaporated in vacuo to leave an oil, which was chromatographed on silica gel (n-hexane–EtOAc, 3:1, as the eluent) to afford diether **11** as a colorless oil: 2.16 g, 81%; R_f 0.30; MS, m/e 266 (M$^+$, 4.1%). Anal. Calcd for $C_8H_{14}N_2O_2S_3$: C, 36.07; H, 5.30; N, 10.52. Found: C, 35.85; H, 5.12; N, 10.63.

3-Oxa-1,5-bis[(2-(methylthio)-1,3,4-thiadiazol-5-yl)thio]pentane (12a). General Procedure. A stirred solution of **13** (328 mg, 2 mmol), bis(2-iodoethyl) ether (**9a**; 326 mg, 1 mmole), and TEA (0.3 mL) in EtOH (5 mL) was refluxed for 1 h. The solvent was evaporated in vacuo, and the residue partitioned between CH_2Cl_2 and water. The organic layer was separated, dried over anhydrous Na_2SO_4, and concentrated. The residual oil was chromatographed on silica gel (eluent C_6H_{12}–EtOAc, 2:1) to give **12a** as a colorless oil, which crystallized on standing: 0.24 g, 60%; R_f 0.35; mp 35–37 °C; MS, m/e 398 (M$^+$, 5.4%). Anal. Calcd for $C_{10}H_{14}N_4OS_6$: C, 30.13; H, 3.54; N, 14.05. Found: C, 29.82; H, 3.44; N, 13.92.

3,6-Dioxa-1,8-bis[(2-(methylthio)-1,3,4-thiadiazol-5-yl)thio]octane (12b). The general procedure was followed except for the substitution of 1,2-bis(2-iodoethoxy)ethane (**9b**; 1 mmol). The usual workup gave **12b** as a pale yellow oil, which crystallized on standing: 0.34 g, 77%; R_f 0.24 (C_6H_{12}–EtOAc, 2:1); mp 30–31.5 °C; MS, m/e 442 (M$^+$, 1.3%). Anal. Calcd for $C_{12}H_{18}N_4O_2S_6$: C, 32.56; H, 4.10; N, 12.66. Found: C, 32.75; H, 4.03; N, 12.51.

3,6,9-Trioxa-1,11-bis[(2-(methylthio)-1,3,4-thiadiazol-5-yl)thio]undecane (12c). The general procedure was followed except for the substitution of bis[2-(2-bromoethoxy)ethyl] ether (**9c**; 1 mmol). The usual workup afforded **12c** as a pale yellow oil, which crystallized on standing: 0.27 g, 55%; R_f 0.12 (C_6H_{12}–EtOAc, 2:1); mp 33–35 °C; MS, m/z 486 (M$^+$, 0.2%). Anal. Calcd for $C_{14}H_{22}N_4O_3S_6$: C, 34.54; H, 4.56; N, 11.51. Found: C, 34.28; H, 4.43; N, 11.45.

X-ray Experimental. Intensity data for **10** were collected on an Enraf-Nonius CAD4 diffractometer equipped with Mo Kα radiation (λ = 0.71073 Å) and a graphite monochromator, by using a crystal of dimensions 0.24 × 0.32 × 0.44 mm at 25 °C. Crystal data: $C_{10}H_{16}N_2O_3S_3$, MW = 308.4, monoclinic space group $C2/c$, a = 15.548 (3) Å, b = 9.480 (1) Å, c = 19.817 (4) Å, β = 105.40 (2)°, V = 2816 (2) Å^3, Z = 8, D_c = 1.455 g cm^{-3}, T = 25 °C, μ(Mo Kα) = 5.1 cm^{-1}. One quadrant of data having $1° < \theta < 25°$ was collected by ω–2θ scans at rates varying 0.53–4.0 deg min^{-1}. Data reduction included corrections for background, Lorentz, polarization, and absorption effects. The latter were based on ψ scans

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of reflections near $\chi = 90°$, and the minimum relative transmission coefficient was 96.09%. Of 2477 unique data, 1842 had $I > 3\sigma(I)$ and were used in the refinement.

The structure was solved by direct methods and refined by full-matrix least squares based on F with $w = \sigma^{-2}(F_o)$. Non-hydrogen atoms were treated anisotropically, while hydrogen atoms were located in difference maps and refined isotropically. Final $R = 0.030$, $R_w = 0.052$ for 228 variables, and the maximum residual density was 0.21 eÅ^{-3}.

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Registry No. 3b, 108345-06-8; **3c**, 108345-07-9; **3d**, 108345-08-0; **3e**, 108345-09-1; **3f**, 108365-56-6; **3g**, 6663-97-4; **3h**, 108345-11-5; **8**, 4628-94-8; **9c**, 31255-26-2; **10**, 108345-10-4; **11**, 108345-12-6; **12a**, 108365-57-7; **12b**, 108345-13-7; **12c**, 108345-14-8; **13**, 6264-40-0; bis(2-iodoethyl) ether, 34270-90-1; 1,2-bis(2-iodoethoxy)ethane, 36839-55-1; 2-chloroethyl methyl ether, 627-42-9.

Supplementary Material Available: Molecular structure of **10** with numbering scheme, tables of bond distances and angles, coordinates for heavy atoms, coordinates and thermal parameters for H atoms, anisotropic thermal parameters, and endocyclic torsion angles (6 pages). Ordering information is given on any current masthead page.

Synthesis and Carbodemetalation Reactions of 4-Methyl- and 5-Aryl-2-(trimethylsilyl)oxazoles. C–C Bond Formation at C_2 of the Oxazole Ring

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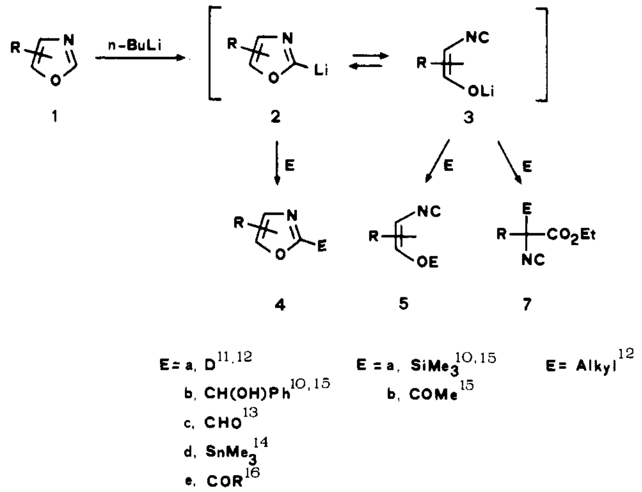
The title compounds **6a–d** have been prepared by sequential lithiation and silylation of the corresponding 2-H oxazoles and isomerization of the resulting α-isocyano silyl enol ethers. Silyloxazoles **6a–d** behave as stable 2-oxazolyl anion equivalents toward various carbon electrophiles (aldehydes, acyl chlorides, ketenes, azolium salts) to give 2-substituted oxazoles in good yields.

Scheme I



Oxazoles[1] continue to attract interest because of the presence of the oxazole ring in numerous biologically active compounds[2] and their use as auxiliaries in synthesis[3] in the form of latent carboxylic acid group equivalents[4] (triamide, ester, ω-cyano anhydride) and aza diene components in Diels–Alder reactions with acetylenes and alkenes[5] to give furans and pyridines as well as poly-

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