$H_{32}N_5O_{12}$, 558.2048; 11 MH^+ m/z 638.

Reductive Deacylation of Liposidomycins with $LiBH_4$. Under an argon atmosphere, to a solution of a crude mixture of liposidomycins (123 mg) in 20 mL THF was added 10 mg of $LiBH_4$. The reaction mixture was refluxed for 3 h. After the reaction mixture was cooled on an ice bath, the solution was adjusted to pH 4 by adding 5% HCl–MeOH. The resulting solution was extracted with EtOAc, and the aqueous layer was evaporated in vacuo. The residue was purified by preparative cellulose TLC (PrOH–1 N NH_4OH (7:3)). Further purification by cellulose TLC (BuOH–MeOH–H_2O (4:1:2)) gave 10.2 mg of a white powder, which was purified by high-voltage paper electrophoresis (0.1 N Py-HCOOH, pH 2 buffer, 2500 V, 170 mA) to give 1 mg of a pure powder 12: FAB-MS MH^+ m/z 656.

Saponification of Liposidomycin A (1) by LiOH. 1 (5–15 μg) was dissolved in 5 μL of 35 mM LiOH (previously purged with N_2 to remove dissolved oxygen). The glass reaction tube was sealed and incubated ca. 5 h at 37 °C (pH > 9), at which point it was neutralized with 0.25 M NH_4OAc (pH 6) and taken to dryness with a Speed-Vac. The dried residue was then taken up in 2–3 μL of H_2O and mixed directly into neat glycerol for analysis by FAB-tandem mass spectrometry.

Preparation of Amino Alcohol Derivatives of Fatty Acid from 1. Derivatives for charge-initiated fragmentation reactions were prepared by the addition of dimethyldioxirane[44] (ca. 100 mM in aqueous acetone) to a dried sample of 1, contained in 5-mm o.d. glass sample tubes. The reagent was added in moderate excess, mixed, and allowed to stand approximately 45 minutes at room temperature. The highly volatile reagent was then removed via Speed-Vac, and the pure, dry epoxides were treated with excess Me_2NH (40% aqueous solution). Sample tubes were then flame sealed and placed in a 105 °C oven (t > 16 h). The tubes were subsequently scored and opened and the reagent removed by Speed-Vac, yielding a dry mixture of dimethylamino alcohols, which were transferred in MeOH to glycerol for FAB-tandem mass spectrometry.

Acknowledgment. We are indebted to Dr. Muneki Ohuchi, JEOL Co., Ltd., for measurement of HMBC, HMQC, and DQF COSY spectra, M. Noguchi, S. C. Pomerantz, M. Seya, J. L. Stauffer, N. Yoshida for technical assistance, and G. Puzo for discussion. This work was supported by Grants GM 21584 and GM 29812 from the National Institutes of Health. J.G. received fellowship support from the American Foundation for Pharmaceutical Education and the University of Utah Research Committee.

Supplementary Material Available: CID mass spectra of m/z 427 and 558 positive ions and m/z 592 negative ion from **2**, ^1H NMR data for 1 and 3, HMBC, DQF COSY, and HMQC spectra of **10**, a HPLC chromatogram of liposidomycin extract, and molecular weights of liposidomycin components (10 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Crown Ether Derivatives of Tetrathiafulvalene. 1

Thomas K. Hansen,* Tine Jørgensen, Paul C. Stein, and Jan Becher

Department of Chemistry, Odense University, DK-5230 Odense M, Denmark

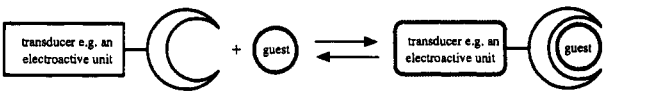
Received May 27, 1992

A synthetic procedure leading to derivatives of tetrathiafulvalene (TTF) incorporating crown ether ligands has been developed. The properties of such redox-active ionophores were studied by cyclic voltammetry (CV), plasma desorption mass spectrometry (PDMS), and ^1H-NMR.

Introduction

In recent years substantial progress has been reported in the fields of redox-active macrocyclic ligand systems,[1-4] that is, systems in which the electronic properties of a redox-active center can be influenced by complexation of a guest molecule in another part (the "antenna") of the molecule or vice versa. Such compounds might be used for redox-controlled release or uptake of guest molecules or as sensor molecules where complexation of ions or molecules is detected by a change in redox properties of the host. At the moment, this area is fairly new and applications are rather few, but the progress in host–guest chemistry, supramolecular chemistry, and general synthetic organic chemistry will undoubtedly lead to an increase of activities in this field. It is now possible to carry out creative design of tailor-made molecules by relatively simple combinations of well-studied ligand systems with redox-active moieties.

Scheme I



Sensormolecule — Complex with altered physical properties

In most of the previously studied cases that are relevant to this study the antenna is of the crown ether type and is situated in close proximity to a redox-active center (the "transducer") which in all cases incorporates a transition metal. Some examples are given in Figure 1. The recent system 1 was reported by van Veggel et al.[2] (M_1: Cu, Ni, Zn; M_2: Ba^{2+}, Cs^+; X: O, S) and showed significant shifts (approx. 90 mV) of redox potentials on substituting Ba^{2+} for Cs^+. The systems 2–5 were reported by Green et al.[3] Surprisingly, the redox potential of 2 (cp = cyclopentadienyl) was insensitive to the presence of alkali metal ions. However, significant shifts were observed in the case of 3–5. The largest shifts were observed when 3 was treated with sodium ions, but 400 equiv of sodium ions were necessary before the maximum shift (110 mV) was reached. The 15-crown-5 derivative 5 reached saturation at 70 mV, but after addition of only 5–7 equiv of sodium ions. A very interesting system 6 based on ferrocene has been reported recently by Gokel et al.[4] In that study the

(1) Gokel, G. W. *Chem. Soc. Rev.* **1992**, *21*, 39.
(2) Van Veggel, F.; Bos, M.; Harkema, S.; van de Bovenkamp, H.; Reedijk, J.; Reinhouldt, D. *J. Org. Chem.* **1991**, *56*, 225.
(3) (a) Green, M. L. H.; Heuer, W. B.; Saunders, G. C. *J. Chem. Soc., Dalton Trans.* **1990**, 3789. (b) Fu, E.; Green, M. L. H.; Lowe, V. J.; Marder, S. R. *J. Organomet. Chem.*, **1988**, C39.
(4) Medina, J. C.; Goodnow, T. T.; Bott, S.; Atwood, J. L.; Kaifer, A. E.; Gokel, G. W. *J. Chem. Soc., Chem. Commun.* **1991**, 290.

0022-3263/92/1957-6403$03.00/0

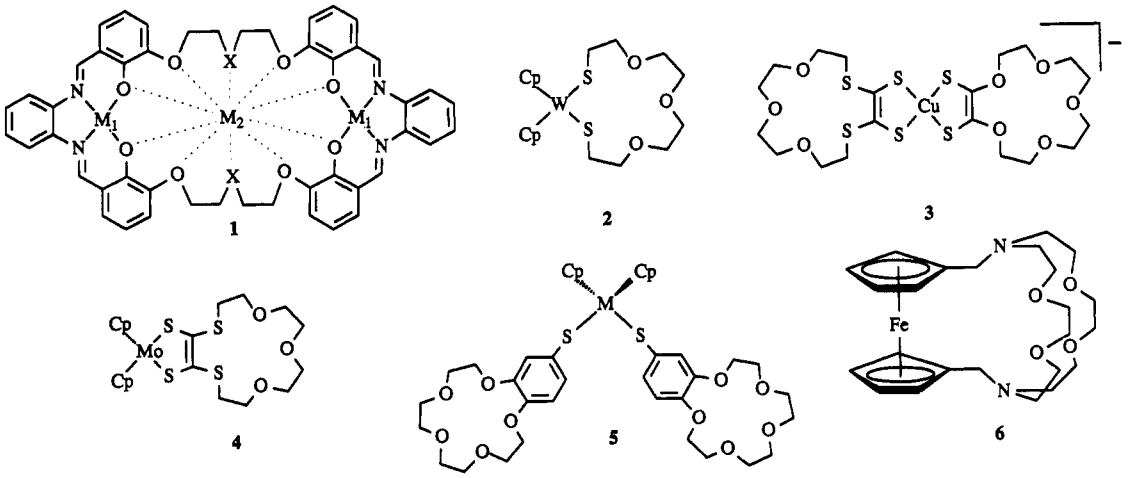


Figure 1.

maximum shift is observed after addition of 1 equiv of sodium (188 mV).

In Scheme I a generalized "sensor molecule" is shown. The "transducer" can be any chemical moiety that (i) serves the purpose of being easy to link to an antenna and (ii) possesses a physical property (UV absorption, redox activity, chemical shift, magnetic spin, etc.) that can be measured easily. (iii) The presence of a guest in the antenna should cause a change in the physical properties of the transducer. However, the reverse situation should also be considered: A physical stimulus (e.g., photoexcitation) might induce a physical change in the transducer and subsequently alter the binding properties of the antenna. Drug delivery, etc. is an obvious application for such systems.

In general, it should be noted that the binding properties of 2–6 are in good agreement with known binding data[5] associated with the parent ligand systems involved. Thus, the ligand incorporated in 6 is known to complex sodium ions better than 5, which again is better than 3. This is reflected in the amount of sodium ions needed to obtain saturation of the shift. On the other hand, the magnitude of the maximum shift is probably a more complex function of the polarizability of the redox system, of the distance to and orientation of the ligand center, as well as other factors. Consequently, it will be less predictable and eventually more interesting to vary the transducer part in order to obtain higher shift values. One such possibility is to use the tetrathiafulvalene (TTF) system as a redox-active unit in such applications.

The unusual behavior of the TTF system has been studied intensively for more than 20 years,[6] mainly because of TTF's ability to form a stable radical cation or dication upon oxidation and to form charge-transfer salts with low dimensional metallic conductivity. The vast majority of papers in this very active field of chemistry have aimed at the physical aspects of the TTF chemistry, especially since the discovery of superconductivity in several salts and CT-complexes of TTF derivatives. However, using TTF as an entirely organic redoxactive unit in host–guest systems seemed attractive to us because the chemistry of TTF is well-known and because the TTF unit shows a fully reversible, two-step oxidation.

Regarding the choice of ligand systems suitable as "antenna" we chose a crown ether for simplicity. Since the first discovery by Pedersen[7] of crown ethers and the ability of such compounds to complex alkali metals, tremendous progress has been made in the number of derivatives and the investigation of properties crown ethers show. It has been shown that the size of the ring and the nature of the heteroatoms in the ring strongly influence complexation constants and the choice of "preferred guest-metal". Generally speaking, a bigger cavity requires bigger cations, and ligands with oxygen as donor atoms have higher affinity for maingroup (I–II) elements than ligands with mainly nitrogen- or sulfur-donor atoms, which preferentially form complexes with transition metals. Crown ethers with mixed oxygen-/sulfur-donor atoms are not the best ligand systems in terms of high complexation constants and specificity toward certain cations. The aim of this study has been to demonstrate whether or not the TTF-unit is a suitable redox-active unit in such applications and to determine the fundamental properties of such systems. The crown ether system has been chosen because of the relatively easy synthesis and the potential for making different ring sizes.

Results and Discussion

The key starting material, dithiolate 7 (dmit, Scheme II),[8] was easily generated from 24 by treatment with a base in tetrahydrofuran (THF) or dimethylformamide (DMF) as noted in our preliminary communication.[9]

Reactions with dibromo glycols 8–12 were generally carried out at room temperature overnight. In most cases a series of mono-, di-, tri-, tetra-, and even pentamers was obtained, and the products 13–23 were separated by chromatography. The distribution could be influenced by the use of high-dilution techniques and variations in solvent. High dilution generally increased the yield of monomer 3–5 times at the expense of "multimers". The reaction and (isolated) yields are given in Scheme II. In Chart I the obtained macrocycles are written in full.

The striking fact that 22 and 23 were isolated in high yields without the use of high dilution (in contrast to the shorter chain examples 13, 17, and 20 appears to us to be

(5) Izatt, R. M.; Pawlak, K.; J. Bradshaw, J. *Chem. Rev.* **1991**, *91*, 1721.

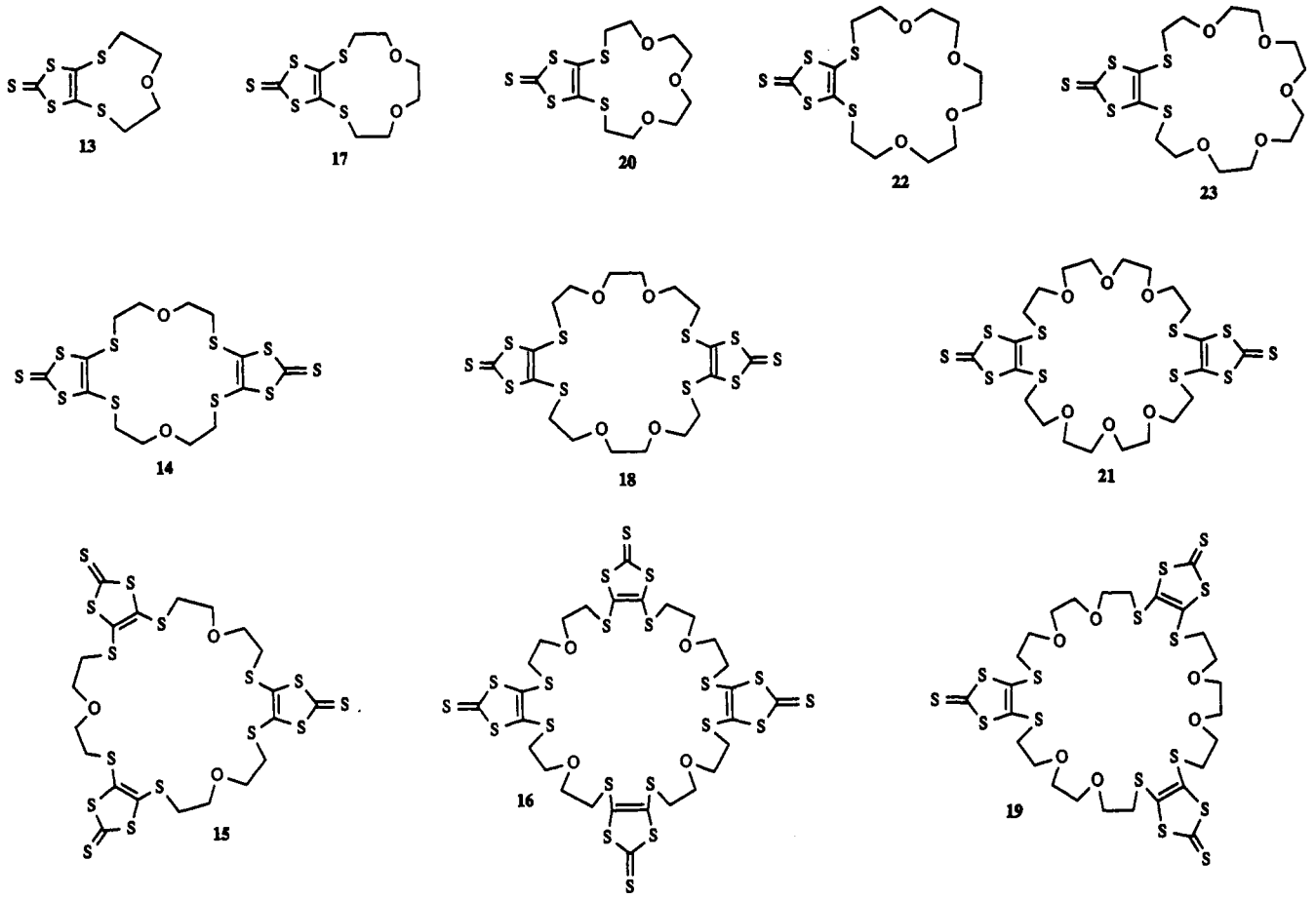
(6) (a) Coleman, L. B.; Cohen, M. J.; Sandman, D. J.; Yamagishi, F. G.; Garito, A. F.; Heeger, A. J. *Solid State Commun.* **1973**, *12*, 1125. (b) Ferraris, J.; Cowan, D. O.; Walatka, V.; Perlstein, J. H. *J. Am. Chem. Soc.* **1973**, *95*, 498. (c) Williams, J. M.; Wang, H. H.; Emge, T. J.; Geiser, U.; Beno, M. A.; Leung, P. C. W.; Carlson, K. D.; Thorn, R. J.; Schultz, A. J.; Whangbo, M. *Prog. Inorg. Chem.* **1987**, 51 (review). (d) Schukat, G.; Richter, A. M.; Fanghänel, E. *Sulfur Rep.* **1987**, 155.

(7) Pedersen, C. J. *J. Am. Chem. Soc.* **1967**, *89*, 2495 and 7017.

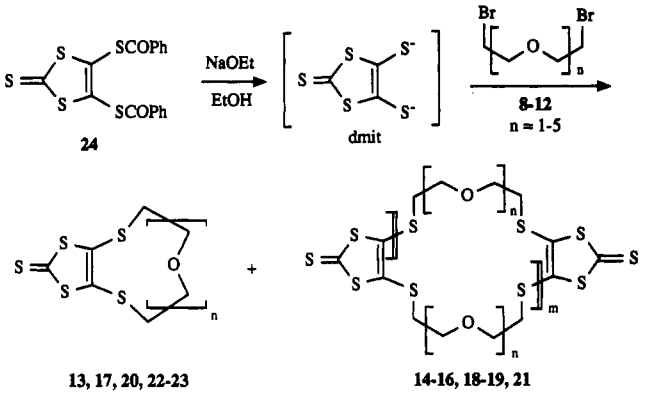
(8) Steimecke, G.; Sieler, H.; Kirmse, R.; Hoyer, E. *Phosphorus Sulfur* **1979**, *7*, 49.

(9) Becher, J.; Hansen, T. K.; Malhotra, N.; Bojesen, G.; Bøwadt, S.; Varma, K. S.; Girmay, B.; Kilburn, J.; Underhill, A. E. *J. Chem. Soc., Perkin Trans. 1* **1990**, 175.

Chart I



Scheme II



	13	14	15	16	17	18	19	20	21	22	23
n	1	1	1	1	2	2	2	3	3	4	5
m	-	1	2	3	-	1	2	-	1	-	-
yield (%)	65	22	4	3	60	25	4	61	25	87	80

a very clear-cut case of the "template effect".[10] Most likely the size of the counterion to 7 is important for the folding of the crown ether chain. Since the effect is so obvious in this case, we made a more thorough investigation of the effect of metal ion in one case (7 + 9) in order to optimize the yield of dimer 18 by changing the counterion, hoping that K^+ might template the formation of 18. In order to determine yields accurately without the loss associated with workup, we used HPLC and determined the yields on samples taken directly from the reaction mixture. Yields were determined according to calibration curves made from isolated samples of 17 and 18. Selected results are given in Table I.

Table I

expt no.	M^+	solvent	17 (% yield)	18 (% yield)	total	ratio
1	Li^+	EtOH	42.9	19.5	62.4	0.45
2	Na^+	EtOH	37.7	26.0	63.7	0.69
3	K^+	EtOH	22.1	16.9	39.0	0.77
4	Na^+	THF	8.2	30.3	38.5	3.70

In experiments 1–3, dibenzoyl ester 24 was suspended in ethanol and treated with LiOEt, NaOEt, or KOEt, respectively, to generate 7 with different counterions. Under inert atmosphere 9 was added. In experiment 4 the solvent was THF. When the reaction was over (24 h) suitable dilution took place, and the reaction mixture was injected on the column.

As can be seen from Table I, the use of a bigger counterion indeed changes the distribution toward a higher proportion of the dimer 18 at the expense of monomer 17. This will obviously also result in a larger amount of multimer. If the purpose is to produce dimer 18, sodium appears to be the best counterion, since when potassium ions were present a higher fraction of the reaction mixture was polymeric or open-chain byproducts. Furthermore, the effect of solvent on the distribution pattern seemed

(10) (a) Vögtle, F.; Weber, E. *Host Guest Complex Chemistry—Macrocycles—Synthesis, Structures, Applications*; Springer: Berlin, Heidelberg, New York, Tokyo, 1985. (b) Sellmann, D.; Frank, P. *Angew. Chem., Int. Ed. Engl.* **1986**, 1107. (c) Buter, J.; Kellogg, R. M. *J. Org. Chem.* **1981**, *46*, 4481. Attempts to use ironcarbonyl as template as in the work of Sellmann[10b] was unsuccessful. Also the approach of Kellogg[10c] to utilize the "cesium effect" did not in our hands lead to any increase in yields compared to using sodium ions as template.

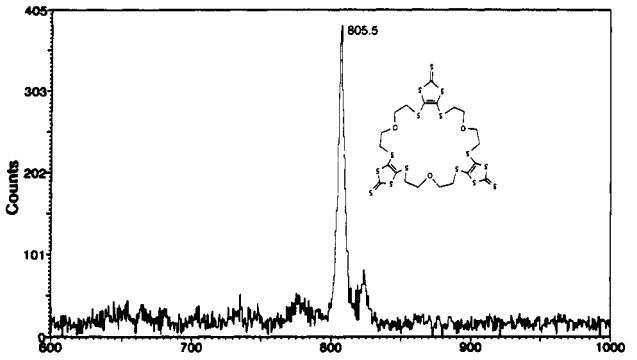
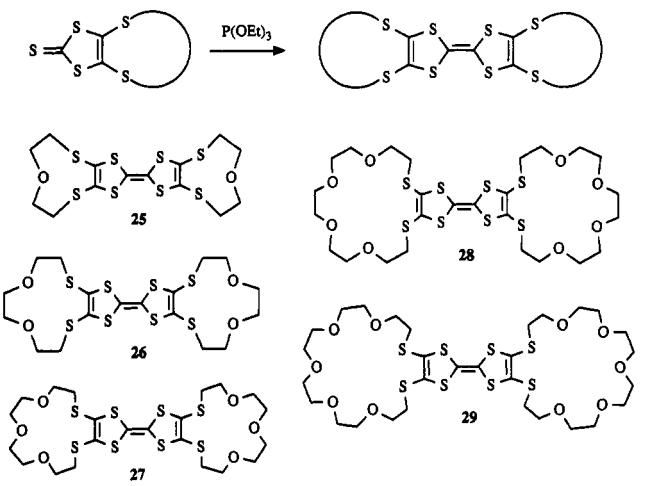


Figure 2. PDMS of 15.

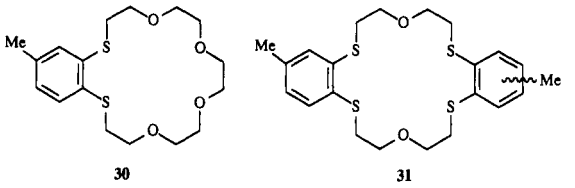
Scheme III



greater than the effect of counterion, as can be concluded from experiment 4. Consequently, since the differences in yields are relatively small, it seems more reasonable to assign the influence of counterion to changes in the reactivity of 7 with different counterions than to a template effect.

Plasma desorption mass spectrometry (PDMS) proved to be an efficient tool in the characterization of the oligomers.[11] Being a relatively new technique, still not widely used by organic chemists, it deserves to be noted that PDMS appears in this context to have several advantages compared to other MS techniques such as EI or FAB. PDMS gives a semiquantitative "overall" picture of the components contained in a reaction mixture with almost no fragmentation. In contrast, EI generally separates components according to volatility and brings about extensive fragmentation. Compared to FAB the main advantage is the ability to produce molecular ions reliably without the need for "the right solvent". In the present case numerous fractions from chromatographic separations had to be identified. Between the fractions containing the oligomers minor fractions could be found containing open-chain products. EI-MS was unable to produce molecular ions for the higher oligomers. However, PDMS afforded spectra like the one shown in Figure 2 (trimer 15) reliably and fast.

Monomers 13, 17, 19, 22, and 23 all underwent the standard coupling reaction generating TTF from 1,3-dithiole-2-thiones in neat triethyl phosphite at 110–130 °C as outlined in Scheme III. In general, the desired products crystallize directly from the reaction mixture and can be



30 31

Figure 3.

filtered off in yields of 30–40%. At this stage in our investigation we discovered that one of the five TTFs (25–29) had been synthesized previously. Compound 27 was prepared in 1985 by Otsubo et al.,[12] who obtained a yield of 0.8% via alkylation directly on the reaction mixture obtained from sodium reduction of carbon disulfide in DMF. However, none of the experiments we wanted to do with the compound were reported.

The metal-binding properties of compounds 25–29 were investigated by cyclic voltammetry, PDMS, and ^{1}H-NMR. Also, the standard picrate extraction technique introduced by Pedersen[13] was attempted because direct comparison to the very similar ligands 30 and 31 (Figure 3) reported by Pedersen[13] would then be possible. However, the picrate technique was not very useful because the absorption maximum of the TTF-chromophore overlaps very much with the picrate absorption band. Since extraction was small, the picrate absorption had to be read as a small shoulder on the TTF-absorption; thus, the obtained results were close to the detection limit. Under the same experimental conditions as described by Pedersen,[13] the K^+ extraction of 28 was found to be comparable with 30 (3.2% extracted from water into methylene chloride) and slightly higher for Na^+ (not determined for 30 by Pedersen), whereas the situation was reversed for 29 where extraction of sodium was below the detection limit whereas a few percent of potassium ions were extracted as expected from the increase in ring size. For the smaller ring systems 25–27 the picrate extraction method could not be used.

Using the PDMS method described by us earlier[11] we could compare the binding of the individual ligands by washing the ligands with equimolar solutions of lithium, sodium, and potassium ions directly on the nitrocellulose target matrix. We found all ligands described here to be less efficient ligands when compared to 18-crown-6 and 15-crown-5 because the $[M + H]^+$ peaks in all cases were higher than the complexed peaks. Compound 17 (and with the same ligand: 27) showed some affinity to sodium ions. Only 22 and 23 (and consequently also 28 and 29) showed substantial binding. The affinity sequence for 22 could be established as $Na^+ > K^+ \gg Li^+$. For 23 the sequence $K^+ > Na^+ \gg Li^+$ was found.

The ^{1}H-NMR spectra of 25 and 28 are given in Figure 4. The spectrum of 25 is independent of the salt concentration for concentrations up to 70 Na^+ ions per molecule. The spectrum of 28, by contrast, shows a dramatic change in resonance position of the $-SCH_2CH_2O-$protons even for relatively low values of r (r is the ratio of Na^+ ions per molecule). The same difference is observed in $T_1(^1H)$: For 25 this is ~1.0 s and independent of the Na^+ concentration, whereas the $T_1(^1H)$ for 28 drops from 1.0 to 0.6 s upon addition of $NaPF_6$ (see Table II). The fact that 25 does not exhibit a change in the NMR values makes us feel confident that the observed changes in 28 are indeed due to complex formation between the ligand and the Na^+ ions. The ^{1}H-NMR spectra suggests that, at the time

(11) Malhotra, N.; Roepstorff, P.; Hansen, T. K.; Becher, J. J. Am. Chem. Soc. 1990, 112, 3709.

(12) Otsubo, T.; Ogura, F. Bull. Chem. Soc. Jpn. 1985, 58, 1343.
(13) Pedersen, C. J. J. Org. Chem. 1971, 36(2), 254.

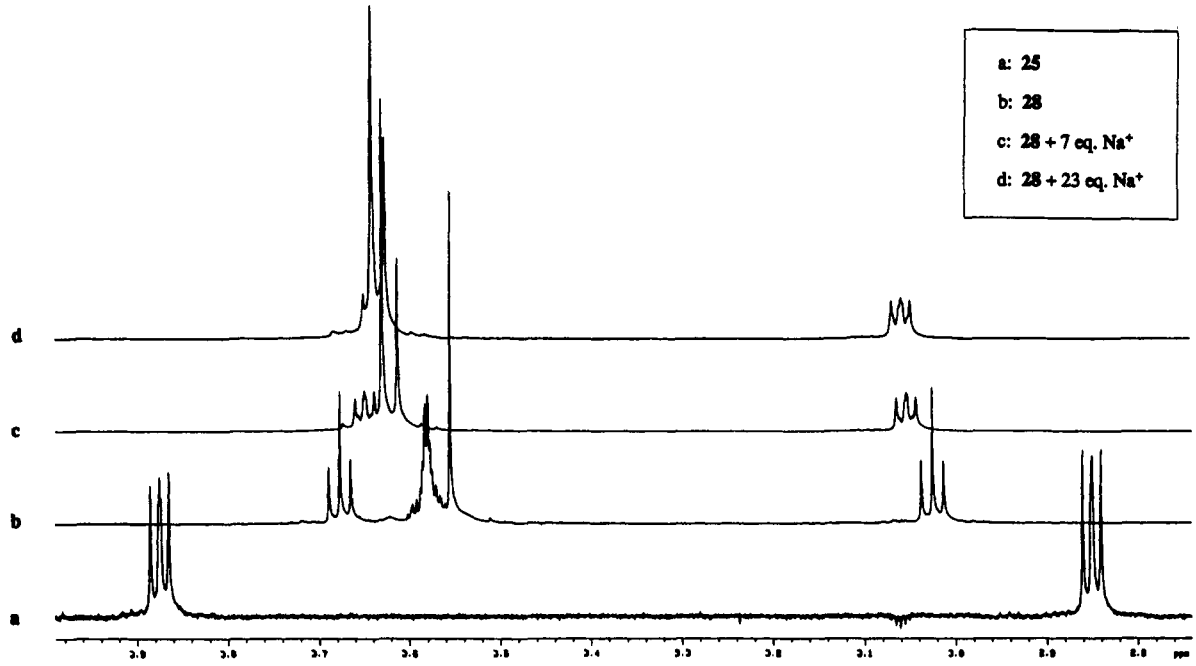
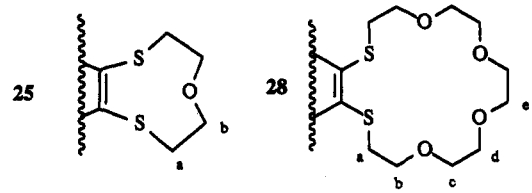


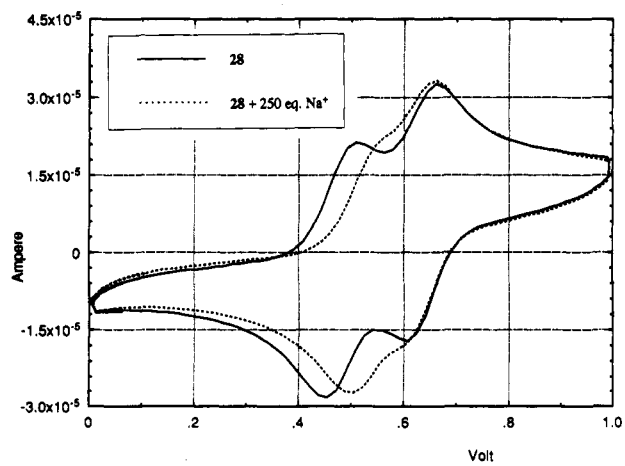
Figure 4.

Table II



	28				25	
	δ (ppm)		T_1 (s)		δ (ppm)	T_1(s)
site	r = 0	r = 0	r = 6.8	r = 23.4	all r	all r
a	3.026	0.97	0.60	0.52	2.850	1.85
e	3.556	1.04	0.65	0.59		
c, d	3.581	1.03	0.66	0.59		
b	3.677	1.01	0.64		3.874	1.00

Table III. Shifts in Redox Potential on Addition of Alkali Ions



250 equiv of	Li^+	Na^+	K^+
25	0	0	0
26	0	0	0
27	0	+10	0
28	+10	+80	+10
29	0	+15	+60

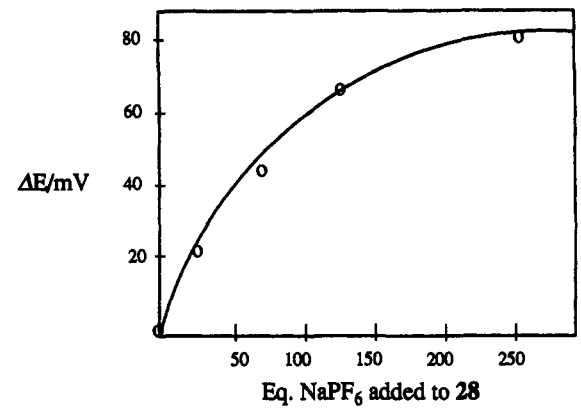


Figure 5.

scale of the experiment at least, all available positions are occupied by Na^+ ions. The changes in line shape and relaxation time occurring upon complexation is due to a stiffening of the ring. A more precise investigation of the behavior of the system for very low Na^+ concentrations is currently under way and will be reported elsewhere.

Complexation was also studied by cyclic voltammetry. We found that **25–29** exhibit a two-electron reversible oxidation–reduction with $E_{1/2(1)}$ = 0.48 V and $E_{1/2(2)}$ = 0.64 V (±5 mV). We then determined the same values by adding controlled amounts of alkali metal ions to the compounds dissolved in acetonitrile and in the presence of 0.1 M tetrabutylammonium hexafluorophosphate. The salts added were either $LiPF_6$, $NaPF_6$, or KPF_6. The shifts observed are summarized in Table III. The shifts observed were always to more anodic (more positive) potential and always affected only $E_{1/2(1)}$, whereas $E_{1/2(2)}$ remained unchanged. Only **28** and **29** showed really significant shifts, and the data seem to be in good agreement with the knowledge on complexation summarized above; thus, the preference of **28** seems to be sodium ions as this ion induces the largest shift, whereas the largest shift for **29** is found when potassium ions are added. The data in Table III are all determined with a large excess (250 equiv) of alkali ions compared to the ligand. The magnitude of the shift was found to be dependent on the concentration

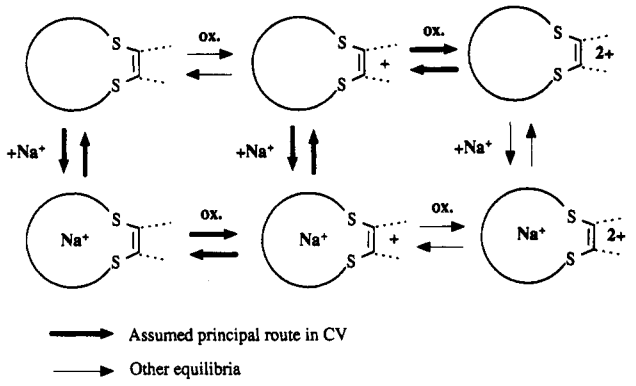


Figure 6.

of the alkali metal ion up to a certain limit. The titration of **28** with sodium ions against the observed shift is shown in Figure 5.

In the case of **28** (CV in Table III) the exact magnitude of the maximum shift was difficult to read because the two peaks merged almost into one. The shift was estimated to be 80 mV, and a computer simulation confirmed this result. When lithium ions or potassium ions were added to **28**, significant but smaller shifts were induced, establishing the order to be $Na^+ > K^+ > Li^+$. Furthermore, the size of the shifts correlated well to the relative "binding power" determined via PDMS found to be Li^+ (1.0), Na^+ (3.8), K^+ (1.5). We assume the reason why only the first oxidation peak is influenced by alkali metal ions should be found in the fact that oxidation of the TTF-unit produces a positive charge situated close to the ligand system, which can be expected to repel the sodium ions, thus lowering the binding constant and eventually "pushing" complexed alkali metal ion out of the ring. The second oxidation peak should then be identical to the neutral species. This is indeed what the CV shows. Figure 6 summarizes the possible equilibria and suggest a principal route for the processes occurring during a CV cycle.

When the shift values are compared to the results obtained by Green[3] for **2–5** it is noteworthy that the maximum shifts are somewhat smaller than Green's, but the specificity is larger. Green found that the order of efficiency to induce the shifts was $Na^+ > Li^+ > K^+$, but the difference in affinity of the alkali metal ions was surprisingly small; that is, the specificity of binding was low. In Green's case binding of the cations actually occurs to a negatively charged ligand system; thus, an effect of ion pairing might be included in the size of the shift. The neutral species **4** indeed showed much smaller shift values than the negatively charged **3**.

That the shifts we have observed are really due to complexation is evidenced by the fact that **25** did not show any significant difference in oxidation potential when Bu_4NPF_6 was used as electrolyte compared to using $LiPF_6$, $NaPF_6$, or KPF_6. The size of the crown in **25** is indeed too small for real complexation as shown by CPK models. Effects due to anions have been excluded by using an alkali metal salt with the same anion as the supporting electrolyte.

Of all four crown ether derivatives we did only succeed to form a tetracyanoquinodimethane (TCNQ) complex with **25**. The conductivity was rather low, 2.14×10^{-4} S, and the temperature characteristics confirmed that the complex was a semiconductor.

In conclusion, the series of compounds presented do indeed show the expected properties when the ligand has a size that allows binding. The specificity of binding is relatively large, and it can be concluded that the TTF unit is useful as an electroactive unit in host–guest systems. It now remains to incorporate TTF into better ligand systems.

Experimental Section

The CV experiments were all made in acetonitrile (0.1 M Bu_4NPF_6 as supporting electrolyte). Counter- and working electrodes were made of platinum, and potentials were referenced versus SCE. Sweep rates were in all experiments 100 mV/s. For the ^{1}H-NMR investigation standard pulse sequences were used. Temperature was stabilized at 25 °C during all experiments, but no independent calibration of the temperature was performed.

The sample of **28** was obtained by dissolving 6.9 mg in 3.2 mL of MeCN, whereafter 2.0 and 4.9 mg of $NaPF_6$ was added to the NMR tube, yielding a ratio of Na^+ ions per molecule (r) of 0, 7, and 23. From the integrals of the ^{1}H-resonances, we estimated the solubility of **25** to be about 1 mg per 3 mL of MeCN. To this sample 2.9 mg and later further 2.1 mg of $NaPF_6$ was added, yielding nominally 0, 40, and 70 Na^+ ions per molecule. All other NMR spectra were recorded in $CDCl_3$ with TMS as internal standard. NMR data are recorded in δ. Melting points are uncorrected. Elemental analyses were carried out by Microanalytical Lab, Copenhagen University. Solvents were dried by standard techniques. The HPLC investigation were done on a standard setup with isocratic elution 83% ethanol/17% water on a reversed-phase (RP-18) column.

13: 5-oxo-2,8,10,12-tetrathiabicyclo[7.3.0]dodec-1(9)-ene-11-thione. **14**: 5,17-dioxa-2,8,10,12,14,20,22,24-octathiatricyclo-[19.3.0.$0^{9,13}$]tetraicosa-1(21),9(13)-diene-11,23-dithione. **15**: 5,17,29-trioxa-2,8,10,12,14,20,22,24,26,32,34,36-dodecathiatetracyclo[31.3.0.$0^{9,13}$.$0^{21,25}$]hexatriaconta-1(33),9(13),21(25)-triene-11,23,35-trithione. **16**: 5,17,29,41-tetraoxa-2,8,10,-12,14,20,22,24,26,32,34,36,38,44,46,48-hexadecathiapentacyclo-[43.3.0.$0^{9,13}$.$0^{21,25}$.$0^{33,37}$]octatetraconta-1(33),9(13),21(25),33(37)-tetraene-11,23,35,47-tetrathione.

Procedure 1. (High Dilution). Optimized for monomer **13**. Sodium (0.52 g; 0.023 mol) in small pieces was dissolved in 30 mL of dry ethanol, and the solution was allowed to cool. This solution was added to a stirred suspension of powdered dibenzoyl ester **24** (4.04 g; 0.01 mol) in 20 mL of dry ethanol under N_2. When an intense red color of **7** had developed and all solid crystals of **24** had disappeared (15–20 min), the solution was sucked into a 50-mL syringe via a piece of Teflon tubing. A solution of diethylene glycol dibromide (**8**) (2.32 g; 0.01 mol) in 50 mL of dry ethanol was sucked into another syringe. The syringes were mounted in a pump (medical Perfusor pump) capable of unloading both simultaneously and very slowly. The two reagents were led into a 250-mL three-necked flask (already loaded with 75 mL of dry ethanol) over 18 h via two Teflon tubings and a rubber septum.

Workup. The solvent was removed in vacuo. The residue was suspended in 150 mL of water and extracted with 3 × 150 mL of chloroform, the chloroform phase was dried with magnesium sulfate, and most of the solvent was evaporated off. The residue was chromatographed on a silica gel column using a mixture of 45% methylene chloride and 55% petroleum ether (bp 65–70 °C) as eluent. Only the first yellow fraction was collected. It contained monomer **13** (1.75 g; 65%). **13**: yellow solid; mp 131 °C; ^{1}H-NMR 2.9 (2, t), 4.0 (2, t); ^{13}C-NMR 205.0, 143.1, 73.7, 36.7; IR (KBr) ν (cm^{-1}) 1068 (C=S), 1134 (–OCH_2); MS m/e 268 (M^+, 100), 196 (8), 164 (18), 88 (88), 76 (92). Anal. Calcd for $C_7H_8OS_5$: C, 31.73; H, 3.02. Found: C, 31.34; H, 2.98.

Procedure 2. Optimized for best yield of **14**. 4.04 g (0.01 mol) of dibenzoyl ester **24** and 2.32 g (0.01 mol) of diethylene glycol dibromide (**8**) was suspended in a mixture of 150 mL of dry ethanol and 50 mL of dry THF. A solution of 0.52 g (0.023 mol) of sodium in 50 mL of dry ethanol was added slowly under inert atmosphere over 8 h. The mixture was left overnight.

Workup. The solvent was removed in vacuo. The residue was suspended in 150 mL of water, extracted with 3 × 150 mL of chloroform, the chloroform phase was dried with magnesium sulfate, and the solvent was evaporated off. The residue was chromatographed on a silica gel column using a mixture of 50% methylene chloride and 50% petroleum ether as eluent. The first yellow band contained monomer **13** (0.48 g; 18%), the second band contained dimer **14** (0.59 g; 22%), and the third poorly separated fraction was applied to PTLC and eluated twice with a mixture

of 65% methylene chloride and 35% petroleum ether (bp 65–70 °C) affording well-separated trimer **15** (107 mg; 4%) and tetramer **16** (80 mg; 3%) with a small contamination of pentamer. **14**: yellow solid; mp 198 °C; ^{1}H-NMR 3.1 (2, t), 3.9 (2, t); IR (KBr) ν (cm^{-1}) 1056 (C=S), 1109 (–OCH$_2$); MS *m/e* 536 (M$^+$, 74), 252 (15), 132 (40), 88 (100). Anal. Calcd for $C_{14}H_{16}O_2S_{10}$: C, 31.15; H, 2.95. Found: C, 31.34; H, 2.98. **15**: yellow oil; ^{1}H-NMR 3.1 (2, t), 3.9 (2, t); IR (KBr) ν (cm^{-1}) 1055 (C=S), 1110 (–OCH$_2$); PDMS 805.5 (M$^+$). **16**: yellow oil; ^{1}H-NMR 3.1 (2, t), 3.9 (2, t); IR (KBr) ν (cm^{-1}) 1056 (C=S), 1109 (–OCH$_2$); PDMS 1074.5 (M$^+$).

17: 5,8-dioxa-2,11,13,15-tetrathiabicyclo[10.3.0]pentadec-1-(12)-ene-14-thione. **18**: 5,8,20,23-tetraoxa-2,11,13,15,-17,26,28,30-octathiatricyclo[25.3.0.0^{12,16}]triaconta-1(27),12(16)-diene-14,29-dithione. **19**: 5,8,20,23,35,38-hexaoxa-2,11,13,15,17,26,28,30,32,41,43,45-dodecathiatetracyclo-[40.3.0.0^{12,16}.0^{27,31}]pentatetraconta-1(42),12(16),27(31)-triene-14,29,44-trithione.

Procedure 1 (High Dilution). Optimized for highest possible yield of monomer **17**. A procedure identical to the one used for **13** was used, substituting diethylene glycol dibromide with triethylene glycol dibromide (**9**) (2.76 g; 0.01 mol). The day after the reaction was started, the solvent was evaporated off and the residue was dissolved in 200 mL of $CHCl_3$, washed with water, and dried ($MgSO_4$). The chloroform phase was concentrated and applied to PTLC (Merck silica gel 60 PF_{254}) using a mixture of 60% dichloroethane and 40% chloroform as eluent (eluting twice). The monomer **17** could in this way be separated from a small amount of the dimer **18**. **17**: yield 1.88 g, 60%; yellow solid; mp 114–15 °C; ^{1}H-NMR 3.72 (4 H, t), 3.64 (4 H, s), 3.08 (4 H, t); ^{13}C NMR 211.4, 137.0, 69.3, 69.0, 36.5. IR (KBr) ν (cm^{-1}) 1034 (C=S), 1115 (–OCH$_2$): MS *m/e* 312 (M$^+$, 100), 196 (20), 148 (19), 120 (37), 88 (96).

Procedure 2. Optimized for highest possible yield of dimer **18**. Powdered dibenzoyl ester **24** (4.04 g; 0.01 mol) was suspended in 20 mL of dry ethanol. A solution of sodium ethoxide (made by dissolving sodium (0.52 g; 0.23 mol) in 30 mL of dry ethanol) was added, and the mixture was stirred under nitrogen for 20 min. The solution was poured slowly, but in a steady stream, into 1 L of dry, degassed diethyl ether with stirring. Immediately after addition the stirring was discontinued and the solution was left for 1 h, protected from air (if a beaker is used, covering with foil and a layer of argon is sufficient. The precipitated red sodium salt Na_2(dmit) **7** was filtered using a Schlenk filter unit and transferred to a 250-mL three-necked flask containing 100 mL of dry THF. To this solution triethylene glycol dibromide (**9**) (2.76 g; 0.01 mol) in 50 mL of dry THF was added over 4 h. keeping the reagents under N_2 at all stages. After stirring overnight the solvents were evaporated off. A workup procedure identical to procedure 1 afforded monomer **17** (150 mg; 5%), dimer **18** (0.78 g; 25%), and trimer **19** (120 mg; 4%). **18**: yellow solid; mp 96–97 °C; ^{1}H-NMR 3.76 (8 H, t), 3.64 (8 H, s), 3.10 (8 H, t); ^{13}C-NMR 211.2, 136.8, 77.0, 70.6, 36.6; IR (KBr) ν (cm^{-1}) 1061 (C=S), 1123 (–OCH$_2$); MS *m/e* 624 (M$^+$, 9), 492 (13), 180 (10), 76 (100). Anal. Calcd for $C_{18}H_{24}O_4S_{10}$: C, 34.70; H, 3.90. Found: C, 34.61; H, 3.84. **19**: yellow oil; ^{1}H-NMR 3.7 (12 H, t), 3.6 (12 H, s), 3.1 (12 H, t); IR (KBr) ν (cm^{-1}) 1060 (C=S), 1125 (–OCH$_2$); PDMS *m/e* 938.2 (M$^+$).

20: 5,8,11-trioxa-2,14,16,18-tetrathiabicyclo[13.3.0]octadec-1-(15)-ene-17-thione. **21**: 5,8,11,23,26,29-hexaoxa-2,14,16,18,20,32,34,36-octathiatricyclo[31.3.0.0^{15,19}]hexatriaconta-1(33),15(19)-diene-17,35-dithione.

The same two procedures were used as for **17** and **18**, substituting glycol **9** with **10**. Under high-dilution conditions (procedure 1) 61% of **20** was obtained. Without high dilution (procedure 2) 23% of **20** and 25% of **21** were obtained. Analytical and spectroscopical data were in good agreement with literature.[12]

22: 5,8,11,14-tetraoxa-2,17,19,21-tetrathiabicyclo[16.3.0]henicos-1(18)-ene-20-thione. **Procedure for 22.** A 2.02-g (0.005-mol) portion of dibenzoyl ester **24** was suspended in dry ethanol. Under inert athmosphere a solution of sodium ethoxide (made by dissolving sodium (0.3 g; 0.13 mol) in 25 mL of dry ethanol) was added. After the solution was stirred for 15 min, 1.82 g (0.005 mol) of pentaethylene glycol dibromide (**11**) was added over 4 h. The next day the solvent was removed in vacuo, and the remaining oil was chromatographed on a short silica column using a mixture of 80% methylene chloride and 20% ethyl acetate as eluent. Collection of the yellow fraction afforded after evaporation of solvent 1.74 g (87%) of a yellow oil **22**. MS: *m/e* 400 (M$^+$, 100), 196 (10), 120 (15), 88 (39); ^{1}H-NMR 3.05 (4 H, t), 3.65 (12 H, s), 3.80 (4 H, t); ^{13}C-NMR 210.0 (C=S), 135.7 (S_2C=CS_2), 69.9, 69.8, 69.5, 68.6 (OCH$_2$), 35.6 (SCH$_2$); IR (KBr) ν (cm^{-1}) 1065 (C=S). Anal. Calcd for $C_{13}H_{20}O_4S_5$: C, 38.98; H, 5.03. Found: C, 39.72; H, 5.01. It was not possible to obtain a better analysis because the compound was an oil.

23: 5,8,11,14,17-pentaoxa-2,20,22,24-tetrathiabicyclo[19.3.0]-tetraicos-1(21)-ene-23-thione. Procedure for **23**. By a procedure similar to **22** substituting **11** with hexaethylene glycol **12** (0.005 mol) and using pure ethyl acetate as eluent 1.78 g (80%) **23** was obtained. **23** (yellow oil): MS *m/e* 444 (M$^+$, 100), 411 (19), 198 (17), 196 (18), 88 (51), 45 (95); HRMS calcd for $C_{15}H_{24}O_5S_5$ (M$^+$) 444.0227, found 444.0168; ^{1}H-NMR 3.77 (4 H, t, J = 3 Hz), 3.68, 3.66 (16 H, s, s) 3.11 (4 H, t, J = 3 Hz); IR (KBr) ν (cm^{-1}) 1062 (C=S).

25: 1,4,5,6-tetrahydro-2(3),6(7)-bis(4-oxa-1,7-dithiaheptan-1,7-yl)-1,4,5,8-tetrathiafulvalene. **26**: 1,4,5,6-tetrahydro-2(3),6-(7)-bis(4,7-dioxa-1,10-dithiadecane-1,10-diyl)-1,4,5,8-tetrathiafulvalene. **27**: 1,4,5,6-tetrahydro-2(3),6(7)-bis(4,7,10-trioxa-1,13-dithiatridecane-1,13-diyl)-1,4,5,8-tetrathiafulvalene. **28**: 1,4,5,6-tetrahydro-2(3),6(7)-bis(4,7,10,13-tetraoxa-1,166-dithiahexadecane-1,16-diyl)-1,4,5,8-tetrathiafulvalene. **29**: 1,4,5,6-tetrahydro-2(3),6(7)-bis(4,7,10,13,16-pentaoxa-1,19-dithianonadecane-1,19-diyl)-1,4,5,8-tetrathiafulvalene.

General Experimental Procedure for 25–29. A monomer (**13**, **17**, **20**, **22**, or **23**) (0.001 mol) was placed in a predried 10-mL round-bottomed two-necked flask with nitrogen-inlet, rubber-septum, and magnetic stirrer. Via the rubber septum 5 mL of freshly distilled triethyl phosphite was added via a syringe. The mixture was heated to 130 °C for 20 min with stirring and then allowed to cool to room temperature. If precipitation did not start, further cooling in an ice bath could be necessary (especially for **28** and **29**). When crystallization was complete, the orange solid was filtered off, washed with 2 × 3 mL of methanol (water in the case of **28** and **29**), and recrystallized. **25**: yield 27% ($CHCl_3$); mp 230–33 °C (dec; MS *m/e* 472 (M$^+$, 100), 280 (35), 88 (38); ^{1}H-NMR 2.85 (8 H, t), 3.90 (8 H t); IR (KBr) ν (cm^{-1}) 1133 (CH_2OCH_2). Anal. Calcd for $C_{14}H_{16}O_2S_8$: C, 35.55; H, 3.57. Found: C, 35.59; H, 3.38. **26**: yield 34% ($CHCl_3$); mp 230–33 °C dec; MS *m/e* 560 (M$^+$, 100); 88 (30); ^{1}H-NMR 3.75 (8 H, s), 3.70 (8 H, t), 3.05 (8 H, t); IR (KBr) ν (cm^{-1}) 1143 (CH_2OCH_2). Anal. Calcd for $C_{18}H_{24}O_4S_8$: C, 38.57; H, 4.29. Found: C, 38.60; H, 4.30. **27**: yield 28% ($CHCl_3$); mp 181 °C. Analytical and spectroscopical data (EIMS, NMR, and IR) were in good agreement with literature.[12] **28**: yield 40% (ethyl acetate); mp 98–99 °C; MS *m/e* 736 (M$^+$, 100), 400 (3), 268 (4); ^{1}H-NMR 3.75 (8 H, t, J = 6 Hz), 3.67 (24 H, s), 3.04 (8 H, t, J = 6 Hz); IR (KBr) ν (cm^{-1}) 1118 (ether). Anal. Calcd for $C_{28}H_{40}O_8S_8$: C, 42.59; H, 5.50; 34.20. Found: C, 42.39; H, 5.43; S, 34.78. **29**: yield 38% (ethyl acetate); mp 59 °C; MS *m/e* 824 (M$^+$, 3), 622 (6), 550 (40), 413 (31), 18 (100); HRMS calcd for $C_{30}H_{48}O_{10}S_8$ (M$^+$) 824.1013, found 824.1043; IR (KBr) ν (cm^{-1}) 1132 (ether); ^{1}H-NMR 3.72 (8 H, t, J = 3 Hz), 3.68, 3.67 (32 H, s, s), 3.05 (8 H, t, J = 3 Hz).

TCNQ Complex (25)$_3$(TCNQ)$_2$. From an equimolar solution of TCNQ and **25** in boiling acetonitrile precipitated black crystals upon cooling which had a 3:2 stoichiometry (determined by elemental analysis). Anal. Calcd for $C_{66}H_{56}O_6N_8S_{24}$: C, 43.42; H, 3.07; N, 6.14; S, 42.10. Found: C, 43.89; H, 3.21; N, 6.68; S, 41.30.

Acknowledgment. We thank the Danish Technical Science Research Council (STVF) and the Danish Natural Science Research Council (SNF) for financial support and Professor Peter Roepstorff, Department of Molecular Biology, Odense University, for kind asistance with PDMS facilities.