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First synthesis and structure of sulfur-containing heterocycles fused to ferrocene

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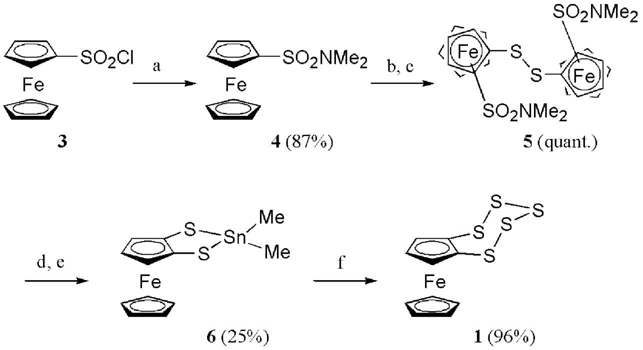
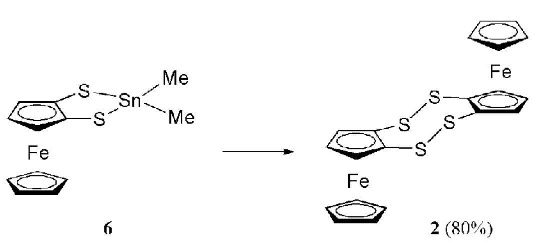
Abstract—Synthesis of a stable pentathiepin fused to a single cyclopentadienyl ring of ferrocene was performed by treatment of the corresponding dithiastannole as a synthetic equivalent of unstable ferrocene 1,2-dithiol with a sulfur source. On the other hand, deprotection of the dithiastannole gave a novel tetrathiocin comprised of two ferrocene units. The single-crystal X-ray diffraction studies revealed the unprecedented sulfur-containing heterocycles bound to ferrocene units. © 2002 Elsevier Science Ltd. All rights reserved.

The synthesis and reactivity of compounds containing multi-sulfur linkage have been studied extensively due to their biological activities and chemical properties.[1] Many methods have been developed to prepare cyclic polysulfides by using either elemental sulfur or other sulfur-transfer reagents, however, these methods often gave poor yields of the desired products and required extreme precaution.[2] Recently, we have succeeded in systematic and selective synthesis of benzene-fused cyclic polysulfides by introduction of bulky substituents on the benzene ring.[3] However, there are no approaches to synthesis of ferrocene-fused cyclic multi-sulfur linkages by synthetic limitation, while the compounds of bridging the cyclopentadienyl (Cp) ligands of ferrocene with multi-sulfur atoms have been developed.[4] In this paper, we report an efficient synthesis and characterization of the crystal structure of novel pentathiepin **1** and tetrathiocin **2** consisting of a ferrocene unit, by X-ray crystallographic analysis, and their electrochemical properties were furnished by cyclic voltammetry technique.

Pentathiepin **1** and tetrathiocin **2** were synthesized as follows (Schemes 1 and 2). We employed ferrocenesulfonyl chloride (**3**)[5] as the starting material to prepare the desired heterocyclic compounds. *N*,*N*-Dimethylaminosulfonylferrocene (**4**) was obtained on treatment of the sulfonyl chloride **3** with dimethylamine in 87%



Scheme 1. *Reagents*: (a) Me_2NH, THF, H_2O. (b) ^nBuLi, ^{n}hexane, THF. (c) S_8. (d) $LiAlH_4$, THF. (e) Me_2SnCl_2, THF. (f) SCl_2, THF.



Scheme 2. *Reagent and conditions*: (a) I_2, $CHCl_3$, room temp., 10 min.

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yield. 2,2″-Bis(*N*,*N*-dimethylaminosulfonylferrocenyl)-1,1″-disulfide (**5**) was obtained quantitatively by *ortho*-lithiation of **4** followed by treatment with elemental sulfur. The disulfide **5** possesses planar chirality due to the two different substituents on the cyclopentadienyl ring of each ferrocene moiety.[6]

Dithiastannole **6**, a synthetic equivalent of unstable ferrocene 1,2-dithiol, was prepared by reduction of a diastereomeric mixture of disulfide **5** with lithium aluminum hydride, followed by stannylation with dimethyltin dichloride in 25% yield. The dithiastannole **6** was identified by ^{1}H, ^{13}C, and ^{119}Sn NMR spectroscopy. There are two singlet peaks of methyl protons in the ^{1}H NMR spectrum indicating that the two methyl groups are unequivalent. The ^{119}Sn NMR spectrum showed 256.9 ppm (relative to Me_4Sn) as a singlet peak, which was similar to the chemical shifts of the corresponding benzo-1,3,2-dithiastannoles previously reported.[3,7] Then, dithiastannole **6** was treated with sulfur dichloride at 0°C and stirred for 1 h at room temperature. After usual work-up, the crude product was purified by column chromatography (silica gel) with hexane as the eluent to give pentathiepin **1**[8] in 96% yield. On the other hand, successive deprotection and dimerization of dithiastannole **6** with iodine in solution gave tetrathiocin **2**[9] in 80% yield as a stable product with only a single diastereoisomer.

The structures of pentathiepin **1** and tetrathiocin **2** have been sufficiently characterized by physical and spectroscopic data, and these solid-state structures were confirmed by X-ray crystallographic analysis.[10,11] The ^{1}H NMR spectrum of pentathiepin **1** in $CDCl_3$ showed a pair of doublet and triplet at 4.53 and 4.42 ppm, assigned to the α and β cyclopentadienyl protons, and a singlet at 4.32 ppm of unsubstituted cyclopentadienyl protons. The ^{13}C NMR spectrum showed the resonance at 70.0, 71.1, and 75.4 ppm assigned to the Cp-H carbons, and at 93.3 ppm assigned to the Cp-S *ipso*-carbon. The remarkable large downfield shift observed for the *ipso*-carbon reflects the deshielding effect of the sulfur substituent.[12]

In the solid-state of pentathiepin **1** (Fig. 1), two sulfur atoms bound to carbon atoms of ferrocene are almost coplanar with the cyclopentadienyl ring, while two sulfur atoms at 2- and 4-position were deviated from this plane (the S–S–C–C torsion angles are 88.1(3) and −88.6(4)°, respectively) to avoid the ferrocene moiety. The S–S–S–S torsion angles of 76.6(3) and −76.0(2)° which are in good agreement with those of reported pentathiepins fused to five-membered heteroaromatic rings.[2c,13]

In the ^{1}H NMR spectrum of tetrathiocin **2**, there were a pair of doublet and triplet at 4.50 and 4.42 ppm assigned to the α and β cyclopentadienyl protons, and a singlet at 4.17 ppm of unsubstituted cyclopentadienyl protons. In the ^{13}C NMR spectrum, four peaks were observed for the Cp carbons, and in particular, the signal for the *ipso*-carbon atom was found at 89.1 ppm. Interestingly, these results indicated a single diastereoisomer of tetrathiocin **2** existed in the solution. Actually, the proposed structure was also detected in the solid-state (Fig. 2). A striking feature in the crystal structure of tetrathiocin **2** is a chair conformation for the eight-membered ring. The C–S–S–C torsion angle was 102.2(6)°, which was smaller than those of the tetrathiocins fused on the benzene ring in the literature.[14] Furthermore, the two intramolecular ferrocene units of tetrathiocin **2** were located in *anti* orientation.

In view of the structure of tetrathiocin annulated with two ferrocenes, the ferrocenes could be arranged in *anti*

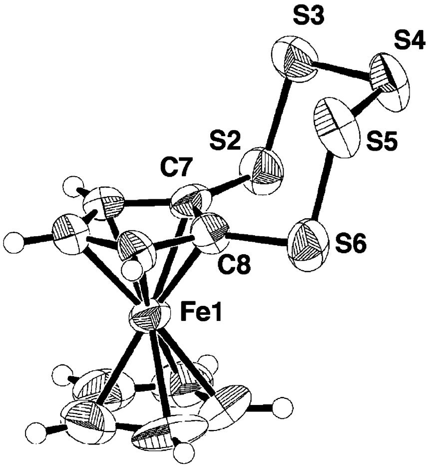

Figure 1. ORTEP drawing of **1**. Selected bond lengths (Å) and bond angles (°): S2–S3 2.057(4), S3–S4 2.051(5), S4–S5 2.045(4), S5–S6 2.053(5), S2–C7 1.75(1), S6–C8 1.754(9), C7–C8 1.47(1), S2–S3–S4 104.7(2), S3–S4–S5 105.4(2), S4–S5–S6 104.6(2), S5–S6–C8 101.8(4), S6–C8–C7 126.1(7), S2–C7–C8 125.6(7).

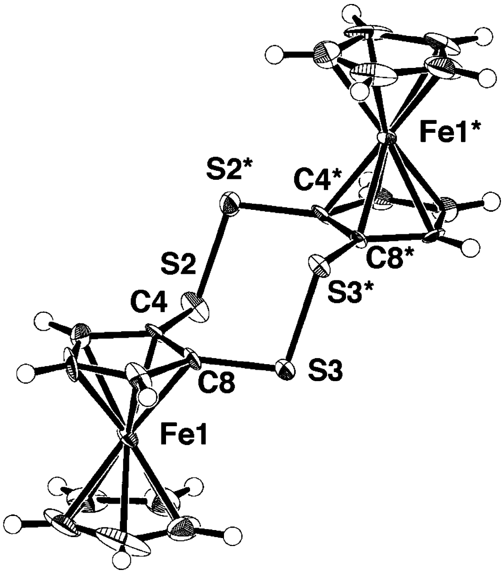

Figure 2. ORTEP drawing of **2**. Selected bond lengths (Å) and bond angles (°): S2–S2* 2.073(4), S3–S3* 2.076(4), S2–C4 1.749(8), S3–C8 1.758(8), C4–C8 1.44(1), S2–S2*–C4* 103.2(3), S3–S3*–C8* 103.0(3), S2–C4–C8 127.6(6), S3–C8–C4 127.8(6).

and *syn* orientations. The crystal data suggest that *anti* orientation is more stable than *syn* orientation kinetically or thermodynamically. Thus, theoretical conformational studies based on density functional theory calculations were carried out using Gaussian 98 program.[15] Two structures were attributed to *anti* and *syn* orientations, which were optimized and characterized by frequency computations and wave function stability checks at B3PW91/3-21G* level, as shown in Fig. 3. The optimized structure of *anti* orientation shows a chair conformation for the eight-membered ring, which is in good agreement with the solid-state structure by X-ray crystallographic analysis. The optimized structure of *syn* orientation shows a twist conformation for the eight-membered ring. The calculation predicts the total energy of the *anti* orientated chair form is 26.7 kJ mol^{-1} lower than that of the *syn* orientated twist form.

Electrochemical studies of pentathiepin **1** (in acetonitrile) and tetrathiocin **2** (in benzonitrile) were performed by cyclic voltammetry.[16] The cyclic voltammograms at 20°C under argon atmosphere showed a well-defined reversible redox wave of **1** ($E_{1/2}$ $=+0.46$ V) and two reversible redox waves of **2** ($E^{1}_{1/2}$ $=+0.35$, $E^{2}_{1/2}=+0.53$ V) vs Ag/0.01 mol dm^{-3} AgNO$_3$, which were in good agreement with those of ferrocenophanes previously reported.[17] Further studies on the unique reversible electrochemical property of novel sulfur-containing heterocycles are in progress.

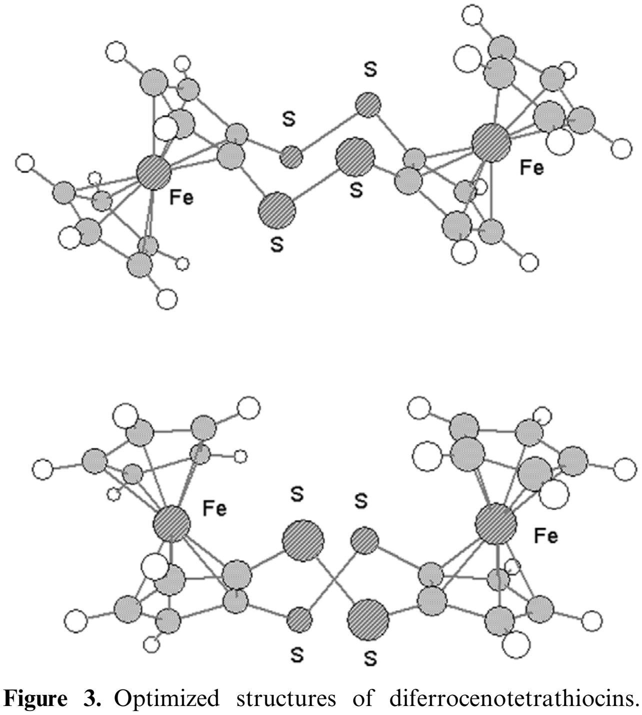

Figure 3. Optimized structures of diferrocenotetrathiocins. *anti*-Orientated chair conformation (upper) and *syn*-orientated twist conformation (lower).

Acknowledgements

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8. Selected data for **1**: Orange crystals; mp 128.5–129.0°C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 4.32 (s, 5H, C$_5$H$_5$), 4.42 (t, $J=2.6$ Hz, 1H, C$_5$H$_3$), 4.53 (d, $J=2.6$ Hz, 2H, C$_5$H$_3$); ^{13}C NMR (101 MHz, CDCl$_3$) δ 70.0, 71.1, 75.4, 93.3; IR (KBr) v 3590, 1712, 1362, 1222, 755, 530 cm^{-1}; MS (70 eV) m/z 344 (M^{+}). Anal. calcd for C$_{10}$H$_8$FeS$_5$: C, 34.88; H, 2.34%. Found: C, 34.61; H, 2.38%.
9. Selected data for **2**: Orange crystals; mp >300°C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 4.17 (s, 10H, C$_5$H$_5$), 4.42 (t, $J=2.8$ Hz, 2H, C$_5$H$_3$), 4.50 (d, $J=2.8$ Hz, 4H, C$_5$H$_3$); ^{13}C

NMR (101 MHz, $CDCl_3$) δ 69.8, 70.8, 76.3, 89.1; IR (KBr) ν 3449, 1194, 1107, 1024, 809, 505 cm^{-1}; MS (70 eV) m/z 496 (M^+). Anal. calcd for $C_{20}H_{16}Fe_2S_4$: C, 48.40; H, 3.25%. Found: C, 48.13; H, 3.28%.

10. Crystal data for **1**: $M=344.32$, $C_{10}H_8FeS_5$, monoclinic, space group $P2_1$, $a=8.6743(7)$, $b=7.5798(8)$, $c=10.4960(9)$ Å, $\beta=110.762(6)°$, $V=645.29(10)$ $Å^3$, $Z=2$, $D_{calc}=1.772$ g cm^{-3}. An orange prismatic crystal of dimensions 0.30×0.10×0.08 nm was used for measurements at 293 K on Rigaku AFC7R diffractometer employing CuKα ($\lambda=1.54178$ Å) radiation using $\omega/2\theta$ scan technique. The structure was solved by direct methods (SIR92) and expanded using Fourier technique (DIRDIF94). All calculations were performed using the teXsan crystallographic software package of Molecular Structure Corporation. The final cycle of full-matrix least-squares refinement was based on 2019 observed reflections ($I>1.50\sigma(I)$) and 144 variable parameters with $R=0.070$, $Rw=0.097$.
11. Crystal data for **2**: $M=496.28$, $C_{20}H_{16}Fe_2S_4$, tetragonal, space group $P4/ncc$, $a=17.950(1)$, $c=11.764(1)$ Å, $V=3790.2(6)$ $Å^3$, $Z=8$, $D_{calc}=1.739$ g cm^{-3}. An orange prismatic crystal of dimensions 0.24×0.20×0.24 nm was used for measurements at 293 K. The structure was solved by the same methods of **1**. The final cycle of full-matrix least-squares refinement was based on 981 observed reflections ($I>1.50\sigma(I)$) and 119 variable parameters with $R=0.051$, $Rw=0.069$.
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