Facile Synthesis of *N,N′*-Ethylenebisthiazolium Salts: Precursors of Dithiadiazafulvalenes†

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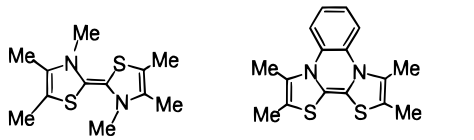
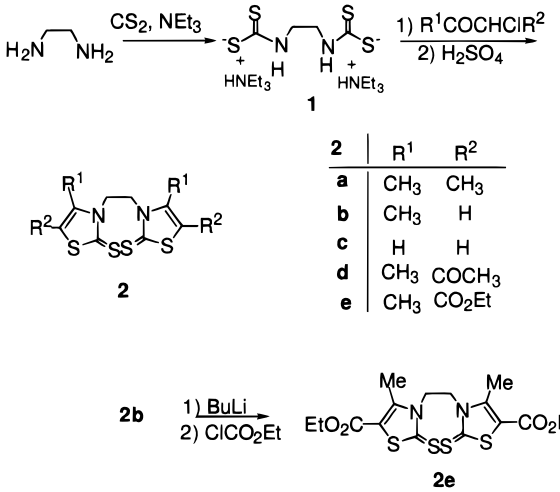
Bis-thiazolium salts, precursors of dithiadiazafulvalene (DTDAF), have been prepared. Electrochemical investigations have been carried out on these salts in order to determine the redox behavior of DTDAF. These bis-thiazolium salts undergo intramolecular coupling, either chemically or electrochemically, to afford *N,N′*-ethylene-bridged DTDAF.

Introduction

Thiazolium salts have received considerable attention with the aim of elucidating biochemical reaction mechanisms such as thiamine activity.[1] For example, N,N′-bridged thiazolium salts, prepared by alkylation of thiazole with α−ω-dibromoalkane, have been studied as catalysts in the benzoin condensation.[2] Another interesting aspect consists of the use of these salts for the synthesis of dithiadiazafulvalenes (DTDAF) which are excellent π-donor molecules for the preparation of organic materials.[3−6] Because DTDAFs generally present very negative oxidation potentials these compounds are highly oxygen-sensitive and therefore have mainly been detected electrochemically.[7,8] Nevertheless, these excellent donors can be used in the formation of charge transfer salts by simply generating the DTDAF in situ and trapping it with an acceptor.[5,6] A peculiar behavior can be observed for the hexamethyl DTDAF as it undergoes important conformational modifications between the neutral state and the dicationic one, particularly in the oxidized state, the two thiazole rings are twisted around the central C−C bond.[6,9] On the contrary, the synthesis of N,N′-phenyl-bridged DTDAF by *intramolecular* coupling of N,N′-phenyl-bridged bisthiazoline selone allowed us to force the thiazole cores to lie in the same plane while the bulky phenyl ring is bent slightly out of the plane.[5] We wish now to present the synthesis of *N,N′*-ethylene-bridged bisthiazolium salts in order to obtain less hindered donor molecules and the electrochemical investigations carried out on these salts. Our synthetic pathway allows the formation of several bisthiazolium salt precursors of N,N′-bridged DTDAF.



Scheme 1



2	R^1	R^2
a	CH_3	CH_3
b	CH_3	H
c	H	H
d	CH_3	$COCH_3$
e	CH_3	CO_2Et

Results and Discussion

The bis(dithiocarbamate) salt **1** was synthesized by adding carbon disulfide to a solution of ethylenediamine and triethylamine as outlined in Scheme 1. Unlike phenylene diamine, where we were not successful in preparing the bis-salt in one pot, we did not encounter this difficulty in the case of ethylenediamine.[10] The reactions of various α-halogenated carbonyl derivatives with salt **1** followed by cyclization and dehydration in the presence of sulfuric acid led to bis-(1,3-thiazoline-2-thiones) **2a**−**c**. Acidic treatment is not always necessary to generate cyclization and dehydration. Indeed, in the presence of electron-withdrawing substituents, bis-(1,3-

† Dedicated to Prof. Albert Robert on the occasion of his 60th birthday.

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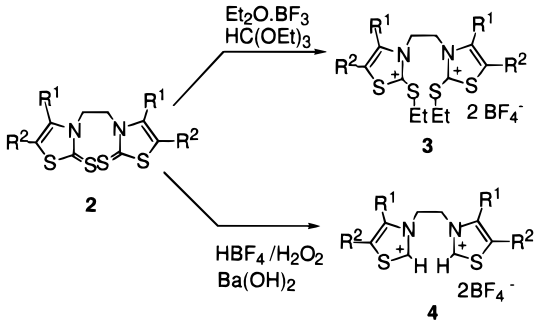
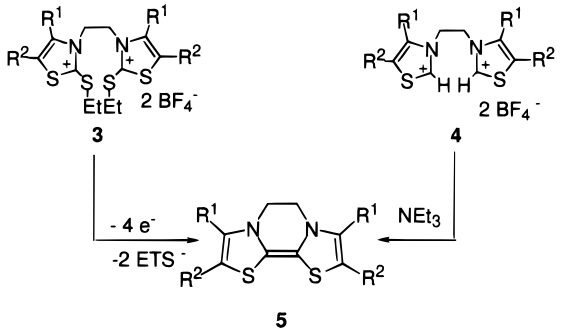
Scheme 2



Scheme 3



thiazoline-2-thiones) **2d** and **2e** were obtained by simply heating the medium after the addition of the α-halogenated carbonyl reactants.

In earlier work we demonstrated that lithiation of the *N*,*N*′-phenyl-bridged bis(thiazoline-2-thione) core can be performed in the presence of BuLi and the resulting lithium salt can react with a range of electrophiles.[10] To test the feasibility of this strategy on **2**, metalation of **2b** was performed and the bis-lithium salt reaction with ethyl chloroformate afforded **2e** (Scheme 1). As attempts to isolate DTDAFs lead to oxidation products,[3,11] this methodology applied on the precursors of DTDAF, such as thiazoline thione, is a very useful route for the introduction of functional groups on the donor core.

Transformation of **2** into bis(2-ethylthio thiazolium salt) **3** was achieved in the presence of boron trifluoride diethyl etherate and triethyl orthoformate.[12] When bisthiazoline thiones **2** were treated with tetrafluoroboric acid and hydrogene peroxyde followed by the addition of Ba(OH)$_2$·8H$_2$O, the corresponding bisthiazolium salts **4** were obtained (Scheme 2).[13] This second strategy was not successful when the thiazole core was substituted with carbonyl groups (**2d**, **2e**). Both salts **3** and **4** are the required precursors for the synthesis of the desired *N*,*N*′-ethylene-bridged DTDAF **5**, either by electroreduction of **3**[14] or basic treatment of **4**[3] (Scheme 3).

To study the redox properties of these DTDAFs we performed two types of electrochemical investigation. The first one consits of the study of the cathodic coupling of bis-(2-ethylthio-1,3-thiazolium fluoroborate) **3**. In an earlier study, we demonstrated that this route was

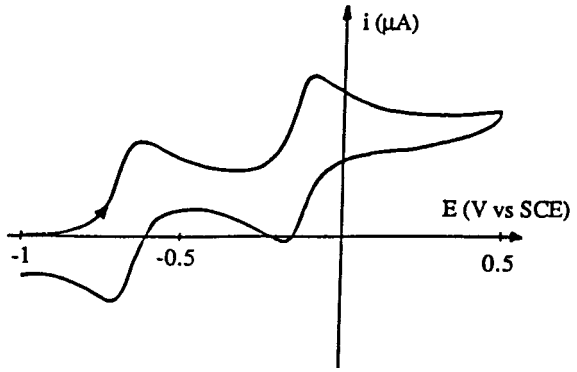


Figure 1. Cyclic voltammogram of **5c** formed in the medium after basic coupling in CH_3CN, 0.1 M $TBAPF_6$, scan speed of 0.1 V·s^{-1}.

Table 1. Cyclic Voltammetry Data of DTDAF 5[a]

R^1	R^2	Epa^1	Epa^2	Δ*E*
5a, CH_3	CH_3	−0.69	−0.22	0.47
5b, CH_3	H	−0.66	−0.12	0.54
5c, H	H	−0.65	−0.10	0.55
5d, CH_3	COMe	−0.24	+0.19	0.43
5e, CH_3	CO_2Et	−0.27	+0.28	0.55
N,*N*′-phenyl-bridged DTDAF		−0.44	−0.03	0.41
6		−0.30	−0.08	0.22
7		−0.17	−0.02	0.15
8		−0.23	+0.26	0.49

[a] *E* in V vs SCE, Pt working electrode with 0.1 M *n*-Bu_4NPF_6 scanning rate 0.1 V/s in CH_3CN.

efficient for the generation and detection of electroactive species such as DTDAF.[14] As previously observed, determination of the oxidation potentials of **5** by cathodic coupling of **3** was easily realized when withdrawing substituents were bound to the thiazole core.[6] Detection of the electroactive species **5** by electroreduction of the thiazolium salts **3a**−**c** was possible only when a catalytic amount of acid was added to the medium. Considering the mechanism involves in this coupling process:[14] generation of a bisradical which couples into an α-bisthioalkyl intermediate, reduction of this intermediate giving DTDAF after elimination of two EtS^- groups, the presence of acid makes the second step easier. We also realized the coupling of the bisthiazolium salt **4** in basic medium and performed cyclic voltammetry experiments, under inert atmosphere, directly on the medium where the donor was formed. Using either the cathodic coupling or the basic one, cyclic voltammograms exhibit two reversible oxidation waves, at very low oxidation potentials, associated with the redox behavior of DTDAF **5** formed in the medium (Figure 1).

Oxidation potentials of the formed DTDAFs **5** are collected in Table 1. If we look at the difference between the two oxidation potentials ($\Delta E = Epa_2 - Epa_1$), we notice larger Δ*E* values in the case of donor molecules **5** than in the case of **6** substituted on the nitrogen by a methyl group (Table 1). This can be explained by the fact that while they are oxidized conformational changes are observed for non bridged DTDAF and this implies an important reduced Coulombic interaction.[6] Contrariwise the N,N′-bridge restrains conformational modifications upon oxidation.[5] Indeed, these observations indicate that the formation of the donor results from an intramolecular coupling of the bis thiazolium salts.

As can be seen in Table 1, the same trends were described by Hünig et al. for the benzo-fused derivatives

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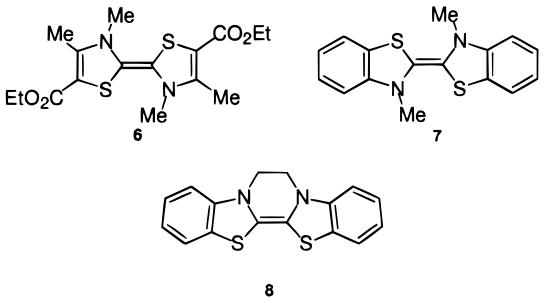
Scheme 4



7 and **8** (Scheme 4).[15] For **7** oxidation to the dicationic state is easier ($\Delta E = 0.15$) than for **8** ($\Delta E = 0.49$). Our results are also consistent with the electrochemical study by Thummel et al. on DTDAF's prepared by diquaternarization of 2,2′-bithiazole followed by electron reduction.[8]

In conclusion, we have described the synthesis of various bisthiazolium salt precursors of *N*,*N*′-ethylene-bridged DTDAF and demonstrated the possibility of functionalizing these derivatives via the metalation procedure. The electrochemical investigations carried out on these salts in order to determine the donor ability of DTDAF indicates that an intramolecular coupling occurred. Furthermore, these derivatives exhibit a larger potential difference than their nonbridged analogues which implies that the cation radical species are stable in a wider potential window. The advantage of this ethylene bridge compared to *N*,*N*′-phenyl-bridged DTDAF lies in the fact that ethylene is less bulky than phenyl. We are now currently examining the in situ approach in order to trap these DTDAF's as their charge tranfer salts.

Experimental Section

^{1}H NMR spectra were recorded at 200 and 300 MHz and ^{13}C NMR spectra at 50 and 75 MHz. Chemical shifts are reported in ppm referenced to tetramethylsilane. Melting points were measured using a Kofler hot stage apparatus. Elemental analyses were obtained from the Laboratoire Central de Microanalyze du CNRS (Lyon). Column chromatography was performed on silica gel 60 (0.040−0.063 mm). For the electrochemical determination of the redox potentials, CH_3CN was dried by refluxing over CaH followed by distillation.

Bis-dithiocarbamate Salt 1. To a stirred solution of ethylenediamine (5 g, 83 mmol) and triethylamine (50 mL) in Et_2O (50 mL) was added carbon disulfide (20 mL) at 0 °C. The reaction mixure was stirred for 48 h at room temperature. The white precipitate was filtered and washed with Et_2O, dried under vacuum, and used without further purification (24.1 g,-70%): mp 100 °C dec; ^{1}H NMR (D_2O) δ 1.38 (t, 18H), 3.30 (q, 12H), 3.86 (s, 4H).

***N*,*N*′-Ethylene-Bridged Bis(thiazoline-2-thione) (2a−c).** Bis-dithiocarbamate salt **1** (5 g, 12 mmol) was slowly added to the α-halogenated carbonyl derivative in excess (20 mL, 3-chlorobutanone, chloroacetone, or chloroacetaldehyde) at 0 °C. The reaction mixture was allowed to reach room temperature and stirred for 12 h. Sulfuric acid 98% (1.3 mL) was added to the cooled medium (0 °C), and after 15 min of stirring, water (30 mL) was added. The mixture was extracted with CH_2Cl_2, and the organic phase was washed with water (3 × 50 mL), dried over Na_2SO_4, and evaporated. The residue was recrystallized from EtOH to give compound **2**.

***N*,*N*′-Ethylene-Bridged Bis(thiazoline-2-thione) (2d−e).** Bis-dithiocarbamate salt **1** (5 g, 12 mmol) was slowly added to the α-halogenated carbonyl derivative in excess (20 mL of chloropentanedione or ethyl-2-chloroacetate) at 0 °C. The reaction mixture was allowed to reach room temperature and heated to 50 °C for 15 min. The solution was cooled to room temperature and bis(thiazoline-2-thione) was precipitated with ethanol, filtered, and dried.

2a: white powder (1.9 g, 50%); mp 253 °C; ^{1}H NMR ($CDCl_3$) δ 2.16 (s, 6H), 2.34 (s, 6H), 4.51 (s, 4H); ^{13}C NMR ($CDCl_3$, CF_3CO_2H) δ 12.04, 13.19, 44.64, 119.56, 136.22, 185.93. Anal. Calcd for $C_{12}H_{16}N_2S_4$: C, 45.54; H, 5.10; N, 8.85; S, 40.52. Found: C, 45.72; H, 5.14; N, 8.83; S, 40.32.

2b: white powder (2.4 g, 69%); mp 232 °C; ^{1}H NMR ($CDCl_3$) δ 2.36 (s, 6H), 4.57 (s, 4H), 6.26 (s, 2H); ^{13}C NMR ($CDCl_3$, CF_3CO_2H) δ 15.75, 44.09, 108.08, 141.43, 188.68. Anal. Calcd for $C_{10}H_{12}N_2S_4$: C, 41.63; H, 4.19; N, 9.71. Found: C, 41.65; H, 4.25; N, 9.49.

2c: white powder (1.9 g 63%); mp 182 °C; ^{1}H NMR ($CDCl_3$) δ 4.70 (s, 4H), 6.53 (d, 2H), 6.91 (d, 2H); ^{13}C NMR ($CDCl_3$, CF_3CO_2H) δ 47.20, 113.82, 133.09, 187.41. Anal. Calcd for $C_8H_8N_2S_4$: C, 36.89; H, 3.09; N, 10.75. Found: C, 36.68; H, 3.01; N, 10.95.

2d: white powder (3.0 g, 67%); mp 259 °C; ^{1}H NMR ($CDCl_3$, CF_3CO_2H) δ 2.55 (s, 6H), 2.95 (s, 6H), 4.72 (s, 4H); ^{13}C NMR ($CDCl_3$, CF_3CO_2H) δ 15.60, 29.86, 44.06, 121.15, 150.88, 189.61, 193.58. Anal. Calcd for $C_{14}H_{16}N_2O_2S_4$: C, 45.14; H, 4.33; N, 7.52. Found: C, 44.98; H, 4.48; N, 7.64.

2e: white powder (3.0 g, 58%); mp 210 °C; ^{1}H NMR ($CDCl_3$) δ 1.35 (t, 6H), 2.79 (s, 6H), 4.31 (q, 4H), 4.58 (s, 4H); ^{13}C NMR ($CDCl_3$, CF_3CO_2H) δ 14.34, 14.75, 44.04, 63.01, 113.23, 149.38, 161.11, 189.86.

***N*,*N*′-Ethylene-Bridged Bis(thiazoline-2-thione) (2e).** To a solution of the *N*,*N*′-ethylene-bridged bis(thiazoline-2-thione) **2b** (0.2 g, 0.7 mmol) in dry THF (25 mL) was added *n*-BuLi (1.1 mL, 1.76 mmol, from a 1.6 M solution in hexane) at −80 °C under an atmosphere of Ar. After the solution was stirred for 0.5 h, ethyl chloroformate (134 μL, 1.4 mmol) was added, and the solution was stirred for an additional 0.5 h at −80 °C. The temperature was slowly allowed to reach room temperature. Solvent was evaporated and CH_2Cl_2 (50 mL) was added to the resulting oil. The organic phase was washed several times with water (3 × 100 mL) and dried over Na_2SO_4, and the solvent was evaporated. The residue was recrystallized from EtOH to give compound **2e** (150 mg, 50%)

***N*,*N*′-Ethylene-Bridged Bis(2-ethylthio Thiazolium Salt) (3).** To a solution of **2** (3.84 mmol) in $CHCl_3$ (100 mL) was added $HC(OEt)_3$ (2.5 mL, 15.4 mmol) and $Et_2O{\cdot}BF_3$ (2 mL, 15.4 mmol). The reaction mixture was refluxed for 3 h and stirred at room temperature for 12 h. The solvent was partially removed and dry ether (25 mL) was added to the solution, the resulting oil was washed several times with Et_2O. The thiazolium salts **3a**−**e** precipitate with the addition of ethanol and then were dried under vacuum, characterized, and used without further purification.

3a: white powder (2.1 g, quantitative yield); mp 136 °C; ^{1}H NMR (CD_3CN) δ 1.47 (t, 6H), 2.44 (s, 6H), 2.49 (s, 6H), 3.39 (q, 4H), 4.66 (s, 4H); ^{13}C NMR (CD_3CN) δ 11.23, 11.34, 12.38, 31.23, 47.90, 129.74, 142.06, 172.39. Anal. Calcd for $C_{16}H_{26}N_2S_4B_2F_8$: C, 35.05; H, 4.78; N, 5.11. Found: C, 35.08; H, 4.15; N, 4.85.

3b: light-brown powder (1.5 g, 76%); mp 140 °C; ^{1}H NMR (CD_3CN) δ 1.26 (t, 6H), 2.33 (s, 6H), 3.21 (q, 4H), 4.46 (s, 4H), 7.43 (s, 2H); ^{13}C NMR (CD_3CN) δ 12.13, 13.12, 31.18, 47.24, 117.41, 146.50, 176.38.

3c: light-brown powder (1.1 g, 58%); mp 96 °C; ^{1}H NMR (CD_3CN) δ 1.67 (t, 6H), 3.63 (q, 4H), 5.00 (s, 4H), 8.13 (d, 2H), 8.23 (d, 2H); ^{13}C NMR (CD_3CN) δ 12.15, 31.61, 50.05, 122.39, 137.12, 176.52.

3d: orange powder (2.2 g, quantitative yield); mp 148 °C; ^{1}H NMR (CD_3CN) δ 1.52 (t, 6H), 2.67 (s, 6H), 2.87 (s, 6H), 3.52 (q, 4H), 4.74 (s, 4H); ^{13}C NMR (CD_3CN) δ 11.92, 13.39, 29.12, 31.91, 47.20, 132.89, 149.41, 179.60, 188.25.

3e: white powder (2.5 g, quantitative yield); mp 162 °C; ^{1}H NMR (CD_3CN) δ 1.47 (t, 6H), 1.60 (t, 6H), 2.97 (s, 6H), 3.61

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(q, 4H), 4.52 (q, 4H), 4.80 (s, 4H); ^{13}C NMR (CD_3CN) δ 11.91, 12.60, 13.01, 31.89, 46.87, 63.18, 122.69, 151.90, 158.02, 179.49.

***N,N*-Ethylenebisthiazolium Salt (4a−c).** To a suspension of **2** (1.2 mmol) in methanol (10 mL) and water (10 mL) at 0 °C were added HBF_4 (0.64 mL, 5.1 mmol, from 50% solution in water) and H_2O_2 (2 mL, 19.2 mmol, from 35% solution in water). The resulting solution was stirred at 0 °C for 0.5 h, and $Ba(OH)_2 \cdot 8H_2O$ was added to the medium. The reaction mixture was allowed to warm to room temperature and stirred for 10 h. The white precipitate was removed by filtration on Celite 521, and the filtrate was concentrated to dryness. The residue was recrystallized from EtOH to give compound **4**.

4a: white powder (100 mg, 20%); mp 190 °C; ^{1}H NMR (D_2O) δ 2.41 (s, 6H), 2.50 (s, 6H), 5.00 (s, 4H), 9.52 (s, 2H); ^{1}H NMR ^{13}C (D_2O) δ 10.80, 12.07, 51.62, 135.93, 142.47, 155.43. Anal. Calcd for $C_{12}H_{18}N_2S_2B_2F_8$: C, 33.67; H, 4.24; N, 6.54; S, 14.98. Found: C, 33.65; H, 4.07; N, 6.41; S, 14.71.

4b: white powder (150 mg, 32%); mp 194 °C; ^{1}H NMR (D_2O) δ 2.51 (s, 6H), 5.03 (s, 4H), 7.91 (s, 2H), 9.71 (s, 2H); ^{13}C NMR (D_2O) δ 12.67, 50.95, 122.92, 147.09, 159.45. Anal. Calcd for $C_{10}H_{14}N_2S_2B_2F_8$: C, 30.03; H, 3.53; N, 7.00; S, 16.03. Found: C, 29.45; H, 3.30; N, 6.70; S, 15.83.

4c: white powder (120 mg, 27%); mp 214−216 °C; ^{1}H NMR (D_2O) δ 5.21 (s, 4H), 8.27 (s, 2H), 9.95 (s, 2H); ^{13}C NMR (D_2O) δ 53.93, 127.65, 137.09.

DTDAF 5. General Procedure. Electrochemical coupling was carried out on a 10^{-3} M solution of *N,N′*-ethylene-bridged bis(2-ethylthiothiazolium salt) **3** in acetonitrile, containing a 1 M tetrabutylammonium hexafluorophosphate as the supporting electrolyte. DTDAF formation was detected immediately after reduction of salt **3** at −1 V vs SCE. Two reversible monoelectronic waves can be observed on the cyclic voltammograms

Basic Coupling. To a solution of *N,N*-ethylenebisthiazolium salt **4** (0.05 mmol) in degassed acetonitrile (2 mL) was added NEt_3 (0.2 mmol) under Ar. The formation of the DTDAF can be visualized by the appearance of an orange color. Under inert atmosphere, a degassed solution of tetrabutylammonium hexafluorophosphate in CH_3CN, was added to the reaction mixture. Electroanalytical investigation was carried out directly. Voltammograms were recorded at 0.1 $V \cdot s^{-1}$ at a platinum disk electrode ($A = 1$ mm^2).

Supporting Information Available: ^{1}H NMR spectra for compounds **3a**−**e** and **4c**. This material is available free of charge via the Internet at http://pubs.acs.org.

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