A Straightforward Access to Mono- and Bis(pyrrolo)tetrathiafulvalenes

Jean-Yves Balandier, Ahmed Belyasmine, Marc Sallé*

Laboratoire de Chimie et Ingénierie Moléculaire des Matériaux d'Angers (CIMMA), Groupe Synthèse Organique et Matériaux Fonctionnels (SOMaF), UMR CNRS 6200, Université d'Angers, 2 Bd Lavoisier, 49045 Angers, France
Fax +33(2)41735405; E-mail: marc.salle@univ-angers.fr

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Abstract: An alternative efficient synthetic procedure to mono- and bis(pyrrolo)tetrathiafulvalenes is proposed starting from 4,4-diethoxybut-2-ynal.

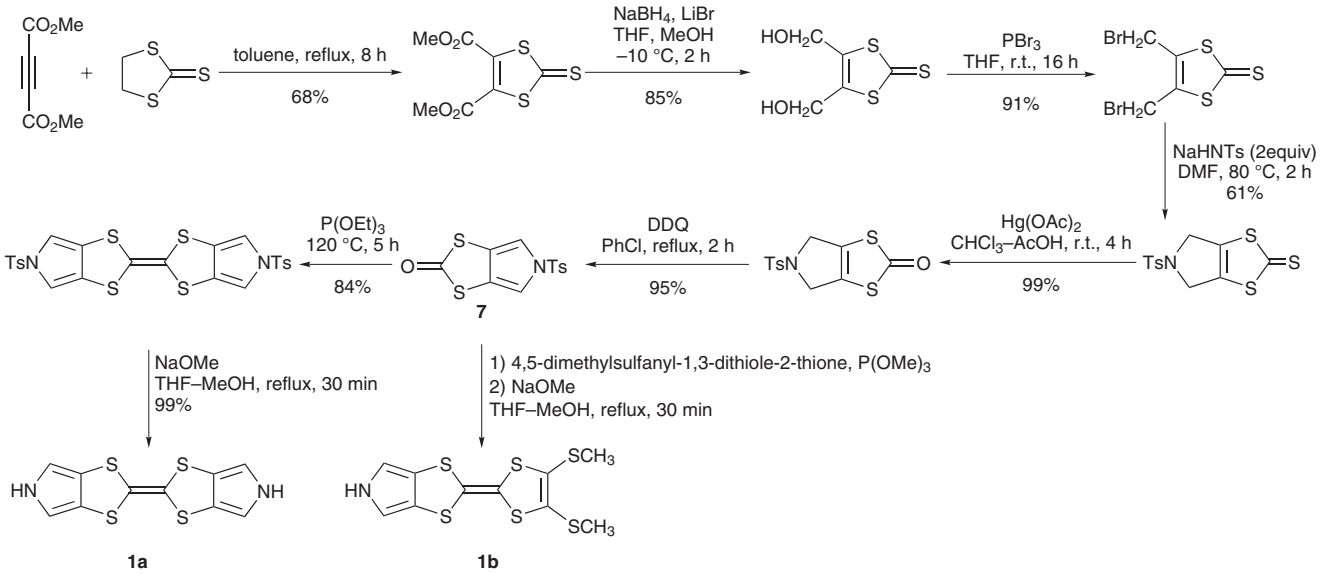
Key words: acetals, ring closure, pyrroles, tetrathiafulvalene, 4,4-diethoxybut-2-ynal

Tetrathiafulvalene (TTF) derivatives have been extensively used as key precursors for molecular materials presenting a rich variety of solid state physical properties.[1] Recently, TTF has appeared as a powerful building block in various molecular or supramolecular architectures, in particular by taking advantage of its remarkable electronic properties (TTF derivatives are easily and reversibly oxidized in two successive one-electron steps).[1,2] In this context, much has been done in order to introduce diverse functionalities onto the periphery of the TTF skeleton.[3] An important step in the design of such TTF derivatives, was achieved by Becher and co-workers, who described[2c,4] an access to bis(pyrrolo)tetrathiafulvalene **1a**. This electroactive derivative exhibits similar electronic properties to TTF, but the corresponding N,N′-disubstituted analogues avoid the well-known problems of *cis*–*trans* isomerization encountered with disubstituted derivatives of the parent TTF. This characteristic puts compound **1a**, as well as the mono(pyrrolo) analogue **1b**, among the most popular TTF derivatives studied in the last few years, in particular for supramolecular assemblies such as bistable rotaxanes,[2c,5] redox-responsive ligands,[2c,6] or as π-extended donors.[7]

The synthetic route developed by the Danish group to reach pyrrolo derivatives **1a** and **1b** is shown in Scheme 1.[2c,4] The key [*c*]-fused 1,3-dithiolepyrrole intermediate **7** was obtained in six steps from dimethylacetylenedicarboxylate and ethylenetrithiocarbonate, in an overall yield of 30% in about one week.

We present here an alternative and straightforward synthetic strategy to reach the key intermediate **7** (Scheme 2).

As for the above-mentioned approach, the first step in our strategy involves a cycloaddition between ethylenetrithiocarbonate and an electrophilic alkyne. In our case, the latter corresponds to the commercially available 4,4-diethoxybut-2-ynal (**2**).[8,9] Our motivation in using this alkyne was based on the idea that the aldehyde oxidation level could be kept throughout the synthetic route, thus avoiding an oxidation step subsequent to the ring closure.



Scheme 1 Access to mono- and bis(pyrrolo)tetrathiafulvalene derivatives according to references 2c and 4.

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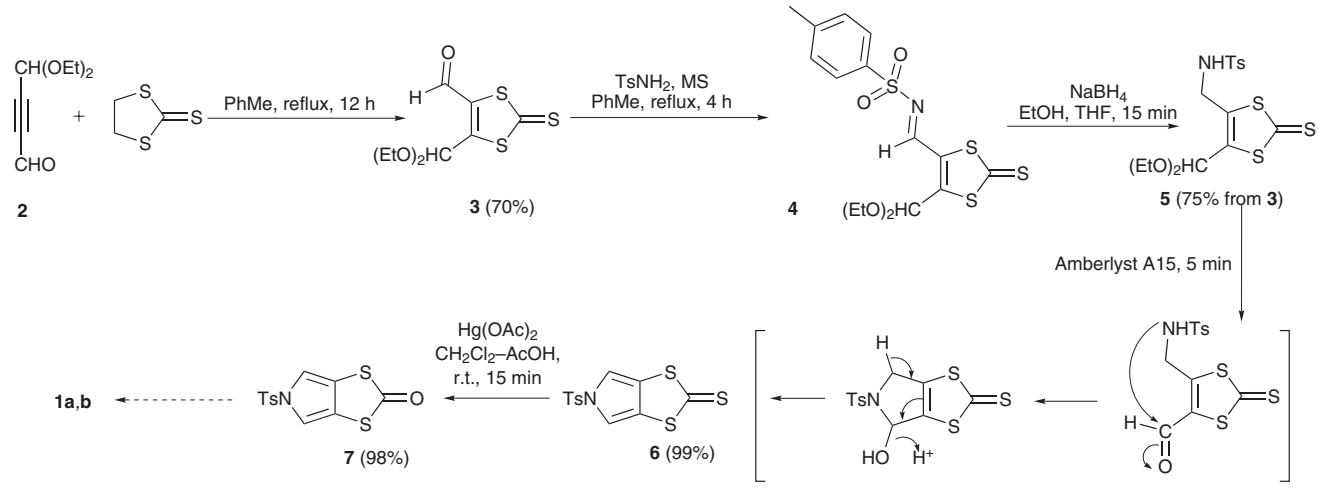

Scheme 2 New route to mono- and bis(pyrrolo)tetrathiafulvalene derivatives

The resulting 1,3-dithiol-2-thione derivative **3**[10] was reacted with tosylamine in refluxing toluene in the presence of molecular sieves. Filtration and evaporation afforded the *N*-tosyl imine **4** which was directly engaged in the subsequent reduction step.[11] Treatment of **4** with sodium borohydride afforded the corresponding *N*-tosyl amino derivative **5** in a global yield of 75% for the two steps (from **3**), after purification of compound **5** by silica gel chromatography.[12] The key step in our strategy was performed by treating compound **5** with Amberlyst® 15 in dichloromethane at room temperature, which allowed the direct and quantitative conversion to the *N*-tosyl protected pyrrole **6**. Three successive elementary reactions are involved in this step: acetal deprotection, ring closure, and dehydration. The intermediates could be detected by TLC, but were not isolated considering the very short reaction time (compound **6** was formed within ten minutes at room temperature in dichloromethane). Key compound **6** was then converted into the keto analogue **7** through transchalcogenation [$Hg(OAc)_2$, CH_2Cl_2–AcOH)] in quantitative yield. Conversion to bis(pyrrolo[3,4-*d*])tetrathiafulvalene **1** was then carried out in two steps, as described,[2c,4] by $P(OEt)_3$-mediated self-coupling to **8**, and subsequent removal of the tosyl protecting group with sodium methoxide.

In conclusion, a quick and efficient synthesis of *N*-tosyl-(1,3)-dithiolo[4,5-*c*]pyrrol-2-one (**7**), the key intermediate for the synthesis of mono- and bispyrrolo(TTF) derivatives **1a** and **1b**, is proposed. Compound **7** could be obtained in less than three days, in a global yield of 51%, starting from commercially available alkyne **2** and ethylenetrithiocarbonate.

^{1}H NMR (500.13 MHz)and ^{13}C NMR (125.75 MHz) spectra were recorded on a Bruker Avance DRX 500 spectrometer. Chemical shifts are reported relative to TMS as internal standard. Mass spectra were carried out on a Varian MAT 311 spectrometer (CRMPO, Rennes). Melting points were determined on a Büchi 510 apparatus. Amberlyst® 15 ion-exchange resin(dry) was purchased from Acros Organics. Chromatography was performed on silica gel.

***N*-{[5-(Diethoxymethyl)-2-thioxo-1,3-dithiol-4-yl]}methyl-4-methylbenzenesulfonamide (5)**

Thione **3** (4.2 g, 15.9 mmol) and *p*-toluenesulfonamide (13.7 g, 5 equiv) were dissolved in anhyd toluene (450 mL) in the presence of molecular sieves (4 Å). The reaction mixture was refluxed under nitrogen for 4 h, [**3** was completely consumed, monitored by TLC, CH_2Cl_2–cyclohexane (6:4), 1% Et_3N]. The molecular sieves were discarded after filtration and the toluene was evaporated in vacuo to afford thione **4**, which was used directly in the following step. The corresponding brown oil was dissolved in anhyd MeOH (300 mL) under nitrogen and reacted with $NaBH_4$ (643 mg, 17 mmol) at r.t. for 15 min. The solvent was removed in vacuo, the resulting material was dissolved in CH_2Cl_2 (300 mL), and washed with H_2O (3 × 400 mL). The organic phase was dried over $MgSO_4$ and evaporated to dryness. The resulting oil was then chromatographed (CH_2Cl_2, 1% Et_3N) to afford the target amine **5** as a dark yellow oil; yield: 4.99 g (11.9 mmol; 75% from **3**); R_f 0.32 (CH_2Cl_2, 4% Et_3N).

^{1}H NMR (acetone-d_6): δ = 7.74 (d, *J* = 7.9 Hz, 2 H, Ar), 7.41 (d, *J* = 7.9 Hz, 2 H, Ar), 7.21 (m, 1 H, NH), 5.64 [s, 1 H, C*H*$(OEt)_2$], 4.26 (m, 2 H, CH_2N), 3.63 (m, 4 H, OCH_2), 2.41 (s, 3 H, $ArCH_3$), 1.17 (t, *J* = 7.1 Hz, 6 H, CH_3).

^{13}C NMR (acetone-d_6): δ = 212.3, 143.6, 141.0, 140.7, 137.7, 129.7, 126.9, 96.3, 61.6, 39.8, 20.5, 14.3.

HRMS (EI): *m*/*z* calcd for $C_{16}H_{21}NO_4S_4$: 419.03535; found: 419.0345.

Anal. Calcd for $C_{16}H_{21}NO_4S_4$: C, 45.80; N, 3.34; O, 15.25. Found: C, 45.58; N, 3.26; O, 15.49.

5-Tosyl-5*H*-[1,3]dithiolo[4,5-*c*]pyrrole-2-thione (6)

Amine **5** (4.99 g, 11.9 mmol) was dissolved in CH_2Cl_2 (400 mL) under nitrogen and Amberlyst® 15 ion-exchange resin (dry, 15 g) was added. The mixture was stirred for 5 min (the reaction was monitored by TLC, CH_2Cl_2), and then the resin was filtered off. The filtrate was concentrated in vacuo and chromatographed (CH_2Cl_2–cyclohexane, 6:4). Evaporation of the solvent afforded thione **6** as a deep yellow powder; yield: 3.85 g (11.8 mmol; 99%); R_f 0.49 (CH_2Cl_2–cyclohexane, 6:4); mp 217–218 °C (Lit.[4] 215.0–215.5 °C).

^{1}H NMR (DMSO-d_6): δ = 7.89 (d, *J* = 8.35 Hz, 2 H, Ar), 7.64 (s, 2 H, $H_{pyrrole}$), 7.48 (d, *J* = 8.3 Hz, 2 H, Ar), 2.39 (s, 3 H, $ArCH_3$).

^{13}C NMR (DMSO-d_6): δ = 221.4, 146.9, 134.5, 131.1, 128.3, 127.5, 112.8, 21.6.

HRMS (EI): *m*/*z* calcd for $C_{12}H_9NO_2S_4$: 326.95162; found: 326.9512.

5-Tosyl-5*H*-[1,3]dithiolo[4,5-*c*]pyrrol-2-one (7)
Thione **6** (1.15 g, 3.52 mmol) was dissolved in a solution of CH_2Cl_2 (250 mL) and glacial AcOH (20 mL). $Hg(OAc)_2$ (2.24 g, 7.03 mmol) was then introduced in one portion and the reaction mixture was stirred for 10 min, causing the yellow solution to turn white.[13] The mercuric salts were removed by filtration through celite, which was washed with CH_2Cl_2 (3 × 50 mL). The filtrate was then treated with a sat. solution of $NaHCO_3$ (3 × 350 mL), H_2O (200 mL), and finally dried over $MgSO_4$. The solvent was evaporated in vacuo, and the resulting material was purified through a short column of silica gel (CH_2Cl_2–cyclohexane, 6:4) to afford compound **7** as white needles after evaporation of the solvent; yield: 1.07 g (98%); R_f 0.47; mp 179–180 °C (Lit.[4a] 178.5–179 °C).

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(11) Attempts to purify imine **4** by silica gel or alumina chromatography invariably led to a partial reverse reaction to the starting products.
(12) Alternatively, compound **5** may be directly engaged in the following step without being chromatographed (no noticeable loss in the yield of **6**). In fact, the purification of **5** by silica gel chromatography is accompanied by formation of compound **6**.
(13) We observed lower yields with longer times.