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New Versatile Building Blocks in Tetrathiafulvalene (TTF) Chemistry : 2,3-*bis*(bromomethyl) and *tetrakis*(bromomethyl)TTFs

P. Hudhomme,[*†] **S.G. Liu, D. Kreher, M. Cariou and A. Gorgues**

Ingénierie Moléculaire et Matériaux Organiques, UMR CNRS 6501, Université d'Angers, 2 Bd Lavoisier, F-49045 Angers

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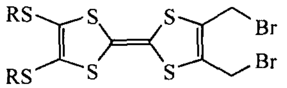
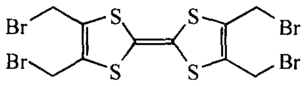
Abstract : Efficient syntheses of novel 2,3-*bis*(bromomethyl)TTF derivatives **1** and *tetrakis*(bromomethyl)TTF **2**, prone to generate corresponding 2,3-dimethylene[2H]-TTF **3** and tetramethylene[4H]-TTF **4** respectively, are reported. © 1999 Published by Elsevier Science Ltd. All rights reserved.

Recent report by J. Becher[1] on **1a** prompts us to present herein our previous syntheses of *bis*(bromomethyl)TTF derivatives **1b-d** and *tetrakis*(bromomethyl)TTF **2** which are of significant interest for their synthetic applications as versatile building blocks for the selective functionalization of the TTF core.[2]



1 **a** : R,R = CH_2CH_2CN **c** : R,R = Pent
b : R,R = CH_3 **d** : R-R = $-CH_2CH_2-$



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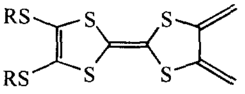
During the past two decades, tetrathiafulvalene derivatives have received considerable attention as electron donors for the preparation of low dimensional organic salts showing specific electrical properties ranging from semiconductive to superconductive behavior.[3] While the synthesis of new π-electron donors based on the TTF core has been particularly fruitful and varied,[4] the possibility of developing chemistry in this family from a diene group able to react through a Diels-Alder cycloaddition was surprisingly missing. Clearly this research area has been restricted by lack of suitable TTF building blocks and to our knowledge, only C. Rovira *et al.* have previously contributed to this field.[5] Their approach used a thermolabile sulfone group as the diene precursor[5a] which was successfully applied to realize cycloadditions of 2,3-dimethylene[2H]-TTF derivatives to C_{60}.[5c,d] Nevertheless, no evidence of the formation of cycloadducts from tetramethylene[4H]-TTF **4** with C_{60} was observed probably due to the drastic experimental conditions inconsistent with respect to the poor stability of the expected cycloadduct (*i.e.* final polymerization of the orthoquinodimethane moiety).[5d]

Our approach was based on the synthesis of precursors which could smoothly generate the formation of these transient dienes. In this context, we have chosen the novel vicinal *bis* and *tetrakis*(bromomethyl)TTFs **1b-d** and **2** able to undergo a reductive elimination upon treatment with naked iodide[6] to give rise to dienes **3** and **4**, by analogy with our previous results in 2-(thi)oxo-1,3-dithiole series.[7]



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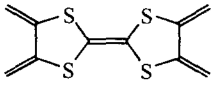

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[†] E-mail : pietrick.hudhomme@univ-angers.fr

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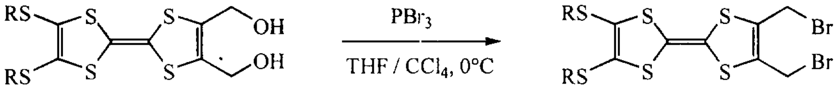
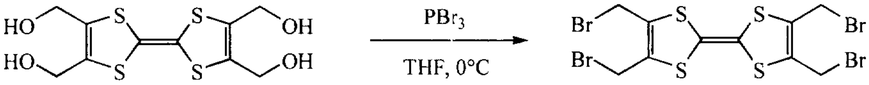
Our starting materials were the corresponding alcohols, 2,3-*bis*(hydroxymethyl)-6,7-*bis*(alkylsulfanyl)-TTF[8] **5** and *tetrakis*(hydroxymethyl)TTF **6**.[9] The unprecedented TTFs bearing two vicinal bromomethyl groups **1** and **2** were then conveniently prepared upon treatment of **5** and **6** with phosphorus tribromide referring to the reaction we had developed on the 4,5-*bis*(hydroxymethyl)-2-thioxo-1,3-dithiole.[10]



5   **b** : R,R = CH_3
c : R,R = Pent
d : R-R = $-CH_2CH_2-$

1



6   **2**

Nevertheless, the isolation of 2,3-*bis*(bromomethyl)TTF derivatives **1b-d** appeared to be highly dependent on the experimental conditions. For instance, we had to optimize some crucial parameters in order to cleanly obtain these target molecules in an average of 70% yield after SiO_2 column chromatography :

i) firstly, we have noted the primordial role of the binary system of solvents (THF/CCl_4) accompanied by a constant bubbling of nitrogen gas in the solution which both seemed to limit the possible protonation of TTF,[11] resulting from the presence of phosphorous acid and probably hydrogen bromide,

ii) in relation with this preliminary observation, we have established that TTF derivatives **1b-d** were not stable in solvents such as dichloromethane or chloroform to realize the extraction step or purification by flash column chromatography either on silica gel or florisil. Of course, the lifetime of **1b-d** in $CDCl_3$ seems to be too short to allow any detection in ^{13}C-nmr,

iii) the rapid degradation of these compounds was observed upon heating *in vacuo* and this kind of instability was confirmed during the mass spectrometry studies. So the EI mass spectrum did not exhibit the molecular ion peak. At the beginning of the acquisition, the spectrum was saturated with the presence of peaks at *m/z* 80 and 82 (1/1) corresponding to the ion of rearrangement $[HBr]^{+\cdot}$. Then the base peak corresponded to 2,3-dimethylene[2H]TTF **3**. Nevertheless, we could efficiently characterize the molecular peak of **1b** using the FAB (+) technique.

*Typical procedure for the preparation of **1 b-d** :*

To 2,3-*bis*(hydroxymethyl)-6,7-*bis*(alkylsulfanyl)-TTF[8] **5** (0.8 mmol) dissolved in dry THF (9 mL) was added dry CCl_4 (9 mL) ; then this well-stirred solution was cooled to 0°C and a constant bubbling of nitrogen gas was adapted. Then 0.11 mL of phosphorus tribromide (1.17 mmol) was slowly added dropwise via a syringe. After stirring for 1 h. at 0°C, the clear purple solution was poured in EtOAc (80 mL). The organic layer was washed with brine (2x50 mL), dried ($MgSO_4$) and the solvent was evaporated *in vacuo* (without heating). The residue was filtered off on a flash silica gel or florisil column using petroleum ether/EtOAc 1/1 as the eluent affording purple crystals in an average yield of 70%. The product could be stored at -10°C under argon atmosphere.

Then we applied this methodology to the preparation of **2** but, due to its poor solubility, the starting material *tetrakis*(hydroxymethyl)TTF **6** was suspended in dry THF. In our first attempts, we have noted the possibility to isolate, in diluted conditions of reaction and in variable yield, the corresponding *bis*(oxydimethylene)TTF in accordance with previous observations using thionyl chloride.[12,13]

Surprisingly, we have rapidly established the better stability of the expected compound **2** obtained in nearly 70% yield after purification by chromatography. To illustrate this higher stability, an alternative route for its preparation was to carry out the reaction in THF/DMSO (5/1) for about 2 h. at 0°C then heat the solution to 45°C. Best confirmation of structure for **2** was supported by its EI mass spectrum which exhibited the molecular ion peak at *m/z* 576 and showed also the successive fragmentation of each bromine atom affording the peak of tetramethylene[4H]-TTF at *m/z* 256 (figure). The isotopic distribution was in agreement with the calculated pattern for each characteristic fragment.

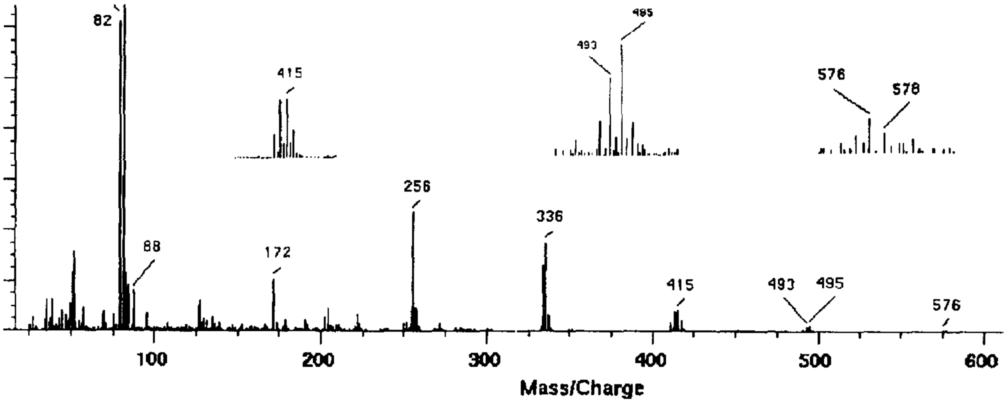


Figure : EI Mass Spectrometry spectrum of *tetrakis*(bromomethyl)TTF **2**

Typical procedure for the preparation of **2** *:*

To a suspension of *tetrakis*(hydroxymethyl)TTF[9] **6** (0.486 g, 1.5 mmol) in 50 mL of dry THF was slowly added via a syringe, at 0°C under a constant bubbling of nitrogen gas, 0.65 mL of phosphorus tribromide (6.9 mmol). After stirring for 4 h. at 0°C, the clear solution was poured in EtOAc (150 mL). The organic layer was washed with brine (3x100 mL), dried ($MgSO_4$) and the solvent was evaporated *in vacuo* (without heating preferentially). The residue was filtered off on a flash silica gel or florisil column using petroleum ether/EtOAc 1/1 as the eluent affording 580 mg of red carmine crystals in 68% yield. The product could be stored at -10°C under argon atmosphere.

Besides usual characterizations using spectroscopic analyses,[14] all compounds **1b-d** and **2** were studied by cyclic voltammetry and display two reversible one-electron oxidation peaks : $Epa_1 = 0.60$ and $Epa_2 = 0.88$ for **1b**, $Epa_1 = 0.58$ and $Epa_2 = 0.86$ for **1c**, $Epa_1 = 0.67$ and $Epa_2 = 1.15$ for **1d**, $Epa_1 = 0.61$ and $Epa_2 = 0.93$ for **2** [Conditions of cyclic voltammetry : [**1** or **2**] $< 10^{-3}$ M in acetonitrile for **1b**, **1c** and **2** (or *o*-dichlorobenzene for **1d**), Bu_4NPF_6 0.1 M (or saturated solution for **1d**) , Pt electrode, v = 100 mVs^{-1}, E_{red} and E_{OX} in V/SCE].

Of course, compounds **1b-d** and **2** are very attractive for synthetic purposes in TTF chemistry. Besides their interaction with nucleophilic derivatives,[15] they also behave as good precursors of the corresponding orthoquinodimethanic dienes **3** and **4** which have been trapped with varied dienophiles.[15] In particular, we have succeeded in the preparation of new donor-acceptor assemblies upon their Diels-Alder reaction with one[2] or two[16] C_{60}.

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14. New compounds gave satisfactory spectral data. Selected data :
    1b : ^1H nmr (C_6D_6) $\delta = 1.98$ (s, 4H, 2 CH_3S), 3.41 (s, 4H, CH_2Br), ^{13}C nmr (C_6D_6) $\delta = 18.70$ (SCH_3), 22.51 (CH_2Br), 109.68, 122.73 and 131.53 (C=C); FAB$^+$ MS : 480/482/484 (M^+), 322. **1c** : ^1H nmr (C_6D_6) $\delta = 0.80$ (t, 6H, $J = 7.2$ Hz, 2 CH_3), 1.12 (m, 8H, 2 $CH_3C\underline{H}_2C\underline{H}_2$), 1.45 (m, 4H, $2C\underline{H}_2CH_2S$), 1.45 (t, 4H, $J = 7.2$ Hz, 2 CH_2S), 3.27 (s, 4H, CH_2Br); ^{13}C nmr (C_6D_6) $\delta = 14.08$ (CH_3), 22.41 ($CH_3\underline{C}H_2CH_2 + \underline{C}H_2Br$), 29.70 ($CH_3CH_2\underline{C}H_2$), 30.81 ($\underline{C}H_2CH_2S$), 36.44 ($CH_2S$), 101.43 and 131.29 (C=C). **1d** : ^1H nmr (C_6D_6) $\delta = 2.33$ (s, 4H, SCH_2CH_2S), 3.41 (s, 4H, CH_2Br). **2** : 130-132°C (dec.); ^1H nmr ($CDCl_3$) $\delta = 4.20$ (CH_2Br); (C_6D_6) $\delta = 3.39$ (CH_2Br); Elem. analysis : $C_{10}H_8S_4Br_4$ M = 576.092 Calc. % C = 20.85, % H = 1.40, % S = 22.26, % Br = 55.49; Found % C = 21.01, % H = 1.55, % S = 21.73, % Br = 51.09.
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