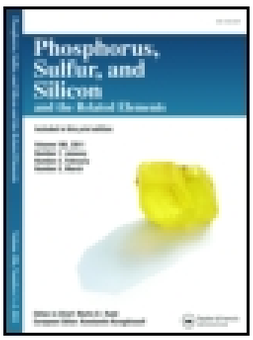

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Synthesis, Characterization and Theoretical Study of the Chemical Reactivity of New Cyclic Sulfamides Linked to Tetrathiafulvalene

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ABSTRACT

The synthesis of the title compounds has been carried out by condensation via a Wittig-type reaction of a pyridinium hexafluorophosphate with a phosphonate ester to give the desired (4-nitrophenyl)tetrathiafulvalene the nitro group of which was reduced to an amino group. Reaction of the amine with chlorosulfonyl isocyanate and subsequently with *tert*-butyl alcohol gave the corresponding open-chain sulfamide. Cyclization under basic conditions and de-protection led to 2-[4-(4′,5′-dipropyltetrathiafulvalen-4-yl)]phenyl-1,2,6-thiadiazinane 1,1-dioxide. Finally, *N*-alkylated and *N*-acylated cyclic sulfamides linked to tetrathiafulvalene were obtained. Their electron donor ability was measured by cyclic voltammetry. A detailed DFT study based on B3LYP/6–31G (d,p) of electronic properties is also presented. The calculated molecular electrostatic potential shows that, the negative charge covers the nitro and sulfamide function, while positive charge is located at the hydrogen atoms of the amine and sulfamide rings. The calculated HOMO and LUMO energy reveals that charge transfer occurs within the molecule. The chemical reactivity parameters reveal that tetrathiafulvalene 1 is highly reactive, which facilitates the desired formation of the cyclic sulfamide. The first hyperpolarizability β_{tot} shows that compounds 1 and 5 are good candidates as a NLO material.

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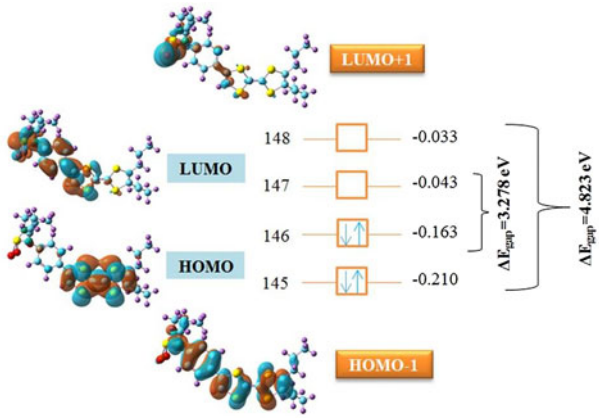
Cyclic sulfamide; tetrathiafulvalene; density functional theory; computational chemistry

GRAPHICAL ABSTRACT



Introduction

Sulfur and nitrogen containing heterocyclic compounds are key building blocks used to develop compounds of biological or medicinal interest. Heterocyclic compounds also have a practical use as components in dyes, antioxidants, copolymers, bases, and ligands. They are not only used as drugs but also in the field of electronics and superconductors.[1] Tetrathiafulvalenes belong to the most representative examples. Due to their unique π-donor properties, tetrathiafulvalene (TTF) and its derivatives represent the basis of the large majority of organic metals and superconductors known so far.[2] One of the trends in TFF research has been and still is the incorporation of various spacer groups into the central double bond as a means to achieve better overlap between the molecules in the solid state, as well as lowering the electron-electron repulsion in the molecule.[3,4] Initially, they were extensively studied in the context of organic electronics due to their ability to form conductive, semi-conductive, and superconductive solid-state phases.[2]

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On the other hand, the discovery of sulfonamides was a significant milestone event in the human chemotherapeutic history. Sulfa drugs (sulfonamides) are used as first drugs among chemotherapeutic agents (together with ampicillin and gentamicin) for the treatment of bacterial infections by *Escherichia coli* in humans.[5] Sulfonamide-based drugs are produced in large quantities, and largely used in medical treatment.[6–10] On the other hand, also heterocyclic sulfonamide derivatives have been reported to show a broad spectrum of pharmacological properties, such as anti-diabetic,[11,12] anti-thyroid,[13] anti-tumor,[14,15] anti-HIV,[16] anti-tubercular,[17] anti-microbial,[18–20] anti-leukemic,[21] anti-inflammatory,[22] anti-convulsive and analgesic[23] activities.

Density functional theory (DFT) adequately takes into account electron correlation contributions, which are especially important in systems containing extensive electron conjugation and/or electron lone pairs.[24] The B3LYP hybrid functional has shown to successfully predict a wide range of molecular properties at a relatively low computational cost. In previous work,[25] we have developed a series of bis-TTF systems which incorporate the cyclic sulfamide moiety in the hope that they may be biologically active. The results are promising.

Taking into account the above and in the continuity of our works, we decided to design and realize a series of cyclic sulfamides linked to tetrathiafulvalene. Here we will report on the investigation of the electrochemical properties and the chemical reactivity via DFT, with the aim to predict some applications of these compounds in the field of material science.

Synthesis

In previous work[25] we have described the synthesis of cyclic sulfamides, where we have incorporated a series of seven-, eight-, nine- and ten-membered heterocyclic rings containing a sulfonamide moiety linked to TTF derivatives. In continuation of our previous work, we describe here a convenient access to a series of cyclic *N*-alkylated sulfonamides linked to TTF derivatives. The synthetic strategies adopted to obtain the target compounds were realized according to the chemical pathway depicted in Scheme 1.

The condensation via Wittig-type reaction of 1,3-dithiole-2-ylidenepiperidinium hexafluorophosphate with a phosphonate ester in the presence of *n*-butyllithium at low temperature in anhydrous tetrahydrofuran under nitrogen, led to the formation of 4′-(4-nitrophenyl)-4,5-dipropyl-tetrathiafulvalene **1** with a good yield of 63% after column chromatography. The nitro group of **1** was reduced with tin and hydrochloric acid at reflux into an amino group in ethanol with a 54% yield of **2** after column chromatography. The open-chained sulfamide **3** was prepared in good yield (85% after recrystallization) in two steps. First chlorosulfonyl isocyanate was reacted with *tert*-butyl alcohol, then the resulting solution of *tert*-butyloxycarbonylsulfamoyl chloride was added in anhydrous dichloromethane to 4′-(4-aminophenyl)-4,5-dipropyltetrathiafulvalene **2**. The cyclization reaction of *N*-[4-(4′,5′-dipropyltetrathiafulvalen-4-yl)]phenyl-*N*′-(*tert*-butoxycarbonyl)sulfamide **3** with dibromopropane under basic conditions in acetone gave the cyclic sulfonamide-TTF **4** with satisfactory yield of 43% after column chromatography. Selective cleavage of the *tert*-butyloxycarbonyl protective group with trifluoroacetic acid gave the sulfamide **5** in 87% yield. Alkylation of **5** with methyl bromide in the presence of potassium carbonate in acetonitrile at 70 °C afforded the *N*-methylsulfamide **6** in 58% yield after purification by flash chromatography. The *N*-propionylsulfamide-TTF derivative **7** was readily prepared in 64% yield from the cyclosulfamide **5** by treatment with propionyl chloride in the presence of triethylamine and catalytic quantities of dimetylaminopyridine.

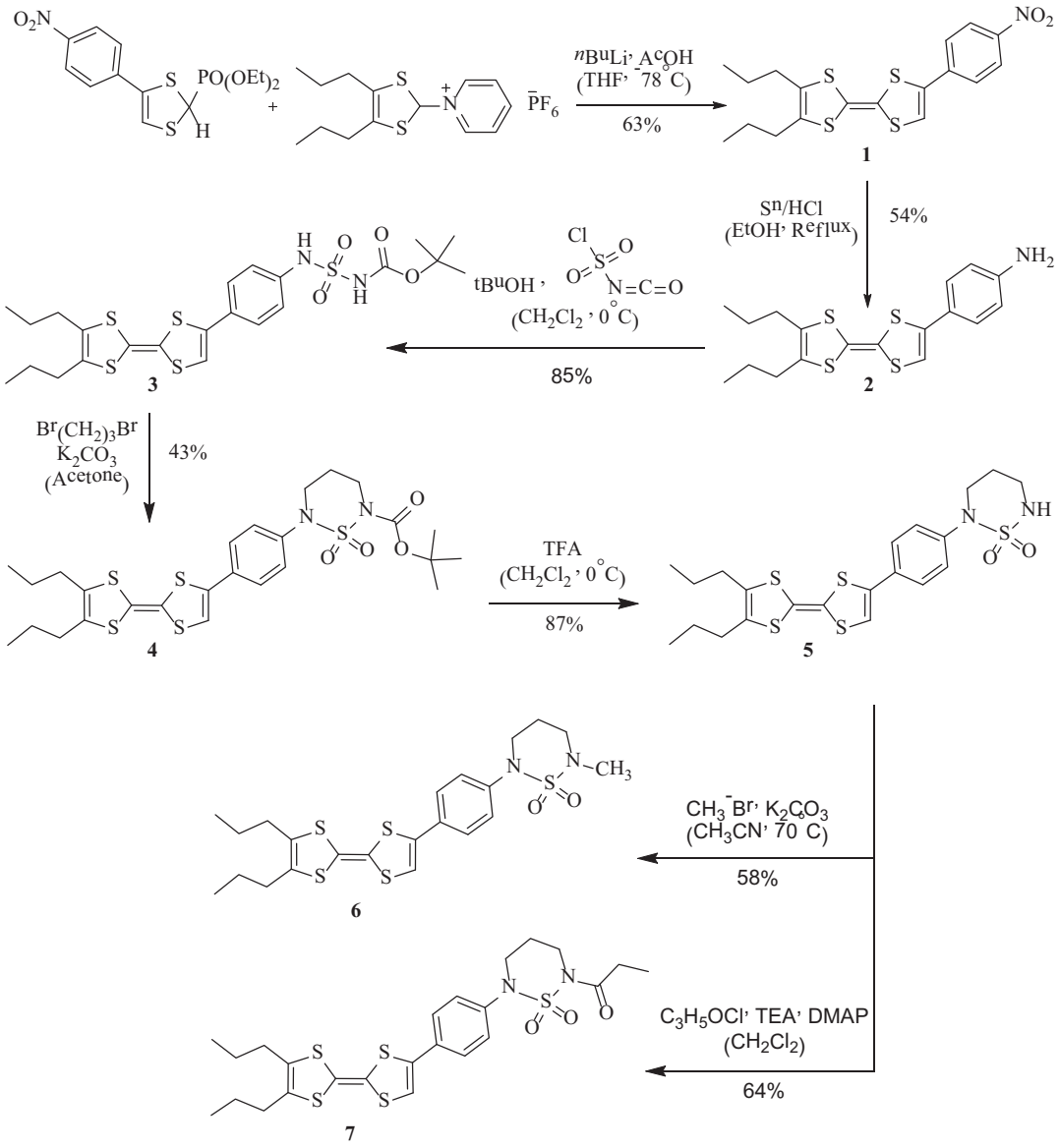
Electrochemical studies

The redox behavior of the cyclic sulfamide-tetrathiafulvalenes **1–7** was studied in solution by cyclic voltammetry (CV). The measurements were performed under nitrogen at room temperature using a glassy carbon working electrode, a Pt counter electrode and a standard calomel electrode (SCE) as reference, with tetrabutylammonium perchlorate (n-Bu_4NClO_4, 0.1 M) in dry acetonitrile as supporting electrolyte. A scan rate of 100 mVs^{-1} was used. The CV measurements showed reversible redox waves for all compounds studied (Figure 1). The corresponding redox potentials $E_{1/2}$ are summarized in Table 1.

From Figure 1 one can clearly see seven oxidation and reduction peaks of the studied compounds **1–7**. The real distinction of the oxidation and reduction waves is obviously due to the difference between the donor and the attractor effects of the substituents carried by the TTF units, which are also visible by cyclic voltammetry. The oxidation potentials of compounds **3–7** are slightly higher than that of compound **2**. On the other hand, compound **1** exhibits a slightly higher potential compared with **3–7**. This can be attributed to the electron-donating capabilities of these compounds by the presence of *p*-nitrophenyl, *p*-aminophenyl and *p*-sulfonamidophenyl groups linked to the donor core. In the same series and specified in compounds **3–7**, the presence of alkyl groups on the TTF skeleton enriches the electron density and facilitates the oxidation of the donor, which is in accordance with these compounds. By a comparison between the phenyl-linked groups that is linked with its role by the TTF core, it is found that the oxidation potentials of the compounds **3–7** ranked from largest to smallest as follows: compound **6** > compound **5** > compound **7** > compound **4** > compound **3**.

Computational results

Quantum chemical calculation is one of the recent emerging tools in unraveling physical and chemical properties of molecules. Among the physical and chemical properties investigated, molecular electrostatic potential, frontier molecular orbitals, global reactivity descriptors and nonlinear optical properties which are calculated by use of the DFT/B3LYP method with 6–31 G (d,p) basis set.



Scheme 1. Synthetic route for the preparation of cyclic sulfamide-tetrathiafulvalenes **1–7**.

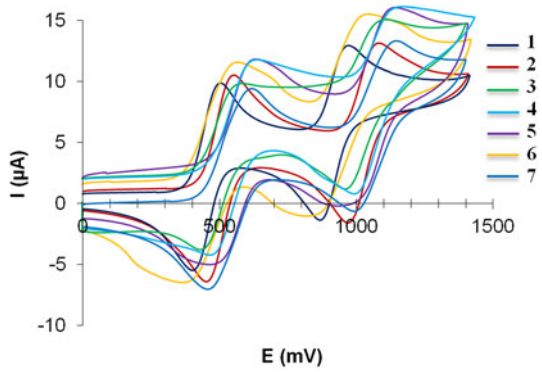


Figure 1. Voltamogram of the cyclic sulfamide-tetrathiafulvalenes **1–7**.

Table 1. Redox potentials of the cyclic sulfamide-tetrathiafulvalenes **1–7**.

Compound	E^1_{ox} (mV)	E^2_{ox} (mV)	ΔE_{ox} (mV)
1	546	1078	532
2	530	1054	524
3	552	1078	526
4	594	1098	504
5	604	1106	502
6	606	1140	534
7	590	1116	526

Molecular electrostatic potential (MEP)

By MEP analysis, the size and shape as well as the site of chemical reactivity and the charge density of the investigated system are explained by an electron density isosurface mapped by the electrostatic potential surface. The MEP surfaces for the title compounds are presented in Figure 2.

Figure 2 demonstrates that the regions exhibiting the negative electrostatic potential are localized near the nitro group for compound **1**, the TTF core for compound **2** and on the sulfamide function for the rest of the compounds. The regions of positive potential are located near the hydrogen bonded directly linked to the TTF core for all compounds and also on the hydrogen atoms of the amine function for compounds **2** and **3** as well as near the hydrogen atoms of the sulfamide rings for the compounds **4–7**.

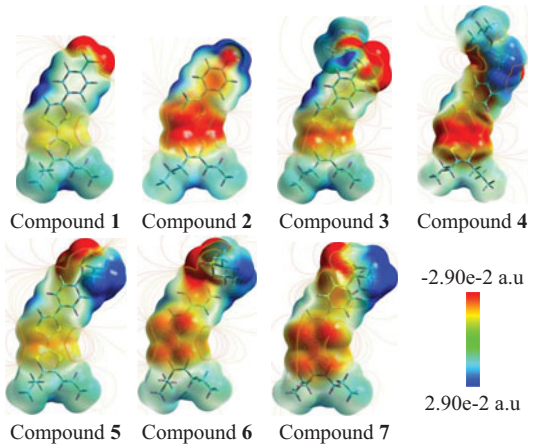


Figure 2. MEP surfaces of compounds **1–7**.

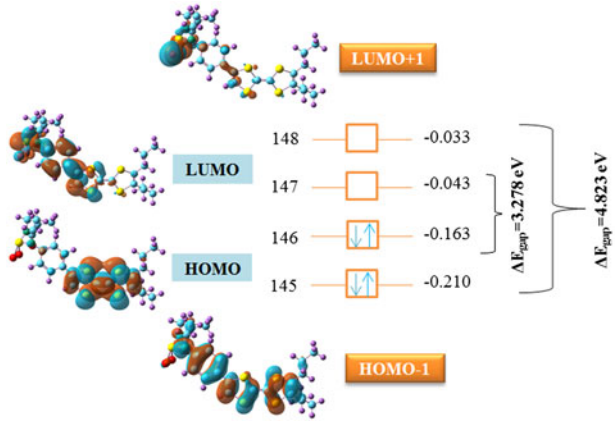


Figure 3. HOMO-LUMO Structure with the energy level diagram of **7**.

Table 2. Quantum chemical descriptors of compounds **1–7**.

Parameters	1	2	3	4	5	6	7
E_{HOMO} (eV)	−4.795	−4.295	−4.509	−4.498	−4.507	−4.469	−4.450
E_{LUMO} (eV)	−2.571	−0.723	−1.213	−1.221	−1.140	−1.080	−1.172
ΔE_{gap} (eV)	2.224	3.572	3.296	3.278	3.367	3.389	3.278
IE (eV)	4.795	4.295	4.509	4.498	4.507	4.469	4.450
A (eV)	2.571	0.723	1.213	1.221	1.140	1.080	1.172
μ (eV)	−3.683	−2.509	−2.861	−2.859	−2.823	−2.774	−2.811
χ (eV)	3.683	2.509	2.861	2.859	2.823	2.774	2.811
(eV)	1.112	1.786	1.648	1.639	1.683	1.694	1.639
S (eV)	0.450	0.280	0.303	0.305	0.297	0.295	0.305
ω (eV)	6.098	1.763	2.484	2.495	2.367	2.271	2.411

According to the above-mentioned conditions, in the case of a chemical reaction or intermolecular interactions the nitro, sulfamide or amine function parts can play important roles.

Frontier molecular orbitals (FMOs)

The electronic absorption corresponds to the transition from the ground to the first excited state, i.e. it is mainly described by the one electron excitation from the HOMO to the LUMO. The HOMO energies, the LUMO energies and the energy gap for the title molecules are given in Table 2 and the pictorial representation of the frontier molecular orbitals for the final product **7** is presented in Figure 3.

The HOMO is confined over the TTF core for all compounds, while the LUMO is located on nitrobenzene part of compound **1**, the aminobenzene part of compound **2** and on the benzosulfonamide group of the remainder compounds which gives charge transfer process in the molecular system.

Global reactivity descriptors

To understand the chemical reactivity and site selectivity of the molecular systems we have calculated global chemical reactivity descriptors such as E_{HOMO}, E_{LUMO}, ΔE_{gap}, A, I, η, μ, *S*, χ and ω of compounds **1–7**. The results are given in Table 2.

Compound **1** exhibits the lowest energy gap (ΔE_{gap} = 2.224 eV). This low gap allows it to be the softest molecule. The compound that has the highest energy gap is **2** (ΔE_{gap} = 3.572 eV). The compound that has the highest HOMO energy is the compound **2** (E_{HOMO} = –4.295 eV). This higher energy allows it to be the best electron donor. Compound **1** has the lowest LUMO energy (E_{LUMO} = –2.571 eV) which signifies that it is the best electron acceptor. The two properties *I* (potential ionization) and *A* (affinity) are very important. The determination of these two properties allows the calculation of the absolute electronegativity χ and the absolute hardness η. These two parameters are related to the one-electron orbital energies of the HOMO and LUMO respectively. Compound **2** has the lowest value of the potential ionization (*I* = 4.295 eV), which makes it the better electron donor. Compound **1** has the largest value of the affinity (*A* = 2.571 eV), which makes it the better electron acceptor. The chemical reactivity varies with the structure of molecules. The chemical hardness (softness) value of compound **1** (η = 1.112 eV, S = 0.450 eV) is lesser (greater) among all the molecules. Thus, compound **1** is found to be more reactive than all the compounds. Compound **1** possesses a higher electronegativity value (χ = 3.683 eV) than all compounds. It is thus the best electron acceptor. The value of ω for compound **1** (ω = 6.098 eV) indicates that it is a stronger electrophile than all compounds. Compound **1** has the smaller frontier orbital gap. So, it is more polarizable and is associated with a high chemical reactivity, low kinetic stability and is also termed as soft molecule.

Nonlinear optical properties (NLO)

The magnitude of the first hyperpolarizability of organic molecules depends on the delocalized π electrons moving through the molecular system. The location of donor and acceptor groups to opposite sides of molecular systems induces the NLO activity. The calculated first hyperpolarizability parameters of compounds **1–7** are given in Table 3.

According to the above mentioned conditions, these compounds can be considered as candidates for NLO materials. Their nonlinear optical properties have been evaluated by the total first hyperpolarizability β, which shows the tendency of the electron donating capacity and extended π-conjugation pattern to be **1** > **5** > **4** > **3** > **7** > **6** > **2**. The calculated values of β_{tot} were found to be 0.85×10^{-30},

Table 3. First hyperpolarizability parameters of compounds **1–7**.

Compound	1	2	3	4	5	6	7
β_{xxx}	620.782	296.453	−230.280	−177.116	511.609	−258.426	−43.742
β_{xxy}	−102.605	55.076	−193.199	−34.915	279.269	271.983	286.336
β_{xyy}	−3.057	41.014	−4.409	−37.836	−74.220	55.698	54.694
β_{yyy}	1.3628	22.738	−34.412	−12.001	14.200	10.387	29.243
β_{xxz}	−36.4761	60.327	183.792	243.777	39.811	−59.796	−66.167
β_{xyz}	6.513	10.122	−11.379	−32.645	−1.884	8.712	19.212
β_{yyz}	4.896	−5.144	13.212	21.443	10.202	12.514	23.712
β_{xzz}	−13.070	−24.304	80.141	−48.429	−34.982	59.751	26.224
β_{yzz}	8.593	2.085	−4.518	7.957	17.974	17.274	27.035
β_{zzz}	16.797	−1.959	16.001	22.342	6.316	2.930	6.574
β_{tot} (esu) $\times 10^{-33}$	858.369	327.548	350.913	391.891	511.958	334.956	346.487

0.32×10^{-30}, 0.35×10^{-30}, 0.39×10^{-30}, 0.51×10^{-30}, 0.33×10^{-30} and 0.34×10^{-30} esu respectively, which are approximately similarly or two and three times higher than the value for urea ($\beta_{tot} = 0.34 \times 10^{-30}$ esu). Urea is one of the prototypical molecules used in the study of the NLO properties of molecular systems. Therefore, it has been used frequently as a threshold value for comparative purposes. So, it is clear that β_{tot} of compounds **1** and **5** are three and two times larger than the value of urea which makes them attractive objects for future studies of nonlinear optical properties and may be a potential applicant in the dipole moment of NLO materials, when compared to compounds **2**, **3**, **4**, **6** and **7**.

Experimental section

General

^{1}H NMR spectra were recorded in DMSO-d6 at 400 MHz on a WP 400-NMR instrument (Bruker BioSpin GmbH, Silberstreifen 4, D-76287 Rheinstetten, Germany). FAB mass spectra were recorded on a JOEL JMS-DX 300 spectrometer (JEOL Europe, Planet II, Gebouw B., Leuvensestreenweg 542, B-1930 Zaventem, Belgium). Uncorrected melting points were measured on a 510 Büchi apparatus (BÜCHI Labortechnik AG, Meierseggstrasse 40, 9230 Flawil, Schweiz). Cyclic voltammetry measurements were carried out on a PAR-273 potentiostat/galvanostat (Alltest Instruments, Inc. 500 Central Ave. Farmingdale, NJ, USA). All solvents were dried by standard methods and all commercial reagents were used without further purification. All reactions were performed under an inert atmosphere of nitrogen.

4′-(4-Nitrophenyl)-4,5-dipropyltetrathiafulvalene 1

Diethyl 4-(4-nitrophenyl)-1,3-dithiolene-2-phosphonate (5.26 g, 16.0 mmol) was dissolved in dry THF (40 ml). The mixture was cooled to −78 °C. *n*-BuLi (10.0 mL, 2.5 m in hexane, 16.0 mmol) was added, resulting in a milky white color of the mixture. After stirring for 10 min, the pyridinium salt (see Scheme 1, 6.97 g, 17 mmol) in dry THF (7 mL) was added in one portion. The mixture was stirred for 15 min at −78 °C, then allowed to reach r.t., and stirred for another 45 min. Then, AcOH (8 mL) was added and stirring was continued for an additional 3 h. The mixture was then concentrated in vacuo to a dark green oil. Et_2O (70 mL) was added and the organic phase was twice washed with $NaHCO_3$ (50 mL) and H_2O (50 mL). The product was subjected to column chromatography on silica gel (hexane/AcOEt 94:6), affording 4.12 g (63%) of **1** as dark green powder. M.p.: 105 °C. TLC: $R_f = 0.78$ (CH_2Cl_2). ^{1}H NMR: 0.97 (t, 6 H, $J = 6.8$ Hz, C**H**$_3$); 1.58 (m, 4 H, CH_3-C**H**$_2$); 2.37 (t, 4 H, $J = 6.8$ Hz, C**H**$_2$-CH=); 6.74 (s, 1 H, C**H**=C); 7.40 (d, $J = 8.85$ Hz, 2 H, nitrophenyl-**H**); 8.10 (d, $J = 8.85$ Hz, 2 H, nitrophenyl-**H**). MS (NOBA, FAB >0): 410 $[M+H]^+$. M = 409. Anal. calcd. for $C_{18}H_{19}O_2S_4N$: C, 52.78%; H, 4.67%; N, 3.42%; S, 31.31%; found: C, 53.08%; H, 4.95%; N, 3.67%; S, 31.41%.

4′-(4-Aminophenyl)-4,5-dipropyltetrathiafulvalene 2

A stirred mixture of **1** (1.63 g, 4 mmol), tin (0.94 g, 8 mmol), and aqueous HCl (35%, 1.8 mL, 20 mmol) in ethanol (30 mL) was refluxed for 4 h under N_2. During this time the initial black solution turned light yellow. The solution was then concentrated in vacuo, treated with an aqueous solution (100 mL) of NaOH (0.1 M) and extracted with ether. The organic phase was washed with water, dried ($MgSO_4$), and concentrated in vacuo. The product was subjected to column chromatography on silica gel (CH_2Cl_2), affording 0.81 g (54%) **2** as orange powder. M.p.: 92 °C. TLC: $R_f = 0.82$ (CH_2Cl_2). ^{1}H NMR: 0.93 (t, 6 H, $J = 6.8$ Hz, C**H**$_3$); 1.52 (m, 4 H, CH_3-C**H**$_2$); 1.94 (t, 4 H, $J = 6.8$ Hz, C**H**$_2$-CH=); 3.45–3.62 (br, 2 H, N**H**$_2$); 6.38 (d, $J = 8.30$ Hz, 2 H, aminophenyl-**H**); 6.58 (s, 1 H, C**H**=C); 6.90 (d, $J = 8.30$ Hz, 2 H, aminophenyl-**H**). MS (NOBA, FAB >0): 380 $[M+H]^+$. M = 379. Anal. calcd. for $C_{18}H_{21}S_4N$: C,56.94%; H,5.57%; N, 3.69%; S, 33.78%; found: C,57.05%; H,5.99%; N, 3.86%; S, 34.11%.

N-[4-(4′,5′-dipropyltetrathiafulvalen-4-yl)]phenyl-N′-(tert-butoxycarbonyl)sulfamide 3

To a stirred solution of 5 mL of chlorosulfonyl isocyanate (8.15 g, 57.6 mmol) in 100 mL of anhydrous CH_2Cl_2 at 0 °C were added 57.6 mmol of absolute *tert*-butyl alcohol in the same solvent. After stirring for 30 min, the resulting solution of BOC-sulfamoyl chloride and 24 mL of triethyl amine (17.40 g, 171.85 mmol) in 100 mL of CH_2Cl_2 were added dropwise to 57.60 mmol of **2** suspended in 120 mL of CH_2Cl_2. The reaction temperature did not rise above 5 °C. The resulting reaction solution was allowed to warm up to

r.t. over 2 h. The reaction mixture was diluted with 100 mL of CH_2Cl_2, washed with 0.1 N HCl and brine. The organic layer was dried (Na_2SO_4) and concentrated in vacuo to give the crude product. Recrystallization from hexane afforded 27.31 g (85%) of **3** as orange powder. M.p.: 87 °C. TLC: $R_f = 0.76$ (CH_2Cl_2). ^{1}H NMR: 0.94 (t, 6 H, $J = 6.8$ Hz, C**H**$_3$); 1.45 (s, 9 H, tBu); 1.52 (m, 4 H, CH_3-C**H**$_2$); 1.96 (t, 4 H, $J = 6.8$ Hz, C**H**$_2$-C=); 5.65 (s, 1 H, N**H**-Ph); 6.48 (d, $J = 8.30$ Hz, 2 H, phenyl-**H**); 6.59 (s, 1 H, C**H**=C); 7.15 (d, $J = 8.30$ Hz, 2 H, phenyl-**H**); 7.35 (s, 1 H, N**H-Boc**). MS (NOBA, FAB > 0): 559 $[M + H]^+$. M = 558. Anal. calcd. for $C_{23}H_{30}O_4S_5N_2$: C,49.43%; H,5.41%; N, 5.01%; S, 28.69%; found: C,49.70%; H,5.70%; N, 5.19%; S, 29.00%.

Tert-butyl 6-[4-(4′,5′-dipropyltetrathiafulvalen-4-yl)] phenyl-1,2,6-thiadiazinane-2-carboxylate 1,1-dioxide 4

The sulfamide **3** (5.58 g, 10 mmol) was dissolved in dry acetone, and anhydrous K_2CO_3 (1.5 equiv.) was added in one portion. Dibromopropane (10 mmol) dissolved in acetone was added dropwise to the solution. The resulting mixture was stirred at r.t. for 8 h, diluted with CH_2Cl_2 (200 mL), and acidified with 5% HCl. The organic layer was washed with water, dried (Na_2SO_4) and concentrated in vacuo. The crude product was purified by silica gel chromatography (CH_2Cl_2) to afford 2.57 g (43%) cyclosulfamide **4** as beige powder. M.p.: 124 °C. TLC: $R_f = 0.55$ (CH_2Cl_2). ^{1}H NMR: 0.94 (t, 6 H, $J = 6.8$ Hz, C**H**$_3$); 1.50 (s, 9 H, *t*Bu); 1.54 (m, 4 H, CH_3-C**H**$_2$);1.80 (m, 2 H, CH_2) 1.99 (t, 4 H, $J = 6.8$ Hz, C**H**$_2$-C=); 3.55 (t, $J = 5.80$ Hz, 2 H, CH_2-N-Ph); 3.98 (t, $J = 5.85$ Hz, 2 H, CH_2-N-*Boc*); 6.60 (s, 1 H, C**H**=C); 6.13 (d, $J = 8.30$ Hz, 2 H, phenyl-**H**); 7.20 (d, $J = 8.30$ Hz, 2 H, phenyl-**H**). MS (NOBA, FAB > 0): 599 $[M + H]^+$. M = 598. Anal. calcd. for $C_{26}H_{34}O_4S_5N_2$: C,52.14%; H,5.72%; N, 4.67%; S, 26.77%; found: C,52.43%; H,5.99%; N, 4.80%; S, 26.95%.

2-[4-(4′,5′-Dipropyltetrathiafulvalen-4-yl)]phenyl-1,2,6-thiadiazinane 1,1-dioxide 5

A solution of trifluoroacetic acid (50% in dry CH_2Cl_2, 3 equiv) was added dropwise into a stirred solution of **4** (6 g, 10 mmol) in dry CH_2Cl_2 (15 mL) at 0 °C. The reaction medium was stirred for 2 h, concentrated under reduced pressure and co-evaporated with diethyl ether. The residue was purified by flash chromatography. Elution with CH_2Cl_2-MeOH (95:5) afforded 4.33 g (87%) of deprotected cyclic sulfamides **5** as beige powder. M.p.: 107 °C. TLC: $R_f = 0.64$ (CH_2Cl_2). ^{1}H NMR: 0.98 (t, 6 H, $J = 8.0$ Hz, C**H**$_3$); 1.60 (m, 4 H, CH_3-C**H**$_2$);1.84 (m, 2 H, CH_2) 2.10 (t, 4 H, $J = 7.10$ Hz, C**H**$_2$-C=); 3.65 (t, $J = 8.30$ Hz, 2 H, CH_2-NH); 4.00 (t, $J = 8.30$ Hz, 2 H, CH_2-N-Ph); 4.35 (t, 1 H, N**H**); 6.60 (s, 1 H, C**H**=C); 6.15 (d, $J = 7.50$ Hz, 2 H, phenyl-**H**); 7.25 (d, $J = 7.50$ Hz, 2 H, phenyl-**H**). MS (NOBA, FAB > 0): 499 $[M + H]^+$. M = 498. Anal. calcd. for $C_{21}H_{26}O_2S_5N_2$: C,50.57%; H,5.25%; N, 5.61%; S, 32.14%; found: C,50.92%; H,5.51%; N, 5.78%; S, 32.27%.

2-[4-(4′,5′-Dipropyltetrathiafulvalen-4-yl)] phenyl-6-methyl-1,2,6-thiadiazinane 1,1-dioxide 6

To a stirred solution of **5** (5 g, 6.65 mmol) in MeCN (150 mL) in a 250 mL round bottom flask was added K_2CO_3 (2.75 g, 20 mmol) and MeBr (2.30 mL, 26.6 mmol). The flask was fitted with a condenser and the mixture was heated to 70 °C for 14 h. The resulting yellow red mixture was filtered by suction, and the solvent removed under reduced pressure to give a yellow oil. Flash chromatography (hexane/CH_2Cl_2, 2:1) afforded 1.97 g (58%) **6** as beige powder. M.p.: 109 °C. TLC: $R_f = 0.58$ (CH_2Cl_2). ^{1}H NMR: 0.94 (t, 6 H, $J = 8.0$ Hz, C**H**$_3$); 1.54 (m, 4 H, CH_3-C**H**$_2$);1.70 (m, 2 H, CH_2) 1.96 (t, 4 H, $J = 7.10$ Hz, C**H**$_2$-C=); 2.85 (t, $J = 8.30$ Hz, 2 H, CH_2-N-Ph); 2.65 (s, 3 H, C**H**$_3$-N); 2.55 (t, $J = 8.30$ Hz, 2 H, CH_2-N-CH_3); 6.59 (s, 1 H, C**H**=C); 6.15 (d, $J = 7.50$ Hz, 2 H, phenyl-**H**); 7.25 (d, $J = 7.50$ Hz, 2 H, phenyl-**H**). MS (NOBA, FAB > 0): 513 $[M + H]^+$. M = 512. Anal. calcd. for $C_{22}H_{28}O_2S_5N_2$: C,51.52%; H,5.50%; N, 5.46%; S, 31.26%; found: C,51.40%; H,5.68%; N, 5.58%; S, 31.43%.

2-[4-(4′,5′-Dipropyltetrathiafulvalen-4-yl)]phenyl-6-propionyl-1,2,6-thiadiazinane 1,1-dioxide 7

To a stirred solution of **5** (5 g, 10 mmol), in CH_2Cl_2 (25 mL) was added triethylamine (1.1 equiv., 11 mmol, 1.11 g, 0.80 mL), and catalytic quantities of 4-dimetylaminopyridine. Propionyl chloride (1.5 equiv., 15 mmol, 1.20 g, 1.28 mL) diluted in the same solvent (10 mL) was added slowly to the resulting solution. When the addition was completed, the reaction mixture was stirred under an atmosphere of dry N_2. TLC revealed the formation of a substituted compound less polar than its precursor. The reaction mixture was concentrated in vacuo. The residue was diluted with CH_2Cl_2 (50 mL), acidified with 0.1 N HCl solution and washed with water. The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure to give the crude **7**, which was purified on silica gel by column chromatography. Elution with CH_2Cl_2 afforded 3.50 g (64%) of pure **7** as beige powder. M.p.: 96 °C. TLC: $R_f = 0.60$ (CH_2Cl_2). ^{1}H NMR: 0.98 (t, 6 H, $J = 6.8$ Hz, C**H**$_3$); 1.00 (t, 3 H, C**H**$_3$-CH_2); 1.54 (m, 4 H, CH_3-C**H**$_2$);1.80 (m, 2 H, CH_2) 1.99 (t, 4 H, $J = 6.8$ Hz, C**H**$_2$-C=); 2.34 (m, 2 H, C**H**$_2$-CH_3); 3.45 (t, $J = 5.80$ Hz, 2 H, CH_2-N-Ph); 3.68 (t, $J = 5.85$ Hz, 2 H, CH_2-N-C = O); 6.60 (s, 1 H, C**H**=C); 6.20 (d, $J = 8.30$ Hz, 2 H, phenyl-**H**); 7.25 (d, $J = 8.30$ Hz, 2 H, phenyl-**H**). MS (NOBA, FAB > 0): 555 $[M + H]^+$. M = 554. Anal. calcd. for $C_{24}H_{30}O_3S_5N_2$: C,51.95%; H,5.45%; N, 5.04%; S, 28.89%; found: C,51.68%; H,5.61%; N, 5.21%; S, 29.11%.

Computational details

Calculations have been performed using Kohn-Sham's Density Functional Theory subjected to the gradient-corrected hybrid density functional B3LYP.[26–28] This functional is a combination of the Beck's three parameters non-local exchange potential with the non-local correlation functional of Lee et al.[29,30] The entire calculations in the

present work were performed using the Gaussian 09 W program package (Gaussian, Inc. 340 Quinnipiac St, Bldg 40, Wallingford, CT, USA)[31] on a personal computer, and the obtained theoretical data were visualized by means of Gauss View 05.[32] DFT was chosen because of the excellent compromise between the computational time and the description of the electronic correlation. The B3LYP method provides a nice balance between cost and accuracy, and is known to perform very well for the prediction of geometries of a number of synthetic and natural products.[33] Computational studies of MEP, FMO_S, quantum chemical descriptors and nonlinear optical properties (NLO) were carried out also by B3LYP/6–31G (d,p) level of DFT.

Conclusions

The synthesis, characterization and theoretical study of new cyclic sulfamides, linked to a TTF moiety (**1**–**7**) is described. The electrochemical behavior of all donors was determined by cyclic voltammetry and they were characterized by 1 H NMR and mass spectroscopy. Theoretical analyses were carried out with the help of density functional theory using B3LYP functional and 6–31 G (d,p) basis set. According to MEP surface and in the case of a chemical reaction or intermolecular interactions, the nitrosulfamide or amine function parts play important roles. The HOMO→LUMO electron transition signifies the electronic movements from the TTF core and benzene part to the nitro or sulfonamide part. According to the quantum chemical parameters, the title compounds are chemically soft systems which can be described as more reactive compounds. The HOMO-LUMO energy gap of **1** is the smallest, which reveals that it is highly reactive and kinetically less stable. This facilitates the desired formation of cyclic sulfamide linked to tetrathiafulvalene and also eases the intramolecular charge transfer, which makes the material to be NLO active. Drug likeness parameters of the synthetized compounds indicate a high potential for industrial therapeutic uses.

Disclosure statement

No potential conflict of interest was reported by the authors.

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