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FULL-LENGTH PAPER

A serendipitous one-step conversion of 3*H*-1,2-dithiole-3-thione to (*E*)-3-[1-(alkylthio)alkylidene]-3*H*-1,2-dithiole: an experimental and theoretical study

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Abstract In the course of our studies on 3*H*-1,2-dithiole-3-thione synthesis, a serendipitous reactivity with α-haloketones, in the presence of excess of potassium iodide, has been observed. Instead of the expected reaction of the nucleophile in a remote point of the molecule, we have obtained a product resulted from the electrophile character of the thiocarbonyl moiety on the 3-position of the 1,2-dithiole. In order to obtain an efficient protocol in terms of energy efficiency, this methodology was studied under conventional and microwave heating with similar or better results in the latter conditions. Simplicity and great efficiency in this one-step transformation are some of the advantages of this reaction. Moreover, the results can be explained according to the Pearson's hard and soft acid base theory.

Keywords 3*H*-1,2-Dithiole-3-thione · (*E*)-3-Alkylidene-3*H*-1,2-dithiole · DFT calculations · HSAB theory

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Introduction

The fascinating biological properties of the 3*H*-1,2-dithiole-3-thione system have attracted the attention of numerous researchers [1,2]. Among these bioactivities, 3*H*-1,2-dithiole-3-thiones have been described as thiol homeostasis modulators (e.g., ACS14, Fig. 1a) [3], as potential anti-cancer agents (e.g., NBS-1120, Fig. 1a) [4], and as schistosomicide or chemopreventive drugs (e.g., oltipraz, Fig. 1a) [5,6]. In some instances the mechanism of action has been associated to the release of H_2S by the dithiolethione heterocycle [7], and in other cases more complex processes have been proposed, i.e., the activation of Nrf2 signaling and induction of phase II enzymes [8].

Since the publication of the preparation of 5-(4-hydroxyphenyl)-3*H*-1,2-dithiole-3-thione (ADT-OH, Fig. 1b) from anethole [9], several applications of ADT-OH as building block have appeared in the literature, in particular its use in the preparation of esters with bioactive frameworks generating hybrid drugs [2,10].

Recently, we reported the use of synthetic chalcones as anti-tumor and chemopreventive agents by induction of phase II enzymes [11,12]. In this context, and as a continuation of our previous work, we are interested in improving this bioactivity developing hybrid chemopreventive agents which combine the chalcone and 3*H*-1,2-dithiole-3-thione moieties (Fig. 1c). To prepare such hybrid compounds we proposed synthetic procedures employing the ADT-OH anion (**I**) as common synthon building block.

Results and discussion

To prepare new hybrid chemopreventive agents, we decided to react ADT-OH with α-chloroacetone to obtain the corre-

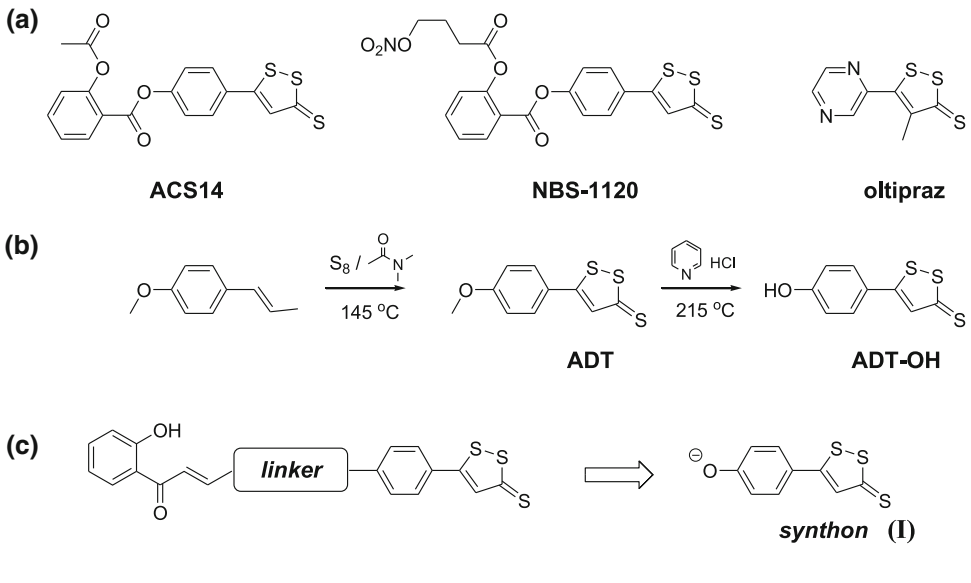
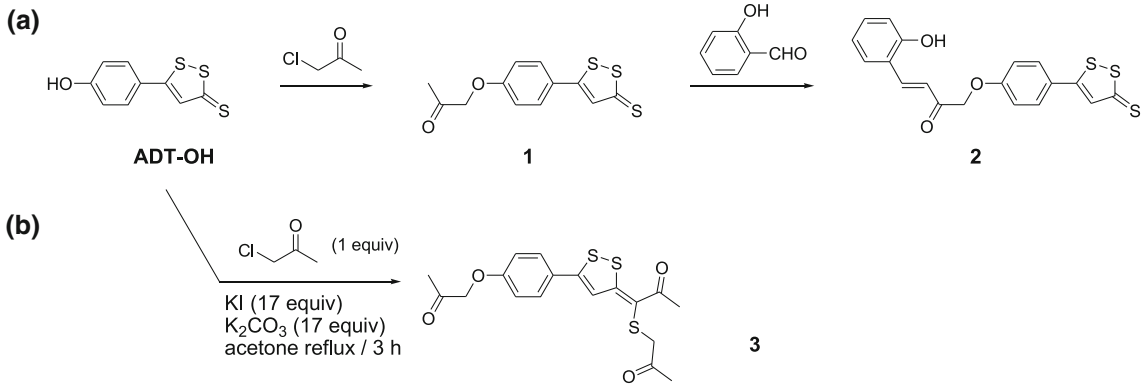


Fig. 1 **a** 3*H*-1,2-Dithiole-3-thiones with different biological activities. **b** Synthesis of ADT-OH. **c** Designed hybrid chemopreventive agents that involve the use of the **ADT-OH** anion (**I**) as synthon



Scheme 1 Synthesis of expected dithiolethiones (**1**, **2**) and unexpected product (**3**)

sponding methylketone **1** (Scheme 1a) that, via aldolic reaction, could generate chalcone-like derivatives, i.e., **2**.

When ADT-OH was subjected to alkylation conditions, using an excess of KI and K_2CO_3 [13,14], we obtained an unexpected final material (Scheme 1b) as the main product (yield 54 %). On the basis of ^{1}H NMR, ^{13}C NMR, and MS spectral data, the product formed was identified as **3**. These spectroscopic data, together with X-ray diffraction, (Fig. 2) unambiguously proved the structure of **3** to be (*E*)-3-[1-(alkylthio)alkylidene]-3*H*-1,2-dithiole.

The generation of this kind of product, using as starting material the corresponding 3*H*-1,2-dithiole-3-thione, has been previously described by Caillaud and Mollier and Brown et al. [15–17] to occur in two steps, via the corresponding 1,2-dithiolylium salts [17–19] in low yields (ca. 27 %).

Encouraged by this result, we tested the scope of this (*E*)-3-[1-(alkylthio)alkylidene]-3*H*-1,2-dithiole formation performing the following experimental studies: (i) modification of the experimental conditions to study the relevance of the reactants, i.e., KI, enolates, and 3*H*-1,2-dithiole-3-thiones; (ii) effects if heating microwave irradiation as heating source. Additionally, we carried out a theoretical study in an attempt to explain the unexpected reactivity in terms of Pearson's hard and soft acid base (HSAB) theory.

First, we analyzed the generation of **3**, from **ADT-OH** in the absence of KI, and the reactivity of 3*H*-1,2-dithiole-3-thiones with other enolates different from α-chloroacetone (Scheme 2) to explore the 3-thiocarbonyl electrophile. The results (Table 1) showed that the incorporation of acetyl moieties in **3** appeared from the α-chloroacetone and not from the other studied enolates (runs 2 and 3, Table 1). Moreover, when KI was not used (run 4, Table 1), the initial expected alkylation, generating product **1**, took place as the only process. When we tested the process with the enolate from phenacyl bromide and with 3*H*-1,2-dithiole-3-thione, **ADT**, in the best condition (Table 1, run 1) we obtained in all the cases the corresponding (*E*)-3-[1-(alkylthio)alkylidene]-3*H*-1,2-dithiole (Table 2). The (*E*)-stereochemistry was assessed using NMR data comparing 4-proton and 4-carbon

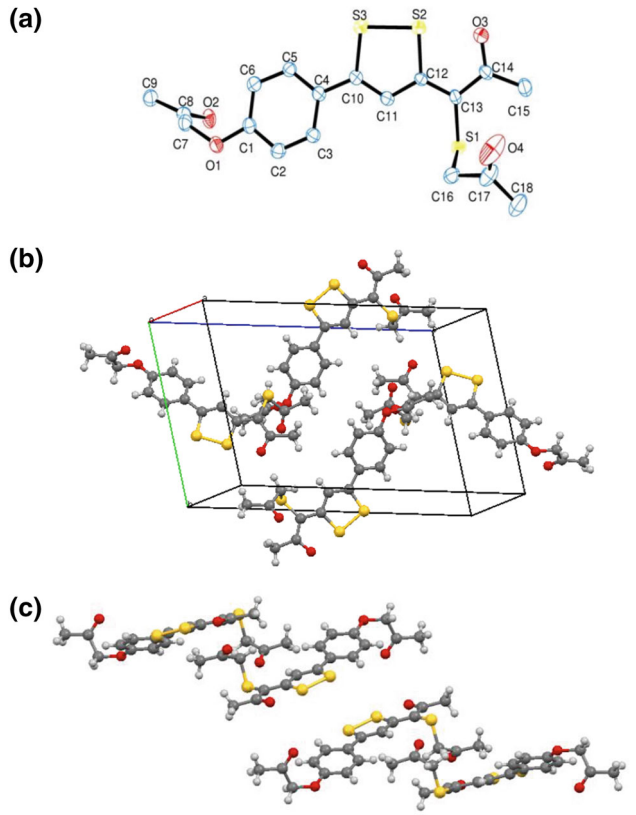


Fig. 2 **a** View of **3** showing the labeling of the non-H atoms and their anisotropic displacement ellipsoids at the 30 % probability level. The plot evidences the (*E*)-arrangement around the alkene moiety. Atoms numbering was arbitrarily assigned. **b** Unit cell content. **c** View of the crystal packing

chemical shifts (H_a and C_a in Table 2) of the different 1,2-dithioles with those values of product **3**.

Secondly, the use of microwave irradiation as heating source was tested (Table 2). Except for product **8**, the yields were significantly improved, more than one and a half higher yields in these conditions.

The low yield during the preparation of compound **6** was due to the fact that the product of *O*-alkylation, via the phenol-moiety (**9**, Fig. 3), was also obtained (14 % yield of *O*-alkylation product via conventional heating and 25 % of *O*-alkylation product via microwave irradiation).

When using **ADT** (as starting 3*H*-1,2-dithiole-3-thione) to obtain compounds **7** and **8**, other products were also detected. The isolation and spectroscopic characterization confirmed that they were the corresponding 1,2-dithiolylium salts (Fig. 3), **10** (7 % yield in conventional heating and 8 % with microwave irradiation) or **11** (11 and 16 % yields). In the case of compound **10**, X-ray diffraction (Fig. 4) unambiguously confirmed the proposed structure. These kind of salts were previously described as main products of reaction between 3*H*-1,2-dithiole-3-thiones and the corresponding α-haloketones [15,16].

To justify the reactivity of 3*H*-1,2-dithiole-3-thione heterocycle observed in these conditions, we relied on the Pearson HSAB theory. For this purpose we applied the following concepts: the molecule reactivity is related to system properties, such as hardness (η) and electronegativity (χ) defined as $\eta = 1/2\ (I - A)$ and $\chi = 1/2\ (I + A)$, where I and A are the ionization potential and electron affinity, respectively [20]. Within the validity of Koopmans' theorem, the frontier orbital energies are given by $I = -E_{\mathrm{HOMO}}$ and $A = -E_{\mathrm{LUMO}}$[21]. Hardness is the resistance of the chemical potential (μ) to the change of electron number (N) [22,23]. The fraction of electrons transferred in a reaction (ΔN)could be determined as follows: $\Delta N = (\chi_A - \chi_B)/2(\eta_A + \eta_B)$ [24], where A and B are the two reactants that participate in the reaction, the electronegativity difference is the driving force of the reaction, while the sum of hardness parameters inhibits electron transfer. The higher ΔN value the greater the chance that the reaction takes place.

We analyzed, for the generation of **3** from ADT-OH as model, different possible intermediates (Scheme 3) and processes calculating for the reactants, at DFT level, the corresponding η and χ values (Table 3), the energy difference GAP $= E_{\mathrm{HOMO}} - E_{\mathrm{LUMO}}$, and ΔN for each one of the processes.

According to the calculations the first step of the process could be understood in terms of the reaction between the ADT-OH phenolate (**I**) and iodoacetone (**II**), generated *in situ* by reaction of KI and chloroacetone (**III**) (first bold-arrow in Scheme 3). The E_{LUMO} of (**II**) is closer to E_{HOMO} of (**I**) than to E_{LUMO} of (**III**) (the highest GAP) additionally the ΔN in the reaction between the phenolate and iodoacetone is the

Scheme 2 Reactivity studies of dithioles from **ADT** and ADT-OH.

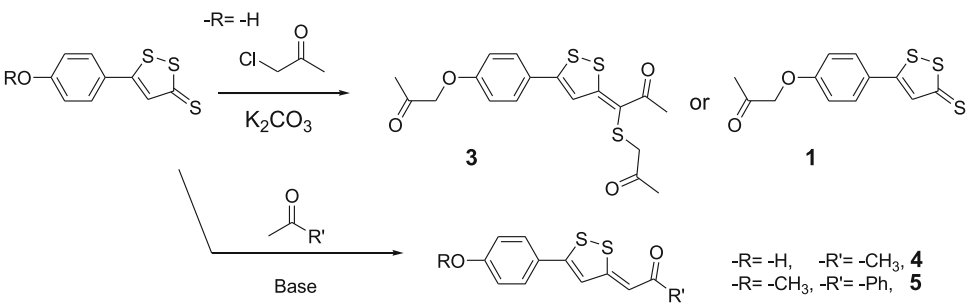
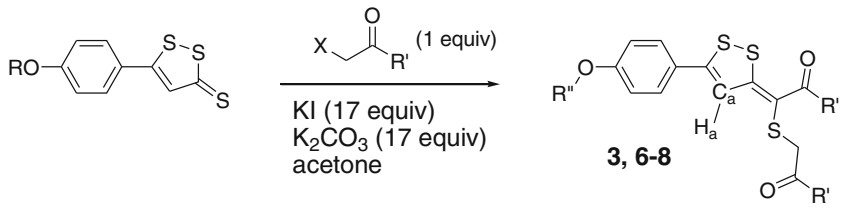


Table 1 Studies according to Scheme 2

Run	–R	KI	Base	Methylketone	time (h)	Yield (%)		
						3	**1**	**4/5**
1[a]	–H	17 equv.[b]	K_2CO_3 (17 equv.)	α-Chloroacetone (1 equv.)	10[c]	54	abs	–
2[a]	–H	17equv.	K_2CO_3 (17 equv.)	Acetone (solvent)	10[c]	-	-	abs
3	$–CH_3$	–	NaH (1 equv.)	Acetophenone (1 equv.)	48[c]	-	-	abs
4[d]	–H	–	K_2CO_3 (1 equv.)	α-Chloroacetone (0.91 equv.)	72[e]	abs	18	-

abs denotes absence of the product, – denotes unexpected product in these processes
[a] According to Scheme 1
[b] Respect to ADT-OH
[c] At reflux
[d] For complete conditions see Experimental section
[e] At room temperature

Table 2 Scope of the transformation 3*H*-1,2-dithiole-3-thione to (*E*)-3-[1-(alkylthio)alkylidene]-3*H*-1,2-dithiole



–R	–X	–R′	Product	–R″	Yield[a] (%) conventional heating	Yield[a] (%) microwave heating[b]	δ^{c}_{Ha} (ppm)	δ^{c}_{Ca} (ppm)
–H	–Cl	$–CH_3$	**3**	$–CH_2COCH_3$	54	82	8.09	123.8
–H	–Br	–Ph	**6**	–H	27	60	8.05	124.4
$–CH_3$	–Cl	$–CH_3$	**7**	$–CH_3$	13	76	8.09	123.3
$–CH_3$	–Br	–Ph	**8**	$–CH_3$	22	22	8.06	124.4

[a] Refers to purified yield, which is >95 % pure as determined by ^{1}H NMR spectroscopy
[b] For conditions see Experimental section
[c] In $CDCl_3$, at 303 K, and respect to TMS

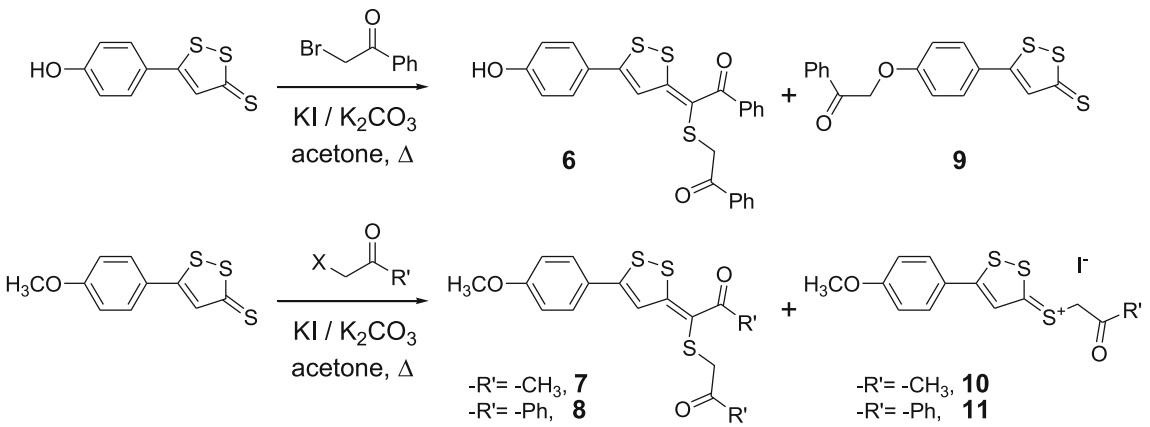


Fig. 3 Secondary products, **9-11**, in the preparation of the desired (*E*)-3-[1-(alkylthio)alkylidene]-3*H*-1,2-dithiole

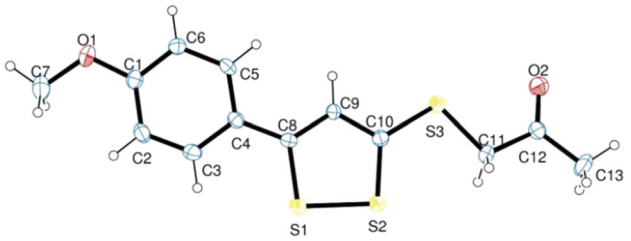


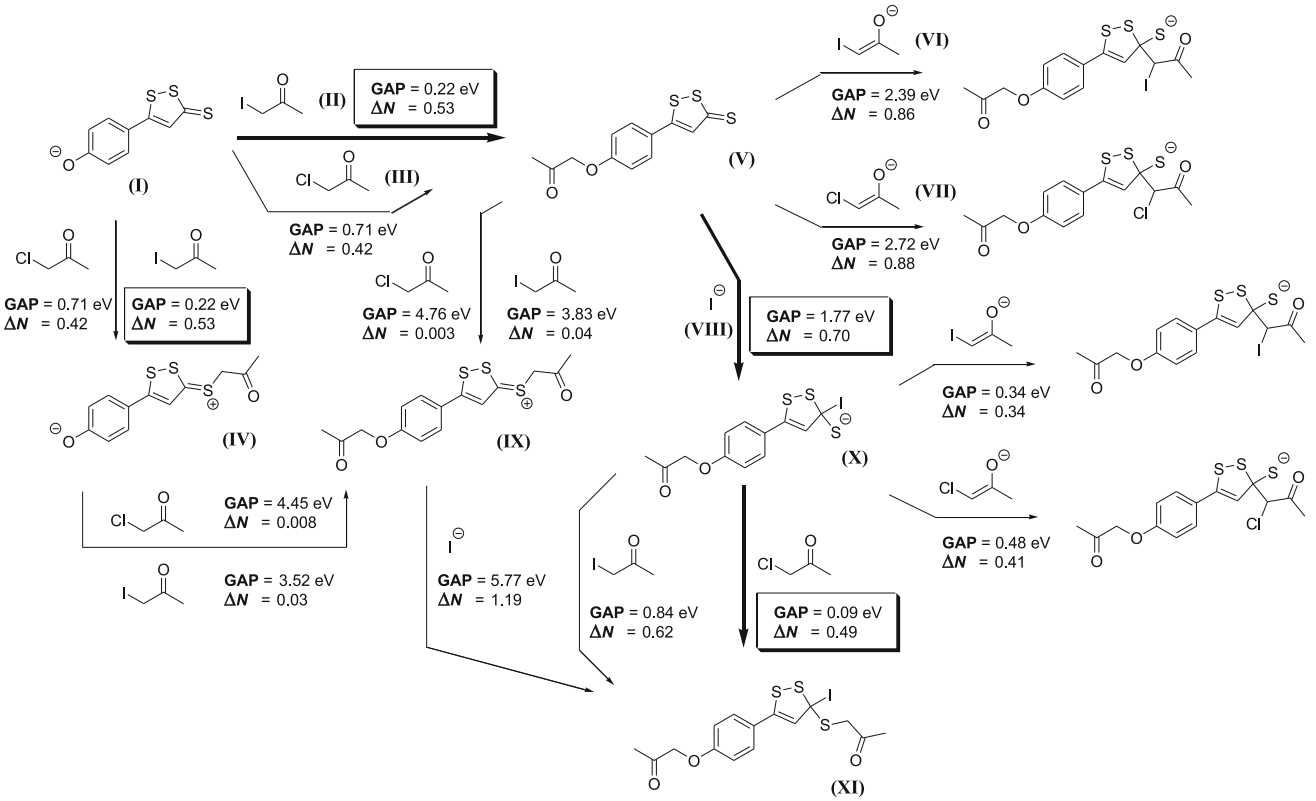
Fig. 4 View of the 3-acylmethylthio-5-(4-methoxyphenyl)-1,2-dithiolium cation in its iodine monohydrate salt **10**

highest of both possible ($\Delta N = 0.53$ vs. $\Delta N = 0.42$). The possible products could be **(IV)** or **(V)**. However, in the reaction of ADT-OH with phenacyl bromide the de-*O*-alkylated **6**, together with the by-product **9** (Fig. 3), was isolated showing the role of intermediate **(IV)** in the process (**(IV')** in the reaction with phenacyl bromide, Fig. 5). In this case, intermediate **(IV')** acted as electrophile and the reaction with iodide **(VIII)** conducted directly to intermediate **(XI')** without acylation. On the other hand, only in the reaction of **ADT** with the different haloketones we were able to isolate the salts **10** and **11** as by-products, in yields around 10 %. These results could indicate *O*-alkylation processes, intermediate **(V)**, are the preferred. Therefore, it was proposed that the generated intermediate **(V)** could react as electrophile, *via* the thiocarbonyl carbon, with different nucleophiles, i.e., enolates **(VI)** and **(VII)**, or iodide (**(VIII)** (Scheme 3), or as nucleophiles, *via* the thiocarbonyl sulfur, with the electrophiles **(II)** or **(III)**. According to the calculations, the dominant pathway corresponded to the iodide nucleophilic attack, with the lowest GAP (1.77 eV versus 2.39–4.76 eV for the other processes) and with adequate ΔN. These results allowed us to explain the participation of iodide during the

Table 3 HOMO/LUMO energies, chemical hardness, and electronegativity of reactants and intermediates according to Scheme 3 (in eV)

Intermediate	E^{a}_{HOMO}	E^{a}_{LUMO}	η	χ
(I)	−2.06	0.72	1.39	0.67
(II)	−7.24	−2.28	2.48	4.76
(III)	−7.50	−1.35	3.08	4.43
(IV)	−5.80	−3.19	1.31	4.50
(V)	−6.11	−2.68	1.72	4.40
(VI)	−0.29	2.92	1.61	−1.31
(VII)	0.04	3.71	1.84	−1.88
(VIII)	−0.91	4.58	2.75	−1.84
(IX)	−9.56	−6.68	1.44	8.12
(X)	−1.44	0.52	0.98	0.46

[a] Calculated at DFT level (B3LYP/6-31+G*)



Scheme 3 Plausible routes for the generation of compound **3** from ADT-OH. *Bold-arrows* show the selected route according to GAP and ΔN values

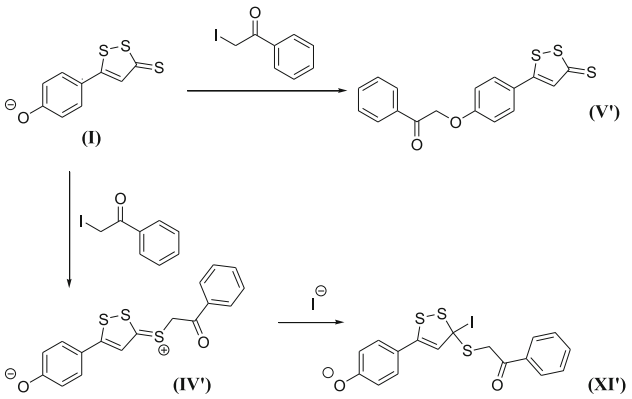
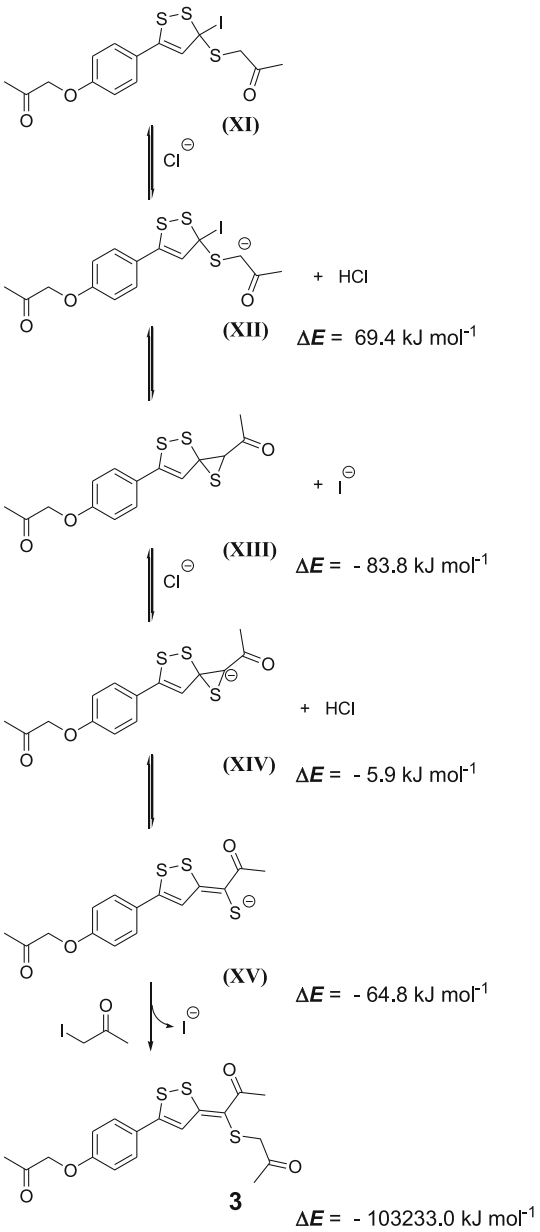


Fig. 5 Plausible routes for the generation of compounds **6** and **9** from ADT-OH and phenacyl bromide

generation of the product **3**. The next intermediate, **(X)**, could act as nucleophiles, *via* the thiolate, or as electrophile, *via* the 1,2-dithiole 3-carbon. The energetically favorable process (of lowest GAP and adequate ΔN) is one in which **(X)** participates as nucleophile reacting with **(III)**. The frontier HOMO of intermediate **(X)** was clearly located in the thiolate moiety being the 1,2-dithiole 3-carbon a poor contributor to the LUMO (Fig. 6) and consequently a poor electrophile.

Finally, the complete process could be rationalized (Scheme 4) from the intermediate **(XI)** reaction with the chloride anion to produce the carbanion **(XII)** that through the intra-molecular S_N2 process produces the episulfide **(XIII)** that after deprotonation and rearrangement of the carbanion **(XIV)** produces the thiolate **(XV)** which in turn leads to the product **3** after reaction with iodoacetone and regenerating the iodine anion that acts as catalyst. Except for the first deprotonation, all of these final steps were exothermic (Scheme 4).

After analyzing the proposed mechanism of this reaction (Schemes 4 and 5) we could infer the relevance of the use of microwave irradiation in the acceleration and yield of the processes. Therefore, the specific microwave effects are reflected in the following aspects: (i) the greater the polarity



Scheme 4 Plausible route for the generation of compound **3** from intermediate (XI)

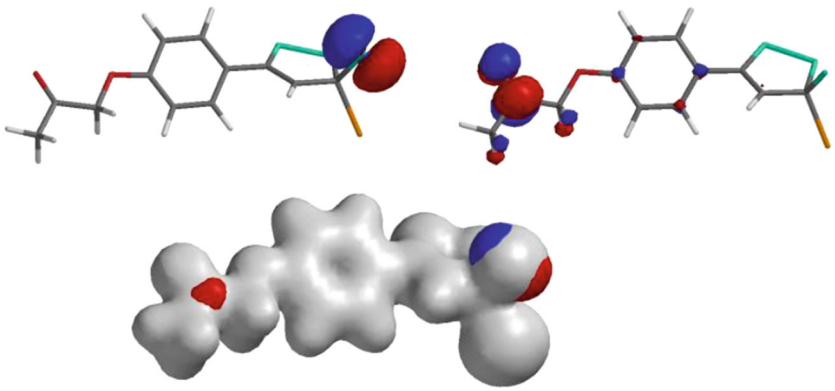


Fig. 6 Frontier molecular orbitals, HOMO (*left*), and LUMO (*right*) (surface isovalue 0.055), and merge both surfaces to electron density one (*center*) (surface isovalue 0.02) for intermediate **(X)**

of the system, for the S_N2 proposed mechanism, the more pronounced the material-wave interactions, due to the dipolar polarization phenomenon, when the rise in temperature is considered [25]; (ii) the proposed nucleophilic attack to the thiocarbonyl or the thiolium salt by iodide (Scheme 3 and Fig. 5) [26]; (iii) the decreasing in the activation energy $\Delta G^{\neq}$, by modification in the entropy term, mainly by the proposed unimolecular cyclization **(XII)** to **(XIII)** (Scheme 4) [27,28].

Conclusions

A serendipitous conversion in one-step of 3*H*-1,2-dithiole-3-thione to (*E*)-3-[1-(alkylthio)alkylidene]-3*H*-1,2-dithiole with α-haloketones and in the presence of excess of potassium iodide has been observed. Instead of the expected reaction of the nucleophile in a remote point of the molecule, we have obtained the product result of the electrophile character of the thiocarbonyl moiety on the 3-position of the 1,2-dithiole. This protocol was optimized, in terms of energy efficiency using microwave irradiation generates a simple and economic procedure. In general, the microwave irradiation allowed us to obtain the desired (*E*)-3-[1-(alkylthio)alkylidene]-3*H*-1,2-dithiole with more than one and a half higher yields (60–82 %) with near to two-hundred lower times of reaction (80–200 s) than the conventional heating procedure. The mechanism of the processes could be explained according to the Pearson's hard and soft acid base theory.

Materials and methods

Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected. Elemental analyses were performed using a Carlo Erba Model EA1108 elemental analyzer instrument. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX-400 spectrometer at 400.13 and 100.77 MHz, respectively, with $CDCl_3$ as solvent and calibrated using residual undeuterated solvent as an internal reference. Chemical shifts are reported in parts per million (ppm) relative to TMS as internal reference, and coupling constants (*J*) are given in Hertz. Multiplicity is abbreviated as: s is the singlet, d is the doublet, dd is the doublet of doublet, t is the triplet, m is the multiplet, and bs is the broad singlet. MS were performed at a Shimadzu QP-2010 spectrometer at 70 eV ionizing voltage. Mass spectra are presented as m/z (% rel int.). For some of the samples, LC/MSD-Serie 100 Hewlett–Packard spectrometer was employed for MALDI-TOF. Analytical TLC was carried out on pre-coated plates (Merck silica gel 60 F254) and visualized with UV light. All chemical reagents were obtained from Merck, Fluka or Acros and were used without further purification. THF was distilled from sodium, and acetone was distilled from potassium carbonate under nitrogen atmosphere. Microwave-assisted syntheses were carried out in 20 mL Teflon sealed vessels in commercial microwave systems, multimode cavity WX-4000 from EU Chemical Instrument Co., power delivery system ranging from 100 to 1,000 W.

The X-ray diffraction measurements were performed on an Oxford Xcalibur Gemini, Eos CCD diffractometer with graphite-monochromated CuKα (λ = 1.54178 Å) radiation for **3** and MoKα (λ = 0.71073 Å) radiation for **10**. X-ray diffraction intensities were collected (ω scans with ϑ and κ-offsets), integrated, and scaled with CrysAlisPro [29] suite of programs. The unit cell parameters for the two crystals were obtained by least-squares refinement based on the angular settings for all collected reflections with intensities larger than seven times the standard deviation of measurement errors using CrysAlisPro. The structures were solved by direct methods using SHELXS-97 [30] and refined by full-matrix least-squares procedure on F^2 with SHELXL-97 [31]. The drawing of the crystal structures were plotted with ORTEP [32].

All computations have been performed with the Spartan'06 package program [33]. The most stable conformers were determined by using the MMFF molecular mechanics method. These conformers were then used as input for density functional theory calculations of geometry optimizations at the B3LYP levels of theory with the 6−31+G* base set [34]. Frequency calculations were performed at the same level of theory as the geometry optimizations to characterize the stationary points as local minima (equilibrium structures).

5-[4-(2-Oxopropyloxy)phenyl]-3H-1,2-dithiole-3-thione (1)

In a 25-mL round-bottom flask equipped with a equalizing addition funnel containing α-chloroacetone (1.82 mL of 111 mM solution in THF, 201 μmol) ADT-OH (50.0 mg, 221 μmol), K_2CO_3(30.5 mg, 243 μmol), 18-crown-6 ether (64.0 mg, 243 μmol), *N*,*N*-dimethyl-*N*-octylbenzenaminium chloride (6.0 mg, 22.1 μmol), and anhydrous THF (5 mL) were placed. The mixture was stirred under a nitrogen atmosphere and then α-chloroacetone was added dropwise during 3 min. The resulting reaction mixture was stirred for 72 h at room temperature. The solvent was evaporated to dryness, and the resulting residue was suspended in CH_2Cl_2(20 mL) and washed with 50 mL of water. Three extractions of the water were performed with CH_2Cl_2 (3 × 20 mL), and the organic layers were dried over Na_2SO_4, evaporated *in vacuo* and purified by column chromatography (SiO_2, hexane:EtOAc, 7:3) to give compound **1** (11.2 mg, 18 %) as an orange solid; m.p. 144–147 °C; [found: C, 50.8; H, 3.5; S, 33.9. $C_{12}H_{10}O_2S_3$ requires C, 51.0; H, 3.6; S, 34.1]; δ_H:

7.65 (2H, d, J = 8.9 Hz, Ar), 7.41 (1H, s, –CC<u>H</u>C(S)SS–), 6.99 (2H, d, J = 8.9 Hz, Ar), 4.66 (2H, s, C<u>H</u>$_2$O), 2.33 (3H, s, C(O)C<u>H</u>$_3$); δ_C: 31.6, 72.4, 115.5, 125.3, 128.8, 134.6, 160.8, 172.4, 203.9, 215.3; m/z (EI) 282 ($M^{+\cdot}$, 100), 239 ($M^{+\cdot}$–CH_3CO, 15), 217 ($M^{+\cdot}$– HS_2, 54), 209 (10).

General procedure for the synthesis of (E)-3-[1-(alkylthio)alkylidene]-3H-1,2-dithioles 3, and 6-8via conventional heating (procedure I)

In a 25-mL round-bottom flask, under nitrogen atmosphere, a mixture of α-haloketone (1 equv.), ADT-OH or **ADT** (1 equv.) 50.0 mg, 221 μmol), K_2CO_3(17 equv.) 519.3 mg, 3.76 mmol), KI (17 equv.) 623.7 mg, 3.76 mmol) and anhydrous acetone (10 mL per 0.2 mmol of ketone) was stirred at reflux for the indicated time. The solvent was then evaporated to dryness, and the resulting residue was suspended in EtOAc(35 mL) and washed with 35 mL of water. Two extractions of the water were performed with EtOAc (2 × 35 mL), and the organic layers were dried over Na_2SO_4, evaporated *in vacuo*, and purified by column chromatography (SiO_2, hexane:AcOEt, 7:3) to give the desired product.

General procedure for the synthesis of (E)-3-[1-(alkylthio)alkylidene]-3H-1,2-dithioles 3, and 6-8via microwave heating (procedure II)

Similar amounts of reactants as for the conventional heating procedure were used. Upon microwave irradiation (100 W) of the mixture during the indicated time, the sample temperature raised to 330 K. This was followed by a similar isolation procedure as describe above to give the desired product.

(E)-5-[4-(2-Oxopropyloxy)phenyl]-3-[2-oxo-1-(2-oxopropylthio)propylidene]-3H-1,2-dithiole (3)

The general procedure I (reacting for 10 h) and II (reacting for 80 sec) using 50.0 mg (0.22 mmol) of ADT-OH gave 54 and 82 %, respectively, of **3** as orange solid; mp 145-149 °C; [found: C, 54.8; H, 4.4; S, 24.1. $C_{18}H_{18}O_4S_3$ requires C, 54.8; H, 4.6; S, 24.4]; δ_H: 8.09 (1H, s, –CC<u>H</u>CSS–), 7.70 (2H, d, J = 8.9 Hz, Ar), 6.97 (2H, d, J = 8.9 Hz, Ar), 4.64 (2H, s, C<u>H</u>$_2$O), 3.46 (2H, s, C<u>H</u>$_2$S), 2.55 (3H, s, C<u>H</u>$_3$C(O)CS), 2,32 (3H, s, C<u>H</u>$_3$C(O)CH$_2$O), 2.26 (3H, s, C<u>H</u>$_3$C(O)CH$_2$S); δ_C: 26.6, 29.1, 46.7, 72.9, 108.8, 115.2, 123.7, 127.0, 129.3, 159.9, 165.4, 177.6, 193.1, 202.9, 204.3; m/z (TOF-ES): 417 $(M+Na)^{+\cdot}$.

(E)-5-(4-Hydroxyphenyl)-3-[2-oxo-1-(2-oxo-2-phenylethylthio)-2-phenylethylidene]-3H-1,2-dithiole (6)

The general procedure I (reacting for 5 h) and II (reacting for 90 s) using 50.0 mg (0.22 mmol) of ADT-OH gave 27 and 60 %, respectively, of **6** as orange oil; [found: C, 65.1; H, 4.0; S, 20.7. $C_{25}H_{18}O_3S_3$ requires C, 64.9; H, 3.9; S, 20.8]; δ_H: 8.05 (1H, s, –CC<u>H</u>CSS–), 7.82 (2H, d, J = 9.6 Hz, Ar), 7.72 (2H, d, J = 8.3, Ar), 7.50 (2H, dd, J = 5.6 Hz, J = 2.9 Hz, Ar), 7.46 (2H, d, J = 8.8, Ar), 7.41 (2H, dd, J = 7.6 Hz, J = 1.8 Hz, Ar), 7.34 (2H, t, J = 7.7, Ar), 6.89 (2H, d, J = 8.7 Hz, Ar), 6.02 (1H, s, O<u>H</u>), 3.73 (2H, s, C<u>H</u>$_2$S); δ_C: 42.2, 107.1, 116.1, 124.4, 125.9, 127.5, 127.7, 128.5, 128.6, 128.8, 128.9, 129.1, 129.4, 130.1, 131.0, 131.6, 133.3, 135.4, 137.4, 158.5, 166.7, 180.7, 188.9, 194.5.

(E)-5-(4-Methoxyphenyl)-3-[2-oxo-1-(2-oxopropylthio)propylidene]-3H-1,2-dithiole (7)

The general procedure I (reacting for 10 h) and II (reacting for 200 s) using 50.0 mg (0.21 mmol) of **ADT** gave 13 and 76 %, respectively, of **7** as orange solid; mp 109-112 °C; [found: C, 54.1; H, 4.3; S, 27.5. $C_{16}H_{16}O_3S_3$ requires C, 54.5; H, 4.6; S, 27.3]; δ_H: 8.09 (1H, s, –CC<u>H</u>CSS–), 7.70 (2H, d, J = 8.9 Hz, Ar), 7.00 (2H, d, J = 8.9 Hz, Ar), 3.89 (3H, s, C<u>H</u>$_3$O), 3.46 (2H, s, C<u>H</u>$_2$S), 2.55 (3H, s, C<u>H</u>$_3$C(O)CS), 2.28 (3H, s, C<u>H</u>$_3$C(O)CH$_2$S); δ_C: 23.4, 29.2, 46.7, 55.5, 108.5, 114.6, 123.3, 126.0, 129.1, 161.9, 166.1, 177.7, 193.0, 203.0; m/z (EI) 352 ($M^{+\cdot}$, 22), 295 ($M^{+\cdot}$– CH_3COCH_2, 100), 264 ($M^{+\cdot}$– CH_3COCH_2– CH_3O, 30), 176 (13), 161 (6), 151 (9), 132 (12).

(E)-5-(4-Methoxyphenyl)- 3-[2-oxo-1-(2-oxo-2-phenylethylthio)-2-phenylethylidene]-3H-1,2-dithiole (8)

The general procedure I (reacting for 5 h) and II (reacting for 90 s) using 50.0 mg (0.21 mmol) of **ADT** gave 22 % in both cases of **8** as yellow oil; [found: C, 65.2; H, 4.0; S, 20.4. $C_{26}H_{20}O_3S_3$ requires C, 65.5; H, 4.2; S, 20.2]; δ_H: 8.06 (1H, s, –CC<u>H</u>CSS–), 7.83 (2H, d, J = 9.6 Hz, Ar), 7.72 (2H, d, J = 8.4, Ar), 7.53 (2H, d, J = 8.9 Hz, Ar), 7.49 (1H, t, J = 1.7, Ar), 7.47 (1H, t, J = 1.3, Ar), 7.41 (2H, dd, J = 6.3 Hz, J = 4.5 Hz, Ar), 7.33 (2H, t, J = 7.7, Ar), 6.95 (2H, d, J = 8.9 Hz, Ar), 3.91 (3H, s, C<u>H</u>$_3$), 3.73 (2H, s, C<u>H</u>$_2$S); δ_C: 42.3, 55.5, 107.3, 114.5, 124.4, 126.0, 127.5, 127.7, 128.5, 128.6, 128.8 (2C), 128.9, 129.1, 129.6, 130.1, 133.2, 134.3, 135.1, 135.5, 137.4, 161.9, 166.5, 180.6, 188.8, 194.

5-[4-(2-Oxo-2-phenylethyloxy)phenyl]-3H-1,2-dithiole-3-thione (9)

Isolated from the chromatographic column in the syntheses of compound **6**, 14 % in procedure I and 25 % in procedure II; as red solid; m.p. 156–159 °C; [found: C, 58.9; H, 3.1; S, 27.5. $C_{17}H_{12}O_2S_3$ requires C, 59.3; H, 3.5; S, 27.9]; δ_H: 8.02 (2H, d, J = 7.1 Hz, Ar), 7.71-7.66 (1H, m, Ar), 7.63(2H, d, J = 9.0 Hz, Ar), 7.56 (2H, t, J = 7.7 Hz, Ar) 7.40 (1H, s, –CC<u>H</u>C(S)SS–), 7.03 (2H, d, J = 9.0 Hz, Ar), 5.42 (2H, s,

C$\underline{H}_2$O); δ_C: 70.5, 115.7, 125.0, 128.1, 128.7, 129.0, 134.1, 134.3, 134.9, 161.2, 172.7, 193.3, 215.3.

3-Acylmethylthio-5-(4-methoxyphenyl)-1,2-dithiolium iodide (10)

Isolated from the chromatographic column in the syntheses of compound **7**, 7 % in procedure I and 8 % in procedure II; red solid; m.p. 132–135 °C; [found: C, 35.6; H, 3.1; S, 22.0. $C_{13}H_{15}IO_3S_3$ requires C, 35.3; H, 3.4; S, 21.8]; δ_H: 8.37 (1H, bs, –CC$\underline{H}$C(S)SS–), 7.68 (1H, d, J = 8.9 Hz, Ar), 6.99 (1H, d, J = 9.0 Hz, Ar), 4.76 (2H, bs, C$\underline{H}_2$S), 4.02 (3H, bs, C$\underline{H}_3$O), 2.60 (3H, bs, C$\underline{H}_3$C(O)); δ_C: 24.0, 35.0, 55.5, 110.0–140.0 (5 C), 162.0, 178.0, 193.7; m/z (EI) 297 ($M^{+\cdot}$, 17), 254 ($M^{+\cdot}$– CH_3CO, 12).

3-Benzoylmethylthio-5-(4-methoxyphenyl)-1,2-dithiolium iodide (11)

Isolated from the chromatographic column in the syntheses of compound **8**, 11 % in procedure I and 16 % in procedure II; red solid; m.p. 177–179 °C; [found: C, 44.1; H, 2.9; S, 19.6. $C_{18}H_{15}IO_2S_3$ requires C, 44.4; H, 3.1; S, 19.8]; δ_H: 8.01 (1H, bs, –CC$\underline{H}$C(S)SS–), 7.80–7.40 (5H, m, Ar), 7.34 (1H, d, J = 8.9 Hz, Ar), 7.01 (1H, d, J = 8.9 Hz, Ar), 5.00 (2H, bs, C$\underline{H}_2$S), 3.92 (3H, bs, C$\underline{H}_3$O); δ_C: 32.0, 55.6, 110.0–140.0 (9 C), 162.1, 167.0, 189.2; m/z (EI) 359 ($M^{+\cdot}$, 17), 254 ($M^{+\cdot}$– PhCO, 12).

Supporting information

For compounds **3** and **10**: tables of crystal data and structure refinement results (Table S1), bond lengths and angles (Tables S2a, b), fractional coordinates and equivalent isotropic displacement parameters of the non-H atoms (Tables S3a, b), atomic anisotropic displacement parameters (Tables S4a, b), and hydrogen atoms positions (Tables S5a, b) are available. Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC 949752, for **3**, and CCDC 949753, for **10**. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.Uk). Copies of the ^{1}H NMR and ^{13}C NMR spectra for compounds **1**, **3**, and **6-8** are available.

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