Unexpected transalkylation on 3-alkyl-2-alkylthio-1,3,4-thiadiazolium-5-thiolates: A computational and experimental mechanistic study†

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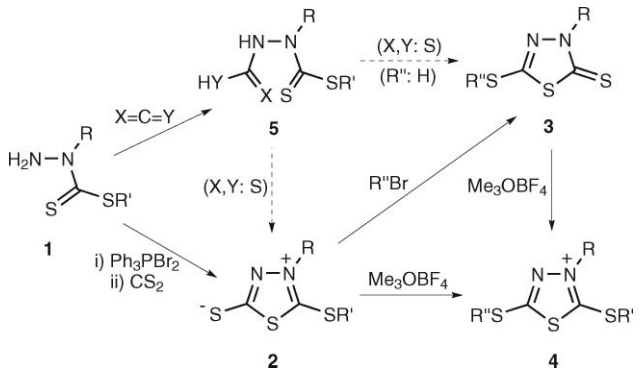
5-Alkylthio-3-methyl-2-thioxo-1,3,4-thiadiazolines have been obtained on heating alkyl 1-methyl-1-hydrazinecarbodithioates with CS_2. A DFT-based computational mechanistic study suggests an initial pseudopericyclic [1,4]H shift as a key step, as well as the intermediacy of the otherwise expected isomers 2-alkylthio-3-methyl-1,3,4-thiadiazolium-5-thiolates, from which the final products are formed by stepwise *S*,*S*-transalkylation.

Introduction

The synthesis of compounds incorporating isolated or fused 1,3,4-thiadiazole rings has attracted widespread attention due to their diverse pharmacological properties such as antiviral, antimicrobial, antiinflammatory, analgesic and antitumoral activities.[1] Although there are a number of such compounds commercially available for medical uses, the synthesis of new therapeutical derivatives is of vital importance due to increasing drug resistance and also looking for less toxic effects.

Based on our endeavors on the synthesis of 2-functionalized[2] and 2,5-difunctionalized[3] derivatives of the 1,3,4-thiadiazole ring system we wanted to explore an easier access to 2,5-bisalkylthio-3-methyl-1,3,4-thiadiazolium salts **4** as useful precursors for other amino- or mercapto-substituted compounds. We reported[3] a synthetic strategy (Scheme 1) to obtain mesoionic thiadiazolium-thiolate **2a** (R = R′ = Me) from the readily available methyl 1-methyl-1-hydrazinecarbodithioate **1a** *via* the corresponding iminophosphorane, whereas S_{C5}-methylation of **2** with trimethyloxonium tetrafluoroborate yielded the expected bismethylthio-thiadiazolium salt **4a** (R = R′ = Me). Conversely, on using an alkyl halide as alkylating agent the nucleophilic soft counteranion promoted the S_{C2}-dealkylation furnishing alkylthio-thiadiazolin-thiones **3**. Such *S*-dealkylating behaviour had been also observed in the reaction of 5-aryl substituted 3-methyl-2-methylthio-1,3,4-thiadiazolium perchlorates with some O-nucleophiles[2b] and theoretically supported on the basis of quantitative Pearson's HSAB principle calculations.[4]



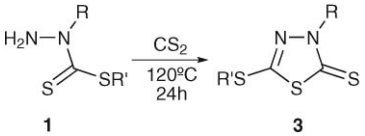
Scheme 1 Synthetic strategy to obtain compounds **2**, **3** and **4**.

On the other hand, *S*-demethylation is a biochemically important reaction within methyl transfer metabolism,[5] which has been very recently studied theoretically.[6] A well-established synthetic *S*-demethylation reactivity was first found with inorganic platinum(II) in 1883[7] and later with related halide compounds of palladium(II) and gold(III), involving a transfer of the methyl group from the metal to an external acceptor.[8] In a wider context, metal-induced S–C bond breaking constitutes an essential step in the important technical process of hydrodesulfurization.[9]

In this paper we focus on the direct reaction of **1** with CS_2, thus avoiding the Kirsanov/aza-Wittig tandem reaction, with the hope that the open-chain product **5a** (X = Y = S) would be obtained analogously than in the reported reactions involving isocyanates or isothiocyanates (X = O, S; Y = NR″) and carbodiimides (X = Y = NR″) (Scheme 1).[2c] The subsequent cyclization would lead to either 5-mercapto-thiadiazolinthione **3** (R″ = H) or thiadiazolium-thiolate **2**.

Results and discussion

Alkyl 1-alkyl-1-hydrazinecarbodithioate **1**, were easily prepared according to the reported procedure,[10] and were heated with CS_2 in a sealed tube to afford, in excellent yields (96–99%), the corresponding 3-alkyl-5-alkylthio-2-thioxo-1,3,4-thiadiazolines **3** (Scheme 2) which were fully characterized spectroscopically (see the ESI†). At lower temperatures or with shorter reaction periods either the conversion decreased or the unaltered starting material



	R	R′
a	CH_3	CH_3
b	CH_3	4-ClC_6H_4-CH_2
c	$C_6H_5CH_2$	CH_3
d	$C_6H_5CH_2$	4-ClC_6H_4-CH_2

Scheme 2 Synthesis of compounds **3**.

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† Electronic supplementary information (ESI) available: Structures, energies and lowest frequencies of all compounds cited in the text. $NICS_{zz}$ variation along the reaction coordinate in steps involving $\mathbf{TS_{1a-10}}$ and $\mathbf{TS_{13syn-2a}}$. See DOI: 10.1039/b923243e

was only recovered. The isomeric nature of these products in comparison with the expected thiadiazolium-thiolates **2** clearly indicated that a transalkylation process must take place at any of the individual steps in the overall transformation. This fact prompted us to look for a detailed mechanistic scheme.

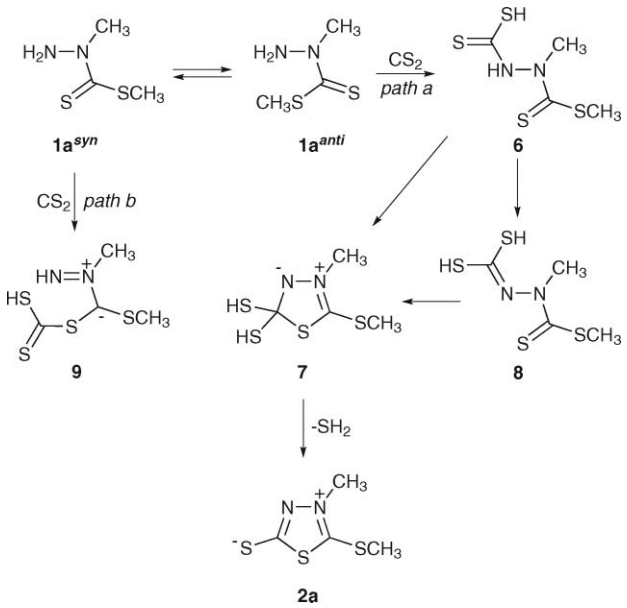
First, the relative stabilities of **2a** and **3a** were calculated using the Gaussian03 package,[11] and the Gibbs free energy change for a hypothetical **2a**→**3a** transformation resulted to be −16.35 or −16.37 Kcal mol^{-1} at the B3LYP/6-311+G** or MP2/6-311+G** levels of theory, respectively. This indicates that **3** could be formed as a thermodynamic control product if **2** was involved as an intermediate in the process. In order to check this possibility, samples of **2a** were heated in either CS_2 or toluene and quantitative conversion in **3a** was observed in both cases.

A thorough inspection of all possible paths connecting **1a** and **3a** in the potential energy surface at the B3LYP/6-311+G** level revealed that actually all reasonable low-energy paths required the intermediacy of **2a**, thus excluding the possibility of a transalkylation taking place on any of the open-chain precursors and pointing to a final transalkylation step.

The obtained energy paths are depicted in Fig. 1, which shows that formation of **2a** is an endergonic process ($\Delta G^{\circ}_{2a} = 10.55$ Kcal mol^{-1}), but formation of the final product **3a** is exergonic ($\Delta G^{\circ}_{3a} =$ −2.14 Kcal mol^{-1}). The expected direct nucleophilic attack of **1a** to CS_2 was observed to proceed from the *anti* rotamer of **1a**, affording intermediate **6** (Fig. 1, path A) (Scheme 3). Compound **6** can then undergo ring-closure to **7**, which is also formed following a lower energy path through tautomer **8**, and readily undergoes dehydrosulfurization to mesoionic compound **2a**. On the contrary, the most stable **1a**$_{syn}$ conformer behaves exclusively as *S*-nucleophile towards carbon disulfide (no path was found for the N-attack to CS_2). This process requires concomitant *N*,*S*-prototropy to yield betaine **9** (path B). Nevertheless no path was found connecting this intermediate to final products **2a** or **3a**. Thermochemical data corresponding to every single step are collected in Table 1.

Both pathways (A and B) for the direct nucleophilic attack of **1a** to CS_2 involve rather high energetic barriers (53.78 and 57.44 Kcal mol^{-1}, respectively).

Instead of that, previous formation of the "pseudo-valence" isomer **10** (Scheme 4)—very much resembling the structure of intermediate **9**—seems to be required, as it proceeds through a much lower energetic barrier (Table 1). Betaine **10** reacts with CS_2 *via* the highly nucleophilic terminal N atom affording **11**.



Scheme 3 Paths A and B.

From this easily accessible key intermediate **11** several low energy paths are possible. First, cyclization of **11** (Scheme 4, path C_1) by the action of its highly nucleophilic S atom affords **12**, from which **2a** is easily formed by dehydrosulfurization. An analogous route (path C_2) can be followed after conversion **11**→**13** by *N*,*S*-prototropy followed by cyclization (**14**) and dehydrosulfurization. This later precursor **14** can also be obtained by *N*,*S*-prototropy of thiadiazolidine **12**, preferably in a intermolecular fashion. Finally, dehydrosulfurization of **13** yields isothiocyanate **15**$_{anti}$ (path D) that easily undergoes pseudopericyclic cyclization to its valence tautomer **2a**. This last step is controlled by the rotation around the N–N bond (**15**$_{anti}$→**15**$_{syn}$) through a rather small energetic barrier, whereas the cyclization of **15**$_{syn}$ resulted to be an almost barrierless process ($\Delta G^{\circ}_{TS} = 0.02$ Kcal mol^{-1} in the gas-phase). Indeed intermediate **15**$_{syn}$ does not exist as such local energy minimum in other lower level potential energy surfaces (*i.e.* B3LYP/6-31+G*). Although path C_2 constitutes the lowest energy access to **2a**, it is important to underline that all steps following intermediate **11** have lower activation energies than formation of the precursor **10** and therefore all three are actually competing pathways.

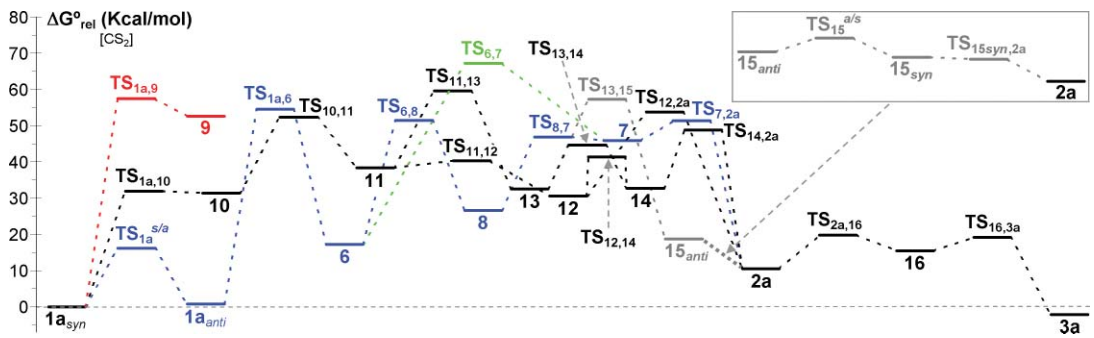
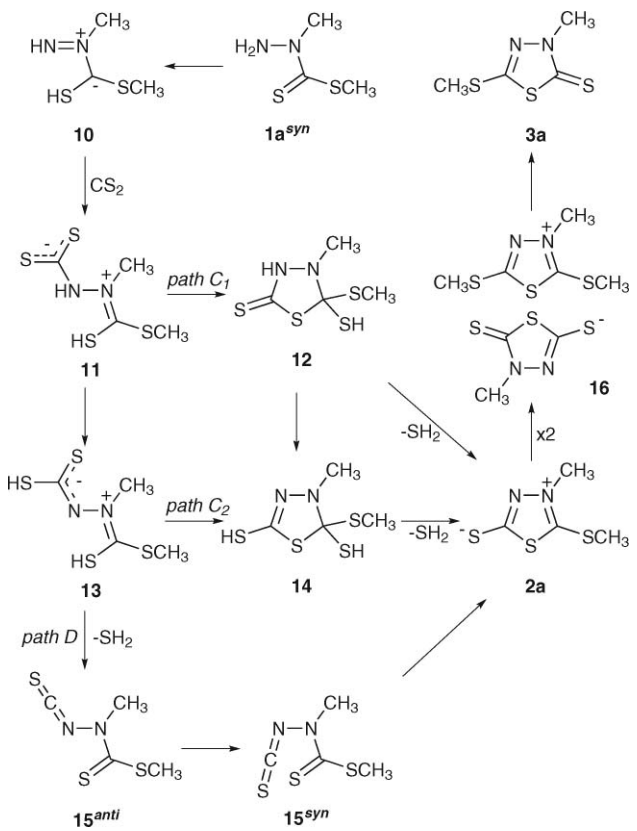


Fig. 1 Calculated (COSMO[CS_2]/B3LYP/6-311+G**) energy paths and activation free energies (Kcal mol^{-1}) for the conversion **1a**→**3a**: A) blue/green, B) red, C) black, D) grey.

Table 1 Thermochemical data[a] for reactions depicted in Schemes 3 and 4

Reaction	ΔG°	ΔG^{TS}
1a$_{syn}$**→1a**$_{anti}$	0.75	16.13
1a$_{anti}$**→6**	16.49	53.78
6→7	28.62	49.94
6→8	9.35	34.18
8→7	19.27	20.28
7→2a	–35.31	5.49
1a$_{syn}$**→9**	52.56	57.44
1a$_{syn}$**→10**	31.40	31.91[b]
		38.71[c]
10→11	6.94	20.91
11→12	–7.77	1.95
12→2a	–20.02	23.18
11→13	–5.81	21.22
12→14	2.11	36.71[b]
		10.80[c]
13→14	0.15	12.10
14→2a	–22.14	16.15
13→15$_{anti}$	–13.80	24.70
15$_{anti}$**→15**$_{syn}$	–1.52	3.80
15$_{syn}$**→2a**	–6.67	–0.54[d]
2a→$\frac{1}{2}$**16**	4.95	9.32
$\frac{1}{2}$**16→3a**	–17.64	3.78
2a→3a	–12.70	63.81[b]
		24.14[c]

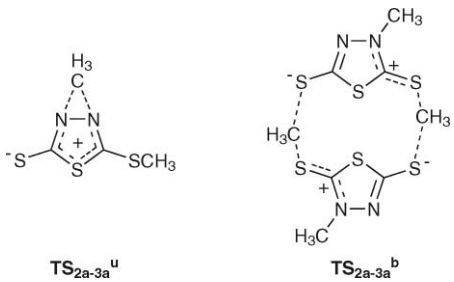
[a] Kcal·mol^{-1}; [b] unimolecular; [c] bimolecular; [d] 0.02 Kcal·mol^{-1} in the gas-phase



Scheme 4 Paths C and D.

Once the thiadiazolium-thiolate **2a** has been formed, the isomerization to **3a** is predicted to take place through a stepwise bimolecular mechanism involving the initial *S*-dealkylation of one molecule of **2a** by means of a nucleophilic attack of the thiolate S-atom of another identical molecule affording the ion-pair **16** (Scheme 4). The thiolate S-atom in **16** again *S*-dealkylates the methylthio group at C-2 of the cation, furnishing two identical molecules of **3a**. This later step is analogous to the above mentioned *S*-demethylation of **4** by the action of soft counter-anions.[3]

A direct one-step transformation **2a→3a** through a bimolecular mechanism (two simultaneous *S*,*S*-*trans*-methylations) would probably compete as it requires only a slightly higher activation energy (see the ESI†) due to the unfavourable entropic contribution. This species is indeed a second-order saddle point with two imaginary frequencies, one related with the required C_1-symmetric vibration (–358.0 cm^{-1}) that corresponds to the aforementioned **2a→3a** transformation (Scheme 5), and having also a second asymmetric vibration (–511.6 cm^{-1}) associated to a degenerated double transmethylation **16→16**. An alternative unimolecular mechanism for the **2a→3a** isomerization could also be envisaged involving a pericyclic (six π-electrons) migration of a methyl group from N-3 to N-4 over all the dienic heterocyclic ring, but according to our calculations this constitutes a nearly energetically forbidden process (Table 1).



Scheme 5 Representations of one-step TS_{2a-3a} structures.

In order to confirm the bimolecular nature of the final transalkylation process, a crossed experiment was performed by heating equimolecular amounts of two different alkyl dithiocarbazates **1a** and **1d** in carbon disulfide, according to the reaction depicted in Scheme 2. After completion and evaporation of the excess of solvent, the composition of the reaction mixture was analyzed by GC-MS (see the ESI†) resulting in roughly equal amounts of all the four possible reaction products **3a** (30.5%), **3b** (22.2%), **3c** (24.4%) and **3d** (22.9%).

It is worth mentioning that the initial prototropy **1a→10** corresponds to the rate-determining step of the overall process when following the proposed path, thus explaining that no intermediate has ever been isolated.

Finally, conversion **1a→10** constitutes, to the best of our knowledge, the first example of a 6-electrons pseudopericyclic [1,4]H *N*-to-*S* rearrangement. At first sight, the pseudopericyclic nature of $\mathbf{TS_{1a-10}}$ is evidenced not only by the very low energetic barrier (ΔG^{TS} = 0.50 Kcal mol^{-1} for the reverse transformation **10→1a**) but also by the almost planar geometry of the transition state ($\mathbf{TS_{1a-10}}$) featuring a characteristic orbital topology with two orbital disconnections (Fig. 2, left).[12] The alternative bimolecular *N*,*S*-prototropy has been also checked and seems to constitute a competitive pathway according to its only slightly higher activation energy (Table 1).

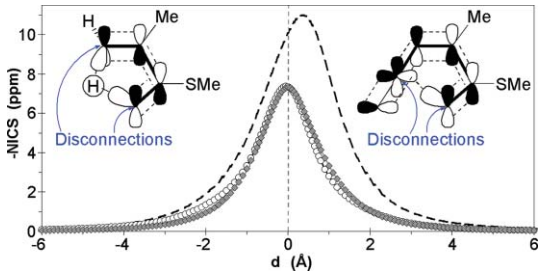


Fig. 2 Calculated NICS values along the perpendicular *z* axis for $\mathbf{TS_{1a-10}}$ (—○—), $\mathbf{TS_{15syn-2a}}$ (—◈—) and $\mathbf{TS_{17-17}}$ (— —). Schematic representation of the pseudopericyclic orbital topology in $\mathbf{TS_{1a-10}}$ (left) and $\mathbf{TS_{15syn-2a}}$ (right).

A deeper insight into the pseudopericyclic character of both $\mathbf{TS_{1a-10}}$ and $\mathbf{TS_{15syn-2a}}$ comes from the observation of the almost symmetric NICS distribution along the perpendicular *z* axis (Fig. 2), which is consistent with the expected σ-aromaticity of such flat TS structures.[13] Their highest negative values (*c.a.* −7.3 ppm, at $z = 0$ Å) are significantly smaller than that calculated for the TS corresponding to a genuine symmetry-allowed pericyclic [1,4]H shift in *Z*-2-butenyl anion (**17**). In this case, the NICS variation for $\mathbf{TS_{17-17}}$ along the *z* axis shows an asymmetric pattern attributable to the π^1-aromaticity behaviour that results, in a formal sense, from only one ring current circulating on the side where the H atom movement allows a close proximity between the terminal *p* atomic orbitals.

Also the NICS(0) and NICS(1)[14] variation along the reaction coordinates **1a→10** and $\mathbf{15}_{syn}\rightarrow\mathbf{2a}$ (Fig. 3) agrees with the classification of these steps as pseudopericyclic,[15] specially for the later where only an smooth maximum is observed for -NICS(0), but far away from the coordinate corresponding to the TS ($d_{C\cdots S}$ = 2.488 Å). On the contrary, the **1a→10** prototropy shows small but not negligible maxima for both NICS(0) and NICS(1) close to the transition state coordinate ($d_{N\cdots H}$ = 1.614 Å), which indicate an aromaticity enhancement and thus pointing to some pericyclic character. Similar results were obtained on using the out-of-plane component of the magnetic shielding tensor ($NICS_{zz}$) (see the ESI) which is reported as a better aromaticity index.[16]

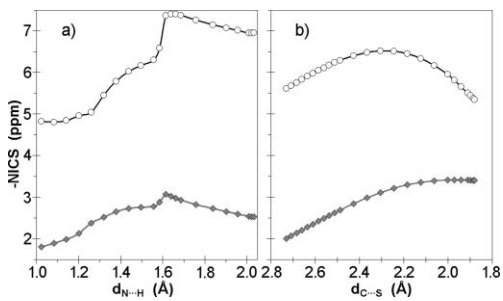


Fig. 3 Calculated NICS values variation along the reaction coordinate for steps **1a→10** (a) and $\mathbf{15}_{syn}\rightarrow\mathbf{2a}$ (b): NICS(0) (—○—); NICS(1) (—◈—).

Conclusions

We report an efficient synthesis of 5-alkylthio-1,3,4-thiadiazolin-2-thiones that, according to DFT calculations, involves an intermolecular double *S*,*S*-transalkylation in the intermediately formed thiadiazolium-thiolate isomer. The key step has been shown to be the unprecedent initial [1,4]H *N*-to-*S* rearrangement of the hydrazinecarbodithioate reagent, whose pseudopericyclic nature was unambiguously established.

Experimental section

Melting points were determined on a hot-plate melting point apparatus and are uncorrected. IR spectra were determined as Nujol emulsions. ^{1}H- and ^{13}C-NMR spectra were recorded at 300 and 75 MHz, respectively. Chemical shifts refer to signals of tetramethylsilane. The following abbreviations for stating the multiplicity of the signals have been used: s (singlet), d (doublet), m (multiplet), q (quaternary carbon). The EI mass spectra were recorded on a Fisons AUTOSPEC 500 VG spectrometer. The coupled GC-MS experiment was performed with 6890 N and 5973 N subunits, fitted with an Agilent 19091*S*-433 HP-5MS column, and using helium (1mL min^{-1}) as carrier and a temperature profile starting at 60 °C (1 min) and warming (10 °C min^{-1}) up to 310 °C (10 min). Microanalyses were performed on a Carlo Erba 1108 instrument.

Computational details

Calculated geometries were fully optimized in the gas-phase with tight convergence criteria at the DFT level with the Gaussian 03 package,[11] using the B3LYP[17] functional and the 6-311+G** basis set for all atoms, unless otherwise stated. Ultrafine grids (99 radial shells and 590 angular points per shell) were employed for numerical integrations. From these gas-phase optimized geometries all reported data were obtained by means of single-point (SP) calculations. Frequency calculations confirmed the nature of ground states and transition states by the existence of none or only one imaginary vibration mode, respectively. Reported electronic energies are uncorrected for the ZPVE (zero-point vibrational energy). Solvent effects were considered by using the Cossi and Barone's CPCM (conductor-like polarizable continuum model) modification[18] of the Tomasi's PCM formalism.[19] With this aim carbon tetrachloride was used as the most similar solvent to CS_2, among those available in Gaussian03, but correcting with available data for CS_2: the dielectric constant was set to 2.2 and the solvent radius to 3.40 Å. The only structure that could not be localised at the working level of theory was that of $\mathbf{TS_{10\text{-}11}}$, for which the fully optimized structure obtained by using the 6-31+G* basis set was employed, although the energy (excepting the thermal correction to the Gibbs free energy) was computed as SP calculation at the final B3LYP/6-311+G** level of theory. Values from the magnetic shielding tensor were obtained using the non-relativistic gauge-including atomic orbital (GIAO) approach.[20] Additionally, the structures of compounds **2a** and **3a** (as well as carbon disulfide) were also further refined at the MP2[21] level of theory with the 6-311+G** basis set.

Alkyl 2-Alkyldithiocarbazes 1 prepared

Compounds **1** were prepared according to the reported[10] procedure. In common solvents these compounds exhibit a hindered rotation around the N-CS bond giving rise to the appearance of the signals belonging to both rotamers in their NMR spectra. Herein only those signals corresponding to the major rotamer are collected.

1a. Colorless prisms, m.p. 94–95 °C (lit.,[10] 92 °C).

1b. White prisms, m.p. 61–62 °C. IR (nujol) ν_{max}: 3297, 1225, 1090, 842 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ^H (ppm): 7.32 (d, 2H, J = 8.47 Hz), 7.27 (d, 2H, J = 8.47 Hz), 4.27 (s, 2H, *S-CH$_2$*), 3.84 (s, 3H, *N-CH$_3$*), 3.73 (s, 2H, *NH$_2$*). ^{13}C NMR ($CDCl_3$) δ^C (ppm): 200.3 (*C=S*), 134.1 (q), 133.6 (q), 130.6 (*CH*), 129.0 (*CH*), 38.8 (*S-CH$_2$*), 36.9 (*N-CH$_3$*). MS (EI): *m/z* (%): 246 (M$^+$, 7), 127 (35), 125 (100), 89 (35). Anal Calcd for $C_9H_{11}N_2S_2Cl$: C, 43.80; H, 4.49; N, 11.35; S, 25.99. Found: C, 43.45; H, 4.31; N, 11.06; S, 26.39.

1c. White needles, m.p. 92–93 °C. IR (nujol) ν_{max}: 3275, 1224 cm^{-1}. ^{1}H NMR (CD_3CN) δ^H (ppm): 7.21–7.01 (m, 5H), 5.20 (s, 2H, *N-CH$_2$*), 4.26 (s, 2H, *NH$_2$*), 1.92 (s, 3H, *S-CH$_3$*). ^{13}C NMR (CD_3CN) δ^C (ppm): 200.1 (*C=S*), 136.6 (q), 130.1 (*CH*), 129.5 (*CH*), 129.2 (*CH*), 61.0 (*N-CH$_2$*), 20.5 (*S-CH$_3$*). MS (EI): *m/z* (%): 213 (M$^+$+1, 6), 121 (36), 91 (100). Anal Calcd for $C_9H_{12}N_2S_2$: C, 50.91; H, 5.70; N, 13.19; S 30.20. Found: C, 50.85; H, 5.70; N, 13.07; S, 30.53.

1d. White prisms, m.p. 109–110 °C. IR (nujol) ν_{max}: 3302, 1222, 1089, 854 cm^{-1}. ^{1}H NMR (CD_3CN) δ^H (ppm): 7.46–7.24 (m, 9H), 5.40 (s, 2H, *N-CH$_2$*), 4.54 (s, 2H, *NH$_2$*), 4.38 (s, 2H, *S-CH$_2$*). ^{13}C NMR (CD_3CN) δ^C (ppm): 200.2 (*C=S*), 136.5 (q), 134.7 (q), 131.9 (q), 130.5 (*CH*), 128.5 (*CH*), 127.9 (*CH*), 127.6 (*CH*), 59.4 (*N-CH$_2$*), 39.5 (*S-CH$_2$*). MS (EI): *m/z* (%): 197 (7), 159 (17), 157 (50), 148 (29), 127 (25), 125 (77), 121 (52), 91 (100). Anal Calcd for $C_{15}H_{15}N_2S_2Cl$: C, 55.80; H, 4.68; N, 8.68; S 19.86. Found: C, 55.62; H, 4.70; N, 8.87; S 19.94.

General procedure for the synthesis of 3-alkyl-5-alkylthio-2-thioxo-1,3,4-thiadiazolines 3

A suspension of the appropiate alkyl 2-alkyldithiocarbazate **1** (10 mmol) in carbon disulfide (10 mL) is heated at 120 °C for 24 h. On cooling, the mixture is evaporated to dryness and the resulting solid is scratched with hexane, filtered off and crystallized from ethanol.

3a. Yellow needles, m.p. 83–84 °C (lit.,[3] 84 °C).

3b. Pale yellow prisms, m.p. 62–63 °C. IR (nujol) ν_{max}: 1596, 1258, 1091, 833 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ^H (ppm): 7.24 (s, 4H), 4.21 (s, 2H, *S-CH$_2$*), 3.77 (s, 3H, *N-CH$_3$*). ^{13}C NMR ($CDCl_3$) δ^C (ppm): 185.6 (*C2*), 154.2 (*C5*), 134.2 (q), 133.6 (q), 130.1 (*CH*), 129.0 (*CH*), 38.8 (*N-CH$_3$*), 37.0 (*S-CH$_2$*). MS (EI): *m/z* (%): 290 (M$^+$+2, 8), 288 (M$^+$, 17), 159 (2), 157 (6), 127 (39), 125 (100), 73 (11). Anal Calcd for $C_{10}H_9N_2S_3Cl$: C, 41.58; H, 3.14; N, 9.70; S, 33.30. Found: C, 41.30; H, 3.07; N, 9.69; S, 33.10.

3c. Yellow oil. IR (nujol) ν_{max}: 1604, 1186 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ^H (ppm): 7.38–7.32 (m, 2H), 7.29–7.21 (m, 3H), 5.36 (s, 2H, *N-CH$_2$*), 2.50 (s, 3H, *S-CH$_3$*) ^{13}C NMR ($CDCl_3$) δ^C (ppm): 185.4 (*C2*), 156.4 (*C5*), 134.6 (q), 128.7 (*CH*), 128.5 (*CH*), 128.2 (*CH*), 53.9 (*N-CH$_2$*), 15.4 (*S-CH$_3$*). MS (EI): *m/z* (%): 254 (M$^+$, 18), 181 (3), 149 (6), 148 (81), 91 (100). Anal Calcd for $C_{10}H_{10}N_2S_3$: C, 47.21; H, 3.96; N, 11.01; S, 37.81. Found: C, 47.34; H, 3.96; N, 11.32; S, 38.07.

3d. White flakes, m.p. 75–76 °C. IR (nujol) ν_{max}: 3303, 1601, 1221, 1089, 854 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ^H (ppm): 7.40–7.23 (m, 9H), 5.45 (s, 2H, *N-CH$_2$*), 4.40 (s, 2H, *S-CH$_2$*). MS (EI): *m/z* (%): 366 (M$^+$+2, 0.5), 364 (M$^+$, 2), 159 (2), 157 (7), 148 (9), 127 (12), 125 (43), 91 (100). Anal Calcd for $C_{16}H_{13}N_2S_3Cl$: C, 52.66; H, 3.60; N, 7.67; S, 26.36. Found: C, 52.96; H, 3.63; N, 7.45; S, 26.60.

Crossed experiment for the synthesis of 3-alkyl-5-alkylthio-2-thioxo-1,3,4-thiadiazolines 3

A suspension of equimolecular amounts of methyl 2-methyldithiocarbazate **1a** (5 mmol) and 4-chlorobencyl 2-benzyldithiocarbazate **1d** (5 mmol) in carbon disulfide (10 mL) is heated at 125 °C for 48 h. On cooling, the mixture is evaporated to dryness and the resulting solid is submitted to GC-MS analysis.

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