New reactions of 4,5-disubstituted 1,2,3-thiadiazoles in the presence of NaH

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Dedicated to Professor A. McKervey on his retirement from Queen's University, Belfast, Ireland

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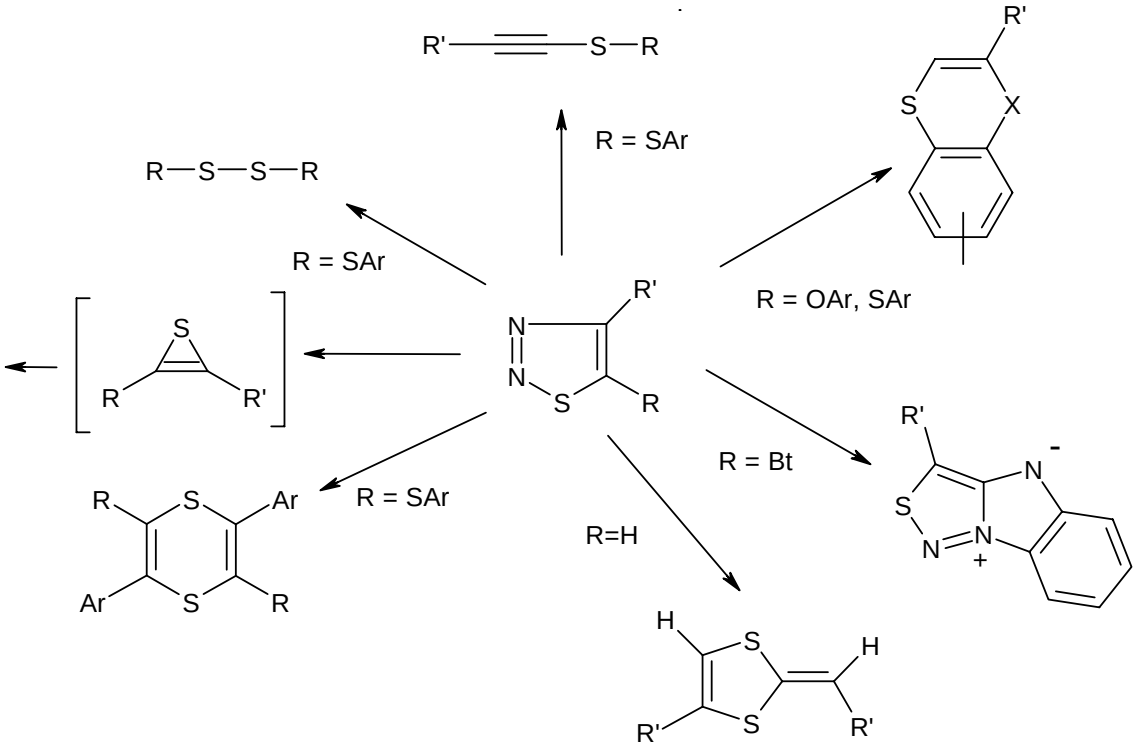
Abstract

1,4-Dithiafulvenes, 1,2,3-thiadiazolylalkylketones, 5-(2-aryl-1-phenylethenyl)-1,2,3-thiadiazole, 1,4-dialkyl-3,6-bis(phenylmethylidene)-2,5-dithiabicyclo[2.2.1]heptane, bis-2,4-(1,2,3-thiadiazol-5-yl)-alkenes and (6-benzyl-3,4-diphenyl-3,4-dihydro-2H-thiopyran-2-ylidene)(phenyl)-methanethiol were formed as a result of transformations of 4,5-disubstituted-1,2,3-thiadiazoles containing an active methylene fragment.

Keywords: 1,2,3-Thiadiazoles, 2,5-dithiabicyclo[2.2.1]heptane, 1,4-dithiafulvenes, 1,2,3-thiadiazolylalkylketones, hydrogen migration

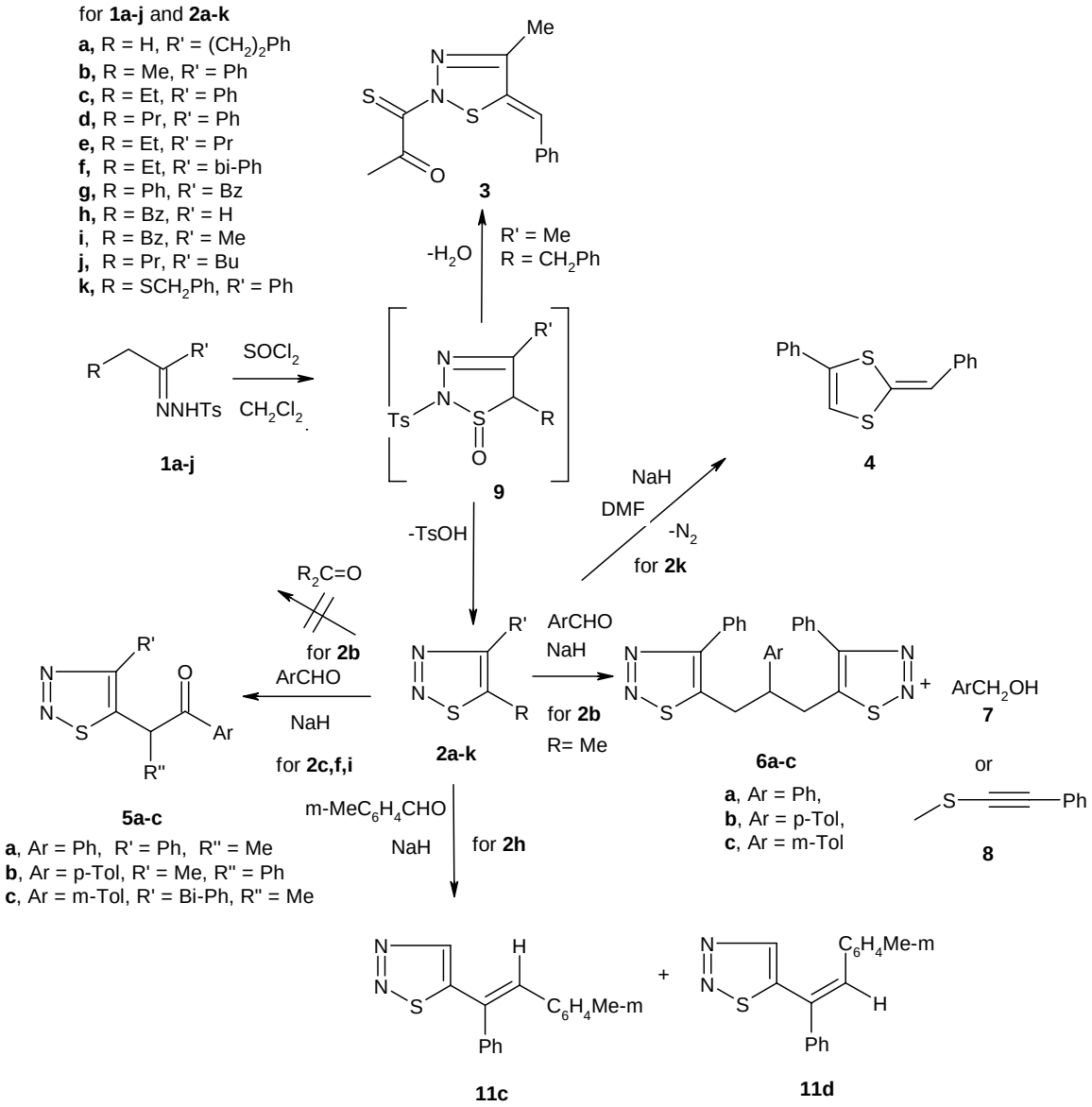
Introduction

It is well documented[1,2a-b] that 1,2,3-thiadiazoles undergo multiple transformations into a wide variety of products. A detailed review of such rearrangements[3] reveals that many proceed by evolution of dinitrogen to form various products depending on the thiadiazole ring substituents. Thus, recently documented thermal transformations of 1-(1,2,3-thiadiazol-5-yl)-1*H*-1,2,3-benzotriazoles involving *intramolecular* heterocyclization lead to 3-R-4*H*-[1,2,3]thiadiazolo[3,4-*a*]benzimidazol-2-ium-4-ides.[4] Heating 4-aryl- and 4-heteroaryl-5-arylthioxy-1,2,3-thiadiazoles in the presence of sodium hydride in DMF forms two isomeric benzo-1,4-dithiines as a result of intramolecular recyclization or as a result of a dimerization process[5] (Scheme 1).



Scheme 1

We now report that 4,5-disubstituted-1,2,3-thiadiazoles **2a-k** containing an active methylene fragment are variously transformed in the presence of NaH into a 1,4-dithiafulvene **4**, 1,2,3-thiadiazolylalkylketones **5a-c**, 5-(2-aryl-1-phenylethenyl)-1,2,3-thiadiazole (**11**), 1,4-dialkyl-3,6-bis(phenylmethylidene)-2,5-dithiabicyclo[2.2.1]heptane **13a,b**, bis-2,4-(1,2,3-thiadiazol-5-yl)-alkenes **12a-c** and (6-benzyl-3,4-diphenyl-3,4-dihydro-2H-thiopyran-2-ylidene)(phenyl)-methanethiol **15** (Schemes 2, 3, 4).



Scheme 2

Results and Discussion

The starting 1,2,3-thiadiazoles **2a-j** were prepared by the previously reported thionyl chloride induced cyclization of tosylhydrazones **1a-j**.[4-6] The yields of **2a-j** were increased compared to the previously reported procedures by using a small excess of thionyl chloride in methylene chloride. 5-Benzylthio-4-phenyl-1,2,3-thiadiazole **2k** was prepared according to an earlier reported procedure.[5]

Compounds **2a** and **2d** both displayed unusual photochromic behavior. Freshly recrystallized samples of these compounds were colorless, but upon exposure to sunlight or UV irradiation they turned to a persistent pink-purple color. Dissolution of either form of the crystals produced apparently identical colorless solutions. Recrystallization of the colored crystals from organic solvents gave colorless crystals, which again upon exposure to irradiation turned into colored crystals. In an attempt to gain insight into the origin of this phenomenon, IR, UV investigation and X-ray structure determinations were carried out on each of the two forms of the crystals of **2a**. However, the two structures were identical within experimental error, and hence the difference in color is not associated with different molecular dimensions. They crystallize in isomorphous space groups ($P2_12_12_1$) with two independent molecules in the asymmetric unit. The complex molecular packing includes some unusually short intermolecular S···N and C-H···N interactions, as shown in Figure 1. The UV and IR spectra were also identical for the crystals of both colors.

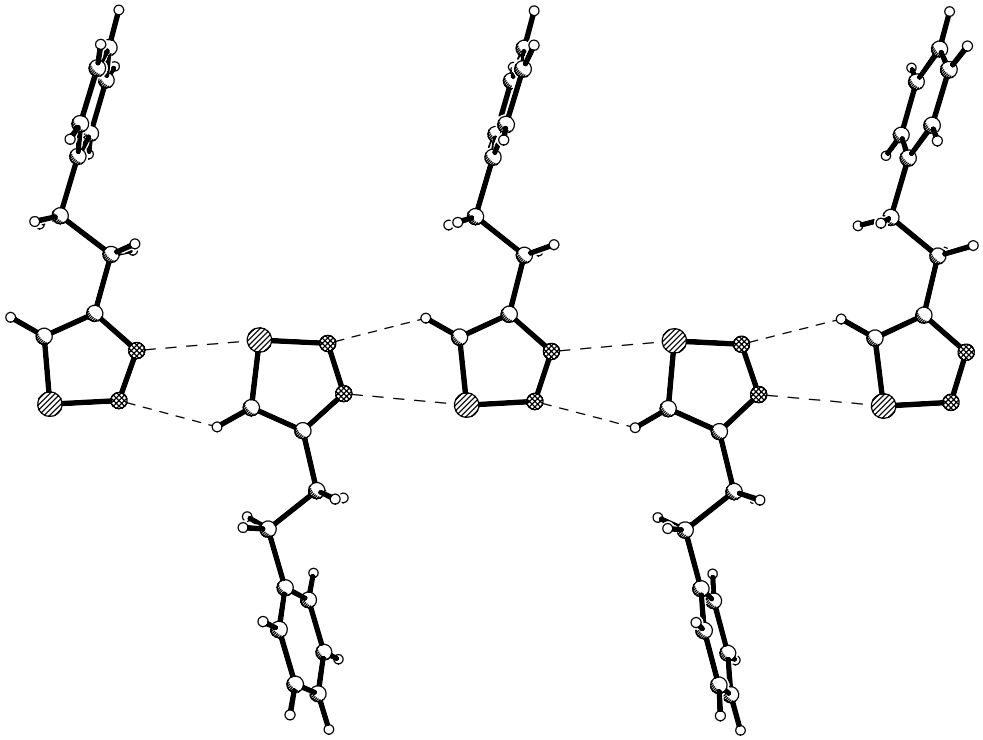


Figure 1. Perspective view showing the short intermolecular S···N and C-H···N interactions (dotted lines) in the X-ray crystal structure of **2a**.

In the preparation of **2i**, when acetone was used to quench excess of thionyl chloride, byproduct **3** was formed probably through intermediate **9**. The structure of compound **3** in solution was established with NMR data. In the ^{1}H NMR spectrum of **3** the signal at 6.84 ppm

was easily assigned to H-6. For the unambiguous chemical shift assignment of the two methyl groups the NOE method was used. Irradiation of the H-6 resonance signal at 6.84 ppm (Figure 2, b) reveals one of the methyl groups at 2.39 ppm (4-CH_3) and the *ortho* protons of the phenyl ring ca. 7.22 ppm. The mutual NOE enhancement effect was observed when the 4-CH_3 resonance signal at 2.39 ppm (Figure 2, c) was irradiated.

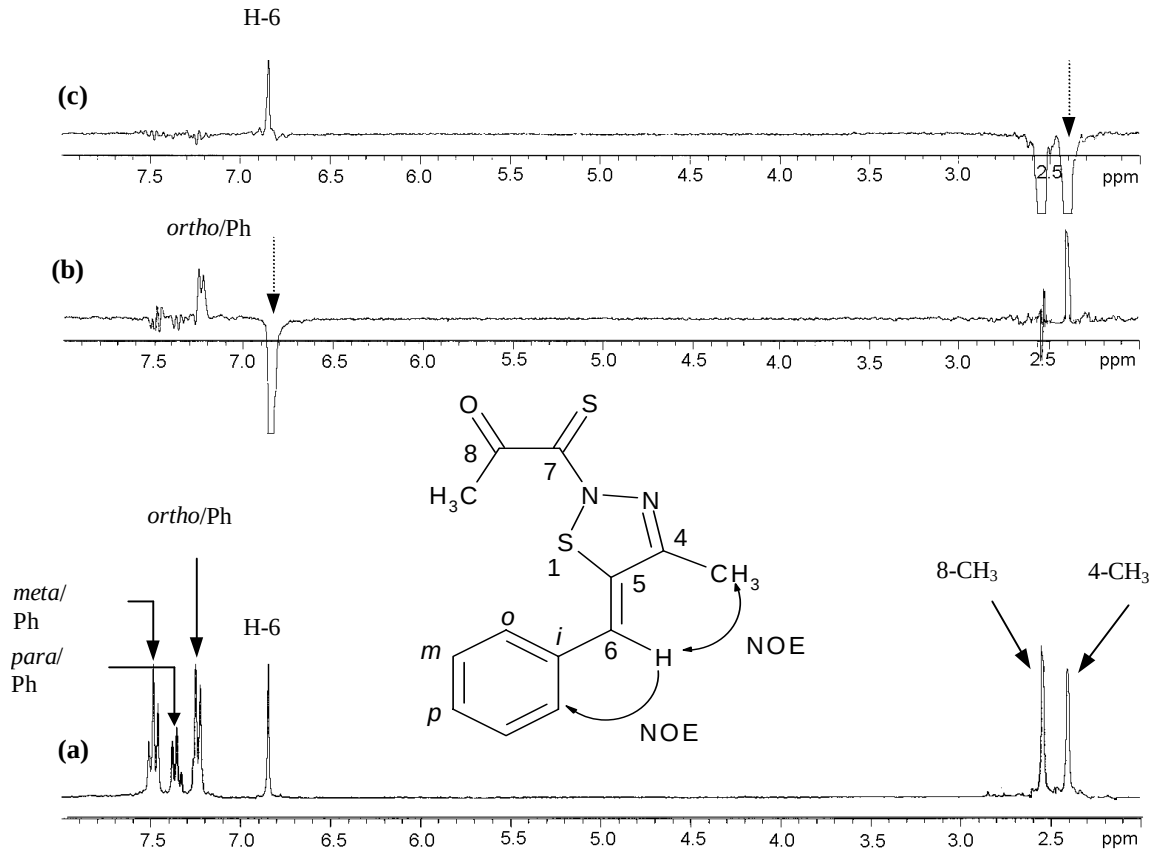


Figure 2. (a) Control ^{1}H NMR spectrum of **3** in $CDCl_3$. NOE difference spectra - **(b)** and **(c)**. Irradiated proton signals are indicated by dotted arrows.

To assign unequivocally the ^{13}C NMR signals of **3**, HETCOR and long-range heterocorrelation HETCOR-LR (Figure 3) were performed. The ^{13}C NMR spectra of **3** showed five quaternary carbon signals at 132.2, 134.4, 162.3, 186.6 and 194.8 ppm. The assignment of these carbon signals is straightforward using long range-heterocorrelation.

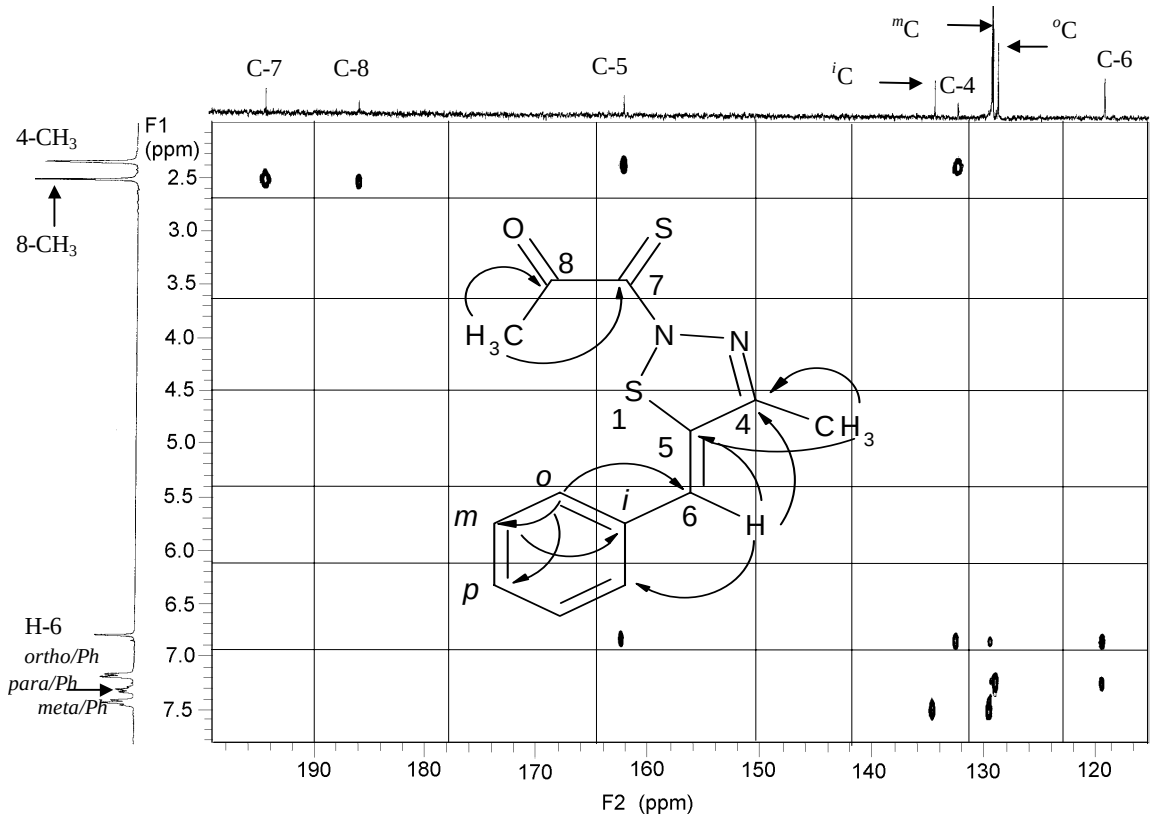


Figure 3. Long-range heterocorrelation spectrum (HETCOR-LR) of **3** in $CDCl_3$; arrows show the long-range correlations *via* two and three bonds which were optimized for 8 Hz.

The structure of **3** was confirmed by X-ray crystal structure determination. The crystals of **3** have a deep red color. Figure 4 shows a perspective view of the molecular structure, which confirms the atom connectivity, the stereochemistry about the exocyclic double bond and establishes the conformations of the side chains in the solid state.

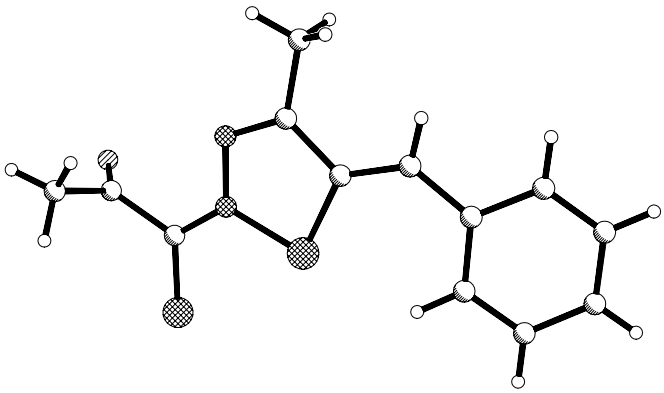
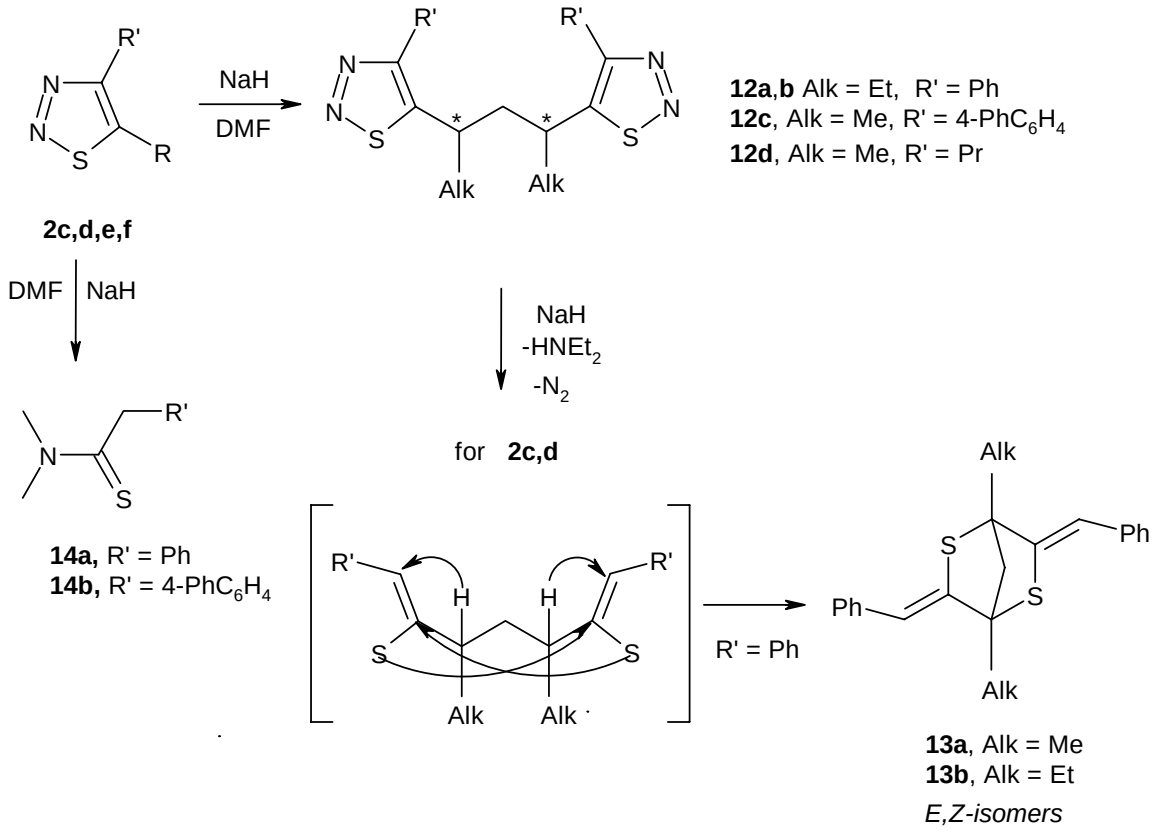


Figure 4. Perspective view of the structure of **3**.

The dithiafulvene **4** was formed on reaction of 5-benzylthio-4-phenyl-1,2,3-thiadiazole (**2k**) with NaH. Compound **4** is well-known: **4** is readily formed (i) by base catalyzed decompositions of 1,2,3-thiadiazoles,[7] (ii) by treatment of 4-phenyl-1,2,3-thiadiazole with base,[8a,b] and (iii) from other precursors.[8c] We believe that in our case the formation of dithiafulvene **4** proceeded by a preliminary proton intramolecular migration from methylene group to thiirene fragment (Scheme 2). The reaction was carried out in DMF in the presence of sodium hydride.

Three different types of compounds were obtained when 1,2,3-thiadiazoles **2** reacted with aromatic aldehydes in the presence of NaH: (i) 1,2,3-thiadiazoles **2c,f,i** gave 5-(α-acylalkyl)-1,2,3-thiadiazoles **5a-c** having a CH_2 linked substituent at the 5-position; (ii) in Knoevenagel type reactions, 5-methyl-1,2,3-thiadiazole **2b** gave bis(1,2,3-thiadiazol-5-yl)alkanes **6a-c** together with arylcarbinol **7** or alkylmercaptoethynes **8** as byproducts; (iii) 1,2,3-thiadiazole **2h** gave E- (**11d**) and Z- (**11c**) isomers of vinyl-substituted 1,2,3-thiadiazole **11** (Scheme 2).

A reaction sequence similar to (ii) took place when DMF was used instead of an aldehyde. Thus, brief heating of thiadiazoles **2d,e,f** in DMF with **3** equivalents of sodium hydride gave bis(1,2,3-thiadiazol-5-yl)alkanes **12a-d** as mixtures of *d,l* and *meso*-forms (Scheme 3).



Scheme 3

Stronger heating of 1,2,3-thiadiazoles, for example **2d,e,f** in DMF in the presence of NaH gave bicyclic compounds 3,6-di-(phenylmethylidene)-2,5-dithiabicyclo[2.2.1]heptanes **13a** and

13b. Thus, after heating **2d**, a mixture of four compounds was obtained, which were then separated by column chromatography into two isomers of **12a,b** (*d,l*- and *meso*-forms) and a mixture of *E,Z*-isomers of 2,5-dithiabicyclo[2.2.1]heptane **13b** (Scheme 3).

The formation of compounds **13a,b** probably occurs *via* **12** as intermediates (Scheme 3). In the next step, double recyclization followed by dinitrogen elimination from the 1,2,3-thiadiazole ring and double migration of a hydrogen atom from a α-methylene fragment affords 3,6-di-(phenylmethylidene)-1,4-diethyl-2,5-dithiabicyclo[2.2.1]heptane **13b**. Heating more strongly or keeping for a longer time in the presence of excess of NaH leads to deep seated degradation of 1,2,3-thiadiazoles; for example, thioamides **14a,b** were obtained when **2c** was stirred at room temperature for two days or **2f** was heated in DMF with NaH.

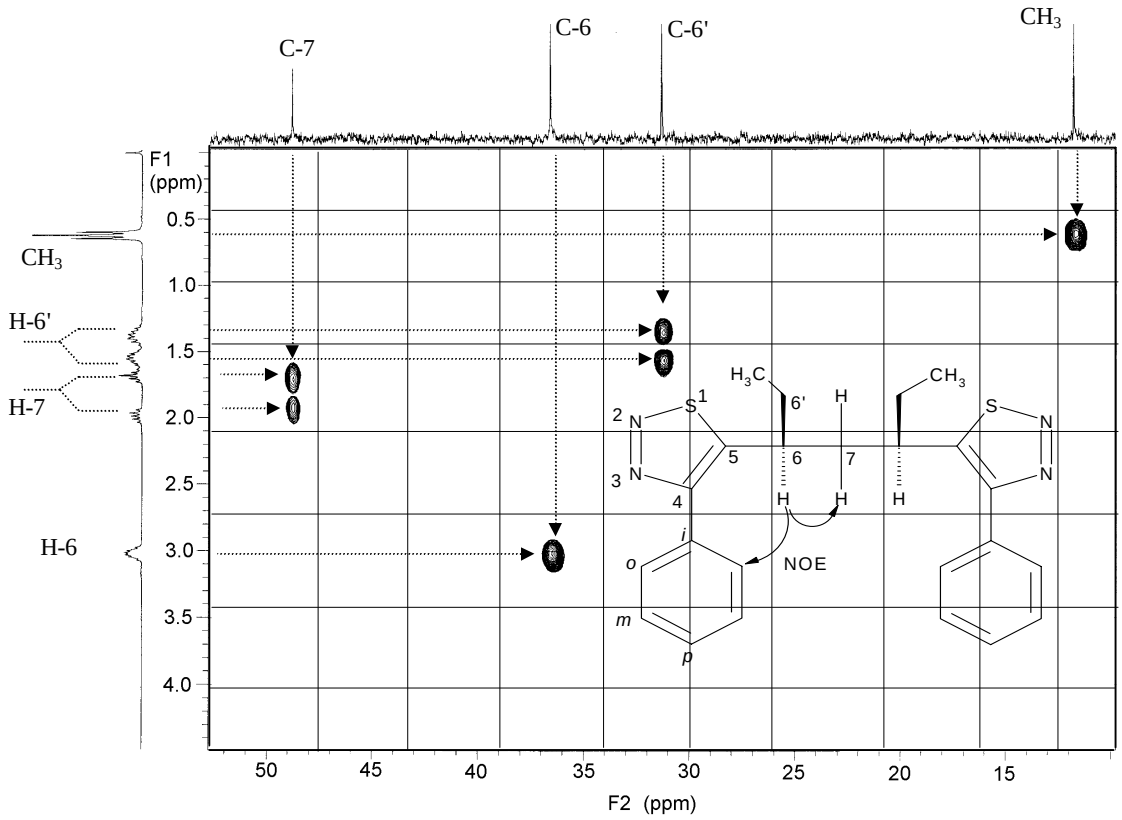


Figure 5. HETCOR spectrum of **12a** in $CDCl_3$ (aliphatic region).

The two isomeric (*meso*-**12a**, and *d,l*-**12b**) 4,5-disubstituted thiadiazoles were characterized by one and two dimensional NMR techniques (DEPT, selective decoupling, COSY, HETCOR). The ^1H NMR spectra of **12a** and **12b** and the protons of 6´-CH_2 and 7-CH_2 groups are non-equivalent, and exhibit different chemical shifts. A useful assignment strategy to distinguish between protons of two types of methylene groups (6´-CH_2 and 7-CH_2) is on the basis of selective decoupling, and HETCOR experiments. The low field (multiplet centered at 3.02 ppm) was assigned to H-6. A representative example of HETCOR spectra is shown for **12a**. The

typical one bond correlation peaks are presented on the contour plot of HETCOR spectrum by dotted arrows (Figure 5).

The DEPT data indicate different forms of the carbon atoms in the aliphatic unit (6-CH_3, 6´-CH_2 and 6-CH). The assignment of quaternary carbon atoms at 130.8 ppm (^{ipso}C), 157.3 ppm (C-5) and 160.3 ppm (C-4) were made by long-range heterocorrelation HETCOR-LR experiments; optimized for 8 Hz long-range J_{CH} coupling.

Characterization of **13a** as $C_{21}H_{20}S_2$ was achieved by high-resolution NMR techniques. The two-fold symmetry of **13a** simplifies both the proton and carbon spectra and thus, only half of the molecule needs to be discussed. The ^{1}H NMR spectrum of **13a** shows three types of singlet signals at 1.96, 2.26 and 6.45 ppm, which belong to CH_3, 7-CH_2 and H-6a, respectively. The ratio of integral intensity in **13a** is 5:1:1:3. The assignment of the o*rtho* protons of the phenyl ring in **13a** was carried out *via* the appropriate NOE experiments (see Figure 6).

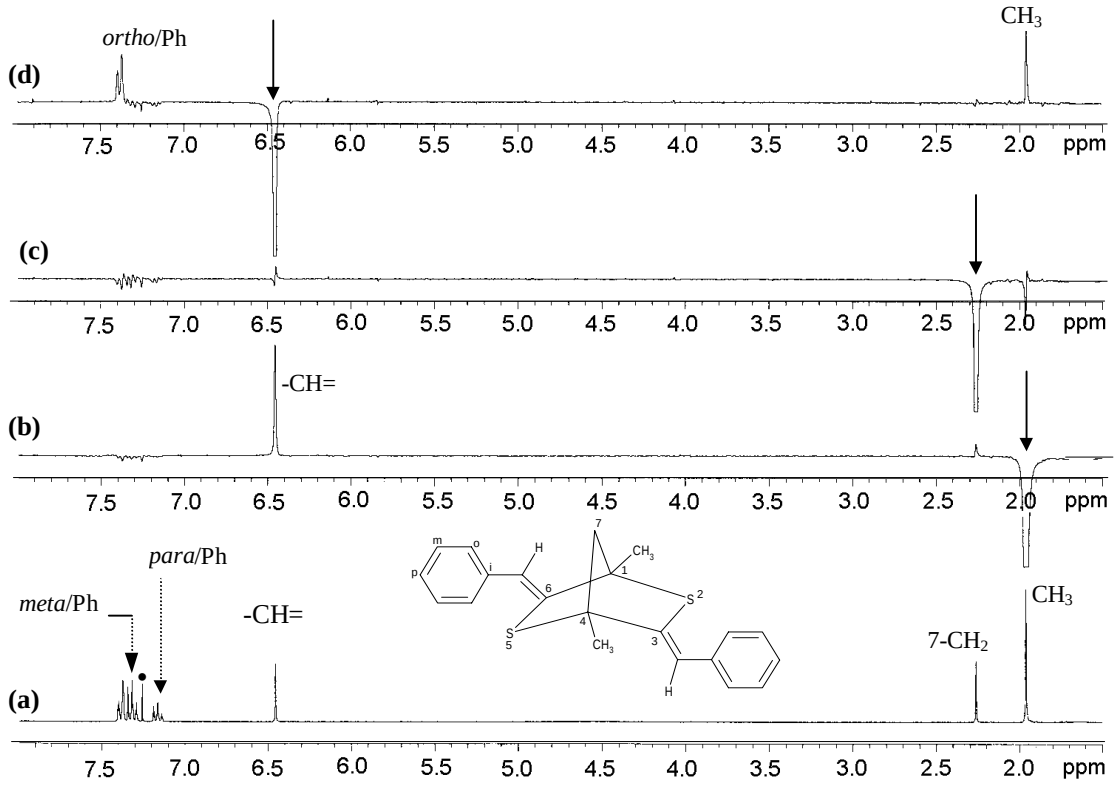


Figure 6. (a) Control ^{1}H NMR spectrum of **13a** in $CDCl_3$. NOE difference spectra - **(b)**, **(c)** and **(d).** Irradiated proton peaks are indicated by arrows (solid); • denotes a solvent peak.

Unequivocal assignments of carbon chemical shifts were made on the basis of coupled ^{13}C NMR, HETCOR (the proton bearing carbon) and long-range correlation HETCOR-LR (to determine the chemical shifts of quaternary carbon atoms) experiments (Figure 7).

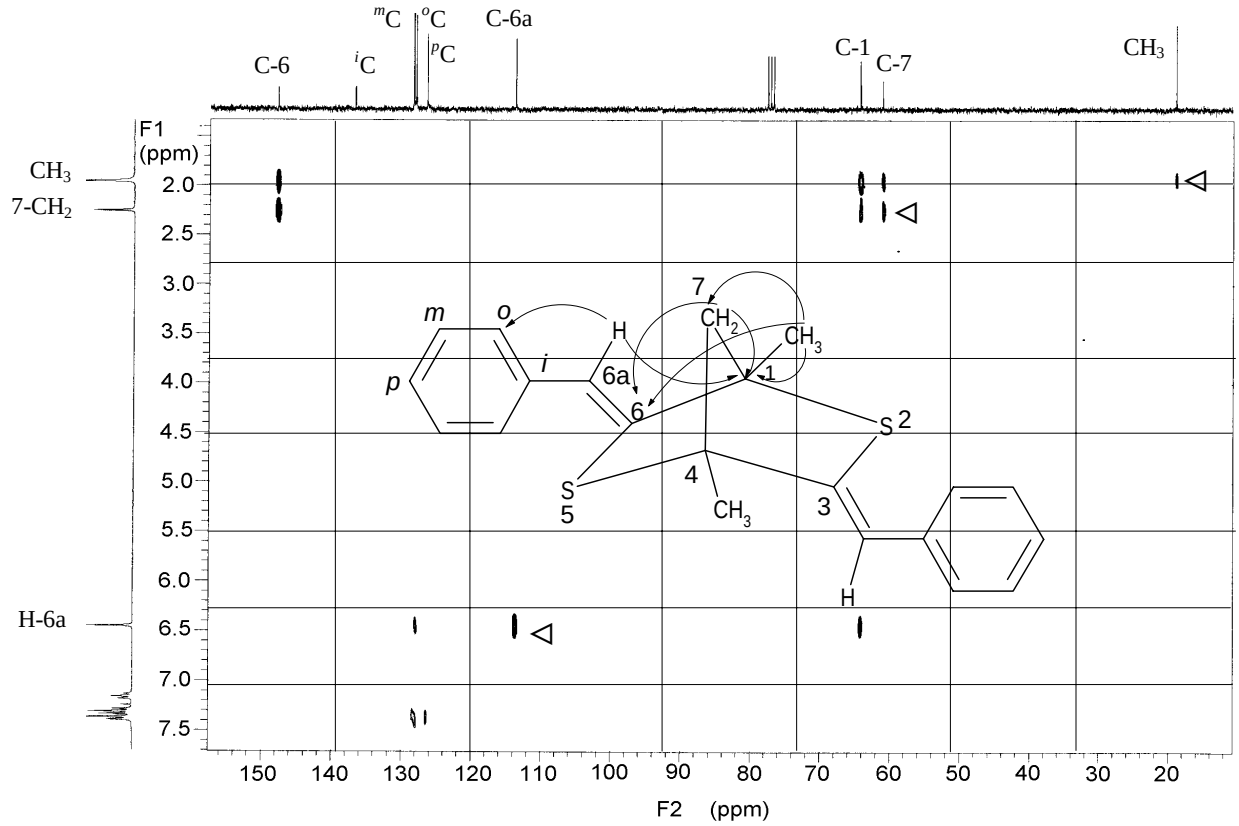


Figure 7. Long-range heterocorrelation spectrum (HETCOR-LR) of **13a**; arrows represent typical C-H long-range ($^{n}J_{CH}$, n = 2 or 3) correlations through two or three bonds (J = 8 Hz) observed in the HETCOR-LR experiment; ◁-denotes the one-bond correlation cross-peaks.

The structure of compound **13** was unambiguously confirmed by single crystal X-ray analysis. Figure 8 shows a perspective view of the molecular structure and confirms the stereochemistry of the benzylidene groups.

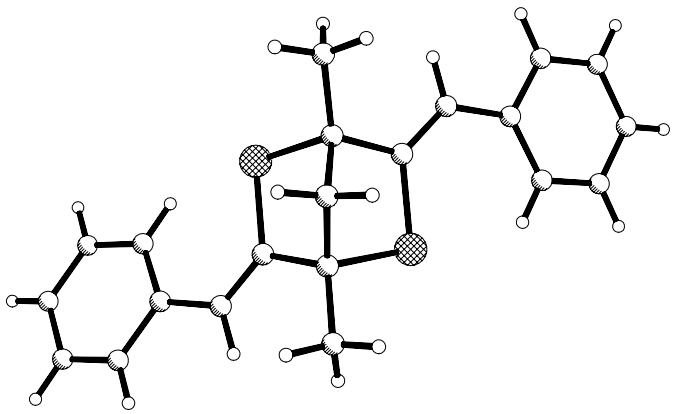
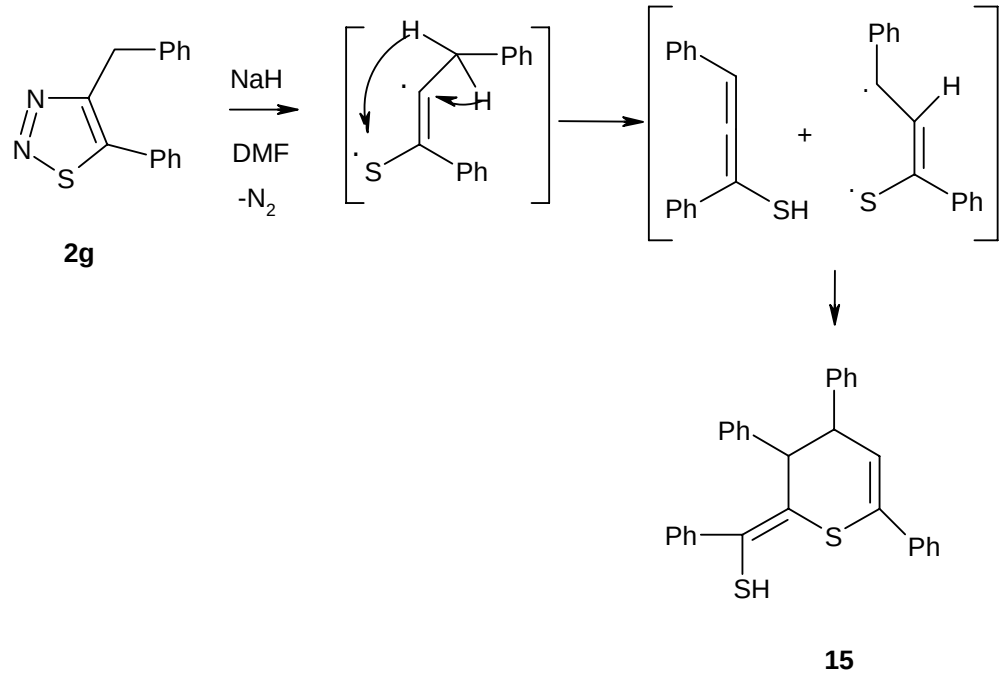


Figure 8. Perspective view of the structure of **13a**.

Another class of 1,2,3-thiadiazole transformations was observed when the methylene fragment of the substituent was in the 4-position of the 1,2,3-thiadiazole rings. Thus, heating of 4-benzyl-5-phenyl-1,2,3-thiadiazole **2g** in DMF in the presence of sodium hydride led to **15** (Scheme 4).



2g **15**

Scheme 4

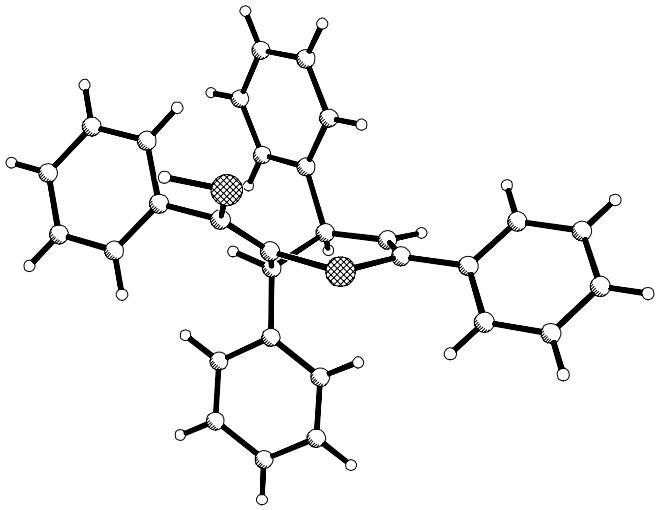


Figure 9. Perspective view of the structure of **15.**

The structure of compound **15** was determined by single crystal X-ray analysis. Figure 9 shows a perspective view of the molecular structure, which establishes the overall structure of

the molecule, along with the stereochemistry of the phenyl substituents and the exocyclic double bond.

The formation of compound **15** can be rationalized by nitrogen elimination followed by a migration of a hydrogen atom from the methylene fragment to the sulfur or carbon atom to form two intermediate fragments. The new C-C bond is formed after the 1,3-cycloaddition of the biradical to the allene.

Conclusions

1,4-Dithiafulvenes, 1,2,3-thiadiazolylalkylketones, 5-(2-aryl-1-phenylethenyl)-1,2,3-thiadiazole, 1,4-dialkyl-3,6-bis(phenylmethylidene)-2,5-dithiabicyclo[2.2.1]heptane, bis(1,2,3-thiadiazol-5-yl)-alkanes and (6-benzyl-3,4-diphenyl-3,4-dihydro-2H-thiopyran-2-ylidene)(phenyl)-methanethiol were formed as a result of the transformation of 4,5-disubstituted-1,2,3-thiadiazoles containing an active methylene fragment.

Experimental Section

Compounds **1a** (mp 124-126 °C, lit. mp 125-126 °C), **1b** (mp 119-120 °C, lit. mp 120-121 °C), **1e** (mp 78-80 °C, lit. mp 80-81 °C), and **1h** were prepared as described in,[9a] **1c** (mp 118-120 °C, lit. mp 119-120 °C)[9b], **1g** – in[9c], **2a** – in[10], **2g** (oil) – in[8b], **2k** – in.[11]

General Procedures. Melting points were determined on a hot stage apparatus without correction. NMR spectra were recorded at 300 MHz for ^{1}H and 75 MHz for ^{13}C NMR spectra with $CDCl_3$-*d* as a solvent if not stated otherwise. Chemical shift values are reported as δ downfield from TMS as the internal standard for ^{1}H and a solvent as the internal standard for ^{13}C.

4-Methyl-*N'*-[(*E*)-1-phenylpentylidene]benzenesulfonohydrazide (1d). A mixture of *p*-tosylhydrazine (22.9 g, 123 mmol) and butyrophenone (20 g, 112 mmol) in MeOH (400 mL) and 4 mL of conc. HCl was reflux for 5 h. The precipitate formed was filtered off and recrystallized from methanol, yield 86 % (35 g), mp 135–136 °C. ^{1}H NMR: δ 7.93 (d, *J* = 8 Hz, 2H), 7.61–7.64 (m, 2H), 7.30–7.33 (m, 5H), 2.59 (t, *J* = 7 Hz, 2H), 2.40 (s, 3H), 1.30–1.42 (m, 4H), 0.83 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR: δ 156.1, 144.0, 143.9, 136.5, 135.4, 129.5, 129.4, 128.3, 127.9, 126.6, 126.3, 28.0, 27.8, 26.7, 22.7, 22.0, 21.5, 13.7. Anal. Calcd for $C_{18}H_{22}N_2O_2S$: C, 65.43; H, 6.71; N, 8.48. Found: C, 65.53; H, 6.98; N. 8.50.

***N'*-[(*E*)-1-[(4-Biphenylyl)butylidene]-4-methylbenzenesulfonohydrazide (1f).** A mixture of *p*-tosylhydrazine (12.5 g, 67 mmol) and 4-biphenylylbutanone (15 g, 39.2 mmol) in benzene (200 mL) was refluxed for 4 h. The benzene was evaporated, the residue was recrystallized from

MeOH. Yield 94 % (24.5 g), mp 118–120 °C. ^{1}H NMR: δ 7.94 (d, *J* = 8.2 Hz, 2H), 7.71 (d, *J* = 8.2 Hz, 2H), 7.59 (t, *J* = 6.1 Hz, 4H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.31–7.35 (m, 3H), 2.58 (t, *J* = 8.1 Hz, 2H), 2.41 (s, 3H), 1.57 (q, *J* = 7.3 Hz, 2H), 0.94 (t, *J* = 7.3 Hz, 3H) (spectral data are given for the major isomer); ^{13}C NMR: δ 155.8, 144.1, 142.2, 140.3, 135.2, 135.4, 129.6, 128.8, 128.3, 128.0, 127.6, 127.0, 128.8, 127.0, 126.8, 21.6, 19.4, 14.1. Anal. Calcd for $C_{23}H_{24}N_2O_2S$: C, 70.38; H, 6.16; N, 7.14. Found: C, 69.74; H, 6.04; N, 7.19.

Crystal data for **2a** (pink form): $C_{10}H_{10}N_2S$, FW 190.26, orthorhombic, space group $P2_12_12_1$, *a* = 6.055(1), *b* = 8.190(2), *c* = 38.639(9) Å, V = 1916.1(8) Å^3, F(000) = 800, Z = 8, T = -105 °C, μ (MoKα) = 0.289 mm^{-1}, D_{calcd} = 1.319 g.cm^{-3}, crystal size 0.60 x 0.54 x 0.43 mm, $2\theta_{max}$ 53° (CCD area detector, MoKα radiation, 98.8% completeness), wR(F^2) = 0.0697 (all 3832 data), R = 0.0301 (3349 data with I > 2σI).

Crystal data for **2a** (colorless form): $C_{10}H_{10}N_2S$, FW 190.26, orthorhombic, space group $P2_12_12_1$, *a* = 6.052(2), *b* = 8.197(2), *c* = 38.581(11) Å, V = 1914.0(10) Å^3, F(000) = 800, Z = 8, T = -105 °C, μ (MoKα) = 0.289 mm^{-1}, D_{calcd} = 1.320 g.cm^{-3}, crystal size 0.68 x 0.46 x 0.24 mm, $2\theta_{max}$ 53° (CCD area detector, MoKα radiation, 99.3% completeness), wR(F^2) = 0.0810 (all 3869 data), R = 0.0352 (3615 data with I > 2σI).

5-Methyl-4-phenyl-1,2,3-thiadiazole (2b). Thionyl chloride (16.5 g, 139 mmol) was added dropwise to 4-methyl-*N*′-[(*E*)-1-phenylpropylidene]benzenesulfonohydrazide (14 g, 46 mmol) in methylene chloride (40 mL). The mixture was stirred at rt overnight, methylene chloride and excess of thionylchloride were removed under reduced pressure and the residue was recrystallized from ether : hexanes 1 : 1. Yield 60 % (4.9 g), white crystals, mp 38–40 °C. ^{1}H NMR: δ 7.69–7.72 (m, 2H), 7.46–7.55 (m, 3H), 2.72 (s, 3H); ^{13}C NMR: δ 159.5, 146.7, 130.9, 128.8, 128.7, 128.6, 10.5. Anal. Calcd for $C_9H_8N_2S$: C, 61.34; H, 4.58; N, 15.90. Found: C, 61.33; H, 4.41; N, 15.85.

5-Ethyl-4-phenyl-1,2,3-thiadiazole (2c). The procedure is similar to **2b**. Yield 58 %, white crystals, mp 65 °C. ^{1}H NMR: δ 7.71 (d, *J* = 6.9 Hz, 2H), 7.45–7.53 (m, 3H), 3.11 (q, *J* = 7.4 Hz, 2H), 1.40 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR: δ 158.6, 154.8, 131.3, 128.7, 19.6, 16.5. Anal. Calcd for $C_{10}H_{10}N_2S$: C, 63.13, H, 5.30; N, 14.72. Found: C, 62.83; H, 5.34; N, 14.90.

4-Phenyl-5-propyl-1,2,3-thiadiazole (2d). The procedure is similar to **2b**. Yield 58 %, white crystals, mp 36–37 °C. ^{1}H NMR: δ 7.69–7.72 (m, 2H), 7.45–7.53 (m, 3H), 3.07 (t, *J* = 7.6 Hz, 2H), 1.72–1.80 (m, 2H), 1.04 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR: δ 159.0, 152.9, 131.4, 128.8, 128.7, 128.6, 27.7, 25.3, 13.8. Anal. Calcd for $C_{11}H_{12}N_2S$: C, 64.67; H, 5.92; N, 13.71. Found: C, 64.60; H, 5.94; N, 13.82.

5-Ethyl-4-propyl-1,2,3-thiadiazole (2e). The procedure is similar to **2b**. Yield 57 %, oil. ^{1}H NMR: δ 2.93 (m, 4H), 1.83 (m, 2H), 1.36 (t, *J* = 7.5 Hz, 3H), 1.00 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR: δ 159.6, 153.6, 28.6, 22.9, 18.6, 16.2, 13.7. Anal. Calcd for $C_7H_{12}N_2S$: C, 53.81; H, 7.74; N, 17.93. Found: C, 53.66; H, 7.75; N, 17.49.

4-Biphenylyl-5-ethyl-1,2,3-thiadiazole (2f). The procedure is similar to **2b**. Yield 72 %, white crystals, mp 82–83 °C. ^{1}H NMR: δ 7.77 (dd, *J* = 8.3, 12.8 Hz, 4H), 7.65 (d, *J* = 7.2 Hz, 2H), 7.38–7.50 (m, 3H), 3.15 (q, *J* = 7.4 Hz, 3H), 1.43 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR: δ 158.3, 154.8,

141.5, 140.3, 130.3, 129.1, 128.9, 127.6, 127.4, 127.1, 19.7, 16.6. Anal. Calcd for $C_{16}H_{14}N_2S$: C, 72.15; H, 5.30; N 10.52. Found: C, 72.06; H, 5.24; N, 10.60.

5-Benzyl-1,2,3-thiadiazole (2h). The procedure is similar to **2b**. Yield 69 %, oil. ^{1}H NMR: δ 8.47 (s, 1H), 7.21–7.34 (m, 5H), 4.33 (s, 2H). ^{13}C NMR: δ 157.2, 147.0, 137.7, 129.2, 129.0, 128.3, 127.4, 127.1, 31.1. Anal. Calcd for $C_9H_8N_2S$: C, 61.34; H, 4.58; N, 15.90. Found: C, 61.09; H, 4.36; N, 15.68.

5-Benzyl-4-methyl-1,2,3-thiadiazole (2i). The procedure is similar to **2b**. Yield 44 %, oil. ^{1}H NMR: δ 7.17–7.32 (m, 5H), 4.18 (s, 2H), 2.64 (s, 3H). ^{13}C NMR δ 156.1, 150.7, 137.7, 128.9, 128.1, 127.2, 30.7, 12.3. Calcd for $C_{10}H_{10}N_2S$: C, 63.13; H, 5.30; N, 14.72. Found: C, 63.29; H, 5.14; N, 14.69.

1-[4-Methyl-5-[(*E*)-phenylmethylidene]-1,2,3-thiadiazol-2-yl]-1-thioxoacetone (3) was obtained as a by-product from reaction of 4-methyl-*N'*-[(*E*)-1-methyl-3-phenylpropylidene]benzenesulfonohydrazide with thionyl chloride after work up of the reaction mixture with acetone and purification by column chromatography. Yield 15 %, red crystals, mp 133-134 °C. ^{1}H NMR: δ 7.50 (m, 2H), 7.34 (t, *J* = 4 Hz, 1H), 7.24–7.21 (m, 2H), 6.83 (s, 1H), 2.56 (s, 3H), 2.39 (s, 3H). ^{13}C NMR: δ 194.8, 186.5, 162.4, 134.4, 132.4, 129.2, 129.1, 128.6, 118.9, 28.1, 13.6. Anal. Calcd for $C_{13}H_{12}N_2OS_2$: C, 56.50; H, 4.38; N, 10.14. Found: C, 56.31; H, 4.30; N, 10.05.

Crystal data for **3**: $C_{13}H_{12}N_2OS_2$, FW 276.37, orthorhombic, space group $Pca2_1$, *a* = 21.383(4), *b* = 8.819(2), *c* = 7.116(1) Å, V = 1341.9(5) Å^3, F(000) = 576, Z = 4, T = -105 °C, μ (MoKα) = 0.385 mm^{-1}, D_{calcd} = 1.368 g.cm^{-3}, crystal size 0.69 x 0.45 x 0.21 mm, $2\theta_{max}$ 53° (CCD area detector, MoKα radiation, 99.6% completeness), wR(F^2) = 0.0981 (all 2425 data), R = 0.0466 (2341 data with I > 2σI).

4-Phenyl-2-[(*E*)-phenylmethylidene]-1,3-dithiole (4). Yield 40 %, white crystals, mp 198 °C.[7,8a,b] ^{1}H NMR δ 7.44–7.17 (m, 10H); 6.66 (s, 1H); 6.60 (s, 0.5H); 6.58 (s, 0.5H); 6.54 (s, 1H) (mixture of *E*- and *Z*-isomers). ^{13}C NMR: δ 144.5, 130.4, 128.6, 128.1, 126.9, 126.7, 122.2, 118.5, 114.8.

1-Phenyl-2-(4-phenyl-1,2,3-thiadiazol-5-yl)-1-propanone (5a). NaH (0.2 g, 8.3 mmol, 60 % suspension in oil) was added to 4-phenyl-5-ethyl-1,2,3-thiadiazole (0.4 g, 2.1 mmol) and benzaldehyde (0.22 g, 2.1 mmol) in THF (10 mL). The reaction mixture was refluxed for 6 h, ether (30 mL) was added, the reaction mixture was washed with water. The organic layer was dried over $MgSO_4$, the solvents were evaporated and the residue was purified by column chromatography (Et_2O : Hexanes 1 : 1). Yield 0.3 g, (48%), oil. ^{1}H NMR: δ 7.87 (d, *J* = 7.3 Hz, 2H), 7.64–7.43 (m, 8H), 5.39 (q, *J* = 7.3 Hz, 1H); 1.62 (d, *J* = 7.3 Hz, 3H). ^{13}C NMR: δ 190.0, 158.9, 150.3, 134.2,134.1, 131.8, 129.2, 129.1, 129.0, 129.04, 128.7, 40.2, 23.2. Anal. Calcd for $C_{17}H_{14}N_2OS$: C, 69.36; H, 4.79; N, 9.52. Found: C, 69.58; H, 4.82; N, 9.13. GCMS Calcd: 294. Found for ms - 2N: 266.

1-(4-Methylphenyl)-2-(4-methyl-1,2,3-thiadiazol-5-yl)-2-phenyl-1-ethanone (5b). The procedure is similar to **5a**. Starting material (yield ~31 %), 4-methylbenzylalcohol (yield 40 %) and **5b** (yield 32 %), white crystals, mp 198 °C, were obtained. ^{1}H NMR: δ 8.03 (d, *J* = 8.1 Hz,

1H), 7.36–7.28 (m, 8H), 6.29 (s, 1H), 2.71 (s, 3H), 2.42 (s, 3H). ^{13}C NMR: δ 194.5, 155.6, 147.4, 145.3, 135.8, 131.8, 129.6, 129.5, 129.3, 128.2, 128.1, 127.7, 52.2, 21.6, 13.2. Anal. Calcd for $C_{16}H_{14}N_2S$: C, 70.10; H, 5.23; N, 9.08. Found: C, 69.51; H, 5.29; N, 9.25.

2-(4-Biphenylyl-1,2,3-thiadiazol-5-yl)-1-(3-methylphenyl)-1-propanone (5c). NaH (0.6 g, 25 mmol, 60 % suspension in oil) was added to **2f** (1.8 g, 6.8 mmol) and 3-methylbenzaldehyde (0.9 g, 7.5 mmol) in THF (30 mL). The reaction mixture was refluxed for 4 h, and stirred overnight at rt, ether (40 mL) was added and the reaction mixture was washed with water. The organic layer was dried over $MgSO_4$, the solvents were evaporated and the residue was purified by column chromatography (Et_2O : Hexanes 1 : 1). Yield 1.3 g, (50 %), oil. ^{1}H NMR: δ 7.81–7.67 (m, 8H), 7.52–7.47 (m, 2H), 7.43–7.33 (m, 3H), 5.43 (q, *J* = 7.2 Hz, 1H), 2.35 (s, 3H), 1.65 (d, *J* = 7.2 Hz, 3H). ^{13}C NMR: δ 198.3, 158.5, 150.9, 142.0, 140.1, 139.0, 135.0, 134.0, 130.3, 129.5, 129.3, 129.0, 128.9, 127.8, 127.7, 127.1, 125.9, 40.2, 23.2, 21.3. Anal. Calcd for $C_{24}H_{20}N_2OS$: MS Calcd 384.50. MS Found: [M+1] 385.1373.

5-[2-(3-Phenyl)-3-(4-phenyl-1,2,3-thiadiazol-5-yl)propyl]-4-phenyl-1,2,3-thiadiazole (6a). NaH (0.6 g, 25 mmol, 60 % suspension in oil) was added to 4-phenyl-5-methyl-1,2,3-thiadiazole (2.21 g, 12.6 mmol) and benzaldehyde (1.4 g, 13.3 mmol) in THF (15 mL) at 20 °C. The reaction mixture was refluxed for 5 h. EtOAc (20 mL) was added; the reaction mixture was washed with water, dried over $MgSO_4$ and purified by column chromatography. Yield 25 % (0.7 g), yellow crystals, mp 126 °C. ^{1}H NMR: δ 7.48 (m, 9H), 7.27–7.25 (m, 4H), 6.92–6.90 (m, 2H), 3.51–3.34 (m, 4H), 3.30–2.97 (m, 1H). ^{13}C NMR: δ 160.2, 148.8, 139.4, 131.0, 129.3, 129.2, 129.0, 128.9, 128.5, 127.9, 49.1, 32.3. Anal. Calcd for $C_{25}H_{20}N_4S_2$: C, 68.15; H, 4.58; N, 12.72. Found: C, 67.93; H, 4.58; N, 12.66.

5-[2-(4-Methylphenyl)-3-(4-phenyl-1,2,3-thiadiazol-5-yl)propyl]-4-phenyl-1,2,3-thiadiazole (6b). The procedure is similar to **6a**. Yield 23 %, yellow crystals, mp 159-160 °C. ^{1}H NMR: δ 7.48 (m, 9H), 7.05 (d, *J* = 7,7 Hz, 2H), 6.79 (d, *J* = 7.7 Hz, 2H), 3.44–3.33 (m, 4H), 2.88–3.00 (m, 1H), 2.33 (s, 3H). ^{13}C NMR: δ 160.0, 148.8, 138.3, 136.1, 131.0, 129.9, 129.0, 128.9, 127.7, 48.6, 32.4, 21.1. Anal. Calcd for $C_{26}H_{22}N_4S_2$: C, 68.69; H, 4.88; N, 12.32. Found: C, 68.89; H, 4.94; N, 11.66.

5-[2-(3-Methylphenyl)-3-(4-phenyl-1,2,3-thiadiazol-5-yl)propyl]-4-phenyl-1,2,3-thiadiazole (6c). The procedure is similar to **6a**. Yield 35 %, white crystals, mp 126 °C. ^{1}H NMR: δ 7.50–7.47 (m, 10H), 7.13–7.07 (m, 2H), 6.71–6.69 (m, 2H), 3.49–3.29 (m, 4H), 2.96–2.91 (m, 1H), 2.24 (s, 3H). ^{13}C NMR: δ 160.0, 148.8, 139.1, 139.0, 130.9, 129.1, 129.0, 128.9, 128.4, 124.8, 49.0, 32.2, 21.3. Anal. Calcd for $C_{26}H_{22}N_4S_2$: C, 68.69; H, 4.88; N, 12.32. Found: C, 68.67; H, 4.87; N, 12.40.

5-[(*E*)-2-(3-Methylphenyl)-1-phenylethenyl]-1,2,3-thiadiazole (11c) and 5-[(*Z*)-2-(3-methyl phenyl)-1-phenylethenyl]-1,2,3-thiadiazole (11d). The procedure is similar to **5a**. The products **11d** and **11e** were isolated by column chromatography as individual compounds. Yield **11d** 56 %, oil. ^{1}H NMR: δ 8.38 (s, 1H), 7.17 (s, 1H), 7.40–7.44 (m, 3H), 7.25–7.29 (m, 2H), 6.91–7.03 (m, 2H), 6.85 (br s, 1H, *ortho*-H/B-ring), 6.77–6.80 (m, 1H), 2.19 (s, 3H). ^{13}C NMR: δ 160.8, 144.5, 138.3, 137.8, 134.8, 134.7, 130.8, 129.5, 129.4, 129.3, 129.0, 128.7, 128.1, 126.7,

21.2. Anal. Calcd for $C_{17}H_{14}N_2S$: C, 73.35; H, 5.07; N, 10.06. Found: C, 73.63; H, 5.04, N, 9.57. GCMS Calcd for $C_{17}H_{14}N_2S$: 278. Found: 278.

Yield **11e** ~10 %, oil. ^{1}H NMR: δ 8.45 (s, 1H), 7.33–7.39 (m, 3H), 7.30–7.32 (m, 2H), 7.08–7.19 (m, 3H), 6.94 (br s, 1H), 6.85–6.88 (m, 1H), 2.27 (s, 3H). ^{13}C NMR: δ 154.3, 148.6, 141.2, 138.5, 135.6, 135.0, 129.7, 129.5, 129.2, 128.9, 128.7, 128.6, 127.3, 125.9, 27.3.

5-[1-Ethyl-3-(4-phenyl-1,2,3-thiadiazol-5-yl)pentyl]-4-phenyl-1,2,3-thiadiazoles (12a,b). NaH (0.72 g, 30 mmol, 60 % suspension in oil) was added to 4-phenyl-5-propyl-1,2,3-thiadiazole (2 g, 9.8 mmol) in DMF (15 mL). The reaction mixture was heated for 10 min at 100 °C. EtOAc (30 mL) was added, the mixture was washed with water, organic layer was dried over $MgSO_4$, the solvent was evaporated and crude product was purified by column chromatography (Et_2O : Hexanes 1 : 1). Yield **22** % (0.45 g), (mixture of *d,l*- and *meso*-forms in ratio ~ 1 : 5). ^{1}H NMR: δ 7.45-7.41 (m, 8H), 7.27-7.24 (m, 6H), 3.26-3.16 (m, 0.7H), 3.11-3.02 (m, 2H), 2.14-1.97 (m, 1.8H), 1.77-1.34 (m, 0.7H), 0.80 (t, *J* = 7.4 Hz, 2.3 H), 0.66 (t, *J* = 7.2 Hz, 6H). ^{13}C NMR: δ 129.0, 128.9, 128.8, 128.8, 128.7, 128.6, 48.8, 45.8, 36.6, 36.5, 31.9, 31.3, 11.7, 11.3 (mixture of *d,l*- and *meso*-forms). Anal. Calcd for $C_{23}H_{24}N_4S_2$: C, 65.68, H, 5.75, N, 13.32. Found: C, 65.41; H, 5.85; N, 13.18.

Heating the reaction mixture for 20 min at 100-110° C gave a mixture of three compounds – **12a**, **12b**, **13b**, which were separated by double column purification.

5-[1-Ethyl-3-(4-biphenylyl-1,2,3-thiadiazol-5-yl)pentyl]-4-(4-biphenylyl-1,2,3-thiadiazole (12c). NaH (0.4 g, 16.7 mmol, 80 % suspension in oil) was added to 4-bi-phenyl-5-ethyl-1,2,3-thiadiazole (2 g, 7.5 mmol) in DMF (10 mL). The reaction mixture was heated for 5 min at 100 °C. EtOAc (30 mL) was added, the mixture was washed with water, the organic layer was dried over $MgSO_4$, evaporated and purified by column chromatography (Et_2O : Hex 1:1). Yield 25 % (0.5 g), mp 120 °C (decomp.) (mixture of *d,l*- and *meso*-form in ratio ~ 1 : 1.5). ^{1}H NMR: δ 7.72–7.62 (m, ArH), 3.48 (q, *J* = 6,8 Hz, 1H), 3.34 (q, *J* = 6.9 Hz, 1.5H), 2.09 (t, *J* = 7.3 Hz, 1H), 1.90 (t, *J* = 7.3 Hz, 1.5H), 1.35 (d, *J* = 6.7 Hz, 3H), 1.23 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR: δ 158.7, 158.4, 158.0, 142.0, 141.9, 140.1, 129.8, 129.7, 129.3, 129.1, 128.9, 127.8, 127.7, 127.5, 127.2, 127.1, 50.9, 50.1, 30.3, 29.9, 24.2, 23.7. Calcd for $C_{33}H_{28}N_4S_2$: C, 72.76; H 5.18; N, 10.28. Found: C, 71.74; H, 5.06; N, 10.27.

5-[1-Methyl-3-(4-propyl-1,2,3-thiadiazol-5-yl)butyl]-4-propyl-1,2,3-thiadiazole (12d). NaH (0.53 g, 17.6 mmol, 80 % suspension in oil) was added to 4-propyl-5-ethyl-1,2,3-thiadiazole (1.38 g, 8.8 mmol) in DMF (10 mL). The reaction mixture was stirred at rt for 12 h and then was heated for a short time at 100 °C. EtOAc (30 mL) was added, the mixture was washed with water, organic layer was dried over $MgSO_4$, evaporated and purified by column chromatography (Et_2O : Hexanes 1 : 1). Yield 21 % (0.3 g), oil. ^{1}H NMR: δ 3.18–2.98 (m, 2H), 2.89–2.68 (m, 3H), 2.51–2.40 (m, 1H), 2.08–1.68 (m, 6H), 1.34 (t, *J* = 7.3 Hz, 6H), 0.99 (t, *J* = 7.3 Hz, 3H), 0.92 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR: δ 159.6, 159.4, 156.8, 156.5, 49.9, 49.8, 30.0, 29.7, 28.9, 28.7, 24.3, 23.8, 23.2, 22.9, 13.8, 13.7. Anal. Calcd for $C_{15}H_{24}N_4S_2$: C, 55.52; H 7.45; N, 17.27. Found: C, 56,21; H, 7.55; N, 16.81.

1,4-Dimethyl-3,6-bis[(*E*)-phenylmethylidene]-2,5-dithiabicyclo[2.2.1]heptane (13a). NaH (0.4 g, 16.7 mmol, 80 % suspension in oil) was added to 4-phenyl-5-ethyl-1,2,3-thiadiazole (1.5 g, 7.9 mmol) in DMF (10 mL). The reaction mixture was heated for 15 min at 100 °C. The completion of the reaction was monitored by TLC. EtOAc (30 mL) was added, the mixture was washed with water, the organic layer was dried over $MgSO_4$, evaporated and purified by column chromatography (EtOAc : Hexanes 1 : 10). Yield 20 %, mp 114 °C, ^{1}H NMR: δ 7.40–7.25 (m, 8H), 7.16 (t, *J* = 7.2 Hz, 2H), 6.46 (s, 2H), 2.26 (s, 2H), 1.96 (s, 6H). ^{13}C NMR: δ 147.7, 136.7, 128.3, 128.0, 126.4, 113.7, 64.2, 60.9, 18.8. Anal. Calcd for $C_{21}H_{20}S$: C, 74.95, H, 5.99. Found: C, 73.76, H, 6.29.

Crystal data for **13a**: $C_{21}H_{20}S_2$, FW 336.49, monoclinic, space group $P2_1/n$, *a* = 10.664(3), *b* = 8.703(2), *c* = 19.273(5) Å, β = 100.589(4) °, V = 1758.2(8) Å^3, F(000) = 712, Z = 4, T = -105 °C, μ (MoKα) = 0.300 mm^{-1}, D_{calcd} = 1.271 g.cm^{-3}, crystal size 0.52 x 0.47 x 0.26 mm, $2\theta_{max}$ 53° (CCD area detector, MoKα radiation, 98.9% completeness), wR(F^2) = 0.0832 (all 3583 data), R = 0.0303 (3053 data with I > 2σI).

1,4-Diethyl-3,6-bis[(*E*)-phenylmethylidene]-2,5-dithiabicyclo[2.2.1]heptane (13b). The procedure is similar to **13a**, oil. ^{1}H NMR: δ 7.38 (d, *J* = 7.6 Hz, 4H), 7.30 (t, *J* = 7.9 Hz, 4H), 7.13 (t, *J* = 7.3 Hz, 2H), 6.42 (s, 2H), 2.32 (t, *J* = 7.0 Hz, 4H), 2.15 (s, 2H), 1.22 (t, *J* = 7.4 Hz, 6H). ^{13}C NMR: δ 146.5, 136.9, 128.3, 128.0, 126.2, 113.9, 68.8, 53.4, 24.8, 10.6. Anal. Calcd for $C_{23}H_{24}S_2$: C, 76.48; H, 7.16. Found: C, 76.57; H, 6.73.

***N*,*N*-Dimethyl-2-phenylethanethioamide (14a).** A mixture of **2c** (0.5 g, 2.6 mmol) and sodium hydride (0.22 g, 9.2 mmol, 60 % suspension in mineral oil) in dry DMF (7 mL) was stirred at rt for 48 h. EtOAc (20 ml) was added and the reaction mixture was washed with water (3 x 20 mL). The organic layer was dried over $MgSO_4$, the solvent was evaporated and the residue was purified twice by column chromatography (EtOAc: Hexanes 1 : 1). Yield 47 % (0.18 g), oil. ^{1}H NMR: δ 7.34–7.26 (m, 5H), 4.32 (s, 2H), 3.50 (s, 3H), 3.20 (s, 3H). ^{13}C NMR: δ 200.5, 129.1, 129.0, 128.9, 128.8, 128.0, 126.9, 50.9, 44.8, 42.2. GCMS Calcd for $C_{10}H_{13}NS$: 179. Found: 179.

2-(4-Biphenylyl)-*N*,*N*-dimethylethanethioamide (14b). The procedure is similar to **14a**. The reaction mixture was heated for 20 min. Starting material (~30 %) and **14b** (32 %), yellow crystals, mp 114 °C, were isolated. ^{1}H NMR: δ 7.58–7.33 (m, 9H), 4.35 (s, 2H), 3.51 (s, 3H), 3.24 (s, 3H). ^{13}C NMR: δ 200.5, 140.6, 139.8, 134.7, 129.0, 128.7, 128.5, 127.4, 127.2, 126.9, 50.5, 44.8, 42.3. Anal. Calcd for $C_{16}H_{17}NS$: C, 75.25, H, 6.71, N, 5.48. Found: C, 74.27, H, 6.62, N, 5.47.

(3,4,6-Triphenyl-3,4-dihydro-2H-thiopyran-2-ylidene)-methanethiol (15). Sodium hydride (0.18 g, 7.6 mmol, 60 % suspension in mineral oil) was added to 4-benzyl-5-phenyl-1,2,3-thiadiazole (1.5 g, 4.1 mmol) in DMF (25 mL). The reaction mixture was heated for 2 min at 100 °C and stirred overnight. EtOAc (20 ml) was added and the reaction mixture was washed with water (3 x 20 mL). The organic layer was dried over $MgSO_4$, the solvent was evaporated and the residue was twice purified by column chromatography (EtOAc: Hexanes 1 : 10). Yield 22 % (0.3 g), white crystals, mp 130–131 °C. ^{1}H NMR: δ 7.58 (d, *J* = 1.8 Hz, 1H), 7.55 (dd, *J* =

1.2, 1.2 Hz, 1H), 7.02–7.38 (m, 18H), 6.38 (br s, 1H), 6.34 (d, *J* = 6.7 Hz, 1H), 4.11 (dd, *J* = 4.9, 1.7 Hz, 1H); 3.91 (s, 1H). ^{13}C NMR: δ 142.9, 142.0, 140.1, 138.7, 134.6, 129.1, 128.5, 128.4, 128.4, 128.3, 128.2, 128.0, 127.7, 127.0, 126.9, 126.7, 125.3, 118.8, 47.5, 46.6. Anal. Calcd for $C_{30}H_{24}S_2$: C, 80.31; H, 5.39. Found: C, 79.69; H, 5.79.

Crystal data for **15**: $C_{30}H_{24}S_2$, FW 448.61, monoclinic, space group $P2_1/c$, *a* = 12.143(5), *b* = 7.212(3), *c* = 27.039(11) Å, β = 99.440(7) °, V = 2336(2) Å^3, F(000) = 944, Z = 4, T = -105 °C, μ (MoKα) = 0.244 mm^{-1}, D_{calcd} = 1.276 g.cm^{-3}, crystal size 0.43 x 0.16 x 0.15 mm, $2\theta_{max}$ 50° (CCD area detector, MoKα radiation, 99.9% completeness), wR(F^2) = 0.0889 (all 4122 data), R = 0.0370 (3037 data with I > 2σI).

Supporting Information available online.

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