

## NOVEL TRIFLUOROMETHYLATED SPIRO-1,3,4-THIADIAZOLES VIA (3+2)-CYCLOADDITIONS OF 2,3-DIPHENYLCYCLOPROPENETHIONE WITH SELECTED IN SITU-GENERATED NITRILE IMINES DERIVED FROM TRIFLUOROACETONITRILE

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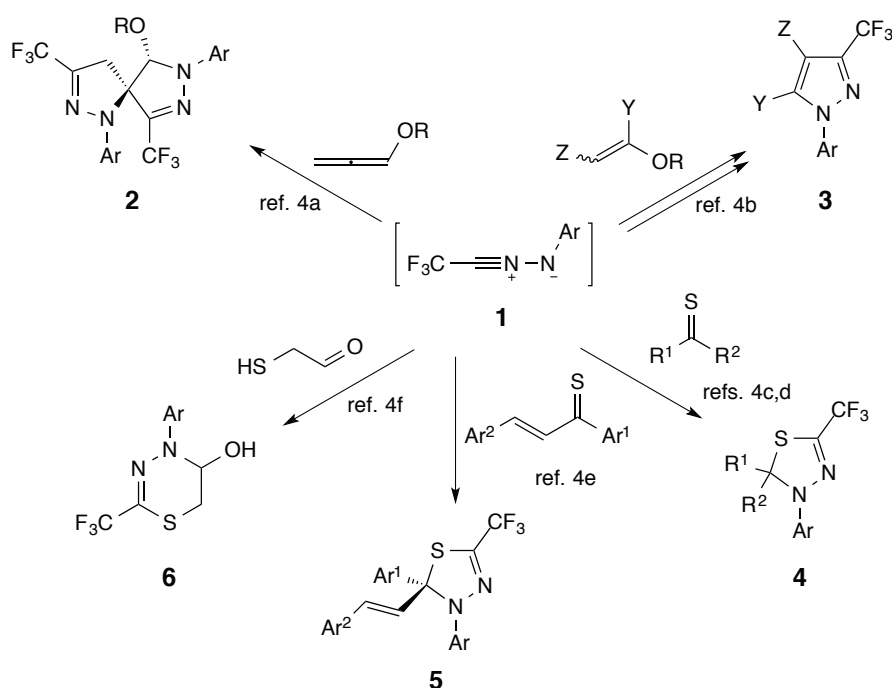
Dedicated to Professor Dr. Kaoru Fuji on the occasion of his 80th birthday

**Abstract** – The in situ-generated N-aryl nitrile imines derived from trifluoroacetonitrile react efficiently with 2,3-diphenylcyclopropenethione to give spirocyclic 1,3,4-thiadiazole derivatives as products of a regio- and chemoselective (3+2)-cycloaddition in good to excellent yields. A stepwise mechanism via initial nucleophilic attack of the S-atom onto the electrophilic C-atom of the electron-deficient 1,3-dipole leading to a zwitterionic intermediate is postulated to explain these formal (3+2)-cycloaddition reactions. The presence of the CF<sub>3</sub> group is necessary to activate the nitrile imine for the efficient trapping of the cyclopropenethione. These are the first examples of a successful reaction of this C=S dipolarophile affording 1,3,4-thiadiazoles as formal (3+2)-cycloadducts.

### INTRODUCTION

One of the most efficient and convenient methods for the synthesis of five-membered heterocyclic compounds is the 1,3-dipolar cycloaddition reaction ((3+2)-cycloaddition reaction, Huisgen reaction).<sup>2</sup> For example, nitrile imines as propargyl-type 1,3-dipoles have frequently been used for the preparation of diverse N-heterocycles.<sup>3</sup> In our recent studies we have shown that the reactions of trifluoromethyl-substituted nitrile imines **1** with C=C and C=S dipolarophiles open access to most

attractive trifluoromethylated N-heterocycles<sup>4</sup> (Scheme 1). Whereas spirobipyrazolines **2** were obtained via double (3+2)-cycloaddition with alkoxyallenes<sup>4a</sup> (for a similar study with allenates and non-fluorinated nitrile imines see ref.<sup>5</sup>), 3-trifluoromethylpyrazoles **3** were formed via a domino cycloaddition/elimination process with enol ethers.<sup>4b</sup> Related studies on reactions of **1** with diverse C=C dipolarophiles and acetylenes have been reported previously by Tanaka and coworkers,<sup>6</sup> and more recently, the cycloaddition with fullerene C<sub>60</sub> was published.<sup>7</sup> The group of Tanaka also described the first cycloadditions of **1** with heterodipolarophiles, i.e. with an isothiocyanate to give 2-methylimino-5-trifluoromethyl-1,3,4-thiadiazoline and with *N,N*-dimethylcyanamide yielding *N,N*-dimethyl-1-phenyl-3-trifluoromethyl-1*H*-1,2,4-triazol-5-amine, respectively.<sup>8</sup> Furthermore, the reaction with the C=N bond of a diazepine derivative led to a 1*H*-1,2,4-triazolo[4,3-*d*][1,4]diazepine.<sup>9</sup>

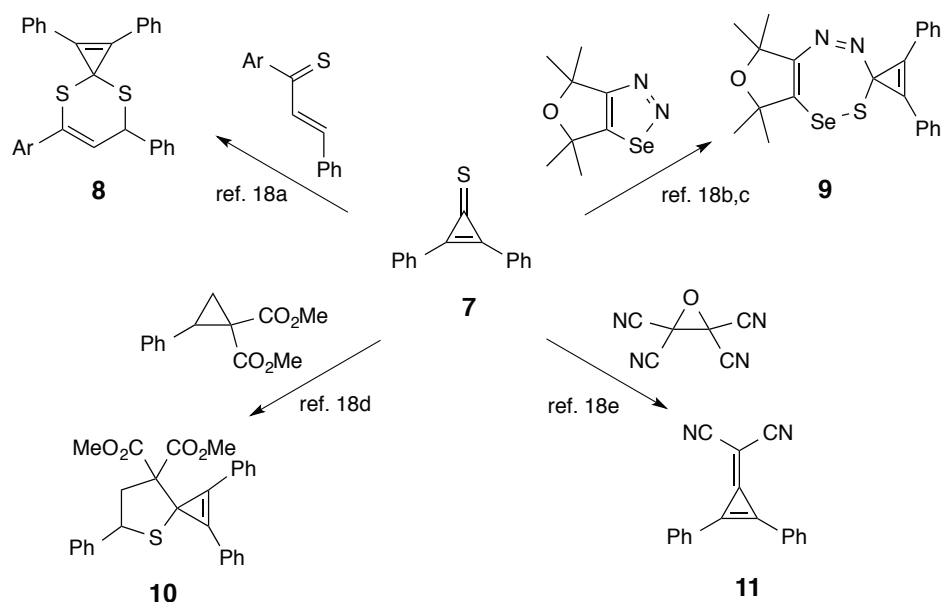


**Scheme 1.** (3+2)-Cycloaddition reactions of trifluoromethylated nitrile imines **1** with alkoxyallenes, enol ethers, and thioketones and (3+3)-annulation with mercaptoacetaldehyde

Within our studies of reactions with thioketones as versatile synthons for the preparation of sulfur-containing heterocycles,<sup>10</sup> 5-trifluoromethyl-2,3-dihydro-1,3,4-thiadiazoles of type **4** and **5** were prepared via (3+2)-cycloaddition of **1** with diarylthioacetones,<sup>4c</sup> cycloaliphatic thioketones,<sup>4d</sup> and thiochalcones,<sup>4e</sup> respectively (Scheme 1). Very recently, we reported that trapping of **1** with mercaptoacetaldehyde leads to 5,6-dihydro-1,3,4-thiadiazine-5-ols **6** via a two-step (3+3)-annulation.<sup>4f</sup> Several reactions of the title 2,3-diphenylcyclopropenethione (**7**) with nucleophilic reagents like enamines,<sup>11</sup> ketene acetals,<sup>12</sup> imines,<sup>13</sup> and other N-nucleophiles<sup>14</sup> have been reported to proceed via a

cascade of steps including nucleophilic addition at C(1) or C(2) and ring opening to give, in most cases, heterocyclic thiones. The reaction with electrophiles such as dimethyl acetylenedicarboxylate also occur via cleavage of the three-membered ring leading to open-chain products,<sup>15</sup> whereas those with an alkyl halide followed by the enolate of a 1,3-dicarbonyl compound yield 5-hydroxy-1-(alkylsulfanyl)cyclopentadienes.<sup>16</sup> Furthermore, a sulfonium ylide<sup>17a</sup> as well as a pyridinium methylene<sup>17b,c</sup> react with **7** in domino reactions via ring opening to form pyran derivatives.

On the other hand, a few reactions of **7** yielding products **8–11** with the preserved cyclopropene ring are known<sup>18</sup> (Scheme 2). The most relevant ones with respect to the following study are the thia-Diels-Alder reaction with thiochalcones to give 4,8-dithiaspiro[2.5]octa-1,5-dienes **8**<sup>18a</sup> and the AlCl<sub>3</sub>-catalyzed addition of dimethyl 2-phenylcyclopropane-1,1-dicarboxylate forming the spirocyclic tetrahydrothiophene derivative **10**.<sup>18d</sup>



**Scheme 2.** Reactions of **7** leading to products **8–11** with preserved cyclopropene ring

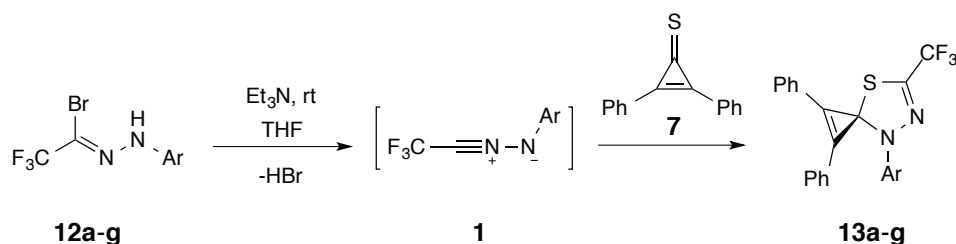
Notably, in contrast to numerous aryl, hetaryl, and cycloaliphatic thioketones known as ‘superdipolarophilic’ reagents,<sup>19</sup> thione **7** has never been studied in (3+2)-cycloaddition reactions with appropriate 1,3-dipoles. Nonetheless, in our earlier studies, a series of non-fluorinated nitrile imines was tested in the (3+2)-cycloadditions with diverse thioketones<sup>20</sup> as well as with heterocyclic thiones, such as rhodanine and 1,3-thiazole-5-thione derivatives,<sup>21</sup> and the respective 1,3,4-thiadiazole derivatives were obtained in good to excellent yields. The goal of the present study was to investigate reactions of **7** with electron-deficient trifluoromethylated nitrile imines of type **1**.

## RESULTS AND DISCUSSION

The fluorinated nitrile imines **1** are not isolable species but they are generated in situ from the corresponding trifluoroacetohydrazonoyl bromides **12** by treatment with an organic base such as triethylamine in CH<sub>2</sub>Cl<sub>2</sub> or THF solution.<sup>4c</sup> In the presence of suitable dipolarophiles, they are trapped to form the respective five-membered cycloadducts, but in the case of less reactive dipolarophiles, dimerization occurs to give, for example, isomeric tetrazine derivatives.<sup>22</sup>

In the present study, the test experiment was performed with **7** and the in situ-generated *para*-nitro-substituted nitrile imine **1a** (Scheme 3). The mixture of substrates **7** and **12a** in THF solution was treated with excess triethylamine at room temperature. After ca. 15 min, the reaction was complete and after filtration and evaporation of the solvent, the crude product was examined by <sup>1</sup>H NMR spectroscopy. The presence of two distinct doublets located at 7.20 and 7.93 ppm (*J* = 9.3 Hz) for the *para*-O<sub>2</sub>N-C<sub>6</sub>H<sub>4</sub> unit as well as two multiplets found at 7.54–7.58 and 7.76–7.77 ppm for 6 and 4 H-atoms, respectively, attributed to two spectroscopically equal phenyl rings indicated the formation of a sole intermolecular 1:1-adduct. After column chromatography, one fraction was isolated, and its spectroscopic properties confirmed the structure of the expected (3+2)-cycloadduct **13a** of **1a** and **7** acting as a C=S dipolarophile. In addition to the already described <sup>1</sup>H NMR signals, the <sup>13</sup>C NMR spectra revealed the presence of the diagnostic resonance for the spiro C-atom at 66.4 ppm and one signal for two sp<sup>2</sup>-hybridized C-atoms for the cyclopropene fragment at 117.7 ppm. Finally, the <sup>19</sup>F NMR spectrum evidenced the presence of one CF<sub>3</sub> group with the typical absorption at –64.59 ppm.

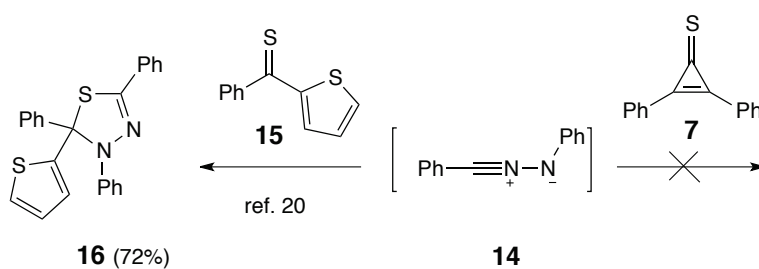
Based on this protocol, analogous reactions were carried out starting with differently substituted hydrazonoyl bromides **12b–g**, and in all cases the desired (3+2)-cycloadducts **13** were isolated as the major product in 64–86% yield. Notably, the type of substituent influenced both the yield and the stability of the obtained product. Thus, the presence of the electron-donating substituents resulted in lower yields, and for this reason, longer reaction times were needed for completion of the reaction. In contrast to **13a**, the 4-methoxy derivative **13g** suffered remarkable instability in CDCl<sub>3</sub> solution and underwent decomposition at room temperature.



	Ar	Yield (%)		Ar	Yield (%)
<b>a</b>	4-O <sub>2</sub> N-C <sub>6</sub> H <sub>4</sub>	95	<b>e</b>	C <sub>6</sub> H <sub>5</sub>	67
<b>b</b>	4-NC-C <sub>6</sub> H <sub>4</sub>	86	<b>f</b>	4-Me-C <sub>6</sub> H <sub>4</sub>	64
<b>c</b>	4-Br-C <sub>6</sub> H <sub>4</sub>	82	<b>g</b>	4-MeO-C <sub>6</sub> H <sub>4</sub>	65
<b>d</b>	4-F-C <sub>6</sub> H <sub>4</sub>	81			

**Scheme 3.** Reaction of in situ-generated nitrile imines **1** with 2,3-diphenylcyclopropenethione (**7**)

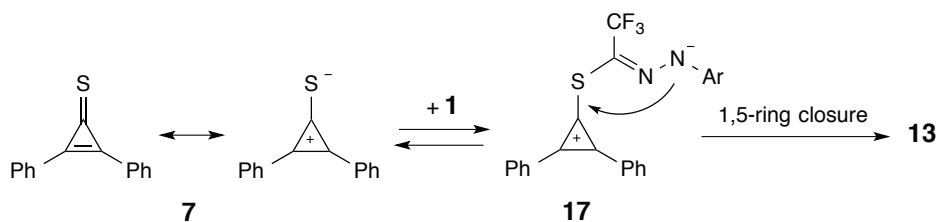
In order to learn more about reactivities in the studied system, two additional experiments were performed. In the first case, the reaction of **7** with diphenyl nitrile imine **14** was carried out under the same conditions (Scheme 4). In contrast to aryl hetaryl thioketones, e.g. **15** yielding **16**,<sup>20</sup> no formation of the (3+2)-cycloadduct onto the C=S bond was observed. In the second experiment, 2,3-diphenylcyclopropenone (O-analogue of **7**) was used for the attempted (3+2)-cycloaddition with **1a**. Also in that case no reaction was observed and the starting ketone was found in the crude mixture.



**Scheme 4.** Attempted reaction of diphenyl nitrile imine **14** with **7**

The (3+2)-cycloadditions with C=S dipolarophiles are known to follow either concerted or non-concerted pathways. In the latter case, diradical intermediates were postulated to explain the course of the reaction.<sup>23</sup> The requirement of a zwitterionic intermediate is a large energy difference between HOMO and LUMO orbitals of 1,3-dipole and dipolarophile. In the classical studies of Huisgen and coworkers, electron-rich thiocarbonyl S-methanides reacted with electron-deficient ethylenic dipolarophiles via a zwitterionic pathway.<sup>24</sup> In contrast, the reaction partners described in the present study can be considered as an

alternative system in which the 1,3-dipole is the electron-deficient component and the dipolarophile the electron-rich one. Therefore, the formation of the zwitterionic intermediate **17** is a plausible explanation for the proposed step-wise (3+2)-cycloaddition leading to the spirocyclic 1,3,4-thiadiazole derivatives **13** (Scheme 5). The obtained results demonstrate that **7** does not display the typical reactivity of thioketones, and instead of dipolarophilic reactivity, in the presence of an appropriate electrophile forms a new bond via nucleophilic attack via the S-atom.



**Scheme 5.** Proposed step-wise reaction mechanism for the formation of **13**

In addition, the reactivity of the nitrile imines **1** is tuned by the substituent in the aryl ring. The more electrophilic this group is, the higher electrophilicity is displayed by the 1,3-dipole as evidenced by the observed reaction times in the described series.

## CONCLUSIONS

The reactions of **7**, observed only with fluorinated nitrile imines **1**, show that it can behave as a C=S dipolarophile. This is the first report of a successful formal (3+2)-cycloaddition performed with this thioketone, and the obtained results demonstrate that a strongly electron-deficient 1,3-dipole is able to trap **7**. This observation allows formulating a stepwise reaction pathway, which is initiated by the nucleophilic attack of the sulfur atom of **7** onto the C-atom of the strongly electron-deficient 1,3-dipolar species **1**. The comparison of the reactivity of **1** and diphenyl nitrile imine **14** evidenced that the presence of the CF<sub>3</sub>-group is necessary to achieve sufficient electrophilicity to perform the formation of the (3+2)-cycloadduct. Moreover, the reaction occurs only with the nucleophilic C=S group of **7**, and the corresponding C=O derivative does not enter the analogous reaction. This difference confirms the assumption that the initiating step is the nucleophilic attack of the ‘dipolarophile’ leading to a zwitterionic intermediate. The described reactions open access to spiro-1,3,4-thiadiazoles functionalized with the CF<sub>3</sub> group at the C(2) atom of this heterocycle and extend possible applications of **7** in organic synthesis as it has mainly been explored as a Michael acceptor, e.g. for rapid labeling of biomolecules as described in a recent publication.<sup>25</sup>

## EXPERIMENTAL

**General remarks.** Reactions were carried out under argon in flame-dried flasks with addition of the

reactants by using syringes; subsequent manipulations were conducted in air. Products were purified by column chromatography on silica gel (230–400 mesh). If not stated otherwise, reported yields refer to analytically pure samples. Melting points were determined using a Mel-Temp II apparatus (*Aldrich*) or with a polarising optical microscope (*Opta-Tech*), and are uncorrected. NMR spectra were recorded on a Bruker Avance III instrument ( $^1\text{H}$  at 600 MHz,  $^{13}\text{C}$  at 151 MHz, and  $^{19}\text{F}$  at 565 MHz) in  $\text{CDCl}_3$  solutions. Chemical shifts ( $\delta$ ) given in ppm are reported relative to solvent residual peaks ( $^1\text{H}$  NMR:  $\delta = 7.26$  ppm [ $\text{CHCl}_3$ ],  $^{13}\text{C}$  NMR:  $\delta = 77.0$  ppm [ $\text{CDCl}_3$ ]) or to  $\text{CFCl}_3$  ( $\delta = 0.00$  ppm) used as external standard in  $^{19}\text{F}$  NMR measurements. Coupling constants ( $J$ ) are given in Hz. The multiplicity of the  $^{13}\text{C}$  signals was deduced from DEPT spectra supplemented with 2D (HMQC, HMBC) measurements. IR spectra were obtained with a Cary 630 FTIR (*Agilent Technologies*) instrument, in neat. The mass spectra were recorded on a Varian 500-MS LC Ion Trap using electrospray ionization (ESI);  $m/z$  (rel. %). Elemental analyses were obtained with a Vario EL III (*Elementar Analysensysteme GmbH*) instrument.

**Starting materials.** Used reagents and starting materials such as arylhydrazines, phenylacetic acid, fluoral hydrate, NBS, inorganic reagents, and solvents are commercially available and were used as received. THF was dried over sodium/benzophenone and freshly distilled before usage. Trifluoroacetaldehyde arylhydrazones were prepared by heating methanolic solutions of excess fluoral hydrate with the appropriate hydrazine in a closed ampoule at 75 °C overnight in the presence of freshly activated molecular sieves 4Å following our earlier report.<sup>26</sup> Hydrazonoyl bromides **12** were obtained by treatment of the above mentioned hydrazones with N-bromosuccinimide (NBS) in dry DMF as described.<sup>4c</sup> 2,3-Diphenylcyclopropenethione (**7**) was prepared by thionation of the respective ketone with Lawesson's Reagent (LR).<sup>27</sup> The latter 2,3-diphenylcyclopropenone was obtained in a three step procedure starting with phenylacetic acid, following the literature protocol.<sup>28</sup>

**Synthesis of spirocyclic thiadiazoles 13a–13g – general procedure.** To a mixture of the respective hydrazonoyl bromide **12** (1.05 mmol) and 2,3-diphenylcyclopropenethione (**7**, 222 mg, 1.00 mmol) in dry THF (5.0 mL) was added dropwise excess  $\text{Et}_3\text{N}$  (0.6 mL) at 0 °C, and the resulting mixture was stirred at room temperature until the starting thione was fully consumed (TLC monitoring, 15–60 min). The precipitate triethylammonium bromide was filtered off, and the solvents were removed in vacuo. The resulting oil was purified by column chromatography (CC) on silica gel using petroleum ether/ $\text{CH}_2\text{Cl}_2$  mixture to give analytically pure products **13**.

*Spiro*-{[1,2-diphenylcyclopropene]-3,2'-[3'-(4-nitrophenyl)-5'-trifluoromethyl-2',3'-dihydro-1',3',4'-thiadiazole]} (**13a**). Reaction time: 15 min; CC petroleum ether/ $\text{CH}_2\text{Cl}_2$  (2:1), yield: 431 mg (95%). Yellow solid, mp 129–131 °C.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.20 ( $d_{br}$ ,  $J \approx 9.3$  Hz, 2 arom. H),

7.54–7.58, 7.76–7.77 (2m, 6 H, 4 H, 2 Ph), 7.93 ( $d_{br}$ ,  $J \approx 9.3$  Hz, 2 arom. H) ppm.  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 151 MHz):  $\delta$  66.4 (s, spiro-C), 117.7 (s, 2 C, cProp), 118.6 (d, 2  $\text{CH}_{\text{arom}}$ ), 119.6 (q,  $^1J_{\text{C,F}} = 271.4$  Hz,  $\text{CF}_3$ ), 124.8 (s, 2  $\text{C}_{\text{arom}}$ , 2 Ph), 124.8 (d, 2  $\text{CH}_{\text{arom}}$ ), 129.7, 130.6, 131.5 (3d, 10  $\text{CH}_{\text{arom}}$ , 2 Ph), 136.9 (q,  $^2J_{\text{C,F}} = 40.7$  Hz, C(5')), 142.9, 147.0 (2s, 2  $\text{C}_{\text{arom}}$ ) ppm.  $^{19}\text{F}$  NMR ( $\text{CDCl}_3$ , 565 MHz):  $\delta$  -64.59 (s,  $\text{CF}_3$ ) ppm. IR (neat):  $\nu$  1590, 1566, 1511, 1340, 1264, 1184, 1137, 1027, 690  $\text{cm}^{-1}$ . ESI-MS ( $m/z$ ): 476.2 (51,  $[\text{M}+\text{Na}]^+$ ), 454.2 (100,  $[\text{M}+\text{H}]^+$ ). Anal. Calcd for  $\text{C}_{23}\text{H}_{14}\text{F}_3\text{N}_3\text{O}_2\text{S}$  (453.44): C 60.92, H 3.11, N 9.27, S 7.07. Found: C 61.11, H 3.22, N 9.29, S 7.09.

4-[Spiro-(1',2'-diphenylcyclopropene)-3',2''-(5''-trifluoromethyl-2'',3''-dihydro-1'',3'',4''-thiadiazol-3''-yl)]benzotrile (**13b**). Reaction time: 15 min; CC petroleum ether/ $\text{CH}_2\text{Cl}_2$  (2:1), yield: 373 mg (86%). Yellow solid, mp 124–126 °C.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.17 ( $d_{br}$ ,  $J \approx 8.8$  Hz, 2 arom. H), 7.33 ( $d_{br}$ ,  $J \approx 8.8$  Hz, 2 arom. H), 7.52–7.58, 7.74–7.75 (2m, 6 H, 4 H, 2 Ph) ppm.  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 151 MHz):  $\delta$  66.7 (s, spiro-C), 106.3 (s, CN), 117.7 (s, 2 C, cProp), 118.9 (s,  $\text{C}_{\text{arom}}$ ), 119.7 (q,  $^1J_{\text{C,F}} = 271.4$  Hz,  $\text{CF}_3$ ), 119.7 (d, 2  $\text{CH}_{\text{arom}}$ ), 124.9 (s, 2  $\text{C}_{\text{arom}}$ , 2 Ph), 129.6, 130.6, 131.4 (3d, 10  $\text{CH}_{\text{arom}}$ , 2 Ph), 132.9 (d, 2  $\text{CH}_{\text{arom}}$ ), 136.2 (q,  $^2J_{\text{C,F}} = 40.6$  Hz, C(5'')), 145.2 (s,  $\text{C}_{\text{arom}}$ ) ppm.  $^{19}\text{F}$  NMR ( $\text{CDCl}_3$ , 565 MHz):  $\delta$  -64.56 (s,  $\text{CF}_3$ ) ppm. IR (neat):  $\nu$  1603, 1556, 1498, 1264, 1197, 1136, 1029, 839, 688  $\text{cm}^{-1}$ . ESI-MS ( $m/z$ ): 434.2 (100,  $[\text{M}+\text{H}]^+$ ). Anal. Calcd for  $\text{C}_{24}\text{H}_{14}\text{F}_3\text{N}_3\text{S}$  (433.45): C 66.50, H 3.26, N 9.69, S 7.40. Found: C 66.40, H 3.41, N 9.78, S 7.15.

Spiro- $\{[1,2\text{-diphenylcyclopropene}]-3,2'\text{-}[3'\text{-(4-bromophenyl)-5'-trifluoromethyl-2',3'-dihydro-1',3',4'\text{-thiadiazole}]\}$  (**13c**). Reaction time: 30 min; CC petroleum ether/ $\text{CH}_2\text{Cl}_2$  (4:1), yield: 400 mg (82%). Pale orange solid, mp 97–99 °C.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ ):  $\delta$  6.95 ( $d_{br}$ ,  $J \approx 8.8$  Hz, 2 arom. H), 7.15 ( $d_{br}$ ,  $J \approx 8.8$  Hz, 2 arom. H), 7.49–7.55, 7.72–7.74 (2m, 6 H, 4 H, 2 Ph) ppm.  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 151 MHz):  $\delta$  68.2 (s, spiro-C), 117.8 (s, C-Br), 118.0 (s, 2 C, cProp), 119.9 (q,  $^1J_{\text{C,F}} = 270.8$  Hz,  $\text{CF}_3$ ), 123.4 (d, 2  $\text{CH}_{\text{arom}}$ ), 125.2 (s, 2  $\text{C}_{\text{arom}}$ , 2 Ph), 129.4, 130.6, 131.0 (3d, 10  $\text{CH}_{\text{arom}}$ , 2 Ph), 131.7 (d, 2  $\text{CH}_{\text{arom}}$ ), 134.6 (q,  $^2J_{\text{C,F}} = 40.2$  Hz, C(5')), 140.2 (s,  $\text{C}_{\text{arom}}$ ) ppm.  $^{19}\text{F}$  NMR ( $\text{CDCl}_3$ , 565 MHz):  $\delta$  -64.35 (s,  $\text{CF}_3$ ) ppm. IR (neat):  $\nu$  1556, 1487, 1329, 1262, 1191, 1133, 1027, 826, 686  $\text{cm}^{-1}$ . (-)-ESI-MS ( $m/z$ ): 487.1 (99,  $[\text{M}\{^{81}\text{Br}\}-\text{H}]^-$ ), 485.1 (100,  $[\text{M}\{^{79}\text{Br}\}-\text{H}]^-$ ). Anal. Calcd for  $\text{C}_{23}\text{H}_{14}\text{BrF}_3\text{N}_2\text{S}$  (487.33): C 56.69, H 2.90, N 5.75, S 6.58. Found: C 56.55, H 3.04, N 5.76, S 6.79.

Spiro- $\{[1,2\text{-diphenylcyclopropene}]-3,2'\text{-}[3'\text{-(4-fluorophenyl)-5'-trifluoromethyl-2',3'-dihydro-1',3',4'\text{-thiadiazole}]\}$  (**13d**). Reaction time: 30 min; CC petroleum ether/ $\text{CH}_2\text{Cl}_2$  (4:1), yield: 345 mg (81%). Yellow solid, mp 131–133 °C.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ ):  $\delta$  6.72–6.75 (m, 2 arom. H), 7.01–7.04 (m, 2



arom. H), 7.48–7.55, 7.71–7.74 (2*m*, 6 H, 4 H, 2 Ph) ppm. <sup>13</sup>C NMR (CDCl<sub>3</sub>, 151 MHz): δ 69.0 (*s*, spiro-C), 115.4 (*d*, <sup>2</sup>*J*<sub>C,F</sub> = 22.6 Hz, 2 CH<sub>arom</sub>), 118.0 (*s*, 2 C, *c*Prop), 120.0 (*q*, <sup>1</sup>*J*<sub>C,F</sub> = 270.7 Hz, CF<sub>3</sub>), 124.3 (*d*, <sup>3</sup>*J*<sub>C,F</sub> = 8.4 Hz, 2 CH<sub>arom</sub>), 125.3 (*s*, 2 C<sub>arom</sub>, 2 Ph), 129.3, 130.6, 130.9 (3*d*, 10 CH<sub>arom</sub>, 2 Ph), 134.2 (*q*, <sup>2</sup>*J*<sub>C,F</sub> = 40.3 Hz, C(5')), 137.0 (*d*, <sup>4</sup>*J*<sub>C,F</sub> = 2.7 Hz, C<sub>arom</sub>), 160.2 (*d*, <sup>1</sup>*J*<sub>C,F</sub> = 244.4 Hz, C–F) ppm. <sup>19</sup>F NMR (CDCl<sub>3</sub>, 565 MHz): δ –64.30 (*s*, CF<sub>3</sub>), –117.23 (*m*, Ar–F) ppm. IR (neat): ν 1566, 1504, 1355, 1330, 1262, 1183, 1129, 1027, 835, 751, 682 cm<sup>-1</sup>. ESI-MS (*m/z*): 427.2 (100, [M+H]<sup>+</sup>). Anal. Calcd for C<sub>23</sub>H<sub>14</sub>F<sub>4</sub>N<sub>2</sub>S (426.43): C 64.78, H 3.31, N 6.57, S 7.52. Found: C 64.69, H 3.31, N 6.71, S 7.39.

*Spiro-[(1,2-diphenylcyclopropene)-3,2'-(3'-phenyl-5'-trifluoromethyl-2',3'-dihydro-1',3',4'-thiadiazole)]* (**13e**). Reaction time: 60 min; CC petroleum ether/CH<sub>2</sub>Cl<sub>2</sub> (9:1), yield: 274 mg (67%). Yellow solid, mp 104–107 °C. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>): δ 6.91–6.94, 7.03–7.08, 7.48–7.53, 7.73–7.74 (4*m*, 1 H, 4 H, 6 H, 4 H, 3 Ph) ppm. <sup>13</sup>C NMR (CDCl<sub>3</sub>, 151 MHz): δ 68.7 (*s*, spiro-C), 118.1 (*s*, 2 C, *c*Prop), 120.1 (*q*, <sup>1</sup>*J*<sub>C,F</sub> = 270.6 Hz, CF<sub>3</sub>), 122.2 (*d*, 2 CH<sub>arom</sub>, Ph), 124.9 (*d*, CH<sub>arom</sub>, Ph), 125.5 (*s*, 2 C<sub>arom</sub>, 2 Ph), 128.6 (*d*, 2 CH<sub>arom</sub>, Ph), 129.3, 130.6, 130.8 (3*d*, 10 CH<sub>arom</sub>, 2 Ph), 133.7 (*q*, <sup>2</sup>*J*<sub>C,F</sub> = 40.1 Hz, C(5')), 141.1 (*s*, C<sub>arom</sub>, Ph) ppm. <sup>19</sup>F NMR (CDCl<sub>3</sub>, 565 MHz): δ –64.30 (*s*, CF<sub>3</sub>) ppm. IR (neat): ν 1556, 1491, 1254, 1183, 1172, 1133, 1021, 749, 680 cm<sup>-1</sup>. ESI-MS (*m/z*): 409.2 (100, [M+H]<sup>+</sup>). Anal. Calcd for C<sub>23</sub>H<sub>15</sub>F<sub>3</sub>N<sub>2</sub>S (408.44): C 67.63, H 3.70, N 6.86, S 7.85. Found: C 67.40, H 3.77, N 6.96, S 7.61.

*Spiro-[[1,2-diphenylcyclopropene]-3,2'-[3'-(4-tolyl)-5'-trifluoromethyl-2',3'-dihydro-1',3',4'-thiadiazole]]* (**13f**). Reaction time: 60 min; CC petroleum ether/CH<sub>2</sub>Cl<sub>2</sub> (9:1), yield: 270 mg (64%). Yellow solid, mp 110–112 °C. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>): δ 2.14 (*s*, 3 H, Me), 6.85, 6.98 (2*d*<sub>br</sub>, *J* = 8.3 Hz, 2 H each, Tol), 7.47–7.54, 7.73–7.77 (2*m*, 6 H, 4 H, 2 Ph) ppm. <sup>13</sup>C NMR (CDCl<sub>3</sub>, 151 MHz): δ 20.7 (*q*, Me), 68.9 (*s*, spiro-C), 118.2 (*s*, 2 C, *c*Prop), 120.1 (*q*, <sup>1</sup>*J*<sub>C,F</sub> = 270.4 Hz, CF<sub>3</sub>), 122.5 (*d*, 2 CH<sub>arom</sub>, Tol), 125.5 (*s*, 2 C<sub>arom</sub>, 2 Ph), 129.22 (*d*, 4 CH<sub>arom</sub>, 2 Ph), 129.23 (*d*, 2 CH<sub>arom</sub>, Tol), 130.6, 130.7 (2*d*, 6 CH<sub>arom</sub>, 2 Ph), 133.1 (*q*, <sup>2</sup>*J*<sub>C,F</sub> = 40.1 Hz, C(5')), 134.7, 138.4 (2*s*, 2 C<sub>arom</sub>, Tol) ppm. <sup>19</sup>F NMR (CDCl<sub>3</sub>, 565 MHz): δ –64.12 (*s*, CF<sub>3</sub>) ppm. IR (neat): ν 1508, 1448, 1329, 1262, 1128, 1027, 822, 751 cm<sup>-1</sup>. ESI-MS (*m/z*): 423.2 (100, [M+H]<sup>+</sup>). Anal. Calcd for C<sub>24</sub>H<sub>17</sub>F<sub>3</sub>N<sub>2</sub>S (422.46): C 68.23, H 4.06, N 6.63, S 7.59. Found: C 68.35, H 4.21, N 6.73, S 7.79.

*Spiro-[[1,2-diphenylcyclopropene]-3,2'-[3'-(4-methoxyphenyl)-5'-trifluoromethyl-2',3'-dihydro-1',3',4'-thiadiazole]]* (**13g**). Reaction time: 60 min; CC petroleum ether/CH<sub>2</sub>Cl<sub>2</sub> (4:1), yield: 285 mg (65%). Thick orange oil. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>): δ 3.63 (*s*, 3 H, OMe), 6.57 (*d*<sub>br</sub>, *J* = 9.0 Hz, 2 arom. H), 6.99 (*d*<sub>br</sub>, *J* = 9.0 Hz, 2 arom. H), 7.46–7.54, 7.72–7.75 (2*m*, 6 H, 4 H, 2 Ph) ppm. <sup>13</sup>C NMR (CDCl<sub>3</sub>, 151 MHz): δ 55.2 (*q*, OMe), 69.4 (*s*, spiro-C), 113.8 (*d*, 2 CH<sub>arom</sub>), 118.3 (*s*, 2 C, *c*Prop), 120.1 (*q*, <sup>1</sup>*J*<sub>C,F</sub> = 270.4 Hz,

CF<sub>3</sub>), 124.6 (*d*, 2 CH<sub>arom</sub>), 125.5 (*s*, 2 C<sub>arom</sub>, 2 Ph), 129.2, 130.6, 130.7 (3*d*, 10 CH<sub>arom</sub>, 2 Ph), 133.1 (*q*, <sup>2</sup>J<sub>C,F</sub> = 40.0 Hz, C(5')), 134.0, 157.3 (2*s*, 2 C<sub>arom</sub>) ppm. <sup>19</sup>F NMR (CDCl<sub>3</sub>, 565 MHz): δ -64.15 (*s*, CF<sub>3</sub>) ppm. (-)-ESI-MS (*m/z*): 437.2 (100, [M-H]<sup>-</sup>). IR (neat): ν 1508, 1355, 1241, 1127, 1023, 831, 758, 685 cm<sup>-1</sup>. Anal. Calcd for C<sub>24</sub>H<sub>17</sub>F<sub>3</sub>N<sub>2</sub>OS (438.46): C 65.74, H 3.91, N 6.39, S 7.31. Found: C 65.70, H 3.94, N 6.46, S 7.30.

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