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[3+2]-Cycloadditions of nitrilimines with heteroaryl thioketones

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ABSTRACT

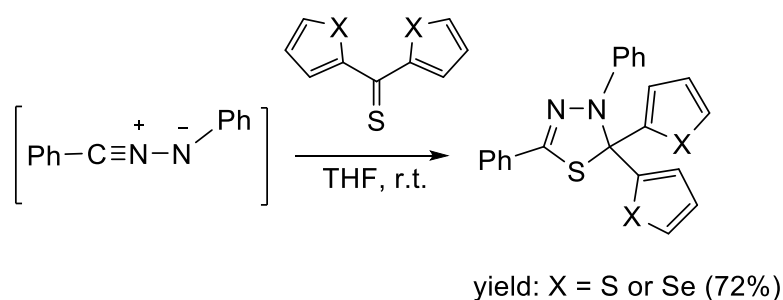
The in situ-generated nitrilimines are trapped efficiently with heteroaryl thioketones bearing thiophen-2-yl or selenophen-2-yl substituents. The exclusive products observed in these reactions are 2,3-dihydro-1,3,4-thiadiazoles formed via regioselective [3+2]-cycloaddition. Competitive head-to-tail dimerization of the intermediate 1,3-dipoles was not observed in any of the studies reactions.

KEYWORDS

[3+2]-Cycloadditions; nitrilimines; thioketones; 1,3,4-thiadiazoles; X-ray crystallography

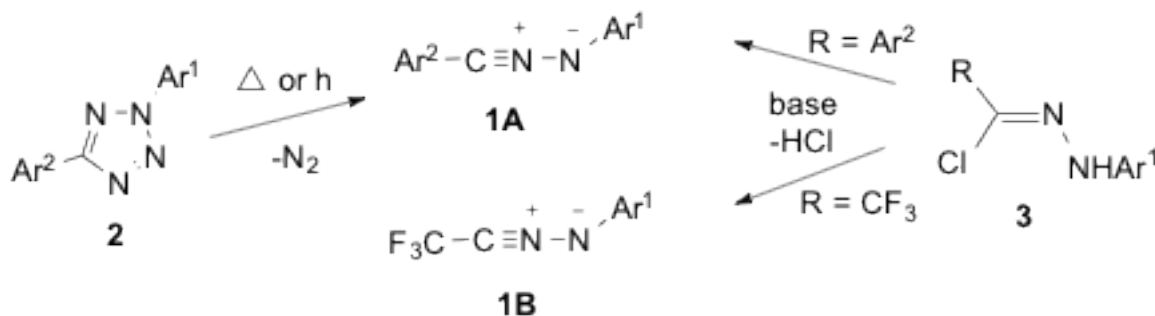
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Graphical abstract



1. Introduction

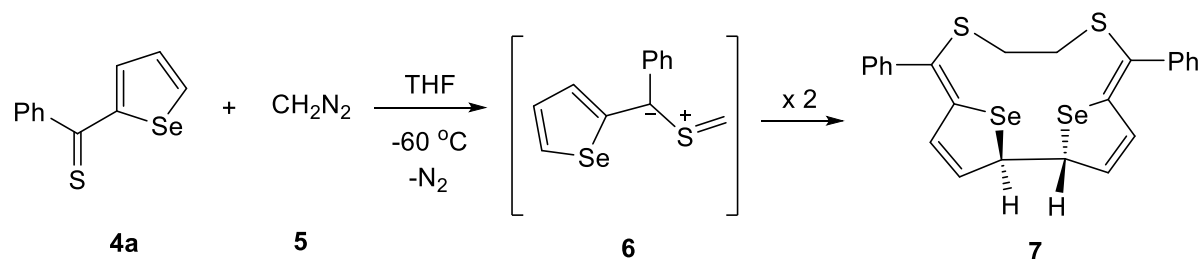
Nitrilimines **1** belong to the group of classical 1,3-dipoles widely applied in [3+2]-cycloadditions with diverse dipolarophiles, mainly activated ethenes, and acetylenes [1,2]. Synthetically important diarylnitrilimines **1A** are generated in situ by thermal or photolytical decomposition of 2,5-disubstituted tetrazoles **2** or by dehydrohalogenation of hydrazonoyl halides **3** in the presence of a base, e.g., triethylamine (TEA, Scheme 1). These reactive 1,3-dipoles have been characterized in a matrix at 12–85 K by UV and IR spectroscopy [3–5], and the structure of the sterically crowded *C,N*-ditritylnitrilimine was confirmed by X-ray crystallography [6]. Other relatively stable nitrilimines, bearing silyl or phosphorus substituents, are also known (e.g. [7–10]).



Scheme 1. Methods for generation of nitrilimines **1**.

Thioketones are known as ‘superdipolarophiles’ [11], and reactions of diarylnitrilimines **1A** with aromatic and cycloaliphatic representatives have been reported [12–15]. Moreover, other thiocarbonyl compounds were also used in cycloadditions with **1** [16–18]. In all cases, 2,3-dihydro-1,3,5-thiadiazoles were obtained in a regioselective manner. In a series of recent papers we reported on diverse cycloadditions using heteroaryl thioketones as dipolaro- and

dienophiles [19]. The studies showed that the presence of a heteroaryl substituent strongly modifies the reactivity of the thioketones. For example, the reaction of phenyl selenophen-2-yl thioketone (**4a**) with diazomethane (**5**) led to the 14-membered cyclodimer **7** of the intermediate thiocarbonyl *S*-methanide **6** via a biradical mechanism [20,21] (Scheme 2).



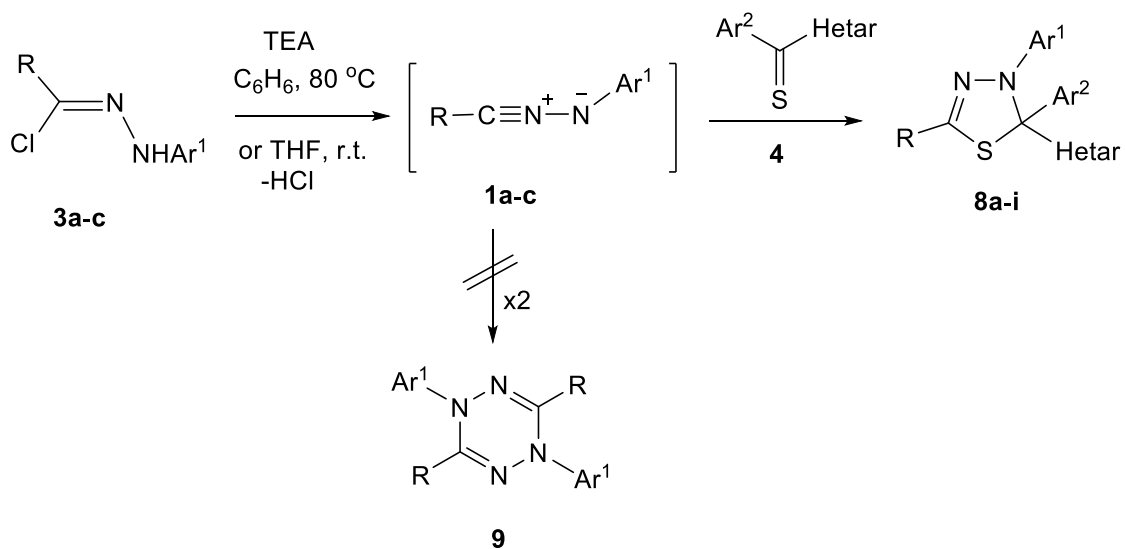
Scheme 2. Head-to-head dimerization of the selenophen-2-yl-substituted thiocarbonyl *S*-methanide **6**.

A very recent study demonstrated that in contrast to diarylnitrilimines **1A**, *N*-aryl-*C*-(trifluoromethyl)nitrilimines **1B** (Scheme 1), derived from trifluoroacetonitrile, react efficiently with thiochalcones as C=S dipolarophiles [22]. The same series of nitrilimines **1B** was used for the synthesis of trifluoromethyl-substituted 2,3-dihydro-1,3,4-thiadiazoles [23]. Considering the importance of these heterocycles [24,25], we have studied [3+2]-cycloadditions of heteroaryl thioketones with *C,N*-diphenyl-, *C*-acetyl-*N*-phenyl-, and *C*-ethoxycarbonyl-*N*-phenylnitrilimines (**1a–1c**).

2. Results and discussion

The reactions of the hydrazonoyl chlorides **3a–c** with heteroaryl thioketones **4** in the presence of an equimolar amount of TEA were performed either in boiling benzene or in THF at room temperature. Characteristically, the reaction times for diphenylnitrilimine (**1a**) were shorter than in the case of **1b** and **1c**. In general, the reactions in boiling benzene required 5–8 h, whereas the experiments in THF at room temperature were complete after 6 h for **1a** and 48 h in the cases of **1b** and **1c**. In a typical experiment with **1a** and phenyl selenophen-2-yl thioketone (**4a**) in THF, the green color of **4a** disappeared after 6 h. After typical workup by chromatography, the product formed was isolated as a yellow solid and characterized by means of spectroscopic methods. The ¹³C NMR spectrum revealed the presence of the expected signals at 118.8 and 153.0 ppm attributed to C(2) and C(5), respectively, of the 2,3-

dihydro-1,3,5-thiadiazole ring. The molecular formula $C_{24}H_{18}N_2SSe$ for the [3+2]-cycloadduct **8a** was confirmed by elemental analysis (Scheme 3).



Scheme 3. [3+2]-Cycloadditions of the in situ-generated nitrilimines **1** with heteroaryl thioketones **4**.

Table 1. Synthesis of 2,3-dihydro-1,3,4-thiadiazoles **8** via [3+2]-cycloadditions.

Hydrazonoyl Chloride		Heteroaryl ^a thioketone		Thiadiazole 8	Yield [%] ^b
3	R	4	Ar ²	Hetar	
a	Ph	a	Ph	Sel	a 76 ^c
a	Ph	b	Ph	Thi	b 72 ^d
a	Ph	c	Sel	Sel	c 73 ^c
a	Ph	d	Thi	Thi	d 71 ^d
b	MeCO	a	Ph	Sel	e 67 ^c
b	MeCO	b	Ph	Thi	f 66 ^c
b	MeCO	c	Sel	Sel	g 72 ^c
b	MeCO	d	Thi	Thi	h 72 ^d
c	EtOCO	d	Thi	Thi	i 72 ^d

^a Ph = Phenyl; Sel = Selenophen-2-yl; Thi = Thiophen-2-yl

^b Yield of isolated product

^c Reaction performed in THF at r.t.

^d Reaction performed in boiling benzene

Similarly, the additional reactions performed with nitrilimines **1a–c** and heteroaryl thioketones **4a–d** afforded 2,3-dihydro-1,3,4-thiadiazoles **8b–i** in 66–76% yield (Table 1). All of these products displayed similar spectroscopic data, which confirmed the structure **8**. In addition, the structures of **8d** and **8h** were unambiguously confirmed by X-ray crystallography (Figure 1).

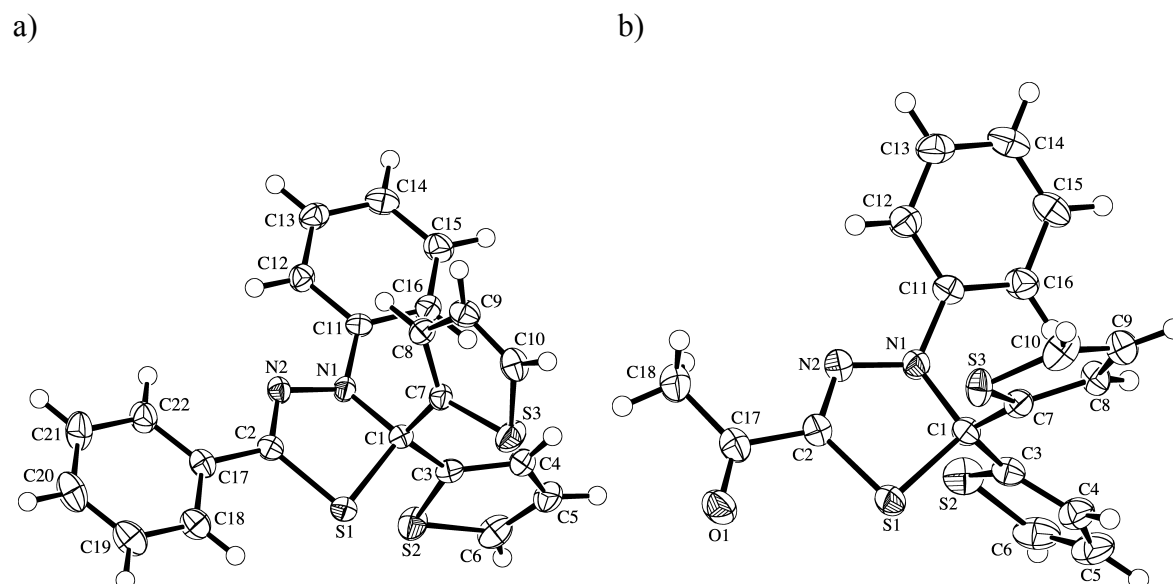


Figure 1. ORTEP plots [26] of the molecular structures of a) **8d** and b) one of the disordered conformations of **8h** (50 % probability ellipsoids; arbitrary numbering of the atoms).

The obtained products **8** were formed via regioselective [3+2]-cycloaddition of the initially generated nitrilimines **1** with thioketones **4** as dipolarophiles. In none of the studied cases were 1,3,4,6-tetrasubstituted 1,4-dihydro-1,2,4,5-tetrazines **9** observed, and this result demonstrated once more that heteroaryl thioketones are ‘superdipolarophilic’ agents. In reactions of **1a** with less reactive ethylenic or acetylenic dipolarophiles, the head-to-tail dimerization leading to **9** was reported as a process competitive with the [3+2]-cycloaddition [27,28].

In contrast to earlier reported formal [3+2]-cycloadditions of heteroaryl thioketones with thiocarbonyl *S*-methanides [29] or diazoalkanes [30], in which the sterically more crowded

1,3-dithiolanes were formed regioselectively, apparently, via an intermediate, delocalized diradical, the reactions with nitrilimines do not offer an experimental indication for a stepwise reaction mechanism. However, the structure of the obtained 1,3,4-thiadiazoles shows that also in this case, the postulated 1,5-diradical could be well stabilized as a likely intermediate within the delocalized system [23].

3. Conclusions

The study showed that heteroaryl thioketones are excellent trapping reagents for in situ-generated nitrilimines bearing phenyl, acetyl or ethoxycarbonyl groups at the C-atom. The 2,3-dihydro-1,3,4-thiadiazoles are formed in high yields in a regioselective manner, regardless of the type of substituents in the transient nitrilimines. In analogy to nitrilimines derived from trifluoroacetonitrile, the [3+2]-cycloadditions with heteroaryl thioketones occur without competitive dimerization of the nitrilimines used in this study.

4. Experimental design

4.1. General

Melting points were determined in a capillary using a Melt-Temp. II (*Aldrich*) apparatus, and they are uncorrected. The IR spectra were recorded on a Nexus FT-IR spectrophotometer as KBr pellets; absorptions in cm^{-1} . The ^1H and ^{13}C NMR spectra were measured in CDCl_3 solution on a Bruker Avance III instrument (600 and 150 MHz, resp.), using the solvent signal as reference. Chemical shifts (δ) are given in ppm and coupling constants J in Hz. The mass spectra were recorded on a Finnigan MAT-95 spectrometer. Elemental analyses were performed in the Microanalytical Laboratory of the Chemistry Faculty in Łódź or of the National Research Centre in Cairo. All crude mixtures were separated by chromatographic methods.

4.2. Starting materials

Aryl heteroaryl (**4a,b**) and diaryl thioketones (**4c,d**) were prepared following the literature procedures based on thionation of the corresponding ketones with Lawesson's reagent [31].

Hydrazonoyl chlorides **3a–c** were prepared either by reaction of the corresponding hydrazone with *N*-chlorosuccinimide-dimethyl sulfide complex according to the known general procedure [32] or by the reaction of aryl diazonium salts with α -chloro- β -ketoesters [33].

4.3. Reactions of thioketons **4** with hydrazonoyl chlorides **3** - General procedures

To a stirred solution of the corresponding thioketone **4** (1 mmol) in dry THF (5 mL), a solution of the appropriate hydrazonoyl chloride **3** (1 mmol) and 2.5 mL of triethylamine in 1 mL of dry THF was added dropwise at room temperature (r.t.) under an argon atmosphere. The resulting mixtures were kept at r.t. until the color of **4** disappeared completely. Triethylamine hydrochloride was filtered off and the solvent was evaporated under reduced pressure. The crude mixtures were purified chromatographically on silica gel using a mixture of petroleum ether with an increasing amount of dichloromethane. The obtained products **8** were additionally purified by crystallization from hexane or petroleum ether with a small amount of CH₂Cl₂.

In the alternative procedure (synthesis of **8b,d,h,i**), the reaction mixtures were refluxed in boiling dry benzene for 5–8 h. After completion of the reactions, the solvent was evaporated under reduced pressure and the obtained products were triturated with methanol to afford solid products (purified by crystallization from EtOH) or yellow-brown oils (purified by column chromatography (SiO₂), using the mixture AcOAEt/CH₂Cl₂ 1:9 as the eluent).

4.3.1. 2,3-Dihydro-2,3,5-triphenyl-2-(selenophen-2-yl)-1,3,4-thiadiazole (**8a**)

Yellow crystals; m.p. 147–149°C (hexane/CH₂Cl₂); yield: 340 mg (76%). ¹H NMR: 6.90–6.94 (*m*, 1CH_{arom}); 7.11–7.18 (*m*, 5CH_{arom}); 7.25 (*dd*, *J*_{H,H} = 3.8 Hz, *J*_{H,H} = 1.0 Hz, 1CH_{arom}); 7.36–7.45 (*m*, 6CH_{arom}); 7.74–7.79 (*m*, 4CH_{arom}); 8.05 (*dd*, *J*_{H,H} = 5.7 Hz, *J*_{H,H} = 1.0 Hz, 1CH_{arom}). ¹³C NMR: 90.3 (C(2)); 118.8, 121.9, 126.7, 127.8, 128.2, 128.3, 128.5, 128.6, 128.9, 129.5, 131.9, 134.0 (18CH_{arom}); 131.2, 141.7, 143.4, 153.0 (4C_{arom}, C=N). IR (KBr): 3063*m*, 3022*m*, 1594*s*, 1553*m*, 1492*s*, 1445*m*, 1328*s*, 1255*s*, 1236*s*, 1122*m*, 1065*m*, 967*s*, 742*s*, 698*s*, 685*s*. Anal. calcd for C₂₄H₁₈N₂SSe (445.44): C 64.71, H 4.07, N 6.29, S 7.20; found: C 64.72, H 4.04, N 6.31, S 7.37.

4.3.2. 2,3-Dihydro-2,3,5-triphenyl-2-(thiophen-2-yl)-1,3,4-thiadiazole (**8b**)

Yellow crystals; m.p. 136–138°C (petroleum ether/CH₂Cl₂); yield: 286 mg (72%). ¹H NMR: 6.76–6.79 (*m*, 2CH_{arom}); 6.95 (*dd*, *J*_{H,H} = 3.7 Hz, *J*_{H,H} = 1.1 Hz, 1CH_{arom}); 6.96–7.00 (*m*, 4CH_{arom}); 7.21 (*dd*, *J*_{H,H} = 5.1 Hz, *J*_{H,H} = 1.1 Hz, 1CH_{arom}); 7.24–7.31 (*m*, 6CH_{arom}); 7.60–7.64 (*m*, 4CH_{arom}). ¹³C NMR: 88.3 (C(2)); 118.6, 121.7, 126.2, 126.6, 127.6, 127.9, 128.1, 128.3, 128.4, 128.5, 129.4, 129.8 (18CH_{arom}); 131.2, 141.7, 141.78, 143.4, 145.6 (4C_{arom}, C=N). IR (KBr): 3079*m*, 3018*m*, 1595*s*, 1553*m*, 1496*vs*, 1448*m*, 1337*s*, 1325*s*, 1255*s*, 1236*s*, 1125*s*, 1068*m*, 967*s*, 821*m*, 739*s*, 720*s*, 685*s*. MS *m/z* (%): 398 [M⁺] (75), 391 (15), 377 (17), 365 (15), 145 (100), 102 (50). Anal. calcd for C₂₄H₁₈N₂S₂ (398.54): C 72.33, H 4.55, N 7.03, S 16.09; found: C 72.34, H 4.57, N 7.02, S 15.92.

4.3.3. 2,3-Dihydro-3,5-diphenyl-2,2-di(selenophen-2-yl)-1,3,4-thiadiazole (8c)

Yellow crystals; m.p. 115–117°C (petroleum ether/CH₂Cl₂); yield: 365 mg (73%). ¹H NMR: 6.98–7.00 (*m*, 1CH_{arom}); 7.14–7.19 (*m*, 4CH_{arom}); 7.25–7.27 (*m*, 2CH_{arom}); 7.34 (*dd*, *J*_{H,H} = 3.9 Hz, *J*_{H,H} = 1.0 Hz, 2CH_{arom}); 7.41–7.46 (*m*, 3CH_{arom}); 7.75–7.78 (*m*, 2CH_{arom}); 8.09 (*dd*, *J*_{H,H} = 5.7 Hz, *J*_{H,H} = 1.4 Hz, 2CH_{arom}). ¹³C NMR: 89.6 (C(2)); 120.7, 123.3, 126.8, 128.2, 128.7, 129.2, 129.7, 130.7, 133.8 (16CH_{arom}); 131.1, 142.4, 143.4, 153.2 (4C_{arom}, C=N). IR (KBr): 3056*m*, 3015*m*, 1594*s*, 1556*m*, 1489*s*, 1445*m*, 1318*s*, 1252*s*, 1239*s*, 1116*s*, 1059*m*, 960*m*, 875*m*, 758*s*, 745*s*, 701*s*, 691*s*, 682*s*. Anal. calcd for C₂₂H₁₆N₂SSe₂ (498.36): C 53.02, H 3.24, N 5.62, S 6.43; found: C 53.02, H 3.22, N 5.55, S 6.38.

4.3.4. 2,3-Dihydro-3,5-diphenyl-2,2-di(thiophen-2-yl)-1,3,4-thiadiazole (8d)

Yellow crystals; m.p. 119–121°C; yield: 287 mg (71%). ¹H NMR: 6.92–7.00 (*m*, 2CH_{arom}); 7.13–7.23 (*m*, 5CH_{arom}); 7.39 (*dd*, *J*_{H,H} = 4.9 Hz, *J*_{H,H} = 1.0 Hz, 1CH_{arom}); 7.42–7.46 (*m*, 2CH_{arom}); 7.77 (*d*, *J*_{H,H} = 6.7 Hz, 1CH_{arom}). ¹³C NMR: 86.1 (C(2)), 120.3, 123.1, 126.7, 126.8, 127.8, 128.2, 128.5, 128.7, 129.7 (16CH_{arom}); 131.2, 142.4, 143.4, 146.1 (4C_{arom}, C=N). IR (KBr): 3075*m*, 3018*m*, 1591*s*, 1559*m*, 1489*s*, 1448*m*, 1426*m*, 1328*s*, 1249*s*, 1236*s*, 1182*m*, 1122*s*, 1065*m*, 1036*m*, 960*s*, 878*m*, 843*m*, 739*s*, 701*vs*, 682*s*. MS *m/z* (%): 404 [M⁺] (100). Anal. calcd for C₂₂H₁₆N₂S₃ (404.57): C 65.31, H 3.99, N 6.92, S 23.78; found: C 65.20, H 4.17, N 6.91, S 23.80.

4.3.5. 1-[4,5-Dihydro-4,5-diphenyl-5-(selenophen-2-yl)-1,3,4-thiadiazol-2-yl]ethanone (8e)

Yellow-brown crystals; m.p. 110–112°C (hexane/CH₂Cl₂); yield: 275 mg (67%). ¹H NMR: 2.63 (s, CH₃); 7.00–7.04 (m, 1CH_{arom}); 7.12–7.18 (m, 5CH_{arom}); 7.21 (dd, *J*_{H,H} = 3.8 Hz, *J*_{H,H} = 1.0 Hz, 1CH_{arom}); 7.39–7.45 (m, 3CH_{arom}); 7.66–7.69 (m, 2CH_{arom}); 8.09 (dd, *J*_{H,H} = 5.8 Hz, *J*_{H,H} = 1.0 Hz, 1CH_{arom}). ¹³C NMR: 26.7 (CH₃); 91.8 (C(2')); 119.8, 123.9, 127.2, 128.4, 128.6, 128.7, 129.0, 132.3, 134.9 (13CH_{arom}); 141.6, 141.7, 142.1, 152.2 (3C_{arom}, C=N); 191.0 (C=O). IR (KBr): 3060m, 3031m, 1666vs (C=O), 1591s, 1527s, 1489s, 1439m, 1252vs, 1144vs, 1046s, 932s, 748s, 691s. Anal. calcd for C₂₀H₁₆N₂OSSe (411.38): C 58.39, H 3.92, N 6.81, S 7.79; found: C 58.40, H 3.93, N 6.82, S 7.87.

4.3.6. 1-[4,5-Dihydro-4,5-diphenyl-5-(thiophen-2-yl)-1,3,4-thiadiazol-2-yl]ethanone (8f)

Yellow crystals; m.p. 113–115°C (hexane/CH₂Cl₂); yield: 240 mg (66%). ¹H NMR: 2.61 (s, CH₃); 6.90 (dd, *J*_{H,H} = 5.0 Hz, *J*_{H,H} = 3.7 Hz, 1CH_{arom}); 6.98–7.02 (m, 1CH_{arom}); 7.06 (dd, *J*_{H,H} = 3.7 Hz, *J*_{H,H} = 1.1 Hz, 1CH_{arom}); 7.14–7.16 (m, 4CH_{arom}); 7.36 (dd, *J*_{H,H} = 5.0 Hz, *J*_{H,H} = 1.1 Hz, 1CH_{arom}); 7.37–7.46 (m, 3CH_{arom}); 7.63–7.65 (m, 2CH_{arom}). ¹³C NMR: 25.7 (CH₃); 89.8 (C(2')); 115.4, 119.6, 123.8, 126.5, 128.4, 128.6, 128.7, 129.5, 130.2 (13CH_{arom}); 141.6, 141.7, 142.2, 145.0 (3C_{arom} and C=N); 191.0 (C=O). IR (KBr): 3066m, 3031m, 1670vs (C=O), 1591s, 1530s, 1492s, 1442m, 1252vs, 1144vs, 1049s, 932s, 821m, 748s, 720s, 691s. Anal. calcd for C₂₀H₁₆N₂OS₂ (364.48): C 65.91, H 4.42, N 7.69, S 17.59; found: C 65.82, H 4.67, N 7.72, S 17.70.

4.3.7. 1-[4,5-Dihydro-4-phenyl-5,5-di(selenophen-2-yl)-1,3,4-thiadiazol-2-yl]ethanone (8g)

Orange crystals; m.p. 116–118°C (petroleum ether/CH₂Cl₂); yield: 335 mg (72%). ¹H NMR: 2.61 (CH₃); 7.06–7.10 (m, 1CH_{arom}); 7.17–7.20 (m, 4CH_{arom}); 7.22–7.24 (m, 2CH_{arom}); 7.32 (dd, *J*_{H,H} = 3.9 Hz, *J*_{H,H} = 1.0 Hz, 2CH_{arom}); 8.12 (d, *J*_{H,H} = 5.6 Hz, 2CH_{arom}). ¹³C NMR: 25.7 (CH₃); 91.2 (C(2')); 121.2, 124.9, 128.5, 129.3, 130.8, 134.5 (11CH_{arom}); 141.5, 142.3, 152.7 (3C_{arom}, C=N); 191.1 (C=O). IR (KBr): 3107m, 3056m, 1670vs (C=O), 1593m, 1530s, 1486s, 1239vs, 1223s, 1141s, 1049m, 1021m, 922m, 891m, 761m, 701s. Anal. calcd for C₁₈H₁₄N₂OSSe₂ (464.30): C 46.56, H 3.04, N 6.03, S 6.91; found: C 46.75, H 3.03, N 6.07, S 6.92.

4.3.8. *1-[4,5-Dihydro-4-phenyl-5,5-di(thiophen-2-yl)-1,3,4-thiadiazol-2-yl]ethanone (8h)*

Yellow crystals; m.p. 130–132°C (EtOH); yield: 265 mg (72%). ¹H NMR: 2.57 (*s*, CH₃); 6.92–6.96 (*m*, 2CH_{arom}); 7.04–7.08 (*m*, 1CH_{arom}); 7.12–7.18 (*m*, 4CH_{arom}); 7.20–7.23 (*m*, 1CH_{arom}); 7.41 (*d*, *J*_{H,H} = 5.0 Hz, 1CH_{arom}); 7.72 (*d*, *J*_{H,H} = 5.0 Hz, 1CH_{arom}); 7.94 (*d*, *J*_{H,H} = 3.7 Hz, 1CH_{arom}). ¹³C NMR: 25.7 (CH₃); 87.3 (C(2')); 120.8, 124.7, 126.8, 128.3, 128.4, 128.6, 141.5, 142.4, 145.6 (11CH_{arom}, 3C_{arom}, C=N); 191.1 (C=O). IR (KBr): 3085*m*, 1665*s* (C=O), 1533*s*, 1490*m*, 1240*s*, 1226*s*, 1137*s*, 1043*m*, 925*m*, 755*m*, 719*s*, 696*m*. MS *m/z* (%): 370 [M⁺] (100). Anal. calcd. for: C₁₈H₁₄N₂OS₃ (370.51): C 58.35, H 3.81, N 7.56, S 25.96; found: C 58.32, H 3.85, N 7.51, S 25.94.

4.3.9. *Ethyl 4,5-dihydro-5,5-di(thiophen-2-yl)-4-(p-tolyl)-1,3,4-thiadiazole-2-carboxylate (8i)*

Yellow-brown oil (AcOEt/CH₂Cl₂ 1:9); yield: 300 mg (72%). ¹H NMR: 1.36 (*t*, *J*_{H,H} = 7.1 Hz, CH₃), 2.22 (*s*, CH₃), 4.35 (*q*, *J*_{H,H} = 7.1 Hz, CH₂O), 6.89–6.92 (*m*, 3CH_{arom}); 6.95–6.98 (*m*, 2CH_{arom}); 7.10 (*dd*, *J*_{H,H} = 3.7 Hz, *J*_{H,H} = 1.1 Hz, 1CH_{arom}); 7.18 (*dd*, *J*_{H,H} = 4.9 Hz, *J*_{H,H} = 3.9 Hz, 1CH_{arom}); 7.37 (*dd*, *J*_{H,H} = 5.1 Hz, *J*_{H,H} = 1.1 Hz, 1CH_{arom}); 7.68 (*dd*, *J*_{H,H} = 4.9 Hz, *J*_{H,H} = 1.1 Hz, 1CH_{arom}); 7.90 (*dd*, *J*_{H,H} = 3.7 Hz, *J*_{H,H} = 1.1 Hz, 1CH_{arom}). ¹³C NMR: 14.1 (CH₃); 20.8 (CH₃); 62.3 (CH₂O); 87.5 (C(2')), 114.5, 121.3, 126.8, 127.9, 128.3, 128.5, 133.2, 133.4 (10CH_{arom}); 134.8, 139.4, 143.0, 145.7, 160.3 (4C_{arom}, C=N); 178.8 (C=O). IR (KBr): 2962*m*, 2923*m*, 1730*s* and 1704*s* (C=O), 1541*s*, 1507*s*, 1463*s*, 1261*vs*, 1090*vs*, 1073*m*, 804*s*, 708*m*. MS *m/z* (%): 414 [M⁺] (100). Anal. calcd for C₂₀H₁₈N₂O₂S₃ (414.56): C 57.94, H 4.38, N 6.76, S 23.20; found: C 57.97, H 4.35, N 6.70, S 23.19.

4.4. *X-Ray Crystal Structure Determination of Compounds 8d and 8h [34]*

All measurements were made on *Nonius KappaCCD* area-detector diffractometer [35] using *MoK α* radiation ($\lambda = 0.71073 \text{ \AA}$) and an *Oxford Cryosystems Cryostream 700* cooler. The data collection and refinement parameters are given below [34] and views of the molecules are shown in Figure 1. Data reduction was performed with *HKL Denzo and Scalepack* [36]. The intensities were corrected for Lorentz and polarization effects, and an absorption correction based on the multi-scan method [37] was applied. Equivalent reflections were merged. Each

structure was solved by direct methods using *SHELXS97* [38], which revealed the positions of all non-hydrogen atoms. In the case of **8h**, one of the five-membered rings is disordered through a rotation of approximately 180° about the ring pivot axis, thus interchanging the positions of the *S*-atom and a *C*-atom. Two positions were defined for each of these atoms and the site occupation factor of the major conformation refined to 0.697(2). Similarity restraints were applied to the chemically equivalent bond lengths involving disordered atoms, while the neighboring disordered atoms were restrained to have similar atomic displacement parameters. The non-hydrogen atoms were refined anisotropically. All of the H-atoms were placed in geometrically calculated positions and refined by using a riding model where each *H*-atom was assigned a fixed isotropic displacement parameter with a value equal to $1.2U_{\text{eq}}$ of its parent atom ($1.5U_{\text{eq}}$ for the methyl group in **8h**). The refinement of each structure was carried out on F^2 by using full-matrix least-squares procedures, which minimized the function $\Sigma w(F_o^2 - F_c^2)^2$. A correction for secondary extinction was applied in the case of **8h**. Neutral atom scattering factors for non-H-atoms were taken from ref. [39], and the scattering factors for *H*-atoms were taken from ref. [40]. Anomalous dispersion effects were included in F_c [41]; the values for f' and f'' were those of ref. [42]. The values of the mass attenuation coefficients are those of ref. [43]. The *SHELXL-2016* program [44] was used for all calculations.

Crystal data for **8d**: $\text{C}_{22}\text{H}_{16}\text{N}_2\text{S}_3$, $M = 404.55$, crystallized from $\text{Et}_2\text{O}/\text{CH}_2\text{Cl}_2$, yellow, prism, crystal dimensions $0.12 \times 0.20 \times 0.28$ mm, triclinic, space group $P\bar{1}$, $Z = 2$, reflections for cell determination 33649, 2θ range for cell determination 4–55°, $a = 9.0252(2)$ Å, $b = 10.2253(2)$ Å, $c = 11.6650(3)$ Å, $\alpha = 94.8910(16)$, $\beta = 110.1558(15)$, $\gamma = 108.0826(16)$ °, $V = 938.12(4)$ Å³, $T = 160(1)$ K, $D_X = 1.432$ g·cm⁻³, $\mu(\text{MoK}\alpha) = 0.405$ mm⁻¹, scan type ω , $2\theta_{(\text{max})} = 54.9$ °, transmission factors (min; max) = 0.863; 0.955, total reflections measured 20152, symmetry independent reflections 4267, reflections with $I > 2\sigma(I)$ 3135, reflections used in refinement 4267, parameters refined 244, $R(F)$ [$I > 2\sigma(I)$ reflections] = 0.0433, $wR(F^2)$ [all data] = 0.1099 ($w = [\sigma^2(F_o^2) + (0.0469P)^2 + 0.4391P]^{-1}$, where $P = (F_o^2 + 2F_c^2)/3$), goodness of fit 1.068, final $\Delta_{\text{max}}/\sigma$ 0.000, $\Delta\rho$ (max; min) = 0.38; -0.44 e Å⁻³.

Crystal data for **8h**: $\text{C}_{18}\text{H}_{14}\text{N}_2\text{OS}_3$, $M = 370.49$, crystallized from hexane/ CH_2Cl_2 , yellow, plate, crystal dimensions $0.07 \times 0.22 \times 0.37$ mm, monoclinic, space group $P2_1/c$, $Z = 4$, reflections for cell determination 61174, 2θ range for cell determination 4–55°, $a = 10.6525(1)$ Å, $b = 15.9217(2)$ Å, $c = 10.3570(2)$ Å, $\beta = 104.7834(9)$, $V = 1698.46(4)$ Å³, $T =$

160(1) K, $D_X = 1.449 \text{ g}\cdot\text{cm}^{-3}$, $\mu(\text{MoK}\alpha) = 0.444 \text{ mm}^{-1}$, scan type ω , $2\theta_{(\text{max})} = 54.9^\circ$, transmission factors (min; max) = 0.890; 0.970, total reflections measured 40626, symmetry independent reflections 3892, reflections with $I > 2\sigma(I)$ 3248, reflections used in refinement 3892, parameters refined 238, restraints 54, $R(F)$ [$I > 2\sigma(I)$ reflections] = 0.0352, $wR(F^2)$ [all data] = 0.0926 ($w = [\sigma^2(F_o^2) + (0.0427P)^2 + 0.8503P]^{-1}$, where $P = (F_o^2 + 2F_c^2)/3$), goodness of fit 1.044, secondary extinction coefficient 0.006(1), final $\Delta_{\text{max}}/\sigma$ 0.001, $\Delta\rho$ (max; min) = 0.37; $-0.48 \text{ e}\ \text{\AA}^{-3}$.

Disclosure statement

No potential conflict of interest was reported by the authors.

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References

- [1] Caramella P, Grünanger P. Nitrile oxides and imines. In: Padwa A, ed. 1,3-Dipolar cycloaddition chemistry. New York: John Wiley & Sons; 1984. pp. 291–392.
- [2] Sharp JT. Nitrile ylides and nitrile imines. In: Padwa A, Pearson WH, eds. Synthetic applications of 1,3-dipolar cycloaddition chemistry toward heterocycles and natural products. New York: John Wiley & Sons; 2002. pp. 473–537.
- [3] Toubro NH, Holm A. Nitrilimines. *J Am Chem Soc.* 1980;102:2093–2094.
- [4] Meier H, Heinzelmann W, Heimgartner H. Direct detection of diphenylnitrilimine in the photolysis of 2,5-diphenyltetrazole. *Chimia.* 1980;34:504–506.
- [5] Bégué D, Qiao GGH, Wentrup C. Nitrile imines: Matrix isolation, IR spectra, structures, and rearrangement to carbodiimides. *J Am Chem Soc.* 2012;134:5339–5350.
- [6] Réau R, Veneziani G, Dahan F, et al. An easy synthesis of nitrilimine. Crystal structure analysis of a unheteroatom substituted stabilized nitrilimine. *Angew Chem Int Ed Engl.* 1992;31:439–440.

- [7] Sicard G, Baceiredo A, Bertrand G. Synthesis and reactivity of a stable nitrile imine. *J Am Chem Soc.* 1988;110:2663–2664.
- [8] Granier M, Baceiredo A, Bertrand G. The first direct proof of a nitrilimine-diaza isomerization. Synthesis of a relatively stable *N*-silylated nitrilimine. *Angew Chem Int Ed Engl.* 1988;27:1350–1351.
- [9] Arthur MP, Baceiredo A, Fischer J, De Cian A, Bertrand G. Substitution reactions at nitrilimine skeletons. *Synthesis.* 1992;43–45.
- [10] Bertrand G, Wentrup C. Nitrile imines: From matrix characterization to stable compounds. *Angew Chem Int Ed Engl.* 1994;33:527–545.
- [11] Huisgen R, Fišera L, Giera H, et al. Thiones as superdipolarophiles. Rates and equilibria of nitron cycloadditions to thioketones. *J Am Chem Soc.* 1995;117:9671–9678.
- [12] Huisgen R, Grashey R, Seidel M, et al. 1,3-Dipolar addition. III. Reaction of diphenylnitrilimine with carbonyl and thiocarbonyl compounds. *Liebigs Ann Chem.* 1962;658:169–180.
- [13] Dunstan JBF, Elsey GM, Russell RA, et al. Dipolar cycloaddition reactions with nitrilimines. *Aust J Chem.* 1998;51:499–510.
- [14] Itto MYA, Feddoui A, Boutalib A, et al. Highly diastereoselective cycloaddition of diarylnitrilimines to the C=S bond of (1*R*)-thiocamphor as a source of chiral spiro-1,3,4-thiadiazoles. *J Sulfur Chem.* 2013;34:250–258.
- [15] Katada T, Eguchi S, Sasaki T. Thermal cycloaddition reactions of thiocarbonyl compounds. Part 2. 1,3-Dipolar cycloaddition reactions of adamantanethione with nitrile oxides, nitrilimines, and diazoalkanes. *J Chem Soc Perkin Trans 1.* 1984;2641–2647.
- [16] Korchevin NA, Usov VA, Voronkov MG, et al. α,β -Unsaturated sulfur compounds. XX. [2 + 3]-Cycloaddition of 3-amino-2-aryl-1-indenethiones to nitrilium betaines and azidobenzene. *Zh Org Khim.* 1986;22:1276–1282.
- [17] Linden A, Awad EMAH, Heimgartner H. A rhodanine derivative and its cycloadduct with diphenyl nitrile imine. *Acta Crystallogr Sect C.* 1999;55:1877–1881.
- [18] Caleb AA, Ballo D, Rachid B, et al. Synthesis and antibacterial activity of new spiro[thiadiazoline-quinoxaline] derivatives. *Arkivoc.* 2011(ii);217–226.
- [19] Mlostoń G, Grzelak P, Hamera-Fałdyga R, et al. Aryl, hetaryl, and ferrocenyl thioketones as versatile building blocks for exploration in the organic chemistry of sulfur. *Phosphorus Sulfur Silicon Relat Elem.* 2017;192:204–211.

- [20] Mlostoń G, Urbaniak K, Linden A, et al. Selenophene-2-yl-substituted thiocarbonyl ylides – at the borderline of dipolar and biradical reactivity. *Helv Chim Acta*. 2015;98:453–461.
- [21] McKee ML, Mlostoń G, Urbaniak K, et al. Dimerization reactions of aryl selenophen-2-yl-substituted thiocarbonyl *S*-methanides as diradical processes: a computational study. *Beilstein J Org Chem*. 2017;13:410–416.
- [22] Grzelak P, Utecht G, Jasiński M. et al. First (3+2)-cycloadditions of thiochalcones as C=S dipolarophiles: Efficient synthesis of 1,3,4-thiadiazoles via reactions with fluorinated nitrile imines. *Synthesis*. 2017;49: 2129–2137.
- [23] Mlostoń G, Urbaniak K, Utecht G, et al. Trifluoromethylated 2,3-dihydro-1,3,4-thiadiazoles via the regioselective [3+2]-cycloadditions of fluorinated nitrile imines with aryl, hetaryl, and ferrocenyl thioketones. *J Fluorine Chem*. 2016;192:147–154.
- [24] Dogan HN, Duran A, Rollas S, et al. Synthesis of new 2,5-disubstituted-1,3,4-thiadiazoles and preliminary evaluation of anticonvulsant and antimicrobial activities. *Bioorg Med Chem*. 2002;10:2893–2898.
- [25] Hu Y, Li C-Y, Wang X-M, et al. 1,3,4-Thiadiazole. Synthesis, reactions, and applications in medicinal, agricultural, and materials chemistry. *Chem Rev*. 2014;114:5572–5610.
- [26] Johnson CK. ORTEP II, Report ORNL-5138, Oak Ridge National Laboratory, Oak Ridge, Tennessee, 1976.
- [27] Huisgen R, Seidel M, Wallbillich G, et al. Diphenylnitrilimine and its 1,3-dipolar additions to alkenes und alkynes. *Tetrahedron*. 1962;17:3–29.
- [28] Spiteri C, Keeling S, Moses JE. New synthesis of 1-substituted-1*H*-indazoles via 1,3-dipolar cycloaddition of *in situ* generated nitrile imines and benzyne. *Org Lett*. 2010;12:3368–3371.
- [29] Mlostoń G, Pipiak P, Linden A, et al. Studies on the reactions of thiocarbonyl *S*-methanides with hetaryl thioketones. *Helv Chim Acta*. 2015;98:462–473.
- [30] Mlostoń G, Pipiak P, Heimgartner H. Diradical reaction mechanism in [3+2]-cycloadditions of hetaryl thioketones with alkyl- or trimethylsilyl-substituted diazomethanes. *Beilstein J Org Chem*. 2016;12:716–724.
- [31] Mlostoń G, Urbaniak K, Gębicki K, et al. Hetaryl thioketones. Synthesis and selected reactions. *Heteroatom Chem*. 2014;25:548–555.

- [32] Patel HV, Vyas KA, Pandey SP, et al. Facile synthesis of hydrazonyl halides by reaction of hydrazones with *N*-halosuccinimide-dimethyl sulfide complex. *Tetrahedron*. 1996;52:661–668.
- [33] Ali KA, Ragab EA, Kamal M, Dawood KM. Synthetic access to some new benzothiazole-based 1,3,4-thiadiazole and 1,3-thiazole derivatives. *Turk J Chem*. 2016;40:277–282.
- [34] CCDC-1544688 and 1544689 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the *Cambridge Crystallographic Data Centre* via www.ccdc.cam.ac.uk/structures.
- [35] Hooft R. KappaCCD Collect Software. Nonius BV, Delft, The Netherlands; 1999.
- [36] Otwinowski Z, Minor W. In: *Methods in Enzymology*, Vol. 276, *Macromolecular Crystallography, Part A*. Carter Jr CW, Sweet RM, editors. New York: Academic Press; 1997. p. 307–326.
- [37] Blessing RH. *Acta Crystallogr Sect A*. 1995;51:33–38.
- [38] Sheldrick GM. *Acta Crystallogr Sect A*. 2008;64:112–122.
- [39] Maslen EN, Fox AG, O'Keefe MA. In: *International tables for crystallography*. Wilson AJC, editor. Vol. C. Dordrecht: Kluwer Academic; 1992. Table 6.1.1.1. p. 477–486.
- [40] Stewart RF, Davidson ER, Simpson WT. Coherent X-ray scattering for the hydrogen atom in the hydrogen molecule. *J Chem Phys*. 1965;42:3175–3187.
- [41] Ibers JA, Hamilton WC. Dispersion corrections and crystal structure refinements. *Acta Crystallogr*. 1964;17:781–782.
- [42] Creagh DC, McAuley WJ. In: *International tables for crystallography*. Wilson AJC, editor. Vol. C. Dordrecht: Kluwer Academic; 1992. Table 4.2.6.8. p. 219–222.
- [43] Creagh DC, Hubbell JH. In: *International tables for crystallography*. Wilson AJC, editor. Vol. C. Dordrecht: Kluwer Academic; 1992. Table 4.2.4.3. p. 200–206.
- [44] Sheldrick GM. Crystal structure refinement with SHELXL. *Acta Crystallogr Sect C* 2015;71:3–8.