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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 studied reactions.



yield: X = S or Se (71–73%)

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

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]).

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Scheme 1. Methods for generation of nitrilimines 1.



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

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).

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**–**3c** 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



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

Hydrazonoyl chloride			Heteroaryl ^a thioketone				
3	R	Ar ¹	4	Ar ²	Hetar	Thiadiazole 8	Yield (%) ^b
a	Ph	Ph	а	Ph	Sel	а	76 ^c
а	Ph	Ph	b	Ph	Thi	b	72 ^d
а	Ph	Ph	с	Sel	Sel	c	73 ^c
а	Ph	Ph	d	Thi	Thi	d	71 ^d
b	MeCO	Ph	а	Ph	Sel	e	67 ^c
b	MeCO	Ph	b	Ph	Thi	f	66 ^c
b	MeCO	Ph	c	Sel	Sel	g	72 ^c
b	MeCO	Ph	d	Thi	Thi	h	72 ^d
c	EtOCO	4-MeC ₆ H ₄	d	Thi	Thi	i	72 ^d

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

^aPh, Phenyl; Sel, Selenophen-2-yl; Thi, Thiophen-2-yl.

^bYield of isolated product.

^cReaction performed in THF at r.t.

^dReaction performed in boiling benzene.

characterized by means of spectroscopic methods. The 13 C 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 C₂₄H₁₈N₂SSe for the [3+2]-cycloadduct **8a** was confirmed by elemental analysis (Scheme 3).

Similarly, the additional reactions performed with nitrilimines **1a–1c** and heteroaryl thioketones **4a–4d** afforded 2,3-dihydro-1,3,4-thiadiazoles **8b–8i** in 66–73% 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).

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].



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).

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 as a likely intermediate could be well stabilized 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 ¹³C NMR spectra were measured in CDCl₃ solution on a Bruker Avance III instrument (600 and 150 MHz, respectively), 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 diheteroaryl thioketones (**4c**,**d**) were prepared following the literature procedures based on thionation of the corresponding ketones with Lawesson's reagent [31].

Hydrazonovl chlorides 3a-3c 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 CH_2Cl_2 .

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 AcOEt/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): 3079m, 3018m, 1595s, 1553m, 1496vs, 1448m, 1337s, 1325s, 1255s, 1236s, 1125s, 1068m, 967s, 821m, 739s, 720s, 685s. 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*, $J_{\rm H,H} = 3.9$ Hz, $J_{\rm H,H} = 1.0$ Hz, 2CH_{arom}); 7.41–7.46 (*m*, 3CH_{arom}); 7.75–7.78 (*m*, 2CH_{arom}); 8.09 (*dd*, $J_{\rm H,H} = 5.7$ Hz, $J_{\rm H,H} = 1.4$ 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): 3075m, 3018m, 1591s, 1559m, 1489s, 1448m, 1426m, 1328s, 1249s, 1236s, 1182m, 1122s, 1065m, 1036m, 960s, 878m, 843m, 739s, 701vs, 682s. 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): 3060*m*, 3031*m*, 1666*vs* (C=O), 1591*s*, 1527*s*, 1489*s*, 1439*m*, 1252*vs*, 1144*vs*, 1046*s*, 932*s*, 748*s*, 691*s*. 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}, C=N); 191.0 (C=O). IR (KBr): 3066*m*, 3031*m*, 1670*vs* (C=O), 1591*s*, 1530*s*, 1492*s*, 1442*m*, 1252*vs*, 1144*vs*, 1049*s*, 932*s*, 821*m*, 748*s*, 720*s*, 691*s*. 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 (**8**g)

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): 3107*m*, 3056*m*, 1670*vs* (C=O), 1593*m*, 1530*s*, 1486*s*, 1239*vs*, 1223*s*, 1141*s*, 1049*m*, 1021*m*, 922*m*, 891*m*, 761*m*, 701*s*. 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*, $J_{\rm H,H} = 7.1$ Hz, CH₃), 2.22 (*s*, CH₃), 4.35 (*q*, $J_{\rm H,H} = 7.1$ Hz, CH₂O), 6.89–6.92 (*m*, 3CH_{arom}); 6.95–6.98 (*m*, 2CH_{arom}); 7.10 (*dd*, $J_{\rm H,H} = 3.7$ Hz, $J_{\rm H,H} = 1.1$ Hz, 1CH_{arom}); 7.18 (*dd*, $J_{\rm H,H} = 4.9$ Hz, $J_{\rm H,H} = 3.9$ Hz, 1CH_{arom}); 7.37 (*dd*, $J_{\rm H,H} = 5.1$ Hz, $J_{\rm H,H} = 1.1$ Hz, 1CH_{arom}); 7.68 (*dd*, $J_{\rm H,H} = 4.9$ Hz, $J_{\rm H,H} = 1.1$ Hz, 1CH_{arom}); 7.90 (*dd*, $J_{\rm H,H} = 3.7$ Hz, $J_{\rm H,H} = 1.1$ 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), 1541s, 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 ($\lambda = 0.71073$ Å) 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 $1.2U_{eq}$ of its parent atom ($1.5U_{eq}$ 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**: C₂₂H₁₆N₂S₃, M = 404.55, crystallized from Et₂O/hexane, 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 33,649, 2θ range for cell determination 4–55°, a = 9.0252(2) Å, b = 10.2253(2) Å, c = 11.6650(3) Å, $\alpha = 94.8910(16)^\circ$, $\beta = 110.1558(15)^\circ$, $\gamma = 108.0826(16)^\circ$, V = 938.12(4) Å³, T = 160(1) K, $D_X = 1.432$ g cm⁻³, μ (MoK α) = 0.405 mm⁻¹, scan type ω , $2\theta_{(max)} = 54.9^\circ$, transmission factors (min; max) = 0.863; 0.955, total reflections measured 20,152, 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 Δ_{max}/σ 0.000, $\Delta\rho$ (max; min) = 0.38; -0.44 e Å^{-3}.

Crystal data for **8h**: C₁₈H₁₄N₂OS₃, M = 370.49, crystallized from hexane/CH₂Cl₂, 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 61,174, 2θ range for cell determination 4–55°, a = 10.6525(1) Å, b = 15.9217(2) Å, c = 10.3570(2) Å, $\beta = 104.7834(9)^\circ$, V = 1698.46(4) Å³, T = 160(1) K, $D_X = 1.449$ g cm⁻³, μ (MoK α) = 0.444 mm⁻¹, scan type ω , $2\theta_{(max)} = 54.9^\circ$, transmission factors (min; max) = 0.890; 0.970, total reflections measured 40,626, 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 Δ_{max}/σ 0.001, $\Delta\rho$ (max; min) = 0.37; -0.48 e Å⁻³.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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