1,3-Dipolar Cycloadditions of α-Diazo Ketones Derived from *N*-Protected (*S*)-Proline with Aromatic and Cycloaliphatic Thioketones

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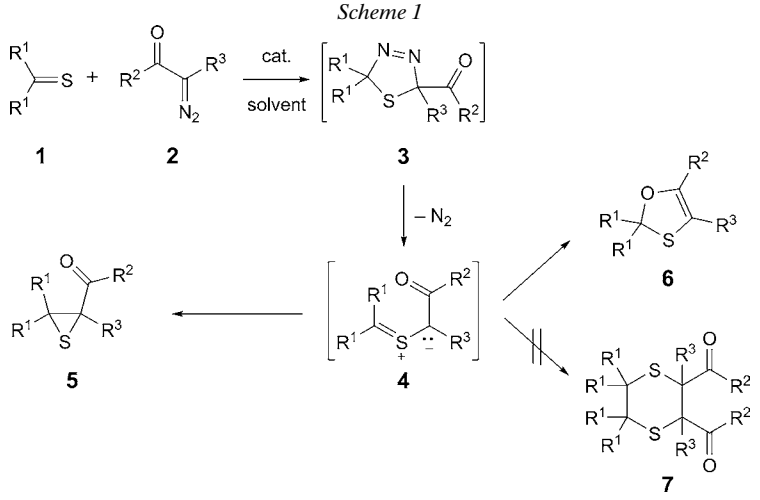
Enantiomerically pure α-oxo diazo compounds derived from (*S*)-proline were used for 1,3-dipolar cycloaddition with aryl and hetaryl thioketones, as well as with cycloalkanethiones. Whereas the reactions with hetaryl thioketones in boiling THF yield α,β-unsaturated ketones *via* a cascade of cycloaddition, 1,3-dipolar electrocyclization, and desulfurization, the analogous reactions with thiobenzophenone and cycloalkanethiones result in the formation of 1,3-oxathiole derivatives. In the latter case, the 1,5-dipolar electrocyclization of the intermediate thiocarbonyl ylide is the key step of the reaction sequence. In all cases, the isolated products are optically active, *i.e.*, the multistep processes occur with retention of the stereogenic center incorporated *via* the use of (*S*)-proline as the precursor of the diazo compounds.

1. Introduction. – Over the last few decades, reactions of diazoalkanes with thioketones have been studied extensively, and both their practical relevance, as well as mechanistic aspects are of current interest. In general, the reactions occur smoothly, even at low temperature, and the kinetic results obtained with diphenyldiazomethane (Ph_2CN_2) inspired *Huisgen* to designate thioketones as 'superdipolarophiles' [1]. Reactions of thioketones **1** with diazoalkanes are especially important, as the [3 + 2] cycloadducts formed can be isolated in some instances and subsequently used for the generation of reactive thiocarbonyl ylides [2]. It is well-known that α-diazocarbonyl compounds **2** are less reactive and, for that reason, their reactions with thioketones must be carried out at enhanced temperature [3] or/and in the presence of a catalyst such as $LiClO_4$ [4] or $Rh_2(OAc)_4$ [4][5]. Characteristically, reactions with α-diazocarbonyl compounds **2** occur with spontaneous elimination of N_2 from the initially formed cycloadducts **3**, and the intermediate thiocarbonyl ylides **4** undergo competitive 1,3-dipolar or 1,5-dipolar electrocyclizations [6] (*Scheme 1*). In the first case, the corresponding 2-carbonyl-substituted thiiranes **5** are the products, and, in the second case, the formation of 1,3-oxathiols **6** is observed. It is worth mentioning that the intermediate α-oxothiocarbonyl ylides **4** do not undergo head-to-head dimerization to give 1,4-dithianes **7**, which is a typical reaction for 1,1-diaryl-substituted thiocarbonyl *S*-methanides [2].

[1]) Part of the planned PhD thesis of *P. P.*, University of Łódź.

Scheme 1



Typical α-diazocarbonyl compounds **2** applied in 1,3-dipolar cycloadditions with thioketones are α-diazo ketones, esters, and amides [6]. To the best of our knowledge, no studies on reactions of thioketones with optically active α-diazo ketones have been reported yet.

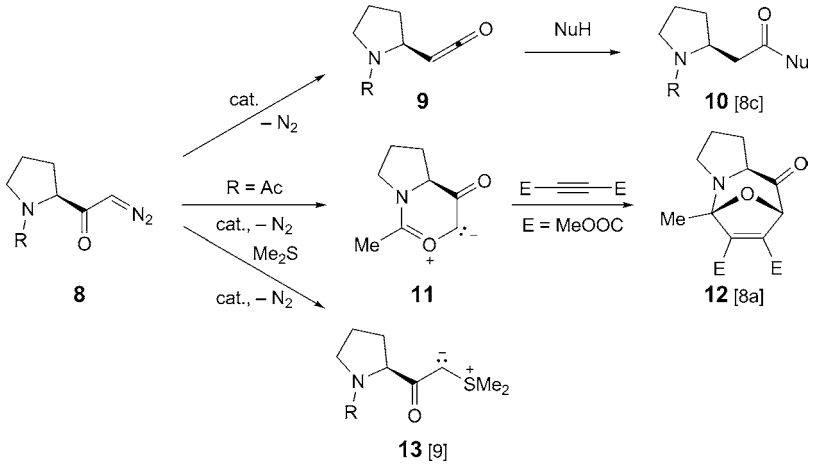
In organic synthesis, natural α-amino acids offer an extremely useful and easily available pool of chiral substrates. Most frequently used examples are (*S*)-proline and its derivatives [7]. However, α-diazo ketones of type **8**, derived from *N*-protected proline, have been investigated only to a limited extent. In the first instance, they were used as precursors of chiral carbenes/carbenoids generated *in situ* by treatment with metal catalysts such as AgOBz or $Rh_2(OAc)_4$ [8]. In some cases, the carbenoid formed thereby undergoes rearrangement to the reactive ketene **9** (*Wolff* rearrangement), which is trapped by nucleophiles to give homoproline derivatives **10** [8c] (*Scheme 2*). On the other hand, the carbenoid attacks the C=O group of the protecting group yielding a reactive carbonyl ylide **11**, which subsequently can be trapped by a suitable dipolarophile, *e.g.*, dimethyl acetylenedicarboxylate, to give **12** [8a]. Another important application is the *in situ* generation of reactive sulfur ylides **13** *via* decomposition of **8** in the presence of Me_2S [9]. However, no 1,3-dipolar cycloadditions with *N*-protected diazo compounds **8** have been reported to date.

The aim of the present study was to test the reactivity of thioketones towards proline-derived α-diazo ketones **8** used as 1,3-dipoles.

2. Results and Discussion. – The starting α-diazo ketones **8** with R = Bz, Bn, and Boc are known compounds, which were obtained by treatment of the corresponding *N*-protected proline chlorides with CH_2N_2 [8a][8b][9]. All of them are relatively stable at room temperature, and in solution they exist as mixtures of two rotamers as evidenced by NMR spectroscopy.

The first series of experiments was perfomed with thiobenzophenone (**1a**) and the benzoyl (Bz) derivative **8a** in order to optimize the reaction conditions. Whereas the reaction carried out in toluene at room temperature required 48 h for full conversion,

Scheme 2



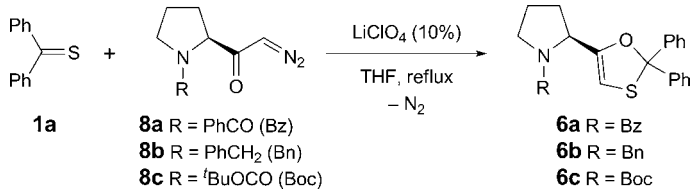
the analogous reaction in THF was complete after only 21 h. The transformation in THF was slightly accelerated by addition of a catalytic amount (*ca.* 10%) of $LiClO_4$ (15 h). However, heating the mixture **1a**, **8a**, and $LiClO_4$ in THF at reflux led to vigorous N_2 evolution, and the reaction was already complete after 3 h. The ^{1}H-NMR analysis of the reaction mixture revealed the presence of only one product, also existing as a mixture of two rotamers. In all of the experiments, the yield of the isolated product was between 80 and 90%.

The structure of the formed compound **6a** was elucidated based on the spectroscopic data. The IR spectrum (KBr) indicated the presence of only one C=O group (1624 cm^{-1}). In the ^{1}H-NMR spectrum ($CDCl_3$), a characteristic *singlet* of the major rotamer at 5.10 ppm is attributed to the =CHS fragment of the 1,3-oxathiole ring [10]. The analogous signal of the minor rotamer appeared at 5.58 ppm. The structure of a 1,3-oxathiole was additionally supported by the ^{13}C-NMR data, and the signals detected at 103.4 and 102.8 ppm for the major and minor rotamer, respectively, are of special importance [3][10]. Furthermore, the ESI-MS provided the molecular formula $C_{26}H_{23}NO_2S$ (*m/z* 436 ($[M + Na]^+$)). The product was optically active, and the $[\alpha]_D^{25}$ value in CH_2Cl_2 was – 135.4. All these data are in accordance with the structure of the expected 1,3-oxathiole derivative **6a** (*Scheme 3*). The analogous structures were determined for the products of the reactions of **2a** with the *N*-benzyl- (Bn) and *N*-Boc-protected α-diazo ketones **8b** and **8c** in comparable yields.

In the case of **6a**, the ^{1}H-NMR spectra in (D_6)DMSO were recorded at 22° and 80°. At room temperature, the presence of two rotamers was evidenced by two broad *singlet*s for =CHS at 4.90 and 4.49 ppm, in a ratio of *ca.* 3 : 2. In addition, two *multiplet*s for H–C(2) of the pyrrolidine ring appeared at 4.15 – 4.00 and 3.70 – 3.55 ppm (ratio *ca.* 3 : 2). In the spectrum recorded at 80°, only two broad signals were detected at 4.95 and 4.20 ppm.

In a recent publication, reactions of selected bis-hetaryl thioketones with CH_2N_2 leading to 4,4,5,5-tetrahetaryl-1,3-dithiolanes were described [11]. To compare the

Scheme 3

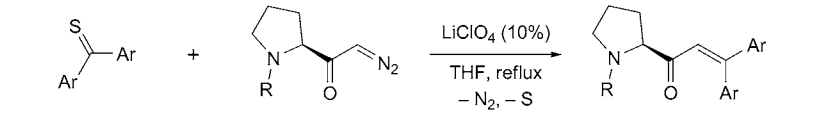


reactivity of hetaryl thioketones containing diverse heteroatoms (O, S, and Se) with that of thiobenzophenone (**1a**), the reactions with α-diazo ketones **8** were performed under optimized conditions (THF, $LiClO_4$, reflux). The reaction with di(thiophen-2-yl) thioketone (**1b**) and **8a** was complete after 4 h, and again the ^{1}H-NMR analysis revealed the formation of a sole product also existing as a mixture of two rotamers. In contrast to 1,3-oxathioles **6** obtained in the reactions with **1a** (*Scheme 3*), no *singlet*s were detected in the region of 5–6 ppm. Instead, characteristic *singlet*s for H–C(sp^2) appeared at 6.85 and 6.36 ppm for the major and minor rotamer, respectively. After chromatographic workup, the ^{13}C-NMR spectrum of the pure product revealed the presence of two C=O groups (196.6 and 169.5 ppm for the major rotamer). In addition, a signal at 121.7 ppm was attributed to a CH=C fragment. The ESI-MS with *m*/*z* 416 ($[M + Na]^+$) provided the molecular formula $C_{22}H_{19}NO_2S_2$. This result established that the formation of the product occurred with loss of a S-atom. On the basis of these findings, we propose that the product formed in the studied reaction was the α,β-unsaturated ketone **14a** (*Scheme 4*).

Analogous products were formed in a series of reactions of thioketones **1c**–**1e** with α-diazo compounds **8a** and **8c**. All of them were isolated as oily materials in good yields.

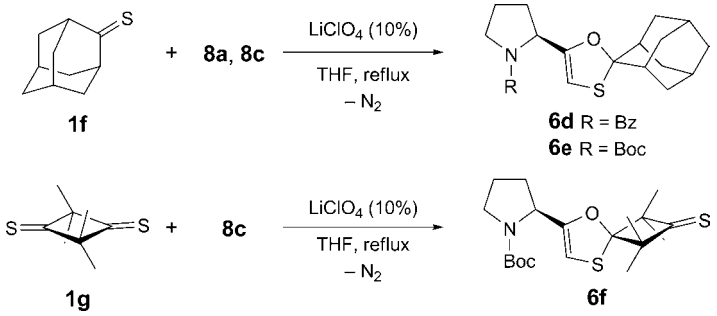
Among cycloaliphatic thioketones (cycloalkanethiones), adamantanethione (**1f**) and 2,2,4,4-tetramethylcyclobutane-1,3-dithione (**1g**) are favorite model compounds, which are frequently used to study the reactivity of the C=S group [12]. In comparison to other α-oxo diazo compounds [3], the reaction of **1f** with **8a** and **8c** in boiling THF occurred smoothly with evolution of N_2. The chromatographic workup led to only one product in each case, identified as the corresponding 1,3-oxathiols **6d** and **6e**, respectively (*Scheme 5*). In an analogous manner, the reaction of **8c** with **1g** was

Scheme 4



	R	Ar
14a	Bz	Thiophen-2-yl
14b	Bz	Selenophen-2-yl
14c	Boc	Thiophen-2-yl
14d	Boc	Selenophen-2-yl
14e	Boc	Furan-2-yl
14f	Boc	Ph, Thiophen-2-yl

Scheme 5



complete after 8 h, and the product **6f** was isolated in 41% yield. Unexpectedly, the reaction of **8c** with the structurally related 2,2,4,4-tetramethyl-3-thioxocyclobutan-1-one led to a complex mixture of products. It is worth mentioning that the ^{1}H-NMR spectra recorded in $CDCl_3$ at room temperature also showed the presence of two rotamers of 1,3-oxathioles **6d**, **6e**, and **6f**.

Finally, the structure of **6f** was established by X-ray crystallography (*Fig.*). The compound in the crystal is enantiomerically pure, and the absolute configuration of the molecule was determined independently by the diffraction experiment. The molecule has the expected proline (*S*)-configuration.

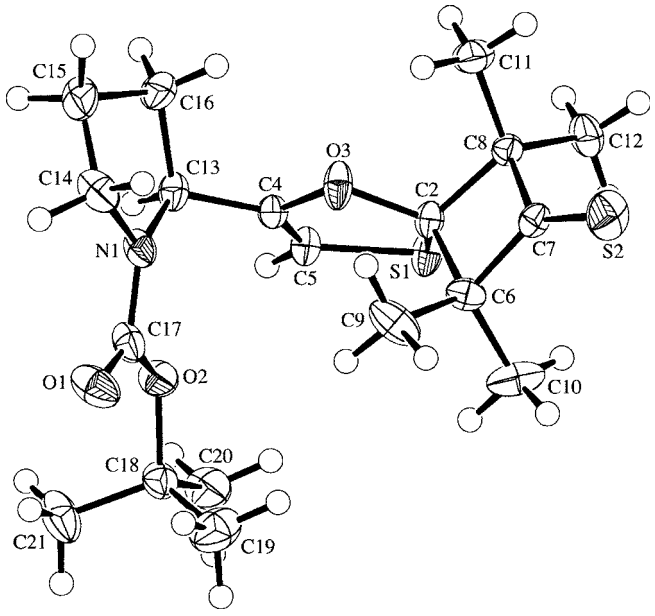


Figure. *ORTEP Plot* [13] *of the molecular structure of* **6f** (with 50% probability ellipsoids; arbitrary numbering of the atoms)

3. Conclusions. – The present study showed that proline-derived α-diazo ketones **8** are useful 1,3-dipoles in reactions with aromatic and cycloaliphatic thioketones **1**. However, the type of the obtained products differs depending on the type of thioketone used. Whereas thiobenzophenone (**1a**), and cycloalkanethiones **1f** and **1g** afford 1,3-oxathioles **6**, the di(hetaryl) thioketones **1b**–**1e** yield α,β-unsaturated ketones **14**. The mechanistic explanation is based on the assumption of the intermediate formation of a reactive thiocarbonyl ylide of type **4** (*Scheme 1*). This type of 1,3-dipoles with an extended π-system is known to undergo preferably electrocyclization reactions, which can occur as 1,3-dipolar or 1,5-dipolar ring closure. In the first case, 2-acylated thiiranes are the expected products. In many instances, however, the spontaneous extrusion of S is observed. Apparently, the hetaryl substituents are decisive for the 1,3-dipolar electrocyclization and the subsequent elimination of S. The replacement of the hetaryl groups by Ph leads to the alternative 1,5-dipolar electrocyclization of the intermediate thiocarbonyl ylide **4**. In contrast to some other 1,3-oxathiols [3], the products **6** do not undergo isomerization *via* ring opening to form thiiranes in solution.

The application of the enantiomerically pure α-diazo ketones **8** allows the preparation of a series of optically active 1,3-oxathiole derivatives **6**, as well as hetaryl-substituted α,β-unsaturated ketones **14**, which are potentially attractive building blocks for asymmetric syntheses, *e.g.*, as activated dieno- and dipolarophiles.

The authors thank the *National Science Center* (PL-Cracow) for financial support within the project *Maestro* (Grant Maestro-3; Dec-2012/06/A/ST5/00219).

Experimental Part

1. *General*. M.p.: *MEL-TEMP. II* (*Aldrich*); uncorrected. Column chromatography (CC): silica gel (SiO_2, 70–230 mesh; *Merck*). IR Spectra: *NEXUS FT-IR* instrument; in KBr or as film; $\tilde{\nu}$ in cm^{-1}. ^1H- and ^{13}C-NMR Spectra: *BRUKER AVANCE III* instrument (at 600 and 150 MHz, resp.) using solvent signal as reference; in $CDCl_3$; chemical shifts (δ) in ppm; coupling constants J in Hz. The majority of the ^{13}C signals were assigned with the aid of DEPT spectra. ESI-MS: *Varian 500-MS LC Ion Trap* spectrometer. Optical rotations: *Perkin-Elmer 241 MC* polarimeter, at 20°.

2. *Starting Materials. 1-(1-Benzoylpyrrolidin-2-yl)-2-diazoethanone* (**8a**), *1-(1-benzylpyrrolidin-2-yl)-2-diazoethanone* (**8b**), and tert-*butyl 2-(diazoacetyl)pyrrolidine-1-carboxylate* (**8c**) were prepared as described in [8b]. *Thiobenzophenone* (=*diphenylmethanethione*; **1a**), the symmetrical heteroaromatic thioketones **1b**, **1c**, and **1d**, and the nonsymmetrical heteroaromatic thioketone **1e** were obtained from the corresponding ketones as described in [11]. *Adamantanethione* (=*tricyclo[3.3.1.1^{3,7}]decane-2-thione*; **1f**) and *2,2,4,4-tetramethylcyclobutane-1,3-dithione* (**1g**) were prepared from the corresponding ketones as described in [12]. Other reagents used in the present study were commercially available. Reported yields refer to isolated products.

3. *Reactions of Aromatic and Heteroaromatic Thioketones* **1a**–**1e** *with Diazo Compounds* **8a**–**8c**. *General Procedure*. To a soln. of **8a**–**8c** (1 mmol) and $LiClO_4$ (10 mol-%) in freshly distilled THF (2.5 ml), **1a** (1.2 mmol) dissolved in a small amount of THF was added portionwise. The mixture was heated at reflux under Ar, and the progress of the reaction was monitored by TLC. The high-field ^1H-NMR spectra recorded for the crude products revealed that products **6** and **14** exist in soln. as mixtures of C–N rotamers.

3.1. *[2-(2,2-Diphenyl-1,3-oxathiol-5-yl)pyrrolidin-1-yl](phenyl)methanone* (**6a**). The reaction of **8a** with **1a** was complete after 3 h. The solvent was evaporated, and the crude product was purified by CC (AcOEt/hexane 1:1). Compound **6a** consisted of a *ca.* 60:40 mixture of two rotamers. Yield: 334 mg (80%). White crystals. M.p. 74.2–77.1° (hexane/Et_2O). $[\alpha]_D = -135.4$ ($c = 1$; CH_2Cl_2). IR (KBr):

2252*m*, 1624*s* (C=O), 1598*m*, 1575*w*, 1447*m*, 1418*m*, 1072*w*, 724*m*. ^{1}H-NMR ($CDCl_3$; values for the minor rotamer in italics): 2.0–2.11 (*m*, CH_2CH_2); 3.40–3.55 (*m*, CH_2N); 4.48, *5.14* (br. *s*, CHN); 5.10, *5.58* (br. *s*, SCH); 7.21–7.57 (*m*, 15 arom. H). ^{13}C-NMR ($CDCl_3$): 22.2 (CH_2); 30.7 (CH_2); 46.1 (CH_2N); 58.0 (CHN); 95.3 (SCH=); 103.4 (C(2′)); 126.4, 128.0, 128.1, 128.4, 129.6, 136.7 (for 15 arom. CH); 143.4, 143.6 (for 3 arom. C); 148.9 (C(5′)); 170.5 (C=O). ESI-MS (MeOH): 436 (100, $[M+Na]^+$).

3.2. *1-Benzyl-2-(2,2-diphenyl-1,3-oxathiol-5-yl)pyrrolidine* (**6b**). The reaction of **8b** with **1a** was complete after 3 h. The solvent was evaporated, and the crude product was crystallized from MeOH. Yield: 352 mg (86%). Colorless crystals. M.p. 93.4–94.5° (MeOH). $[\alpha]_D = -40.8$ ($c = 0.5$; CH_2Cl_2). IR (KBr): 2964*m*, 2808*s*, 1656*m*, 1494*s*, 1447*s*, 1328*m*, 1173*m*, 1110*s*, 1081*m*, 1003*s*, 742*s*, 700*s*. ^{1}H-NMR ($CDCl_3$): 1.72–2.05 (*m*, CH_2CH_2); 2.15–2.25, 2.90–3.05 (2*m*, CH_2N); 3.21–3.25 (*m*, CHN); 3.61 (*AB*, $^2J_{AB} = 12$, PhCH_2); 5.51 (*s*, SCH); 7.23–7.65 (*m*, 15 arom. H). ^{13}C-NMR ($CDCl_3$): 22.7 (CH_2); 29.4 (CH_2); 53.2 (CH_2N); 58.2 (CHN); 62.7 (PhCH_2); 94.2 (SCH=); 102.8 (C(2′)); 126.6, 126.7, 127.9, 128.0 (br.), 128.1, 128.6 (for 15 arom. CH); 139.5, 143.9, 144.3 (3 arom. C); 150.9 (C(5′)). ESI-MS (MeOH): 400 (100, $[M+H]^+$).

3.3. tert-*Butyl 2-(2,2-Diphenyl-1,3-oxathiol-5-yl)pyrrolidine-1-carboxylate* (**6c**). The reaction of **8c** with **1a** was complete after 3 h. The solvent was evaporated, and the crude product was purified by CC (CH_2Cl_2). Compound **6c** consisted of a 71:29 mixture of two rotamers. Yield: 230 mg (56%). Pale-yellow oil. $[\alpha]_D = -90.2$ ($c = 1$; CH_2Cl_2). IR (film): 2975*s*, 1694*s* (C=O), 1447*s*, 1390*s*, 1170*s*, 1110*s*, 994*s*, 917*m*, 878*m*, 753*s*, 698*s*. ^{1}H-NMR ($CDCl_3$; values for the minor rotamer in italics): 1.32 (br. *s*, ^{t}Bu); 1.84–1.98 (*m*, CH_2CH_2); 3.44–3.50 (*m*, CH_2); 4.45–4.60 (br. *m*, CHN); 5.28, *5.37* (br. *s*, SCH); 7.28–7.53 (*m*, 10 arom. H). ^{13}C-NMR ($CDCl_3$): 23.2 (CH_2N); 28.2 (Me_3C); 30.4 (CH_2); 46.1 (CH_2N); 55.4 (CHN); 79.5 (Me_3C); 93.3 (SCH=); 103.1 (C(2′)); 126.2, 126.4, 128.0 (for 10 arom. CH); 143.8 (for 2 arom. C); 149.7 (C(5′)); 154.1 (C=O). ESI-MS (MeOH): 448 (30, $[M+K]^+$), 432 (100, $[M+Na]^+$), 410 (15, $[M+H]^+$).

3.4. *1-[1-Benzoylpyrrolidin-2-yl]-3,3-di(thiophen-2-yl)prop-2-en-1-one* (**14a**). The reaction of **8a** with *di(thiophen-2-yl)methanethione* (**1b**) was complete after 4 h. The solvent was evaporated, and the crude product was purified by CC (AcOEt/hexane 1:1). Compound **14a** consisted of a 78:22 mixture of two rotamers. Yield: 312 mg (80%). Yellow, viscous oil. $[\alpha]_D = -46$ ($c = 1$; CH_2Cl_2). IR (KBr): 2971*w*, 2872*w*, 1688*m* (C=O), 1625*s*, 1575*s*, 1417*s*, 1251*m*, 1216*m*, 1078*m*, 852*m*, 701*s*. ^{1}H-NMR ($CDCl_3$; values for the minor rotamer in italics): 1.82–2.20 (*m*, CH_2CH_2); 3.50–3.82 (*m*, CH_2N); 4.35–4.91 (*m*, CHN); 6.85, *6.36* (*s*, HC=); 7.02–7.57 (*m*, 11 arom. H). ^{13}C-NMR ($CDCl_3$): 25.3 (CH_2); 28.6 (CH_2); 50.2 (CH_2N); 65.3 (CHN); 121.7 (=CH); 126.8, 127.3, 127.6, 127.9, 128.2, 128.5, 130.0, 130.2, 130.4 (for 11 arom. CH); 136.4, 138.1, 141.1, 145.4 (3 arom. C, Ar_2C); 169.5 (C=O); 196.9 (C=O). ESI-MS (MeOH): 416 (100, $[M+Na]^+$).

3.5. *1-(1-Benzoylpyrrolidin-2-yl)-3,3-di(selenophen-2-yl)prop-2-en-1-one* (**14b**). The reaction of **8a** with *di(selenophen-2-yl)methanethione* (**1c**) was complete after 1 d. The solvent was evaporated, and the crude product was purified by CC (AcOEt/hexane 1:1). Compound **14b** consisted of a 78:22 mixture of two rotamers. Yield: 340 mg (70%). Yellow, viscous oil. $[\alpha]_D = -36.8$ ($c = 1$; CH_2Cl_2). IR (KBr): 2949*w*, 2969*w*, 1684*m* (C=O), 1625*s*, 1575*s*, 1417*s*, 1243*w*, 1075*m*, 1017*w*, 698*s*. ^{1}H-NMR ($CDCl_3$; values for the minor rotamer in italics): 1.81–2.18 (*m*, CH_2CH_2); 3.48–3.78 (*m*, CH_2N); 4.38–4.80 (*m*, CHN); 6.76, *6.25* (*s*, HC=); 7.02–8.16 (*m*, 11 arom. H). ^{13}C-NMR ($CDCl_3$): 25.4 (CH_2); 29.7 (CH_2); 49.7 (CH_2N); 65.3 (CH); 121.6 (=CH); 127.9, 128.4, 129.1, 129.0, 130.4, 132.4, 132.7, 133.9, 134.0 (for 11 arom. CH); 136.6, 144.1, 145.3, 151.7 (3 arom. C, Ar_2C); 169.4 (C=O), 197.2 (C=O). ESI-MS (MeOH): 510 (100, $[M+Na]^+$).

3.6. tert-*Butyl 2-[3,3-Di(thiophen-2-yl)acryloyl]pyrrolidine-1-carboxylate* (**14c**). The reaction of **8c** with **1b** was complete after 3 h. The solvent was evaporated, and the crude product was purified by CC (AcOEt/hexane 1:1). Compound **14c** consisted of a 78:22 mixture of two rotamers. Yield: 264 mg (68%). Yellow, viscous oil. $[\alpha]_D = -56.2$ ($c = 1$; CH_2Cl_2). IR (KBr): 2975*m*, 1694*s* (C=O), 1570*s*, 1394*s*, 1254*w*, 1162*s*, 1119*s*, 706*m*. ^{1}H-NMR ($CDCl_3$; values for the minor rotamer in italics): 1.49 (br. *s*, ^{t}Bu); 1.85–2.16 (*m*, CH_2CH_2); 3.40–3.58 (*m*, CH_2N); 4.27–4.49 (*m*, CHN); 6.71, *6.78* (*s*, HC=): 7.04–7.49 (*m*, 6 arom. H). ^{13}C-NMR ($CDCl_3$): 23.6 (CH_2); 28.4 (Me_3C); 30.3 (CH_2); 46.2 (CH_2N); 65.7 (CHN); 80.2 (Me_3C); 119.9 (=CH); 126.7, 127.8, 128.0, 128.5, 130.1, 130.4 (6 arom. CH); 138.0, 141.4, 145.5 (2 arom. C, Ar_2C); 154.0 (C=O); 198.2 (C=O). ESI-MS (MeOH): 412 (100, $[M+Na]^+$).

3.7. tert-*Butyl 2-[3,3-Di(selenophen-2-yl)acryloyl]pyrrolidine-1-carboxylate* (**14d**). The reaction of **8c** with **1c** was complete after 1 d. The solvent was evaporated, and the crude product was purified by CC (AcOEt/hexane 1:1). Compound **14d** consisted of a 62:38 mixture of two rotamers. Yield: 430 mg (88%). Yellow, viscous oil. $[\alpha]_D = -35.4$ ($c = 1$; CH_2Cl_2). IR (KBr): 2976*s*, 1698*s* (C=O), 1569*s*, 1397*s*, 1365*s*, 1162*s*, 1120*s*, 1014*m*, 839*m*, 736*s*, 696*s*. ^{1}H-NMR ($CDCl_3$; values for the minor rotamer in italics): 1.39 (br. *s*, ^{t}Bu); 1.85–2.18 (*m*, CH_2CH_2); 3.42–3.59 (*m*, CH_2N); 4.28–4.50 (*m*, CHN); 6.60, *6.68* (*s*, HC=); 7.28–7.44 (*m*, 4 arom. CH); 8.00–8.22 (*m*, 2 arom. CH). ^{13}C-NMR ($CDCl_3$): 23.6 (CH_2); 28.4 (Me_3C); 30.6 (CH_2); 46.8 (CH_2N); 65.7 (CHN); 80.0 (Me_3C); 119.9 (=CH); 128.9, 130.3, 132.2, 133.1, 133.8, 134.5 (6 arom. CH); 143.7, 145.6, 151.8 (2 arom. C, CAr_2); 153.9 (C=O); 198.3 (C=O). ESI-MS (MeOH): 506 (100, $[M+Na]^+$). Anal. calc. for $C_{20}H_{23}NO_3Se_2$ (483.32): C 49.70, H 4.80, N 2.90; found: C 49.76 H 5.03 N 2.71.

3.8. tert-*Butyl 2-[3,3-Di(furan-2-yl)acryloyl]pyrrolidine-1-carboxylate* (**14e**). The reaction of **8c** with *di(furan-2-yl)methanethione* (**1d**) was complete after 3 d. The solvent was evaporated, and the crude product was purified by CC (AcOEt/hexane 1:1). Compound **14e** consisted of a 70:30 mixture of two rotamers. Yield: 146 mg (40%). Yellow, viscous oil. $[\alpha]_D = -23$ ($c = 1$; CH_2Cl_2). IR (KBr): 2977*s*, 1689*s* (C=O), 1542*s*, 1404*s*, 1258*w*, 1162*s*, 1121*s*, 1020*m*, 924*w*, 885*w*, 747*m*. ^{1}H-NMR ($CDCl_3$; values for the minor rotamer in italics): 1.38 (br. *s*, ^{t}Bu); 1.86–2.20 (*m*, CH_2CH_2); 3.41–3.58 (*m*, CH_2N); 4.32–4.52 (*m*, CHN); 6.49–6.90 (*m*, 6 arom. CH); 7.49, *7.51* (br. *s*, HC=). ^{13}C-NMR ($CDCl_3$): 23.6 (CH_2); 27.6 (Me_3C); 31.0 (CH_2); 47.0 (CH_2N); 66.0 (CHN); 80.0 (Me_3C); 111.2, 112.3, 114.3, 115.6, 118.1, 118.4, 144.5 (6 arom. CH, =CH); 131.0, 146.7, 148.2 (2 arom. C, Ar_2C); 154.1 (C=O); 198.4 (C=O). ESI-MS (MeOH): 396 (27, $[M+K]^+$), 380 (100, $[M+Na]^+$).

3.9. tert-*Butyl 2-[3-(Furan-2-yl)-3-phenylprop-2-enoyl]pyrrolidine-1-carboxylate* (**14f**). The reaction of **8c** with *phenyl(thiopen-2-yl)methanethione* (**1e**) was complete after 1 d. The solvent was evaporated, and the crude product was purified by CC (AcOEt/petroleum ether (PE) 2:3). Compound **14f** consisted of a 63:37 mixture of two rotamers. Yield: 278 mg (73%). Yellow oil. $[\alpha]_D = -48$ ($c = 1$; CH_2Cl_2). IR (KBr): 2976*m*, 1690*s* (C=O), 1570*s*, 1478*m*, 1492*m*, 1396*s*, 1265*m*, 1162*m*, 735*m*, 700*m*. ^{1}H-NMR ($CDCl_3$; values for the minor rotamer in italics): 1.42 (br. *s*, ^{t}Bu); 1.82–2.06 (*m*, CH_2CH_2); 3.37–3.52 (*m*, CH_2N); 4.18–4.43 (*m*, CHN); 6.75, *6.81* (br. *s*, HC=); 6.89–7.42 (*m*, 8 arom. CH). ^{13}C-NMR ($CDCl_3$): 23.5 (CH_2); 28.4 (Me_3C); 30.4 (CH_2); 46.7 (CH_2N); 65.4 (CHN); 79.9 (Me_3C); 118.4 (=CH); 128.0, 128.5, 128.6, 128.7, 128.9, 130.8 (for 8 arom. CH); 138.1, 145.5, 149.3 (2 arom. C, Ar*C*Ph); 154.0 (C=O), 198.2 (C=O). ESI-MS (MeOH): 422 (27, $[M+K]^+$), 406 (100, $[M+Na]^+$), 384(15, $[M+H]^+$). Anal. calc. for $C_{22}H_{25}NO_3S$ (383.50): C 68.90, H 6.57, N 3.65, S 8.36; found: C 68.23, H 6.77, N 3.58, S 7.99.

4. *Reactions of Cycloalkanethiones* **1f** *and* **1g** *with Diazo Compounds* **8a** *and* **8c**. – *General Procedure.* To a soln. of **8a** or **8c** (1 mmol) and $LiClO_4$ (10 mol-%) in freshly dist. THF (2.5 ml) was added in portions **1f** or **1g** (1.05 mmol). The mixture was heated at reflux under Ar, and the progress of the reaction was monitored by TLC. The high-field NMR spectrum indicated that compounds **6d**–**6f** consisted of a mixture of C–N rotamers.

4.1. *Phenyl[2-(spiro[1,3-oxathiole-2,2′-tricyclo[3.3.1.1^{3,7}]decan]-5-yl)pyrrolidin-1-yl]methanone* (**6d**). The reaction of **8a** with **1f** was complete after 4 d. The solvent was evaporated, and the crude product was purified by CC (AcOEt/hexane 1:1). Compound **6d** consisted of a 53:47 mixture of two rotamers. Yield: 140 mg (37%). Yellow, viscous oil. $[\alpha]_D = -68.6$ ($c = 1$; CH_2Cl_2). IR (KBr): 2907*s*, 2854*s*, 1633*s* (C=O), 1578*m*, 1448*s*, 1401*s*, 1100*m*, 1061*m*, 1000*m*, 725*m*, 699*m*. ^{1}H-NMR ($CDCl_3$; values for the minor rotamer in italics): 1.59–1.82 (*m*, 5 CH_2); 2.00–2.43 (*m*, CH_2CH_2, 4 CH); 3.43, 3.57, *3.69*, *3.79* (2 br. *s*, CH_2N); 4.38, *4.98* (br. *s*, CHN); 4.91, *5.40* (br. *s*, SCH); 7.38–7.49 (*m*, 5 arom. H). ^{13}C-NMR ($CDCl_3$): 22.3 (CH_2); 26.3, 26.5 (2 CH); 31.1 (CH_2); 33.8, 35.4, 37.3 (2:1:1, 4 CH_2); 39.4 (2 CH); 46.1 (CH_2N); 58.0 (CHN); 93.7 (SCH=); 107.4 (C(2′)); 126.8, 127.1, 129.7 (for 5 arom. CH); 137.0 (1 arom. C); 149.3 (C(5′)); 170.5 (C=O). ESI-MS (MeOH): 420 (100, $[M+K]^+$).

4.2. tert-*Butyl 2-(Spiro[1,3-oxathiole-2,2′-tricyclo[3.3.1.1^{3,7}]decan]-5-yl)pyrrolidine-1-carboxylate* (**6e**). The reaction of **8c** with **1f** was complete after 3 d. The solvent was evaporated, and the crude product was purified by CC (CH_2Cl_2/PE 2:3). Compound **6e** consisted of a 61:39 mixture of two rotamers. Yield: 171 mg (45%). Yellow viscous oil. $[\alpha]_D = -41.2$ ($c = 1$; CH_2Cl_2). IR (KBr): 2912*s*, 1698*s* (C=O), 1453*m*, 1394*s*, 1255*w*, 1167*m*, 1000*m*, 916*w*, 904*w*, 736*m*. ^{1}H-NMR ($CDCl_3$; values for the minor rotamer in italics): 1.44 (br. *s*, ^{t}Bu); 1.65–2.35 (*m*, CH_2CH_2, 4 CH, 5 CH_2); 3.38–3.45 (*m*, CH_2N); 4.32–

Table. *Crystallographic Data for Compound* **6f**

Crystallized from		$MeOH/CH_2Cl_2$	D_x [g cm^{-3}]	1.220
Empirical formula		$C_{19}H_{29}NO_3S_2$	$\mu(MoK_\alpha)$ [mm^{-1}]	0.272
Formula weight [g mol^{-1}]		383.56	Scan type	ω
Crystal color, habit		pale-pink, plate	$2\theta_{(max)}$ [°]	56.9
Crystal dimensions [mm]		$0.05 \times 0.19 \times 0.20$	Transmission factors (min; max)	0.871; 1.000
Temp. [K]		160(1)	Total reflections measured	20424
Crystal system		monoclinic	Symmetry-independent reflections	4649
Space group		$P2_1$	Reflections with $I > 2\sigma(I)$	4442
Z		2	Reflections used in refinement	4649
Reflections for cell determination		13733	Parameters refined; restraints	233; 1
2θ Range for cell determination [°]		5–57	Final $R(F)$ [$I > 2\sigma(I)$ reflections]	0.0261
Unit cell parameters	a [Å]	6.92133(11)	$wR(F^2)$ (all data)	0.0641
	b [Å]	9.82205(13)	Weights	$w = [\sigma^2(F_o^2) + (0.0336P)^2 + 0.1546P]^{-1}$
	c [Å]	15.5729(2)		where $P = (F_o^2 + 2F_c^2)/3$
	β [°]	99.6213(14)	Goodness-of-fit	1.041
V [Å^3]		1043.78(3)	Final Δ_{max}/σ	0.001
			$\Delta\rho$ (max; min) [e Å^{-3}]	0.28; −0.25

4.44 (*m*, CHN); 5.10, *5.20* (br. *s*, SCH). ^{13}C-NMR ($CDCl_3$): 23.3 (CH_2); 26.4, 26.6 (2 CH); 28.4 (Me_3C); 30.8 (CH_2); 33.7, 35.2, 37.4 (2 : 1 : 1, 4 CH_2); 39.4 (2 CH); 46.1 (CH_2N); 55.4 (CHN); 79.4 (Me_3C); 92.0 (SCH=); 107.1 (C(2′)); 150.3 (C(5′)); 154.2 (C=O). ESI-MS (MeOH): 416 (100, $[M+K]^+$).

4.3. tert-*Butyl 2-(1,1,3,3-Tetramethyl-2-thioxo-5-oxa-8-thiaspiro[3.4]oct-6-en-6-yl)pyrrolidine-1-carboxylate* (**6f**). The reaction of **8c** with **1g** was complete after 8 h. The solvent was evaporated, and the crude product was purified by CC (CH_2Cl_2). Compound **6f** consisted of a 59 : 41 mixture of two rotamers. Yield: 158 mg (41%). Pale-pink crystals. M.p. 72.0–74.3° (CH_2Cl_2). $[\alpha]_D = -79.2$ ($c = 1$; CH_2Cl_2). IR (KBr): 2968*s*, 2925*m*, 2882*w*, 1686*s* (C=O), 1459*m*, 1397*s*, 1368*m*, 1306*w*, 1165*s*, 1125*m*, 1042*s*, 1012w, 706*w*. ^{1}H-NMR ($CDCl_3$; values for the minor rotamer in italics): 1.27, 1.34, 1.35, 1.36 (4*s*, 4 Me); 1.47 (br. *s*, ^{t}Bu); 1.88–2.02 (*m*, CH_2CH_2); 3.38–3.45 (*m*, CH_2N); 4.41–4.52 (*m*, CHN); 5.15, *5.25* (br. *s*, SCH). ^{13}C-NMR ($CDCl_3$): 23.3 (CH_2); 26.7 (br. *s*, 4 Me); 28.5 (Me_3C); 30.3 (CH_2); 46.1 (CH_2N); 55.2 (CHN); 69.6, 70.1 (C(1′), C(3′)); 79.6 (Me_3C); 91.8 (SCH=); 108.3 (C(4′)); 150.5 (C(6′)); 154.1 (C=O); 280.7 (C=S). ESI-MS (MeOH): 422 (65, $[M+K]^+$), 406 (100, $[M+Na]^+$).

Suitable crystals for the X-ray crystal-structure determination were growm from MeOH/CH_2Cl_2 in the refrigerator.

5. *X-Ray Crystal-Structure Determination of* **6f** (*Table* and *Fig.*)[2]). All measurements were made on an *Agilent Technologies SuperNova* area-detector diffractometer [14] using MoK_α radiation (λ 0.71073 Å) from a micro-focus X-ray source and an *Oxford Instruments Cryojet XL* cooler. Data reduction was performed with *CrysAlisPro* [14]. The intensities were corrected for *Lorentz* and polarization effects, and an empirical absorption correction using spherical harmonics [14] was applied. The space group was determined by the systematic absences, packing considerations, a statistical analysis of intensity distribution, and the successful solution and refinement of the structure. Equivalent reflections, other than *Friedel* pairs, were merged. The data collection and refinement parameters are compiled in the *Table*. A view of the molecule is shown in the *Figure*. The structure was solved by direct methods using *SHELXS-2013* [15], which revealed the positions of all non-H-atoms. The non-H-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 1.2 U_{eq} of its parent C-atom (1.5 U_{eq} for the Me groups). The refinement of the 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 not applied. Refinement of the absolute structure parameter [16] yielded a value of 0.01(1), which confidently confirmed that the refined model represents the true enantiomorph. Neutral atom scattering factors for non-H-atoms were taken from [17a], and the scattering factors for H-atoms were taken from [18]. Anomalous dispersion effects were included in F_c [19]; the values for f' and f'' were those of [17b]. The values of the mass attenuation coefficients are those of [17c]. The *SHELXL-2014* program [20] was used for all calculations.

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[2]) CCDC-1028924 contains the supplementary crystallographic data for this article. These data can be obtained free of charge from the *Cambridge Crystallographic Data Centre*, *via* www.ccdc.cam.ac.uk/data_request/cif.

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Received October 17, 2014