Monatshefte für Chemie 138, 1257–1266 (2007)
DOI 10.1007/s00706-007-0654-x
Printed in The Netherlands

Monatshefte für Chemie
Chemical Monthly

Synthesis of Polycyclic Monothioimides *via* a Domino Reaction of β-Aminocycloalkenethioamides

Artur Budzowski[1,*], **Mateusz Pitak**[2], and **Katarzyna Stadnicka**[2]

[1] Department of Organic Chemistry, Faculty of Chemistry, Jagiellonian University, Kraków, Poland
[2] Department of Crystal Chemistry and Crystal Physics, Faculty of Chemistry, Jagiellonian University, Kraków, Poland

Received February 14, 2007; accepted (revised) March 1, 2007; published online August 27, 2007

Summary. Tricyclic cyclopenta[*b*]pyrrolo[3,4-*c*]pyridine-3,5-dione and pyrrolo[3,4-*d*]quinoline-3,5-diones with stable hemiaminal function or bicyclic azaspiro[4.4]nonanes and azaspiro[4.5]decanes were obtained in a domino reaction of cycloalkenecarbothioamides with maleimides. The proposed mechanism involves *Michael* addition, ring transformation, aqueous hydrolysis of the imine, and additional ring closure which is observed exclusively for one diastereoisomer.

Keywords. Heterocycles; *Michael* addition; Thioamides; Spiro compounds; X-Ray structure determination.

Introduction

The α,β-unsaturated thiocarbonyl compounds are valuable building blocks for the construction of various heterocycles [1]. They can serve as heterodienes or heterodienophiles for *Diels-Alder* reactions leading to thiopyrane derivatives [2]. We have found that 2-furyl- and 2-thienyl-substituted enaminothiones undergo the hetero-*Diels-Alder* reaction with electron-deficient alkenes [3]. Similarly, *N*-aryl-3-(2-furyl)- and *N*-aryl-3-(2-thienyl)-2-propenethioamides react with maleimides affording the cycloadducts with high diastereoselectivity [4]. Besides, α,β-unsaturated thioamides react as *Michael* acceptors with secondary amines [5] or thiols [6]. On the other hand, simple thioamides undergo *Michael*-type addition to maleimide derivatives affording 4-hydroxy-1,3-thiazoles [7]. The reactivity of maleimides as *Michael* acceptors has been observed in the reactions of substituted 2-vinylpyrroles with two molecules of *N*-phenylmaleimide. The originally formed cycloadducts reacted with another molecule affording the *Michael* adducts [8].

Maleimides and their polycyclic derivatives have important biological properties, *e.g.* 1,3-dioxo-2-azaspiro[4.4]nonanes and 1,3-dioxo-2-azaspiro-[4.5]decanes have been successfully tested for anticonvulsant activity [9]. Similar imide hydroxamic acid derivatives have been evaluated for histone deacetylase inhibition and tumor cell antiproliferation, and were active in both assays [10].

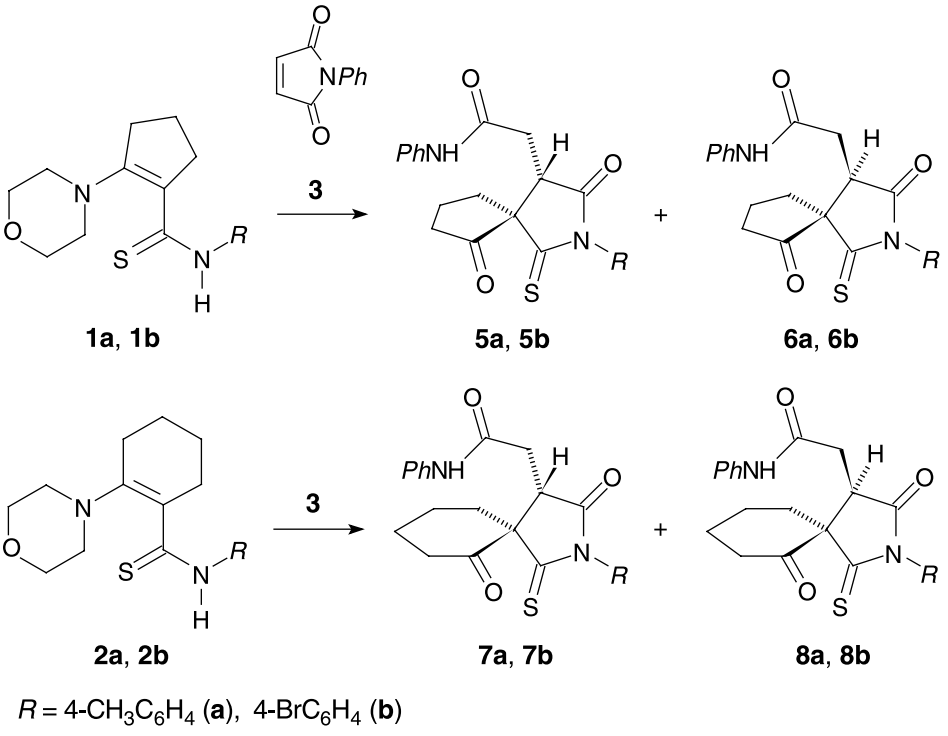
Results and Discussion

Synthesis and Characterization

In this work, we studied the reactions of maleimides with thiocarbonyl compounds, which have structural features of both thioamides and enamines. The cyclic enaminothioanilides are readily available by addition of enamines to aryl isothiocyanates [11].

We report the results of the reactions of *N*-aryl-2-(morpholin-4-yl)cycloalkenecarbothioamides **1** and **2** with *N*-phenylmaleimide (**3**) and maleimide (**4**) [12]. We prepared the enaminotioanilides with unstrained, five- and six-membered rings. The reactions of the thioamides **1a**, **1b**, **2a**, and **2b** with **3** proceeded at room temperature, with low to moderate diastereoselectivity, affording mixtures of diastereoisomeric

* Corresponding author. E-mail: budzowsk@chemia.uj.edu.pl



Scheme 1

Table 1. Results of the reaction of the thioamides with *N*-phenylmaleimide (**3**) (see Scheme 1)

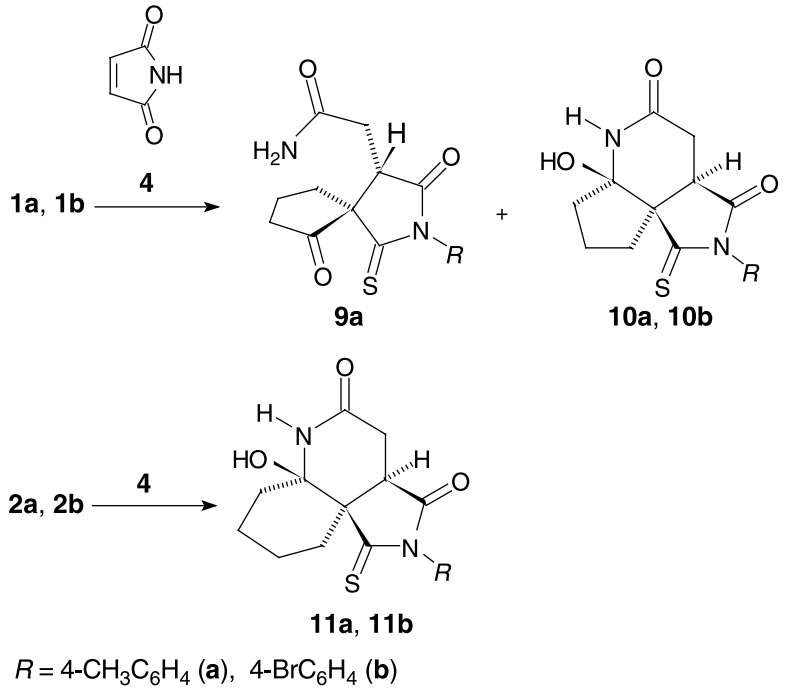
Thioamide	*R*	Yield of mixture/%[a]	Ratio[b]	Isolated yield/%[c]
1a	4-CH_3-C_6H_4	50	6:1	**5a**: 17, **6a**: 10
1b	4-Br-C_6H_4	74	5:1	**5b**: 17
2a	4-CH_3-C_6H_4	76	2:1	**7a**: 23, **8a**: 31
2b	4-Br-C_6H_4	43	2.5:1	**7b**: 10, **8b**: 16

[a] Yields of the diastereoisomeric mixtures. [b] The ratio of diastereoisomers was calculated from ^{1}H NMR spectra of crude reaction mixtures. [c] Yields of the product isolated after separation

monothioimides **5a** and **6a**, **5b** and **6b**, **7a** and **8a**, or **7b** and **8b** (Scheme 1). The mixtures of products were formed in moderate to good yields (43–76%). The products were separated by fractional crystallization (Table 1). The minor isomers **6a**, **8a**, and **8b** were additionally purified by PTLC.

The best results were achieved using a twofold excess of **3** and addition of a small amount of water, which was necessary for the enamine hydrolysis. The evolved morpholine reacted with the excess of **3** affording 3-(morpholin-4-yl)-1-phenylsuccinimide [13].

The structures of the products were established by NMR studies, including COSY, HSQC, and HMBC measurements for two pairs of diastereoisomers: **5a**, **6a** and **7b**, **8b**. The chemical shifts of carbonyl carbons C-6: $\delta = 214.4$, 213.4 ppm for **5a** and **6a** and $\delta = 205.9$ ppm for **7b** and **8b** are characteristic for 5- and 6-membered cycloalkanones. The distinction between the diastereoisomers was resolved by N*O*ESY experiments. The N*O*ESY spectrum of **5a** showed steric proximity of proton 9-H and protons of the pendant arm $CH_2CONHPh$, but the proton 9-H of **6a** showed steric proximity to proton 4-H. Similarly, the N*O*ESY spectrum of **7b** revealed a correlation between protons 10-H and $CH_2CONHPh$ and the spectrum of **8b** showed the correlation between protons 4-H and 10-H. Thus, the acetanilide fragments and the carbonyl groups of the cycloalkanone rings in the isomers **5** and **7** are in a *trans*-relationship, while in the isomers **6** and **8** they are in a *cis*-relationship with respect to the pyrrolidine rings.



Scheme 2

The thioamides **1a**, **1b**, **2a**, and **2b** were treated with maleimide (**4**) under conditions similar to those described above. The reaction of **1a** with **4** afforded a mixture of two isomeric products **9a** and **10a** in a ratio 9:1 in moderate 60% yield (Scheme 2), however only the major product **9a** was isolated (33%). The structure of **9a** was analogous to **5a**. The presence of **10a** and the ratio in the reaction mixture were based on characteristic signals of N–H, O–H, and 3a-H protons in the ^{1}H NMR spectrum, at $\delta = 8.40$, 6.47, and 3.55 ppm. The reactions of **1b**, **2a**, and **2b** with **4** afforded exclusively the tricyclic products **10b**, **11a**, and **11b**, in low yields of 9–21%. The bicyclic products similar to **9a** were unstable,

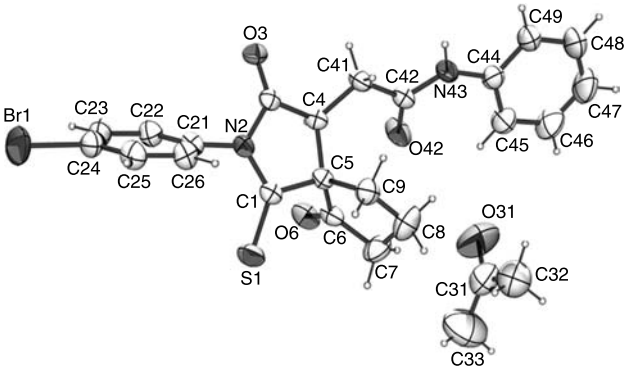


Fig. 1. ORTEP view of the asymmetric unit containing (4*S*,5*R*)-**5b** and acetone molecules; displacement ellipsoids are scaled to enclose 50% electron density; the atom numbering is arbitrary and different from that used for the assignment of the NMR spectra. Selected distances, bond angles, and torsion angles: C1–C5 1.516(4), C4–C5 1.548(4), C6–C5 1.543(4), and C5–C9 1.543(4) Å; C4–C5–C9 118.3(3), C41–C4–C5–C6 −100.3(3)°

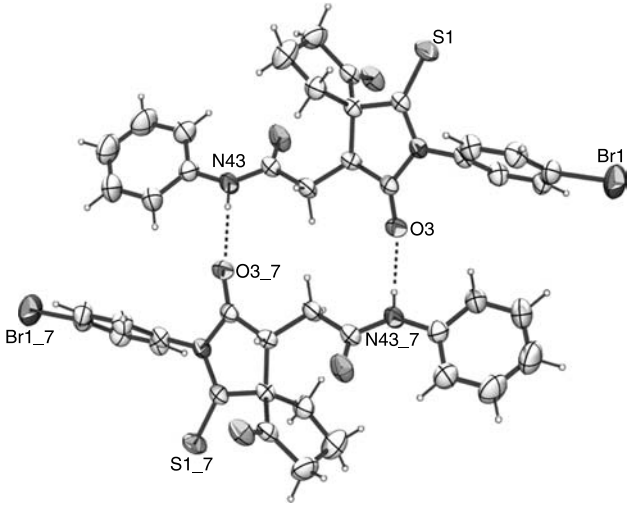


Fig. 2. The enantiomers (4*S*,5*R*) and (4*R*,5*S*) of **5b** related by the centre of symmetry form dimers due to strong linear hydrogen bonds N(43)–H(43) ··· O(3)_7($-x+1/2$, $-y-1/2$, $-z+1/2$) with geometrical parameters *D*–H 0.83(4), H ··· *A* 2.10(4), *D* ··· *A* 2.925(4) Å; ∠*DHA* 176(4)°

probably due to the unusual reactivity of the amide group (see below).

The mass spectrum of **11a** contained a base peak at $m/z = 326$ due to ejection of water from the molecular ion $m/z = 344$. The HMBC spectrum showed correlations of the characteristic hemiaminal carbon C-6a ($\delta = 82.1$ ppm) with N–H, O–H, and 3a-H protons, at $\delta = 8.35$, 6.25, 3.19 ppm.

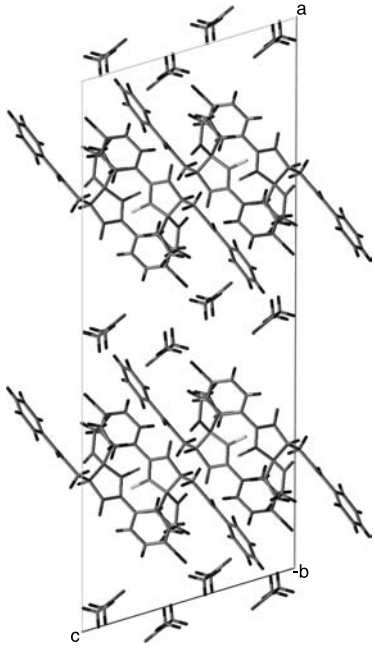


Fig. 3. Packing in the crystal structure of **5b** viewed along [010]: the layers built of **5b** molecules at $x = 0.250$ and 0.750 are separated by the layers of the solvent molecules (acetone) at $x = 0.000$ and 0.500

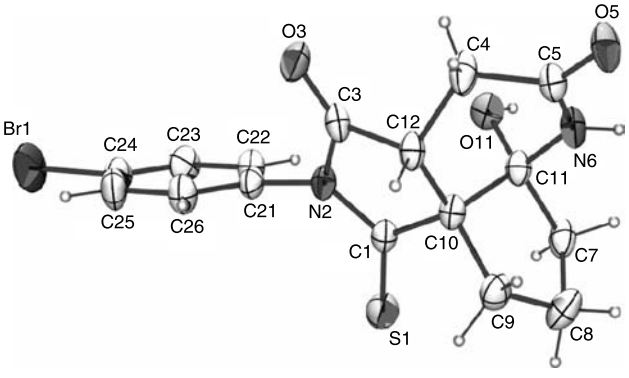


Fig. 4. ORTEP view of the asymmetric unit containing **10b** of configuration (3a*R*,6a*R*,9a*R*) [(12*R*,11*R*,10*R*)-**10b** in the drawing respectively, because the atom numbering is arbitrary and different from that used for the assignment of the NMR spectra]. Selected distances, bond angles, and torsion angles: C1 – C10 1.543(3), C12–C10 1.535(3), C11–C10 1.559(3), and C10–C9 1.541(3) Å; C12–C10–C9 116.7(2), C4–C12–C10–C11 −25.1(3)°

*X-Ray Crystal Structures of **5b** and **10b***

Figure 1 shows the asymmetric unit of **5b** consisting of (4*S*,5*R*)-isomer and one acetone molecule (the structure contains a racemic mixture of the (4*S*,5*R*)- and (4*R*,5*S*)-isomers, centrosymmetric space group $C\ 2/c$). Thus, the X-ray crystal structure of **5b** revealed that the 4-bromophenyl group is connected to the N2 atom of the pyrrolidine ring. The *trans*-configuration of the pendant arm ($CH_2CONHPh$) and the C6=O6 carbonyl group with regard to the pyrrolidine ring was confirmed. The spiro-system is strained with the elongated bond lengths between C5 and neigh-

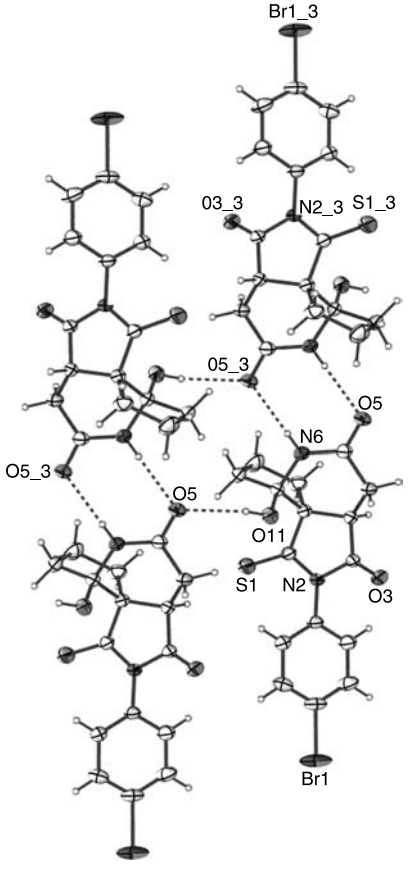
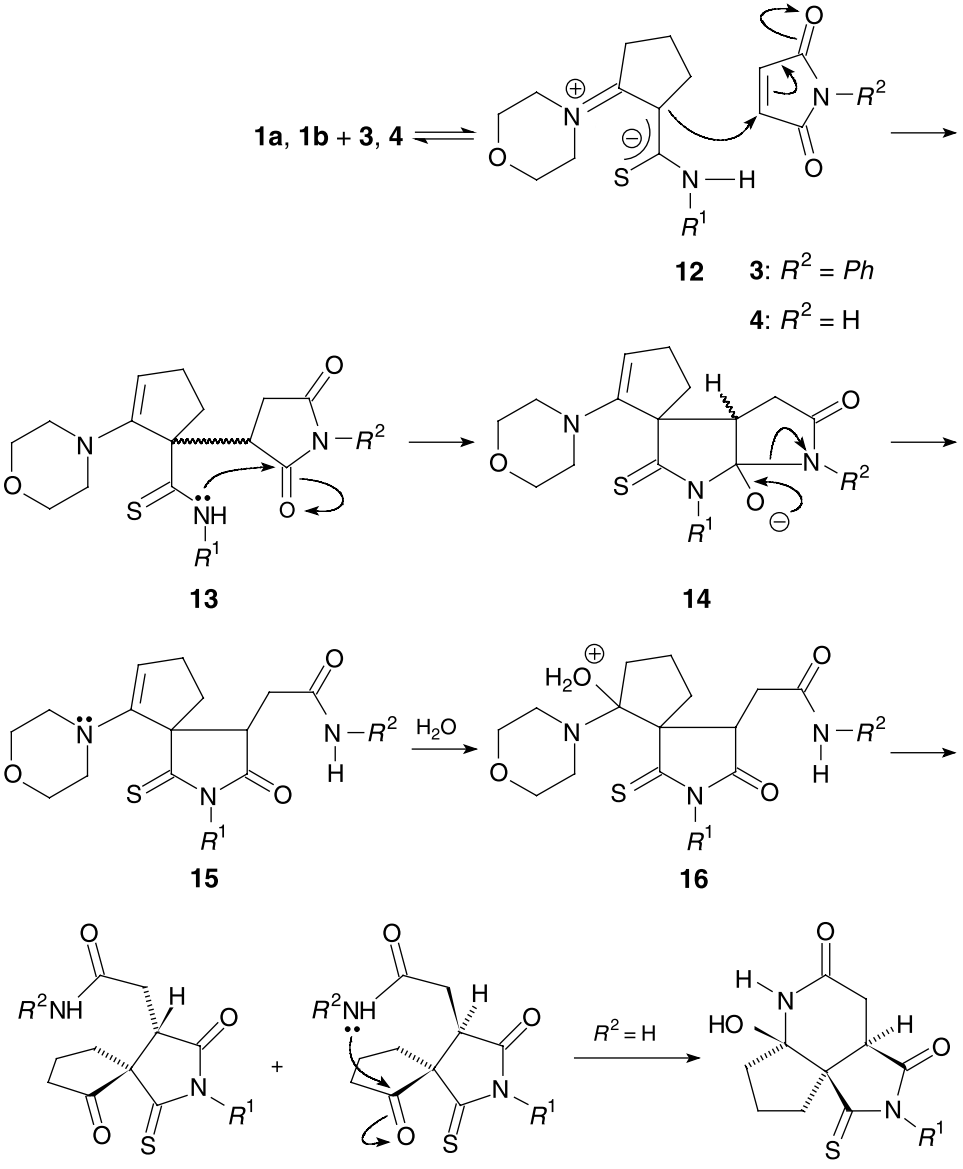


Fig. 5. The enantiomers of **10b** related by the centre of symmetry form dimers through the strong linear hydrogen bonds N(6)–H(2) ··· O(5)_3 ($-x+1$, $-y$, $-z+1$) with geometrical parameters *D*–H 0.80(4), H ··· *A* 2.13(4), *D* ··· *A* 2.923(3) Å; ∠*DHA* 176(3)°. The mutual packing of the dimers along **b** is determined by O(11) – H(11) ··· O(5) (x, $y+1$, z) hydrogen bonds [*D*–H 0.85(4), H ··· *A* 2.15(4), *D* ··· A 2.970(3) Å; ∠*DHA* 163(3)°]

bouring carbon atoms. A steric hindrance between C41-H41a and H9a-C9 (H41a $\cdots$ H9a = 2.12 Å) additionally influences the significant distortion of C4–C5–C9 from the tetrahedral angle.

The (4*S*,5*R*)- and (4*R*,5*S*)-enantiomers related by the center of symmetry form dimers through strong linear hydrogen bonds of N–H $\cdots$ O type (Fig. 2). The hydrogen bonds force the specific conformation of the pendant arm. The structure consists of layers built of **5b** molecules separated by layers formed by acetone molecules (Fig. 3).

The crystal structure of **10b** confirmed that the molecule has three fused rings with the C10 atom as a vertex of all three rings (Fig. 4). The piperidine and pyrrolidine rings as well as the piperidine and cyclopentane rings are in *cis*-relationship. The tricyclic system is highly strained with particularly elongated C10–C11 bond length. The pyrrolidine ring adopts



Scheme 3

an envelope conformation with the C12 atom out of C10C1N2C3 plane similarly to that observed in **5b**. The cycloalkane ring has the envelope conformation with the C11 atom out of C7C8C9C10 plane, whereas the cycloalkanone ring of **5b** has a different envelope conformation with the C8 atom above C9C5C6C7 plane. The conformational switch with significant changes of the appropriate torsion angles is forced by the formation of the piperidine ring. The six-membered ring adopts a *pseudo*-twist-boat conformation with the hydroxyl substituent almost perpendicular to the best plane of the ring (*e.g.* 93° between C11–O11 and C11 ⋯ C4). The packing in the crystal structure is determined by relatively strong hydrogen bonds formed by N–H and O–H from the hemiaminal moiety (Fig. 5). The centrosymmetric dimers with strong linear N6–H2 ⋯ O5 $(-x+1, -y, -z+1)$ hydrogen bonds stabilize the observed hemiaminal moiety in the crystalline state. The acceptance of two strong hydrogen bonds by the carbonyl oxygen O5 indicates an excess of electron density at O5, and the withdrawing effect could increase the stability of the hemiaminal moiety. An interesting geometric relation is observed between C1=S1 and O3=C3 $(x+3/2,\ y-1/2,\ -z+1/2)$ with the torsion angle C1–S1 ⋯ O3–C3 = 111.4° indicating dipol–dipol interaction.

Mechanism of the Reactions

The formation of the bicyclic and tricyclic products might be explained by a mechanism involving *Michael* addition of the substituted maleimide **3** or **4** to the enaminothioanilide, as shown in Scheme 3 for **1a** and **1b**. The negative charge of **12** is stabilized by the thiocarbonyl group. The alternative for this step could be an ene reaction; however, the typical ene reactions involving maleimides require much higher temperatures, at least 180°C [14], which does not match our conditions. The *Michael* adduct **13** is then converted by the nucleophilic attack of the thioamide nitrogen on the imide carbonyl group and ring opening of the polycyclic intermediate **14**, affording the monothioimide **15**. Spontaneous water hydrolysis of the enamine fragment of **15** provides a pair of stable products **5** and **6** when R^2 = phenyl. In the case of the products derived from **4**, a pair of diastereoisomers **10** and **17** is formed. However, only for the minor isomer **17** the proximity between the N-unsubstituted amide moiety and newly formed carbonyl group leads to the additional cyclization and formation of **9a** and **9b** with a hemiaminal function. The syntheses of hemiaminals by the direct attack of an amide-nitrogen on a carbonyl group have been published so far only for fluorinated or chlorinated ketones [15]. However, there are some other examples of 6-hydroxypiperidin-2-one ring formation in multi-step reactions. The six-membered rings stabilize considerably the hemiaminal functions [16].

Conclusion

In conclusion, we have shown the first examples of domino reactions of β-amino-α,β-unsaturated thioamides with maleimides, providing an easy access to polycyclic monothioimides, which have potential biological properties. The reaction with unsubstituted maleimide proceeded *via* an additional stereoselective ring closure affording tricyclic compounds with hemiaminal function.

Experimental

Melting points were determined on a Boetius hot-stage apparatus and are corrected. IR spectra were run in KBr pellets on a Bruker IFS 48 spectrometer. Mass spectra were obtained on a Finnigan Mat 95 (70 eV) mass spectrometer. NMR spectra were recorded on a Bruker AMX 500 spectrometer (^{1}H: 500.14 MHz, ^{13}C: 125.76 MHz) or Mercury-300 Varian in $CDCl_3$ or *DMSO*-d_6 using *TMS* as an internal standard. Elemental analyses (C, H, N) were conducted using the Euro EA 3000 Elemental Analyzer, their results were found to be in good agreement (±0.3%) with the calculated values. Diffraction data were collected using diffractometer Nonius Kappa CCD with graphite monochromated Mo-K_α radiation.

The *N*-aryl-2-(morpholin-4-yl)cyclopent-1-ene-1-carbothioamides **1a**, **1b**, and *N*-aryl-2-(morpholin-4-yl)cyclohex-1-ene-1-carbothioamides **2a**, **2b** were synthesized according to Ref. [11].

*Reactions of **1a**, **1b**, **2a**, and **2b** with N-Phenylmaleimide* (**3**)
To a solution of the appropriate thioanilide **1a**, **1b**, **2a**, or **2b** (2 mmol) in acetonitrile (90 cm^3, for **2b**: 160 cm^3), *N*-phenylmaleimide (692 mg, 4 mmol), and 2 drops of water were added. The mixture was stirred at room temperature for 3 d. The solvent was evaporated, and *ca.* 4 cm^3 *Me*OH were added, and the yellow precipitate was filtered off. The mixture of diastereoisomers was separated by fractional crystallization from $CHCl_3$. The major isomers **5a**, **5b**, **7a**, and **7b** were crystallized from *Me*OH/acetone 1/1. The minor diastereoisomers **6a**, **8a**, and **8b** were additionally purified by PTLC on silica gel ($CHCl_3$:acetone, 12:1) and crystallized from *Me*OH.

*Reaction of **1a** with **3***

A crude mixture of **5a** and **6a** was obtained according to the general procedure. Yellow powder (813 mg, 50%); m.p.: 217–223°C.

(4RS,5SR)-[2-(4-Methylphenyl)-3,6-dioxo-N-phenyl-1-thioxo-2-azaspiro[4.4]nonane-4-acetamide (**5a**, $C_{23}H_{22}N_2O_3S$)

After fractional crystallization the compound was obtained as a pale yellow powder (138 mg, 17%); m.p.: 225–228°C; ^{1}H NMR (300 MHz, *DMSO*-d_6): $\delta = 10.21$ (s, NH), 7.53 (d, $^3J = 7.7$ Hz, 2H^2-*Ph*), 7.35–7.28 (m, 2H^3-*Ph*, 2H^3-*Ar*), 7.13–7.02 (m, 2H^2-*Ar*, H^4-*Ph*), 3.42 (dd, $^3J = 5.1$ Hz, H-4), 3.10–2.95 (m, $\underline{H}_2$C–CONH*Ph*), 2.62–2.46 (m, 2H-7, H-9), 2.36 (s, CH_3), 2.41–2.21 (m, H-8, H-9), 2.03–1.90 (m, H-8) ppm; ^{13}C NMR (75 MHz, *DMSO*-d_6): $\delta = 214.4$ (C^6=O), 212.8 (C^1=S), 179.4 (C^3=O), 168.5 (C$\underline{O}$NH*Ph*), 138.5 (C^1–*Ph*, C^1-*Ar*), 132.3 (C^4-*Ar*), 129.7 (C^3-*Ar*), 128.7 (C^3-*Ph*), 127.3 (C^2-*Ar*), 123.3 (C^4-*Ph*), 119.1 (C^2-*Ph*), 68.3 (C-5), 44.1 (C-4), 36.7 (C-7), 34.1 (C$\underline{H}_2$CONH*Ph*), 31.3 (C-9), 20.7 (CH_3), 19.6 (C-8) ppm; IR (KBr): $\bar{\nu} = 3341$, 3036, 2954, 2919, 1759, 1737, 1688, 1601, 1547, 1511, 1499, 1443, 1419, 1383, 1323, 1282, 1195, 1169 cm^{-1}; MS (70 eV): m/z (%) = 406.0 (M$^+$, 38), 285.0 (18), 257.0 (100, M − *Ar*NCS), 230.0 (12), 228.0 (11), 202.0 (10), 91.0 (16), 77.0 (10).

(4RS,5RS)-[2-(4-Methylphenyl)-3,6-dioxo-N-phenyl-1-thioxo-2-azaspiro[4.4]nonane-4-acetamide (**6a**, $C_{23}H_{22}N_2O_3S$)

Yellow crystals (79 mg, 10%); m.p.: 218–221°C; ^{1}H NMR (300 MHz, *DMSO*-d_6,): $\delta = 10.18$ (s, NH), 7.59 (d, $^3J = 7.6$ Hz, 2H^2-*Ph*), 7.34–7.28 (m, 2H^3-*Ph*, 2H^3-*Ar*), 7.10–7.02 (m, 2H^2-*Ar*, H^4-*Ph*), 3.84 (dd, $^3J = 7.0$, 6.4 Hz, H-4), 3.03–2.90 (m, H-9), 2.84 (dd, $^2J = 15.9$, $^3J = 6.4$ Hz, $\underline{H}$C–CONH*Ph*), 2.60–2.47 (m, 2H-7, $\underline{H}$C–CONH*Ph*), 2.35 (s, CH_3), 2.39–2.21 (m, H-8, H-9), 2.05–1.90 (m, H-8) ppm; ^{13}C NMR (75 MHz, *DMSO*-d_6): $\delta = 213.4$ (C^6=O), 210.3 (C^1=S), 178.0 (C^3=O), 168.2 (C$\underline{O}$NH*Ph*), 138.8, 138.6 (C^1-*Ph*, C^1-*Ar*), 132.3 (C^4-*Ar*), 129.7, 128.7 (C^3-*Ar*, C^3-*Ph*), 127.2 (C^2-*Ar*), 123.2 (C^4-*Ph*), 119.0 (C^2-*Ph*), 69.8 (C-5), 46.2 (C-4), 37.9 (C-7), 33.4 (C-9), 32.3 (C$\underline{H}_2$CONH*Ph*), 20.7 (CH_3), 19.7 (C-8) ppm; IR (KBr): $\bar{\nu} = 3349$, 3052, 2978, 2921, 2889, 1742, 1688, 1600, 1532, 1513, 1497, 1439, 1426, 1381, 1326, 1285, 1191, 1157 cm^{-1}; MS (70 eV): m/z (%) = 406.1 (M$^+$, 63), 285.0 (22), 257.0 (100, M − *Ar*NCS), 230.0 (11), 93.0 (13), 91.0 (13), 77.0 (9).

*Reaction of **1b** with **3***

A crude mixture of **5b** and **6b** was obtained according to the general procedure. Yellow crystals (701 mg, 74%); m.p.: 225–230°C. After fractional crystallization only **5b** was isolated in pure form.

(4RS,5SR)-[2-(4-Bromophenyl)-3,6-dioxo-N-phenyl-1-thioxo-2-azaspiro[4.4]nonane-4-acetamide (**5b**, $C_{22}H_{19}BrN_2O_3S$)

Pale yellow crystals (158 mg, 17%); m.p.: 228–232°C; ^{1}H NMR (500 MHz, *DMSO*-d_6): $\delta = 10.2$ (s, NH), 7.76 (d, $^3J = 8.4$ Hz, 2H$^{2/3}$-*Ar*), 7.52 (d, $^3J = 7.8$ Hz, 2H^2-*Ph*), 7.30 (dd, $^3J = 7.8$ Hz, 2H^3-*Ph*), 7.21 (d, $^3J = 8.4$ Hz, H$^{2/3}$-*Ar*), 7.06 (t, $^3J = 7.4$ Hz, H^4-*Ph*), 3.45 (dd, $^3J = 5.0$ Hz, H-4), 3.08–2.99 (m, $\underline{H}_2$C–CONH*Ph*), 2.61–2.54 (m, 1H), 2.53–2.47 (m, 2H), 2.39–2.24 (m, 2H), 2.01–1.93 (m, 1H) ppm; ^{13}C NMR (126 MHz, *DMSO*-d_6): $\delta = 214.1$, 212.5, 179.0, 168.5, 138.5, 134.1, 132.3, 129.9, 128.6, 123.4, 122.2, 119.2, 68.5, 44.1, 36.7, 34.1, 31.2, 19.5 ppm; IR (KBr): $\bar{\nu} = 3367$, 3097, 3054, 2973, 2886, 1756, 1684, 1598, 1538, 1498, 1486, 1442, 1386, 1321, 1283, 1240, 1193, 1159, 1124 cm^{-1}; MS (70 eV): m/z (%) = 472.1 (M + 2, 55), 470.1 (M$^+$, 50), 351.1 (18), 349.1 (17), 323.1 (100), 321.1 (96), 296.0 (9), 294.0 (15), 186.1 (9).

*Reaction of **2a** with **3***

A crude mixture of **7a** and **8a** was obtained according to the general procedure. Yellow powder (635 mg, 76%); m.p.: 186–198°C.

(4RS,5SR)-2-(4-Methylphenyl)-N-phenyl-3,6-dioxo-1-thioxo-2-azaspiro[4.5]decane-4-acetamide (**7a**, $C_{24}H_{24}N_2O_3S$)

The title compound was obtained as pale yellow needles (195 mg, 23%); m.p.: 206–209°C; ^{1}H NMR (300 MHz, *DMSO*-d_6): $\delta = 10.20$ (s, NH), 7.53 (d, $^3J = 7.6$ Hz, 2H^2-*Ph*), 7.34–7.28 (m, 2H^3-*Ph*, 2H^3-*Ar*), 7.11 (d, $^3J = 8.2$ Hz, 2H^2-*Ar*), 7.05 (t, $^3J = 7.4$ Hz, H^4-*Ph*), 3.93 (dd, $^3J = 6.4$, 5.2 Hz, H-4), 3.04–2.93 (m, $\underline{H}_2$C–CONH*Ph*), 2.81 (ddd, $^2J = 16.1$, $^3J = 9.4$, 6.2 Hz, H-7), 2.61 (ddd, $^2J = 16.1$, $^3J = 5.6$ Hz, H-7), 2.41 (ddd, $^2J = 14.2$, $^3J = 6.8$, 4.2 Hz, H-10), 2.36 (s, CH_3), 2.31–2.22 (m, 1H), 2.13 (ddd, $^2J = 14.2$, $^3J = 9.2$, 4.2 Hz, H-10), 1.94–1.85 (m, 2H), 1.75–1.68 (m, 1H) ppm; ^{13}C NMR (75 MHz, *DMSO*-d_6): $\delta = 212.7$, 206.0, 178.5, 168.5, 138.6, 138.5, 132.3, 129.6, 128.6, 127.4, 123.3, 119.1, 67.3, 44.5, 33.5, 30.9, 23.5, 20.6, 20.5 ppm; IR (KBr): $\bar{\nu} = 3340$, 3037, 2941, 2875, 1756, 1737, 1699, 1685, 1598, 1544, 1512, 1498, 1441, 1424, 1379, 1325, 1284, 1253, 1165 cm^{-1}; MS (70 eV): m/z (%) = 420.2 (M$^+$, 100), 404.3 (14), 359.2 (16), 299.2 (26), 286.1 (20), 271.2 (85, M − *Ar*NCS), 266.2 (20), 243.1 (16), 230.1 (15), 169.0 (19), 151.1 (27), 123.1 (15), 93.1 (51), 91.1 (27), 77.0 (18).

(4RS,5RS)-2-(4-Methylphenyl)-N-phenyl-3,6-dioxo-1-thioxo-2-azaspiro[4.5]decane-4-acetamide (**8a**, $C_{24}H_{24}N_2O_3S$)

Yellow crystals (255 mg, 31%); m.p.: 206–208°C; ^{1}H NMR (300 MHz, *DMSO*-d_6): $\delta = 10.19$ (s, NH), 7.60 (d, $^3J = 7.6$ Hz, 2H^2-*Ph*), 7.34–7.27 (m, 2H^3-*Ph*, 2H^3-*Ar*), 7.08–7.01 (m, 2H^2-*Ar*, H^4-*Ph*), 3.67 (dd, $^3J = 6.8$, 5.8 Hz, H-4), 2.95 (dd, $^2J = 15.9$, $^3J = 6.8$ Hz, $\underline{H}$C–CONH*Ph*), 2.79–2.64 (m, 2H), 2.58 (dd, $^2J = 15.9$, $^3J = 5.8$ Hz, $\underline{H}$C–CONH*Ph*), 2.48–2.36 (m, 2H), 2.34 (s, CH_3), 2.08 (ddd, $J = 13.9$, 11.0, 4.8 Hz, H-10), 1.99–1.79 (m, 2H-8), 1.78–1.68 (m, H-9) ppm; ^{13}C NMR (75 MHz, *DMSO*-d_6): $\delta = 210.6$, 206.0, 177.6, 168.5, 138.9, 138.5, 132.3, 129.6, 128.6, 127.1, 123.2, 119.0, 69.7, 48.2, 38.4, 33.6, 32.6, 22.6, 21.3, 20.7 ppm; IR (KBr): $\bar{\nu} = 3357$, 3049, 2930, 2859, 1750, 1689, 1599, 1530, 1512, 1496, 1437, 1381, 1283, 1251, 1185, 1154, 1096 cm^{-1}; MS (70 eV): m/z (%) = 420.1 (M$^+$, 100), 402.1 (12), 359.2 (20), 299.1 (28), 271.1 (96, M − *Ar*NCS), 266.1 (24), 255.1 (17), 238.1 (65), 230.1 (16), 211.1 (18), 195.1 (41), 185.1 (51), 167.1 (31), 151.1 (31), 123.1 (22), 93.0 (36), 91.0 (20), 77.0 (16).

*Reaction of **2b** with **3***

A crude mixture of **7b** and **8b** was obtained according to the general procedure. Yellow powder (206 mg, 43%); m.p.: 205–216°C. The mixture of diastereoisomers was analytically pure.

(4RS,5SR)-2-(4-Bromophenyl)-3,6-dioxo-N-phenyl-1-thioxo-2-azaspiro[4.5]decane-4-acetamide (**7b**, $C_{23}H_{21}BrN_2O_3S$)

After fractional crystallization the title compound was obtained as pale yellow crystals (45 mg, 10%); m.p.: 229–231°C; ^{1}H NMR (300 MHz, *DMSO*-d$_6$): $\delta = 10.19$ (s, NH), 7.75 (d, $^3J = 8.6$ Hz, 2H$^{2/3}$-*Ar*), 7.53 (d, $^3J = 7.6$ Hz, 2H^2-*Ph*), 7.31 (dd, $^3J = 8.5$, 7.3 Hz, 2H^3-*Ph*), 7.23 (d, $^3J = 8.6$ Hz, 2H$^{2/3}$-*Ar*), 7.05 (t, $^3J = 7.3$ Hz, H^4-*Ph*), 3.94 (dd, $^3J = 6.2$, 5.3 Hz, H-4), 3.09–2.96 (m, $\underline{H}_2$C–CONH*Ph*), 2.86–2.71 (m, H-7), 2.68–2.57 (m, H-7), 2.45–2.38 (m, H-10), 2.32–2.21 (m, H-9), 2.12 (ddd, $J = 13.8$, 8.9, 3.3 Hz, H-10), 1.95–1.85 (m, 2H-8), 1.77–1.68 (m, H-9) ppm; ^{13}C NMR (75 MHz, *DMSO*-d$_6$): $\delta = 212.5$ (C^1=S), 205.9 (C^6=O), 178.3 (C^3=O), 168.5 ($\underline{C}$ONH*Ph*), 138.6 (C^1-*Ph*), 134.1, 132.3 (*Ar*), 130.0 (*Ar*), 128.7 (C^3-*Ph*), 123.3 (C^4-*Ph*), 122.2, 119.2 (C^2-*Ph*), 67.5 (C-5), 44.5 (C-4), 38.6 (C-7), 33.6 ($\underline{C}$H$_2$CONH*Ph*), 30.8 (C-10), 23.6 (C-8), 20.6 (C-9) ppm; IR (KBr): $\bar{\nu} = 3361$, 3056, 2945, 2879, 1753, 1705, 1675, 1598, 1538, 1499, 1486, 1442, 1375, 1339, 1279, 1251, 1164 cm^{-1}; MS (70 eV): m/z (%) = 486.0 (M + 2, 86), 484.0 (M$^+$, 81), 425.0 (15), 423.0 (16), 392.9 (19), 391.0 (18), 365.0 (48), 363.0 (47), 352.0 (32), 350.0 (33), 337.0 (100), 335.0 (97), 332.0 (32), 330.0 (30), 308.9 (27), 307.0 (25), 304.0 (22), 293.9 (30), 271.1 (27), 257.0 (22), 174.0 (20), 151.1 (26), 135.0 (21), 123.1 (17), 93.0 (98), 92.0 (26), 91.0 (19), 77.0 (43), 55.0 (25).

(4RS,5RS)-2-(4-Bromophenyl)-3,6-dioxo-N-phenyl-1-thioxo-2-azaspiro[4.5]decane-4-acetamide (**8b**, $C_{23}H_{21}BrN_2O_3S$)

Yellow crystals (74 mg, 16%); m.p.: 202–204°C; ^{1}H NMR (300 MHz, *DMSO*-d$_6$): $\delta = 10.20$ (s, NH), 7.73 (d, $^3J = 8.7$ Hz, Hz, 2H$^{2/3}$-*Ar*), 7.60 (d, $^3J = 8.5$ Hz, 2H^2-*Ph*), 7.31 (dd, $^3J = 8.5$, 7.4 Hz, 2H^3-*Ph*), 7.15 (d, $^3J = 8.7$ Hz, 2H$^{2/3}$-*Ar*), 7.05 (t, $^3J = 7.4$ Hz, H^4-*Ph*), 3.71 (dd, $^3J = 6.9$, 5.7 Hz, H-4), 2.94 (dd, $^2J = 15.9$, $^3J = 6.9$ Hz, $\underline{H}$C–CONH*Ph*), 2.79–2.64 (m, H-7, H-10), 2.58 (dd, $^2J = 15.9$, $^3J = 5.7$ Hz, $\underline{H}$C–CONH*Ph*), 2.48–2.31 (m, H-7, H-9), 2.08 (ddd, $J = 13.9$, 11.0, 4.8 Hz, H-10), 2.01–1.81 (m, 2H-8), 1.78–1.69 (m, H-9) ppm; ^{13}C NMR (75 MHz, *DMSO*-d$_6$): $\delta = 210.3$ (C^1=S), 205.9 (C^6=O), 177.3 (C^3=O), 168.5 ($\underline{C}$ONH*Ph*), 138.9 (C^1-*Ph*), 134.1, 132.3 (C$^{2/3}$-*Ar*), 129.7 (C$^{2/3}$-*Ar*), 128.7 (C^3-*Ph*), 123.2 (C^4-*Ph*), 122.2, 119.0 (C^2-*Ph*), 69.8 (C-5), 48.2 (C-4), 38.4 (C-7), 33.4 (C-10), 32.5 ($\underline{C}$H$_2$CONH*Ph*), 22.6 (C-8), 21.3 (C-9) ppm; IR (KBr): $\bar{\nu} = 3356$, 3051, 2926, 2858, 1748, 1690, 1599, 1531, 1487, 1438, 1373, 1308, 1285, 1185, 1155, 1098, 1068 cm^{-1}; MS (70 eV): m/z (%) = 486.0 (M + 2, 83), 484.0 (M$^+$, 76), 425.0 (18), 423.0 (17), 420.1 (21), 406.1 (29), 364.9 (24), 363.0 (22), 348.0 (18), 337.0 (81), 335.0 (82), 332.0 (21), 293.9 (17), 271.1 (39), 257.0 (52), 238.1 (17), 206.0 (35), 174.0 (94), 151.1 (46), 146.0 (100), 123.1 (27), 102.0 (29), 93.0 (95), 91.0 (26), 77.0 (33), 57.0 (29), 55.0 (25).

*Reactions of **1a** and **1b** with Maleimide* (***4***)

To a solution of the appropriate thioanilide **1a** or **1b** (1 mmol) in acetonitrile (40 cm^3), maleimide (194 mg, 2 mmol) and 2 drops of water were added. The mixture was stirred at room temperature for 3 d. The solvent was evaporated, and *ca.*, 2 cm^3 *Me*OH were added. The oily residue was cooled overnight, the precipitated crystals were collected by filtration, and recrystallized from acetone/*Me*OH 4/1.

(4RS,5SR)-2-(4-Methylphenyl)-3,6-dioxo-1-thioxo-2-azaspiro[4.4]nonane-4-acetamide (**9a**, $C_{17}H_{18}N_2O_3S$)

According to the procedure a mixture of **9a** and **10a** (199 mg, 60%) was obtained. After fractional crystallization (acetone/*Me*OH 4/1) pure **9a** was isolated as yellow crystals (107 mg, 33%); m.p.: 206–209°C; ^{1}H NMR (300 MHz, *DMSO*-d$_6$): $\delta = 7.59$ (s, NH), 7.31 (d, $^3J = 8.2$ Hz, 2H^3-*Ar*), 7.08 (d, $^3J = 8.2$ Hz, 2H^2-*Ar*), 7.02 (s, NH), 3.42 (dd, $^3J = 5.0$ Hz, H-4), 2.81–2.67 (m, H_2C–CONH$_2$), 2.65–2.42 (m, 3H), 2.36 (s, CH$_3$), 2.37–2.14 (m, 2H), 2.02–1.87 (m, 1H) ppm; ^{13}C NMR (75 MHz, *DMSO*-d$_6$): $\delta = 214.6$, 213.0, 179.7, 171.7, 138.5, 132.5, 129.7, 127.4, 68.4, 44.1, 36.8, 33.0, 31.2, 20.7, 19.7 ppm; IR (KBr): $\bar{\nu} = 3362$, 3164, 2973, 2941, 2920, 2880, 1766, 1742, 1677, 1512, 1431, 1377, 1322, 1270, 1179, 1156, 1084 cm^{-1}; MS (70 eV): m/z (%) = 330.1 (M$^+$, 96), 285.1 (17), 257.1 (100), 230.1 (20), 91.0 (11).

(3aRS,6aRS,9aRS)-2-(4-Bromophenyl)-6a-hydroxy-1-thioxo-decahydro-1H-cyclopenta[b]pyrrolo[3,4-c]pyridine-3,5-dione (**10b**, $C_{16}H_{15}BrN_2O_3S$)

Pale yellow crystals (168 mg, 21%); m.p.: 195–195°C; ^{1}H NMR (300 MHz, *DMSO*-d$_6$): $\delta = 8.39$ (s, NH), 7.72 (d, $^3J = 8.5$ Hz, 2H$^{2/3}$-*Ar*), 7.18 (d, $^3J = 8.5$ Hz, 2H$^{2/3}$-*Ar*), 6.50 (s, OH), 3.56 (dd, $^3J = 10.1$, 6.7 Hz, H-3a), 2.69 (dd, $^2J = 17.1$, $^3J = 6.7$ Hz, H-4), 2.57 (dd, $^2J = 17.1$, $^3J = 10.1$ Hz, H-4), 2.54–2.47 (m, 1H), 2.41–2.35 (m, 1H), 1.99 (dd, 1H, $^3J =$ 12.2, 8.3 Hz), 1.91–1.82 (m, 2H), 1.74–1.64 (m, 1H) ppm; ^{13}C NMR (75 MHz, *DMSO*-d$_6$): $\delta = 216.4$ (C=S), 178.5, 169.3 (C=O), 134.6, 132.1, 130.0, 121.9, 91.1 (C-6a), 63.9, 41.9, 35.1, 33.3, 27.7, 19.2 ppm; IR (KBr): $\bar{\nu} = 3341$, 3287, 3191, 3081, 2956, 2925, 2857, 1768, 1653, 1487, 1442, 1405, 1379, 1333, 1278, 1243, 1183, 1151, 1095, 1032 cm^{-1}; MS (70 eV): m/z (%) = 396.2 (M + 2, 66), 394.1 (M$^+$, 66), 378.1 (38), 376.2 (34), 363.1 (63), 361.1 (64), 351.2 (26), 349.1 (26), 323.1 (100), 321.1 (96), 296.1 (18), 294.1 (22), 215.0 (19), 213.0 (17), 169.1 (23), 135.1 (35), 134.1 (32).

*Reactions of **2a** and **2b** with Maleimide* (***4***)

To a solution of the appropriate thioanilide **2a** or **2b** (1 mmol) in acetonitrile (40 cm^3 for **2a**, 85 cm^3 for **2b**), maleimide (194 mg, 2 mmol) and 2 drops of water were added. The mixture was stirred at room temperature for 3 d. The solvent was evaporated, the resulting oil was dissolved in $CHCl_3$, washed with 1 *M* HCl, water, dried ($MgSO_4$), and chromatographed on silica gel ($CHCl_3$:*Me*OH, 20:1). The resulting oil was treated with *Me*OH, the precipitated crystals were collected by filtration, and recrystallized from acetone/*Me*OH 2/1.

(3aRS,6aRS,10aRS)-6a-Hydroxy-2-(4-methylphenyl)-1-thioxododecahydro-pyrrolo[3,4-d]quinoline-3,5-dione (**11a**, $C_{18}H_{20}N_2O_3S$)

Yellow crystals (59 mg, 9%); m.p.: 252–254°C; ^{1}H NMR (500 MHz, *DMSO*-d_6): $\delta = 8.35$ (s, NH), 7.27 (d, $^3J = 8.2$ Hz, 2H^3-*Ar*), 7.03 (d, $^3J = 8.2$ Hz, 2H^2-*Ar*), 6.25 (s, OH), 3.19 (dd, $^3J = 10.3$, 6.7 Hz, H-3a), 2.74–2.64 (m, $^2J = 17.1$, $^3J = 6.7$ Hz, H-4, H-9), 2.57–2.48 (m, H-4, H-7), 2.35 (s, CH_3), 2.04–1.98 (m, H-10), 1.70–1.53 (m, H-7, 2H-8, H-10), 1.45–1.39 (m, H-9) ppm; ^{13}C NMR (126 MHz, *DMSO*-d_6): $\delta = 215.5$ (C^1=S), 178.9 (C^3=O), 169.1 (C^5=O), 138.1 (C^4-*Ar*), 132.8 (C^1-*Ar*), 129.4 (C^3-*Ar*), 127.5 (C^2-*Ar*), 82.1 (C-6a), 57.0 (C-10a), 44.3 (C-3a), 33.6 (C-10), 31.4 (C-7), 28.1 (C-4), 21.6 (C-8), 20.6 (CH_3), 19.9 (C-9) ppm; IR (KBr): $\bar{\nu} = 3550$, 3374, 3212, 2965, 2921, 1753, 1650, 1513, 1441, 1383, 1277, 1253, 1200, 1162, 1081 cm^{-1}; MS (70 eV): m/z (%) = 344.1 (M$^+$, 42) 326.1 (100), 298.1 (24), 297.1 (66), 293.2 (31), 271.1 (23), 169.0 (16), 149.1 (62), 148.1 (48), 91.1 (29).

(3aRS,6aRS,10aRS)-2-(4-Bromophenyl)-6a-hydroxy-1-thioxododecahydro-pyrrolo[3,4-d]quinoline-3,5-dione (**11b**, $C_{17}H_{17}BrN_2O_3S$)

Yellow crystals (68 mg, 17%); m.p.: 238–241°C; ^{1}H NMR (500 MHz, *DMSO*-d_6): $\delta = 8.35$ (s, NH), 7.72 (d, $^3J = 8.6$ Hz, 2H$^{2/3}$-*Ar*), 7.14 (d, $^3J = 8.6$ Hz, 2H$^{2/3}$-*Ar*), 6.28 (s, OH), 3.22 (dd, $^3J = 10.4$, 6.7 Hz, H-3a), 2.74–2.64 (m, $^2J = 16.9$, $^3J = 6.7$ Hz, H-4 + 1H), 2.56 (dd, $^2J = 16.9$, $^3J = 10.4$ Hz, H-4), 2.52–2.47 (m, 1H), 2.05–2.00 (m, 1H), 1.71–1.55 (m, 4H), 1.46–1.40 (m, 1H) ppm; ^{13}C NMR (126 MHz, *DMSO*-d_6): $\delta = 215.3$ (C=S), 178.7, 169.1 (C=O), 134.7, 132.2, 130.2, 121.9 (CH arom), 82.1 (C(6a)), 57.2, 44.4, 33.4, 31.4, 28.0, 21.6, 19.9 ppm; IR (KBr): $\bar{\nu} = 3568$–3294, 3207, 2963, 2933, 1758, 1654, 1489, 1442, 1370, 1280, 1253, 1199, 1161, 1067, 1037 cm^{-1}; MS (70 eV): m/z (%) = 410.0 (M + 2, 17), 408.0 (M$^+$, 18), 392.0 (100), 390.0 (96), 363.0 (70), 361.0 (64), 359 (35), 357.1 (35), 335.0 (18), 169.0 (13), 149.1 (69), 148.1 (60), 134.1 (16).

Table 2. Crystal data and structure refinement details for **5b** and **10b**

Identification code	**5b**	**10b**
Crystal data		
Chemical formula	$C_{22}H_{19}BrN_2O_3S \cdot C_3H_6O$	$C_{16}H_{15}BrN_2O_3S$
Molecular weight	529.44	395.27
Mo-K_α, λ/Å	0.71073	0.71073
Crystal system	Monoclinic	Monoclinic
a/Å	35.4610(11)	10.2053(2)
b/Å	9.9774(3)	6.5168(1)
c/Å	14.3751(4)	23.4182(5)
β/°	106.908(2)	96.986(1)
V/Å^3	4866.2(3)	1545.89(5)
Temperature/K	293(2)	293(2)
Space group	*C* 2/*c*	*P* 2(1)/*n*
Z, *Dx*/Mg/m^3	8, 1.445	4, 1.698
μ/mm^{-1}	1.809	2.811
F(000)	2176	800
Crystal size/mm^3	0.37 × 0.25 × 0.01	0.40 × 0.15 × 0.02
θ range/°	3.34–27.93	3.11–27.43
Data collection		
Diffractometer	Nonius Kappa CCD	Nonius Kappa CCD
Data collection method	ϕ scans ($\kappa = 0$) + ω scans	ϕ scans ($\kappa = 0$) + ω scans
N_{meas}, N_{unique}, R_{int}	9274, 5774, 0.0471	5633, 3504, 0.0383
$N_{observed}$ [$I > 2\sigma(I)$]	3555	2745
Absorption correction	Multi-scan [17]	Multi-scan [17]
T_{min}, T_{max}	0.5541, 0.9821	0.3994, 0.9459
Refinement		
Data/restraints/parameters	5774/0/302	3504/0/217
Goodness-of-fit (*S*)	1.048	1.021
R indices [$I > 2\sigma(I)$]	$R_1 = 0.0550$, $wR_2 = 0.1088$	$R_1 = 0.0401$, $wR_2 = 0.0935$
R indices (all data)	$R_1 = 0.1075$, $wR_2 = 0.1327$	$R_1 = 0.0582$, $wR_2 = 0.1026$
A, *B* in *w* scheme[a]	0.0364, 10.0630	0.0399, 1.3834
Extinction coefficient	none	SHELXL, 0.0034(7)
$\Delta\rho_{max}$, $\Delta\rho_{min}$/eÅ^{-3}	0.360, −0.532	0.490, −0.555

[a] Weighting scheme: $w = 1/[\sigma 2(F_o^2) + (AP)^2 + BP]$ where $P = (F_o^2 + 2F_c^2)/3$

X-Ray Structure Analysis

Crystals suitable for X-ray diffraction experiment were obtained from acetone solutions by slow evaporation at room temperature. Table 2 gives details of data collections and refinements for **5b** and **10b**. *Lorentz*, polarization and absorption corrections were introduced.

The structures were solved by direct methods using SIR-92 [18] and refined by full-matrix least squares based on F^2 using SHELXL-97 [19]. The positions of hydrogen atoms were calculated from geometrical constraints: methine C–H = 0.98, methylene C–H = 0.97, methyl C–H = 0.96, aromatic C–H = 0.93 Å, and were introduced into refinement in the riding model. Molecular graphics: ORTEP-3 for Windows [20] and POV-Ray [21]. Software used to prepare supplementary material SHELXL-97 [19]. For deposition of supplementary material Ref. [22].

Acknowledgements

The Authors thank the Joint X-ray Laboratory Faculty of Chemistry, and SLAFIBS, Jagiellonian University, for making the Nonius Kappa CCD diffractometer available. We are also indebted to Dr. *E. Szneler*, Dr. *K. Czarnecki*, and Dr. *K. Jamroży*, for recording the NMR spectra.

References

[1] Jagodziński TS (2003) Chem Rev **103**: 197

[2] For reviews see: (a) Tietze LF, Kettschau G (1997) Hetero Diels-Alder Reactions in Organic Chemistry. In: Metz P (ed) Stereoselective Heterocyclic Synthesis I, Topics Curr Chem, vol 189, Springer, Berlin Heidelberg, p 1; (b) Metzner P (1999) Thiocarbonyl Compounds as Specific Tools for Organic Synthesis. In: Page PCB (ed) Organosulfur Chemistry I, Topics Curr Chem, vol 204, Springer, Berlin Heidelberg, p 127; (c) Bogdanowicz-Szwed K, Budzowski A (2003) Wiad Chem **57**: 435

[3] (a) Bogdanowicz-Szwed K, Budzowski A (2001) Monatsh Chem **132**: 947; (b) Bogdanowicz-Szwed K, Budzowski A (2002) Z Naturforsch **57b**: 637

[4] Bogdanowicz-Szwed K, Budzowski A, (2004) Monatsh Chem **135**: 97

[5] Sośnicki JG, Jagodziński TS, Hansen PE (2001) Tetrahedron **57**: 8705

[6] Sośnicki JG, Jagodziński TS, Liebscher J (1997) J Heterocyclic Chem **34**: 643

[7] Takido T, Tamura S, Sato K, Kamijo H, Nakazawa T, Hata T, Seno M (1998) J Heterocyclic Chem **35**: 437

[8] Ohno M, Shimizu S, Eguchi S (1990) Tetrahedron Lett **31**: 4613

[9] (a) Obniska J, Zejc A (2003) Acta Polon Pharm-Drug Res **60**: 383; (b) Obniska J (2004) Acta Polon Pharm-Drug Res **61**: 467

[10] Curtin ML, Garland RB, Heyman HR, Frey RR, Michaelides MR, Li J, Pease LJ, Glaser KB, Marcotte PA, Davidsen SK (2002) Bioorg Med Chem Lett **12**: 2919

[11] (a) Ried W, Käppeler W (1964) Liebigs Ann Chem **673**: 132; (b) Bogdanowicz-Szwed K (1982) Monatsh Chem **113**: 583

[12] Maleic anhydride was examined as a reagent as well, however it was excluded after initial experiments, because no desired products were detected

[13] Samples of the by-product were isolated from filtrates, its spectral data were consistent with the literature: Medion-Simon M, Pindur U (1991) Helv Chim Acta **74**: 430

[14] Cunningham ID, Brownhill A, Hamerton I, Howlin BJ (1997) Tetrahedron **53**: 13473

[15] (a) Sewald N, Seymour L, Burger K, Osipov SN, Kolomiets AF, Fokin AV (1994) Tetrahedron: Asymmetry **5**: 1051; (b) Hoess E, Rudolph M, Seymour L, Schierlinger C, Burger K (1993) J Fluorine Chem **61**: 163; (c) Aksinenko AY, Pushin AN, Sokolov VB (2002) Russ Chem Bl **51**: 2136

[16] (a) O'Callaghan CN, McMurry TBH, Draper SM, Champeil E (1999) J Chem Res, Miniprint **12**: 2901; (b) O'Callaghan CN, McMurry TBH, O'Brien JE, Draper SM, Gormley FK (1997) J Chem Res, Miniprint **2**: 453; (c) Sawada D, Takahashi H, Shiro M, Ikegami S (2005) Tetrahedron Lett **46**: 2399; (d) Vonhoff S, Piens K, Pipelier M, Braet C, Claeyssens M, Vasella A (1999) Helv Chim Acta **82**: 963; (e) Granier T, Vasella A (1998) Helv Chim Acta **81**: 865; (f) Soto JL, Seoane C, Zamorano P, Rubio MJ, Monforte A, Quinteiro M (1985) J Chem Soc Perkin Trans 1, 1681

[17] Otwinowski Z, Minor W (1997) Methods in Enzymology. In: Carter CW Jr, Sweet RM (eds) Macromolecular Crystallography, Part A, vol 276, Academic Press, New York, p 307

[18] Altomare A, Cascarano G, Giacovazzo C, Guagliardi A, Burla MC, Polidori G, Camalli M (1994) J Appl Cryst **27**: 435

[19] Sheldrick GM (1997) SHELXL97, A Program for the Refinement of Crystal Structures, University of Göttingen, Germany

[20] Farrugia L (1999) J Appl Cryst **32**: 837

[21] POV-Ray © POV-Team™ 1991–2002

[22] Crystallographic Data (excluding structure factors) for structures reported in this paper have been deposited with Cambridge Crystallographic Data Centre as Supplementary Publication No. CSD-605376 (**5b**) and CSD-605377 (**10b**). Copies of the data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) +44-1223-336-033; E-mail: deposit@ccdc.cam.ac.uk