2-Thioxopyrano[2,3-\textit{d}][1,3]thiazoles by Diels-Alder reaction of arylidenerhodanines under microwave irradiation

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Dedicated on the occasion of the jubilee of academician Irina P. Beletskaya

Abstract
The cycloaddition reaction of 5-arylidene rhodanine derivatives with dienophiles under microwave irradiation afforded the title compounds within short reaction times and in good yields.

Keywords: Rhodanine, benzylidene rhodanines, dienophiles, cycloaddition, microwave irradiation

Introduction
The chemistry of rhodanine and its derivatives has been studied for over half a century because of important chemical and biological applications. Rhodanine derivatives exhibit antibacterial, antiviral, anticonvulsant, antidiabetic and anti-HIV-1 activities,\textsuperscript{1-4} and have been reported as uridine diphospho-N-acetylmuramate/L-alanine ligase inhibitors.\textsuperscript{5} Therefore, the synthesis of new rhodanine derivatives is of considerable interest.

Diels-Alder reactions of arylidenerhodanines are a convenient route to fused thiazoles. The reactions of 5-arylidene-1,3-thiazolidine-2,4-dithiones with dimethyl acetylenedicarboxylate (DMAD), maleic anhydride, maleimide, and acrylonitrile in acetic acid at room temperature have been reported to yield thiopyrano[2,3-\textit{d}]thiazolidine-2-thiones.\textsuperscript{6}

Results and Discussion
Recently we have reported a convenient method for the synthesis of rhodanines 1. The reaction of amines, hydrazides, or oxamic acid thiohydrazides with thioicarboxyldiglycolic acid in the
presence of carbonyldiimidazole affords N-substituted rhodanines 1, which upon reaction with arylaldehydes form the corresponding arylidene derivatives 2 (Scheme 1).

\[
\begin{align*}
S &= C(SCH_2CO_2H)_2 \\
&\xrightarrow{1. 1,1'-\text{carbonyldiimidazole}} \text{THF, rt, 1.5 h} \\
&\xrightarrow{2. R-NH_2, \text{reflux, 4 h}} 1 \\
&\xrightarrow{\text{ArCH=O}} \xrightarrow{H_2NCH_2CH_2NH_2+2 \text{AcOH}} \xrightarrow{\text{MeOH, rt, 1–2 h}} 2
\end{align*}
\]

Scheme 1

We investigated the Diels-Alder reaction of arylidenerhodanines 2 with maleic anhydride, N-phenylmaleimide, and DMAD under various conditions: at room temperature, under reflux in various solvents (benzene, toluene, xylenes, acetic acid, acetic anhydride), and under high pressure (10–15 kbar) at various temperatures (from 20 to 150 °C). However, under these reaction conditions either the starting materials were recovered or tarry products were formed.

\[
\begin{align*}
R &\quad \text{Ar} = \text{Ph} \\
1a &\quad \text{PhNHC(S)(O)NH-} \\
1b &\quad 4-\text{ClC}_6\text{H}_4\text{NHC(S)(O)NH-} \\
1c &\quad 4-\text{ClC}_6\text{H}_4\text{NHC(S)(O)NH-} \\
1d &\quad \text{Ph-} \\
1e &\quad \text{S-CONH-}
\end{align*}
\]

Scheme 2
The wide applicability of microwave irradiation for chemical reaction enhancement is due to high reaction rates, formation of cleaner products, and operational simplicity.\(^9,^{10}\) A favorable effect of microwave irradiation on the formation of arylidenerhodanines in the course of the reaction of rhodanines with aromatic aldehydes has been noted previously.\(^{11,12}\) So far, microwave-induced cycloaddition reactions of 5-arylidenerhodanines have not been studied.

In fact, we found that the reactions of arylidenerhodanines 2a–e with maleic anhydride, \(N\)-phenylmaleimide, and DMAD under 210 W microwave radiation smoothly formed the respective cycloaddition products 3, 4, and 5 within 15–30 min in 72–90% yield (Scheme 2).

In conclusion, we developed a facile synthesis of pyrano[2,3-\(d\)][1,3]thiazoles 3–5 resulting from the cycloaddition reaction of arylidenerhodanines 2 with some dienophiles. Employing microwave irradiation was crucial for the progress of this reaction and provided good yields of pyrano[2,3-\(d\)][1,3]thiazoles.

**Experimental Section**

**General Procedures.** \(^1\)H and \(^13\)C NMR spectra were recorded on a Bruker AC-200 instrument in DMSO-\(d_6\). Mass spectra were obtained with a Kratos instrument using a direct inlet system; the ionization energy was 70 eV, the accelerating voltage was 1.75 kV. Melting points were measured on a Boetius hot-stage apparatus. The reactions were carried out with a microwave oven (Rolsen MS1770SA, 700W) in sealed vessels without external cooling. The purity of the products was checked by TLC (Merck Kieselgel 60 F\(_{254}\), EtOAc/ hexane).

2-Thioxo-1,3-thiazolidin-4-ones (1a–c) have been reported previously,\(^7\) likewise, starting materials 5-arylidene-4-oxo-2-thioxo-1,3-thiazolidines 2a–c have been prepared previously.\(^{8a,b}\)

2-Thioxo-1,3-thiazolidin-4-ones (1d,e). **General procedure**\(^7\)

A solution of trithiocarbonyldiglycolic acid (0.24 g, 1 mmol) and carbonyldiimidazole (0.32 g, 2 mmol) in tetrahydrofuran (10 mL) was stirred at room temperature for 1.5 h. The appropriate amine or hydrazide (1 mmol) was added, and the reaction mixture was refluxed for 4 h. Then 2 M hydrochloric acid (30 mL) was added, and the mixture was extracted with ethyl acetate (4×15 mL). The organic phases were combined, dried with MgSO\(_4\), and concentrated. The residue was purified by flash chromatography (silica gel, EtOAc/hexane, 1:3 v/v).

3-Phenyl-2-thioxo-1,3-thiazolidin-4-one (1d). The reaction with aniline (93 mg, 1 mmol) furnished yellow crystals 1d (0.19 g, 91%); mp 192–193 °C (EtOH/hexanes); \(R_f = 0.47\) (EtOAc–hexane, 1:1 v/v). \(^1\)H NMR (200 MHz, DMSO-\(d_6\)): \(\delta \) 7.59–7.45 (m, 3H), 7.39 (d, \(J = 7.3\) Hz, 2H), 4.41 (s, 2H). EI-MS: \(m/z\) (%) 209 (100, M\(^+\)).

N-(4-Oxo-2-thioxo-1,3-thiazolidin-3-yl)thiophene-2-carboxamide (1e). The reaction with 2-thiophene-carboxylic acid hydrazide (0.14 g, 1 mmol) furnished yellow crystals 1e (0.22 g, 87%); mp 172–173 °C; \(R_f = 0.55\) (EtOAc–hexane, 1:1 v/v). \(^1\)H NMR (200 MHz, DMSO-\(d_6\)): \(\delta \) 11.52 (s, 1H), 8.01–7.92 (m, 2H), 7.27 (t, \(J = 4.3\) Hz, 1H), 4.51 (s, 2H). EI-MS: \(m/z\) (%) 258 [M\(^+\)] (100).

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3-Substituted-5-arylidene-2-thioxo-1,3-thiazolidin-4-ones (2d–h). General procedure
A mixture of rhodanine 1 (1 mmol), araldehyde (1 mmol), and ethylenediammonium diacetate (18 mg, 0.1 mmol) in methanol (15 mL) was stirred at room temperature for 1–2 h. After evaporation of the solvent under reduced pressure, and the residue was purified by flash chromatography (sila gel, EtOAc/hexane, 1:3 v/v).

5-Benzylidene-3-phenyl-2-thioxo-1,3-thiazolidin-4-one (2d). The reaction of 1d (0.21 g, 1 mmol) with benzaldehyde (0.1 g, 1 mmol) furnished yellow crystals 2d (0.28 g, 95%); mp 185–186 °C; R_f = 0.69 (EtOAc/hexane, 1:1 v/v). 1H NMR (200 MHz, DMSO-d6): δ 7.82 (s, 1H), 7.63–7.45 (m, 6H), 7.42–7.33 (m, 3H), 7.13 (t, J = 7.3 Hz, 1H). EI-MS: m/z (%) 297 (100, M+).

Anal. calcd. for C_{16}H_{11}NOS_2: C, 64.62; H, 3.73; N, 4.71; S, 21.56. Found: C, 64.66; H, 3.65; N, 4.79; S, 21.50.

N-[5-Benzylidene-4-oxo-2-thioxo-1,3-thiazolidin-3-yl]thiophene-2-carboxamide (2e). The reaction of 1e (0.25 g, 1 mmol) with benzaldehyde (0.1 g, 1 mmol) furnished yellow crystals 2e (0.3 g, 87%); mp 167–168 °C; R_f = 0.75 (EtOAc/hexane, 1:1 v/v). 1H NMR (200 MHz, DMSO-d6): δ 10.51 (s, 1H), 8.05 (d, J = 4.7 Hz, 1H), 7.80 (s, 1H), 7.59 (t, J = 7.3 Hz, 2H), 7.51 (d, J = 7.3 Hz, 1H), 7.41 (t, J = 4.1 Hz, 1H), 7.29 (d, J = 3.5 Hz, 1H), 7.14 (t, J = 7.3 Hz, 1H). EI-MS: m/z (%) 346 (87, M+). Anal. calcd. for C_{15}H_{10}N_2O_2S_3: C, 52.00; H, 2.91; N, 8.09; S, 27.76. Found: C, 52.13; H, 2.83; N, 8.01; S, 27.79.

N-[5-(2-Hydroxybenzylidene)-4-oxo-2-thioxo-1,3-thiazolidin-3-yl]thiophene-2-carboxamide (2f). The reaction of 1f (0.25 g, 1 mmol) with salicylic aldehyde (0.1 g, 1 mmol) furnished yellow crystals 2f (0.3 g, 87%); mp 193–194 °C; R_f = 0.86 (EtOAc/hexane, 1:1 v/v). 1H NMR (200 MHz, DMSO-d6): δ 10.21 (s, 1H), 9.08 (s, 1H), 8.03 (d, J = 4.7 Hz, 1H), 7.95 (s, 1H), 7.49–7.42 (m, 2H), 7.31–7.22 (m, 3H), 6.84 (d, J = 7.7 Hz, 1H). EI-MS: m/z (%) 362 (98, M+). Anal. calcd. for C_{15}H_{10}N_2O_3S_3: C, 49.71; H, 2.78; N, 7.73; S, 26.54. Found: C, 49.71; H, 2.62; N, 7.79; S, 26.55.

N-[5-(2-Nitrobenzylidene)-4-oxo-2-thioxo-1,3-thiazolidin-3-yl]thiophene-2-carboxamide (2g). The reaction of 1g (0.25 g, 1 mmol) with 2-nitrobenzaldehyde (0.15 g, 1 mmol) furnished yellow crystals 2g (0.31 g, 79%); mp 201–202 °C; R_f = 0.86 (EtOAc/hexane, 1:1 v/v). 1H NMR (200 MHz, DMSO-d6): δ 10.55 (s, 1H), 8.25 (d, J = 7.9 Hz, 1H), 8.09 (s, 1H), 8.01 (d, J = 4.7 Hz, 1H), 7.89–7.80 (m, 2H), 7.44 (t, J = 4.1 Hz, 1H), 7.26 (d, J = 3.5 Hz, 1H), 7.12 (t, J = 7.6 Hz, 1H). EI-MS: m/z (%) 391 (85, M+). Anal. calcd. for C_{15}H_{9}N_3O_4S_3: C, 46.03; H, 2.32; N, 10.73; S, 24.57. Found: C, 46.16; H, 2.27; N, 10.79; S, 24.62.

N-[5-(4-Methoxybenzylidene)-4-oxo-2-thioxo-1,3-thiazolidin-3-yl]thiophene-2-carboxamide (2h). The reaction of 1h (0.25 g, 1 mmol) with 4-methoxybenzaldehyde (0.14 g, 1 mmol) furnished yellow crystals 2h (0.35 g, 92%); mp 177–178 °C (EtOH/hexanes); R_f = 0.75 (EtOAc/hexane, 1:1 v/v). 1H NMR (200 MHz, DMSO-d6): δ 10.52 (s, 1H), 8.02 (d, J = 4.7 Hz, 1H), 7.80 (s, 1H), 7.52–7.44 (m, 3H), 7.31–7.20 (m, 3H), 3.77 (s, 3H). EI-MS: m/z (%) 376 (88, M+). Anal. calcd. for C_{16}H_{12}N_2O_3S_3: C, 51.05; H, 3.21; N, 7.44; S, 25.55. Found: C, 51.15; H, 3.22; N, 7.38; S, 25.59.
2-Thioxopyrano[2,3-d][1,3]thiazoles (3 - 5). General procedure
5-Arylidenerhodanine 2 (0.1 mmol), dienophile (0.1 mmol), and acetic acid (2 mL) were mixed in a tightly closed tube with a heat-resistant lid. The tube was placed in a microwave oven and irradiated at 210 W for 15–30 min. The reaction mixture was cooled and poured into water (20 mL). The yellow precipitate formed was filtered off, washed with water and recrystallized from EtOH/hexanes mixtures.

2-[(5,7-Dioxo-8-phenyl-2-thioxo-4a,5,7a,8-tetrahydro-2H-furo[3′,4′:5,6]pyrano[2,3-d][1,3]thiazol-3(7H)-yl)amino]-N-phenyl-2-thioxoacetamide (3a). The reaction of 2a\(^{8a}\) (0.04 g, 0.1 mmol) with maleic anhydride (0.01 g, 0.1 mmol) furnished light yellow crystals 3a (42 mg, 82%); mp 285–286 °C (EtOH/hexanes); \( R_f = 0.68 \) (EtOAc/hexane, 1:1 v/v). \(^{1}\)H NMR (200 MHz, DMSO-\(d_6\)): \( \delta 10.38 \) (s, 1H), 7.75–7.01 (m, 10 H), 5.45 (d, \( J = 9.1 \) Hz, 1H), 4.83 (d, \( J = 6.2 \) Hz, 1H), 3.75–3.60 (m, 1 H). \(^{13}\)C NMR (50 MHz, DMSO-\(d_6\)): \( \delta 187.7, 174.6, 173.1, 170.6, 167.8, 148.3, 141.8, 140.9, 132.3, 127.9, 126.8, 125.0, 125.6, 121.7, 101.9, 79.6, 49.3, 39.5. EI-MS: \( m/z \) (%) 319 (48), 179 (32). Anal. calcd. for C\(_{22}\)H\(_{15}\)N\(_3\)O\(_5\)S\(_3\): C, 53.11; H, 3.04; N, 8.44; S, 19.33. Found: C, 53.21; H, 3.00; N, 8.29; S, 19.48.

N-(4-Chlorophenyl)-2-[(5,7-dioxo-8-phenyl-2-thioxo-4a,5,7a,8-tetrahydro-2H-furo[3′,4′:5,6]pyrano[2,3-d][1,3]thiazol-3(7H)-yl)amino]-2-thioxoacetamide (3b). The reaction of 2b\(^{8a}\) (43 mg, 0.1 mmol) with maleic anhydride (0.01 g, 0.1 mmol) furnished light yellow crystals 3b (39 mg, 74%); mp 302–303 °C (EtOH/hexanes); \( R_f = 0.59 \) (EtOAc/hexane, 1:1 v/v). \(^{1}\)H NMR (200 MHz, DMSO-\(d_6\)): \( \delta 10.03 \) (s, 1H), 7.68–7.03 (m, 9 H), 5.45 (d, \( J = 9.1 \) Hz, 1H), 4.65 (d, \( J = 6.2 \) Hz, 1H), 3.73–3.62 (m, 1 H). \(^{13}\)C NMR (50 MHz, DMSO-\(d_6\)): \( \delta 187.7, 174.6, 173.1, 170.6, 167.7, 148.3, 140.9, 138.9, 130.6, 129.6, 127.8, 126.8, 125.6, 121.2, 101.9, 79.6, 49.3, 39.5. EI-MS: \( m/z \) (%) 319 (53), 214 (41). Anal. calcd. for C\(_{22}\)H\(_{14}\)ClN\(_3\)O\(_5\)S\(_3\): C, 49.67; H, 2.65; Cl, 6.66; N, 7.90; S, 18. Found: C, 53.35; H, 2.85; N, 8.15; S, 19.63.

2-[(5,7-Dioxo-8-phenyl-2-thioxo-4a,5,7a,8-tetrahydro-2H-furo[3′,4′:5,6]pyrano[2,3-d][1,3]thiazol-3(7H)-yl)amino]-N-(4-methoxyphenyl)-2-thioxoacetamide (3c). The reaction of 2c\(^{8a,b}\) (0.043 g, 0.1 mmol) with maleic anhydride (0.01 g, 0.1 mmol) furnished light yellow crystals 3c (0.047 g, 89%); mp 257–258 °C (EtOH/hexanes); \( R_f = 0.71 \) (EtOAc/hexane, 1:1 v/v). \(^{1}\)H NMR (200 MHz, DMSO-\(d_6\)): \( \delta 10.67 \) (s, 1H), 7.68–6.92 (m, 9 H), 5.35 (d, \( J = 9 \) Hz, 1H), 4.63 (d, \( J = 6.1 \) Hz, 1H), 3.75–3.61 (m, 1 H), 3.75 (s, 3H). \(^{13}\)C NMR (50 MHz, DMSO-\(d_6\)): \( \delta 187.9, 174.6, 173.1, 170.6, 173.0, 167.8, 156.1, 148.3, 140.9, 135.6, 127.8, 126.8, 125.6, 121.2, 101.9, 79.6, 49.3, 39.5. EI-MS: \( m/z \) (%) 319 (39), 210 (30). Anal. calcd. for C\(_{23}\)H\(_{17}\)N\(_3\)O\(_6\)S\(_3\): C, 52.36; H, 3.25; N, 7.96; S, 18.23. Found: C, 52.49; H, 3.05; N, 7.80; S, 18.46.

3,8-Diphenyl-2-thioxo-3,4a,7a,8-tetrahydro-2H-furo[3′,4′:5,6]pyrano[2,3-d][1,3]thiazole-5,7-dione (3d). The reaction of 2d (0.03 g, 0.1 mmol) with maleic anhydride (0.01 g, 0.1 mmol) furnished light yellow crystals 3d (35 mg, 90%); mp 237–238 °C (EtOH/hexanes); \( R_f = 0.50 \) (EtOAc–hexane, 1:1 v/v). \(^{1}\)H NMR (200 MHz, DMSO-\(d_6\)): \( \delta 7.88–7.01 \) (m, 10 H), 5.23 (d, \( J = 9.1 \) Hz, 1H), 4.63 (d, \( J = 6.1 \) Hz, 1H), 3.75–3.61 (m, 1 H), 3.75 (s, 3H). \(^{13}\)C NMR (50 MHz, DMSO-\(d_6\)): \( \delta 185.3, 174.8, 171.2, 151.7, 142.9, 140.9, 129.9, 128.2, 126.3, 125.2, 123.1, 120.2, 97.6, 78.6, 49.3, 39.5.
EI-MS: m/z (%) 395 (74, M⁺). Anal. calcd. for C₂₀H₁₄N₂O₅S₂: C, 56.33; H, 3.31; N, 6.57; S, 15.04. Found: C, 56.30; H, 3.21; N, 6.42; S, 15.18.

N-(5,7-Dioxo-8-phenyl-2-thioxo-4a,5,7a,8-tetrahydro-2-furo[3′,4′:5,6]pyrano[2,3-d][1,3]thiazol-3(7H)-yl)thiophene-2-carboxamide (3e). The reaction of 2e (35 mg, 0.1 mmol) with maleic anhydride (0.01 g, 0.1 mmol) furnished light yellow crystals 3e (37 mg, 83%); mp 268−269 °C (EtOH/hexanes); Rf = 0.50 (EtOAc/hexane, 1:1 v/v). ¹H NMR (200 MHz, DMSO-d₆): δ 9.89 (s, 1H), 7.91−7.05 (m, 8H), 5.15 (d, J = 9 Hz, 1H), 4.83 (d, J = 6.1 Hz, 1H), 3.78−3.65 (m, 1H). ¹³C NMR (50 MHz, DMSO-d₆): δ 182.4, 174.7, 171.2, 158.3, 154.2, 139.9, 139.2, 137.7, 128.9, 127.1, 126.8, 125.3, 124.8, 103.9, 76.4, 49.3, 36.2. EI-MS: m/z (%) 444 (57, M⁺). Anal. calcd. for C₂₀H₁₄N₂O₅S₂: C, 56.33; H, 3.31; N, 6.57; S, 15.04. Found: C, 56.30; H, 3.21; N, 6.42; S, 15.18.

2-[(5,7-Dioxo-6,8-diphenyl-2-thioxo-4a,5,6,7a,8-hexahydropyrrolo[3′,4′:5,6]pyrano[2,3-d][1,3]thiazol-3(2H)-yl)amino]-N-phenyl-2-thiooxacetamide (4a). The reaction of 2a (0.04 g, 0.1 mmol) with N-phenylmaleimide (17 mg, 0.1 mmol) furnished light yellow crystals 4a (49 mg, 86%); mp 271−272 °C (EtOH/hexanes); Rf = 0.55 (EtOAc/hexane, 1:1 v/v). ¹H NMR (200 MHz, DMSO-d₆): δ 10.25 (s, 1H), 7.76−6.82 (m, 15H), 5.38 (d, J = 9 Hz, 1H), 4.74 (d, J = 6 Hz, 1H), 4.29−4.05 (m, 1H). ¹³C NMR (50 MHz, DMSO-d₆): δ 187.2, 174.5, 172.9, 168.5, 167.7, 147.2, 143.2, 141.2, 133.7, 132.2, 129.4, 128.6, 128.2, 126.8, 126.2, 125.7, 124.9, 121.8, 101.0, 87.7, 51.5, 41.6. EI-MS: m/z (%) 394 (25), 179 (37). Anal. calcd. for C₂₈H₂₀N₄O₅S₃: C, 58.73; H, 3.52; N, 9.78; S, 16.80. Found: C, 58.89; H, 3.41; N, 9.62; S, 16.95.

N-(4-Chlorophenyl)-2-[(5,7-dioxo-6,8-diphenyl-2-thioxo-4a,5,6,7a,8-hexahydropyrrolo[3′,4′:5,6]pyrano[2,3-d][1,3]thiazol-3(2H)-yl)amino]-2-thiooxacetamide (4b). The reaction of 2b (0.04 g, 0.1 mmol) with N-phenylmaleimide (17 mg, 0.1 mmol) furnished light yellow colored crystals 4b (0.048 g, 80%) after recrystallization; mp 292−293 °C (EtOH/hexanes); Rf = 0.50 (EtOAc/hexane, 1:1 v/v). ¹H NMR (200 MHz, DMSO-d₆): δ 10.45 (s, 1H), 7.78−7.05 (m, 14H), 5.46 (d, J = 9.0 Hz, 1H), 4.65 (d, J = 6.0 Hz, 1H), 4.15−4.02 (m, 1H). ¹³C NMR (50 MHz, DMSO-d₆): δ 187.5, 174.4, 173.1, 168.3, 167.7, 147.0, 143.4, 138.8, 133.7, 130.7, 129.6, 129.2, 128.6, 128.2, 126.9, 126.2, 124.9, 121.2, 100.7, 87.6, 51.6, 41.6. EI-MS: m/z (%) 394 (37), 214 (46). Anal. calcd. for C₂₈H₁₉ClN₄O₅S₃: C, 55.39; H, 3.15; Cl, 5.84; N, 9.23; S, 15.84. Found: C, 55.55; H, 3.10; Cl, 5.70; N, 9.11; S, 16.04.

2-[(5,7-Dioxo-6,8-diphenyl-2-thioxo-4a,5,6,7a,8-hexahydropyrrolo[3′,4′:5,6]pyrano[2,3-d][1,3]thiazol-3(2H)-yl)amino]-N-(4-methoxyphenyl)-2-thiooxacetamide (4c). The reaction of 2c (43 mg, 0.1 mmol) with N-phenylmaleimide (17 mg, 0.1 mmol) furnished light yellow crystals 4c (47 mg, 78%); mp 267−268 °C (EtOH/hexanes); Rf = 0.55 (EtOAc/hexane, 1:1 v/v). ¹H NMR (200 MHz, DMSO-d₆): δ 10.55 (s, 1H), 7.68−6.82 (m, 14H), 5.37 (d, J = 9.0 Hz, 1H), 4.65 (d, J = 6 Hz, 1H), 4.29−4.05 (m, 1H), 3.75 (s, 3H). ¹³C NMR (50 MHz, DMSO-d₆): δ 187.4, 174.5, 173.2, 168.4, 167.7, 156.1, 147.2, 143.3, 135.7, 133.7, 129.2, 128.6, 128.3, 126.8, 126.4, 124.9, 121.3, 116.7, 100.6, 87.6, 55.4, 51.6, 41.5. EI-MS: m/z (%) 409 (15), 210 (25). Anal. calcd. for C₂₉H₂₂N₄O₅S₃: C, 57.79; H, 3.68; N, 9.30; S, 15.96. Found: C, 57.92; H, 3.52; N, 9.19; S, 16.10.
3,6,8-Triphenyl-2-thioxo-3,4a,7a,8-tetrahydropyrrolo[3',4':5,6]pyrano[2,3-d][1,3]thiazole-5,7(2H,6H)-dione (4d). The reaction of 2d (0.03 g, 0.1 mmol) with N-phenylmaleimide (17 mg, 0.1 mmol) furnished light yellow crystals 4d (0.04 g, 86%); mp 229–230 °C (EtOH/hexanes); Rf = 0.50 (EtOAc/hexane, 1:1 v/v). ¹H NMR (200 MHz, DMSO-d₆): δ 7.78–6.92 (m, 15 H), 5.23 (d, J = 8.9 Hz, 1H), 4.37 (d, J = 6.1 Hz, 1H), 4.28–4.12 (m, 1H). ¹³C NMR (50 MHz, DMSO-d₆): δ 183.2, 174.6, 170.9, 150.9, 143.2, 142.8, 138.2, 129.9, 129.2, 128.9, 128.5, 126.8, 125.6, 124.9, 122.8, 119.8, 96.9, 86.2, 51.5, 38.3. EI-MS: m/z (%) 470 (63, M⁺). Anal. calcd. for C₂₆H₁₈N₂O₃S₂: C, 66.36; H, 3.86; N, 5.95; S, 13.63. Found: C, 66.48; H, 3.75; N, 6.01; S, 13.75.

N-(5,7-Dioxo-6,8-diphenyl-2-thioxo-4a,5,6,7,7a,8-hexahydropyrrolo[3',4':5,6]pyrano[2,3-d][1,3]thiazol-3(2H)-yl)thiophene-2-carboxamide (4e). The reaction of 2e (0.03 g, 0.1 mmol) with N-phenylmaleimide (17 mg, 0.1 mmol) furnished light yellow crystals 4e (0.04 g, 86%); mp 229–230 °C (EtOH/hexanes); Rf = 0.50 (EtOAc/hexane, 1:1 v/v). ¹H NMR (200 MHz, DMSO-d₆): δ 7.78–6.92 (m, 15 H), 5.23 (d, J = 8.9 Hz, 1H), 4.37 (d, J = 6.1 Hz, 1H), 4.28–4.12 (m, 1H). ¹³C NMR (50 MHz, DMSO-d₆): δ 183.2, 174.6, 170.9, 150.9, 143.2, 142.8, 138.2, 129.9, 129.2, 128.9, 128.5, 126.8, 125.6, 124.9, 122.8, 119.8, 96.9, 86.2, 51.5, 38.3. EI-MS: m/z (%) 470 (63, M⁺). Anal. calcd. for C₂₆H₁₈N₂O₃S₂: C, 66.36; H, 3.86; N, 5.95; S, 13.63. Found: C, 66.48; H, 3.75; N, 6.01; S, 13.75.

Dimethyl 3-[{(2-anilino-2-oxoethanethioyl)amino]-7-phenyl-2-thioxo-3,7-dihydro-2H-pyrano[2,3-d][1,3]thiazole-5,6-dicarboxylate (5a). The reaction of 2a (0.04 g, 0.1 mmol) with DMAD (14 mg, 0.1 mmol) furnished light yellow crystals 5a (0.04 g, 86%); mp 229–230 °C (EtOH/hexanes); Rf = 0.50 (EtOAc/hexane, 1:1 v/v). ¹H NMR (200 MHz, DMSO-d₆): δ 9.82 (s, 1H), 8.05–6.92 (m, 13 H), 4.62 (s, 1H). ¹³C NMR (50 MHz, DMSO-d₆): δ 182.6, 174.6, 170.9, 150.9, 143.2, 142.8, 138.2, 129.9, 129.2, 128.9, 128.5, 126.7, 126.3, 125.2, 124.7, 103.8, 83.3, 51.7, 37.3. EI-MS: m/z (%) 519 (25, M⁺). Anal. calcd. for C₂₅H₁₇N₃O₄S₃: C, 57.79; H, 3.30; N, 8.09; S, 18.51. Found: C, 57.91; H, 3.25; N, 8.19; S, 18.67.

Dimethyl 3-[(2-anilino-2-oxoethanethioyl)amino]-7-phenyl-2-thioxo-3,7-dihydro-2H-pyrano[2,3-d][1,3]thiazole-5,6-dicarboxylate (5b). The reaction of 2b (0.04 g, 0.1 mmol) with DMAD (14 mg, 0.1 mmol) furnished light yellow crystals 5b (0.04 g, 86%); mp 229–230 °C (EtOH/hexanes); Rf = 0.50 (EtOAc/hexane, 1:1 v/v). ¹H NMR (200 MHz, DMSO-d₆): δ 9.82 (s, 1H), 8.05–6.92 (m, 13 H), 4.62 (s, 1H). ¹³C NMR (50 MHz, DMSO-d₆): δ 182.6, 174.6, 170.9, 150.9, 143.2, 142.8, 138.2, 129.9, 129.2, 128.9, 128.5, 126.7, 126.3, 125.2, 124.7, 103.8, 83.3, 51.7, 37.3. EI-MS: m/z (%) 519 (25, M⁺). Anal. calcd. for C₂₅H₁₇N₃O₄S₃: C, 57.79; H, 3.30; N, 8.09; S, 18.51. Found: C, 57.91; H, 3.25; N, 8.19; S, 18.67.
123.3, 121.3, 118.2, 116.7, 96.8, 55.5, 52.4, 51.6, 42.2. EI-MS: m/z (%) 363 (33), 210 (29). Anal. calcd. for C_{25}H_{23}N_{3}O_{7}S_{3}: C, 52.34; H, 4.04; N, 7.32; S, 16.77. Found: C, 52.52; H, 3.88; N, 7.20; S, 16.90.

**Dimethyl 3,7-diphenyl-2-thioxo-3,7-dihydro-2H-pyrano[2,3-d][1,3]thiazole-5,6-dicarboxylate (5d).** The reaction of 2d (0.03 g, 0.1 mmol) with DMAD (14 mg, 0.1 mmol) furnished light yellow crystals 5d (0.034 g, 78%); mp 215–216 °C (EtOH/hexanes); R_f = 0.65 (EtOAc/hexane, 1:1 v/v). ¹H NMR (200 MHz, DMSO-d_6): δ 7.79–7.01 (m, 10 H), 4.55 (s, 1 H), 3.75 (s, 3H), 3.62 (s, 3H). EI-MS: m/z (%) 439 (75, M+).

13C NMR (50 MHz, DMSO-d_6): δ 183.5, 166.2, 164.7, 146.4, 145.2, 143.1, 139.8, 130.9, 129.9, 129.2, 123.9, 122.6, 120.8, 120.1, 92.6, 52.5, 51.6, 40.9. Anal. calcd. for C_{22}H_{19}NO_{5}S_{2}: C, 59.85; H, 4.34; N, 3.17; S, 14.52. Found: C, 59.99; H, 4.23; N, 3.07; S, 14.64.

**Dimethyl 7-phenyl-3-[(2-thienylcarbonyl)amino]-2-thioxo-3,7-dihydro-2H-pyrano[2,3-d][1,3]thiazole-5,6-dicarboxylate (5e).** The reaction of 2e (35 mg, 0.1 mmol) with DMAD (14 mg, 0.1 mmol) furnished light yellow crystals 5e (0.04 g, 82%); mp 257–258 °C (EtOH/hexanes); R_f = 0.63 (EtOAc/hexane, 1:1 v/v). ¹H NMR (200 MHz, DMSO-d_6): δ 9.37 (s, 1H), 8.15 (d, J = 4.5 Hz, 1H), 7.45-7.31 (m, 3H), 7.25–7.1 (m, 2H), 7.0 (d, J = 6.9 Hz, 1H) 4.62 (s, 1H), 3.81 (s, 3H), 3.75 (s, 3H). EI-MS: m/z (%) 488 (38, M+). Anal. calcd. for C_{21}H_{16}N_{2}O_{6}S_{3}: C, 51.63; H, 3.30; N, 5.73; S, 19.69. Found: C, 51.80; H, 3.25; N, 5.60; S, 19.82.

**Dimethyl 7-(2-hydroxyphenyl)-3-[(2-thienylcarbonyl)amino]-2-thioxo-3,7-dihydro-2H-pyrano[2,3-d][1,3]thiazole-5,6-dicarboxylate (5f).** The reaction of 2f (36 mg, 0.1 mmol) with DMAD (14 mg, 0.1 mmol) furnished light yellow crystals 5f (31 mg, 62%); mp 273–274 °C (EtOH/hexanes); R_f = 0.60 (EtOAc/hexane, 1:1 v/v). ¹H NMR (200 MHz, DMSO-d_6): δ 10.35 (s, 1H), 9.23 (s, 1H), 8.15 (d, J = 4.7 Hz, 1H), 7.45 (t, J = 4.8 Hz, 1H), 7.33 (d, J = 7.9 Hz, 1H), 7.21 (d, J = 3.55 Hz, 1H), 7.03 (t, J = 8.0 Hz, 2H), 6.80 (d, J = 8.3 Hz, 1H), 4.65 (s, 1H), 3.84 (s, 3H), 3.75 (s, 3H). EI-MS: m/z (%) 504 (15, M+). Anal. calcd. for C_{21}H_{16}N_{2}O_{7}S_{3}: C, 49.99; H, 3.20; N, 5.55; S, 19.06. Found: C, 51.80; H, 3.25; N, 5.60; S, 19.82.

**Dimethyl 7-(2-nitrophenyl)-3-[(2-thienylcarbonyl)amino]-2-thioxo-3,7-dihydro-2H-pyrano[2,3-d][1,3]thiazole-5,6-dicarboxylate (5g).** The reaction of 2g (39 mg, 0.1 mmol) with DMAD (14 mg, 0.1 mmol) furnished light yellow crystals 5g (0.03 g, 57%); mp 287–288 °C (EtOH/hexanes); R_f = 0.60 (EtOAc/hexane, 1:1 v/v). ¹H NMR (200 MHz, DMSO-d_6): δ 10.35 (s, 1H), 9.23 (s, 1H), 8.15 (d, J = 4.7 Hz, 1H), 7.45 (t, J = 4.8 Hz, 1H), 7.33 (d, J = 7.9 Hz, 1H), 7.21 (d, J = 3.55 Hz, 1H), 7.03 (t, J = 8.0 Hz, 2H), 6.80 (d, J = 8.3 Hz, 1H), 4.65 (s, 1H), 3.84 (s, 3H), 3.75 (s, 3H). EI-MS: m/z (%) 533 (31, M+). Anal. calcd. for C_{21}H_{16}N_{3}O_{8}S_{3}: C, 47.27; H, 2.83; N, 7.88; S, 18.03. Found: C, 47.37; H, 2.75; N, 7.99; S, 18.17.
Dimethyl 7-(4-methoxyphenyl)-3-[(2-thienylcarbonyl)amino]-2-thioxo-3,7-dihydro-2H-pyrano[2,3-d][1,3]thiazole-5,6-dicarboxylate (5h). The reaction of 2h (38 mg, 0.1 mmol) with DMAD (14 mg, 0.1 mmol) furnished light yellow crystals 5h (0.039 g, 68%); mp 287–288 °C (EtOH/hexanes); Rf = 0.65 (EtOAc/hexane, 1:1 v/v). $^1$H NMR (200 MHz, DMSO-d$_6$): δ 9.32 (s, 1H), 8.05 (d, $J = 4.7$ Hz, 1H), 7.45 (t, $J = 4.6$ Hz, 1H), 7.23 (d, $J = 3.6$ Hz, 1H), 7.15 (d, $J = 8.2$ Hz, 2H), 6.93 (d, $J = 8.2$ Hz, 2H), 4.82 (s, 1H), 3.85 (s, 6H), 3.70 (s, 3H). $^{13}$C NMR (50 MHz, DMSO-d$_6$): δ 184.2, 166.1, 163.2, 159.8, 148.9, 138.6, 137.2, 135.6, 127.6, 124.9, 118.2, 117.1, 99.7, 55.3, 52.4, 51.6, 37.9. EI-MS: $m/z$ (%) 518 (40, M$^+$). Anal. calcd. for C$_{22}$H$_{18}$N$_2$O$_7$S$_3$: C, 50.95; H, 3.50; N, 5.40; S, 18.55. Found: C, 51.12; H, 3.61; N, 5.31; S, 18.60.

References and Notes

8. (a) Yarovenko, V. N.; Nikitina, A. S.; Zavarzin, I. V.; Krayushkin, M. M.; Kovalenko, L. V. Russ. Chem. Bull. 2007, 56, 1624. (b) Compound 2e has been reported in lit. 8 (a); in this article, structure 2e in Scheme 1 has been incorrectly drawn (Me should read MeO).