Effect of microwave irradiation on reaction of furo[3,2-*b*]pyrrole and furo[2,3-*b*]pyrrole-2-carbaldehydes with some active methylene compounds

Alzbeta Krutosíková,[a] Margita Lácová,[b] Miloslava Dandárová,[c] and Jarmila Chovancová[b]

[a] *Department of Chemistry, Faculty of Natural Sciences, University of St. Cyril and Methodius, SK 917 01 Trnava, Slovak Republic*
[b] *Department of Organic Chemistry, Natural Sciences Faculty, Comenius University, SK 842 15 Bratislava, Slovak Republic*
[c] *Department of Organic Chemistry, Slovak University of Technology SK 812 37 Bratislava, Slovak Republic*
E-mail: krutosik@ucm.sk

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Abstract

The synthesis of methyl 4-(methoxymethyl)furo[3,2-*b*]pyrrole-5-carboxylate (1d) and methyl 2-formyl-4-(methoxymethyl)furo[3,2-*b*]pyrrole-5-carboxylate (2d) is described. The effect of microwave irradiation on the condensation reactions of methyl 2-formylfuro[3,2-*b*]pyrrole-5-carboxylates 2a-2d and methyl 2-formylfuro[2,3-*b*]pyrrole-5-carboxylates 3a-3d with active methylene compounds as are: 2-thioxothiazolidine-4-one (rhodanine), 2-thioxoimidazolidine-4-one (thiohydantoine), and 3-amino-2-thioxothiazolidine-4-one (3-aminorhodanine) was studied and compared with "classical" conditions. The results show that microwave irradiation shortens the reaction time while maintaining comparable yields.

Keywords: Furo[2,3-*b*]pyrroles, furo[3,2-*b*]pyrroles, 2-thioxoimidazolidine-4-one, 2-thioxothiazolidine-4-one and 3-amino-2-thioxothiazolidine-4-one, ^{1}H NMR

Introduction

Investigations of indole (furopyrroles, thienopyrroles) isosters, in which the benzene ring is replaced by furan or thiophene ring, have resulted in the discovery of many biologically active compounds.[1] Therefore, efficient synthetic routes to these types of heterocycle are of great interest.[1] In continuation of our program aimed at developing efficient syntheses of fused oxygen-nitrogen containing heterocycles we have reported the use of substituted furo[3,2-*b*] and furo[2,3-*b*]pyrroles in the synthesis.[2-8] In our previous studies,[6] comparing the course of Diels-Alder reactions of furo[3,2-*b*]pyrroles with their [2,3-*b*] isomers, we concluded that the [2,3-*b*]

system is the more reactive diene than its [3,2-*b*] isomer. This observation is supported by the high-level ab initio calculations.[8] We have also reported[7] the results of the use of substituted furo[3,2-*b*]pyrrole and furo[2,3-*b*]pyrrole-type aldehydes in the synthesis.[7] A formyl substituent at C2 results in the reactivity of both systems being comparable.

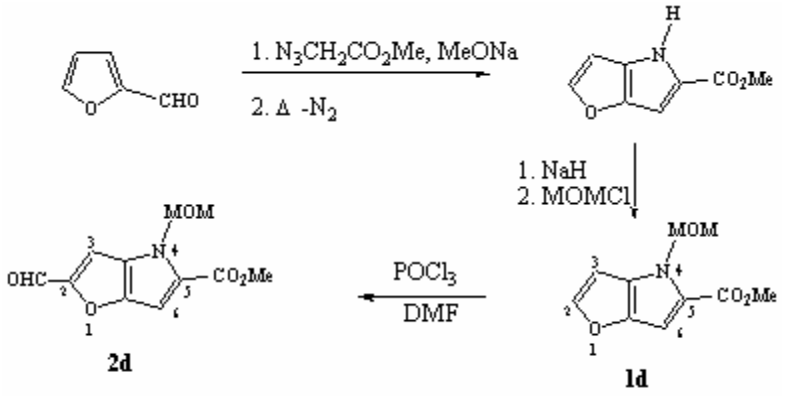
R for 2,3, a = H, b = Me, c = Bn, d = MOM

The aim of this study was to synthesise some new condensation products of furo[3,2-*b*]pyrrole (2) and furo[2,3-*b*]pyrrole-type aldehydes (3) by reaction with active methylene compounds (Schemes 2 and 3) and to compare the "classical" method with the effect of microwave irradiation and to find conditions in to increase the yield of the condensations.

As it was shown before,[9] microwave irradiation can shorten the duration of condensation reactions. For example condensations of thiohydantoin with aromatic aldehydes without solvents[10] and substituted 3-formylchromones in acetic anhydride[11] under microwave irradiation have been described.

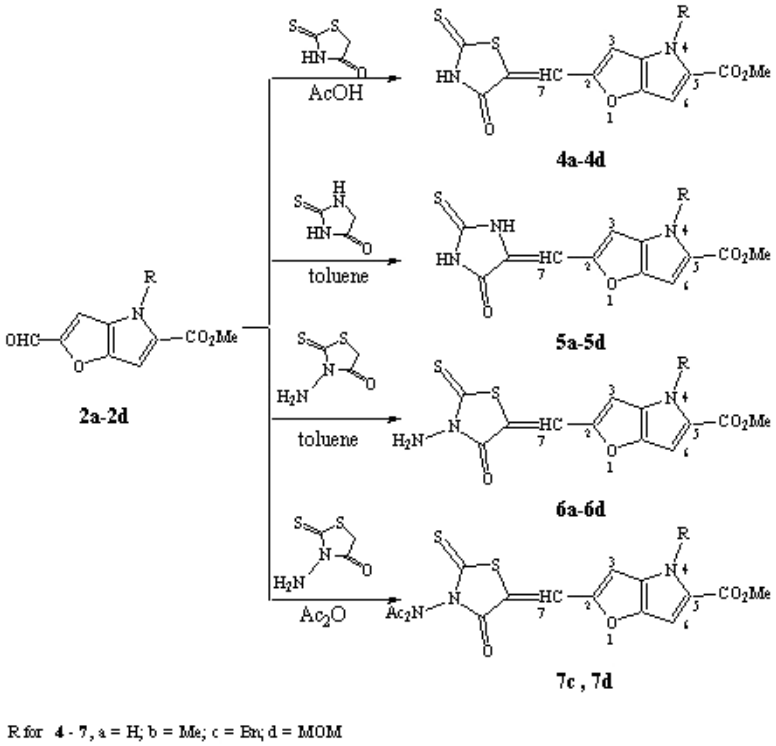
Results and Discussion

In our previous paper[2], we described the preparation of 1b and 1c from methyl 4*H*-furo[3,2-*b*]pyrrole-5-carboxylate (1a) under phase transfer catalysis conditions and the formylation of these compounds under conditions of the Vilsmeier reaction. This paper presents a synthesis of methyl 6-(methoxymethyl)furo[3,2-*b*]pyrrole-5-carboxylate (1d), which was obtained more effectively by direct substitution of *in situ* prepared sodium salt of 1a in DMF, and its formylation under the condition used in ref.[2] In this reaction, 2-formylated product 2d was obtained (Scheme 1).



Scheme 1

Methyl 2-(4-oxo-2-thioxothiazolidin-5-ylidene)methyl-4*H*-furo[3,2-*b*]pyrrole-5-carboxylate (4a) and its 4-Me, 4-Bn and 4-MOM derivatives 4b-4d were obtained by reactions of 2a-2d with 2-thioxothiazolidine-4-one (rhodanine) in acetic acid in the presence of freshly fused potassium acetate (Scheme 2).

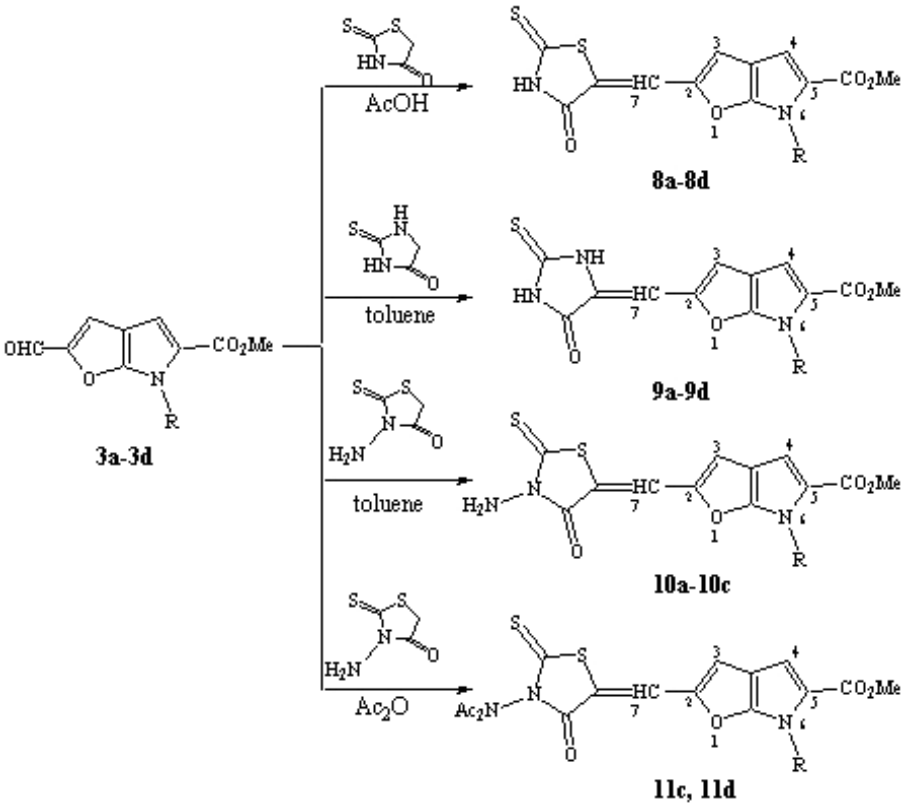


Scheme 2

Analogously 3a-3d gave 8a-8d (Scheme 3). 2a and 2c were used for the preparation of 4a and 4d using microwave irradiation. Although the yields by both methods were almost the same, the reactions in a microwave oven were considerably faster.

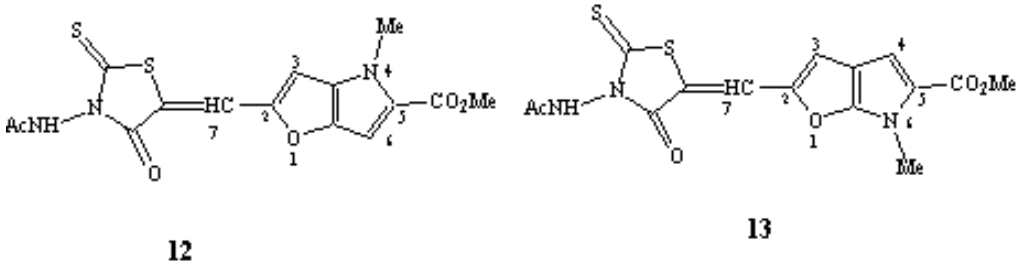
Methyl 2-(4-oxo-2-thioxoimidazolidin-5-ylidene)methyl-4*H*-furo[3,2-*b*]pyrro-le-5-carboxylate (5a) and its 4-Me, 4-Bn and 4-MOM derivatives 5b-5d were obtained by reactions of 2a-2d with 2-thioxoimidazolidine-4-one (thiohydantoine) in a mixture of toluene with DMF in the presence of freshly fused potassium acetate (Scheme 2). 3a-3d similarly gave 9a-9d (Scheme 3). Compounds 5b, 9b and 9d were prepared using microwave irradiation.

The reactions of compounds 2a-2d and 3a–3d with 3-amino-2-thioxothiazolidine-4-one (3-aminohydantoin) were studied in various conditions.



Scheme 3

With toluene as the solvent and potassium acetate from 2a-2d methyl 2-(3-amino-4-oxo-2-thioxothiazolidin-5-ylidene)methyl-4*H*-furo[3,2-*b*]pyrrole-5-carboxylate and its methyl, benzyl, methoxymethyl derivatives (6a-6d) were obtained. Analogously 3a-3c gave 10a-10c. If this reaction was effected in acetic anhydride in the presence of potassium carbonate, the *N*,*N*-diacetylated compounds 7c, 7d and 11c, 11d were formed. Starting from 3c under microwave irradiation compound 11c was obtained. Finally, if acetic acid was used as the solvent in "classical" conditions, *N*-monoacetylated compounds 12 and 13 were obtained.



12 **13**

All synthesised compounds are stable solids, which are rather sparingly soluble in common solvents, and with high melting points. The structures of the studied compounds have been confirmed by ^{1}H NMR spectra, which display signals of furo[3,2-*b*]pyrrole and furo[2,3-*b*]pyrrole protons, respectively and the double bond H-7 signals.

In conclusion, we can state, on the basis of the present studies and our previous reaction studies of both fused ring systems, that the 1,4-system is more stable than its 1,6 positional isomer. In the described experiments we ascertained that if the formyl group occupies the C2 position, the reactivity as well as stability of both systems is comparable. We noticed a remarkable difference in solubility of the two types of aldehyde. Compounds 3a-3d are less soluble than 2a-2d. This observation can be explained by the 1,4-system having a significantly larger calculated dipole moment,[5] which may result in the greater solubility. Although the yields by both "classical" and microwave oven procedures were almost the same, the reactions in a microwave oven were faster.

Experimental Section

General Procedures. Melting points were determined on a Kofler hot plate apparatus and are uncorrected. Samples for analysis were dried over P_4O_{10} at 60 ^{o}C and 30 Pa for 8-10 h. ^{1}H NMR (80 MHz) spectra were recorded on a Tesla BS 587 spectrometer and on a 300 MHz spectrometer VARIAN GEMINI 200. TMS was used as an internal standard; chemical shifts are given in ppm (d-scale), coupling constants (*J*) in Hz. The reaction progress and purity of all prepared compounds was followed by TLC (SILUFOL UV_{254}, Kavalier, Votice, Czech Republic) in the system chloroform-methanol 9:1 visualising spots with UV lamp or iodine vapour. Solvents were purified by published methods. All microwave assisted reactions were carried out in a Lavis - 1000 multi Quant microwave oven. The apparatus was adapted for laboratory applications with magnetic stirring and an external reflux condenser.

The following starting compounds were prepared: methyl 6-(methoxymethyl)furo[2,3-*b*]pyrrole-5-carboxylate,[3] methyl 2-formylfuro[2,3-*b*]pyrrole-5-carboxylates 1a-1c ref.,[2] methyl 2-formylfuro[3,2-*b*]pyrrole-5-carboxylates 2a-2c ref.[4]

Methyl 6-(methoxymethyl)furo[3,2-*b*]pyrrole-5-carboxylate (1d). A solution of methyl furo[3,2-*b*]pyrrole-5-carboxylate (1a) (3.3 g, 20 mmol) in *N*,*N*-dimethylformamide (40 mL) was added slowly to a mixture of sodium hydride (60% in mineral oil, 0.96 g, 24 mmol) in *N*,*N*-dimethylformamide (20 mL). The mixture was stirred at 20 ^{o}C till the evolution of hydrogen ceased, then chloromethyl methyl ether (1.8 mL, 1.9 g, 24 mmol) was added and the stirring at room temperature continued for 1 h. The solution was poured into ice water (150 mL), the precipitate was filtered off and crystallised. Yield: 3.0 g (72%), m.p. 76-78 ^{o}C(hexane). For $C_{10}H_{11}NO_4$ (209.2) calculated: 57.41% C, 5.30% H, 6.70% N; found: 57.28% C, 5.34% H,

6.76% N. ^{1}H NMR (80 MHz, DMSO-d_6) δ 7.54 (d, 1H, J = 2.2 Hz, H-2), 6.95 (s, 1H, H-6), 6.60 (d, 1H, J = 2.2 Hz, H-3), 5.77 (s, 2H, N-CH_2), 3.93 (s, 3H, CO_2CH_3), 3.30 (s, 3H, OCH_3).

Methyl 2-formyl-6-(methoxymethyl)furo[3,2-*b*]pyrrole-5-carboxylate (2d). A mixture of *N*,*N*-dimethylformamide (11.7 g, 160 mmol) and phosphorus oxychloride (4.6 g, 30 mmol) was stirred at 0 °C for 20 min. 1d (2.5 g, 12 mmol) dissolved in *N*,*N*-dimethylformamide (12 mL) was added at temperature not exceeding 10 °C. The mixture was stirred at 60 °C for 5 h, poured into ice-cold water, neutralized with sodium hydrogencarbonate, allowed to stand overnight and the precipitate was filtered off and crystallized from a hexane-toluene 3:1 mixture to give 2.9 g (84%) 2d, m.p. 118-120 °C. For $C_{11}H_{11}NO_5$ (237.21) calculated: 55.70% C, 4.67% H, 5.90% N; found: 55.65% C, 4.82% H, 6.15% N. ^{1}H NMR (80 MHz, DMSO-d_6) δ 9.72 (s, 1H, CH=O), 7.37 (s, 1H, H-3), 6.96 (s, 1H, H-6), 5.82 (s, 2H, N-CH_2), 3.95 (s, 3H, CO_2CH_3), 3.33 (s, 3H, OCH_3).

Methyl 2-(4-oxo-2-thioxothiazolidin-5-ylidene)methyl-4*H*-furo[3,2-*b*]pyrrole-5-carboxylate (4a). Methyl 2-formyl-4*H*-furo[3,2-*b*]pyrrole-5-carboxylate (2a) (0.6 g, 3 mmol) and 2-thioxoimidazolidine-4-one (0.4 g, 3 mmol) were dissolved in glacial acetic acid (4 mL) and potassium acetate (0.3 g, 3 mmol) was added into the refluxing mixture. After 30 min fine crystals were filtered off after cooling, washed with cold EtOH and crystallised from acetic acid to give 0.80 g (87%) of 4a, m.p. 292-296 °C. For $C_{12}H_8N_2O_4S_2$(308.34) calculated: 46.74% C, 2.62% H, 9.09% N, 20.80% S; found: 46.54% C, 2.65% H, 9.00% N, 20.69% S. ^{1}H NMR (80 MHz, DMSO-d_6) δ 13.65 (br s, 1H, NH), 12.09 (br s, 1H, NH), 7.49 (s, 1H, H-7), 7.28 (s, 1H, H-3), 6.86 (s, 1H, H-6), 3.81 (s, 3H, CO_2CH_3).

The following compounds were prepared by this procedure:

Methyl 4-methyl-2-(4-oxo-2-thioxothiazolidin-5-ylidene)methyl-furo[3,2-*b*]pyrrole-5-carboxylate (4b). Yield: 93%, m.p. 274-278°C(AcOH). For $C_{13}H_{10}N_2O_4S_2$ (322.36) calculated: 48.44% C, 3.13% H, 8.69% N, 19.85% S; found: 48.54% C, 3.25% H, 8.80% N, 19.69% S. ^{1}H NMR (80 MHz, DMSO-d_6) δ 13.50 (br s, 1H, NH), 7.47 (s, 1H, H-7), 7.39 (s, 1H, H-3), 6.88 (s, 1H, H-6), 3.95 (s, 3H, N-CH_3), 3.81 (s, 3H, CO_2CH_3).

Methyl 4-benzyl-2-(4-oxo-2-thioxothiazolidin-5-ylidene)methyl-furo[3,2-*b*]pyrrole-5-carboxylate (4c). Yield: 90%, m.p. 240-243°C(AcOH). For $C_{19}H_{14}N_2O_4S_2$ (398.04) calculated: 57.27% C, 3.54% H, 7.03% N, 16.10% S; found: 57.32% C, 3.43% H, 7.23% N, 16.37% S. ^{1}H NMR (80 MHz, DMSO-d_6) δ 13.60 (br s, 1H, NH), 7.47 (s, 1H, H-7), 7.00-7.40 (m, 5H, H_{arom}), 7.27 (s, 1H, H-3), 7.01 (s, 1H, H-6), 5.69 (s, 2H, N-CH_2), 3.78 (s, 3H, CO_2CH_3).

Methyl 4-methoxymethyl-2-(4-oxo-2-thioxothiazolidin-5-ylidene)-methylfuro[3,2-*b*]pyrrole-5-carboxylate (4d). Yield: 86%, m.p. 240-244°C(AcOH). For $C_{14}H_{12}N_2O_4S_2$(352.39) calculated: 47.72% C, 3.43% H, 7.95% N, 18.20% S; found: 47.52% C, 3.48% H, 7.99% N, 18.34% S. ^{1}H NMR (80 MHz, DMSO-d_6) δ 13.36 (br s, 1H, NH), 7.50 (s, 1H, H-7), 7.45 (s, 1H, H-3), 7.03 (s, 1H, H-6), 5.74 (s, 2H, N-CH_2), 3.82 (s, 3H, CO_2CH_3), 3.20 (s, 3H, OCH_3).

From 3a-3d the following compounds were prepared by this procedure:

Methyl 2-(4-oxo-2-thioxothiazolidin-5-ylidene)methyl-6*H*-furo-[2,3-*b*]pyrrole-5-carboxylate (8a). Yield: 71%, m.p. 280-282°C(AcOH). For $C_{12}H_8N_2O_4S_2$ (308.34) calculated: 46.74% C, 2.62% H, 9.09% N, 20.80% S; found: 46.62% C, 2.69% H, 9.18% N, 20.88% S.^{1}H NMR (80 MHz, DMSO-d_6) δ 13.57 (br s, 1H, NH), 13.00 (br s, 1H, NH), 7.49 (s, 1H, H-7), 7.37 (s, 1H, H-3), 6.86 (s, 1H, H-4), 3.81 (s, 3H, CO_2CH_3).

Methyl 6-methyl-2-(4-oxo-2-thioxothiazolidin-5-ylidene)methyl-furo[2,3-*b*]pyrrole-5-carboxylate (8b). Yield: 68%, m.p. 258-251 °C (AcOH). For $C_{13}H_{10}N_2O_4S_2$ (322.36) calculated: 48.44% C, 3.13% H, 8.69% N, 19.85% S; found: 48.56% C, 3.08% H, 8.72% N, 19.94% S. ^{1}H NMR (80 MHz, DMSO-d_6) δ 13.47 (br s, 1H, NH), 7.45 (s, 1H, H-7), 7.34 (s, 1H, H-3), 6.91 (s, 1H, H-4), 3.91 (s, 3H, N-CH_3), 3.78 (s, 3H, CO_2CH_3).

Methyl 6-benzyl-2-(4-oxo-2-thioxothiazolidin-5-ylidene)methyl-furo[2,3-*b*]pyrrole-5-carboxylate (8c). Yield: 81%, m.p. 235-238 °C(AcOH). For $C_{19}H_{14}N_2O_4S_2$ (398.04) calculated: 57.27% C, 3.54% H, 7.03% N, 16.10% S; found: 57.42% C, 3.38% H, 7.12% N, 16.27% S. ^{1}H NMR (80 MHz, DMSO-d_6) δ 13.58 (br s, 1H, NH), 7.50 (s, 1H, H-7), 7.40 (s, 1H, H-3), 7.34 (m, 5H, H_{arom}), 7.04 (s, 1H, H-4), 5.70 (s, 2H, N-CH_2), 3.79 (s, 3H, CO_2CH_3).

Methyl 6-methoxymethyl-2-(4-oxo-2-thioxothiazolidin-5-ylidene)methylfuro[2,3-*b*]pyrrole-5-carboxylate (8d). Yield: 86%, m.p. 227-231°C(AcOH). For $C_{14}H_{12}N_2O_4S_2$ (352.39) calculated: 47.72% C, 3.43% H, 7.95% N, 18.20% S; found: 47.68% C, 3.55% H, 8.12% N, 18.28% S. ^{1}H NMR (80 MHz, DMSO-d_6) δ 13.62 (br s, 1H, NH), 7.53 (s, 1H, H-7), 7.41 (s, 1H, H-3), 7.06 (s, 1H, H-4), 5.78 (s, 2H, N-CH_2), 3.80 (s, 3H, CO_2CH_3), 3.29 (s, 3H, OCH_3).

Methyl 2-(4-oxo-2-thioxoimidazolidin-5-ylidene)methyl-4*H*-furo[3,2-*b*]pyrrole-5-carboxylate (5a). Potassium acetate (0.2 g, 2 mmol) was added into the refluxing mixture of 2a (0.4 g, 2 mmol) and 2-thioxoimidazolidine-4-one (0.236 g, 2 mmol) in a mixture of toluene (8 mL) and DMF (2 mL) and the reaction mixture was refluxed for 4 h. After cooling was added ethanol (5 mL) and fine crystals were filtered off, washed with cold EtOH and crystallised from toluene to give 0.44 g (75%) of 5a, m.p. 360 °C. For $C_{12}H_9N_3O_4S$ (291.28) calculated: 49.48% C, 3.11% H, 14.43% N, 11.01% S; 49.52% C, 3.19% H, 14.62% N, 10.85% S. ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.30 (br s, 1H, NH), 11.90 (br s, 2H, NH), 7.21 (s, 1H, H-7), 6.70 (d, 1H, J = 0.9 Hz, H-3), 6.38 (s, 1H, H-6), 3.82 (s, 3H, CO_2CH_3).

The following compounds were prepared by this procedure:

Methyl 4-methyl-2-(4-oxo-2-thioxoimidazolidin-5-ylidene)methylfuro[3,2-*b*]pyrrole-5-carboxylate (5b). Yield: 75%, m.p. 285-287 °C(toluene). For $C_{13}H_{11}N_3O_4S$ (305.31) calculated: 51.14% C, 3.63% H, 13.76% N, 10.50% S; found: 51.32% C, 3.67% H, 13.56% N, 10.45% S. ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.60-12.00 (br s, 2H, NH), 7.33 (s, 1H, H-7), 6.80 (s, 1H, H-3), 6.50 (s, 1H, H-6), 3.94 (s, 3H, N-CH_3), 3.79 (s, 3H, CO_2CH_3).

Methyl 4-benzyl-2-(4-oxo-2-thioxoimidazolidin-5-ylidene)methylfuro[3,2-*b*]pyrrole-5-carboxylate (5c). Yield: 74%, m.p. 278-280 °C(toluene). For $C_{19}H_{15}N_3O_4S$ (381.41) calculated: 59.83% C, 3.96% H, 11.02% N, 8.41% S; found: 59.92% C, 3.76% H, 10.93% N, 8.30% S. ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.27-7.33 (m,

4H, H-7, H_{arom}), 7.16-7.20 (m, 2H, H_{arom}), 6.85 (s, 1H, H-3), 6.41 (s, 1H, H-6), 5.67 (s, 2H, N-CH_2), 3.77 (s, 3H, CO_2CH_3).

Methyl 4-methoxymethyl-2-(4-oxo-2- thioxoimidazolidin -5-ylidene)methylfuro[3,2-*b*]pyrrole-5-carboxylate (5d). Yield: 73%, m.p. 272–274 °C(toluene). For $C_{14}H_{13}N_3O_5S$ (335.34) calculated: 50.14% C, 3.91% H, 12.53% N, 9.56% S; found: 50.37% C, 3.81% H, 12.70% N, 9.76% S. ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.39 (br s, 1H, NH), 11.30 (br s, 1H, NH), 7.40 (s, 1H, H-7), 6.89 (s,1H, H-3), 6.45 (s,1H, H-6), 5.73 (s, 2H, N-CH_2), 3.81 (s, 3H, CO_2CH_3), 3.20 (s, 3H, OCH_3).

From 3a-3d the following compounds were prepared by this procedure:

Methyl 2-(4-oxo-2-thioxoimidazolidin-5-ylidene)methyl-6*H*-furo-[2,3-*b*]pyrrole-5-carboxylate (9a). Yield:75%, m.p.360 °C(toluene). For $C_{12}H_9N_3O_4S$ (291.28) calculated: 49.48% C, 3.11% H, 14.43% N, 11.01% S; found: 49.67% C, 3.01% H, 14.23% N, 11.22% S. ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.80 (br s, 1H, NH), 12.30 (s, 1H, NH), 11.70 (s, 1H, NH), 7.45 (s, 1H, H-7), 6.84 (s, 1H, H-3), 6.42 (s, 1H, H-4), 3.80 (s, 3H, CO_2CH_3).

Methyl 6-methyl-2-(4-oxo-2-thioxoimidazolidin-5-ylidene)methyl-furo[2,3-*b*]pyrrole-5-carboxylate (9b). Yield: 74%, m.p. 360 °C(toluene). For $C_{13}H_{11}N_3O_4S$(305.31) calculated: 51.14% C, 3.63% H, 13.76% N, 10.50% S; found: 51.52% C, 3.57% H, 13.69% N, 10.61% S. ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.60-12.00 (br s, 2H, NH), 7.18 (s, 1H, H-7), 6.89 (s, 1H, H-3), 6.36 (s, 1H, H-4), 4.05 (s, 3H, N-CH_3), 3.78 (s, 3H, CO_2CH_3).

Methyl 6-benzyl-2-(4-oxo-2-thioxoimidazolidin-5-ylidene)methyl-furo[2,3-*b*]pyrrole-5-carboxylate (9c). Yield: 70%, m.p.285-287 °C(toluene). For $C_{19}H_{15}N_3O_4S$(381.41) calculated: 59.83% C, 3.96% H, 11.02% N, 8.41% S; found: 59.72% C, 3.92% H, 11.13% N, 8.38% S. ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.36 (br s, 1H, NH), 11.91 (s, 1H, NH), 7.28-7.36 (m, 3H, H_{arom}), 7.26 (s, 1H, H-7), 7.15-7.17 (m, 2H, H_{arom}), 6.99 (s, 1H, H-3), 6.48 (s, 1H, H-4), 5.91 (s, 2H, N-CH_2), 3.72 (s, 3H, CO_2CH_3).

Methyl 6-methoxymethyl-2-(4-oxo-2-thioxoimidazolidin-5-ylide-ne)methylfuro[2,3-*b*]pyrrole-5-carboxylate (9d). Yield: 73%, m.p. 292-294 °C(toluene). For $C_{14}H_{13}N_3O_5S$(335.34) calculated: 50.14% C, 3.91% H, 12.53% N, 9.56% S; found: 50.26% C, 3.87% H, 12.49% N, 9.60% S. ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.34 (br s, 1H, NH), 11.94 (br s, 1H, NH), 7.25 (s, 1H, H-7), 7.03 (s, 1H, H-3), 6.47 (s, 1H, H-4), 5.99 (s, 2H, N-CH_2), 3.79 (s, 3H, CO_2CH_3), 3.21 (s, 3H, OCH_3).

Methyl 2-(3-amino-4-oxo-2-thioxothiazolidin-5-ylidene)methyl-4*H*-furo[3,2-*b*]pyrrole-5-carboxylate (6a). 2a (0.4 g, 2 mmol) and 3-amino-2-thioxothiazolidine-4-one (0.296 g, 2 mmol) were dissolved in toluene (10 mL) and potassium acetate (0.2 g, 2 mmol) was added into the refluxing mixture. After 5 h reflux into the cold reaction mixture was added ethanol (5 mL) and fine crystals were filtered off, washed with cold EtOH and crystallised from toluene to give 80%of 6a, m.p. 288-290 °C. For $C_{12}H_9N_3O_4S_2$(323.35) calculated: 44.57% C, 2.81% H, 13.00% N, 19.83% S; found: 44.72% C, 2.94% H, 12.94% N, 19.73% S. ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.95 (br s, 1H, NH), 7.70 (s, 1H, H-7), 7.34 (s, 1H, H-3), 6.86 (s, 1H, H-6), 5.94 (s, 2H, NH_2), 3.84 (s, 3H, CO_2CH_3).

The following compounds were prepared by this procedure:

Methyl 4-methyl-2-(3-amino-4-oxo-2-thioxothiazolidin-5-ylidene)methylfuro[3,2-*b*]pyrrole-5-carboxylate (6b). Yield: 84%, m.p.268–270 °C(toluene). For $C_{13}H_{11}N_3O_5S_2$(337.38) calculated: 46.28% C, 3.29% H, 12.46% N, 19.01% S; found: 46.42% C, 3.33% H, 12.64% N, 19.17% S. ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.66 (s, 1H, H-7), 7.43 (s, 1H, H-3), 6.87 (s, 1H, H-6), 5.84 (s, 2H, NH_2), 3.95 (s, 3H, N-CH_3), 3.82 (s, 3H, CO_2CH_3).

Methyl 4-benzyl-2-(3-amino-4-oxo-2-thioxothiazolidin-5-ylidene)methylfuro[3,2-*b*]pyrrole-5-carboxylate (6c). Yield:87%, m.p.242–245 °C(toluene). For $C_{19}H_{15}N_3O_5S_2$(413.05) calculated: 55.19% C, 3.66% H, 10.16% N, 15.51% S; found: 55.14% C, 3.62% H, 10.06% N, 15.55% S. ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.69 (s, 1H, H-7), 7.36 (s, 1H, H-3), 7.30-7.32 (m, 3H, H_{arom}), 7.14-7.16 (m, 2H, H_{arom}), 7.02 (s, 1H, H-6), 5.93 (s, 2H, NH_2), 5.71 (s, 2H, N-CH_2), 3.79 (s, 3H, CO_2CH_3).

Methyl 4-methoxymethyl-2-(3-amino-4-oxo-2-thioxothiazolidin-5-ylidene)methylfuro[3,2-*b*]pyrrole-5-carboxylate (6d). Yield: 86%, m.p. 212-214 °C (toluene). For $C_{14}H_{13}N_3O_5S_2$(367.40) calculated: 45.77% C, 3.57% H, 11.44% N, 17.46% S; found: 45.89% C, 3.75% H, 11.48% N, 17.49% S. ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.71 (s, 1H, H-7), 7.50 (s, 1H, H-3), 7.01 (s,1H, H-6), 5.84 (s, 2H, NH_2), 5.78 (s, 2H, N-CH_2), 3.82 (s, 3H, CO_2CH_3), 3.01 (s, 3H, OCH_3).

From 3a-3c the following compounds were prepared by this procedure:

Methyl 2-(3-amino-4-oxo-2-thioxothiazolidin-5-ylidene)methyl-6*H*-furo[2,3-*b*]pyrrole-5-carboxylate (10a). Yield: 88%, m.p. 360 °C(decomp.) (toluene). For $C_{12}H_9N_3O_4S_2$(323:35) calculated: 44.57% C, 2.81% H, 13.00% N, 19.83% S; found: 44.39% C, 2.84% H, 12.99% N, 19.96% S. ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.05 (br s, 1H, NH), 7.65 (s, 1H, H-7), 7.39 (s, 1H, H-3), 6.84 (s, 1H, H-4), 5.85 (br s, 2H, NH_2), 3.82 (s, 3H, CO_2CH_3).

Methyl 6-methyl-2-(3-amino-4-oxo-2-thioxothiazolidin-5-ylidene)methylfuro[2,3-*b*]pyrrole-5-carboxylate (10b). Yield: 78%, m.p. 244-247 °C (toluene). For $C_{13}H_{11}N_3O_5S_2$(337.38) calculated: 46.28% C, 3.29% H, 12.46% N, 19.01% S; found: 46.42% C, 3.33% H, 12.64% N, 19.30% S. ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.72 (s,1H, H-7), 7.45 (s,1H, H-3), 6.96 (s, 1H, H-4), 5.93 (s, 2H, NH_2), 3.94 (s, 3H, N-CH_3), 3.79 (s, 3H, CO_2CH_3).

Methyl 6-benzyl-2-(3-amino-4-oxo-2-thioxothiazolidin-5-ylidene)methylfuro[2,3-*b*]pyrrole-5-carboxylate (10c). Yield: 88%, m.p. 241-244 °C(toluene). For $C_{19}H_{15}N_3O_5S_2$(413.05) calculated: 55.19% C, 3.66% H, 10.16% N, 15.51% S; found: 55.28% C, 3.83% H, 10.22% N, 15.69% S. ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.73 (s, 1H, H-7), 7.47 (s, 1H, H-3), 7.32-7.34 (m, 5H, H_{arom}), 7.07 (s, 1H, H-4), 5.92 (s, 2H, NH_2), 5.72 (s, 2H, N-CH_2), 3.80 (s, 3H, CO_2CH_3).

Methyl 4-benzyl-2-(3-diacetylamino-4-oxo-2-thioxothiazolidin-5-ylidene)methylfuro[3,2-*b*]pyrrole-5-carboxylate (7c). 2c (0.283 g, 1 mmol) and 3-amino-2-thioxothiazolidine-4-one (0.148 g, 1 mmol) were dissolved in dry acetic anhydride (3 mL) and dry potassium carbonate (0.138 g, 1 mmol) was added into the refluxing mixture. After 5 h heating at 80 °C into the cool reaction mixture was added ethanol (3 mL) and fine crystals were filtered off, washed with cold EtOH and crystallised from toluene to give 0.447 g (90%) of 7c, m.p. 199-201 °C(ethanol). For $C_{23}H_{19}N_3O_6S_2$(497.55) calculated: 55.52% C,

3.85% H, 8.45% N, 12.89% S; found: 55.43% C, 3.76% H, 8.70% N, 12.75% S. ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.92 (s, 1H, H-7), 7.48 (s, 1H, H-3), 7.30 (m, 3H, H_{arom}), 7.16 (m, 2H, H_{arom}), 7.05 (s, 1H, H-6), 5.73 (s, 2H, N-CH_2), 3.80 (s, 3H, CO_2CH_3), 2.38 (s, 3H, CH_3CON), 2.08 (s, 3H, CH_3CON).

From 2d, 3c and 3d the following compounds were prepared by this procedure:

Methyl 6-methoxymethyl-2-(3-diacetylamino-4-oxo-2-thioxothiazolidin-5-ylidene)methyl-furo[3,2-*b*]pyrrole-5-carboxylate (7d). Yield: 86%, m.p. 235-238 °C(ethanol). For $C_{18}H_{17}N_3O_7S_2$(451.48) calculated: 47.89% C, 3.80% H, 9.31% N, 14.20% S; found: 47.73% C, 3.66% H, 9.23% N, 14.11% S. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (s,1H, H-7), 6.99 (s, 1H, H-3), 6.91 (s, 1H, H-6), 5.81 (s, 2H, N-CH_2), 3.89 (s, 3H, CO_2CH_3), 3.33 (s, 3H, OCH_3), 2.42 (s, 6H, CH_3CON).

Methyl 6-benzyl-2-(3-diacetylamino-4-oxo-2-thioxothiazolidin-5-ylidene)methylfuro[2,3-*b*]pyrrole-5-carboxylate (11c). Yield: 63%, m.p. 189-191 °C(ethanol). For $C_{23}H_{19}N_3O_6S_2$(497.55) calculated: 55.52% C, 3.85% H, 8.45% N, 12.89% S; found: 55:60% C, 3.71% H, 8.55% N, 12. 76% S. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (s, 1H, H-7), 7.37-7.39 (m, 5H, H_{arom}), 7.06 (s, 1H, H-3), 6.99 (s, 1H, H-4), 5.72 (s, 2H, N-CH_2), 3.87 (s, 3H, CO_2CH_3), 2.41 (s, 6H, CH_3CON).

Methyl 6-methoxymethyl-2-(3-diacetylamino-4-oxo-2-thioxothiazolidin-5-ylidene)methyl-furo[2,3-*b*]pyrrole-5-carboxylate (11d). Yield: 64%, m.p. 215-218 °C(ethanol). For $C_{18}H_{17}N_3O_7S_2$(451.48) calculated: 47.89% C, 3.80% H, 9.31% N, 14.20% S; found: 47.92% C, 3.73% H, 9.19% N, 14.31% S. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (s, 1H, H-7), 7.09 (s, 1H, H-3), 7.01 (s, 1H, H-4), 5.85 (s, 2H, N-CH_2), 3.89 (s, 3H, CO_2CH_3), 3.42 (s, 3H, OCH_3), 2.42 (s, 6H, CH_3CON).

Methyl 4-methyl-2-(3-acetylamino-4-oxo-2-thioxothiazolidin-5-ylidene)methylfuro[3,2-*b*]pyrrole-5-carboxylate (12). 2b (0.207 g, 1 mmol) and 3-amino-2-thioxothiazolidine-4-one (0.148 g, 1 mmol) were dissolved in dry acetic anhydride (2.5 mL) and dry potassium carbonate (0.138 g, 1 mmol) was added into the refluxing mixture. After 2 h heating at 60 °C into the cool reaction mixture was added ethanol (3 mL) and fine crystals were filtered off, washed with cold EtOH and crystallised from toluene to give 0.293 g (65%) of 12, m.p. 214-216 °C(ethanol). For $C_{15}H_{13}N_3O_7S_2$(451.48) calculated: 47.89% C, 3.80% H, 9.31% N, 14.20% S; found: 47.92% C, 3.73% H, 9.19% N, 14.31% S. ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.96 (s, 1H, H-7), 7.72 (br s, 1H, NH), 6.95 (s, 1H, H-3), 6.93 (s, 1H, H-6), 3.95 (s, 3H, N-CH_3), 3.82 (s, 3H, CO_2CH_3), 2.39 (s, 3H, CH_3CO).

Methyl 6-methyl-2-(3-acetylamino-4-oxo-2-thioxothiazolidin-5-ylidene)methylfuro[2,3-*b*]pyrrole-5-carboxylate (13). Yield: 65%, m.p. 212-215 °C(ethanol). For $C_{15}H_{13}N_3O_7S_2$(451.48) calculated: 47.89% C, 3.80% H, 9.31% N, 14.20% S; found: 47.95% C, 3.92% H, 9.29% N, 14.36% S. ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.87 (s, 1H, H-7), 7.55 (s, 1H, H-3), 6.96 (s, 1H, H-4), 3.97 (s, 3H, N-CH_3), 3.80 (s, 3H, CO_2CH_3), 3.09 (s, 3H, CH_3CON).

Synthesis of 4a, 4c, 5b, 7d, 9b, 11c. Reactions in microwave oven

A mixture of the corresponding aldehyde 2 or 3 (2 mmol), 2-thioxothiazolidine-4-one (or 2-thioxoimidazolidine-4-one or 3-amino-2-thioxothiazolidine-4-one) (2 mmol) in dry acetic acid anhydride (2 mL) in the presence of freshly fused potassium acetate

(2 mmol) was stirred and irradiated in a microwave oven at 500 W for 2-8 min. After cooling and adding of diethylether (10 mL) the reaction mixture was allowed to stand overnight and the precipitate was filtered off and crystallised from solvents which were described in "classical" procedures.

The following compounds were prepared by this procedure:

Compound	tr (min)	Yield (%)
4a	3	88
4c	4	89
5b	2	75
7d	3	50
9b	4	80
9d	8	85
11c	3	65

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