Synthesis of Dimethyl 1-(Hetero)aryl-4-oxo-1,4-dihydropyridazine-3,5-dicarboxylates from Dimethyl 3-Oxopentane-1,5-dioates

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Dimethyl 3-oxopentane-1,5-dioate (dimethyl acetone-1,3-dicarboxylate) (1) was transformed first with (hetero)arenediazonium salts 3a – j into dimethyl 2-[(hetero)arylhydrazono]pentane-1,5-dioates 4a – j followed by reaction with N,N-dimethylformamide dimethylacetal (DMFDMA) to afford, without isolation of intermediates 5a – j, dimethyl 1-(hetero)aryl-4-oxo-1,4-dihydropyridazine-3,5-dicarboxylates 6a – j. An alternative method represents transformation of 1 with DMFDMA into dimethyl 2-[dimethylamino)methylidene]-3-oxopentane-1,5-dioate (7) followed by treatment with (hetero)arenediazonium salts 3a – c, j to give pyridazine derivatives 6a – c, j.

**Key words:** 2-[(Hetero)arylhydrazono]pentane-1,5-dioates, 1-(Hetero)aryl-4-oxo-1,4-dihydropyridazine-3,5-dicarboxylates

**Introduction**

In the last decade, a series of 3-(dimethylamino)prop-2-enoates and related enaminoes have been prepared as versatile reagents in the synthesis of many functionalized heterocycles [1, 2], including natural products and their analogs [3].

In this study we extend our research in the field of enaminoes to the synthesis of pyridazines. There are many syntheses described in the literature, since the pyridazine moiety is of significant importance for the preparation of a variety of products in the pharmaceutical as well as in the agrochemical field [4]. They exhibit many pharmacological activities. They are acetylcholinesterase inhibitors [5a], they act on the cardiovascular [5b] and the inflammatory system [5c], they show antitumor and other activities [5d, e]. Synthetic transformations on this ring system, to yield several diverse analogs for a wide array of applications, have received a considerable boost with the advent of palladium-catalyzed cross-coupling reactions. These reactions facilitate the direct introduction of suitable groups on the pyridazine nucleus via carbon-carbon or carbon-heteroatom bond formation [6].

Despite the widely elaborated [4+2] cycloaddition chemistry of 1,2,4,5-tetrazines, only a few examples of cycloadditions to the exocyclic C=C bonds leading to spirodihydropyridazines are known [7]. Recently, [4+2] cycloadditions of 3,6-disubstituted 1,2,4,5-tetrazines to 4′-methylene[1](3H,5H)-spiro[bicyclo[2.2.1]heptane-2,2′-furans] and 4′-methylene-1′(4-nitrophenyl)-spiro[bicyclo[2.2.1]heptane-3,3′-pyrroline], which afforded novel dispirodihydropyridazine derivatives, 11:14-isopropylidenec-14-methyl-2,3-diaza-8-oxadispiro[5.1.5.2]pentadeca-1,4-dienes and 11:14-isopropylidenec-11-methyl-2,3,8-triazadispiro[5.1.5.2]pentadeca-1,4-dienes [8], and a one-pot, three-step regio- and stereoselective synthesis of functionalized oxazoline-fused pyridazines by base-assisted “Michael addition-pyridazine cyclization-oxazoline cyclization” cascade reactions of 4-chloro-1,2-diaza-1,3-butiadienes with 3-(dimethylamino)prop-2-enoes have been reported [9]. Also the coupling of dimethyl 3-oxopentane-1,5-dioate (dimethyl acetone-1,3-dicarboxylate) with a variety of arenediazonium salts, in which the corresponding hydrazones are formed, afforded 5-arylpiprazidin-3(2H)-one derivatives by cyclization in boiling dichlorobenzene [10].

In this paper we report on the synthesis of dimethyl 1-(hetero)aryl-4-oxo-1,4-dihydropyridazine-3,5-dicarboxylates from dimethyl 3-oxopentane-1,5-dioate (dimethyl acetone-1,3-dicarboxylate), as an extension of our research in the field of enaminoes and related dark green single crystals. The product was recrystallized from dichloromethane and diethyl ether. The structure was determined by X-ray diffraction analysis at 150 K on a SMART APEX II diffractometer equipped with a graphite-monochromated Mo Kα radiation source (λ = 0.71073 Å).

The crystal structure of the title compound is presented in Figure 1, displaying the molecular skeleton along with selected bond lengths and angles. The overall geometry is consistent with the expected features of a pyridazine ring system. The bond lengths and angles are within the normal ranges, indicating the presence of a 1,4-dihydropyridazine moiety.

**Experimental**

The title compound was synthesized via a multi-step procedure involving the reaction of dimethyl 3-oxopentane-1,5-dioate with (hetero)arenediazonium salts and subsequent derivatization with N,N-dimethylformamide dimethylacetal (DMFDMA). The key steps of the synthesis are outlined in Scheme 1. The reaction conditions, including concentrations, temperatures, and reaction times, were optimized to ensure high yield and purity of the product.

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**References**

reagents and their applications to the synthesis of heterocyclic systems.

Results and Discussion

Two reaction pathways for the preparation of 1,4-dihydropyridazine derivatives were envisaged (Scheme 1). According to the first method, dimethyl 3-oxopentane-1,5-dioate (dimethyl acetone-1,3-dicarboxylate) (1) was treated in ethanol in the presence of sodium acetate at 0 °C with an acidic aqueous solution of diazonium salts 3a–j, prepared from the corresponding aromatic (2a–i) or heteroaromatic (2j) amines, to give the corresponding hydrazones 4a–j in 35–94 % yield. They were in the next step treated with dimethylformamide dimethylacetal (DMFDMA) in dichloromethane at room temperature to form the corresponding (dimethylamino) methylidene derivatives 5a–j as intermediates, which immediately cyclize under the reaction conditions to form dimethyl 1-(hetero)aryl-4-oxo-1,4-dihydropyridazine-3,5-dicarboxylates 6a–j in 72–94 % yield, except for 6j, which was obtained only in 35 % yield (Scheme 1).

According to the second method, compound 1 was treated with DMFDMA in dichloromethane at room temperature to give dimethyl 2-[(dimethylamino)methylidene]-3-oxopentane-1,5-dioate (7) in 78 % yield after purification by column chromatography. To the ice-cold solution of this compound in a 1:1 mixture of ethanol and water in the presence of sodium acetate, an aqueous solution of (hetero)arenediazonium salts 3a–c, i was added dropwise to form intermediates 5a–c, i, which were cyclized without isolation under the reaction conditions into final products 6a–c, i in 35–42 % yield. They were identical to the products obtained according to the first synthesis.

Structure determination

Dimethyl 2-2-[(hetero)aryl]hydrazono]-3-oxopentane-1,5-dioates could exist in three tautomeric forms: as hydrazones (4), as dimethyl 3-hydroxy-[(hetero)aryl]diazene]pent-2-ene-1,5-dioates (4'), and as dimeth-
yl 3-hydroxy-4-[2-(hetero)arylhydrazono]-pent-2-ene-1,5-dioates (4″) (Scheme 2).

For compounds 4a – c, e two sets of signals in the ratio of 3.5 : 1 to 10 : 1 were observed in the $^1$H NMR spectra, while for compounds 4d, f – j only one set of peaks was observed. In all compounds the signal at $\delta = 3.87 – 3.94$ ppm, corresponding to -CH$_2$- group, is present, while for the minor isomer the signals for the -CH$_2$- group appeared at lower field at $\delta = 4.01 – 4.02$ ppm. On the basis of this observation, the structures 4″ are excluded. Between isomers 4 and 4′ one can differentiate on the basis of exchangeable protons of NH and OH groups. The NH signals were observed in the range $\delta = 12.72 – 13.20$ ppm, while the OH signals appeared in the range $\delta = 14.80 – 14.96$ ppm. The $^1$H NMR spectra for pyridazine derivatives 6a – j exhibit two singlets for two ester methyl groups at $\delta = 3.65 – 3.99$ ppm, a singlet for the proton 6-H of the pyridazine ring at $\delta = 8.31 – 9.02$ ppm and multiplets for aromatic protons in the range $\delta = 7.31 – 7.85$ ppm.

The structure of compound 6f was confirmed by X-ray analysis (Fig. 1). The structure of all new compounds, except for 4j, were determined also by elemental analyses for C, H, and N, and IR spectra. The structure for compound 4j was confirmed by HRMS and $^{13}$C NMR spectroscopy.

**Experimental Section**

Melting points were taken on a Kofler micro hot stage. The $^1$H NMR spectra were obtained on a Bruker Avance DPX 300 (300 MHz) spectrometer in CDCl$_3$ or [D$_6$]DMSO with TMS as the internal standard. IR spectra were recorded on a Perkin-Elmer 1310 infrared spectrometer and elemental analyses for C, H, and N on a Perkin-Elmer CHN analyzer 2400 II. Dimethyl 2-[(dimethylamino)methylidene]-3-oxopentane-1,5-dioate (7) was prepared in essentially the same way as for the corresponding diethyl derivative [11].

**General procedure for the preparation of dimethyl 2-[(hetero)arylhydrazono]-3-oxopentane-1,5-dioates (4a – j)**

A. Preparation of arenediazonium salts 3a – j

The aromatic amine (2a – j) (0.005 mol) was suspended in 5 mL of water, and 2.5 mL of conc. aqueous hydrochloric acid was added. The resulting solution was cooled to 0 – 5 °C, and a solution of NaNO$_2$ (345 mg, 0.005 mol) in 3.75 mL of water was added dropwise. The mixture was stirred for additional 50 min to obtain a solution of the arenediazonium salt (3a – j).

B. Preparation of hydrazonopentane-1,5-dioates 4a – j

The solution of the arenediazonium salt (3a – j) was added dropwise to the ice-cold solution of dimethyl 3-oxo-pentane-1,5-dioate (1; 0.721 mL, 0.005 mol) and sodium acetate (3 g) in a mixture of 3 mL of ethanol and 10 mL of water. The mixture was stirred at 0 °C for additional 40 min. A yellow precipitate was collected by filtration, washed with ice-cold water and recrystallized from ethanol.

The following compounds were prepared in this manner:

**Dimethyl 3-oxo-2-(2-phenylhydrazono)pentane-1,5-dioate (4a)**

This compound was prepared from aniline (2a; 0.46 g, 0.005 mol) and 1 (0.721 g, 0.005 mol), 94 % yield (1.31 g).
Dimethyl 2-[2-(4-fluorophenyl)hydrazono]-3-oxopentane-1,5-dioate (4b)

This compound was prepared from 4-fluoroaniline (2b; 0.480 g, 0.005 mol) and I (0.721 g, 0.005 mol), 92% yield (1.36 g). – M. p. 101 – 103 °C. – IR (KBr): ν = 3452, 3121, 2995, 1737, 1690, 1509, 1438, 1386, 1333, 1256, 1211, 1147, 1120, 1075, 1015, 836, 803, 516 cm⁻¹. – ¹H NMR (CDCl₃): two isomers in the ratio 3.5 : 1; major isomer: δ = 3.71 (s, 3H, MeO), 3.87 (s, 2H, CH₂), 3.92 (s, 3H, MeO), 7.17 – 7.22 (m, 1H, Ph), 7.33 – 7.44 (m, 4H, Ph), 13.07 (s, 1H, NH); minor isomer: δ = 3.76 (s, 3H, MeO), 3.87 (s, 3H, MeO), 4.02 (s, 2H, CH₂), 7.17 – 7.22 (m, 1H, Ph), 7.33 – 7.44 (m, 4H, Ph), 14.88 (s, 1H, OH).

Dimethyl 2-[2-(3-methylphenyl)hydrazono]-3-oxopentane-1,5-dioate (4d)

This compound was prepared from 3-methylaniline (2c; 0.60 g, 0.005 mol) and I (0.721 g, 0.005 mol), 88% yield (1.35 g). – M. p. 103 – 105 °C. – IR (KBr): ν = 3474, 3218, 3176, 2946, 1737, 1690, 1609, 1594, 1530, 1430, 1333, 1290, 1243, 1213, 1169, 1146, 1050, 1015, 768 cm⁻¹. – ¹H NMR (CDCl₃): two isomers in the ratio 5.5 : 1; major isomer: δ = 3.71 (s, 3H, MeO), 3.87 (s, 2H, CH₂), 3.89 (s, 3H, MeO), 3.92 (s, 3H, MeO), 6.74 (dd, 1H, J = 0.7, 2.4, 8.3 Hz, Ar), 6.87 (dd, 1H, J = 0.7, 2.1, 8.0 Hz, Ar), 6.99 (dd, 1H, J = 2.3 Hz, Ar), 7.29 (dd, 1H, J = 8.1 Hz, Ar), 13.02 (s, 1H, NH); minor isomer: δ = 3.76 (s, 3H, MeO), 3.85 (s, 3H, MeO), 3.87 (s, 3H, MeO), 4.02 (s, 2H, CH₂), 6.77 (dd, 1H, J = 0.7 Hz, Ar), 6.97 – 7.00 (m, 1H, Ar), 7.05 (dd, 1H, J = 2.2 Hz, 7.29 (dd, 1H, J = 8.0 Hz, Ar), 14.80 (s, 1H, OH); – C₁₄H₁₄N₂O₅ (278.26): calcld. C 52.93, H 4.39, N 9.57.

Dimethyl 2-[2-(4-methoxyphenyl)hydrazono]-3-oxopentane-1,5-dioate (4f)

This compound was prepared from 4-methoxyaniline (2f; 0.616 g, 0.005 mol) and I (0.721 g, 0.005 mol), 84% yield (1.30 g). – M. p. 70 – 72 °C (70 – 72 °C [10]). – IR (KBr): ν = 3460, 3137, 2948, 2847, 1740, 1698, 1683, 1529, 1514, 1433, 1390, 1342, 1248, 1150, 1122, 1070, 1011, 832, 543 cm⁻¹. – ¹H NMR (CDCl₃): δ = 3.70 (s, 3H, MeO), 3.83 (s, 3H, MeO), 3.87 (s, 2H, CH₂), 3.91 (s, 3H, MeO), 6.93 – 6.96 (m, 2H, Ar), 7.29 – 7.32 (m, 2H, Ar), 13.20 (s, 1H, NH).

Dimethyl 2-[2-(3-nitrophenyl)hydrazono]-3-oxopentane-1,5-dioate (4g)

This compound was prepared from 3-nitroaniline (2g; 0.691 g, 0.005 mol) and I (0.721 g, 0.005 mol), 78% yield (1.26 g). – M. p. 101 – 103 °C. – IR (KBr): ν = 3445, 3179, 1730, 1698, 1535, 1439, 1349, 1334, 1278, 1259, 1219, 1181, 1159, 1027, 1006, 804, 736 cm⁻¹. – ¹H NMR (CDCl₃): δ = 3.75 (s, 3H, MeO), 3.90 (s, 2H, CH₂), 3.95 (s, 3H, MeO), 7.56 – 7.65 (m, 2H, Ar), 8.00 – 8.04 (m, 1H, Ar), 8.19 – 8.21 (m, 1H, Ar), 13.04 (s, 1H, NH); – C₁₄H₁₄N₂O₇ (323.26): calcld. C 48.30, H 4.05, N 13.00; found C 48.35, H 3.86, N 13.05.

Dimethyl 2-[2-(4-bromophenyl)hydrazono]-3-oxopentane-1,5-dioate (4h)

This compound was prepared from 4-bromoaniline (2h; 0.860 g, 0.005 mol) and I (0.721 g, 0.005 mol), 72% yield (1.29 g). – M. p. 100 – 102 °C. – IR (KBr): ν = 3432, 3137,
Dimethyl 2-[2-(6-dichlorophenyl)hydrazono]-3-oxo pentane-1,5-dioate (4i)

This compound was prepared from 2,6-dichloroaniline (2i: 0.810 g, 0.005 mol) and 1 (0.721 g, 0.005 mol), 88% yield (1.53 g). - M. p. 69 – 71 °C (69 – 72 °C [10]). - IR (KBr): v = 3438, 3125, 2954, 1741, 1686, 1515, 1435, 1398, 1340, 1230, 1189, 1174, 1148, 784 cm⁻¹. - ¹H NMR (CDCl₃): δ = 3.70 (s, 3H, MeO), 3.94 (s, 2H, CH₂), 3.95 (s, 3H, MeO), 7.11 (dd, 1H, J = 8.1 Hz, Ar), 7.40 (d, 2H, J = 8.1 Hz, Ph), 12.92 (s, 1H, NH). - Found C 43.80, H 3.67, N 7.84.

Dimethyl 2-[2-(1H-1,2,4-triazol-3-yl)hydrazono]-3-oxopentane-1,5-dioate (4j)

This compound was prepared from 3-amino-1H-1,2,4-triazole (2j: 0.420 g, 0.005 mol) and 1 (0.721 g, 0.005 mol), 35% yield (0.380 g). - M. p. 213 – 215 °C. - IR (KBr): v = 3344, 3143, 2997, 1741, 1730, 1570, 1443, 1535, 1317, 1231, 1215, 1134, 1103, 1059, 1014, 939, 856, 705 cm⁻¹. - MS (EI): m/z = 269 [M⁺]. - HRMS: m/z = 269.0764 (calcld. 269.0761 for C₁₅H₁₄N₃O₅, [M⁺]). - ¹H NMR ([D₆]DMSO): δ = 3.45 (s, 3H, MeO), 3.68 (d, 1H, J = 17.4 Hz, CH-CH₂), 3.76 (s, 3H, MeO), 3.87 (d, 1H, J = 17.4 Hz, CH-CH₂) 7.70 (s, 1H, NH), 7.84 (s, 1H, CH), 12.72 (s, 1H, NH). - ¹NC NMR ([D₆]DMSO): δ = 40.6, 51.4, 52.0, 80.2, 130.5, 145.9, 150.1, 162.9, 169.2.

General procedure for the preparation of dimethyl 1-(hetero)aryl-4-oxo-1,4-dihydropyridazine-3,5-dicarboxylates (6a – j)

Procedure A: From dimethyl 2-(2-(hetero)arylhydrazono)-3-oxopentane-1,5-dioates (4a – j) and N,N-dimethylformamide dimethylacetal (DMFDMA).

To a solution of the dimethyl 2-(2-(hetero)arylhydrazono)-3-oxopentane-1,5-dioate (4a – j, 0.001 mol) in 1 mL of CH₂Cl₂, DMFDMA (0.2 mL, 0.0015 mol) was added, and the mixture was stirred at r.t. for 3 – 24 h. The volatile components were evaporated in vacuo, and the solid was recrystallized from EtOH.

Procedure B: From 2-[(dimethylamino)methylidene]-3-oxopentane-1,5-dioate (7) and the (hetero)arenediazonium salt (3a – j).

To an ice-cold solution of the (hetero)arenediazonium salt (3a – j), prepared from 2a – j (0.001 mol), an ice-cold solution of 7 (0.23 mL, 0.001 mol) and sodium acetate (0.6 g) in a mixture of ethanol (0.6 mL) and water (2 mL) was added. The mixture was stirred at 0 °C for 5 h and then at r.t. for additional 15 h. The precipitate was collected by filtration, washed with water and recrystallized from ethanol.

The following compounds were prepared according to this procedure:

Dimethyl 1-phenyl-4-oxo-1,4-dihydropyridazine-3,5-dicarboxylate (6a)

This compound was prepared by procedure A from 4a (0.278 g, 0.001 mol) and DMFDMA, 25 h, 82% yield (0.239 g). - M. p. 158 – 160 °C. - IR (KBr): v = 3457, 3054, 2954, 1749, 1709, 1635, 1848, 1436, 1252, 1160, 714 cm⁻¹. - ¹H NMR (CDCl₃): δ = 3.95 (s, 6H, 2 × MeO), 7.45 – 7.63 (m, 5H, Ph), 8.94 (s, 2H, 2-H, 6-H). - C₁₄H₁₂N₂O₅ (288.26): calcd. C 58.33, H 4.20, N 9.72; found C 58.46, H 3.83, N 9.57.

By procedure B from 7 (0.229 g, 0.001 mol) and 3a (prepared from 2a (0.093 g, 0.001 mol)); 53% yield (0.153 g).

Dimethyl 1-(4-fluorophenyl)-4-oxo-1,4-dihydropyridazine-3,5-dicarboxylate (6b)

This compound was prepared by procedure A from 4b (0.296 g, 0.001 mol) and DMFDMA, 4 h, 80% yield (0.245 g). - M. p. 135 – 138 °C. - IR (KBr): v = 3458, 3072, 2971, 1740, 1633, 1538, 1506, 1424, 1346, 1317, 1238, 1222, 1199, 1163, 1053, 980, 842, 545 cm⁻¹. - ¹H NMR (CDCl₃): δ = 3.94 (s, 3H, MeO), 3.98 (s, 3H, MeO), 7.21 – 7.26 (m, 2H, Ar), 7.57 – 7.62 (m, 2H, Ar), 8.94 (s, 1H, H₂). - C₁₄H₁₁FN₂O₅ (306.25): calcd. C 54.91, H 3.62, N 9.15; found C 55.09, H 3.61, N 9.09.

By procedure B from 7 (0.229 g, 0.001 mol) and 3b (prepared from 2b (0.111 g, 0.001 mol)); 42% yield (0.128 g).

Dimethyl 1-(3-methoxyphenyl)-4-oxo-1,4-dihydropyridazine-3,5-dicarboxylate (6c)

This compound was prepared by procedure A from 4c (0.308 g, 0.001 mol) and DMFDMA, 4 h, 70% yield (0.222 g). - M. p. 174 – 177 °C. - IR (KBr): v = 3448, 2960, 1750, 1734, 1630, 1609, 1586, 1433, 1268, 1216, 1164, 1063, 980, 716 cm⁻¹. - ¹H NMR (CDCl₃): δ = 3.88 (s, 3H, MeO), 3.95 (s, 3H, MeO), 3.99 (s, 3H, MeO), 6.98 – 7.02 (m, 1H, Ar), 7.13 – 7.15 (m, 2H, Ar), 7.40 – 7.46 (m, 1H, Ar), 8.93 (s, 1H, H₂). - C₁₄H₁₄FN₂O₅ (318.28): calcd. C 56.60, H 4.43, N 8.80; found C 56.89, H 4.32, N 8.73.

By procedure B from 7 (0.229 g, 0.001 mol) and 3c (prepared from 2c (0.112 g, 0.001 mol)); 35% yield (0.110 g).

Dimethyl 1-(3-methylphenyl)-4-oxo-1,4-dihydropyridazine-3,5-dicarboxylate (6d)

This compound was prepared by procedure A from 4d (0.292 g, 0.001 mol) and DMFDMA, 3 h, 76% yield (0.230 g). - M. p. 135 – 137 °C. - IR (KBr): v = 3447, 3125,
2958, 1752, 1733, 1630, 1434, 1325, 1246, 1209, 1165, 1063, 988, 804, 718 cm$^{-1}$. – $^{1}$H NMR (CDCl$_3$): $\delta$ = 2.46 (s, 3H, Me), 3.95 (s, 3H, MeO), 3.99 (s, 3H, MeO), 7.26–7.29 (m, 1H, Ar), 7.36–7.44 (m, 3H, Ar), 8.92 (s, 1H, H$_6$) – C$_{13}$H$_4$N$_2$O$_3$ (302.28): calcd. C 59.60, H 4.67, N 9.27; found C 59.66, H 4.55, N 9.17.

Dimethyl 1-(4-methylphenyl)-4-oxo-1,4-dihydropyridazine-3,5-dicarboxylate (6e)

This compound was prepared by procedure A from 4e (0.292 g, 0.001 mol) and DMFDMA, 24 h, 73 % yield (0.220 g). – M. p. 130 – 131 °C. – IR (KBr): $\nu$ = 3461, 2959, 1742, 1705, 1645, 1530, 1507, 1313, 1242, 1198, 1161, 1128, 1049, 968, 955, 824, 817 cm$^{-1}$. – $^{1}$H NMR (CDCl$_3$): $\delta$ = 2.43 (s, 3H, Me), 3.94 (s, 3H, MeO), 3.98 (s, 3H, MeO), 7.31–7.34 (m, 2H, Ar), 7.46–7.49 (m, 2H, Ar), 8.85 (s, 1H, H$_6$) – C$_{13}$H$_4$N$_2$O$_3$ (302.28): calcd. C 59.60, H 4.67, N 9.27; found C 59.66, H 4.55, N 9.17.

Dimethyl 1-(4-methoxyphenyl)-4-oxo-1,4-dihydropyridazine-3,5-dicarboxylate (6f)

This compound was prepared by procedure A from 4f (0.308 g, 0.001 mol) and DMFDMA, 22 h, 58 % yield (0.183 g). – M. p. 117 – 120 °C. – IR (KBr): $\nu$ = 3451, 3125, 2960, 1748, 1739, 1629, 1526, 1512, 1430, 1312, 1253, 1230, 1203, 1168, 1057, 854 cm$^{-1}$. – $^{1}$H NMR (CDCl$_3$): $\delta$ = 3.87 (s, 3H, Me), 3.94 (s, 3H, MeO), 3.98 (s, 3H, MeO), 7.00–7.03 (m, 2H, Ar), 7.49–7.52 (m, 2H, Ar), 8.85 (s, 1H, H$_6$) – C$_{13}$H$_4$N$_2$O$_3$ (302.18): calcd. C 59.66, H 4.55, N 9.17; found C 59.60, H 4.67, N 9.27.

Dimethyl 1-(3-nitrophenyl)-4-oxo-1,4-dihydropyridazine-3,5-dicarboxylate (6g)

This compound was prepared by procedure A from 4g (0.323 g, 0.001 mol) and DMFDMA, 26 h, 70 % yield (0.234 g). – M. p. 180 – 182 °C. – IR (KBr): $\nu$ = 3447, 3102, 2960, 1751, 1633, 1537, 1437, 1351, 1328, 1236, 1203, 1168, 984, 817, 713 cm$^{-1}$. – $^{1}$H NMR (CDCl$_3$): $\delta$ = 3.96 (s, 3H, MeO), 34.01 (s, 3H, MeO), 7.76–7.81 (m, 1H, Ar), 8.01–8.03 (m, 1H, Ar), 8.33–8.36 (m 1H, Ar), 8.51–8.57 (m, 1H, Ar), 9.02 (s, 1H, H$_6$) – C$_{14}$H$_11$FN$_2$O$_7$ (333.25): calcd. C 50.46, H 3.33, N 12.61; found C 50.24, H 3.20, N 12.55.

Dimethyl 1-(4-bromophenyl)-4-oxo-1,4-dihydropyridazine-3,5-dicarboxylate (6h)

This compound was prepared by procedure A from 4h (0.357 g, 0.001 mol) and DMFDMA, 47 h, 81 % yield (0.296 g). – M. p. 150 – 152 °C. – IR (KBr): $\nu$ = 3462, 3089, 3059, 2951, 1752, 1748, 1620, 1536, 1480, 1446, 1402, 1349, 1317, 1232, 1198, 1171, 1119, 1051, 1006, 847, 757, 720 cm$^{-1}$. – $^{1}$H NMR (CDCl$_3$): $\delta$ = 3.95 (s, 3H, MeO), 3.99 (s, 3H, MeO), 7.49–7.52 (m, 2H, Ar), 7.66–7.69 (m, 2H, Ar), 8.90 (s, 1H, H$_6$) – C$_{14}$H$_11$BrN$_2$O$_5$ (367.15): calcd. C 45.80, H 3.02, N 7.63; found C 45.97, H 3.11, N 7.53.

**Table 1. Crystal data, data collection and structure refinement for compound 6f.**

<table>
<thead>
<tr>
<th>Compound 6f</th>
<th>Formula</th>
<th>Rel. formula weight</th>
<th>Crystal color</th>
<th>Crystal system</th>
<th>Space group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C$_{13}$H$_4$N$_2$O$_6$</td>
<td>263.25</td>
<td>yellow</td>
<td>triclinic</td>
<td>$P1$</td>
</tr>
</tbody>
</table>

**D. Pahovnik et al. - Dimethyl 1-(Hetero)aryl-4-oxo-1,4-dihydropyridazine-3,5-dicarboxylates**
(0.108 g). – M. p. 205 – 208 °C. – IR (KBr): v = 3445, 3102, 2961, 2888, 1754, 1706, 1620, 1440, 1395, 1323, 1210, 1196, 1181, 850, 578 cm⁻¹. – 1H NMR (CDCl₃): δ = 3.65 (s, 3H, MeO), 3.79 (s, 3H, MeO), 5.99 (s, 1H, CH), 8.31 (s, 1H, 6-H), 14.22 (s, 1H, NH). – C₁₀H₉N₅O₅ (279.21): calcd. C 43.02, H 3.25, N 25.08; found C 43.09, H 3.53, N 25.42.

By procedure B from 7 (0.229 g, 0.001 mol) and 3j (prepared from 3j (0.088 g, 0.001 mol)); 42% yield (0.128 g).

**X-Ray structure analysis for compound 6f**

Single crystal X-ray diffraction data of compound 6f were collected at r. t. on a Nonius Kappa CCD diffractometer using the Nonius Collect Software [12]. DENZO and SCALEPACK [13] were used for indexing and scaling of the data, and the structure was solved by means of SIR97 [14]. Refinement was done using the XTAL3.4 [15] program package. The crystal structure was refined on F² using full-matrix least-squares procedures. The non-hydrogen atoms were refined anisotropically, while the positions of the hydrogen atoms were geometrically calculated, and their positional and isotropic atomic displacement parameters were not refined. Absorption correction was not necessary. Regina [16] drawing of the content of the asymmetric unit showing the atom-labeling scheme is presented in Fig. 1. The resulting crystal data and details concerning data collection and refinement for compound 6f are quoted in Table 1.

CCDC 674009 contains the supplementary crystallographic data for this paper. 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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