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ORIGINAL PAPER

Cyclisation reactions of hydrazones XXXII. Synthesis of some pyrazolylhydrazones and study of their cyclisation

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Abstract Several variously substituted 1*H*-pyrazol-5-yl hydrazones were prepared in order to study their cyclisation reactions. It has been found that the pathway of the cyclisation depends on the nature of the cyclisation medium and the position of substitution in the pyrazole ring.

Keywords Heterocycles · Isomers · Pyrazolo[5,1-*c*][1,2,4]triazine · Pyrazolo[5,1-*c*]pyrimido[4,5-*e*][1,2,4]triazine

Introduction

The regioselectivity of the cyclisation of the functional derivatives of 2-[2-(1*H*-pyrazol-5-yl)hydrazono]malonic acid was intensively studied [1–10]. It was observed that the pathway of cyclisation depended on the nature of substrate functional groups. For example, a nitrile group is usually more susceptible to a cyclisation reaction than an amide group [9]. However, the cyclisation medium also plays a very important role. For example, the treatment of ethyl 2-[2-(1*H*-pyrazol-5-yl)hydrazono]-2-cyanoacetate in an alkaline solvent leads to a different product in contrast to an acid solvent [2]. In pyridine, the cyclisation reaction proceeds via the ester group, whereas in acetic acid, the nitrile group is involved.

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Our previous study revealed that the direction of the cyclisation reaction of the hydrazone **2** (R^1 = Me, R^2 = H) [10] was strictly influenced by the nature of the cyclisation medium. This communication is focused on the correlation between the course of the cyclisation reaction at hydrazone **2** with corresponding R^1 and R^2 substitutions on the pyrazole ring.

An application to this cyclisation study is the synthesis of the heterocyclic systems mimicking naturally occurring compounds. The pyrazolo[5,1-*c*][1,2,4]triazine skeleton is isosteric to the purine system. Many pyrazolo[5,1-*c*]-[1,2,4]triazines similar to derivative **3** have been prepared to investigate their potential biological activity [11]. Derivative **5** can, in fact, be the aza-analog of uracil or thymine. Pyrazolopyrimidotriazine **4** could also potentially mimic the heterocyclic system in 5,10-methylenetetrahydrofolate (Fig. 1).

This hypothesis could be supported by examples of biologically active derivatives with similar heterocyclic skeletons, including pyrazolo[1,2-*a*][1,2,4]benzotriazine [12, 13], benzo[*g*]indole [14], imidazo[1,5-*a*]quinoxaline [15], and benzo[*e*]pyrazolo[5,1-*c*][1,2,4]triazine [16, 17]. For this reason, the hydrazones **2** could be considered as useful and versatile starting materials for the synthesis of the structurally diverse heterocyclic compounds with potential biological effects.

Results and discussion

Diazotation of 3-aminopyrazoles **1a**–**1d** and subsequent in situ coupling of the diazonium salt with ethyl (2-cyanoacetyl)carbamate afforded the corresponding hydrazones **2a**–**2d** in high yields (Scheme 1). The stability of these hydrazones in solution is relatively low due to their

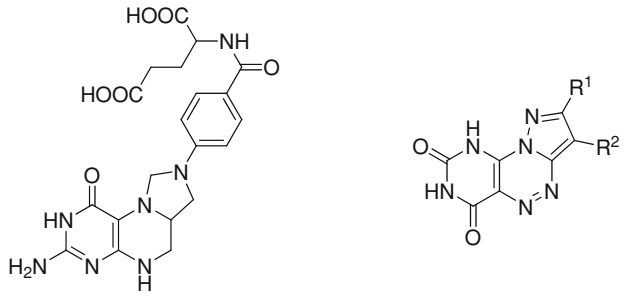


Fig. 1 Structural comparison of heterocyclic systems between tetrahydrofolate and compound **4**

spontaneous cyclisation to the pyrazolo[5,1-*c*][1,2,4]triazines **3a**–**3d**.

Pyrazolo[5,1-*c*][1,2,4]triazines **3a**–**3d** were easily prepared by the thermal cyclisation of hydrazones **2a**–**2d** in boiling ethanol. This cyclisation occurs if the *E*-isomer of the corresponding hydrazone is present. Under these cyclisation conditions, the interconversion between *E* and *Z* isomers is fast due to azo-hydrazono tautomerism. This dynamic equilibrium of geometric isomers enabled us to obtain good yields.

Subsequent treatment of pyrazolo[5,1-*c*][1,2,4]triazine **3** with an aqueous solution of sodium carbonate resulted in pyrazolo[5,1-*c*]pyrimido[4,5-*e*][1,2,4]triazine **4**, which is, in fact, a constitutional isomer of the 6-azauracil **5**. In the case of **3d**, during cyclisation, the ethoxy group was susceptible to hydrolysis to a carboxy group in a boiling aqueous solution of sodium carbonate, producing derivative **4e**. If the cyclisation reaction was carried out at ambient temperature, the ethoxy group was stable under these reaction conditions for at least 14 h, and derivative **4d** was isolated.

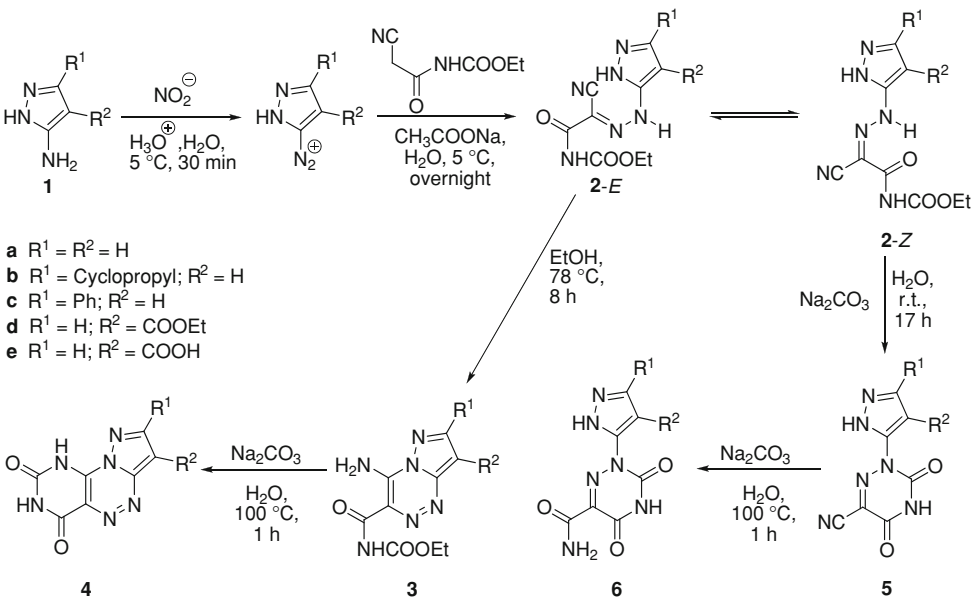
Hydrazone **2** was also treated with an aqueous solution of sodium carbonate to study the direction of the cyclisation reaction in relation to the substitution of the pyrazole ring. In this case, the cyclisation obviously proceeded via an anionic mesomeric intermediate in which the *Z* isomer should undergo ring closure to form 6-azauracil derivative **5**. It was found that the applied procedure was only successful in the case of the hydrazone **2a**. If the temperature was not elevated, then 6-azauracil **5a** was isolated. At a higher temperature, the cyclisation of the hydrazone **2a** in boiling aqueous sodium carbonate solution was accompanied by the subsequent transformation of the nitrile group to an amide group, resulting in the 6-azauracil **6a**.

Hydrazone **2d**, when treated with aqueous sodium carbonate solution at room temperature, unexpectedly only afforded the isomeric tricyclic derivative **4d**. The direction of the cyclisation is, therefore, influenced by the ethoxycarbonyl group on the pyrazole ring. Even if the temperature of the reaction mixture was elevated to the boiling point, the course of the cyclisation remained the same. Specifically, in this case, only the ethoxycarbonyl group was hydrolysed to yield carboxylic acid **4e**.

The applied cyclisation method using aqueous sodium carbonate solution was not suitable for hydrazones **2b** and **2c**. In both cases, the desired 6-azauracils **5b** and **5c** were present in the reaction mixture but were always accompanied with impurities that were difficult to separate.

Variously substituted hydrazones **2a**–**2d** were treated in aqueous sodium carbonate solution and ethanol to gain a deeper insight into the course of their cyclisation. The result of this reaction was dictated by both the substitution

Scheme 1



of the pyrazole ring and the nature of the cyclisation medium. If hydrazones **2a**–**2d** were heated in boiling ethanol, the thermal cyclisation was favoured, and pyrazolo[5,1-*c*][1,2,4]triazines **3a**–**3d** were obtained. The situation was more complex when aqueous sodium carbonate solution was used. The cyclisation then proceeded via a mesomeric anionic intermediate, and, therefore, the substitution on the pyrazole ring played a very important role in determining the direction of the cyclisation and the potential for side reactions. From this aspect, only hydrazones **2a** and **2d** furnished pure compounds. Interestingly, the ethoxycarbonyl group in hydrazone **2d** completely changed the course of the cyclisation, resulting in derivatives **4d** or **4e**, depending on the temperature of the cyclisation medium.

Experimental

Pyrazoles **1a**–**1c** were purchased from Aldrich (Milwaukee, IL, USA) and pyrazole **1d** from Fluorochem (UK). Melting points were determined on a Boetius stage. Infrared spectra were measured on an ATI Unicam Genesis FTIR instrument in KBr. The LC/MS analyses were carried out on an UHPLC-MS system consisting of an UHPLC chromatograph Accela with a photodiode array detector and triple quadrupole mass spectrometer TSQ Quantum Access (both Thermo Scientific, CA, USA), using a Nucleodur Gravity C18 column at 30 °C with a flow rate of 800 mm^3/min (Macherey–Nagel, 1.8 μm, 2.1 × 50 mm, Germany). The APCI source operated at a discharge current of 5 μA, vaporizer temperature of 400 °C and capillary temperature of 200 °C. ^1H and ^{13}C NMR spectra were measured in DMSO-d_6 at 20 °C on a Bruker Avance 300 FT NMR spectrometer. Elemental analyses were performed with an EA 1108 Elemental Analyser (Fison Instruments). The results were found to be in good agreement (±0.4%) with the calculated values.

General synthesis of hydrazones 2

A solution of 0.69 g sodium nitrite (10 mmol) in 5 cm^3 ice water was slowly added to an ice-cooled and stirred solution of aminopyrazole **1** (10 mmol) in 14 cm^3 water and 6 cm^3 conc. hydrochloric acid so that the temperature was maintained between 0 and 5 °C. After 30 min of continuous stirring and cooling, the reaction mixture of a diazonium salt was poured in portions into a cold solution of 1.72 g ethyl cyanoacetylcarbamate (11 mmol) and 11.5 g sodium acetate in 630 cm^3 water. Then, the reaction mixture was stirred for 30 min under ice-cooling and placed in a refrigerator overnight. The precipitated hydrazone **2** was collected by filtration, washed with water and dried on air.

Ethyl N-[2-cyano-2-[(1H-pyrazol-3-yl)hydrazono]acetyl]-carbamate (**2a**, $C_9H_{10}N_6O_3$)
Yield 2.21 g (88%); m.p.: 216–218 °C; ^1H NMR (300 MHz, DMSO-d_6): $\delta = 1.25$ (t, $J = 7$ Hz, 3H), 4.18 (q, $J = 7$ Hz, 2H), 6.41 (s, 1H), 7.64 (s, 1H), 10.22 (s, NH), 12.61 (bs, NH) ppm; IR (KBr): $\bar{\nu} = 3{,}541$, 3,257, 2,219, 1,763, 1,506, 1,192, 1,030, 929, 779, 686 cm^{-1}; MS (-APCI): $m/z = 249.0$ (M−1).

Ethyl N-[2-cyano-2-[(5-cyclopropyl-1H-pyrazol-3-yl)-hydrazono]acetyl]carbamate (**2b**, $C_{12}H_{14}N_6O_3$)
Yield 2.36 g (81%); m.p.: 206–207 °C; ^1H NMR (300 MHz, DMSO-d_6): $\delta = 0.65$–0.72 (m, 2H), 0.89–0.99 (m, 2H), 1.25 (t, $J = 7.14$ Hz, 3H), 1.82–1.94 (m, 1H), 4.17 (q, $J = 7.14$ Hz, 2H), 6.11 (s, 1H), 10.17 (bs, NH), 12.54 (bs, NH) ppm; IR (KBr): $\bar{\nu} = 3{,}289$, 3,100, 2,982, 2,229, 1,765, 1,697, 1,512, 1,492, 1,320, 1,206, 1,030, 928, 762 cm^{-1}; MS (-APCI): $m/z = 289.0$ (M−1).

Ethyl N-[2-cyano-2-[(5-phenyl-1H-pyrazol-3-yl)-hydrazono]acetyl]carbamate (**2c**, $C_{15}H_{14}N_6O_3$)
The diazotation reaction was carried out in a suspension. Yield 3.05 g (94%); m.p.: 219–221 °C; ^1H NMR (300 MHz, DMSO-d_6): $\delta = 1.28$ (t, $J = 7$ Hz, 3H), 4.21 (q, $J = 7$ Hz, 2H), 6.76 (s, 1H), 7.30–7.45 (m, 3H), 7.78 (d, $J = 7.3$ Hz, 2H), 10.34 (s, NH), 12.76 (bs, NH) ppm; IR (KBr): $\bar{\nu} = 3{,}320$, 2,219, 2,161, 1,772, 1,707, 1,575, 1,490, 1,270, 1,211, 1,028, 764, 695 cm^{-1}; MS (-APCI): $m/z = 325.0$ (M−1).

Ethyl N-[2-cyano-2-[(4-ethoxycarbonyl-1H-pyrazol-3-yl)-hydrazono]acetyl]carbamate (**2d**, $C_{12}H_{14}N_6O_5$)
Yield 3.36 g (99%, isolated as monohydrate); m.p.: 232–234 °C; ^1H NMR (300 MHz, DMSO-d_6): $\delta = 1.27$ (t, $J = 7$ Hz, 3H), 1.31 (t, $J = 7$ Hz, 3H), 4.20 (q, $J = 7$ Hz, 2H), 4.26 (q, $J = 7$ Hz, 2H), 8.05 (s, 1H), 10.34 (s, NH), 11.02 (bs, NH) ppm; IR (KBr): $\bar{\nu} = 3{,}656$, 3,165, 2,216, 1,756, 1,717, 1,561, 1,535, 1,331, 1,232, 1,089, 771 cm^{-1}; MS (-APCI): $m/z = 321.1$ (M−1).

General synthesis of pyrazolo[5,1-c][1,2,4]triazines 3

A solution of hydrazone **2** (3 mmol) in 200 cm^3 ethanol was refluxed for 8 h. Then, the solution was concentrated to about half of its volume and the precipitated pyrazolo[5,1-*c*][1,2,4]triazine **3** was collected by filtration, washed with a small amount of ethanol and dried on air.

Ethyl N-[(4-aminopyrazolo[5,1-c][1,2,4]triazin-3-yl)-carbonyl]carbamate (**3a**, $C_9H_{10}N_6O_3$)
Yield 0.58 g (77%); m.p.: 233–234 °C; ^1H NMR (300 MHz, DMSO-d_6): $\delta = 1.27$ (t, $J = 7$ Hz, 3H), 4.20

(q, $J = 7$ Hz, 2H), 7.13 (d, $J = 2.3$ Hz, 1H), 8.43 (d, $J = 2.3$ Hz, 1H), 8.94 (s, NH), 9.44 (s, NH), 10.47 (s, NH) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): $\delta = 14.1$, 61.3, 98.6, 117.6, 141.8, 146.6, 149.3, 150.2, 163.7 ppm; IR (KBr): $\bar{\nu} = 3{,}441$, 3,378, 3,275, 2,989, 1,768, 1,630, 1,489, 1,224, 1,162, 1,022, 791, 648 cm^{-1}; MS (-APCI): $m/z = 249.0$ (M−1).

Ethyl N-[(4-amino-7-cyclopropylpyrazolo[5,1-c]-[1,2,4]triazin-3-yl)carbonyl]carbamate
(**3b**, $C_{12}H_{14}N_6O_3$)
Yield 0.75 g (86%); m.p.: 213–214 °C; ^{1}H NMR (300 MHz, DMSO-d_6): $\delta = 0.92$–0.99 (m, 2H), 1.06–1.14 (m, 2H), 1.27 (t, $J = 7.1$ Hz, 3H), 2.11–2.22 (m, 1H), 4.20 (q, $J = 7.1$ Hz, 2H), 6.81 (s, 1H), 8.77 (s, NH), 9.12 (s, NH), 10.36 (s, NH) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): $\delta = 9.5$, 9.8, 14.0, 61.2, 94.4, 117.5, 140.9, 149.6, 150.1, 163.1, 163.6 ppm; IR (KBr): $\bar{\nu} = 3{,}443$, 3,380, 3,281, 3,142, 1,763, 1,676, 1,626, 1,565, 1,493, 1,387, 1,218, 1,023, 793, 650 cm^{-1}; MS (-APCI): $m/z = 289.1$ (M−1).

Ethyl N-[(4-amino-7-phenylpyrazolo[5,1-c][1,2,4]triazin-3-yl)carbonyl]carbamate (**3c**, $C_{15}H_{14}N_6O_3$)
Yield 0.76 g (78%); m.p.: 205–208 °C; ^{1}H NMR (300 MHz, DMSO-d_6): $\delta = 1.28$ (t, $J = 7$ Hz, 3H), 4.21 (q, $J = 7$ Hz, 2H), 7.46–7.58 (m, 3H), 7.64 (s, 1H), 8.17 (d, $J = 6.6$ Hz, 2H), 8.95 (s, NH), 9.34 (s, NH), 10.48 (s, NH) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): $\delta = 14.1$, 61.3, 95.2, 118.1, 126.7, 128.9, 129.9, 131.3, 141.4, 150.2, 150.4, 156.7, 163.6 ppm; IR (KBr): $\bar{\nu} = 3{,}449$, 3,294, 2,985, 1,765, 1,674, 1,621, 1,562, 1,496, 1,259, 1,164, 1,028, 683 cm^{-1}; MS (-APCI): $m/z = 325.1$ (M−1).

Ethyl N-[(4-amino-8-ethoxycarbonylpyrazolo-[5,1-c][1,2,4]triazin-3-yl)carbonyl]carbamate
(**3d**, $C_{12}H_{14}N_6O_5$)
Yield 0.92 g (90%); m.p.: 246–249 °C; ^{1}H NMR (300 MHz, DMSO-d_6): $\delta = 1.28$ (t, $J = 7.1$ Hz, 3H), 1.34 (t, $J = 7.1$ Hz, 3H), 4.22 (q, $J = 7.1$ Hz, 2H), 4.34 (q, $J = 7.1$ Hz, 2H), 8.75 (s, 1H), 9.09 (s, 1H), 9.68 (s, 1H), 10.62 (s, 1H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): $\delta = 14.1$, 14.3, 60.1, 61.4, 103.3, 121.1, 141.7, 147.4, 148.1, 150.3, 161.2, 163.3 ppm; IR (KBr): $\bar{\nu} = 3{,}357$, 3,173, 2,985, 1,784, 1,635, 1,579, 1,498, 1,438, 1,213, 1,155, 1,043, 704, 667 cm^{-1}; MS (-APCI): $m/z = 321.1$ (M−1).

*General synthesis of pyrazolo[5,1-c]pyrimido[4,5-e]-[1,2,4]triazines **4***

The pyrazolo[5,1-*c*][1,2,4]triazine **3** (1 mmol) was mixed with 30 cm^3 water and 0.21 g sodium carbonate (2 mmol). The reaction mixture was stirred for 10 min at room temperature, then refluxed for 1 h and, finally, was allowed to cool to room temperature (except the pyrazolo[5,1-*c*][1,2,4]triazine **3c**, which was treated with sodium carbonate only at room temperature for 14 h). After acidification by diluted hydrochloric acid (1:10), the reaction mixture was stirred for 2 h. The precipitate was collected by filtration, washed with water and dried on air.

Pyrazolo[5,1-c]pyrimido[4,5-e][1,2,4]triazin-2,4(1H,3H)-dione (**4a**, $C_7H_4N_6O_2$)
Yield 0.15 g (75%); m.p.: >360 °C; ^{1}H NMR (300 MHz, DMSO-d_6): $\delta = 4.04$ (bs, NH), 7.40 (d, $J = 2.3$ Hz, 1H), 8.59 (d, $J = 2.3$ Hz, 1H), 11.84 (s, NH) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): $\delta = 99.9$, 120.5, 137.6, 147.6, 148.9, 150.1, 159.8 ppm; IR (KBr): $\bar{\nu} = 3{,}138$, 3,105, 3,035, 2,825, 1,738, 1,698, 1,607, 1,420, 1,327, 1,279, 820, 463 cm^{-1}; MS (-APCI): $m/z = 203.2$ (M−1).

8-Cyclopropylpyrazolo[5,1-c]pyrimido[4,5-e][1,2,4]-triazin-2,4(1H,3H)-dione (**4b**, $C_{10}H_8N_6O_2$)
Yield 0.25 g (99%); m.p.: 313–315 °C; ^{1}H NMR (300 MHz, DMSO-d_6): $\delta = 0.96$–1.05 (m, 2H), 1.11–1.20 (m, 2H), 2.18–2.29 (m, 1H), 7.08 (s, 1H), 11.75 (s, NH) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): $\delta = 9.9$, 10.0, 95.4, 120.3, 136.6, 148.8, 150.5, 159.8, 164.5 ppm; IR (KBr): $\bar{\nu} = 3{,}551$, 3,481, 3,072, 2,872, 1,729, 1,710, 1,600, 1,541, 1,478, 1,422, 1,310, 1,187, 1,052, 834, 595, 463 cm^{-1}; MS (-APCI): $m/z = 243.0$ (M−1).

8-Phenylpyrazolo[5,1-c]pyrimido[4,5-e][1,2,4]-triazin-2,4(1H,3H)-dione (**4c**, $C_{13}H_8N_6O_2$)
Yield 0.27 g (95%); m.p.: 358–360 °C; ^{1}H NMR (300 MHz, DMSO-d_6): $\delta = 7.42$–7.55 (m, 3H), 7.43 (s, 1H), 8.11 (d, $J = 7$ Hz, 2H), 10.54 (s, NH) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): $\delta = 94.5$, 122.5, 126.4, 128.8, 129.1, 132.3, 145.9, 151.6, 155.0, 157.2, 162.5 ppm; IR (KBr): $\bar{\nu} = 3{,}635$, 3,470, 3,060, 2,845, 1,751, 1,692, 1,610, 1,419, 1,270, 780, 696 cm^{-1}; MS (-APCI): $m/z = 278.9$ (M−1).

Ethyl 1,2,3,4-tetrahydro-2,4-dioxopyrazolo[5,1-c]-pyrimido[4,5-e][1,2,4]triazin-7-carboxylate
(**4d**, $C_{10}H_8N_6O_4$)
Pyrazolo[5,1-*c*][1,2,4]triazine **3c** was treated with sodium carbonate at room temperature for 14 h. Yield 0.18 g (64%); m.p.: 303-305 °C; ^{1}H NMR (300 MHz, DMSO-d_6): $\delta = 1.37$ (t, $J = 7$ Hz, 3H), 4.40 (q, $J = 7$ Hz, 2H), 5.72 (bs, NH), 8.92 (s, 1H), 11.96 (s, NH) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): $\delta = 14.2$, 60.4, 104.1, 123.5, 138.5, 147.5, 148.7, 149.3, 159.3, 160.8 ppm; IR (KBr): $\bar{\nu} = 3{,}552$, 3,472, 3,222, 3,088, 2,836, 1,742, 1,711, 1,600, 1,543, 1,408, 1,259, 1,219, 1,187, 1,144, 1,046, 790, 574 cm^{-1}; MS (-APCI): $m/z = 275.0$ (M−1).

1,2,3,4-Tetrahydro-2,4-dioxopyrazolo[5,1-c]pyrimido-[4,5-e][1,2,4]triazin-7-carboxylic acid (**4e**, $C_8H_4N_6O_4$)
Yield 0.21 g (85%); m.p.: 343–345 °C; ^{1}H NMR (300 MHz, DMSO-d_6): $\delta = 4.63$ (bs, NH), 8.85 (s, 1H),

11.96 (s, NH) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): $\delta = 105.1$, 123.4, 138.6, 147.5, 149.1, 149.4, 159.4, 162.3 ppm; IR (KBr): $\bar{\nu} = 3{,}510$, 3,205, 2,810, 1,722, 1,610, 1,535, 1,408, 1,225, 1,200, 738, 588, 457 cm^{-1}; MS (-APCI): $m/z = 202.9$ (M−1).

3,5-Dioxo-2,3,4,5-tetrahydro-2-(1H-pyrazol-3-yl)-1,2,4-triazin-6-carbonitrile (**5a**, $C_7H_4N_6O_2$)

Hydrazone **2a** (0.5 g, 2 mmol) was dissolved in a solution of 0.21 g sodium carbonate (2 mmol) and 20 cm^3 water at room temperature. The reaction mixture was stirred for 17 h at room temperature, then acidified to pH ~1 by diluted hydrochloric acid (10:1) and stirred for 1 h. The precipitate was collected by filtration, washed with water and dried. Yield 0.22 g (54%); m.p.: 283–285 °C; ^{1}H NMR (300 MHz, DMSO-d_6): $\delta = 6.42$ (d, $J = 2.3$ Hz, 1H), 7.84 (d, $J = 2.3$ Hz, 1H), 12.94 (s, NH), 13.13 (s, NH) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): $\delta = 100.9$, 112.3, 122.9, 130.1, 146.4, 146.7, 154.4 ppm; IR (KBr): $\bar{\nu} = 3{,}281$, 3,163, 3,131, 3,059, 2,850, 2,248, 1,756, 1,697, 1,568, 1,530, 1,486, 1,421, 1,312, 1,270, 1,229, 1,110, 1,043, 798, 603 cm^{-1}; MS (-APCI): $m/z = 203.0$ (M−1).

3,5-Dioxo-2,3,4,5-tetrahydro-2-(1H-pyrazol-3-yl)-1,2,4-triazin-6-carboxamide (**6a**, $C_7H_6N_6O_3$)

Hydrazone **2a** (0.5 g, 2 mmol) was dissolved in a solution of 0.42 g sodium carbonate (4 mmol) and 50 cm^3 water at room temperature. The reaction mixture was stirred for 30 min at room temperature, then refluxed for 1 h and, finally, two-thirds of the water was evaporated off. After cooling to room temperature, the reaction mixture was acidified to pH ~1 by diluted hydrochloric acid (10:1) and stirred for 3 h. The precipitate was collected by filtration, washed with water and dried. Yield 0.28 g (57%); m.p.: 266–269 °C; ^{1}H NMR (300 MHz, DMSO-d_6): $\delta = 6.41$ (d, $J = 2.5$ Hz, 1H), 7.82 (d, $J = 2.5$ Hz, 1H), 7.86 (s, NH), 8.00 (s, NH), 12.60 (s, NH), 13.05 (s, NH) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): $\delta = 101.2$, 129.8, 137.5, 146.8, 147.5, 155.8, 160.9 ppm; IR (KBr): $\bar{\nu} = 3{,}543$, 3,344, 3,171, 2,993, 2,784, 1,738, 1,709, 1,484, 1,415, 1,309, 1,043, 783, 588 cm^{-1}; MS (-APCI): $m/z = 221.0$ (M−1).

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