Scientific paper

Transformations of Dialkyl Acetone-1,3-dicarboxylates *via* Their Dimethylaminomethylidene Derivatives Into 1-substituted 4-ethoxycarbonyl-5-(ethoxycarbonylmethyl)pyrazoles, 7-amino-2-ethoxycarbonyl-1*H*, 2*H*-pyrazolo[2,3-*c*]pyrimidin-5-one, 4-hydroxypyridin-2(1*H*)-ones and 6-substituted 3-benzoylamino-2,5-dioxo-5,6-dihydro-2*H*-pyrano[3,2-*c*]pyridine-8-carboxylates.

Silvo Zupančič, Jurij Svete and Branko Stanovnik*

Faculty of Chemistry and Chemical Technology, University of Ljubljana, Aškerčeva 5, P. O. box 537, 1000 Ljubljana, Slovenia

** Corresponding author: E-mail: branko.stanovnik@fkkt.uni-lj.si*

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Dedicated to the memory of Professor Ljubo Golič

Abstract

Diethyl 1-dimethylamino-3-oxobut-1-ene-2,4-dicarboxylate (**2a**), prepared from diethyl acetone-1,3-dicarboxylate and *N,N*-dimethylformamide dimethylacetal (DMFDMA), was transformed with hydrazines **3a-g** into 1-susbtituted 4-ethoxycarbonyl-5-(ethoxycarbonylmethyl)pyrazoles **5a-g**, with aminoguanidine (**6**) into 7-amino-2-ethoxycarbonyl-1*H*,2*H*-pyrazolo[2,3-*c*]pyrimidin-5-one (**9**), and with amines **10a-k** into 4-hydroxypyridin-2(1*H*)-ones **11a-k**. Compounds **11** were treated with methyl (*Z*)-2-benzoylamino-3-dimethylaminopropenoate (**12**) to give 6-substituted 3-benzoylamino-2,5-dioxo-5,6-dihydro-2*H*-pyrano[3,2-*c*]pyridine-8-carboxylates **14**, while in the reaction with methyl 3-dimethylamino-2-(methoxycarbonyl)propenoate (**15**) decarboxylation of one of the ester groups took place producing alkyl (*E*)-1-alkyl-4-hydroxy-5-(3-methoxy-3-oxoprop-1-enyl)-6-oxo-1,6-dihydropyridine-3-carboxylates **17.**

Keywords: 1-substituted 4-ethoxycarbonyl-5-(ethoxycarbonylmethyl)pyrazoles, 1*H*,2*H*-pyrazolo[2,3-*c*]pyrimidin-5-one, 4-hydroxypyridin-2(1*H*)-ones, 6-substituted 2*H*-pyrano[3,2-*c*]pyridine-8-carboxylates.

1. Introduction

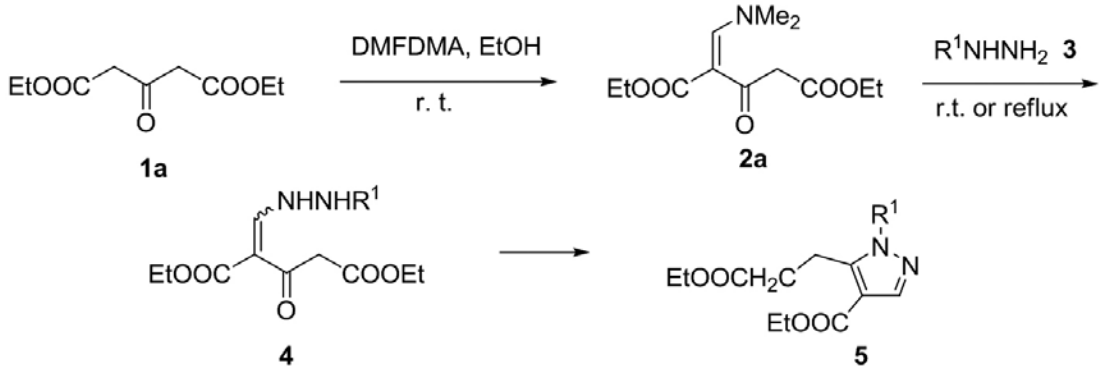
There are many methods for the synthesis of pyrazoles,[1] pyrazolopyrimidines,[2] and pyranopyridines[3] described in the literature.

In connection with our interest in enaminones and related compounds, as building blocks for the preparation of various heterocyclic systems[4] including also some natural products,[5,6] dialkyl acetone-1,3-dicarboxylates have been recently employed for the synthesis of heteroaryl substituted pyrimidines,[7] dialkyl 1-substituted 4-oxo-1,4-dihydropyridine-3,5-dicarboxylates,[8] pyrazolo[4,3-*d*]pyridine-7-carboxylates,[9] pyrazolyl substituted pyridopyrimidines, pyranopyranediones, and chromenediones,[10] and pyrazolo[4,3-*d*][1,2]diazepines.[11,12]

In this paper the following transformations were studied:

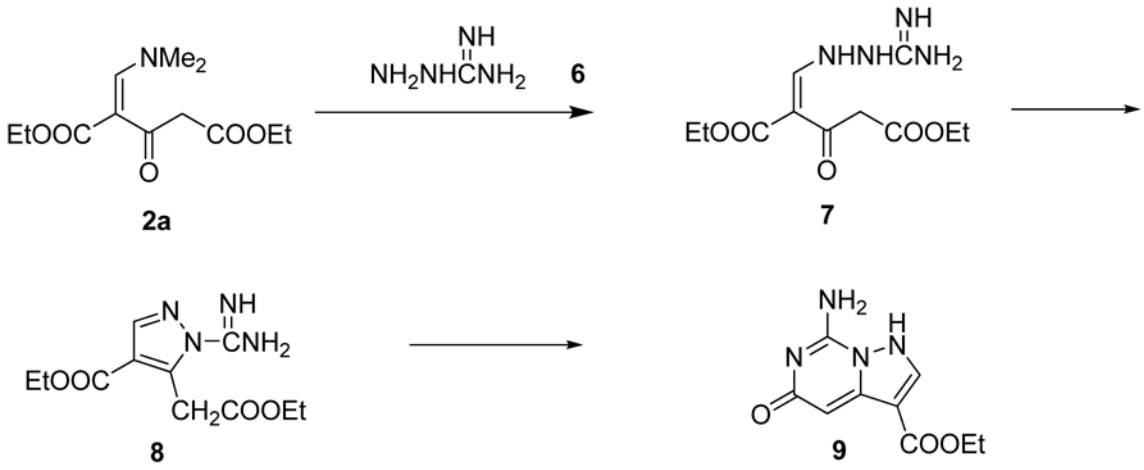
1. 1. Transformations of Diethyl 1-dimethylamino-3-oxobut-1-ene-2,4-dicarboxylate (2) with Hydrazines Into 1-substituted 4-ethoxycarbonyl-5-(ethoxycarbonylmethyl)-pyrazoles (5)

Diethyl acetone-1,3-dicarboxylate (**1a**) reacts with *N,N*-dimethylformamide dimethylacetal (DMFDMA) in ethanol at room temperature to give diethyl 1-dimethylamino-3-oxobut-1-ene-2,4-dicarboxylate (**2a**), which was used without isolation and purification for further reaction. To this reaction mixture an equivalent amount of monosubstituted hydrazine was added and the reaction mixture was stirred at room temperature or heated at reflux for several hours to form the intermediate **4**, which was without isolation cyclised into 1-substituted 4-ethoxycarbonyl-5-(ethoxycarbonylmethyl)pyrazoles **5**. (Scheme 1). Structures of compounds **5** were determined on the basis of elemental analyses for C, H, and N, and ^{1}H NMR spectra. The chemical shift for H_3 appears in the range δ_{H3} = 7.80–8.30 ppm, while CH_2 group appears at δ_{CH2} = 4.15–4.68 ppm.



5	Reaction conditions	R^1	Yield (%)	Mp (^{o}C) solvent
a	Reflux, 2 h	Me	66.1	59–66 (MTBE)
b	Reflux, 1 h	benzyl	23.7	67–69 (Hex)
c	RT, 1h	2-pyridyl	47.0	60–61 (EtOH)
d	RT, 1h	2-pyrimidinyl	49.3	56–65 (Hex)
e	RT, 1h	6-chloro-3-pyridazinyl	61.2	91–93 (EtOH)
f	RT, 1.5 h	6-phenyl-3-pyridazinyl	57.4	111–114 (EtOH)
g	RT, 1h	imidazo[1,2-b]pyridazin-6-yl	71.1	138–139 (EtOH)

Scheme 1. Preparation of 1-substituted 4-ethoxycarbonyl-5-(ethoxycarbonylmethyl)-pyrazoles (**5**).



Scheme 2. The synthesis of 7-amino-2-ethoxycarbonyl-1*H*,2*H*-pyrazolo[2,3-*c*]pyrimidin-5-one (**9**).

1. 2. The Synthesis of 7-amino-2-ethoxycarbonyl-1*H*,2*H*-pyrazolo[2,3-c]pyrimidin-5-one (9).

In the reaction of diethyl 1-dimethylamino-3-oxobut-1-ene-2,4-dicarboxylate (**2a**) with aminoguanidine (**6**) first a substitution intermediate **7** is formed, which cyclises into pyrazole derivative **8**, followed by cyclisation into the bicyclic 7-amino-2-ethoxycarbonyl-1*H*,2*H*-pyrazolo[2,3-*c*]pyrimidin-5-one (**9**). The intermediates **7** and **8** were not isolated. (Scheme 2).

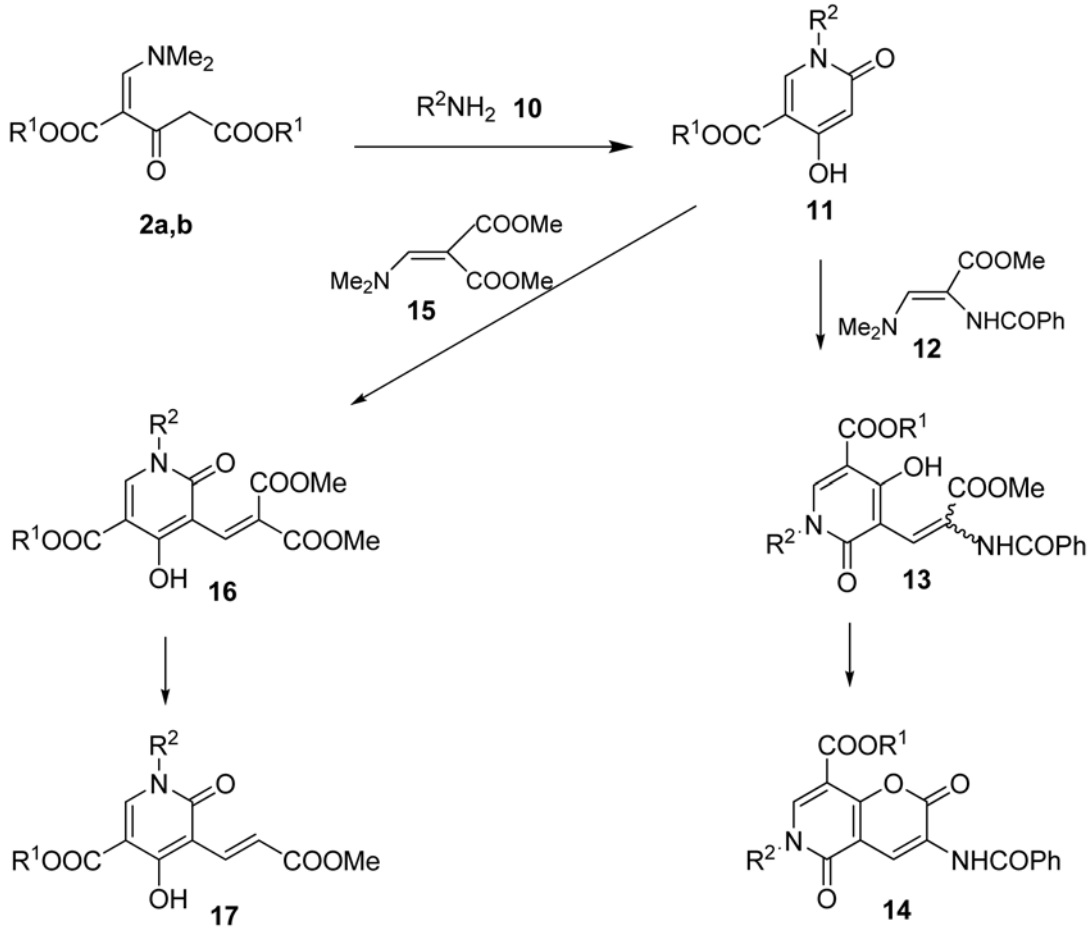
1. 3. The Synthesis of 4-hydroxypyridin-2 (1H)-ones (11) and 6-substituted 3-benzoylamino-2,5-dioxo-5,6-dihydro-2H -pyrano[3,2-c]pyridine-8-carboxylates (14).

The dimethylamino group in diethyl (**2a**) and dimethyl 1-dimethylamino-3-oxobut-1-ene-2,4-dicarboxylates (**2b**) can be exchanged very easily with nitrogen nucleophiles. In the reaction with primary amines in methanol or ethanol under reflux for several hours first the substitution of the dimethylamino group by an amine is taking place followed by

intramolecular nucleophilic attack of the amino group to the ester group to afford the corresponding 1-substituted 5-alkoxycarbonyl-4-hydroxypyridin-2(1*H*)-ones (**11**) in 16–93% yields. (Scheme 3). In the reaction of **11a,b,e,f** with methyl (*Z*)-2-benzoylamino-3-dimethylaminopropenoate (**12**) first the intermediate **13** was formed, which cyclised into 6-substituted 3-benzoylamino8-ethoxycarbonyl-2*H*,5*H*-pyrido[4,3-*b*]pyran-2,5-diones (**14**). On the other hand, reaction with 3-dimethylamino-2-(methoxycarbonyl)propenoate (**15**) first the intermediate **16** is formed, which did not produce the corresponding pyranopyridine derivative, instead hydrolysis and decarboxylation of one of the ester groups took place to give 4-hydroxy-5-methoxycarbonyl-1-methyl-3-(2-methoxycarbonyl)ethenylpyridin-2(1*H*)-one (**17**).

2. Experimental

Melting points were determined on a Kofler micro hot stage. ^{1}H and ^{13}C NMR spectra were obtained on a



Scheme 3. The synthesis of 4-hydroxypyridin-2(1*H*)-ones (**11**) and 6-substituted 3-benzoylamino-2,5-dioxo-5,6-dihydro-2*H*-pyrano[3,2-*c*]pyridine-8-carboxylates (**14**).

11	**Reaction condition**	**R^1**	**R^2**	**Yield (%)**	**Mp (°C) solvent**
a	Reflux, MeOH , 13.5h	Me	H	51.7	247–253 (MeOH)
b	RT, EtOH , 20 h	Et	H	52.3	219–221(EtOH)
c	Reflux, MeOH , 1.5 h	Me	Me	93.0	148–151(MeOH)
d	Reflux, EtOH , 1 h	Et	Me	62.9	109–113 (MTBE)
e	Reflux, EtOH , 24 h	Et	CH_2CH_2OH	21.9	157–161(toluene)
f	Reflux, EtOH , 3.5 h	Et	*i*-Pr	56.0	130–156 (MTBE)
g	Reflux, EtOH , 2.5 h	Et	Bn	16.4	105–112 (*n*BuCl)
h	Reflux, EtOH , 2.0 h	Et	$N(Me)_2$	17.7	95–105 (MTBE)
i	Reflux, EtOH , 24 h	Et	Ph	22.8	95–97(*n*-BuCl)
j	Reflux, EtOH , 2.5 h	Et	A	32.2	264–268(DMF)
k	RT, EtOH , 1 h	Et	B	28.8	268–270(DMF)

A) R^2 = (phthalazin-1-yl)amino
B) R^2 = (4-chlorophthalazin-1-yl)amino

14	**Reaction condition**	**R^1**	**R^2**	**Yield (%)**	**Mp (°C) solvent**
a	Reflux, 16 h	Me	Me	18.9	277–290
b	Reflux, 1 h	Et	Me	47.5	267–270(AcOH)
c	Reflux, 9 h	Et	*i*-Pr	38.8	192–194 (Ether)
d	Reflux, 9 h	Et	$CH_2CH_2OCOCH_3$	81.8	218–224 (AcOH)

17	**Reaction condition**	**R^1**	**R^2**	**Yield (%)**	**Mp (°C) solvent**
a	Reflux, 16 h	Me	Me	22.6	210–214 (toluene)
b	Reflux, 1 h	Et	*i*-Pr	55.8	140–147 (MeOH)

Bruker Avance DPX 300 at 300 MHz for ^{1}H and 75.5 MHz for ^{13}C nucleus, using DMSO-d_6 and $CDCl_3$ with TMS as the internal standard. Mass spectra were recorded on an AutoSpecQ spectrometer, IR spectra on a Perkin-Elmer Spectruim BX FTIR spectrophotometer. Microanalyses were performed on a Perkin-Elmer CHN Analyser 2400.

Diethyl 2-((dimethylamino)methylene)-3-oxopentanedioate (2a)

To a solution of diethyl acetone-1,3-dicarboxylate (**1a**; 0.95 ml, 5 mmol) in ethanol (10 ml) DMFDMA (0.72 ml, 5 mmol) was added and the mixture was stirred at room temperature for 45 min. The reaction mixture was concentrated and the residue was chromatographed on a column of Al_2O_3. Elution with hexane / aceton (2 : 1, v:v) gave 750 mg (58%) of the title product as a yellow oil. ^{1}H NMR (300 MHz, DMSO-d_6/TMS) δ: 1.28 (m, 6H: 2 × OCH_2CH_3), 2.91 (bs, 3H: NCH_3), 3.29 (bs, 3H: NCH_3), 3.79 (s, 2H: CH_2), 4.18 (m, 4H: 2 × OCH_2CH_3), 7.83 (s, 1H: H_2); ^{13}C NMR (75.5 MHz, DMSO-d_6/TMS), δ: 14.11 (OCH_2CH_3), 14.38 (OCH_2CH_3), 42.60, 47.89, 48.59, 59.94 (OCH_2CH_3), 60.68 (OCH_2CH_3), 101.05, 159.34, 167.35 (COOEt), 169.23 (COOEt), 189.60 (CO); IR (NaCl) ν (cm^{-1}): 2981, 1735, 1686, 1641, 1580; MS (MH+) m /z: 258. HRMS for $C_{12}H_{19}NO_5$: calcd: 257.126323, found: 257.126650.

This compound was prepared *in situ* and was used without isolation and purification in further experiments,

Dimethyl 2-((dimethylamino)methylidene)-3-oxopentanedioate (2b)

To a solution of dimethyl acetone-1,3-dicarboxylate (**1b**; 0.72 ml, 5 mmol) in methanol (10 ml) DMFDMA (0.72 ml, 5 mmol) was added and the mixture was stirred at room temperature for 45 min. The reaction mixture was concentrated in reduced pressure. The residue was chromatographed on a column of Al_2O_3. Elution with hexane / aceton (2 : 1, v:v) gave 412 mg (36%) of the title product as a yellow oil. ^{1}H NMR (300 MHz, DMSO-d_6/TMS) δ: 2.92 (bs, 3H: NCH_3), 3.30 (bs, 3H: NCH_3), 3.71 (s, 3H: CH_3), 3.72 (s, 3H: CH_3), 3,80 (s, 2H: $COCH_2COOMe$), 7.85 (s, 1H: H_1); IR (NaCl) ν (cm^{-1}): 2982, 1733, 1680, 1647, 1586; HRMS for $C_{10}H_{15}NO_5$: calcd: 229.095023, found: 229.095560. This compound was prepared *in situ* and was used without isolation and purification in further experiments,

2. 1. General Procedure for the Synthesis of Pyrazoles 5

To a solution of diethyl acetone-1,3-dicarboxylate (**1a**; 0.38 ml, 2.0 mmol) in ethanol (4 ml) DMFDMA (0.29 ml, 2.0 mmol) was added and the mixture was stirred at room temperature for 45 min. Then hydrazine (**3**; 2 mmol) was added and the reaction mixture was stirred to complete the reaction. The mixture was then cooled to 0°C and the product was separated by filtration. The crude products were purified by recrystallisation form an appropriate solvent.

Ethyl 5-(2-ethoxy-2-oxoethyl)-1-methyl-1H-pyrazole-4-carboxylate (5a)

This compound was prepared from diethyl acetone-1,3-dicarboxylate (**1a**; 0.38 ml, 2.0 mmol), ethanol (4 ml), DMFDMA (0.29 ml, 2.0 mmol) and methylhydrazine (**3a**; 0.11 ml, 2.0 mmol), 2 hours of reflux in 66% yield, mp = 59–61 °C (from TBME). ^{1}H NMR (300 MHz, DMSO-d_6/TMS) δ: 1.19 (t, 3H: OCH_2CH_3, J = 7.2 Hz), 1.25 (t, 3H: OCH_2CH_3, J = 7.2 Hz), 3.80 (s, 3H: NCH_3), 4.11 (q, 2H: OCH_2CH_3, J = 7.2 Hz), 4.15 (s, 2H: CH_2COOEt), 4.18 (q, 2H: OCH_2CH_3, J = 7.2 Hz), 7.80 (s, 1H: H_3); ^{13}C NMR (75.5 MHz, DMSO-d_6/TMS), δ: 13.99 (OCH_2CH_3), 14.12 (OCH_2CH_3), 30.13 (CH_2COOEt), 36.62 (NCH_3), 59.52 (OCH_2CH_3), 60.82 (OCH_2CH_3), 111.92 (C_4), 139.56 (C_5), 139.60 (C_3), 162.60 (COOEt), 168.38 (CH_2COOEt); IR (KBr) ν (cm^{-1}): 3432, 2994, 1723, 1703, 1562, 1248; MS (MH^+) m/z: 241; elemental analysis: calcd (%) for $C_{11}H_{16}N_2O_4$ (240.3): C 54.99, H 6.71, N 11.66; found: C 54.93, H 6.75, N 11.43.

Ethyl 1-benzyl-5-(2-ethoxy-2-oxoethyl)-1H-pyrazole-4-carboxylate (5b)

This compound was prepared from diethyl acetone-1,3-dicarboxylate (**1a**; 0.38 ml, 2.0 mmol), ethanol (4 ml), DMFDMA (0.29 ml, 2.0 mmol) and benzylhydrazine dihydrochloride (**3**; 390 mg, 2.0 mmol), 1 hour of reflux in 24% yield, mp = 67- 69 °C (from hexane). ^{1}H NMR (300 MHz, DMSO-d_6/TMS) δ: 1.11 (t, 3H: OCH_2CH_3, J = 7.2 Hz), 1.24 (t, 3H: OCH_2CH_3, J = 7.2 Hz), 4.00 (q, 2H: OCH_2CH_3, J = 7.2 Hz), 4.14 (s, 2H: CH_2COOEt), 4.18 (q, 2H: OCH_2CH_3, J = 7.2 Hz), 5.42 (s, 2H: CH_2Ph), 7.16-7.19 (m, 2H: Ph), 7.27–7.32 (m, 3H: Ph), 7.90 (s, 1H: H_3)); ^{13}C NMR (300 MHz, DMSO-d_6/TMS, δ: 13.89 (OCH_2CH_3), 14.12 (OCH_2CH_3), 30.38 (CH_2COOEt), 52.32 (CH_2Ph), 59.57 (OCH_2CH_3), 60.68 (OCH_2CH_3), 112.40 (C_4), 127.33, 127.58, 128.42, 136.40, 139.88, 140.32, 162.52(COOEt), 168.13 (COOEt); IR (KBr) ν (cm^{-1}): 3456, 2980, 1734, 1703, 1563, 1242; elemental analysis: calcd (%) for $C_{17}H_{20}N_2O_4$ (316.4): C 64.54, H 6.37, N 8.86; found: C 64.56, H 6.41, N 8.83.

Ethyl 5-(2-ethoxy-2-oxoethyl)-1-(pyridin-2-yl)-1H-pyrazole-4-carboxylate (5c)

This compound was prepared from diethyl acetone-1,3-dicarboxylate (**1a**; 0.38 ml, 2.0 mmol), ethanol (4 ml), DMFDMA (0.29 ml, 2.0 mmol) and 2-hydrazinopyridine (**3c**; 218 mg, 2.0 mmol), 1 hour of reflux in 47% yield, mp = 60–61 °C (from ethanol). ^{1}H NMR (300 MHz, DMSO-d_6/TMS) δ: 1.10 (t, 3H: OCH_2CH_3, J = 7.2 Hz), 1.30 (t, 3H: OCH_2CH_3, J = 7.2 Hz), 4.03 (q, 2H: OCH_2CH_3, J = 7.2 Hz), 4.27 (q, 2H: OCH_2CH_3, J = 7.2 Hz), 4.58 (s, 2H: CH_2COOEt), 7.44 (ddd, 1H: H_5 (Het), J = 7.2 Hz, J = 4.8 Hz, J = 0.9 Hz), 7.94 (bd, 1H: H_3 (Het), J = 8.4Hz), 8.06 (ddd, 1H: H_4 (Het) J = 8.4 Hz, J = 7.2 Hz, J = 1.8 Hz), 8.16 (s, 1H: H_3), 8.45 (ddd, 1H: H_6 (Het), J = 4.8 Hz, J = 1.8 Hz, J = 0.9 Hz); ^{13}C NMR (75.5 MHz, DMSO-d_6/TMS), δ: 13.96 (OCH_2CH_3), 14.13 (OCH_2CH_3), 32.26 (CH_2COOEt), 60.07 (OCH_2CH_3), 60.43 (OCH_2CH_3), 114.75, 115.95, 122.93, 139.70, 140.60, 141.76, 147.50, 152.04, 162.52 (COOEt), 168.48 (COOEt); IR (KBr) ν (cm^{-1}): 3411, 2984, 1728, 1707, 1405, 1243; elemental analysis: calcd (%) for $C_{15}H_{17}N_3O_4$ (303.3): C 59.40, H 5.65, N 13.85; found: C 59.45, H 5.76, N 13.77.

Ethyl 5-(2-ethoxy-2-oxoethyl)-1-(pyrimidin-2-yl)-1H-pyrazole-4-carboxylate (5d)

This compound was prepared from diethyl acetone-1,3-dicarboxylate (**1a**; 0.38 ml, 2.0 mmol), ethanol (4 ml), DMFDMA (0.29 ml, 2.0 mmol) and 2-hydrazinopyrimidine (**3d**; 220 mg, 2.0 mmol), 1 hour of reflux in 49% yield, mp = 63–65 °C (from hexane). ^{1}H NMR (300 MHz, DMSO-d_6/TMS) δ: 1.10 (t, 3H: OCH_2CH_3, J = 7.2Hz), 1.30 (t, 3H: OCH_2CH_3, J = 7.2Hz), 4.03 (q, 2H: OCH_2CH_3, J = 7.2 Hz), 4.27 (q, 2H: OCH_2CH_3, J = 7.2 Hz), 4.55 (s, 2H: CH_2COOEt), 7.59 (dd, 1H: H_5 (Het), J = 5.1 Hz, J = 5.1 Hz), 8.17 (s, 1H: H_3), 8.92 (d, 2H: H_4, H_6 (Het) J = 5.1 Hz); ^{13}C NMR (75.5 MHz, DMSO-d_6/TMS), δ:13.96 (OCH_2CH_3), 14.09 (OCH_2CH_3), 32.20 (CH_2COOEt), 60.16 (OCH_2CH_3), 60.51 (OCH_2CH_3), 114.98, 120.56, 141.79, 142.03, 156.09, 158.34, 159.13, 162.42 (COOEt), 168.40 (COOEt); IR (KBr) ν (cm^{-1}): 3443, 2982, 1732, 1716, 1567, 1428, 1266; elemental analysis: calcd (%) for $C_{14}H_{16}N_4O_4$ (304.3): C 55.26, H 5.30, N 18.41; found: C 54.85, H 5.26, N 18.79.

Ethyl 1-(6-chloropyridazin-3-yl)-5-(2-ethoxy-2-oxoethyl)-1H-pyrazole-4-carboxylate (5e)

This compound was prepared from diethyl acetone-1,3-dicarboxylate (**1a**; 0.38 ml, 2.0 mmol), ethanol (4 ml), DMFDMA (0.29 ml, 2.0 mmol) and 6-chloro-3-hydrazinopyridazine (**3e**; 288 mg, 2.0 mmol), 1 hour of reflux in 61% yield, mp = 91–93 °C (from ethanol). ^{1}H NMR (300 MHz, DMSO-d_6/TMS) δ: 1.13 (t, 3H: OCH_2CH_3, J = 7.2 Hz), 1.30 (t, 3H: OCH_2CH_3, J = 7.2 Hz), 4.07 (q, 2H: OCH_2CH_3, J = 7.2 Hz), 4.29 (q, 2H: OCH_2CH_3, J = 7.2 Hz), 4.58 (s, 2H: CH_2COOEt), 8.17 (d, 1H: (Het), J = 9.3 Hz), 8.30 (d, 1H: (Het), J = 9.3 Hz), 8.31 (s, 1H: H_3); ^{13}C NMR (75.5 MHz, DMSO-d_6/TMS), δ: 13.97 (OCH_2CH_3), 14.08 (OCH_2CH_3), 32.23 (CH_2COOEt), 60.34 (OCH_2CH_3), 60.66 (OCH_2CH_3), 115.79, 124.44, 132.05, 141.52, 143.10, 155.06, 155.40, 162.18 (COOEt), 168.17 (COOEt); IR (KBr) ν (cm^{-1}): 3418, 2981, 1736, 1710, 1582, 1546, 1271; elemental analysis: calcd (%) for $C_{14}H_{15}ClN_4O_4$ (338.8): C 49.64, H 4.46, N 16.54; found: C 49.90, H 4.60, N 16.52.

Ethyl 5-(2-ethoxy-2-oxoethyl)-1-(6-phenylpyridazin-3-yl)-1H-pyrazole-4-carboxylate (5f)

This compound was prepared from diethyl acetone-1,3-dicarboxylate (**1a**; 0.38 ml, 2.0 mmol), ethanol (4 ml), DMFDMA (0.29 ml, 2.0 mmol) and 3-hydrazino-6-phenylpyridazine (**3f**; 372 mg, 2.0 mmol), 1.5 hours of

reflux in 57% yield, mp = 111–114 °C (from ethanol). ^{1}H NMR (300 MHz, DMSO-d_6/TMS) δ: 1.12 (t, 3H: OCH_2CH_3, J = 7.2 Hz), 1.32 (t, 3H: OCH_2CH_3, J = 7.2 Hz), 4.07 (q, 2H: OCH_2CH_3, J = 7.2 Hz), 4.29 (q, 2H: OCH_2CH_3, J = 7.2 Hz), 4.68 (s, 2H: CH_2COOEt), 7.50–7.65 (m, 3H: Ph), 8.15–8.25 (m, 2H: Ph), 8.29 (d, 1H: (Het), J = 9.3 Hz), 8.30 (s, 1H: H_3), 8.51 (d, 1H: (Het), J = 9.3 Hz); ^{13}C NMR (75.5 MHz, DMSO-d_6/TMS), δ: 13.95 (OCH_2CH_3), 14.09 (OCH_2CH_3), 32.30 (CH_2COOEt), 60.25 (OCH_2CH_3), 60.60 (OCH_2CH_3), 115.49, 121.60, 126.88, 127.51, 129.11, 130.41, 134.95, 141.18, 142.78, 155.04, 157.86, 162.30 (COOEt), 168.30 (COOEt); IR (KBr) ν (cm^{-1}): 3422, 2984, 1731, 1709, 1549, 1180; elemental analysis: calcd (%) for $C_{20}H_{20}N_4O_4$ (380.4): C 63.15, H 5.30, N 14.73; found: C 63.04, H 5.35, N 14.66.

Ethyl 5-(2-ethoxy-2-oxoethyl)-1-(imidazo[1,2-b]pyridazin-6-yl)-1H-pyrazole-4-carboxylate (5g)

This compound was prepared from diethyl acetone-1,3-dicarboxylate (**1a**; 0.38 ml, 2.0 mmol), ethanol (4 ml), DMFDMA (0.29 ml, 2.0 mmol) and 6-hydrazinoimidazo[1,2-*b*]pyridazine (**3g**; 298 mg, 2.0 mmol), 1 hour of reflux in 71% yield, mp = 138–139 °C (from ethanol). ^{1}H NMR (300 MHz, DMSO-d_6/TMS) δ: 1.09 (t, 3H: OCH_2CH_3, J = 7.2 Hz), 1.31 (t, 3H: OCH_2CH_3, J = 7.2 Hz), 4.08 (q, 2H: OCH_2CH_3, J = 7.2 Hz), 4.29 (q, 2H: OCH_2CH_3, J = 7.2 Hz), 4.55 (s, 2H: CH_2COOEt), 7.76 (d, 1H: H_5 (Het), J = 9.8 Hz), 7.89 (d, 1H: H_2 (Het), J = 1.1 Hz), 8.15 (dd, 1H: H_1 (Het), J = 1.1Hz, J = 0.7 Hz), 8.27 (s, 1H: H_3), 8.37 (dd, 1H: H_6 (Het), J = 9.8 Hz, J = 0.7 Hz); ^{13}C NMR (75.5 MHz, DMSO-d_6/TMS), δ: 13.93 (OCH_2CH_3), 14.09 (OCH_2CH_3), 31.96 (CH_2COOEt), 60.29 (OCH_2CH_3), 60.78 (OCH_2CH_3), 113.14, 115.32, 117.39, 128.10, 134.98, 137.43, 141.27, 142.57, 147.99, 162.23 (COOEt), 168.31 (COOEt); IR (KBr) ν (cm^{-1}): 2990, 1740, 1716, 1537, 1270; elemental analysis: calcd (%) for $C_{16}H_{17}N_5O_4$ (343.3): C 55.97, H 4.99, N 20.40; found: C 56.01, H 4.91, N 20.29.

Ethyl 7-amino-2-oxo-1,2-dihydropyrazolo[1,5-c]pyrimidine-4-carboxylate (9)

To a solution of diethyl acetone-1,3-dicarboxylate (**1a**; 0.38 ml, 2 mmol) in ethanol (4 ml) DMFDMA (0.29 ml, 2 mmol) was added and the mixture was stirred at room temperature for 45 min. Then aminoguanidine hydrogen carbonate (**6**; 816 mg, 6 mmol) was added and the mixture was stirred under reflux for 15 hours. The reaction mixture was cooled, diluted with ethyl acetate (100 ml), washed with water (100 ml) and brine (3 × 100 ml) and dried over Na_2SO_4. The mixture was filtered and filtrate concentrated to 5 ml, cooled to 0 °C and the product separated. Yield 13%, mp = 293–295 °C (from methanol). ^{1}H NMR (300 MHz, $CDCl_3$/TMS) δ: 1.30 (t, 3H: OCH_2CH_3, J = 6.9 Hz), 4.23 (q, 2H: OCH_2CH_3, J = 6.9 Hz), 6.27 (s, 1H: H_3), 7.83 (s, 2H: NH_2), 8.23 (s, 1H: H_5), 11.00 (bs, 1H: NH); ^{13}C NMR (75.5 MHz, $CDCl_3$/TMS), δ: 14.42 (OCH_2CH_3), 59.05 (OCH_2CH_3), 80.28, 100.06, 145.62, 146.53, 147.55, 162.15, 162.67; IR (KBr) ν (cm^{-1}): 3364, 3166, 1693, 1597, 1514, 1317, 1036; MS (M+) m /z: 222; elemental analysis: calcd (%) for $C_9H_{10}N_4O_3$ (222.2): C 48.65, H 4.54, N 25.21; found: C 48.45, H 4.37, N 24.67.

2. 2. General Procedure for the Synthesis of Pyridones 11

To a solution of dialkyl acetone-1-3-dicarboxylate (**1a**; 0.95 ml, **1b**; 0.72 ml; 5 mmol) in an alcohol (10 ml) was added DMFDMA (0.72 ml, 5.0 mmol) and the mixture was stirred at room temperature for 45 min. Then amine (**10**; 6 mmol) and one drop of concentrated HCl were added and stirred under reflux to complete the reaction. After that, the mixture was concentrated under reduced pressure to the oily residue. To this residue *tert*-buthylmethyl ether was added and the mixture was cooled to 0 °C. The product was separated by filtration and purified by recrystallisation from an appropriate solvent.

Methyl 4-hydroxy-6-oxo-1,6-dihydropyridine-3-carboxylate (11a)

This compound was prepared from dimethyl acetone-1,3-dicarboxylate (**1b**; 0.72 ml, 5.0 mmol), methanol (10 ml), DMFDMA (0.72 ml, 5.0 mmol) and ammonia (**10a**; 25%, 0,40 ml, 6 mmol), 13.5 h of reflux, in 52% yield, mp = 247–253 °C (from methanol), lit.[13] mp = 237–240 °C. ^{1}H NMR (300 MHz, DMSO-d_6/TMS) δ: 3.79 (s, 3H: OCH_3), 5.61 (s, 1H: H_3), 8.02 (s, 1H: H_6), 10.00–12.00 (bs, 2H: NH, OH); ^{13}C NMR (75.5 MHz, DMSO-d_6/TMS), δ: 51.98 (OCH_3), 98.49 (C_3), 100.15 (C_5), 142.63 (C_6), 163.50, 165.83, 166.22; IR (KBr) ν (cm^{-1}): 3443, 3076, 2686, 1694, 1651, 1440; elemental analysis: calcd (%) for $C_7H_7NO_4$ (169.1): C 49.71, H 4.17, N 8.28; found: C 49.86, H 4.31, N 8.17.

Ethyl 4-hydroxy-6-oxo-1,6-dihydropyridine-3-carboxylate (11b)

This compound was prepared from diethyl acetone-1,3-dicarboxylate (**1a**; 0.95 ml, 5.0 mmol), ethanol (10 ml), DMFDMA (0.72 ml, 5.0 mmol) and ammonia (**10a**; 25%, 0,40 ml, 6 mmol), 20 hours at r.t., in 52% yield, mp = 219–221 °C (from ethanol), lit.[14] mp = 213 °C. ^{1}H NMR (300 MHz, DMSO-d_6/TMS) δ: 1.28 (t, 3H: OCH_2CH_3, J = 7.2 Hz), 4.26 (q, 2H: OCH_2CH_3, J = 7.2 Hz), 5.61 (s, 1H: H_3), 8.02 (s, 1H: H_6), 10.81 (bs, 1H: OH), 11.75 (bs, 1H: NH); ^{13}C NMR (75.5 MHz, DMSO-d_6/TMS), δ: 14.01 (OCH_2CH_3), 60.90 (OCH_2CH_3), 98.50 (C_3), 99.99 (C_5), 142.50 (C_6), 163.58, 165.96, 166.11; IR (KBr) ν (cm^{-1}): 3421, 3068, 1661, 1316; elemental analysis: calcd (%) for $C_8H_9NO_4$ (183.2): C 52.46, H 4.95, N 7.65; found: C 52.52, H 4.80, N 7.53.

Methyl 4-hydroxy-1-methyl-6-oxo-1,6-dihydropyridine-3-carboxylate (11c)

This compound was prepared from dimethyl acetone-1,3-dicarboxylate (**1b**; 0.72 ml, 5.0 mmol), methanol (10 ml), DMFDMA (0.72 ml, 5.0 mmol) and methylamine (**10c**; 12 M, 0.50 ml, 6 mmol), 1.5 h of reflux, in 93% yield, mp = 148–151 °C (from methanol) ^{1}H NMR (300 MHz, DMSO-d_6/TMS) δ: 3.42 (s, 3H: NCH_3), 3.80 (s, 3H: OCH_3), 5.66 (s, 1H: H_3), 8.47 (s, 1H: H_6), 10.00–12.00 (bs, 1H: OH); ^{13}C NMR (75.5 MHz, DMSO-d_6/TMS), δ: 36.48 (NCH_3), 51.99 (OCH_3), 97.67 (C_3), 99.78 (C_5), 146.51 (C_6), 162.71, 165.14, 166.19; IR (KBr) ν (cm^{-1}): 3418, 3054, 1693, 1453; elemental analysis: calcd (%) for $C_8H_9NO_4$ (183.2): C 52.46, H 4.95, N 7.65; found: C 52.37, H 5.01, N 7.75.

Ethyl 4-hydroxy-1-methyl-6-oxo-1,6-dihydropyridine-3-carboxylate (11d)

This compound was prepared from diethyl acetone-1,3-dicarboxylate (**1**; 0.95 ml, 5.0 mmol), methanol (10 ml), DMFDMA (0.72 ml, 5.0 mmol) and methylamine (**10c**; 12 M, 0.50 ml, 6 mmol), 1 hour of reflux, in 63% yield, mp = 109–113 °C (from MTBE), lit.[15] mp (not reported). ^{1}H NMR (300 MHz, DMSO-d_6/TMS) δ: 1.30 (t, 3H: OCH_2CH_3, J = 7.2 Hz), 3.43 (s, 3H: NCH_3), 4.29 (q, 2H: OCH_2CH_3, J = 7.2 Hz), 5.68 (s, 1H: H_3), 8.49 (s, 1H: H_6), 10.60–10.85 (bs, 1H: OH); ^{13}C NMR (75.5 MHz, DMSO-d_6/TMS), δ: 14.09 (OCH_2CH_3), 36.52 (NCH_3), 60.94 (OCH_2CH_3), 97.66 (C_3), 99.68 (C_5), 146.34 (C_6), 162.76, 165.29, 166.11; IR (KBr) ν (cm^{-1}): 3422, 1694, 1560, 1307; elemental analysis: calcd (%) for $C_9H_{11}NO_4$ (197.2): C 54.82, H 5.62, N 7.10; found: C 54.79, H 5.58, N 7.12.

Ethyl 4-hydroxy-1-(2-hydroxyethyl)-6-oxo-1,6-dihydropyridine-3-carboxylate (11e)

This compound was prepared from diethyl acetone-1,3-dicarboxylate (**1a**; 0.95 ml, 5.0 mmol), ethanol (10 ml), DMFDMA (0.72 ml, 5.0 mmol) and ethanolamine (**10e**; 0.37 ml, 6 mmol), 24 hours of reflux, in 23% yield, mp = 157–161 °C (from toluene). ^{1}H NMR (300 MHz, DMSO-d_6/TMS) δ: 1.30 (t, 3H: OCH_2CH_3, J = 6.9Hz), 3.58 (m, 2H: NCH_2), 3.97 (m, 2H: CH_2OH), 4.29 (q, 2H: OCH_2CH_3, J = 6.9 Hz), 4.91 (t, 1H: CH_2OH, J = 5.4 Hz), 5.69 (s, 1H: H_3), 8.34 (s, 1H: H_6), 10.75 (bs, 1H: OH); ^{13}C NMR (75.5 MHz, DMSO-d_6/TMS), δ: 14.34 (OCH_2CH_3), 51.44, 58.63, 61.36, 98.14, 99.93, 146.93, 162.88, 165.57, 166.31; IR (KBr) ν (cm^{-1}): 3268, 3055, 1685, 1317, 844; elemental analysis: calcd (%) for $C_{10}H_{13}NO_5$ (227.2): C 52.86, H 5.77, N 6.16; found: C 52.86, H 5.42, N 5.84.

Ethyl 4-hydroxy-1-isopropyl-6-oxo-1,6-dihydropyridine-3-carboxylate (11f)

This compound was prepared from diethyl acetone-1,3-dicarboxylate (**1b**; 0.95 ml, 5.0 mmol), ethanol (10 ml), DMFDMA (0.72 ml, 5.0 mmol) and isopropylamine (**10f**; 0.52 ml, 6 mmol), 3.5 hours of reflux, in 56% yield, mp = 152–156 °C (from MTBE). ^{1}H NMR (300 MHz, DMSO-d_6/TMS) δ: 1.31 (m, 9H: OCH_2CH_3, 2 × CH_3), 4.29 (q, 2H: OCH_2CH_3, J = 7.2 Hz), 4.95 (p, 1H: CH J = 6.9 Hz), 5.69 (s, 1H: H_3), 8.25 (s, 1H: H_6), 10.76 (bs, 1H: OH); ^{13}C NMR (75.5 MHz, DMSO-d_6/TMS), δ: 14.07 (OCH_2CH_3), 21.02 (2 × CH_3), 46.96 (CH), 60.96 (OCH_2CH_3), 98.01 (C_3), 100.74 (C_5), 141.27 (C_6), 162.01, 164.48, 165.78; IR (KBr) ν (cm^{-1}): 3448, 1693, 1659, 1318, 1241, 780; elemental analysis: calcd (%) for $C_{11}H_{15}NO_4$ (225.2): C 58.66, H 6.71, N 6.22; found: C 58.82, H 6.67, N 6.26.

Ethyl 1-benzyl-4-hydroxy-6-oxo-1,6-dihydropyridine-3-carboxylate (11g)

This compound was prepared from diethyl acetone-1,3-dicarboxylate (**1a**; 0.95 ml, 5.0 mmol), ethanol (10 ml), DMFDMA (0.72 ml, 5.0 mmol) benzylamine (**10g**; 0.65 ml, 6 mmol), 2.5 hours of reflux, in 16% yield, mp = 108–112 °C (from *n*-butyl chloride). ^{1}H NMR (300 MHz, DMSO-d_6/TMS) δ: 1.29 (t, 3H: OCH_2CH_3, J = 6.9 Hz), 4.28 (q, 2H: OCH_2CH_3, J = 6.9 Hz), 5.16 (s, 2H: CH_2Ph), 5.74 (s, 1H: H_3), 7.25–7.35 (m, 5H: Ph), 8.59 (s, 1H: H_6), 10.65–10.90 (bs, 1H: OH); ^{13}C NMR (75.5 MHz, DMSO-d_6/TMS), δ: 14.06 (OCH_2CH_3), 50.82 (CH_2Ph), 60.96 (OCH_2CH_3), 98.23 (C_3), 100.84 (C_5), 127.43, 127.51, 128.56, 137.0, 145.67, 162.22, 165.25, 165.75; IR (KBr) ν (cm^{-1}): 2985, 1687, 1655, 1560, 1321; elemental analysis: calcd (%) for $C_{15}H_{15}NO_4$ (273.3): C 65.92, H 5.53, N 5.13; found: C 65.72, H 5.42, N 5.31.

Ethyl 1-(dimethylamino)-4-hydroxy-6-oxo-1,6-dihydropyridine-3-carboxylate (11h)

This compound was prepared from diethyl acetone-1,3-dicarboxylate (**1a**; 0.95 ml, 5.0 mmol), ethanol (10 ml), DMFDMA (0.72 ml, 5.0 mmol) and 1,1-dimethylhydrazine (**10h**; 0.46 ml, 6 mmol), 2 hours of reflux, in 18% yield, mp = 95–105 °C (from MTBE). ^{1}H NMR (300 MHz, DMSO-d_6/TMS) δ: 1.29 (t, 3H: OCH_2CH_3, J = 7.2 Hz) , 2.95 (s, 6H: $N(CH_3)_2$), 4.26 (q, 2H: OCH_2CH_3, J = 7.2 Hz), 5.67 (s, 1H: H_3), 8.21 (s, 1H: H_6), 10.80 (bs, 1H: OH); ^{13}C NMR (75.5 MHz, DMSO-d_6/TMS), δ: 13.98 (OCH_2CH_3), 44.07 ($N(CH_3)_2$), 60.96 (OCH_2CH_3), 99.73 (C_3), 100.02 (C_5), 147.05 (C_6), 162.24, 164.85, 165.05; IR (KBr) ν (cm^{-1}): 3463, 3050, 1693, 1557, 1278, 1234, 1139, 776; elemental analysis: calcd (%) for $C_{10}H_{14}N_2O_4$ (226.2): C 53.09, H 6.24, N 12.38; found: C 52.68, H 6.02, N 11.80.

Ethyl 4-hydroxy-6-oxo-1-phenyl-1,6-dihydropyridine-3-carboxylate (11i)

This compound was prepared from diethyl acetone-1,3-dicarboxylate (**1a**; 0.95 ml, 5.0 mmol), ethanol (10 ml), DMFDMA (0.72 ml, 5.0 mmol) and aniline (**10i**; 0.55 ml, 6 mmol), 24 hours of reflux, in 23% yield, mp = 95–97 °C (from *n*-butyl chloride). ^{1}H NMR (300 MHz,

DMSO-d_6/TMS) δ: 1.26 (t, 3H: OCH_2CH_3 , J = 7.2 Hz), 4.26 (q, 2H: OCH_2CH_3, J = 7.2 Hz), 5.78 (s, 1H: H_3), 7.40–7.55 (m, 5H: Ph), 8.23 (s, 1H: H_6), 10.50–11.40 (bs, 1H: OH); ^{13}C NMR (75.5 MHz, DMSO-d_6/TMS), δ: 13.98 (OCH_2CH_3), 60.97 (OCH_2CH_3), 98.35 (C_3), 101.38 (C_5), 126.97, 128.57, 129.05, 139.80, 145.29, 161.94, 165.32, 165.45; IR (KBr) ν (cm^{-1}): 3100, 1673, 1551, 1455, 1102; elemental analysis: calcd (%) for $C_{14}H_{13}NO_4$ (259.3): C 64.86, H 5.05, N 5.40; found: C 64.91, H 4.91, N 5.39.

Ethyl 4-hydroxy-6-oxo-1-(phthalazin-1-ylamino)-1,6-dihydropyridine-3-carboxylate (11j)

This compound was prepared from diethyl acetone-1,3-dicarboxylate (**1a**; 0.95 ml, 5.0 mmol), ethanol (10 ml), DMFDMA (0.72 ml, 5.0 mmol) and 1-hydrazinophthalazine (**10j**; 961 mg, 6 mmol), 2.5 hours of reflux, in 32% yield, mp = 264–268 °C (from DMF). ^{1}H NMR (300 MHz, CF_3COOD/ TMS) δ: 1.28 (t, 3H: OCH_2CH_3, J = 7.2 Hz), 4.27 (q, 2H: OCH_2CH_3, J = 7.2 Hz), 5.80 (s, 1H: H_3), 7.80–7.95 (m, 3H: Het), 8.23 (s, 1H: H_6), 8.29 (s, 1H: Het), 8.36 (d, 1H: Het), 10.66 (bs, 1H: OH), 12.02 (bs, 1H: NH); ^{13}C NMR (75.5 MHz, CF_3COOD/TMS), δ: 13.99 (OCH_2CH_3), 60.90 (OCH_2CH_3), 99.08 (C_3), 99.43 (C_5), 124.28, 124.46, 126.64, 126.72, 132.12, 133.14, 138.97, 143.44, 150.89, 159.46, 164.17, 166.19; IR (KBr) ν (cm^{-1}): 3173, 1689, 1658, 1536, 1467, 1282; MS (M^+) m/z: 326; elemental analysis: calcd (%) for $C_{16}H_{14}N_4O_4$ (326.3): C 58.89, H 4.32, N 17.17; found: C 58.90, H 4.38, N 17.26.

Ethyl 1-(4-chlorophthalazin-1-ylamino)-4-hydroxy-6-oxo-1,6-dihydropyridine-3-carboxylate (11k)

This compound was prepared from diethyl acetone-1,3-dicarboxylate (**1a**; 0.95 ml, 5.0 mmol), ethanol (10 ml), DMFDMA (0.72 ml, 5.0 mmol) and 1-chloro-4-hydrazinophthalazine (**10k**; 1168 mg, 6 mmol), 1 hour at r.t. in 29% yield, mp = 268–270 °C (from DMF). ^{1}H NMR (300 MHz, CF_3COOD/ TMS) δ: 1.47 (t, 3H: OCH_2CH_3 , J = 7.2 Hz), 4.58 (q, 2H: OCH_2CH_3, J = 7.2 Hz), 6.56 (s, 1H: H_3), 8.50–8.55 (m, 2H: Het), 8.70–8.75 (m, 2H: Het), 8.76 (s, 1H: H_6), 11.51 (bs, 2H: OH , NH); ^{13}C NMR (75.5 MHz, CF_3COOD/ TMS), δ: 14.51 (OCH_2CH_3), 66.46 (OCH_2CH_3), 102.74, 107.90, 122.09, 126.48, 129.77, 131.01, 140.65, 141.22, 148.06, 154.00, 156.53, 166.78, 169.09, 173.24; IR (KBr) ν (cm^{-1}): 3411, 1693, 1662, 1536, 1468, 1279; MS (MH^+) m/z: 361; elemental analysis: calcd (%) for $C_{16}H_{13}ClN_4O_4$ (360.8): C 53.27, H 3.63, N 15.53; found: C 53.49, H 3.65, N 15.43.

2. 3. General Procedure for the Synthesis of Compounds 14.

To the solution of compound **11** (1 mmol) in glacial acetic acid (4 ml) was added methyl 2-benzoylamino-3-dimethylaminopropenoate (**12**; 248 mg, 1 mmol) and the resulting solution was stirred under reflux to complete the reaction. The mixture was cooled and the product was separated by filtration and purified by recrystallisation from an appropriate solvent.

Methyl 3-benzamido-6-methyl-2,5-dioxo-5,6-dihydro-2H-pyrano[3,2-c]pyridine-8-carboxylate (14a)

This compound was prepared from methyl 4-hydroxy-6-oxo-1,6-dihydropyridine-3-carboxylate (**11a**; 169mg, 1.0 mmol), 16 hours of reflux, in 19% yield, mp = 287–290 °C (from acetic acid). ^{1}H NMR (300 MHz, DMSO-d_6/TMS) δ: 3.60 (s, 3H: NCH_3), 3.84 (s, 3H: OCH_3), 7.50–7.70 (m, 3H: Ph), 7.95 (m, 2H: Ph), 8.61 (s, 1H: H_4 or H_7), 8.66 (s, 1H: H_4 or H_7), 9.74 (bs, 1H: NH); ^{13}C NMR (75.5 MHz, DMSO-d_6/TMS), δ: 37.34 (NCH_3), 52.06 (OCH_3), 100.70, 107.43, 122.95, 123.55, 127.72, 128.57, 132.26, 133.39, 146.19, 155.42, 156.52, 159.54, 161.96, 166.04; IR (KBr) ν (cm^{-1}): 3397, 3070, 1726, 1703, 1676, 1649, 1547, 1313; elemental analysis: calcd (%) for $C_{18}H_{14}N_2O_6$ (354.3): C 61.02, H 3.98, N 7.91; found: C 61.04, H 3.56, N 7.78.

Ethyl 3-benzamido-6-methyl-2,5-dioxo-5,6-dihydro-2H-pyrano[3,2-c]pyridine-8-carboxylate (14b)

This compound was prepared from ethyl 4-hydroxy-6-oxo-1,6-dihydropyridine-3-carboxylate (**11b**; 183 mg, 1.0 mmol), 1 hour of reflux, in 48% yield, mp = 267–270 °C (from acetic acid). ^{1}H NMR (300 MHz, DMSO-d_6/TMS) δ: 1.33 (t, 3H: OCH_2CH_3, J = 6.9 Hz), 3.61 (s, 3H: NCH_3), 4.31 (q, 2H: OCH_2CH_3, J = 6.9 Hz), 7.50–7.70 (m, 3H: Ph), 7.95 (m, 2H: Ph), 8.62 (s, 1H: H_4 or H_7), 8.65 (s, 1H: H_4 or H_7), 9.77 (bs, 1H: NH); ^{13}C NMR (75.5 MHz, DMSO-d_6/TMS), δ: 14.14 (OCH_2CH_3), 37.33 (NCH_3), 60.76 (OCH_2CH_3), 100.93, 107.44, 122.94, 123.49, 127.69, 128.56, 132.24, 133.38, 145.97, 155.46, 156.51, 159.52, 161.38, 166.00; IR (KBr) ν (cm^{-1}): 3396, 3071, 1726, 1650, 1519, 1307; elemental analysis: calcd (%) for $C_{19}H_{16}N_2O_6$ (368.3): C 61.96, H 4.38, N 7.61; found: C 62.04, H 4.37, N 7.43.

Ethyl 3-benzamido-6-isopropyl-2,5-dioxo-5,6-dihydro-2H-pyrano[3,2-c]pyridine-8-carboxylate (14c)

This compound was prepared from ethyl 4-hydroxy-1-isopropyl-6-oxo-1,6-dihydropyridine-3-carboxylate (**11f**; 225mg, 1.0 mmol), 9 hours of reflux, in 39% yield, mp = 192–194 °C (from diethyl ether). ^{1}H NMR (75.5 MHz, DMSO-d_6/TMS) δ: 1.34 (t, 3H: OCH_2CH_3, J = 7.2 Hz), 1.40 (d, 6H: 2 × CH_3 J = 6.9 Hz), 4.33 (q, 2H: OCH_2CH_3, J = 7.2 Hz), 5.07 (p, 1H: CH, J = 6.9 Hz), 7.50–7.70 (m, 3H: Ph), 7.95 (m, 2H: Ph), 8.41 (s, 1H: H_4 or H_7), 8.64 (s, 1H: H_4 or H_7), 9.77 (bs, 1H: NH); ^{13}C NMR (300 MHz, DMSO-d_6/TMS), δ: 14.12 (OCH_2CH_3), 20.94 (2 × CH_3), 48.89 (CH), 60.95 (OCH_2CH_3), 101.89, 107.72, 123.05, 123.76, 127.72, 128.58, 132.26, 133.38, 140.98, 154.90, 156.53, 158.94, 161.57, 166.01; IR (KBr) ν (cm^{-1}): 3408, 1654, 1521, 1248; MS (M^+) m/z: 396; elemental analysis: calcd (%)

for $C_{21}H_{20}N_2O_6$ (396.4): C 63.63, H 5.09, N 7.07; found: C 63.23, H 4.76, N 6.99.

Ethyl 6-(2-acetoxyethyl)-3-benzamido-2,5-dioxo-5,6-dihydro-2H-pyrano[3,2-c]pyridine-8-carboxylate (14d)

This compound was prepared from ethyl 4-hydroxy-1-(2-hydroxyethyl)-6-oxo-1,6-dihydropyridine-3-carboxylate (**11e**; 227 mg, 1.0 mmol), 9 hours of reflux, in 82% yield, mp = 218–224 °C (from acetic acid). ^{1}H NMR (300 MHz, DMSO-d_6/TMS) δ: 1.33 (t, 3H: OCH_2CH_3, J = 6.9 Hz), 1.98 (s, 3H: $COCH_3$), 4.35 (m, 6H: NCH_2CH_2O, OCH_2CH_3), 7.50–7.70 (m, 3H: Ph), 7.95 (m, 2H: Ph), 8.60 (s, 1H: H_4 or H_7), 8.62 (s, 1H: H_4 or H_7), 9.79 (bs, 1H: NH); ^{13}C NMR (75.5 MHz, DMSO-d_6/TMS), δ: ?14.12 (OCH_2CH_3), 20.49, 48.21, 60.87, 61.13, 101.41, 107.76, 123.15, 123.39, 127.74, 128.59, 132.29, 133.38, 145.56, 155.47, 156.45, 159.24, 161.31, 166.05, 170.06; IR (KBr) ν (cm^{-1}): 3383, 3071, 1742, 1699, 1528, 1235; MS (M^+) m/z: 440; elemental analysis: calcd (%) for $C_{22}H_{20}N_2O_8$ (440.4): C 60.00, H 4.58, N 6.36; found: C 59.83, H 4.58, N 6.02.

2. 4. General Procedure for Preparation of Compounds 17

To the solution of dimethyl malonate (0.46 ml, 2 mmol) in toluene (8 ml) was added DMFDMA (0.66 ml) and stirred under reflux for 0.5 h. Toluene was evaporated to obtain crude compound **15**, which was without purification used in further experiments. Then glacial acetic acid (8 ml) and compound **11** (2 mmol) were added and stirred under reflux to complete the reaction. The mixture was cooled and the product was separated by filtration and purified by recrystallisation from an appropriate solvent.

Methyl (E)-4-hydroxy-5-(3-methoxy-3-oxoprop-1-enyl)-1-methyl-6-oxo-1,6-dihydropyridine-3-carboxylate (17a)

This compound was prepared from methyl 4-hydroxy-1-methyl-6-oxo-1,6-dihydropyridine-3-carboxylate (**11c**; 366 mg, 2.0 mmol), 16 hours of reflux, in 23% yield, mp = 210–214 °C (from toluene). ^{1}H NMR (300 MHz, DMSO-d_6/TMS) δ: 3.52 (s, 3H: NCH_3), 3.69 (s, 3H: OCH_3), 3.90 (s, 3H: OCH_3), 7.09 (d, 1H: CH= CHCOOMe, J = 15.9 Hz), 7.83 (d, 1H: CH=CHCOOMe, J = 15.9 Hz), 8.72 (s, 1H: H_6), 11.70 (bs, 1H: OH); ^{13}C NMR (75.5 MHz, DMSO-d_6/TMS), δ: 37.35 (NCH_3), 51.22 (OCH_3), 52.67 (OCH_3), 97.49, 104.23, 117.45, 134.52, 146.85, 161.26, 165.27, 167.78, 168.13; IR (KBr) ν (cm^{-1}): 3420, 3084, 1702, 1681, 1552, 1449; MS (MH+) m /z: 268; elemental analysis: calcd (%) for $C_{12}H_{13}NO_6$ (267.2): C 53.93, H 4.90, N 5.24; found: C 54.23, H 4.84, N 5.20.

Ethyl (E)-4-hydroxy-1-isopropyl-5-(3-methoxy-3-oxoprop-1-enyl)-6-oxo-1,6-dihydropyridine-3-carboxylate (17b)

This compound was prepared from ethyl 4-hydroxy-1-isopropyl-6-oxo-1,6-dihydropyridine-3-carboxylate (**11f**; 450 mg, 2.0 mmol), 1 hour of reflux, in 56% yield, mp = 140–147 °C (from methanol). ^{1}H NMR (300 MHz, DMSO-d_6/TMS) δ: 1.35 (m, 9H: OCH_2CH_3, 2 × CH_3), 3.69 (s, 3H: NCH_3), 4.38 (q, 2H: OCH_2CH_3, J = 7.2 Hz), 5.04 (p, 1H: CH J = 6.9 Hz), 7.09 (d, 1H: CH=CHCOOMe, J = 15.9 Hz), 7.84 (d, 1H: CH=CHCOOMe, J = 15.9 Hz), 8.41 (s, 1H: H_6), 11.80 (bs, 1H: OH); ^{13}C NMR (75.5 MHz, DMSO-d_6/TMS), δ: 13.91 (OCH_2CH_3), 21.00 (2 × CH_3), 48.36 (CH), 51.19 (OCH_3), 61.95 (OCH_2CH_3), 98.25, 104.43, 117.66, 134.62, 141.90, 160.59, 164.80, 167.70, 167.75; IR (KBr) ν (cm^{-1}): 2987, 1706, 1612, 1334, 1277; elemental analysis: calcd (%) for $C_{15}H_{19}NO_6$ (309.3): C 58.25, H 6.19, N 4.53; found: C 58.43, H 6.10, N 4.58.

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Povzetek

V članku so opisane pretvorbe dietil 1-dimetilamino-3-oksobut-1-en-2,4-dicarboksilata (**2a**) s hidrazini **3a-g** v 1-substituirane 4-etoksikarbonil-5-(etoksikarbonilmetil)pirazole **5a-g**, z aminogvanidinom (**6**) v 7-amino-2-etoksikarbonil-1*H,2H*-pirazolo[2,3-c]pirimidin-5-on (**9**) in z amini **10a-k** v 4-hidroksipiridin-2(1H)-one **11a-k**. Iz spojin **11** nastanejo pri reakciji z (*Z*)-2-benzoilamino-3-dimetuilaminopropenoatom (**12**) 6-substituirani 3-benzoilamino-2,5-diokso-5,6-dihidro-2*H*-pirano[3,2-c]piridin-8-karboksilati.