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Diethyl Acetonedicarboxylate – a Precursor for the Synthesis of New Substituted 4-Aminoquinolines and Fused 4-Aminopyridines*

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Summary. The reaction of cyclic enaminonitriles **1** with diethyl acetonedicarboxylate (**2**) affords fused 4-amino-3-ethoxycarbonyl-2-ethoxycarbonylmethyl-pyridines **4**. The course of the reaction and the yield of cyclic products were promoted by tin(IV)chloride. N-substituted diethyl 3-aminoglutaconates **3** seem to be intermediates of the cyclization reaction.

Keywords. Cyclization; Enamines; Enaminonitriles; Tin(IV)chloride.

Diethylacetondicarboxylat – ein Precursor für die Synthese neuer substituierter 4-Aminochinoline und kondensierter 4-Aminopyridine

Zusammenfassung. Die Reaktion der cyclischen Enaminonitrile **1** mit Diethylacetondicarboxylat (**2**) ergibt kondensierte 4-Amino-3-ethoxycarbonyl-2-ethoxycarbonylmethyl-pyridine **4**. Der Reaktionsablauf und die Ausbeute werden durch Zusatz von Zinn(IV)chlorid gefördert. Wahrscheinlich verläuft die Reaktion über N-substituierte Diethyl-3-amino-glutaconate **3** als Zwischenprodukte.

Introduction

Cyclic α,β-enaminonitriles **1** are suitable synthons for various cyclization reactions, *e.g.* with diethyl acetonedicarboxylate (**2**). It has been shown that 2-amino-3-cyanopyrroles and ethyl acetoacetate give the corresponding enamines in the presence of *p*-toluenesulfonic acid which cyclize under base catalysis to ethyl 4-amino-2-methylpyrrolo[2,3-b]pyridine-3-carboxylates [1]. Any other attempts to prepare fused pyridines with other aromatic and heterocyclic compounds bearing amino and cyano-groups failed. Another reagent was used for the conversion of substituted 2-amino-3-cyanothiophenes. These compounds react with ethyl aminocrotonate in the presence of *p-TSA* to 2-[N-(3′-ethoxycarbonyl-2′-propenylamino)]-3-cyanothiophenes which then were treated with sodium ethoxide to give the desired ethyl 4-amino-2-methylthieno[2,3-*b*]pyridine-3-carboxylates [2]. Recently, tin(IV)

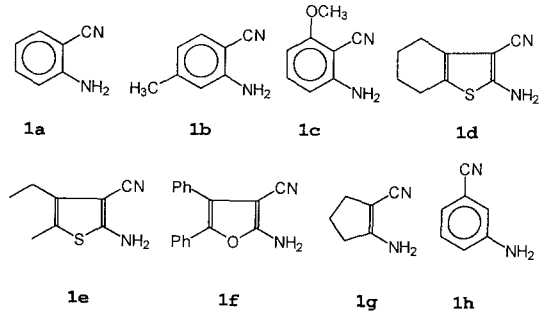
* Dedicated to Prof. *Milan Kratochvíl* on the occasion of his 70th birthday

chloride-promoted reactions of β-dicarbonyl compounds with nitriles have been described [3–5].

We attempted to find conditions for the reactions of diethyl acetonedicarboxylate (**2**) with several cyclic α,β-enaminonitriles (**1a–g**, Scheme 1).

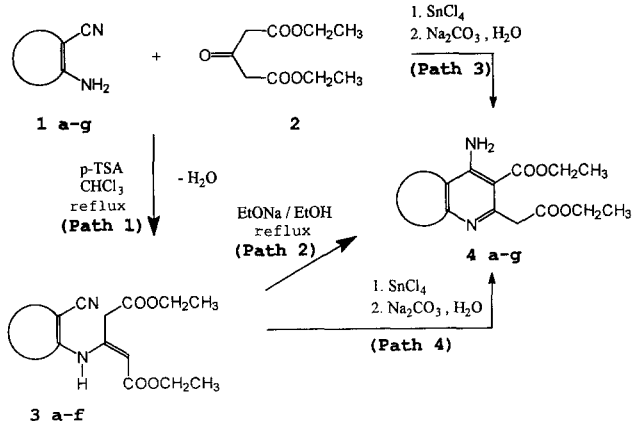
Results and Discussion

The starting aminobenzonitriles **1a–c** and **1h** were prepared by reduction of the corresponding nitro derivatives [6]. The heterocyclic α,β-enaminonitriles **1d–f** were prepared by *Gewald*'s method [7, 8], and the nonaromatic 1-amino-2-cyano-1-cyclopentene (**1g**) was obtained by an acid catalyzed cyclization of the corresponding 1,6-hexandinitrile [9].



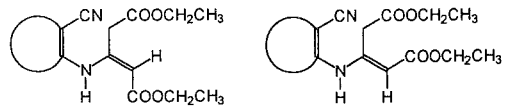
Scheme 1

All aromatic α,β-enaminonitriles **1a–f** gave the corresponding N-substituted diethyl 3-aminoglutaconates **3a–f** in good yields in the presence of *p-TSA* (Scheme 2, path 1; Table 1). The temperature of the reaction mixture had to be kept below 80 °C. Any higher temperature gives rise to undesired amides. The nonaromatic 1-amino-2-cyano-1-cyclopentene (**1g**) did not react even at higher temperature.



Scheme 2

The presence of a double bond in **3a–f** and **3h** allows two isomeric forms (Scheme 3). The isomers can interchange by acid or base catalysis in a suitable polar solvent. The equilibrium constant is dependent on solvent polarity and temperature. In a nonpolar solvent (chloroform), only *Z* isomers were observed even in the presence of a catalyst.



3 a–f

Z isomer *E* isomer

Scheme 3

Table 1. Characteristics and yields of *Z* isomers of enamines **3a–f, h**

	Yield (%)	m.p. (°C) (ethanol)	IR ($CHBr_3$) $\tilde{\nu}$ (cm^{-1})	^1H NMR ($CDCl_3$) δ (ppm), J (Hz)
3a	42	82–84.5	760, 800, 1025, 1045, 1590, 1620, 1650, 1720, 2210, 3150	1.18 (t, 3H, $J = 7.0$), 1.29 (t, 3H, $J = 7.0$), 3.33 (s, 2H), 4.07 (q, 2H, $J = 7.0$), 4.20 (q, 2H, $J = 7.0$), 4.99 (s, 1H), 7.16–7.72 (m, 4H), 10.66 (br, 1H)
3b	39	85–86	800, 820, 1030, 1050, 1605, 1650, 1730, 2210, 3240	1.20 (t, 3H, $J = 7.0$), 1.29 (t, 3H, $J = 7.0$), 2.40 (s, 3H), 3.32 (s, 2H), 4.08 (q, 2H, $J = 7.0$), 4.19 (q, 2H, $J = 7.0$), 4.97 (s, 1H), 7.03–7.56 (m, 3H), 10.52 (br, 1H)
3c	41	114–115	790, 1025, 1040, 1590, 1620, 1645, 1725, 2210, 3280	1.20 (t, 3H, $J = 7.0$), 1.29 (t, 3H, $J = 7.0$), 3.36 (s, 2H), 3.93 (s, 3H), 4.10 (q, 2H, $J = 7.0$), 4.20 (q, 2H, $J = 7.0$), 4.97 (s, 1H), 6.28–6.85 (m, 2H), 7.29–7.55 (m, 1H), 10.53 (br, 1H)
3d	63	oil	800, 1025, 1045, 1260, 1620, 1650, 1725, 2210, 3300	1.22 (t, 3H, $J = 7.0$), 1.28 (t, 3H, $J = 7.0$), 1.84 (m, 4H), 2.62 (m, 4H), 3.39 (s, 2H), 4.10 (q, 2H, $J = 7.0$), 4.19 (q, 2H, $J = 7.0$), 4.96 (s, 1H), 10.55 (br, 1H)
3e	52	oil	800, 1025, 1040, 1260, 1605, 1650, 1725, 2210, 3260	1.17 (t, 3H, $J = 7.5$), 1.18 (t, 3H, $J = 7.0$), 1.29 (t, 3H, $J = 7.0$), 2.63 (q, 2H, $J = 7.5$), 3.39 (s, 2H), 4.13 (q, 2H, $J = 7.0$), 4.21 (q, 2H, $J = 7.0$), 4.95 (s, 1H), 10.60 (br, 1H)
3f	78	140–141	770, 805, 1025, 1040, 1260, 1605, 1640, 1730, 2210, 3260	1.10 (t, 3H, $J = 7.0$), 1.30 (t, 3H, $J = 7.0$), 3.70 (s, 2H), 4.07 (q, 2H, $J = 7.0$), 4.17 (q, 2H, $J = 7.0$), 5.06 (s, 1H), 7.26–7.40 (m, 5H), 7.41 (s, 5H), 11.79 (br, 1H)
3h	53	80–81	800, 1025, 1045, 1620, 1645, 1725, 2210, 3210	1.20 (t, 3H, $J = 7.0$), 1.29 (t, 3H, $J = 7.0$), 3.31 (s, 2H), 4.10 (q, 2H, $J = 7.0$), 4.17 (q, 2H, $J = 7.0$), 4.89 (s, 1H), 7.40–7.49 (m, 4H), 10.40 (br, 1H)

In the solid state, **3a–f** and **3h** exist as *Z* isomers. The structure of diethyl 3-[N-(2-cyanophenyl)]aminoglutaconate (**3a**) was determined by X-ray analysis (Figure 1). The double bond is located between carbons C(5) and C(6) (cf. Table 2).

The structures of **3b–f** and **3h** in the solid state have been established by the comparison of X-ray data and the ^1H NMR spectrum of **3a** in dimethylsulfoxide

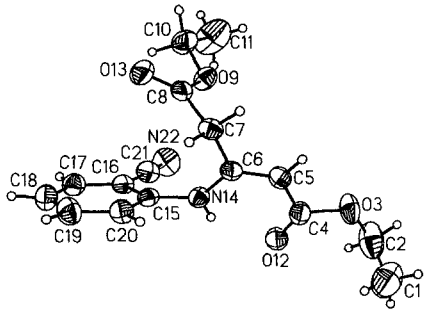


Fig. 1. X-ray structure of **3a**

Table 2. Selected bond lengths and angles [15] of **3a**

Bond lengths	(Å)	Bond angles	(deg)
C(4)–C(5)	1.435(5)	C(4)–C(5)–C(6)	123.7(3)
C(5)–C(6)	1.354(7)	C(5)–C(6)–C(7)	120.7(2)
C(6)–C(7)	1.504(3)	C(5)–C(6)–N(14)	121.6(4)
C(6)–N(14)	1.354(4)		

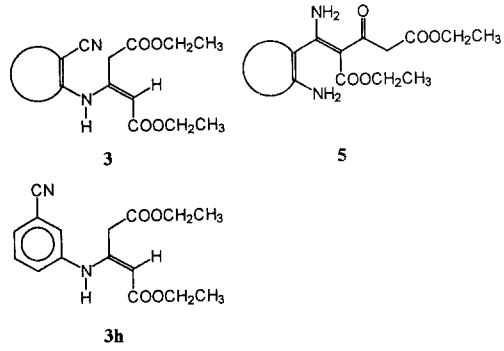
with the ^{1}H NMR spectra of compounds **3b–f** and **3h** in the same solvent. The chemical shifts of the protons of the *E* and *Z* isomers differ significantly in *DMSO*. For example, the chemical shift of the hydrogen atom bound to nitrogen varies between 8 and 10.5 ppm for *E* isomers and between 9.5 and 12 ppm for *Z* isomers. The N–H bond vibrations in the IR spectrum are significant for strong intramolecular hydrogen bonds.

Reflux of enamines **3a–f** in the presence of an equimolar amount of sodium ethoxide in anhydrous ethanol (Scheme 2, path 2) led to the formation of fused 4-amino-3-ethoxycarbonyl-2-ethoxycarbonylmethyl-pyridines **4a–f**, although only in low yields (Table 3). We therefore used tin(IV)chloride as a catalyst. Reactions of diethyl acetonedicarboxylate with **1a–g** in the presence of a twofold stoichiometric amount of tin(IV)chloride in 1,2-dichloroethane (Scheme 2, path 3) were successful. The corresponding fused substituted 4-aminopyridines and 4-aminoquinolines **4a–g** were obtained in good yields (Table 3).

Table 3. Comparison of yields of **4a–g** synthesized by various methods

	Yield (%)				m.p. (°C)
	Path 1+2	Path 2	Path 3	Path 4	
4a	12.6	30	66	66	126–127
4b	13.7	35	51	58	115.5–116.5
4c	10.3	25	45	55	138–139
4d	12.6	20	61	60	130–130.5
4e	10.4	20	63	63	120.5–121.5
4f	23.4	30	43	40	179–180
4g	–	–	49	–	103–103.5

The formation of heterocycles **4a–g** might be expected *via* two intermediates (**3** and **5**, Scheme 4), but none of them could be detected in the reaction mixture.



Scheme 4

We suppose that hydrochloric acid formed during the decomposition of the tin complexes and by hydrolysis of the remaining tin(IV)chloride with water causes decomposition of the intermediate **3** to give **2** and the corresponding α,β-enaminonitriles **1a–f**.

In order to establish the course of the reaction we repeated the reaction with 3-aminobenzonitrile (**1h**) because its condensation product (diethyl 3-[N-(3-cyanophenyl)]-aminoglutaconate, **3h**), as we have found, is more stable in acidic environment than **3a–f** and because it cannot cyclize intramolecularly. Indeed, a small amount of the corresponding enamine **3h** could be isolated from the reaction mixture. The possible intermediate **5** could not be detected in the reaction mixture. Therefore, we assume that the formation of the fused 4-amino-3-ethoxycarbonyl-2-ethoxycarbonylmethyl-pyridines **4a–g** also proceeds *via* enamine intermediates.

All isolated enamines **3a–f** gave the corresponding cyclic products **4a–f** in good yields on treatment with stoichiometric amount of tin(IV)chloride (Scheme 2, path 4; Table 3).

The tin(IV)chloride promoted reaction of **2** with various α,β-enaminonitriles seems to be a suitable method for the preparation of fused 4-amino-3-ethoxycarbonyl-2-ethoxycarbonylmethylpyridines – suitable precursors for syntheses of many other interesting heterocyclic compounds. We suppose that the promotion of the synthesis by tin(IV)chloride is caused by its well known ability to coordinate to nitriles [10] and β-ketoesters [11], enhancing their nucleophilic and electrophilic nature, respectively. The mechanism of this promotion has not yet been studied.

Experimental

Melting points: VEB Wagetechnik RAPIDO 79/2106 melting point apparatus; IR spectra: Unicam SP 1000 spectrometer; ^{1}H NMR spectra: Tesla BS 587A (80 MHz) or Tesla BS 567 (100 MHz) spectrometers; ^{13}C NMR spectra: Tesla BS 587A (20 MHz). Selected chemical shifts are reported in ppm relative to tetramethylsilane as internal standard. X-ray analysis: crystals of **3a** were obtained by crystallization from ethanol. The crystals were found to be monoclinic (space group $P2_1/C$; unit cell constants: $a = 32.125(8)$, $b = 7.701(4)$, $c = 13.521(4)$ Å, $\beta = 101.46(2)°$, $U = 3278(2)$ Å^3, $F(000) = 1280$, $\mu(MoK_\alpha) = 0.83\,cm^{-3}$, $T = 295$ K, $D_x = 1{,}225\,g \cdot cm^{-3}$, $Z = 8$). Final values of the lattice parameters were determined on a KUMA diffractometer. The dimensions of the crystal used 0.25 × 0.55 × 0.55 nm.

Diffraction intensities were measured with $\omega = 2\theta$ scan techniques using graphite monochromatized MoK_α radiation. The crystal stability during the data collection was checked by measuring two standard reflections after every fifty one; no significant decreases in their intensities was detected. The intensities were corrected for the *Lp*-factor; no absorption correction was applied. The structure was solved by direct methods. The refinements were performed on $|F_0|$. All atoms, except hydrogens, were refined anisotropically by a block-diagonal matrix least-squared procedure with weight $1/w = \sigma^2(F_0) + (k \cdot |F_0|)^2$ ($k = 0.0001$). Hydrogen atoms were positioned theoretically and refined isotropically. Final residuals R and R_w are 0.0498 and 0.0658, resp., for observed reflections, and 0.1957 and 0.0737, resp., for all data. The programs used were SHELXS-86 [12] for the structure solution and SHELXS-76 [13] for the refinement including atomic scattering factors and geometry calculation. The figure was drawn by ORTEP [14].

Diethyl 3-[N-(2-cyanophenyl)]aminoglutaconate (**3a**); *General procedure for the synthesis of enamines* **3a–f** *and* **3h**

A mixture of 2-aminobenzonitrile (**1a**; 1.32 g, 10 mmol), diethyl acetonedicarboxylate (**2**; 2 g, 10 mmol), and a catalytic amount of *p*-toluenesulfonic acid were refluxed in chloroform (30 ml) in a *Dean-Stark* apparatus for chloroform. After 3 hours, the chloroform solution was washed with sodium carbonate (50 ml of 0.1 *M* aqueous solution) and finally with water (50 ml). Then the solution was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was placed in a refrigerator; the formed colourless crystals were filtered off and crystallized from ethanol. Yield, 42%; m.p. (*Z* isomer), 82–84.5 °C; IR ($CHBr_3$): $\tilde{\nu} = 760$, 1025, 1045, 1590, 1620, 1650, 1720, 2210, 3150 cm^{-1}; ^1H NMR (*DMSO*-d_6): *Z* isomer, $\delta = 1.00$ (t, 3H, $J = 7.0$ Hz), 1.23 (t, 3H, $J = 7.0$ Hz), 3.60 (s, 2H), 3.89 (q, 2H, $J = 7.0$ Hz), 4.13 (q, 2H, $J = 7.0$ Hz), 5.00 (s, 1H), 7.34–7.87 (m, 4H), 10.43 (br, 1H) ppm; *E* isomer $\delta = 1.10$ (t, 3H, $J = 7.0$ Hz), 1.23 (t, 3H, $J = 7.0$ Hz), 3.91 (q, 2H, $J = 7.0$ Hz), 3.93 (s, 2H), 4.13 (q, 2H, $J = 7.0$ Hz), 4.81 (s, 1H), 7.34–7.87 (m, 4H), 8.86 (br, 1H) ppm.

4-Amino-3-ethoxycarbonyl-2-ethoxycarbonylmethylquinoline (**4a**); *General procedure for the synthesis of cyclic products* **4b–f** *(Scheme 2, path 3)*

2-Aminobenzonitrile (**1a**; 3 g, 25.4 mmol) and diethyl acetonedicarboxylate (**2**; 5.14 g, 25.4 mmol) were dissolved in 1,2-dichloroethane (20 ml) under a nitrogen atmosphere. Then tin(IV)chloride (13.24 g, 51 mmol) was added and the reaction mixture was refluxed for 6 h. After removal of the solvent the residue was dissolved in acetone (100 ml) and the *pH* of the mixture was adjusted to 8.5–9 by the addition of aqueous sodium carbonate solution (1g in 50 ml water). The resulting suspension was filtered and the precipitate extracted with dichloromethane (200 ml). Acetone was removed under reduced pressure and the remainder extracted with dichloromethane (100 ml). The exctracts were combined and dried over $MgSO_4$; after removal of the solvent, the residue was crystallized from 60% aqueous ethanol to give a light yellow product. Yield, 66%; m.p. 126–127 °C; IR($CHBr_3$): $\tilde{\nu} = 760$, 1595, 1660, 1715, 3275, 3365 cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 1.26$ (t, 3H, $J = 7.0$ Hz), 1.39 (t, 3H, $J = 7.0$ Hz), 4.19 (q, 2H, $J = 7.0$ Hz), 4.24 (s, 2H), 4.34 (q, 2H, $J = 7.0$ Hz), 7.27 (br, 2H), 7.29–7.80 (m, 4H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 14.13$, 14.27 (CH_3), 47.25 (CH_2), 60.70, 60.98 (OCH_2), 120.75, 125.39, 129.46, 131.21 (CH), 102.02, 117.61, 147.37, 154.51, 155.37 (C), 168.64, 171.46 (C=O) ppm.

4-Amino-3-ethoxycarbonyl-2-ethoxycarbonylmethyl-7-methylquinoline (**4b**)

IR($CHBr_3$): $\tilde{\nu} = 790$, 1605, 1655, 1710, 3260, 3360 cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 1.26$ (t, 3H, $J = 7.0$ Hz), 1.39 (t, 3H, $J = 7.0$ Hz), 2.47 (s, 3H), 4.18 (q, 2H, $J = 7.0$ Hz), 4.22 (s, 2H), 4.35 (q, 2H, $J = 7.0$ Hz), 6.91 (br, 2H), 7.14–7.67 (m, 3H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 14.13$, 14.27 (CH_3), 21.59 (CH_3), 47.28 (CH_2), 60.66, 60.84 (OCH_2), 120.68, 127.32, 128.74 (CH), 101.59, 115.51, 141.70, 147.58, 154.58, 155.43 (C), 168.71, 171.63 (C=O) ppm.

4-Amino-3-ethoxycarbonyl-2-ethoxycarbonylmethyl-5-methoxyquinoline (**4c**)

IR ($CHBr_3$): $\tilde{\nu} = 765, 820, 1595, 1610, 1630, 1670, 1725, 3230, 3360\,cm^{-1}$; ^1H NMR ($CDCl_3$): $\delta = 1.26$ (t, 3H, $J = 7.0$ Hz), 1.35 (t, 3H, $J = 7.0$ Hz), 4.14 (s, 3H), 4.20 (q, 2H, $J = 7.0$ Hz), 4.38 (q, 2H, $J = 7.0$ Hz), 4.49 (s, 2H), 7.25–7.95 (m, 3H), 9.53 (br, 2H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 13.88, 14.13$ (CH_3), 57.13 (OCH_3), 41.00 (CH_2), 61.73, 62.34 (OCH_2), 107.76, 114.68, 135.10 (CH), 101.30, 140.48, 153.47, 158.29, 159.32, 162.04 (C), 166.60, 168.49 (C=O) ppm.

4-Amino-3-ethoxycarbonyl-2-ethoxycarbonylmethyl-5,6,7,8-tetrahydrobenzo[b]thieno[2,3-b]pyridine (**4d**)

IR ($CHBr_3$): $\tilde{\nu} = 1235, 1555, 1585, 1660, 1715, 2920, 3290, 3450\,cm^{-1}$; ^1H NMR ($CDCl_3$): $\delta = 1.23$ (t, 3H, $J = 7.0$ Hz), 1.37 (t, 3H, $J = 7.0$ Hz), 1.86–1.94 (m, 4H), 2.79–3.00 (m, 4H), 4.10 (s, 2H), 4.15 (q, 2H, $J = 7.0$ Hz), 4.33 (q, 2H, $J = 7.0$ Hz), 6.75 (br, 2H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 14.10, 14.27$ (CH_3), 22.30, 22.66, 25.66, 26.55 (CH_2), 46.35 (CH_2), 60.59, 60.51 (OCH_2), 104.12, 118.75, 126.92, 133.70, 152.62, 152.62, 161.64 (C), 168.74, 171.21 (C=O) ppm.

4-Amino-3-ethoxycarbonyl-2-ethoxycarbonylmethyl-5-ethyl-6-methylthieno[2,3-b]pyridine (**4e**)

IR ($CHBr_3$): $\tilde{\nu} = 1235, 1545, 1580, 1655, 1710, 2940, 3270, 3430\,cm^{-1}$; ^1H NMR ($CDCl_3$): $\delta = 1.25$ (t, 3H, $J = 7.5$ Hz), 1.25 (t, 3H, $J = 7.0$ Hz), 1.37 (t, 3H, $J = 7.0$ Hz), 2.41 (s, 2H), 2.82 (q, 2H, $J = 7.5$ Hz), 4.11 (s, 2H), 4.16 (q, 2H, $J = 7.0$ Hz), 4.43 (q, 2H, $J = 7.0$ Hz), 6.85 (br, 2H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 13.17, 14.06, 14.24, 14.99$ (CH_3), 21.52, 46.32 (CH_2), 60.59, 60.95 (OCH_2), 104.37, 118.75, 130.60, 131.24, 152.01, 152.44, 161.65 (C), 168.62, 171.14 (C=O) ppm.

4-Amino-3-ethoxycarbonyl-2-(ethoxycarbonyl)methyl-5,6-diphenylfuro[2,3-b]pyridine (**4f**)

IR ($CHBr_3$): $\tilde{\nu} = 700, 710, 770, 775, 1280, 1610, 1665, 1720, 3300, 3420\,cm^{-1}$; ^1H NMR ($CDCl_3$): $\delta = 1.27$ (t, 3H, $J = 7.0$ Hz), 1.35 (t, 3H, $J = 7.0$ Hz), 4.18 (s, 2H), 4.19 (q, 2H, $J = 7.0$ Hz), 4.31 (q, 2H, $J = 7.0$ Hz), 6.20 (br, 2H), 7.18–7.71 (m, 10H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 14.10, 14.24$ (CH_3), 46.35 (CH_2), 60.70, 60.98 (OCH_2), 126.28, 126.28, 128.28, 128.46, 128.46, 128.92, 129.64, 129.64, 130.14, 130.14 (CH), 104.84, 105.84, 116.33, 129.81, 132.67, 140.17, 147.55, 152.44, 153.97 (C), 168.21, 170.99 (C=O) ppm.

4-Amino-3-ethoxycarbonyl-2-ethoxycarbonylmethylcyclopenta[2,3-b]pyridine (**4g**)

IR ($CHBr_3$): $\tilde{\nu} = 1600, 1665, 1720, 3320, 3440\,cm^{-1}$; ^1H NMR ($CDCl_3$): $\delta = 1.25$ (t, 3H, $J = 7.0$ Hz), 1.36 (t, 3H, $J = 7.0$ Hz), 2.03–3.06 (m, 6H), 4.11 (s, 2H), 4.15 (q, 2H, $J = 7.0$ Hz), 4.31 (q, 2H, $J = 7.0$ Hz), 5.94 (br, 2H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 14.10, 14.24$ (CH_3), 21.98, 27.37, 34.97, 46.03 (CH_2), 60.59, 60.91 (OCH_2), 107.02, 119.97, 152.19, 156.08, 165.75 (C), 168.43, 171.35 (C=O) ppm.

4-Amino-3-ethoxycarbonyl-2-ethoxycarbonylmethylquinoline (**4a**); *General procedure for the synthesis of cyclic derivatives* **4b–f** *(Scheme 2, path 4)*

Enamine **3a** (3 g, 9.9 mmol) was dissolved in 1,2-dichloroethane (20 ml) under a nitrogen atmosphere. Then, tin(IV)chloride (2.60 g, 9.9 mmol) was added and the reaction mixture was refluxed for 6 h. The product was isolated as described above (see procedure for path 3). Yield: 66%.

4-Amino-3-ethoxycarbonyl-2-ethoxycarbonylmethylquinoline (**3a**); *General procedure for the synthesis of cyclic products* **4b–f** *(Scheme 2, path 2)*

A solution of enamine **3a** (0.5 g, 1.7 mmol) in ethanol (20 ml) containing 1.7 mmol of sodium ethoxide was refluxed for 8 h. Then, the reaction mixture was concentrated to one half of the original volume

and diluted with water (100 ml). The white precipitation was filtered off and recrystallized from 30% aqueous ethanol to give 0.14 g of cyclic product **4a**. Yield, 30%; spectral data: see above.

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