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A Simple and Expeditious Synthesis of Substituted 3-Aminoindolizines

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Summary. Treatment of easily available 2-formyl-1,4-dihydropyridines with 3-oxo-3-phenylpropanenitrile offers a simple and efficient one-pot method for the preparation of substituted 3-aminoindolizines.

Keywords. 1,4-Dihydropyridines; 3-Aminoindolizines; *Knoevenagel* reaction.

Eine einfache und rasche Synthese substituierter 3-Aminoindolizine

Zusammenfassung. Die Umsetzung der einfach zugänglichen 2-Formyl-1,4-dihydropyridine mit 3-Oxo-3-phenylpropannitrilen stellt eine einfache und effiziente Eintopfmethode zur Darstellung substituierter 3-Aminoindolizine dar.

Introduction

Synthetic indolizines are relatively well known as photographic sensitizers, fabric brighteners, and dyes [1, 2]. They are also known to exhibit pharmacological effects on the central nervous system [2] as well as depressant [3] and anti-inflammatory activities [4]. Some indolizine derivatives have shown effectiveness in the treatment of angina pectoris [5].

Methods for the preparation of indolizine are based on the 1,3-dipolar cycloaddition of a reactive dipole prepared from substituted pyridinium salts and alkynes [6], thermal intramolecular cyclization of 3-acetoxy-3-(2-pyridyl)-2-methylenepropionate esters [7], intramolecular cyclocondensation of N-pyridinium aldehydes [8], *Chichibabin* reaction of 1-(ethoxycarbonylmethyl)-2-methylpyridinium chloride [2], or on the reaction of β-ketoesters and β-diketones with 2-halopyridinium salts in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene [9].

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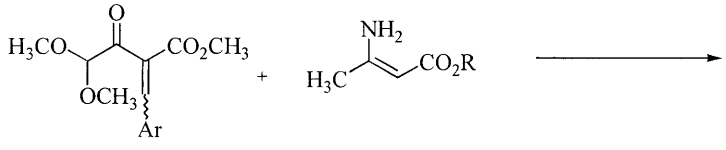
3-Aminoindolizines can also be prepared by reaction 2-bromomethylpyridine with benzyl cyanide in the presence of sodium amide [10], *Michael* addition of substituted acetonitriles on 2-pyridylchalcones followed by intramolecular cyclization [11], electrochemical reduction of appropriate substituted pyridines and pyridinium salts [12], or reduction of the corresponding nitro, azo, or nitrosoindolizine [13].

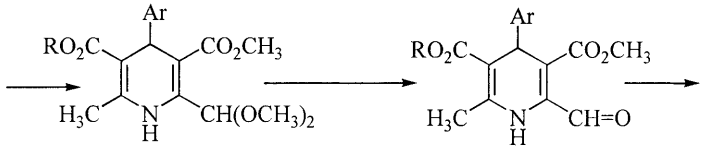
In this paper we report a novel simple and efficient synthetic method for the preparation of 3-aminoindolizines derivatives from easily obtainable 2-formyl-1,4-dihydropyridines by treatment with 3-phenyl-3-oxopropanenitrile.

Results and Discussion

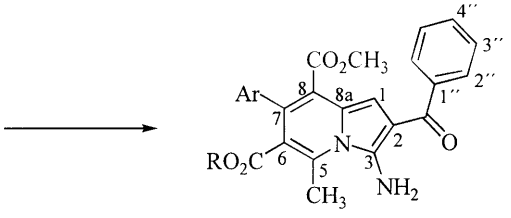
The 2-formyl-1,4-dihydropyridines **13**–**22** (Scheme 1) were prepared in 51–94% yield by acidic hydrolysis of the corresponding 2-dimethoxymethyl-1,4-dihydropyridines **3**–**12** [14] which were obtained from alkyl 3-aminocrotonates **2** and methyl 2-arylmethylene-4,4-dimethoxy-3-oxobutanoates **1** according to the



1 **2**



3 - 12 **13 - 22**



23 - 32

3, 13, 23: Ar = 2-NO_2Ph, *R* = Et
4, 14, 24: Ar = 2-NO_2Ph, *R* = *i*-Pr
5, 15, 25: Ar = 3-NO_2Ph, *R* = Et
6, 16, 26: Ar = 3-NO_2Ph, *R* = *i*-Pr
7, 17, 27: Ar = 4-NO_2Ph, *R* = Et
8, 18, 28: Ar = 4-NO_2Ph, *R* = *i*-Pr
9, 19, 29: Ar = 5-NO_2-2-furyl, *R* = Et
10, 20, 30: Ar = 5-NO_2-2-furyl, *R* = *i*-Pr
11, 21, 31: Ar = 2-furyl, *R* = Et
12, 22, 32: Ar = 2-furyl, *R* = *i*-Pr

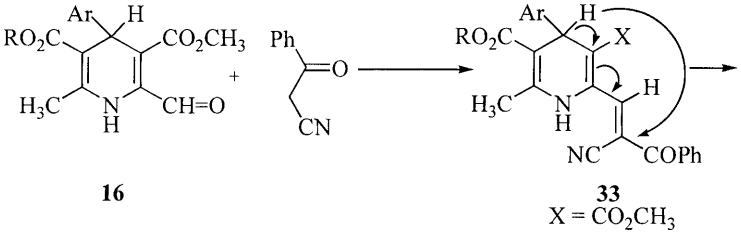
Scheme 1

modified *Hantzsch* method (Scheme 1). α,β-Unsaturated esters **1** were prepared through *Knoevenagel* reaction of methyl 4,4-dimethoxy-3-oxobutanoate and arylaldehydes with a catalytic amount of piperidine in benzene under azeotropic dehydration [14].

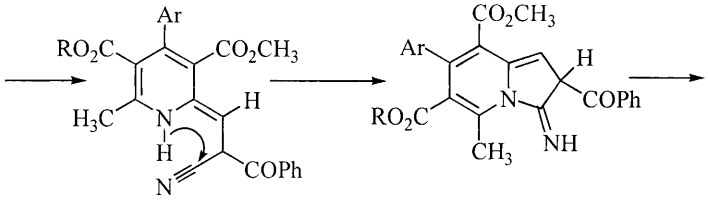
The treatment of 2-formyl-1,4-dihydropyridines **13–22** with 3-phenyl-3-oxopropanenitrile and a catalytic amount of piperidine in anhydrous ethanol under reflux gave dark violet crystalline 3-aminoindolizines in 72–93% yield (Scheme 1). In contrast to simple aminoindolizines [13b,c], indolizines **23–32** are stable at normal conditions.

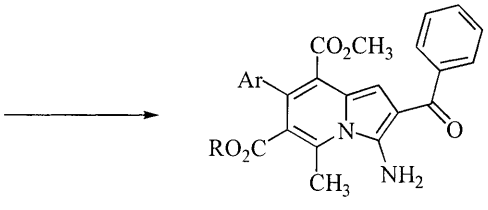
The structure of the 1,4-dihydropyridines **3–22** was determined based on NMR and IR spectroscopic analyses. Especially diagnostic for the formation of **3–22** were the signals of the proton at C-4 of the 1,4-dihydropyridine ring at $\delta = 5.0$–6.0 ppm and of the NH group at $\delta = 6.9$–7.3 ppm in the ^{1}H NMR spectra [14].

The structural elucidation of the 3-aminoindolizines was accomplished by NMR (including DEPT, COSY, and HETCOR experiments) and mass spectroscopic analyses. The ^{1}H NMR spectra of **23–32** showed a proton signal at $\delta = 6.55$–6.86 ppm, typical for 3-aminoindolizines [12], and no signal for a proton



16 **33** X = CO_2CH_3





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Scheme 2

in position 4 of 1,4-dihydropyridine at about 5.5 ppm. Also we didn't find any signal of a cyano group in the ^{13}C NMR and IR spectra of **23–32**. On the other hand, the IR spectra of **23–32** pointed at the presence of a primary amino group at 3400–3500 cm^{-1}. The signals of all carbon atoms in the ^{13}C NMR spectra of compounds **3–32** were assigned using 2D CH-correlation techniques.

In a preliminary communication [15], the treatment of 2-formyl-1,4-dihydropyridine **16** with 3-phenyl-3-oxopropanenitrile and a catalytic amount of piperidine in anhydrous ethanol at room temperature has been described to give the corresponding 2-vinyl substituted 1,4-dihydropyridine derivative **33** in 78% yield. We found that compound **26** can be prepared also from **33** by simple reflux in ethanol. Although no mechanistic studies have been undertaken, we suppose that the first step of this process is a *Knoevenagel* reaction of aldehyde **16** with 3-phenyl-3-oxopropanenitrile. The product of the condensation undergoes a subsequent [1, 5]-sigmatropic rearrangement followed by intramolecular addition of the NH group to the nitrile function and tautomerization to the aforementioned 3-aminoindolizine (Scheme 2).

In conclusion, the reported synthesis of substituted 3-aminoindolizines **23–32** from 2-formyl-1,4-dihydropyridines **13–22** is efficient (72–93% yield) and convenient from both a chemical (standard transformations are employed) and economic point of view (1,4-dihydropyridine derivatives are readily available starting materials).

Experimental

Melting points were measured on a Boetius micro hot-stage and are uncorrected. The infrared spectra were recorded on a Philips analytical PV 9 800 FT IR spectrophotometer (KBr), the NMR spectra on a Bruker AC-500 spectrometer in $CDCl_3$ using tetramethylsilane as internal standard. Ascending thin layer chromatography was performed on precoated silica gel plates (60 F254, Merck), and the spots were visualized using a UV lamp or iodine vapour. Mass spectroscopic measurements were performed on an AEI MS 902 S spectrometer. The elemental analyses agreed favourably with the calculated values.

General procedure for the preparation of 2-dimethoxymethyl-1,4-dihydropyridines (**3–12**)

A mixture of methyl 4,4-dimethoxy-2-(arylmethylene)-3-oxobutanoate (**1**, 0.016 mol) and alkyl 3-aminocrotonate (**2**, 0.017 mol) was refluxed in 40 cm^3 2-propanol for 10 h. After cooling, the solvent was removed *in vacuo* to give an oil which was triturated in MeOH or subjected to column chromatography (silica gel, CH_2Cl_2) to afford **3–12**. The separated solid was collected by suction and recrystallized from 2-propanol.

Ethyl 2-dimethoxymethyl-3-methoxycarbonyl-6-methyl-4-(2-nitrophenyl)-1,4-dihydropyridine-5-carboxylate (**3**; $C_{20}H_{24}N_2O_8$)

Yield: 54%; m.p.: 123–124°C; ^1H NMR ($CDCl_3$, δ, 500 MHz): 7.71–7.28 (m, $4H_{ar}$), 6.76 (s, NH), 6.00 (s, CH), 5.84 (s, H-4), 4.04 (q, OCH_2), 3.62 (s, OCH_3), 3.42, 3.43 (s, OCH_3), 2.39 (s, CH_3), 1.16 (t, CH_3) ppm; ^{13}C NMR ($CDCl_3$, δ, 75 MHz): 167.0 (CO_2CH_3), 166.4 (CO), 147.7 (C2′), 144.8 (C6), 143.9 (C2), 142.0 (C1′), 133.0 (C4′), 131.3 (C6′), 127.3 (C5′), 124.0 (C3′), 105.0 (C3), 103.4 (C5), 99.0 (OCHO), 60.0 (OCH_2), 55.6, 55.2 (OCH_3), 51.4 (OCH_3), 34.7 (C4), 19.6, 14.1 (CH_3) ppm; IR (KBr): $\nu = 3345$ (N–H), 1697 (C=O) cm^{-1}.

Isopropyl 2-dimethoxymethyl-3-methoxycarbonyl-6-methyl-4-(2-nitrophenyl)-1,4-dihydropyridine-5-carboxylate (**4**; $C_{21}H_{26}N_2O_8$)

Yield: 56%; m.p.: 145–147°C (Ref. [14]: 143–145°C); ^{1}H NMR ($CDCl_3$, δ, 500 MHz): 7.75–7.26 (m, $4H_{ar}$), 6.71 (s, NH), 5.96 (s, CH), 5.88 (s, H-4), 4.96 (m, OCH), 3.60 (s, OCH_3), 3.38, 3.46 (s, OCH_3), 2.39 (s, CH_3), 1.24, 0.98, (d, CH_3, $J = 6.2$ Hz) ppm; ^{13}C NMR ($CDCI_3$, δ, 75 MHz): 166.7 (CO_2CH_3), 166.6 (CO), 147.7 (C2′), 144.6 (C6), 143.7 (C2), 142.3 (C1′), 133.0 (C4′), 131.3 (C6′), 127.2 (C5′), 124.1 (C3′), 105.0 (C3), 103.7 (C5), 98.5 (OCHO), 67.4 (OCH), 55.6, 55.1 (OCH_3), 51.4 (OCH_3), 34.8 (C4), 21.8, 21.4 19.6 (CH_3) ppm; IR (KBr): $\nu = 3359$ (N–H), 1697 (C=O) cm^{-1}.

Ethyl 2-dimethoxymethyl-3-methoxycarbonyl-6-methyl-4-(3-nitrophenyl)-1,4-dihydropyridine-5-carboxylate (**5**; $C_{20}H_{24}N_2O_8$)

Yield: 63%; m.p.: 88–90°C; ^{1}H NMR ($CDCl_3$, δ, 500 MHz): 8.16–7.40 (m, $4H_{ar}$), 6.96 (s, NH), 6.03 (s, CH), 5.17 (s, H-4), 4.10 (q, OCH_2), 3.68 (s, OCH_3), 3.49, 3.45 (s, OCH_3), 2.40 (s, CH_3), 1.24 (t, CH_3) ppm; ^{13}C NMR ($CDCl_3$, δ, 75 MHz): 166.7 (CO_2CH_3), 166.3 (CO), 149.1 (C1′), 148.7 (C3′), 144.8 (C6), 144.1 (C2), 134.0 (C6′), 128.7 (C5′), 122.6 (C2′), 121.3 (C4′), 104.0 (C3), 102.5 (C5), 98.4 (OCHO), 59.8 (OCH_2), 55.4, 54.9 (OCH_3), 51.2 (OCH_3), 39.7 (C4), 19.3, 14.0 (CH_3) ppm; IR (KBr): $\nu = 3372$ (N–H), 1682 (C=O) cm^{-1}.

Isopropyl 2-dimethyoxymethyl-3-methoxycarbonyl-6-methyl-4-(3-nitrophenyl)-1,4-dihydropyridine-5-carboxylate (**6**; $C_{21}H_{26}N_2O_8$)

Yield: 49%; m.p.: 100–102°C (Ref. [14]: oil); ^{1}H NMR ($CDCl_3$, δ, 500 MHz): 8.14–7.39 (m, $4H_{ar}$), 6.81 (s, NH), 6.02 (s, CH), 5.12 (s, H-4), 4.97 (m, OCH), 3.67 (s, OCH_3), 3.49, 3.46 (s, OCH_3), 2.38 (s, CH_3), 1.26, 1.12 (d, CH_3 $J = 6.2$ Hz), ppm; ^{13}C NMR ($CDCl_3$, δ, 75 MHz): 166.6 (CO_2CH_3), 166.4 (CO), 149.4 (C1′), 148.2 (C3′), 144.6 (C6), 144.2 (C2), 134.3 (C6′), 128.8 (C5′), 123.0 (C2′), 121.5 (C4′), 104.2 (C3), 103.2 (C5), 98.6 (OCHO), 67.4 (OCH), 55.7, 55.1 (OCH_3), 51.5 (OCH_3), 40.0 (C4), 22.1, 21.8, 19.6 (CH_3) ppm; IR (KBr): $\nu = 3359$ (N–H), 1697 (C=O) cm^{-1}.

Ethyl 2-dimethoxymethyl-3-methoxycarbonyl-6-methyl-4-(4-nitrophenyl)-1,4-dihydropyridine-5-carboxylate (**7**; $C_{20}H_{24}N_2O_8$)

Yield: 55% ; yellow oil; ^{1}H NMR ($CDCl_3$, δ, 500 MHz): 8.09 (d, $2H_{ar}$), 7.52 (d, $2H_{ar}$, $J = 8.8$ Hz), 7.19 (s, NH), 6.04 (s, CH), 5.21 (s, H-4), 4.10 (q, OCH_2), 3.68 (s, OCH_3), 3.47, 3.42 (s, OCH_3), 2.43 (s, CH_3), 1.23 (t, CH_3), ppm; ^{13}C NMR ($CDCl_3$, δ, 75 MHz): 167.0 (CO_2CH_3), 166.7 (CO), 154.8 (C1′), 146.7 (C4′), 145.6 (C6), 144.5 (C2), 128.9 (C6′, C2′), 123.5 (C5′, C3′), 104.1 (C3), 102.5 (C5), 99.0 (OCHO), 60.0 (OCH_2), 55.6, 55.4 (OCH_3), 51.4 (OCH_3), 40.4 (C4), 19.3, 14.4 (CH_3) ppm; IR (KBr): $\nu = 3393$ (N–H), 1697 (C=O) cm^{-1}.

Isopropyl 2-dimethoxymethyl-3-methoxycarbonyl-6-methyl-4-(4-nitrophenyl)-1,4-dihydropyridine-5-carboxylate (**8**; $C_{21}H_{26}N_2O_8$)

Yield: 57%; yellow oil; ^{1}H NMR ($CDCl_3$, δ, 500 MHz): 8.09 (d, $2H_{ar}$), 7.53 (d, $2H_{ar}$, $J = 8.8$ Hz), 7.15 (s, NH), 6.04 (s, CH), 5.19 (s, H-4), 4.98 (m, OCH), 3.68 (s, OCH_3), 3.46, 3.42 (s, OCH_3), 2.43 (s, CH_3), 1.25, 1.13 (d, CH_3, $J = 6.2$ Hz) ppm; ^{13}C NMR ($CDCl_3$, δ, 75 MHz): 166.7 (CO_2CH_3), 166.4 (CO), 154.9 (C1′), 146.7 (C4′), 145.3 (C6), 144.5 (C2), 129.0 (C6′, C2′), 123.4 (C5′, C3′), 104.1 (C3), 102.8 (C5), 99.0 (OCHO), 67.4 (OCH), 55.6, 55.3 (OCH_3), 51.4 (OCH_3), 40.4 (C4), 22.1, 21.9, 19.3 (CH_3) ppm; IR (KBr): $\nu = 3383$ (N–H), 1697 (C=O) cm^{-1}.

Ethyl 2-dimethoxymethyl-3-methoxycarbonyl-6-methyl-4-(5-nitro-2-furyl)-1,4-dihydropyridine-5-carboxylate (**9**; $C_{18}H_{22}N_2O_9$)

Yield: 73%; m.p.: 109–111°C; ^{1}H NMR ($CDCl_3$, δ, 500 MHz): 7.16 (d, H-4′), 7.03 (s, NH), 6.24 (d, H-3′, $J = 3.7$ Hz), 5.96 (s, CH), 5.25 (s, H-4), 4.14 (q, OCH_2), 3.68 (s, OCH_3), 3.43, 3.37 (s, OCH_3), 2.33 (s, CH_3), 1.25 (t, CH_3) ppm; ^{13}C NMR ($CDCl_3$, δ, 75 MHz): 166.4 (CO_2CH_3), 166.0 (CO), 161.8 (C2′), 151.1 (C5′), 146.2 (C6), 145.8 (C2), 112.9 (C4′), 108.7 (C3′), 99.5 (C3), 98.7 (C5), 98.2 (OCHO), 60.2 (OCH_2), 55.7, 54.2 (OCH_3), 51.6 (OCH_3), 34.5 (C4), 19.5, 14.3 (CH_3) ppm; IR (KBr): $\nu = 3314$ (N–H), 1701 (C=O) cm^{-1}.

Isopropyl 2-dimethoxymethyl-3-methoxycarbonyl-6-methyl-4-(5-nitro-2-furyl)-1,4-dihydropyridine-5-carboxylate (**10**; $C_{19}H_{24}N_2O_9$)

Yield: 65%; m.p.: 94.5–97°C; ^{1}H NMR ($CDCl_3$, δ, 500 MHz): 7.18 (d, H-4′), 7.00 (s, NH), 6.28 (d, H-3′, $J = 3.7$ Hz), 6.00 (s, CH), 5.28 (s, H-4), 5.07 (m, OCH), 3.74 (s, OCH_3), 3.50, 3.45 (s, OCH_3), 2.37 (s, CH_3), 1.28, 1.25 (d, CH_3, $J = 6.2$ Hz) ppm; ^{13}C NMR ($CDCl_3$, δ, 75 MHz): 166.4 (CO_2CH_3), 166.0 (CO), 161.8 (C2′), 151.1 (C5′), 146.2 (C6), 145.9 (C2), 112.9 (C4′), 108.7 (C3′), 99.5 (C3), 98.7 (C5), 98.2 (OCHO), 67.7 (OCH), 55.7, 54.2 (OCH_3), 51.6 (OCH_3), 34.5 (C4), 23.1, 22.0, 19.5 (CH_3) ppm; IR (KBr): $\nu = 3337$ (N–H), 1674 (C=O) cm^{-1}.

Ethyl 2-dimethoxymethyl-4-(2-furyl)-3-methoxycarbonyl-6-methyl-1,4-dihydropyridine-5-carboxylate (**11**; $C_{18}H_{23}NO_7$)

Yield: 70%; yellow oil; ^{1}H NMR ($CDCl_3$, δ, 500 MHz): 7.20 (dd, H-5′), 6.84 (s, NH), 6.20 (dd, H-4′, $J_1 = 3.2$, $J_2 = 1.8$ Hz), 6.04 (s, CH), 5.97 (dd, H-3′, $J_1 = 3.2$, $J_2 = 0.8$ Hz), 5.23 (s, H-4), 4.17 (q, OCH_2), 3.72 (s, OCH_3), 3.46, 3.39 (s, OCH_3), 2.35 (s, CH_3), 1.27 (t, CH_3) ppm; ^{13}C NMR ($CDCl_3$, δ, 75 MHz): 167.1 (CO_2CH_3), 166.9 (CO), 158.2 (C2′), 145.5 (C6), 144.6 (C2), 141.1 (C5′), 110.2 (C4′), 104.7 (C3′), 101.7 (C3), 100.2 (C5), 98.5 (OCHO), 59.8 (OCH_2), 55.4, 54.4 (OCH_3), 51.3 (OCH_3), 33.6 (C4), 19.2, 14.4 (CH_3) ppm; IR (KBr): $\nu = 3340$ (N–H), 1680 (C=O) cm^{-1}.

Isopropyl 2-dimethoxymethyl-4-(2-furyl)-3-methoxycarbonyl-6-methyl-1,4-dihydropyridine-5-carboxylate (**12**; $C_{19}H_{25}NO_7$)

Yield: 71%; yellow oil; ^{1}H NMR ($CDCl_3$, δ, 500 MHz): 7.21 (dd, H-5′), 6.82 (s, NH), 6.25 (dd, H-4′, $J_1 = 3.2$, $J_2 = 1.8$ Hz), 6.08 (dd, H-3′, $J_1 = 3.2$, $J_2 = 0.8$ Hz), 6.03 (s, CH), 5.21 (s, H-4), 5.05 (m, OCH), 3.72 (s, OCH_3), 3.47, 3.40 (s, OCH_3), 2.34 (s, CH_3), 1.26, 1.21 (d, CH_3, $J = 6.2$ Hz) ppm; ^{13}C NMR ($CDCl_3$, δ, 75 MHz): 166.8 (CO_2CH_3), 166.6 (CO), 158.4 (C2′), 145.2 (C6), 147.0 (C5′), 144.7 (C2), 110.2 (C4′), 104.7 (C3′), 101.5 (C3), 100.5 (C5), 98.6 (OCHO), 66.9 (OCH), 55.3, 54.4 (OCH_3), 51.2 (OCH_3), 33.6 (C4), 22.0, 21.8, 19.0 (CH_3) ppm; IR (KBr): $\nu = 3361$ (N–H), 1685 (C=O) cm^{-1}.

General procedure for the preparation of 2-formyl-1,4-dihydropyridines (**13**–**22**)

To a solution of **3**–**12** (2.3 mmol) in 10 cm^3 acetone, 1.5 cm^3 6 *N* HCl were added, and the mixture was stirred for 3 h at room temperature. After the reaction was completed, the solvent was removed to give a residue which was pulverized by addition of 10 cm^3 H_2O. The suspension was extracted with 20 cm^3 ethyl acetate, and the extract was washed with 15 cm^3 aqueous solution of $NaHCO_3$ (10%) and then twice with 10 cm^3 H_2O. The dried solution was concentrated to give **13**–**22** as an oil which was crystallized from a mixture of AcOEt and hexane. The crystals were collected by filtration and dried.

Ethyl 2-formyl-3-methoxycarbonyl-6-methyl-4-(2-nitrophenyl)-1,4-dihydropyridine-5-carboxylate (**13**; $C_{18}H_{18}N_2O_7$)

Yield: 94%; m.p.: 148–150°C; ^{1}H NMR ($CDCl_3$, δ, 500 MHz): 10.38 (s, CHO), 7.79–7.33 (m, $4H_{ar}$), 6.94 (s, NH), 5.99 (s, H-4), 4.08 (q, OCH_2), 3.72 (s, OCH_3), 2.43 (s, CH_3), 1.16 (t, CH_3) ppm; ^{13}C NMR ($CDCl_3$, δ, 75 MHz): 186.4 (CHO), 166.7 (CO_2CH_3), 165.8 (CO), 147.8 (C2′), 144.8 (C6), 140.5 (C1′), 138.9 (C2), 133.3 (C5′), 131.3 (C6′), 127.9 (C4′), 124.3 (C3′), 116.2 (C3), 103.0 (C5), 60.3 (OCH_2), 52.3 (OCH_3) 35.5 (C4), 19.6, 14.1 (CH_3) ppm; IR (KBr): $\nu = 3337$ (N–H), 1696 (C=O) cm^{-1}.

Isopropyl 2-formyl-3-methoxycarbonyl-6-methyl-4-(2-nitrophenyl)-1,4-dihydropyridine-5-carboxylate (**14**; $C_{19}H_{20}N_2O_7$)

Yield: 92%; m.p.: 125–127°C; ^{1}H NMR ($CDCl_3$, δ, 500 MHz): 10.34 (s, CHO), 7.80–7.33 (m, $4H_{ar}$), 6.90 (s, NH), 5.99 (s, H-4), 4.98 (m, OCH), 3.71 (s, OCH_3), 2.45 (s, CH_3), 1.24, 0.98 (d, CH_3, $J = 6.2$ Hz) ppm; ^{13}C NMR ($CDCl_3$, δ, 75 MHz): 186.0 (CHO), 166.1 (CO_2CH_3), 165.8 (CO), 147.7 (C2′), 144.7 (C6), 140.8 (C1′), 138.7 (C2), 133.3 (C5′), 131.5 (C6′), 127.9 (C4′), 124.4 (C3′), 116.1 (C3), 103.2 (C5), 67.7 (OCH), 52.3 (OCH_3), 35.6 (C4), 21.7, 21.4, 19.6 (CH_3) ppm; IR (KBr): $\nu = 3345$ (N–H), 1705 (C=O) cm^{-1}.

Ethyl 2-formyl-3-methoxycarbonyl-6-methyl-4-(3-nitrophenyl)-1,4-dihydropyridine-5-carboxylate (**15**; $C_{18}H_{18}N_2O_7$)

Yield: 95%; m.p.: 143–145°C; ^{1}H NMR ($CDCl_3$, δ, 500 MHz): 10.49 (s, CHO), 8.12–7.43 (m, $4H_{ar}$), 7.04 (s, NH), 5.25 (s, H-4), 4.13 (q, OCH_2), 3.79 (s, OCH_3), 2.45 (s, CH_3), 1.25 (t, CH_3) ppm; ^{13}C NMR ($CDCl_3$, δ, 75 MHz): 186.4 (CHO), 166.4 (CO_2CH_3), 165.7 (CO), 148.4 (C3′), 147.7 (C1′), 144.9 (C6), 139.0 (C2), 134.2 (C6′), 129.2 (C5′), 123.0 (C2′), 122.1 (C4′), 114.5 (C3), 102.2 (C5), 60.3 (OCH_2), 52.3 (OCH_3), 40.7 (C4), 19.5, 14.2 (CH_3) ppm; IR (KBr): $\nu = 3344$ (N–H), 1701 (C=O) cm^{-1}.

Isopropyl 2-formyl-3-methoxycarbonyl-6-methyl-4-(3-nitrophenyl)-1,4-dihydropyridine-5-carboxylate (**16**; $C_{19}H_{20}N_2O_7$)

Yield: 91%; m.p.: 147–149°C; ^{1}H NMR ($CDCl_3$, δ, 500 MHz): 10.49 (s, CHO) 8.12–7.43 (m, $4H_{ar}$), 7.00 (s, NH), 5.23 (s, H-4), 4.98 (m, OCH), 3.78 (s, OCH_3), 2.44 (s, CH_3), 1.27, 1.11 (d, CH_3, $J = 6.2$ Hz) ppm; ^{13}C NMR ($CDCl_3$, δ, 75 MHz): 186.5 (CHO), 166.1 (CO_2CH_3), 165.8 (CO), 148.3 (C3′), 147.9 (C1′), 144.6 (C6), 139.1 (C2), 134.3 (C6′), 129.2 (C5′), 123.1 (C2′), 122.1 (C4′), 114.5 (C3), 102.6 (C5), 67.8 (OCH), 52.4 (OCH_3), 40.9 (C4), 22.1, 21.8, 19.6 (CH_3) ppm; IR (KBr): $\nu = 3366$ (N–H), 1701 (C–O) cm^{-1}.

Ethyl 2-formyl-3-methoxycarbonyl-6-methyl-4-(4-nitrophenyl)-1,4-dihydropyridine-5-carboxylate (**17**; $C_{18}H_{18}N_2O_7$)

Yield: 93%; orange oil; ^{1}H NMR ($CDCl_3$, δ, 500 MHz): 10.48 (s, CHO), 8.11 (d, $2H_{ar}$), 7.44 (d, $2H_{ar}$, $J = 8.9$ Hz), 7.03 (s, NH), 5.25 (s, H-4), 4.11 (q, OCH_2), 3.78 (s, OCH_3), 2.44 (s, CH_3), 1.23 (t, CH_3) ppm; ^{13}C NMR ($CDCl_3$, δ, 75 MHz): 186.4 (CHO), 166.5 (CO_2CH_3), 165.8 (CO), 152.7 (C1′), 147.0 (C4′), 144.8 (C6), 139.1 (C2), 128.9 (C6′, C2′), 123.7 (C5′, C3′), 114.5 (C3), 102.2 (C5), 60.4 (OCH_2), 52.4 (OCH_3), 41.0 (C4), 19.6, 14.3 (CH_3) ppm; IR (KBr): $\nu = 3354$ (N–H), 1701 (C=O) cm^{-1}.

Isopropyl 2-formyl-3-methoxycarbonyl-6-methyl-4-(4-nitrophenyl)-1,4-dihydropyridine-5-carboxylate (**18**; $C_{19}H_{20}N_2O_7$)

Yield: 95%; m.p.: 126–128°C; ^{1}H NMR ($CDCl_3$, δ, 500 MHz): 10.48 (s, CHO), 8.11 (d, $2H_{ar}$), 7.47 (d, $2H_{ar}$, $J = 8.9$ Hz), 7.14 (s, NH), 5.24 (s, H-4), 4.98 (m, OCH), 3.79 (s, OCH_3), 2.45 (s, CH_3), 1.26, 1.13 (d, CH_3, $J = 6.2$ Hz) ppm; ^{13}C NMR ($CDCl_3$, δ, 75 MHz): 186.6 (CHO), 167.0 (CO_2CH_3), 165.8 (CO), 153.0 (C1′), 146.9 (C4′), 144.8 (C6), 139.9 (C2), 129.0 (C6′, C2′), 123.6 (C5′, C3′), 114.4 (C3), 102.4 (C5), 67.8 (OCH), 52.3 (OCH_3), 41.0 (C4), 22.1, 21.8, 19.5 (CH_3) ppm; IR (KBr): $\nu = 3370$ (N–H), 1697 (C=O) cm^{-1}.

Ethyl 2-formyl-3-methoxycarbonyl-6-methyl-4-(5-nitro-2-furyl)-1,4-dihydropyridine-5-carboxylate (**19**; $C_{16}H_{16}N_2O_8$)

Yield: 75%; m.p.: 101–103°C; ^{1}H NMR ($CDCl_3$, δ, 500 MHz): 10.52 (s, CHO), 7.19 (d, H-4′), 7.17 (s, NH), 6.30 (d, H-3′, $J = 3.7$ Hz), 5.41 (s, H-4), 4.21 (q, OCH_2), 3.86 (s, OCH_3), 2.44 (s, CH_3), 1.29 (t, CH_3) ppm; ^{13}C NMR ($CDCl_3$, δ, 75 MHz): 186.0 (CHO), 166.1 (CO_2CH_3), 165.4 (CO), 160.1 (C2′), 151.5 (C5′), 146.3 (C6), 140.1 (C2), 112.7 (C4′), 109.7 (C3), 109.5 (C3′), 98.3 (C5), 60.6 (OCH_2), 52.6 (OCH_3), 35.3 (C4), 19.6, 14.3 (CH_3) ppm; IR (KBr): $\nu = 3343$ (N–H), 1689 (C=O) cm^{-1}.

Isopropyl 2-formyl-3-methoxycarbonyl-6-methyl-4-(5-nitro-2-furyl)-1,4-dihydropyridine-5-carboxylate (**20**; $C_{17}H_{18}N_2O_8$)

Yield: 79%; m.p.: 128–130°C; ^{1}H NMR ($CDCl_3$, δ, 500 MHz): 10.51 (s, CHO), 7.20 (d, H-4′), 7.17 (s, NH), 6.30 (d, H-3′, $J = 3.7$ Hz), 5.38 (s, H-4), 5.07 (m, OCH), 3.86 (s, OCH_3), 2.43 (s, CH_3), 1.30, 1.24 (d, CH_3, $J = 6.2$ Hz) ppm; ^{13}C NMR ($CDCl_3$, δ, 75 MHz): 186.1 (CHO), 165.6 (CO_2CH_3), 165.5 (CO), 160.3 (C2′), 151.5 (C5′), 146.0 (C6), 140.1 (C2), 112.7 (C4′), 109.6 (C3), 109.5 (C3′), 98.8 (C5), 67.7 (OCH), 52.6 (OCH_3), 35.3 (C4), 22.1, 21.9, 19.5 (CH_3) ppm; IR (KBr): $\nu = 3345$ (N–H), 1705 (C=O) cm^{-1}.

Ethyl 2-formyl-4-(2-furyl)-3-methoxycarbonyl-6-methyl-1,4-dihydropyridine-5-carboxylate (**21**; $C_{16}H_{17}NO_6$)

Yield: 54%; m.p.: 118–119°C; ^{1}H NMR ($CDCl_3$, δ, 500 MHz): 10.49 (s, CHO), 7.24 (dd, H-5′), 7.09 (s, NH), 6.24 (dd, H-4′, $J_1 = 3.2$, $J_2 = 1.8$ Hz), 6.02 (dd, H-3′, $J_1 = 3.2$, $J_2 = 0.8$ Hz), 5.32 (s, H-4), 4.18 (q, OCH_2), 3.83 (s, OCH_3), 2.41 (s, CH_3), 1.27 (t, CH_3) ppm; ^{13}C NMR ($CDCl_3$, δ, 75 MHz): 186.6 (CHO), 166.8 (CO_2CH_3), 166.1 (CO), 156.5 (C2′), 145.2 (C6), 141.8 (C5′), 139.5 (C2), 112.1 (C3), 110.4 (C4′), 105.7 (C3′), 99.7 (C5), 60.1 (OCH_2), 52.3 (OCH_3), 34.4 (C4), 19.4, 14.3 (CH_3) ppm; IR (KBr): $\nu = 3360$ (N–H), 1696 (C=O) cm^{-1}.

Isopropyl 2-formyl-4-(2-furyl)-3-methoxycarbonyl-6-methyl-1,4-dihydropyridine-5-carboxylate (**22**; $C_{17}H_{19}NO_6$)

Yield: 51%; m.p.: 96–98°C; ^{1}H NMR ($CDCl_3$, δ, 500 MHz): 10.49 (s, CHO), 7.24 (dd, H-5′), 7.00 (s, NH), 6.25 (dd, H-4′, $J_1 = 3.2$, $J_2 = 1.8$ Hz), 6.03 (dd, H-3′, $J_1 = 3.2$, $J_2 = 0.8$ Hz), 5.29 (s, H-4), 5.05 (m, OCH), 3.83 (s, OCH_3), 2.40 (s, CH_3), 1.27, 1.21 (d, CH_3, $J = 6.2$ Hz) ppm; ^{13}C NMR ($CDCl_3$, δ, 75 MHz): 186.7 (CHO), 166.3 (CO_2CH_3), 166.2 (CO), 156.7 (C2′), 144.7 (C6), 141.7 (C5′), 139.5 (C2), 112.1 (C3), 110.4 (C4′), 105.7 (C3′), 100.2 (C5), 67.3 (OCH), 52.3 (OCH_3), 34.5 (C4), 22.1, 21.9, 19.5 (CH_3) ppm; IR (KBr): $\nu = 3349$ (N–H), 1697 (C=O) cm^{-1}.

General procedure for the preparation of 3-amino-2-benzoylindolizines **23–32**

A mixture of 1.3 mmol **13–22** 0.19 g 3-phenyl-3-oxopropanenitrile (1.3 mmol) and 3 drops piperidine in 3 cm^3 EtOH was refluxed for 3–6 h. After standing at 0°C overnight, the precipitates were filtered, dried, and recrystallized from ethanol.

3-Amino-2-benzoyl-5-methyl-7-(2-nitrophenyl)indolizine-6,8-dicarboxylic acid 6-ethyl-8-methyl ester (**23**; $C_{27}H_{23}N_3O_7$)

Yield: 93%; m.p.: 159–161°C; ^{1}H NMR ($CDCl_3$, δ, 500 MHz): 8.32–7.33 (m, $9H_{ar}$), 6.81 (s, H-1), 6.07 (s, NH_2), 3.82 (q, OCH_2), 3.48 (s, OCH_3), 2.96 (s, CH_3), 0.91 (t, CH_3) ppm; ^{13}C NMR ($CDCl_3$, δ, 75 MHz): 193.2 (COPh), 166.8 (CO), 165.3 (CO_2CH_3), 148.3 (C2′), 142.9 (C3), 140.1 (C1″), 136.6 (C1′), 136.2 (C5), 132.8 (C5′), 131.5 (C6′), 131.3 (C4″), 128.9 (C4′), 128.8 (C2″), 128.2 (C3″), 127.2 (C7), 124.2 (C3′), 123.2 (C8), 120.6 (C6), 120.0 (C8a), 109.5 (C2), 103.4 (C1), 61.5 (OCH_2), 51.9 (OCH_3), 18.2 (CH_3), 13.5 (CH_3) ppm; IR (KBr): $\nu = 3474$ (N–H), 1721 (C=O) cm^{-1}; MS: *m/z* (%) = 501 ($M^{+\bullet}$, 59), 411 (9), 396 (9), 395 (9), 106 (11), 105 (100), 77 (56).

3-Amino-2-benzoyl-5-methyl-7-(2-nitrophenyl)indolizine-6,8-dicarboxylic acid 6-isopropyl-8-methyl ester (**24**; $C_{28}H_{25}N_3O_7$)

Yield: 88%; m.p.: 169–172°C; ^{1}H NMR ($CDCl_3$, δ, 500 MHz): 8.35–7.33 (m, $9H_{ar}$), 6.85 (s, H-1), 6.05 (s, NH_2), 4.76 (m, OCH), 3.47 (s, OCH_3), 2.97 (s, CH_3), 0.99 (d, CH_3, $J = 6.3$ Hz) ppm; ^{13}C NMR ($CDCl_3$, δ, 75 MHz): 193.2 (COPh), 166.2 (CO), 165.3 (CO_2CH_3), 148.5 (C2′), 142.8 (C3), 140.2 (C1″), 135.8 (C5), 133.6 (C1′), 132.8 (C5′), 131.7 (C6′), 131.3 (C4″), 128.9 (C4′), 128.8 (C2″), 128.3 (C3″), 127.2 (C7), 124.3 (C3′), 123.3 (C8), 120.7 (C6), 120.3 (C8a), 109.6 (C2), 103.3 (C1), 69.5 (OCH), 51.9 (OCH_3), 18.1, 20.9 (CH_3) ppm; IR (KBr): $\nu = 3425$ (N–H), 1723 (C=O) cm^{-1}; MS: *m/z* (%) = 515 ($M^{+\bullet}$, 58), 473 (29), 410 (12), 395 (22), 106 (10), 105 (100), 77 (56).

3-Amino-2-benzoyl-5-methyl-7-(3-nitrophenyl)indolizine-6,8-dicarboxylic acid 6-ethyl-8-methyl ester (**25**; $C_{27}H_{23}N_3O_7$)

Yield: 75%; m.p.: 177–179°C; ^{1}H NMR ($CDCl_3$, δ, 500 MHz): 8.33–7.33 (m, $9H_{ar}$), 6.72 (s, H-1), 6.33 (s, NH_2), 3.92 (q, OCH_2), 3.53 (s, OCH_3), 2.94 (s, CH_3), 0.97 (t, CH_3) ppm; ^{13}C NMR ($CDCl_3$, δ, 75 MHz): 193.0 (COPh), 166.0 (CO), 165.8 (CO_2CH_3), 147.9 (C3′), 143.1 (C3), 140.0 (C1″), 139.6 (C5), 135.3 (C6′), 134.8 (C1′), 131.4 (C4″), 129.0 (C2′), 128.8 (C2″), 128.3 (C3″), 125.8 (C7), 123.6 (C4′), 123.5 (C8), 123.2 (C6), 122.6 (C5′), 120.4 (C8a), 109.5 (C2), 103.4 (C1), 61.7 (OCH_2), 52.2 (OCH_3), 17.9 (CH_3), 13.6 (CH_3) ppm; IR (KBr): $\nu = 3428$ (N–H), 1721 (C=O) cm^{-1}; MS: *m/z* (%) = 501 ($M^{+\bullet}$, 87), 471 (15), 469 (10), 468 (20), 368 (8), 339 (23), 106 (10), 105 (100), 85 (20), 77 (48).

3-Amino-2-benzoyl-5-methyl-7-(3-nitrophenyl)indolizine-6,8-dicarboxylic acid 6-isopropyl-8-methyl ester (**26**; $C_{28}H_{25}N_3O_7$)

Yield: 72%; m.p.: 158–160°C; ^{1}H NMR ($CDCl_3$, δ, 500 MHz): 8.32–7.33 (m, $9H_{ar}$), 6.71 (s, H-1), 6.02 (s, NH_2), 4.80 (m, OCH), 3.52 (s, OCH_3), 2.94 (s, CH_3), 0.96 (d, CH_3, $J = 6.3$ Hz) ppm; ^{13}C NMR ($CDCl_3$, δ, 75 MHz): 193.1 (COPh), 166.5 (CO), 165.8 (CO_2CH_3), 147.9 (C3′), 143.0 (C3), 140.0 (C1″), 139.5 (C5), 134.9 (C6′), 134.9 (C1′), 131.4 (C4″), 129.0 (C2′), 128.7 (C2″), 128.3 (C3″), 125.8 (C7), 123.7 (C4′), 123.5 (C8), 123.2 (C6), 122.6 (C5′), 120.6 (C8a), 109.5 (C2), 102.9 (C1), 69.7 (OCH), 52.2 (OCH_3), 21.2, 17.8 (CH_3) ppm; IR (KBr): $\nu = 3501$ (N–H), 1728

(C=O) cm^{-1}; MS: *m/z* (%) = 515 ($M^{+\bullet}$, 44), 474 (14), 473 (42), 410 (8), 368 (12), 106 (9), 105 (100), 77 (56).

3-Amino-2-benzoyl-5-methyl-7-(4-nitrophenyl)indolizine-6,8-dicarboxylic acid 6-ethyl-8-methyl ester (**27**; $C_{27}H_{23}N_3O_7$)

Yield: 73%; m.p.: 154–155°C; ^{1}H NMR ($CDCl_3$, δ, 500 MHz): 8.31–7.34 (m, $9H_{ar}$), 6.72 (s, H-1), 6.33 (s, NH_2), 3.91 (q, OCH_2), 3.52 (s, OCH_3), 2.96 (s, CH_3), 0.92 (t, CH_3) ppm; ^{13}C NMR ($CDCl_3$, δ, 75 MHz): 193.0 (COPh), 167.0 (CO), 165.8 (CO_2CH_3), 147.2 (C4′), 145.1 (C1′), 143.2 (C3), 140.0 (C1″), 135.5 (C5), 131.4 (C4″), 129.5 (C2′, C6′), 128.7 (C2″), 128.3 (C3″), 126.0 (C7), 123.4 (C8), 123.2 (C6), 123.2 (C3′, C5′), 120.1 (C8a), 109.6 (C2), 103.1 (C1), 61.7 (OCH_2), 52.2 (OCH_3), 17.9, 13.6 (CH_3) ppm; IR (KBr): ν = 3399 (N–H), 1722 (C=O) cm^{-1}; MS: *m/z* (%) = 501 ($M^{+\bullet}$, 41), 396 (20), 106 (10), 105 (100), 77 (49).

3-Amino-2-benzoyl-5-methyl-7-(4-nitrophenyl)indolizine-6,8-dicarboxylic acid 6-isopropyl-8-methyl ester (**28**; $C_{28}H_{25}N_3O_7$)

Yield: 75%; m.p.: 183–185°C; ^{1}H NMR ($CDCl_3$, δ, 500 MHz): 8.33–7.34 (m, $9H_{ar}$), 6.71 (s, H-1), 6.33 (s, NH), 4.80 (m, OCH), 3.51 (s, OCH_3), 2.94 (s, CH_3), 0.93 (d, CH_3, J = 6.3 Hz) ppm: ^{13}C NMR ($CDCl_3$, δ, 75 MHz): 193.0 (COPh), 167.5 (CO), 165.8 (CO_2CH_3), 147.2 (C4′), 144.9 (C1′), 143.2 (C3), 140.0 (C1″), 135.1 (C5), 131.4 (C4″), 129.7 (C2′, C6′), 128.7 (C2″), 128.3 (C3″), 125.9 (C7), 123.4 (C8), 123.2 (C6), 123.2 (C3′, C5′), 120.3 (C8a), 109.5 (C2), 103.0 (C1), 69.7 (OCH), 52.2 (OCH_3), 21.2, 17.7 (CH_3) ppm; IR (KBr): ν = 3426 (N–H), 1718 (C=O) cm^{-1}; MS: *m/z* (%) = 515 ($M^{+\bullet}$, 34), 501 (17), 473 (37), 410 (15), 396 (10), 368 (17), 106 (10), 105 (100), 77 (44).

3-Amino-2-benzoyl-5-methyl-7-(5-nitro-2-furyl)indolizine-6,8-dicarboxylic acid 6-ethyl-8-methyl ester (**29**; $C_{25}H_{21}N_3O_8$)

Yield: 91%; m.p.: 176–178°C; ^{1}H NMR ($CDCl_3$, δ, 500 MHz): 7.81–7.32 (m, $6H_{ar}$), 6.71 (s, H-1), 6.51 (d, H-3′, J = 3.7 Hz), 6.42 (s, NH_2), 4.25 (q, OCH_2), 3.80 (s, OCH_3), 2.94 (s, CH_3), 1.24 (t, CH_3) ppm; ^{13}C NMR ($CDCl_3$, δ, 75 MHz): 192.8 (COPh), 167.1 (CO), 165.7 (CO_2CH_3), 152.4 (C2′), 151.5 (C5′), 144.0 (C3), 139.7 (C1″), 135.1 (C5), 131.6 (C4″), 128.7 (C2″), 128.2 (C3″), 126.0 (C7), 122.8 (C8a), 117.7 (C8), 113.1 (C4′), 112.3 (C6), 111.7 (C3′), 110.0 (C2), 105.4 (C1), 62.4 (OCH_2), 53.0 (OCH_3), 17.6, 13.9 (CH_3) ppm; IR (KBr): ν = 3474 (N–H), 1723 (C=O) cm^{-1}; MS: *m/z* (%) = 491 ($M^{+\bullet}$, 35), 459 (11), 430 (11), 357 (11), 106 (11), 105 (100), 77 (54).

3-Amino-2-benzoyl-5-methyl-7-(5-nitro-2-furyl)indolizine-6,8-dicarboxylic acid 6-isopropyl-8-methyl ester (**30**; $C_{26}H_{23}N_3O_8$)

Yield: 93%; m.p.: 217–219°C; ^{1}H NMR ($CDCl_3$, δ, 500 MHz): 7.81–7.32 (m, $6H_{ar}$), 6.74 (s, H-1), 6.54 (d, H-3′, J = 3.7 Hz), 6.13 (s, NH_2), 5.10 (m, OCH), 3.80 (s, OCH_3), 2.96 (s, CH_3), 1.24 (d, CH_3, J = 6.2 Hz) ppm; ^{13}C NMR ($CDCl_3$, δ, 75 MHz): 193.0 (COPh), 166.4 (CO), 165.7 (CO_2CH_3), 152.5 (C2′), 151.6 (C5′), 143.8 (C3), 139.8 (C1″), 134.7 (C5), 131.6 (C4″), 128.7 (C2″), 128.2 (C3″), 126.2 (C7), 122.9 (C8a), 118.3 (C8), 113.0 (C4′), 112.5 (C6), 111.9 (C3′), 110.1 (C2), 105.4 (C1), 69.1 (OCH), 53.0 (OCH_3), 21.6, 17.6 (CH_3) ppm; IR (KBr): ν = 3472 (N–H), 1720 (C=O) cm^{-1}; MS: *m/z* (%) = 505 ($M^{+\bullet}$, 38), 464 (20), 358 (9), 357 (10), 106 (10), 105 (100).

3-Amino-2-benzoyl-7-(2-furyl)-5-methylindolizine-6,8-dicarboxylic acid 6-ethyl-8-methyl ester (**31**; $C_{25}H_{22}N_2O_6$)

Yield: 82%; m.p.: 142–144°C; ^{1}H NMR ($CDCl_3$, δ, 500 MHz): 7.83–7.32 (m, $5H_{ar}$), 6.55 (s, H-1), 6.42 (dd, H-4′, J_1 = 3.2, J_2 = 1.8 Hz), 6.33 (s, NH_2), 6.30 (dd, H-3′, J_1 = 3.2, J_2 = 0.8 Hz), 4.13 (q,

OCH_2), 3.69 (s, OCH_3), 2.88 (s, CH_3), 1.13 (t, CH_3) ppm; ^{13}C NMR ($CDCl_3$, δ, 75 MHz): 192.8 (COPh), 167.8 (CO), 166.6 (CO_2CH_3), 149.2 (C2′), 143.6 (C3), 142.5 (C5′), 140.1 (C1″), 134.8 (C5), 131.2 (C4″), 128.6 (C2″), 128.2 (C3″), 123.3 (C8a), 123.2 (C7), 118.8 (C8), 116.0 (C6), 111.5 (C4′), 109.4 (C2), 109.1 (C3′), 102.6 (C1), 61.8 (OCH_2), 52.4 (OCH_3), 17.5, 13.5 (CH_3) ppm; IR (KBr): $\nu = 3474$ (N–H), 1723 (C=O) cm^{-1}; MS: *m/z* (%) = 446 ($M^{+\bullet}$, 100), 419 (9), 387 (15), 359 (10), 342 (26), 106 (9), 105 (78), 77 (38).

3-Amino-2-benzoyl-7-(2-furyl)-5-methylindolizine-6,8-dicarboxylic acid 6-isopropyl-8-methyl ester (**32**; $C_{26}H_{24}N_2O_6$)

Yield: 90%; m.p.: 153–155°C; ^1H NMR ($CDCl_3$, δ, 500 MHz): 7.83–7.32 (m, $5H_{ar}$), 6.57 (s, H-1), 6.42 (dd, H-4′, $J_1 = 3.2$, $J_2 = 1.8$ Hz), 6.35 (s, NH_2), 6.31 (dd, H-3′, $J_1 = 3.2$, $J_2 = 0.8$ Hz), 5.02 (m, OCH), 3.70 (s, OCH_3), 2.90 (s, CH_3), 1.15 (d, CH_3, $J = 6.2$ Hz) ppm; ^{13}C NMR ($CDCl_3$, δ, 75 MHz): 192.9 (COPh), 167.0 (CO), 166.6 (CO_2CH_3), 149.2 (C2′), 143.3 (C3), 142.4 (C5′), 140.1 (C1″), 134.2 (C5), 131.2 (C4″), 128.7 (C2″), 128.3 (C3″), 123.4 (C8a), 123.4 (C7), 119.4 (C8), 116.1 (C6), 111.4 (C4′), 109.4 (C2), 109.2 (C3′), 102.6 (C1), 69.6 (OCH), 52.4 (OCH_3), 21.5, 17.5 (CH_3) ppm; IR (KBr): $\nu = 3467$ (N–H), 1717 (C=O) cm^{-1}; MS: *m/z* (%) = 460 ($M^{+\bullet}$, 55), 419 (13), 418 (44), 359 (11), 313 (10), 113 (14), 111 (10), 105 (78), 99 (18), 97 (21), 77 (36).

Isopropyl 2-(2-benzoylvinyl-2-cyano)-3-methoxycarbonyl-6-methyl-4-(3-nitrophenyl)-1,4-dihydropyridine-5-carboxylate (**33**; $C_{28}H_{25}N_3O_7$)

To a solution of 388 mg **16** (1 mmol) in 18 cm^3 anhydrous ethanol, 145 mg 3-phenyl-3-oxopropanenitrile (1 mmol) and 1 drop piperidine were added, and then the mixture was stirred at room temperature until no starting material could be detected (TLC). After standing at 0°C overnight the precipitate was filtered, dried, and recrystallized from 2-propanol.

Yield: 78%; m.p.: 176–178°C; ^1H NMR (*DMSO*-d_6, δ, 500 MHz): 0.95 and 1.15 (d, d, 6H, $J = 6.2$ Hz, $CH(CH_3)_2$), 2.22 (s, 3H, C-6–CH_3), 3.67 (s, 3H, OCH_3), 4.75 (m, 1H, $CH(CH_3)_2$), 5.11 (s, 1H, C-4–H), 7.56–8.11 (m, 9H, H), 8.12 (s, 1H, =C–H), 8.43 (s, 1H, NH) ppm; IR (KBr): $\nu = 3348$ (NH), 2228 (CN), 1699 and 1676 (C=O) cm^{-1}; MS: *m/z* = 515 ($M^{+\bullet}$), 473, 428, 105.

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