A Novel Approach for the Synthesis of 5-Pyridylindolizine Derivatives *via* 2-(2-Pyridyl)pyridinium Ylides

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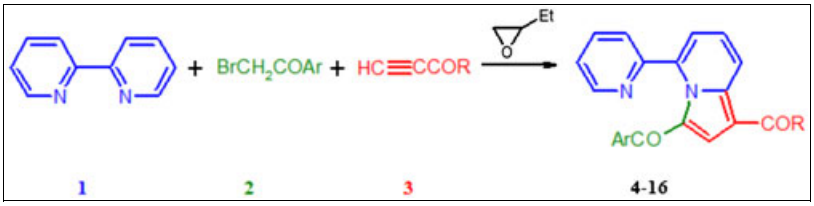

New indolizine derivatives were synthesized by an efficient one-pot three-component procedure starting from commercially available materials such as 2,2′-dipyridyl, substituted bromoacetophenones, and electron-poor alkynes in 1,2-epoxybutane as reaction solvent and acid scavenger.

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INTRODUCTION

Indolizine is a simple heteroaromatic isomeric with 1*H*-indole molecule. The variety of biological activities [1–9] and the well-known fluorescence properties of indolizine derivatives [10–12] and of pyridyl indolizines in particular [13–17] make them important synthetic targets.

Two general ways of indolizine synthesis are known [18–20]. The first way is based on intramolecular condensation of suitable substituted pyridine precursors [18–20]. The second route is based on 1,3-dipolar cycloaddition reactions of pyridinium-ylides with activated carbon—carbon multiple bonds [14–22]. Monosubstituted pyridinium *N*-ylides dipols are generally unstable compounds, and they are generated *in situ* by treatment of pyridinium salts with an organic or inorganic base.

Sequential transformations, multicomponent processes, and one-pot procedures have become increasingly interesting because they offer simple and efficient synthetic ways to pyrroloazines [23–30].

Herein, we present an efficient one-pot three-component synthesis of 5-(2-pyridyl)indolizines on the basis of consecutive quaternization, *N*-ylide generation, and 1,3-dipolar cycloaddition sequence.

RESULTS AND DISCUSSIONS

The synthesis of several 5-(2-pyridyl)indolizines by 1,3-dipolar cycloaddition reactions of pyridinium-*N*-ylides with activated carbon—carbon multiple bonds was already described [16,21,22]. The synthesis of 5-(2′-pyridyl) indolizines via 2-(2-pyridyl)-pyridinium-*N*-ylides implies two steps. In the first step, 2-(2-pyridyl)pyridinium salts are prepared starting from 2,2′-dipyridyl **1** and substituted bromoacetophenones **2**. Subsequently, 2-(2-pyridyl) pyridinium salts are converted into 2-(2-pyridyl)pyridinium-*N*-ylides by the treatment with an organic or inorganic base in the presence of the acetylenic dipolarophile.

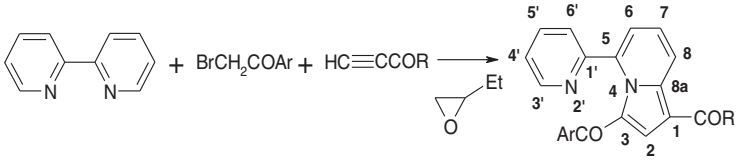
The new 5-(2-pyridyl)indolizine derivatives were synthesized by a one-pot three-component procedure. The key components of the one-pot, three-component pathway are 2,2′-dipyridyl **1**, substituted bromoacetophenones **2**, and electron-deficient alkynes **3** in 1,2-epoxybutane that acts both as solvent and proton scavenger. The reaction conditions are mild, involving only mixing of the components at reflux temperature, followed by solvent evaporation and subsequent purification by column chromatography (Scheme 1).

In the one-pot, three-component pathway, the reaction mechanism implies the intermediate formation of the 2-(2-pyridyl)pyridinium salt **17** from the corresponding 2,2′-dipyridyl **1** and 2-bromoacetophenone **2**. In the next step, the bromide ion from the 2-(2-pyridyl)pyridinium salt attacks the oxirane ring of epoxide resulting in the generation of an alkoxide. The alkoxide substracts one of the methylene protons in the bromide salt with the *in situ* generation of the *N*-ylide **18**. The *N*-ylide reacts with the activated alkyne **3** to give the corresponding dihydroindolizine that is dehydrogenated to the 5-(2-pyridyl) indolizines **4–16** (Scheme 2).

The new compounds are presented in the table as follows: Table 1

The structure of the compounds **4–16** was determined by IR and NMR spectroscopy.

Scheme 1. One-pot three-component synthesis of 5-(2-pyridyl)indolizines **4–16**.



1 2 3 4-16

4: Ar = C_6H_5, R = Me; **5**: Ar = 4-$C_6H_5C_6H_4$, R = Me; **6**: Ar = 3-$NO_2C_6H_4$, R = Me; **7**: Ar = 4-ClC_6H_4, R = Me; **8**: Ar = C_6H_5, R = OMe; **9**: Ar = 4-$C_6H_5C_6H_4$, R = OMe; **10**: Ar = 4-BrC_6H_4, R = OMe; **11**: Ar = 4-MeC_6H_4, R = OEt; **12**: Ar = 1-naphthyl, R = OEt; **13**: Ar = 2-naphthyl, R = OEt; **14**: Ar = 2-$NO_2C_6H_4$, R = OEt; **15**: Ar = 3-$NO_2C_6H_4$, R = OEt; **16**: Ar = 4-FC_6H_4, R = OEt.

Scheme 2. The reaction mechanism (R = Me, OMe, OEt).

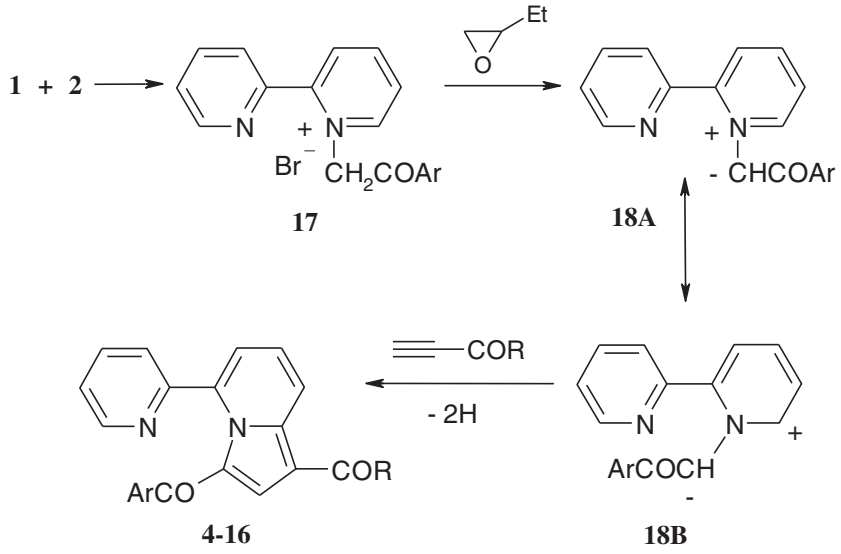


Table 1

New 5-(2-pyridyl)indolizines.

Compd.	Ar	R	mp (°C)	Yield (%)
4	C_6H_5	Me	183–185	54
5	4-$C_6H_5C_6H_4$	Me	212–214	61
6	3-$NO_2C_6H_4$	Me	212–214	44
7	4-ClC_6H_4	Me	238–240	42
8	C_6H_5	OMe	181–182	52
9	4-$C_6H_5C_6H_4$	OMe	190–192	47
10	4-BrC_6H_4	OMe	184–186	59
11	4-MeC_6H_4	OEt	202–204	43
12	1-naphthyl	OEt	199–201	46
13	2-naphthyl	OEt	166–168	43
14	2-$NO_2C_6H_4$	OEt	234–236	51
15	3-$NO_2C_6H_4$	OEt	173–175	49
16	4-FC_6H_4	OEt	186–188	48

The IR spectra of the compounds show the characteristic bands for the carbonyl groups. For all the compounds, the carbonyl group in the aroyl moiety appears in the range 1620–1647 cm^{-1}. The band for the carbonyl groups in the acetyl moiety for compounds **4–7** appears superimposed in the same range because of electronic effects that decrease the double C=O bond character. The carbonyl groups in the ester for compounds **8–16** appear in the range 1679–1703 cm^{-1}. Also, for the compounds **6**, **14**, and **15**, the vibration bands of the NO_2 group are present in the ranges 1514–1534 cm^{-1} and 1346–1356 cm^{-1}, respectively. The ^{1}H-NMR spectra show as main characteristics the signals of the hydrogen atoms H-6, H-7, and H-8 attached on the pyridine moiety of the indolizine skeleton, which appear as doublets of doublets ($J_{7,8}$ = 9.0 Hz,

$J_{6,7}$ = 7.0 Hz, and $J_{6,8}$ = 1.3 Hz). The hydrogen atom H-2 appears as a sharp singlet at ~7.20 ppm. All the signals for the aroyl and pyridine moieties attached to positions 3 and 5 respectively are in good accordance with the proposed structures and were confirmed by COSY and HETCOR experiments. The ^{13}C-NMR spectra of the compounds **4–16** present the signals of the carbon atom C-1 strongly shielded. The signal of C-1 appears in the range 114–116 ppm for compounds **4–7** because of the influence of the acetyl moiety. By replacing acetyl with a carbomethoxy group, the shielding effect is greater C-1 signal being observed at 105–106 ppm. The carbon atoms C-5, C-6, C-8, and C-8a are deshielded because of their α and γ positions in respect with the nitrogen atom. The carbon atoms in the carbonyl groups appear in expected ranges.

CONCLUSION

In conclusion, the one-pot three-component reaction of 2,2′-dipyridyl with 2-bromoacetophenones and nonsymmetrical electron-deficient alkynes in 1,2-epoxybutane is an efficient procedure for the preparation of 5-(2-pyrydil)indolizines by sequential quaternization, ylide generation, and 1,3-dipolar cycloaddition.

EXPERIMENTAL

Melting points were determined on a Boëtius hot plate microscope. The elemental analysis was carried out on a COSTECH Instruments EAS32 apparatus. The IR spectra were recorded on a Nicolet Impact 410 spectrometer in KBr pellets. The NMR spectra were recorded on a Varian Gemini 300 BB instrument, operating at 300 MHz for ^{1}H-NMR and 75 MHz for ^{13}C-NMR, using $CDCl_3$ as solvent and TMS as internal standard. Supplementary evidence was given by COSY and HETCOR experiments.

2,2′-Dipyridyl, 2-bromoacetophenones, methyl propiolate, ethyl propiolate, 3-butin-2-one, 1,2-epoxybutane, and neutral alumina were purchased from Aldrich and used without further purification.

General procedure for the synthesis of 5-(2-pyridyl) indolizines (4–16). A suspension of 2,2′-dipyridyl **1** (0.4 g, 2.5 mmol), phenacyl bromide **2** (2.5 mmol), and a nonsymmetrical acetylene **3** (3.5 mmol) in 20 mL 1,2-epoxybutane was heated at reflux temperature for 40 h. The solvent was evaporated under reduced pressure, and the residue was purified by column chromatography on neutral alumina [benzene : ethyl acetate (4:1)]. The recovered solid was crystallized from $CHCl_3$/MeOH.

1-Acetyl-3-benzoyl-5-(2-pyridyl)indolizine (4). This compound was obtained as yellow crystals; IR (ATR): 3058, 1636, 1586, 1503, 1233 cm^{-1}; ^{1}H-NMR: δ 2.53 (s, 3H, Me); 7.12–7.17 (m, 2H, 6-H, 4′-H); 7.45–7.63 (m, 5H, 2-H, 7-H, phenyl); 7.71 (dt, 1H, 6′-H, *J* = 7.7, 1.2 Hz); 7.83–7.90 (m, 3H, 5-H, phenyl); 8.22 (ddd, 1H, 3′-H, *J* = 4.8, 1.7, 0.9 Hz); 8.73 (dd, 8-H, *J* = 9.0, 1.3 Hz,); ^{13}C-NMR: δ 28.1 (Me); 114.2 (1-C); 118.7, 120.9, 122.0, 123.9, 127.2, 127.9, 138.2, 148.7 (2-C, 6-C, 7-C, 8-C, 3′-C, 4′-C, 5′-C, 6′-C); 126.4, 138.0, 139.1, 140.9, 155.1 (3-C, 5-C, 8a-C, 1′-C, 1″-C); 128.5, 129.7 (2″-C, 3″-C, 5″-C, 6″-C); 184.2 (COAr); 193.2 (COMe). *Anal*. Calcd for $C_{22}H_{16}N_2O_2$: C 77.63; H 4.74; N 8.23; Found: C 77.92; H 4.51; N 8.58.

1-Acetyl-3-(4-phenylbenzoyl)-5-(2-pyridyl)indolizine (5). This compound was obtained as yellow crystals; IR (ATR): 3065, 1642, 1625, 1570, 1507, 1236 cm^{-1}; ^{1}H-NMR: δ 2.53 (s, 3H, Me); 7.13–7.16 (m, 2H, 6-H, H-4′); 7.39–7.57 (m, 5H, 2-H, 7-H, biphenylyl); 7.66–7.74 (m, 5H, 6′-H, biphenylyl); 7.87 (td, 1H, 5′-H, *J* = 7.7, 1.7, 1.2 Hz); 7.97 (d, 2H, biphenylyl, *J* = 8.5 Hz); 8.25 (ddd, 1H, 3′-H, *J* = 4.8, 1.7, 0.9 Hz); 8.73 (dd, 8-H, *J* = 9.0, 1.3 Hz);^{13}C-NMR: δ 28.1 (Me); 114.2 (1-C); 118.6, 120.9, 122.1, 123.8, 127.2, 127.4, 127.9, 128.3, 128.6, 129.1, 130.3, 138.2, 148.7 (2-C, 6-C, 7-C, 8-C, 3′-C, 4′-C, 5′-C, 6′-C, biphenylyl); 126.5, 136.6, 139.1, 140.0, 140.9, 145.2, 148.7, 155.3 (3-C, 5-C, 8a-C, 2′-C, biphenylyl); 183.7 (COAr); 193.2 (COMe). *Anal*. Calcd for $C_{28}H_{20}N_2O_2$: C 80.75; H 4.84; N 6.73; Found: C 80.51; H 5.12; N 7.04.

1-Acetyl-3-(3-nitrobenzoyl)-5-(2-pyridyl)indolizine (6). This compound was obtained as yellow crystals; IR (ATR): 1653, 1631, 1526, 1510, 1352, 1234 cm^{-1}; ^{1}H-NMR: δ 2.52 (s, 3H, Me); 7.15–7.20 (m, 2H, 6-H, 4′-H); 7.48 (s, 1H, 2-H); 7.60 (dd, 1H, 7-H, *J* = 9.0, 7.0 Hz); 7.69 (t, 1H, 5″-H, *J* = 7.9 Hz); 7.74 (dt, 1H, 6′-H, *J* = 7.7, 1.2 Hz); 7.89 (td, 1H, H-5′, *J* = 7.7, 1.7, 1.2 Hz); 8.19–8.24 (m, 2H, 3′-H, 6″-H); 8.42–8.35 (m, 1H, 4″-H); 8.70 (t, 1H, 2″-H, *J* = 1.9 Hz); 8.75 (dd, 8-H, *J* = 9.0, 1.3 Hz); ^{13}C-NMR: δ 28.1 (Me); 114.6 (1-C); 119.1, 121.0, 122.2, 124.1, 124.3, 126.8, 127.2, 128.6, 129.7, 135.2, 138.3, 148.6 (2-C, 6-C, 7-C, 8-C, 3′-C, 4′-C, 5′-C, 6′-C, 2″-C, 4″-C, 5″-C, 6″-C); 125.6, 139.1, 139.7, 141.4, 148.4, 155.0 (3-C, 5-C, 8a-C, 2′-C, 1″-C, 3″-C); 181.3 (COAr); 193.0 (COMe); *Anal*. Calcd for $C_{22}H_{15}N_3O_4$: C 68.57; H 3.92; N 10.90; Found: C 68.89; H 4.17; N 11.21.

1-Acetyl-3-(4-chlorobenzoyl)-5-(2-pyridyl)indolizine (7). This compound was obtained as yellow crystals; IR (ATR): 1640, 1620, 1584, 1510, 1423, 1233 cm^{-1}; ^{1}H-NMR: δ 2.50 (s, 3H, Me); 7.13–7.18 (m, 2H, 6-H, 4′-H); 7.46 (d, 2H, 3″-H, 5″-H, *J* = 8.5 Hz); 7.48 (s, 1H, 2-H); 7.54 (dd, 1H, 7-H, *J* = 9.0, 7.0 Hz); 7.71 (dt, 1H, 6′-H, *J* = 7.7, 1.2 Hz); 7.83 (d, 2H, 2″-H, 6″-H, *J* = 8.5 Hz); 7.87 (td, 1H, 5′-H, *J* = 7.7, 1.7, 1.2 Hz); 8.21 (ddd, 1H, 3′-H, *J* = 4.8, 1.7, 0.9 Hz); 8.73 (dd, 8-H, *J* = 9.0, 1.3 Hz); ^{13}C-NMR: δ 28.1 (Me); 114.6 (1-C); 119.1, 120.9, 122.1, 124.0, 126.9, 128.1, 138.3, 148.6 (2-C, 6-C, 7-C, 8-C, 3′-C, 4′-C, 5′-C, 6′-C); 126.0, 136.3, 138.7, 139.0, 141.0, 155.1 (3-C, 5-C, 8a-C, 1′-C, 1″-C, 4″-C); 128.8, 131.0 (2″-C, 3″-C, 5″-C, 6″-C); 182.9 (COAr); 193.1 (COMe); *Anal*. Calcd for $C_{22}H_{15}ClN_2O_2$: C 70.50; H 4.03; Cl 9.46; N 7.47; Found: C 70.71; H 4.39; Cl 9.81; N 7.69.

Methyl 3-benzoyl-5-(2-pyridyl)indolizine-1-carboxylate (8). This compound was obtained as yellow crystals; IR (ATR): 3047, 1685, 1626, 1594, 1517 1245 cm^{-1}; ^{1}H-NMR: δ 3.89 (s, 3H, Me); 7.09 (dd, 1H, 6-H, *J* = 7.0, 1.3 Hz); 7.14 (ddd, 4′-H, *J* = 7.7, 4.8, 1.2 Hz); 7.43–7.51 (m, 3H, 7-H, 3″-H, 5″-H); 7.54–7.59 (m, 1H, 4″-H); 7.60 (s, 1H, 2-H); 7.71 (dt, 1H, 6′-H, *J* = 7.7, 1.2 Hz); 7.83–7.89 (m, 3H, 5′-H, 2″-H, 6″-H); 8.23 (ddd, 1H, 3′-H, *J* = 4.8, 1.7, 0.9 Hz); 8.47 (dd, 8-H, *J* = 9.0, 1.3 Hz); ^{13}C-NMR: δ 51.3 (Me); 105.2 (1-C); 118.0, 119.9, 122.0, 123.8, 126.7, 127.5, 138.2, 148.7 (2-C, 6-C, 7-C, 8-C, 3′-C, 4′-C, 5′-C, 6′-C); 126.2, 138.0, 139.3, 141.5, 155.4 (3-C, 5-C, 8a-C, 1′-C, 1″-C); 128.4, 129.7 (2″-C, 3″-C, 5″-C, 6″-C); 132.4 (4″-C); 164.7 (COO); 184.1 (COAr); *Anal*. Calcd for $C_{22}H_{16}N_2O_3$: C 74.15; H 4.53; N 7.86; Found 74.42; H 4.81; N 7.69.

Methyl 3-(4-phenylbenzoyl)-5-(2-pyridyl)indolizine-1-carboxylate (9). This compound was obtained as yellow crystals; IR (ATR): 3055, 1697, 1624, 1596, 1522, 1220 cm^{-1}; ^{1}H-NMR: δ 3.89 (s, 3H, Me); 7.09 (dd, 1H, 6-H, *J* = 7.0, 1.3 Hz); 7.13 (ddd, 4′-H, *J* = 7.7, 4.8, 1.2 Hz); 7.37–7.51 (m, 4H, 7-H, biphenylyl); 7.62–7.73 (m, 6H, 2-H, 6′-H, biphenylyl); 7.87 (td, 1H, 5′-H, *J* = 7.7, 1.7, 1.2 Hz); 7.96 (d, 2H, biphenylyl, *J* = 8.5 Hz); 8.25

(ddd, 1H, 3′-H, J = 4.8, 1.7, 0.9 Hz); 8.67 (dd, 8-H, J = 9.0, 1.3 Hz); ^{13}C-NMR: δ 51.3 (Me); 105.2 (1-C); 117.9, 119.9, 122.0, 123.8, 126.6, 127.1, 127.3, 127.4, 128.2, 129.0, 130.3, 138.2, 148.7 (2-C, 6-C, 7-C, 8-C, 3′-C, 4′-C, 5′-C, 6′-C, biphenylyl); 126.8, 136.6, 139.3, 140.1, 141.5, 145.1, 148.7, 155.4 (3-C, 5-C, 8a-C, 2′-C, biphenylyl); 164.7 (COOMe); 183.7 (COAr); *Anal*. Calcd for $C_{28}H_{20}N_2O_3$: C 77.76; H 4.66; N 6.48; Found: C 77.49; H 4.92; N 6.78.

Methyl 3-(4-bromobenzoyl)-5-(2-pyridyl)indolizine-1-carboxylate (10). This compound was obtained as yellow crystals; IR (ATR): 3053, 1678, 1645, 1578, 1522, 1220 cm^{-1}; ^{1}H-NMR: δ 3.89 (s, 3H, Me); 7.08 (dd, 1H, 6-H, J = 7.0, 1.3 Hz); 7.14 (ddd, 1H, 4′-H, J = 7.7, 4.8, 1.2 Hz); 7.47 (dd, 1H, 7-H, J = 9.0, 7.0 Hz); 7.58 (s, 1H, 2-H); 7.70 (dt, 1H, 6′-H, J = 7.7, 1.2 Hz); 7.60, 7.79 (2d, 4H, 2″-H, 3″-H, 5″-H, 6″-H, J = 8.5 Hz); 7.87 (td, 1H, 5′-H, J = 7.7, 1.7, 1.2 Hz); 8.21 (ddd, 1H, 3′-H, J = 4.8, 1.7, 0.9 Hz); 8.47 (dd, 8-H, J = 9.0, 1.3 Hz); ^{13}C-NMR: δ 51.3 (Me); 105.3 (1-C); 118.0, 119.9, 122.0, 123.9, 126.8, 127.1, 138.2, 148.6 (2-C, 6-C, 7-C, 8-C, 3′-C, 4′-C, 5′-C, 6′-C); 126.2, 127.4, 136.7, 139.2, 141.5, 155.2 (3-C, 5-C, 8a-C, 1′-C, 1″-C, 4″-C); 131.3, 131.7 (2″-C, 3″-C, 5″-C, 6″-C); 164.5 (COO); 182.9 (COAr); *Anal*. Calcd for $C_{22}H_{15}BrN_2O_3$: C 60.71; H 3.47; Br 18.66; N 6.44. Found: C 61.06; H 3.81; Br 18.79; N 6.79;

Ethyl 3-(4-methylbenzoyl)-5-(2-pyridyl)indolizine-1-carboxylate (11). This compound was obtained as yellow crystals; IR (ATR): 3071, 1686, 1630, 1518 1350, 1242 cm^{-1}; ^{1}H-NMR: δ 1.38 (t, 3H, J = 7.1 Hz, Me-ester, J = 7.1 Hz); 2.45 (s, 3H, Me); 4.37 (q, 2H, CH_2O, J = 7.1 Hz); 7.06 (dd, 1H, 6-H, J = 7.0, 1.3 Hz); 7.11 (ddd, 4′-H, J = 7.7, 4.8, 1.2 Hz); 7.26 (d, 2H, 3″-H, 5″-H, J = 8.2 Hz); 7.45 (dd, 1H, 7-H, J = 9.0, 7.0 Hz); 7.60 (s, 1H, 2-H); 7.69 (dt, 1H, 6′-H, J = 7.7, 1.2 Hz); 7.79 (d, 2H, 2″-H, 6″-H, J = 8.2 Hz); 7.83 (td, 1H, 5′-H, J = 7.7, 1.7, 1.2 Hz); 8.23 (ddd, 1H, 3′-H, J = 4.8, 1.7, 0.9 Hz); 8.46 (dd, 8-H, J = 9.0, 1.3 Hz); ^{13}C-NMR: δ 14.4, 21.7 (2Me); 60.1 (CH_2); 105.4 (1-C); 117.7, 119.9, 121.8, 123.7, 126.3, 127.0, 138.0, 148.6 (2-C, 6-C, 7-C, 8-C, 3′-C, 4′-C, 5′-C, 6′-C); 126.6, 135.2, 139.2, 141.2, 143.1,155.4 (3-C, 5-C, 8a-C, 1′-C, 1″-C, 4″-C); 129.1, 129.8 (2″-C, 3″-C, 5″-C, 6″-C); 164.3 (COO); 184.0 (COAr); *Anal*. Calcd for $C_{24}H_{20}N_2O_3$: C 74.98; H 5.24; N 7.29; Found: C 75.12; H 5.41; N 7.60.

Ethyl 3-(1-naphthoyl)-5-(2-pyridyl)indolizine-1-carboxylate (12). This compound was obtained as yellow crystals; IR (ATR): 3047, 1686, 1628, 1519, 1349, 1238 cm^{-1}; ^{1}H-NMR: δ 1.32 (t, 3H, Me, J = 7.1 Hz); 4.37 (q, 2H, CH_2O, J = 7.1 Hz); 7.10–7.16 (m, 2H, 6-H, 4′-H); 7.42 (s, 1H, 2-H); 7.43–7.76 (m, 6H, 7-H, 6′-H, naphthyl); 7.83–7.91 (m, 2H, 5′-H, naphthyl); 7.96–7.99 (m, 1H, naphthyl); 8.31–8.38 (m, 2H, 3′-H, naphthyl); 8.46 (dd, 8-H, J = 9.0, 1.3 Hz); ^{13}C-NMR: δ 14.5 (Me); 60.0 (CH_2); 105.9 (1-C); 118.2, 119.8, 121.7, 123.7, 126.8, 127.1, 138.0, 148.5 (2-C, 6-C, 7-C, 8-C, 3′-C, 4′-C, 5′-C, 6′-C); 124.5, 125.8, 126.2, 128.1, 128.4, 128.5, 131.5 (2″-C, 3″-C, 4″-C, 5″-C, 6″-C, 7″-C, 8″-C); 128.6, 139.7, 141.8, 155.4 (3-C, 5-C, 8a-C, 1′-C); 131.1, 133.6, 136.3 (1″-C, 5a″-C, 8a″-C); 164.1 (COO); 184.4 (COAr); *Anal*. Calcd for $C_{27}H_{20}N_2O_3$: C 77.13, H 4.79, N 7.29; Found: C 77.42, H 5.04, N 7.58.

Ethyl 3-(2-naphthoyl)-5-(2-pyridyl)indolizine-1-carboxylate (13). This compound was obtained as yellow crystals; IR (ATR): 3055, 1679, 1623, 1523, 1357, 1231 cm^{-1}; ^{1}H-NMR: δ 1.37 (t, 3H, Me, J = 7.1 Hz); 4.36 (q, 2H, CH_2O, J = 7.1 Hz); 7.06–7.10 (m, 2H, 6-H, 4′-H); 7.48 (dd, 1H, 7-H, J = 9.0, 7.0 Hz); 7.53–7.63 (m, 3H, naphthyl); 7.66 (s, 1H, 2-H); 7.72 (dt, 1H, 6′-H, J = 7.7, 1.2 Hz); 7.83 (td, 1H, 5′-H, J = 7.7, 1.7, 1.2 Hz); 7.87–7.92, 7.96–7.99 (m, 3H, naphthyl); 8.18 (ddd, 1H, 3′-H, J = 4.8, 1.7, 0.9 Hz); 8.48–8.52 (m, 2H, 8-H, naphthyl); ^{13}C-NMR: δ 14.5 (Me); 60.0 (CH_2); 105.5 (1-C); 117.7, 119.8, 121.8, 123.6, 126.6, 127.2, 138.0, 148.5 (2-C, 6-C, 7-C, 8-C, 3′-C, 4′-C, 5′-C, 6′-C); 125.4, 126.4, 128.0, 128.1, 129.4, 131.0, 131.1 (1″-C, 3″-C, 4″-C, 5″-C, 6″-C, 7″-C, 8″-C); 126.5, 139.1, 141.3, 155.2 (3-C, 5-C, 8a-C, 1′-C); 132.4, 135.1, 135.3 (2″-C, 4a″-C, 8a″-C); 164.2 (COO); 184.0 (COAr); *Anal*. Calcd for $C_{27}H_{20}N_2O_3$: C 77.13, H 4.79, N 7.29; Found C 76.88, H 4.91, N 7.61.

Ethyl 3-(2-nitrobenzoyl)-5-(2-pyridyl)indolizine-1-carboxylate (14). This compound was obtained as yellow crystals; IR (ATR): 2976, 1692, 1644, 1534, 1356, 1235 cm^{-1}; ^{1}H-NMR: δ 1.37 (t, 3H, Me, J = 7.1 Hz); 4.37 (q, 2H, CH_2O, J = 7.1 Hz); 7.17 (dd, 1H, 6-H, J = 7.0, 1.3 Hz); 7.23 (ddd, 1H, 4′-H, J = 7.7, 4.8, 1.2 Hz); 7.51–7.75 (m, 5H, 7-H, 6′-H, 3″-H, 4″-H, 6″-H); 7.54 (s, 1H, 2-H); 7.87 (td, 1H, 5′-H, J = 7.7, 1.7, 1.2 Hz); 8.23 (ddd, 1H, 3′-H, J = 4.8, 1.7, 0.9 Hz); 8.46–8.50 (m, 2H, 8-H, 5″-H); ^{13}C-NMR: δ 14.6 (Me); 60.3 (CH_2); 106.8 (1-C); 119.1, 119.8, 122.1, 123.8, 124.6, 127.8, 129.4, 130.0, 133.1, 135.9, 137.7, 148.5 (2-C, 6-C, 7-C, 8-C, 3′-C, 4′-C, 5′-C, 6′-C, 3″-C, 4″-C, 5″-C, 6″-C); 125.9, 135.8, 140.3, 142.4, 147.8, 155.3 (3-C, 5-C, 8a-C, 1′-C, 1″-C, 2″-C); 163.9 (COO); 179.0 (COAr); *Anal*. Calcd for $C_{23}H_{17}N_3O_5$: C 66.50, H 4.12, N 10.12; Found: C 66.26, H 4.37, N 9.87.

Ethyl 3-(3-nitrobenzoyl)-5-(2-pyridyl)indolizine-1-carboxylate (15). This compound was obtained as yellow crystals; IR (ATR): 3097, 1703, 1629, 1526, 1348, 1240 cm^{-1}; ^{1}H-NMR: δ 1.37 (t, 3H, Me, J = 7.1 Hz); 4.37 (q, 2H, CH_2O, J = 7.1 Hz); 7.11 (dd, 1H, 6-H, J = 7.0, 1.3 Hz); 7.15 (ddd, 1H, 4′-H, J = 7.7, 4.8, 1.2 Hz); 7.51 (dd, 1H, 7-H, J = 9.0, 7.0 Hz); 7.55 (s, 1H, 2-H); 7.65 (t, 1H, 5″-H, J = 7.9 Hz); 7.71 (dt, 1H, 6′-H, J = 7.7, 1.2 Hz); 7.87 (td, 1H, 5′-H, J = 7.7, 1.7, 1.2 Hz); 8.16–8.22 (m, 2H, 3′-H, 6″-H); 8.38–8.42 (m, 1H, 4″-H); 8.47 (dd, 8-H, J = 9.0, 1.3 Hz); 8.66 (t, 1H, 2″-H, J = 1.9 Hz); ^{13}C-NMR: δ 14.4 (Me); 60.1 (CH_2); 106.1 (1-C); 118.1, 119.9, 121.9, 123.8, 124.2, 126.4, 127.0, 127.3, 129.4, 135.0, 138.0, 148.3 (2-C, 6-C, 7-C, 8-C, 3′-C, 4′-C, 5′-C, 6′-C, 2″-C, 4″-C, 5″-C, 6″-C); 125.5, 138.0, 139.2, 141.7, 148.2, 155.0 (3-C, 5-C, 8a-C, 1′-C, 1″-C, 3″-C); 163.8 (COO); 181.0 (COAr); *Anal*. Calcd for $C_{23}H_{17}N_3O_5$: C 66.50, H 4.12, N 10.12; Found: C 66.82, H 4.49, N 10.40.

Ethyl 3-(4-fluorobenzoyl)-5-(2-pyridyl)indolizine-1-carboxylate (16). This compound was obtained as yellow crystals; IR (ATR): 3075, 1684, 1640, 1592, 1518, 1237 cm^{-1}; ^{1}H-NMR: δ 1.40 (t, 3H, Me, J = 7.1 Hz); 4.38 (q, 2H, CH_2O, J = 7.1 Hz); 7.08 (dd, 1H, 6-H, J = 7.0, 1.3 Hz); 7.11–7.17 (m, 3H, 4′-H, 3″-H, 5″-H); 7.47 (dd, 1H, 7-H, J = 9.0, 7.0 Hz); 7.57 (s, 1H, 2-H); 7.70 (dt, 1H, 6′-H, J = 7.7, 1.2 Hz); 7.84–7.93 (m, 3H, 5′-H, 2″-H, 6″-H); 8.17 (ddd, 1H, 3′-H, J = 4.8, 1.7, 0.9 Hz); 8.47 (dd, 1H, 8-H, J = 9.0, 1.3 Hz); ^{13}C-NMR: δ 14.7 (Me); 60.1 (CH_2); 105.7 (1-C); 115.5 (d, 3″-C, 5″-C, J = 21.8 Hz); 117.9, 120.0, 122.0, 123.9, 126.6, 127.0, 138.3, 148.6 (2-C, 6-C, 7-C, 8-C, 3′-C, 4′-C, 5′-C, 6′-C); 126.3, 139.2, 141.4, 155.4 (3-C, 5-C, 8a-C); 132.2 (d, 2″-C, 6″-C, J = 9.2 Hz,); 134.2 (d, 1″-C, J = 2.8 Hz); 163.8 (COO); 165.7 (d, 4″-C, J = 252.2 Hz); 182.8 (COAr); *Anal*. Calcd for $C_{23}H_{17}FN_2O_3$: C 71.13, H 4.41, N 7.21; Found: C 71.02, H 4.78, N 7.53.

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