A Simple and Effective Approach to the Synthesis of Isoquinoline Derivatives Under Solvent-Free Conditions

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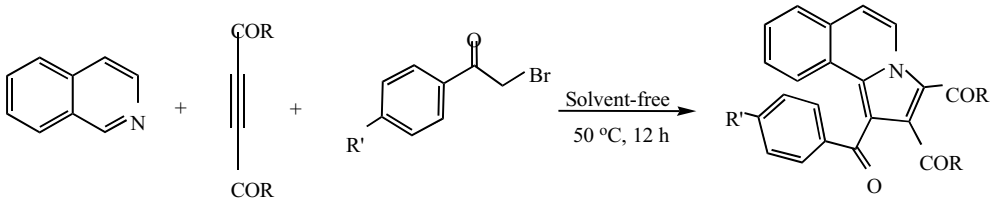
Abstract: An efficient synthesis of dialkyl pyrrolo[2,1-a]isoquinoline-2,3-dicarboxylates, pyrrolo[1,2-a]quinoline-1,2-dicarboxylates and indolizines is described via one-pot reactions of isoquinoline, quinoline or pyridine and phenacyl bromids with dialkyl acetylenedicarboxylates or diaryloylacetylene under solvent-free conditions at 50°C. The mild reaction conditions and high yields of the products exhibit the good synthetic advantage of these methods.



Keywords: Indolizine, isoquinoline, one-pot reactions, phenacyl bromides, solvent-free.

1. INTRODUCTION

Multicomponent reactions (MCRs), with three or more reactants merge in a one-pot method to provide a single product, have gradually become more popular during the last decade [1-7]. They are efficiently and environmentally valuable because multi-step syntheses generate large amounts of waste mainly due to complex isolation procedures often including costly, toxic, and unsafe solvents after each step. Bridgehead nitrogen heterocycles are of fascination because they compose a main class of natural and non-natural products, many of which display valuable biological activity [8-10]. The isoquinoline frame is set up in a large number of naturally occurring and synthetic biologically active heterocyclic compounds [9]. Thus, as part of a related study on multicomponent reactions, we wish to report a simple synthesis of functionalized pyrrolo[2,1-a]isoquinolines, pyrrolo[1,2-a]quinoline and indolizine [11]. The reaction of isoquinoline **1** and dialkyl acetylenedicarboxylate **2** in the presence of phenacyl bromides **3** proceeds smoothly under solvent-free conditions at 50°C to produce pyrrolo[2,1-a]isoquinoline **4** in excellent yields (Scheme **1**).

2. RESULTS AND DISCUSSION

Isoquinoline reacts with the electron deficient acetylenic compound **2** in the presence of phenacyl bromids under solvent-free conditions at 50°C. The products were separated by column chromatography and characterized on the basis of their elemental analyses and their IR, ^{1}H NMR and ^{13}C NMR spectra. The mass spectrum of **4a** displayed the molecular ion peak (M^+) at m/z = 417, which confirmed the 1:1:1 adduct of isoquinoline, dimethyl acetylenedicarboxylate (DMAD) and 4-methoxy phenacyl bromid. The ^{1}H NMR spectrum of **4a** showed three methoxy groups (δ = 3.62, 3.93 and 3.98), along with multiplets at δ = 6.52-8.22 for the aromatic moiety. The ^{13}C NMR spectrum of **4a** showed 24 different resonances in agreement with the proposed structure. Although we have not established the mechanism of the reaction between isoquinoline and activated acetylenes in the presence of phenacyl bromids in an experimental manner, a possible explanation is proposed in Scheme **2**. The first step may involve addition of isoquinoline to the activated acetylenic ester and formation of the 1:1 adducts **5**. Subsequent nucleophilic attack of **5** to phenacyl bromides yields the 1:1:1 adducts **6**, which is converted to **4** by elimination of hydrogen.

Under similar conditions, reaction of quinoline **9** and pyridin **11** with dialkyl acetylenedicarboxylates in the presence of phenacyl bromids proceeds smoothly at 50°C to produce quinoline derivatives **10a-b** and pyridine derivatives **12a-b** in 87-93% yields (Scheme **3**).

3. CONCLUSION

In conclusion, we have developed a convenient and one-pot method for preparing stabilized pyrrolo[2,1-a]isoquinolines, pyrrolo[1,2-a]quinolines and indolizines.

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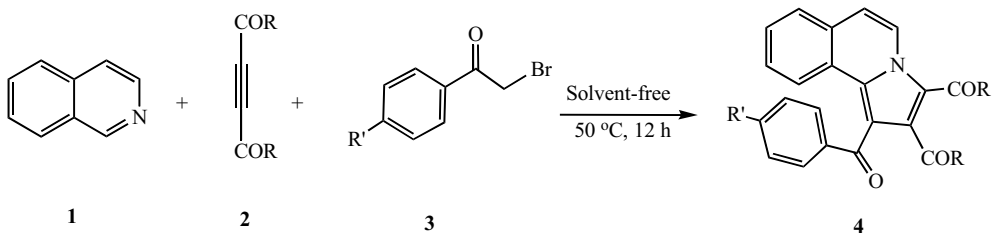
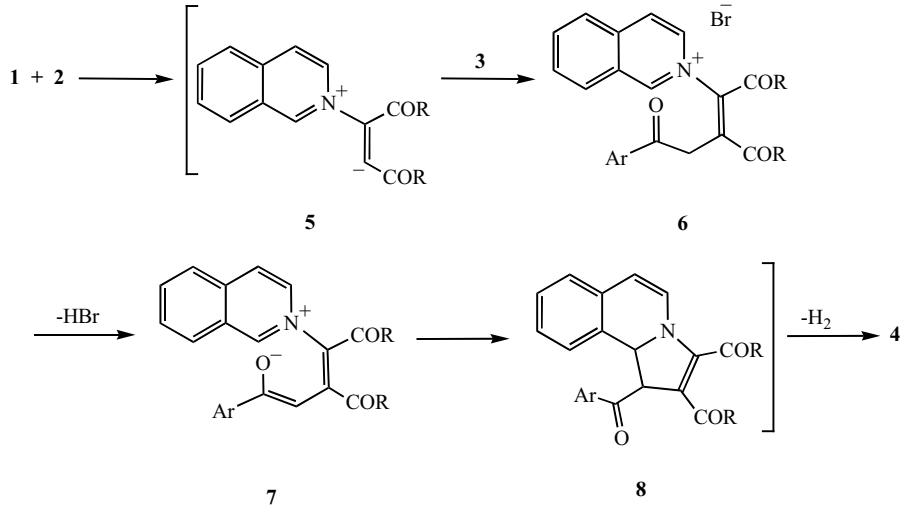


1 2 3 4

2, 3, 4	R	R'	Yield (%) of **4**
a	OMe	MeO	90
b	OEt	MeO	92
c	O-*i*-pro	MeO	87
d	O′Bt	MeO	85
e	C_6H_5	MeO	90
f	4-CH_3-C_6H_4	MeO	93
g	OMe	Br	89
h	OEt	Br	85
i	O-*i*-pro	Br	87
j	O′Bt	Br	90
k	C_6H_5	Br	83
l	4-CH_3-C_6H_4	Br	83

Scheme 1. Reactions of isoquinoline and dialkyl acetylenedicarboxylate in the presence of phenacyl bromides.



Scheme 2. Possible mechanism for the formation of compound **4**.

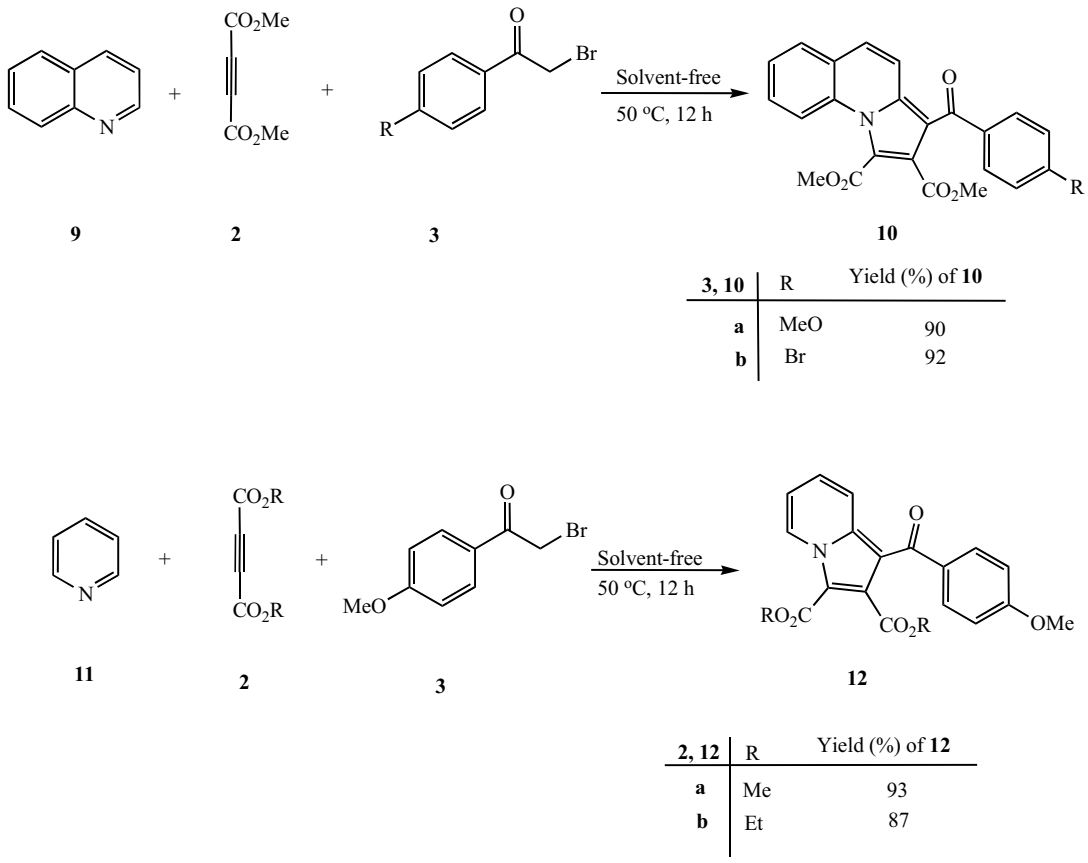
The present method carries the advantage that these reactions are performed under solvent-free conditions and the substrates can be reacted without any prior activation or modification. The simplicity of the present procedure makes it an interesting alternative to complex multistep approaches. The procedure described here provides an acceptable one-pot method for the preparation of functionalized pyrrolo [2,1-a]isoquinolines, pyrrolo[1,2-a]quinoline and indolizine.

MATERIALS AND METHODS

Dibenzoylacetylene and 4,4'-dimethylphenoylacetylen were prepared by a known procedure [12, 13]. Other chemicals used in this work were purchased from Fluka and used without further purification. Melting points were measured on a Kofler hot stage apparatus and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were obtained with a Bruker FT-500 spectrometer in chloroform-d1, and tetramethylsilane (TMS) was used as an internal standard. Mass spectra were recorded with a Finnigan Mat TSQ-70 spectrometer. Infrared (IR) spectra were acquired on a Nicollet Magna 550-FT spectrometer. Elemental analyses were carried out with a Perkin-Elmer model 240-C apparatus. The results of elemental analyses (C, H, N) were within ±0.4% of the calculated values.

General Procedure for Preparation of Compounds 4a-l, 10 and 12

A mixture of phenacyl bromides **3** (2 mmol) and activated acetylenes **2** (2 mmol) was warmed about 50°C. Then, isoquinoline **1**, quinoline **9** or pyridine **11** (2 mmol)



Scheme 3. Reactions of quinoline or pyridine and dialkyl acetylenedicarboxylate in the presence of phenacyl bromides.

was added slowly. The reaction mixture was stirred for 12 h at 50°C, and then poured into 15 mL of water. The resulting precipitate was separated by filtration and using EtOH to afford the pure title compounds.

Dimethyl 1-(4-methoxybenzoyl)pyrrolo[2,1-a]isoquinoline-2,3-dicarboxylate (4a)

Pale yellow crystals, yield: 0.75 g (90%), m.p. 112-114°C. IR (KBr): ν = 1729, 1713, 1697 and 1534 cm^{-1}.^{1}H NMR (500 MHz, $CDCl_3$): 3.62 (MeO), 3.93 (3 H, s, MeO), 3.98 (3 H, s, MeO), 6.52 (1 H, d, $^3J_{HH}$ = 7.5 Hz, CH), 6.75 (1 H, d, $^3J_{HH}$ = 7.4 Hz, CH), 6.93 (1 H, d, $^3J_{HH}$ = 7.5 Hz, CH), 7.00-7.07 (4 H, m, 4 CH), 7.13-7.20 (2 H, m, 2 CH), 8.22 (1 H, d, $^3J_{HH}$ = 7.8 Hz, CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 52.3 (MeO), 53.3 (MeO), 53.8 (MeO), 105.7 (C), 108.9 (CH), 113.8 (CH), 113.9 (2 CH), 115.4 (C), 123.6 (CH), 124.7 (CH), 126.6 (C), 126.9 (CH), 128.0 (CH), 130.1 (C), 130.5 (C), 131.3 (2 CH), 131.5 (2 C), 160.6 (C=O), 163.9 (C), 164.2 (C=O), 192.3 (C=O) ppm. MS (EI, 70 eV): *m*/*z* (%) = 417 (M^+, 20), 386 (68), 310 (100), 107 (100), 31 (84). Anal. Calcd for $C_{24}H_{19}NO_6$ (417.42): C, 69.06; H, 4.59; N, 3.36. Found: C, 68.97; H, 4.48; N, 3.27 %.

Diethyl 1-(4-methoxybenzoyl)pyrrolo[2,1-a]isoquinoline-2,3-dicarboxylate (4b)

Yellow powder, yield: 0.82 g (92%), m.p. 142-144°C. IR (KBr): ν = 1722, 1715, 1700 and 1579 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.95 (3 H, t, $^3J_{HH}$ = 7.2 Hz, CH_3), 1.40 (3 H, t, $^3J_{HH}$ = 7.2 Hz, CH_3), 3.92 (3 H, s, MeO), 4.02 (2 H, q, $^3J_{HH}$ = 7.2 Hz, OCH_2), 4.43 (2 H, q, $^3J_{HH}$ = 7.2 Hz, OCH_2), 5.86 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH), 6.52 (1 H, d, $^3J_{HH}$ = 7.4 Hz, CH), 6.76 (1 H, d, $^3J_{HH}$ = 7.4 Hz, CH), 7.02-7.06 (4 H, m, 4 CH), 7.19 (2 H, t, $^3J_{HH}$ = 7.5 Hz, 2 CH), 8.23 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 13.8 (Me), 14.0 (Me), 55.6 (MeO), 62.7 (CH_2O), 66.4 (CH_2O), 105.7 (C), 108.6 (CH), 113.8 (C), 113.9 (2 CH), 123.6 (CH), 124.2 (CH), 124.7 (CH), 126.8 (CH), 128.0 (CH), 130.2 (C), 130.5 (C), 131.4 (2 CH), 131.5 (2 C), 132.5 (C), 161.2 (C=O), 163.7 (C=O), 164.0 (C), 199.0 (C=O) ppm. Anal. Calcd for $C_{26}H_{23}NO_6$ (445.47): C, 70.10; H, 5.20; N, 3.14. Found: C, 69.98; H, 5.10; N, 3.04 %.

*Di(***iso***-propyl) 1-(4-methoxybenzoyl)pyrrolo[2,1-a]isoquinoline-2,3-dicarboxylate (4c)*

Yellow powder, yield: 0.82 g (87%), m.p. 137-139°C. IR (KBr): ν = 1739, 1714, 1705 and 1574 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.35 (6 H, d, $^3J_{HH}$ = 6.7 Hz, 2 CH_3), 1.42 (6 H, d, $^3J_{HH}$ = 6.7 Hz, 2 CH_3), 3.90 (3 H, s, MeO), 5.18 (1 H, m, CH), 5.42 (1 H, m, CH), 6.86 (1 H, d, $^3J_{HH}$ = 7.5 Hz, CH), 7.19 (1 H, d, $^3J_{HH}$ = 7.7 Hz, CH), 7.32 (2 H, d, $^3J_{HH}$ = 7.4 Hz, 2 CH), 7.53 (1 H, t, $^3J_{HH}$ = 7.4 Hz, CH), 7.62 (1 H, t, $^3J_{HH}$ = 7.4 Hz, CH), 7.72 (1 H, d, $^3J_{HH}$ = 7.5 Hz, CH), 8.45 (2 H, d, $^3J_{HH}$ = 7.5 Hz, 2 CH), 9.25 (1 H, d, $^3J_{HH}$ = 7.7 Hz, CH) ppm.^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 21.6 (2 CH_3), 22.4 (2 CH_3), 53.4 (MeO), 68.8 (*C*HMe$_2$), 70.5 (*C*HMe$_2$), 108.6 (C), 113.2 (C), 117.0 (2 CH), 119.6 (C), 124.2 (2 C), 124.5 (CH), 125.3 (CH), 126.4 (CH), 127.5 (2 CH), 128.4 (CH), 129.0 (C), 129.6 (2 CH), 130.1 (C), 132.6 (C), 163.2 (C=O), 163.7 (C=O), 189.8 (C=O) ppm. Anal. Calcd for $C_{28}H_{27}NO_6$

(473.52): C, 71.02; H, 5.75; N, 2.96. Found: C, 70.92; H, 5.67; N, 2.88 %.

Di(*tert*-butyl) 1-(4-methoxybenzoyl)pyrrolo[2,1-a]isoquinoline-2,3-dicarboxylate (4d)

Pale yellow crystal, yield: 0.85 g (85%), m.p. 190-192 °C. IR (KBr): ν = 1736, 1715, 1710 and 1586 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.62 (9 H, s, 3 CH_3), 1.73 (9 H, s, 3 CH_3), 3.87 (3 H, s, MeO), 7.18 (2 H, d, $^3J_{HH}$ = 7.5 Hz, 2 CH), 7.32 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH), 7.52 (2 H, d, $^3J_{HH}$ = 7.7 Hz, 2 CH), 7.74 (1 H, d, $^3J_{HH}$ = 7.2 Hz, CH), 7.75 (1 H, t, $^3J_{HH}$ = 7.2 Hz, CH), 7.94 (1 H, t, $^3J_{HH}$ = 7.5 Hz, CH), 8.57 (1 H, d, $^3J_{HH}$ = 7.5 Hz, 1 CH), 9.22 (1 H, d, $^3J_{HH}$ = 7.7 Hz, CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 28.5 (3 CH_3), 28.7 (3 CH_3), 53.0 (MeO), 83.5 (CMe_3), 84.2 (CMe_3), 106.7 (C), 115.0 (C), 117.4 (2 CH), 120.18 (C), 124.5 (C), 125.0 (CH), 125.7 (CH), 127.5 (CH), 128.5 (CH), 129.5 (2 CH), 130.2 (C), 130.3 (2 CH), 131.8 (2 C), 132.4 (C), 164.0 (C=O), 164.7 (C=O), 190.2 (C=O) ppm. Anal. Calcd for $C_{30}H_{31}NO_6$ (501.58): C, 71.84; H, 6.23; N, 2.79. Found: C, 71.75; H, 6.17; N, 2.68 %.

Dibenzoyl 1-(4-methoxybenzoyl)pyrrolo[2,1-a]isoquinoline-2,3-dicarboxylate (4e)

Yellow powder, yield: 0.92 g (90%), m.p. 188-190°C. IR (KBr): ν = 1715, 1710, 1690 and 1548 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 3.85 (3 H, s, MeO), 7.15 (2 H, d, $^3J_{HH}$ = 7.6 Hz, CH), 7.30 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.38 (5 H, m, 5 CH), 7.50 (1 H, d, $^3J_{HH}$ = 7.4 Hz, CH), 7.53 (1 H, t, $^3J_{HH}$ = 7.4 Hz, CH), 7.62 (1 H, t, $^3J_{HH}$ = 7.2 Hz, CH), 7.64 (4 H, m, 4 CH), 7.74 (1 H, d, $^3J_{HH}$ = 7.2 Hz, CH), 8.05 (1 H, t, $^3J_{HH}$ = 7.9 Hz, CH), 8.12 (1 H, d, $^3J_{HH}$ = 7.9 Hz, CH), 9.24 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 53.4 (MeO), 118.0 (2 CH), 120.5 (2 C), 121.2 (C), 122.5 (CH), 123.4 (CH), 124.5 (C), 125.6 (CH), 126.5 (CH), 128.4 (CH), 129.3 (2 CH), 129.5 (CH), 129.7 (2 CH), 130.6 (2 CH), 130.8 (C), 131.2 (2 CH), 131.5 (2 CH), 134.5 (CH), 134.8 (C), 135.0 (CH), 137.5 (C), 139.0 (C), 139.5 (C), 142.4 (C), 189.8 (C=O), 192.2 (C=O), 193.8 (C=O) ppm. MS (EI, 70 eV): *m/z* (%) = 509 (M^+, 25), 380 (84), 129 (48), 107 (100), 77 (100). Anal. Calcd for $C_{34}H_{23}NO_4$ (509.56): C, 80.14; H, 4.55; N, 2.75. Found: C, 80.04; H, 4.46; N, 2.68 %.

Di(4-methylbenzoyl)-1-(4-methoxybenzoyl)pyrrolo[2,1-a]isoquinoline-2,3-dicarboxylate (4f)

Yellow crystals, yield: 0.99 g (93%), m.p. 182-184°C. IR (KBr): ν = 1720, 1715, 1669 and 1587 cm^{-1}. ^1H NMR (500.13 MHz, $CDCl_3$): δ = 2.35 (3 H, s, Me), 2.37 (3 H, s, Me), 3.98 (3 H, s, MeO), 7.07(2 H, d, $^3J_{HH}$ = 7.5 Hz, 2 CH), 7.15 (1 H, d, $^3J_{HH}$ = 7.5 Hz, CH), 7.25 (1 H, t, $^3J_{HH}$ = 7.4 Hz, CH), 7.38 (2 H, t, $^3J_{HH}$ = 7.3 Hz, 2 CH), 7.45 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.47 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.62 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.85 (2 H, d, $^3J_{HH}$ = 7.5 Hz, 2 CH), 8.15 (2 H, t, $^3J_{HH}$ = 7.9 Hz, 2 CH), 8.27 (1 H, d, $^3J_{HH}$ = 7.9 Hz, CH), 9.42 (1 H, d, $^3J_{HH}$ = 7.5 Hz, CH) ppm.^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 21.5 (CH_3), 22.0 (CH_3), 52.8 (MeO), 117.2 (2 C), 120.0 (CH), 122.5 (CH), 124.2 (C), 125.0 (C), 125.7 (CH), 127.3 (2 CH), 128.6 (2 CH), 129.0 (CH), 130.4 (2 CH), 130.6 (C), 130.8 (2 CH), 131.0 (2 CH), 131.4 (C), 133.8 (2 CH), 135.6 (2 CH), 136.2 (C), 137.4 (C), 144.5 (C), 144.8 (2 C), 145.6 (C), 190.4 (C=O), 192.0 (C=O), 193.6 (C=O) ppm. Anal. Calcd for $C_{36}H_{27}NO_4$ (537.61): C, 80.43; H, 5.06; N, 2.61. Found: C, 80.37; H, 4.89; N, 2.57%.

Dimethyl 1-(4-bromobenzoyl)pyrrolo[2,1-a]isoquinoline-2,3-dicarboxylate (4g)

Pale yellow crystals, yield: 0.83 g (89%), m.p. 104-106°C. IR (KBr): ν = 1729, 1716, 1705 and 1657 cm^{-1}.^1H NMR (500.13 MHz, $CDCl_3$): δ = 3.53 (3 H, s, CH_3O), 3.98 (3 H, s, CH_3O), 5.89 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH), 6.51 (1 H, d, $^3J_{HH}$ = 7.2 Hz, CH), 6.68 (1 H, d, $^3J_{HH}$ = 7.2 Hz, CH), 7.02-7.21 (3 H, m, 3 CH), 7.72 (2 H, d, $^3J_{HH}$ = 7.2 Hz, 2 CH), 8.10 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 53.4 (MeO), 53.9 (MeO), 105.3 (C), 109.1 (CH), 123.4 (CH), 124.0 (CH), 124.9 (CH), 127.1 (CH), 128.3 (CH), 129.0 (C), 130.2 (C), 130.4 (2 CH), 131.2 (C), 131.4 (C), 131.9 (C), 132.2 (2 CH), 135.8 (C), 145.7 (C), 161.5 (C=O), 164.0 (C=O), 193.4 (C=O) ppm. MS (EI, 70 eV): *m/z* (%) = 466 (M^+, 15), 435 (68), 312 (48), 129 (84), 154 (100), 31 (84). Anal. Calcd for $C_{23}H_{16}BrNO_5$ (466.29): C, 59.25; H, 3.46; N, 3.00. Found: C, 59.18; H, 3.38; N, 2.94%.

Diethyl 1-(4-bromobenzoyl)pyrrolo[2,1-a]isoquinoline-2,3-dicarboxylate (4h)

Yellow powder, yield: 0.84 g (85%), m.p. 145-147°C. IR (KBr): ν = 1727, 1710, 1708 and 1630 cm^{-1}. ^1H NMR (500.13 MHz, $CDCl_3$): δ = 1.37 (3 H, t, $^3J_{HH}$ = 7.2 Hz, CH_3), 1.45 (3 H, t, $^3J_{HH}$ = 7.2 Hz, CH_3), 4.42 (2 H, q, $^3J_{HH}$ = 7.2 Hz, OCH_2), 4.46 (2 H, q, $^3J_{HH}$ = 7.2 Hz, OCH_2), 6.31 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH), 7.03-7.05 (2 H, m, 2 CH), 7.19 (1 H, d, $^3J_{HH}$ = 7.2 Hz, CH), 7.41 (2 H, d, $^3J_{HH}$ = 7.2 Hz, 2 CH), 7.58 (2 H, d, $^3J_{HH}$ = 7.2 Hz, 2 CH), 7.61-7.65 (2 H, m, 2 CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 14.1 (CH_3), 14.2 (CH_3), 62.5 (OCH_2), 62.7 (OCH_2), 105.3 (C), 109.1 (CH), 123.4 (CH), 124.0 (CH), 124.9 (CH), 127.1 (CH), 128.3 (CH), 129.0 (C), 130.2 (C), 130.4 (2 CH), 131.2 (C), 131.4 (C), 131.9 (C), 132.2 (2 CH), 135.8 (C), 145.7 (C), 161.5 (C=O), 164.0 (C=O), 191.5 (C=O) ppm. Anal. Calcd for $C_{25}H_{20}BrNO_5$ (494.29): C, 60.74; H, 4.08; N, 2.83. Found: C, 60.67; H, 3.92; N, 2.76%.

Di(iso-propyl)1-(4-bromobenzoyl)pyrrolo[2,1-a]isoquinoline-2,3-dicarboxylate (4i)

Yellow powder, yield: 0.91 g (87%), m.p. 136-138°C. IR (KBr): ν = 1717, 1712, 1710 and 1620 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.36 (6 H, d, $^3J_{HH}$ = 7.0 Hz, 2 CH_3), 1.45 (6 H, d, $^3J_{HH}$ = 7.0 Hz, 2 CH_3), 5.23 (1 H, m, CH), 5.42 (1 H, m, CH), 6.24 (1 H, d, $^3J_{HH}$ = 7.7 Hz, CH), 6.64 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH), 6.75 (1 H, d, $^3J_{HH}$ = 7.8 Hz, CH), 7.02-7.21 (3 H, m, 3 CH), 7.75 (2 H, d, $^3J_{HH}$ = 7.5 Hz, 2 CH), 8.12 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 21.5 (2 CH_3), 22.6 (2 CH_3), 69.2 ($CHMe_2$), 71.4 ($CHMe_2$), 108.7 (C), 111.4 (CH), 123.5 (CH), 124.4 (CH), 125.2 (CH), 127.5 (CH), 128.6 (CH), 129.2 (C), 130.4 (C), 130.8 (2 CH), 131.5 (C), 131.7 (C), 132.4 (C), 132.5 (2 CH), 136.0 (C), 145.6 (C), 162.5 (C=O), 164.3 (C=O), 193.7 (C=O) ppm. Anal. Calcd for $C_{27}H_{24}BrNO_5$ (522.39): C, 62.08; H, 4.63; N, 2.68. Found: C, 61.97; H, 4.58; N, 2.56%.

Di(tert-butyl) 1-(4-bromobenzoyl)pyrrolo[2,1-a]isoquinoline-2,3-dicarboxylate (4j)

Pale yellow crystals, yield: 0.99 g (90%), m.p. 191-193°C. IR (KBr): ν = 1710, 1700, 1697 and 1657 cm^{-1}. ^1H

NMR (500 MHz, $CDCl_3$): δ = 1.52 (9 H, s, 3 CH_3), 1.68 (9 H, s, 3 CH_3), 6.30 (1 H, d, $^3J_{HH}$ = 7.5 Hz, CH), 6.65 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH), 6.78 (1 H, d, $^3J_{HH}$ = 7.5 Hz, CH), 7.12-7.25 (3 H, m, 3 CH), 7.82 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 8.15 (2 H, d, $^3J_{HH}$ = 7.5 Hz, 2 CH) ppm.^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 28.5 (3 CH_3), 29.2 (3 CH_3), 83.6 (*C*Me_3), 84.4 (*C*Me_3), 107.5 (C), 112.4 (CH), 122.8 (CH), 124.5 (CH), 125.6 (CH), 127.4 (CH), 128.5 (CH), 129.6 (C), 130.4 (C), 130.8 (2 CH), 131.7 (2 C), 132.2 (C), 132.6 (2 CH), 136.3 (C), 146.2 (C), 162.4 (C=O), 164.2 (C=O), 192.7 (C=O) ppm. Anal. Calcd for $C_{29}H_{28}BrNO_5$ (550.45): C, 63.28; H, 5.13; N, 2.54. Found: C, 63.17; H, 5.04; N, 2.48%.

Dibenzoyl 1-(4-bromobenzoyl)pyrrolo[2,1-a]isoquinoline-2,3-dicarboxylate (4k)

Yellow powder, yield: 0.93 g (83%), m.p. 188-190°C. IR (KBr): ν = 1715, 1700, 1690 and 1659 cm^{-1}. ^{1}H NMR (500.13 MHz, $CDCl_3$): δ = 7.18 (2 H, d, $^3J_{HH}$ = 7.5 Hz, 2 CH), 7.35 (2 H, d, $^3J_{HH}$ = 7.4 Hz, 2 CH), 7.42 (4 H, m, 4 CH), 7.53 (1 H, d, $^3J_{HH}$ = 7.5 Hz, CH), 7.60 (1 H, t, $^3J_{HH}$ = 7.2 Hz, CH), 7.68 (1 H, t, $^3J_{HH}$ = 7.2 Hz, CH), 7.72 (4 H, m, 4 CH), 7.78 (1 H, d, $^3J_{HH}$ = 7.5 Hz, CH), 8.24 (2 H, t, $^3J_{HH}$ = 7.8 Hz, 2 CH), 8.32 (1 H, d, $^3J_{HH}$ = 7.8 Hz, CH), 9.30 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 117.8 (CH), 118.6 (CH), 120.3 (C), 120.8 (C), 123.4 (CH), 124.5 (C), 125.5 (CH), 126.7 (2 CH), 128.4 (CH), 129.3 (2 CH), 129.6 (2 CH), 130.3 (2 CH), 130.6 (2 CH), 131.0 (C), 131.5 (2 CH), 132.2 (CH), 134.2 (CH), 134.3 (2 C), 134.7 (CH), 137.6 (2 C), 138.9 (C), 139.3 (C), 190.4 (C=O), 192.5 (C=O), 194.3 (C=O) ppm. Anal. Calcd for $C_{33}H_{20}BrNO_3$ (558.43): C, 70.98; H, 3.61; N, 2.51. Found: C, 70.86; H, 3.54; N, 2.45%.

Di(4-methylbenzoyl)-1-(4-bromobenzoyl)pyrrolo[2,1-a]isoquinoline-2,3-dicarboxylate (4l)

Yellow crystals, yield: 0.97 g (83%), m.p. 182-184°C. IR (KBr): ν = 1714, 1710, 1658 and 1624 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.37 (3 H, s, Me), 2.42 (3 H, s, Me), 7.10 (2 H, d, $^3J_{HH}$ = 7.5 Hz, 2 CH), 7.27 (1 H, t, $^3J_{HH}$ = 7.6 Hz, CH), 7.34 (1 H, t, $^3J_{HH}$ = 7.5 Hz, CH), 7.42 (1 H, t, $^3J_{HH}$ = 7.6 Hz, CH), 7.48 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.52 (2 H, d, $^3J_{HH}$ = 7.8 Hz, 2 CH), 7.63 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.82 (2 H, d, $^3J_{HH}$ = 7.5 Hz, 2 CH), 8.12 (2 H, t, $^3J_{HH}$ = 7.9 Hz, 2 CH), 8.21 (2 H, d, $^3J_{HH}$ = 7.9 Hz, 2 CH), 9.45 (1 H, d, $^3J_{HH}$ = 7.5 Hz, CH) ppm.^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 21.5 (CH_3), 22.4 (CH_3), 116.9 (2 C), 119.2 (CH), 122.4 (CH), 124.0 (C), 124.5 (C), 125.7 (2 CH), 126.4 (CH), 127.5 (CH), 128.6 (2 CH), 129.0 (2 CH), 129.2 (CH), 129.6 (C), 130.0 (CH), 130.5 (2 CH), 130.9 (C), 134.2 (2 CH), 135.6 (2 CH), 136.3 (C), 137.5 (C), 144.6 (C), 144.9 (2 C), 145.6 (C), 193.7 (C=O), 194.2 (C=O), 194.8 (C=O) ppm. Anal. Calcd for $C_{35}H_{24}BrNO_3$ (586.48): C, 71.68; H, 4.12; N, 2.39. Found: C, 71.56; H, 4.00; N, 2.26%.

Dimethyl 1-(4-methoxybenzoyl)pyrrolo[2,1-a]quinoline-2,3-dicarboxylate (10a)

Yellow powder, yield: 0.75 g (90%), m.p. 108-110°C. IR (KBr): ν = 1719, 1712, 1710 and 1635 cm^{-1}.^{1}H NMR (500.13 MHz, $CDCl_3$): δ = 3.85 (3 H, s, MeO), 3.90 (3 H, s, MeO), 3.95 (3 H, s, MeO), 7.19 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.45 (2 H, d, $^3J_{HH}$ = 7.5 Hz, 2 CH), 7.52 (1 H, d, $^3J_{HH}$ = 7.5 Hz, CH), 7.60 (1 H, t, $^3J_{HH}$ = 7.8 Hz, CH), 7.65 (1 H, t, $^3J_{HH}$ = 7.6 Hz, CH), 7.82 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH), 8.16 (1 H, d, $^3J_{HH}$ = 7.8 Hz, CH), 8.25 (1 H, d, $^3J_{HH}$ = 7.5 Hz, CH) ppm.^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 51.9 (MeO), 52.8 (MeO), 53.4 (MeO), 117.0 (2 C), 117.6 (2 CH), 119.7 (2 CH), 124.2 (C), 125.2 (2 CH), 126.5 (C), 129.0 (2 CH), 129.5 (CH), 129.8 (C), 130.2 (CH), 132.4 (C), 132.8 (C), 133.5 (C), 163.5 (C=O), 165.2 (C=O), 189.8 (C=O) ppm. Anal. Calcd for $C_{24}H_{19}NO_6$ (417.42): C, 69.06; H, 4.59; N, 3.36. Found: C, 68.95; H, 4.50; N, 3.25%.

Dimethyl 1-(4-bromobenzoyl)pyrrolo[2,1-a]quinoline-2,3-dicarboxylate (10b)

Yellow powder, yield: 92%, m.p. 124-126°C. ^{1}H NMR (500.13 MHz, $CDCl_3$): δ = 3.82 (3 H, s, MeO), 3.87 (3 H, s, MeO), 7.14 (2 H, d, $^3J_{HH}$ = 7.5 Hz, 2 CH), 7.36 (2 H, d, $^3J_{HH}$ = 7.5 Hz, 2 CH), 7.47 (1 H, d, $^3J_{HH}$ = 7.5 Hz, CH), 7.52 (1 H, t, $^3J_{HH}$ = 7.6 Hz, CH), 7.58 (1 H, t, $^3J_{HH}$ = 7.6 Hz, CH), 7.65 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH), 8.07 (1 H, d, $^3J_{HH}$ = 7.8 Hz, CH), 8.17 (1 H, d, $^3J_{HH}$ = 7.8 Hz, CH) ppm.^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 52.0 (MeO), 52.6 (MeO), 116.7 (2 C), 118.4 (2 CH), 120.2 (2 CH), 123.8 (C), 125.4 (2 CH), 125.8 (C), 128.3 (2 CH), 129.0 (CH), 130.1 (C), 130.5 (CH), 131.9 (C), 132.6 (C), 132.8 (C), 163.7 (C=O), 166.0 (C=O), 190.2 (C=O) ppm.

Dimethyl 1-(4-methoxybenzoyl)-2,3-indolizinedicarboxylate (12a)

Yellow crystal, yield: 0.68 g (93%), m.p. 112-114°C.IR (KBr): ν = 1725, 1716, 1711 and 1642 cm^{-1}.^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.87 (3 H, s, MeO), 3.90 (3 H, s, MeO), 3.93 (3 H, s, MeO), 7.14 (2 H, t, $^3J_{HH}$ = 7.5 Hz, 2 CH), 7.35 (2 H, d, $^3J_{HH}$ = 7.4 Hz, 2 CH), 7.46 (2 H, d, $^3J_{HH}$ = 7.8 Hz, 2 CH), 8.40 (1 H, d, $^3J_{HH}$ = 7.3 Hz, CH), 9.34 (1 H, d, $^3J_{HH}$ = 7.5 Hz, CH) ppm.^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 52.3 (MeO), 52.8 (MeO), 53.0 (MeO), 113.8 (2 C), 117.4 (2 CH), 120.5 (C), 121.4 (CH), 126.4 (CH), 128.3 (2 CH), 129.4 (C), 130.2 (2 CH), 139.2 (2 C), 163.4 (C=O), 164.2 (C=O), 190.4 (C=O) ppm. Anal. Calcd for $C_{20}H_{17}NO_6$ (367.36): C, 65.39; H, 4.66; N, 3.81. Found: C, 65.28; H, 4.58; N, 3.75%.

Diethyl 1-(4-methoxybenzoyl)-2,3-indolizinedicarboxylate (12b)

Yellow powder, yield: 87%, m.p. 118-120°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.35 (3 H, t, $^3J_{HH}$ = 7.3 Hz, CH_3), 1.42 (3 H, t, $^3J_{HH}$ = 7.3 Hz, CH_3), 3.87 (3 H, s, MeO), 4.38 (2 H, q, $^3J_{HH}$ = 7.2 Hz, OCH_2), 4.45 (2 H, q, $^3J_{HH}$ = 7.3 Hz, OCH_2), 7.15 (2 H, t, $^3J_{HH}$ = 7.4 Hz, 2 CH), 7.38 (2 H, d, $^3J_{HH}$ = 7.4 Hz, 2 CH), 7.52 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 8.34 (1 H, d, $^3J_{HH}$ = 7.5 Hz, CH), 8.94 (1 H, d, $^3J_{HH}$ = 7.5 Hz, CH) ppm.^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 13.7 (CH_3), 14.2 (CH_3), 52.8 (MeO), 62.6 (OCH_2), 63.0 (OCH_2), 114.0 (2 C), 116.8 (2 CH), 121.2 (C), 121.8 (CH), 125.7 (CH), 128.0 (2 CH), 129.6 (C), 130.4 (2 CH), 140.2 (2 C), 163.5 (C=O), 164.4 (C=O), 190.4 (C=O) ppm.

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CONFLICT OF INTEREST

Declared none.

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