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Synthesis of pyrrolo[2,1-*a*]isoquinolines from activated acetylenes, benzoylnitromethanes, and isoquinoline

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ABSTRACT

Isoquinoline reacts smoothly with aroylnitromethanes in the presence of dialkyl acetylenedicarboxylates and dibenzoylacetylene to produce pyrrolo[2,1-*a*]isoquinolines in good yields. Quinoline and benzothiazole also react in a similar way. Pyridine and *N*-methylimidazole catalyze the reaction between nitromethane derivatives with electron-deficient acetylenes to produce highly functionalized isoxazoles.

1. Introduction

In recent years, nitroalkanes have proved to be very useful building blocks for the one-pot synthesis of a variety of important targets. A one-pot process can be planned by the right choice of different parameters such as (i) reaction conditions, (ii) catalyst, (iii) addition sequence of reactants, or (iv) use of starting materials with a high chemical versatility, e.g., nitroalkanes. Nitroalkanes are a valuable source of stabilized carbanions since the high electron-withdrawing power of the nitro group provides an outstanding enhancement of the hydrogen acidity at the α-position.[1–5] Nitronate anions can be generated from nitroalkanes using a wide range of bases and act as carbon nucleophiles with common electrophiles, including aldehydes[6,7] and electron-poor alkenes,[8] leading to carbon–carbon bond formation. The nitro group can be removed from the molecule by replacing it with hydrogen[9,10] or by elimination as nitrous acid, introducing a double bond.[11,12]

As part of our current interest in the application of nitroalkanes in organic synthesis,[13–16] we describe a simple synthesis of functionalized pyrrolo[2,1-*a*]isoquinolines, pyrrolo[1,2-*a*]quinoline, pyrrolo[2,1-*b*][1,3]benzothiazole, and highly functionalized isoxazole derivatives. The reaction forming fused pyrroles is complementary to the cycloadditions of quinolinium and isoquinolinium ylides with electron-deficient acetylenes.[17]

2. Results and discussion

The reaction of isoquinoline (**1**) with dialkyl acetylenedicarboxylates (**2a–d**) or dibenzoylacetylene (**2e**) in the presence of aroylnitromethanes (**3**) proceeded smoothly in H_2O/MeCN (5:1) mixture and was complete within 3 h. The ^1H and ^{13}C NMR spectra of the crude products clearly indicated the formation of pyrrolo[2,1-*a*]isoquinolines (**4a–g**) in 71–85% yields (Table 1).

The structures of compounds **4a–g** were deduced from their IR, ^1H NMR, and ^{13}C NMR spectra. For example, the ^1H NMR spectrum of **4a** exhibited signals for methoxy (δ=3.48 and 3.90 ppm) protons, along with multiplets (δ=7.16–9.18 ppm) for the aromatic region. The proton-decoupled ^{13}C NMR spectrum of **4a** showed 21 distinct resonances in agreement with the proposed structure. The IR spectrum of **4a** displayed characteristic carbonyl bands (1735, 1732, and 1680 cm^{-1}). The ^1H NMR and ^{13}C NMR spectra of **4b–g** were similar to those for **4a** except for the ester moieties, which exhibited characteristic resonances in the appropriate regions of the spectrum. The tribenzol derivative **4g** is reported before. However, the melting point reported[18] for **4g** (218–220 °C) is far from 135–137 °C of the present paper.

Although the mechanistic details of the reaction are not known, a plausible rationalization may be advanced to explain the product formation (Scheme 1). Presumably, the zwitterionic intermediate[19–21] formed from isoquinoline and **2** is protonated by **3** to furnish intermediate **6**, which is attacked by carbanion **7** to produce **8**. This intermediate undergoes a series of cyclization and elimination reactions to generate product **4**.

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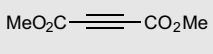
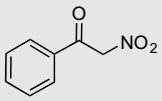
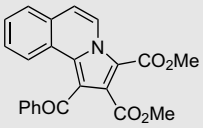
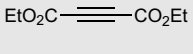
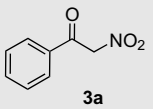
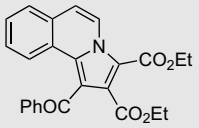
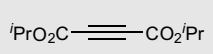
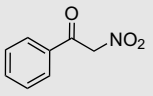
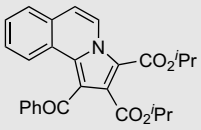
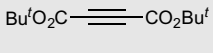
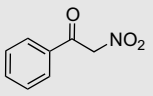
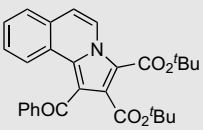
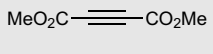
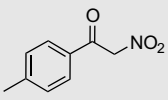
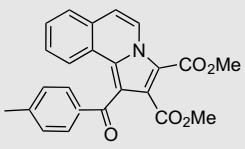
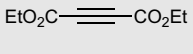
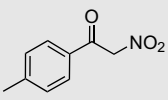
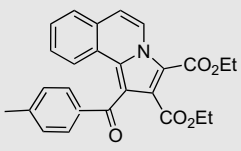
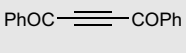
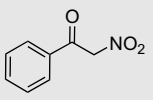
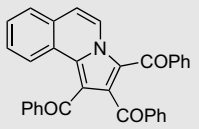
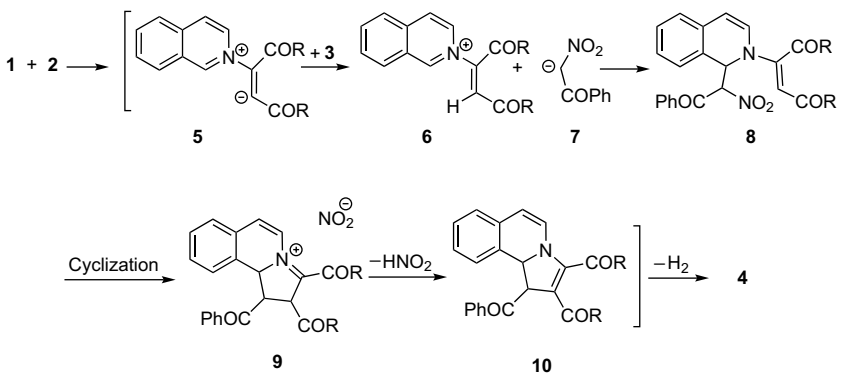
Table 1
Reaction of isoquinoline (**1**) with activated acetylenic compounds **2** in the presence of aroylnitromethanes **3** in aqueous media

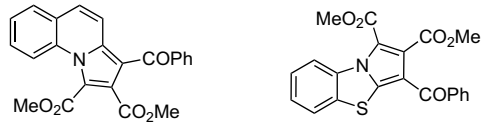
Entry	Activated acetylene	Nitro compound	Product	Yield[a]/%
a	 **2a**	 **3a**	 **4a**	80
b	 **2b**	 **3a**	 **4b**	78
c	 **2c**	 **3a**	 **4c**	75
d	 **2d**	 **3a**	 **4d**	76
e	 **2a**	 **3b**	 **4e**	75
f	 **2b**	 **3b**	 **4f**	71
g	 **2e**	 **3a**	 **4g**	85

[a] Yield after recrystallization.



Scheme 1. Proposed mechanism for the formation of compounds **4**.

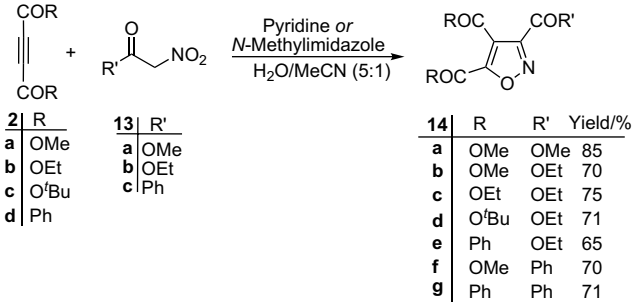
Under similar reaction conditions, DMAD reacts with benzoylnitromethane in the presence of quinoline and benzothiazole to produce dimethyl 3-benzoylpyrrolo[1,2-*a*]quinoline-1,2-dicarboxylate (**11**) and dimethyl 3-benzoylpyrrolo[2,1-*b*][1,3]benzothiazole-1,2-dicarboxylate (**12**) (Scheme 2). Compounds **11** and **12** were again fully characterized according to their elemental analyses and their IR, ^{1}H NMR, and ^{13}C NMR spectra.



11 (63%) **12** (56%)

Scheme 2.

To extend our knowledge of this reaction, we performed the reaction between DMAD and nitromethane derivatives **13** in the presence of pyridine and *N*-methylimidazole in H_2O/MeCN (5:1) mixture. Surprisingly, this reaction led to functionalized isoxazoles **14a–g** in good yields (Scheme 3). Pyridine and *N*-methylimidazole act as a catalyst in this transformation and the reaction proceeds smoothly at rt in the presence of 20 mol % of the catalyst. Recently, we reported[16] the synthesis of similar isoxazoles through the reaction of activated acetylenes and alkyl 2-nitroethanoates in the presence of triphenylphosphine under reflux condition in toluene.[13] However, pyridine and *N*-methylimidazole are found to be more effective catalysts for formation of isoxazoles **14** in aqueous media.



2	R
a	OMe
b	OEt
c	O^{t}Bu
d	Ph

13	R'
a	OMe
b	OEt
c	Ph

14	R	R'	Yield/%
a	OMe	OMe	85
b	OMe	OEt	70
c	OEt	OEt	75
d	O^{t}Bu	OEt	71
e	Ph	OEt	65
f	OMe	Ph	70
g	Ph	Ph	71

Scheme 3. Synthesis of compounds **14**.

A synthesis of compound **14f** from benzoylnitromethane and DMAD in refluxing xylene in the presence of a catalytic amount of *p*-toluenesulfonic acid is reported[22] before; the melting point and spectroscopic data are in good agreement with our results.

In summary, we have reported a transformation involving isoquinoline, activated acetylenes, and benzoylnitromethane to produce pyrrolo[2,1-*a*]isoquinolines in good yields. Quinoline and benzothiazole also react in a similar way. Alternatively, pyridine and *N*-methylimidazole catalyzed the reaction between nitromethane derivatives with electron-deficient acetylenes to produce highly functionalized isoxazoles.

3. Experimental

3.1. General

Dibenzoylacetylene was prepared by a known procedure.[23,24] The reagents and solvents used in this work were obtained from Aldrich and Fluka and were used without further purification. Mp: Electrothermal-9100 apparatus. IR Spectra: Shimadzu IR-460 spectrometer; in cm^{-1}. ^{1}H NMR and ^{13}C NMR spectra: Bruker DRX-500 AVANCE instrument; in $CDCl_3$ at 500.1 and 125.7 MHz, respectively; δ in parts per million, J in hertz. EIMS: Finnigan-MAT-8430 mass spectrometer, at 70 eV; in m/z. Elemental analyses: Heraeus CHN-O-Rapid analyzer.

3.2. General procedure for the synthesis of functionalized pyrrolo[2,1-*a*]isoquinolines 4

To a stirred solution of **2** (2 mmol) and **3** (2 mmol) in 5 mL of H_2O/MeCN (5:1) was added isoquinoline (0.26 g, 2 mmol) at rt. The reaction mixture was then stirred for 3 h. The precipitates were filtered and recrystallized from methanol to give **4**.

*3.2.1. Dimethyl 1-benzoylpyrrolo[2,1-a]isoquinoline-2,3-dicarboxylate (**4a**)*

Pale yellow crystals, mp 196–198 °C, 0.62 g, yield 80%. IR (KBr) (ν_{max}/cm^{-1}): 1735 (C=O), 1732 (C=O), 1680 (C=O), 1641, 1366, 1210. MS, m/z (%): 387 (M$^+$, 10), 310 (100), 284 (10), 105 (30), 77 (60). Anal. Calcd for $C_{23}H_{17}NO_5$ (387.38): C, 71.31; H, 4.42; N, 3.62%. Found: C, 71.78; H, 4.54; N, 3.78%. ^{1}H NMR: δ 3.48 (3H, s, OMe), 3.90 (3H, s, OMe), 7.16 (1H, d, ^3J=7.6 Hz, CH), 7.33 (1H, t, ^3J=7.5 Hz, CH), 7.41 (2H, t, ^3J=7.5 Hz, 2CH), 7.47 (1H, t, ^3J=7.0 Hz, CH), 7.54 (1H, t, ^3J=7.0 Hz, CH), 7.65 (1H, d, ^3J=7.8 Hz, CH), 7.87 (2H, d, ^3J=7.5 Hz, 2CH), 8.04 (1H, d, ^3J=8.3 Hz, CH), 9.18 (1H, d, ^3J=7.6 Hz, CH) ppm. ^{13}C NMR: δ 52.0 (OMe), 52.1 (OMe), 114.2 (C), 115.6 (CH), 117.0 (C), 123.9 (CH), 124.1 (C), 125.2 (CH), 127.0 (C), 127.2 (CH), 128.0 (CH), 128.5 (2CH), 128.6 (CH), 129.0 (C), 129.7 (2CH), 132.0 (C), 133.3 (CH), 138.4 (C), 160.8 (C=O), 164.8 (C=O), 193.4 (C=O) ppm.

*3.2.2. Diethyl 1-benzoylpyrrolo[2,1-a]isoquinoline-2,3-dicarboxylate (**4b**)*

Pale yellow crystals, mp 137–139 °C, 0.65 g, yield 78%. IR (KBr) (ν_{max}/cm^{-1}): 1736 (C=O), 1732 (C=O), 1684 (C=O), 1640, 1398, 1203. MS, m/z (%): 415 (M$^+$, 5), 338 (100), 312 (15), 105 (35), 77 (62). Anal. Calcd for $C_{25}H_{21}NO_5$ (415.44): C, 72.28; H, 5.09; N, 3.37%. Found: C, 72.61; H, 5.20; N, 3.48%. ^{1}H NMR: δ 1.06 (3H, t, ^3J=7.2 Hz, Me), 1.33 (3H, t, ^3J=7.2 Hz, Me), 3.91 (2H, q, ^3J=7.2 Hz, OCH_2), 4.36 (2H, q, ^3J=7.2 Hz, OCH_2), 7.16 (1H, d, ^3J=7.6 Hz, CH), 7.33 (1H, t, ^3J=8.1 Hz, CH), 7.41 (2H, t, ^3J=7.8 Hz, 2CH), 7.47 (1H, t, ^3J=7.5 Hz, CH), 7.53 (1H, t, ^3J=7.4 Hz, CH), 7.66 (1H, d, ^3J=7.9 Hz, CH), 7.90 (2H, d, ^3J=8.1 Hz, 2CH), 8.04 (1H, d, ^3J=8.3 Hz, CH), 9.22 (1H, d, ^3J=7.6 Hz, CH) ppm. ^{13}C NMR: δ 13.7 (Me), 14.0 (Me), 61.1 (OCH_2), 61.5 (OCH_2), 114.3 (C), 115.4 (CH), 116.7 (C), 124.0 (CH), 124.2 (C), 125.2 (CH), 127.2 (CH), 127.3 (C), 128.0 (CH), 128.5 (2CH), 128.6 (CH), 129.1 (C), 129.9 (2CH), 131.9 (C), 133.4 (CH), 138.4 (C), 160.4 (C=O), 164.5 (C=O), 193.4 (C=O) ppm.

*3.2.3. Diisopropyl 1-benzoylpyrrolo[2,1-a]isoquinoline-2,3-dicarboxylate (**4c**)*

Yellow crystals, mp 150–152 °C, 0.66 g, yield 75%. IR (KBr) (ν_{max}/cm^{-1}): 1726 (C=O), 1723 (C=O), 1682 (C=O), 1648, 1376, 1213. MS, m/z (%):443 (M$^+$, 6), 366 (100), 340 (12), 105 (20), 77 (57). Anal. Calcd for $C_{27}H_{25}NO_5$ (443.49): C, 73.12; H, 5.68; N, 3.16%. Found: C, 73.42; H, 5.53; N, 3.38%. ^{1}H NMR: δ 1.05 (6H, d, ^3J=6.3 Hz, CHMe_2), 1.38 (6H, d, ^3J=6.5 Hz, CHMe_2), 4.80–4.85 (1H, m, CH), 5.28–5.33 (1H, m, CH), 7.16 (1H, d, ^3J=7.6 Hz, CH), 7.35 (1H, t, ^3J=7.5 Hz, CH), 7.44 (2H, t, ^3J=7.8 Hz, 2CH), 7.47 (1H, t, ^3J=7.8 Hz, CH), 7.49 (1H, t, ^3J=7.7 Hz, CH), 7.58 (1H, d, ^3J=7.8 Hz, CH), 7.96 (2H, d, ^3J=7.2 Hz, 2CH), 7.89 (1H, d, ^3J=7.8 Hz, CH), 9.25 (1H, d, ^3J=7.6 Hz, CH) ppm. ^{13}C NMR: δ 21.3 (CHMe_2), 21.8 (CHMe_2), 69.1 (*C*HMe_2), 69.5 (*C*HMe_2), 114.2 (C), 115.0 (C), 115.1 (CH), 123.5 (CH), 124.1 (C), 125.1 (CH), 127.1 (C), 127.2 (CH), 128.0 (CH), 128.4 (2CH), 128.6 (C), 129.1 (2CH), 130.0 (C), 131.2 (CH), 133.6 (CH), 138.2 (C), 160.1 (C=O), 164.0 (C=O), 193.4 (C=O) ppm.

*3.2.4. Di(tert-butyl) 1-benzoylpyrrolo[2,1-a]isoquinoline-2,3-dicarboxylate (**4d**)*

Yellow crystals, mp 164–166 °C, 0.71 g, yield 76%. IR (KBr) (ν_{max}/cm^{-1}): 1723 (C=O), 1717 (C=O), 1681 (C=O), 1659, 1368, 1201. MS, *m*/*z* (%): 471 (M$^+$, 9), 394 (100), 368 (14), 105 (31), 77 (59). Anal. Calcd for $C_{29}H_{29}NO_5$ (471.55): C, 73.87; H, 6.20; N, 2.97%. Found: C, 74.08; H, 6.03; N, 3.16%. ^{1}H NMR: δ 1.28 (9H, s, C*Me*$_3$), 1.58 (9H, s, C*Me*$_3$), 7.00 (1H, d, ^3J=7.6 Hz, CH), 7.25 (1H, t, ^3J=7.7 Hz, CH), 7.37 (1H, t, ^3J=7.9 Hz, CH), 7.39 (2H, t, ^3J=7.6 Hz, 2CH), 7.52 (1H, t, ^3J=7.7 Hz, CH), 7.57 (1H, d, ^3J=7.7 Hz, CH), 7.82 (1H, d, ^3J=8.3 Hz, CH), 7.96 (2H, d, ^3J=7.5 Hz, 2CH), 9.10 (1H, d, ^3J=7.6 Hz, CH) ppm. ^{13}C NMR: δ 27.3 (C*Me*$_3$), 28.1 (C*Me*$_3$), 82.0 (*C*Me$_3$), 82.6 (*C*Me$_3$), 114.6 (CH), 116.4 (C), 116.5 (C), 123.8 (CH), 124.2 (C), 124.4 (CH), 126.1 (C), 127.0 (CH), 127.8 (CH), 127.9 (CH), 128.6 (C), 128.7 (2CH), 129.9 (2CH), 130.2 (C), 133.6 (CH), 138.0 (C), 160.1 (C=O), 162.4 (C=O), 193.9 (C=O) ppm.

*3.2.5. Dimethyl 1-(4-methyl)benzoylpyrrolo[2,1-a]isoquinoline-2,3-dicarboxylate (**4e**)*

Pale yellow crystals, mp 207–209 °C, 0.60 g, yield 75%. IR (KBr) (ν_{max}/cm^{-1}): 1732 (C=O), 1729 (C=O), 1692 (C=O), 1637, 1361, 1213. MS, *m*/*z* (%): 401 (M$^+$, 6), 324 (100), 298 (10), 105 (20), 77 (70). Anal. Calcd for $C_{24}H_{19}NO_5$ (401.41): C, 71.81; H, 4.77; N, 3.49%. Found: C, 71.78; H, 4.54; N, 3.78%. ^{1}H NMR: δ 2.43 (3H, s, Me), 3.56 (3H, s, OMe), 3.94 (3H, s, OMe), 7.18 (1H, d, ^3J=7.5 Hz, CH), 7.25 (2H, d, ^3J=7.6 Hz, 2CH), 7.37 (1H, t, ^3J=7.5 Hz, 1CH), 7.50 (1H, t, ^3J=7.3 Hz, CH), 7.68 (1H, d, ^3J=7.7 Hz, CH), 7.83 (2H, d, ^3J=7.6 Hz, 2CH), 8.05 (1H, d, ^3J=7.4 Hz, 1CH), 9.21 (1H, d, ^3J=7.5 Hz, CH) ppm. ^{13}C NMR: δ 22.2 (Me), 52.5 (OMe), 52.7 (OMe), 114.7 (C), 116.0 (CH), 117.8 (C), 124.4 (CH), 124.8 (C), 125.7 (CH), 127.3 (C), 127.7 (CH), 128.6 (CH), 129.1 (CH), 129.6 (C), 129.7 (2CH), 130.4 (2CH), 132.3 (C), 136.4 (C), 144.9 (C), 161.4 (C=O), 165.4 (C=O), 193.6 (C=O) ppm.

*3.2.6. Diethyl 1-(4-methyl)benzoylpyrrolo[2,1-a]isoquinoline-2,3-dicarboxylate (**4f**)*

Pale yellow crystals, mp 165–167 °C, 0.61 g, yield 71%. IR (KBr) (ν_{max}/cm^{-1}): 1733 (C=O), 1732 (C=O), 1683 (C=O), 1638, 1362, 1211. MS, *m*/*z* (%): 429 (M$^+$, 8), 352 (100), 326 (14), 105 (25), 77 (65). Anal. Calcd for $C_{26}H_{23}NO_5$ (429.44): C, 72.72; H, 5.36; N, 3.26%. Found: C, 72.68; H, 5.27; N, 3.48%. ^{1}H NMR: δ 1.12 (3H, t, ^3J=7.3 Hz, Me), 1.45 (3H, t, ^3J=7.3 Hz, Me), 2.40 (3H, s, Me), 3.90 (2H, q, ^3J=7.3 Hz, OCH_2), 4.06 (2H, q, ^3J=7.3 Hz, OCH_2), 7.19 (1H, d, ^3J=7.5 Hz, CH), 7.27 (2H, d, ^3J=7.6 Hz, 2CH), 7.35 (1H, t, ^3J=7.5 Hz, 1CH), 7.48 (1H, t, ^3J=7.3 Hz, CH), 7.61 (1H, d, ^3J=7.7 Hz, CH), 7.80 (2H, d, ^3J=7.6 Hz, 2CH), 8.10 (1H, d, ^3J=7.4 Hz, 1CH), 9.23 (1H, d, ^3J=7.5 Hz, CH) ppm. ^{13}C NMR: δ 13.9 (Me), 14.4 (Me), 22.4 (Me), 61.1 (OCH_2), 62.3 (OCH_2), 114.8 (C), 116.1 (CH), 118.7 (C), 124.6 (CH), 125.0 (C), 125.4 (CH), 126.9 (C), 127.6 (CH), 128.4 (CH), 128.9 (CH), 129.3 (C), 129.9 (2CH), 131.3 (2CH), 131.9 (C), 135.4 (C), 144.7 (C), 160.8 (C=O), 164.9 (C=O), 192.8 (C=O) ppm.

*3.2.7. 1,2,3-Tribenzoylpyrrolo[2,1-a]isoquinoline (**4g**)*

Pale yellow crystals, mp 135–137 °C, 0.81 g, yield 85%. IR (KBr) (ν_{max}/cm^{-1}): 1674 (C=O), 1640 (C=O), 1593 (C=O), 1232, 958, 557. MS, *m*/*z* (%): 479 (M$^+$, 10), 402 (100), 376 (16), 105 (33), 77 (63). Anal. Calcd for $C_{33}H_{21}NO_3$ (479.53): C, 82.66; H, 4.41; N, 2.92%. Found: C, 82.88; H, 4.54; N, 3.06%. ^{1}H NMR: δ 7.54 (2H, t, ^3J=7.7 Hz, 2CH), 7.57–7.63 (4H, m, 4CH), 7.68 (1H, t, ^3J=7.4 Hz, CH), 7.74–7.80 (3H, m, 3CH), 7.84 (1H, d, ^3J=7.2 Hz, CH), 7.88 (2H, d, ^3J=8.3 Hz, CH), 7.97 (1H, d, ^3J=8.2 Hz, CH), 8.06 (2H, d, ^3J=8.3 Hz, 2CH), 8.15 (1H, d, ^3J=8.1 Hz, CH), 8.17 (2H, d, ^3J=7.3 Hz, 2CH), 8.52 (1H, d, ^3J=7.5 Hz, CH), 9.33 (1H, d, ^3J=7.4 Hz, CH) ppm. ^{13}C NMR: δ 115.4 (C), 123.8 (C), 126.3 (CH), 127.1 (C), 125.5 (C), 128.7 (2CH), 128.9 (2CH), 129.0 (2CH), 129.2 (2CH), 129.8 (2CH), 130.0 (C), 130.3 (2CH), 130.7 (CH), 134.2 (CH), 134.4 (CH), 134.5 (CH), 134.9 (CH), 135.1 (CH), 135.2 (CH), 136.1 (CH), 142.4 (C), 152.1 (C), 159.8 (C), 164.9 (C), 180.8 (C=O), 184.2 (C=O), 186.5 (C=O) ppm.

3.3. General procedure for the synthesis of compounds 11 and 12

To a stirred solution of **2a** (0.28 g, 2 mmol) and **3a** (2 mmol) in 5 mL of H_2O/MeCN (5:1) was added quinoline or benzothiazole (2 mmol) at rt. The reaction mixture was then stirred for 5 h. The precipitates were filtered and recrystallized from methanol to give the title compounds.

*3.3.1. Dimethyl 3-benzoylpyrrolo[1,2-a]quinoline-1,2-dicarboxylate (**11**)*

Pale yellow powder, mp 100–102 °C, 0.49 g, yield 63%. IR (KBr) (ν_{max}/cm^{-1}): 1734 (C=O), 1730 (C=O), 1681 (C=O), 1643, 1356, 1205. MS, *m*/*z* (%): 387 (M$^+$, 8), 310 (100), 284 (11), 105 (36), 77 (68). Anal. Calcd for $C_{23}H_{17}NO_5$ (387.38): C, 71.31; H, 4.42; N, 3.62%. Found: C, 71.39; H, 4.57; N, 3.77%. ^{1}H NMR: δ 3.72 (3H, s, OMe), 4.03 (3H, s, OMe), 7.43 (1H, d, ^3J=7.5 Hz, CH), 7.45 (2H, t, ^3J=7.5 Hz, 2CH), 7.48 (1H, t, ^3J=7.5 Hz, 2CH), 7.50 (1H, t, ^3J=7.6 Hz, CH), 7.77 (1H, t, ^3J=8.1 Hz, CH), 7.80 (1H, d, ^3J=8.2 Hz, 1CH), 7.87 (1H, d, ^3J=8.1 Hz, 2CH), 8.10 (2H, d, ^3J=7.7 Hz, 2CH), 8.21 (1H, d, ^3J=7.5 Hz, CH) ppm. ^{13}C NMR: δ 51.8 (OMe), 53.2 (OMe), 117.5 (C), 117.7 (CH), 121.1 (CH), 125.4 (C), 125.8 (CH), 125.9 (C), 126.7 (CH), 128.3 (C), 128.4 (2CH), 128.8 (C), 128.9 (2CH), 129.1 (CH), 129.2 (C), 129.6 (CH), 129.9 (CH), 130.5 (C), 159.9 (C=O), 163.4 (C=O), 191.3 (C=O) ppm.

*3.3.2. Dimethyl 3-benzoylpyrrolo[2,1-b][1,3]benzothiazole-1,2-dicarboxylate (**12**)*

Pale yellow powder, mp 100–102 °C, 0.44 g, yield 56%. IR (KBr) (ν_{max}/cm^{-1}): 1722 (C=O), 1719 (C=O), 1679 (C=O), 1654, 1355, 1200. MS, *m*/*z* (%): 393 (M$^+$, 9), 316 (100), 290 (20), 105 (28), 77 (57). Anal. Calcd for $C_{21}H_{15}NO_5S$ (393.41): C, 64.11; H, 3.84; N, 3.56%. Found: C, 64.36; H, 3.65; N, 3.68%. ^{1}H NMR: δ 3.53 (3H, s, OMe), 3.93 (3H, s, OMe), 7.45 (2H, t, ^3J=7.7 Hz, CH), 7.49 (1H, t, ^3J=7.7 Hz, CH), 7.52 (1H, t, ^3J=7.7 Hz, CH), 7.69 (2H, d, ^3J=8.4 Hz, 2CH), 7.72 (1H, t, ^3J=7.7 Hz, CH), 7.87 (1H, d, ^3J=7.7 Hz, CH), 8.95 (1H, d, ^3J=8.3 Hz, CH) ppm. ^{13}C NMR: δ 51.8 (OMe), 51.9 (OMe), 117.6 (C), 123.0 (C), 125.2 (CH), 126.3 (C), 127.9 (2CH), 128.7 (2CH), 129.0 (C), 129.9 (CH), 131.2 (CH), 132.9 (C), 133.1 (C), 134.4 (CH), 138.3 (CH), 142.5(C), 159.6 (C=O), 164.2 (C=O), 188.8 (C=O) ppm.

3.4. General procedure for the synthesis of functionalized isoxazoles 14

To a stirred solution of **2** (2 mmol) and **13** (2 mmol) in 5 mL of H_2O/MeCN (5:1) was added pyridine or *N*-methylimidazole (20 mol %) at rt. The reaction mixture was then stirred for 6 h. The solvent was removed under reduced pressure and the viscous residue was purified by column chromatography (Merck 230–400 mesh) using *n*-hexane/EtOAc (4:1) as eluent. Compounds **14a**–**e** are reported previously.[16]

*3.4.1. Dimethyl 3-benzoyl-isoxazole-4,5-dicarboxylate (**14f**)*

Pale yellow powder, mp 91–93 °C [lit.[22] 88–89 °C] 0.41 g, yield 70%. IR (KBr) (ν_{max}/cm^{-1}): 1746 (C=O), 1743 (C=O), 1738 (C=O), 1646, 1580, 1282. MS, *m*/*z* (%): 289 (M$^+$, 10), 212 (100), 186 (22), 105 (57), 77 (75). Anal. Calcd for $C_{14}H_{11}NO_6$ (289.24): C, 58.14; H, 3.83; N, 4.84%. Found: C, 59.78; H, 5.60; N, 6.98%. ^{1}H NMR: δ 3.87 (3H, s, OMe), 4.00 (3H, s, OMe), 7.50 (2H, t, ^3J=6.6 Hz, 2CH), 7.65 (1H, t, ^3J=6.8 Hz, CH), 8.13 (2H, d, ^3J=7.17 Hz, 2CH) ppm. ^{13}C NMR: δ 53.2 (OMe), 53.6 (OMe), 117.6 (C), 128.8 (2CH), 130.5 (2CH), 134.8 (CH), 134.9 (C), 155.9 (C), 159.1 (C), 159.9 (C=O), 160.1 (C=O), 183.7 (C=O) ppm.

*3.4.2. 3,4,5-Tribenzoyl-isoxazole (**14g**)*

White powder, mp 145–147 °C, 0.53 g, yield 80%. IR (KBr) (ν_{max}/cm^{-1}): 1670, 1647, 1569, 1250, 870, 673. MS, *m*/*z* (%): 381 (M^+, 12), 304 (100), 278 (26), 105 (50), 77 (82). Anal. Calcd for $C_{24}H_{15}NO_4$ (381.38): C, 75.58; H, 3.96; N, 3.67%. Found: C, 75.77; H, 3.80; N, 3.78%. ^{1}H NMR: δ 7.43 (2H, t, ^3J=7.8 Hz, 2CH), 7.51–7.59 (5H, m, 5CH), 7.66–7.69 (2H, m, 2CH), 7.85 (2H, d, ^3J=7.3 Hz, 2CH), 8.12 (2H, d, ^3J=7.4 Hz, 2CH), 8.28 (2H, d, ^3J=7.4 Hz, 2CH) ppm. ^{13}C NMR: δ 125.3 (C), 128.7 (2CH), 128.8 (2CH), 128.9 (2CH), 129.1 (2CH), 130.1 (2CH), 130.7 (2CH), 133.9 (CH), 134.6 (C), 134.7 (CH), 134.8 (CH), 134.9 (C), 136.5 (C), 160.6 (C), 165.0 (C), 180.3 (C=O), 183.6 (C=O), 186.9 (C=O) ppm.

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