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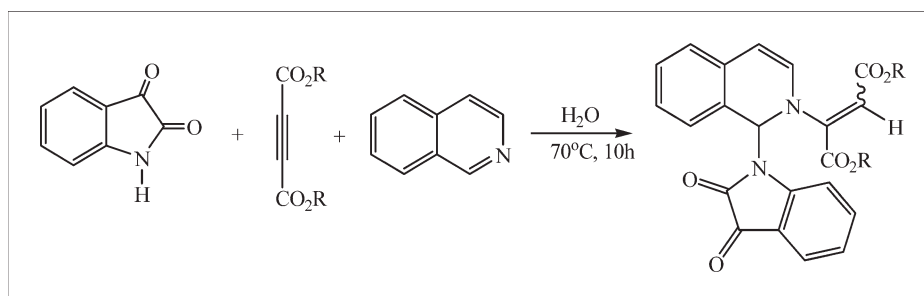
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A straightforward and efficient method for the synthesis of 1,2-dihydroisoquinolines *via* a one-pot, three-component reaction of isoquinoline, activated acetylenes, and NH-acids in water at 70°C without using any catalyst is reported. The method offers several advantages including high yields of products and an easy workup procedure.

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INTRODUCTION

The organic reactions in aqueous media have attracted much attention in synthetic organic chemistry, not only because water is one of the most abundant, cheap, and environmentally friendly solvents but also because water exhibits unique reactivity and selectivity properties that are different from those of conventional organic solvents. Thus, development of novel reactivity as well as selectivity that cannot be attained in conventional organic solvents is one of the challenging goals of aqueous chemistry. Multicomponent reactions (MCRs) are fast and appropriate solutions for the synthesis of different classes of compounds and are important in synthetic organic chemistry [1–4]. 1,2-Dihydroisoquinolines, as basic scaffolds in many natural products and pharmaceuticals that show significant biological activities [5–11] have promoted considerable efforts toward their synthesis [12–17]. Thus, it is desired to increase novel methods to buildup the new 1,2-dihydroisoquinoline-based structures. At the present, it has been expected that chemical reactions in aqueous solutions frequently give better results than in organic solvents and often the insolubility of the last products facilitates their isolation [18,19].

As part of our continuing interest in the development of new synthetic methods in heterocyclic chemistry and our interest in isoquinoline-based multicomponent reactions [20–22], we describe an efficient synthesis of 1,2-

dihydroisoquinolines **4** *via* the reaction of isatin **1** with activated acetylenes **2** and isoquinoline **3** in water at 70°C (Scheme 1).

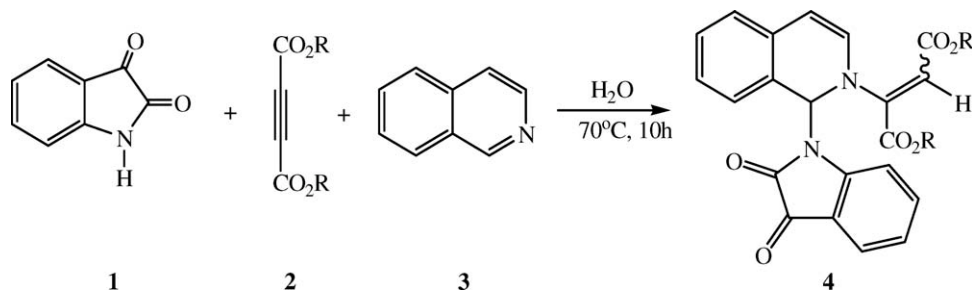
RESULT AND DISCUSSION

As indicated in Scheme 1, isatin **1**, activated acetylenes **2**, and isoquinoline **3** undergo a smooth 1:1:1 addition reaction in water at 70°C (the activated acetylenes and isatin are mixed first, and then isoquinoline is added) to produce 1,2-dihydroisoquinolines **4** in 82–96% yields (Scheme 1). We examined the diversity of reaction with different substitution as indicated in the Table 1.

Under similar conditions, the reaction of quinoline, pyridine, or phenanthridine with DMAD in the presence of various NH-acids led to dimethyl 2-[1(2*H*)-quinolinyl]-2-butenedioate (**7**), dimethyl 2-[1(2*H*)-pyridinyl]-2-butenedioate (**8**), or dimethyl 2-[1(2*H*)-phenanthridinyl]-2-butenedioate (**9**) in excellent yields (Table 2).

The reactions between isoquinoline, quinoline, pyridine, or phenanthridine with dimethyl acetylenedicarboxylate as a Michael acceptor [23–30] in the presence of heterocyclic NH acids were carried out in water and finished after ~10 h at room temperature. Products **4h–4j** and **9a–9e** are known compounds [30]. Structures of compounds **4a–4i**, **7a–7c**, **8a–8c**, and **9a–9e** were deduced from their IR, mass, ¹H-NMR, and ¹³C-NMR spectra.

Scheme 1



The mass spectra of these compounds displayed molecular ion peaks at the appropriate m/z values.

The $^1\text{H-NMR}$ spectrum of **4a** exhibited four singlets for the methoxy (δ 3.88 and 3.94 ppm), olefinic (δ 5.39 ppm), and methin (δ 7.82 ppm) protons along with multiplets for the isoquinoline moiety. The proton-decoupled $^{13}\text{C-NMR}$ spectrum of **4a** showed 23 distinct resonances in agreement with the proposed structure. Partial assignments of these resonances are given in Experimental Section.

Although the mechanistic details of the reaction are not known, a plausible rationalization may be advanced to explain the product formation. Presumably, the reaction involves the initial formation of a 1:1 zwitterionic intermediate **5** between isoquinoline and the activated acetylene, [31–36]. This intermediate is protonated by NH-acids and then attacked by the conjugate base of the NH-acids to produce **4** (Scheme 2).

In conclusion, we have reported an efficient and environmentally friendly approach for the synthesis of 1,2-disubstituted nitrogen containing heterocycles *via* condensation of activated acetylenes and isoquinoline, quinoline, pyridine, or phenanthridine in the presence of NH-acids using water as the solvent. To the best of our knowledge, this is the first report on the synthesis of compounds of type **4**, **7**, **8**, or **9** in water and this new procedure opens an important alternative to the use of volatile organic solvents.

EXPERIMENTAL

All chemicals were obtained from commercial sources. Melting points were measured on a Kofler hot stage apparatus and are uncorrected. $^1\text{H-NMR}$ and $^{13}\text{C-NMR}$ spectra were obtained with a Bruker FT-500 spectrometer in chloroform- d_1 , 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 Nicolet Magna 550-FT spectrometer. Elemental analyses were carried out with a Perkin-Elmer model 240-C apparatus. The results of elemental analyses (C, H, and N) were within $\pm 0.4\%$ of the calculated values.

General procedure for the preparation of compounds 4, 7, 8, and 9. To a magnetically stirred solution of NH-acids (2 mmol) and dialkyl acetylenedicarboxylate (2 mmol) in H_2O (20 mL), isoquinoline, quinoline, pyridine, or phenanthridine

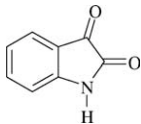
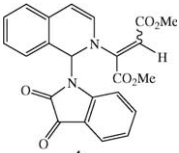
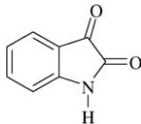
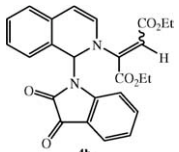
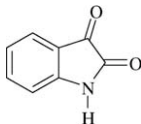
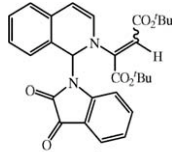
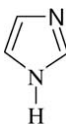
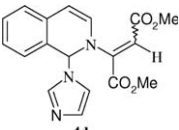
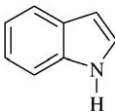
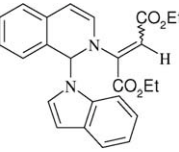
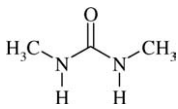
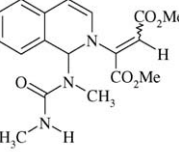
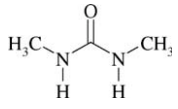
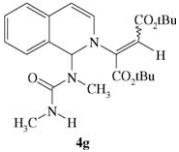
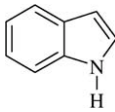
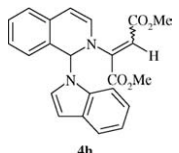
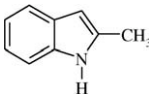
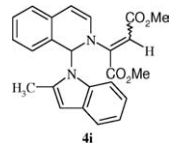
(2 mmol) was added, and the reaction was heated for 10 h at 70°C . The completion of reaction was confirmed by TLC (EtOAc–hexane 6:1). The resulting precipitate was separated by filtration and recrystallized from EtOH to afford the pure title compounds.

Dimethyl 2-[1-(2,3-dioxo-2,3-dihydro-1H-indol-1-yl)-2(1H)-isoquinolinyl]-2-butenedioate (4a). Pale yellow powder, mp $162\text{--}164^\circ\text{C}$, yield: 0.74 g (89%). IR(KBr) ν_{max} (cm^{-1}): 1738, 1732, 1723, 1692, and 1245 cm^{-1} . $^1\text{H-NMR}$: δ = 3.88 (3 H, s, MeO), 3.94 (3 H, s, MeO), 5.39 (1 H, s, CH), 7.54 (1 H, d, 3J = 7.6 Hz, CH), 7.69 (2 H, t, 3J = 7.2 Hz, 2 CH), 7.73 (2 H, t, 3J = 7.2 Hz, 2 CH), 7.82 (1 H, s, CH), 7.93 (2 H, d, 3J = 7.5 Hz, 2 CH), 8.69 (2 H, d, 3J = 7.5 Hz, 2 CH), 9.31 (1 H, d, 3J = 7.6 Hz, CH) ppm. $^{13}\text{C-NMR}$: δ = 51.6 (MeO), 52.3 (MeO), 58.8 (CH), 94.6 (CH), 108.2 (CH), 122.4 (CH), 123.5 (2 CH), 124.7 (2 CH), 126.2 (2 CH), 128.4 (CH), 128.5 (C), 128.6 (C), 134.5 (CH), 1365.4 (C), 148.5 (C), 152.7 (C), 159.7 (C=O), 160.6 (C=O), 163.4 (C=O), 185.7 (C=O) ppm. MS: m/z (%) = 418 (M $^+$, 15), 387 (45), 272 (58), 146 (94), 129 (100), 31(100). Anal. Calc. for $\text{C}_{23}\text{H}_{18}\text{N}_2\text{O}_6$ (418.40): C, 66.03; H, 4.34; N, 6.70; found: C, 65.94; H, 4.23; N, 6.62%.

Diethyl 2-[1-(2,3-dioxo-2,3-dihydro-1H-indol-1-yl)-2(1H)-isoquinolinyl]-2-butenedioate (4b). Yellow powder, mp $140\text{--}142^\circ\text{C}$, yield: 0.84 g (94%). IR(KBr) ν_{max} (cm^{-1}): 1738, 1735, 1724, 1682, and 1195 cm^{-1} . $^1\text{H-NMR}$: δ = 1.41 (3 H, t, 3J = 7.2 Hz, Me), 1.47 (3 H, t, 3J = 7.2 Hz, Me), 4.50 (2 H, q, 3J = 7.2 Hz, CH_2O), 4.57 (2 H, q, 3J = 7.2 Hz, CH_2O), 5.27 (1 H, s, CH), 7.49 (1 H, d, 3J = 7.6 Hz, CH), 7.56 (1 H, s, CH), 7.65 (2 H, t, 3J = 7.3 Hz, 2 CH), 7.68 (2 H, t, 3J = 7.3 Hz, 2 CH), 7.88 (2 H, d, 3J = 7.5 Hz, 2 CH), 8.65 (2 H, d, 3J = 7.5 Hz, 2 CH), 9.27 (1 H, d, 3J = 7.6 Hz, CH) ppm. $^{13}\text{C-NMR}$: δ = 14.3 (Me), 14.5 (Me), 58.5 (CH), 60.3 (CH_2O), 61.4 (CH_2O), 95.2 (CH), 108.5 (CH), 123.4 (2 CH), 124.7 (CH), 125.1 (CH), 126.7 (2 CH), 127.2 (CH), 128.4 (CH), 129.2 (C), 134.5 (CH), 135.3 (C), 137.6 (C), 147.8 (C), 152.6 (C), 160.4 (C=O), 161.2 (C=O), 164.5 (C=O), 185.5 (C=O) ppm. MS: m/z (%) = 446 (M $^+$, 15), 368 (62), 290 (100), 253 (38), 146 (88), 129 (100), 31 (100). Anal. Calc. for $\text{C}_{25}\text{H}_{22}\text{N}_2\text{O}_6$ (446.46): C, 67.26; H, 4.97; N, 6.27; found: C, 67.14; H, 4.85; N, 6.13%.

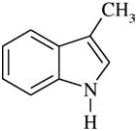
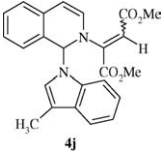

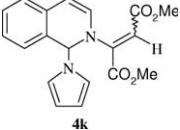
Di(tert-butyl) 2-[1-(2,3-dioxo-2,3-dihydro-1H-indol-1-yl)-2(1H)-isoquinolinyl]-2-butenedioate (4c). Yellow powder, mp $145\text{--}147^\circ\text{C}$, yield: 0.92 g (92%). IR(KBr) ν_{max} (cm^{-1}): 1735, 1730, 1725, 1687, and 1278 cm^{-1} . $^1\text{H-NMR}$: δ = 1.59 (9 H, s, 3 Me), 1.71 (9 H, s, 3 Me), 5.48 (1 H, s, CH), 7.48 (1 H, s, CH), 7.50 (1 H, d, 3J = 7.7 Hz, CH), 7.71 (2 H, d, 3J = 7.2 Hz, 2 CH), 7.73 (2 H, t, 3J = 7.2 Hz, 2 CH), 7.93 (2 H, t, 3J = 7.5 Hz, 2 CH), 8.55 (2 H, d, 3J = 7.5 Hz, 2 CH), 9.22

Table 1
Synthesis of 1,2-dihydroisoquinoline derivatives in water.

Entry	NH-acid	R	Product	Yield (%)
1		Me	 4a	89
2'		Et	 4b	94
3		tBu	 4c	92
4		Me	 4d	94
5		Et	 4e	84
6		Me	 4f	89
7		tBu	 4g	94
8		Me	 4h	82
9		Me	 4i	95

(Continued)

Table 1
(Continued)

Entry	NH-acid	R	Product	Yield (%)
10		Me		96
11		Me		92

(1 H, d, $^3J = 7.7$ Hz, CH) ppm. $^{13}\text{C-NMR}$: $\delta = 28.3$ (CMe₃), 28.4 (CMe₃), 59.4 (CH), 83.4 (CMe₃), 84.0 (CMe₃), 96.0 (CH), 109.2 (CH), 123.7 (2 CH), 125.4 (CH), 125.8 (CH), 127.2 (2 CH), 127.8 (CH), 128.8 (CH), 129.5 (C), 134.6 (CH), 135.5 (C), 136.8 (C), 147.2 (C), 151.7 (C), 160.5 (C=O), 161.4 (C=O), 164.3 (C=O), 186.0 (C=O) ppm. Anal. Calc. for C₂₉H₃₀N₂O₆ (502.56): C, 69.31; H, 6.02; N, 5.57; found: C, 69.24; H, 5.89; N, 5.46%.

Dimethyl 2-[1-(1H-midazol-1-yl)-2-(1H-isoquinolinyl)]-2-butenedioate (4d). Yellow powder, mp 124–126°C, yield: 0.64 g (94%). IR(KBr) ν_{max} (cm⁻¹): 1732, 1725, 1557, 1410, and 1127 cm⁻¹. $^1\text{H-NMR}$: $\delta = 3.75$ (3 H, s, MeO), 3.82 (3 H, s, MeO), 5.98 (1 H, s, CH), 7.05 (1 H, d, $^3J = 5.7$ Hz, CH), 7.24 (1 H, d, $^3J = 7.5$ Hz, CH), 7.42 (1 H, d, $^3J = 5.7$ Hz, CH), 7.52 (1 H, t, $^3J = 7.5$ Hz, CH), 7.58 (1 H, t, $^3J = 7.5$ Hz, CH), 7.67 (1 H, s, CH), 7.70 (1 H, d, $^3J = 7.4$ Hz, CH), 7.85 (1 H, d, $^3J = 7.4$ Hz, CH), 8.02 (1 H, d, $^3J = 7.5$ Hz, CH), 8.25 (1 H, s, CH) ppm. $^{13}\text{C-NMR}$: $\delta = 51.5$ (MeO), 52.2 (MeO), 60.4 (CH), 98.2 (CH), 103.0 (CH), 118.2 (CH), 120.7 (CH), 127.5 (2 CH), 127.9 (CH), 129.3 (CH), 130.1 (CH), 137.5 (CH), 138.2 (C), 140.0 (C), 141.2 (C), 165.4 (C=O), 167.2 (C=O) ppm. Anal. Calc. for C₁₈H₁₇N₃O₄ (339.35): C, 63.71; H, 5.05; N, 12.38; found: C, 63.58; H, 4.92; N, 12.27%.

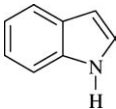
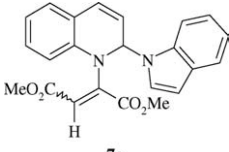
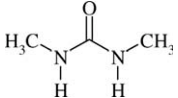
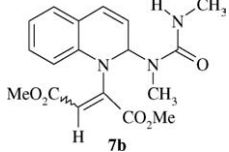

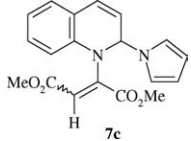
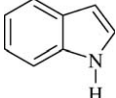
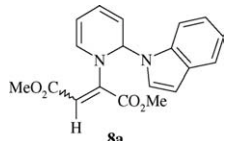


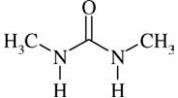
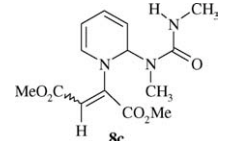
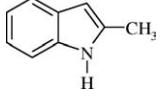
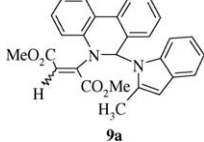
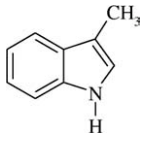
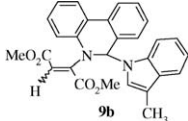
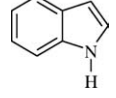
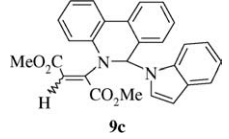
Diethyl 2-[1-(1H-indol-1-yl)-2-(1H-isoquinolinyl)]-2-butenedioate (4e). Yellow powder, mp 115–117°C, yield: 0.75 g (84%). IR(KBr) ν_{max} (cm⁻¹): 1738, 1732, 1545, 1412, and 1175 cm⁻¹. $^1\text{H-NMR}$: $\delta = 1.25$ (3 H, t, $^3J = 7.3$ Hz, Me), 1.34 (3 H, t, $^3J = 7.3$ Hz, Me), 4.21 (2 H, q, $^3J = 7.3$ Hz, CH₂O), 4.32 (2 H, q, $^3J = 7.3$ Hz, CH₂O), 5.95 (1 H, s, CH), 6.87 (1 H, d, $^3J = 6.2$ Hz, CH), 7.23 (1 H, d, $^3J = 7.7$ Hz, CH), 7.38 (1 H, d, $^3J = 6.2$ Hz, CH), 7.56 (2 H, t, $^3J = 7.4$ Hz, 2 CH), 7.63 (2 H, t, $^3J = 7.4$ Hz, 2 CH), 7.67 (1 H, s, CH), 7.74 (2 H, d, $^3J = 7.4$ Hz, 2 CH), 8.40 (2 H, d, $^3J = 7.4$ Hz, 2 CH), 9.25 (1 H, d, $^3J = 7.7$ Hz, CH) ppm. $^{13}\text{C-NMR}$: $\delta = 13.8$ (Me), 14.3 (Me), 60.0 (CH), 61.4 (CH₂O), 62.6 (CH₂O), 97.2 (CH), 103.4 (CH), 110.2 (CH), 115.6 (CH), 119.7 (2 CH), 121.3 (CH), 122.8 (CH), 125.5 (2 CH), 127.1 (CH), 128.6 (2 CH), 132.5 (C), 134.7 (C), 136.2 (C), 138.8 (C), 142.3 (C), 167.2 (C=O), 168.4 (C=O) ppm. MS: m/z (%) = 416 (M⁺, 15), 371 (54), 272 (52), 129 (100), 116 (86), 45(100). Anal. Calc. for C₂₅H₂₄N₂O₄ (416.47): C, 72.10; H, 5.81; N, 6.73; found: C, 72.00; H, 5.74; N, 6.67%.

Dimethyl 2-[1-[methyl[(methylamino)carbonylamino]-2-(1H-isoquinolinyl)]-2-butenedioate (4f). Pale yellow powder, mp 120–122°C, yield: 0.64 g (89%). IR(KBr) ν_{max} (cm⁻¹): 1730, 1727, 1717, 1712, and 1232 cm⁻¹. $^1\text{H-NMR}$: $\delta = 3.17$ (3 H, s, NMe), 3.19 (3 H, s, NMe), 3.74 (3 H, s, MeO), 3.82 (3 H, s, MeO), 5.94 (1 H, s, CH), 6.52 (1 H, s, NH), 7.25 (1 H, d, $^3J = 7.5$ Hz, CH), 7.48 (1 H, t, $^3J = 7.5$ Hz, CH), 7.57 (1 H, t, $^3J = 7.6$ Hz, CH), 7.62 (1 H, s, CH), 7.75 (1 H, d, $^3J = 7.6$ Hz, CH), 8.42 (1 H, d, $^3J = 7.5$ Hz, CH), 8.97 (1 H, d, $^3J = 7.5$ Hz, CH) ppm. $^{13}\text{C-NMR}$: $\delta = 27.8$ (NMe), 33.4 (NMe), 52.4 (MeO), 53.6 (MeO), 65.4 (CH), 98.2 (CH), 102.3 (CH), 118.2 (CH), 124.3 (2 CH), 126.7 (CH), 128.5 (CH), 134.2 (C), 135.8 (C), 141.8 (C), 159.7 (C=O), 161.4 (C=O), 164.8 (C=O) ppm. MS: m/z (%) = 359 (M⁺, 5), 230 (45), 129 (100), 31(100). Anal. Calc. for C₁₈H₂₁N₃O₅ (359.38): C, 60.16; H, 5.89; N, 11.69; found: C, 60.04; H, 5.75; N, 11.58%.

Di(tert-butyl)2-[1-[methyl[(methylamino)carbonylamino]-2-(1H-isoquinolinyl)]-2-butenedioate (4g). Yellow powder, mp 147–149°C, yield: 0.83 g (94%). IR(KBr) ν_{max} (cm⁻¹): 1728, 1718, 1654, and 1258 cm⁻¹. $^1\text{H-NMR}$: $\delta = 1.54$ (9 H, s, 3 Me), 1.68 (9 H, s, 3 Me), 2.65 (3 H, s, NMe), 2.97 (3 H, s, NMe), 5.58 (1 H, s, CH), 6.38 (1 H, s, NH), 7.48 (1 H, s, CH), 7.52 (1 H, d, $^3J = 7.5$ Hz, CH), 7.65 (1 H, d, $^3J = 7.2$ Hz, CH), 7.74 (1 H, t, $^3J = 7.3$ Hz, CH), 7.84 (1 H, t, $^3J = 7.4$ Hz, CH), 8.58 (1 H, d, $^3J = 7.5$ Hz, CH), 9.18 (1 H, d, $^3J = 7.7$ Hz, CH) ppm. $^{13}\text{C-NMR}$: $\delta = 27.6$ (CMe₃), 28.2 (CMe₃), 32.4 (NMe), 33.8 (NMe), 59.5 (CH), 82.8 (CMe₃), 83.6 (CMe₃), 96.4 (CH), 102.5 (CH), 118.6 (CH), 124.0 (2 CH), 127.2 (CH), 128.6 (CH), 134.4 (C), 136.0 (C), 142.2 (C), 160.4 (C=O), 162.3 (C=O), 165.7 (C=O) ppm. Anal. Calc. for C₂₄H₃₃N₃O₅ (443.54): C, 64.99; H, 7.50; N, 9.47; found: C, 64.84; H, 7.42; N, 9.35%.

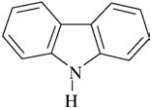
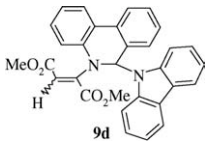
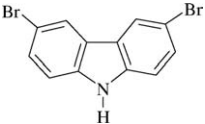
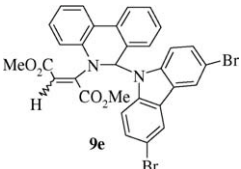
Dimethyl 2-[1-(1H-pyrrol-1-yl)-2-(1H-isoquinolinyl)]-2-butenedioate (4k). Yellow powder, mp 134–136°C, yield: 0.62 g (92%). IR(KBr) ν_{max} (cm⁻¹): 1730, 1722, 1545, 1425, and 1167 cm⁻¹. $^1\text{H-NMR}$: $\delta = 3.80$ (3 H, s, OMe), 3.85 (3 H, s, OMe), 5.95 (1 H, s, CH), 6.84 (1 H, d, $^3J = 6.7$ Hz, CH), 6.97 (2 H, t, $^3J = 5.8$ Hz, 2 CH), 7.24 (1 H, d, $^3J = 7.2$ Hz, CH), 7.32 (2 H, t, $^3J = 6.2$ Hz, 2 CH), 7.38 (1 H, t, $^3J = 6.7$ Hz, CH), 7.54 (1 H, d, $^3J = 7.5$ Hz, CH), 7.68 (1 H, s, CH), 7.78 (1 H, d, $^3J = 7.5$ Hz, CH), 8.02 (1 H, d, $^3J = 7.5$ Hz, CH) ppm. $^{13}\text{C-NMR}$: $\delta = 51.5$ (OMe), 52.7 (OMe),

Table 2
Synthesis of 1,2-dihydroquinoline, 1,2-dihydropyridine, or 1,2-dihydrophenanthridine derivatives in water.

Entry	NH-acid	R	Product	Yield (%)
1		Me	 7a	88
2		Me	 7b	86
3		Me	 7c	89
4		Me	 8a	86
5		Me	 8b	90
6		Me	 8c	89
7		Me	 9a	92
8		Me	 9b	94
9		Me	 9c	97

(Continued)

Table 2
(Continued)

Entry	NH-acid	R	Product	Yield (%)
10		Me		95
11		Me		96

58.7 (CH), 98.4 (CH), 104.2 (CH), 120.4 (CH), 122.8 (2 CH), 123.3 (2 CH), 127.5 (2 CH), 128.4 (CH), 131.5 (CH), 135.4 (C), 137.3 (C), 14.08 (C), 163.8 (C=O), 165.7 (C=O) ppm. Anal. Calc. for $C_{19}H_{18}N_2O_4$ (338.36): C, 67.45; H, 5.36; N, 8.28; found: C, 67.32; H, 5.28; N, 8.19%.

Dimethyl 2-[2-(1H-indol-1-yl)-1(2H)-quinolinyl]-2-butenedioate (7a). Yellow powder, mp 135–137°C, yield: 0.68 g (88%). IR(KBr) ν_{\max} (cm^{-1}): 1732, 1728, 1694, 1548, and 1243 cm^{-1} . 1H -NMR: δ = 3.85 (3 H, s, OMe), 3.90 (3 H, s, OMe), 5.47 (1 H, s, CH), 6.38 (1 H, d, 3J = 5.8 Hz, CH), 6.85 (1 H, d, 3J = 6.5 Hz, CH), 7.35 (1 H, d, 3J = 6.5 Hz, CH), 7.55 (1 H, d, 3J = 7.4 Hz, CH), 7.56 (2H, t, 3J = 7.2 Hz, 2 CH), 7.60 (2 H, t, 3J = 7.2 Hz, 2 CH), 7.79 (2 H, d, 3J = 7.7 Hz, 2 CH), 8.15 (2 H, d, 3J = 7.2 Hz, 2 CH), 8.21 (1 H, d, 3J = 7.7 Hz, CH) ppm. ^{13}C -NMR: δ = 51.5 (OMe), 52.5 (OMe), 59.2 (CH), 97.5 (CH), 102.5 (CH), 113.4 (CH), 117.8 (2 CH), 120.4 (CH), 121.8 (2 CH), 122.5 (2 CH), 125.4 (CH), 127.6 (CH), 129.8 (C), 131.6 (CH), 133.2 (C), 136.3 (C), 138.7 (C), 141.8 (C), 165.4 (C=O), 166.8 (C=O) ppm. MS: m/z (%) = 388 (M^+ , 15), 357 (45), 129 (100), 116 (94), 31 (100). Anal. Calc. for $C_{23}H_{20}N_2O_4$ (388.42): C, 71.12; H, 5.19; N, 7.21; found: C, 70.98; H, 5.05; N, 7.12%.

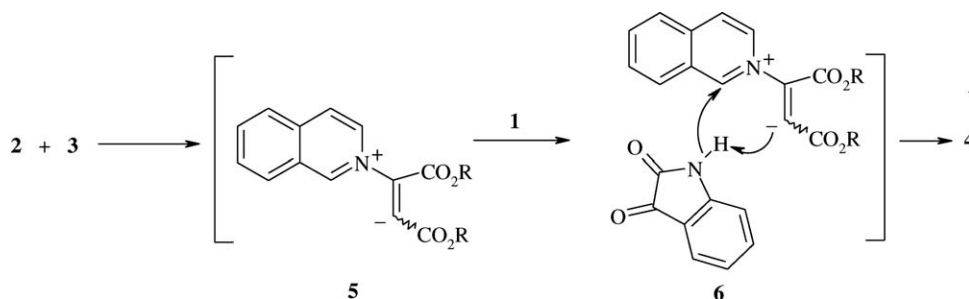
Dimethyl 2-[2-[methyl(methylamino)carbonylamino]-1(2H)-quinolinyl]-2-butenedioate (7b). Yellow powder, mp 128–130°C, yield: 0.64 g (86%). IR(KBr) ν_{\max} (cm^{-1}): 1735, 1727, 1695, 1547, and 1194 cm^{-1} . 1H -NMR: δ = 3.22 (3 H, s, NMe), 3.25 (3 H, s, NMe), 3.83 (3 H, s, OMe), 3.87 (3 H, s, OMe), 5.86 (1 H, s, CH), 6.38 (1H, d, 3J = 8.2, NH), 7.35 (1 H, d, 3J = 7.3 Hz, CH), 7.40 (1 H, t, 3J = 7.5 Hz, CH), 7.52 (1 H, t,

3J = 7.5 Hz, CH), 7.57 (1 H, m, CH), 7.62 (1 H, d, 3J = 7.5 Hz, CH), 7.75 (1 H, d, 3J = 7.5 Hz, CH), 7.82 (1 H, d, 3J = 7.5 Hz, CH) ppm. ^{13}C -NMR: δ = 27.5 (NMe), 33.6 (NMe), 51.4 (OMe), 52.8 (OMe), 68.2 (CH), 98.5 (CH), 114.8 (CH), 117.5 (CH), 121.4 (CH), 126.7 (C), 128.5 (CH), 131.4 (CH), 133.8 (CH), 135.6 (C), 142.7 (C), 159.6 (C=O), 163.8 (C=O), 165.2 (C=O) ppm. MS: m/z (%) = 359 (M^+ , 10), 328 (45), 230 (52), 129 (100), 31 (100). Anal. Calc. for $C_{18}H_{21}N_3O_5$ (359.38): C, 60.16; H, 5.89; N, 11.69; found: C, 60.23; H, 5.94; N, 11.76%.

Dimethyl 2-[2-(1H-pyrrol-1-yl)-1(2H)-quinolinyl]-2-butenedioate (7c). Yellow powder, mp 131–133°C, yield: 0.60 g (89%). IR(KBr) ν_{\max} (cm^{-1}): 1728, 1720, 1587, 1457, and 1168 cm^{-1} . 1H -NMR: δ = 3.82 (3 H, s, MeO), 3.87 (3 H, s, MeO), 5.87 (1 H, s, CH), 6.38 (2 H, t, 3J = 5.7 Hz, 2 CH), 6.85 (1 H, d, 3J = 6.2 Hz, CH), 6.96 (2 H, t, 3J = 5.9 Hz, 2 CH), 7.23 (1 H, d, 3J = 7.4 Hz, CH), 7.32 (1 H, t, 3J = 7.2 Hz, CH), 7.40 (1 H, t, 3J = 7.2 Hz, CH), 7.64 (1 H, d, 3J = 6.8 Hz, CH), 7.75 (1 H, d, 3J = 7.2 Hz, CH), 8.25 (1 H, d, 3J = 7.5 Hz, CH) ppm. ^{13}C -NMR: δ = 52.3 (MeO), 52.7 (MeO), 60.3 (CH), 100.4 (CH), 117.4 (CH), 119.2 (CH), 121.5 (2 CH), 122.6 (2 CH), 124.3 (2 CH), 128.4 (CH), 131.4 (CH), 132.0 (C), 138.7 (C), 143.2 (C), 167.2 (C=O), 169.0 (C=O) ppm. Anal. Calc. for $C_{19}H_{18}N_2O_4$ (338.36): C, 67.45; H, 5.36; N, 8.28; found: C, 67.35; H, 5.30; N, 8.22%.

Dimethyl 2-[2-(1H-indol-1-yl)-1(2H)-pyridinyl]-2-butenedioate (8a). Yellow powder, mp 119–121°C, yield: 0.58 g (86%). IR(KBr) ν_{\max} (cm^{-1}): 1740, 1735, 1674, 1453, and 1153 cm^{-1} .

Scheme 2



¹H-NMR: δ = 3.73 (3 H, s, OMe), 3.80 (3 H, s, OMe), 5.56 (1 H, s, CH), 6.42 (1 H, d, ³J = 6.3 Hz, CH), 6.52 (1 H, d, ³J = 6.8 Hz, CH), 6.68 (1 H, t, ³J = 7.4 Hz, CH), 6.75 (1 H, t, ³J = 7.5 Hz, CH), 7.14 (1 H, t, ³J = 7.4 Hz, CH), 7.35 (1 H, d, ³J = 6.8 Hz, CH), 7.48 (1 H, d, ³J = 7.4 Hz, CH), 7.55 (1 H, d, ³J = 7.4 Hz, CH), 7.63 (1 H, t, ³J = 7.3 Hz, 2 CH), 7.95 (1 H, d, ³J = 7.7 Hz, CH), 8.22 (2 H, d, ³J = 6.9 Hz, 2 CH) ppm. ¹³C-NMR: δ = 51.2 (OMe), 52.4 (OMe), 59.6 (CH), 98.2 (CH), 114.5 (CH), 119.2 (CH), 120.4 (2 CH), 121.5 (CH), 122.2 (CH), 122.8 (2 CH), 125.6 (CH), 132.6 (C), 134.7 (CH), 136.5 (C), 138.5 (C), 167.2 (C=O), 169.2 (C=O) ppm. Anal. Calc. for C₁₉H₁₈N₂O₄ (338.36): C, 67.45; H, 5.36; N, 8.28; found: C, 67.38; H, 5.27; N, 8.16%.

Dimethyl 2-[2-(imidazol-1-yl)-1(2H)-pyridinyl]-2-butenedioate (8b). Yellow powder, mp 115–117°C, yield: 0.52 g (90%). IR(KBr) ν_{\max} (cm⁻¹): 1728, 1724, 1525, and 1147 cm⁻¹. ¹H-NMR: δ = 3.75 (3 H, s, MeO), 3.82 (3 H, s, MeO), 5.92 (1 H, s, CH), 6.75 (1 H, t, ³J = 7.3 Hz, CH), 7.18 (1 H, t, ³J = 7.4 Hz, CH), 7.27 (1 H, d, ³J = 6.5 Hz, CH), 7.38 (1 H, d, ³J = 6.5 Hz, CH), 7.75 (1 H, d, ³J = 6.4 Hz, CH), 7.86 (1 H, s, CH), 8.35 (1 H, d, ³J = 7.3 Hz, CH), 9.12 (1 H, d, ³J = 7.3 Hz, CH) ppm. ¹³C-NMR: δ = 51.6 (OMe), 52.4 (OMe), 62.2 (CH), 98.7 (CH), 116.8 (CH), 120.4 (2 CH), 123.2 (CH), 125.2 (CH), 129.8 (CH), 134.5 (C), 138.3 (CH), 162.4 (C=O), 164.8 (C=O) ppm. Anal. Calc. for C₁₄H₁₅N₃O₅ (289.29): C, 58.13; H, 5.23; N, 14.53; found: C, 58.25; H, 5.32; N, 15.61%.

Dimethyl 2-[2-{methyl(methylamino)carbonylamino}-1(2H)-pyridinyl]-2-butenedioate (8c). Yellow powder, mp 117–119°C, yield: 0.55 g (89%). IR(KBr) ν_{\max} (cm⁻¹): 1738, 1736, 1730, 1625, 1584, and 1185 cm⁻¹. ¹H-NMR: δ = 3.27 (3 H, s, NMe), 3.32 (3 H, s, NMe), 3.78 (3 H, s, OMe), 3.85 (3 H, s, OMe), 5.86 (1 H, s, CH), 6.34 (1 H, d, ³J = 8.5, NH), 6.78 (1 H, t, ³J = 7.3 Hz, CH), 7.03 (1 H, m, CH), 7.37 (1 H, t, ³J = 7.5 Hz, CH), 7.42 (1 H, m, CH), 7.97 (1 H, d, ³J = 7.5 Hz, CH) ppm. ¹³C-NMR: δ = 28.2 (NMe), 32.5 (NMe), 51.5 (OMe), 52.6 (OMe), 67.4 (CH), 100.2 (CH), 109.4 (CH), 113.5 (CH), 120.8 (CH), 133.8 (C), 135.7 (CH), 159.8 (C=O), 160.2 (C=O), 165.2 (C=O) ppm. Anal. Calc. for C₁₄H₁₉N₃O₅ (309.32): C, 54.36; H, 6.19; N, 13.58; found: C, 54.27; H, 6.04; N, 13.47%.

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