Phenanthridine or isoquinoline are good reagents for the synthesis of enamino esters

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A new class of enamino esters has been isolated in excellent yields from the 1:1:1 addition reaction between phenanthridine or isoquinoline and activated acetylenic esters in the presence of heterocyclic NH compounds (succinimide, 5-nitroindazole, benzoxazolinone, 6-chlorobenzoxazolinone, carbazole and 3,6-dibromocabazole) or 1,3-dicarbonyl compounds such as 1,3-dimethylbarbituric acid and 1,3-diethyl-2-thiobar- bituric acid.

Keywords: enamino esters, phenanthridine, isoquinoline, activated acetylenic esters, heterocyclic NH or 1,3-dicarbonyl compounds

Heterocyclic rings are present as fundamental components in the skeleton of more than half of the biologically active compounds produced naturally.[1] Phenanthridines are important core structures found in a variety of natural products and other biologically important molecules with a wide rang of biological activities and applications,[2–5] including antibacterial, antiprotozoal, anticancer, antimicrobial, anti-inflammatory, antivirial, antioxidant[7–13] and also with applications as drugs,[6] DNA targeting agents,[14] dyes,[15] and probes.[16] Isoquinoline is also present in various natural products such as cryptaustoline and cryptowoline.[17] They are known to exhibit various biological activities[18–22] such as antileukaemic,[23] tubulin polymerisation inhibitory[24] and anti-tumour activities.[25] As previously reported,[26] the reaction between phenanthridine and 2 mol equiv. dimethyl acetylenedicarboxylate, led to the formation of a new ring on the phenanthridine compound. We now describe an efficient synthesis of a new class of enamino esters (see Scheme 1).

Results and discussion

An efficient synthesis of a new class of enamino esters from reaction between phenanthridine **1** or isoquinoline **5** and activated acetylenic esters **2** or **6** as a Michael acceptor[27–34] was undertaken in the presence of heterocyclic NH compounds (succinimide, 5-nitroindazole, benzoxazole, 6-chlorobenzoxazole, carbazole and 3,6-dibromocarbazole) or 1,3-dicarbonyl compounds such as 1,3-dimethylbarbituric acid and 1,3-diethyl-2-thiobarbituric acid at ambient temperature. Reactions were carried out by first mixing the phenanthridine or isoquinoline and heterocyclic NH or 1,3-dicarbonyl compounds and then the acetylenic ester was added slowly. The reactions proceeded smoothly in CH_2Cl_2 and then the whole reaction mixture solidified into yellow solid within a few hours. The ^{1}H and ^{13}C NMR spectra of the crude products clearly indicated the formation of enamino esters **4a–h** and **8i–l**. No product other than **4a–h** and **8i–l** could be detected by NMR spectroscopy. The structures of compounds **4a–h** and **8i–l** were confirmed by elemental analyses, mass, IR, ^{1}H NMR and ^{13}C NMR spectra. The ^{1}H NMR 500 MHz spectrum of **4a** exhibited a signal for two methylene (δ = 2.81, s, 4H, $2CH_2$, O=C–CH_2–CH_2–C=O), two sharp line (δ = 3.67 and 3.77) arising from methoxy protons, olefinic proton, which appear as a singlet (δ = 7.04, 1H, s, C=C*H*–CO_2CH_3), and also a sharp line for methine proton (δ = 9.26, 1H, s, NCHN). Aromatic protons, along with multiplets at δ = 7.19–8.48 ppm for the phenanthridine moiety. The ^{13}C NMR spectrum of **4a** showed 23 distinct resonances in agreement with the proposed structure. In addition, product **4a** displayed ^{13}C NMR resonances at δ 121.86, 122.30 and 124.10 ppm, respectively for the N*C*HN, N–C=*C*H–CO_2CH_3, N–*C*=CH–CO_2CH_3 units. The carbonyl groups resonances in the ^{13}C NMR spectra of **4a** appear at δ = 161.73, 162.91, 174.78 and 178.57 ppm. The ^{1}H and ^{13}C NMR spectra of compounds **4b–h** and **8i–l** are similar to those of **4a.** The ^{1}H NMR of each of the isolated product **4 (a**, **c**, **d** and **g)** exhibited a N–C=CH proton signal at about 7.04–7.28 ppm, which is in agreement with the (*E*) configuration for the vinyl moiety in **4**. Compounds **4 (b**, **e**, **f** and **h)** and **8 (i–l)** exhibited a N–C=CH proton signal at about 5.29–6.73 ppm, which is in agreement with the (*Z*) configuration[18, 35,36] (see Scheme 2).

Briefly, we have developed a new method to access a novel class of heterocyclic derivatives. The present method has the advantage that, not only is the reaction performed under neutral conditions, but also the substances can be mixed without any activation or modifications. It seems that, the simplicity of recent procedure makes it as an interesting alternative method in comparison with other approaches.

Experimental

Melting points and IR spectra of all compounds were measured on an Electrothermal 9100 apparatus and a Shimadzu IR-460 spectrometer, respectively. The ^{1}H, ^{13}C, and ^{31}P NMR spectra were obtained with a Bruker DRX-500 Avance instrument using $CDCl_3$ as applied solvent and TMS as internal standard at 500.1, 125.8, and 202.4 MHz respectively. In addition, the mass spectra were recorded on a GCMS-QP5050A mass spectrometer operating at an ionization potential of 70 eV. Elemental analysis for C, H and N were performed using a Heraeus CHN–O-Rapid analyser. Activated acetylenic esters, Phenanthridine, isoquinoline, succinimide, 5-nitroindazole, benzoxazole, 5-chlo-robenzoxazole, carbazole, 3,6-dibromocarbazole, 1,3-dimethylbarbituric acid and 1,3-diethyl-2-thiobarbituric acid were purchased from Fluka, (Buchs, Switzerland) and used without further purifications.

Typical procedure (exemplified by **(4a***)*

*Dimethyl 2-[6-(2,5-dioxopyrrolidin-1-yl)phenanthridin-5(6*H*)-yl] fumarate* (**4a**): To a magnetically stirred solution of phenanthridine (0.18 g, 1 mmol) and succinimide (0.09 g, 1 mmol) in CH_2Cl_2 (10 mL) was added, dropwise, a mixture of dimethyl acetylenedicarboxylate (0.14g 1 mmol) in CH_2Cl_2 (5 mL) at –10 °C over 10 min. After approximately a few hours stirring at ambient temperature, the whole reaction mixture solidified into a brown solid, the solvent was then removed under reduced pressure and product washed with cold diethyl ether (2 × 5 mL) and it was obtained as brown powder, yield 93%, 0.39g m.p. 100–102 °C, IR (ν_{max}, cm^{-1}): 1743 (C=O). MS, *m/z* (%) = 420 (M^+, 4), 389 (M–OCH_3, 54), 361 (M–CO_2CH_3, 41), 358 (M–2OCH_3, 43), 322($C_4H_4NO_2$, 61). Anal. Calcd for $C_{23}H_{20}N_2O_6$ (420.16): C, 65.69; H, 4.80; N, 6.66. Found: C, 65.78; H, 4.76; N, 6.73%. ^{1}H NMR (500.1 MHz, $CDCl_3$), δ_H 2.82 (4H, s, O=C–CH_2–CH_2–C=O), 3.67 and 3.77 (6H, 2s, 2OCH_3), 7.04 (1H, s, N–C=C*H*–CO_2CH_3), 7.19–8.48 ($8H_{aro}$, m, 8CH, phenanthridine), 9.26 (1H, s, NCHN). ^{13}C NMR (125.8 MHz,

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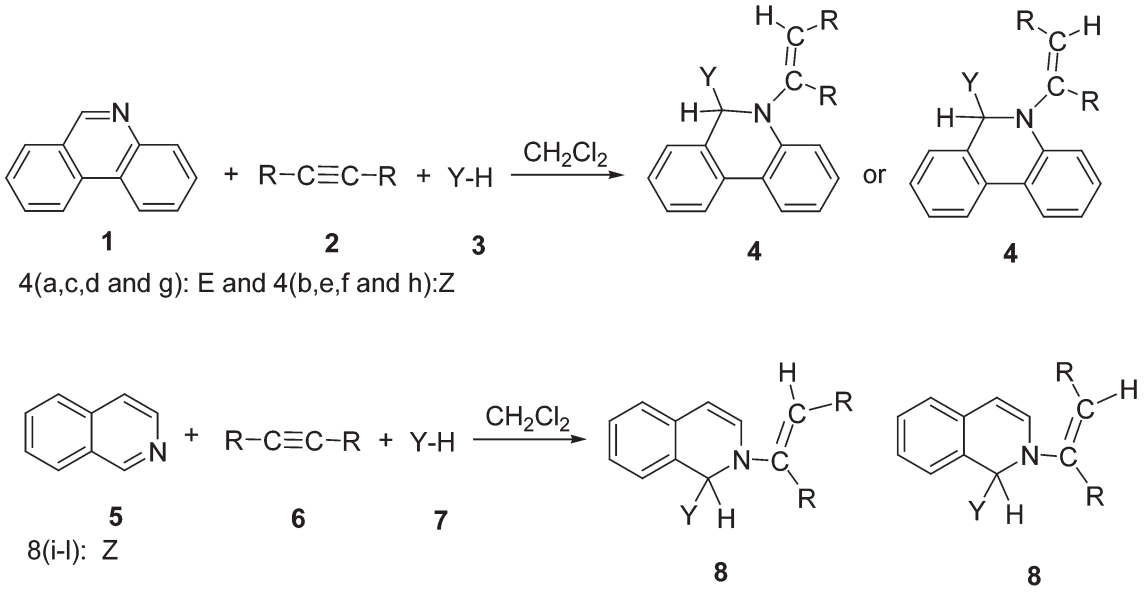

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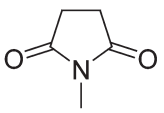
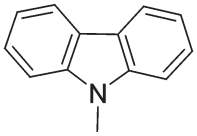
4a		CO_2Me	93	4h		CO_2Bu^t	96
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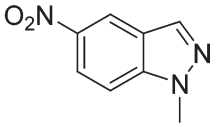
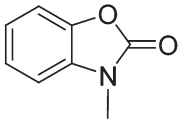
4c		CO_2Me	93	8i		CO_2Me	92
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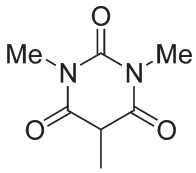
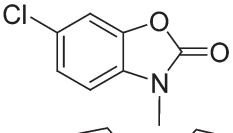
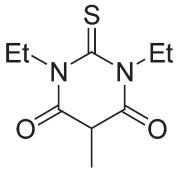
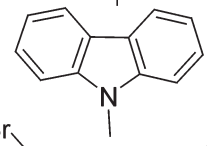
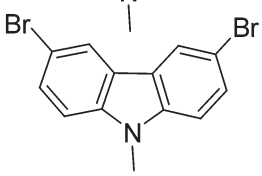
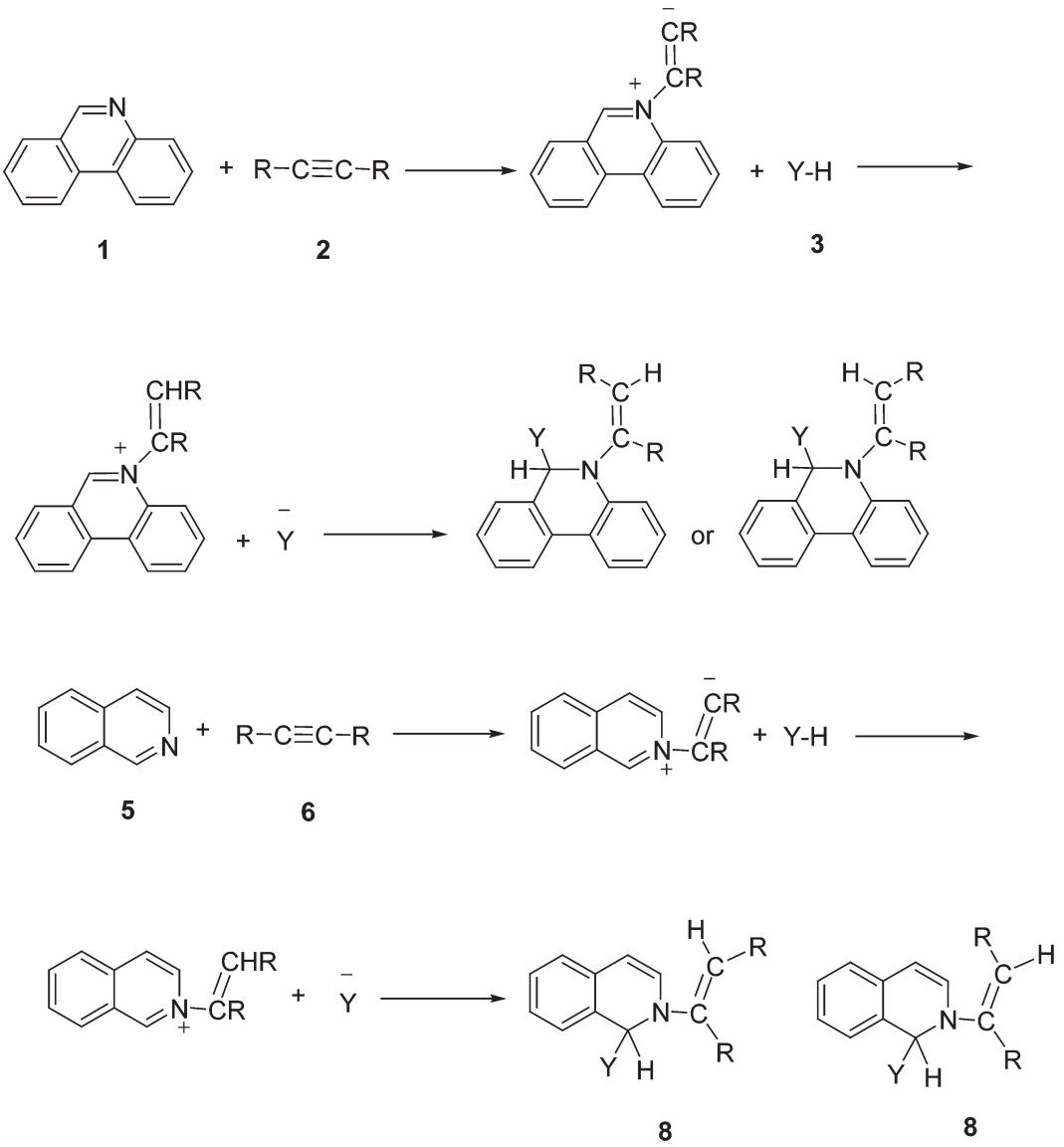
4e		CO_2Et	92	8j		CO_2Me	92
4f		CO_2Me	94	8k		CO_2Me	93
4g		CO_2Et	91	8l		CO_2Me	95

Scheme 1

$CDCl_3$), 28.88 and 29.62 ($2CH_2$, O=C–CH_2–CH_2–C=O), 52.50 and 53.49 ($2OCH_3$), 121.86 (NCHN), 122.30 (N–C=*C*H–CO_2CH_3), 124.10 (N–C=CH–CO_2CH_3), 125.86, 127.62, 127.86, 128.30, 128.71, 129.11, 129.37, 132.09, 132.52, 132.72, 142.00 and 152.60 (12C, phenanthridine), 161.73 and 162.91 (2NC=O), 174.78 and 178.57 (2C=O, ester).

Di-tert-*butyl 2-[6-(2,5-dioxopyrrolidin-1-yl)phenanthridin-5(6*H*)-yl] maleate* (**4b**): Yellow powder, yield 95%, 0.48g m.p. 102–104 °C, IR (ν_{max}, cm^{-1}): 1717 (C=O). MS, *m/z* (%) = 504 (M^+, 3), 431 (M–$OC(CH_3)_3$, 63), 358 (M–$2OC(CH_3)_3$, 24), 302 (M–$2CO_2C(CH_3)_3$, 17), 134 ($C_7H_4NO_2$, 23). Anal. Calcd for $C_{29}H_{32}N_2O_6$ (504.25): C, 69.01; H, 6.40; N, 5.55. Found: C, 68.92; H, 6.47; N, 5.61%. ^{1}H NMR (500.1 MHz, $CDCl_3$), δH 1.44 and 1.48 (18H, 2s, $2OC(CH_3)_3$), 2.83 (4H, s, O=C–CH_2–CH_2–C=O), 6.01 (1H, s, N–C=C*H*–$CO_2C(CH_3)_3$), 7.66–8.62 ($8H_{aro}$, m, 8CH, phenanthridine), 9.28 (1H, s, NCHN).^{13}C NMR (125.8 MHz, $CDCl_3$), 26.75 and 26.58 ($6CH_3$), 27.73 and 27.79 ($2CH_2$, O=C–CH_2–CH_2–C=O), 81.50 and 82.79 (2C, $2CO2C(CH_3)_3$), 120.82 (NCHN), 121.18 (1C, N–C=*C*H–$CO_2C(CH_3)_3$), 123.05 (1C, N–C=CH–$CO_2C(CH_3)_3$), 125.31, 126.07, 126.47, 127.67, 127.75, 128.97, 129.04, 130.02, 131.18, 131.51, 143.34 and 152.50 (12C, phenanthridine), 159.25 and 160.94 (2NC=O), 173.52 and 173.93 (2C=O, ester).

*Dimethyl 2-[6-(5-nitro-1H-indazole-1-yl)phenanthridin-5(6*H*)-yl] fumarate* (**4c**): Brown powder, yield 93%, 0.45g m.p. 120–122 °C, IR (ν_{max}, cm^{-1}): 1740 (C=O). MS, *m/z* (%) = 484 (M^+, 3), 425 (M–CO_2CH_3, 41), 422 (M–$2OCH_3$, 51), 366 (M–$2CO_2CH_3$, 22). Anal. Calcd for $C_{26}H_{20}N_4O_6$ (484.16): C, 64.44; H, 4.16; N, 11.57. Found: C, 64.32; H, 4.21; N, 11.63%. ^{1}H NMR (500.1 MHz, $CDCl_3$), δH 3.59 and 3.88



Scheme 2

(6H, 2s, 2OCH$_3$), 7.24 (1H, s, N–C=C*H*–CO$_2$CH$_3$), 7.68–8.71 (11H$_{aro}$, m, 11CH), 8.36 (1H, s, N=CH), 9.36 (1H, s, NCHN). ^{13}C NMR (125.8 MHz, CDCl$_3$), δC 52.60 and 53.76 (2OCH$_3$), 110.79 (NCHN), 118.85 (N–C=*C*H–CO$_2$CH$_3$), 122.05, 122.41, 121.42 and 123.81 (4C, phenanthridine), 124.34 (N–C=CH–CO$_2$CH$_3$), 125.05, 125.75, 127.25, 127.90, 128.08, 128.20, 129.35 and 129.65 (8C, phenanthridine), 132.46, 133.11, 136.24, 138.45, 141.71, 142.45,143.16 and 152.51 (7C, nitroindazol), 162.51 and 162.95 (2C=O, ester).

Di-tert-*butyl 2-[6-(5-nitro-1H-indazole-1-yl)phenanthridin-5(6*H*)-yl] fumarate* (**4d**): Yellow powder, yield 94%, 0.53g m.p. 103–105 °C, IR (ν$_{max}$, cm^{-1}): 1715 (C=O). MS, *m/z* (%) = 568 (M$^+$, 5), 511 (M–C(CH$_3$)$_3$, 19), 495 (M–OC(CH$_3$)$_3$, 27), 467 (M–CO$_2$C(CH$_3$)$_3$, 46). Anal. Calcd for C$_{32}$H$_{32}$N$_4$O$_6$ (568.25): C, 67.58; H, 5.68; N, 9.85. Found: C, 67.70; H, 5.61; N, 9.97%. ^{1}H NMR (500.1 MHz, CDCl$_3$), δH 1.16 and 1.49 (18H, 2s, 2OC(*CH*$_3$)$_3$), 7.11 (1H, s, N–C=C*H*–CO$_2$C(CH$_3$)$_3$), 7.26–8.62 (10H$_{aro}$, m, 10CH), 8.35 (1H, s, N=CH), 8.74 (1H, s, O2N–C=CH), 9.29 (1H, s, NCHN).^{13}C NMR (125.8 MHz, CDCl$_3$), 26.57and 26.81 (6CH$_3$), 81.96 and 83.35 (2C, 2CO2*C*(CH$_3$)$_3$), 109.80 (NCHN), 117.64 (1C, N–C=*C*H–CO$_2$C(CH$_3$)$_3$), 121.20 (1C, N–C=CH–CO$_2$C(CH$_3$)$_3$), 123.06, 125.32, 126.07, 126.48, 127.70, 127.79, 128.33, 129.04 and 130.02 (12C, phenanthridine), 131.52, 134.87, 136.71, 141.44 and 141.92 (5C, nitroindazol), 143.35 (N=CH), 152.51 (O2N–C), 159.98 and 161.03 (2C=O, ester).

Diethyl 2-(6-(1,3-dimethyl-2,4,6-trioxo-hexahydropyrimidin-5-yl) phenanthridin-5(6H)-yl)maleate (**4e**): Brown powder, yield 92%, 0.46g m.p. 109–111 °C, IR (ν$_{max}$, cm^{-1}): 1618, 1635 and 1743 (C=O). MS, *m/z* (%) = 359 (M–2CO$_2$Et, 41), 350 (M–C$_6$H$_7$N$_2$O$_3$, 72), 305 (M–C$_6$H$_7$N$_2$O$_3$ and OEt, 14), 321 (M–C$_6$H$_7$N$_2$O$_3$ and Et, 10), 292 (M–C$_6$H$_7$N$_2$O$_3$ and 2Et, 100), 277 (M–C$_6$H$_7$N$_2$O$_3$ and CO$_2$Et, 15), 264 (M–C$_6$H$_7$N$_2$O$_3$ and CH–CO$_2$Et, 36), 179 (C$_{13}$H$_9$N, 92). Anal. Calcd for C$_{27}$H$_{27}$N$_3$O$_7$ (505.21): C, 64.13; H, 5.39; N, 8.31. Found: C, 64.21; H, 5.46; N, 8.35%. ^{1}H NMR (500.1 MHz, CDCl$_3$), δ$_H$ 1.15 and 1.40 (6H, 2t, $^3J_{HH}$ = 7.1 Hz, 2OCH$_2$*CH*$_3$), 2.72 and 3.40 (6H, 2s, 2NCH$_3$), 4.16 and 4.38 (4H, 2m, 2ABX3system, 2O*CH*$_2$CH$_3$), 4.81 (1H, d, $^3J_{HH}$ = 7.3 Hz, O=C–C*H*–C=O), 5.22 (1H, d, 3*J*HH = 7.2 Hz, NC*H*CH), 5.63 (1H, s, N–C=C*H*–CO$_2$CH$_2$CH$_2$CH$_3$), 6.69-7.83 (8H$_{aro}$, m, 8CH, phenanthridine). ^{13}C NMR (125.8 MHz, CDCl$_3$), 13.87 and 14.20 (2OCH$_2$*CH*$_3$), 27.68 and 29.03 (2NCH$_3$), 52.85 (2O*CH*$_2$CH$_3$), 62.17 (N*C*HCH), 67.06 (O=C–CH–C=O), 74.45 (1C, N–C=*C*H–CO$_2$CH$_2$CH$_2$CH$_3$), 112.55, 117.24 and 119.62 (5C, phenanthridine), 122.12 (1C, N–C=CH–CO$_2$CH$_2$CH$_2$CH$_3$), 125.00, 125.33, 127.07, 130.01, 130.24, 130.63 and 144.36 (7C, phenanthridine), 166.10 and 168.06 (O=*C*–C–C=O), 169.07 and 171.72 (2C=O, ester).

*Dimethyl 2-[6-(1,3-diethyl-4,6-dioxo-2-thioxohexahydropyrimidin-5-yl)phenanthridin-5(6*H*)-yl]maleate* (**4f**): Brown powder, yield 94%, 0.48 g m.p. 109–111 °C, IR (ν$_{max}$, cm^{-1}): 1620, 1634 and 1729 (C=O). MS, *m/z* (%) = 403 (M–2CO$_2$Me, 22), 342 (M–C$_{13}$H$_9$N, 28), 323 (M–C$_8$H$_{10}$N$_2$O$_2$S, 32), 322 (M–C$_8$H$_{11}$N$_2$O$_2$S, 100), 264 (M–C$_8$H$_{10}$N$_2$O$_2$S and CO$_2$Me, 30), 204 (M–C$_8$H$_{11}$N$_2$O$_2$S and 2CO$_2$Me, 38), 179 (C$_{13}$H$_9$N, 92). Anal. Calcd for C$_{27}$H$_{27}$N$_3$O$_6$S (521.21): C, 62.16; H, 5.22; N, 8.06.

Found: C, 62.35; H, 5.18; N, 8.12%. ^{1}H NMR (500.1 MHz, $CDCl_3$), δH 0.64 and 1.37 (6H, 2t, $^3J_{HH}$ = 6.7 Hz, 2NCH$_2$*CH$_3$*), 3.63 and 3.92 (6H, 2s, 2OCH$_3$), 4.47 (4H, bro, 2N*CH$_2$*CH$_3$), 4.87 (1H, d, $^3J_{HH}$ = 7.2 Hz, O=C–*CH*–C=O), 5.27 (1H, d, $^3J_{HH}$ = 7.2 Hz, N*CH*CH), 5.67 (1H, s, N–C=*CH*–CO_2CH_3), 6.74–7.88 (8H$_{aro}$, m, 8CH, phenanthridine). ^{13}C NMR (125.8 MHz, $CDCl_3$), δC 10.31 and 10.95 (2NCH$_2$*CH$_3$*), 42.08 and 43.15 (2N*CH$_2$*CH$_3$), 51.89 and 52.13 (2OCH$_3$), 65.30 (N*C*HCH), 66.22 (O=C–CH–C=O), 73.97 (N–C=*C*H–CO_2CH_3), 111.12., 111.15, 116.15, 118.43, 121.07 and 12113 (6C, phenanthridine), 123.24 (N–C=CH–CO_2CH_3), 124.86, 126.28, 128.86, 129.15, 129.51, and 142.80 (6C, phenanthridine), 164.04 and 165.12 (O=*C*–C–C=O), 168.50 and 170.99 (2C=O, ester), 177.08 (C=S).

*Diethyl 2-[6-(1,3-diethyl-4,6,dioxo-2-thioxohexahydropyrimidin-5-yl) phenanthridin-5(6*H*)-yl)fumarate* (**4g**): Brown powder, yield 91%, 0.49g m.p. 163–165 °C, IR (ν_{max}, cm^{-1}): 1627, 1641 and 1732(C=O). MS, *m/z* (%) = 306 (M–$C_8H_{10}N_2O_2S$ and OEt, 37), 276 (M–$C_8H_{11}N_2O_2S$, OEt and Et, 10), 264 (M–$C_8H_{11}N_2O_2S$ and CH–CO_2Et, 34), 248 (M–$C_8H_{11}N_2O_2S$, Et and CO_2Et, 18), 204 (M–$C_8H_{11}N_2O_2S$ and 2CO_2Et, 64), 179 ($C_{13}H_9N$, 100), 167 ($C_6H_3N_2O_2S$, 38). Anal. Calcd for $C_{29}H_{31}N_3O_6S$ (549.24): C, 63.36; H, 5.69; N, 7.65. Found: C, 63.42; H, 5.73; N, 7.71%. ^{1}H NMR (500.1 MHz, $CDCl_3$), δ_H 1.07 and 1.22 (12H, 2t, $^3J_{HH}$ = 6.9 Hz, 2OCH$_2$*CH$_3$* and 2NCH$_2$*CH$_3$*), 4.32 and 4.50 (8H, 2m, 2ABX3system, 2O*CH$_2$*CH$_3$ and 2N*CH$_2$*CH$_3$), 5.03 (1H, d, $^3J_{HH}$ = 8.4 Hz, O=C–*CH*–C=O), 6.24 (1H, d, $^3J_{HH}$ = 8.4 Hz, N*CH*CH), 7.28 (1H, s, N–C=*CH*–$CO_2CH_2CH_3$), 7.31-8.18 (8H$_{aro}$, m, 8CH, phenanthridine). ^{13}C NMR (125.8 MHz, $CDCl_3$), 12.30, 12.33, 12.41 and 12.69 (2OCH$_2$*CH$_3$* and 2NCH$_2$*CH$_3$*), 42.97 and 44.16 (2N*CH$_2$*CH$_3$), 51.31 and 53.65 (2O*CH$_2$*CH$_3$), 63.48 (N*C*HCH), 65.14 (O=C–CH–C=O), 86.30 (1C, N–C=*C*H–$CO_2CH_2CH_3$), 114.95, 117.07, 117.63, 119.87, 120.20, 120.57, 120.17 and 122.85 (8C, phenanthridine), 124.58 (1C, N–C=CH–$CO_2CH_2CH_3$), 125.36, 129.04, 132.96 and 142.38 (4C, phenanthridine), 163.06 and 165.80 (O=*C*–C–C=O), 167.87 and 169.99 (2C=O, ester), 177.13 (C=S).

Di-tert-*butyl 2-(6-(9H-carbazole-9-yl)phenanthridin-5(6*H*)-yl)maleate* (**4h**): Yellow powder, yield 96%, 0.54g m.p. 185–187 °C, IR (ν_{max}, cm^{-1}): 1684 and 1713 (C=O). MS, *m/z* (%) = 350 (M–$C_{12}H_8N$ and CMe_3, 100), 292 (M–$C_{12}H_8N$ and 2CMe_3, 65), 204 (M–$C_{12}H_8N$ and 2CO_2CMe_3, 64), 179 ($C_{13}H_9N$, 56), 167 ($C_{12}H_9N$, 81). Anal. Calcd for $C_{37}H_{36}N_2O_4$ (572.28): C, 77.58; H, 6.34; N, 4.89. Found: C, 77.65; H, 6.41; N, 4.94%. ^{1}H NMR (500.1 MHz, $CDCl_3$), δH 0.84 and 1.19 (18H, 2s, 2OC(*CH$_3$*)$_3$), 5.29 (1H, s, N–C=C*H*–$CO_2C(CH_3)_3$), 7.29 (1H, s, NC*H*CH), 6.75–8.06 (16H$_{aro}$, m, 16CH, phenanthridine and carbazol).^{13}C NMR (125.8 MHz, $CDCl_3$), 26.11 and 26.57 (6C, 2CO_2C(*CH$_3$*)$_3$), 68.63 (1C, N*C*HN), 81.35 and 81.39 (2C, 2CO2*C*(CH$_3$)$_3$), 109.57(1C, N–C=*C*H–$CO_2C(CH_3)_3$), 114.40, 114.43, 118.22, 118.76 118.89 and 119.18 (6C, phenanthridine), 120.98, 122.36 and 122.74 (3C, carbazol), 124.05 (1C, N–C=CH–$CO_2C(CH_3)_3$), 126.53, 127.52, 127.69, 128.10 and 130.69 (5C, phenanthridine), 138.50, 139.21, 140.28 and 141.62 (9C, carbazol), 141.90 (1C, phenanthridine), 161.49 and 162.47 (2C=O, ester).

*Dimethyl 2-[1-(2-oxobenzo[*d*]oxazol-3(*2H*)-yl)isoquinoline-2(1*H*)-yl] maleate* (**8i**): Brown powder, yield 92%, 0.37g m.p. 112–114 °C, IR (ν_{max}, cm^{-1}): 1634 and 1727 (C=O). MS, *m/z* (%) = 406 (M^+, 5), 347 (M–CO_2CH_3, 59), 344 (M–2OCH$_3$, 16), 134 ($C_7H_4NO_2$, 29). Anal. Calcd for $C_{22}H_{18}N_2O_6$ (406.14): C, 65.00; H, 4.47; N, 6.89. Found: C, 64.95; H, 4.52; N, 6.94%. ^{1}H NMR (500.1 MHz, $CDCl_3$), δH 3.70 and 3.87 (6H, 2s, 2OCH$_3$), 6.19 (1H, d, $^3J_{HH}$ = 7.7 Hz, N–CH=C*H*), 6.57 (1H, d, $^3J_{HH}$ = 7.7 Hz, N–C*H*=CH), 6.73 (1H, s, N–C=C*H*–CO_2CH_3), 7.12–8.53 (8H$_{aro}$, m, 8CH,), 9.36 (1H, s, NC*H*N). ^{13}C NMR (125.8 MHz, $CDCl_3$), δC 51. 90 and 52.23 (2OCH$_3$), 96.34 (N–C=*C*H–CO_2CH_3), 124.80 (N–C=CH–CO_2CH_3), 124.19, 125.76, 126.21, 126.94, 127.57, 127.79, 128.63, 128.90, 129.00, 129.16, 129.87, 130.11, 130.41 and 131,79 (13C, 13CH, isoquinolin and benzoxazolinon), 142.85 (1C, N–C=O), 152.00 (1C, *C*H–O–C=O), 164.52 and 165.18 (2C=O, ester).

Dimethyl 2-[1-(6-chloro-2-oxobenzo[d]oxazol-3(2H)-yl)isoquinoline-2(1H)-yl]maleate (**8j**): Brown powder, yield 92%, 0.40g m.p. 106–108 °C, IR (ν_{max}, cm^{-1}): 1641 and 1730 (C=O). MS, *m/z* (%) = 440 (M^+, 4), 409 (M–OCH_3, 18), 381 (M–CO_2CH_3, 54), 378 (M–2OCH_3, 29). Anal. Calcd for $C_{22}H_{17}ClN_2O_6$ (440.63): C, 59.91; H, 3.89; N, 6.35. Found: C, 60.02; H, 3.83; N, 6.41%. ^{1}H NMR (500.1 MHz, $CDCl_3$), δH 3.73 and 3.89 (6H, 2s, 2OCH$_3$), 5.97 (1H, d, $^3J_{HH}$ = 7.8 Hz, N–CH=C*H*), 6.45 (1H, d, $^3J_{HH}$ = 7.8 Hz, N–C*H*=CH), 6.54 (1H, s, N–C=C*H*–CO_2CH_3), 7.13–8.54 (7H$_{aro}$, m, 7CH,), 9.41 (1H, s, NC*H*N). ^{13}C NMR (125.8 MHz, $CDCl_3$), δC 52. 60 and 53.21 (2OCH$_3$), 110.34 (N–C=*C*H–CO_2CH_3), 123.72 (N–C=CH–CO_2CH_3), 124.69, 125.34, 126.20, 126.44, 127.50, 128.00, 128.25, 128.93, 129.11, 129.26, 130.27, 130.89 and 132,19 (12C, 12CH, isoquinolin and benzoxazolinon), 142.77 (1C, N–C=O), 151.32 (1C, C–Cl), 152.38 (1C, *C*H–O–C=O), 162.46 and 163.79 (2C=O, ester).

Dimethyl 2-[1-(9H-carbazole-9-yl) isoquinoline-2(1H)-yl]maleate (**8k**): Brown powder, yield 93%, 0.41g m.p. 112–114 °C, IR (ν_{max}, cm^{-1}): 1619 and 1738 (C=O). MS, *m/z* (%) = 438 (M^+, 7), 379 (M–CO_2CH_3, 44), 320(M–2CO_2CH_3, 33), 166 ($C_{12}H_8N$, 27). Anal. Calcd for $C_{27}H_{22}N_2O_4$ (438.17): C, 73.94; H, 5.06; N, 6.39. Found: C, 74.02; H, 5.11; N, 6.43%. ^{1}H NMR (500.1 MHz, $CDCl_3$), δH 3.52 and 3.69 (6H, 2s, 2OCH$_3$), 5.39 (1H, s, N–C=C*H*–CO_2CH_3), 6.15 (1H, d, $^3J_{HH}$ = 7.9 Hz, N–CH=C*H*, isoiquinolin), 6.66 (1H, d, $^3J_{HH}$ = 7.9 Hz, N–C*H*=CH, isoiquinolin), 7.81 (1H, s, NCHN), 6.91–8.17 (12H$_{aro}$, m, 12CH, isoiquinolin and carbazol), ^{13}C NMR (125.8 MHz, $CDCl_3$), 51.42 and 52.24 (2OCH$_3$), 66.18 (N*C*HN), 96.93 (N–C=*C*H–CO_2CH_3), 106.18, 109.95, 110.76, 110.88, 119.08, 120.15, 120.37 and 120.52 (9C, isoquinoline and carbazol), 123.87 (N–C=CH–CO_2CH_3), 125.03, 125.38, 125.80, 126.18, 126.61, 126.77, 127.69, 127.76, 129.23, 138.67 and 149.24 (11C, isoquinoline and carbazol), 164.09 and 166.55 (2C=O, ester).

*Dimethyl 2-[1-(3,6-dibrmo-9*H*-carbazole-9-yl)isoquinoline-2(1*H*)-yl] maleate*(**8l**): Brown powder, yield 95%, 0.57g m.p. 130–132 °C, IR (ν_{max}, cm^{-1}): 1623 and 1743 (C=O). MS, *m/z* (%) = 596 (M^+, 6), 565 (M–OCH_3, 64), 537 (M–CO_2CH_3, 61), 326 ($C_{12}H_8Br_2N$, 34). Anal. Calcd for $C_{27}H_{20}Br_2N_2O_4$ (596.15): C, 54.35; H, 3.38; N, 4.70. Found: C, 54.31; H, 3.44; N, 4.78%. ^{1}H NMR (500.1 MHz, $CDCl_3$), δH 3.74 and 3.88 (6H, 2s, 2OCH$_3$), 6.19 (1H, d, $^3J_{HH}$ = 7.8 Hz, N- CH=C*H*, isoiquinolin), 6.46 (1H, s, N–C=C*H*–CO_2CH_3), 6.97 (1H, d, $^3J_{HH}$ = 7.8 Hz, N–C*H*=CH, isoiquinolin), 7.14–8.45 (10H$_{aro}$, m, 10CH, isoiquinolin and carbazol), ^{13}C NMR (125.8 MHz, $CDCl_3$), 51.44 and 53.15 (2OCH$_3$), 69.34 (N*C*HN), 98.74 (N–C=*C*H–CO_2CH_3), 107.12, 110.36, 110.70, 110.85, 119.07, 120.11, 120.36, 120.40 and 120.52 (9C, isoquinoline and carbazol), 124.82 (N–C=CH–CO_2CH_3), 124.19, 125.57, 125.80, 126.20, 127.14, 126.77, 128.69, 136.36, 139.35, 140.37 and 156.15 (11C, isoquinoline and carbazol), 164.79 and 165.85 (2C=O, ester).

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