

Blaise Reaction: Synthesis, skeletal diversification of C(4) substituted 5-ylidenepyrrol-(5H)-ones and the role of the strategically located ester on the reactivity of the nitriles

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Experimental Section

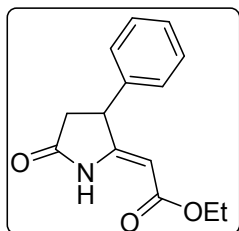
General experimental procedure

All reactions were carried out in flame-dried glassware. Solvents were dried according to the standard procedure given in the literature. Thin layer chromatography (TLC) was used for monitoring the reactions. Silica gel G and GF 254 coated glass plates were used for making TLC plates. Purification was done by using a column chromatography technique by using 100-200 mesh silica from Avra Synthesis Pvt. Ltd and hexanes and ethyl acetate. Centrifugation was carried out by using REMI centrifuge at 700 rpm. Melting points were uncorrected and were recorded on the VEEGO VMP-DS instrument by using open-ended capillary tubes. IR spectra were recorded as KBr pellets on a Nicolet-6700 spectrometer. NMR (¹H, ¹³C, and DEPT-135) spectra were recorded by using Bruker – Avance 400 MHz spectrometer with tetramethylsilane (TMS) as internal standard and (CDCl₃ and CDCl₃ + CCl₄, 1:1) solutions; *J*-values are noted in Hz. ¹H-NMR data are reported as follows: chemical shift (multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublet and br s = broad singlet), coupling constant (*J*) and integrations). High-resolution mass spectra (HRMS) were recorded on an Agilent 6350 B Q-TOF mass spectrometer using electrospray ionization mode. Ethyl 3-cyano-3-aryl propionate derivatives were prepared by modification of the existing method/literature procedure ^[23]. The diethyl-2-benzylidene malonates were prepared using the literature method^[23] from corresponding aldehydes and diethyl malonate. All aldehydes were purchased either from Sigma Aldrich Chemicals or AVRA Synthesis Private Limited. Zn powder was bought from Spectrum Chemicals Pvt. Ltd. Chlorotrimethylsilane (TMSCl) was purchased from Sigma Aldrich Chemicals Private Limited.

Experimental procedure for conducting the Blaise reaction

A solution of TMSCl (3 mol %) in dry THF (1 mL) was added to the suspension of Zn (2 equiv) in dry THF (3 mL). The resulting suspension was refluxed under vigorous stirring for 20 min under argon atmosphere. To the resulting suspension under reflux conditions, nitrile (1 mmol) in dry THF (2 mL) and EBA (2 equiv) in dry THF (2 mL) were added drop-wise slowly and simultaneously for 10 min using two separate syringes. After addition, the reaction mixture turned light green in color which was continued to reflux till color changed to brown (TLC; 3-6 h) which indicates all the starting material had been consumed. Then, the reaction mixture was cooled to rt (30 °C), centrifuged at 700 rpm and the upper solution was decanted. Residual solid was washed with THF (4 mL; 4 x 1 mL). The Combined THF solutions were concentrated to about 1 mL under reduced pressure in a rotavap and the residue was treated with 3 N HCl till the pH became 2 (about 5 mL). The resulting mixture was stirred for 30 min at rt (30 °C), the mixture was then diluted with 10 mL ethyl acetate and 10 mL water. The organic layer (ethyl acetate) was separated and washed with water (2 x 10 mL) brine (10 mL). The solution was dried over anhydrous Na₂SO₄ and concentrated under reduced pressure to provide the crude product, which was subsequently purified by column chromatography using silica gel (100-200 mesh) as stationary phase and 20-60% ethyl acetate in hexane as mobile phase.

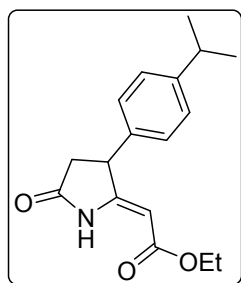
Ethyl (Z)-2-(5-oxo-3-phenylpyrrolidin-2-ylidene)acetate 12a.



Following the general experimental procedure, the reaction of ethyl 3-cyano-3-phenylpropanoate **10a** (200 mg, 1.02 mmol) with EBA (340 mg, 2.04 mmol) in presence of Zn (132 mg, 2.04 mmol),

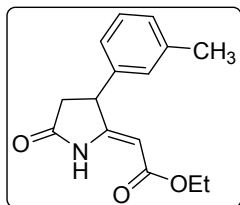
and trimethylsilyl chloride (7 mg, 3 mol %) in THF (5 mL) for 6 h, then treatment with 3 *N* HCl (5 mL) afforded, ethyl (*Z*)-2-(5-oxo-3-phenylpyrrolidin-2-ylidene)acetate **12a** as a light brown color solid in 78% yield (194 mg). Mp. 70-80 °C; Rf = 0.3 (hexanes: EtOAc 8:2); IR Data (ν): 3341, 2925, 2858, 1752, 1683, 1638, 1429, 1261, 1188, 761, 702 cm⁻¹; ¹H NMR (400 MHz, CDCl₃+CCl₄) δ 9.93 (s, 1H), 7.28 (t, *J* = 7.2 Hz, 2H), 7.23 (d, *J* = 7.0 Hz, 1H), 7.12 (d, *J* = 7.0 Hz, 2H), 4.67 (s, 1H), 4.10 (d, *J* = 3.9 Hz, 1H), 4.06 (m, 2H), 2.92 (dd, *J* = 18.2, 9.8 Hz, 1H), 2.51 (dd, *J* = 18.2, 5.8 Hz, 1H), 1.17 (t, *J* = 7.3 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃+CCl₄) δ 175.58 (C), 168.25 (C), 160.98 (C), 140.56 (C), 129.40 (CH), 127.99 (CH), 127.65 (CH), 91.72 (CH), 60.08 (CH₂), 44.89 (CH), 37.83 (CH₂), 14.50 (CH₃) ppm; HRMS (ESI): *m/z* calcd for C₁₄H₁₅NO₃ [M + H] 246.1130, found, 246.1126.

Ethyl (*Z*)-2-(3-(4-isopropylphenyl)-5-oxopyrrolidin-2-ylidene)acetate **12b.**



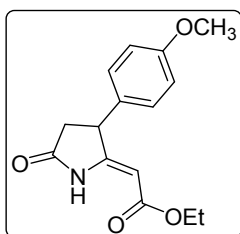
Following the general experimental procedure, the reaction of ethyl 3-cyano-3-(4-isopropylphenyl) propionate **10b** (100 mg, 0.41 mmol) with EBA (67 mg, 0.82 mmol) in presence of Zn (53 mg, 0.82 mmol), and trimethylsilyl chloride (7 mg, 5 mol %) in THF (5 mL) for 7 h followed by hydrolysis with 3 *N* HCl (5 mL) afforded, ethyl (*Z*)-2-(3-(4-isopropylphenyl)-5-oxopyrrolidin-2-ylidene)acetate **12b** as a light yellow color solid in 77% yield (90 mg). Mp. 85-90 °C; Rf = 0.5 (hexanes: EtOAc 8:2); IR Data (ν): 3338, 2965, 1754, 1684, 1639, 1427, 1261, 1188, 1046, 821, 705 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 9.98 (s, 1H), 7.20 (d, *J* = 8.2 Hz, 2H), 7.10 (d, *J* = 8.2 Hz, 2H), 4.77 (s, 1H), 4.16-4.13 (m, 1H), 4.12 (q, *J* = 7.1, 2.7 Hz, 2H), 2.97 (dd, *J* = 18.2, 9.8 Hz, 1H), 2.89 (m, 1H), 2.58 (dd, *J* = 18.2, 5.9 Hz, 1H), 1.23 (m, 9H) ppm; ¹³C NMR (100 MHz, CDCl₃+CCl₄) δ 176.04 (C), 168.36 (C), 161.26 (C), 148.60 (C), 127.46 (CH), 127.36 (CH), 91.62 (CH), 60.11 (CH₂), 44.50 (CH), 37.84 (CH₂), 33.91 (CH), 24.09 (CH₃), 24.09 (CH₃), 14.42 (CH₃) ppm; HRMS (ESI): *m/z* calcd for C₁₇H₂₁NO₃ [M + H] 288.3668, found 288.1589.

Ethyl (*Z*)-2-(5-oxo-3-(*m*-tolyl)pyrrolidin-2-ylidene)acetate **12c.**



Following the general experimental procedure, the reaction of ethyl 3-cyano-3-(*m*-tolyl)propanoate **10c** (100 mg, 0.46 mmol) with EBA (76 mg, 0.92 mmol) in presence of Zn (60 mg, 0.92), and trimethylsilyl chloride (7 mg, 3 mol %) in THF (5 mL) for 7 h, then treatment with 3 *N* HCl (5mL) afforded, ethyl (*Z*)-2-(5-oxo-3-(*m*-tolyl)pyrrolidin-2-ylidene)acetate **12c** as a light yellow color liquid in 77% yield (92 mg); *R*_f = 0.6 (hexanes: EtOAc 8:2); IR Data (ν) 3344, 2942, 1751, 1683, 1653, 1506, 1461, 1260, 1189, 1038, 813, 704, 631 cm^{-1} ; ^1H NMR (400 MHz, $\text{CDCl}_3+\text{CCl}_4$) δ 9.99 (s, 1H), 7.22 (t, $J = 7.9$ Hz, 1H), 7.09 (d, $J = 7.6$ Hz, 1H), 7.00 – 6.95 (m, 2H), 4.74 (d, $J = 1.4$ Hz, 1H), 4.19 – 4.13 (m, 1H), 4.13 – 4.09 (m, 2H), 2.96 (dd, $J = 18.2, 9.8$ Hz, 1H), 2.57 (dd, $J = 18.2, 5.7$ Hz, 1H), 2.35 (s, 3H), 1.24 (t, $J = 7.1$ Hz, 3H) ppm; ^{13}C NMR (100 MHz, $\text{CDCl}_3+\text{CCl}_4$) δ 175.69 (C), 168.29 (C), 161.13 (C), 140.54 (C), 139.07 (C), 129.27 (CH), 128.75 (CH), 128.24 (CH), 124.75 (CH), 91.63 (CH), 60.06 (CH₂), 44.84 (CH), 37.82 (CH₂), 21.64 (CH₃), 14.51 (CH₃) ppm; HRMS (ESI): *m/z* calcd for C₁₅H₁₇NO₃ [M + H] 260.1286, found, 260.1288.

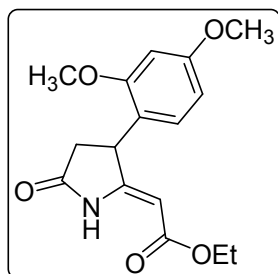
Ethyl (*Z*)-2-(3-(4-methoxyphenyl)-5-oxopyrrolidin-2-ylidene)acetate **12d.**



Following the general experimental procedure, the reaction of ethyl 3-cyano-3-(4-methoxyphenyl)propanoate **10d** (200 mg, 0.83 mmol) with EBA (272 mg, 1.65 mmol) in presence of Zn (107mg, 1.65 mmol), and trimethylsilyl chloride (7 mg, 3 mol %) in THF (5 mL) for 7 h, then treatment with 3 *N* HCl (5mL) afforded, ethyl (*Z*)-2-(3-(4-methoxyphenyl)-5-oxopyrrolidin-2-ylidene)acetate **12d** as a light yellow color liquid in 63% yield (143 mg); *R*_f = 0.4 (hexanes: EtOAc 8:2); IR Data (ν): 3333, 2978, 1752, 1684, 1638, 1432, 1257, 1189, 1038, 821, 756 cm^{-1} ; ^1H NMR (400 MHz, $\text{CDCl}_3+\text{CCl}_4$) δ 9.98 (s, 1H), 7.23 (d, $J = 7.9$ Hz, 1H), 6.82 – 6.77 (m, 1H), 6.75 (d, $J = 7.6$ Hz, 1H), 6.70 – 6.67 (m, 1H), 4.75 (d, $J = 1.5$ Hz, 1H), 4.13-4.13 (m, , 1H), 4.11

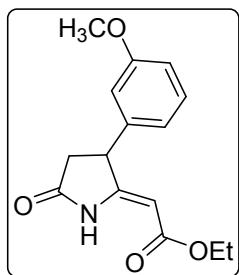
(m, 2H), 3.79 (s, 3H), 2.96 (dd, $J = 18.2, 9.8$ Hz, 1H), 2.57 (dd, $J = 18.2, 5.8$ Hz, 1H), 1.23 (t, $J = 7.1$ Hz, 3H) ppm; ^{13}C NMR (100 MHz, $\text{CDCl}_3 + \text{CCl}_4$) δ 175.47 (C), 168.08 (C), 161.24 (C), 159.12 (C), 132.21 (CH), 128.51 (CH), 114.53 (CH), 91.32 (CH), 59.84 (CH₂), 55.15 (CH₃), 44.00 (CH), 37.72 (CH₂), 14.30 (CH₃); HRMS (ESI): m/z calcd for $\text{C}_{15}\text{H}_{17}\text{NO}_4$ [$\text{M} + \text{H}$] 276.1236, found, 276.1220.

Ethyl (Z)-2-(3-(2,4-dimethoxyphenyl)-5-oxopyrrolidin-2-ylidene)acetate 12e.



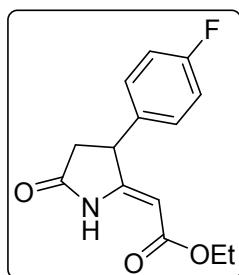
Following the general experimental procedure, the reaction of ethyl 3-cyano-3-(2,4-dimethoxyphenyl)propanoate **10e** (200 mg, 0.78 mmol) with EBA (256 mg, 1.56 mmol) in presence of Zn (101mg, 1.56 mmol), and trimethylsilyl chloride (7 mg, 3 mol %) in THF (5 mL) for 7 h, then treatment with 3 *N* HCl (5mL) afforded, ethyl (Z)-2-(3-(2,4-dimethoxyphenyl)-5-oxopyrrolidin-2-ylidene)acetate **12e** as a light brown solid in 62% yield (147 mg); Mp. 110-115 °C; $R_f = 0.6$ (hexanes: EtOAc 8:2); IR Data (ν): 3344, 2942, 1751, 1683, 1653, 1506, 1461, 1260, 1189, 1038, 813, 704, 631 cm^{-1} ; ^1H NMR (400 MHz, $\text{CDCl}_3 + \text{CCl}_4$) δ 9.93 (s, 1H), 6.99 (d, $J = 8.2$ Hz, 1H), 6.41 (t, $J = 3.1$ Hz, 1H), 6.40 – 6.37 (m, 1H), 4.69 (s, 1H), 4.21 (m, 5.2 Hz, 1H), 4.09 (q, $J = 7.1, 3.8$ Hz, 2H), 3.77 (s, 3H), 3.75 (s, 3H), 2.80 (dd, $J = 18.0, 10.0$ Hz, 1H), 2.56 (dd, $J = 18.0, 5.5$ Hz, 1H), 1.21 (t, $J = 7.1$ Hz, 3H) ppm; ^{13}C NMR (100 MHz, $\text{CDCl}_3 + \text{CCl}_4$) δ 176.71 (C), 168.40 (C), 162.15 (C), 160.72 (C), 158.12 (C), 129.94 (C), 120.73 (CH), 104.28 (CH), 99.40 (CH), 89.78 (CH), 59.75 (CH₂), 55.44 (OCH₃), 55.37 (OCH₃), 40.57 (CH), 35.87 (CH₂), 14.43 (CH₃) ppm; HRMS (ESI): m/z calcd for $\text{C}_{16}\text{H}_{19}\text{NO}_5$ [$\text{M} + \text{H}$] 306.1341, found, 306.1293.

Ethyl (Z)-2-(3-(3-methoxyphenyl)-5-oxo-2,5-dihydro-1H-pyrrol-2-yl)acetate 12f.



Following the general experimental procedure, the reaction of ethyl 3-cyano-3-(3-methoxyphenyl)propanoate **10f** (100 mg, 0.445 mmol) with EBA (150 mg, 0.881 mmol) in presence of Zn (57 mg, 3.88 mmol), and trimethylsilyl chloride (7 mg, 3 mol %) in THF (5 mL) for 7 h, then treatment with 3 N HCl (5 mL) afforded, ethyl (*Z*)-2-(3-(3-methoxyphenyl)-5-oxo-2,5-dihydro-1*H*-pyrrol-2-yl)acetate **12f** as a light yellow color liquid in 77% yield (96 mg); R_f = 0.3 (hexanes: EtOAc 8:2); IR Data (ν): 3333, 2977, 1751, 1685, 1693, 1436, 1261, 1192, 1403, 700, 533 cm⁻¹; ¹H NMR (400 MHz, CDCl₃+CCl₄) δ 9.98 (s, 1H), 7.24 (t, *J* = 6.4 Hz, 1H), 6.82 – 6.77 (m, 1H), 6.75 (d, *J* = 7.6 Hz, 1H), 6.70 – 6.67 (m, 1H), 4.75 (d, *J* = 1.5 Hz, 1H), 4.13 (dd, *J* = 3.8, 1.8 Hz, 1H), 4.11 (dd, *J* = 7.1, 1.6 Hz, 2H), 3.79 (s, 3H), 2.96 (dd, *J* = 18.2, 9.8 Hz, 1H), 2.57 (dd, *J* = 18.2, 5.8 Hz, 1H), 1.22 (t, *J* = 7.1 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃+CCl₄) δ 175.59 (C), 168.25 (C), 160.77 (C), 160.30 (C), 141.97 (C), 130.42 (CH), 119.84 (CH), 113.62 (CH), 112.99 (CH), 91.68 (CH), 60.07 (CH₂), 55.32 (CH₃), 44.85 (CH), 37.68 (CH₂), 14.49 (CH₃) ppm; HRMS (ESI): *m/z* calcd for C₁₅H₁₇NO₄ [M + H] 276.1236, found, 276.1230.

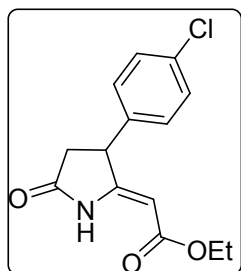
Ethyl (*Z*)-2-(3-(4-fluorophenyl)-5-oxopyrrolidin-2-ylidene)acetate **12g.**



Following the general experimental procedure, the reaction of ethyl 3-cyano-3-(4-fluorophenyl)propanoate **10g** (200 mg, 0.92 mmol) with EBA (310 mg, 0.92 mmol) in presence of Zn (112 mg, 0.92), and trimethylsilyl chloride (9 mg, 3 mol %) in THF (5 mL) for 5 h, then treatment with 3 N HCl (5 mL) afforded, ethyl (*Z*)-2-(3-(4-fluorophenyl)-5-oxopyrrolidin-2-ylidene)acetate **12g** as a light yellow color liquid in 75% yield (181 mg); R_f = 0.4 (hexanes: EtOAc 8:2); IR Data (ν): 3335, 2981, 1752, 1686, 1640, 1510, 1427, 1262, 1191, 1042, 833 cm⁻¹; ¹H NMR

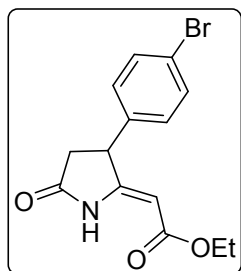
(400 MHz, CDCl₃+CCl₄) δ 10.02 (s, 1H), 7.17 (dd, J = 8.7, 5.1 Hz, 2H), 7.04 (t, J = 8.6 Hz, 2H), 4.72 (d, J = 1.5 Hz, 1H), 4.19 – 4.16 (m, 1H), 4.13 (q, J = 14.1, 6.9 Hz, 2H), 2.99 (dd, J = 18.2, 9.9 Hz, 1H), 2.53 (dd, J = 18.2, 5.9 Hz, 1H), 1.24 (t, J = 7.1 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 175.42 (C), 168.15 (C), 163.66 (C), 160.90 (d, J = 196.4 Hz) (C), 136.29 (d, J = 13.6 Hz) (C), 129.26 (d, J = 32.4 Hz) (CH), 116.50 (d, J = 86 Hz) (CH), 91.88 (CH), 60.20 (CH₂), 44.15 (CH), 37.90 (CH₂), 14.49 (CH₃) ppm.

Ethyl (Z)-2-(3-(4-chlorophenyl)-5-oxopyrrolidin-2-ylidene)acetate 12h.



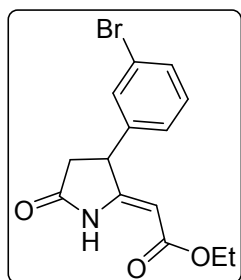
Following the general experimental procedure, the reaction of ethyl 3-(4-chlorophenyl)-3-cyanopropanoate **10h** (500 mg, 1.831 mmol) with EBA (611 mg, 3.66 mmol) in presence of Zn (273 mg, 3.66 mmol), and trimethylsilyl chloride (7mg, 3 mol %) in THF (5 mL) for 5 h, then treatment with 3 N HCl (5mL) afforded, Ethyl (Z)-2-(3-(4-chlorophenyl)-5-oxopyrrolidin-2-ylidene)acetate **12h** as a light brown color liquid in 80% yield (408 mg); R_f = 0.4 (hexanes: EtOAc 7:3); IR Data (ν): 3331, 2982, 1754, 1686, 1639, 1489, 1263, 1190, 1043, 823, 711 cm⁻¹; ¹H NMR (400 MHz, CDCl₃+CCl₄) δ 10.00 (s, 1H), 7.30 (d, J = 8.4 Hz, 2H), 7.12 (d, J = 8.4 Hz, 2H), 4.69 (s, 1H), 4.17 – 4.13 (m, 1H), 4.12 – 4.07 (m, 2H), 2.96 (dd, J = 18.1, 9.8 Hz, 1H), 2.50 (dd, J = 18.1, 5.8 Hz, 1H), 1.21 (t, J = 7.1 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃+CCl₄) δ 175.15 (C), 168.00 (C), 160.34 (C), 139.00 (C), 133.91 (C), 129.50 (CH), 128.96 (CH), 91.77 (CH), 60.07 (CH₂), 44.15 (CH), 37.61 (CH₂), 14.40 (CH₃) ppm; HRMS (ESI): m/z calcd for C₁₄H₁₄ClNO₃ [M + H] 280.0740, found, 280.0736.

Ethyl (Z)-2-(3-(4-bromophenyl)-5-oxopyrrolidin-2-ylidene)acetate 12i.



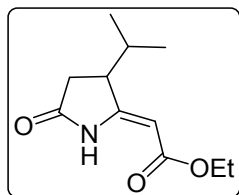
Following the general experimental procedure, the reaction of ethyl 3-(4-bromophenyl)-3-cyanopropanoate **10i** (200 mg, 0.980 mmol) with EBA (329 mg, 1.970 mmol) in presence of Zn (128 mg, 1.970), and trimethylsilyl chloride (7mg, 3 mol %) in THF (5 mL) for 6 h, then treatment with 3 N HCl (5mL) afforded, Ethyl (*Z*)-2-(3-(4-bromophenyl)-5-oxopyrrolidin-2-ylidene)acetate **12i** as a light yellow color Semisolid in 77% yield (243 mg); R_f = 0.4 (hexanes: EtOAc 8:2); IR Data (ν): 3333,2980, 1749, 1683, 1639, 1483, 1261, 1188, 1040, 708, 450 ppm; ¹H NMR (400 MHz, CDCl₃+CCl₄) δ 9.99 (s, 1H), 7.48 (d, *J* = 8.3 Hz, 2H), 7.08 (d, *J* = 8.3 Hz, 2H), 4.71 (s, 1H), 4.18 (dd, *J* = 12.9, 5.6 Hz, 1H), 4.12 (d, *J* = 7.1 Hz, 2H), 2.98 (dd, *J* = 18.2, 9.9 Hz, 1H), 2.52 (dd, *J* = 18.2, 5.8 Hz, 1H), 1.24 (d, *J* = 7.0 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 175.20, 168.12, 160.28, 139.52, 132.57, 129.36, 122.06, 91.92, 60.21, 44.29, 37.65, 14.47 ppm; HRMS (ESI): *m/z* calcd for C₁₄H₁₄BrNO₃ [M + H] 324.0150, found, 324.0232 and 326.0214.

Ethyl (*Z*)-2-(3-(3-bromophenyl)-5-oxopyrrolidin-2-ylidene)acetate **12j.**



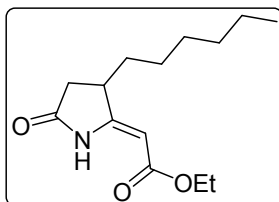
Following the general experimental procedure, the reaction of ethyl 3-(3-bromophenyl)-3-cyanopropanoate **10j** (200 mg, 0.711 mmol) with EBA (234 mg, 1.423 mmol) in presence of Zn (92 mg, 1.423), and trimethylsilyl chloride (5 mg, 3 mol %) in THF (5 mL) for 6 h, then treatment with 3 N Cl (5mL) afforded, ethyl (*Z*)-2-(3-(3-bromophenyl)-5-oxopyrrolidin-2-ylidene)acetate **12j** as a light brown oil in 78% yield (179 mg); R_f = 0.4 (hexanes: EtOAc 8:2); IR Data (ν): 3333,2980, 1749, 1683, 1639, 1483, 1261, 1188, 1040, 708, 450 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 9.99 (s, 1H), 7.44 (ddd, *J* = 8.0, 1.9, 1.0 Hz, 1H), 7.35 (t, *J* = 1.8 Hz, 1H), 7.23 (d, *J* = 7.9 Hz, 1H), 7.18 – 7.09 (m, 1H), 4.77 (d, *J* = 1.5 Hz, 1H), 4.21 – 4.15 (m, 1H), 4.15 – 4.11 (m, 2H), 3.00 (dd, *J* = 18.3, 9.9 Hz, 1H), 2.55 (dd, *J* = 18.2, 5.7 Hz, 1H), 1.25 (d, *J* = 7.1 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 175.41 (C), 168.20 (C), 159.99 (C), 142.67 (C), 131.18 (CH), 130.86 (CH), 130.87(CH), 126.27 (CH), 121 (CH), 92.11 (CH), 60.31 (CH₂), 44.32 (CH), 37.61 (CH₂), 14.38 (CH₃) ppm; HRMS (ESI): *m/z* calcd for C₁₄H₁₄BrNO₃ [M + H] 324.0150, found, 324.0241.

Ethyl (*Z*)-2-(3-isopropyl-5-oxopyrrolidin-2-ylidene)acetate **12q.**



Following the general experimental procedure, the reaction of ethyl 3-cyano-4-methylpentanoate **10q** (100 mg, 0.59 mmol) with EBA (98 mg, 1.17 mmol) in the presence of Zn (78 mg, 1.17 mmol), and trimethylsilyl chloride (7mg, 3 mol %) in THF (5 mL) for 6 h, then treatment with 3 *N* HCl (5mL) afforded, ethyl (*Z*)-2-(3-isopropyl-5-oxopyrrolidin-2-ylidene)acetate **12q** as a light brown semisolid in 77% yield (95 mg); *R*_f = 0.6 (hexanes: EtOAc 7:3); IR Data (ν): 3349, 2978, 1746, 1684, 1638, 1513, 1462, 1256, 1189, 1032, 737, 557 ¹H NMR (400 MHz, CDCl₃+CCl₄) δ 9.87 (s, 1H), 4.96 (s, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 3.05 – 3.00 (m, 1H), 2.45 (dd, *J* = 18.2, 9.5 Hz, 1H), 2.26 (dd, *J* = 18.2, 4.3 Hz, 1H), 2.07 – 2.01 (m, 1H), 1.28 (t, *J* = 7.1 Hz, 3H), 0.98 (d, *J* = 6.9 Hz, 3H), 0.85 (d, *J* = 6.8 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 176.53 (C), 168.33 (C), 161.06 (C), 90.05 (CH), 60.02 (CH₂), 44.41 (CH), 31.30 (CH), 29.70 (CH₂), 20.43 (CH₃), 16.24 (CH₃), 14.59 (CH₃) ppm.

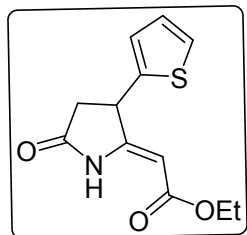
Ethyl (*Z*)-2-(3-hexyl-5-oxopyrrolidin-2-ylidene)acetate **12r.**



Following the general experimental procedure, the reaction of ethyl 3-cyanononanoate **10r** (200 mg, 1.21 mmol) with EBA (404 mg, 2.42 mmol) in presence of Zn (157 mg 2.42 mmol), and trimethylsilyl chloride (7mg, 3 mol %) in THF (5 mL) for 6 h, then treatment with 3 *N* HCl (5mL) afforded, ethyl (*Z*)-2-(3-hexyl-5-oxopyrrolidin-2-ylidene)acetate **12r** as a light brown color liquid in 63% yield (192 mg); *R*_f = 0.5 (hexanes: EtOAc 8:2); IR Data (ν): 3343, 2929, 2861, 1751, 1685, 1637, 1431, 1258, 1191, 1401, 807, 716, cm⁻¹; ¹H NMR (400 MHz, CDCl₃+CCl₄) δ 9.80 (s, 1H), 4.95 (s, 1H), 4.14 (q, *J* = 14.2, 7.1 Hz, 2H), 3.03 – 2.96 (m, 1H), 2.60 (dd, *J* = 18.0, 9.2 Hz, 1H), 2.18 (dd, *J* = 18.0, 4.5 Hz, 1H), 1.69-1.59 (m, 2H), 1.28-1.25 (m, 11H), 0.87-0.86 (m, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃+CCl₄) δ 176.27 (C), 168.30 (C), 162.00 (C), 89.71 (CH), 59.96 (CH₂), 38.62 (CH), 34.68 (CH₂), 34.33 (CH₂), 31.77 (CH₂), 29.25 (CH₂), 26.54 (CH₂), 22.74 (CH₂), 14.54

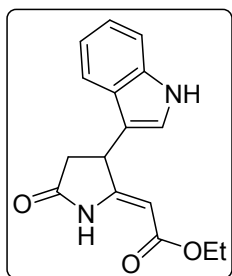
(CH₃), 14.20 (CH₃); HRMS (ESI): *m/z* calcd for C₁₄H₂₃NO₃ [M + H] 254.1756, found, 254.1749.

Ethyl (Z)-2-(5-oxo-3-(thiophen-2-yl)pyrrolidin-2-ylidene)acetate 12k.



Following the general experimental procedure, the reaction of ethyl 3-cyano-3-(thiophen-2-yl)propanoate **10k** (500 mg, 2.39 mmol) with EBA (798 mg, 4.78 mmol) in presence of Zn (310 mg 4.78 mmol), and trimethylsilyl chloride (7mg, 3 mol %) in THF (5 mL) for 5 h, then treatment with 3 *N* HCl (5mL) afforded, Ethyl (Z)-2-(5-oxo-3-(thiophen-2-yl)pyrrolidin-2-ylidene)acetate **12k** as a brown color semisolid in 83% yield (497 mg); *R_f* = 0.7 (hexanes: EtOAc 8:2); IR Data (*v*): 3331, 2982, 1749, 1686, 1640, 1429, 1259, 1189, 1043, 816, 704 cm⁻¹; ¹H NMR (400 MHz, CDCl₃+CCl₄) δ 9.93 (s, 1H), 7.25 – 7.22 (m, 2H), 6.95 (d, *J* = 4.9 Hz, 1H), 4.93 (s, 1H), 4.53 – 4.47 (m, 2H), 4.14 (q, *J* = 13.8, 2H), 3.02 (dd, *J* = 18.0, 9.7 Hz, 2H), 2.66 (dd, *J* = 18.0, 6.2 Hz, 2H), 1.25 (t, *J* = 7.1 Hz, 7H) ppm; ¹³C NMR (100 MHz, CDCl₃+CCl₄) δ 174.73 (C), 168.12 (C), 159.61 (C), 142.41 (C), 127.29 (CH), 125.89 (CH), 125.36 (CH), 91.89 (CH), 60.20 (CH₂), 39.91 (CH), 38.37 (CH₂), 14.47 (CH₃)ppm; HRMS (ESI): *m/z* calcd for C₁₂H₁₃NO₃S [M + H] 252.0694, found, 252.0690.

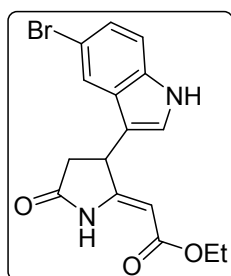
Ethyl (Z)-2-(3-(1*H*-indol-3-yl)-5-oxopyrrolidin-2-ylidene)acetate 12n.



Following the general experimental procedure, the reaction of ethyl 3-cyano-3-(1*H*-indol-3-yl)propanoate **10n** (500 mg, 2.07 mmol) with EBA (375 mg, 2.27 mmol) in presence of Zn (267 mg, 4.14 mmol), and trimethylsilyl chloride (10 mg, 3 mol %) in THF (5 mL) for 5 h, then treatment with 3 *N* HCl (5mL) afforded, Ethyl (Z)-2-(3-(1*H*-indol-3-yl)-5-oxopyrrolidin-2-ylidene)acetate **12n** as a brown color solid in 83% yield (414 mg). Mp. 160-170 °C; *R_f* = 0.4

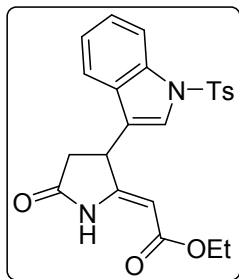
(hexanes: EtOAc 6:4); IR Data (ν): 3347, 2925, 1743, 1681, 1638, 1429, 1261, 1196, 1151, 1043, 769, 675, 539 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 10.07 (s, 1H), 8.35 (s, 1H), 7.42 (dd, $J = 12.5$, 8.1 Hz, 2H), 7.24 – 7.21 (m, 1H), 7.16 – 7.10 (m, 2H), 4.94 (d, $J = 1.6$ Hz, 1H), 4.51 (dd, $J = 9.7$, 6.2, 1.5 Hz, 1H), 4.12 (q, $J = 7.1$, 3.7 Hz, 2H), 2.98 (dd, $J = 9.8$ Hz, 1H), 2.79 (dd, $J = 6.2$ Hz, 1H), 1.21 (t, $J = 7.1$ Hz, 3H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 176.4(C), 168.5(C), 160.7(C), 136.8(C), 125.4(C), 122.8(CH), 122.4(CH), 120.1(CH), 118.7(CH), 114.3(C), 111.7(C), 91.2(CH), 60.0(OCH₂), 36.6(CH), 36.5(CH), 14.3(CH₃) ppm; HRMS (ESI): m/z calcd for $\text{C}_{16}\text{H}_{16}\text{N}_2\text{O}_3$ [M + H] 285.1239, found, 285.1247.

Ethyl (*Z*)-2-(3-(5-bromo-1*H*-indol-3-yl)-5-oxopyrrolidin-2-ylidene)acetate **12o.**



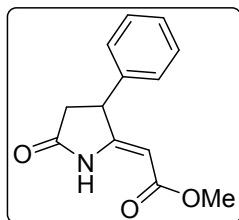
Following the general experimental procedure, the reaction of ethyl 3-(5-bromo-1*H*-indol-3-yl)-3-cyanopropanoate **10o** (100 mg, 0.31 mmol) with EBA (103 mg, 0.62 mmol) in presence of Zn (40 mg, 0.624 mmol), and trimethylsilyl chloride (7mg, 3 mol %) in THF (5 mL) for 5 h, then treatment with 3 *N* HCl (5mL) afforded, ethyl (*Z*)-2-(3-(5-bromo-1*H*-indol-3-yl)-5-oxopyrrolidin-2-ylidene)acetate **12o** as a light brown color oil in 85% yield (96 mg); $R_f = 0.4$ (hexanes: EtOAc 6:4); IR Data (ν): 3335, 2980, 1742, 1680, 1640, 1460, 1261, 1196, 1042, 805, 752 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 10.05 (s, 1H), 8.41 (s, 1H), 7.54 (s, 1H), 7.34 – 7.27 (m, 2H), 7.13 (d, $J = 2.4$ Hz, 1H), 4.90 (s, 1H), 4.49 – 4.43 (m, 1H), 4.13 (dt, $J = 7.1$, 4.1 Hz, 2H), 3.00 (dd, $J = 18.1$, 9.8 Hz, 1H), 2.70 (dd, $J = 18.1$, 6.3 Hz, 1H), 1.23 (t, $J = 7.1$ Hz, 3H) ppm; ^{13}C NMR (101 MHz, CDCl_3) δ 176.12 (C), 168.39 (C), 160.17 (C), 135.43 (C), 127.29 (C), 125.83 (C), 123.62 (C), 121.21 (CH), 114.07 (CH), 113.48 (CH), 113.28 (CH), 91.35 (CH), 60.20 (CH₂), 36.61 (CH), 36.40 (CH₂), 14.37 (CH₃) ppm; HRMS (ESI): m/z calcd for $\text{C}_{16}\text{H}_{15}\text{N}_2\text{O}_3$ [M + H] 363.0344, found, 363.0345 and 365.0329.

Ethyl (*Z*)-2-(5-oxo-3-(1-tosyl-1*H*-indol-3-yl)pyrrolidin-2-ylidene)acetate **12p.**



Following the general experimental procedure, the reaction of ethyl 3-cyano-3-(1-tosyl-1*H*-indol-3-yl)propanoate **10p** (100 mg, 0.252 mmol) with EBA (83 mg, 0.505 mmol) in presence of Zn (32 mg, 0.505 mmol), and trimethylsilyl chloride (~ 4 mg, 3 mol %) in THF (5 mL) for 5 h, then treatment with 3 *N* HCl (5mL) afforded, ethyl (*Z*)-2-(5-oxo-3-(1-tosyl-1*H*-indol-3-yl)pyrrolidin-2-ylidene)acetate **12p** as a light brown color oil in 82% yield (90 mg); *R*_f = 0.4 (hexanes: EtOAc 7:3); IR Data (ν): 3120, 2980, 1742, 1680, 1640, 1460, 1330, 1261, 1196, 1042, 805, 752 cm⁻¹; ¹H NMR (400 MHz, CDCl₃+CCl₄) δ 9.99 (s, 1H), 7.91 (d, *J* = 8.3 Hz, 1H), 7.69 (d, *J* = 8.4 Hz, 2H), 7.42 (s, 1H), 7.28 – 7.23 (m, 1H), 7.21 – 7.12 (m, 4H), 4.74 (d, *J* = 1.6 Hz, 1H), 4.33 (ddd, *J* = 9.8, 6.1, 1.2 Hz, 1H), 4.08 – 4.01 (m, 2H), 2.87 (dd, *J* = 18.1, 10.0 Hz, 1H), 2.56 (dd, *J* = 18.1, 6.2 Hz, 1H), 2.29 (s, 3H), 1.17 (s, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃+CCl₄) δ 175.05, 168.04, 158.74, 145.11, 135.87, 135.48, 130.15, 128.49, 127.10 (s), 125.52 (s), 124.15 (s), 123.79 (s), 120.64 (s), 119.49 (s), 114.39 (s), 91.51 (s), 60.15 (s), 36.27, 35.71, 21.82, 14.51 ppm; HRMS (ESI): *m/z* calcd for C₂₃H₂₂N₂O₅S [M -H] 437.1171, found, 437.1139.

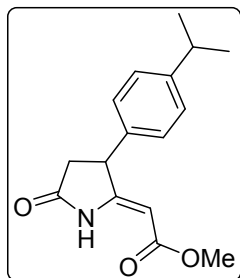
Methyl (*Z*)-2-(5-oxo-3-phenylpyrrolidin-2-ylidene)acetate **12q**.



Following the general experimental procedure, the reaction of ethyl 3-cyano-3-phenylpropanoate **10a** (100 mg, 0.510 mmol) with EBA (155 mg, 1.02 mmol) in presence of Zn (64 mg, 1.02 mmol), and trimethylsilyl chloride (4 mg, 3 mol %) in THF (5 mL) for 6 h, then treatment with 3 *N* HCl (5mL) afforded, methyl (*Z*)-2-(5-oxo-3-phenylpyrrolidin-2-ylidene)acetate **12q** as a light brown color viscous liquid in 78 % yield (91 mg); *R*_f = 0.5 (hexanes: EtOAc 7:3); IR Data (ν): 3335, 2980, 1742, 1680, 1640, 1460, 1261, 1196, 1042, 805, 752 cm⁻¹; ¹H NMR (400 MHz, CDCl₃+CCl₄) δ 9.91 (s, 1H), 7.30 – 7.25 (m, 2H), 7.23 (dd, *J* = 5.0, 3.6 Hz, 1H), 7.12 (dd, *J* = 6.9,

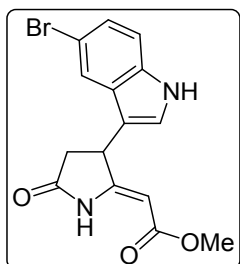
1.5 Hz, 2H), 4.68 (d, $J = 1.5$ Hz, 1H), 4.11 (ddd, $J = 9.8, 5.7, 1.4$ Hz, 1H), 3.60 (s, 3H), 2.93 (dd, $J = 18.2, 9.8$ Hz, 1H), 2.51 (dd, $J = 18.2, 5.8$ Hz, 1H) ppm; ^{13}C NMR (100 MHz, $\text{CDCl}_3 + \text{CCl}_4$) δ 175.58, 168.61, 161.17, 140.53, 129.42, 128.03, 127.63, 91.34, 51.32, 44.88, 37.84 ppm; HRMS (ESI): m/z calcd for $\text{C}_{13}\text{H}_{13}\text{NO}_3$ [M + H] 232.0973 found, 232.0975.

Methyl (Z)-2-(3-(4-isopropylphenyl)-5-oxopyrrolidin-2-ylidene)acetate 12r.



Following the general experimental procedure, the reaction of ethyl 3-cyano-3-(4-isopropylphenyl)propanoate **10b** (100 mg, 0.41 mmol) with EBA (124 mg, 0.82 mmol) in presence of Zn (54 mg, 0.82 mmol), and trimethylsilyl chloride (7 mg, 3 mol %) in THF (5 mL) for 7 h, then treatment with 3 *N* HCl (5 mL) afforded, methyl (Z)-2-(5-oxo-3-phenylpyrrolidin-2-ylidene)acetate **12r** as a pale yellow color liquid in 77% yield (85 mg); $R_f = 0.5$ (hexanes: EtOAc 7:3); 3335, 2980, 1742, 1680, 1640, 1460, 1261, 1196, 1042, 805, 752 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 9.98 (s, 1H), 7.18 (d, $J = 8.1$ Hz, 2H), 7.09 (d, $J = 8.2$ Hz, 2H), 4.75 (d, $J = 1.5$ Hz, 1H), 4.14 (ddd, $J = 9.7, 5.7, 1.3$ Hz, 1H), 3.65 (s, 3H), 2.95 (dd, $J = 18.2, 9.8$ Hz, 1H), 2.90 – 2.84 (m, 1H), 2.55 (dd, $J = 18.2, 5.8$ Hz, 1H), 1.24 (s, 3H), 1.23 (s, 3H) ppm; ^{13}C NMR (100 MHz $\text{CDCl}_3 + \text{CCl}_4$) δ 175.74 (s), 168.57 (s), 161.40 (s), 148.51 (s), 137.74 (s), 127.42 (d, $J = 16.2$ Hz), 91.13 (s), 51.20 (s), 44.48 (s), 37.79 (s), 33.92 (s), 24.10 (s) ppm; HRMS (ESI): m/z calcd for $\text{C}_{16}\text{H}_{19}\text{NO}_3$ [M + H] 274.1443 found, 274.1399.

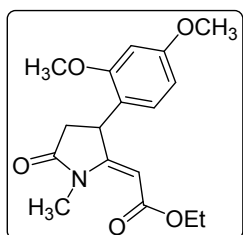
Methyl (Z)-2-(3-(5-bromo-1H-indol-3-yl)-5-oxopyrrolidin-2-ylidene)acetate 12s.



Following the general experimental procedure, the reaction of ethyl 3-(5-bromo-1H-indol-3-yl)-3-cyanopropanoate **10o** (100 mg, 0.31 mmol) with EBA (94 mg, 0.62 mmol) in presence of Zn (40

mg, 0.62 mmol), and trimethylsilyl chloride (5 mg, 3 mol %) in THF (5 mL) for 5 h then treatment with 3 *N* HCl (5mL) afforded, methyl (*Z*)-2-(3-(5-bromo-1*H*-indol-3-yl)-5-oxopyrrolidin-2-ylidene)acetate **12s** as a light brown color semisolid in 82% yield (89 mg); *R*_f = 0.4 (hexanes: EtOAc 6:4); IR Data (ν): 3335, 2980, 1742, 1680, 1640, 1460, 1261, 1196, 1042, 805, 752 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 10.03 (s, 1H), 8.45 (s, 1H), 7.53 (d, *J* = 1.5 Hz, 1H), 7.29 (dd, *J* = 5.5, 1.0 Hz, 2H), 7.13 (d, *J* = 2.4 Hz, 1H), 4.91 (d, *J* = 1.5 Hz, 1H), 4.46 (ddd, *J* = 9.7, 6.2, 1.3 Hz, 1H), 3.67 (s, 3H), 3.00 (dd, *J* = 18.1, 9.8 Hz, 1H), 2.70 (dd, *J* = 18.2, 6.3 Hz, 1H) ppm; ¹³C NMR (100 MHz, CDCl₃+CCl₄) δ 176.16, 168.73, 160.37, 135.44, 127.24, 125.83, 123.65, 121.16, 114.00, 113.47, 113.31, 90.97, 51.39, 36.61, 36.41 ppm; HRMS (ESI): *m/z* calcd for C₁₅H₁₃BrN₂O₃ [M + H] 349.0188 found , 349.0193.

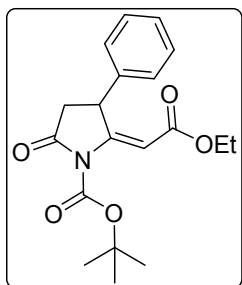
Ethyl (*Z*)-2-(3-(2,4-dimethoxyphenyl)-1-methyl-5-oxopyrrolidin-2-ylidene)acetate **15.**



The compound ethyl (*Z*)-2-(3-(2,4-dimethoxyphenyl)-1-methyl-5-oxopyrrolidin-2-ylidene)acetate **12e** (1.0 equiv, 100 mg, 0.32 mmol) was taken in a 2N RBF equipped with septa and nitrogen inlet , the RB was evacuated and flushed with nitrogen three times. This was followed by addition of potassium *t*-butoxide (2.0 equiv, 73 mg, 0.65 mmol) under nitrogen atmosphere, to this reaction mixture, anhydrous THF (6 mL) was added at 0 °C. The reaction was kept as such for 30 minutes then Methyl iodide dissolved in THF (2 mL) was added via syringe to the reaction mixture and the reaction was continued at room temperature for 12h. The progress of reaction was followed by TLC pattern. The reaction mixture was diluted with ethyl acetate (10 mL) and water (10 mL), The aqueous layer was extracted with ethyl acetate (10×2 mL). the combined organic phase was washed with brine and dried over Na₂SO₄ and concentrated under reduced pressure. the residual oily liquid was purified with flash chromatography 60/120 mesh silica using 30% ethyl acetate in hexane as eluent to give ethyl (*Z*)-2-(3-(2,4-dimethoxyphenyl)-1-methyl-5-oxopyrrolidin-2-ylidene)acetate as light brown semisolid **15**; *R*_f = 0.8 (hexanes: EtOAc, 7:3) Yield 90% ; IR Data (ν): 2942, 2841, 1737, 1703, 1621, 1504, 1461, 1299, 1169, 1118, 1037, 830, 537 cm⁻¹; ¹H NMR (400 MHz, CDCl₃+CCl₄) δ 6.95 (d, *J* = 8.4 Hz, 1H), 6.41 – 6.28 (m, 2H), 5.21 (s, 1H), 4.90 (d, *J*

= 9.6 Hz, 1H), 3.96 (dd, $J = 7.1, 4.9$ Hz, 2H), 3.77 (s, 3H), 3.76 (s, 3H), 3.08 (s, 3H), 2.95 (dd, $J = 18.0, 9.8$ Hz, 1H), 2.33 (dd, $J = 18.0, 2.1$ Hz, 1H), 1.12 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 176.00(C), 165.88(C), 162.81(C), 159.90(C), 157.65(C), 123.36(C), 103.79(CH), 98.95(CH), 93.16(CH), 59.53(OCH_2), 55.53(OCH_3), 55.35(OCH_3), 37.80(CH_2), 37.55(CH), 27.05(CH), 14.42(CH_3) ppm; HRMS (ESI): m/z calcd for $\text{C}_{17}\text{H}_{21}\text{NO}_5$ [$\text{M} + \text{H}$] 320.1500, found, 320.1498.

***tert*-Butyl (*E*)-2-(2-ethoxy-2-oxoethylidene)-5-oxo-3-phenylpyrrolidine-1-carboxylate **16**.**

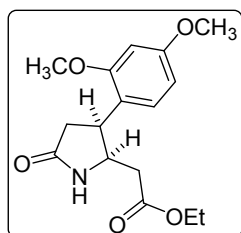


The ethyl (*Z*)-2-(5-oxo-3-phenylpyrrolidin-2-ylidene)acetate **12a** (100 mg, 0.41 mmol) was taken in a 2N RBF equipped with nitrogen inlet containing anhydrous MeCN (7 ml) was cooled to 0 °C then a solution of di-*t*-butyl dicarbonate (1.1 equiv, 97 g, 0.45 mmol) in MeCN (2 ml) was added via syringe dropwise DMAP (5 mg, 0.04 mmol) was added and the cooling bath was removed. After 12 h the reaction was concentrated in vacuum and the crude was partitioned between water (with a little amount of 1 M HCl added in order to perform the extraction from pH \approx 7) and AcOEt and extracted. After drying over Na_2SO_4 and solvent removal, the crude was purified by chromatography using 60/120 mesh silica using 20% ethyl acetate in hexane as eluent to give light brown liquid to give *tert*-butyl (*E*)-2-(2-ethoxy-2-oxoethylidene)-5-oxo-3-phenylpyrrolidine-1-carboxylate **16**; $R_f = 0.6$ (hexanes: EtOAc, 8:2) Yield 90%; IR Data (ν): 2926, 1753, 1683, 1455, 1369, 1258, 1183, 1146, 1046, 770, 700 cm^{-1} ; ^1H NMR (400 MHz, $\text{CDCl}_3 + \text{CCl}_4$) δ 7.33 – 7.27 (m, 2H), 7.25 – 7.19 (m, 3H), 6.24 (d, $J = 1.0$ Hz, 1H), 5.10 (d, $J = 9.7$ Hz, 2H), 4.10 – 4.05 (m, 1H), 4.01 (ddd, $J = 10.9, 7.1, 4.7$ Hz, 2H), 3.06 (dd, $J = 17.8, 9.8$ Hz, 1H), 2.53 (dd, $J = 17.8, 1.5$ Hz, 1H), 1.61 (s, 8H), 1.15 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 172.79, 166.17, 155.92, 148.75, 142.37, 129.02, 127.24, 126.60, 100.95, 85.89, 60.04, 40.59, 39.52, 28.02, 14.29 ppm; HRMS (ESI): m/z calcd for $\text{C}_{19}\text{H}_{23}\text{NO}_5$ [$\text{M} + \text{H}$] 346.1654, found, 346.1636.

General experimental procedure for reduction of **12 with LAH**

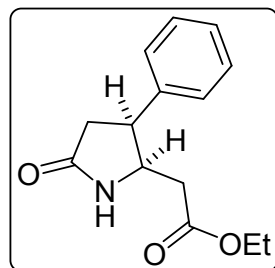
In a 50 mL, two neck round bottom flask equipped with N₂ inlet, 2-pyrrolidinone derivative (0.50 mmol) dissolved in THF (7 mL) was taken. The reaction mixture was cooled to 0° C. To this reaction mixture, 2 M LAH (1.50 mmol) in THF was added dropwise for a period of 10 minutes. The reaction was kept at 0°C for 30 minutes and then brought to room temperature continued for 2h. The progress of the reaction was followed by TLC pattern using 30% ethyl acetate in hexane as mobile phase. The reaction was cooled to rt (30 °C) and then quenched by 5% KOH (5 mL) solution. The reaction mixture was then filtered by celite and the filtrate was concentrated by rotavap, the crude so obtained was subjected to column chromatography for purification by using 100/200 mesh silica involving 30% ethyl acetate in hexane as eluent to give a light brown oil.

Ethyl 2-((2*R*,3*S*)-3-(2,4-dimethoxyphenyl)-5-oxopyrrolidin-2-yl)acetate 17b.



Following the experimental procedure, the reaction of ethyl (*Z*)-2-(3-(2,4-dimethoxyphenyl)-5-oxopyrrolidin-2-ylidene)acetate **12e** (50 mg, 0.163 mmol) with 2 M LAH (19 mg, 0.491 mmol) **6** in THF (5 mL) for 3h followed by quenching with by 5% KOH (4 mL) solution afforded, ethyl 2-((2*R*,3*S*)-3-(2,4-dimethoxyphenyl)-5-oxopyrrolidin-2-yl)acetate **17b** as a light brown oil 60% yield (30 mg); R_f = 0.6 (hexanes: EtOAc 7:3); IR Data (ν): 3373, 2943, 1660, 1609, 1505, 1463, 1236, 1154, 1045, 836, 781 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.04 (s, 1H), 7.02 (d, *J* = 8.4 Hz, 1H), 6.46 – 6.42 (m, 2H), 4.30 – 4.19 (m, 2H), 4.15 – 4.08 (m, 1H), 4.06 (s, 2H), 3.79 (s, 6H), 3.62 (td, *J* = 8.9, 4.1 Hz, 1H), 3.57 – 3.48 (m, 1H), 2.38 – 2.27 (m, 1H), 1.98 (dq, *J* = 12.4, 8.2 Hz, 1H), 1.21 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 171.25, 169.73, 159.94, 158.32, 129.42, 121.69, 104.51, 98.80, 76.84, 58.52, 55.55, 55.56, 46.08, 43.74, 31.07, 14.76ppm.

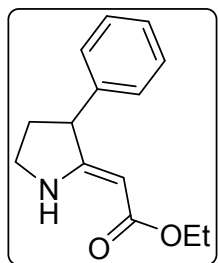
Ethyl 2-((2*R*,3*S*)-5-oxo-3-phenylpyrrolidin-2-yl)acetate 17a.



Following the experimental procedure B, the reaction of Ethyl (*Z*)-2-(5-oxo-3-phenylpyrrolidin-2-ylidene)acetate **12a** (50 mg, 0.20 mmol) with 2 *M* LAH (23 mg, 0.61 mmol) 6 in THF (5 mL) for 3h followed by quenching with by 5% KOH (5 mL) solution afforded, ethyl 2-((2*R*,3*S*)-5-oxo-3-phenylpyrrolidin-2-yl)acetate **17a** as a light brown oil 59% yield (29 mg); *R*_f = 0.6 (hexanes: EtOAc 7:3); IR Data (ν): 3373, 2943, 1660, 1609, 1505, 1463, 1236, 1154, 1045, 836, 781 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.99 (s, 1H), 7.26 – 7.20 (m, 2H), 7.18 (dd, J = 5.5, 4.2 Hz, 1H), 7.14 – 7.11 (m, 2H), 4.12 (s, 1H), 4.03 – 3.94 (m, 2H), 3.82 (t, J = 8.6 Hz, 1H), 3.62 (dd, J = 13.2, 5.4 Hz, 1H), 3.51 (dd, J = 16.8, 8.3 Hz, 1H), 2.44 – 2.28 (m, 1H), 2.00 (dd, J = 12.5, 9.1 Hz, 1H), 1.14 (t, J = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 171.04, 168.84, 141.09, 128.88, 128.40, 127.29, 78.92, 58.65, 50.77, 46.09, 32.91, 14.83 ppm.

General experimental procedure for reduction of **12** with NaBH_4

Ethyl (*Z*)-2-(3-phenylpyrrolidin-2-ylidene)acetate **18**.



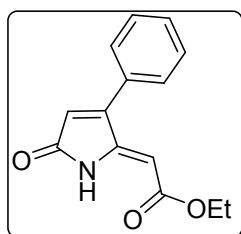
In a 25 mL, two neck round bottom flask equipped with N_2 inlet, the **12a** derivative (100 mg, 0.510 mmol) was dissolved in THF: MeOH (5:1, 6 mL) and the reaction mixture was cooled to 0°C . To this reaction mixture, NaBH_4 (3 equiv.) was added in aliquots. The reaction was kept at 0°C for 30 minutes and then brought to room temperature and continued for 3h. The progress of the reaction was followed by TLC pattern using 30% ethyl acetate in hexane as mobile phase. The reaction was cooled to rt (30°C) and then quenched by adding ice-cooled water and then work up using DCM, the organic layer was treated with anhydrous NaSO_4 and then concentrated under vacuum to give oily liquid, which was subjected to column chromatography for purification by using 100/200 mesh silica involving 30% ethyl acetate in hexane as eluent to give ethyl (*Z*)-2-(3-phenylpyrrolidin-2-ylidene)acetate **18** as light brown oil. *R*_f = 0.5 (hexanes: EtOAc, 7:3); IR Data (ν): 3343, 2943, 1660, 1505, 1403, 1230, 1130, 836, 781 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.29 – 7.24 (m, 2H), 7.23– 7.16 (m, 3H), 4.67(s, 1H), 4.07(dd, J = 7.3, 4.8 Hz, 1H), 4.03 (q, J = 7.1 Hz, 2H), 3.66–3.57 (m, 1H), 3.57–3.46 (m, 2H), 2.18–2.06 (m, 1H), 2.02 (ddd, J = 13.7, 7.5, 3.8 Hz, 1H),

1.19(t, $J = 7.1$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.49, 164.89, 140.37, 129.00, 127.86, 127.54, 83.95, 60.37, 58.91, 47.73, 35.48, 14.65 ppm.

Experimental condition for dehydrogenation of **12a**

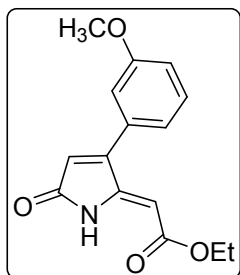
A 2N RBF was charged with ethyl (*Z*)-2-(5-oxo-3-phenylpyrrolidin-2-ylidene)acetate **12a** (50 mg, 0.204 mmol), $\text{Pd}(\text{OAc})_2$ (10 mol%), K_2CO_3 (28 mg, 0.408 mmol) and the tube was then evacuated and backfilled with nitrogen three times. And then dichloroethane (DCE) was added to it under nitrogen influx and the reaction was heated to reflux conditions. The progress of the reaction was followed by TLC pattern analysis. The reaction mixture was cooled down to rt (30 °C) and filtered through celite. The filtrate was diluted with ethyl acetate and washed with water, the aqueous layer was washed with ethyl acetate (3 times). The combined organic phases were treated with brine solution, the organic layer so obtained was dried over Na_2SO_4 and concentrated under reduced pressure, and the purification of the residue was done by flash column chromatography using 100/200 mesh silica using 30% ethyl acetate in hexane as eluent to give light brown oil for the title compound.

Ethyl (*Z*)-2-(5-oxo-3-phenyl-1,5-dihydro-2*H*-pyrrol-2-ylidene)acetate **20a**.



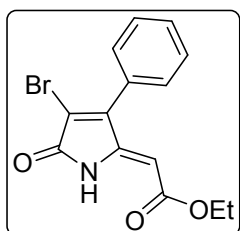
Following the experimental procedure, the reaction of ethyl (*Z*)-2-(5-oxo-3-phenylpyrrolidin-2-ylidene)acetate **12a** (50 mg, 0.20 mmol), $\text{Pd}(\text{OAc})_2$ (10 mol %), K_2CO_3 (28 mg, 0.40 mmol) in DCE (5 mL) afforded ethyl (*Z*)-2-(5-oxo-3-phenyl-1,5-dihydro-2*H*-pyrrol-2-ylidene)acetate **20a** as a white soft crystalline solid yield 70 % (35 mg); $R_f = 0.6$ (hexanes: EtOAc, 6:4); IR Data (ν): 3340, 2920, 2800, 1715, 1680, 1638, 1565, 1429, 1260, 1188, 761, 705 cm^{-1} ; ^1H NMR (400 MHz, $\text{CDCl}_3 + \text{CCl}_4$) δ 9.31 (s, 1H), 7.47 (ddd, $J = 3.7, 3.2, 1.8$ Hz, 3H), 7.43 – 7.37 (m, 2H), 6.31 (d, $J = 1.8$ Hz, 1H), 5.49 (s, 1H), 4.24 (q, $J = 7.1$ Hz, 2H), 1.30 (t, $J = 7.1$ Hz, 3H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 170.21, 167.11, 152.21, 150.02, 130.79, 130.13, 129.10, 128.59, 123.67, 98.41, 61.04, 14.36 ppm; HRMS (ESI): m/z calcd for $\text{C}_{14}\text{H}_{13}\text{NO}_3$ [$\text{M} + \text{H}$] 244.2620, found, 244.0978.

Ethyl (*Z*)-2-(3-(3-methoxyphenyl)-5-oxo-1,5-dihydro-2*H*-pyrrol-2-ylidene)acetate **20b**.



Following the experimental procedure, the reaction of ethyl 2-(3-(3-methoxyphenyl)-5-oxo-2,5-dihydro-1*H*-pyrrol-2-yl)acetate **12f** (50 mg, 0.15 mmol), Pd(OAc)₂ (10 mol %), K₂CO₃ (42 mg, 0.31 mmol) in DCE (5 mL) afforded ethyl (*Z*)-2-(5-oxo-3-phenyl-1,5-dihydro-2*H*-pyrrol-2-ylidene)acetate **20b** as a white crystalline solid (Mp = 69 °C) yield 70% (35 mg); R_f = 0.6 (hexanes: EtOAc, 6:4); IR Data (ν): 3340, 2925, 2800, 1710, 1680, 1638, 1536, 1420, 1260, 1188, 761, 705 cm⁻¹; ¹H NMR (400 MHz, CDCl₃+CCl₄) δ 9.29 (s, 1H), 7.42 – 7.34 (m, 1H), 7.03 – 6.96 (m, 2H), 6.93 – 6.89 (m, 1H), 6.31 (d, *J* = 1.8 Hz, 1H), 5.52 (s, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.85 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 170.18, 167.14, 159.97, 152.09, 149.96, 132.04, 130.24, 123.76, 120.95, 115.42, 114.38, 98.45, 61.05, 55.57, 14.37 ppm; HRMS (ESI): *m/z* calcd for C₁₅H₁₅NO₄ [M + H] 274.1000, found, 274.1042.

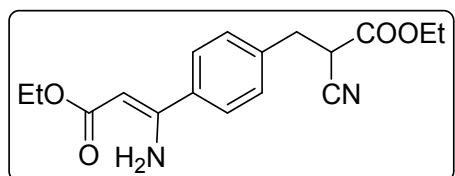
Ethyl (*Z*)-2-(4-bromo-5-oxo-3-phenyl-1,5-dihydro-2*H*-pyrrol-2-ylidene)acetate **19**.



N-Bromosuccinimide (NBS; 1.1 equiv, 399 mg, 2.44 mmol) was added to ethyl (*Z*)-2-(5-oxo-3-phenylpyrrolidin-2-ylidene)acetate **12a** (1 equiv, 500 mg, 2.04 mmol) in anhydrous CCl₄ (5 mL). The temperature of reaction mixture was raised to reflux conditions with vigorous stirring and the reaction was kept as such for 3h. The progress of reaction was followed by TLC pattern. The reaction mixture was cooled down to rt (30 °C) and then poured into water (10 mL), followed by extraction with DCM (20 mL). The extract was washed with brine (30 mL), dried over Na₂SO₄, filtered, and concentrated in vacuum to leave an orange oily residue. The purification of residue was done by flash column chromatography using 60/120 mesh silica using 20% ethyl acetate in hexane as eluent to give ethyl(*Z*)-2-(4-bromo-5-oxo-3-phenyl-1,5-dihydro-2*H*-pyrrol-2-ylidene)acetate **19** as a light brown oil; R_f = 0.6 (hexanes: EtOAc, 6:4); IR Data (ν): 3320, 2935,

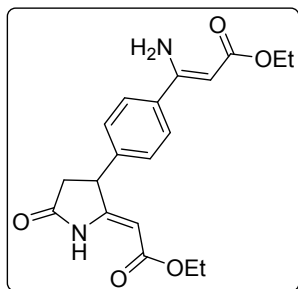
2830, 1710, 1680, 1638, 1536, 1420, 1260, 1188, 761, 706 cm^{-1} ; ^1H NMR (400 MHz, $\text{CDCl}_3+\text{CCl}_4$) δ 9.51 (s, 1H), 7.51 (dd, $J=4.3, 2.4$ Hz, 3H), 7.46 – 7.40 (m, 2H), 5.42 (s, 1H), 4.24 (q, $J=7.1$ Hz, 2H), 1.29 (t, $J=7.1$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 166.94 (C), 165.21 (C), 149.25 (C), 147.10 (C), 130.19 (CH), 129.23 (CH), 128.98 (CH), 126.37(CH), 119.82 (C), 99.19 (CH), 61.24 (OCH_2), 14.32 (CH_3) ppm; HRMS (ESI): m/z calcd for $\text{C}_{14}\text{H}_{12}\text{BrNO}_3$ [$\text{M} + \text{H}$] 322.0010, found, 322.0082 and 324.0063.

Ethyl (Z)-4-amino-4-(4-(2-cyano-3-ethoxy-3-oxopropyl)phenyl)-2-oxobut-3-enoate 25.



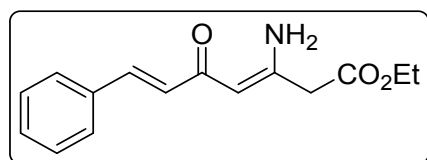
Following the general experimental procedure, the reaction of ethyl 2-cyano-3-(4-cyanophenyl)propanoate **24** (50 mg, 0.22 mmol) with EBA (28 mg, 0.44 mmol) in presence of Zn (28 mg, 0.44 mmol), and trimethylsilyl chloride (~ 6 mg, 3 mol %) in THF (5 mL) for 3 h, then treatment with 3 N HCl (5mL) afforded, ethyl (Z)-4-amino-4-(4-(2-cyano-3-ethoxy-3-oxopropyl)phenyl)-2-oxobut-3-enoate **25** as a light brown color liquid in 80% yield (55 mg); $R_f = 0.4$ (hexanes: EtOAc 6:4); IR Data (ν): 2928, 2240, 1736, 1683, 1608, 1572, 1415, 1266, 1190, 854, 807, 526 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.51 (d, $J=8.2$ Hz, 2H), 7.31 (d, $J=8.2$ Hz, 2H), 4.91 (s, 1H), 4.24 (q, $J=7.1$ Hz, 2H), 4.15 (q, $J=7.1$ Hz, 2H), 3.70 (dd, $J=8.3, 5.8$ Hz, 1H), 3.28 (dd, $J=13.9, 5.7$ Hz, 1H), 3.21 (dd, $J=13.7, 8.4$ Hz, 1H), 1.32 (t, $J=7.1$, 3H), 1.28 (t, $J=7.1$, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.32, 165.28, 159.69, 137.56, 137.57, 129.75, 126.87, 115.86, 85.20, 63.15, 59.01, 39.46, 35.49, 14.81, 14.18 ppm. HRMS(ESI): m/z calcd for $\text{C}_{17}\text{H}_{20}\text{N}_2\text{O}_4$ [$\text{M}+2\text{H}$] 318.1400, found 318.1302.

Ethyl (Z)-3-amino-3-(4-((Z)-2-(2-ethoxy-2-oxoethylidene)-5-oxopyrrolidin-3-yl)phenyl)acrylate 23.



Following the experimental procedure, the reaction of ethyl 2-cyano-3-(4-cyanophenyl)propanoate **10s** (100 mg, 0.38 mmol) with EBA (126 mg, 0.77 mmol) in presence of Zn (49 mg, 0.77 mmol), and trimethylsilyl chloride (~6 mg, 3 mol %) in THF (5 mL) for 3 h, then treatment with 3 *N* HCl (5mL) afforded, ethyl(*Z*)-3-amino-3-(4-((*Z*)-2-(2-ethoxy-2-oxoethylidene)-5-oxopyrrolidin-3-yl)phenyl)acrylate **23** as a light brown color liquid in 75% yield (102 mg); *R*_f = 0.4 (hexanes: EtOAc 6:4); IR Data (ν): 3340, 2925, 2825, 1752, 1715, 1683, 1639, 1429, 1261, 1187, 761cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 10.00 (s, 1H), 7.53 (d, *J* = 8.4 Hz, 2H), 7.24 (d, *J* = 8.3 Hz, 2H), 4.94 (s, 1H), 4.75 (d, *J* = 1.5 Hz, 1H), 4.22 (dd, *J* = 5.5, 4.1 Hz, 1H), 4.20 – 4.11 (m, 4H), 3.01 (dd, *J* = 18.2, 9.9 Hz, 1H), 2.56 (dd, *J* = 18.2, 5.7 Hz, 1H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.23 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 175.55, 170.41, 168.17, 160.26, 159.61, 142.60, 137.37, 133.18, 128.51, 128.12, 127.16, 91.98, 85.09, 60.24, 59.12, 44.42, 37.60, 14.67, 14.35ppm; HRMS(ESI): *m/z* calcd for C₁₉H₂₂N₂O₅[M+H] 359.1500, found 359.1592.

Ethyl (3*Z*, 6*E*)-3-amino-5-oxo-7-phenylhepta-3,6-dienoate **30**.



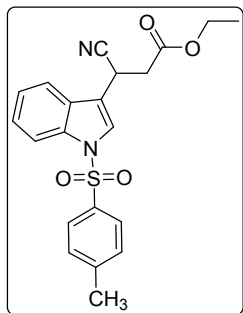
Following the experimental procedure, the reaction of (*E*)-4-(4-cyano-3-oxobut-1-en-1-yl)benzene-1-ylum **29** (200 mg, 1.17 mmol) with EBA (192 mg, 1.17 mmol) in presence of Zn (152 mg, 2.34 mmol), and trimethylsilyl chloride (6 mg, 5 mol %) in THF (7mL) for 3 h, then treatment with 3 *N* HCl (5mL) afforded, ethyl (3*Z*,6*E*)-3-amino-5-oxo-7-phenylhepta-3,6-dienoate **30** as a light brown liquid in 51% yield (154 mg); *R*_f = 0.4 (hexanes: EtOAc 6:4); IR Data (ν): 3340, 2925, 2854, 1728, 1683, 1635, 1449, 1374, 1275, 1167, 753, 690 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ ¹H NMR (400 MHz, CDCl₃) δ 10.12 (s, 1H), 7.53 (dd, *J* = 7.7, 1.5 Hz, 3H), 7.38 – 7.32 (m, 4H), 6.68 (d, *J* = 15.9 Hz, 1H), 5.26 (s, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.23 (s, 2H), 1.29 (t, *J* = 7.1 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 188.17, 169.12, 157.72, 138.94, 135.72, 129.54,

128.89, 128.25, 128.04, 97.28, 61.90, 40.80, 14.23ppm; HRMS(ESI): m/z calcd for $C_{15}H_{17}NO_3[M+H]$ 260.1208, found 260.1289.

General procedure for the synthesis of 3-aryl-3-cyanopropionate esters

The diethyl 2-arylidene malonates (2.4 mmol) were dissolved in a mixture of ethanol (16 mL) and water (4 mL) in the ratio of 4:1. To this solution at 0 °C (ice-water bath), solid KCN (1.5 equiv, 158 mg, 3.6 mmol; CAUTION) was added in one-lot. The reaction was kept at 0 °C for 10 min and then stirred at rt for 3 h by which time the TLC indicated that the malonates were absent. The reaction mixture was then filtered with the help of 10 mL more EtOH. The filtrate was concentrated under reduced pressure in a Rotary evaporator and the water bath was kept at rt. The residue was diluted with 15 mL of *tert*-butyl methyl ether (TBME) and treated with glacial acetic acid (1.0 equiv) in water (1 volume) in a fume-cupboard. The layers were separated, the aqueous phase was extracted with 10 x 3 mL of TBME. Combined organic phases were washed with brine (10 mL x 2) and dried over anhydrous Na_2SO_4 . The solvent was removed by Rotary evaporator under reduced pressure (5 mm). The purification of crude was done by column chromatography with 100-200 mesh silica as stationary phase and eluting with 20-30% ethyl acetate in hexane as mobile phase. Solvent from pooled column fractions was removed under reduced pressure using a Rotary evaporator to provide nitrile esters.

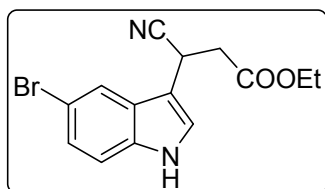
Ethyl 3-cyano-3-(1-(*tosyl*-1*H*-indol-3-yl)propanoate 10n.



Following the general experimental procedure, the reaction of diethyl-2-((1-(*tosyl*oxy)-1*H*-indol-3-yl)methylene)malonate **31n** (500 mg, 1.1 mmol) was taken in a mixture of ethanol (12 mL) and water (3 mL) with solid KCN (112 mg, 1.6 mmol), afforded -3-cyano-3-(1-(*tosyl*oxy)-1*H*-indol-3-yl)propanoate **10n** as a colorless liquid. $R_f = 0.5$ (hexanes: EtOAc, 8:2) Yield 69% (299 mg); IR Data (ν): 2924, 2230, 1735, 1672, 1696, 1483, 1448, 1374, 1285, 1263, 1120, 1097, 1020, 1000, 969, 813, 747, 704, 672 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3 + CCl_4$, 1:1) δ 7.99 (d, $J = 8.3$ Hz, 1H), 7.76 (d, $J = 8.4$ Hz, 2H), 7.61 (d, $J = 0.6$ Hz, 1H), 7.58 (d, $J = 7.8$ Hz, 1H), 7.39 – 7.32 (m, 1H),

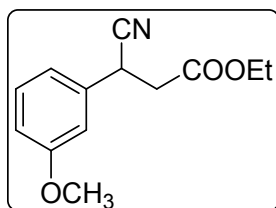
7.30 – 7.26 (m, 1H), 7.23 (d, $J = 8.0$ Hz, 2H), 4.47 (ddd, $J = 8.1, 6.5, 0.8$ Hz, 1H), 4.18 (dd, $J = 7.2, 3.9$ Hz, 2H), 3.04 (dd, $J = 16.6, 8.2$ Hz, 1H), 2.93 (dd, $J = 16.6, 6.5$ Hz, 1H), 2.35 (s, 3H), 1.26 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (100 MHz; $\text{CDCl}_3 + \text{CCl}_4$, 1:1; CH_3 , CH_2 , CH, C were assigned by deduction from DEPT-135) δ 169.0 (C), 145.3 (C), 135.44 (C), 135.40 (C), 130.2 (CH), 127.9, 127.1 (CH), 125.7 (CH), 124.6 (CH), 123.9 (CH), 119.3 (CH), 118.8 (C), 115.6 (C), 114.2 (CH), 61.7 (CH_2), 37.9 (CH_2), 24.9 (CH), 21.8 (CH_3), 14.3 (CH_3) ppm; HRMS(ESI): m/z calcd for $\text{C}_{21}\text{H}_{20}\text{N}_2\text{O}_4\text{S}[\text{M}+\text{H}]$ 396.1222, found 397.1223.

Ethyl 3-(5-bromo-1H-indol-3-yl)-3-cyanopropanoate **10o**.



Following the general experimental procedure, the reaction of diethyl 2-((5-bromo-1H-indol-3-yl)methylene)malonate **31o** (500 mg, 1.56 mmol) was taken in a mixture of ethanol (12 mL) and water (3 mL) with solid KCN (155 mg, 2.34 mmol), afforded ethyl 3-(5-bromo-1H-indol-3-yl)-3-cyanopropanoate **10o** as a light brown solid. Mp = 110-120 °C; Rf = 0.4 (hexanes: EtOAc, 7:3) Yield 72% (359 mg); IR Data (ν): 3376, 2980, 2246, 1729, 1459, 1379, 1258, 1280, 1026, 806, 557 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.43 (s, 1H), 7.76 (d, $J = 1.6$ Hz, 1H), 7.31 (dd, $J = 8.7, 1.7$ Hz, 1H), 7.24 (dd, $J = 3.9, 2.4$ Hz, 2H), 4.51 (dd, $J = 8.0, 6.8$ Hz, 1H), 4.17 (dd, $J = 10.4, 3.9$ Hz, 2H), 3.05 (dd, $J = 16.5, 8.2$ Hz, 1H), 2.95 (dd, $J = 16.6, 6.6$ Hz, 1H), 1.23 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 169.60, 135.13, 126.72, 126.06, 124.10, 120.99, 119.98, 113.80, 113.34, 61.65, 38.63, 24.96, 14.21 ppm.

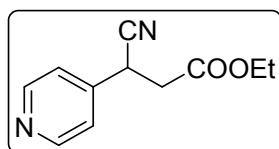
Ethyl 3-cyano-3-(3-methoxyphenyl)propanoate **10f**.



Following the experimental procedure, the reaction of diethyl-2-(3-methoxybenzylidene)malonate (500 mg, 1.7 mmol) **31f** was taken in a mixture of ethanol (12 mL) and water (3 mL) with solid KCN (178 mg, 2.5 mmol), afforded ethyl-3-cyano-3-(3-methoxyphenyl)propanoate **10f** as a colorless liquid. Rf = 0.5 (hexanes: EtOAc, 8:2) Yield 67%

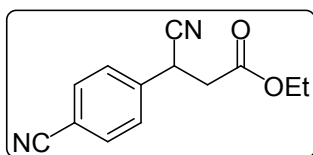
(265 mg); IR Data (ν): 2934, 2242, 1736, 1671, 1599, 1455, 1380, 1259, 1159, 1039, 866, 786, 699, 603 cm^{-1} ; ^1H NMR (400 MHz, $\text{CDCl}_3+\text{CCl}_4$) δ 7.26 (dd, $J = 9.4, 6.5$ Hz, 1H), 6.91 (dd, $J = 7.7, 0.4$ Hz, 1H), 6.86 (t, $J = 2.0$ Hz, 1H), 6.83 (ddd, $J = 8.3, 2.5, 0.7$ Hz, 1H), 4.25 – 4.22 (m, 1H), 4.16 (dd, $J = 7.1, 2.4$ Hz, 2H), 3.80 (s, 3H), 2.97 (dd, $J = 16.5, 8.3$ Hz, 1H), 2.79 (dd, $J = 16.5, 6.7$ Hz, 1H), 1.25 (s, 3H). ^{13}C NMR (100 MHz, $\text{CDCl}_3+\text{CCl}_4$) δ 169.07, 160.33, 136.16, 130.45, 119.69, 119.60, 114.18, 113.18, 61.48, 55.32, 40.26, 33.35, 14.35 ppm; HRMS(ESI): m/z calcd for $\text{C}_{13}\text{H}_{15}\text{NO}_3$ [M+H] 234.1052, found 234.1136.

Ethyl 3-cyano-3-(pyridin-4-yl)propanoate **10l**.



Following the experimental procedure, the reaction of diethyl 2-(pyridin-4-ylmethylene)malonate **31l** (1.0 g, 4.0 mmol) was taken in a mixture of ethanol (12 mL) and water (3 mL) with solid KCN (397 mg, 6.0 mmol). With small modification in the work up, in place of using glacial acetic acid, sodium bicarbonate washing was done after filtration as the product was going in the aqueous layer then organic layer was concentrated under reduced pressure followed by flash chromatography to give ethyl 3-cyano-3-(pyridin-4-yl)propanoate **10l** as a colorless liquid. $R_f = 0.3$ (hexanes: EtOAc, 7:3) Yield 56% (456 mg); IR Data (ν): 3032, 2939, 2247, 1735, 1652, 1596, 1563, 1446, 1265, 1194, 821, 773, 627 cm^{-1} ; ^1H NMR (400 MHz, $\text{CDCl}_3+\text{CCl}_4$) δ 8.56 (dd, $J = 4.5, 1.6$ Hz, 2H), 7.26 (dd, $J = 4.5, 1.7$ Hz, 2H), 4.25 (t, $J = 7.3$ Hz, 1H), 4.09 (dd, $J = 7.1, 1.8$ Hz, 2H), 2.95 (dd, $J = 16.8, 7.7$ Hz, 1H), 2.78 (dd, $J = 16.8, 6.8$ Hz, 1H), 1.17 (t, $J = 7.1$ Hz, 3H) ppm; ^{13}C NMR (100 MHz, $\text{CDCl}_3+\text{CCl}_4$) δ 168.47, 150.61, 143.34, 122.29, 61.58, 38.96, 32.47, 14.09 ppm.

Ethyl 3-cyano-3-(4-cyanophenyl)propanoate **10s**.



Following the experimental procedure, the reaction of diethyl 2-(4-cyanobenzylidene)malonate (500 mg, 1.81 mmol) **31s** was taken in a mixture of ethanol (12 mL) and water (3 mL) with solid KCN (1.5 equiv, 2.74 mmol) afforded ethyl 3-cyano-3-(4-cyanophenyl)propanoate **10s** as a colorless liquid; $R_f = 0.4$ (hexanes: EtOAc, 7:3), yield 58% (239 mg); IR Data (ν): 2922, 2852, 2229, 1736, 1610, 1505, 1408, 1214, 1022, 838, 546 cm^{-1} ; ^1H NMR (400 MHz, $\text{CDCl}_3+\text{CCl}_4$) ^1H

NMR (400 MHz, CDCl₃) δ 7.70 (d, J = 8.5 Hz, 2H), 7.53 (d, J = 8.3 Hz, 2H), 4.36 (t, J = 7.3 Hz, 1H), 4.16 (dt, J = 10.6, 3.5 Hz, 2H), 3.02 (dd, J = 16.7, 7.3 Hz, 1H), 2.83 (dd, J = 16.7, 7.3 Hz, 1H), 1.25 (t, J = 7.1 Hz, 3H) ; ¹³C NMR (100 MHz, CDCl₃) δ 168.57, 139.79, 133.15, 128.59, 118.73, 117.86, 113.25, 61.85, 39.67, 33.25, 14.28 ppm.

References

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