An efficient synthetic route to carbocyclic enaminonitriles via Lewis acid catalysed domino-ring-opening-cyclisation (DROC) of donor-acceptor cyclopropanes with malononitrile

Manas K. Ghorai,* Ranadeep Talukdar* and Deo Prakash Tiwari*
Department of Chemistry, Indian Institute of Technology, Kanpur, 208016, India

E-mail: mkghorai@iitk.ac.in

Supporting Information

<table>
<thead>
<tr>
<th>SL No.</th>
<th>Contents</th>
<th>Page No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>General Experimental</td>
<td>S-2</td>
</tr>
<tr>
<td>2.</td>
<td>Spectral Data</td>
<td>S-2</td>
</tr>
<tr>
<td>3.</td>
<td>X-ray Crystallographic Analysis Table</td>
<td>S-9</td>
</tr>
<tr>
<td>4.</td>
<td>NMR Spectra</td>
<td>S-12</td>
</tr>
<tr>
<td>5.</td>
<td>Crystal Structures of 3a, 3e and 3k</td>
<td>S-27</td>
</tr>
</tbody>
</table>
**General Experimental:**

Analytical thin layer chromatography (TLC) was carried out using silica gel 60 F$_{254}$ pre-coated plates. Visualization was accomplished with UV lamp or I$_2$ stain. Silica gel 230-400 mesh size were used for column chromatography using the combination of ethyl acetate and petroleum ether as an eluent. Unless noted, all reactions were carried out in oven-dried glassware under an atmosphere of nitrogen using anhydrous solvents. Where appropriate, solvents and all reagents were purified prior to use following the guidelines of Perrin and Armarego$^1$ and Vogel.$^2$ Yb(OTf)$_3$ was purchased from Sigma-Aldrich and was used directly. NaH and malononitrile were purchased from Spectrochem India Pvt. Ltd. and were used directly. All racemic 2-arylcyclopropane-1,1-dicarboxylates were prepared using reported method.$^3$ All commercial reagents were used as received.

**General procedure for the ring opening cyclization of dialkyl-2-arylcyclopropane-1,1-dicarboxylates to dialkyl-2-amino-3-cyano-4-arylcyclopent-2-ene-1,1-dicarboxylates:** To a suspension of NaH (1.275 mmol) in THF (1.0 mL), malononitrile 2 (1.275 mmol) was added at room temperature under nitrogen atmosphere and the reaction mixture was stirred until evolution of H$_2$ ceased. Dialkyl-2-arylcyclopropane-1,1-dicarboxylate 1 (0.425 mmol) dissolved in THF (1.0 mL) and Yb(OTf)$_3$ (0.085 mmol) dissolved in THF (1.0 mL) were added sequentially to the reaction mixture and it was stirred at 60 °C for appropriate time. After complete consumption of the starting material (monitored by TLC) the reaction was quenched with saturated aqueous NH$_4$Cl solution (2.0 mL). After separating the organic layer, the aqueous layer was extracted with ethyl acetate (5 × 2.0 mL). The combined organic extract was washed with brine, dried over anhydrous sodium sulphate and the solvent was removed under reduced pressure. The crude concentrate was purified by flash column chromatography on silica gel (230-400 mesh) using ethyl acetate in petroleum ether (10-20%) as the eluent to afford the pure products (3) as white crystalline solids.

**Spectral Data:**

**Dimethyl-2-amino-3-cyano-4-phenylcyclopent-2-ene-1,1-dicarboxylate (3a)** The general method described above was followed when 1a (100 mg, 0.425 mmol) was reacted with malononitrile (80 μL, 1.275 mmol) in the presence of NaH (51 mg, 1.275 mmol) using 20 mol % of Yb(OTf)$_3$ (53 mg, 0.085 mmol) at 60 °C for 15 min to afford 3a (124 mg, 0.412 mmol) as a white crystalline solid in 88% yield. mp 127-129 °C. R$_f$ 0.35 (40% EtOAc/hexanes). IR
(KBr, cm$^{-1}$) 3459, 3360, 3275, 3232, 3028, 2956, 2923, 2851, 2817, 2196, 1737, 1647, 1603, 1495, 1454, 1435, 1393, 1354, 1279, 1212, 1178, 1066, 1030, 944, 905, 877, 797, 766. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.33 (t, $J = 7.3$ Hz, 2H), 7.26-7.22 (m, 3H), 5.16 (s, 2H), 4.12 (t, $J = 7.8$ Hz, 1H), 3.83 (s, 3H), 3.77 (s, 3H), 3.01 (dd, $J = 13.8, 7.7$ Hz, 1H), 2.27 (dd, $J = 13.7, 7.9$ Hz, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 169.0, 168.5, 156.7, 141.9, 128.9, 127.5, 127.4, 117.0, 84.1, 64.9, 53.8, 53.5, 46.8, 41.6; HRMS (ESI) Calcd for C$_{16}$H$_{16}$N$_2$O$_4$ (M+H)$^+$ 301.1188, found 301.1180.

Dimethyl-2-amino-3-cyano-4-p-toly cyclopent-2-ene-1,1-dicarboxylate (3b) The general method described above was followed when 1b (100 mg, 0.404 mmol) was reacted with malononitrile (76 $\mu$L, 1.212 mmol) in the presence of NaH (48 mg, 1.212 mmol) using 20 mol % of Yb(OTf)$_3$ (50 mg, 0.081 mmol) at 60 °C for 15 min to afford 3b (108 mg, 0.343 mmol) as a white crystalline solid in 85% yield. mp 139-140 °C. R$_f$ 0.39 (40% EtOAc/hexanes). IR (neat, cm$^{-1}$) 3414, 3349, 3279, 3243, 2955, 2871, 2196, 1742, 1726, 1664, 1613, 1514, 1435, 1319, 1274, 1251, 1217, 1182, 1073, 942, 881, 821, 766. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.3 (t, $J = 7.3$ Hz, 2H), 6.86 (d, $J = 8.9$ Hz, 2H), 5.13 (s, 2H), 4.07 (t, $J = 7.8$ Hz, 1H), 3.82 (s, 3H), 3.83 (s, 3H), 3.78 (s, 3H), 3.77 (s, 3H), 2.97 (dd, $J = 13.5, 7.7$ Hz, 1H), 2.23 (dd, $J = 13.8, 8.0$ Hz, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 169.1, 168.6, 156.4, 156.1, 127.2, 127.4, 127.3, 121.7, 117.0, 84.1, 64.9, 53.8, 53.5, 46.5, 41.7, 31.7, 22.7, 21.1, 14.2; HRMS (ESI) Calcd for C$_{17}$H$_{14}$N$_2$O$_4$ (M+H)$^+$ 315.1345, found 315.1344.

Dimethyl-2-amino-3-cyano-4-(4-methoxyphenyl)cyclopent-2-ene-1,1-dicarboxylate (3c) The general method described above was followed when 1c (100 mg, 0.430 mmol) was reacted with malononitrile (82 $\mu$L, 1.290 mmol) in the presence of NaH (52 mg, 1.290 mmol) using 20 mol % of Yb(OTf)$_3$ (53 mg, 0.086 mmol) at 60 °C for 15 min to afford 3c (103 mg, 0.387 mmol) as a white crystalline solid in 90% yield. mp 109-111 °C. R$_f$ 0.31 (40% EtOAc/hexanes). IR (neat, cm$^{-1}$) 3459, 3360, 2957, 2925, 2854, 2196, 1738, 1651, 1610, 1514, 1436, 1390, 1249, 1215, 1176, 1069, 1033, 880, 833. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.15 (d, $J = 8.6$ Hz, 2H), 6.86 (d, $J = 8.9$ Hz, 2H), 5.13 (s, 2H), 4.07 (t, $J = 7.8$ Hz, 1H), 3.82 (s, 3H), 3.83 (s, 3H), 3.78 (s, 3H), 3.77 (s, 3H), 2.97 (dd, $J = 13.5, 7.7$ Hz, 1H), 2.23 (dd, $J = 13.8, 8.0$ Hz, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 169.1, 168.6, 158.9, 156.4, 134.0, 128.4,
Dimethyl-2-amino-3-cyano-4-(2,3-dimethoxyphenyl)cyclopent-2-ene-1,1-dicarboxylate (3d) The general method described above was followed when 1d (100 mg, 0.340 mmol) was reacted with malononitrile (64 μL, 1.020 mmol) in the presence of NaH (41 mg, 1.020 mmol) using 20 mol % of Yb(OTf)₃ (42 mg, 0.068 mmol) at 60 °C for 15 min to afford 3d (110 mg, 0.306 mmol) as a white crystalline solid in 90% yield. mp 113-115 °C. Rf 0.28 (40% EtOAc/hexanes). IR (KBr, cm⁻¹) 3427, 3342, 3272, 3233, 2956, 2832, 2195, 1733, 1656, 1599, 1478, 1439, 1334, 1283, 1201, 1003, 938, 901, 840, 797, 752. ¹H NMR (500 MHz, CDCl₃): δ 7.03 (t, J = 8.1 Hz, 1H), 6.82-6.78 (m, 2H), 5.10 (s, 2H), 4.49 (t, J = 7.7 Hz, 1H), 3.85 (s, 3H), 3.74 (s, 3H), 3.04 (dd, J = 13.8, 7.9 Hz, 1H), 2.29 (dd, J = 13.8, 2.1 Hz, 1H). ¹³C NMR (125 MHz, CDCl₃): δ 169.6, 168.8, 156.6, 152.8, 147.1, 135.7, 124.5, 119.6, 117.3, 111.4, 83.6, 65.1, 61.2, 55.8, 53.5, 40.4, 40.3; HRMS (ESI) Calcd for C₁₇H₁₈N₂O₅ (M+H)⁺ 331.1294, found 331.1290.

Dimethyl-2-amino-4-(4-fluorophenyl)-3-cyanocyclopent-2-ene-1,1-dicarboxylate (3e) The general method described above was followed when 1e (100 mg, 0.395 mmol) was reacted with malononitrile (75 μL, 1.185 mmol) in the presence of NaH (48 mg, 1.185 mmol) using 20 mol % of Yb(OTf)₃ (49 mg, 0.079 mmol) at 60 °C for 30 min to afford 3e (100 mg, 0.316 mmol) as a white crystalline solid in 80% yield. mp 143-145 °C. Rf 0.34 (40% EtOAc/hexanes). IR (KBr, cm⁻¹) 3472, 3328, 3264, 3219, 2961, 2897, 2200, 1736, 1652, 1596, 1510, 1438, 1395, 1283, 1239, 1213, 1110, 1073, 939, 911, 872, 840, 785. ¹H NMR (500 MHz, CDCl₃): δ 7.21-7.18 (m, 2H), 7.02 (t, J = 8.7 Hz, 2H), 5.15 (s, 2H), 4.10 (t, J = 7.6 Hz, 1H), 3.83 (s, 3H), 3.79 (s, 3H), 3.00 (dd, J = 13.8, 7.6 Hz, 1H), 2.22 (dd, J = 13.7, 7.9 Hz, 1H). ¹³C NMR (125 MHz, CDCl₃): δ 169.0, 168.4, 163.7, 161.6, 156.7, 137.6, 129.0, 128.9, 116.9, 115.9, 115.7, 84.0, 64.8, 53.8, 53.6, 46.1, 41.7; HRMS (ESI) Calcd for C₁₉H₁₉FNO₄ (M+H)⁺ 319.1094, found 319.1096.
Dimethyl-2-amino-4-(4-chlorophenyl)-3-cyanocyclopent-2-ene-1,1-dicarboxylate (3f) The general method described above was followed when 1f (100 mg, 0.392 mmol) was reacted with malononitrile (74 μL, 1.176 mmol) in the presence of NaH (47 mg, 1.176 mmol) using 20 mol % of Yb(OTf)$_3$ (49 mg, 0.078 mmol) at 60 °C for 25 min to afford 3f (110 mg, 0.329 mmol) as a white crystalline solid in 84% yield. mp 148-150 °C. R$_f$ 0.34 (40% EtOAc/hexanes). IR (KBr, cm$^{-1}$) 3460, 3358, 2955, 2196, 1736, 1647, 1603, 1490, 1435, 1411, 1277, 1249, 1212, 1089, 1068, 1014, 828. $^1$H NMR (500 MHz, CDCl$_3$): δ 7.30 (d, $J$ = 8.6 Hz, 2H), 7.17 (d, $J$ = 8.6 Hz, 2H), 5.16 (s, 2H), 4.09 (t, $J$ = 7.8 Hz, 1H), 3.83 (s, 3H), 3.78 (s, 3H), 3.00 (dd, $J$ = 13.8, 7.7 Hz, 1H), 2.22 (dd, $J$ = 13.7, 7.9 Hz, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$): δ 168.9, 168.3, 156.8, 141.0, 133.2, 129.1, 128.8, 116.8, 83.6, 64.8, 53.9, 53.6, 46.2, 41.5; HRMS (ESI) Calcd for C$_{16}$H$_{15}$ClN$_2$O$_4$ (M+H)$^+$ 335.0799, found 335.0794.

Dimethyl-2-amino-4-(2-bromophenyl)-3-cyanocyclopent-2-ene-1,1-dicarboxylate (3g) The general method described above was followed when 1g (100 mg, 0.320 mmol) was reacted with malononitrile (60 μL, 0.960 mmol) in the presence of NaH (39 mg, 0.960 mmol) using 20 mol % of Yb(OTf)$_3$ (40 mg, 0.064 mmol) at 60 °C for 1 hr to afford 3g (95 mg, 0.250 mmol) as a white crystalline solid in 78% yield. mp 122-123 °C. R$_f$ 0.36 (40% EtOAc/hexanes). IR (KBr, cm$^{-1}$) 3478, 3359, 2956, 2195, 1752, 1733, 1653, 1602, 1467, 1431, 1392, 1280, 1243, 1209, 1054, 758. $^1$H NMR (500 MHz, CDCl$_3$): δ 7.54 (d, $J$ = 8.0 Hz, 1H), 7.32-7.29 (m, 1H), 7.27-7.25 (m, 1H), 7.12-7.10 (m, 1H), 5.21 (s, 2H), 4.58 (t, $J$ = 7.5 Hz, 1H), 3.84 (s, 3H), 3.72 (s, 3H), 3.18 (dd, $J$ = 13.8, 8.3 Hz, 1H), 2.17 (dd, $J$ = 13.9, 6.6 Hz, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$): δ 168.9, 168.5, 157.5, 141.0, 133.1, 128.9, 128.1, 124.2, 116.9, 82.2, 64.7, 53.9, 53.5, 46.0, 39.7; HRMS (ESI) Calcd for C$_{16}$H$_{15}$BrN$_2$O$_4$ (M+H)$^+$ 379.0293, found 379.0298.
Dimethyl-2-amino-4-(3-bromophenyl)-3-cyanocyclopent-2-ene-1,1-dicarboxylate (3h) The general method described above was followed when 1h (100 mg, 0.320 mmol) was reacted with malononitrile (60 μL, 0.960 mmol) in the presence of NaH (39 mg, 0.960 mmol) using 20 mol % of Yb(OTf)$_3$ (40 mg, 0.064 mmol) at 60 °C for 45 min to afford 3h (98 mg, 0.256 mmol) as a white crystalline solid in 80% yield. mp 128-130 °C. R$_f$ 0.37 (40% EtOAc/hexanes). IR (KBr, cm$^{-1}$) 3472, 3332, 3258, 2954, 2198, 1733, 1647, 1592, 1438, 1283, 1237, 1211, 1073, 938, 886, 790. $^1$H NMR (500 MHz, CDCl$_3$): δ 7.39-7.37 (m, 2H), 7.12-7.04 (m, 2H), 5.17 (s, 2H), 4.08 (t, $J$ = 7.7 Hz, 1H), 3.83 (s, 3H), 3.78 (s, 3H), 3.01 (dd, $J$ = 13.9, 7.8 Hz, 1H), 2.21 (dd, $J$ = 13.8, 8.0 Hz, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$): δ 168.8, 168.3, 157.0, 144.3, 130.7, 130.5, 130.4, 126.1, 123.0, 116.7, 83.3, 64.8, 53.9, 53.6, 46.5, 41.4; HRMS (ESI) Calcd for C$_{16}$H$_{15}$BrN$_2$O$_4$ (M+H)$^+$ 379.0293, found 379.0299.

Dimethyl-2-amino-4-(3-bromophenyl)-3-cyanocyclopent-2-ene-1,1-dicarboxylate (3i) The general method described above was followed when 1i (100 mg, 0.320 mmol) was reacted with malononitrile (60 μL, 0.960 mmol) in the presence of NaH (39 mg, 0.960 mmol) using 20 mol % of Yb(OTf)$_3$ (40 mg, 0.064 mmol) at 60 °C for 30 min to afford 3i (111 mg, 0.294 mmol) as a white crystalline solid in 92% yield. mp 138-140°C. R$_f$ 0.32 (40% EtOAc/hexanes). IR (KBr, cm$^{-1}$) 3462, 3328, 3263, 3219, 2955, 2198, 1753, 1743, 1654, 1597, 1487, 1437, 1410, 1281, 1251, 1179, 1107, 1071, 1009, 940, 881, 823. $^1$H NMR (500 MHz, CDCl$_3$): δ 7.45 (d, $J$ = 8.3 Hz, 2H), 7.11 (d, $J$ = 8.2 Hz, 2H), 5.17 (s, 2H), 4.08 (t, $J$ = 7.6 Hz, 1H), 3.83 (s, 3H), 3.78 (s, 3H), 3.00 (dd, $J$ = 13.9, 7.8 Hz, 1H), 2.21 (dd, $J$ = 13.8, 8.0 Hz, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$): δ 168.9, 168.3, 156.9, 141.0, 132.0, 129.1, 121.3, 116.8, 83.5, 64.8, 53.9, 53.6, 46.3, 41.4; HRMS (ESI) Calcd for C$_{16}$H$_{15}$BrN$_2$O$_4$ (M+H)$^+$ 379.0293, found 379.0292.

Dimethyl-2-amino-3-cyano-4-(naphthalen-1-yl)cyclopent-2-ene-1,1-dicarboxylate (3j) The general method described above was followed when 1j (100 mg, 0.350 mmol) was reacted with malononitrile (66 μL, 1.050 mmol)
in the presence of NaH (42 mg, 1.050 mmol) using 20 mol % of Yb(OTf)$_3$ (43 mg, 0.070 mmol) at 60 °C for 2 hr to afford 3j (79 mg, 0.228 mmol) as a white crystalline solid in 65% yield. mp 112-115 °C. R$_f$ 0.34 (40% EtOAc/hexanes). IR (KBr, cm$^{-1}$) 3356, 2924, 2852, 2196, 1736, 1647, 1595, 1435, 1396, 1274, 1205, 1067, 780. $^1$H NMR (500 MHz, CDCl$_3$): δ 8.05 (d, J = 8.6 Hz, 1H), 7.87 (d, J = 7.9 Hz, 1H), 7.76 (d, J = 7.9 Hz, 1H), 7.56-7.42 (m, 4H), 5.23 (s, 2H), 4.96 (t, J = 8.0 Hz, 1H), 3.88 (s, 3H), 3.67 (s, 3H), 2.30 (dd, J = 13.7, 8.7 Hz, 1H), 2.29 (dd, J = 13.8, 8.8 Hz, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$): δ 168.9, 168.6, 157.1, 137.8, 134.1, 131.4, 129.1, 127.9, 126.3, 125.8, 125.7, 123.7, 122.9, 117.2, 82.7, 64.9, 53.9, 53.4, 42.5, 40.7. HRMS (ESI) Calcd for C$_{20}$H$_{18}$N$_2$O$_4$ (M+H)$^+$ 351.1345, found 351.1348.

![Dimethyl-2-amino-3-cyano-4-(naphthalen-2-yl)cyclopent-2-ene-1,1-dicarboxylate (3k)](image)

**Dimethyl-2-amino-3-cyano-4-(naphthalen-2-yl)cyclopent-2-ene-1,1-dicarboxylate (3k)** The general method described above was followed when 1k (100 mg, 0.350 mmol) was reacted with malononitrile (66 μL, 1.050 mmol) in the presence of NaH (42 mg, 1.050 mmol) using 20 mol % of Yb(OTf)$_3$ (43 mg, 0.070 mmol) at 60 °C for 45 min to afford 3k (100 mg, 0.287 mmol) as a white crystalline solid in 82% yield. mp 143-145 °C. R$_f$ 0.34 (40% EtOAc/hexanes). IR (KBr, cm$^{-1}$) 3429, 3339, 3265, 2924, 2854, 2187, 1753, 1734, 1655, 1594, 1507, 1436, 1268, 1202, 1072, 895, 856, 823, 804, 752. $^1$H NMR (500 MHz, CDCl$_3$): δ 7.84-7.80 (m, 3H), 7.70 (s, 1H), 7.49-7.43 (s, 2H), 7.35 (dd, J = 8.6, 1.8 Hz, 1H), 4.30 (t, J = 7.8 Hz, 1H), 3.85 (s, 3H), 3.78 (s, 3H), 3.08 (dd, J = 13.9, 7.8 Hz, 1H), 2.37 (dd, J = 13.8, 7.7 Hz, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$): δ 169.1, 168.5, 156.8, 139.3, 133.6, 132.9, 128.9, 127.9, 127.8, 126.3, 125.9, 125.2, 117.1, 84.1, 65.0, 53.9, 53.6, 47.0, 41.5. HRMS (ESI) Calcd for C$_{20}$H$_{18}$N$_2$O$_4$ (M+H)$_+$ 351.1345, found 351.1346.

![Diethyl-2-amino-3-cyano-4-phenylcyclopent-2-ene-1,1-dicarboxylate (3l)](image)

**Diethyl-2-amino-3-cyano-4-phenylcyclopent-2-ene-1,1-dicarboxylate (3l)** The general method described above was followed when 1l (100 mg, 0.381 mmol) was reacted with malononitrile (72 μL, 1.143 mmol) in the presence of NaH (46 mg, 1.143 mmol) using 20 mol % of Yb(OTf)$_3$ (47 mg, 0.076 mmol) at 60 °C for 20 min to afford 3l (104 mg, 0.316 mmol) as a white crystalline solid in 83% yield. mp 92-94 °C. R$_f$ 0.50 (40% EtOAc/hexanes). IR (KBr, cm$^{-1}$) 3457, 3338, 3262, 3220, 3058, 3031, 3007, 2985, 2941, 2894, 2194, 1728, 1651, 1594, 1497, 1454, 1394, 1369, 1301, 1283, 1253, 1238, 1209, 1096, 1065, 1051, 1020, 924, 856, 811, 773. $^1$H NMR (500 MHz, CDCl$_3$): δ
Dimethyl-2-amino-3-cyano-4-(furan-2-yl)cyclopent-2-ene-1,1-dicarboxylate (3m) The general method described above was followed when 1m (100 mg, 0.446 mmol) was reacted with malononitrile (84 µL, 1.338 mmol) in the presence of NaH (54 mg, 1.338 mmol) using 20 mol % of Yb(OTf)$_3$ (55 mg, 0.089 mmol) at 60 °C for 25 min to afford 3m (118 mg, 0.406 mmol) as a white crystalline solid in 91% yield. mp 107-109 °C. R$_f$ 0.30 (40% EtOAc/hexanes). IR (KBr, cm$^{-1}$) 3466, 3335, 3274, 3224, 2959, 2204, 1756, 1732, 1651, 1598, 1506, 1435, 1401, 1338, 1296, 1281, 1238, 1217, 1182, 1144, 1070, 1013, 990, 939, 928, 904, 883, 838, 816, 789. $^1$H NMR (500 MHz, CDCl$_3$): δ 7.33 (t, $J$ = 5.9 Hz, 1H), 6.30-6.28 (m, 1H), 6.17 (d, $J$ = 3.4 Hz, 1H), 5.16 (s, 2H), 4.18 (t, $J$ = 7.3 Hz, 1H), 3.81 (s, 3H), 3.77 (s, 3H), 2.92 (dd, $J$ = 13.8, 7.7 Hz, 1H), 2.54 (dd, $J$ = 13.8, 6.8 Hz, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$): δ 168.6, 168.0, 157.0, 142.1 128.9, 127.4, 117.1, 84.0, 65.1, 62.9, 62.6, 46.8, 41.6, 14.1, 14.0; HRMS (ESI) Calcd for C$_{18}$H$_{30}$N$_2$O$_4$ (M+H)$^+$ 329.1501, found 329.1502.

Dimethyl-2-amino-3-cyano-4-(thiophen-2-yl)cyclopent-2-ene-1,1-dicarboxylate (3n) The general method described above was followed when 1n (100 mg, 0.417 mmol) was reacted with malononitrile (79 µL, 1.251 mmol) in the presence of NaH (50 mg, 1.251 mmol) using 20 mol % of Yb(OTf)$_3$ (52 mg, 0.083 mmol) at 60 °C for 30 min to afford 3n (119 mg, 0.389 mmol) as a white crystalline solid in 93% yield. mp 147-149 °C. R$_f$ 0.30 (40% EtOAc/hexanes). IR (KBr, cm$^{-1}$) 3460, 3333, 3271, 3224, 2955, 2927, 2205, 1733, 1684, 1650, 1598, 1435, 1404, 1373, 1321, 1292, 1280, 1219, 1200, 1173, 1105, 1072, 982, 939, 909, 837, 811, 779. $^1$H NMR (500 MHz, CDCl$_3$): δ 7.20-7.19 (m, 1H), 6.94-6.92 (m, 2H), 5.18 (s, 2H), 4.41 (t, $J$ = 7.5 Hz, 1H), 3.82 (s, 3H), 3.79 (s, 3H), 3.05 (dd, $J$ = 14.5, 7.6 Hz, 1H), 2.41 (dd, $J$ = 13.8, 7.4 Hz, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$): δ 168.8, 168.3, 156.4, 145.9, 127.1, 124.8, 124.6, 116.8, 84.1, 64.6, 53.9, 53.6, 41.9, 41.7; HRMS (ESI) Calcd for C$_{18}$H$_{31}$N$_2$O$_4$S (M+H)$^+$ 307.0753, found 307.0757.
(E)-dimethyl-2-amino-3-cyano-4-styrylcyclopent-2-ene-1,1-dicarboxylate (3o) The general method described above was followed when 10 (100 mg, 0.384 mmol) was reacted with malononitrile (72 μL, 1.153 mmol) in the presence of NaH (46 mg, 1.153 mmol) using 20 mol % of Yb(OTf)₃ (48 mg, 0.077 mmol) at 60 °C for 30 min to afford 3o (116 mg, 0.357 mmol) as a white crystalline solid in 93% yield. mp 101-103 °C. Rf 0.37 (40% EtOAc/hexanes). IR (KBr, cm⁻¹) 3463, 3440, 3345, 3273, 2954, 2196, 1737, 1661, 1601, 1497, 1445, 1433, 1395, 1278, 1243, 1216, 1200, 1106, 1066, 985, 967, 936, 912, 789. ¹H NMR (500 MHz, CDCl₃): δ 7.35 (d, J = 7.4 Hz, 1H), 7.29 (t, J = 7.5 Hz, 2H), 7.22 (t, J = 7.3 Hz, 2H), 6.52 (d, J = 15.6 Hz, 1H), 6.05 (dd, J = 15.6, 8.5 Hz, 1H), 5.80 (s, 2H), 3.81 (s, 3H), 3.81 (s, 3H), 3.68 (q, J = 7.5 Hz, 1H), 2.83 (dd, J = 13.8, 7.7 Hz, 1H), 2.27 (dd, J = 13.8, 6.7 Hz, 1H). ¹³C NMR (125 MHz, CDCl₃): δ 169.0, 168.6, 156.0, 136.7, 132.0, 130.2, 128.6, 127.7, 126.5, 117.1, 83.5, 64.9, 53.7, 53.6, 44.6, 38.5; HRMS (ESI) Calcd for C₁₆H₁₈N₂O₄ (M+Na)+ 349.1164, found 349.1162.

4. X-ray Crystallographic Analysis:

Single crystal X-ray data of compounds 3a, 3e and 3k were collected at 100 K on a CCD diffractometer using graphite-monochromated MoKα radiation (λ = 0.71073 Å). Linear absorption coefficients, scattering factors for the atoms and the anomalous dispersion corrections were taken from International Tables for X-ray Crystallography. Data integration and reduction were processed with SAINT⁴ software. An empirical absorption correction was applied to the collected reflections with SADABS⁵ using XPREP.⁶ The structure was solved by the direct method using SHELXTL⁷ and refined on F² by full-matrix least-squares technique using the SHELXL-97 program package. Non-hydrogen atoms were refined anisotropically. The H atoms have been refined as follows; the hydrogen atoms attached to carbon and oxygen atoms were positioned geometrically and treated as riding atoms using SHELXL default parameters.

Table 1. Crystal and structure refinement data for compounds 3a, 3e and 3k

<table>
<thead>
<tr>
<th>Compound</th>
<th>3a</th>
<th>3e</th>
<th>3k</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empirical formula</td>
<td>C₁₆H₁₆N₂O₄</td>
<td>C₁₆H₁₅FN₂O₄</td>
<td>C₂₀H₁₉N₂O₄</td>
</tr>
<tr>
<td>Formula weight</td>
<td>300.31</td>
<td>318.30</td>
<td>350.36</td>
</tr>
<tr>
<td>Crystal system</td>
<td>Triclinic</td>
<td>Triclinic</td>
<td>Triclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>P -1</td>
<td>P -1</td>
<td>P -1</td>
</tr>
<tr>
<td></td>
<td>1, Å</td>
<td>2, Å</td>
<td>3, Å</td>
</tr>
<tr>
<td>----------------</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
</tr>
<tr>
<td>a</td>
<td>7.9815(8)</td>
<td>8.060(5)</td>
<td>7.632(5)</td>
</tr>
<tr>
<td>b</td>
<td>9.9504(10)</td>
<td>10.050(5)</td>
<td>10.273(5)</td>
</tr>
<tr>
<td>c</td>
<td>10.0645(10)</td>
<td>10.085(5)</td>
<td>11.899(5)</td>
</tr>
<tr>
<td>α (°)</td>
<td>96.580(2)</td>
<td>96.045(5)</td>
<td>82.050(5)</td>
</tr>
<tr>
<td>β (°)</td>
<td>101.994(2)</td>
<td>103.961(5)</td>
<td>84.145(5)</td>
</tr>
<tr>
<td>γ (°)</td>
<td>100.214(2)</td>
<td>99.238(5)</td>
<td>84.145(5)</td>
</tr>
<tr>
<td>U, Å³</td>
<td>759.89(13)</td>
<td>773.6(7)</td>
<td>870.8(8)</td>
</tr>
<tr>
<td>Z</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>ρ&lt;sub&gt;calc&lt;/sub&gt; Mg/m&lt;sup&gt;3&lt;/sup&gt;</td>
<td>1.312</td>
<td>1.366</td>
<td>1.336</td>
</tr>
<tr>
<td>μ, mm&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>0.096</td>
<td>0.107</td>
<td>0.094</td>
</tr>
<tr>
<td>F(000)</td>
<td>316</td>
<td>332</td>
<td>368</td>
</tr>
<tr>
<td>Refl. collected</td>
<td>3962</td>
<td>5962</td>
<td>4557</td>
</tr>
<tr>
<td>Independent refl.</td>
<td>2615 [R(int) = 0.0190]</td>
<td>3070 [R(int) = 0.0380]</td>
<td>3005 [R(int) = 0.0339]</td>
</tr>
<tr>
<td>GOOF</td>
<td>1.035</td>
<td>1.008</td>
<td>1.022</td>
</tr>
<tr>
<td>[I&gt;2σ(I)]</td>
<td>R1 = 0.0470, wR2 = 0.1192</td>
<td>R1 = 0.0513, wR2 = 0.0956</td>
<td>R1 = 0.0630, wR2 = 0.1389</td>
</tr>
<tr>
<td>R indices (all data)</td>
<td>R1 = 0.0572, wR2 = 0.1344</td>
<td>R1 = 0.0930, wR2 = 0.1092</td>
<td>R1 = 0.1046, wR2 = 0.1697</td>
</tr>
<tr>
<td>CCDC deposition No.</td>
<td>CCDC 939509</td>
<td>CCDC 939510</td>
<td>CCDC 939511</td>
</tr>
</tbody>
</table>
5. References:


6. NMR Spectra:

Fig 1: $^1$H NMR (500 MHz, CDCl$_3$) of 3a

Fig 2: $^{13}$C NMR (125 MHz, CDCl$_3$) of 3a
Fig 3: $^1$H NMR (500 MHz, CDCl$_3$) of $3b$

Fig 4: $^{13}$C NMR (125 MHz, CDCl$_3$) of $3b$
Fig 5: $^1$H NMR (500 MHz, CDCl$_3$) of 3c

Fig 6: $^{13}$C NMR (125 MHz, CDCl$_3$) of 3c
Fig 7: $^1$H NMR (500 MHz, CDCl$_3$) of 3d

Fig 8: $^{13}$C NMR (125 MHz, CDCl$_3$) of 3d
Fig 9: $^1$H NMR (500 MHz, CDCl$_3$) of 3e

Fig 10: $^{13}$C NMR (125 MHz, CDCl$_3$) of 3e
Fig 11: $^1$H NMR (500 MHz, CDCl$_3$) of 3f

Fig 12: $^{13}$C NMR (125 MHz, CDCl$_3$) of 3f
Fig 13: $^1$H NMR (500 MHz, CDCl$_3$) of 3g

Fig 14: $^{13}$C NMR (125 MHz, CDCl$_3$) of 3g
Fig 15: $^1$H NMR (500 MHz, CDCl$_3$) of 3h

Fig 16: $^{13}$C NMR (125 MHz, CDCl$_3$) of 3h
Fig 17: $^1$H NMR (500 MHz, CDCl$_3$) of 3i

Fig 18: $^{13}$C NMR (125 MHz, CDCl$_3$) of 3i
Fig 19: $^1$H NMR (500 MHz, CDCl$_3$) of 3j

Fig 20: $^{13}$C NMR (125 MHz, CDCl$_3$) of 3j
Fig 21: $^1$H NMR (500 MHz, CDCl$_3$) of 3k

Fig 22: $^{13}$C NMR (125 MHz, CDCl$_3$) of 3k
Fig 23: $^1$H NMR (500 MHz, CDCl$_3$) of $3l$

Fig 24: $^{13}$C NMR (125 MHz, CDCl$_3$) of $3l$
Fig 25: $^1$H NMR (500 MHz, CDCl$_3$) of 3m

Fig 26: $^{13}$C NMR (125 MHz, CDCl$_3$) of 3m
Fig 27: $^1$H NMR (500 MHz, CDCl$_3$) of 3n

Fig 28: $^{13}$C NMR (125 MHz, CDCl$_3$) of 3n
Fig 29: $^1$H NMR (500 MHz, CDCl$_3$) of 3o

Fig 30: $^{13}$C NMR (125 MHz, CDCl$_3$) of 3o
7. Crystal Structures of 3a, 3e and 3k:

Figure 31: X-ray crystal structure (Diamond view) of 3a
Figure 32. X-ray crystal structure of compound 3a with 50% thermal ellipsoids
Figure 3: X-ray crystal structure (Diamond view) of 3e
Figure 34. X-ray crystal structure of compound 3e with 50% thermal ellipsoids
Figure 35: X-ray crystal structure (Diamond view) of 3k
Figure 36. X-ray crystal structure of compound 3k with 50% thermal ellipsoids