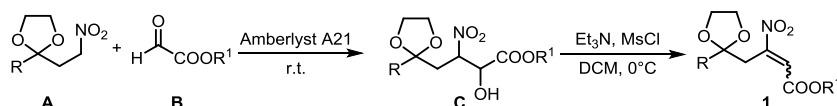


Supporting Information

General Remarks

¹H-NMR were recorded at 400 MHz on a VarianMercury Plus 400. ¹³C-NMR were recorded at 100 MHz. IR spectra were recorded with a PerkinElmer Paragon 500 FT-IR. Mass spectra were performed on a GC/MS system by means of the EI technique (70 eV). Microanalyses were performed with a CHNS-O analyzer Model EA 1108 from Fisons Instruments.

Synthesis of compounds 1.



Compounds **1** were synthesized by a nitroaldol-dehydration process, starting from protected nitroketone **A** and aldehydes **B**.¹ In turn, compounds **A** can be easily synthesized by Curran² or Ono³ methodologies, and compounds **B** can be prepared by Shing procedure.⁴

1) R. Ballini, D. Fiorini, A. Palmieri, *Tetrahedron Lett.* 2004, **45**, 7027. 2) D. P. Curran and T. A. Heffner, *J. Org. Chem.* 1990, **55**, 4585. 3) N. Ono, M. Fujii and A. Kaji, *Synthesis* 1987, 532. 4) Y.-L. Zhong and T. K. M. Shing, *J. Org. Chem.* 1997, **62**, 2622.

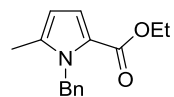
General procedure for the preparation of pyrrole-2-carboxylates 6.

A mixture of β -nitroacrylate **1** (1 mmol) and amine **2** (1 mmol) was stirred at room temperature for the appropriate time (Time1, see Table 2). Then, 2-MeTHF (10 mL) and Amberlyst 15 (200 mg) were added and the resulting mixture was stirred at 60°C for the needed time (Time2, see Table 2). Finally, after the reaction was completed, Amberlyst 15 was filtered off washing with fresh 2-MeTHF (5 mL) and, after removing the solvent at reduced pressure, the crude product **6** was purified by flash chromatography column (hexanes:EtOAc = 95:5).

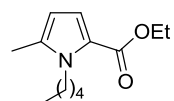
General procedure for the flow preparation of pyrrole-2-carboxylates 6ab and 6ac.

The solutions of starting materials **1a** (0.2 M in 2-MeTHF) and **2b** (or **2c**) (0.2 M in 2-MeTHF) were pumped by means of HPLC pumps (model: Hewlett-Packard HPLC pump series 1050; flow rate of 0.05 mL/min) to the T-mixing piece **T1**, and then passed into the reactors **R1** (internal volume of 10 mL) and **R2** (heated at 60°C and packed with Amberlyst 15, 1.5 g/mmol) maintained under controlled pressure by a back pressure regulator (~2 atm). Finally, after removing the solvent at reduced pressure, the crude product **6** was purified by flash chromatography column (hexanes:EtOAc = 95:5).

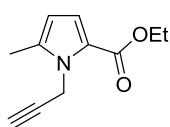
General procedure for the preparation of pyrrolebenzoxazinone 7. A mixture of β -nitroacrylate **1** (1 mmol) and aminophenole **2** (1 mmol) in 2-MeTHF (0.3 mL) was stirred at room temperature for 7 hours. Then, 2-MeTHF (9.7 mL) and Amberlyst 15 (200 mg) were added and the resulting mixture was stirred at 60°C for further 7 h. After the reaction was completed, Amberlyst 15 was filtered off washing with fresh 2-MeTHF (5 mL) and, after the solvent evaporation, the crude product **6** was dissolved in toluene (10 mL), treated with *p*-TSA-H₂O (0.3 mmol, 57 mg) and heated at reflux for 1.5 hours. Then, the solution was treated with a saturated solution of sodium bicarbonate (10 mL) and the mixture was extracted with EtOAc (3 x 20 mL). Finally, the organic phase was dried over Na₂SO₄ and after the filtration and solvent evaporation, the crude product **7** was purified by flash chromatography column (hexanes:EtOAc = 95:5).



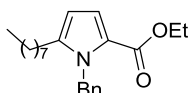
Compound **6aa**. Yield 68%. Colourless oil. IR (cm⁻¹, neat): 694, 728, 759, 1029, 1132, 1232, 1267, 1482, 1694. ¹H-NMR (CDCl₃, 400MHz) δ : 1.30 (t, 3H, *J* = 7.3 Hz), 2.20 (s, 3H), 4.23 (q, 2H, *J* = 7.3 Hz), 5.64 (s, 2H), 6.02 (d, 1H, *J* = 3.8 Hz), 6.90-6.99 (m, 2H), 7.03 (d, 1H, *J* = 3.8 Hz), 7.17-7.37 (m, 3H). ¹³C-NMR (CDCl₃, 100MHz) δ : 12.8, 14.6, 48.3, 59.8, 108.4, 118.1, 122.1, 126.0, 127.1, 128.8, 137.4, 138.6, 161.4. GC-MS (70 eV): *m/z*: 243 ([M⁺], 69), 197 (21), 170 (14), 108 (14), 91 (100), 65 (15). Anal. Calcd. for C₁₅H₁₇NO₂ (243.31): C, 74.05; N, 5.76; H, 7.04. Found: C, 74.11; N, 5.72; H, 7.09.



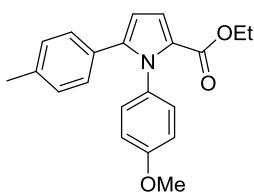
Compound **6ab**. Yield 72%. Colourless oil. IR (cm⁻¹, neat): 750, 1112, 1238, 1470, 1483, 1469. ¹H-NMR (CDCl₃, 400MHz) δ : 0.84-0.98 (m, 3H), 1.24-1.42 (m, 7H), 1.58-1.80 (m, 2H), 2.28 (s, 3H), 4.20-4.33 (m, 4H), 5.91 (d, 1H, *J* = 3.8 Hz), 6.92 (d, 1H, *J* = 3.8 Hz). ¹³C-NMR (CDCl₃, 100MHz) δ : 12.8, 14.2, 14.7, 22.7, 29.2, 31.1, 45.4, 59.6, 107.9, 117.7, 121.5, 136.4, 161.3. GC-MS (70 eV): *m/z*: 223 ([M⁺], 35), 178 (18), 167 (35), 150 (100), 138 (22), 108 (26), 94 (47). Anal. Calcd. for C₁₃H₂₁NO₂ (223.32): C, 69.92; N, 6.27; H, 9.48. Found: C, 70.00; N, 6.22; H, 9.53.



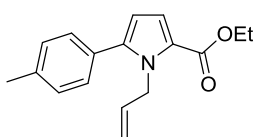
Compound **6ac**. Yield 68% White solid, m.p. = 37-39°C. IR (cm⁻¹, neat): 672, 747, 1043, 1139, 1257, 1484, 1677, 2122, 3269. ¹H-NMR (CDCl₃, 400MHz) δ: 1.34 (t, 3H, *J* = 7.3 Hz), 2.26 (t, 1H, *J* = 2.5 Hz), 2.34 (s, 3H), 4.28 (q, 2H, *J* = 7.3 Hz), 5.18 (d, 2H, *J* = 2.5 Hz), 5.93 (d, 1H, *J* = 3.8 Hz), 6.92 (d, 1H, *J* = 3.8 Hz). ¹³C-NMR (CDCl₃, 100MHz) δ: 12.6, 14.7, 34.3, 60.0, 72.0, 79.0, 108.5, 118.2, 121.4, 137.1, 161.4. GC-MS (70 eV): *m/z*: 191 ([M⁺], 65), 163 (57), 162 (83), 146 (53), 134 (29), 118 (100), 117 (49), 91 (30), 78 (19), 65 (23), 52 (29), 39 (43). Anal. Calcd. for C₁₁H₁₃NO₂ (191.23): C, 69.09; N, 7.32; H, 6.85. Found: C, 69.14; N, 7.29; H, 6.89.



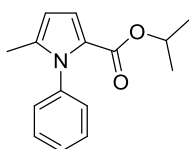
Compound **6ba**. Yield 70%. White solid, m.p. = 29-31°C. IR (cm⁻¹, neat): 699, 732, 751, 1115, 1129, 1260, 1452, 1468, 1691. ¹H-NMR (CDCl₃, 400MHz) δ: 0.88 (t, 3H, *J* = 7.3 Hz), 1.19-1.35 (m, 13H), 1.50-1.62 (m, 2H), 2.47 (t, 2H, *J* = 7.7 Hz), 4.20 (q, 2H, *J* = 7.3 Hz), 5.63 (s, 2H), 6.03 (d, 1H, *J* = 3.8 Hz), 6.90 (d, 2H, *J* = 7.7 Hz), 7.04 (d, 1H, *J* = 3.8 Hz), 7.17-7.30 (m, 3H). ¹³C-NMR (CDCl₃, 100MHz) δ: 14.3, 14.6, 22.9, 26.7, 28.6, 29.4, 29.6, 32.1, 48.1, 59.8, 107.3, 118.1, 122.0, 125.9, 127.1, 128.8, 138.9, 142.1, 161.4. GC-MS (70 eV): *m/z*: 341 ([M⁺], 21), 242 (16), 170 (24), 91 (100), 65 (7). Anal. Calcd. for C₂₂H₃₁NO₂ (341.49): C, 77.38; N, 4.10; H, 9.15. Found: C, 77.44; N, 4.08; H, 9.18.



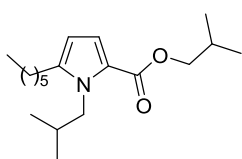
Compound **6cd**. Yield 60%. Pale yellow solid, m.p. = 127-129°C. IR (cm⁻¹, neat): 753, 821, 1026, 1089, 1153, 1232, 1462, 1512, 1611, 1706. ¹H-NMR (CDCl₃, 400MHz) δ: 1.23 (t, 3H, *J* = 7.3 Hz), 2.28 (s, 3H), 3.81 (s, 3H), 4.16 (q, 2H, *J* = 7.3 Hz), 6.38 (d, 1H, *J* = 4.3 Hz), 6.86 (d, 2H, *J* = 8.6 Hz), 7.01 (s, 4H), 7.09-7.17 (m, 3H). ¹³C-NMR (CDCl₃, 100MHz) δ: 14.6, 21.4, 55.6, 59.9, 109.6, 113.8, 118.4, 125.1, 128.9, 129.0, 129.4, 129.8, 132.3, 137.3, 141.8, 159.2, 160.8. GC-MS (70 eV): *m/z*: 335 ([M⁺], 100), 290 (14), 262 (83), 248 (22), 129 (21). Anal. Calcd. for C₂₁H₂₁NO₃ (335.40): C, 75.20; N, 4.18; H, 6.31. Found: C, 75.14; N, 4.21; H, 6.28.



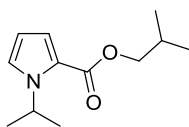
Compound **6ce**. Yield 70%. Colourless oil. IR (cm⁻¹, neat): 751, 823, 1118, 1133, 1218, 1260, 1443, 1465, 1544, 1695. ¹H-NMR (CDCl₃, 400MHz) δ: 1.35 (t, 3H, *J* = 7.3 Hz), 2.40 (s, 3H), 4.29 (q, 2H, *J* = 7.3 Hz), 4.73-4.81 (m, 1H), 4.91-4.97 (m, 2H), 5.07-5.14 (m, 1H), 5.91-6.06 (m, 1H), 6.20 (d, 1H, *J* = 3.8 Hz), 7.09 (d, 1H, *J* = 3.8 Hz), 7.22 (d, 2H, *J* = 8.1 Hz), 7.31 (d, 2H, *J* = 8.1 Hz). ¹³C-NMR (CDCl₃, 100MHz) δ: 14.7, 21.5, 48.2, 60.0, 109.5, 115.4, 118.3, 122.9, 129.3, 129.5, 129.6, 136.0, 138.3, 141.9, 161.3. GC-MS (70 eV): *m/z*: 269 ([M⁺], 100), 240 (10), 224 (31), 196 (45), 172 (17), 156 (12), 129 (30), 115 (10), 80 (13). Anal. Calcd. for C₁₇H₁₉NO₂ (269.34): C, 75.81; N, 5.20; H, 7.11. Found: C, 75.87; N, 5.18; H, 7.15.



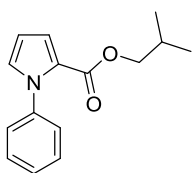
Compound **6df**. Yield 75%. White solid, m.p. = 61-63°C. IR (cm⁻¹, neat): 698, 750, 1039, 1104, 1152, 1274, 1362, 1485, 1550, 1595, 1678. ¹H-NMR (CDCl₃, 400MHz) δ: 1.10 (d, 6H, *J* = 6.4 Hz), 2.02 (s, 3H), 4.91-5.03 (m, 1H), 6.04 (d, 1H, *J* = 3.8 Hz), 7.02 (d, 1H, *J* = 3.8 Hz), 7.18-7.23 (m, 2H), 7.38-7.49 (m, 3H). ¹³C-NMR (CDCl₃, 100MHz) δ: 13.3, 22.0, 66.9, 108.2, 117.9, 124.5, 128.1, 128.3, 128.9, 137.5, 139.8, 160.3. GC-MS (70 eV): *m/z*: 243 ([M⁺], 78), 201 (100), 184 (50), 156 (66), 128 (16), 108 (35), 77 (28), 51 (14). Anal. Calcd. for C₁₅H₁₇NO₂ (243.31): C, 74.05; N, 5.76; H, 7.04. Found: C, 74.11; N, 5.73; H, 7.09.



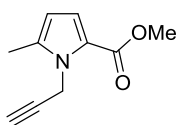
Compound **6eg**. Yield 73%. Colourless oil. IR (cm⁻¹, neat): 750, 1113, 1232, 1256, 1469, 1478, 1697. ¹H-NMR (CDCl₃, 400MHz) δ: 0.83-0.93 (m, 9H), 0.98 (d, 6H, *J* = 6.8 Hz), 1.26-1.44 (m, 6H), 1.59-1.71 (m, 2H), 1.95-2.13 (m, 2H), 2.55 (t, 2H, *J* = 7.7 Hz), 3.96 (d, 2H, *J* = 6.8 Hz), 4.02-4.17 (m, 2H), 5.94 (d, 1H, *J* = 3.8 Hz), 6.96 (d, 1H, *J* = 3.8 Hz). ¹³C-NMR (CDCl₃, 100MHz) δ: 14.3, 19.5, 20.1, 22.8, 27.1, 28.2, 28.8, 29.4, 30.6, 31.9, 51.8, 69.8, 106.5, 118.0, 121.6, 142.0, 161.6. GC-MS (70 eV): *m/z*: 307 ([M⁺], 57), 264 (69), 236 (76), 234 (47), 208 (27), 206 (100), 182 (45), 180 (83), 164 (26), 162 (64), 138 (67), 136 (55), 124 (43), 106 (73), 94 (34), 80 (27), 57 (33), 41 (45), 29 (27). Anal. Calcd. for C₁₉H₃₃NO₂ (307.48): C, 74.22; N, 4.56; H, 10.82. Found: C, 74.29; N, 4.52; H, 10.87.



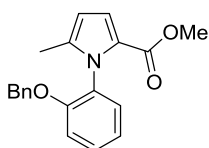
Compound **6fh**. Yield 64%. Pale yellow oil. IR (cm⁻¹, neat): 731, 1067, 1106, 1208, 1227, 1415, 1698. ¹H-NMR (CDCl₃, 400MHz) δ: 1.00 (d, 6H, *J* = 6.8 Hz), 1.44 (d, 6H, *J* = 6.4 Hz), 1.97-2.10 (m, 1H), 4.00 (d, 2H, *J* = 6.4 Hz), 5.40-5.54 (m, 1H), 6.16 (t, 1H, *J* = 3.4 Hz), 6.96-7.00 (m, 1H), 7.02-7.06 (m, 1H). ¹³C-NMR (CDCl₃, 100MHz) δ: 19.5, 24.0, 28.2, 48.6, 70.0, 108.3, 118.1, 122.0, 123.8, 161.5. GC-MS (70 eV): *m/z*: 210 ([M+1⁺], 4), 209 ([M⁺], 34), 153 (41), 138 (40), 136 (44), 111 (100), 94 (70), 93 (49), 66 (15), 41 (14). Anal. Calcd. for C₁₂H₁₉NO₂ (209.29): C, 68.87; N, 6.69; H, 9.15. Found: C, 68.94; N, 6.65; H, 9.19.



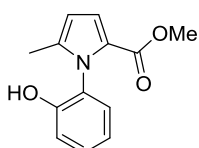
Compound **6ff**. Yield 63%. Pale yellow oil. IR (cm⁻¹, neat): 696, 737, 757, 1119, 1264, 1417, 1498, 1598, 1710. ¹H-NMR (CDCl₃, 400MHz) δ: 0.86 (d, 6H, *J* = 6.8 Hz), 1.78-1.93 (m, 1H), 3.89 (d, 2H, *J* = 6.4 Hz), 6.28-6.31 (m, 1H), 6.93-6.95 (m, 1H), 7.12-7.15 (m, 1H), 7.30-7.34 (m, 2H), 7.38-7.46 (m, 3H). ¹³C-NMR (CDCl₃, 100MHz) δ: 19.3, 28.0, 70.4, 109.3, 119.1, 124.0, 126.6, 128.0, 128.8, 129.9, 140.8, 160.9. GC-MS (70 eV): *m/z*: 243 ([M⁺], 30), 187 (100), 170 (88), 143 (39), 115 (60), 94 (49), 77 (18), 51 (12), 39 (12). Anal. Calcd. for C₁₅H₁₇NO₂ (243.31): C, 74.05; N, 5.76; H, 7.04. Found: C, 74.00; N, 5.79; H, 6.99.



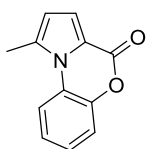
Compound **6gc**. Yield 53%. Pale yellow solid, m.p. = 40-42°C. IR (cm⁻¹, neat): 666, 750, 1041, 1135, 1225, 1256, 1435, 1482, 1694, 2122, 3264. ¹H-NMR (CDCl₃, 400MHz) δ: 2.26 (t, 1H, *J* = 2.5 Hz), 2.35 (s, 3H), 3.81 (s, 3H), 5.18 (d, 2H, *J* = 2.5 Hz), 5.94 (d, 1H, *J* = 3.8 Hz), 6.91 (d, 1H, *J* = 3.8 Hz). ¹³C-NMR (CDCl₃, 100MHz) δ: 12.6, 34.3, 51.3, 72.1, 79.0, 108.7, 118.3, 121.0, 137.2, 161.8. GC-MS (70 eV): *m/z*: 177 ([M⁺], 91), 162 (100), 146 (45), 134 (36), 118 (60), 117 (51), 91 (28), 78 (18), 65 (19), 52 (25), 39 (35). Anal. Calcd. for C₁₀H₁₁NO₂ (177.20): C, 67.78; N, 7.90; H, 6.26. Found: C, 67.84; N, 7.84; H, 6.30.



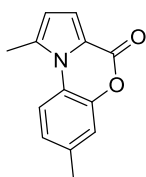
Compound **6gi**. Yield 63%. Yellow viscous oil. IR (cm⁻¹, neat): 699, 753, 1032, 1101, 1153, 1270, 1481, 1593, 1682. ¹H-NMR (CDCl₃, 400MHz) δ: 2.05 (s, 3H), 3.67 (s, 3H), 5.07 (s, 2H), 6.13 (d, 1H, *J* = 3.8 Hz), 7.05-7.14 (m, 3H), 7.18-7.45 (m, 7H). ¹³C-NMR (CDCl₃, 100MHz) δ: 13.0, 51.0, 70.5, 108.3, 114.1, 118.0, 121.3, 123.4, 126.8, 127.9, 128.7, 129.0, 129.6, 129.9, 137.2, 138.1, 154.7, 161.1. GC-MS (70 eV): *m/z*: 321 ([M⁺], 29), 289 (11), 262 (79), 239 (28), 198 (20), 170 (47), 91 (100), 65 (18). Anal. Calcd. for C₂₀H₁₉NO₃ (321.38): C, 74.75; N, 4.36; H, 5.96. Found: C, 74.81; N, 4.33; H, 6.00.



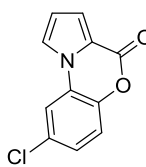
Compound **6gj**. Yield 57%. White solid, m.p. = 131-133°C. IR (cm⁻¹, neat): 701, 749, 1033, 1104, 1151, 1272, 1485, 1598, 1691, 3352. ¹H-NMR (CDCl₃, 400MHz) δ: 2.01 (s, 3H), 3.67 (s, 3H), 5.22 (bs, 1H), 6.12 (d, 1H, *J* = 3.8 Hz), 6.96-7.08 (m, 4H), 7.30-7.36 (m, 1H). ¹³C-NMR (CDCl₃, 100MHz) δ: 12.8, 51.4, 109.3, 117.0, 119.0, 121.0, 123.5, 126.4, 128.9, 130.4, 138.7, 152.3, 161.1. GC-MS (70 eV): *m/z*: 231 ([M⁺], 89), 200 (33), 199 (59), 198 (36), 172 (100), 171 (21), 170 (84), 154 (21), 144 (18), 130 (14), 115 (19), 77 (14), 65 (20), 63 (17), 53 (22), 51 (18), 39 (25). Anal. Calcd. for C₁₃H₁₃NO₃ (231.25): C, 67.52; N, 6.06; H, 5.67. Found: C, 67.60; N, 6.01; H, 5.71.



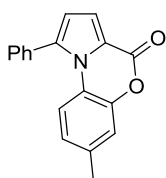
Compound **7gj**. Yield 98% from **6gj**, yield 54% from **1g** and **2j**. White solid, m.p. = 170-172°C. IR (cm⁻¹, neat): 717, 731, 751, 792, 967, 1102, 1216, 1290, 1414, 1489, 1500, 1604, 1716. ¹H-NMR (CDCl₃, 400MHz) δ: 2.81 (s, 3H), 6.37 (d, 1H, *J* = 3.8 Hz), 7.21-7.31 (m, 3H), 7.34-7.39 (m, 1H), 7.90-7.94 (m, 1H). ¹³C-NMR (CDCl₃, 100MHz) δ: 17.3, 115.6, 115.9, 117.6, 118.1, 118.9, 124.7, 124.9, 126.1, 133.8, 143.5, 154.3. GC-MS (70 eV): *m/z*: 199 ([M⁺], 100), 170 (87), 154 (19), 130 (14), 115 (10), 63 (9). Anal. Calcd. for C₁₂H₉NO₂ (199.21): C, 72.35; N, 7.03; H, 4.55. Found: C, 72.41; N, 6.99; H, 4.58.



Compound **7gk**. Yield 56%. White solid, m.p. = 163-166°C. IR (cm⁻¹, neat): 732, 778, 793, 979, 1039, 1107, 1352, 1415, 1487, 1516, 1712. ¹H-NMR (CDCl₃, 400MHz) δ: 2.37 (s, 3H), 2.76 (s, 3H), 6.34 (d, 1H, *J* = 3.8 Hz), 7.02 (dd, 1H, *J* = 8.5, 1.8 Hz), 7.14 (d, 1H, *J* = 0.9 Hz), 7.27 (d, 1H, *J* = 4.3 Hz), 7.77 (d, 1H, *J* = 8.5 Hz). ¹³C-NMR (CDCl₃, 100MHz) δ: 17.2, 21.0, 113.3, 115.2, 115.6, 116.2, 117.3, 119.0, 125.3, 133.5, 136.4, 143.3, 154.5. GC-MS (70 eV): *m/z*: 213 ([M⁺], 100), 184 (57), 168 (15), 154 (14), 144 (19), 116 (10), 77 (9), 39 (7). Anal. Calcd. for C₁₃H₁₁NO₂ (213.24): C, 73.23; N, 6.57; H, 5.20. Found: C, 73.29; N, 6.52; H, 5.25.



Compound **7fl**. Yield 54%. White solid, m.p. = 214-216°C. IR (cm⁻¹, neat): 729, 746, 761, 805, 867, 978, 1184, 1346, 1508, 1608, 1718. ¹H-NMR (CDCl₃, 400MHz) δ: 6.66-6.77 (m, 1H), 7.20-7.43 (m, 3H), 7.54-7.64 (m, 2H). ¹³C-NMR (CDCl₃, 100MHz) δ: 114.6, 114.7, 117.7, 118.3, 118.7, 119.7, 123.6, 126.5, 130.3, 142.0, 153.3. GC-MS (70 eV): *m/z*: 221 ([M+2⁺], 32), 219 ([M⁺], 100), 191 (20), 164 (12), 140 (15), 128 (20), 75 (8), 63 (9), 51 (8). Anal. Calcd. for C₁₁H₆NCIO₂ (219.62): C, 60.16; N, 6.38; H, 2.75. Found: C, 60.21; N, 6.33; H, 2.77.



Compound **7hk**. Yield 42%. Pale yellow solid, m.p. = 121-123°C. IR (cm⁻¹, neat): 702, 729, 768, 800, 856, 1099, 1347, 1508, 1736. ¹H-NMR (CDCl₃, 400MHz) δ: 2.32 (s, 3H), 6.54 (d, 1H, *J* = 3.8 Hz), 6.66-6.72 (m, 1H), 6.91 (d, 1H, *J* = 8.5 Hz), 7.14 (s, 1H), 7.41 (d, 1H, *J* = 3.8 Hz), 7.46-7.53 (m, 5H). ¹³C-NMR (CDCl₃, 100MHz) δ: 21.0, 116.4, 116.9, 117.6, 118.7, 118.8, 121.5, 124.9, 129.1, 129.5, 129.9, 132.7, 136.6, 136.8, 143.5, 154.9. GC-MS (70 eV): *m/z*: 276 ([M+1⁺], 20), 275 ([M⁺], 100), 230 (31), 216 (12), 115 (19), 77 (7), 51 (7). Anal. Calcd. for C₁₈H₁₃NO₂ (275.31): C, 78.53; N, 5.09; H, 4.76. Found: C, 78.59; N, 5.04; H, 4.79.