Convenient synthesis of 2-[2-Aryl-2-oxo-1-(2-indolin-3-ylidene)ethyl]fumarates via a One-Pot Two-Step Reaction

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Supporting Information

Characterization data of new compounds 2-4

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General procedure for the three-component reaction of 4-picoline, dialkyl acetylenedicarboxylate and 2-oxindolin-3-ylidene derivatives

A mixture of 4-picoline (1.2 mmol), dialkyl acetylenedicarboxylate (1.2 mmol) and 3-phenacylideneoxindole (1.0 mmol) in 10.0 mL of DME was stirred at room temperature for six hours. Then the mixture was refluxed for additional six hours. The solvent was removed by evaporation and the residue was subjected to thin-layer chromatography with a mixture of light petroleum and ethyl acetate (V/N = 3:1) as developing reagent. The product was separated from silicon gel by eluting with ethanol.

**Dimethyl 2-(1-(1-benzyl-5-fluoro-2-oxoindolin-3-ylidene)-2-oxo-2-phenylethyl)fumarate (1a)**

red solid, 0.219g, 44%, m.p. 138.6-139.3°C; ¹H NMR (600 MHz, CDCl₃) δ: major: 8.09 (d, J = 7.2Hz, 2H, ArH), 7.60 (t, J = 7.2Hz, 1H, ArH), 7.46 (t, J = 7.8Hz, 2H, ArH), 7.36-7.32 (m, 2H, ArH), 7.29-7.28 (m, 3H, ArH), 7.05 (s, 1H, CH), 6.84-6.80 (m, 1H, ArH), 6.78-6.77 (m, 1H, ArH), 6.58-6.56 (m, 1H, ArH), 4.90 (s, 2H, CH₂), 3.84 (s, 3H, OCH₃), 3.71 (s, 3H, OCH₃); minor: 8.26 (d, J = 7.2Hz, 2H, ArH), 7.68-7.67 (m, 1H, ArH), 7.55 (t, J = 7.2Hz, 2H, ArH), 6.63-6.62 (m, 1H, ArH), 3.78 (brs, 3H, OCH₃). major/minor = 7:1. ¹³C NMR (150 MHz, CDCl₃) δ: 192.6, 166.8, 165.2, 165.0, 140.3, 139.8, 136.0, 135.2, 134.1, 131.6, 130.2, 130.1, 129.8, 128.9, 128.9, 127.8, 127.3, 127.2, 117.7, 117.6, 113.8, 113.6, 109.8, 109.7, 53.0, 52.2, 43.8; IR (KBr) υ: 2951, 1727, 1671, 1599, 1485, 1453, 1344, 1249, 1176, 1018, 966, 822, 765 cm⁻¹; MS (m/z): 522.53 ([M+Na]+) (96%); HRMS (ESI) Calcd. for C₂₉H₂₂FNNaO₆ ([M+Na]+): 522.1323. Found: 522.1313.

**Dimethyl 2-(1-(1-benzyl-5-chloro-2-oxoindolin-3-ylidene)-2-(4-chlorophenyl)-2-oxoethyl)fumarate (1b)**

red solid, 0.220g, 40%, m.p. 190.2-191.0°C; ¹H NMR (600 MHz, CDCl₃) δ: major: 8.03 (d, J = 7.8Hz, 2H, ArH), 7.45 (d, J = 8.4Hz, 2H, ArH), 7.34-7.32 (m, 2H, ArH), 7.25 (s, 1H, ArH), 7.12-7.09 (m, 1H, ArH), 7.05 (s, 1H, CH), 7.01 (s, 1H, ArH), 6.60 (d, J = 8.4Hz, 1H, ArH), 4.89 (s, 2H, CH₂), 3.84 (s, 3H, OCH₃), 3.71 (s, 3H, OCH₃); minor: 8.22 (d, J = 7.8Hz, 2H, ArH), 7.53 (d, J = 8.4Hz, 2H, ArH), 7.20-7.19 (m, 2H, ArH), 6.82 (brs, 1H, ArH), 6.56 (brs, 1H, ArH), 3.78 (brs, 3H, OCH₃). Major/minor: 9:1. ¹³C NMR (150 MHz, CDCl₃) δ: 191.5, 166.5, 165.2, 165.0, 142.7, 140.7, 140.3, 139.3, 134.9, 134.5, 131.3, 131.2, 131.1, 129.3, 128.9, 127.9, 127.2, 126.3, 121.0, 110.3, 53.1, 52.2, 43.8; IR (KBr) υ: 2952, 1724, 1671, 1593, 1490, 1438, 1347, 1246, 1124, 1088, 1016, 861, 822, 765 cm⁻¹; MS (m/z): 572.52 ([M+Na]+) (100%); HRMS (ESI) Calcd. for C₂₉H₂₁Cl₂NNaO₆ ([M+Na]+): 572.0638. Found: 572.0635.

**Dimethyl 2-(1-(1-benzyl-5-methyl-2-oxoindolin-3-ylidene)-2-(4-chlorophenyl)-2-oxoethyl)fumarate (1c)**

red solid, 0.222g, 42%, m.p. 190.2-191.0°C; ¹H NMR (600 MHz, CDCl₃) δ: major: 8.07-8.06 (m, 2H, ArH), 7.43-7.42 (m, 2H, ArH), 7.31-7.27 (m, 5H, ArH), 7.05 (s, 1H, CH), 6.93-6.92 (m, 1H, ArH), 6.75 (brs, 1H, ArH), 6.56-6.54 (m, 1H, ArH), 4.88 (s, 2H, CH₂), 3.82 (s, 3H, OCH₃), 3.70 (s, 3H, OCH₃), 2.02 (s, 3H, CH₃); minor: 7.51-7.49 (m, 2H, ArH), 6.67 (brs, 1H, ArH), 3.78 (brs, 3H, OCH₃). major/minor: 7:1. ¹³C NMR (150 MHz, CDCl₃) δ: 192.2, 167.0, 165.3, 165.2, 142.2, 140.7, 140.3, 137.2, 135.5, 134.8, 132.4, 131.9, 131.8, 131.3, 129.8, 129.1, 128.8, 127.7, 127.3, 127.2, 127.0, 119.7, 109.3, 109.1, 53.0, 52.1, 43.7, 20.9; IR (KBr) υ: 2950, 2317, 1727, 1671, 1593, 1490, 1438, 1347, 1246, 1124, 1088, 1017, 961, 900, 845, 812, 765 cm⁻¹; MS (m/z): 552.68 ([M+Na]+) (61%); HRMS (ESI) Calcd. for C₃₀H₂₅Cl₂NNaO₆ ([M+Na]+): 552.1184. Found: 552.0635.
Dimethyl

2-(1-(benzyl-5-fluoro-2-oxoindolin-3-ylidene)-2-(4-chlorophenyl)-2-oxoethyl)fumarate (1d)
red solid, 0.240g, 45%, m.p. 161.2-162.5°C; ¹H NMR (600 MHz, CDCl₃) δ: major: 8.04 (d, J = 8.4Hz, 2H, ArH), 7.44 (d, J = 8.4Hz, 2H, ArH), 7.34-7.32 (m, 2H, ArH), 7.29-7.27 (m, 2H, ArH), 7.26 (brs, 1H, ArH), 7.05 (s, 1H, CH), 6.87-6.84 (m, 1H, ArH), 6.81-6.80 (m, 1H, ArH), 6.60-6.58 (m, 1H, ArH), 4.89 (s, 2H, CH₂), 3.85 (s, 3H, OCH₃), 3.71 (s, 3H, OCH₃); minor: 8.22 (d, J = 7.8Hz, 2H, ArH), 7.52 (d, J = 7.8Hz, 2H, ArH), 7.27 (brs, 1H, ArH), 6.56 (brs, 1H, ArH), 3.78 (brs, 3H, OCH₃). Major/minor = 9:1. ¹³C NMR (150 MHz, CDCl₃) δ: 191.5, 166.7, 165.2, 165.0, 159.3, 157.7, 140.7, 140.4, 140.2, 139.2, 135.1, 134.4, 131.8, 131.5, 131.2, 130.2, 130.0, 129.3, 128.9, 127.9, 127.3, 120.7, 118.0, 117.8, 113.7, 113.6, 110.0, 109.9, 53.1, 52.2, 43.8; IR (KBr) υ: 3035, 2954, 1729, 1673, 1592, 1484, 1458, 1375, 1343, 1246, 1166, 1135, 1088, 1015, 965, 884, 847, 819, 769 cm⁻¹; MS (m/z): 556.52 ([M+Na]⁺) (100%); HRMS (ESI) Calcd. for C₂₉H₂₁ClFNNaO₆ ([M+Na]⁺): 556.0934. Found: 556.0927.

Diethyl

2-(1-(benzyl-5-fluoro-2-oxoindolin-3-ylidene)-2-(4-chlorophenyl)-2-oxoethyl)fumarate (1e)
red solid, 0.252g, 45%, m.p. 141.2-142.0°C; ¹H NMR (600 MHz, CDCl₃) δ: major: 8.07 (d, J = 6.6Hz, 2H, ArH), 7.44 (d, J = 6.6Hz, 2H, ArH), 7.32-7.27 (m, 5H, ArH), 7.05 (s, 1H, CH), 6.85 (brs, 1H, ArH), 6.79 (d, J = 7.2Hz, 1H, ArH), 6.58 (brs, 1H, ArH), 4.90 (brs, 2H, CH₂), 4.30 (brs, 2H, CH₂), 4.17-4.16 (m, 2H, CH₂), 1.31 (brs, 3H, CH₃), 1.17 (brs, 3H, CH₃); minor: 8.24 (d, J = 6.0Hz, 2H, ArH), 7.51 (d, J = 6.0Hz, 2H, ArH), 7.32-7.27 (m, 2H, ArH), 1.31 (brs, 3H, CH₃). Major/minor = 9:1. ¹³C NMR (150 MHz, CDCl₃) δ: 191.5, 166.6, 164.8, 164.5, 159.3, 157.7, 140.7, 140.3, 139.2, 139.5, 135.1, 134.3, 131.5, 131.1, 130.5, 129.3, 128.9, 127.9, 127.8, 127.7, 117.7, 117.5, 113.6, 113.4, 109.9, 109.8, 62.3, 61.3, 43.8, 41.3, 13.9; IR (KBr) υ: 2983, 1712, 1671, 1589, 1486, 1457, 1374, 1339, 1246, 1168, 1136, 1088, 1023, 968, 854, 822, 768 cm⁻¹; MS (m/z): 584.54 ([M+Na]⁺) (100%); HRMS (ESI) Calcd. for C₃₁H₂₅ClFNNaO₆ ([M+Na]⁺): 584.1247. Found: 584.1242.

Diethyl 2-(1-(benzyl-5-chloro-2-oxoindolin-3-ylidene)-2-oxo-2-p-tolylethyl)fumarate (1f)
red solid, 0.223g, 40%, m.p. 157.2-158.2°C; ¹H NMR (600 MHz, CDCl₃) δ: major: 8.03 (d, J = 7.2Hz, 2H, ArH), 7.32-7.31 (m, 7H, ArH), 7.06 (brs, 2H, ArH), 6.92 (brs, 1H, CH), 6.58-6.56 (m, 1H, ArH), 4.90 (s, 2H, CH₂), 4.30-4.29 (m, 2H, CH₂), 4.16 (d, J = 6.6Hz, 2H, CH₂), 2.44-2.42 (m, 3H, CH₃), 1.29 (brs, 3H, CH₃), 1.16 (brs, 3H, CH₃); minor: 8.16-8.15 (m, 2H, ArH), 7.32-7.31 (m, 1H, ArH), 6.58-5.56 (m, 1H, ArH), 6.86 (brs, 1H, ArH), 1.29 (brs, 3H, CH₃). Major/minor = 7:1. ¹³C NMR (150 MHz, CDCl₃) δ: 192.2, 166.5, 164.9, 164.4, 145.4, 142.5, 140.6, 139.9, 135.2, 133.4, 130.6, 130.5, 130.3, 130.2, 130.1, 129.7, 128.9, 127.8, 127.7, 127.3, 127.2, 126.1, 121.3, 110.1, 62.2, 61.2, 43.7, 21.8, 14.1, 13.9; IR (KBr) υ: 3066, 3031, 2982, 2933, 2926, 1626, 1604, 1474, 1443, 1372, 1338, 1243, 1178, 1144, 1119, 1089, 1025, 960, 896, 865, 828, 773 cm⁻¹; MS (m/z): 580.53 ([M+Na]⁺) (100%); HRMS (ESI) Calcd. for C₃₂H₂₉ClFNNaO₆ ([M+Na]⁺): 580.1497. Found: 580.1489.

Diethyl 2-(1-(benzyl-5-methyl-2-oxoindolin-3-ylidene)-2-(4-chlorophenyl)-2-oxoethyl)fumarate (1g)
red solid, 0.289g, 52%, m.p. 144.2-145.2°C; ¹H NMR (600 MHz, CDCl₃) δ: major: 8.08 (d, J = 7.8Hz, 2H, ArH), 7.43-7.41 (d, J = 7.8Hz, 2H, ArH), 7.31-7.30 (m, 5H, ArH), 7.05 (s, 1H, CH), 6.92 (d, J = 7.2Hz, 1H, ArH), 6.75 (s, 1H, ArH), 6.55-6.54 (m, 1H, ArH), 4.88 (s, 2H, CH₂), 4.29
(brs, 2H, CH₂), 4.15 (d, \( J = 6.0\text{Hz}, 2\text{H}, \text{CH}_2 \)), 2.02 (s, 3H, CH₃), 1.29 (brs, 3H, CH₃), 1.16 (brs, 3H, CH₃); minor: 8.25-8.23 (m, 2H, ArH), 7.50-7.49 (m, 2H, ArH), 6.66 (brs, 1H, ArH), 1.29 (brs, 3H, CH₃). Major/minor = 10:1.

\(^{13}\text{C\ NMR\ (150 MHz, CDCl}_3\) δ: 192.2, 166.8, 165.0, 164.6, 142.1, 140.6, 140.3, 137.5, 135.6, 134.7, 132.1, 131.7, 131.6, 131.4, 130.2, 128.8, 127.7, 127.3, 127.2, 119.8, 109.0, 62.1, 61.1, 43.7, 20.9, 14.1, 13.9; IR (KBr) ν: 2982, 2349, 1726, 1672, 1588, 1539, 1488, 1454, 1369, 1344, 1248, 1129, 1092, 1031, 964, 817 cm⁻¹; MS (m/z): 580.56 ([M+Na⁺]⁺ (100%); HRMS (ESI) Calcd. for C\(_{32}\)H\(_{28}\)ClNNaO\(_6\) ([M+Na⁺]): 580.1497. Found: 580.1489.

3-Ethyl 1,2-dimethyl 3-(1-benzyl-5-chloro-2-oxoindolin-3-ylidene)prop-1-ene-1,2,3-tricarboxylate (1h)
red solid, 0.362g, 75%, m.p. 153.2-154.4°C; \(^1\text{H\ NMR\ (600 MHz, CDCl}_3\) δ: 8.54 (s, 1H, ArH), 7.29-7.26 (m, 3H, ArH), 7.20 (brs, 3H, ArH) , 7.07 (s, 1H, CH), 6.60 (d, \( J = 7.8\text{Hz}, 1\text{H}, \text{ArH} \)), 4.86-4.84 (m, 2H, CH₂), 4.40 (brs, 1H, CH), 4.30 (brs, 1H, CH), 3.79 (s, 3H, OCH₃), 3.72 (s, 3H, OCH₃), 1.30 (t, \( J = 6.0\text{Hz}, 3\text{H}, \text{CH}_3 \)); \(^{13}\text{C\ NMR\ (150 MHz, CDCl}_3\) δ: 167.0, 165.7, 164.7, 164.3, 143.6, 143.1, 135.0, 134.6, 132.2, 131.4, 128.8, 128.2, 127.8, 127.1, 121.0, 62.0, 52.9, 52.1, 43.7; IR (KBr) ν: 2987, 2949, 1720, 1643, 1603, 1469, 1437, 1341, 1245, 1175, 1139, 1086, 1030, 886, 782 cm⁻¹; MS (m/z): 506.43 ([M+Na⁺]⁺ (100%); HRMS (ESI) Calcd. for C\(_{25}\)H\(_{22}\)ClNNaO\(_7\) ([M+Na⁺]): 506.0977. Found: 506.0972.

3-Ethyl 1,2-dimethyl 3-(1-benzyl-5-fluoro-2-oxoindolin-3-ylidene)prop-1-ene-1,2,3-tricarboxylate (1i)
orange solid, 0.373g, 80%, m.p. 132.4-133.1°C; \(^1\text{H\ NMR\ (600 MHz, CDCl}_3\) δ: 8.33 (dd, \( J_1 = 6.0\text{Hz}, \ J_2 = 2.4\text{Hz}, 1\text{H}, \text{ArH} \)), 7.31-7.29 (m, 4H, ArH), 7.26 (s, 1H, ArH), 6.95 (td, \( J_1 = 0.6\text{Hz}, \ J_2 = 1.8\text{Hz}, 1\text{H}, \text{ArH} \)), 6.59-6.57 (m, 1H, ArH), 4.89-4.81 (m, 2H, CH₂), 4.38-4.37 (m, 1H, CH), 4.30-4.29 (m, 1H, CH), 3.80 (s, 3H, OCH₃), 3.72 (s, 3H, OCH₃), 1.29 (t, \( J = 7.2\text{Hz}, 3\text{H}, \text{CH}_3 \)); \(^{13}\text{C\ NMR\ (150 MHz, CDCl}_3\) δ: 167.2, 165.7, 164.7, 164.3, 143.7, 140.8, 135.1, 134.4, 132.8, 128.8, 127.8, 127.7, 127.1, 121.0, 120.9, 118.2, 118.0, 116.4, 116.2, 109.4, 109.3, 62.0, 52.9, 52.1, 43.7, 13.9; IR (KBr) ν: 3126, 2951, 1723, 1643, 1614, 1476, 1342, 1274, 1248, 1217, 1179, 1152, 1104, 1022, 935, 892, 837, 809, 753 cm⁻¹; MS (m/z): 490.48 ([M+Na⁺]⁺ (93%); HRMS (ESI) Calcd. for C\(_{25}\)H\(_{22}\)FNNaO\(_7\) ([M+Na⁺]): 490.1273. Found: 490.1274.

3-Ethyl 1,2-dimethyl 3-(1-butyl-5-chloro-2-oxoindolin-3-ylidene)prop-1-ene-1,2,3-tricarboxylate (1j)
orange solid, 0.368g, 82%, m.p. 142.5-143.4°C; \(^1\text{H\ NMR\ (600 MHz, CDCl}_3\) δ: 8.54 (s, 1H, ArH), 7.32 (d, \( J = 7.8\text{Hz}, 1\text{H}, \text{ArH} \)), 7.03 (s, 1H, CH), 6.72 (d, \( J = 8.4\text{Hz}, 1\text{H}, \text{ArH} \)), 4.38 (brs, 1H, CH), 4.28 (brs, 1H, CH), 3.78 (s, 3H, OCH₃), 3.70 (s, 3H, OCH₃), 3.63 (d, \( J = 6.6\text{Hz}, 2\text{H}, \text{CH}_2 \)), 1.58-1.57 (m, 2H, CH₂), 1.34-1.31 (m, 2H, CH₂), 1.29 (t, \( J = 7.2\text{Hz}, 3\text{H}, \text{CH}_3 \)); \(^{13}\text{C\ NMR\ (150 MHz, CDCl}_3\) δ: 166.7, 165.6, 164.7, 164.3, 143.8, 143.5, 134.1, 132.4, 131.4, 128.8, 127.8, 127.4, 121.2, 109.1, 61.9, 52.8, 52.1, 39.8, 29.3, 20.0, 13.9, 13.7; IR (KBr) ν: 3129, 2951, 1725, 1643, 1602, 1465, 1437, 1347, 1239, 1172, 1139, 1109, 1075, 1016, 930, 884, 828, 778, 751 cm⁻¹; MS (m/z): 472.40 ([M+Na⁺]⁺ (100%); HRMS (ESI) Calcd. for C\(_{22}\)H\(_{24}\)ClNNaO\(_7\) ([M+Na⁺]): 472.1134. Found: 472.1135.
Dimethyl 2-(1-(1-benzyl-5-fluoro-2-oxoindolin-3-ylidene)-2-oxo-2-phenylethyl)fumarate (1a):
Dimethyl 2-(1-(1-benzyl-5-fluoro-2-oxoindolin-3-ylidene)-2-oxo-2-phenylethyl)fumarate (1b):
Dimethyl 2-(1-(1-benzyl-5-methyl-2-oxoindolin-3-ylidene)-2-(4-chlorophenyl)-2-oxoethyl)fumarate (1c):
Dimethyl 2-(1-(1-benzyl-5-fluoro-2-oxoindolin-3-ylidene)-2-(4-chlorophenyl)-2-oxoethyl)fumarate (1d):
Diethyl 2-(1-(1-benzyl-5-fluoro-2-oxoindolin-3-ylidene)-2-(4-chlorophenyl)-2-oxoethyl)fumarate (1e):
Diethyl 2-(1-(1-benzyl-5-chloro-2-oxoindolin-3-ylidene)-2-oxo-2-p-tolylethyl)fumarate (1f):
Diethyl 2-(1-(1-benzyl-5-methyl-2-oxoindolin-3-ylidene)-2-(4-chlorophenyl)-2-oxoethyl)fumarate (1g):
3-Ethyl 1,2-dimethyl 3-(1-benzyl-5-chloro-2-oxoindolin-3-ylidene)prop-1-ene-1,2,3-tricarboxylate (1h):
3-Ethyl 1,2-dimethyl 3-(1-benzyl-5-fluoro-2-oxoindolin-3-ylidene)prop-1-ene-1,2,3-tricarboxylate (1i):
3-Ethyl 1,2-dimethyl 3-(1-butyl-5-chloro-2-oxoindolin-3-ylidene)prop-1-ene-1,2,3-tricarboxylate (1j):