



Supporting Information

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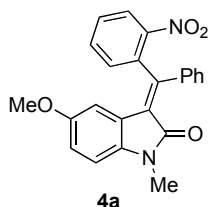
69451 Weinheim, Germany

Palladium-Catalyzed Three-component Synthesis of 3-(Diarylmethylenyl)oxindole by a Domino Sonagashira/Carbopalladation/C-H Activation/C-C bond Forming Process

Artur Pinto, Luc Neuville, Jieping Zhu*

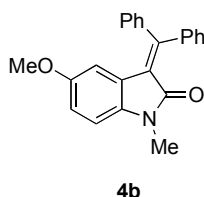
Institut de Chimie des Substances Naturelles, CNRS, 91198 Gif-sur-Yvette Cedex, France

General procedure for the palladium-catalyzed three components reaction :
Synthesis of (3E)-5-methoxy-1-methyl-3-[(2-nitrophenyl)(phenyl)methylene]-1,3-dihydro-2H-indol-2-one (4a). A mixture of anilide **1a** (50 mg, 0.27 mmol), and phenyl iodide **2a** (27 μ L, 0.24 mmol) in DMF was purged under an Argon flow for 30 min. After CuI (1mg, 0.0055 mmol), NaOAc (54mg, 0.66 mmol) and Pd(Ph₃)₄ (12.7 mg, 0,011 mmol) was added. The mixture was heated at 60°C for 1 hour and iodo-2-nitrobenzene **3a** (66 mg, 0.27 mmol) was introduced and the reaction was further heated at 110°C for 28 hours. After cooling the mixture, saturated NaCl was added. The mixture was then extracted with EtOAc. The organic layers were then combined, washed with brine, dried (Na₂SO₄) and concentrated. The residue was purified by flash chromatography column (2:1 heptanes-EtOAc) to give **4a** (72 mg, 77 %)

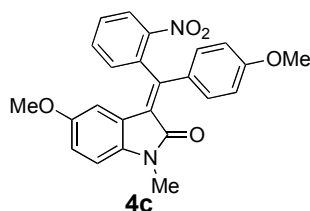


Red solid: mp 197-200°C; ¹H NMR (300 MHz, CDCl₃) δ 8.19 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.77 (dt, *J* = 7.5, 1.1 Hz, 1H), 7.65 (dt, *J* = 8.2, 1.5 Hz, 1H), 7.55 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.44-7.39 (m, 2H), 7.36-7.31 (m, 3H), 6.73 (dd, *J* = 8.5, 2.4 Hz, 1H), 6.65 (d, *J* = 8.5 Hz, 1H), 5.60 (d, *J* = 2.4 Hz, 1H), 3.48 (s, 3H), 3.17 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 166.0, 155.0, 149.4, 147.5, 137.6, 136.4, 136.2, 134.3, 131.3, 130.2, 129.9, 129.5, 127.6, 125.6, 125.0,

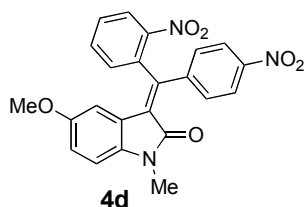
123.4, 114.1, 110.0, 108.17, 55.5, 25.9. IR (CH₂Cl₂) ν 1697, 1524, 1493, 1345 cm⁻¹. HRMS for C₂₃H₁₈N₂O₄Na [M+Na]⁺ calcd 409.1164, found 409.1182.



3-(diphenylmethylene)-5-methoxy-1-methyl-1,3-dihydro-2H-indol-2-one (4b): Red solid; mp 135-137°C. ¹H NMR (300 MHz, CDCl₃) δ 7.49-7.43 (m, 3H), 7.40-7.32 (m, 7H), 6.74 (dd, J = 8.5, 2.5 Hz, 1H), 6.66 (d, J = 8.46 Hz, 1H), 6.00 (d, J = 2.5 Hz, 1H), 3.47 (s, 3H), 3.18 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 166.7, 154.8, 154.7, 141.2, 139.7, 137.4, 130.0, 129.3, 129.2, 129.1, 129.0, 127.8, 124.7, 124.0, 114.4, 109.5, 108.0, 55.4, 25.9. IR (CH₂Cl₂) ν 1695, 1493, 1286, 698 cm⁻¹. HRMS for C₂₃H₁₉NO₂Na [M+Na]⁺ calcd 364.1313, found 364.1349.

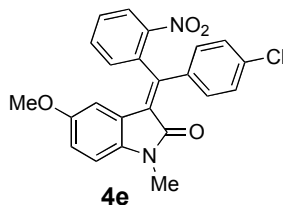


(3E)-5-methoxy-1-methyl-3-[(4-methoxyphenyl)(2-nitrophenyl)methylene]-1,3-dihydro-2H-indol-2-one (4c): orange solid; yield 82%; mp 204-206°C; ¹H NMR (300 MHz, CDCl₃) δ 8.19 (dd, J = 8.1, 0.9 Hz, 1H), 7.75 (dt, J = 7.5, 0.9 Hz, 1H), 7.65 (dt, J = 8.1, 1.3 Hz, 1H), 7.53 (dd, J = 7.5, 1.3 Hz, 1H), 7.36 (d, J = 8.8 Hz, 2H), 6.83 (d, J = 8.8 Hz, 2H), 6.71 (dd, J = 8.5, 2.3 Hz, 1H), 6.65 (d, J = 8.5 Hz, 1H), 5.57 (d, J = 2.3 Hz, 1H), 3.80 (s, 3H), 3.46 (s, 3H), 3.19 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 166.2, 160.9, 154.9, 149.6, 147.9, 137.3, 136.7, 134.1, 132.4, 131.5, 130.0, 128.3, 125.5, 123.9, 123.8, 113.7, 113.0, 109.8, 108.1, 55.5, 55.2, 21.1. IR (CH₂Cl₂) ν 1693, 1505, 1344, 1245 cm⁻¹. HRMS for C₂₄H₂₀N₂O₅Na [M+Na]⁺ calcd 409.1270, found 409.1243.

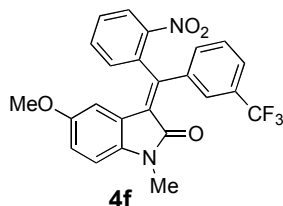


(3E)-5-methoxy-1-methyl-3-[(2-nitrophenyl)(4-nitrophenyl)methylene]-1,3-dihydro-2H-indol-2-one (4d): red solid; yield 71%; mp 215-218°C; ¹H NMR (300 MHz, CDCl₃) δ 8.27 (d, J = 8.1 Hz, 2H), 8.18 (dd, J = 8.4, 0.8 Hz, 1H), 7.85 (dt, J = 7.5, 0.8 Hz, 1H), 7.73 (dt, J = 8.4, 1.1 Hz, 1H), 7.64-7.54 (m, 3H), 6.77 (dd, J = 8.5, 2.4 Hz, 1H), 6.68 (d,

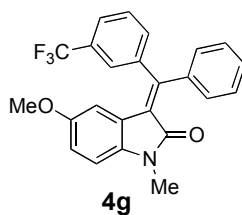
$J = 8.5$ Hz, 1H), 5.59 (d, $J = 2.4$ Hz, 1H), 3.49 (s, 3H), 3.16 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 165.6, 155.2, 147.9, 147.2, 145.7, 143.0, 138.0, 135.0, 134.8, 131.3, 131.1, 130.6, 126.7, 125.9, 122.9, 122.6, 115.0, 110.4, 108.6, 55.5, 26.0. IR (CH_2Cl_2) ν 1699, 1511, 1341, 700 cm^{-1} . HRMS for $\text{C}_{23}\text{H}_{17}\text{N}_3\text{O}_6\text{Na}$ $[\text{M}+\text{Na}]^+$ calcd 454.1015, found 454.1044.



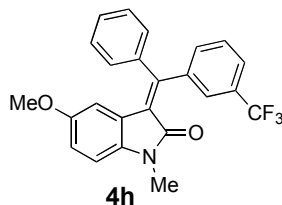
(3E)-3-[(4-chlorophenyl)(2-nitrophenyl)methylene]-5-methoxy-1-methyl-1,3-dihydro-2H-indol-2-one (4e): orange solid; yield 76%; mp 176-178°C; ^1H NMR (300 MHz, CDCl_3) δ 8.24 (dd, $J = 8.1, 0.8$ Hz, 1H), 7.82 (dt, $J = 7.4, 0.8$ Hz, 1H), 7.77-7.64 (m, 2H), 7.63-7.54 (m, 3H), 7.47 (t, $J = 8.0$ Hz, 1H), 7.30 (d, $J = 8.6$ Hz, 2H), 6.75 (dd, $J = 8.5, 2.3$ Hz, 1H), 6.67 (d, $J = 8.5$ Hz, 1H), 5.57 (d, $J = 2.3$ Hz, 1H), 3.49 (s, 3H), 3.18 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 165.9, 155.1, 147.8, 147.5, 137.6, 135.9, 135.6, 134.6, 134.5, 131.7, 131.3, 130.2, 127.9, 125.7, 125.3, 123.2, 114.3, 110.1, 108.3, 55.5, 26.0. IR (CH_2Cl_2) ν 1698, 1513, 1343, 805 cm^{-1} . HRMS for $\text{C}_{23}\text{H}_{17}\text{N}_2\text{O}_4\text{NaCl}$ $[\text{M}+\text{Na}]^+$ calcd 443.0775, found 443.0781.



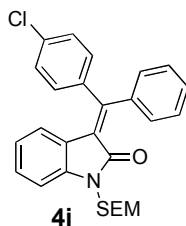
(3E)-5-methoxy-1-methyl-3-[(2-nitrophenyl)[3-(trifluoromethyl)phenyl]methylene]-1,3-dihydro-2H-indol-2-one (4f): orange solid; yield 76%; mp 213-215°C; ^1H NMR (300 MHz, CDCl_3) δ 8.27 (dd, $J = 8.1, 0.7$ Hz, 1H), 7.75 (dt, $J = 7.5, 0.7$ Hz, 1H), 7.65 (dt, $J = 8.1, 1.1$ Hz, 1H), 7.53 (dd, $J = 7.5, 1.1$ Hz, 1H), 7.38 (d, $J = 8.6$ Hz, 2H), 7.30 (d, $J = 8.6$ Hz, 2H), 6.75 (dd, $J = 8.5, 2.3$ Hz, 1H), 6.67 (d, $J = 8.5$ Hz, 1H), 5.60 (d, $J = 2.3$ Hz, 1H), 3.49 (s, 3H), 3.18 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 165.7, 155.1, 147.2, 147.0, 137.8, 137.0, 135.5, 134.7, 134.2, 131.3, 130.3, 129.8, 128.0, 126.4, 126.3, 126.0, 125.9, 125.8, 122.9, 114.6, 110.2, 108.4, 55.5, 26.0. IR (CH_2Cl_2) ν 1698, 1526, 1348, 1328, 1107, 1057, 662 cm^{-1} . HRMS for $\text{C}_{24}\text{H}_{17}\text{N}_2\text{O}_4\text{F}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ calcd 477.1038, found 477.1074.



(3E)-5-methoxy-1-methyl-3-{phenyl[3-(trifluoromethyl)phenyl]methylene}-1,3-dihydro-2H-indol-2-one (4g): orange solid; yield 66%; mp 106-109°C; ^1H NMR (300 MHz, CDCl_3) δ 7.73 (d, J = 7.6 Hz, 1H), 7.66 (s, 1H), 7.60 (t, J = 7.6 Hz, 1H), 7.54 (d, J = 7.6 Hz, 1H), 7.42-7.31 (m, 5H), 6.77 (dd, J = 8.5, 2.4 Hz, 1H), 6.68 (d, J = 8.5 Hz, 1H), 5.90 (d, J = 2.4 Hz, 1H), 3.45 (s, 3H), 3.18 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 166.3, 154.9, 152.1, 141.9, 139.0, 137.7, 132.9, 130.0, 129.7, 129.4, 128.0, 126.2, 126.1, 125.8, 125.8, 125.7, 123.3, 115.4, 109.2, 108.3, 55.4, 26.0. IR (CH_2Cl_2) ν 1696, 1334, 1103, 817, 695 cm^{-1} . HRMS for $\text{C}_{24}\text{H}_{18}\text{NO}_2\text{F}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ calcd 432.1187, found 432.1205.

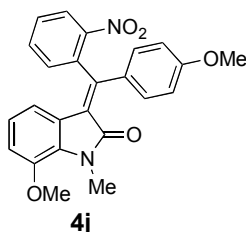


(3Z)-5-methoxy-1-methyl-3-{phenyl[3-(trifluoromethyl)phenyl]methylene}-1,3-dihydro-2H-indol-2-one (4h): red oil; yield 43%; ^1H NMR (300 MHz, CDCl_3) δ 7.65-7.57 (m, 2H), 7.55 (s, 1H), 7.52-7.45 (m, 4H), 7.36-7.31 (m, 2H), 6.76 (dd, J = 8.5, 2.5 Hz, 1H), 6.67 (d, J = 8.5 Hz, 1H), 6.01 (d, J = 2.5 Hz, 1H), 3.47 (s, 3H), 3.17 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 166.4, 154.9, 152.9, 140.4, 137.6, 133.4, 130.5, 130.1, 129.5, 129.2, 129.2, 128.2, 126.7, 126.6, 125.6, 125.6, 123.5, 114.9, 109.8, 108.1, 55.4, 26.0. IR (CH_2Cl_2) ν 1695, 1331, 1104, 1121, 697 cm^{-1} . HRMS for $\text{C}_{24}\text{H}_{18}\text{NO}_2\text{F}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ calcd 432.1187, found 432.1199.

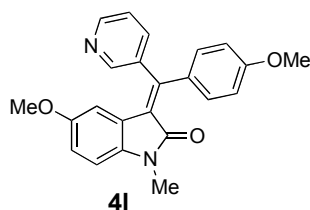


1-(2-Dimethylsilanyl-ethoxymethyl)-5-methoxy-3-[1-(4-chlorophenyl)-1-phenyl-meth-(E)-ylidene]-1,3-dihydro-indol-2-one (4i): orange oil; yield 59%; ^1H NMR (300 MHz, CDCl_3) δ 7.46-7.28 (m, 9H), 7.23 (t, J = 7.7 Hz, 1H), 7.05 (d, J = 7.7 Hz, 1H), 6.79 (t, 7.7 Hz, 1H), 6.58 (d, J = 7.7 Hz, 1H), 5.19 (s, 1H), 3.60 (t, J = 8.2 Hz, 1H), 0.94 (t, J = 8.2 Hz, 1H), 0.00 (s, 9H). ^{13}C NMR (75 MHz, CDCl_3) δ 168.2, 154.9, 143.4, 141.0, 140.9, 136.9, 132.4, 131.6, 131.5, 130.8, 130.7, 130.6, 129.3, 124.4, 124.2, 123.3, 110.9, 70.8, 67.5, 19.3, 0.02.

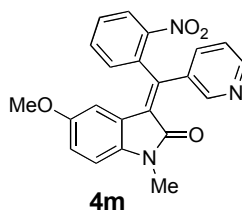
IR (CH₂Cl₂) ν 1705, 1468, 1339, 1245, 1073, 829 cm⁻¹. HRMS for C₂₇H₂₈NO₂NaSiCl [M+Na]⁺ calcd 484.1476, found 484.1462.



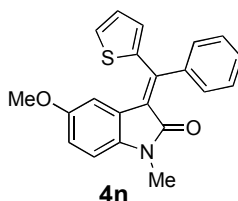
(3E)-7-methoxy-1-methyl-3-[(2-nitrophenyl)(4-methoxyphenyl)methylene]-1,3-dihydro-2H-indol-2-one (4j): orange solid; yield 67%; mp 199-202°C; ¹H NMR (300 MHz, CDCl₃) δ 8.17 (d, J = 8.0 Hz, 1H), 7.73 (t, J = 7.5 Hz, 1H), 7.65 (t, J = 8.0 Hz, 1H), 7.52 (d, 7.5 Hz, 1H), 7.34 (dd, J = 8.8, 1.9 Hz, 1H), 6.84 (dd, J = 8.8, 1.9 Hz, 1H), 6.75 (d, J = 7.6 Hz, 1H), 6.58 (t, J = 7.6 Hz, 1H), 5.68 (d, J = 7.6 Hz, 1H), 3.84 (s, 3H), 3.81 (s, 3H), 3.52 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 166.5, 160.9, 149.6, 148.0, 145.2, 137.0, 134.0, 132.4, 131.6, 131.6, 129.8, 128.6, 125.5, 124.5, 123.8, 121.8, 115.8, 113.0, 112.9, 56.1, 55.2, 29.1. IR (CH₂Cl₂) ν 1694, 1522, 1330, 1241, 1069, 794, 724 cm⁻¹. HRMS for C₂₄H₂₀N₂O₅Na [M+Na]⁺ calcd 439.1270, found 439.1255.



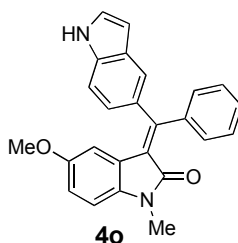
(3E)-5-methoxy-3-[(4-methoxyphenyl)(pyridin-3-yl)methylene]-1-methyl-1,3-dihydro-2H-indol-2-one (4l): red solid; yield 69%; mp 146-149°C; ¹H NMR (300 MHz, CDCl₃) δ 8.70 (dd, J = 4.8, 1.8 Hz, 1H), 8.59 (d, J = 1.8 Hz, 1H), 7.62 (td, J = 7.8, 1.8 Hz, 1H), 7.39 (dd, J = 7.8, 4.8 Hz, 1H), 7.29 (d, J = 8.8 Hz, 2H), 6.88 (d, J = 8.8 Hz, 2H), 6.72 (dd, J = 8.5, 2.4 Hz, 1H), 6.66 (d, J = 8.5 Hz, 1H), 5.87 (d, J = 2.4 Hz, 1H), 3.83 (s, 3H), 3.47 (s, 3H), 3.18 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 166.4, 161.1, 154.8, 150.5, 150.4, 150.2, 137.5, 137.3, 137.3, 132.6, 130.9, 124.8, 124.0, 123.7, 114.3, 113.3, 109.3, 108.2, 55.5, 55.3, 26.0. IR (CH₂Cl₂) ν 1689, 1493, 1281, 1028, 802 cm⁻¹. HRMS for C₂₃H₂₁N₂O₃ [M+H]⁺ calcd 373.1552, found 373.1537.



(3Z)-5-methoxy-1-methyl-3-[(2-nitrophenyl)(pyridin-3-yl)methylene]-1,3-dihydro-2H-indol-2-one (4m): red solid; yield 81%; mp 215-217°C; ^1H NMR (300 MHz, CDCl_3) δ 8.54 (m, 2H), 8.26 (dd, $J = 8.2, 1.1$ Hz, 1H), 7.88 (td, $J = 7.9, 1.8$ Hz, 1H), 7.82 (dt, $J = 7.5, 1.1$ Hz, 1H), 7.70 (dt, $J = 8.2, 1.4$ Hz, 1H), 7.56 (dd, $J = 7.5, 1.4$ Hz, 1H), 7.27 (dd, $J = 7.9, 5.0$ Hz, 1H), 6.74 (dd, $J = 8.5, 2.4$ Hz, 1H), 6.66 (d, $J = 8.5$ Hz, 1H), 5.56 (d, $J = 2.4$ Hz, 1H), 3.46 (s, 3H), 3.15 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 165.8, 155.1, 150.1, 150.0, 147.2, 145.2, 138.2, 137.8, 135.4, 134.7, 132.5, 131.3, 130.4, 126.1, 125.9, 122.8, 122.4, 114.7, 110.2, 108.4, 55.5, 26.0. IR (CH_2Cl_2) ν 1682, 1522, 1343, 703 cm^{-1} . HRMS for $\text{C}_{22}\text{H}_{18}\text{N}_3\text{O}_4$ $[\text{M}+\text{H}]^+$ calcd 388.1297, found 388.1325.

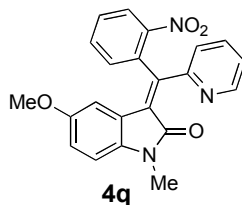


(3E)-5-methoxy-1-methyl-3-[phenyl(2-thienyl)methylene]-1,3-dihydro-2H-indol-2-one (4n): red solid; yield 61%; mp 120-123; ^1H NMR (300 MHz, CDCl_3) δ 7.61 (dd, $J = 3.9, 1.2$ Hz, 1H), 7.55 (dd, $J = 5.0, 1.2$ Hz, 1H), 7.52 (m, 3H), 7.36 (m, 2H), 7.06 (dd, $J = 5.0, 3.9$ Hz, 1H), 6.69 (dd, $J = 8.5, 2.4$ Hz, 1H), 6.63 (d, $J = 8.5$ Hz, 1H), 5.36 (d, $J = 2.4$ Hz, 1H), 3.39 (s, 3H), 3.26 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 166.6, 154.7, 146.0, 141.6, 141.3, 136.7, 135.0, 131.7, 129.3, 129.2, 129.1, 126.7, 124.5, 122.4, 114.2, 109.7, 107.7, 55.3, 26.0. IR (CH_2Cl_2) ν 1667, 1554, 1056, 1030, 728 cm^{-1} . HRMS for $\text{C}_{21}\text{H}_{16}\text{NO}_2\text{S}$ $[\text{M}+\text{H}]^+$ calcd 348.1058, found 348.1081.

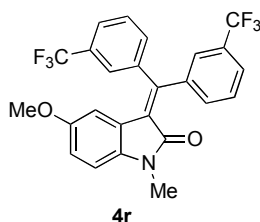


(3E)-3-[1H-indol-6-yl(phenyl)methylene]-5-methoxy-1-methyl-1,3-dihydro-2H-indol-2-one (4o): orange solid; yield 45%; mp 226-228°C; ^1H NMR (300 MHz, CDCl_3) δ 8.55 (br, 1H), 7.60, (s, 1H), 7.40-7.35 (m, 6H), 7.20 (dd, $J = 3.0, 2.7$ Hz, 1H), 7.16 (dd, $J = 8.4, 1.6$ Hz, 1H), 6.72 (dd, $J = 8.5, 2.4$ Hz, 1H), 6.66 (d, $J = 8.5$ Hz, 1H), 6.52 (ddd, $J = 3.0, 1.9,$

0.8 Hz, 1H), 6.16 (d, $J = 2.4$ Hz, 1H), 3.34 (s, 3H), 3.21 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 167.2, 157.3, 154.7, 140.9, 137.1, 136.5, 132.5, 130.5, 129.1, 128.1, 127.7, 125.3, 124.8, 124.0, 123.7, 123.0, 113.8, 111.4, 109.4, 107.7, 103.2, 55.4, 26.0. IR (CH_2Cl_2) ν 1672, 1494, 1101, 748.4, 658.6 cm^{-1} . HRMS for $\text{C}_{25}\text{H}_{20}\text{N}_2\text{O}_2\text{Na}$ $[\text{M}+\text{Na}]^+$ calcd 403.1422, found 403.1440.



(3Z)-5-methoxy-1-methyl-3-[(2-nitrophenyl)(pyridin-2-yl)methylene]-1,3-dihydro-2H-indol-2-one (4q): orange solid; yield 51%; mp ; ^1H NMR (300 MHz, CDCl_3) δ 8.54 (ddd, $J = 4.9, 1.9, 1.0$ Hz, 1H), 8.24 (dd, $J = 8.2, 1.1$ Hz, 1H), 7.95 (ddd, $J = 7.9, 1.0, 1.0$ Hz, 1H), 7.82 (dt, $J = 7.7, 1.1$ Hz, 1H), 7.79-7.62 (m, 3H), 7.22 (ddd, $J = 7.9, 4.9, 1.0$ Hz), 6.74 (dd, $J = 8.5, 2.5$ Hz, 1H), 6.66 (d, $J = 8.5$ Hz, 1H), 5.60 (d, $J = 2.5$ Hz, 1H), 3.47 (s, 3H), 3.16 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 165.9, 155.1, 154.9, 154.9, 149.0, 137.9, 135.1, 135.1, 134.5, 134.0, 132.3, 129.7, 127.9, 127.3, 125.0, 123.2, 123.0, 114.7, 110.2, 108.3, 55.5, 25.9. IR (CH_2Cl_2) ν 1700, 1522, 1490, 1342, 668 cm^{-1} . HRMS for $\text{C}_{22}\text{H}_{17}\text{N}_3\text{O}_4\text{Na}$ $[\text{M}+\text{Na}]^+$ calcd 410.1117, found 410.1118.



3-[Bis-(3-trifluoromethyl-phenyl)-methylene]-5-methoxy-1-methyl-1,3-dihydro-2H-indol-2-one (4r): red oil; yield 57%. ^1H NMR (300 MHz, CDCl_3) δ 7.75 (d, $J = 7.7$ Hz, 1H), 7.69-7.50 (m, 7H), 6.79 (dd, $J = 8.5, 2.5$ Hz, 1H), 6.70 (d, $J = 8.5$ Hz, 1H), 5.91 (d, $J = 2.5$ Hz, 1H), 3.46 (s, 3H), 3.18 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 166.1, 155.0, 149.5, 141.1, 139.7, 137.9, 133.3, 133.3, 132.8, 129.9, 128.5, 126.8, 126.6, 126.5, 126.2, 126.1, 126.1, 126.0, 125.9, 122.8, 115.9, 109.4, 108.6, 55.8, 26.0. IR (CH_2Cl_2) ν 1695, 1328, 1166, 1116, 1072, 700 cm^{-1} . HRMS for $\text{C}_{25}\text{H}_{17}\text{NO}_2\text{F}_6\text{Na}$ $[\text{M}+\text{Na}]^+$ calcd 500.1061, found 500.1043.

