5-Bromo-norborn-2-en-7-one Derivatives as a Carbon Monoxide Source for Palladium Catalyzed Carbonylation Reactions

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Two-chamber glassware

Chamber A = CO generation chamber
Chamber B = Carbonylation reaction chamber

Conversion of starting material to Carbonylated product

Figure SI1: ^1^H NMR spectrum (400 MHz, CDCl$_3$) of the aromatic region for the crude reaction mixture of 8a with that of iodoanisole (Entry 1, Table 1).
**2,5-Dimethyl-3,4-diphenylcyclopentadien-1-one** (diene dimer) (3)

Benzil (10.0 g, 47.6 mmol) and pentan-3-one (7.59 mL, 71.4 mmol) in isopropanol (150 mL) were combined with KOH (3.47 g, 61.8 mmol) in isopropanol (100 mL) and the reaction mixture was stirred for 3 h at rt. Isopropanol was removed under reduced pressure, the residue was acidified with aqueous 5% HCl and extracted into EtOAc. The organic layer was washed with water and brine, and dried over anhydrous MgSO$_4$. The filtrate was concentrated under reduced pressure. The residue was cooled to 0 °C, acetic anhydride (16 mL) and conc. H$_2$SO$_4$ (1.0 mL) were slowly added and the mixture stirred at rt o/n. The solution was added to cold water (100 mL) with stirring. The precipitate was collected, washed with H$_2$O, and dried under vacuum to afford the title compound 3 (8.98 g, 73%) as a white powder.

1H NMR (400 MHz, CDCl$_3$) $\delta$ 0.58 (s, 3H), 1.25 (s, 3H), 1.64 (s, 3H), 2.25 (s, 3H), 6.70 (m, 2H), 6.89 - 7.00 (m, 8H), 7.04 - 7.12 (m, 5H), 7.20 - 7.29 (m, 5H); 13C NMR (101 MHz, CDCl$_3$) $\delta$ 10.0, 12.5, 12.6, 18.2, 58.6, 59.9, 61.2, 66.9, 127.00, 127.04, 127.2, 127.36, 127.43, 128.0, 129.0, 129.4, 130.3, 131.0, 132.0, 133.6, 134.1, 134.2, 140.2, 143.0, 143.3, 144.5, 166.0, 203.3, 209.6; HRMS-ESI m/z [M+Na]$^+$ calc. for C$_{38}$H$_{32}$O$_2$Na$: 543.2295, found: 543.2278.

**N-Phenyl-3-bromomaleimide** (4a)

A solution of N-phenylmaleimide (6.80 g, 39.3 mmol) in CCl$_4$ (60 ml) was added slowly to a solution of bromine (2.50 ml, 48.5 mmol) in CCl$_4$ (40 ml) at room temperature. The reaction mixture was refluxed for 1 hour, and then cooled to room temperature. The precipitate was filtered and washed with CCl$_4$ (ca. 20 ml) to give 2,3-dibromo-N-phenylmaleimide. The intermediate was dissolved in dry THF (120 ml) and added dropwise to a solution of triethylamine (5.63 ml, 40.4 mmol) in dry THF (20 ml) at 0 C° and the mixture was stirred for 2 hours. The solution was warmed to room temperature and concentrated in vacuo. Afterwards the residue was dissolved in EtOAc and washed with water and brine, and dried over anhydrous Na$_2$SO$_4$. The organic layer was concentrated in vacuo to give a pale brown residue which was purified by column chromatography (EtOAc/Pet. ether 1:9) to give the title compound 4a (7.70 g, 78 %) as a pale brown solid. m.p. 159-161 °C (EtOAc/Pet. ether 1:9) (lit m.p. = 161-163 °C). 1H NMR (500 MHz, CDCl$_3$) $\delta$ 7.02 (s, 1H), 7.33–7.35 (m, 2H), 7.38–7.41 (m, 1H), 7.46–7.49 (m, 2H). 13C NMR (125 MHz, CDCl$_3$) $\delta$ 126.2, 128.5, 129.4, 131.1, 131.96, 132.02, 164.3, 167.5; $\nu_{\text{max}}$ (cm$^{-1}$) 1708 (C=O); Anal. calc. for C$_{10}$H$_6$BrNO$_2$: C, 47.65; H, 2.40; N, 5.56. Found: C, 47.89; H, 2.39; N, 5.54.

**3a-Bromo-3a,4,7,7a-tetrahydro-4,7-dimethyl-2,5,6-triphenyl-4,7-methano-1H-isoindole-1,3,8(2H)-trione** (5a)

Diene dimer 3 (393 mg, 1.51 mmol) and N-phenyl-2-bromomaleimide (4a) (418 mg, 1.66 mmol) were refluxed in benzene (20 ml) for 6 h. The solution was concentrated in vacuo to afford a brown oil which was recrystallised in ether to afford the title compound 5a (551 mg, 1.07 mmol, 71 %) as white crystals. m.p. 173-177 °C (ether); 1H NMR (500 MHz, CDCl$_3$) $\delta$ 1.68 (s, 3H), 1.71 (s, 3H), 3.71 (s, 1H),
6.97-7.00 (m, 4H), 7.16-7.29 (m, 8H), 7.43-7.51 (m, 3H); 13C NMR (125 MHz, CDCl₃) δ 11.7, 12.6, 56.9, 59.0, 60.4, 61.1, 126.21 128.3, 128.4, 128.5, 129.2, 129.5, 129.6, 129.8, 131.3, 132.5, 132.6, 140.6, 144.8, 171.4, 172.0, 196.8 νₘₐₓ (cm⁻¹) 1780 (C=O), 1720 (C=O); HRMS-ESI [M+Na]⁺ calc. for C₂₉H₂₂BrNO₃Na⁺: 534.0699, Found: 534.0675.

3a,4,7,7a-Tetrahydro-7a-bromo-4,7-dimethyl-5,6-diphenyl-4,7-methanoisobenzofuran-1,3,8-trione³ (5b)

Diene dimer (3) (999 mg, 0.192 mmol) and bromomaleic anhydride (1.295 mL, 3.84 mmol) were refluxed in toluene (60 mL) for 4 h. The orange solution was concentrated in vacuo. The product was triturated in ether and petrol to afford the title compound 5b as an inseparable 6:1 mixture of the endo and exo isomers (808 mg, 96%) as a white solid. νₘₐₓ (cm⁻¹) 1775 (C=O), 1218 (C-O-C), 697 (C-Br); HRMS-ESI m/z [M+Na]⁺ calc. for C₂₉H₁₇BrO₄Na⁺: 459.0202, Found: 459.0171.

For the endo isomer; ¹H NMR (400 MHz, CDCl₃) δ inter alia 1.62 (s, 3H), 1.65 (s, 3H), 3.74 (s, 1H), 6.93 - 6.97 (m, 4H), 7.20 - 7.22 (dt, J = 6.2, 2.1 Hz, 6H); ¹³C NMR (101 MHz, CDCl₃) δ inter alia 11.3, 12.1, 56.7, 57.5, 61.1, 128.5, 128.6, 128.69, 128.71, 129.5, 129.8, 131.8, 131.9, 141.2, 145.6, 166.9, 167.0, 195.6. For the exo isomer; ¹H NMR (400 MHz, CDCl₃) δ inter alia 1.25 (s, 3H), 1.59 (s, 3H), 3.52 (s, 1H), 6.93 - 6.97 (m, 4H), 7.20 - 7.22 (dt, J = 6.2, 2.1 Hz, 6H).

4,7-Dimethyl-5,6-diphenyl-1,3-isobenzofurandione⁴ (9)

Et₃N (0.096 mL, 0.686 mmol) was added to cycloadduct 5b (100 mg, 0.229 mmol) in toluene (4 mL) and heated at reflux for 3 h. The solvent was concentrated in vacuo and the residue extracted into EtOAc, then washed with 1M HCl and dried over MgSO₄. The solvent was concentrated in vacuo to afford the title compound 9 (73.7 mg, 98%) as a pale solid. νₘₐₓ (cm⁻¹) 1763 (C=O), 1685 (C=O), 1209 (C-O-C); HRMS-ESI m/z [M+Na]⁺ calc. for C₂₂H₁₆O₃Na⁺: 351.0992, found: 351.0964.

Diethyl 3,6-dimethyl-4,5-diphenylphthalate⁵ (12)

Diethyl acetylenedicarboxylate (0.110 mL, 0.748 mmol) and diene dimer 3 (334 mg, 0.641 mmol) were added to a Kimax® tube, followed by 1,4-dioxane (6 mL). The Kimax® tube was sealed with a screwcap fitted with a silicon seal. The sealed system was heated to 80 °C for 20 h. The reaction mixture was cooled to rt and the solvent concentrated in vacuo. The crude product was purified by silica column chromatography (EtOAc/PE 1:4-1:1) to afford the title compound 12 (275 mg, 91%) as white crystals. ¹H NMR (400 MHz, CDCl₃) δ 1.39 (t, J = 7.1 Hz, 6H), 2.08 (s, 6H), 4.38 (q, J = 7.1 Hz, 4H), 6.88 (m, 4H), 7.11 (m, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 14.3, 18.5, 61.7, 126.6, 127.8, 129.8, 131.8, 132.1, 139.9, 144.4, 168.9; νₘₐₓ (cm⁻¹) 1723 (C=O); HRMS-ESI m/z [M+Na]⁺ calc. for C₂₉H₂₆O₄Na⁺: 425.1723, Found: 425.1736.
**N-butyl-4-methoxybenzamide** (8a)

*Diethyl acetylenedicarboxylate as CO source - two-chamber system*

Following General Procedure A: Chamber A: diethyl acetylenedicarboxylate (0.110 mL, 0.748 mmol), diene dimer 3 (334 mg, 0.641 mmol) and 1,4-dioxane. Chamber B: Pd$_2$(dba)$_3$ (9.78 mg, 10.68 µmol), PPh$_3$ (11.21 mg, 0.043 mmol), p-iodoanisole (100 mg, 0.427 mmol), n-butylamine (0.097 mL, 0.983 mmol), 1,4-dioxane (4 mL) and Et$_3$N (0.137 mL, 0.983 mmol). The system was sealed and heated to 80 °C for 20 h. The reaction mixture was cooled to rt, and the solvent in Chamber B was concentrated *in vacuo*. The crude product was purified by silica column chromatography (EtOAc/PE 1:4-1:1) to afford the title compound 10a (84.5 mg, 95%) as white crystals. 1H NMR (400 MHz, CDCl$_3$) δ 0.96 (t, J = 7.3 Hz, 3H), 1.39 - 1.44 (m, 2H), 1.56 - 1.63 (m, 2H), 3.42 - 3.47 (m, 2H), 3.85 (s, 3H), 5.98 (bs, 1H), 6.92 (d, J = 8.9 Hz, 2H), 7.72 (d, J = 8.9 Hz, 2H); 13C NMR (101 MHz, CDCl$_3$) δ 13.8, 20.2, 31.8, 39.7, 55.4, 113.7, 127.1, 128.5, 162.0, 167.0; ν$_{max}$ (cm$^{-1}$) 3319 (N-H stretch), 2963 (C-H stretch), 2839 (O-Me), 1627 (C=O), 1501 (N-H bend), 1237 (C-N stretch); HRMS-ESI m/z [M+Na]$^+$ calc. for C$_{12}$H$_{17}$NO$_2$Na$: 230.1151$, Found: 230.1129.

**Using 5b as CO source**

Following General Procedure B: Chamber A: cycloadduct 5b (280 mg, 0.641 mmol), 1,4-dioxane (5 mL) and Et$_3$N (0.137 mL, 0.983 mmol). Chamber B: Pd$_2$(dba)$_3$ (9.78 mg, 10.68 µmol), PPh$_3$ (11.21 mg, 0.043 mmol), p-iodoanisole (100 mg, 0.427 mmol), n-butylamine (0.097 mL, 0.983 mmol), 1,4-dioxane (4 mL) and Et$_3$N (0.089 mL, 0.641 mmol). The two-chamber system was sealed and heated to 80 °C for 20 h. The reaction mixture was cooled to rt, and the solvent in Chamber B was concentrated *in vacuo*. The crude product was purified by silica column chromatography (EtOAc/PE 1:4 - 1:1) to afford the title compound 10a (78.2 mg, 88%) as a white solid. 1H NMR (400 MHz, CDCl$_3$) δ 0.94 (t, J = 7.3 Hz, 3H), 1.35 - 1.38 (m, 2H), 1.54-1.61 (m, 2H) 3.40 - 3.45 (q, J = 7.1 Hz, 2H), 6.15 (bs, 1H), 6.89 (d, J = 8.9 Hz, 2H), 7.72 (d, J = 8.9 Hz, 2H). 13C NMR (101 MHz, CDCl$_3$) δ 13.8, 20.2, 31.8, 39.7, 55.4, 113.8, 127.3, 128.7, 162.2, 167.1; ν$_{max}$ (cm$^{-1}$) 3311 (N-H stretch), 2839 (C-H), 1623 (C=O), 1502 (N-H bend), 1237 (C-N stretch); HRMS-ESI m/z [M+Na]$^+$ calc. for C$_{12}$H$_{17}$NO$_2$Na$: 230.1168$, Found: 230.1164.

**N-butyl-4-nitrobenzamide** (8b)

*Diethyl acetylenedicarboxylate as CO source*

Following General Procedure A: Chamber A: Diethyl acetylenedicarboxylate (0.088 mL, 0.602 mmol), diene dimer 3 (157 mg, 0.301 mmol) and 1,4-dioxane (5 mL). Chamber B: Pd$_2$(dba)$_3$ (9.19 mg, 10.04 µmol), PPh$_3$ (10.53 mg, 0.040 mmol), 1-iodo-4-nitrobenzene (100 mg, 0.427 mmol), n-butylamine (0.097 mL, 0.983 mmol), 1,4-dioxane (4 mL) and Et$_3$N (0.089 mL, 0.641 mmol). The system was sealed and heated to 80 °C for 20 h. The reaction mixture was cooled to rt, and the solvent in Chamber B was concentrated *in vacuo*. The crude product was purified by silica column chromatography (EtOAc/PE 1:4-1:1) to afford the title compound 10a (73.1 mg, 82%) as a pale yellow solid. 1H NMR (400 MHz, CDCl$_3$) δ 0.98 (t, J = 7.3 Hz, 3H), 1.38 - 1.48 (dq, J = 15.6, 7.3 Hz, 2H), 1.59 - 1.67 (m, 2H), 3.47 - 3.52 (td, J = 7.2, 5.3 Hz, 2H), 6.15 (bs, 1H), 7.92...
(d, J = 9.0 Hz, 2H), 8.29 (d, J = 8.3 Hz, 2H); 13C NMR (101 MHz, CDCl3) δ 13.9, 20.3, 31.7, 40.3, 124.0, 128.2, 140.6, 149.6, 165.6. νmax (cm⁻¹) 3302 (N-H stretch), 1634 (C=O), 1537 (N-H bend), 1510 (NO2), 1346 (NO2), 1295 (C-N stretch); HRMS-ESI m/z [M+Na]+ calc. for C12H14N2O3Na+: 245.0897, Found: 245.0874

CORM as CO source

Following General Procedure B: Chamber A: cycloadduct 5b (263 mg, 0.602 mmol), 1,4-dioxane (5 mL) and Et3N (0.129 mL, 0.924 mmol). Chamber B: Pd2(dba)3 (9.19 mg, 10.04 µmol), PPh3 (10.53 mg, 0.040 mmol), 1-iodo-4-nitrobenzene (100 mg, 0.402 mmol), n-butylamine (0.091 mL, 0.924 mmol), 1,4-dioxane (4 mL) and Et3N (0.129 mL, 0.924 mmol. The two-chamber system was sealed and heated to 80 °C for 20 h. The reaction mixture was cooled to rt, and the solvent in Chamber B was concentrated in vacuo. The crude product was purified by silica column chromatography (EtOAc/PE 1:4 - 1:1) to afford the title compound 10b (88.6 mg, 99%) as a pale yellow solid. 1H NMR (400 MHz, CDCl3) δ 0.98 (t, J = 7.3 Hz, 3H), 1.39 - 1.48 (m, 2H), 1.60 - 1.67 (m, 2H), 3.47 - 3.52 (m, 2H), 6.12 (bs, 1H), 7.92 (d, J = 8.7 Hz, 2H), 8.29 (d, J = 8.7 Hz, 2H); 13C NMR (101 MHz, CDCl3) δ 13.7, 20.1, 31.6, 40.1, 123.8, 128.0, 140.4, 149.5, 165.4; νmax (cm⁻¹) 3302 (N-H stretch), 1634 (C=O), 1537 (N-H bend), 1510 (NO2), 1346 (NO2), 1295 (C-N stretch); HRMS-ESI m/z [M+Na]+ calc. for C12H14N2O3Na+: 245.0897, Found: 245.0874.

4-bromo-N-butylbenzamide (8c)

Following General Procedure B: Chamber A: cycloadduct 5b (150 mg, 0.343 mmol), 1,4-dioxane (5 mL) and Et3N (0.072 mL, 0.515 mmol). Chamber B: Pd2(dba)3 (7.85 mg, 8.58 µmol), PPh3 (9.00 mg, 0.034 mmol), 1-bromo-4-iodobenzene (97 mg, 0.343 mmol), n-butylamine (0.078 mL, 0.789 mmol), 1,4-dioxane (4 mL) and Et3N (0.110 mL, 0.789 mmol). The two-chamber system was sealed and heated to 80 °C for 20 h. The reaction mixture was cooled to rt, and the solvent in Chamber B was concentrated in vacuo. The crude product was purified by silica column chromatography (EtOAc/PE 1:6 - 2:1) to afford the title compound 10c (73.1 mg, 81%) as an off white solid. 1H NMR (400 MHz, CDCl3) δ 0.96 (t, J = 7.3 Hz, 3H), 1.37 - 1.46 (m, 2H), 1.57 - 1.64 (m, 2H), 3.43 - 3.48 (m, 2H), 6.02 (bs, 1H), 7.63 (d, J = 8.7 Hz, 2H), 7.86 (d, J = 8.7 Hz, 2H); 13C NMR (101 MHz, CDCl3) δ 13.9, 31.0, 31.8, 40.0, 125.9, 128.6, 131.8, 133.8, 166.7; νmax (cm⁻¹) 3321 (N-H stretch), 1631 (C=O), 1535 (N-H bend), 1297 (C-N stretch), 644 (C-Br); HRMS-ESI m/z [M+H]+ calc. for C11H15NO79Br+: 256.0332, found: 256.0324.

N-butylbenzamide (8d)

Following General Procedure B: Chamber A: cycloadduct 5b (322 mg, 0.735 mmol), 1,4-dioxane (5 mL) and Et3N (0.157 mL, 1.127 mmol). Chamber B: Pd2(dba)3 (11.22 mg, 0.012 mmol), PPh3 (12.86 mg, 0.049 mmol), iodobenzene (0.055 mL, 0.490 mmol), n-butylamine (0.111 mL, 1.127 mmol), 1,4-dioxane (4 mL) and Et3N (0.157 mL, 1.127 mmol). The two-chamber system was sealed and heated to 80 °C for 20 h. The reaction mixture was cooled to rt, and the solvent in Chamber B was concentrated in vacuo. The crude product was purified by silica column chromatography (EtOAc/PE 1:6 - 2:1) to afford the title compound 10d (163 mg, 91%) as a pale yellow solid. 1H NMR (400 MHz, CDCl3) δ 0.94 (t, J = 7.3 Hz, 3H), 1.37 - 1.46 (m, 2H), 1.53 - 1.60 (m, 2H), 3.29 - 3.34 (m, 2H), 6.02 (bs, 1H), 7.63 (d, J = 8.7 Hz, 2H), 7.86 (d, J = 8.7 Hz, 2H); 13C NMR (101 MHz, CDCl3) δ 13.9, 31.0, 31.8, 40.0, 125.9, 128.6, 131.8, 133.8, 166.7; νmax (cm⁻¹) 3321 (N-H stretch), 1631 (C=O), 1535 (N-H bend), 1297 (C-N stretch), 644 (C-Br); HRMS-ESI m/z [M+H]+ calc. for C11H15NO79Br+: 256.0332, found: 256.0324.

N-butylbenzamide (8d)
was purified by silica column chromatography (EtOAc/PE 0:1 - 1:4) to afford the title compound **10d** (84.1 mg, 97%) as an oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 0.96 (t, $J = 7.3$ Hz, 3H), 1.43 (m, 2H), 1.61 (m, 2H), 3.47 (td, $J = 7.2$, 5.7 Hz, 2H), 6.09 (bs, 1H), 7.43 (m, 2H), 7.48 (m, 1H), 7.75 (m, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 13.8, 31.0, 31.8, 39.9, 127.0, 128.5, 131.3, 134.9, 167.7; $\nu_{\text{max}}$ (cm$^{-1}$) 3317 (N-H stretch), 1634 (C=O), 1539 (N-H bend), 1307 (C-N stretch); HRMS-ESI m/z [M+Na]$^+$ calc. for C$_{11}$H$_{15}$NONa$^+$: 200.1046; Found: 200.1030.

**N-butyl-1-naphthamide**$^\circledast$ **(8e)**

Following General Procedure B: Chamber A: cycloadduct **30** (367.5 mg, 0.840 mmol), 1,4-dioxane (5 mL) and Et$_3$N (0.137 mL, 0.984 mmol). Chamber B: Pd$_2$(dba)$_3$ (9.01 mg, 9.84 µmol), PPh$_3$ (10.32 mg, 0.039 mmol), 1-iodonaphthalene (0.057 mL, 0.394 mmol), n-butylamine (0.089 mL, 0.905 mmol), 1,4-dioxane (4 mL) and Et$_3$N (0.126 mL, 0.905 mmol). The two-chamber system was sealed and heated to 80 °C for 20 h. The reaction mixture was cooled to rt, and the solvent in Chamber B was concentrated in vacuo. The crude $^1$H NMR indicated that 90% of the starting material was converted to the title compound. The crude product was purified by silica column chromatography (EtOAc/PE 1:6 - 1:3) to give a pale orange solid. This was then triturated in DCM and petrol to afford the title compound **8e** (78 mg, 88%) as a white solid. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 0.99 (t, $J = 7.35$ Hz, 3H), 1.46 (m, 2H), 1.65 (m, 2H), 3.56 (m, 2H), 5.95 (bs, 1H), 7.45 (dd, $J = 8.3$, 7.0 Hz, 1H), 7.56 (m, 2H), 7.89 (m, 3H), 8.30 (ddd, $J = 7.8$, 1.9, 0.8 Hz, 1H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 13.8, 20.2, 31.8, 39.8, 124.7, 124.7, 125.4, 126.4, 127.0, 128.3, 130.1, 130.4, 133.7, 134.9, 169.5; $\nu_{\text{max}}$ (cm$^{-1}$) 3293 (N-H stretch), 3061 (C-H), 1653 (C=O), 1553 (N-H stretch), 1298 (C-N stretch); HRMS-ESI m/z [M+Na]$^+$ calc. for C$_{15}$H$_{17}$NONa$^+$: 250.1194; Found: 250.1202.

**Morpholino(4-methoxyphenyl)methanone**$^{11}$ **(10a)**

Following General Procedure B: Chamber A: cycloadduct **5b** (280 mg, 0.641 mmol), 1,4-dioxane (5 mL) and Et$_3$N (0.137 mL, 0.983 mmol). Chamber B: Pd$_2$(dba)$_3$ (9.78 mg, 10.68 µmol), PPh$_3$ (11.21 mg, 0.043 mmol), p-iodoanisole (100 mg, 0.427 mmol), morpholine (0.086 mL, 0.983 mmol), 1,4-dioxane (4 mL) and Et$_3$N (0.137 mL, 0.983 mmol). The two-chamber system was sealed and heated to 100 °C for 25 h. The reaction mixture was cooled to rt, and the solvent in Chamber B was concentrated in vacuo. The crude product was purified by silica column chromatography (EtOAc/PE 2:1 - 6:1) to afford the title compound **10a** (70.8 mg, 75%) as a yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.64 - 3.70 (b, 8H), 3.83 (s, 3H), 6.90 - 6.94 (m, 2H), 7.37 - 7.41 (m, 2H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 43.7, 48.7, 55.5, 67.1, 113.9, 127.5, 129.3, 161.0, 170.5; $\nu_{\text{max}}$ (cm$^{-1}$) 2857, 1627 (C=O), 1277 (C-N stretch), 1107 (C-O-C); HRMS-ESI m/z [M+Na]$^+$ calc. for C$_{12}$H$_{15}$NO$_3$Na$^+$: 244.0944; found: 244.0929.
Morpholino(4-nitrophenyl)methanone<sup>12</sup> (10b)

Following General Procedure B: Chamber A: cycloadduct 5b (263 mg, 0.602 mmol) 1,4-dioxane (5 mL) and Et<sub>3</sub>N (0.129 mL, 0.924 mmol). Chamber B: Pd<sub>2</sub>(dba)<sub>3</sub> (9.19 mg, 10.04 µmol), PPh<sub>3</sub> (10.53 mg, 0.040 mmol), 1-iodo-4-nitrobenzene (100 mg, 0.402 mmol), morpholine (0.081 mL, 0.924 mmol) 1,4-dioxane (4 mL) and Et<sub>3</sub>N (0.129 mL, 0.924 mmol). The two-chamber system was sealed and heated to 100 °C for 25 h. The reaction mixture was cooled to rt, and the solvent in Chamber B was concentrated in vacuo. The crude product was purified by silica column chromatography (EtOAc/PE 1:1 - 6:1) to afford the title compound 10b (83.1 mg, 88%) as an orange solid.

1H NMR (400 MHz, CDCl<sub>3</sub>) δ 3.39 - 3.81 (m, 8H), 7.57 - 7.60 (m, 2H), 8.28 - 8.31 (m, 2H); 13C NMR (101 MHz, CDCl<sub>3</sub>) δ 42.8, 48.2, 66.9, 124.1, 128.3, 141.6, 148.7, 168.2; ν<sub>max</sub> (cm<sup>-1</sup>) 2920 (C-H bend), 1631 (C=O), 1515 (NO<sub>2</sub>), 1350 (NO<sub>2</sub>), 1279 (C-N), 1105 (C-O-C); HRMS-ESI m/z [M+H]<sup>+</sup> calc. for C<sub>12</sub>H<sub>13</sub>NO<sub>3</sub>: 237.0870, found: 237.0876.

Morpholino(4-bromophenyl)methanone<sup>13</sup> (10c)

Following General Procedure B: Chamber A: cycloadduct 5b (232 mg, 0.530 mmol) 1,4-dioxane (5 mL) and Et<sub>3</sub>N (0.113 mL, 0.813 mmol). Chamber B: Pd<sub>2</sub>(dba)<sub>3</sub> (8.09 mg, 8.84 µmol), PPh<sub>3</sub> (9.27 mg, 0.035 mmol), 1-bromo-4-iodobenzene (100 mg, 0.353 mmol), morpholine (0.071 mL, 0.813 mmol), 1,4-dioxane (4 mL) and Et<sub>3</sub>N (0.113 mL, 0.813 mmol). The two-chamber system was sealed and heated to 100 °C for 25 h. The reaction mixture was cooled to rt, and the solvent in Chamber B was concentrated in vacuo. The crude product was purified by silica column chromatography (EtOAc/PE 1:1 - 4:1) to afford the title compound 10c as an pale orange oil (67.5 mg, 72%).

1H NMR (400 MHz, CDCl<sub>3</sub>) δ 3.46 - 3.70 (m, 8H), 7.28 - 7.30 (m, 2H), 7.55 - 7.57 (m, 2H); 13C NMR (101 MHz, CDCl<sub>3</sub>) δ 42.8, 48.2, 67.0, 124.4, 129.0, 132.0, 134.2, 169.5; ν<sub>max</sub> (cm<sup>-1</sup>) 1628 (C=O), 1276 (C-N stretch), 1111 (C-O-C); HRMS-ESI m/z [M+H]<sup>+</sup> calc. for C<sub>11</sub>H<sub>13</sub>NO<sub>2</sub>Br: 270.0124, found: 270.0122.

Morpholino(phenyl)methanone<sup>12</sup> (10d)

Following General Procedure B: Chamber A: cycloadduct 30 (322 mg, 0.735 mmol), 1,4-dioxane (5 mL) and Et<sub>3</sub>N (0.157 mL, 1.127 mmol). Chamber B: Pd<sub>2</sub>(dba)<sub>3</sub> (11.22 mg, 0.012 mmol), PPh<sub>3</sub> (12.86 mg, 0.049 mmol), iodobenzene (0.055 mL, 0.55 mL, 0.490 mmol), morpholine (0.099 mL, 1.127 mmol), 1,4-dioxane (4 mL) and Et<sub>3</sub>N (0.157 mL, 1.127 mmol). The two-chamber system was sealed and heated to 100 °C for 25 h. The reaction mixture was cooled to rt, and the solvent in Chamber B was concentrated in vacuo. The crude product was purified by silica column chromatography (EtOAc/PE 1:1 - 4:1) to afford the title compound 10d (93 mg, 99%).

1H NMR (400 MHz, CDCl<sub>3</sub>) δ 3.46 - 3.75 (m, 8H), 7.39 - 7.43 (m, 5H); 13C NMR (101 MHz, CDCl<sub>3</sub>) δ 42.7, 48.3, 67.0, 127.2, 128.7, 130.0, 135.5, 170.6; ν<sub>max</sub> (cm<sup>-1</sup>) 1625 (C=O), 1275 (C-N stretch), 1110 (C-O-C); 544 (C-Br); HRMS-ESI m/z [M+Na]<sup>+</sup> calc. for C<sub>11</sub>H<sub>13</sub>NO<sub>2</sub>Na+: 214.0838, found: 214.0839.
Morpholino(naphthalen-1-yl)methanone\(^{13}\) (10e)

Following General Procedure B: Chamber A: cycloadduct 5b (258 mg, 0.590 mmol), 1,4-dioxane (5 mL) and Et\(_3\)N (0.126 mL, 0.905 mmol). Chamber B: Pd\(_2\)(dba)\(_3\) (9.01 mg, 9.84 µmol), PPH\(_3\) (10.32 mg, 0.039 mmol), 1-iodonaphthalene (0.057 mL, 0.394 mmol), morpholine (0.079 mL, 0.905 mmol), 1,4-dioxane (4 mL) and Et\(_3\)N (0.126 mL, 0.905 mmol). The two-chamber system was sealed and heated to 100 °C for 25 h. The reaction mixture was cooled to rt, and the solvent in Chamber B was concentrated \textit{in vacuo}. The crude \(^1\)H NMR indicated that only 80% of the starting material was converted into the title compound. The crude product was purified by silica column chromatography (EtOAc/PE 1:2 - 4:1) to afford the title compound 10e (71.2 mg, 75%).

\[^1\]H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 3.16 - 3.25 (m, 2H), 3.47 - 3.56 (m, 2H), 3.83 - 4.04 (m, 4H), 7.41 - 7.43 (dd, \(J = 7.0, 1.3\) Hz, 1H), 7.47 - 7.57 (m, 4H), 7.84 - 7.90 (m, 3H); \[^13\]C NMR (101 MHz, CDCl\(_3\)) \(\delta\); 42.3, 47.8, 67.1, 67.2, 124.1, 124.7, 125.3, 126.7, 127.3, 128.6, 129.5, 129.7, 133.6, 133.8, 169.6; \(\nu_{\text{max}}\) (cm\(^{-1}\)) 1629 (C=O), 1247 (C-N stretch), 1111 (C-O-C); HRMS-ESI m/z [M+Na\(^+\)] calcd. for C\(_{15}\)H\(_{15}\)NO\(_2\)Na\(^+\): 264.0995, found: 264.0994.

\(^{N}\)-butyl-2-(4-methoxyphenyl)-2-oxoacetamide (13)

Chamber A: Cycloadduct 5b (654 mg, 1.496 mmol) was added followed by Toluene (6 mL). Chamber B: Pd\(_2\)(dba)\(_3\) (19.56 mg, 0.021 mmol), tri-\textit{tert}-butylphosphonium tetrafluoroborate (12.40 mg, 0.043 mmol), p-iodoanisole (100 mg, 0.427 mmol) were added followed by toluene (5 mL), butylamine (0.063 mL, 0.641 mmol) and DBU (0.128 mL, 0.855 mmol). The system was flushed with argon then DBU (0.256 mL, 1.709 mmol) was added to Chamber A, the system was then sealed with screwcaps fitted with silicon seals. The sealed system was left to stir for 25 h. The solvent in Chamber B was concentrated \textit{in vacuo}. The crude product was purified by silica column chromatography (EtOAc/PE: 1:9 - 2:3) to afford the title compound 13 (64.7 mg, 64%) as a pale yellow solid. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 0.94 (t, \(J = 7.3\) Hz, 3H), 1.34 - 1.44 (m, 2H), 1.54 - 1.61 (m, 2H), 3.34 - 3.40 (m, 2H), 3.87 - 3.88 (m, 3H), 6.93 (dt, \(J = 9.0, 1.3\) Hz, 2H), 7.15 (bs, 1H), 8.40 (dt, \(J = 9.2, 1.8\) Hz, 2H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\); 13.8, 20.2, 31.5, 39.2, 55.7, 113.9, 126.6, 134.0, 162.4, 164.8, 186.0; \(\nu_{\text{max}}\) (cm\(^{-1}\)) 3242 (NH), 2933 (OMe), 1667, 1630 (C=O); HRMS-ESI m/z [M+Na\(^+\)] calc. for C\(_{13}\)H\(_{17}\)NO\(_3\)Na\(^+\): 258.1101, Found: 258.1118.

(4-methoxyphenyl)(phenyl)methanone\(^{14}\) (15a)

Following General Procedure C: Chamber A: Cycloadduct 5b (561 mg, 1.282 mmol) was added, followed by 1,4-dioxane (5 mL). Chamber B: Pd\(_2\)(dba)\(_3\) (7.83 mg, 8.55 µmol), phenylboronic acid (78 mg, 0.641 mmol), p-iodoanisole (100 mg, 0.427 mmol) and K\(_2\)CO\(_3\) (177 mg, 1.282 mmol) were added, followed by anisole (4 mL). The system was flushed with argon then Et\(_3\)N (0.208 mL, 1.496 mmol) was added to Chamber A, the system was then sealed with screwcaps fitted with silicon seals. The system was allowed to sit for 30 min to release CO before being heated to 80 °C for 25 h. The reaction mixtures were cooled to rt and the solvent in Chamber B was concentrated \textit{in vacuo}. The crude product was purified by silica column chromatography (EtOAc/PE) to afford the title compound 15a (67.5 mg, 74%) as a yellow oil. \(^1\)H NMR (400 MHz, CDCl\(_3\))
δ 3.89 (s, 3H), 6.97 (d, J = 8.6 Hz, 2H), 7.47 (t, J = 7.6 Hz, 2H), 7.57 (t, J = 7.5 Hz, 1H), 7.76 (d, J = 8.1 Hz, 2H), 7.83 (d, J = 8.5 Hz, 2H); 13C NMR (101 MHz, CDCl3) δ 55.6, 113.7, 128.3, 129.9, 130.3, 132.0, 132.7, 138.4, 163.3, 195.8; νmax (cm⁻¹) 2841 (OMe), 1649 (C=O); HRMS-ESI m/z [M+Na]+ calc. for C14H12O2Na+: 235.0729, Found: 235.0730.

Benzophenone (15b)

Following General Procedure C: Chamber A: Cycloadduct 5b (643 mg, 1.471 mmol) was added, followed by 1,4-dioxane (5 mL). Chamber B: Pd2(dba)3 (8.98 mg, 9.80 µmol), phenylboronic acid (90 mg, 0.735 mmol) and K2CO3 (203 mg, 1.471 mmol) were added, followed by anisole (5 mL) and iodobenzene (0.055 mL, 0.490 mmol). The system was flushed with argon then Et3N (0.239 mL, 1.716 mmol) was added to Chamber A, the system was then sealed with screwcaps fitted with silicon seals. The system was allowed to sit for 30 min to release CO before being heated to 80 °C for 24 h. The reaction mixtures were cooled to rt and the solvent in Chamber B concentrated in vacuo. The crude product was purified by silica column chromatography to afford the title compound 15b (69.3 mg, 78%) as a yellow oil. 1H NMR (400 MHz, CDCl3) δ 7.49 (m, 4H), 7.59 (m, 2H), 7.81 (m, 4H). 13C NMR (101 MHz, CDCl3) δ 128.4, 130.2, 132.5, 137.7, 196.9; νmax (cm⁻¹) 1655 (C=O); HRMS-ESI m/z [M+Na]+ calc. for C13H10ONa+: 205.0622, Found: 205.0624.

(4’-chlorophenyl)-(4-methoxyphenyl)methanone15 (15c)

Following General Procedure C: Chamber A: Cycloadduct 5b (561 mg, 1.282 mmol) was added, followed by 1,4-dioxane (5 mL). Chamber B: Pd2(dba)3 (7.83 mg, 8.55 µmol), 4-chlorophenylboronic acid (100 mg, 0.641 mmol), p-iodoanisole (100 mg, 0.427 mmol) and K2CO3 (177 mg, 1.282 mmol) were added, followed by anisole (4 mL). The system was flushed with argon then Et3N (0.208 mL, 1.496 mmol) was added to Chamber A, the system was then sealed with screwcaps fitted with silicon seals. The system was allowed to sit for 30 min to release CO before being heated to 80 °C for 24 h. The reaction mixtures were cooled to rt and the solvent in Chamber B concentrated in vacuo. The crude product was purified by silica column chromatography (EtOAc/PE) to afford the title compound 15c (98.8 mg, 94%) as a yellow solid. 1H NMR (400 MHz, CDCl3) δ 3.90 (s, 3H), 6.97 (d, J = 8.9 Hz, 2H), 7.45 (d, J = 8.6 Hz, 2H), 7.71 (d, J = 8.5 Hz, 2H), 7.80 (d, J = 8.9 Hz, 2H); 13C NMR (101 MHz, CDCl3) δ 55.7, 113.8, 128.7, 129.7, 131.3, 132.6, 136.7, 138.4, 163.5, 194.5; νmax (cm⁻¹) 2842 (OMe), 1639 (C=O); HRMS-ESI m/z [M+Na]+ calc. for C14H1135ClO2Na+: 269.0335, Found: 269.0340.

Ethyl 2-(4-iodophenoxy)acetate16 (6f)

To a solution of 4-iodophenol (1 g, 4.55 mmol) in acetone (100 mL), K2CO3 (1.885 g, 13.64 mmol) and ethyl 2-bromoacetate (0.553 mL, 5.00 mmol) were added. The mixture was heated at reflux o/n. The reaction progress was monitored by TLC until no starting material was observed. The reaction was allowed to cool to rt and the solution was concentrated in vacuo. The residue was dissolved in DCM and washed with water (2 x 40 mL). The organic layer was dried with MgSO4, filtered and concentrated in vacuo. The crude

product was purified by silica column chromatography (DCM 100%) to afford the title compound 6f (1.390 g, 99%) as a white crystalline solid. $^1$H NMR (400 MHz, CDCl$_3$) δ 1.29 (t, J = 7.1 Hz, 3H), 4.27 (q, J = 7.1 Hz, 2H), 6.69 (d, J = 8.9 Hz, 2H), 7.57 (d, J = 8.9 Hz, 2H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 14.3, 61.6, 65.6, 84.2, 117.2, 138.5, 157.9, 168.7; $\nu_{\text{max}}$ (cm$^{-1}$) 1754 (C=O), 1198 (C-O-C); HRMS-ESI m/z [M+Na]$^+$ calc. for C$_{10}$H$_{11}$IO$_3$Na+: 328.9645, found: 328.9645.

**Ethyl 2-(4-(4-chlorobenzoyl)phenoxy)acetate (15d)**

Following General Procedure C: Chamber A: Cycloadduct 5b (643 mg, 1.470 mmol) was added, followed by 1,4-dioxane (4 mL). Chamber B: Ethyl 2-(4-iodophenoxy)acetate (150 mg, 0.490 mmol), (4-chlorophenyl)boronic acid (115 mg, 0.735 mmol), K$_2$CO$_3$ (203 mg, 1.470 mmol) and Pd$_2$(dba)$_3$ (8.97 mg, 9.80 µmol) were added, followed by anisole (4 mL). The system was flushed with argon then Et$_3$N (0.239 mL, 1.715 mmol) was added to Chamber A, the system was then sealed with screwcaps fitted with silicon seals. The system was allowed to sit for 30 min to release CO before being heated to 80 °C for 30 h. The reaction mixtures were cooled to rt and the solvent in Chamber B concentrated in vacuo. The crude product was purified by silica column chromatography (EtOAc/PE 1:15 - 1:5) to afford the title compound 15d (117.6 mg, 75%).

$^1$H NMR (400 MHz, CDCl$_3$) δ 1.31 (t, J = 7.1 Hz, 3H), 4.29 (q, J = 7.1 Hz, 2H), 4.71 (s, 2H), 6.98 (d, J = 8.6 Hz, 2H), 7.45 (d, J = 8.3 Hz, 2H), 7.71 (d, J = 8.4 Hz, 2H), 7.80 (d, J = 8.6 Hz, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 14.3, 61.8, 65.3, 114.4, 128.7, 130.9, 131.3, 132.6, 136.4, 138.6, 161.5, 168.4, 194.4; $\nu_{\text{max}}$ (cm$^{-1}$) 1755 (C=O), 1615 (C=O aryl), 1201 (C-O-C), 760 (Ar-Cl); HRMS-ESI m/z [M+Na]$^+$ calc. for C$_{17}$H$_{15}$I$_3$ClO$_4$Na+: 341.0551, found: 341.0549

**Isopropyl 2-(4-iodophenoxy)-2-methylpropanoate (6g)**

4-iodophenol (200 mg, 0.909 mmol) and anhydrous K$_2$CO$_3$ (377 mg, 2.73 mmol) were mixed in dry acetonitrile (20 mL). Isopropyl 2-bromo-2-methylpropanoate (0.184 mL, 1.091 mmol) was introduced to the suspension, and the reaction mixture was heated at reflux for 18 h. The reaction progress was monitored by TLC. After the mixture was cooled to rt, the reaction was terminated by addition of 1 M HCl (30 mL), and the product was extracted with ethyl acetate (50 mL). The organic layer was washed with water and brine and dried over MgSO$_4$ filtered and concentrated in vacuo. The crude product was purified by silica column chromatography to afford the title compound 6g (172.6 mg, 54.5%).

$^1$H NMR (400 MHz, CDCl$_3$) δ 1.21 (d, J = 6.3 Hz, 6H), 1.57 (s, 6H), 5.07 (hept, J = 6.3 Hz, 1H), 6.59 - 6.63 (m, 2H), 7.49 - 7.53 (m, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 21.7, 25.4, 69.3, 79.4, 84.6, 121.2, 138.1, 155.6, 173.6; $\nu_{\text{max}}$ (cm$^{-1}$) 1724 (C=O), 1100 (C-O-C); HRMS-ESI m/z [M+Na]$^+$ calc. for C$_{17}$H$_{16}$I$_3$ClO$_4$Na+: 371.0115, found: 371.0111.
Isopropyl 2-(4-(4-chlorobenzoyl)phenoxy)-2-methylpropanoate\(^{17}\) (15e)

Following General Procedure C: Chamber A: Cycloadduct 5b (565 mg, 1.292 mmol) was added, followed by 1,4-dioxane (4 mL). Chamber B: isopropyl 2-(4-iodophenoxy)-2-methylpropanoate (150 mg, 0.431 mmol), (4-chlorophenyl)boronic acid (81 mg, 0.517 mmol), K\(_2\)CO\(_3\) (179 mg, 1.292 mmol) and Pd\(_2\)(dba)\(_3\) (7.89 mg, 8.62 \(\mu\)mol) were added, followed by anisole (4 mL). The system was flushed with argon then Et\(_3\)N (0.210 mL, 1.508 mmol) was added to Chamber A, the system was then sealed with screwcaps fitted with silicon seals. The system was allowed to sit for 30 min to release CO before being heated to 80 °C for 65 h. The reaction mixtures were cooled to rt and the solvent in Chamber B concentrated \textit{in vacuo}. The crude product was purified by silica column chromatography (DCM/PE 10% - 100%) to afford the title compound 15e (124.9 mg, 80%).

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 1.20 (d, \(J = 6.3\) Hz, 6H), 1.66 (s, 6H), 5.09 (sept, \(J = 6.1\) Hz, 1H), 6.86 (d, \(J = 8.3\) Hz, 2H), 7.45 (d, \(J = 8.4\) Hz, 2H), 7.70 (d, \(J = 8.7\) Hz, 2H), 7.73 (d, \(J = 8.7\) Hz, 2H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 21.7, 25.5, 69.5, 76.8, 117.4, 128.7, 130.4, 131.3, 132.1, 136.6, 138.5, 159.9, 173.2, 194.4; \(\nu_{\text{max}}\) (cm\(^{-1}\)) 1727 (C=O), 1653 (C=O aryl), 1144 (C-O-C), 762 (C-Cl); HRMS-ESI \(m/z\) [M+Na]\(^+\) calc. for C\(_{20}\)H\(_{21}\)ClO\(_4\)Na: 383.1021, found: 383.0997.

3-iodo-1H-indole\(^{18}\) (16)

A solution of iodine (4.38 g, 17.24 mmol) in DMF (30 mL) was added dropwise to a solution of 1H-indole (2 g, 17.07 mmol) and KOH (2.395 g, 42.7 mmol) in DMF (30 mL) and stirred at rt for one hour. The reaction mixture was poured into ice and water (400 mL) containing ammonia (0.5%) and sodium metabisulfite (0.1% aqueous solution). The resulting precipitate was filtered and washed with water to give the title compound 16b (3.2 g, 77%) as a crystalline solid which was used without further purification. Warning: strong unpleasant odour associated with this compound (similar to that of skatole).\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.18 - 7.24 (m, 2H), 7.30 (d, \(J = 2.5\) Hz, 1H), 7.37 (d, \(J = 7.9\), 1H), 7.47 (d, \(J = 7.7\), 1H), 7.30 (d, \(J = 2.5\) Hz, 1H), 7.37 (d, \(J = 7.9\), 1H), 7.47 (d, \(J = 7.7\), 1H), 8.34 (bs, 1H).

1H-indol-3-ylphenylmethanone\(^{19}\) (17)

Following General Procedure C: Chamber A: Cycloadduct 5b (0.656 g, 1.500 mmol) was added, followed by 1,4-dioxane (4 mL). Chamber B: 3-iodo-1H-indole (0.122 g, 0.5 mmol), phenylboronic acid (0.073 g, 0.600 mmol), K\(_2\)CO\(_3\) (0.207 g, 1.500 mmol) and Pd\(_2\)(dba)\(_3\) (9.16 mg, 10.00 \(\mu\)mol) were added, followed by anisole (4 mL). The system was flushed with argon then Et\(_3\)N (0.244 mL, 1.750 mmol) was added to Chamber A, the system was then sealed with screwcaps fitted with silicon seals. The system was allowed to sit for 30 min to release CO before being heated to 80 °C for 25 h. The reaction mixtures were cooled to rt and the solvent in Chamber B concentrated \textit{in vacuo}. The crude product was purified by silica column chromatography (PE: EtOAc 9:1 - 1:1) to afford the title compound 17 (55.4 mg, 50%). \(^1\)H NMR (400 MHz, DMSO-d\(_6\)) \(\delta\) 7.22 - 7.29 (m, 2H), 7.51 - 7.57 (m, 3H), 7.59 - 7.64 (m, 1H), 7.79 (d, \(J = 6.8\) Hz, 2H), 7.93 (s, 1H), 8.26 (d, \(J = 6.9\) Hz, 1H), 12.06 (s, 1H); \(^{13}\)C NMR (101 MHz, DMSO) \(\delta\) 112.2, 115.0, 121.4,
121.9, 123.1, 126.2, 128.36, 131.0, 135.8, 136.7, 140.5, 189.9; \( \nu_{\text{max}} \) (cm\(^{-1}\)) 3142 (N-H), 2922 (C-H), 1596 (C=O), 1427.

(1H-indol-3-yl)(naphthalen-2-yl)methanone (18)

Following General Procedure C: Cycloadduct 5b (656 mg, 1.5 mmol) was added, followed by 1,4-dioxane (4 mL). In Chamber B: 3-iodo-1H-indole (122 mg, 0.50 mmol), 2-naphthylboronic acid (103 mg, 0.600 mmol), \( \text{K}_2\text{CO}_3 \) (207 mg, 1.50 mmol) and \( \text{Pd}_2\text{(dba)}_3 \) (9.16 mg, 10.00 µmol) were added, followed by anisole (4 mL). The system was flushed with argon then Et\(_3\)N (0.244 mL, 1.750 mmol) was added to Chamber A, the system was then sealed with screwcaps fitted with silicon seals. The system was allowed to sit for 30 min to release CO before being heated to 80 °C for 25 h. The reaction mixtures were cooled to rt and the solvent in Chamber B concentrated \textit{in vacuo}. The crude product was purified by silica column chromatography (PE: EtOAc 9:1 - 1:1) to afford the title compound 18 (59.9 mg, 44%).

\( ^1\text{H} \) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.38 - 7.33 (m, 2H), 7.50 - 7.46 (m, 1H), 7.63 - 7.54 (m, 2H), 7.77 (d, \( J = 3.0 \) Hz, 1H), 7.98 - 7.90 (m, 4H), 8.34 (s, 1H), 8.48 - 8.41 (m, 1H), 8.62 (s, 1H); \( ^{13}\text{C} \) NMR (101 MHz, DMSO) \( \delta \) 112.3, 115.2, 121.5, 121.9, 123.2, 125.3, 126.3, 126.7, 127.64, 127.64, 128.1, 132.2, 134.2, 136.0, 136.7, 137.7, 189.90; \( \nu_{\text{max}} \) (cm\(^{-1}\)) 3147 (N-H stretch), 1596 (C=O); HRMS-ESI \( m/z \) [M+Na]\(^+\) calc. for C\(_{19}\)H\(_{13}\)NONa\(^+\): 294.0889, found: 294.0868.

2-morpholinoethyl methanesulfonate (19)

A solution of 2-morpholinoethanol (1 mL, 8.26 mmol) and Et\(_3\)N (3.45 mL, 24.77 mmol) in THF (50 mL) was cooled to 0 °C. Methanesulfonyl chloride (0.959 mL, 12.38 mmol) was added dropwise over 5 min to the mixture which was then stirred at 0 °C for 10 min. The reaction mixture was filtered through Celite® 545 with THF and concentrated under reduced pressure. The crude 2-morpholinoethyl methanesulfonate 19 was used without further purification. \( ^1\text{H} \) NMR (400 MHz, CDCl\(_3\)) \textit{inter alia} \( \delta \) 2.55 (t, \( J = 4.6 \) Hz, 4H), 2.74 (t, \( J = 5.5 \) Hz, 2H), 3.09 (s, 3H), 3.74 - 3.70 (m, 4H), 4.35 (t, \( J = 5.5 \) Hz, 2H).

4-(2-(3-iodo-1H-indol-1-yl)ethyl)morpholine (20)

To 3-iodo-1H-indole (0.610 g, 2.510 mmol) in DMF (30 mL) at 0 °C was added NaH (60% dispersion in mineral oil, 0.502 g, 12.55 mmol) portion wise over 5 min. The mixture was stirred for 10 min at 0 °C and then was allowed to warm to ambient temperature. The mixture was stirred for 1 h at ambient temperature and then was cooled to 0 °C. The 2-morpholinoethyl methanesulfonate (1.0 g, 4.78 mmol) in 2 mL of THF was added rapidly \textit{via} cannula. After the addition was complete, the ice bath was removed and the mixture was stirred for 4 h at ambient temperature. The mixture was then cooled to 0 °C, was quenched with 30 mL of saturated, aqueous NH\(_4\)Cl and was diluted with 30 mL of EtOAc. The layers were separated, and the aqueous layer was extracted EtOAc (3 x 15 mL). The combined organic extracts were washed with water (4 x 10 mL) and brine (4 x 10 mL) and then were dried over anhydrous MgSO\(_4\),
filtered, concentrated under reduced pressure, and purified by silica column chromatography (CHCl₃: EtOAc 1:0 - 1:1) to afford the title compound 20 (808.4 mg, 90%) as a pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 2.55 - 2.45 (m, 4H), 2.74 (t, J = 6.8 Hz, 2H), 3.77 - 3.67 (m, 4H), 4.25 (t, J = 6.8 Hz, 2H), 7.20 (dd, J = 8.0, 6.9, 1.2 Hz, 1H), 7.24 - 7.30 (m, 2H), 7.33 (dt, J = 8.3, 0.9 Hz, 1H), 7.45 (dt, J = 7.8, 1.0 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 44.3, 54.0, 58.3, 67.0, 109.5, 120.5, 121.5, 122.8, 130.6, 132.1, 136.2; ν max (cm⁻¹) 1141 (C-O-C), 726 (C-I); HRMS-ESI m/z [M+H]+ calc. for C₁₄H₁₈N₂O⁺: 357.0458, found: 357.0458.

(4-methoxyphenyl)(1-(2-morpholinoethyl)-1H-indol-3-yl)methanone (21)

Following General Procedure C: Chamber A: Cycloadduct 5b (552 mg, 1.263 mmol) was added, followed by 1,4-dioxane (4 mL). In Chamber B: 4-(2-(3-iodo-1H-indol-1-yl)ethyl)morpholine (150 mg, 0.421 mmol) in 0.2 mL anisole, (4-methoxyphenyl)boronic acid (77 mg, 0.505 mmol), K₂CO₃ (175 mg, 1.263 mmol) and Pd₂(dba)₃ (7.71 mg, 8.42 µmol) were added, followed by anisole (3.8 mL). The system was flushed with argon then Et₃N (0.205 mL, 1.474 mmol) was added to Chamber A, the system was then sealed with screwcaps fitted with silicon seals. The system was allowed to stir for 30 min to release CO before being heated to 80 °C for 25 h. The reaction mixtures were cooled to rt and the solvent in Chamber B concentrated in vacuo. The crude product was purified by silica column chromatography (CHCl₃: EtOAc 2:1 - 1:2) to afford the title compound 21 (65.4 mg, 43%) as a pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 2.51 (t, J = 4.4 Hz, 4H), 2.79 (d, J = 6.3 Hz, 2H), 3.71 (t, J = 4.8 Hz, 2H), 3.90 (s, 3H), 4.27 (d, J = 6.6 Hz, 2H), 6.99 (d, J = 8.7 Hz, 2H), 7.29 - 7.37 (m, 2H), 7.40 (m, 1H), 7.70 (s, 1H), 7.85 (d, J = 8.7 Hz, 2H), 8.35 - 8.43 (m, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 44.2, 53.8, 55.6, 57.8, 66.9, 109.6, 113.6, 115.9, 122.6, 122.9, 123.6, 127.5, 131.1, 133.5, 136.8, 137.0, 162.4, 189.9; ν max (cm⁻¹) 2850 (C-H), 1598 (C=O), 1252 (C-N); HRMS-ESI m/z [M+H]+ calc. for C₂₂H₂₅N₂O₃+: 365.1860; found: 365.1837.

(1-(2-morpholinoethyl)-1H-indol-3-yl)(naphthalen-1-yl)methanone (22)

Following General Procedure C: Chamber A: Cycloadduct 5b (552 mg, 1.263 mmol) was added, followed by 1,4-dioxane (4 mL). In Chamber B: 4-(2-(3-iodo-1H-indol-1-yl)ethyl)morpholine (150 mg, 0.421 mmol), naphthalen-1-ylboronic acid (87 mg, 0.505 mmol), K₂CO₃ (175 mg, 1.263 mmol) and Pd₂(dba)₃ (7.71 mg, 8.42 µmol) were added, followed by anisole (4 mL). The system was flushed with argon then Et₃N (0.205 mL, 1.474 mmol) was added to Chamber A, the system was then sealed with screwcaps fitted with silicon seals. The system was allowed to stir for 30 min to release CO before being heated to 80 °C for 30 h. The reaction mixtures were cooled to rt and the solvent in Chamber B concentrated in vacuo. The crude product was purified by silica column chromatography (CHCl₃: EtOAc 2:1 - 1:2) to afford the title compound 22 as a 3:1 mixture of product to the non-carbonylative Suzuki side product (101.5 mg, 63%). ¹H NMR (400 MHz, CDCl₃) δ 3.04 (s, 4H), 3.29 (t, J = 7.1 Hz, 2H), 3.90 (t, J = 4.7 Hz, 4H), 4.57 - 4.66 (m, 2H), 7.36 - 7.57 (m, 6H), 7.64 (d, J = 7.5 Hz, 1H), 7.91 (d, J = 7.5 Hz, 1H), 7.98 (d, J = 8.2 Hz, 1H), 8.14 (d, J = 8.5 Hz, 1H), 8.45 - 8.52 (m,
1H), $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 41.5, 52.7, 56.1, 64.1, 109.5, 119.2, 123.5, 123.8, 124.7, 124.8, 125.8, 126.1, 126.5, 127.07, 127.11, 128.5, 130.6, 130.7, 133.9, 135.6, 137.3, 138.5, 192.3; $\nu_{\text{max}}$ (cm$^{-1}$) 1672 (C=O), 1196 (C-N stretch), 1133 (C-O-C); HRMS-ESI m/z [M+H]$^+$ calc. for C$_{21}$H$_{25}$N$_2$O$_2^+$: 385.1911, found: 358.1882.
2,5-Dimethyl-3,4-diphenylcyclopentadien-1-one (diene dimer) (3) (400 MHz, CDCl₃)
**N-Phenyl-3-bromomaleimide (4a)** (400 MHz, CDCl$_3$)

![N-Phenyl-3-bromomaleimide (4a) (400 MHz, CDCl$_3$)](image1)

(100 MHz, CDCl$_3$)

![N-Phenyl-3-bromomaleimide (4a) (100 MHz, CDCl$_3$)](image2)
3a-Bromo-3a,4,7,7a-tetrahydro-4,7-dimethyl-2,5,6-triphenyl-4,7-methano-1H-isoindole-1,3,8(2H)-trione endo (5a) (500 MHz, CDCl₃)

(125 MHz, CDCl₃)
3a,4,7,7a-Tetrahydro-7a-bromo-4,7-dimethyl-5,6-diphenyl-4,7-methanoisobenzofuran-1,3,8-trione (5b) (400 MHz, CDCl$_3$)

(100 MHz, CDCl$_3$)
4,7-Dimethyl-5,6-diphenyl-1,3-isobenzofurandione (9) (400 MHz, CDCl$_3$)

(100 MHz, CDCl$_3$)
Diethyl 3,6-dimethyl-4,5-diphenylphthalate (12) (400 MHz, CDCl₃)

(100 MHz, CDCl₃)
$N$-butyl-4-methoxybenzamide (8a) (400 MHz, CDCl$_3$)

(100 MHz, CDCl$_3$)
N-butyl-4-nitrobenzamide (8b) (400 MHz, CDCl₃)
(100 MHz, CDCl₃)

4-bromo-N-butylbenzamide (8c) (400 MHz, CDCl₃)
"N-butylbenzamide (8d) (400 MHz, CDCl₃)"
(100 MHz, CDCl₃)

N-butyl-1-naphthamide (8e) (400 MHz, CDCl₃)
(100 MHz, CDCl₃)

(4-methoxyphenyl)(morpholino)methanone (10a) (400 MHz, CDCl₃)
Morpholino(4-nitrophenyl)methanone (10b) (400 MHz, CDCl₃)
(100 MHz, CDCl$_3$)

(4-bromophenyl)(morpholino)methanone (10c) (400 MHZ, CDCl$_3$)
(100 MHz, CDCl₃)
Morpholino(phenyl)methanone (10d) (400 MHz, CDCl₃)

(100 MHz, CDCl₃)
Morpholino(naphthalen-1-yl)methanone (10e) (400 MHz, CDCl₃)

(100 MHz, CDCl₃)
N-butyl-2-(4-methoxyphenyl)-2-oxoacetamide (13) (400 MHz, CDCl₃)

(100 MHz, CDCl₃)
(4-methoxyphenyl)(phenyl)methanone (15a) (400 MHz, CDCl₃)

(100 MHz, CDCl₃)
Benzophenone (15b) (400 MHz, CDCl₃)

\[
\begin{align*}
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\end{align*}
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(100 MHz, CDCl₃)
(4’-chlorophenyl)(4-methoxyphenyl)methanone (15c) (400 MHz, CDCl₃)

(100 MHz, CDCl₃)
Ethyl 2-(4-iodophenoxy)acetate (6f) (400 MHz, CDCl$_3$)

(100 MHz, CDCl$_3$)
Ethyl 2-(4-(4-chlorobenzoyl)phenoxy)acetate (15d) (400 MHz, CDCl₃)

(100 MHz, CDCl₃)
Isopropyl 2-(4-iodophenoxy)-2-methylpropanoate (6g) (400 MHz, CDCl₃)

(100 MHz, CDCl₃)
Isopropyl 2-(4-(4-chlorobenzoyl)phenoxy)-2-methylpropanoate (15e) (400 MHz, CDCl$_3$)

(100 MHz, CDCl$_3$)
3-iodo-1H-indole (16) (400 MHz, CDCl₃)
1H-indol-3-ylphenylmethanone (17) (400 MHz, CDCl$_3$)

(100 MHz, CDCl$_3$)
(1H-indol-3-yl)(naphthalen-2-yl)methanone (18) (400 MHz, CDCl₃)

(100 MHz, CDCl₃)
4-(2-(3-iodo-1H-indol-1-yl)ethyl)morpholine (20) (400 MHz, CDCl₃)

(100 MHz, CDCl₃)
(4-methoxyphenyl)(1-(2-morpholinoethyl)-1H-indol-3-yl)methanone (21) (400 MHz, CDCl₃)

(100 MHz, CDCl₃)
(1-(2-morpholinoethyl)-1H-indol-3-yl)(naphthalen-1-yl)methanone (22) (400 MHz, CDCl₃)

(100 MHz, CDCl₃)
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