Nickel-Catalyzed Reductive Cross-Coupling of Aryl Halides with Alkyl Halides

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Supporting Information

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I. General Chemicals.

$\text{NiI}_2 \cdot x\text{H}_2\text{O}$ ($x = 3.5$ by elemental analysis), $\text{Ni}(\text{cod})_2$ and 1,2-bis(diphenylphosphino)benzene were purchased from Strem Chemicals and used as received. $\text{NiCl}_2(\text{dme})$ was either purchased from Strem or made according to the literature procedure.¹ It is important to note that the stoichiometry of both NiI_2 hydrate and $\text{NiCl}_2(\text{dme})$ are variable (our $\text{NiCl}_2(\text{dme})$ varied from 0.1 to 0.7 dme and the dme is easily lost upon exposure to vacuum). We found that *excess nickel is not detrimental to the isolated yield of product*, but we obtained lower yields in reactions employing excess ligands. Therefore, we employed slight excess (0.107 equiv $[\text{Ni}]$ to 0.100 mol% $[\text{ligands}]$) in our reactions to account for the variable nickel stoichiometry.

4,4'-Di-*tert*-butyl-2,2'-dipyridyl, manganese powder (325 mesh), anhydrous pyridine, dichloromethane, DMF, pinacol, di-*tert*-butyl dicarbonate, benzyl chloroformate, thionyl chloride and acetic anhydride were purchased from Aldrich and used as received.

DMPU (1,3-Dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone, absolute, over molecular sieve ($\text{H}_2\text{O} \leq 0.03\%$), $\geq 99.0\%$ (GC) was purchased from Aldrich and sparged with nitrogen after use for ~ 30 seconds. Although sequential drying of DMPU over 4 Å molecular sieve before use could reduce water content to as low as 16 ppm, successful reactions were observed in DMPU containing as much as 1000 ppm water. All other dry solvents were prepared from ACS grade, inhibitor free solvents by passage through activated alumina and molecular sieves in a Vacuum Atmospheres solvent purification system. Water content was routinely measured using Karl-Fisher titration (Metrohm) and was less than 30 ppm in all cases.

Iodobenzene, 4'-iodoacetophenone, 4-iodoanisole, 2-bromotoluene, 4-iodobenzonitrile, ethyl-4-bromobutyrate, 4-iodobenzoic acid, 3-bromopropylamine hydrobromide, 5-bromoindole, 2-bromoheptane (technical grade), 5-bromo-2-methyl-2-pentene, and 4-bromophenylboronic acid were purchased from Aldrich and used without further purification. 4-iodobenzotrifluoride, and *neo*-pentyl iodide, were purchased from Aldrich and filtered through a short pad of activated basic alumina (1.5 cm) under nitrogen before use. 3-bromopropyl-carbamic acid *tert*-butyl ester [83948-53-2],² (3-bromopropyl)carbamic acid benzyl ester [39945-54-5],³ *p*-bromophenylboronic pinacol ester,⁴ and *N*-acetyl-5-bromoindole⁵ were synthesized according to the literature procedures and spectral data were in agreement with the reported values. Organic iodides that had been stored on the bench for long periods of time did not always provide consistently high results. In these cases, filtration of the organic iodide through basic alumina or silica gel provided material that could again be coupled in high yield.

Methods.

NMR chemical shifts are reported in ppm and referenced to the residual solvent peak CDCl_3 ($\delta = 7.26$ ppm ^1H or $\delta = 77.16$ ppm ^{13}C) as an internal standard and trifluorotoluene ($\delta = 0.000$ ppm) as an external standard (^{19}F). NMR spectra were recorded on Bruker model Avance NMR spectrometer operating at 400.13 MHz or 500.13 MHz proton NMR frequency, and data analysis was performed using the iNMR software package (version 3.1.5).

GC analyses were performed on an Agilent 7890A GC equipped with dual DB-5 columns (20 m x 180 μm x 0.18 μm), dual FID detectors and using hydrogen as the carrier gas. The

analysis method used in all cases was 1 μL inj. of sample, inj. temp of 300 $^{\circ}\text{C}$, 100:1 split ratio, initial inlet pressure was 20.3 psi but varied as the column flow was held constant at 1.8 mL/min for the duration of the run. Initial oven temperature of 50 $^{\circ}\text{C}$ was held for 0.46 min followed by a temperature ramp up to 300 $^{\circ}\text{C}$ at 65 $^{\circ}\text{C}/\text{min}$ and finally the temperature was held at 300 $^{\circ}\text{C}$ for 0.69 min. Total run time was ~ 5 min. FID temperature was 325 $^{\circ}\text{C}$.

GC/MS analyses were performed on a Shimadzu GCMS-QP2010 equipped with an RTX-XLB column (30 m x 0.25 mm x 0.28 μm) with a quadrupole mass analyzer using helium as the carrier gas. The analysis method used in all cases was 5 μL inj. of sample, inj. temp of 225 $^{\circ}\text{C}$, 25:1 split ratio, initial inlet pressure was 7.8 psi, but varied as the column flow was held constant at 1.0 mL/min for the duration of the run, the interface temperature was held at 250 $^{\circ}\text{C}$, and the ion source (EI, 30 eV) was held at 250 $^{\circ}\text{C}$. Initial oven temperature was held at 50 $^{\circ}\text{C}$ for 3 min with the detector off followed by a temperature ramp, with the detector on, to 280 $^{\circ}\text{C}$ at 40 $^{\circ}\text{C}/\text{min}$, and finally the temperature was held at 280 $^{\circ}\text{C}$ for 3 min. Total run time was 11.75 min.

Chromatography was performed on silica gel (EMD, silica gel 60, particle size 0.040-0.063 mm) using standard flash techniques or on a Biotage Isolera One (KP-SIL 50 g Biotage snap cartridge with samplet, 40 mL/min flow rate, detection at 254 nm and 280 nm). Products were visualized by one of the following methods: UV stain, ninhydrin stain, KMnO_4 stain or by GC.

Elemental Analyses were performed by Robertson Microlit Laboratories, Inc. (Madison, NJ).

II. Optimization and Control Reactions

Typical procedure for optimization screens and control reactions. Reactions were set up in a nitrogen filled glove box. To an oven-dried 1-dram vial containing a teflon-coated stir-bar was added the required amount of appropriate catalyst and ligand(s) followed by DMPU (2 mL), pyridine (if used), organohalide(s) (0.500 mmol each), Mn^0 (2.00 equiv), and dodecane (10.0 μL internal standard). The reaction vials were capped with a PTFE-faced silicone septum, removed from the glove box and heated in a reaction block on the benchtop. After 15-24 h reaction time, 50 μL aliquots of reaction mixture were removed with a 50 μL gas-tight syringe and quenched with 50 μL of 1 M aqueous NaHSO_4 , diluted with ethyl ether or ethyl acetate (1 mL), and filtered through a short silica pad (1.5 cm) in a pipette packed with glass wool. The filtrate was analyzed by gas chromatography and percent yield or percent conversion based on unreacted starting material were calculated.

Table S1: Direct Insertion of Mn^0 .

R = C_8H_{17} or Ph

Substrate	T ($^\circ\text{C}$)	Consumption of RI (%) ^{a,b}
$\text{C}_8\text{H}_{17}\text{-I}$	60	0
$\text{C}_8\text{H}_{17}\text{-I}$	80	19
Ph-I	60	0
Ph-I	80	0

^a Based on unreacted iodide (corrected vs. dodecane). ^b Catalytic cross coupling of Ph-I and $\text{C}_8\text{H}_{17}\text{-I}$ is complete in 3 hours

Table S2: Direct Insertion of Mn^0 in the Presence of Pyridine.

R = C_8H_{17} or Ph

Substrate	T ($^\circ\text{C}$)	Consumption of RI (%) ^{a,b}
$\text{C}_8\text{H}_{17}\text{-I}$	60	9
$\text{C}_8\text{H}_{17}\text{-I}$	80	59
Ph-I	60	0
Ph-I	80	0

^a Based on unreacted iodide (corrected vs. dodecane). ^b Catalytic cross coupling of Ph-I and $\text{C}_8\text{H}_{17}\text{-I}$ is complete in 3 hours

Table S3: Solvent Effect.

Solvent	Yield (%) ^a
DMPU	87
DMAc	71
NMP	64
DMF	60
DMI	65
THF	37
Toluene	trace
DCM	trace
DMSO	19

^a GC yield corrected vs. dodecane internal standard after 14 h reaction time.
 Reaction is complete in 14 h.

Table S4: GC Product Distribution Data for Substrates **3a-p**

Entry	Product	3 ^a (% yield)	3 ^b (A%)	Biaryl ^b (A%)	β-Hydride Elimination ^b (A%)	Bialkyl ^b (A%)	Reduced Arene ^b (A%)
1	3a	77	82	4	5	0	4
2	3b	75	75	7	6	1	1
3	3c	75	63	11	2	0.5	2
4	3d	69	72	7	2	0.5	5
5 ^d	3e	55	48	ND ^c	6	0	ND ^c
6	3f	82	88	ND ^c	2	1	ND ^c
7	3g	82	63	ND ^c	4	2	ND ^c
8	3h	78	73	ND ^c	0	3	ND ^c
9	3i	77	91	ND ^c	0	0.5	ND ^c
10	3j	77	61	6	4	18	5
11	3k	85	87	3	3	1	2
12	3l	65	44	5	ND ^c	13	2
13	3m	64	62	12	ND ^c	6	2
14	3n	75	73	ND ^c	0	6	3
15	3o	38	56	19	0	0	3
16	3p	88	64	0.5	5	3	5

^a Isolated yield of purified product, average of two runs. ^b Area percent determined by GC from crude reaction mixtures, average of two runs. In cases where the A% is 0, a peak of <0.5 A% is present or no peak is observed and the retention time of the compound is known. ^c Not detected by GC analysis. No assignable peak and retention time of compound is unknown. ^d Data from run 1 only, no final data point collected for run 2.

Table S5: Substrate scope using a single ligand (**1**) *versus* a combination of ligands **1** and **2**.^a

1

2

Entry	Product	X ¹	X ²	T (°C)	Yield (%) ^b Ligand (1)	Yield (%) ^c Ligands (1) and (2)	
1	R = OMe	3b	I	I	80	70	75
2	R = CF ₃	3c	I	I	80	60	75
3	R = C(O)Me	3d	I	I	80	54	69
4	R =	3f	Br	I	60	74	82
5		3g	Br	I	80	62	82
6		3i	Br	I	60	83	77
7 ^d		3j	I	Br	80	57	64
8		3o	I	I	80	29	38

^a Organohalides (1.00 mmol each), 0.107 mmol NiI₂·xH₂O, 0.100 mmol ligand(s), 0.099 mmol pyridine, 2.00 mmol Mn⁰ powder, and 4 mL of DMPU are heated for 3-21 hours, ^b Isolated yield of purified product using only 4,4'-di-*t*-butylbipyridine **1** (0.100 mmol), ^c Isolated yield of purified product using 0.0499 mmol 4,4'-di-*t*-butylbipyridine (**1**) and 0.0499 mmol 1,2-Bis(diphenylphosphino)benzene (**2**). Average of two runs, ^d Longer reaction time required (37 h).

III. Preparation of Organohalides

4-iodo(phenyl)methanol [CAS: 18282-51-4].⁶ To a stirred suspension of 4-iodobenzoic acid (5.00 g, 20.0 mmol, 1.00 equiv) in dichloromethane (65 mL) was added thionyl chloride (13 mL, 179 mmol, 9.0 equiv) before heating to 70 °C overnight. The resulting pale yellow solution was evaporated to dryness under reduced pressure to afford a pale yellow solid. The pale yellow solid, 4-iodobenzoyl chloride, was dissolved in 30 mL dioxane, and added dropwise to a stirred suspension of sodium borohydride (1.5 g, 40 mmol, 2.0 equiv) in dioxane (30 mL) at 0 °C over 25 min. The resulting mixture was heated to 100 °C for 90 min, then cooled to room temperature. Finally, H₂O (30 mL) was added slowly. **Caution: Evolves Hydrogen Gas!** The mixture was extracted with dichloromethane (3 x 50 mL). Organic layers were combined, washed with H₂O (2 x 50 mL), HCl (1N, 2 x 50 mL), NaOH (1N, 2 x 50 mL), H₂O (1 x 50 mL), and brine (1 x 50 mL), dried over MgSO₄, filtered and evaporated under reduced pressure to give a white powder (4.54 g, 97% two steps).

¹H NMR (400 MHz, CDCl₃) δ 7.69 (d, *J* = 8.3 Hz, 2H), 7.11 (d, *J* = 8.3 Hz, 2H), 4.64 (d, *J* = 5.2 Hz, 2H), 1.73 (t, *J* = 5.5 Hz, 1H).

¹³C NMR (100 MHz, CDCl₃) δ 140.6, 137.8, 128.9, 93.1, 64.8.

GC-MS *m/z* (% relative intensity, ion): 234.85 (1.900, M⁺), 107.05 (31.30, M⁺ - I), 79.00 (100.0, M⁺ - CHIO).

NOTE: Long-term storage of 4-iodo(phenyl)methanol on benchtop resulted in diminished yields of reductive coupling reactions with the reagent. Purification of the compound immediately before use helped to observe reproducible results with reductive coupling reactions (**Table 1, entry 8**). The product could be purified passing through a short silica gel column (hexanes: ethyl acetate 80:20).

IV. Reductive Cross-Coupling Reactions

General procedure for preparative reactions (Table 1).

On the benchtop, NiI₂·xH₂O (*x* = 3.5, MW = 375.56, 40.3 mg, 0.107 mmol, 0.107 equiv), 1,2-bis(diphenylphosphino)benzene (22.3 mg, 0.0499 mmol, 0.0499 equiv), 4,4'-di-*tert*-butyl-2,2'-dipyridyl (13.4 mg, 0.0499 mmol, 0.0499 equiv), and solid substrates (1.00 mmol, 1.00 equiv) were weighed on weigh paper and transferred to a flame dried 10 mL Schlenk flask equipped with a magnetic stir bar. The flask was then capped with a rubber septum and purged with N₂ gas (~ 30 sec.). DMPU (4 mL), pyridine (8.0 μL, 0.099 mmol, 0.099 equiv), and liquid substrates (1.00 mmol, 1.00 equiv) were injected into the flask. The generally deep purple solution was sparged with N₂ gas (~ 30 - 60 sec.), and manganese powder (110 mg, 2.00 mmol, 2.00 equiv) was added. The reaction flask was placed in a 60 or 80 °C oil bath and stirred under positive pressure of nitrogen.

The reaction progress was followed by GC analysis. At appropriate times 50 μL aliquots of reaction mixture were removed with a 50 μL gas-tight syringe and quenched with 50 μL of 1 M aqueous NaHSO₄, diluted with ethyl ether or ethyl acetate (1 mL), and filtered through a short

silica pad (1.5 cm) in a pipette packed with glass wool. The filtrate was analyzed by gas chromatography.

The reactions generally turn from orange/brown to black when complete (Figure S1). Upon completion (judged as <1 Area % of starting materials remaining by GC analysis) the reaction mixture was filtered through a short plug of silica gel to remove metal salts and DMPU, eluted with diethyl ether, and concentrated under reduced pressure followed by purification on a silica gel. Alternatively, the entire reaction mixture was loaded onto a silica gel column for purification. Column fractions were analyzed by GC for compounds **3a**, **3l-3p** and by TLC for compounds **3b-3k**. The compounds on TLC were visualized using KMnO_4 stain for **3g** and **3h**, ninhydrin stain for **3k** and iodine for compounds **3b-3f**, **3i**, and **3j**.

Figure S1. Reaction completion is accompanied by color change from orange (left) to black (right).

1-octylbenzene (3a) (Table 1, entry 1) [CAS: 2189-60-8].⁶ The general procedure was followed with iodobenzene (112 μ L, 1.00 mmol, 1.00 equiv) and 1-iodooctane (181 μ L, 1.00 mmol, 1.00 equiv) at 80 °C for 3 h. The product was isolated by chromatography (pentane) as a colorless oil. First run 146 mg (77%). Second run 146 mg (77%).

¹H NMR (500 MHz, CDCl₃) δ 7.36-7.23 (m, 5H), 2.68 (t, J = 8.4 Hz, 2H), 1.72-1.66 (m, 2H), 1.39-1.35 (m, 10H), 0.97 (t, J = 6.6 Hz, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 143.0, 128.5, 128.4, 125.7, 36.2, 32.1, 31.7, 29.7, 29.6, 29.5, 22.9, 14.3.

GC-MS m/z GC-MS m/z (% relative intensity, ion): 190.15 (14.30, M⁺), 92.00 (100.0, M⁺⁺- C₇H₁₄), 91.00 (67.20, M⁺- C₇H₁₅)

1-methoxy-4-octylbenzene (3b) (Table 1, entry 2) [CAS: 3307-19-5].⁷ The general procedure was followed with 4-iodoanisole (234 mg, 1.00 mmol, 1.00 equiv) and 1-iodooctane (181 μ L, 1.00 mmol, 1.00 equiv) at 80 °C for 15 h. The product was isolated by chromatography (90:10 pentane:ether) as colorless oil. First run 170 mg (77%). Second run 160 mg (72%).

¹H NMR (500 MHz, CDCl₃) δ 7.09 (d, J = 8.6 Hz, 2H), 6.83 (d, J = 8.6 Hz, 2H), 3.79 (s, 3H), 2.55 (t, J = 7.5 Hz, 2H), 1.62-1.55 (m, 2H), 1.33-1.28 (m, 10H), 0.89 (t, J = 6.7 Hz, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 157.8, 135.2, 129.4, 113.8, 55.4, 35.2, 32.1, 31.9, 29.9, 29.7, 29.4, 22.8, 14.3.

GC-MS m/z (% relative intensity, ion): 220.10 (10.70, M⁺), 121.05 (100.0, M⁺- C₇H₁₅).

1-(trifluoromethyl)-4-octylbenzene. (3c) (Table 1, entry 3). The general procedure was followed with 4-iodobenzotrifluoride (147 μ L, 1.00 mmol, 1.00 equiv) and 1-iodooctane (181 μ L, 1.00 mmol, 1.00 equiv) at 80 °C for 19 h. The product was isolated by chromatography (hexanes) as pale yellow oil. First run 180 mg (70%). Second run 204 mg (79%).

¹H NMR (500 MHz, CDCl₃) δ 7.55 (d, J = 8.1 Hz, 2H), 7.30 (d, J = 8.1 Hz, 2H), 2.68 (t, J = 7.6 Hz, 2H), 1.68-1.62 (m, 2H), 1.34-1.30 (m, 10H), 0.91 (t, J = 6.8 Hz, 3H)

¹³C NMR (125 MHz, CDCl₃) δ 147.2, 128.8, 128.4 (q, J = 32.0 Hz), 125.3 (q, J = 3.8 Hz), 124.6 (q, J = 217.7 Hz), 36.0, 32.1, 31.4, 29.9, 29.6, 29.4, 22.9, 14.2.

¹⁹F NMR (375 MHz, C₆D₆) δ 0.567

GC-MS m/z (% relative intensity, ion): 258.05 (19.90, M⁺), 160.15 (100.0, M⁺- C₇H₁₄), 91.00 (19.80, M⁺- C₈H₁₅F₃).

1-(4-octylphenyl)ethanone (3d) (Table 1, entry 4) [CAS: 10541-56-7].⁸ The general procedure was followed and the reaction was run with 4'-iodoacetophenone (246 mg, 1.00 mmol, 1.00

equiv) and 1-iodooctane (181 μ L, 1.00 mmol, 1.00 equiv) at 80 °C for 8 h. The product was isolated by chromatography (80:20 pentane:ether) as pale yellow oil. First run 158 mg (68%). Second run 159 mg (69%).

^1H NMR (500 MHz, CDCl_3) δ 7.88 (d, J = 8.2 Hz, 2H), 7.26 (d, J = 8.2 Hz, 2H), 2.66 (t, J = 7.5 Hz, 2H), 2.58 s, (3H), 1.62-1.59 (m, 2H), 1.31-1.26 (m, 10H), 0.88 (t, J = 6.6 Hz, 3H).

^{13}C NMR (125 MHz, CDCl_3) δ 197.9, 148.9, 135.0, 128.7, 128.6, 36.1, 32.0, 31.2, 29.5, 29.4, 29.3, 26.6, 22.8, 14.2.

GC-MS m/z (% relative intensity, ion): 232.05 (16.90, M^+), 217.05 (100.0, $\text{M}^+ - \text{CH}_3$), 105.00 (17.70, $\text{M}^+ - \text{C}_9\text{H}_{20}$), 91.00 (23.40, $\text{M}^+ - \text{C}_9\text{H}_{15}\text{O}$).

4-octylbenzonitrile (3e) (Table 1, entry 5).⁹ The general procedure was followed with 4-iodobenzonitrile (229 mg, 1.00 mmol, 1.00 equiv) and 1-iodooctane (181 μ L, 1.00 mmol, 1.00 equiv) at 80 °C for 15 h. The product was isolated by chromatography (80:20 pentane:ether, first run and 90:10 pentane:ether, second run) as faintly yellow oil. First run 138 mg (64%). Second run 101 mg (47%, reaction did not proceed to completion).

^1H NMR (500 MHz, CDCl_3) δ 7.54 (d, J = 8.2 Hz, 2H), 7.26 (d, J = 8.1 Hz, 2H), 2.65 (t, J = 7.6 Hz, 2H), 1.64-1.57 (m, 2H), 1.30-1.25 (m, 10H), 0.87 (t, J = 5.5 Hz, 3H).

^{13}C NMR (125 MHz, CDCl_3) δ 148.7, 132.1, 129.3, 119.2, 109.6, 36.2, 31.9, 31.0, 29.8, 29.4, 29.3, 22.7, 14.2.

GC-MS m/z (% relative intensity, ion): 215.05 (14.30, M^+), 117.05 (100.0, $\text{M}^+ - \text{C}_7\text{H}_{14}$).

4,4,5,5-tetramethyl-2-(4-octylphenyl)-1,2,3-dioxaborolane (3f) (Table 1, entry 6). The general procedure was followed with *p*-bromophenylboronic pinacol ester (283 mg, 1.00 mmol, 1.00 equiv) and 1-iodooctane (181 μ L, 1.00 mmol, 1.00 equiv) at 60 °C for 16 h. The product was isolated by chromatography (hexanes: *tert*-butyl methyl ether 95: 5) as yellow oil. First run 271 mg (86%). Second run 245 mg (78%).

^1H NMR (500 MHz, CDCl_3) δ 7.82 (d, J = 7.9 Hz, 2H), 7.28 (d, J = 7.6 Hz, 2H), 2.70 (t, J = 7.5 Hz, 2H), 1.73-1.68 (m, 2H), 1.43-1.35 (m, 22H), 0.97 (t, J = 7.0 Hz, 3H).

^{13}C NMR (125 MHz, CDCl_3) δ 146.5, 134.9, 128.0, 83.7, 36.3, 32.0, 31.5, 29.9, 29.6, 29.5, 29.4, 25.0, 22.8, 14.2.

GC-MS m/z (% relative intensity, ion): 316.20 (38.50, M^+), 301.20 (37.70, $\text{M}^+ - \text{CH}_3$), 230.10 (100.0, $\text{M}^+ - \text{C}_5\text{H}_{11}\text{O}$), 217.05 (63.29, $\text{M}^+ - \text{C}_7\text{H}_{15}$).

1-methyl-2-octylbenzene (3g) (Table 1, entry 7) [CAS: 79835-99-7]. The general procedure was followed with 2-bromotoluene (120 μ L, 1.00 mmol, 1.00 equiv) and 1-iodooctane (181 μ L,

1.00 mmol, 1.00 equiv) at 80 °C for 15 h. The product was isolated by chromatography (pentane) as colorless oil. First run 162 mg (79%). Second run 169 mg (83%).

^1H NMR (500 MHz, CDCl_3) δ 7.13-7.11 (m, 4H), 2.59 (t, J = 7.8 Hz, 2H), 2.31 (s, 3H), 1.60-1.53 (m, 2H), 1.39-1.28 (m, 10H), 0.89 (t, J = 6.6 Hz, 3H).

^{13}C NMR (125 MHz, CDCl_3) δ 141.3, 135.9, 130.2, 128.9, 126.0, 125.8, 33.5, 32.1, 30.5, 29.9, 29.7, 29.5, 22.9, 19.4, 14.3.

GC-MS m/z (% relative intensity, ion): 204.10 (11.90, M^+), 105.05 (100.0, $\text{M}^+ - \text{C}_7\text{H}_{15}$), 91.00 (9.500, $\text{M}^+ - \text{C}_8\text{H}_{17}$).

(4-octylphenyl)methanol (3h) (Table 1, entry 8) [CAS: 40016-25-9]. The general procedure was followed with 4-iodo(phenyl)methanol (234 mg, 1.00 mmol, 1.00 equiv) and 1-iodooctane (181 μL , 1.00 mmol, 1.00 equiv) at 80 °C for 15 h. The product was isolated by chromatography (50:50 pentane:ether, first run and 80:20 hexanes:EtOAc, second run) as colorless oil. First run 165 mg (75%). Second run 179 mg (81%).

^1H NMR (500 MHz, CDCl_3) δ 7.32 (d, J = 8.0 Hz, 2H), 7.23 (d, J = 8.0 Hz, 2H), 4.68 (s, 2H), 2.67 (t, J = 7.6 Hz, 2H), 2.15 (br s, 1H), 1.69-1.66 (m, 2H), 1.38-1.34 (m, 10H), 0.96 (t, J = 5.0 Hz, 3H).

^{13}C NMR (125 MHz, CDCl_3) δ 142.6, 138.2, 128.7, 127.2, 65.3, 35.8, 32.0, 31.7, 29.6, 29.44, 29.39, 22.8, 14.2.

GC-MS m/z (% relative intensity, ion): 220.05 (19.70, M^+), 121.05 (70.50, $\text{M}^+ - \text{C}_7\text{H}_{15}$), 107.00 (100.0, $\text{M}^+ - \text{C}_8\text{H}_{17}$), 91.00 (41.6, $\text{M}^+ - \text{C}_8\text{H}_{18}\text{O}$).

1-(5-octyl-1H-indol-1-yl)ethanone (3i) (Table 1, entry 9). The reaction was run according to the general procedure except 4,4'-di-*tert*-butyl-2,2'-dipyridyl (26.8 mg, 0.100 mmol, 0.100 equiv) was used and no 1,2-bis(diphenylphosphino)benzene was used. Accordingly, *N*-acetyl-5-bromoindole (239 mg, 1.00 mmol, 1.00 equiv), and 1-iodooctane (181 μL , 1.00 mmol, 1.00 equiv) were heated at 60 °C for 14 h. The product was isolated by chromatography (hexanes:EtOAc 85:15) as yellow oil. First run 227 mg (84%). Second run 189 mg (70%).

^1H NMR (500 MHz, CDCl_3) δ 8.32 (s, br., 1H), 7.39-7.36 (m, 2H), 7.18 (dd, 1H, J = 8.5 Hz and 1.6 Hz), 6.59 (d, J = 3.7 Hz, 1H), 2.70 (t, J = 7.6 Hz, 2H), 2.62 (s, 3H), 1.68-1.62 (m, 2H), 1.34-1.27 (m, 10H), 0.88 (t, J = 7.1 Hz, 3H).

^{13}C NMR (125 MHz, CDCl_3) δ 168.5, 138.6, 134.0, 130.7, 126.0, 125.3, 120.3, 116.3, 109.2, 36.0, 32.1, 32.0, 29.6, 29.44, 29.40, 24.0, 22.8, 14.2.

GC-MS m/z (% relative intensity, ion): 271.10 (14.50, M^+), 229.10 (14.10, $\text{M}^+ - \text{C}_2\text{H}_2\text{O}$), 172.15 (10.50, $\text{M}^+ - \text{C}_7\text{H}_{17}$), 130.10 (100.0, $\text{M}^+ - \text{C}_9\text{H}_{17}\text{O}$).

Ethyl 4-phenylbutanoate (3j) (Table 1, entry 10) [CAS: 10031-93-3].¹⁰ The general procedure was followed with iodobenzene (112 μ L, 1.00 mmol, 1.00 equiv) and ethyl-4-bromobutyrate (145 μ L, 1.00 mmol, 1.00 equiv) at 80 °C for 7 h. The product was isolated by chromatography (80:20 pentane:ether, first run and 95:5 pentane:ether, second run) as colorless oil. First run 162 mg (84%). Second run 135 mg (70%).

¹H NMR (500 MHz, CDCl₃) δ 7.31-7.27 (m, 2H), 7.21-7.18 (m, 3H), 4.13 (q, 2H, J = 7.1 Hz), 2.65 (t, J = 7.4 Hz, 2H), 2.32 (t, J = 7.4 Hz, 2H), 1.99-1.92 (m, 2H), 1.26 (t, J =7.1 Hz, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 173.6, 141.6, 128.6, 128.5, 126.1, 60.4, 35.3, 33.8, 26.7, 14.4.

GC-MS m/z (% relative intensity, ion): 192.10 (21.20, M⁺), 147.10 (42.50, M⁺ - C₂H₅O), 104.00 (90.00, M⁺ - C₄H₈O₂), 91.00 (100.0, M⁺ - C₅H₉O₂).

tert-butyl 3-phenylpropylcarbamate (3k) (Table 1, entry 11) [CAS: 147410-39-7]. The general procedure was followed with iodobenzene (112 μ L, 1.00 mmol, 1.00 equiv) and 3-bromopropyl-carbamic acid *tert*-butyl ester (238 mg, 1.00 mmol, 1.00 equiv) at 60 °C for 16 h. The product was isolated by chromatography (hexanes:EtOAc 1-10% EtOAc) as yellow oil. First run 193 mg (83%). Second run 206 mg (89%).

¹H NMR (500 MHz, CDCl₃) δ 7.36-7.33 (m, 2H), 7.26-7.23 (m, 3H), 4.86 (s, br., 1H), 3.22-3.21 (m, br., 2H), 2.70 (t, J = 7.6 Hz, 2H), 1.90-1.84 (m, 2H), 1.53 (s, 9H).

¹³C NMR (125 MHz, CDCl₃) δ 156.0, 141.6, 128.40, 128.36, 125.9, 19.0, 40.2, 33.1, 31.7, 28.4.

GC-MS m/z (% relative intensity, ion): 179.10 (23.30, M⁺ - C₄H₈+), 118.05 (100.0, M⁺ - C₅H₁₁NO₂), 91.00 (15.70, M⁺ - C₇H₁₄NO₂), 57.00 (77.50, M⁺ - C₁₁H₁₄O₂).

Benzyl 3-phenylpropylcarbamate (3l) (Table 1, entry 12) [CAS: 302569-84-2].¹¹ The general procedure was followed with iodobenzene (112 μ L, 1.00 mmol, 1.00 equiv) and 3-bromopropyl-carbamic acid benzyl ester (272 mg, 1.00 mmol, 1.00 equiv) at 60 °C for 14 h. The product was isolated by chromatography (hexanes:EtOAc 3 – 35% EtOAc) as yellow oil. First run 158 mg (59%). Second run 191 mg (71%).

¹H NMR (400 MHz, CDCl₃) δ 7.38-7.18 (m, 10 H), 5.13 (s, 2H), 4.90 (s, br., 1H), 3.28-3.20 (m, 2H), 2.66 (t, J = 7.7 Hz, 2H), 1.89-1.82 (m, 2H).

¹³C NMR (101 MHz, CDCl₃) δ 156.5, 141.4, 136.6, 128.47, 128.45, 128.4, 128.3, 128.0, 125.9, 66.5, 40.6, 33.0, 31.5.

GC-MS m/z (% relative intensity, ion): 269.10 (0.800, M⁺), 178.15 (30.20, M⁺ - C₇H₇), 91.00 (100.0, M⁺ - C₁₀H₁₂NO₂).

1-(4-methylpent-3-enyl)benzene (3m) (Table 1, entry 13) [CAS: 33501-90-5].¹² The general procedure was followed with iodobenzene (112 μ L, 1.00 mmol, 1.00 equiv) and 5-bromo-2-methyl-2-pentene (133 μ L, 1.00 mmol, 1.00 equiv) at 60 °C for 37 h. The product was isolated by chromatography (hexanes) as yellow oil. First run 111 mg (69%). Second run 93.1 mg (58%).

¹H NMR (400 MHz, CDCl₃) δ 7.40-7.26 (m, 5H), 5.32-5.28 (m, 1H), 2.75 (t, J = 7.5 Hz, 2H), 2.43 (q, J = 7.7 Hz, 2H), 1.81 (s, 3H), 1.68 (s, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 142.5, 132.2, 128.6, 128.3, 125.8, 123.9, 36.3, 30.2, 25.8, 17.8.

GC-MS m/z (% relative intensity, ion): 160.20 (27.30, M⁺), 91.00 (44.40, M⁺-C₅H₉), 69.05 (100.0, M⁺-C₇H₇).

2-ethylhexylbenzene (3n) (Table 1, entry 14).¹³ The general procedure was followed with iodobenzene (112 μ L, 1.00 mmol, 1.00 equiv) and 2-ethylhexylbromide (178 μ L, 1.00 mmol, 1.00 equiv) at 80 °C for 7 h. The product was isolated by preparative TLC (hexanes, R_f = 0.8) as a yellow oil. First run 134 mg (71%). Second run 149 mg (78%).

¹H NMR (400 MHz, CDCl₃) δ 7.39-7.36 (m, 2H), 7.29-7.26 (m, 3H), 2.71-2.62 (m, 2H), 1.75-1.66 (m, 1H), 1.45-1.372 (m, 8H), 1.03-0.99 (m, 6H)

¹³C NMR (101 MHz, CDCl₃) δ 142.0, 129.3, 128.2, 125.6, 41.3, 40.3, 32.5, 29.0, 25.6, 23.2, 14.3, 10.9.

GC-MS m/z (% relative intensity, ion): 190.20 (15.70, M⁺), 98.00 (15.90, M⁺-C₇H₁₄), 91.01 (55.60, M⁺-C₇H₇), 57.02 (100.0, M⁺-C₄H₉)

neo-pentylbenzene (3o) (Table 1, entry 15) [CAS: 1007-26-7].¹⁴ The general procedure was followed with iodobenzene (112 μ L, 1.00 mmol, 1.00 equiv) and neo-pentyl iodide (159 μ L, 1.00 mmol, 1.00 equiv) at 80 °C for 21 h. The product was isolated by chromatography (hexanes) as colorless oil. First run 54 mg (36%). Second run 60 mg (41%).

¹H NMR (400 MHz, CDCl₃) δ 7.33-7.17 (m, 5H), 2.55 (s, 2H), 0.97 (s, 9H).

¹³C NMR (101 MHz, CDCl₃) δ 139.9, 130.6, 127.7, 125.9, 50.4, 31.9, 29.6.

GC-MS m/z (% relative intensity, ion): 148.20 (21.20, M⁺), 133.15 (12.10, M⁺-CH₃), 92.00 (100.0, M⁺-C₄H₈), 57.00 (94.40, M⁺-C₇H₇).

1-(heptan-2-yl)benzene (3p) (Table 1, entry 16) [CAS: 2132-84-5].¹⁵ The general procedure was followed with iodobenzene (112 μ L, 1.00 mmol, 1.00 equiv) and 2-bromoheptane (188 μ L, 1.20 mmol, 1.20 equiv) at 60 °C for 26 h. The product was isolated by chromatography (hexanes)

as colorless oil. First run 152 mg (86%, isolated as a 95:5 mixture with (heptan-3-yl)benzene). Second run 159 mg (90% yield, isolated as a 95:5 mixture with (heptan-3-yl)benzene). Reaction selectivity determined to be 89:7:4 **3p**:branched isomer:linear isomer by GC analysis of the crude reaction mixture.

¹H NMR (400 MHz, CDCl₃) δ 7.42-7.26 (m, 5H), 2.86-2.77 (m, 1H), 1.74-1.69 (m, 2H), 1.39-1.37 (m, 9H), 1.00 (t, *J* = 6.7 Hz, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 148.1, 128.4, 127.1, 125.9, 40.2, 38.6, 32.2, 27.6, 22.8, 22.5, 14.2.

GC-MS *m/z* (% relative intensity, ion): 176.20 (8.8, M⁺), 105.00 (100.0, M⁺ - C₅H₁₁), 91.00 (9.9, M⁺ - C₆H₁₄).

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S16

S17

S18

3a

S19

3a

S20

S21

S22

3c

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7.260

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0.913
0.898

S23

3c

S24

3c

-0.567

S25

7.888
7.868

7.273
7.260
7.252

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1.604
1.593
1.312
1.308
1.302
1.282
1.275
1.261
0.893
0.876
0.858

3d

S26

3d

S27

3e

S28

3e

S29

7.829
7.814

7.283
7.268

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2.697
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0.952

3f

S30

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3f

S31

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3g

S32

3g

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S33

3h

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S34

3h

S35

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S36

S37

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S38

3j

S39

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3k

S40

3k

S41

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3l

S42

3l

S43

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3m

S44

3m

S45

3n

S46

S47

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1.91

9

S48

S49

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3p

S50

3p