

Supporting Information:

Functional Group Tolerant Kumada-Corriu-Tamao Coupling of Non-activated Alkyl Halides with Aryl and Heteroaryl Nucleophiles: Catalysis by a Nickel Pincer Complex Permits the Coupling of Functionalized Grignard Reagents

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Additional Experimental Details

Chemicals and Reagents

The following starting materials in **Tables 3-5** were prepared according to literature procedures: 5-iodopentanenitrile (entry **1**),¹ [(3-bromopropyl)sulfanyl]benzene (entry **5**),² 2-(3-iodopropyl)furan (entry **13**),³ 1-(3-iodopropyl)-3-methyl-1*H*-indole (entry **14**), methyl 1-(3-iodopropyl)-1*H*-indole-3-carboxylate (entry **15**) and 1-[1-(3-iodopropyl)-1*H*-pyrrol-2-yl]ethanone (entry **16**),⁴ ethyl 4-iodobutanoate (entry **17**),⁵ *tert*-butyl 4-iodopiperidine-1-carboxylate (entry **19**),⁶ 4-iodo-2-phenyltetrahydro-2*H*-pyran (table **4**, entry **20**) and 2-(4-bromophenyl)-4-iodotetrahydro-2*H*-pyran (entry **20**),⁷ 4-iodo-1-phenylbutan-1-one (entry **21**).⁸ The following starting materials for Grignard formation were prepared according to literature procedures: N,N-diethyl-4-iodobenzamide **4b** and (4-ethylpiperazin-1-yl)(4-iodophenyl)methanone **4e**,⁹ dimethyl 5-iodoisophthalate **4c**,¹⁰ 2-chloro-5-iodothiophene (table **5**, entry **5**),¹¹ 4-iodo-1-methyl-1*H*-pyrazole **5d**.¹²

¹ K. Yasui, K. Fugami, S. Tanaka, and Y. Tamaru, *J. Org. Chem.* **1995**, 60 (5), 1365-1380.

² X. Zhou, R. G. Carter, *Angew. Chem., Int. Ed.* **2006**, 45(11), 1787-1790.

³ G. Gomez, H. Rivera, I. Garcia, L. Estevez, Y. Fall, *Tetrahedron Letters* **2005**, 46(35), 5819-5822.

⁴ D. R. Artis, I. Cho, S. Jaime-Figueroa, J. M. Muchowski, *J. Org. Chem.* **1994**, 59 (9), 2456-2466.

⁵ S. M. Sparks, C. P. Chow, L. Zhu, and K. J. Shea, *J. Org. Chem.* **2004**, 69 (9), 3025-3035.

⁶ E. G. Corley, K. Conrad, J. A. Murry, C. Savarin, J. Holko, G. Boice, *J. Org. Chem.*, **2004**, 69 (15), 5120-5123.

⁷ G. Sabitha, K. B. Reddy, G. S. Reddy, N. Fatima, J. S. Yadav, *Synlett* **2005**, No. 15, 2347-2351.

⁸ R. Giovannini, T. Stdemann, A. Devasagayaraj, G. Dussin, P. Knochel, *J. Org. Chem.* **1999**, 64 (10), 3544-3553.

⁹ PCT Int. Appl., 2006014133, 09 Feb 2006.

¹⁰ M. Mazik, and A. Knig, *J. Org. Chem.* **2006**, 71 (20), 7854-7857.

¹¹ O. Bayh et al., *Tetrahedron* **2005**, 61, 4779-4784.

¹² M. M. Kim, R. T. Ruck, D. Zhao, M. A. Huffman, *Tetrahedron Letters* **2008**, 49, 4026-4028.

Additional Entries for Table 1

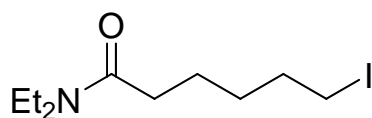
Table 1. Kumada-Corriu-Tamao Coupling of Octyl Bromide with PhMgCl.^a

Octyl-Br + PhMgCl $\xrightarrow[\text{conditions}]{\text{cat. 1}}$ Octyl-Ph

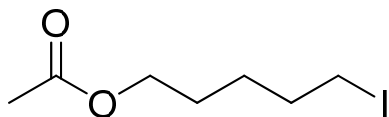
Entry	Solvent	Cat. (mol%)	T (°C)	Additive	Yield (%) ^b
1	DMA	9	0	-	30
2	DMA	9	20	-	42
3	NMP	9	-35	-	46
4	DMF	9	-35	-	0
5	THF	9	-35	-	13
6	DMA+THF (2:1)	9	-35	-	41
7	DMA	9	-30	1 equiv. TMEDA	20
8	THF	9	-30	1 equiv. TMEDA	43
9	THF	5	20	1 equiv. NEt ₃	34
10	THF	5	20	1 equiv. NEt ⁱ Pr ₂	31
11	THF	5	20	1 equiv. HMTA	59
12	THF	3	20	0.3 equiv. TMEDA	86
13	THF	3	20	0.1 equiv. TMEDA	90

^a 0.6 mmol (1.2 equivalent) of PhMgCl in THF (3 mL, 2 M) was added dropwise via a syringe pump (1h) to a solution (1 mL) of **1** and octyl-Br (0.5 mmol) according to the conditions specified in Table 1. The reaction time was 30 minutes to 1 hour. ^b GC yields relative to the organic halides.

Synthesis of substrates



N,N-diethyl-6-iodohexanamide was synthesized from N,N-diethyl-6-bromohexanamide¹³ by the same method as for 4-iodo-1-phenylbutan-1-one (table 3, entry 21). ¹H NMR (400MHz, CDCl₃): 3.30 (q, *J* = 7.3 Hz, 2H), 3.24 (q, *J* = 7.0 Hz, 2H), 3.14 (t, *J* = 7.0 Hz, 2H), 2.24 (t, *J* = 7.3 Hz, 2H), 1.79 (m, 2H), 1.61 (m, 2H), 1.38 (m, 2H), 1.11 (t, *J* = 7.3 Hz, 3H), 1.04 (t, *J* = 7.0 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): 171.5, 41.7, 39.9, 33.1, 32.6, 30.1, 24.1, 14.2, 12.9, 6.7. HRCI-MS: calculated for (C₁₀H₂₀NOI, M+H), 298.0668; found, 298.0669.



5-iodopentyl acetate was synthesized from 5-bromopentyl acetate by the same method as for 4-iodo-1-phenylbutan-1-one (table 3, entry 21). ¹H NMR (400MHz, CDCl₃): 4.01 (t, *J* = 6.7 Hz, 2H), 3.14 (t, *J* = 6.7 Hz, 2H), 2.00 (s, 3H), 1.80 (m, 2H), 1.60 (m, 2H), 1.44 (m, 2H). ¹³C NMR

¹³ J. Zhou, F. C. Fu, *J. Am. Chem. Soc.* **2003**, 125(41), 12527-12530.

(100 MHz, CDCl₃): 170.8, 63.9, 32.8, 27.3, 26.7, 20.8, 6.4. HRCI-MS: calculated for (C₇H₁₃O₂I, M+H), 257.0038; found, 257.0036.

Detailed descriptions for products

Note: For all entries in Tables 3-5 of main text, the coupling products were all isolated and the yields were determined by the masses of the products. Their identification was achieved by one of the following two methods:

Method I. For previously reported or commercially available compounds, their identity and purity were confirmed by comparing their ¹H and/or ¹³C NMR spectra with the reported values. The references to literature data are given.

Method II. For new compounds, their ¹H and ¹³C data are reported together with elemental analysis or high resolution mass spectrometric data (within 5 ppm of calculated value).

Below are the details for the coupling procedure, separation method, spectroscopic and analytical data for all the products

Typical procedure for reactions shown in Table 3

A mixture of an alkyl halide (1 mmol), [(^{Me}NN₂)Ni-Cl] (10.4 mg, 0.03 mmol) and TMEDA (50 μL, 0.34 mmol) or O-TMEDA (114 μL, 0.6 mmol) were dissolved in 2ml of THF (O-TMEDA was used for substrates containing ester or ketone functional group). A solution of an aryl Grignard reagent (1.2 mmol) in 6 mL of THF was added dropwise with a syringe pump (1h) to

the above solution. After the addition was completed, the reaction mixture was stirred for 1h. The reaction was then quenched with a saturated solution of NH_4Cl (30 mL). The resulting solution mixture was then extracted with ether (3 times, 20 mL each), dried over Na_2SO_4 , filtered, and finally evaporated under a reduced pressure. The residue was purified by flash chromatography on silica-gel.

Typical procedure for reactions shown in Tables 4 and 5, including the preparation of functionalized Grignard reagents in situ

Method A

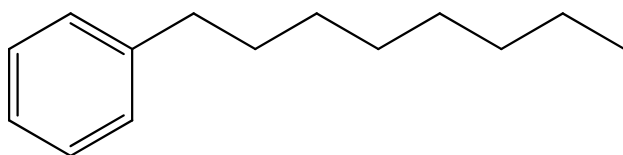
To a solution of O-TMEDA (228 μL , 1.2 mmol) in 6ml of THF was added a 2.0 M solution of $^{i\text{iso}}\text{PrMgCl}$ (600 μL , 1.2 mmol) at 0°C . The mixture was stirred for 20min and a solution of an aryl iodide or aryl bromide (1 mmol) in 2ml of THF was added by one portion. The resulting mixture was stirred at room temperature for 10 min and then is added by syringe pump (1h) to a solution containing an alkyl halide (5 mmol) and $[(^{\text{Me}}\text{NN}_2)\text{Ni-Cl}]$ (10.4 mg, 0.03 mmol) in THF (2 mL). After the addition was completed, the reaction mixture was stirred for 1h. The reaction was then quenched with a saturated solution of NH_4Cl (30 mL). The resulting solution mixture was extracted with ether (3 times, 20 mL each), dried over Na_2SO_4 , filtered, and finally evaporated under a reduced pressure. The residue was purified by flash chromatography on silica-gel.

Method B

Magnesium turnings (122 mg, 5 mmol) were placed in a vial to which a 0.5M solution of LiCl (5.0 mL, 2.5 mmol) was added. The magnesium was activated by adding a small amount of

diisobutylaluminum hydride (20 μ L, 1M in THF, 0.02mmol). The resulting mixture was stirred for 5min and a solution of an aryl iodide or aryl bromide (2 mmol) in 2 mL of THF was added at room temperature. The reaction mixture was stirred for 30min (or 2h in case of 4-bromobenzonitrile) and added by syringe pump (1h) to a solution of an alkyl halide (1 mmol), and [(^{Me}NN₂)Ni-Cl] (10.4 mg, 0.03 mmol) and TMEDA (50 μ L, 0.34 mmol) or O-TMEDA (114 μ L, 0.6 mmol) in 2 mL of THF (O-TMEDA was used for substrates containing ester or ketone functional group). After the addition was completed, the reaction mixture was stirred for 1h. The reaction was quenched with a saturated solution of NH₄Cl (30 mL). The resulting solution mixture was then extracted with ether (3 times, 20 mL each), dried over Na₂SO₄, filtered, and finally evaporated under a reduced pressure. The residue was purified by flash chromatography on silica-gel.

Separation and characterization data for products



octylbenzene (table 2, entry 1):¹⁴

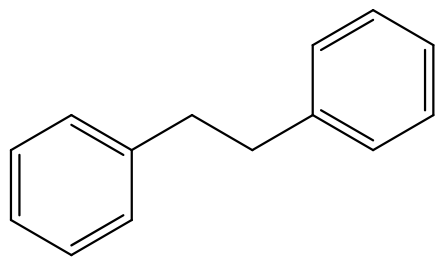
Synthesized with TMEDA as an additive.

Eluted from the column with hexane-diethyl ether (100:1) in 92% yield as a colorless liquid:

¹H NMR (400MHz, CDCl₃): 7,32 (m, 2H), 7,23 (m, 3H), 2,65 (t, *J* = 8,5 Hz, 2H), 1,66 (m, 2H), 1,33 (m, 10H), 0,93 (t, *J* = 6,7 Hz, 3H).

¹³C NMR (100 MHz, CDCl₃): 142.9, 128.3, 128.1, 125.5, 36.0, 31.9, 31.5, 29.5, 29.3, 29.2, 22.6, 14.1.

¹⁴ R. E. Merrill, and Eiichi Negishi, *J. Org. Chem.* **1974**, 39 (23), 3452-3453.



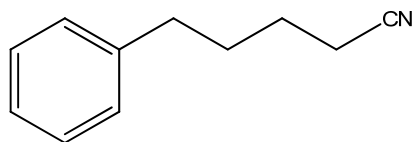
1,2-diphenylethane (table 2, entry 11):¹⁵

Synthesized with TMEDA as an additive.

Eluted from the column with hexane-diethyl ether (100:1) in 90% yield as a white solid:

¹H NMR (400MHz, CDCl₃): 7,37 (m, 4H), 7,28 (m, 6H), 3,01 (s, 4H).

¹³C NMR (100 MHz, CDCl₃): 141.7, 128.4, 128.2, 125.8, 37.9.



5-phenylpentanenitrile (table 3, entry 1):¹⁶

Synthesized with TMEDA as an additive.

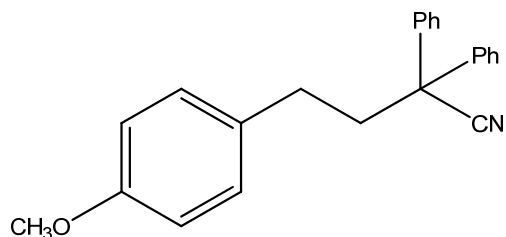
Eluted from the column with hexane-diethyl ether (30:1 to 10:1) in 80% yield as a colorless liquid:

¹H NMR (400MHz, CDCl₃): 7.31 (m, 2H), 7.20 (m, 3H), 2.67 (t, *J* = 7.3 Hz, 2H), 2.35 (t, *J* = 7.0 Hz, 2H), 1.80 (m, 2H), 1.69 (m, 2H).

¹³C NMR (100 MHz, CDCl₃): 141.1, 128.3, 128.2, 125.9, 119.5, 34.9, 30.1, 24.7, 16.9.

¹⁵ J. C. Sheehan, and F. S. Guziec Jr., *J. Org. Chem.* **1973**, 38 (17), 3034-3040.

¹⁶ P. Shukla, Y. C. Hsu, and C. H. Cheng, *J. Org. Chem.* **2006**, 71 (2), 655-658.



4-(4-methoxyphenyl)-2,2-diphenylbutanenitrile (table 3, entry 2):

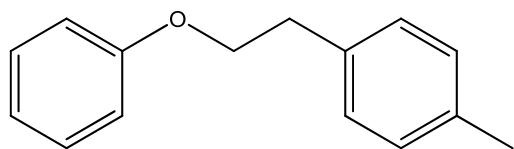
Synthesized with TMEDA as an additive.

Eluted from the column with hexane-diethyl ether (30:1 to 10:1) in 89% yield as a colorless oil:

¹H NMR (400MHz, CDCl₃): 7.30-7.46 (m, 8H), 7.31 (m, 2H), 7.08 (d, *J* = 8.5 Hz, 2H), 6.83 (d, *J* = 8.5 Hz, 2H), 3.79 (s, 3H), 2.66 (m, 4H).

¹³C NMR (100 MHz, CDCl₃): 158.0, 139.9, 132.6, 129.2, 128.9, 127.9, 126.8, 122.1, 113.9, 55.2, 51.6, 41.9, 31.1.

HRCI-MS: calculated for (C₂₃H₂₁NO, M+H), 328.1701; found, 328.1700.



1-methyl-4-(2-phenoxyethyl)benzene (table 3, entry 3):

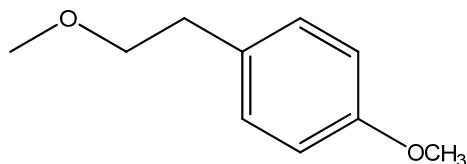
Synthesized with TMEDA as an additive.

Eluted from the column with hexane-diethyl ether (30:1) in 99% yield as a colorless liquid:

¹H NMR (400MHz, CDCl₃): 7.34 (m, 2H), 7.22 (m, 4H), 6.99 (m, 3H), 4.21 (t, *J* = 7.3 Hz, 2H), 3.13 (t, *J* = 7.3 Hz, 2H), 2.40 (s, 3H).

^{13}C NMR (100 MHz, CDCl_3): 158.7, 135.9, 135.0, 129.3, 129.1, 128.8, 120.6, 114.5, 68.6, 35.3, 21.0.

Elemental analysis: Anal. Calcd for $\text{C}_{15}\text{H}_{16}\text{O}$: C, 84.87; H, 7.60. Found: C, 84.34; H, 7.58.



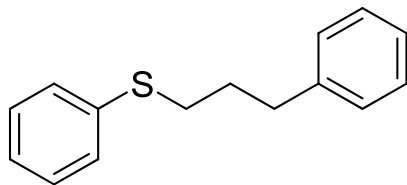
1-methoxy-4-(2-methoxyethyl)benzene (table 3, entry 4):¹⁷

Synthesized with TMEDA as an additive.

Eluted from the column with hexane-diethyl ether (10:1) in 89% yield as a colorless liquid:

^1H NMR (400MHz, CDCl_3): 7.15 (d, $J = 8.5$ Hz, 2H), 6.85 (d, $J = 8.5$ Hz, 2H), 3.79 (s, 3H), 3.58 (t, $J = 7.3$ Hz, 2H), 3.37 (s, 3H), 2.84 (t, $J = 7.0$ Hz, 2H).

^{13}C NMR (100 MHz, CDCl_3): 158.0, 130.9, 129.6, 113.7, 73.8, 58.5, 55.1, 35.2.



phenyl(3-phenylpropyl)sulfane (table 3, entry 5):¹⁸

Synthesized with TMEDA as an additive.

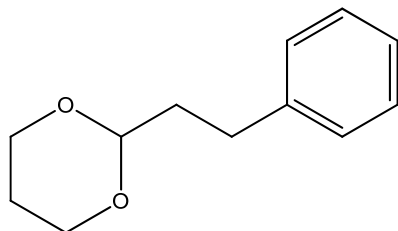
Eluted from the column with hexane-diethyl ether (100:1) in 66% yield as a colorless liquid:

¹⁷ C. W. Bird, A. L. Brown and C. C. Chan, *Tetrahedron* **1985**, 41 (20), 4685-4690.

¹⁸ C. G. Screttas, and M. Micha-Screttas, *J. Org. Chem.* **1978**, 43 (6), 1064-1071.

$^1\text{H NMR}$ (400MHz, CDCl_3): 7.15-7.40 (m, 10H), 2.94 (m, 2H), 2.78 (t, $J = 7.3$ Hz, 2H), 1.99 (m, 2H).

$^{13}\text{C NMR}$ (100 MHz, CDCl_3): 141.2, 136.5, 129.0, 128.8, 128.4, 128.3, 125.9, 125.7, 34.6, 32.8, 30.5.



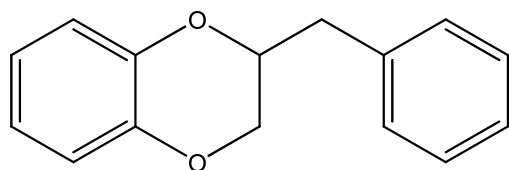
2-phenethyl-1,3-dioxane (table 3, entry 6):¹⁹

Synthesized with TMEDA as an additive.

Eluted from the column with hexane-diethyl ether (10:1) in 96% yield as a colorless liquid:

$^1\text{H NMR}$ (400MHz, CDCl_3): 7.28 (m, 2H), 7.20 (m, 3H), 4.52 (t, $J = 5.3$ Hz, 1H), 4.13 (dd, $J_1 = 11.4$ Hz, $J_2 = 5.0$ Hz, 2H), 3.76 (m, 2H), 2.73 (m, 2H), 2.11 (m, 1H), 1.93 (m, 2H), 1.35 (m, 1H).

$^{13}\text{C NMR}$ (100 MHz, CDCl_3): 141.6, 128.4, 128.3, 125.7, 101.4, 66.8, 36.6, 30.0, 25.8.



2-benzyl-2,3-dihydrobenzo[b][1,4]dioxine (table 3, entry 7):²⁰

Synthesized with TMEDA as an additive.

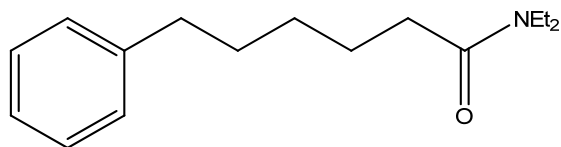
¹⁹ Y. S. Hon, C. F. Lee, R. J. Chen, and Y. F. Huang, *Synthetic Communications* **2003**, 33:16, 2829-2842.

²⁰ C. Chowdhury, G. Chaudhuri, S. Guha, A. K. Mukherjee, and N. G. Kundu, *J. Org. Chem.* **1998**, 63 (6), 1863-1871.

Eluted from the column with hexane-diethyl ether (20:1) in 85% yield as a colorless liquid:

¹H NMR (400MHz, CDCl₃): 7.28-7.38 (m, 5H), 6.84-6.94 (m, 4H), 4.38 (m, 1H), 4.20 (dd, $J_1 = 11.2$ Hz, $J_2 = 2.1$ Hz, 1H), 3.93 (dd, $J_1 = 11.4$ Hz, $J_2 = 7.0$ Hz, 1H), 3.14 (dd, $J_1 = 13.8$ Hz, $J_2 = 6.5$ Hz, 1H), 2.91 (dd, $J_1 = 14.1$ Hz, $J_2 = 7.3$ Hz, 1H).

¹³C NMR (100 MHz, CDCl₃): 143.2, 143.1, 136.3, 129.3, 128.5, 126.7, 121.5, 121.2, 117.3, 117.0, 73.6, 66.9, 37.5.



N,N-diethyl-6-phenylhexanamide (table 3, entry 8):

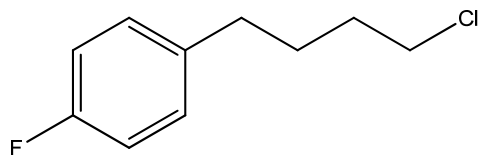
Synthesized with TMEDA as an additive.

Eluted from the column with hexane-diethyl ether (4:6) in 84% yield as a colorless liquid:

¹H NMR (400MHz, CDCl₃): 7.25 (d, $J = 7.3$ Hz, 2H), 7.17 (d, $J = 6.5$ Hz, 3H), 3.36 (q, $J = 7.0$ Hz, 2H), 3.28 (q, $J = 7.3$ Hz, 2H), 2.61 (m, 2H), 2.27 (m, 2H), 1.66 (m, 4H), 1.38 (m, 2H), 1.15 (t, $J = 7.0$ Hz, 3H), 1.10 (t, $J = 7.0$ Hz, 3H).

¹³C NMR (100 MHz, CDCl₃): 172.0, 142.5, 128.3, 128.1, 125.5, 41.8, 39.9, 35.7, 32.9, 31.2, 29.0, 25.2, 14.3, 13.0.

HRCI-MS: calculated for (C₁₆H₂₅NO, M+H), 248.2014; found, 248.2012.



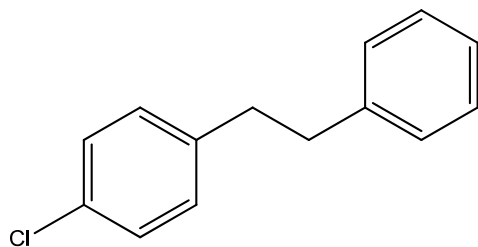
1-(4-chlorobutyl)-4-fluorobenzene (table 3, entry 9):²¹

Synthesized with TMEDA as an additive.

Eluted from the column with hexane-diethyl ether (30:1) in 76% yield as a colorless liquid:

¹H NMR (400MHz, CDCl₃): 7.14 (m, 2H), 6.98 (m, 2H), 3.55 (t, *J* = 6.2 Hz, 2H), 2.63 (t, *J* = 7.3 Hz, 2H), 1.79 (m, 4H).

¹³C NMR (100 MHz, CDCl₃): 161.3 (d, *J* = 243.1 Hz), 137.4 (d, *J* = 3.2 Hz), 129.7 (d, *J* = 8.1 Hz), 115.1 (d, *J* = 20.9 Hz), 44.7, 34.2 (d, *J* = 0.4 Hz), 31.9, 28.7 (d, *J* = 1.1 Hz).



1-chloro-4-phenethylbenzene (table 3, entry 10):²²

Synthesized with TMEDA as an additive.

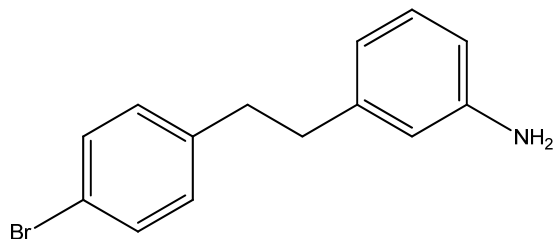
Eluted from the column with hexane-diethyl ether (60:1) in 98% yield as a white solid:

¹H NMR (400MHz, CDCl₃): 7.10-7.35 (m, 9H), 2.93 (s, 4H).

²¹ G. A. Olah, V. V. Krishnamurthy, B. P. Singh, and P. S. Iyer, *J. Org. Chem.*, **1983**, 48 (7), 955-963.

²² G. A. Molander, C. S. Yun, *Tetrahedron* **2002**, 58, 1465-1470.

^{13}C NMR (100 MHz, CDCl_3): 141.2, 140.0, 131.5, 129.7, 128.4, 128.35, 128.33, 125.9, 37.7, 37.1.



3-(4-bromophenethyl)aniline (table 3, entry 11):

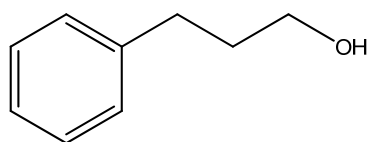
Synthesized with TMEDA as an additive.

Eluted from the column with hexane-diethyl ether (60:1 to 2:1) in 98% yield as a colorless liquid:

^1H NMR (400MHz, CDCl_3): 7.40 (d, $J = 8.2$ Hz, 2H), 7.07 (m, 3H), 6.55 (m, 3H), 3.64 (br, 2H), 2.84 (m, 4H).

^{13}C NMR (100 MHz, CDCl_3): 146.2, 142.5, 140.7, 131.2, 130.1, 129.2, 119.5, 118.8, 115.2, 112.9, 37.6, 37.0.

HRCI-MS: calculated for ($\text{C}_{14}\text{H}_{14}\text{NBr}$, $\text{M}+\text{H}$), 276.0388 and 278.0368; found, 276.0385 and 278.0377.



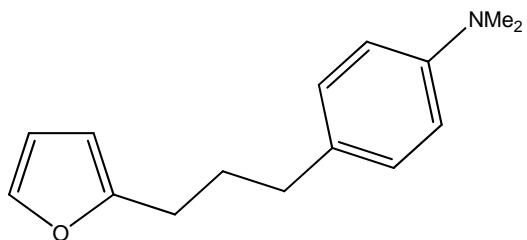
3-phenylpropan-1-ol (table 3, entry 12):²³

Synthesized with TMEDA as an additive.

Eluted from the column with hexane-diethyl ether (1:1) in 74% yield as a colorless liquid:

¹H NMR (400MHz, CDCl₃): 7.30 (m, 2H), 7.20 (m, 3H), 3.68 (t, *J* = 6.5 Hz, 2H), 2.72 (m, 2H), 1.91 (m, 2H), 1.52 (br, 1H).

¹³C NMR (100 MHz, CDCl₃): 141.7, 128.36, 128.38, 125.8, 62.2, 34.1, 32.0.



4-(3-(furan-2-yl)propyl)-N,N-dimethylaniline (table 3, entry 13):

Synthesized with TMEDA as an additive.

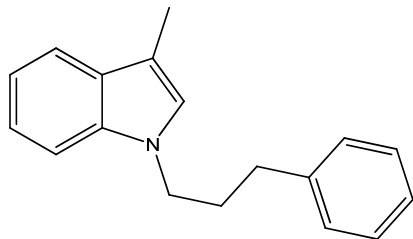
Eluted from the column with hexane-diethyl ether (60:1 to 30:1) in 83% yield as a colorless oil:

¹H NMR (400MHz, CDCl₃): 7.32 (m, 1H), 7.09 (d, *J* = 8.5 Hz, 2H), 6.72 (d, *J* = 8.5 Hz, 2H), 6.29 (m, 1H), 6.00 (m, 1H), 2.93 (s, 6H), 2.66 (t, *J* = 7.3 Hz, 2H), 2.59 (t, *J* = 7.3 Hz, 2H), 1.95 (m, 2H).

¹³C NMR (100 MHz, CDCl₃): 156.2, 148.9, 140.6, 130.2, 129.0, 113.0, 110.0, 104.7, 40.9, 34.1, 29.8, 27.4,

²³ I. Fleming, R. Henning, D. C. Parker, H. E. Plaut and P. E. J. Sanderson, *J. Chem. Soc. Perkin Trans. I.*, **1995**, 317-337.

HRCI-MS: calculated for (C₁₅H₁₉NO, M+H), 230.1545; found, 230.1552.



3-methyl-1-(3-phenylpropyl)-1H-indole (table 3, entry 14):

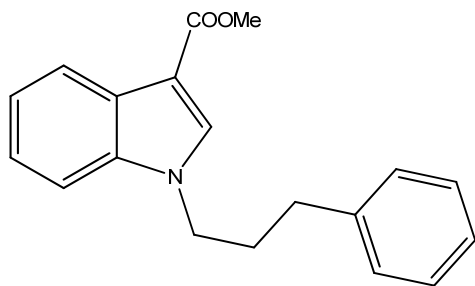
Synthesized with TMEDA as an additive.

Eluted from the column with hexane-diethyl ether (50:1) in 81% yield as a colorless oil:

¹H NMR (400MHz, CDCl₃): 7.62 (d, *J* = 7.9 Hz, 1H), 7.20-7.35 (m, 7H), 7.14 (m, 1H), 6.90 (s, 1H), 4.10 (t, *J* = 7.3 Hz, 2H), 2.67 (t, *J* = 7.3 Hz, 2H), 2.38 (s, 3H), 2.19 (m, 2H).

¹³C NMR (100 MHz, CDCl₃): 141.0, 136.2, 128.7, 128.4, 128.3, 126.0, 125.3, 121.2, 118.9, 118.4, 110.2, 109.1, 45.3, 33.0, 31.6, 9.5.

HRCI-MS: calculated for (C₁₈H₁₉N, M+H), 250.1596; found, 250.1596.



methyl 1-(3-phenylpropyl)-1H-indole-3-carboxylate (table 3, entry 15):

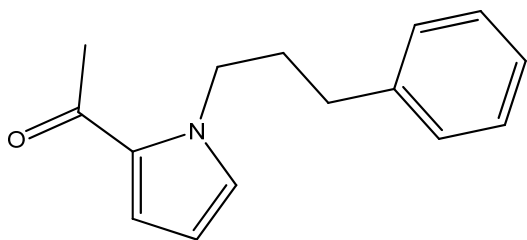
Synthesized with O-TMEDA as an additive.

Eluted from the column with hexane-diethyl ether (2:1) in 81% yield as a slightly yellow liquid:

¹H NMR (400MHz, CDCl₃): 8.20 (m, 1H), 7.82 (s, 1H), 7.28 (m, 6H), 7.16 (m, 2H), 4.16 (t, *J* = 7.0 Hz, 2H), 3.92 (s, 3H), 2.66 (t, *J* = 7.3 Hz, 2H), 2.23 (m, 2H).

¹³C NMR (100 MHz, CDCl₃): 165.4, 140.3, 136.4, 134.1, 128.5, 128.3, 126.7, 126.2, 122.6, 121.8, 121.7, 109.9, 107.0, 50.9, 46.1, 32.7, 31.0.

HRCI-MS: calculated for (C₁₉H₁₉NO₂, M+H), 294.1494; found, 294.1492.



1-(1-(3-phenylpropyl)-1H-pyrrol-2-yl)ethanone (table 3, entry 16):

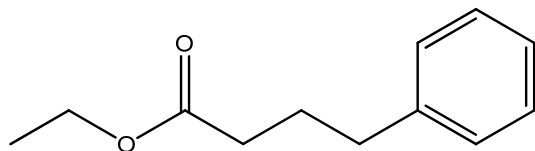
Synthesized with O-TMEDA as an additive.

Eluted from the column with hexane-diethyl ether (20:1 to 10:1) in 62% yield as a colorless liquid:

¹H NMR (400MHz, CDCl₃): 7.28 (m, 2H), 7.19 (m, 3H), 6.98 (dd, *J*₁ = 4.1 Hz, *J*₂ = 1.5 Hz, 1H), 6.83 (m, 1H), 6.14 (dd, *J*₁ = 3.8 Hz, *J*₂ = 2.3 Hz, 1H), 4.35 (t, *J* = 7.0 Hz, 2H), 2.63 (m, 2H), 2.45 (s, 3H), 2.09 (m, 2H).

¹³C NMR (100 MHz, CDCl₃): 188.1, 141.2, 130.1, 130.0, 128.3, 128.2, 125.8, 120.2, 107.8, 49.2, 32.7, 27.2.

HRCI-MS: calculated for (C₁₅H₁₇NO, M+H), 228.1388; found, 228.1379.



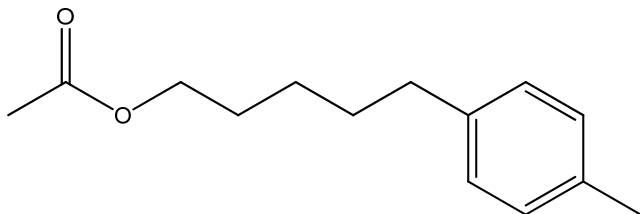
ethyl 4-phenylbutanoate (table 3, entry 17):²⁴

Synthesized with O-TMEDA as an additive.

Eluted from the column with hexane-diethyl ether (20:1) in 75% yield as a colorless liquid:

¹H NMR (400MHz, CDCl₃): 7.30 (m, 2H), 7.20 (m, 3H), 4.14 (q, *J* = 7.3 Hz, 2H), 2.67 (t, *J* = 7.6 Hz, 2H), 2.33 (t, *J* = 7.6 Hz, 2H), 1.97 (quint, *J* = 7.9 Hz, 2H), 1.26 (t, *J* = 7.0 Hz, 3H).

¹³C NMR (100 MHz, CDCl₃): 173.3, 141.3, 128.4, 128.2, 125.8, 60.1, 35.0, 33.6, 26.4, 14.1.



5-p-tolylpentyl acetate (table 3, entry 18):

Synthesized with O-TMEDA as an additive.

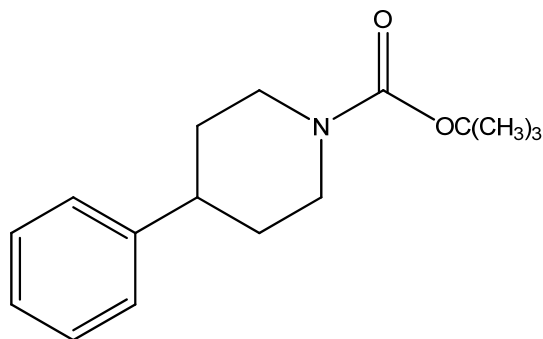
Eluted from the column with hexane-diethyl ether (30:1 to 10:1) in 63% yield as a colorless liquid:

¹H NMR (400MHz, CDCl₃): 7.09 (m, 4H), 4.07 (t, *J* = 6.7 Hz, 2H), 2.59 (t, *J* = 7.6 Hz, 2H), 2.33 (s, 3H), 2.05 (s, 3H), 1.65 (m, 4H), 1.40 (m, 2H).

²⁴ N. Kurono, K. Sugita, S. Takasugi, and M. Tokuda, *Tetrahedron* **1999**, 55, 6097-6108.

^{13}C NMR (100 MHz, CDCl_3): 171.1, 139.2, 135.0, 128.9, 128.2, 64.4, 35.2, 31.1, 28.4, 25.5, 20.97, 20.95.

Elemental analysis: Anal. Calcd for $\text{C}_{14}\text{H}_{20}\text{O}_2$: C, 76.33; H, 9.15. Found: C, 76.44; H, 9.18.



tert-butyl 4-phenylpiperidine-1-carboxylate (table 3, entry 19):

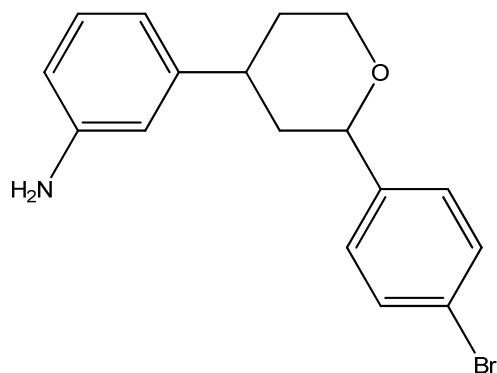
Synthesized with O-TMEDA as an additive.

Eluted from the column with hexane-diethyl ether (30:1 to 10:1) in 65% yield as a colorless liquid:

^1H NMR (400MHz, CDCl_3): 7.31 (m, 2H), 7.21 (m, 3H), 4.24 (m, 2H), 2.81 (m, 2H), 2.63 (m, 1H), 1.82 (m, 2H), 1.62 (qd, $J_1 = 12.6$ Hz, $J_2 = 3.5$ Hz, 2H), 1.49 (s, 9H).

^{13}C NMR (100 MHz, CDCl_3): 154.8, 145.7, 128.4, 126.7, 126.3, 79.3, 44.3, 42.7, 33.1, 28.4.

HRCI-MS: calculated for ($\text{C}_{16}\text{H}_{23}\text{NO}_2$, M+H), 262.1807; found, 262.1819.



3-(2-(4-bromophenyl)tetrahydro-2H-pyran-4-yl)aniline (table 3, entry 20):

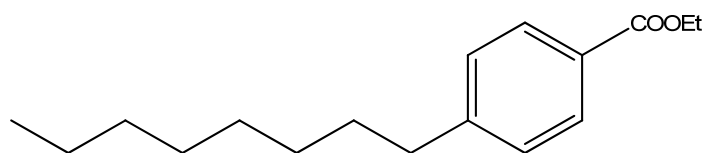
Synthesized with TMEDA as an additive.

Eluted from the column with hexane-diethyl ether (20:1 to 1:1) in 73% yield as a slightly yellow liquid:

¹H NMR (400MHz, CDCl₃): 7.47 (d, *J* = 8.5 Hz, 2H), 7.27 (d, *J* = 8.2 Hz, 2H), 7.11 (t, *J* = 7.6 Hz, 1H), 6.65 (d, *J* = 7.3 Hz, 1H), 6.55 (m, 2H), 4.44 (m, 1H), 4.28 (m, 1H), 3.45-3.80 (m, 3H), 2.85 (m, 1H), 2.04 (m, 1H), 1.76 (m, 3H).

¹³C NMR (100 MHz, CDCl₃): 146.5, 146.4, 141.8, 131.3, 129.4, 127.4, 121.0, 117.0, 113.4, 113.2, 79.1, 68.6, 41.9, 41.2, 33.1.

HRCI-MS: calculated for (C₁₇H₁₈NBrO, M+H), 332.0650 and 334.0631; found, 332.0639 and 334.0642.



ethyl 4-octylbenzoate (table 4, entry 2):

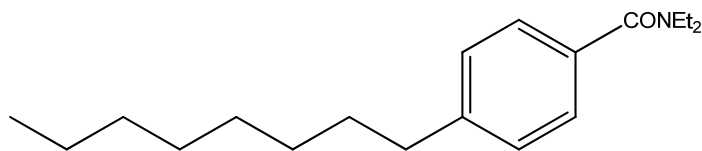
Synthesized by Method A with O-TMEDA as an additive.

Eluted from the column with hexane-diethyl ether (100:1 to 60:1) in 83% yield as a colorless liquid:

¹H NMR (400MHz, CDCl₃): 7.96 (d, *J* = 8.2 Hz, 2H), 7.23 (d, *J* = 8.4 Hz, 2H), 4.36 (q, *J* = 7.0 Hz, 2H), 2.65 (m, 2H), 1.62 (m, 2H), 1.38 (t, *J* = 7.2 Hz, 3H), 1.20-1.35 (m, 10H), 0.88 (m, 3H).

¹³C NMR (100 MHz, CDCl₃): 166.6, 148.3, 129.5, 128.3, 126.3, 60.6, 35.9, 31.8, 31.1, 29.3, 29.2, 29.1, 22.6, 14.3, 14.0.

HRCI-MS: calculated for (C₁₇H₂₆O₂, M+H), 263.2011; found, 263.2019.



N,N-diethyl-4-octylbenzamide (table 4, entry 3):

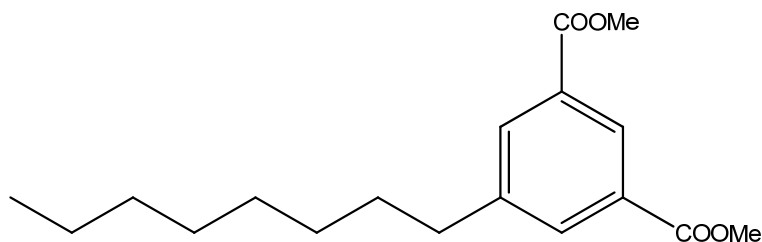
Synthesized by Method A with O-TMEDA as an additive.

Eluted from the column with hexane-diethyl ether (30:1 to 2:1) in 75% yield as a colorless liquid:

¹H NMR (400MHz, CDCl₃): 7.28 (m, 2H), 7.18 (d, *J* = 7.9 Hz, 2H), 3.14-3.60 (br, 4H), 2.61 (m, 2H), 1.59 (m, 2H), 1.10-1.35 (m, 16H), 0.87 (m, 3H).

¹³C NMR (100 MHz, CDCl₃): 171.4, 144.0, 134.4, 128.2, 126.2, 43.2, 39.2, 35.7, 31.8, 31.2, 29.4, 29.22, 29.21, 22.6, 14.1, 14.0, 12.9.

HRCI-MS: calculated for (C₁₉H₃₁ON, M+H), 290.2484; found, 290.2475.



dimethyl 5-octylisophthalate (table 4, entry 4):

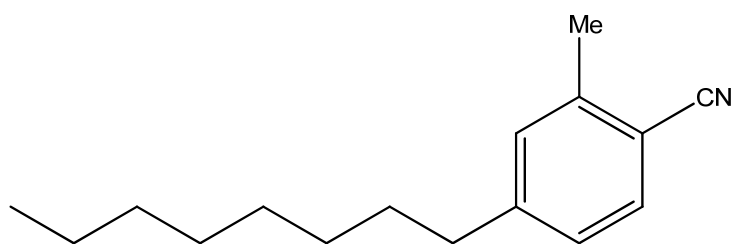
Synthesized by Method A with O-TMEDA as an additive.

Eluted from the column with hexane-diethyl ether (30:1 to 10:1) in 70% yield as a colorless liquid:

$^1\text{H NMR}$ (400MHz, CDCl_3): 8.49 (s, 1H), 8.04 (s, 2H), 3.94 (s, 6H), 2.69 (t, $J = 7.3$ Hz, 2H), 1.64 (m, 2H), 1.22-1.35 (m, 10H), 0.87 (t, $J = 6.7$ Hz, 3H).

$^{13}\text{C NMR}$ (100 MHz, CDCl_3): 166.4, 143.7, 133.8, 130.4, 128.1, 52.2, 35.5, 31.8, 31.2, 29.3, 29.18, 29.16, 22.6, 14.0.

HRCI-MS: calculated for ($\text{C}_{18}\text{H}_{26}\text{O}_4$, M+H), 307.1909; found, 307.1923.



2-methyl-4-octylbenzonitrile (table 4, entry 5):

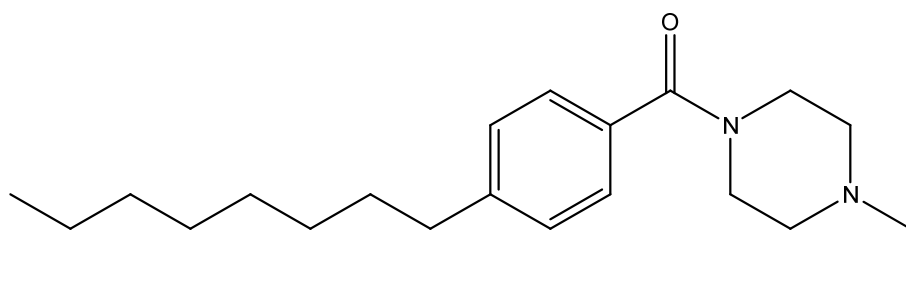
Synthesized by Method A with O-TMEDA as an additive.

Eluted from the column with hexane-diethyl ether (60:1) in 58% yield as a colorless liquid:

¹H NMR (400MHz, CDCl₃): 7.49 (d, *J* = 7.9 Hz, 1H), 7.11 (s, 1H), 7.06 (d, *J* = 7.9 Hz, 1H), 2.60 (t, *J* = 7.6 Hz, 2H), 2.51 (s, 3H), 1.59 (m, 2H), 1.23-1.35 (m, 10H), 0.88 (t, *J* = 6.2 Hz, 3H).

¹³C NMR (100 MHz, CDCl₃): 148.3, 141.7, 132.3, 130.3, 126.3, 118.4, 109.8, 36.0, 31.8, 30.9, 29.3, 29.2, 29.1, 22.6, 20.4, 14.0.

HRCI-MS: calculated for (C₁₆H₂₃N, M+H), 230.1909; found, 230.1912.



(4-ethylpiperazin-1-yl)(4-octylphenyl)methanone (table 4, entry 6):

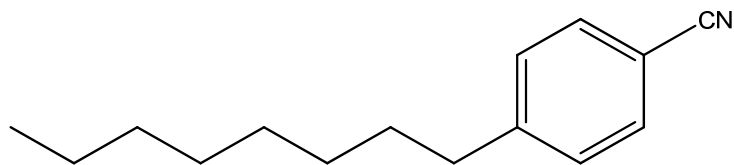
Synthesized by Method A with O-TMEDA as an additive.

Eluted from the column with hexane-ethyl acetate (1:99) in 86% yield as a slightly yellow oil:

¹H NMR (400MHz, CDCl₃): 7.32 (m, 2H), 7.20 (d, *J* = 8.2 Hz, 2H), 3.40-3.90 (br, 4H), 2.30-2.70 (m, 8H), 1.60 (m, 2H), 1.27 (m, 10H), 1.11 (t, *J* = 7.0 Hz, 3H), 0.87 (m, 3H).

¹³C NMR (100 MHz, CDCl₃): 170.4, 144.7, 133.0, 128.3, 127.1, 53.1, 52.5, 52.2, 47.7, 42.2, 35.7, 31.8, 31.2, 29.3, 29.20, 29.19, 22.6, 14.0, 11.8.

HRCI-MS: calculated for (C₂₁H₃₄N₂O, M+H), 331.2749; found, 331.2751.



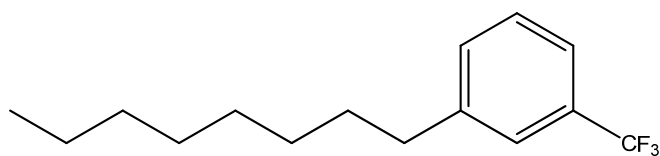
4-octylbenzonitrile (table 4, entry 7): ²⁵

Synthesized by Method B with TMEDA as an additive.

Eluted from the column with hexane-diethyl ether (100:1) in 62% yield as a colorless liquid:

¹H NMR (400MHz, CDCl₃): 7.56 (d, *J* = 7.9 Hz, 2H), 7.27 (d, *J* = 7.9 Hz, 2H), 2.65 (m, 2H), 1.61 (m, 2H), 1.25-1.35 (m, 10H), 0.87 (t, *J* = 6.5 Hz, 3H).

¹³C NMR (100 MHz, CDCl₃): 148.6, 132.1, 129.2, 119.2, 109.4, 36.1, 31.8, 30.9, 29.3, 29.21, 29.20, 22.6, 14.1.



1-octyl-3-(trifluoromethyl)benzene (table 4, entry 8): ²⁶

Synthesized by Method B with TMEDA as an additive.

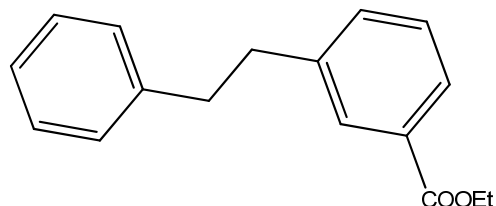
Eluted from the column with hexane-diethyl ether (100:1) in 70% yield as a colorless liquid:

¹H NMR (400MHz, CDCl₃): 7.35-7.46 (m, 4H), 2.66 (t, *J* = 7.6 Hz, 2H), 1.63 (m, 2H), 1.24-1.36 (m, 10H), 0.89 (t, *J* = 6.5 Hz, 3H).

²⁵ S. Huo, *Org. Lett.*, **2003** 5 (4), 423-425.

²⁶ G. A. Molander, and T. Ito, *Org. Lett.* **2001**, 3 (3), 393-396.

^{13}C NMR (100 MHz, CDCl_3): 143.7, 131.7 (q, $J = 1.3$ Hz), 128.5, 125.0 (q, $J = 3.8$ Hz), 122.4 (q, $J = 3.8$ Hz), 35.8, 31.8, 31.3, 29.4, 29.23, 29.22, 22.6, 14.1.



ethyl 3-phenethylbenzoate (table 4, entry 9):

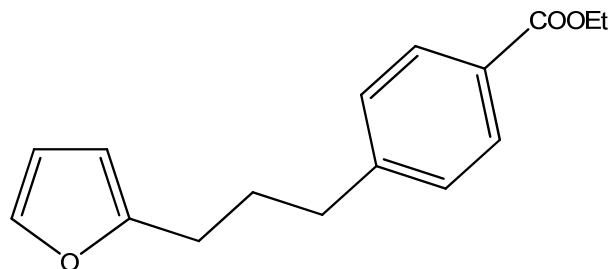
Synthesized by Method A with O-TMEDA as an additive.

Eluted from the column with hexane-diethyl ether (100:1 to 60:1) in 88% yield as a colorless liquid:

^1H NMR (400MHz, CDCl_3): 7.90 (m, 2H), 7.31 (m, 4H), 7.20 (m, 3H), 4.39 (q, $J = 7.3$ Hz, 2H), 2.98 (m, 4H), 1.41 (t, $J = 7.0$ Hz, 3H).

^{13}C NMR (100 MHz, CDCl_3): 166.7, 141.9, 141.2, 133.0, 130.5, 129.4, 128.4, 128.3, 128.2, 127.1, 125.9, 60.8, 37.7, 37.6, 14.3.

HRCI-MS: calculated for ($\text{C}_{17}\text{H}_{18}\text{O}_2$, M+H), 255.1385; found, 255.1387.



ethyl 4-(3-(furan-2-yl)propyl)benzoate (table 4, entry 10):

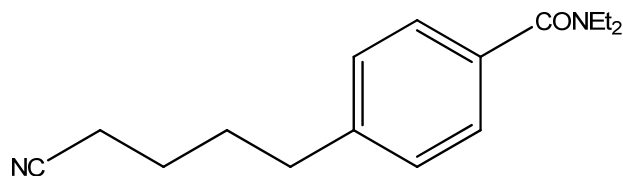
Synthesized by method A with O-TMEDA as an additive, 3.3 of 5eq of Alkyl-I was recovered after reaction with 99% purity.

Eluted from the column with hexane-diethyl ether (100:1 to 30:1) in 74% yield as a colorless liquid:

¹H NMR (400MHz, CDCl₃): 7.96 (d, *J* = 8.2 Hz, 2H), 7.31 (d, *J* = 1.2 Hz, 1H), 7.25 (m, 2H), 6.29 (dd, *J*₁ = 2.6 Hz, *J*₂ = 1.8 Hz, 1H), 6.00 (d, *J* = 2.9 Hz, 1H), 4.37 (q, *J* = 7.0 Hz, 2H), 2.71 (m, 2H), 2.65 (t, *J* = 7.3 Hz, 2H), 1.99 (m, 2H), 1.39 (t, *J* = 7.0 Hz, 3H).

¹³C NMR (100 MHz, CDCl₃): 166.6, 155.5, 147.3, 140.8, 129.6, 128.4, 128.2, 110.0, 105.0, 60.7, 35.1, 29.3, 27.3, 14.3.

HRCI-MS: calculated for (C₁₆H₁₈O₃, M+H), 259.1334; found, 259.1341.



4-(4-cyanobutyl)-N,N-diethylbenzamide (table 4, entry 11):

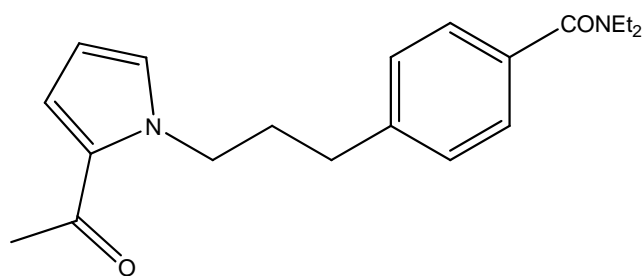
Synthesized by method A with O-TMEDA as an additive, 2.7 of 5eq of Alkyl-I was recovered after reaction with 99% purity.

Eluted from the column with hexane-diethyl ether (10:1 to 1:2) in 70% yield as a colorless liquid:

¹H NMR (400MHz, CDCl₃): 7.30 (d, *J* = 8.4 Hz, 2H), 7.18 (d, *J* = 7.6 Hz, 2H), 3.20-3.60 (br, 4H), 2.67 (t, *J* = 7.2 Hz, 2H), 2.35 (t, *J* = 7.0 Hz, 2H), 1.79 (m, 2H), 1.67 (m, 2H), 1.05-1.30 (br, 6H).

¹³C NMR (100 MHz, CDCl₃): 171.1, 142.2, 135.0, 128.2, 126.5, 119.4, 43.2, 39.2, 34.7, 30.0, 24.7, 17.0, 14.1, 12.9.

HRCI-MS: calculated for (C₁₆H₂₂ON₂, M+H), 259.1810; found, 259.1821.



4-(3-(2-acetyl-1H-pyrrol-1-yl)propyl)-N,N-diethylbenzamide (table 4, entry 12):

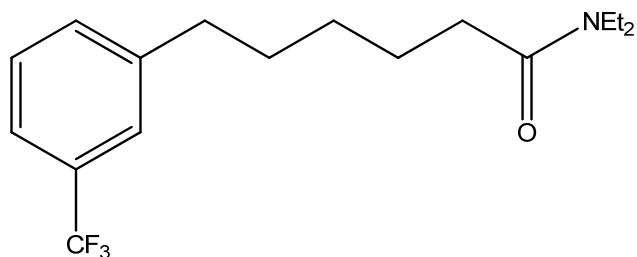
Synthesized by method A with O-TMEDA as an additive, 2.8 of 5eq of Alkyl-I was recovered after reaction with 99% purity.

Eluted from the column with hexane-diethyl ether (20:1 to 3:1) in 72% yield as a slightly yellow liquid:

¹H NMR (400MHz, CDCl₃): 7.29 (d, *J* = 7.3 Hz, 2H), 7.19 (d, *J* = 7.3 Hz, 2H), 6.97 (dd, *J*₁ = 4.1 Hz, *J*₂ = 1.8 Hz, 1H), 6.82 (m, 1H), 6.13 (dd, *J*₁ = 4.1 Hz, *J*₂ = 2.6 Hz, 1H), 4.33 (t, *J* = 7.3 Hz, 2H), 3.20-3.60 (br, 4H), 2.63 (m, 2H), 2.44 (s, 3H), 2.07 (m, 2H), 1.05-1.25 (br, 6H).

¹³C NMR (100 MHz, CDCl₃): 188.2, 171.3, 142.4, 134.9, 130.1, 130.0, 128.2, 126.4, 120.3, 107.9, 49.2, 43.2, 39.1, 32.5, 27.3, 14.1, 12.8.

HRCI-MS: calculated for (C₂₀H₂₆O₂N₂, M+H), 327.2072; found, 327.2073.



N,N-diethyl-6-(3-(trifluoromethyl)phenyl)hexanamide (table 4, entry 13):

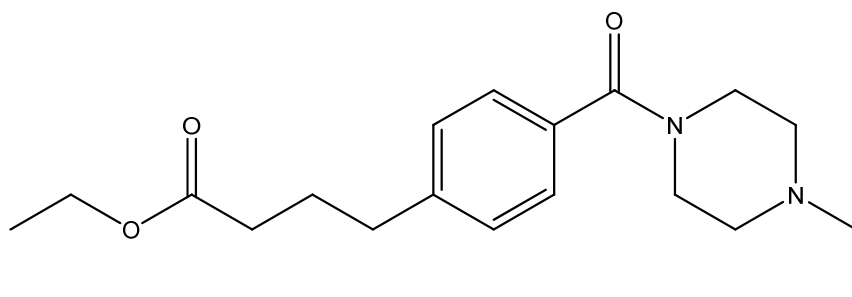
Synthesized by method B with TMEDA as an additive.

Eluted from the column with hexane-diethyl ether (1:1 to 1:2) in 69% yield as a yellow liquid:

¹H NMR (400MHz, CDCl₃): 7.38 (m, 4H), 3.36 (q, *J* = 7.0 Hz, 2H), 3.28 (q, *J* = 7.0 Hz, 2H), 2.67 (t, *J* = 7.6 Hz, 2H), 2.28 (t, *J* = 7.3 Hz, 2H), 1.67 (m, 4H), 1.38 (m, 2H), 1.15 (t, *J* = 7.0 Hz, 3H), 1.09 (t, *J* = 7.0 Hz, 3H).

¹³C NMR (100 MHz, CDCl₃): 171.9, 143.4, 131.7, 128.6, 125.0 (q, *J* = 3.7 Hz), 122.4 (q, *J* = 3.8 Hz), 41.8, 40.0, 35.5, 32.8, 31.0, 28.9, 25.1, 14.3, 13.0.

HRCI-MS: calculated for (C₁₇H₂₄F₃NO, M+H), 316.1888; found, 316.1891.



ethyl 4-(4-(4-ethylpiperazine-1-carbonyl)phenyl)butanoate (table 4, entry 14):

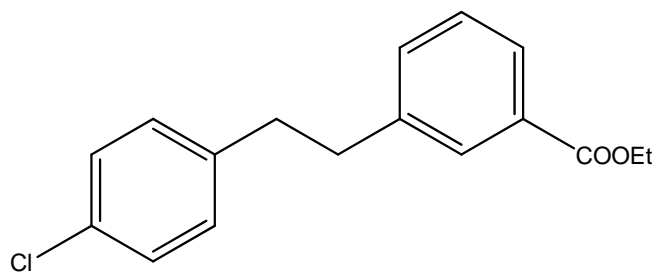
Synthesized by method A with O-TMEDA as an additive, 2.7 of 5eq of Alkyl-I was recovered after reaction with 99% purity.

Eluted from the column with hexane-ethanol (60:1 to 2:1) in 86% yield as a yellow oil:

¹H NMR (400MHz, CDCl₃): 7.30 (d, *J* = 6.5 Hz, 2H), 7.17 (d, *J* = 6.5 Hz, 2H), 4.09 (q, *J* = 7.0 Hz, 2H), 3.35-3.85 (br, 4H), 2.64 (t, *J* = 7.0 Hz, 2H), 2.30-2.55 (br, 6H), 2.28 (t, *J* = 7.6 Hz, 2H), 1.92 (m, 2H), 1.22 (t, *J* = 7.0 Hz, 3H), 1.06 (t, *J* = 7.0 Hz, 3H).

¹³C NMR (100 MHz, CDCl₃): 173.1, 170.1, 143.1, 133.4, 128.4, 127.1, 60.1, 53.0, 52.4, 52.1, 47.6, 42.2, 34.8, 33.4, 26.2, 14.1, 11.8.

HRCI-MS: calculated for (C₁₉H₂₈N₂O₃, M+H), 333.2178; found, 333.2191.



ethyl 3-(4-chlorophenethyl)benzoate (table 4, entry 15):

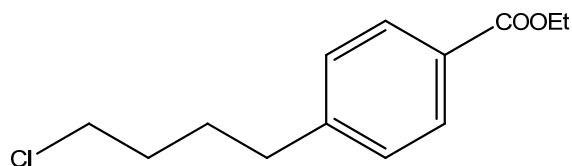
Synthesized by method A with O-TMEDA as an additive, 3.6 of 5eq of Alkyl-I was recovered after reaction with 99% purity.

Eluted from the column with hexane-diethyl ether (60:1 to 30:1) in 76% yield as a colorless liquid:

¹H NMR (400MHz, CDCl₃): 7.88 (m, 2H), 7.32 (m, 2H), 7.24 (d, *J* = 8.2 Hz, 2H), 7.08 (d, *J* = 8.5 Hz, 2H), 4.38 (q, *J* = 7.3 Hz, 2H), 2.92 (m, 4H), 1.40 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, CDCl_3): 166.6, 141.4, 139.6, 133.0, 131.7, 130.5, 129.7, 129.4, 128.4, 128.3, 127.2, 60.9, 37.4, 36.9, 14.3.

HRCI-MS: calculated for ($\text{C}_{17}\text{H}_{17}\text{ClO}_2$, M+H), 289.0995; found, 289.0987.



ethyl 4-(4-chlorobutyl)benzoate (table 4, entry 16):

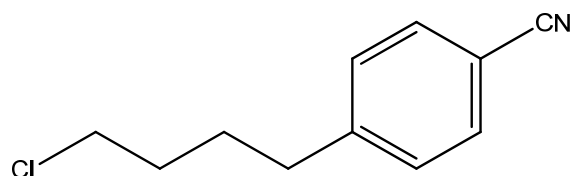
Synthesized by method A with O-TMEDA as an additive, 3.0 of 5eq of Alkyl-I was recovered after reaction with 99% purity.

Eluted from the column with hexane-diethyl ether (60:1 to 30:1) in 86% yield as a colorless liquid:

^1H NMR (400MHz, CDCl_3): 7.96 (d, $J = 8.2$ Hz, 2H), 7.24 (d, $J = 8.4$ Hz, 2H), 4.36 (q, $J = 7.0$ Hz, 2H), 3.54 (m, 2H), 2.70 (t, $J = 7.2$ Hz, 2H), 1.79 (m, 4H), 1.39 (t, $J = 7.2$ Hz, 3H).

^{13}C NMR (100 MHz, CDCl_3): 166.5, 147.1, 129.6, 128.3, 125.2, 60.7, 44.7, 35.0, 31.9, 28.1, 14.3.

HRCI-MS: calculated for ($\text{C}_{13}\text{H}_{17}\text{ClO}_2$, M+H), 241.0995; found, 241.0985.



4-(4-chlorobutyl)benzonitrile (table 4, entry 17):

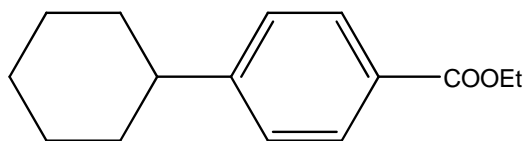
Synthesized by method B with TMEDA as an additive.

Eluted from the column with hexane-diethyl ether (20:1 to 10:1) in 72% yield as a colorless liquid:

$^1\text{H NMR}$ (400MHz, CDCl_3): 7.57 (d, $J = 8.2$ Hz, 2H), 7.28 (d, $J = 8.2$ Hz, 2H), 3.55 (m, 2H), 2.70 (t, $J = 7.2$ Hz, 2H), 1.80 (m, 4H).

$^{13}\text{C NMR}$ (100 MHz, CDCl_3): 147.4, 132.1, 129.1, 118.9, 109.7, 44.5, 35.1, 31.8, 27.9.

HRCI-MS: calculated for ($\text{C}_{11}\text{H}_{12}\text{ClN}$, M+H), 194.0737; found, 194.0745.



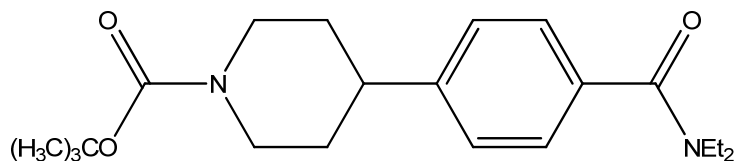
ethyl 4-cyclohexylbenzoate (table 4, entry 18):²⁷

Synthesized by method A with O-TMEDA as an additive.

Eluted from the column with hexane-diethyl ether (30:1) in 61% yield as a colorless liquid:

$^1\text{H NMR}$ (400MHz, CDCl_3): 7.96 (d, $J = 8.2$ Hz, 2H), 7.27 (m, 2H), 4.36 (q, $J = 7.0$ Hz, 2H), 2.55 (m, 1H), 1.82 (m, 4H), 1.35-1.45 (m, 6H), 1.38 (t, $J = 7.0$ Hz, 3H).

$^{13}\text{C NMR}$ (100 MHz, CDCl_3): 166.6, 153.2, 129.6, 126.7, 126.3, 60.6, 44.6, 34.1, 26.7, 26.0, 14.3.



²⁷ X. Luo, H. Zhang, H. Duan, Q. Liu, L. Zhu, T. Zhang, and A. Lei, *Org. Lett.* **2007**, 9 (22), 4571-4574.

tert-butyl 4-(4-(diethylcarbamoyl)phenyl)piperidine-1-carboxylate (table 4, entry 19):

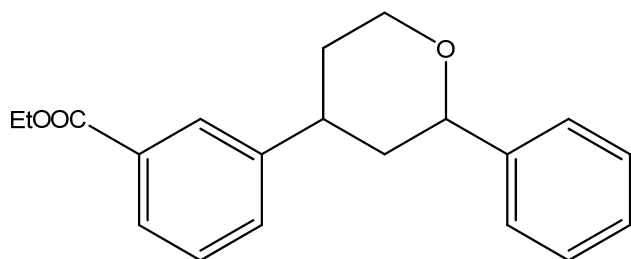
Synthesized by method A with O-TMEDA as an additive, 2.6 of 5eq of Alkyl-I was recovered after reaction with 99% purity.

Eluted from the column with hexane-diethyl ether (10:1 to 1:2) in 60% yield as a colorless liquid:

$^1\text{H NMR}$ (400MHz, CDCl_3): 7.29 (m, 2H), 7.19 (m, 2H), 4.22 (br, 2H), 3.15-3.60 (br, 4H), 2.70 (m, 3H), 1.80 (m, 2H), 1.61 (m, 2H), 1.46 (s, 9H), 1.05-1.25 (br, 6H).

$^{13}\text{C NMR}$ (100 MHz, CDCl_3): 171.2, 154.7, 146.8, 135.3, 126.7, 126.5, 79.4, 44.2, 43.2, 42.5, 39.1, 33.0, 28.4, 14.1, 12.8.

HRCI-MS: calculated for ($\text{C}_{21}\text{H}_{32}\text{N}_2\text{O}_3$, M+H), 361.2491; found, 361.2481.



ethyl 3-(2-phenyltetrahydro-2H-pyran-4-yl)benzoate (table 4, entry 20):

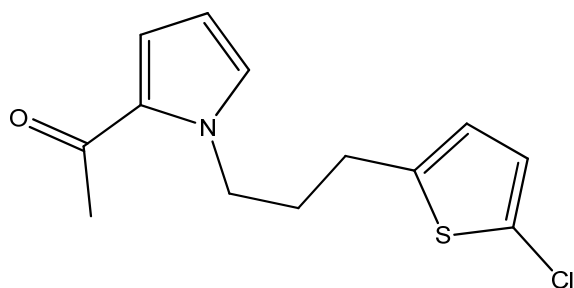
Synthesized by method A with O-TMEDA as an additive, 3.6 of 5eq of Alkyl-I was recovered after reaction with 99% purity.

Eluted from the column with hexane-diethyl ether (20:1 to 10:1) in 58% yield as a colorless oil:

¹H NMR (400MHz, CDCl₃): 7.95 (s, 1H), 7.91 (d, *J* = 7.6 Hz, 1H), 7.40 (m, 6H), 7.28 (m, 1H), 4.51 (dd, *J*₁ = 11.2 Hz, *J*₂ = 1.8 Hz, 1H), 4.39 (q, *J* = 7.0 Hz, 2H), 4.31 (m, 1H), 3.79 (td, *J*₁ = 11.4 Hz, *J*₂ = 2.9 Hz, 1H), 3.05 (m, 1H), 2.10 (m, 1H), 1.85 (m, 3H), 1.40 (t, *J* = 7.3 Hz, 3H).

¹³C NMR (100 MHz, CDCl₃): 166.6, 145.6, 142.5, 131.2, 130.7, 128.5, 128.3, 127.8, 127.6, 127.4, 125.7, 79.8, 68.5, 60.9, 41.9, 41.2, 33.1, 14.3.

HRCI-MS: calculated for (C₂₀H₂₂O₃, M+H), 311.1647; found, 311.1658.



1-(1-(3-(5-chlorothiophen-2-yl)propyl)-1H-pyrrol-2-yl)ethanone (table 5, entry 5):

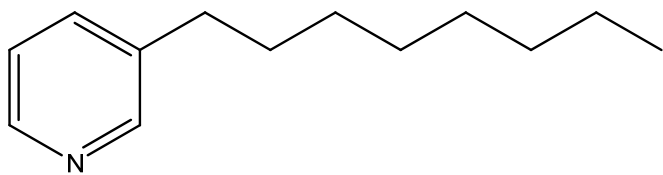
Synthesized by method B with O-TMEDA as an additive.

Eluted from the column with hexane-diethyl ether (30:1 to 20:1) in 62% yield as a slightly yellow liquid:

¹H NMR (400MHz, CDCl₃): 6.97 (dd, *J*₁ = 4.1 Hz, *J*₂ = 1.8 Hz, 1H), 6.82 (m, 1H), 6.71 (d, *J* = 3.8 Hz, 1H), 6.57 (m, 1H), 6.14 (dd, *J*₁ = 3.8 Hz, *J*₂ = 2.3 Hz, 1H), 4.35 (t, *J* = 7.0 Hz, 2H), 2.71 (t, *J* = 7.3 Hz, 2H), 2.44 (s, 3H), 2.08 (m, 2H).

¹³C NMR (100 MHz, CDCl₃): 188.2, 142.9, 130.2, 130.0, 126.9, 125.7, 123.7, 120.4, 108.0, 48.7, 32.5, 27.3, 27.2.

HRCI-MS: calculated for (C₁₃H₁₄OCINS, M+H), 268.0563; found, 268.0574.



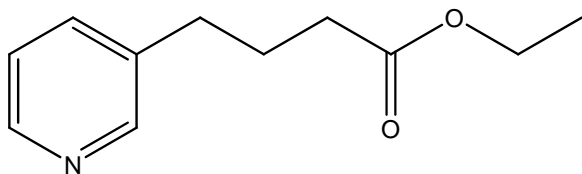
3-octylpyridine (table 5, entry 6):²⁸

Synthesized by method B with TMEDA as an additive.

Eluted from the column with hexane-diethyl ether (20:1 to 1:1) in 76% yield as a colorless liquid:

¹H NMR (400MHz, CDCl₃): 8.42 (m, 2H), 7.48 (m, 1H), 7.19 (dd, $J_1 = 7.6$ Hz, $J_2 = 4.8$ Hz, 1H), 2.59 (m, 2H), 1.61 (m, 2H), 1.24-1.36 (m, 10H), 0.87 (m, 3H).

¹³C NMR (100 MHz, CDCl₃): 149.8, 147.0, 137.9, 135.7, 123.2, 33.0, 31.8, 31.1, 29.3, 29.2, 29.1, 22.6, 14.0.



ethyl 4-(pyridin-3-yl)butanoate (table 5, entry 7):

Synthesized by method B with O-TMEDA as an additive.

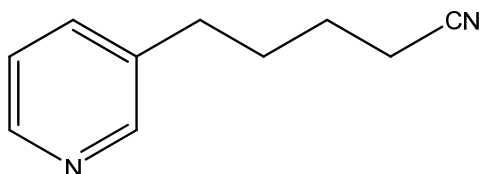
Eluted from the column with hexane-diethyl ether (1:1 to 1:4) in 69% yield as a colorless liquid:

¹H NMR (400MHz, CDCl₃): 8.44 (m, 2H), 7.50 (m, 1H), 7.20 (dd, $J_1 = 7.4$ Hz, $J_2 = 5.0$ Hz, 1H), 4.12 (q, $J = 7.0$ Hz, 2H), 2.65 (m, 2H), 2.32 (t, $J = 7.4$ Hz, 2H), 1.95 (m, 2H), 1.24 (t, $J = 7.2$ Hz, 3H).

²⁸ I. Kondolff, H. Doucet and M. Santelli, *Tetrahedron* **2004**, 60, 3813–3818.

^{13}C NMR (100 MHz, CDCl_3): 173.0, 149.8, 147.5, 136.6, 135.8, 123.3, 60.3, 33.4, 32.1, 26.1, 14.1.

HRCI-MS: calculated for ($\text{C}_{11}\text{H}_{15}\text{O}_2\text{N}$, $\text{M}+\text{H}$), 194.1181; found, 194.1183.



5-(pyridin-3-yl)pentanenitrile (table 5, entry 8):

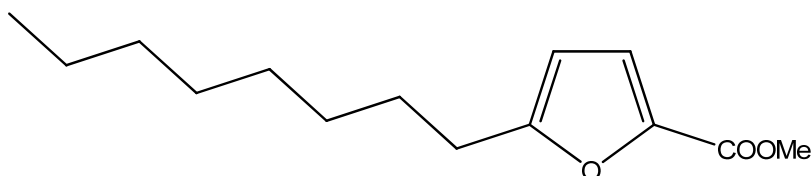
Synthesized by method B with TMEDA as an additive.

Eluted from the column with hexane-ethyl acetate (1:1 to 1:99) in 78% yield as a slightly yellow liquid:

^1H NMR (400MHz, CDCl_3): 8.45 (m, 2H), 7.49 (d, $J = 7.6$ Hz, 1H), 7.22 (dd, $J_1 = 7.2$ Hz, $J_2 = 5.0$ Hz, 1H), 2.66 (t, $J = 7.6$ Hz, 2H), 2.36 (t, $J = 7.0$ Hz, 2H), 1.79 (m, 2H), 1.69 (m, 2H).

^{13}C NMR (100 MHz, CDCl_3): 149.7, 147.6, 136.3, 135.6, 123.3, 119.3, 32.0, 29.9, 24.7, 17.0.

HRCI-MS: calculated for ($\text{C}_{10}\text{H}_{12}\text{N}_2$, $\text{M}+\text{H}$), 161.1079; found, 161.1074.



methyl 5-octylfuran-2-carboxylate (table 5, entry 9):

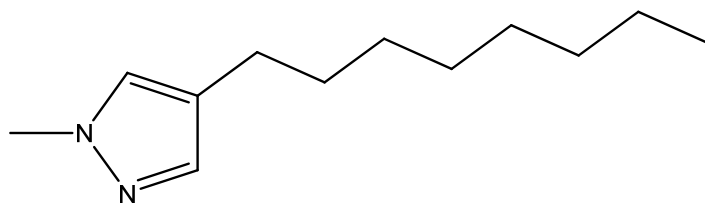
Synthesized by method A with O-TMEDA as an additive.

Eluted from the column with hexane-diethyl ether (60:1 to 30:1) in 65% yield as a slightly yellow liquid:

¹H NMR (400MHz, CDCl₃): 7.09 (d, *J* = 3.2 Hz, 1H), 6.11 (d, *J* = 3.2 Hz, 1H), 3.87 (s, 3H), 2.67 (t, *J* = 7.3 Hz, 2H), 1.66 (m, 2H), 1.20-1.35 (m, 10H), 0.87 (t, *J* = 6.7 Hz, 3H).

¹³C NMR (100 MHz, CDCl₃): 161.6, 159.2, 142.7, 119.2, 107.4, 51.6, 31.7, 29.2, 29.14, 29.12, 28.3, 27.7, 22.6, 14.0.

HRCI-MS: calculated for (C₁₄H₂₂O₃, M+H), 239.1647; found, 239.1653.



1-methyl-4-octyl-1H-pyrazole (table 5, entry 10):

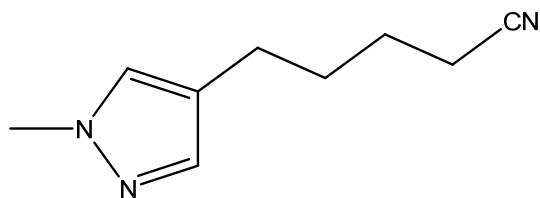
Synthesized by method A with O-TMEDA as an additive.

Eluted from the column with hexane-diethyl ether (1:1) in 91% yield as a slightly yellow liquid:

¹H NMR (400MHz, CDCl₃): 7.28 (s, 1H), 7.10 (s, 1H), 3.83 (s, 3H), 2.41 (t, *J* = 7.6 Hz, 2H), 1.51 (m, 2H), 1.20-1.35 (m, 10H), 0.86 (t, *J* = 6.5 Hz, 3H).

¹³C NMR (100 MHz, CDCl₃): 138.5, 127.9, 122.0, 38.6, 31.8, 30.9, 29.3, 29.2, 24.0, 22.5, 14.0.

HRCI-MS: calculated for (C₁₂H₂₂N₂, M+H), 195.1861; found, 195.1859.



5-(1-methyl-1H-pyrazol-4-yl)pentanenitrile (table 5, entry 11):

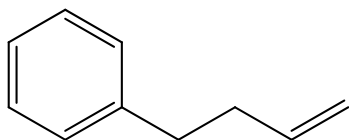
Synthesized by method A with O-TMEDA as an additive, 3.4 of 5eq of Alkyl-I was recovered after reaction with 99% purity.

Eluted from the column with hexane-diethyl ether (20:1 to 1:15) in 74% yield as a colorless liquid:

$^1\text{H NMR}$ (400MHz, CDCl_3): 7.27 (s, 1H), 7.14 (s, 1H), 3.83 (s, 3H), 2.48 (t, $J = 7.0$ Hz, 2H), 2.33 (t, $J = 6.5$ Hz, 2H), 1.68 (m, 4H).

$^{13}\text{C NMR}$ (100 MHz, CDCl_3): 138.4, 128.1, 120.5, 119.5, 38.6, 29.8, 24.6, 23.1, 16.8.

HRCI-MS: calculated for ($\text{C}_9\text{H}_{13}\text{N}_3$, M+H), 164.1188; found, 164.1194.

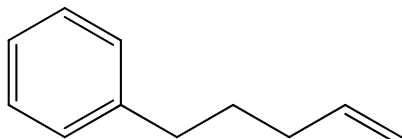


4-phenyl-1-butene (mechanistic investigations, entry 1):²⁹

Eluted from the column with hexane-diethyl ether (100:1) in 78% yield as a colorless liquid:

$^1\text{H NMR}$ (400MHz, CDCl_3): 7.31 (m, 2H), 7.20 (m, 3H), 5.88 (m, 1H), 5.04 (m, 2H), 2.73 (t, $J = 7.3$ Hz, 2H), 2.40 (q, $J = 7.6$ Hz, 2H).

$^{13}\text{C NMR}$ (100 MHz, CDCl_3): 141.8, 138.0, 128.4, 128.2, 125.7, 114.8, 35.5, 35.3.



²⁹ D. Crich, and X. S. Mo, *J. Am. Chem. Soc.* **1998**, 120 (33), 8298-8304.

5-phenyl-1-pentene (mechanistic investigations, entry 2):³⁰

Eluted from the column with hexane-diethyl ether (100:1) in 87% yield as a colorless liquid:

¹H NMR (400MHz, CDCl₃): 7.30 (m, 2H), 7.20 (m, 3H), 5.87 (m, 1H), 5.04 (m, 2H), 2.65 (m, 2H), 2.12 (q, $J = 7.0$ Hz, 2H), 1.75 (m, 2H).

¹³C NMR (100 MHz, CDCl₃): 142.4, 138.5, 128.4, 128.2, 125.6, 114.6, 35.3, 33.2, 30.6.

³⁰ J. C. Anderson, and R. H. Munday, *J. Org. Chem.* **2004**, 69 (25), 8971-8974.

