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AN IMPROVED COPPER-CATALYZED CROSS-COUPLING REACTION OF ALKYL TRIFLATES WITH PRIMARY ALKYL GRIGNARD REAGENTS

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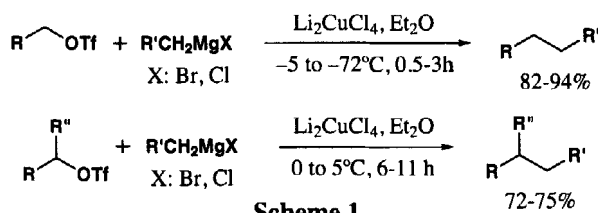
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Metal-catalyzed cross-coupling reactions are powerful carbon-carbon bond formation processes that have received a great deal of attention over the past three decades.¹ This methodology has been extensively used as a convenient tool to synthesize various natural products, biologically active compounds, and many other highly complex organic fine chemicals.² This method includes reactions of tosylates with Grignard reagents catalyzed by different metals ranging from expensive and physiologically suspicious noble metals to inexpensive and toxicologically benign iron salts.³ The primary limitation of this method has been that displacements of tosylates often require drastic reaction conditions. Triflates have been recognized as one of the most reactive leaving groups in solvolytic displacement reactions⁴ and indeed showed much higher activity than the corresponding tosylates in cross-coupling reactions with alkynyllithium reagents.⁵ This suggests that triflates should be more easily coupled with organometallic nucleophiles and, consequently, would extend the range of electron-deficient substrates that can be involved in cross-coupling reactions. As previously noted,⁶ the cross-coupling reaction of tosylates with Grignard reagents has been improved by the use of copper catalyst dilithium tetrachlorocuprate (Li_2CuCl_4). An attempt to replace the tosylates with the triflates under the same conditions has been reported; however, the required presence of equimolar quantities of cuprous bromide (CuBr) as co-catalyst, diminishes the value of this method.⁷ Herein, we report that alkyl-alkyl cross-coupling reactions can be efficiently catalyzed in the presence of dilithium tetrachlorocuprate as the only catalyst using mild conditions and diethyl ether as solvent (*Scheme 1*).



Scheme 1

Table 1 shows that primary alkyl triflates (Entries 1-12) can be efficiently cross-coupled with Grignard reagents to afford the desired coupling products in 82-94% yield. It should be noted that steric hindrance at the β -position of primary triflates required higher temperatures and longer reaction times to furnish the coupling product (see 2,2-dimethylpentyl triflate,

Table 1. Cross-coupling Reactions of Triflates with Grignard Reagents

Entry	R-OTf	Grignard	Products	Temp. (°C)	Time (h)	Yield (%)
1		$\text{C}_4\text{H}_9\text{MgCl}$		-72	1.0	93
2		$\text{C}_4\text{H}_9\text{MgCl}$		-70	1.0	94
3		$\text{C}_3\text{H}_7\text{MgCl}$		-56	3.0	91
4		$\text{C}_2\text{H}_5\text{MgBr}$		-54	3.0	92
5		$\text{C}_4\text{H}_9\text{MgCl}$		-62	1.0	93
6		$\text{C}_4\text{H}_9\text{MgCl}$		-65	0.9	92
7		$\text{C}_4\text{H}_9\text{MgCl}$		-65	1.0	90
8		$\text{C}_2\text{H}_5\text{MgBr}$		-20	0.5	92
9		$\text{C}_4\text{H}_9\text{MgCl}$		-65	0.5	94
10		$\text{C}_4\text{H}_9\text{MgCl}$		-65	0.5	92
11		$\text{C}_4\text{H}_9\text{MgCl}$		-65	1.0	91
12		$\text{C}_4\text{H}_9\text{MgCl}$		-5	7.0	82
13		$\text{C}_3\text{H}_7\text{MgBr}$		5	11.0	72
14		$\text{C}_4\text{H}_9\text{MgCl}$		0	6.0	75
15		$\text{C}_4\text{H}_9\text{MgCl}$		-60	1.0	94
16		$\text{C}_4\text{H}_9\text{MgCl}$		-60	1.0	90

Entry 12). The effect of steric hindrance near the site of reaction slows down the reaction rate as is further evidenced in the reactions of the secondary triflates (*Entries 13 and 14*). Attempted coupling of cyclohexyl triflate and cycloheptyl triflate with C_4H_9MgCl did not result in formation of the expected coupling products; instead, only alkenes were produced (*Entries 15 and 16*). Evidently, under the strongly basic conditions α -hydrogen elimination is more favorable than cross-coupling.^{8,9} The alkyl-alkyl cross-coupling reaction with retention of alkene geometry has successfully been demonstrated in the reaction of *Entry 6*, where the allylic triflate, *cis*-2-hexenyl triflate, was regioselectively converted into *cis*-4-decene by an S_N2 -type reaction. It is similar to its acetate analog under the same reaction conditions,⁶ but requires a shorter reaction time and affords a higher yield. Attempts to prepare triflates from highly conjugated allylic alcohols, such as 2,4-hexadien-1-ol and cinnamyl alcohol, and from a tertiary alcohol, such as 3-methylpentan-3-ol, were unsuccessful; sticky masses were obtained during the triflation process from conjugated allylic alcohols, even with careful management of reagents, solvents, and reaction conditions. We assume that the highly conjugated triflates have high carbonium ion character and initiate polymerization at ambient temperature. The failure to generate tertiary triflates, however, appeared to be the direct result of spontaneous, β -hydrogen elimination, probably induced by the presence of pyridine as a non-nucleophilic proton trap.¹⁰ Triflation of primary alcohols can be completed within 30-60 min at -5 to $0^\circ C$ with triflic anhydride and pyridine in dichloromethane (CH_2Cl_2);^{4c,9,11} for secondary alcohols, triflation can be accomplished within 2 h under the same conditions. Although all triflates (*Entries 1-16*) are sufficiently stable at room temperature to be easily checked by GC and GC-MS, most triflates are very reactive and thermally labile compounds,¹² and therefore, were prepared *in situ* and used directly for coupling without further purification.

Although tetrahydrofuran (THF) is the most common solvent for the cross coupling reactions,^{2h,11a,13} there are problems during addition of the triflate-THF solution to the Grignard reagents, which is the commonly used procedure in the literature.^{11a,13a} The triflate-THF solutions became more and more viscous at ambient temperature and it was impossible to add to the Grignard reagent solutions by dropping funnel or syringe. Inverse addition (Grignard reagent to the triflate THF solution)^{2h,13b} did not improve matters much, even using an ice bath to cool the triflate-THF solution. It is likely that THF polymerization occurs during the preparation of the triflate-THF solutions, because many different triflates have been reported as efficient initiators of the cationic ring-opening living polymerization of THF.^{10a,14} This problem was easily overcome by replacing THF with diethyl ether as solvent and the two addition methods (normal and inverse) resulted in similar yields.

In conclusion, we have shown that cross-coupling reactions of alkyl triflates with alkyl Grignard reagents catalyzed by copper catalyst, Li_2CuCl_4 , can be carried out in diethyl ether (*Table 2*).

EXPERIMENTAL SECTION

^1H and ^{13}C NMR spectra were recorded at 400 MHz for ^1H and 100 MHz for ^{13}C using CDCl_3 as the solvent. The chemical shifts are reported as δ -values using tetramethylsilane (0 ppm) for proton spectra and carbon spectra as an internal standard. Gas chromatography electron impact (EI) mass spectrometry (GC-MS) was conducted using a 30 m x 0.25 mm id, 0.25 μm film-thickness capillary column (DB-5) with helium as carrier gas (38 cm/s). The initial temperature of the column was 50°C for 2 min, then programmed to 250°C at 15°C/min and held for 20 min. A 70 eV electron beam was employed for sample ionization. GC analyses were performed in the splitless mode using a 30 m x 0.32 mm id, 0.25 μm film-thickness capillary column (HB-5) with hydrogen as carrier gas (38 cm/s). The initial temperature of the column was 50°C for 2 min, then programmed to 250°C at 10°C/min and held for 20 min. All reactions were performed under an atmosphere of dry nitrogen with magnetic stirring. Reactions were monitored by GC and GC-MS. Silica gel 60 was used for flash chromatography. The copper catalyst (Li_2CuCl_4 , 0.1 M in THF solution) and Grignard reagents used in coupling reactions ($\text{C}_2\text{H}_5\text{MgBr}$, 3.0 M Et_2O solution, $\text{C}_3\text{H}_7\text{MgCl}$, 2.0 M Et_2O solution, and $\text{C}_4\text{H}_9\text{MgCl}$, 2.0 M THF solution) were purchased from Aldrich. Solvents were distilled prior to use: diethyl ether was distilled from sodium-benzophenone ketyl under nitrogen; CH_2Cl_2 was distilled from calcium hydride; hexane was distilled from sodium; and pentane was distilled from calcium hydride.

General Procedure for Preparation of Triflates.- To a mixture of alcohol (1 mmol) and pyridine (1 mmol) in CH_2Cl_2 (4 mL per mmol alcohol) was added triflic anhydride (1.2 mmol) at about -20°C. The solution was then kept at -5 to 0°C by an ice-salt bath. The reaction progress was monitored by GC until the alcohol was consumed. The mixture was diluted with hexanes (double the volume of CH_2Cl_2) and filtered through a pad of Celite. For highly volatile triflates, (Entries 6, 8-12, and 15-16), pentane was used. The solvent was evaporated to afford the crude triflates that were used directly for the coupling reaction.

General Procedure for Cross-Coupling Reactions of Triflates with Grignard Reagents.- To a freshly prepared crude triflate and Li_2CuCl_4 (1.5 mol%, 0.1 M in THF) solution in anhydrous diethyl ether (4 mL per mmol triflate) was added the Grignard reagent (1.4 equiv) at the temperatures given in Table 1. The reaction mixture was stirred for the times listed in Table 1. The reaction progress was monitored by GC until the triflate was consumed. The reaction was quenched by adding 2 mL of H_2O at -20°C, warmed to ambient temperature and then further acidified to pH 3 with 2 N HCl. The organic layer was separated, and the aqueous layer was extracted with hexanes. The combined organic layers were washed with water, brine, dried (Na_2SO_4), and concentrated to afford the crude materials that were purified by flash chromatography on silica gel using hexanes as eluent.

(3Z,6Z,9Z)-3,6,9-Docosatriene (Entry 1): (9Z,12Z,15Z)-9,12,15-Octadecantrieneol (100 mg, 0.379 mmol) was treated sequentially with 1.2 equiv of triflic anhydride (0.468 mmol, 128.3 mg, 77 μL), 0.015 equiv of Li_2CuCl_4 (0.0057 mmol, 0.1 M solution in THF, 57 μL) and 1.4 equiv of $\text{C}_4\text{H}_9\text{MgCl}$ (0.531 mmol, 2 M ether solution, 0.27 mL). The workup and purification by flash chromatography afforded 107 mg (93%) of the target compound as a colorless oil.

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1-Pentadecene (Entry 2): 10-Undecenol (500 mg, 2.94 mmol) was treated sequentially with 1.2 equiv of triflic anhydride (3.53 mmol, 1.0 g, 0.59 mL), 0.015 equiv of Li_2CuCl_4 (0.0441 mmol, 0.1 M solution in THF, 441 μL) and 1.4 equiv of $\text{C}_4\text{H}_9\text{MgCl}$ (4.95 mmol, 2 M ether solution, 2.47 mL). The workup and purification by flash chromatography yielded 581 mg (94%) of the title compound as a colorless oil.

Heptadecane (Entry 3): Tetradecanol (514 mg, 2.40 mmol) was treated sequentially with 1.2 equiv of triflic anhydride (2.88 mmol, 0.813 g, 0.49 mL), 0.015 equiv of Li_2CuCl_4 (0.036 mmol, 0.1 M solution in THF, 360 μL) and 1.4 equiv of $\text{C}_3\text{H}_7\text{MgCl}$ (3.36 mmol, 2 M ether solution, 1.68 mL). The workup and purification by flash chromatography afforded 524 mg (91%) of the title compound as a colorless oil.

Hexadecane (Entry 4): Tetradecanol (455 mg, 2.12 mmol) was treated sequentially with 1.2

Table 2. Spectral Data of Coupling Products

Compounds	^1H NMR δ	^{13}C NMR δ	MS m/z (%)
(3Z,6Z,9Z)-3,6,9- Docosatriene	0.87 (t, $J = 6.8$ Hz, 3H), 0.96 (t, $J = 7.4$ Hz, 3H), 1.25-1.34 (m, 20 H), 2.02-2.10 (m, 4H), 2.80 (t, $J = 6.0$ Hz, 4H), 5.27-5.41 (m, 6H)	14.1, 14.3, 20.6, 22.7, 25.5, 25.6, 27.25, 29.33, 29.37, 29.57, 29.65, 29.66, 29.67, 29.68, 29.7, 31.9, 127.1, 127.6, 128.2, 128.3, 130.4, 131.9	304 (M^+) (4), 275 (2), 248 (15), 194 (1), 163 (2), 149 (6), 135 (12), 121 (16), 108 (82), 95 (42), 93 (39), 79 (100), 67 (50), 55 (27)
1-Pentadecene	0.87 (t, $J = 6.8$ Hz, 3H), 1.19-1.32 (br, 20H), 1.36 (m, 2H), 2.02 (qt, $J = 7.6$, 1.2 Hz, 2H), 4.91 (m, 1H), 4.98 (m, 1H), 5.80 (m, 1H)	14.1, 22.7, 29.0, 29.2, 29.4, 29.55, 29.66, 29.69, 29.70, 29.71, 29.73, 32.0, 33.9, 114.1, 139.3	210 (M^+) (13), 182 (9), 168 (3), 154 (4), 140 (9), 125 (21), 111 (50), 97 (100), 83 (95), 69 (73), 55 (72)
Heptadecane	0.85 (t, $J = 6.4$ Hz, 6H), 1.20-1.39 (br, 30H)	14.1, 22.7, 29.4, 29.7, 29.8, 32.0	240 (M^+) (5), 197 (1), 183 (2), 169 (3), 155 (3), 141 (4), 127 (6), 113 (9), 99 (16), 85 (53), 71 (74), 57 (100)
Hexadecane	0.87 (t, $J = 8.0$ Hz, 6H), 1.21-1.32 (br, 28H)	14.1, 22.7, 29.4, 29.7, 29.8, 32.0	226 (M^+) (4), 155 (3), 141 (3), 127 (5), 113 (8), 99 (14), 85 (51), 71 (71), 57 (100), 55 (19)
6-Tridecyne	0.86 (t, $J = 7.2$ Hz, 3H), 0.87 (t, $J = 7.2$ Hz, 3H), 1.20-1.38 (br, 10H), 1.41-1.49 (br, 4H), 2.11 (t, $J = 6.8$ Hz, 4H)	13.97, 14.02, 18.71, 18.75, 22.2, 22.6, 28.5, 29.0, 29.1, 31.1, 31.4, 80.2	151 ($\text{M}^+ - 29$) (8), 137 (3), 123 (5), 109 (36), 95 (80), 81 (96), 67 (100), 54 (54)
<i>cis</i> -4-Decene	0.87 (t, $J = 6.8$ Hz, 3H), 0.94 (t, $J = 7.6$ Hz, 3H), 1.21-1.37 (br, 8H), 1.96-2.06 (br, 4H), 5.27-5.38 (m, 2H)	14.1, 14.4, 20.5, 22.7, 27.1, 29.0, 29.8, 31.8, 129.4, 131.6	140 (M^+) (46), 111 (9), 97 (22), 84 (21), 83 (21), 70 (66), 69 (87), 56 (72), 55 (100)

Table 2. Continued...

Compounds	¹ H NMR δ	¹³ C NMR δ	MS <i>m/z</i> (%)
1-(2-Ethoxy-ethoxy)hexane	0.83 (t, <i>J</i> = 6.8 Hz, 3H), 1.16 (t, <i>J</i> = 6.8 Hz, 3H), 1.20-1.33 (br, 6H), 1.53 (<i>J</i> = 6.8 Hz, 2H), 3.40 (t, <i>J</i> = 6.8 Hz, 2H), 3.48 (q, <i>J</i> = 6.8 Hz, 2H), 3.52 (s, 4H)	13.9, 15.1, 22.5, 25.7, 29.5, 31.6, 66.6, 69.8, 70.0, 71.5	175 (M ⁺ -15) (1), 145 (1), 130 (4), 115 (3), 101 (7), 91 (36), 85 (100), 83 (38), 74 (31), 69 (14), 59 (73), 55 (22)
4-Propylcyclohexene	0.88 (t, <i>J</i> = 7.2 Hz, 3H), 1.21 (m, 3H), 1.32 (m, 2H), 1.58 (m, 2H), 1.71 (m, 1H), 2.00-2.10 (br, 3H), 5.64 (m, 2H)	14.3, 20.0, 25.3, 29.0, 31.9, 33.2, 39.1, 126.7, 126.9	124 (M ⁺) (29), 109 (5), 96 (15), 95 (30), 91 (4), 83 (12), 82 (85), 81 (100), 79 (31), 77 (14), 67 (52), 55 (31), 54 (59)
4-Pentylcyclohexene	0.87 (t, <i>J</i> = 7.2 Hz, 3H), 1.13-1.38 (br, 9H), 1.50 (m, 1H), 1.61 (m, 1H), 1.72 (m, 1H), 1.90-2.10 (br, 3H), 5.64 (m, 2H)	14.1, 22.7, 25.3, 26.6, 29.0, 32.0, 32.2, 33.5, 36.7, 126.8, 127.0, 4 (41)	152 (M ⁺) (19), 124 (4), 109 (10), 96 (57), 95 (20), 91 (8), 82 (43), 81 (100), 79 (25), 77 (11), 67 (46), 55 (26)
3-Ethyl-octane	0.82 (t, <i>J</i> = 8.0 Hz, 6H), 0.88 (t, <i>J</i> = 8.0 Hz, 3H), 1.15 (m, 1H), 1.11-1.33 (m, 12H)	10.9, 14.1, 22.8, 25.5, 26.5, 32.4, 32.8, 40.4	142 (M ⁺) (2), 113 (18), 112 (41), 98 (2), 83 (5), 71 (100), 70 (28), 57 (87), 55 (18)
4-Methyl-nonane	0.83 (d, <i>J</i> = 8.0 Hz, 3H), 0.86 (t, <i>J</i> = 8.0 Hz, 3H), 0.87 (t, <i>J</i> = 8.0 Hz, 3H), 1.08 (br, 2H), 1.20-1.40 (br, 11H)	14.1, 14.4, 19.7, 20.2, 22.8, 26.8, 32.3, 32.6, 37.1, 39.5	142 (M ⁺) (5), 127 (2), 112 (3), 99 (15), 98 (35), 85 (7), 71 (51), 70 (46), 57 (100), 55 (18)
4,4-Dimethyl-nonane	0.81 (s, 6H), 0.87 (t, <i>J</i> = 8.0 Hz, 3H), 0.88 (t, <i>J</i> = 8.0 Hz, 3H), 1.10-1.31 (br, 12H)	14.1, 15.1, 17.2, 22.8, 23.7, 27.3, 32.7, 33.0, 42.1, 44.6	141 (M ⁺ -15) (4), 113 (23), 85 (100), 84 (28), 71 (53), 57 (64)
4-Methyl-octadecane	0.82 (d, <i>J</i> = 8.0 Hz, 3H), 0.86 (t, <i>J</i> = 8.0 Hz, 3H), 0.87 (t, <i>J</i> = 8.0 Hz, 3H), 1.04-1.08 (br, 2H), 1.20-1.35 (br, 29H)	14.1, 14.4, 19.7, 20.2, 22.7, 27.1, 29.4, 29.7, 29.8 (high intensity), 29.9, 30.1, 32.0, 32.5, 37.1, 39.5	268 (M ⁺) (2), 253 (4), 239 (4), 225 (53), 211 (1), 197 (9), 196 (12), 183 (4), 169 (8), 155 (11), 141 (14), 127 (18), 113 (22), 99 (32), 85 (93), 71 (100), 57 (98), 55 (47)
5-Methyl-dodecane	0.83 (d, <i>J</i> = 6.8 Hz, 3H), 0.87 (t, <i>J</i> = 6.8 Hz, 3H), 0.88 (t, <i>J</i> = 6.9 Hz, 3H), 1.04-1.12 (br, 2H), 1.18-1.40 (br, 17H)	14.1, 14.2, 19.7, 22.7, 23.1, 27.1, 29.4, 29.5, 30.1, 32.0, 32.8, 36.8, 37.2	184 (M ⁺) (2), 169 (2), 154 (2), 140 (2), 127 (14), 126 (26), 113 (2), 98 (7), 85 (100), 71 (74), 57 (81)

equiv of triflic anhydride (2.54 mmol, 0.718 g, 0.43 mL), 0.015 equiv of Li₂CuCl₄, (0.0318 mmol, 0.1 M solution in THF, 318 μ L) and 1.4 equiv of C₂H₅MgBr (2.97 mmol, 3 M ether solu-

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tion, 0.99 mL). The workup and purification by flash chromatography yielded 443 mg (92%) of the title compound as a colorless oil.

6-Tridecyne (Entry 5): 3-Nonynol (430 mg, 3.06 mmol) was treated sequentially with 1.2 equiv of triflic anhydride (3.68 mmol, 1.04 g, 0.62 mL), 0.015 equiv of Li_2CuCl_4 , (0.0459 mmol, 0.1 M solution in THF, 459 μL) and 1.4 equiv of $\text{C}_4\text{H}_9\text{MgCl}$ (4.29 mmol, 2 M ether solution, 2.15 mL). The workup and purification by flash chromatography yielded 511 mg (93%) of the title compound as a colorless oil.

cis-4-Decene (Entry 6): *cis*-2-Hexenol (500 mg, 4.99 mmol) was treated sequentially with 1.2 equiv of triflic anhydride (5.99 mmol, 1.69 g, 1.01 mL), 0.015 equiv of Li_2CuCl_4 , (0.0749 mmol, 0.1 M solution in THF, 749 μL) and 1.4 equiv of $\text{C}_4\text{H}_9\text{MgCl}$ (6.99 mmol, 2 M ether solution, 3.5 mL). The workup and purification by flash chromatography yielded 643 mg (92%) of the title compound as a colorless oil.

1-(2-Ethoxyethoxy)hexane (Entry 7): 2-(2-Ethoxyethoxy)ethanol (510 mg, 3.80 mmol) was treated sequentially with 1.2 equiv of triflic anhydride (4.57 mmol, 1.29 g, 0.77 mL), 0.015 equiv of Li_2CuCl_4 , (0.0578 mmol, 0.1 M solution in THF, 578 μL) and 1.4 equiv of $\text{C}_4\text{H}_9\text{MgCl}$ (5.34 mmol, 2 M ether solution, 2.67 mL). The workup and purification by flash chromatography yielded 635 mg (96%) of the title compound as a colorless oil.

4-Propylcyclohexene (Entry 8): 3-Cyclohexene-1-methanol (400 mg, 3.56 mmol) was treated sequentially with 1.2 equiv of triflic anhydride (4.28 mmol, 1.27 g, 0.72 mL), 0.015 equiv of Li_2CuCl_4 , (0.0534 mmol, 0.1 M solution in THF, 534 μL) and 1.4 equiv of $\text{C}_2\text{H}_5\text{MgBr}$ (4.98 mmol, 3 M ether solution, 1.67 mL). The workup and purification by flash chromatography yielded 408 mg (92%) of the title compound as a colorless oil.

4-Pentylcyclohexene (Entry 9): 3-Cyclohexene-1-methanol (400 mg, 3.56 mmol) was treated sequentially with 1.2 equiv of triflic anhydride (4.28 mmol, 1.27 g, 0.72 mL), 0.015 equiv of Li_2CuCl_4 , (0.0534 mmol, 0.1 M solution in THF, 534 μL) and 1.4 equiv of $\text{C}_4\text{H}_9\text{MgCl}$ (4.98 mmol, 2 M ether solution, 2.50 mL). The workup and purification by flash chromatography yielded 506 mg (94%) of the title compound as a colorless oil.

3-Ethyloctane (Entry 10): 2-Ethylbutanol (506 mg, 4.95 mmol) was treated sequentially with 1.2 equiv of triflic anhydride (5.94 mmol, 1.68 g, 1.0 mL), 0.015 equiv of Li_2CuCl_4 , (0.0743 mmol, 0.1 M solution in THF, 743 μL) and 1.4 equiv of $\text{C}_4\text{H}_9\text{MgCl}$ (6.93 mmol, 2 M ether solution, 3.47 mL). The workup and purification by flash chromatography yielded 645 mg (92%) of the title compound as a colorless oil.

4-Methylnonane (Entry 11): 2-Methylpentanol (504 mg, 4.92 mmol) was treated sequentially with 1.2 equiv of triflic anhydride (5.91 mmol, 1.67 g, 1.0 mL), 0.015 equiv of Li_2CuCl_4 , (0.0738 mmol, 0.1 M solution in THF, 738 μL) and 1.4 equiv of $\text{C}_4\text{H}_9\text{MgCl}$ (6.90 mmol, 2 M ether solution, 3.45 mL). The workup and purification by flash chromatography yielded 634 mg (91%) of the title compound as a colorless oil.

4,4-Dimethylnonane (Entry 12): 2,2-Dimethylpentanol (500 mg, 4.30 mmol) was treated sequentially with 1.2 equiv of triflic anhydride (5.17 mmol, 1.46 g, 0.87 mL), 0.015 equiv of Li_2CuCl_4 , (0.0645 mmol, 0.1 M solution in THF, 645 μL) and 1.4 equiv of $\text{C}_4\text{H}_9\text{MgCl}$ (6.03 mmol, 2 M ether solution, 3.01 mL). The workup and purification by flash chromatography yielded 552 mg (82%) of the title compound as a colorless oil.

4-Methyloctadecane (Entry 13): 2-Hexadecanol (500 mg, 2.06 mmol) was treated sequentially with 1.2 equiv of triflic anhydride (2.47 mmol, 0.70 g, 0.42 mL), 0.015 equiv of Li_2CuCl_4 , (0.0309 mmol, 0.1 M solution in THF, 309 μL) and 1.4 equiv of $\text{C}_3\text{H}_7\text{MgBr}$ (2.98 mmol, 2 M ether solution, 1.45 mL). The workup and purification by flash chromatography yielded 399 mg (72%) of the title compound as a colorless oil.

5-Methyldodecane (Entry 14): 2-Nonanol (501 mg, 3.47 mmol) was treated sequentially with 1.2 equiv of triflic anhydride (4.16 mmol, 1.18 g, 0.70 mL), 0.015 equiv of Li_2CuCl_4 , (0.0521 mmol, 0.1 M solution in THF, 521 μL) and 1.4 equiv of $\text{C}_4\text{H}_9\text{MgCl}$ (4.86 mmol, 2 M ether solution, 2.43 mL). The workup and purification by flash chromatography yielded 476 mg (75%) of the title compound as a colorless oil.

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