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COPPER(I)-CATALYZED DIRECT ARYLATION OF 1,4-DISUBSTITUTED 1,2,3-TRIAZOLES WITH ARYL IODIDES

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Abstract – Treatment of 1,4-disubstituted 1,2,3-triazoles with aryl iodides in the presence of a catalytic amount of copper chloride and lithium *tert*-butoxide (stoichiometric) in DMF at 140 °C leads to arylation at the 5-position. Various combinations of substituted aryl iodides and 1,4-disubstituted 1,2,3-triazoles bearing functional groups were found to be compatible.

INTRODUCTION

Heteroaromatic compounds such as azoles have received much attention and found wide application in medicinal chemistry and materials science. Direct arylation of the C–H bonds of heterocycles—i.e., functionalization of aromatic heterocycles—is of current interest because it represents a possible alternative approach to conventional cross-coupling reactions with organometallic reagents and would not require reactive functional groups such as halogens or metal moieties.[1]

As 1,2,3-triazoles are often found in biologically active compounds, they are important heterocycles in medicinal as well as organic chemistry.[2] The reaction of terminal alkynes with organic azides gives 1,4- or 1,5-disubstituted 1,2,3-triazoles using copper and ruthenium catalysts, respectively.[3] 1,4,5-Trisubstituted 1,2,3-triazoles, which also show biological activity,[4] may be prepared by reaction of internal alkynes, but with a lack of regioselectivity and/or generality.[4b, 5] Two traditional cross-coupling reactions have been proposed for regioselective synthesis of 1,4,5-trisubstituted 1,2,3-triazoles; the Negishi coupling reaction of 4-metallated (zinc)-1,2,3-triazoles with aryl halides,[6] and the Suzuki coupling reaction of 5-iodo-1,2,3-triazoles with arylboric acids.[7] The possibility of taking advantage of the ready availability of 1,4-disubstituted 1,2,3-triazoles via the copper-catalyzed reaction—i.e., click chemistry—renders direct arylation with aryl halides preferable. Using this reaction, Gevorgyan reported palladium-catalyzed direct arylation of 1,2,3-triazoles with aryl bromides.[8] Recently, Oshima and Ackerman independently reported palladium-catalyzed direct arylation of 1,2,3-triazoles with aryl

chlorides using microwave[9] and conventional heating,[10] respectively, and using tricyclohexylphosphine as a ligand. These reactions are effective for synthesis of 1,4,5-trisubstituted 1,2,3-triazoles; however, the development of an inexpensive catalyst to use instead of expensive palladium is desirable. Quite recently, copper-catalyzed direct arylation of 1,2,3-triazoles has been reported by Ackerman *et al.*[11] while we are preparing this paper. We have independently examined similar copper-catalyzed (combination of CuI/LiOBu^t/DMF catalyst system)[12] direct C-5 arylation of 1,4-disubstituted 1,2,3-triazoles with aryl iodides and would like to report our original results including preliminary mechanistic considerations.[13]

RESULTS AND DISCUSSION

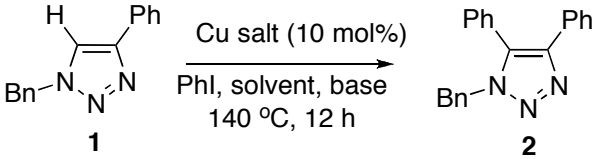
At the outset, we optimized the Cu-catalyzed direct phenylation reaction of 1-benzyl-4-phenyl-1,2,3-triazole **1** with iodobenzene using CuI as a catalyst and LiOBu^t as a base in DMF at 140 °C (Scheme 1). The results are shown in Table 1. Analysis of the reaction mixture by GC/MS revealed the presence of the 5-phenylated product **2** (entry 4). The product was isolated in 74% yield after purification by preparative TLC. The use of other bases—K_2CO_3, KOBu^t, and NaOBu^t—gave negligible amounts of the product (entries 1 – 3). Solvents other than DMF were also examined (DMSO,

Table 1. Optimization of Cu-catalyzed direct phenylation of 1-benzyl-4-phenyl-1,2,3-triazole **1** with iodobenzene[a]

entry	Cu salt	base	solvent	yield (%)[b] of **2**
1	CuI	K_2CO_3	DMF	0
2	CuI	KOBu^t	DMF	trace
3	CuI	NaOBu^t	DMF	trace
4	CuI	LiOBu^t	DMF	74
5	CuI	LiOBu^t	DMSO	15[c]
6	CuI	LiOBu^t	NMP	29
7	CuI	LiOBu^t	dioxane	12
8	CuCl	LiOBu^t	DMF	74
9	CuCl	LiOBu^t	DMF	75[d]
10	CuBr	LiOBu^t	DMF	73
11	CuCN	LiOBu^t	DMF	68
12	$CuCl_2$	LiOBu^t	DMF	70

[a]**1** (0.5 mmol), PhI (1.5 mmol), solvent (1.0 mL), Cu salt (0.05 mmol), base (1.0 mmol); 140 °C, 12 h. [b]Isolated yield. [c]A diphenylated product was detected by GC/MS. [d]Reaction time 9 h.

NMP, dioxane), but these were found not to be suitable for the reaction (entries 5 – 7). CuCl, CuBr, and CuCN and even $CuCl_2$ were found to be effective as Cu catalysts for direct arylation, giving the product in moderate to good yields (entries 8 – 12). When the reaction time was shortened from 12 h to 9 h,



Scheme 1

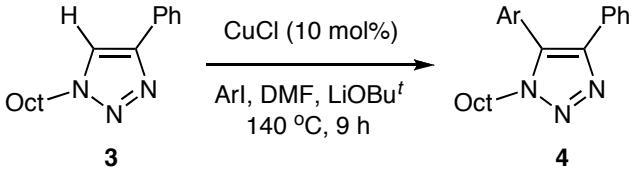
a good yield was still obtained (entry 9). The corresponding reactions with chloro- and bromobenzene did not proceed, and unreacted **1** was recovered.

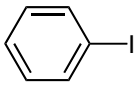
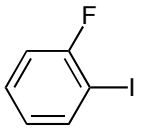
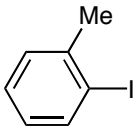
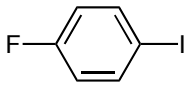
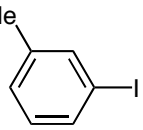
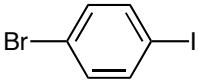
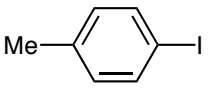
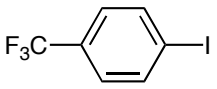
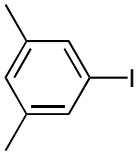
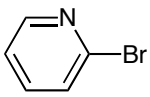
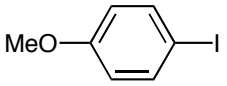
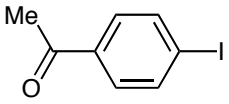
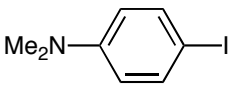
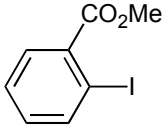
After optimizing the reaction conditions, we then examined the scope with respect to aryl iodides; the results of these experiments are summarized in Table 2. It is notable that in the reaction of **1** with iodobenzene, small amounts (2 – 3%) of diphenylated product (probably both 4- and benzylic phenylated product) were often detected by GC/MS analysis. In order to prevent the diphenylation reaction, 1-*n*-octyl-4-phenyl-1,2,3-triazole **3** was used as a 1,4-disubstituted triazole for the coupling reaction. The reactions of **3** with various aryl iodides were carried out under optimized conditions, using CuCl/LiOBu^t in DMF at 140 °C for 9 h (CuCl was the choice of catalyst for economical reasons). The coupling reactions with *o*-, *m*-, and *p*-iodotoluene and 1-iodo-3,5-xylene proceeded smoothly to give the corresponding 5-arylated products **4** in excellent yields (entries 2 – 5). *p*-Iodoanisole also reacted with **3** to give the product in high yield (entry 6). In contrast, the reaction with halogeno-substituted iodobenzenes gave the corresponding products in low to moderate yields (entries 8 – 10).

Coupling with *p*-bromoiodobenzene occurred chemoselectively at the iodo-substituted carbon with moderate yield (entry 10), while the reaction with *p*-trifluoromethyl iodobenzene gave a low yield (entry 11). These results may suggest that the reactivity of electron-rich iodobenzene was high enough to give the corresponding coupling products in satisfactory yields, while electron-deficient aryl iodides tended to show lower reactivity toward the coupling reaction. Indeed, the reactions with methyl *o*-iodobenzoate and *p*-iodoacetophenone gave negligible amounts of the relevant coupling products (entries 13 – 14), while the use of *p*-iodo-*N*,*N*-dimethylaniline gave the product in good yield (entry 7). It is surprising that the coupling reaction with 2-bromopyridine proceeded to give the corresponding product in moderate yield despite the fact that the reaction with bromobenzene did not proceed (entry 12).

The scope of the reaction with respect to 1,4-disubstituted 1,2,3-triazole **5** (Scheme 2) is shown in Table 3. Investigation of phenylation reactions of 1-*n*-octyl-4-alkyl- or 4-aryl-substituted **5** (R^1 = *n*-octyl) showed that the reactions with these substrates were successful, giving the corresponding products in high yield (entries 1, 3 – 7). The reaction with the 4-TMS derivative was the exception, giving a low yield, probably due to the steric hindrance (entry 2). The presence of an electron-donating or withdrawing group as a substituent of the phenyl group did not significantly affect the yield. The reaction with 1-substituted 1,2,3-triazole gave the the 5-arylated product as a single product showing that arylation occurred at only

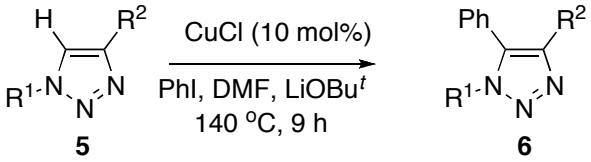
Table 2. Scope of the phenylation reaction with aryl iodides[a]



entry	ArI	4	yield (%)[b]	entry	ArI	4	yield (%)[b]
1		**4a**	98	8		**4h**	67
2		**4b**	99	9		**4i**	49
3		**4c**	95	10		**4j**	64
4		**4d**	99	11		**4k**	30
5		**4e**	80	12		**4l**	54
6		**4f**	99	13		**4m**	0[c]
7		**4g**	96	14		**4n**	–[d]

[a]**3** (0.5 mmol), ArI (1.5 mmol), DMF (1.0 mL), CuCl (0.05 mmol), LiOBu^t (1.0 mmol).
[b]Isolated yield. [c]Acetophenone was detected (~10%). [d]The coupling product was detected (~3%).

C-5 position (entry 8). The reactions with 1-*p*-methylphenyl derivatives bearing a phenyl or *n*-butyl group at the 4-position were also successful, giving the corresponding products in reasonable yields (entries 9 – 10). Combining these results with those shown in Table 1, it can be seen that the reaction does not favor any particular substituents at the 1- and 4-positions of the starting 1,4-disubstituted 1,2,3-triazoles: any substituents may be compatible with the reaction.



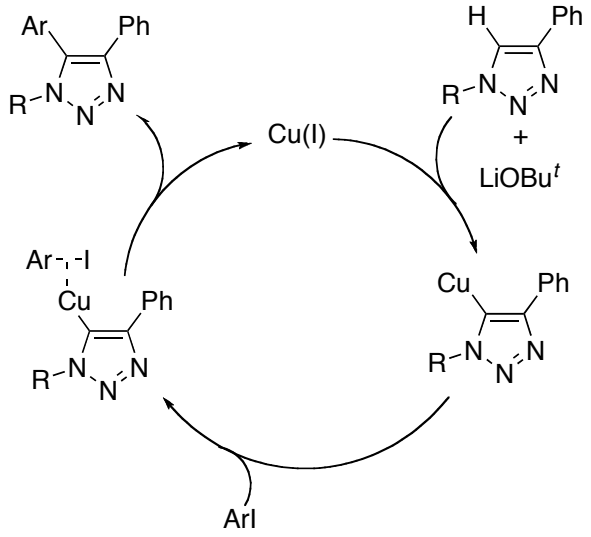
Scheme 2

Table 3. Scope of the phenylation reaction with respect to 1,4-disubstituted-1,2,3-triazole **5**[a]

entry	R^1	R^2	**6**	yield (%)[b]
1	Oct	*n*-Bu	**6a**	81
2	Oct	TMS	**6b**	23
3	Oct	*p*-MeC_6H_4	**6c**	91
4	Oct	ferrocenyl	**6d**	63
5	Oct	*p*-$CF_3C_6H_4$	**6e**	99
6	Oct	*o*-FC_6H_4	**6f**	99
7	Oct	*p*-FC_6H_4	**6g**	99
8	Oct	H	**6h**	91
9	*p*-MeC_6H_4	Ph	**6i**	73
10	*p*-MeC_6H_4	*n*-Bu	**6j**	84

[a]**3** (0.5 mmol), PhI (1.5 mmol), DMF (1.0 mL), CuCl (0.05 mmol), $LiOBu^t$ (1.0 mmol).
[b]Isolated yield.

The reaction presumably proceeds via deprotonation at C-5 position by $LiOBu^t$ followed by cupration via lithium-copper transmetallation; coupling of the resulting organocopper species with aryl iodide leads to the corresponding 5-aryl 1,2,3-triazole (Scheme 3).[14] An electrophilic mechanism may be ruled out because the reaction was not affected by the presence of C-4 electron-rich and -poor substituents. Kinetic isotope effect was examined in the reaction of iodobenzene with C-5-deuterated 1,2,3-triazole. No isotope effect was observed suggesting that C-H activation mechanisms is not plausible in the reaction.[8]



Scheme 3

In conclusion, the copper-catalyzed reaction of 1,4-disubstituted 1,2,3-triazoles with aryl iodides was examined. The reaction with electron-rich aryl iodides gave the corresponding 1,4,5-trisubstituted 1,2,3-triazoles in a good yield, but the reaction with electron-poor aryl iodides gave the coupling products in low yield. Several types of the starting 1,4-disubstituted 1,2,3-triazoles bearing various substituents were used successfully.

EXPERIMENTAL

General. ^{1}H- and ^{13}C-NMR spectra were recorded using a Varian Mercury 300 NMR (300 MHz) spectrometer as solutions in $CDCl_3$. The chemical shifts are reported in δ units downfield from the internal reference, Me_4Si. The GC/MS analyses were carried out using a Hewlett-Packard 5975B/6890N instrument equipped with a capillary column (helium as carrier gas). Flash column chromatography was performed on a Yamazen YFLC-254 equipped with a UV detector using Merck Silica Gel 60. Preparative TLC was conducted using a 20 x 20 cm glass sheet coated with a 2 mm thick layer of Merck Kieselgel 60 PF_{254}. Starting 1,4-disubsituted 1,2,3-triazoles were prepared by the Sharpless' Cu catalyzed *Click* reaction of organic azides with alkynes.[3] All commercial aryl iodides are used without further purification.

General procedure for the coupling reaction of triazole with aryl iodide. In a 20 mL Schlenk tube containing a magnetic stirring bar were charged CuCl (5.0 mg, 0.05 mmol), triazole **3** (129 mg, 0.5 mmol), LiOBu^t (80.0 mg, 1.0 mmol) and dry DMF (1 mL) under a slight pressure of nitrogen. *p*-Iodotoluene (163 mg, 1.5 mmol) was then added using a syringe through the septum with stirring at rt. The tube was stirred at rt for 5 min and placed in a preheated oil bath (140 °C) for 9 h. The reaction mixture was allowed to cool to rt and diluted with EtOAc (50 mL). The solution was washed with brine (25 mL x 2), dried over $MgSO_4$, filtered, and the solvent was removed using a rotary evaporator that left a yellow residue. The GC/MS analysis revealed the presence of 1,4,5-trisubstituted triazole **4d**. The mixture containing the product was subjected to flash chromatography on silica gel (hexane/EtOAc = 10/1 as eluent) to afford the pure product. Yield, 172 mg, 99%.

2: White solid; mp 103-104 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.39 (s, 2H), 7.00-7.57 (m, 15H); ^{13}C NMR ($CDCl_3$) δ 52.0, 126.7, 127.4, 127.6, 127.8, 128.1, 128.4, 128.6, 129.1, 129.6, 130,0, 130.9, 133.8, 135.3, 144.5. Anal. Calcd for $C_{21}H_{17}N_3$: C, 81.00; H, 5.50; N, 13.49. Found: C, 80.66; H, 5.54; N, 13.37 EI MS m/z 311.2.

4a: Colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.86 (t, 3H, *J* = 7.0 Hz), 1.20 (m, 10 H), 1.75-1.77 (m, 2H), 4.19 (t, 2H, *J* = 7.4 Hz), 7.2-7.4 (m, 5H), 7.5-7.6 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 14.0, 22.4, 26.2, 28.7, 28.8, 29.9, 31.5, 48.1, 126.6, 127.4, 128.1, 128.3, 129.2, 129.5, 129.8, 131.0, 133.5, 144.0. ESI HRMS calcd for $C_{22}H_{27}N_3$ [M+ H] 334.2266, found 334.2307. EI MS m/z 333.2.

4b: Colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.86 (t, 3H, *J* = 7.0 Hz), 1.20 (m, 10 H), 1.70-1.77 (m, 2H), 2.00 (s, 3H), 4.03 (dt, 1H, *J* = 7.4, 13.5 Hz), 4.15 (dt, 1H, *J* = 7.4, 13.5 Hz), 7.2-7.6 (m, 9H); ^{13}C NMR ($CDCl_3$) δ 13.9, 19.4, 22.4, 26.2, 28.7, 28.8, 29.7, 31.5, 47.9, 125.6, 126.6, 127.4, 127.5, 128.4, 129.9, 130.2, 130.8, 131.2, 132.6, 137.7, 143.9. Anal. Calcd for $C_{23}H_{29}N_3$: C, 79.50; H, 8.41; N, 12.09. Found: C, 79.66; H, 8.54; N, 12.17. EI MS m/z 347.3.

4c: Colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.85 (t, 3H, *J* = 7.0 Hz), 1.20 (m, 10 H), 1.73-1.80 (m, 2H), 2.40 (s, 3H), 4.17 (t, 2H, *J* = 7.3 Hz), 7.1-7.6 (m, 7H), 7.5-7.6 (d, 2H); ^{13}C NMR ($CDCl_3$) δ 14.0, 21.3, 22.5, 26.3, 28.7, 28.9, 30.0, 31.6, 48.1, 126.6, 127.0, 127.4, 128.1, 128.3(C), 128.3(CH), 129.1, 130.3. 131.1, 133.7, 139.1, 143.9. Anal. Calcd for $C_{23}H_{29}N_3$: C, 79.50; H, 8.41; N, 12.09. Found: C, 79.19; H, 8.73; N, 12.22. EI MS m/z 347.3.

4d: Colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.86 (t, 3H, *J* = 7.0 Hz), 1.20 (m, 10 H), 1.75-1.78 (m, 2H), 2.46 (s, 3H), 4.19 (t, 2H, *J* = 7.3 Hz), 7.18-7.32 (m, 7H), 7.5-7.6 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 13.9, 21.3, 22.4, 26.2, 28.7, 28.8, 29.9, 31.5, 48.0, 124.9, 126.5, 127.3, 128.2, 129.6, 129.9, 131.1, 133.5, 139.5, 143.8. ESI HRMS calcd for $C_{23}H_{29}N_3$ [M+ H] 348.2422, found 348.220. EI MS m/z 347.3.

4e: White solid; mp 54-55 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.85 (t, 3H, *J* = 7.0 Hz), 1.20 (m, 10 H), 1.76-1.81 (m, 2H), 2.36 (s, 6H), 4.17 (t, 2H, *J* = 7.3 Hz), 6.92 (s, 2H), 7.18 (s, 1H), 7.2-7.3 (m, 3H), 7.56-7.59 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 14.1, 21.2, 22.5, 26.3, 28.7, 28.9, 30.0, 31.6, 48.0, 126.5, 127.4, 127.5, 128.0, 128.3(C), 128.3(CH), 131.2, 133.9. 138.9, 143.8. Anal. Calcd for $C_{24}H_{31}N_3$: C, 79.73; H, 8.64; N, 11.62. Found: C, 79.76; H, 8.74; N, 11.26. EI MS m/z 361.3.

4f: Colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.86 (t, 3H, *J* = 7.0 Hz), 1.21 (m, 10 H), 1.77-1.78 (m, 2H), 3.88 (s, 3H), 4.18 (t, 2H, *J* = 7.3 Hz), 7.02 (d, 2H, *J* = 8.6 Hz), 7.2-7.3 (m, 5H), 7.57 (d, 2H, *J* = 6.5 Hz); ^{13}C NMR ($CDCl_3$) δ 14.0, 22.5, 26.3, 28.8, 28.9, 30.0, 31.6, 48.0, 55.3, 114.7, 119.9, 126.6, 127.4, 128.3, 131.2, 133.4, 144.0, 155.7, 160.4. Anal. Calcd for $C_{23}H_{29}N_3O$: C, 76.00; H, 8.04; N, 11.56, O, 4.40. Found: C, 75.96; H, 8.02; N, 11.64; O, 4.39 EI MS m/z 363.3.

4g: Colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.86 (t, 3H, *J* = 7.0 Hz), 1.21 (m, 10 H), 1.77-1.80 (m, 2H), 3.03 (s, 6H), 4.18 (t, 2H, *J* = 7.3 Hz), 6.78 (d, 2H, *J* = 8.8 Hz), 7.14 (d, 2H, *J* = 8.8Hz), 7.2-7.3 (m, 3H), 7.61 (d, 2H, *J* = 6.7 Hz); ^{13}C NMR ($CDCl_3$) δ 14.0, 22.5, 26.3, 28.8, 28.9, 30.0, 31.6, 40.1, 48.0, 112.3, 114.4, 126.6, 127.1, 128.2, 130.6, 131.6, 134.2, 143.7, 150.7. Anal. Calcd for $C_{24}H_{32}N_4$: C, 76.55; H, 8.57; N, 14.88. Found: C, 76.66; H, 8.54; N, 14.87. EI MS m/z 376.3.

4h: Colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.86 (t, 3H, *J* = 7.0 Hz), 1.21 (m, 10 H), 1.77-1.82 (m, 2H), 4.19 (t, 2H, *J* = 7.3 Hz), 7.22-7.32 (m, 6H), 7.52-7.58 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 14.0, 22.5, 26.2,

28.7, 28.8, 29.6, 31.5, 48.5, 116.0 (d, $J_{C\text{-}F}$ = 15.3 Hz), 116.5 (d, $J_{C\text{-}F}$ = 21.1), 124.9 (d, $J_{C\text{-}F}$ = 3.9 Hz), 126.5, 127.6, 127.7, 128.4, 130.8, 132.0, 132.1 (d, $J_{C\text{-}F}$ = 8.1 Hz), 145.1, 160.0 (d, $J_{C\text{-}F}$ = 249.7 Hz). ESI HRMS calcd for $C_{22}H_{26}FN_3$ [M+ H] 352.2188, found 352.2285. EI MS m/z 351.2.

4i: Colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.86 (t, 3H, *J* = 7.0 Hz), 1.20 (m, 10 H), 1.76-1.78 (m, 2H), 4.18 (t, 2H, *J* = 7.3 Hz), 7.18-7.34 (m, 7H), 7.5-7.6 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 13.9, 22.5, 26.3, 28.7, 28.8, 29.9, 31.5, 48.1, 116.6 (d, $J_{C\text{-}F}$ = 21.9 Hz), 124.1 (d, $J_{C\text{-}F}$ = 18.7 Hz), 126.6, 127.6, 128.4, 130.8, 131.8 (d, $J_{C\text{-}F}$ = 8.3 Hz), 132.5, 144.2, 163.2 (d, $J_{C\text{-}F}$ = 250.6 Hz). ESI HRMS calcd for $C_{22}H_{26}FN_3$ [M+ H] 352.2188, found 352.2185. EI MS m/z 351.2.

4j: Colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.86 (t, 3H, *J* = 7.0 Hz), 1.20 (m, 10 H), 1.76-1.80 (m, 2H), 4.19 (t, 2H, *J* = 7.3 Hz), 7.21 (d, 2H, *J* = 8.4 Hz), 7.2-7.3 (m, 5H), 7.66 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR ($CDCl_3$) δ 14.0, 22.5, 26.3, 28.7, 28.9, 30.0, 31.6, 48.2, 124.0, 126.7, 127.0, 127.7, 128.4, 130.6, 131.4, 132.6, 138.5, 144.2. Anal. Calcd for $C_{22}H_{26}BrN_3$: C, 64.08; H, 6.36; N, 10.19. Found: C, 63.86; H, 6.64; N, 10.17. EI MS m/z 411.2, 413.2.

4k: Colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.86 (t, 3H, *J* = 7.0 Hz), 1.25 (m, 10 H), 1.74-1.81 (m, 2H), 4.25 (t, 2H, *J* = 7.4 Hz), 7.27-7.32 (m, 3H), 7.47-7.50 (m, 4H), 7.78 (d, 2H, *J* = 8.1 Hz); ^{13}C NMR ($CDCl_3$) δ 14.0, 22.5, 26.3, 28.8, 28.9, 30.1, 31.6, 48.4, 123.6 (q, $J_{C\text{-}F}$ = 272.6 Hz), 126.3 (q, $J_{C\text{-}F}$ = 3.6 Hz), 126.9, 127.9, 128.5, 130.5, 131.7 (q, $J_{C\text{-}F}$ = 33.5 Hz), 132.1, 144.7, 146.9, 155.6. ESI HRMS calcd for $C_{23}H_{26}F_3N_3$ [M+ H] 402.2188, found 402.2260. EI MS m/z 401.2.

4l: Colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.85 (t, 3H, *J* = 7.0 Hz), 1.21 (m, 10 H), 1.73-1.80 (m, 2H), 4.54 (t, 2H, *J* = 7.3 Hz), 7.27-7.37 (m, 5H), 7.52 (m, 2H), 7.69 (m, 1H), 8.79 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 14.0, 22.5, 26.3, 28.8, 28.9, 30.0, 31.6, 49.1, 123.5, 125.5, 127.7, 127.9, 128.5, 130.9, 132.1, 136.8, 145.3, 148.1, 150.2. Anal. Calcd for $C_{21}H_{26}N_4$: C, 75.41; H, 7.84; N, 16.75. Found: C, 75.16; H, 7.54; N, 16.67. EI MS m/z 334.2.

6a: Colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.81-0.86 (m, 6H), 1.17-1.34 (m, 12 H), 1.56-1.73 (m, 4H), 2.62 (t, 2H, *J* = 7.8 Hz), 4.19 (t, 2H, *J* = 7.3 Hz), 7.28 (m, 2H), 7.50 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 13.6, 13.9, 22.2, 22.4, 24.6. 26.2, 28.7, 28.8, 29.9, 31.5, 31.7, 48.1, 127.9, 128.8, 129.0, 129.4, 147.2, 155.6. Anal. Calcd for $C_{20}H_{31}N_3$: C, 76.63; H, 9.97; N, 13.40. Found: C, 76.56; H, 10.04; N, 13.28. EI MS m/z 313.3.

6b: Colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.13 (s, 9H), 0.86 (t, 3H, *J* = 7.0 Hz), 1.18 (m, 10 H), 1.72-1.75 (m, 2H), 4.14 (t, 2H, *J* = 7.4 Hz), 7.24-7.27 (m, 2H), 7.47-7.53 (m, 3H); ^{13}C NMR ($CDCl_3$) δ –0.95, 14.0, 22.5, 26.4, 28.8, 28.9, 30.2, 31.6, 47.6, 126.7, 128.6, 129.0, 129.3, 129.8, 143.2. Anal. Calcd for $C_{19}H_{31}N_3Si$: C, 69.25; H, 9.48; N, 12.75. Found: C, 68.96; H, 9.74; N, 12.35. EI MS m/z 329.2.

6c: White solid; mp 50-51 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.85 (t, 3H, *J* = 7.0 Hz), 1.19 (m, 10 H), 1.75-1.78 (m, 2H), 2.29 (s, 3H), 4.18 (t, 2H, *J* = 7.3 Hz), 7.05 (d, 2H, *J* = 8.0 Hz), 7.31 (m, 2H), 7.45 (d, 2H, *J* = 8.0 Hz), 7.50 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 13.9, 21.0, 22.4, 26.2, 28.7, 28.8, 29.9, 31.5, 48.0, 126.5, 128.1, 128.9, 129.1, 129.4, 129.8, 133.1, 137.1, 144.0, 147.2. ESI HRMS Calcd for $C_{23}H_{29}N_3$ [M+ H] 348.2422, found 348.4220. EI MS m/z 347.3.

6d: Brown oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.85 (t, 3H, *J* = 7.0 Hz), 1.19 (m, 10 H), 1.7-1.8 (m, 2H), 3.99 (s, 5H), 4.13-4.16 (m, 4H), 4.44 (t, 2H, *J* = 1.9 Hz), 7.35-7.39 (m, 2H), 7.55-7.58 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 14.0, 22.5, 26.3, 28.8, 28.9, 29.9, 31.6, 48.1, 66.5, 68.2, 69.2, 75.9, 128.3, 129.0, 129.6, 130.1, 132.2, 143.4. Anal. Calcd for $C_{26}H_{31}FeN_3$: C, 70.75; H, 7.08; N, 9.52. Found: C, 70.66; H, 6.84; N, 9.17

6e: White solid; mp 53-54 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.85 (t, 3H, *J* = 7.0 Hz), 1.25 (m, 10 H), 1.77-1.81 (m, 2H), 4.20(t, 2H, *J* = 7.4 Hz), 7.33-7.35 (m, 2H), 7.48-7.55 (m, 4H), 7.67 (d, 2H, *J* = 8.1 Hz); ^{13}C NMR ($CDCl_3$) δ 13.9, 22.4, 26.2, 28.7, 28.8, 29.9, 31.5, 48.2, 124.1 (q, $J_{C\text{-}F}$ = 272.7 Hz), 125.2 (q, $J_{C\text{-}F}$ = 3.6 Hz), 126.6, 127.6, 129.4, 129.7, 129.9, 134.5 (d, $J_{C\text{-}F}$ = 13.1 Hz), 142.6, 147.2, 155.6. ESI HRMS calcd for $C_{23}H_{26}F_3N_3$ [M+ H] 402.2188, found 402.2260. EI MS m/z 401.2.

6f: Colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.86 (t, 3H, *J* = 7.0 Hz), 1.21 (m, 10 H), 1.82 (m, 2H), 4.29 (t, 2H, *J* = 7.5 Hz), 6.97 (d, 1H, *J* = 8.9 Hz), 7.15 (d, 1H, *J* = 7.5 Hz), 7.26-7.28 (m, 3H), 7.45 (m, 3H), 7.61 (d, 1H, *J* = 7.5 Hz); ^{13}C NMR ($CDCl_3$) δ 13.9, 22.4, 26.2, 28.7, 28.8, 29.8, 31.5, 48.4, 115.6 (d, $J_{C\text{-}F}$ = 21.7 Hz), 118.9 (d, $J_{C\text{-}F}$ = 14.5 Hz), 123.9 (d, $J_{C\text{-}F}$ = 3.8 Hz), 127.7, 128.7, 129.1, 129.2, 129.7 (d, $J_{C\text{-}F}$ = 8.7 Hz), 131.1 (d, $J_{C\text{-}F}$ = 2.4 Hz), 135.4, 146.0, 159.2 ($J_{C\text{-}F}$ = 245.8 Hz). ESI HRMS calcd for $C_{22}H_{26}FN_3$ [M+ H] 352.2188, found 352.2285. EI MS m/z 351.2.

6g: White solid; mp 68-69 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.86 (t, 3H, *J* = 7.0 Hz), 1.20 (m, 10 H), 1.76-1.78 (m, 2H), 4.20 (t, 2H, *J* = 7.3 Hz), 6.92 (t, 2H, 8.8 Hz), 7.26-7.32 (m, 2H), 7.5-7.6 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 14.0, 22.5, 26.3, 28.7, 28.9, 30.0, 31.6, 48.2, 115.3 (d, $J_{C\text{-}F}$ = 21.6 Hz), 127.2 (d, $J_{C\text{-}F}$ = 2.9 Hz), 127.9, 128.3 (d, $J_{C\text{-}F}$ = 8.1 Hz), 129.3, 129.7, 129.8, 133.3, 143.3, 162.2 (d, $J_{C\text{-}F}$ = 247.0 Hz). ESI HRMS calcd for $C_{22}H_{26}FN_3$ [M+ H] 352.2188, found 352.2271. EI MS m/z 351.2.

6h: Colorless oil. ^{1}H-NMR($CDCl_3$, 300 MHz) δ 0.83 (t, 3H, J = 7.0 Hz), 1.20 (m, 10 H), 1.80-1.85 (m, 2H), 4.32 (t, 2H, J = 7.3 Hz), 7.37 (m, 5H), 7.68 (s, 1H); ^{13}C-NMR ($CDCl_3$) δ 13.9, 22.4, 26.2, 28.6, 28.8, 29.6, 31.4, 48.1, 127.1, 128.5, 128.8, 129.2, 132.8, 137.5. Anal. Calcd for $C_{16}H_{23}N_3$: C, 74.67; H, 9.01; N, 16.33. Found: C, 74.58; H, 8.91; N, 15.97. EI MS m/z 257.2.

6i: White solid; mp 203-205 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.35 (s, 3H), 7.1-7 .6 (m, 14H); ^{13}C NMR ($CDCl_3$) δ 21.1, 120.3, 124.9, 127.3, 127.8, 128.4, 129.0. 129.4, 129.7, 130.1, 134.0, 139.0, 144.6. Anal.

Calcd for $C_{21}H_{17}N_3$: C, 81.00; H, 5.50; N, 13.49. Found: C, 80.79; H, 5.44; N, 13.17. EI MS m/z 311.1.

6j: Colorless oil. White solid; mp 89-90 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.88 (t, 3H, *J* = 7.6 Hz), 1.36 (sext, 2 H, *J* = 7.6 Hz), 1.71 (quint, 2H, *J* = 7.6 Hz), 2.34 (s, 3H), 2.73 (t, 2H, *J* = 7.6 Hz), 7.17 (m, 6H), 7.36 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 13.7, 21.1, 22.4, 24.8. 31.7, 124.6, 127.8, 128.6, 128.7, 129.5, 129.6, 133.7, 134.3, 138.6, 146.1. Anal. Calcd for $C_{19}H_{21}N_3$: C, 78.32; H, 7.26; N, 14.42. Found: C, 78.16; H, 7.44; N, 14.17. EI MS m/z 291.2.

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