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SYNTHESIS OF *N*–HETEROCYCLIC CARBENE LIGANDS FOR SITE-SELECTIVE C–H ALKYLATION BY COOPERATIVE NICKEL/ALUMINUM CATALYSIS

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Abstract – We report synthesis of *N*-heterocyclic carbenes (NHCs), *N*,*N*′-bis{2,6-bis(3,5-dialkylphenyl)methy-4-methoxyphenyl}imidazol-2-ylidenes {alkyl = ethyl (**L2**) or *n*-propyl (**L3**)} and their applications to nickel-catalyzed C–H alkylation reactions of arenes. They showed site-selectivities and/or yields higher than NHCs used previously for the reactions.

INTRODUCTION

Direct C–H functionalization of arenes is efficient transformation for the preparation of poly-substituted benzenes. It is necessary to control *ortho*/*meta*/*para*-selectivity when mono-substituted benzenes are starting materials. Although *ortho*-selective C–H functionalization has been well developed in the last two decades,[1] selective functionalization of *meta*- and *para*-, i.e. remote, C–H bonds of mono-substituted benzenes is limited. For example, substrate-controlled *meta*- and *para*-selective functionalization has been developed by Yu[2] and Maiti[3] using precisely designed directing groups, which require installation and removal steps. On the other hand, the development of catalyst-controlled site-selective remote C–H functionalization of common arene substrates remains less explored.[4] One of the most effective strategies for the catalyst-controlled C–H functionalization can be bifunctional catalysis,[5] where non-covalent interaction of polar functional groups of arene substrates with catalysts, such as hydrogen bonding, ion-pairing, and Lewis-pairing directs either *meta*- or *para*-selective C–H functionalization.[6] One of the other possible strategies to control remote, in particular *para*-selective, C–H functionalization relies on steric repulsion as demonstrated with silylation and borylation using rhodium or iridium catalysts ligated by bulky bidentate diphosphines reported by Hartwig[7] and Itami,[8] respectively. However, only a limited number of arene substrates bearing a bulky substituent can be successfully reacted in high

para-selectivity. Recently, we have reported *para*-selective alkylation of benzamides and aromatic ketones by cooperative nickel/aluminum catalysis. The combination of a bulky *N*-heterocyclic carbene (NHC) ligand on nickel and a bulky aluminum co-catalyst successfully controls the site-selectivity (Figure 1).[9] Although steric repulsion plays a key role also in our system, arene substrates do not require much steric bulkiness because an arene/aluminum Lewis-pair serves as a "tentatively bulky arenes" to control the selectivity. In addition, the coordination of a carbonyl group to Lewis acid renders the arenes electron-poor and accelerates the C–H activation by an electron-rich nickel(0)/NHC catalyst to avoid background less site-selective reactions. This strategy can be applied to other arenes bearing a Lewis basic substituent including pyridines,[10] sulfonyl arenes,[11] and anilides,[12] and also to *para*-selective iridium-catalyzed C–H borylation of benzamides and pyridines.[13] Thus, we have demonstrated that our strategy has allowed a broader scope of arenes to participate in different types of *para*-selective C–H functionalization. Nevertheless, the *para*-selectivity of the alkylation reaction is not always satisfactory, particularly when the amount of the aluminum co-catalyst is reduced, or less sterically hindered substrates are reacted. Herein, we report the synthesis of new NHC ligands having bis(3,5-dialkylphenyl)methyl groups, the evaluation of their steric properties based on $\%V_{bur}$ values,[14] which are widely used to describe steric properties of NHC ligands,[15] and their effects on the nickel-catalyzed *para*-selective C–H alkylation reactions.

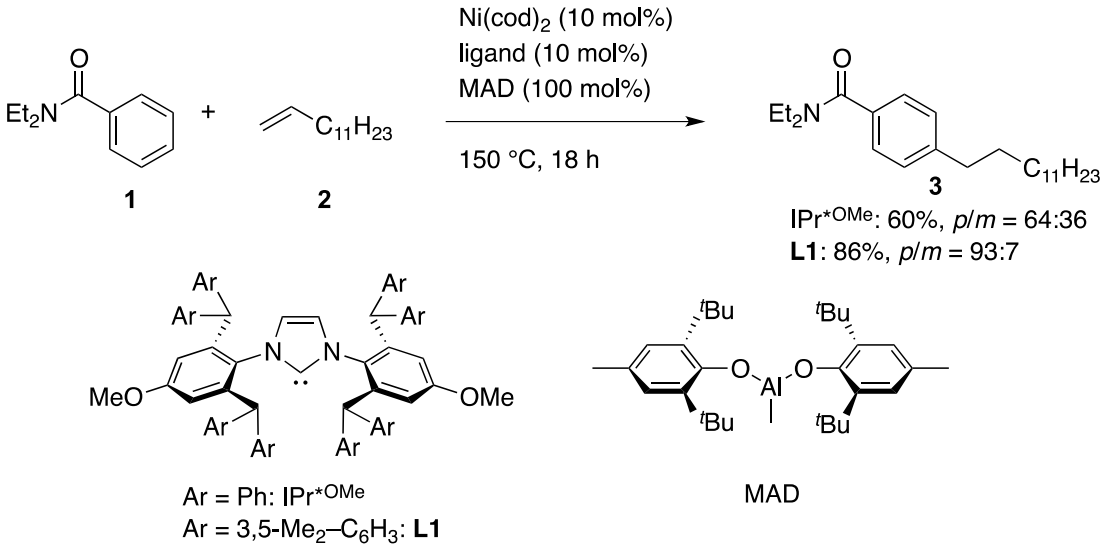
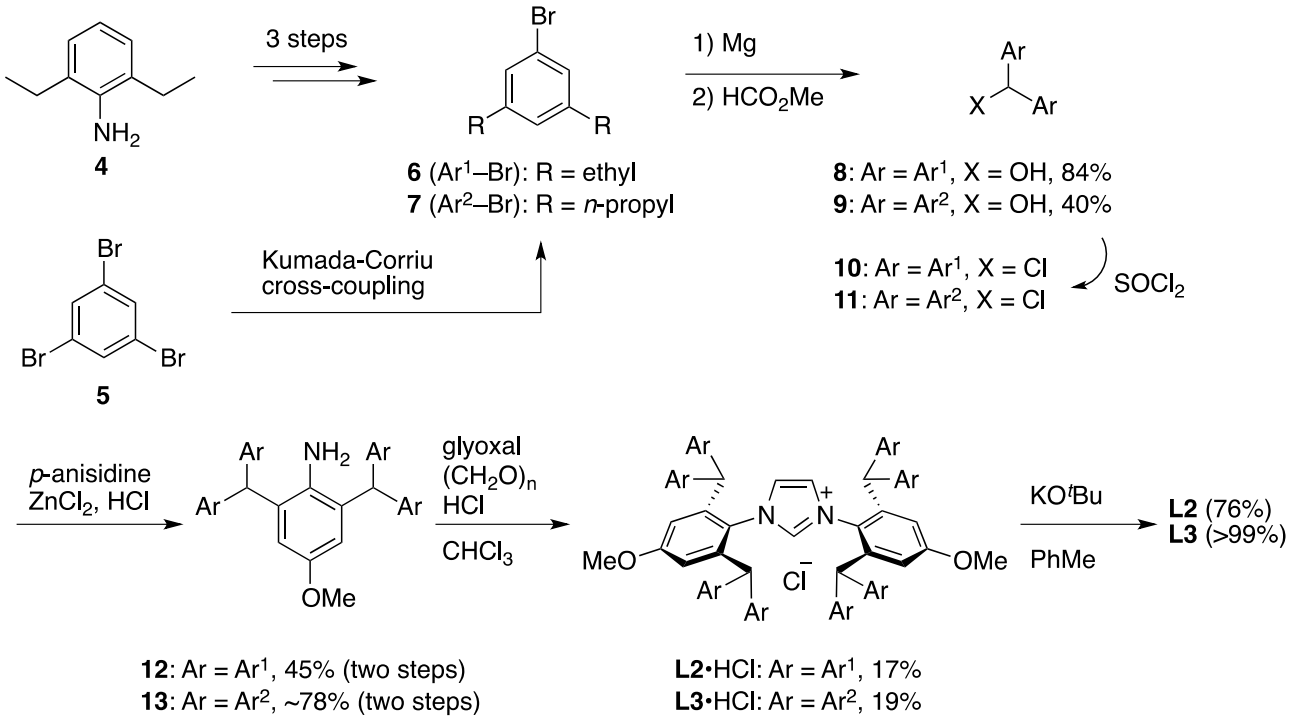


Figure 1



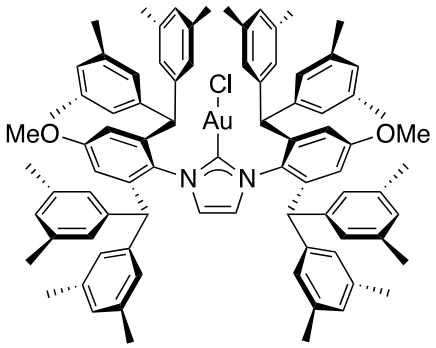
Scheme 1

RESULTS AND DISCUSSION

In the previous works, we found that the replacement of the diphenylmethyl groups in IPr*^{OMe}[16] to bis(3,5-dimethylphenyl)methyl groups dramatically enhanced the yield and *para*-selectivity of the alkylation of *N*,*N*-diethylbenzamide (Figure 1).[9] Theoretical calculations with DFT showed that the *para*-selectivity was ascribed to steric repulsion between the methyl groups of the 3,5-dimethylphenyl groups of **L1** and the substituents on aluminum. Hence, we decided to synthesize NHCs bearing 3,5-diethylphenyl (**L2**) and 3,5-di(*n*-propyl)phenyl (**L3**). 1-Bromo-3,5-dialkylbenzenes (**6** and **7**) were prepared from 2,6-diethylaniline according to the literatures,[17] or from 1,3,5-tribromobenzene through the Kumada-Corriu cross-coupling reaction (Scheme 1). They were converted to arylmagnesium bromide, which reacted with ~0.50 equivalent of methyl formate to give bis(3,5-dialkylphenyl)methanols **8** and **9**. After chlorination of the alcohols by thionyl chloride, the double diarylmethylation of *p*-anisidine in the presence of $ZnCl_2$/HCl afforded anilines **12** and **13**. They were treated with glyoxal and paraformaldehyde in the presence of hydrochloric acid to undergo cyclization reaction, affording imidazolium chloride **L2**·HCl and **L3**·HCl. Finally, free carbenes **L2** and **L3** were obtained through the deprotonation of these imidazolium chlorides by KO^{t}Bu in toluene.

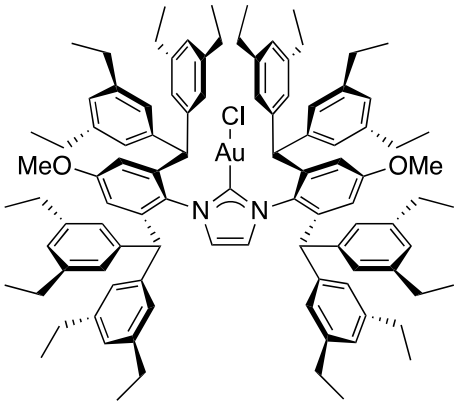
The (**L1**)AuCl and (**L2**)AuCl complexes were prepared by following the reported procedures,[18] and their single crystals were obtained through recrystallization from a saturated EtOAc solution of (**L1**)AuCl, or by slow diffusion of *n*-pentane into a Et_2O solution of (**L2**)AuCl, respectively. The single crystal X-ray analysis revealed their crystal structures (Figure 2). Two kinds of conformations were observed with

(**L2**)AuCl in the crystal. The space-filled model of the complexes showed that the alkyl groups surround the metal centers to make reaction pockets, which may limit the access of sterically congested C–H bonds of arene substrates by the steric repulsion in C–H functionalization reactions.[9,19] To evaluate the bulkiness of **L1** and **L2** quantitatively, $\%V_{bur}$ values were calculated.[20] The $\%V_{bur}$ values were larger with **L1** {54.6 (d = 2.00), 50.8 (d = 2.28)} than with IPr* {50.4 (d = 2.00), 45.7 (d = 2.28)}[15,21] and unexpectedly also with **L2** {47.2 and 53.5 (d = 2.00), 42.9 and 47.6 (d = 2.28)}, due presumably to crystal packings.



Au–C(carbene): 1.975(3) Å, Au–Cl: 2.2760(10) Å
C(carbene)–Au–Cl: 180.0º

(**L1**)AuCl



Au–C(carbene): 1.967(4) Å, Au–Cl: 2.2804(12) Å
C(carbene)–Au–Cl: 179.50(15)º

(**L2**)AuCl

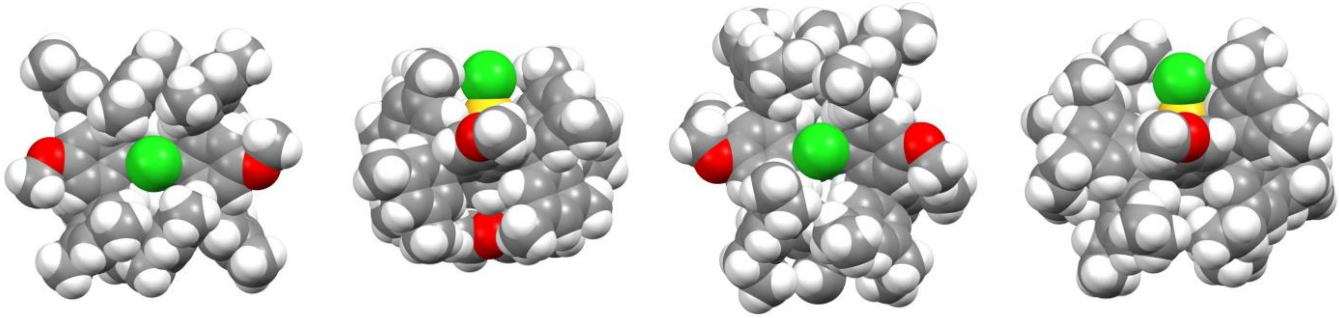
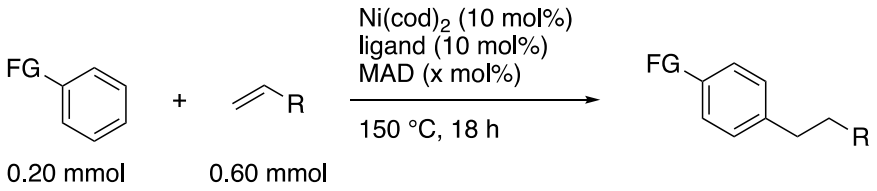


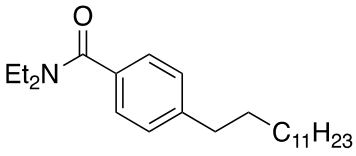
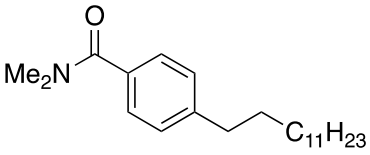
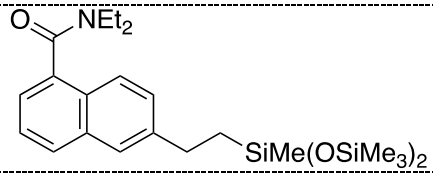
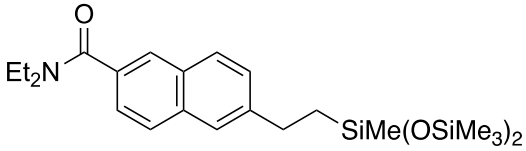
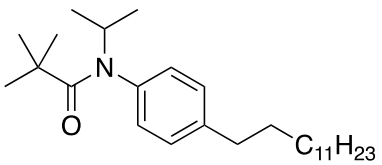
Figure 2. Crystal Structures of (**L1**)AuCl and (**L2**)AuCl

The alkylation of *N*,*N*-diethylbenzamide with 1-tridecene by using several NHC ligands was carried out to evaluate the effects of **L2** and **L3** on the catalytic reactions. In the presence of 40 mol% MAD, the use of IPr*^{OMe} and **L1** resulted in poor or moderate *para*-selectivities and moderate yields (Table 1, entries 1 and 2). However, **L2** showed good *para*-selectivity (entry 3, *para*/*meta* = 94:6). Besides, the yield was also substantially improved to 88%. The time course of the reaction revealed that **L2** accelerated the alkylation reaction (Figure 3). It could be caused by the acceleration of the C–H bond cleavage, which would be the rate-determining step based on our previous study,[9] by sterically demanding **L2**.[22,23]

Unfortunately, poorer yield and *para*-selectivity were observed with decreased catalyst loadings (entries 4 and 5), and thus 40 mol% of MAD was still necessary for practical yield and *para*-selectivity. Bulkier **L3** slightly increased the *para*-selectivity, whereas a decreased 48% yield was noted (entry 6).

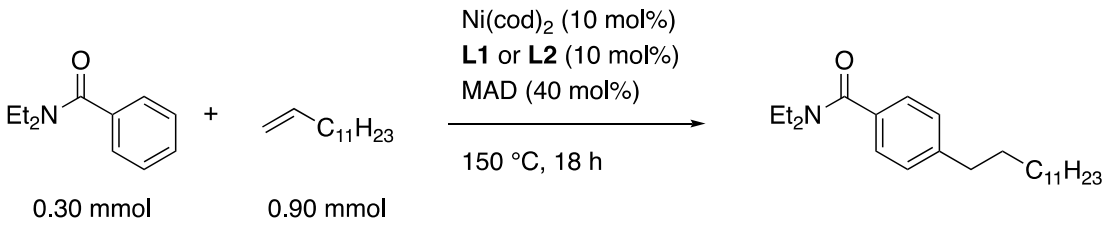
Table 1



entry	arene	ligand	x (mol%)	yield (%)[1]	*para*/*meta*[2]
1[3]		IPr*^{OMe}	40	48	56:44
2[3]		**L1**	40	62	86:14
3[3]		**L2**	40	88	94:6
4[3]		**L2**	20	74	90:10
5[3]		**L2**	10	44	83:17
6[4]		**L3**	40	48	95:5
7		IPr*^{OMe}	40	63	31:69
8		**L1**	40	78	73:27
9		**L2**	40	85	88:12
10		**L3**	40	29	92:8
11[5,6]		**L1**	100	47[7]	78:22[8]
12[4,9]		**L2**	100	86	92:8[8]
13[4,9]		**L3**	100	53	91:9[8]
14[5]		**L1**	100	88[7]	57:35:8[10]
15[4]		**L2**	100	91	70:29:1[10]
16		IPr*^{OMe}	40	43	49:51
17[11]		**L1**	40	66	76:24
18		**L2**	40	78	86:14
19		**L3**	40	53	91:9

[1] Determined by ^{1}H NMR analysis. [2] Determined by GC analysis. [3] Run on 0.50 mmol scale. [4] Run on 0.10 mmol scale. [5] Run on 1.0 mmol scale. [6] ref. 9. [7] Isolated yield. [8] C6/other isomers. [9] With 3.5 eq of the alkene. [10] C6/C7/other isomers. [11] Run on 0.60 mmol (ref. 12).

We then investigated the alkylation of other arenes. The alkylation of *N*,*N*-dimethylbenzamide gave similar results as those of *N*,*N*-diethylbenzamide; ligands bearing longer alkyl groups resulted in better *para*-selectivities although the highest yield was observed with **L2** (entries 7–10). A dramatic enhancement of the C6-selectivity by using **L2** or **L3** was observed in the alkylation of *N*,*N*-diethyl-1-naphthamide, compared with the previous result with **L1** (entries 11–13).[9] This is a rare example of the remote C–H functionalization of 1-substituted naphthalenes with high site-selectivity.[24] In the case of *N*,*N*-diethyl-2-naphthamide, moderate C6-selectivity was observed with **L2** (C6/C7/others = 70:29:1, entry 15), which was clearly higher than that with **L1** (57:35:8, entry 14). These C6-selectivities were much lower than the case of *N*,*N*-diethyl-1-naphthamide due probably to the longer distance between the aminocarbonyl group of the substrates and the reaction sites. In the alkylation of *N*-alkylanilides, a 3-methyl-2-butyl group on nitrogen of anilides was necessary to achieve high *para*-selectivity with **L1** in our previous report.[12] However, *N*-isopropylanilide could participate in the *para*-selective alkylation with **L2** or **L3** with good site-selectivities (entries 18 and 19). The use of **L3** resulted in yields lower than those by the using **L2** in all the cases, presumably because **L3** was too bulky to destabilize the nickel center coordinated by substrates.[22] The *para*-selective alkylation of aromatic ketones was also examined using 4-(*N*,*N*-dimethylamino)benzophenone and 1-octene, but yields were lower than 10% under the similar reaction conditions using IPr*^{OMe}, **L1**, or **L2** with slightly better site-selectivity by **L2**.



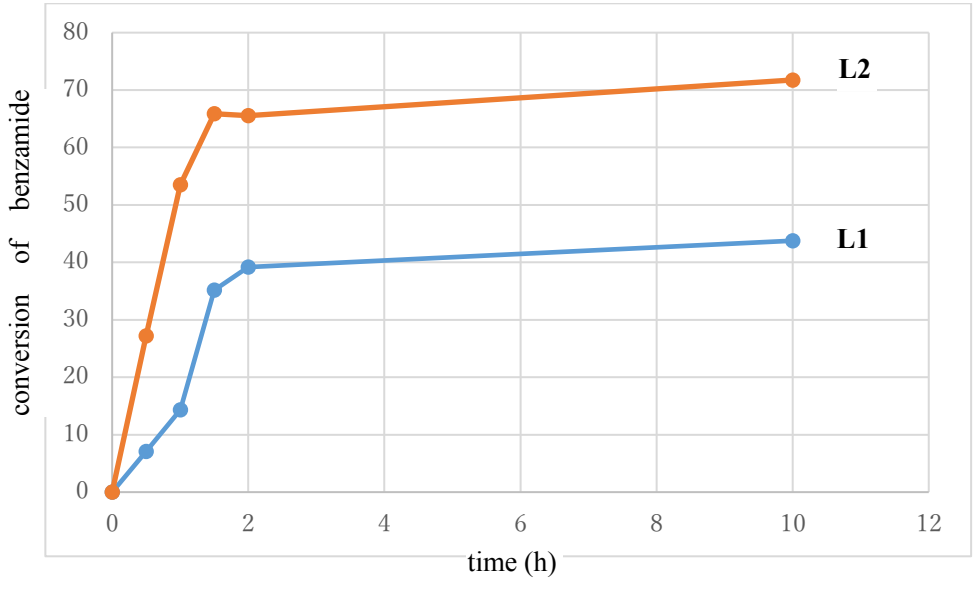


Figure 3. Time course of the alkylation of *N*,*N*-diethylbenzamide

In summary, we have synthesized the new bulky NHCs **L2** and **L3** having longer alkyl chains at their peripheral region. The use of **L2** and **L3** as ligands has improved the site-selectivities and/or yields of the alkylation reactions of aromatic amides by cooperative nickel/aluminum catalysis.

EXPERIMENTAL

General. All manipulations of oxygen- and moisture-sensitive materials were conducted with a standard Schlenk technique under an argon atmosphere or in a glove box under a nitrogen atmosphere. Medium pressure liquid chromatography (MPLC) was performed using Kanto Chemical silica gel 60 (spherical, 40–50 μm) or Biotage® SNAP Ultra. Analytical thin layer chromatography (TLC) was performed on Merck TLC silica gel 60 F_{254} (0.25 mm) plates. Visualization was accomplished with UV light (254 nm) and/or an aqueous alkaline $KMnO_4$ solution followed by heating.

Apparatus. Proton and carbon nuclear magnetic resonance spectra (^{1}H and ^{13}C NMR) were recorded on a JEOL ECS-400 (^{1}H NMR, 400 MHz; ^{13}C NMR 101 MHz) spectrometer with solvent resonance as the internal standard (^{1}H NMR, $CDCl_3$ at 7.26 ppm, C_6D_6 at 7.16 ppm; ^{13}C NMR, $CDCl_3$ at 77.0 ppm, C_6D_6 at 128.0 ppm, THF-d_8 at 67.57 ppm. NMR data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sext = sextet, sept = septet, br = broad, m = multiplet), coupling constants (Hz), and integration. High-resolution mass spectra were obtained with Thermo Scientific Exactive (ESI) and Thermo Scientific™ MALDI LTQ Orbitrap (MALDI). GC analysis was performed on a Shimadzu GC-2014 equipped with a BP1 column (SGE Analytical Science, 0.25 mm x 30 m, pressure = 149.0 kPa, detector = FID, 290 °C) with helium gas as a carrier. Medium pressure liquid chromatography (MPLC) was performed with a Yamazen EPLC-W-Prep 2XY or SHOKO SCIENTIFIC Purif-espoir2.

Chemicals. Unless otherwise noted, commercially available chemicals were distilled and degassed before use. If commercially available chemicals are solids, the chemicals are used without purification. IPr*^{OMe25} **L1**,[9] MAD,[26] *N*,*N*-diethyl-1-naphthamide,[27] and *N*-isopropyl-*N*-phenylpivalamide[28] were prepared according to the literature procedures. Anhydrous toluene for catalytic reactions was purchased from Wako Pure Chemical Industries. Anhydrous toluene and hexane were purchased from Kanto Chemical and further purified by passage through activated alumina under positive argon pressure as described by Grubbs *et al*.[29]

Preparation of 4-bromo-2,6-diethylaniline. A solution of 2,6-diethylaniline (19.2 g, 129 mmol) in CH_2Cl_2 (400 mL) was cooled to –78 °C under argon atmosphere. To the solution was added dropwise Br_2

(21 g, 136 mmol) over 10 min at –78 °C. After warmed up to room temperature, the solution was stirred overnight at room temperature. The resulting mixture was quenched with a 10% aqueous solution of $NaHSO_4$. The mixture was extracted with CH_2Cl_2 (50 mL x 3) and the combined organic layers were washed with brine (300 mL), dried over Na_2SO_4, and then concentrated in *vacuo* to give 4-bromo-2,6-diethylaniline (30 g) as a light brown oil, which was used directly in the next step without further purifications. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.07 (s, 2H), 3.62 (br s, 2H), 2.49 (q, *J* = 7.3 Hz, 4H), 1.25 (t, *J* = 7.6 Hz, 6H).

Preparation of 1-bromo-3,5-diethylbenzene. To 4-bromo-2,6-diethylaniline (35 g, 155 mmol) was added an aqueous solution of HBF_4 (50 wt%, 22 mL). The resulting solution was cooled to 0 °C. To the resulting solution was added dropwise an ice-cold solution of $NaNO_2$ (10.7 g, 155 mmol) in H_2O (21 mL). The mixture was stirred for a few minutes at 0 °C and filtered. The residue was washed with Et_2O to give 4-bromo-2,6-diethylbenzenediazonium tetrafluoroborate (29 g, 90 mmol) as a yellow powder. The yellow powder was added to a solution of NaOMe (9.7 g, 180 mmol) in MeOH (120 mL) at room temperature and the mixture was refluxed for 5 min. To the resulting mixture was added ice-cooled water and EtOAc. The organic layer was washed with water (50 mL x 3), washed with brine (100 mL), and then dried over $MgSO_4$. All the volatiles were removed in *vacuo*. The residue was purified by MPLC on silica gel (*n*-hexane) to afford 1-bromo-3,5-diethylbenzene (10.8 g) as a red oil, which was used for the next step without further purifications. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.16 (s, 2H), 6.94 (s, 1H), 2.59 (q, *J* = 7.7 Hz, 4H), 1.22 (t, *J* = 7.6 Hz, 6H).

Preparation of bis(3,5-diethylphenyl)methanol. A three-necked round-bottomed flask equipped with a reflux condenser was charged with magnesium turnings (4.1 g, 169 mmol) and THF (200 mL) under argon atmosphere. To the mixture was added a solution of 1-bromo-3,5-diethylbenzene (15.3 g, 72 mmol) in THF (100 mL). The resulting mixture was stirred for 3 h at room temperature, and then refluxed for 3 h. The solution was cooled to room temperature. To the resulting solution was slowly added a solution of methyl formate (1.98 g, 33 mmol) in THF (20 mL) at 0 °C. The mixture was stirred overnight at room temperature. The resulting mixture was quenched with H_2O at 0 °C and the organic layer was extracted with EtOAc (100 mL x 3). The combined organic layers were washed with brine (300 mL) and dried over Na_2SO_4. All the volatiles were removed in *vacuo*. The residue was purified by MPLC on silica gel (*n*-hexane/EtOAc = 96:4) to give bis(3,5-diethylphenyl)methanol (9.0 g, 30 mmol, 84%) as a yellow oil, Rf 0.81 (*n*-hexane/EtOAc = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.05 (s, 4H), 6.94 (s, 2H), 5.76 (d, *J* = 3.2 Hz, 1H), 2.61 (q, *J* = 7.7 Hz, 8H), 2.12 (d, *J* = 3.2 Hz, 1H), 1.22 (t, *J* = 7.6 Hz, 12H); ^{13}C NMR (101

MHz, $CDCl_3$): δ 144.4, 143.9, 126.6, 123.4, 76.6, 28.8, 15.6; HRMS[ESI(+)] calcd for $C_{21}H_{28}ONa$ $[M+Na]^+$: 319.2032. Found: *m/z* 319.2038.

Preparation of 2,6-bis{bis(3,5-diethylphenyl)methyl}-4-anisidine. Bis(3,5-diethylphenyl)methanol (2.1 g, 7.1 mmol) was dissolved in CH_2Cl_2 (50 mL). To the solution was added dropwise $SOCl_2$ (0.57 mL, 7.8 mmol). The mixture was stirred for 1 h at room temperature. To the resulting mixture was added a saturated $NaHCO_3$ aq. The mixture was extracted with CH_2Cl_2 (50 mL x 3) and the combined organic layers were washed with brine (100 mL). All volatiles were removed in *vacuo* to afford bis(3,5-diethylphenyl)methyl chloride as a light brown oil, which was used as soon as possible for the next step without further purification.

To a recovery flask were added bis(3,5-diethylphenyl)methyl chloride (2.2 g, 7.1 mmol) and *p*-anisidine (0.44 g, 3.6 mmol). The mixture was heated at 150 °C to melt. To the hot liquid was added a mixture of $ZnCl_2$ (0.24 g, 1.78 mmol) and conc. HCl aq. (0.30 mL, 3.6 mmol). The resulting mixture was stirred for 1.0 h at 185 °C. The mixture was cooled to room temperature, dissolved in CH_2Cl_2 (30 mL), washed with water (15 mL x 3), and then dried over $MgSO_4$. The organic layer was concentrated in *vacuo* to give a black sticky solid. The crude was purified by MPLC on silica gel (*n*-hexane/Et_2O = 98:2) to give 2,6-bis{bis(3,5-diethylphenyl)methyl}-4-anisidine (1.09 g, 1.60 mmol, 45%) as a brown solid, Rf 0.73 (*n*-hexane/EtOAc = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.86 (s, 4H), 6.74 (s, 8H), 6.21 (s, 2H), 5.36 (s, 2H), 3.45 (s, 3H), 3.19 (s, 2H), 2.53 (q, *J* = 7.5 Hz, 16H), 1.15 (t, *J* = 7.6 Hz, 24 H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 151.5, 144.1, 142.6, 136.3, 131.0, 126.5, 125.6, 114.2, 55.1, 52.6, 28.8, 15.6; HRMS[ESI(+)] calcd for $C_{49}H_{61}ONNa$ $[M+Na]^+$: 702.4645. Found: *m/z* 702.4648.

Preparation of L2·HCl. The mixture of 2,6-bis{bis(3,5-diethylphenyl)methyl}-4-anisidine (1.09 g, 1.60 mmol), 40 wt% glyoxal in water (0.55 g, 3.80 mmol), paraformaldehyde (54 mg, 1.80 mmol), and $CHCl_3$ (3.4 mL) was heated at 60 °C, and to the mixture conc. HCl aq. (0.22 mL, 2.7 mmol) was added. The mixture was stirred for 13 h at 60 °C before concentration in *vacuo* to afford a brown solid. To the brown solid was added water. The organic layer was extracted with CH_2Cl_2 three times, and dried over Mg_2SO_4. All the volatiles were removed in *vacuo*. The residue was purified by MPLC on silica gel (CH_2Cl_2/MeOH = 96:4) to give **L2**·HCl (196 mg, 0.137 mmol, 17%) as a white powder [mp 240–244 °C (decomposed)], Rf 0.61 (EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 13.47 (s, 1H), 6.90 (s, 8H), 6.81 (s, 4H), 6.74 (s, 4H), 6.47 (s, 4H), 6.28 (s, 8H), 5.41 (s, 2H), 5.27 (s, 4H), 3.56 (s, 6H), 2.57–2.43 (m, 16H), 2.28–2.12 (m, 16H), 1.05 (t, *J* = 7.3 Hz, 24H), 0.82 (t, *J* = 7.3 Hz, 24H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 160.3, 144.3, 144.2, 142.5, 142.2, 127.2, 126.3, 125.7, 125.4, 123.1, 115.6, 55.2, 51.6, 28.8, 28.5, 15.8, 15.6; HRMS[ESI(+)] calcd for $C_{101}H_{121}N_2O_2$ $[M-Cl^-]^+$: 1393.9423. Found: *m/z* 1393.9400.

Preparation of L2. In a glove box, the mixture of **L2**·HCl (3.6 g, 2.5 mmol), KO^{t}Bu (0.31 g, 2.8 mmol), and toluene (30 mL) was stirred at room temperature for 3 h. The mixture was filtered through a pad of Celite® and concentrated in *vacuo* to afford a white solid. The recrystallization from a saturated solution of the solid in hot *n*-hexane afforded **L2** (2.6 g, 1.90 mmol, 76%) as a white powder. ^{1}H NMR (400 MHz, C_6D_6): δ 7.17 (s, 8H), 6.99 (s, 4H), 6.85 (s, 8H), 6.79 (s, 4H), 6.77 (s, 4H), 6.29 (s, 4H), 5.87 (s, 2H), 3.11 (s, 6H), 2.40–2.26 (m, 32H), 0.96 (m, J = 7.5 Hz, 48H); ^{13}C NMR (101 MHz, THF-d_8): δ 222.0, 159.5, 146.1, 144.9, 144.6, 144.5, 143.9, 134.7, 128.1, 127.7, 126.0, 122.5, 115.1, 55.3, 52.3, 29.9, 29.7, 16.5, 16.4. HRMS[MALDI(+)] calcd for $C_{101}H_{121}N_2O_2$ $[M+H]^+$: 1393.9423. Found: *m/z* 1393.9363.

Preparation of bis{3,5-di(*n*-propyl)phenyl}methanol. To a flame-dried schlenk flask filled with argon was added magnesium turnings (3.2 g, 131 mmol) and Et_2O (30 mL). To the mixture was added a solution of 1-iodopropane (18.6 g, 110 mmol) in Et_2O (20 mL), and the resulting solution was stirred for 1 h to give a Grignard reagent. To a flame-dried three-necked round-bottomed flask filled with argon and equipped with a refluxing condenser was added a solution of 1,3,5-tribromobenzene (6.9 g, 22 mmol) and [1,1'-bis(diphenylphosphino)ferrocene]palladium(II) dichloride (88 mg, 0.12 mmol) in Et_2O (200 mL). To the stirred mixture, the Grignard reagent was added dropwise by an addition funnel over 1.5 h at 35 °C. The resulting mixture was stirred at 35 °C for 4 h, cooled to 0 °C, and then quenched with a saturated solution of NH_4Cl aq. The organic layer was washed with water (100 mL x 3) and brine (100 mL), dried over Na_2SO_4, and then concentrated in *vacuo* to give a yellow oil. The crude was dissolved in *n*-hexane and filtered through silica gel to afford a crude containing 1-bromo-3,5-di(*n*-propyl)benzene and 1,3,5-tri(*n*-propyl)benzene as a colorless oil. The crude was used directly in the next step without further purification.

To a flame-dried three-necked round-bottomed flask filled with argon and equipped with a refluxing condenser was added magnesium turnings (0.33 g, 13.5 mmol) and THF (30 mL). To the mixture was added 1,2-dibromoethane (0.169 g, 0.90 mmol) and the crude containing 1-bromo-3,5-di(*n*-propyl)benzene in THF (20 mL). The resulting mixture was stirred for 1 h at room temperature, and then refluxed for 1 h. The solution was slowly cooled to 0 °C. To the resulting solution was added slowly a solution of methyl formate (0.30 g, 5.0 mmol) in THF (15 mL). The mixture was stirred overnight at room temperature. The resulting mixture was quenched with conc. HCl aq. at 0 °C. The organic layer was extracted with Et_2O (10 mL x 3). The combined organic layers were washed with brine (20 mL) and dried over Na_2SO_4. All the volatiles were removed in *vacuo*. The residue was purified by MPLC on silica gel (*n*-hexane/EtOAc = 97:3) to give bis{3,5-di(*n*-propyl)phenyl}methanol (0.70 g, 2.0 mmol, 40% based on methyl formate) as a light yellow oil, Rf 0.64 (*n*-hexane/EtOAc = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.00 (s, 4H), 6.89 (s, 2H), 5.74 (d, J = 3.7 Hz, 1H), 2.54 (t, J = 7.8 Hz, 8H), 2.10 (d,

J = 3.7 Hz, 1H), 1.66–1.56 (m, 8H), 0.92 (t, *J* = 7.3 Hz, 12H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 143.7, 142.7, 127.8, 124.1, 76.6, 38.0, 24.6, 13.9; HRMS[ESI(+)] calcd for $C_{25}H_{36}ONa$ $[M+Na]^+$: 375.2658. Found: *m/z* 375.2662.

Preparation of 2,6-bis[bis{3,5-di(*n*-propyl)phenyl}methyl]-4-anisidine. To the solution of bis{3,5-di(*n*-propyl)phenyl}methanol (1.11 g, 3.2 mmol) in CH_2Cl_2 (15 mL) was added dropwise $SOCl_2$ (0.41 g, 3.2 mmol). The mixture was stirred for 1 h at room temperature. To the resulting mixture was added sat. $NaHCO_3$ aq. and the organic layer was extracted with CH_2Cl_2 (10 mL x 3), and then washed with brine (20 mL). All the volatiles were removed in *vacuo* to afford a crude mixture containing bis{3,5-di(*n*-propyl)phenyl}methyl chloride as a light yellow oil, which was used quickly in the next step without further purification.

To a round-bottom flask, the crude containing bis{3,5-di(*n*-propyl)phenyl}methyl chloride and *p*-anisidine (0.155 g, 1.26 mmol) were added. The mixture was heated at 150 °C to melt. To the hot liquid was added a mixture of $ZnCl_2$ (0.108 g, 0.79 mmol) and conc. HCl aq. (0.50 mL, 6.0 mmol). The resulting mixture was stirred for 1 h at 190 °C. The mixture was cooled to room temperature, dissolved in CH_2Cl_2 (20 mL), washed with water (10 mL x 3) and dried over Na_2SO_4. The organic layer was concentrated in vacuo to give a black sticky solid. The crude was purified by MPLC on silica gel (*n*-hexane/Et_2O = 98:2) to give a crude containing 2,6-bis[bis{3,5-di(*n*-propyl)phenyl}methyl]-4-anisidine as a light brown solid (0.97 g, ~1.2 mmol, ~78%). The crude was used directly in the next step without further purification.

Preparation of L3·HCl. The mixture of 2,6-bis[bis{3,5-di(*n*-propyl)phenyl}methyl]-4-anisidine (0.97 g, 1.22 mmol), 40% glyoxal (0.21 g, 1.45 mmol) in water, and paraformaldehyde (40 mg, 1.34 mmol) in $CHCl_3$ (3.0 mL) was heated at 60 °C. To the resulting mixture was added conc. HCl aq. (0.112 mL, 1.34 mmol). The mixture was stirred for 20 h at 60 °C before concentration in *vacuo* to give a brown solid. The brown solid was washed with a solution of *n*-hexane/EtOAc = 80:20 and purified by MPLC on silica gel (CH_2Cl_2/MeOH = 92:8) to afford **L3**·HCl (0.191 g, 0.118 mmol, 19%) as a brown sticky solid [mp 176–181 °C], Rf 0.09 (EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 13.46 (s, 1H), 6.85 (s, 8H), 6.77 (s, 4H), 6.70 (s, 4H), 6.41 (s, 4H), 6.27 (s, 8H), 5.38 (s, 2H), 5.32 (s, 4H), 3.52 (s, 6H), 2.49–2.37 (m, 16H), 2.21–2.14 (m, 8H), 2.10–2.03 (m, 8H), 1.51–1.42 (m, 16H), 1.29–1.20 (m, 16H), 0.75 (t, *J* = 6.9 Hz, 24H), 0.65 (t, *J* = 7.3 Hz, 24H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 160.1, 142.6, 142.5, 142.4, 142.1, 127.7, 127.0, 126.9, 126.7, 125.5, 122.9, 115.6, 55.1, 51.4, 37.8, 37.6, 24.5, 24.4, 13.7, 13.5. HRMS[ESI(+)] calcd for $C_{117}H_{153}N_2O_2$ $[M–Cl]^+$: 1618.1927. Found: *m/z* 1618.1932.

Preparation of L3. In a glove box, KO^{t}Bu (15.0 mg, 0.130 mmol) was added to a solution of **L3**·HCl (0.191 g, 0.120 mmol) in benzene (8.1 mL), and the resulting solution was stirred at room temperature for 1 h. All the volatiles were removed in *vacuo* to give a brown solid, which was dissolved in toluene. The solution was filtered through a pad of Celite® and concentrated in *vacuo* to afford **L3** as a brown solid (0.191 g, 0.120 mmol, >99%). ^{1}H NMR (400 MHz, C_6D_6): δ 7.07 (s, 8H), 6.94 (s, 4H), 6.85 (s, 8H), 6.80 (s, 4H), 6.78 (s, 4H), 6.31 (s, 4H), 5.84 (s, 2H), 3.19 (s, 6H), 2.41–2.25 (m, 32H), 1.48–1.38 (m, 32H), 0.78 (m, J = 6.9 Hz, 48H); ^{13}C NMR (101 MHz, C_6D_6): δ 220.5, 159.0, 145.6, 144.0, 143.8, 142.6, 142.3, 134.4, 126.93, 126.85, 122.1, 115.2, 54.5, 51.9, 38.2, 25.0, 14.0, 13.9. HRMS[MALDI(+)] calcd for $C_{117}H_{153}N_2O_2$ $[M+H]^+$: 1618.1927. Found: *m/z* 1618.1875.

Preparation of (L1)AuCl. In a glove box, $AuCl(SMe_2)$ (30 mg, 0.100 mmol) was added to the solution of **L1** (0.117 g, 0.100 mmol) in THF (4.0 mL). The resulting solution was stirred overnight at room temperature in dark. Out of the glove box, the mixture was filtered through a pad of Celite® and a membrane filter (pore size: 0.45 μm). The filtrate was concentrated in *vacuo*. The recrystallization from a saturated EtOAc solution of the obtained solid afforded (**L1**)AuCl (29 mg, 21%) as a colorless solid Rf 0.48 (*n*-hexane/EtOAc = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.77 (s, 8H), 6.75 (s, 4H), 6.73 (s, 4H), 6.50 (s, 4H), 6.35 (s, 8H), 5.79 (s, 2H), 5.17 (s, 4H), 3.61 (s, 6H), 2.17 (s, 24H), 2.06 (s, 24H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.7, 142.9, 142.8, 142.8, 137.7, 137.4, 129.2, 128.2, 128.1, 127.4, 127.1, 123.1, 115.0, 55.1, 50.9, 21.2. HRMS[ESI(+)] calcd for $C_{85}H_{88}AuClN_2O_2Na$ $[M+Na]^+$: 1423.6092. Found: *m/z* 1423.6133. Deposition number is CCDC-1865712.

Preparation of (L2)AuCl. In a glove box, $AuCl(SMe_2)$ (52 mg, 0.175 mmol) was added to the solution of **L2**·HCl (0.25 g, 0.175 mmol) in CH_2Cl_2 (7.5 mL), and the resulting solution was stirred for 15 min at room temperature. K_2CO_3 (0.48 g, 3.5 mmol) was added to the mixture, and the resulting solution was stirred overnight, and then filtered through a pad of Celite®. The filtrate was concentrated in *vacuo*. Recrystallization by slow diffusion of *n*-pentane into an Et_2O solution of the obtained solid afforded (**L2**)AuCl (61 mg, 21%) as a white solid [mp 160–185 °C (decomp)], Rf 0.57 (*n*-hexane/EtOAc = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.84 (s, 8H), 6.80 (s, 4H), 6.72 (s, 4H), 6.48 (s, 4H), 6.29 (s, 8H), 5.49 (s, 2H), 5.44 (s, 4H), 3.60 (s, 6H), 2.46–2.51 (m, 16H), 2.16–2.31 (m, 16H), 1.04 (t, J = 7.6 Hz, 24H), 0.83 (t, J = 7.6 Hz, 24H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.6, 144.3, 143.8, 143.1, 143.0, 142.3, 129.2, 126.8, 126.4, 125.5, 123.0, 115.1, 55.1, 51.5, 28.7, 28.6, 15.7, 15.5. HRMS[ESI(+)] calcd for $C_{101}H_{120}AuClN_2O_2Na$ $[M+Na]^+$: 1647.8596. Found: *m/z* 1647.8605. Deposition number is CCDC-1865713.

Preparation of *N*,*N*-diethyl-2-naphthamide. To a mixture of 2-naphthoic acid (1.72 g, 10 mmol) and DMF (10 mL) was added thionyl chloride (0.76 mL, 1.25 g, 10.5 mmol) at room temperature. The resulting solution was stirred for 30 min at 60 °C, and then cooled to room temperature before diethylamine (1.46 g, 2.1 mL, 20 mmol) and triethylamine (3.0 g, 4.2 mL, 30 mmol) were added. The resulting mixture was stirred for 10 h at room temperature, and then extracted by EtOAc (50 mL x 3). The combined organic layers were washed with water (50 mL x 3) and dried over Na_2SO_4. All the volatiles were removed in *vacuo*. The residue was purified by MPLC on silica gel (*n*-hexane/EtOAc = 90:10 to 60:40) to give *N*,*N*-diethyl-2-naphthamide (1.26 g, 5.5 mmol, 55%) as a colorless oil. The ^{1}H NMR and ^{13}C NMR spectra were consistent with a previous report.[30] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85–7.88 (m, 4H), 7.51–7.53 (m, 2H), 7.47 (d, *J* = 9.2 Hz, 1H), 3.60 (br s, 2H), 3.31 (br s, 2H), 1.28 (br s, 3H), 1.14 (br s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 171.2, 134.6, 133.3, 132.7, 128.3, 128.2, 127.7, 126.7, 126.5, 125.7, 123.9, 43.3, 39.3, 14.2, 13.0.

Procedure for Table 1. In a glove box, a 4 mL vial was charged with $Ni(cod)_2$ (10 mol%), an NHC ligand (10 mol%), and alkene (3.0–3.5 equiv), and the resulting mixture was stirred for 5 min at room temperature. Then, mono-substituted arene (1.0 equiv) and MAD (10–40 mol%) were added to the reaction mixture in this order. The resulting mixture was stirred at 150 °C for 18 h. After cooled to room temperature, EtOAc was added to the mixture. The site-selectivity was determined by GC analysis of the crude product. After 1,3,5-trimethoxybenzene was added to the mixture as an internal standard for ^{1}H NMR analysis, the solution was filtered through a pad of silica gel and concentrated in *vacuo*. The yield was determined by ^{1}H NMR analysis.

Purification of *N*,*N*-dimethyl-4-tridecylbenzamide. The crude product obtained in the entry 9 of Table 1 was purified by MPLC (25 g of silica gel, *n*-hexane/EtOAc = 90:10 to 50:50) to give *N*,*N*-dimethyl-4-tridecylbenzamide (43 mg, 0.130 mmol, 65%) and *N*,*N*-dimethyl-3-tridecylbenzamide (2.0 mg, 6.0 μmol, 3%).

***N*,*N*-Dimethyl-4-tridecylbenzamide.** A pale yellow oil, Rf 0.15 (*n*-hexane/EtOAc = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, *J* = 7.3 Hz, 2H), 7.19 (d, *J* = 7.8 Hz, 2H), 3.09 (br s, 3H), 2.99 (br s, 3H), 2.61 (t, *J* = 7.8 Hz, 2H), 1.58–1.61 (m, 2H), 1.25–1.29 (m, 20H), 0.87 (t, *J* = 6.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 171.8, 144.6, 133.5, 128.3, 127.1, 39.7, 35.8, 35.4, 31.9, 31.3, 29.6, 29.6, 29.5, 29.3, 29.2, 22.7, 14.1 (Three peaks overlap.). HRMS[ESI(+)] calcd for $C_{22}H_{37}NONa$ $[M+Na]^+$: 354.2767. Found: *m/z* 354.2779.

***N*,*N*-Dimethyl-3-tridecylbenzamide.** A pale yellow oil, Rf 0.21 (*n*-hexane/EtOAc = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27–7.31 (m, 1H), 7.19–7.22 (m, 3H), 3.11 (br s, 3H), 2.97 (br s, 3H), 2.61 (t, *J* = 7.6 Hz, 2H), 1.70–1.58 (m, 2H), 1.25–1.29 (m, 20H), 0.88 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 171.9, 143.2, 136.2, 129.6, 128.1, 127.0, 124.2, 39.4, 35.8, 35.3, 31.9, 31.3, 29.6, 29.6, 29.5, 29.3, 29.3, 22.7, 14.1 (Three peaks overlap). HRMS[ESI(+)] calcd for $C_{22}H_{37}NONa$ $[M+Na]^+$: 354.2767. Found: *m/z* 354.2779.

Purification of *N*,*N*-diethyl-6-{2-(1,1,1,3,5,5,5-heptamethyltrisiloxan-3-yl)ethyl}-2-naphthamide. The crude product obtained in the entry 14 of Table 1 was separated by MPLC (25 g of silica gel, *n*-hexane/EtOAc = 90:10 to 70:30) to give isomer mixture of alkylation products (0.42 g, 0.88 mmol, 88%, C6/C7/others = 57:35:8), which was further purified by HPLC (*n*-hexane/EtOAc = 80:20).

***N*,*N*-Diethyl-6-{2-(1,1,1,3,5,5,5-heptamethyltrisiloxan-3-yl)ethyl}-2-naphthamide.** A pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.76–7.81 (m, 2H), 7.63 (s, 1H), 7.43 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.39 (dd, *J* = 8.2, 1.8 Hz, 1H), 3.59 (s, 2H), 3.31 (s, 2H), 2.78–2.83 (m, 2H), 1.28 (s, 3H), 1.13 (s, 3H), 0.89–0.94 (m, 2H), 0.12 (s, 18H), 0.05 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.5, 143.8, 133.7, 131.1, 128.2, 127.8, 127.7, 125.5, 125.3, 123.9, 43.4, 39.3, 29.5, 19.5, 14.3, 13.0, 1.9, –0.3 (One peak overlap.). HRMS[ESI(+)] calcd for $C_{24}H_{42}NO_3Si_3$ $[M+H]^+$: 476.2467. Found: *m/z* 476.2453.

***N*,*N*-Diethyl-7-{2-(1,1,1,3,5,5,5-heptamethyltrisiloxan-3-yl)ethyl}-2-naphthamide.** A pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.2 Hz, 1H), 7.79 (s, 1H), 7.77 (d, *J* = 8.7 Hz, 1H), 7.63 (s, 1H), 7.40 (m, 2H), 3.60 (br s, 2H), 3.30 (br s, 2H), 2.79–2.83 (m, 2H), 1.28 (br s, 3H), 1.12 (br s, 3H), 0.90–0.94 (m, 2H), 0.12 (s, 18H), 0.06 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.5, 143.5, 134.5, 133.0, 131.8, 128.0, 127.9, 127.6, 125.8, 125.2, 123.0, 43.3, 39.3, 29.4, 19.5, 14.2, 12.9, 1.9, –0.3; HRMS[ESI(+)] calcd for $C_{24}H_{41}NO_3Si_3Na$ $[M+Na]^+$: 498.2286. Found: *m/z* 498.2283.

Procedure for Figure 3. In a glove box, a 4 mL vial was charged with $Ni(cod)_2$ (8.3 mg, 30 μmol), **L1** (35 mg, 30 μmol) or **L2** (42 mg, 30 μmol), and 1-tridecene (164 mg, 0.21 mL, 0.90 mmol), and the resulting mixture was stirred for 5 min at room temperature. Then, *N*,*N*-diethylbenzamide (53.2 mg, 0.30 mmol) and MAD (58 mg, 0.120 mmol) were added to the reaction mixture in this order. The resulting mixture was stirred at 150 °C and analyzed by GC after 0.50 h, 1.0 h, 1.5 h, 2.0 h, 10 h, and 18 h. In each analysis, the vial was cooled in an ice bath, and approximately 10 μL of the reaction mixture was taken for GC analysis. The vial was heated at150 °C again.

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REFERENCES AND NOTES

1. S. Murai, F. Kakiuchi, S. Sekine, Y. Tanaka, A. Kamatani, M. Sonoda, and N. Chatani, *Nature*, 1993, **366**, 529; X. Chen, K. M. Engle, D.-H. Wang, and J.-Q. Yu, *Angew. Chem. Int. Ed.*, 2009, **48**, 5094.
2. D. Leow, G. Li, T.-S. Mei, and J.-Q. Yu, *Nature*, 2012, **486**, 518; L. Wan, N. Dastbaravardeh, G. Li, and J.-Q. Yu, *J. Am. Chem. Soc.*, 2013, **135**, 18056; Y.-F. Yang, G.-J. Cheng, P. Liu, D. Leow, T.-Y. Sun, P. Chen, X. Zhang, J.-Q. Yu, Y.-D. Wu, and K. N. Houk, *J. Am. Chem. Soc.*, 2014, **136**, 344; R.-Y. Tang, G. Li, and J.-Q. Yu, *Nature*, 2014, **507**, 215; G. Yang, P. Lindovska, D. Zhu, J. Kim, P. Wang, R.-Y. Tang, M. Movassaghi, and J.-Q. Yu, *J. Am. Chem. Soc.*, 2014, **136**, 10807; Y. Deng and J.-Q. Yu, *Angew. Chem. Int. Ed.*, 2015, **54**, 888; L. Chu, M. Shang, K. Tanaka, Q. Chen, N. Pissarnitski, E. Streckfuss, and J.-Q. Yu, *ACS Cent. Sci.*, 2015, **1**, 394; H.-J. Xu, Y. Lu, M. E. Farmer, H.-W. Wang, D. Zhao, Y.-S. Kang, W.-Y. Sun, and J.-Q. Yu, *J. Am. Chem. Soc.*, 2017, **139**, 2200; L. Fang, T. G. Saint-Denis, B. L. H. Taylor, S. Ahlquist, K. Hong, S. Liu, L. Han, K. N. Houk, and J.-Q. Yu, *J. Am. Chem. Soc.*, 2017, **139**, 10702; Z. Jin, L. Chu, Y.-Q. Chen, and J.-Q. Yu, *Org. Lett.*, 2018, **20**, 425; G. Yang, D. Zhu, P. Wang, R.-Y. Tang, and J.-Q. Yu, *Chem. Eur. J.*, 2018, **24**, 3434.
3. S. Bag, T. Patra, A. Modak, A. Deb, S. Maity, U. Dutta, A. Dey, R. Kancherla, A. Maji, A. Hazra, M. Bera, and D. Maiti, *J. Am. Chem. Soc.*, 2015, **137**, 11888; T. Patra, S. Bag, R. Kancherla, A. Mondal, A. Dey, S. Pimparkar, S. Agasti, A. Modak, and D. Maiti, *Angew. Chem. Int. Ed.*, 2016, **55**, 7751; A. Maji, S. Guin, S. Feng, A. Dahiya, V. K. Singh, P. Liu, and D. Maiti, *Angew. Chem. Int. Ed.*, 2017, **56**, 14903; A. Maji, A. Dahiya, G. Lu, T. Bhattacharya, M. Brochetta, G. Zanoni, P. Liu, and D. Maiti, *Nat. Commun.*, 2018, **9**, 3582.
4. L. Ping, D. S. Chung, J. Bouffard, and S.-g. Lee, *Chem. Soc. Rev.*, 2017, **46**, 4299.
5. Y. Kuninobu, H. Ida, M. Nishi, and M. Kanai, *Nat. Chem.*, 2015, **7**, 712; H. J. Davis, M. T. Mihai, and R. J. Phipps, *J. Am. Chem. Soc.*, 2016, **138**, 12759; Z. Zhang, K. Tanaka, and J.-Q. Yu, *Nature*, 2017, **543**, 538.
6. M. E. Hoque, R. Bisht, C. Haldar, and B. Chattopadhyay, *J. Am. Chem. Soc.*, 2017, **139**, 7745.
7. C. Cheng and J. F. Hartwig, *Science*, 2014, **343**, 853.

8. Y. Saito, Y. Segawa, and K. Itami, *J. Am. Chem. Soc.*, 2015, **137**, 5193.
9. S. Okumura, S. Tang, T. Saito, K. Semba, S. Sakaki, and Y. Nakao, *J. Am. Chem. Soc.*, 2016, **138**, 14699.
10. Y. Nakao, Y. Yamada, N. Kashihara, and T. Hiyama, *J. Am. Chem. Soc.*, 2010, **132**, 13666.
11. S. Okumura and Y. Nakao, *Org. Lett.*, 2017, **19**, 584.
12. S. Okumura, T. Komine, E. Shigeki, K. Semba, and Y. Nakao, *Angew. Chem. Int. Ed.*, 2018, **57**, 929.
13. L. Yang, K. Semba, and Y. Nakao, *Angew. Chem. Int. Ed.*, 2017, **56**, 4853.
14. A. C. Hillier, W. J. Sommer, B. S. Yong, J. L. Petersen, L. Cavallo, and S. P. Nolan, *Organometallics*, 2003, **22**, 4322.
15. A. Gómez-Suárez, D. J. Nelson, and S. P. Nolan, *Chem. Commun.*, 2017, **53**, 2650.
16. S. Meiries, K. Speck, D. B. Cordes, A. M. Z. Slawin, and S. P. Nolan, *Organometallics*, 2013, **32**, 330.
17. F. Shi, J. K. Shen, D. Chen, K. Fog, K. Thirstrup, M. Hentzer, J.-J. Karlsson, V. Menon, K. A. Jones, K. E. Smith, and G. Smith, *ACS Med. Chem. Lett.*, 2011, **2**, 303.
18. A. Collado, A. Gómez-Suárez, A. R. Martin, A. M. Z. Slawin, and S. P. Nolan, *Chem. Commun.*, 2013, **49**, 5541.
19. B. E. Haines, Y. Saito, Y. Segawa, K. Itami, and D. G. Musaev, *ACS Catal.*, 2016, **6**, 7536.
20. ScambVca application was used for the calculation of $\%V_{bur}$, which is available on web: http://www.molnac.unisa.it/OMtools/sambvca.php. Calculation parameters: sphere radius, 3.50 Å; distances for the metal−ligand bond (*d*), 2.00 Å or 2.28 Å; hydrogen atoms were omitted; scaled Bondi radii were used as recommended by Cavallo, see: A. Poater, B. Cosenza, A. Correa, S. Giudice, F. Ragone, V. Scarano, and L. Cavallo, *Eur. J. Inorg. Chem.*, 2009, 1759.
21. Because the $\%V_{bur}$ of IPr*^{OMe} has never been measured with (IPr*^{OMe})AuCl, the $\%V_{bur}$ of IPr*,[15] which is structurally similar with IPr*^{OMe}, was used for the comparison.
22. Computational study of C–H bond cleavage steps by nickel catalysis, see: S. Tang, O. Eisenstein, Y. Nakao, and S. Sakaki, *Organometallics*, 2017, **36**, 2761.
23. It cannot be excluded that **L2** accelerates the reductive elimination as well as the C–H bond cleavage. The selected examples for reductive elimination accelerated by sterically hindered ligands, see: (a) B. C. Hamann and J. F. Hartwig, *J. Am. Chem. Soc.*, 1997, **119**, 12382; (b) G. Mann, C. Incarvito, A. L. Rheingold, and J. F. Hartwig, *J. Am. Chem. Soc.*, 1999, **121**, 3224; (c) D. A. Culkin and J. F. Hartwig, *Organometallics*, 2004, **23**, 3398.
24. Remote C5, C6, and C7-selective C–H functionalization of 1-substituted naphthalenes has been highly limited compared to C2, C3, C4, and C8-selective C-H functionalization. Selected examples

of C5-selective reactions: W. F. Short and H. Wang, *J. Chem. Soc.*, 1950, 991; C6-selective reactions: K. Mikoshiba, K. Hamada, A. Terauchi, S. Ozaki, J. Goto, E. Ebii, and A. Suzuki, Jpn. Kokai Tokkyo Koho JP 2010195768, 2010; C7-selective reactions: M. Prakash, S. Muthusamy, and V. Kesavan, *J. Org. Chem.*, 2014, **79**, 7836; N. Misawa, M. Nodate, T. Otomatsu, K. Shimizu, C. Kaido, M. Kikuta, A. Ideno, H. Ikenaga, J. Ogawa, S. Shimizu, and K. Shindo, *Appl. Microbiol. Biotechnol.*, 2011, **90**, 147; To the best of our knowledge, the only example of C(6)–H functionalization of naphthalene bearing a C1-electron-withdrawing group is the reaction of 1-naphthaldehyde with trioxane to give 6,6'-methylenebis(1-napthaldehyde), but the site-selectivity is not shown in the literature. M. A. Mughal, A. Mughal, G. Z. Memon, M. Y. Khuhawar, and S. Qureshi, *Asian J. Chem.*, 2013, **25**, 9931.

25. S. Meiries, K. Speck, D. B. Cordes, A. M. Z. Slawin, and S. P. Nolan, *Organometallics*, 2013, **32**, 330.
26. T. Adachi, H. Sugimoto, T. Aida, and S. Inoue, *Macromolecules*, 1993, **26**, 1238.
27. R. G. Harvey, C. Cortez, and S. A. Jacobs, *J. Org. Chem.*, 1982, **47**, 2120.
28. L. Zhang, C. Chen, J. Han, Z.-B. Huang, and Y. Zhao, *Org. Chem. Front.*, 2016, **3**, 1271.
29. A. B. Pangborn, M. A. Giardello, R. H. Grubbs, R. K. Rosen, and F. J. Timmers, *Organometallics*, 1996, **15**, 1518.
30. R. Salvio, L. Moisan, D. Ajami, and J. Rebek Jr., *Eur. J. Org. Chem.*, 2007, 2722.