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FULL PAPER

Copper-Catalyzed Oxidative Dehydrogenative C(sp^3)–H Bond Amination of (Cyclo)Alkanes using *NH*-Free Heterocycles as Amine Sources

Chang-Sheng Wang,[a] Xiao-Feng Wu,[b] Pierre H. Dixneuf[a] and Jean-François Soulé*[a]

Abstract: A copper-catalyzed oxidative C(sp^3)–H/N–H coupling of *NH*-heterocycles with affordable (cyclo)alkanes was developed. This protocol involved C(sp^3)–N bond formation *via* a radical pathway generated by a homolytic cleavage of di-*tert*-butyl peroxide and trapping of the radical(s) by copper catalysts. The reaction tolerated a series of functional groups, such as bromo, fluoro, ester, ketone, nitrile, methyl and methoxy. *NH*-free indoles, pyroles, pyrazoles, indazoles and benzotriazoles have been successfully *N*-alkylated.

Introduction

N-alkyl heterocycle derivatives constitute an important class of organic compounds, which have been widely used in biology, synthetic and polymer chemistry.[1] As example, The *N*-alkyl indole **I** displays biological activity for the treatment of neurodegenerative diseases.[2] The *N*-cycloalkyl pyrrole **II** is an analogue of BN1212 exhibiting antitubercular properties.[3] The *N*-cyclopentylindazole **III** was used as a selective inhibitor of EZH2.[4] The *N*-(*tert*-butoxymethyl)indole **IV** has shown inhibition properties on vascular endothelial growth factors, which are important signaling proteins involved in both vasculogenesis and angiogenesis (Figure 1).[5]

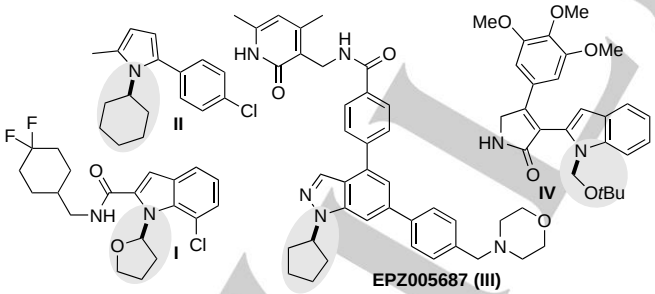

Figure 1. Examples of *N*-Alkyl heterocycles Displaying Biological Activities.

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Despite this wide applicability, ecofriendly routes for the synthesis of *N*-alkyl heterocycles are limited. One of the most common synthetic pathway involves SN_2 reaction using a stoichiometric amount of a strong base and an appropriate alkylating agent (e.g., alkyl halide, alkyl triflate, *etc.*) generation a lot of waste (Figure 2a).[6] Since the discovery of transition-metal catalyzed C–H bond functionalizations,[7] catalytic C–H amination provides an appealing method for the straightforward construction of C–N bonds.[8] General protocols for the transition-metal catalyzed C–H amination required electrophilic amines, *via* an internal oxidant strategy (e.g., azides,[9] *N*-haloamines[10] or oximes[11]). However, such protocols could not be employed for the *N*-functionalization of *NH*-heterocycles. Amines can be directly used, although an external oxidant is required.[12] However, only rare examples of C–H amination with *NH*-heterocycles have been reported.[13] This lack of exploitation is probably due to the presence of competitive C(sp^2)–H bonds on *NH*-heterocycles, which are generally more reactive.[14] Although synthetic tools enabling C(sp^2)–N bond formation have been well established,[15] facile intermolecular amination of C(sp^3)–H bonds under mild conditions still remains a challenge in synthetic chemistry.[4, 11d, 16]

Recently, cross-dehydrogenative coupling reactions have attracted increasing attention owing to the use of abundant hydrocarbons (i.e., arenes, olefins, or cycloalkanes) as unreactive coupling partners for the C–C, C–O, and C–N bond formation.[17] Warren and co-workers reported the oxidative dehydrogenative amination of alkanes with unactivated amines using copper(II) as catalyst associated to di-*tert*-butyl peroxide (DTBP) (Figure 2b).[18] Outstanding achievements are emerging in this area[19] although only amines with low nucleophilicity were successfully alkylated. For example, Hartwig and co-workers reported C(sp^3)–H amination of cyclohexane with phthalimide and sulfonamides.[19c] Cai and co-workers have reported that with *NH*-indole, using nickel catalyst, regiospecific C2- or C3-products were obtained without the formation of *N*–alkylated indole (Figure 2c).[20] In addition, Yi and co-workers have reported that under metal-free conditions in the presence of DTBP, the cross-dehydrogenative coupling between *NH*-indoles and (cyclo)alkanes took place at the C7 position of the indole unit, and in some cases C2 or C4 regioselectivity was overserved (Figure 2d).[21] To the best of our knowledge, oxidative dehydrogenative amination of (cyclo)alkanes using electron-rich *NH*-heteroarenes as amine sources has not been reported yet owing to the chemoselectivity issue between C–H or N–H reactivity.[22] Inspired by previous works on the generation of alkyl radical in the presence of coordinated amines,[18, 19c] we herein report a general method for the C−N bond formation *via* C−H/N−H cross-coupling of *NH*-free

indoles, pyrroles, benzotriazoles, indazoles, and pyrazoles with (cyclo)alkanes to afford the corresponding *N*-alkylated heterocycles in good yields with a high chemoselectivity (Figure 2e).

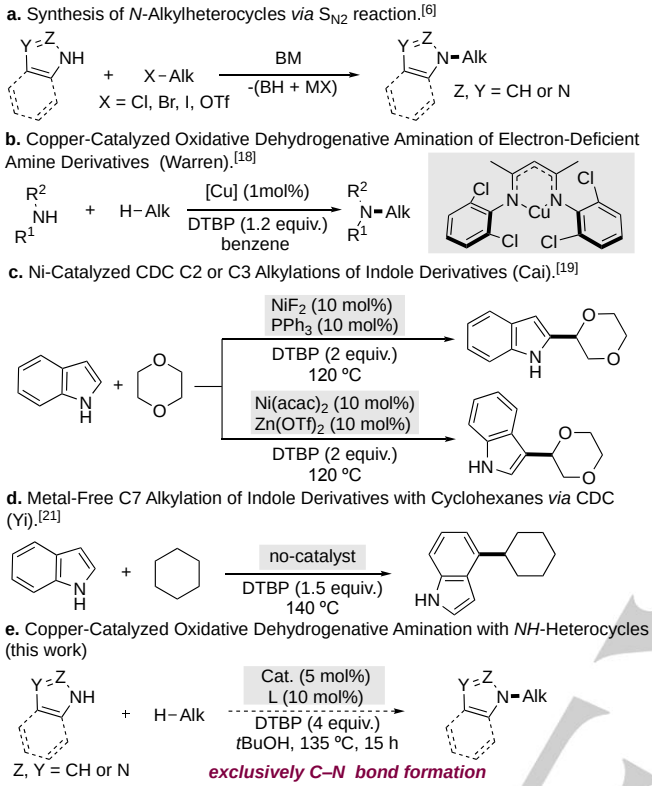
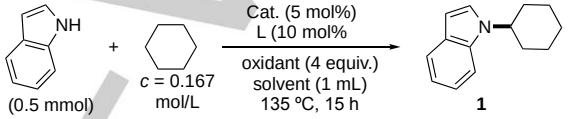


Figure 2. *N*-Alkylation of amines and *NH*–Heterocycles

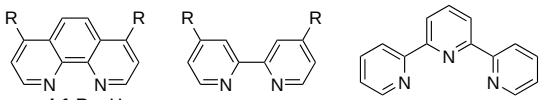
Results and Discussion

We started our investigation using *NH*-free indole and cyclohexane as model substrates. The reaction was initially studied with DTBP as an oxidant, in *t*BuOH without catalyst. As reported by Yi,[21] we have not observed the formation of the amination product **1** after heating at 135 °C over 15 h, but we did observe the formation of C-alkylated products (Table 1, entry 1). When $FeCl_3$ (5 mol%) in the presence of phenanthroline (**L1**) (10 mol%) was used as the catalytic system, the amination product **1** was obtained in low yield with predominant formation of other C2, C3 and C7–alkylated products (Table 1, entry 2). $FeCl_2$, in concert with **L1**, gave a similar result (Table 1, entry 3). In contrast, when copper (II or I) oxides, combined with **L1**, were used as catalysts, **1** was selectively obtained in 41% and 50% yield, respectively without the formation of other C2, C3 and C7–alkylated products (Table 1, entries 4 and 5). Encouraged by these results, a number of other copper sources, including CuBr, CuI, $[MeCN]_4Cu(I)PF_6$, $Cu(I)Br(Me_2S)$, and $Cu(OAc)_2.n\text{-}H_2O$ were evaluated in the presence of **L1** (Table 1, entries 6−10). The results showed that $Cu(I)Br(Me_2S)$ displayed the highest catalytic activity for this reaction and *N*-cyclohexylindole (**1**) was isolated in 67% yield (Table 1, entry 10). Next, we evaluated without success the influence of other *N,N*-bidentate ligands, such as 4,7-diphenyl-1,10-phenanthroline (**L2**), 2,2'-bipyridine (**L3**), 4,4'-di-*tert*-butyl-2,2'-bipyridine (**L4**) and 2,2':6',2''-terpyridine (**L5**) (Table 1, entries 11-14). When the reaction is performed in absence of phenanthroline (**L1**), the yield in **1** dropped to 10% concurrent with the formation of other C2, C3 and C7–alkylated products (Table 1, entry 15). Other oxidants such as TBHP, BPO were inefficient for the coupling of cyclohexane bonds with *NH*-indole; whereas, DCP give a lower yield of 32% in the desired product **1** (Table 1, entries 16−18). It is important to note that using a lower amount of cyclohexane the yield of **1** decreased (Table 1, entry 19). The reaction is less efficient in other solvents such as benzene, trifluorotoluene, or 1,2-dichloroethane (Table 1, entries 20-22).

Table 1 Optimization of Oxidative Dehydrogenative Amination of Cyclohexane with *NH*-free Indole.



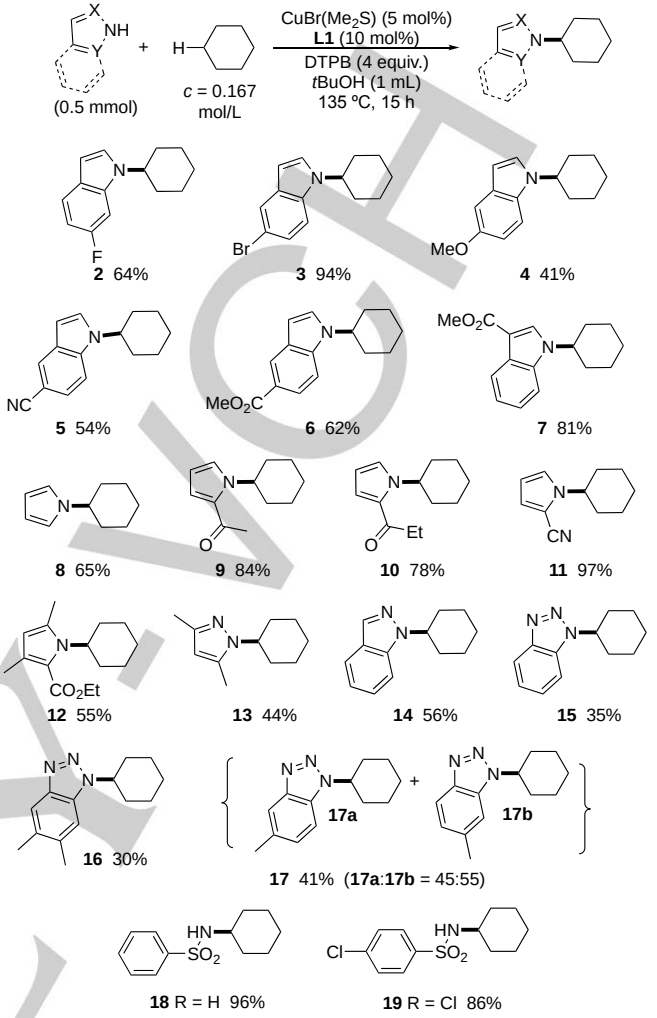
Entry	Cat.	L	oxidant	solvent	Yield in **1** (%)[a]
1	–	**–**	DTBP	–	0[b]
2	$FeCl_3$	**L1**	DTBP	*t*BuOH	5[b]
3	$FeCl_2$	**L1**	DTBP	*t*BuOH	8[b]
4	CuO (II)	**L1**	DTBP	*t*BuOH	41
5	Cu_2O (I)	**L1**	DTBP	*t*BuOH	50
6	CuBr	**L1**	DTBP	*t*BuOH	77
7	CuI	**L1**	DTBP	*t*BuOH	62
8	$Cu(OAc)_2.n\text{-}H_2O$	**L1**	DTBP	*t*BuOH	65
9	$Cu(CH_3CN)_4PF_6$	**L1**	DTBP	*t*BuOH	52
10	**$CuBr(Me_2S)$**	**L1**	DTBP	*t*BuOH	**87 (67)**
11	$CuBr(Me_2S)$	**L2**	DTBP	*t*BuOH	55
12	$CuBr(Me_2S)$	**L3**	DTBP	*t*BuOH	22
13	$CuBr(Me_2S)$	**L4**	DTBP	*t*BuOH	39
14	$CuBr(Me_2S)$	**L5**	DTBP	*t*BuOH	13
15	$CuBr(Me_2S)$	**–**	DTBP	*t*BuOH	10[b]
16	$CuBr(Me_2S)$	**L1**	TBHP	*t*BuOH	NR
17	$CuBr(Me_2S)$	**L1**	BPO	*t*BuOH	NR
18	$CuBr(Me_2S)$	**L1**	DCP	*t*BuOH	32
19[c]	$CuBr(Me_2S)$	**L1**	DTBP	*t*BuOH	46
20	$CuBr(Me_2S)$	**L1**	DTBP	C_6H_6	28
21	$CuBr(Me_2S)$	**L1**	DTBP	$CF_3C_6H_5$	35
22	$CuBr(Me_2S)$	**L1**	DTBP	DCE	45



[a] Determined by GC-analysis using *n*-dodecane as internal standard, isolated yield is shown in parentheses. [b] Formation of of other C2, C3 and C7-alkylated products. [c] Reaction performed at 0.5 mol/L of cyclohexane.

With the optimized reaction conditions in hands, we then explored the substrate scope. Firstly, we investigated the reactivity of *NH*-heterocycles with cyclohexane using Cu/**L1**/DTBP system (Scheme 1). *NH*-6-Fluoroindole and *NH*-5-bromoindole were successfully *N*-alkylated to deliver the corresponding *N*-cyclohexylindoles **2** and **3** in 64% and 94% yield, respectively. It should be mentioned that for these reactions, no cleavage of the C–halogen bonds were observed, allowing further transformations. An electron-donating group on the indole moiety,

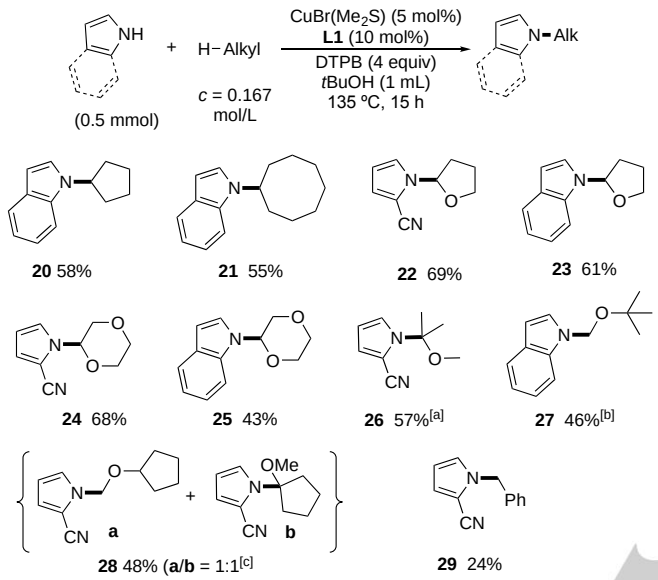
such as 5-methoxyl, slightly affected the yield in the coupling product **4**; while an electron-withdrawing group such as nitrile or methyl ester allowed the formation of the desired *N*-alkylindoles **5** and **6** in 54% and 62% yields, respectively. The reaction conditions tolerate a C3 substituent on the indole moiety such as ester. Indeed, from methyl *NH*-indole-3-carboxylate the optimized reaction conditions gave exclusively the *N*-alkylation product **7** in 81%. Whereas, indole bearing a C2-substituent such as methyl or phenyl did not allow the formation of the corresponding *N*-alkylation product. Under these reaction conditions, *NH*-pyrrole was also alkylated affording *N*-cyclohexylpyrrole **8** in 65% yield, without the formation of C2 or C3 alkylation products. Cu/**L1**/DTBP-catalyzed oxidative dehydrogenative amination tolerated functional groups such as ketone and nitrile. Indeed, 2-acetyl, 2-propionyl, and 2-nitrile pyrroles successfully reacted with cyclohexane to afford the *N*-cyclohexylpyrroles **9**–**11** in 84–97% yields. A trisubstituted pyrrole including ethyl ester group was also *N*-alkylated to afford **12** in 55% yield. Poly-nitrogen heterocyclic compounds are ubiquitous structural elements important to a wide range of fine and bulk chemical fields.[23] Therefore, we investigated their reactivity in oxidative dehydrogenative amination. *NH*-3,5-Dimethylpyrazole and *NH*-indazole smoothly reacted in the presence of cyclohexane to give the corresponding *N*-alkylated products **13** and **14** in moderate yields, but without the formation of C-alkylation products. *NH*-Benzotriazole displayed poor reactivity, as the *N*-alkylated products **15**–**17** were isolated in moderate to low yields. In the case of 5-methylbenzo[1,2,3]triazole, the product was isolated as mixture of two regioisomers **17a** and **17b** in 55:45 ratio. Finally, our catalytic system displayed similar performance than other protocols[19a] for the *N*-alkylation of sulfonamides, as **18** and **19** were obtained in 96% and 86% yields. It is important to note that some functional groups on the heterocycle moiety such as nitro, amino, or hydroxyl are not compatible with the reaction conditions.



Scheme 1. Scope of *NH*-Heterocycle in Cu-catalyzed C(sp^3)–H Amination of Cyclohexane.

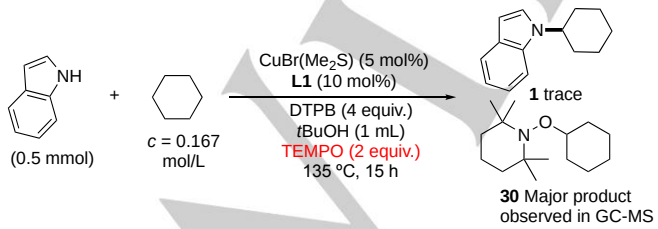
Substrate scope studies were also carried out on other hydrocarbons using *NH*-pyrrole or *NH*-indole as amine sources (Scheme 2). As expected, the reaction between *NH*-indole with linear alkanes (*e.g.*, pentane or hexane) leads to a variety of *N*-alkylated product at C1, C2, C3 carbons. The direct amination of other cycloalkanes (*e.g.*, cyclopentane and cyclooctane) with *NH*-indole allowed the formation of **20** and **21** in 58% and 55% yields, respectively. Tetrahydrofuran can be also used as suitable alkylating agent through the regioselective C(sp^3)–H bond activation.[24] The amination occurred at the *α*-position of the oxygen atom to afford **22** and **23** in 69% and 61% yields from *NH*-2-cyanopyrrole and *NH*-indole. Similarly, 1,4-dioxane was successfully coupled with 2-cyanopyrrole and indole giving the *N*-alkylated products **24** and **25** in 68% and 43% yield, respectively. Interestingly, the reaction of 2-cyanopyrrole with 2,2-dimethoxypropane led selectively to the formation of *N*-(2-methoxypropan-2-yl)-2-cyanopyrrole (**26**) in 57% yield. This product results from the substitution of one methoxy group. Methyl *tert*-butyl ether reacted at the methoxy position to afford

regioselectively the *N*-alkylated heterocycle **27** in 46% yield. In contrast, cyclopentyl methyl ether provided a mixture of two regioisomers **28a** and **28b** in 1:1 ratio. These regioselectivities are in line with a radical pathway, in which the radical is stabilized by the oxygen atom. Finally, from toluene, pyrrole was *N*-benzylated in moderate yield.



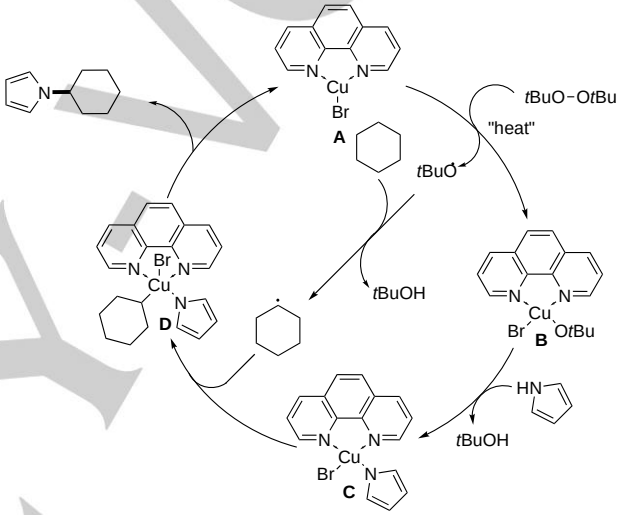
Scheme 2. Scope of (Cyclo)Alkanes in Cu-catalyzed C(sp^3)–H Amination with *NH*-Heterocycle. [a] Using 2,2-dimethoxypropane as alkane source; [b] Using methyl *tert*-butyl ether as alkane source; [c] Using methyl cyclopentyl ether as alkane source

To obtain a better understanding of the mechanism, a radical control experiment was carried out in the presence of a radical scavenger (Scheme 3). When 2 equivalents of 2,2,6,6-tetramethylpiperidine1-oxyl (TEMPO) was added to the reaction under the standard conditions, no desired product **1** was detected. However, we have observed the formation of the adduct cyclohexane–TEMPO **30** (determined by GC−MS), which implied that a radical process is involved in the oxidative dehydrogenative amination of (cyclo)alkanes with *NH*-heterocycles.



Scheme 3. Radical Trapping Experiment with TEMPO.

Based on our experimental results and previous reports,[19] a possible mechanism is described in Scheme 4. First, homolytic cleavage of the DTBP peroxide under heating allowed the formation of *tert*-butoxyl radical (*t*BuO•) which is trapped by the copper(I) **A** to generate the copper(II) alkoxide **B.** σ-Bond metathesis of **B** with an *NH*-heterocycle regenerates intermediate **C**. The coordination of the *N*-heterocycle to the copper centre renders the N atom particularly reactive toward reaction with C-based radicals (R•), which are generated by abstracting a hydrogen atom from (cyclo)alkane by *tert*-butoxyl radical (*t*BuO•). Reaction of the alkyl radical (R•) with Cu(II) **C** should allow the formation of the Cu(III) intermediate **D**, which undergoes a reductive elimination to release the desired *N*-alkylated heterocycle and reduce the Cu center to regenerate active copper(I) **A.**



Scheme 4. Proposed Mechanism.

Conclusions

In summary, we have described a copper-catalyzed oxidative dehydrogenative amination of unactivated alkanes with *NH*-heterocycles to produce exclusively the corresponding *N*-alkylated products without formation of a C–C bond. Choice of copper source as well as the phenanthroline ligand were found to be critical to suppress the formation of C-alkylated heterocycles. A wide variety of *NH*-heterocycles including poly-nitrogen heterocyclic compounds were successfully *N*-alkylated. Moreover, the reaction conditions tolerate a broad variety of substituents of the heterocycles such as methyl, methoxy, fluoro, bromo, ketone, ester, and nitrile. This method employs abundant and cheap feedstock under oxidative conditions, without any pre-functionalization or the production of stoichiometric metal salt waste, making it very attractive for practical use in the preparation of useful *N*–alkylated heterocyclic derivatives.

Experimental Section

General Remarks: All reactions were run in Schlenk tubes without the use of an inert atmosphere. Commercial *NH*-free heterocycles and (cyclo)alkanes were used without purification. The reactions were followed by GC and NMR. ^{1}H and ^{13}C spectra were recorded with a Bruker 400 MHz spectrometer in $CDCl_3$ solutions. Chemical shifts are reported in ppm relative to $CDCl_3$ (7.26 for ^{1}H NMR and 77.0 for ^{13}C NMR). Flash chromatography was performed on silica gel (230–400 mesh).

General Procedure for Copper-Catalyzed Oxidative Dehydrogenative C(sp^3)–H Bond Amination of (Cyclo)Alkanes with *NH*-free Heterocycles: In a dried 25 mL Schlenk tube equipped with a magnetic stirrer, CuBr(Me_2S) (5.0 mg, 0.025 mmol, 5 mol%) and 1,10-phenanthroline (9.0 mg, 0.05 mmol, 10 mol%) were dissolved in *t*-BuOH (1 mL) and (cyclo)alkane (1 mL). Then, *NH*-free heterocycles (0.5 mmol) and additional (cyclo)alkane (2 mL) were successfully added before addition of DTBP (292 mg, 2.0 mmol, 4 equiv.). The resulting solution mixture was stirred at 135 ºC over 15 h. After evaporation of solvent, the product was purified using flash column chromatography on silica gel.

***N*-Cyclohexylindole (1):** Following the general procedure using *NH*-indole (58 mg, 0.5 mmol) and cyclohexane (3 mL), **1** was isolated in 67% yield (66 mg) as a colorless oil after purification using flash column chromatography with pentane : ethyl acetate = 40 : 1. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.70 (d, *J* = 7.8 Hz, 1H), 7.45 (d, *J* = 8.2 Hz, 1H), 7.30 – 7.22 (m, 2H), 7.16 (d, *J* = 7.2 Hz, 1H), 4.28 (tt, *J* = 3.7, 11.8 Hz, 1H), 2.28 – 2.12 (m, 2H), 2.08 – 1.92 (m, 3H), 1.74 (td, *J* = 3.1, 12.3 Hz, 2H), 1.56 (tdd, *J* = 3.3, 8.1, 12.9 Hz, 3H), 1.44 – 1.25 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 135.6, 128.5, 124.1, 121.1, 121.0, 119.3, 109.5, 101.0, 55.1, 33.6, 26.1, 25.8. MS(EI) m/z(%) = 199 ([M]$^+$,49), 156 (30), 130 (10),117 (100), 90 (14), 55 (13).

***N*-Cyclohexyl-6-fluoroindole (2)**: Following the general procedure using 6-Fluoro-*NH*-indole (68 mg, 0.5 mmol) and cyclohexane (3 mL), **2** was isolated in 64% yield (69 mg) as a light yellow oil after purification using flash column chromatography with pentane : ethyl acetate = 40 : 1. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.55 (dd, *J* = 8.6, 5.5 Hz, 1H), 7.22 (d, *J* = 3.2 Hz, 1H), 7.08 (dd, *J* = 10.2, 1.7 Hz, 1H), 6.89 (dd, *J* = 9.4, 2.2 Hz, 1H), 6.51 (d, *J* = 3.1 Hz, 1H), 4.12 (tt, *J* = 11.8, 3.6 Hz, 1H), 2.23 – 2.06 (m, 2H), 2.04 – 1.90 (m, 2H), 1.76 – 1.64 (m, 2H), 1.60 – 1.44 (m, 2H), 1.40 – 1.24 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ(ppm) -121.6. ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 159.6 (d, *J* = 236.6 Hz), 135.5 (d, *J* = 12.0 Hz), 124.9, 124.5 (d, *J* = 3.6 Hz), 121.5 (d, *J* = 10.2 Hz), 108.0 (d, *J* = 24.6 Hz), 101.2, 95.9 (d, *J* = 26.3 Hz), 55.4, 33.4, 25.9, 25.6. MS(EI) m/z(%) = 217 ([M]$^+$,36), 174 (11), 135 (100), 108 (14), 55 (19).

5-Bromo-*N*-cyclohexylindole (3): Following the general procedure using 5-bromo-*NH*-indole (97 mg, 0.5 mmol) and cyclohexane (3 mL), **3** was isolated in 94% yield (130 mg) as a light yellow oil after purification using flash column chromatography with pentane : ethyl acetate = 40 : 1. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.75 (dd, *J* = 1.4, 1.0 Hz, 1H), 7.28 – 7.24 (m, 2H), 7.22 (d, *J* = 3.2 Hz, 1H), 6.45 (d, *J* = 3.2 Hz, 1H), 4.17 (tt, *J* = 11.8, 3.7 Hz, 1H), 2.19 – 2.03 (m, 2H), 2.01 – 1.86 (m, 2H), 1.87 – 1.75 (m, 1H), 1.75 – 1.62 (m, 2H), 1.61 – 1.40 (m, 2H), 1.40 – 1.21 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 134.2, 130.1, 125.2, 123.9, 123.4, 112.4, 110.9, 100.6, 55.4, 33.5, 25.9, 25.6. MS(EI) m/z (%) = 277 ([M]$^+$,100), 236 (20), 197 (82), 168 (8), 155 (37), 116 (62), 89 (35), 55(73).

***N*-Cyclohexyl-5-methoxyindole (4)**. Following the general procedure using 5-methoxy-*NH*-indole (74 mg, 0.5 mmol) and cyclohexane (3 mL), **4** was isolated in 41% yield (46 mg) as a light yellow oil after purification using flash column chromatography with pentane : ethyl acetate = 40 : 1. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.29 (d, *J* = 8.9 Hz, 1H), 7.21 (d, *J* = 3.2 Hz, 1H), 7.12 (d, *J* = 2.4 Hz, 1H), 6.91 – 6.85 (m, 1H), 6.44 (d, *J* = 3.1 Hz, 1H), 4.17 (tt, *J* = 11.7, 3.6 Hz, 1H), 3.87 (s, 3H), 2.23 – 2.10 (m, 2H), 2.01 – 1.87 (m, 2H), 1.85 – 1.75 (m, 1H), 1.75 – 1.65 (m, 2H), 1.54 – 1.43 (m, 2H), 1.38 – 1.23 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 153.9, 130.9, 128.7, 124.6, 111.5, 110.1, 102.6, 100.5, 55.9, 55.3, 33.6, 26.0, 25.7. MS(EI) m/z(%) = 229 ([M]$^+$,100), 214 (8), 186 (26), 147 (57), 132 (63), 104 (14), 55(18).

***N*-Cyclohexylindole-5-carbonitrile (5):** Following the general procedure **A**. using *NH*-indole-5-carbonitrile (71 mg, 0.5 mmol) and cyclohexane 3 mL, **5** was isolated in 54 % yield (60 mg) as a light yellow oil, after purification using flash column chromatography with pentane : ethyl acetate = 40 : 1. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.96 (s, 1H), 7.43 – 7.39 (m, 2H), 7.34 (d, *J* = 3.3 Hz, 1H), 6.58 (d, *J* = 3.3 Hz, 1H), 4.23 (tt, *J* = 3.7, 11.9 Hz, 1H), 2.16 – 2.08 (m, 2H), 2.01 – 1.92 (m, 2H), 1.86 – 1.78 (m, 1H), 1.72 (ddd, *J* = 3.2, 12.5, 24.7 Hz, 2H), 1.57 – 1.44 (m, 2H), 1.36 – 1.23 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 137.0, 128.2, 126.6, 126.5, 124.1, 120.9, 110.3, 102.3, 102.2, 55.6, 33.5, 25.8, 25.5. MS(EI) m/z(%) = 224 ([M]$^+$,41), 181 (18), 142 (100),115 (9), 83 (10), 55 (26).

Methyl *N*-cyclohexylindole-5-carboxylate (6): Following the general procedure **A**. using methyl *NH*-indole-5-carboxylate (88 mg, 0.5 mmol) and cyclohexane 3 mL, **6** was isolated in 62 % yield (80 mg) as a light yellow oil, after purification using flash column chromatography with pentane : ethyl acetate = 30 : 1. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.40 (d, *J* = 1.3 Hz, 1H), 7.91 (dd, *J* = 1.6, 8.7 Hz, 1H), 7.38 (d, *J* = 8.7 Hz, 1H), 7.28 (d, *J* = 3.3 Hz, 1H), 6.60 (d, *J* = 3.2 Hz, 1H), 4.24 (tt, *J* = 3.7, 11.9 Hz, 1H), 3.93 (s, 3H), 2.13 (d, *J* = 11.3 Hz, 2H), 1.95 (d, *J* = 13.5 Hz, 2H), 1.81 (d, *J* = 13.1 Hz, 1H), 1.71 (qd, *J* = 3.2, 12.5 Hz, 2H), 1.58 – 1.44 (m, 2H), 1.36 – 1.22 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 168.3, 138.0, 128.0, 125.5, 124.0, 122.5, 121.3, 109.0, 102.8, 55.4, 51.8, 33.5, 25.9, 25.6. MS(EI) m/z(%) = 257 ([M]$^+$,100), 226 (14), 214 (19),175 (45), 144 (97), 116 (31), 89 (11), 55 (31).

Methyl 1-cyclohexyl-*1H*-indole-3-carboxylate (7): Following the general procedure **A**. using methyl *1H*-indole-3-carboxylate (88 mg, 0.5 mmol) and cyclohexane 3 mL, **7** was isolated in 81% yield (104 mg) as a light yellow oil, after purification using flash column chromatography with pentane : ethyl acetate = 30 : 1. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.24 – 8.19 (m, 1H), 7.97 (s, 1H), 7.45 – 7.38 (m, 1H), 7.31 – 7.25 (m, 2H), 4.23 (tt, *J* = 3.6, 11.8 Hz, 1H), 3.93 (s, 3H), 2.16 (d, *J* = 11.5 Hz, 2H), 2.00 – 1.91 (m, 2H), 1.81 (d, *J* = 13.1 Hz, 1H), 1.76 – 1.64 (m, 2H), 1.58 – 1.43 (m, 2H), 1.36 – 1.23 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 165.6, 136.2, 131.0, 126.7, 122.4 121.8, 121.8, 110.0, 106.9, 55.6, 50.9, 33.4, 25.8, 25.5. MS(EI) m/z(%) = 257 ([M]$^+$,88), 226 (14), 175 (43),144 (100), 116 (12), 55 (23).

***N*-Cyclohexylpyrrole (8)**. Following the general procedure using *NH*-pyrrole (34 mg, 0.5 mmol) and cyclohexane (3 mL), **8** was isolated in 65% yield (48 mg) as a light yellow oil after purification using flash column chromatography with pentane : ethyl acetate = 40 : 1. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 6.79 – 6.74 (m, 2H), 6.20 – 6.15 (m, 2H), 3.83 (tt, *J* = 11.6, 3.6 Hz, 1H), 2.20 – 2.06 (m, 2H), 1.97 – 1.87 (m, 2H), 1.81 – 1.70 (m, 1H), 1.70 – 1.57 (m, 2H), 1.52 – 1.37 (m, 2H), 1.33 – 1.19 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 118.4, 107.4, 58.7, 34.7, 25.8, 25.5. MS(EI) m/z(%) = 149 ([M]$^+$,67), 106 (19), 94 (23), 67 (100), 55 (23).

2-Acetyl-*N*-Cyclohexylpyrrole (9). Following the general procedure using 2-acetyl-*NH*-pyrrole (55 mg, 0.5 mmol) and cyclohexane (3

mL), **9** was isolated in 84% yield (80 mg) as a light yellow oil after purification using flash column chromatography with pentane : ethyl acetate = 40 : 1. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.11 – 7.07 (m, 1H), 6.96 (dd, *J* = 4.0, 1.6 Hz, 1H), 6.14 (dd, *J* = 4.0, 2.7 Hz, 1H), 5.17 – 5.06 (m, 1H), 2.43 (s, 3H), 2.17 – 1.95 (m, 2H), 1.92 – 1.81 (m, 2H), 1.77 – 1.68 (m, 1H), 1.54 – 1.42 (m, 4H), 1.27 – 1.12 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 188.4, 130.0, 125.5, 120.4, 108.1, 56.6, 34.6, 27.8, 25.9, 25.7. MS(EI) m/z(%) = 191 ([M]$^+$,38), 176 (62), 148 (10), 120 (7), 109 (46), 94 (100) 55 (25).

***N*-Cyclohexyl-2-propionylpyrrole (10)**. Following the general procedure using 2-propionyl-*NH*-pyrrole (62 mg, 0.5 mmol) and cyclohexane (3 mL), **10** was isolated in 78% yield (80 mg) as a light yellow oil after purification using flash column chromatography with pentane : ethyl acetate = 40 : 1. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.10 – 7.07 (m, 1H), 6.98 (dd, J = 1.6, 4.0 Hz, 1H), 6.14 (dd, J = 2.7, 4.0 Hz, 1H), 5.22 – 5.05 (m, 1H), 2.82 (q, J = 7.4 Hz, 2H), 2.14 – 2.00 (m, 2H), 1.92 – 1.78 (m, 2H), 1.79 – 1.67 (m, 1H), 1.54 – 1.44 (m, 4H), 1.20- – 1.17 (m, 1H), 1.17 (t, J = 7.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 191.9, 129.7, 125.2, 119.3, 108.0, 56.7, 34.6, 32.7, 25.9, 25.7, 9.0. MS(EI) m/z(%) = 205 ([M]$^+$,24), 176 (42), 162 (3), 148 (8), 123 (14), 94(100), 81 (5),55(16).

***N*-Cyclohexylpyrrole-2-carbonitrile (11)**. Following the general procedure using *NH*-pyrrole-2-carbonitrile (46 mg, 0.5 mmol) and cyclohexane (3 mL), **11** was isolated in 97% yield (84 mg) as a light yellow oil after purification using flash column chromatography with pentane : ethyl acetate = 40 : 1. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 6.91 (dd, *J* = 2.6, 1.6 Hz, 1H), 6.74 (dd, *J* = 3.9, 1.6 Hz, 1H), 6.15 (dd, *J* = 3.9, 2.8 Hz, 1H), 4.08 (tt, *J* = 11.9, 3.8 Hz, 1H), 2.14 – 2.03 (m, 2H), 1.96 – 1.84 (m, 2H), 1.80 – 1.69 (m, 1H), 1.69 – 1.57 (m, 2H), 1.52 – 1.35 (m, 2H), 1.30 – 1.18 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 123.1, 119.6, 114.1, 109.2, 102.8, 58.4, 34.2, 25.6, 25.2. MS(EI) m/z(%) = 174 ([M]$^+$,59), 93 (84), 83 (38), 67 (52), 55 (100).

Ethyl-*N*-cyclohexyl-3,5-dimethylpyrrole-2-carboxylate (12). Following the general procedure using ethyl 3,5-dimethyl-*NH*-pyrrole-2-carboxylate (84 mg, 0.5 mmol) and cyclohexane (3 mL), **12** was isolated in 55% yield (68 mg) as a light yellow oil after purification using flash column chromatography with pentane : ethyl acetate = 40 : 1. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 5.73 (s, 1H), 5.08 – 4.77 (m, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 2.33 (s, 3H), 2.25 (s, 3H), 2.14 – 1.96 (m, 2H), 1.91 – 1.80 (m, 4H), 1.76 – 1.62 (m, 2H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.30 – 1.16 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 162.3, 135.4, 129.6, 119.5, 112.5, 59.4, 57.1, 31.9, 26.6, 25.5, 15.2, 14.7, 14.5. MS(EI) m/z(%) = 249 ([M]$^+$,96), 204 (23), 176 (68), 167 (72), 138 (82), 121 (100), 95 (76), 55 (36).

***N*-Cyclohexyl-3,5-dimethylpyrazole (13)**. Following the general procedure using 3,5-dimethyl-*1H*-pyrazole (48 m, 0.5 mmol) and cyclohexane (3 mL), **13** was isolated in 44% yield (39 mg) as a light yellow oil after purification using flash column chromatography with pentane : ethyl acetate = 40 : 1. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 5.75 (s, 1H), 3.96 – 3.74 (m, 1H), 2.23 (s, 3H), 2.22 (s, 3H), 1.93 – 1.81 (m, 6H), 1.74 – 1.64 (m, 1H), 1.43 – 1.27 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 146.8, 137.6, 104.5 (d, *J* = 11.9 Hz), 57.2 (d, *J* = 10.7 Hz), 32.9, 25.9, 25.2, 13.6 (d, *J* = 8.9 Hz), 11.0 (d, *J* = 9.1 Hz). MS(EI) m/z(%) = 178 ([M]$^+$,30), 163 (9), 135 (9), 123 (14), 109 (63), 97 (100), 81 (9).

***N*-Cyclohexylindazole (14)**. Following the general procedure using *NH*-indazole (59 mg, 0.5 mmol) and cyclohexane (3 mL), **14** was isolated in 56% yield (56 mg) as a light yellow oil after purification using flash column chromatography with pentane : ethyl acetate = 40 : 1. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.02 (s, 1H), 7.73 (d, *J* = 8.1 Hz, 1H), 7.47 (d, *J* = 8.4 Hz, 1H), 7.36 (t, *J* = 7.9 Hz, 1H), 7.13 (t, *J* = 7.5 Hz, 1H), 4.60 – 4.26 (m, 1H), 2.11 – 1.99 (m, 2H), 1.99 – 1.92 (m, 2H), 1.84 – 1.74 (m, 1H), 1.63 – 1.59 (m, 1H), 1.54 – 1.41 (m, 2H), 1.41 – 1.30 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 138.6, 132.5, 125.8, 124.0, 121.2, 120.4, 109.2, 58.2, 32.5, 25.9, 25.5. MS(EI) m/z(%) = 200 ([M]$^+$,37), 171 (13), 157 (37), 131(59), 118 (100), 91 (23), 77 (13).

***N*-Cyclohexylbenzo[*d*][1,2,3]triazole (15)**. Following the general procedure using *NH*-benzo[*d*][1,2,3]triazole (60 mg, 0.5 mmol) and cyclohexane (3 mL), **15** was isolated in 35% yield (35 mg) as a light yellow oil after purification using flash column chromatography with pentane : ethyl acetate = 40 : 1. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.06 (d, *J* = 8.3 Hz, 1H), 7.57 (d, *J* = 8.3 Hz, 1H), 7.45 (t, *J* = 6.6 Hz, 1H), 7.34 (d, *J* = 6.9 Hz, 1H), 4.72 – 4.59 (m, 1H), 2.23 – 2.15 (m, 2H), 2.06 – 1.94 (m, 2H), 1.87 – 1.77 (m, 1H), 1.62 – 1.34 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 146.1, 132.2, 126.7, 123.7, 120.1, 109.8, 59.1, 32.6, 25.6, 25.3. MS(EI) m/z(%) = 201 ([M]$^+$,26), 147 (12), 133 (27), 120 (100), 91 (57), 64(29), 55(25). mp 102-104 °C.

***N*-Cyclohexyl-5,6-dimethylbenzo[*d*][1,2,3]triazole (16)**. Following the general procedure using 5,6-dimethyl-*NH*-benzo[d][1,2,3]triazole (74 mg, 0.5 mmol) and cyclohexane (3 mL), **16** was isolated in 30% yield (35 mg) as a light yellow solid after purification using flash column chromatography with pentane : ethyl acetate = 40 : 1. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.79 (s, 1H), 7.33 (s, 1H), 4.68 – 4.52 (m, 1H), 2.44 (s, 3H), 2.41 (s, 3H), 2.21 – 2.14 (m, 4H), 2.07 – 1.96 (m, 2H), 1.86 – 1.77 (m, 1H), 1.61 – 1.34 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 145.4, 136.9, 133.4, 131.2, 119.1, 109.3, 58.9, 32.5, 25.6, 25.3, 20.9, 20.4. MS (EI) m/z(%) = 229 ([M]$^+$,26), 158 (9), 119(100), 91 (13), 55 (36). mp 122-124 °C.

***N*-Cyclohexyl-5-methylbenzo[*d*][1,2,3]triazole (17a) and *N*-cyclohexyl-6-methylbenzo[*d*][1,2,3]triazole (17b).** Following the general procedure using 5-methyl-*NH*-benzo[d][1,2,3]triazole (74 mg, 0.5 mmol) and cyclohexane (3 mL), **17a and 17b** was isolated in 41% yield (44 mg) in 45:55 ratio as a light yellow oil after purification using flash column chromatography with pentane : ethyl acetate = 40 : 1. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.92 (d, *J* = 8.5 Hz, 1H, **17b**), 7.81 (s, 1H, **17a**), 7.46 (d, *J* = 8.5 Hz, 1H, **17a**), 7.34 (s, 1H, **17b**), 7.31 – 7.26 (m, 1H, **17a**), 7.17 (dd, *J* = 1.4, 8.5 Hz, 1H, **17b**), 4.76 – 4.47 (m, 1H, **17a**+**17b**), 2.54 (s, 3H, **17b**), 2.51 (s, 3H, **17a**), 2.23 – 2.09 (m, 4H, **17a**+**17b**), 2.08 – 1.92 (m, 2H, **17a**+**17b**), 1.87 – 1.75 (m, 1H, **17a**+**17b**), 1.61 – 1.46 (m, 2H, **17a**+**17b**), 1.45 – 1.33 (m, 1H, **17a**+**17b**). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 146.7 (**17a**), 144.7 (**17b**), 137.2 (**17b**), 133.7 (**17a**), 132.7 (**17a**), 130.7 (**17b**), 129.1 (**17a**), 126.0 (**17b**), 119.4 (**17b**), 118.9 (**17a**), 109.3 (**17b**), 109.0 (**17a**), 59.0 (**17a**), 58.8 (**17b**), 32.5 (**17a**), 32.5 (**17b**), 25.6 (**17a** and **17b**), 25.3 (**17a** and **17b**), 22.0 (**17a** or **17b**), 21.4 (**17a** or **17b**). MS (EI) m/z(%) = 215 ([M]$^+$,74), 186 (15), 172(28), 158 (75), 144 (53), 105 (100), 91 (38), 55 (76).

***N*-Cyclohexylbenzenesulfonamide (18)**. Following the general procedure using benzenesulfonamide (79 mg, 0.5 mmol) and cyclohexane (3 mL), **18** was isolated in 96 % yield (114 mg) as a light yellow oil after purification using flash column chromatography with pentane : ethyl acetate = 10 : 1. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.93 – 7.86 (m, 2H), 7.57 – 7.51 (m, 1H), 7.51 – 7.43 (m, 2H), 5.14 (d, *J* = 7.5 Hz, 1H), 3.18 – 3.03 (m, 1H), 1.74 – 1.66 (m, 2H), 1.64 – 1.56 (m, 2H), 1.51 – 1.41 (m, 1H), 1.27 – 1.19 (m, 1H), 1.19 – 1.12 (m, 3H), 1.12 – 1.00 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 141.5, 132.4, 129.0, 126.9, 52.7, 33.8, 25.1, 24.6. MS (EI) m/z(%) = 239 ([M]$^+$,32), 210 (7), 196 (87), 158 (9), 141(72), 98 (46), 77 (100), 51 (23).

4-Chloro-*N*-Cyclohexylbenzenesulfonamide (19). Following the general procedure using 4-chlorobenzenesulfonamide (95 mg, 0.5 mmol) and cyclohexane (3 mL), **19** was isolated in 86% yield (117 mg) as a light yellow solid after purification using flash column chromatography with pentane : ethyl acetate = 10 : 1. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.83 (d, *J* = 8.4 Hz, 1H), 7.45 (d, *J* = 8.4 Hz, 1H), 5.15 (d, *J* = 7.6 Hz, 1H), 3.12 (tt, *J* = 6.8, 13.5 Hz, 1H), 1.76 – 1.67 (m, 2H), 1.64 – 1.56 (m, 2H), 1.53 – 1.42 (m, 1H), 1.26 – 1.05 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 140.1, 138.8, 129.3, 128.4, 52.8, 33.8, 25.1, 24.6. MS (EI) m/z(%) = 273 ([M]$^+$,34), 244 (7), 230 (100), 175 (70), 153 (8), 111(84), 75 (33), 55(21).

***N*-Cyclopentylindole (20)**. Following the general procedure using *NH*-indole (58 mg, 0.5 mmol) and cyclopentane (3 mL), **20** was isolated in 58 % yield (54 mg) as a light orange oil after purification using flash column chromatography with pentane : ethyl acetate = 40 : 1. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.69 (d, *J* = 7.8 Hz, 1H), 7.46 (d, *J* = 8.2 Hz, 1H), 7.30–7.23 (m, 2H), 7.20–7.12 (m, 1H), 6.56 (d, *J* = 3.2 Hz, 1H), 4.91–4.79 (m, 1H), 2.32 – 2.21 (m, 2H), 2.06–1.90 (m, 4H), 1.86–1.77 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 136.2, 128.6, 124.5 (d, *J* = 6.9 Hz), 121.2 (d, *J* = 1.8 Hz), 120.9 (d, *J* = 4.2 Hz), 119.3, 109.9, 101.0, 57.0, 32.6, 24.1. MS (EI) m/z(%) = 185 ([M]$^+$,40), 156 (24), 117 (100), 90 (16).

***N*-Cyclooctylindole (21)**. Following the general procedure using *NH*-indole (58 mg, 0.5 mmol) and cyclooctane (3 mL), **21** was isolated in 55% yield (62 mg) as a light yellow oil after purification using flash column chromatography with pentane : ethyl acetate = 40 : 1. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.69 (d, *J* = 7.9 Hz, 1H), 7.43 (d, *J* = 8.2 Hz, 1H), 7.28 (d, *J* = 3.3 Hz, 1H), 7.24 (d, *J* = 7.5 Hz, 1H), 7.15 (t, *J* = 7.5 Hz, 1H), 6.55 (d, *J* = 3.1 Hz, 1H), 4.63 – 4.53 (m, 1H), 2.21 – 1.99 (m, 2H), 1.94 – 1.83 (m, 2H), 1.82 – 1.65 (m, 10H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 135.3, 128.5, 124.7, 121.1, 121.0, 119.2, 109.6, 101.0, 56.0, 33.4, 26.9, 26.1, 24.9. MS (EI) m/z(%) = 227 ([M]$^+$,67), 156 (54), 143 (37), 130 (23), 117 (100), 90 (14), 69 (15), 14 (55).

***N*-(Tetrahydrofuran-2-yl)pyrrole-2-carbonitrile (22)**. Following the general procedure using *NH*-pyrrole-2-carbonitrile (46 mg, 0.5 mmol) and tetrahydrofuran (3 mL), **22** was isolated in 69% yield (56 mg) as a light yellow oil after purification using flash column chromatography with pentane : ethyl acetate = 40 : 1. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 6.97 (dd, *J* = 1.7, 2.5 Hz, 1H), 6.83 (dd, *J* = 1.5, 3.8 Hz, 1H), 6.17 (t, *J* = 3.4 Hz, 1H), 6.00 (dd, *J* = 3.7, 6.5 Hz, 1H), 4.21 (dd, *J* = 7.4, 14.1 Hz, 1H), 3.99 (dd, *J* = 7.2, 15.3 Hz, 1H), 2.54 – 2.35 (m, 1H), 2.28 – 2.17 (m, 1H), 2.16 – 2.00 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 123.6, 121.4, 113.7, 109.6, 101.6, 88.3, 69.5, 33.6, 24.5. MS(EI) m/z(%) = 162 ([M]$^+$,12), 131 (5), 92 (10), 71 (100).

***N*-(Tetrahydrofuran-2-yl)indole (23)**. Following the general procedure using *NH*-indole (58 mg, 0.5 mmol) and tetrahydrofuran (3 mL), **23** was isolated in 61% yield (57 mg) as a colorless yellow oil after purification using flash column chromatography with pentane : ethyl acetate = 40 : 1. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.69 (d, *J* = 7.8 Hz, 1H), 7.53 (d, *J* = 8.3 Hz, 1H), 7.31 – 7.26 (m, 2H), 7.20 (t, *J* = 7.5 Hz, 1H), 6.60 (d, *J* = 3.1 Hz, 1H), 6.60 (d, *J* = 3.1 Hz, 1H), 6.29 (dd, *J* = 6.1, 4.3 Hz, 1H), 4.18 (td, *J* = 7.9, 6.0 Hz, 1H), 4.05 (dd, *J* = 15.3, 7.3 Hz, 1H), 2.47 – 2.39 (m, 2H), 2.26 – 2.11 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 135.7, 129.2, 124.0, 121.8, 121.0, 120.0, 110.0, 102.3, 85.8, 68.4, 31.6, 24.8. MS(EI) m/z (%) = 187 ([M]$^+$,21), 117 (100), 89 (10), 71 (22).

***N*-(1,4-Dioxan-2-yl)pyrrole-2-carbonitrile (24)**. Following the general procedure using *NH*-pyrrole-2-carbonitrile (46 mg, 0.5 mmol) and 1,4-dioxane (3 mL), **24** was isolated in 68% yield (60 mg) as a light yellow oil after purification using flash column chromatography with pentane : ethyl acetate = 40 : 1. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.20 (dd, *J* = 2.7, 1.5 Hz, 1H), 6.85 (dd, *J* = 3.9, 1.4 Hz, 1H), 6.23 (t, *J* = 3.6 Hz, 1H), 5.55 (dd, *J* = 6.7, 3.0 Hz, 1H), 4.01 (dd, *J* = 11.8, 3.0 Hz, 1H), 3.93 – 3.71 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 125.1, 121.2, 113.2, 110.1, 103.6, 80.6, 68.7, 66.0, 64.9. MS(EI) m/z(%) = 178 ([M]$^+$,20), 118 (7), 86 (100), 59 (12).

***N*-(1,4-Dioxan-2-yl)indole (25)**. Following the general procedure **A**. using *NH*-indole (58 mg, 0.5 mmol) and 1,4-dioxane (3 mL), **25** was isolated in 43% yield (44 mg) as a white solid after purification using flash column chromatography with pentane : ethyl acetate = 40 : 1. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.68 (d, *J* = 7.8 Hz, 1H), 7.52 (d, *J* = 8.2 Hz, 1H), 7.47 (d, *J* = 3.4 Hz, 1H), 7.32 – 7.26 (m, 1H), 7.23 – 7.16 (m, 1H), 6.61 (d, *J* = 3.2 Hz, 1H), 5.80 – 5.74 (m, 1H), 4.14 – 4.10 (m, 2H), 3.97 – 3.81 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 136.1, 128.8, 125.5, 122.2, 121.1, 120.4, 110.1, 103.0, 79.2, 68.7, 66.4, 64.6. MS (EI) m/z (%) = 203([M]$^+$,18), 117(100), 90 (12). mp 76-78 ^{o}C.

***N*-(2-Methoxypropan-2-yl)pyrrole-2-carbonitrile (26)**. Following the general procedure using *NH*-pyrrole-2-carbonitrile (46 mg, 0.5 mmol) and 2,2-dimethoxypropane (3 mL), **26** was isolated in 57% yield (47 mg) as a light yellow oil after purification using flash column chromatography with pentane : ethyl acetate = 40 : 1. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 6.93 (dd, *J* = 2.8, 1.7 Hz, 1H), 6.91 (dd, *J* = 3.8, 1.6 Hz, 1H), 6.15 (dd, *J* = 3.7, 3.0 Hz, 1H), 3.12 (s, 3H), 1.81 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 124.3, 123.4, 114.7, 108.7, 101.4, 89.8, 50.1, 27.0. MS(EI) m/z(%) = 164 ([M]$^+$,4), 133 (11), 92(11), 73 (100).

***N*-(*Tert*-butoxymethyl)indole (27)**. Following the general procedure using *NH*-indole (58 mg, 0.5 mmol) and 2-methoxy-2-methylpropane (3 mL), **27** was isolated in 46% yield (47 mg) as a light yellow oil after purification using flash column chromatography with pentane : ethyl acetate = 40 : 1. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.66 (d, *J* = 7.9 Hz, 1H), 7.53 (d, *J* = 8.2 Hz, 1H), 7.31 – 7.25 (m, 1H), 7.22 (d, *J* = 3.2 Hz, 1H), 7.20 – 7.14 (m, 1H), 6.56 (d, *J* = 3.2 Hz, 1H), 5.56 (s, 2H), 1.29 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 136.1, 129.1, 127.5, 121.9, 120.9, 119.9, 110.1, 102.4, 74.2, 70.3, 28.0. MS(EI) m/z(%) = 203 ([M]$^+$,20), 130 (35), 117(100), 57 (22).

***N*-((Cyclopentyloxy)methyl)pyrrole-2-carbonitrile (28a) and 1-(1-methoxycyclopentyl)pyrrole-2-carbonitrile (28b)**. Following the general procedure using *NH*-pyrrole-2-carbonitrile (46 mg, 0.5 mmol) and methoxycyclopentane (3 mL), **28a** was isolated in 24% yield (23 mg) as pure form as a light yellow oil, and **28b** was isolated in 24% yield (23 mg) as pure form as a light yellow oil after purified using flash column chromatography with pentane : ethyl acetate = 40 : 1. **28a** ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.00 (dd, *J* = 2.6, 1.6 Hz, 1H), 6.83 (dd, *J* = 3.9, 1.5 Hz, 1H), 6.24 (dd, *J* = 3.8, 2.9 Hz, 1H), 5.35 (s, 2H), 4.01 – 3.91 (m, 1H), 1.68 (ddd, *J* = 6.9, 4.2, 1.7 Hz, 4H), 1.63 – 1.44 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 126.7, 120.9, 113.4, 110.4, 104.0, 80.2, 76.1, 32.3, 23.5. MS(EI) m/z(%) = 190 ([M]$^+$,51), 159 (43), 145 (15), 132 (25), 106 (100), 97 (25), 71 (48), 67 (52).

28 b ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 6.97 (dd, *J* = 2.8, 1.7 Hz, 1H), 6.90 (dd, *J* = 3.8, 1.6 Hz, 1H), 6.13 (dd, *J* = 3.8, 2.9 Hz, 1H), 2.96 (s, 3H), 2.59 – 2.47 (m, 2H), 2.20 – 2.06 (m, 2H), 1.92 – 1.73 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 125.3, 123.2, 114.7, 108.4, 102.5, 99.1, 50.0, 35.9, 22.2. MS(EI) m/z(%) = 190 ([M]$^+$,4), 119 (3), 106 (4), 92 (100), 78 (77), 69(44), 51(12).

***N*-Benzylpyrrole-2-carbonitrile (29)**. Following the general procedure using *NH*-pyrrole-2-carbonitrile (46 mg, 0.5 mmol,) and toluene (3 mL), **29** was isolated in 24% yield (22 mg) as a light yellow oil after purification using flash column chromatography with pentane : ethyl acetate = 40 : 1. ^{1}H NMR (400 MHz, $CDCl_3$) δ (m) 7.41 – 7.31 (m, 3H), 7.22 – 7.16 (m, 2H), 6.87 – 6.81 (m, 2H), 6.21 (dd, *J* = 3.9, 2.8 Hz, 1H), 5.21 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 136.0, 129.0, 128.4, 127.4, 126.6, 120.3, 113.8, 109.9, 104.2, 52.4. MS(EI) m/z(%) = 182 ([M]$^+$,18), 91 (100), 65 (14).

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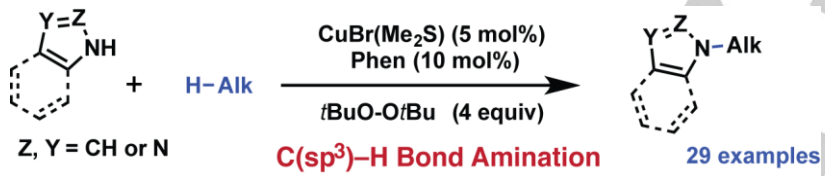

A variety of *N*-alkylated heterocycles is facilely synthesized by direct C−H bond amination of low cost (cyclo)alkanes catalyzed by inexpensive copper salts. A broad *NH*-free heterocycles scope has been used as amine sources and the reaction displayed a good functional group compatibility.

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Copper-Catalyzed Oxidative Dehydrogenative C(sp3)–H Bond Amination of (Cyclo)Alkanes using *NH*-Free Heterocycles as Amine Sources