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N-Alkylation of Amines with Alcohols Catalyzed by Manganese(II) Chloride or Bromopentacarbonylmanganese(I)

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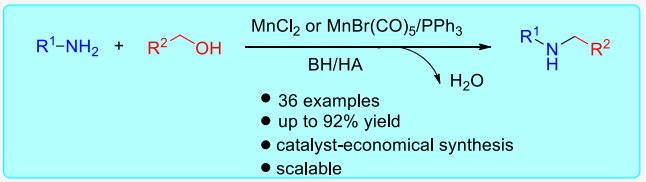
ABSTRACT: A manganese-catalyzed *N*-alkylation reaction of amines with alcohols via hydrogen autotransfer strategy has been demonstrated. The developed practical catalytic system including an inexpensive, nontoxic, commercially available $MnCl_2$ or $MnBr(CO)_5$ as the metal salt and triphenylphosphine as a ligand provides access to diverse aromatic, heteroaromatic, and aliphatic secondary amines in moderate-to-high yields. In addition, this operationally simple protocol is scalable to the gram level and suitable for synthesizing heterocycles such as indole and resveratrol-derived amines known to be active for Alzheimer's disease.



INTRODUCTION

Regarding the current important concerns about environmental issues and energy crisis, the development of new, efficient, and sustainable methodologies for the construction of chemical compounds using abundantly available metals instead of rare noble metals and renewable feedstocks is nowadays a central topic in green chemistry. In this context, catalytic alkylation reaction of amines with readily available alcohols,[1] following mostly the borrowing-hydrogen or hydrogen-autotransfer (BH/HA) concept first reported by Winans and Adkins in 1932,[2] is an environmentally friendly and atom-economical strategy since the utilized alcohol starting material can be obtained from biomass, which is a sustainable alternative to finite fossil resources, and the only generated byproduct of this transformation is water. To date, a diverse range of catalytic systems based on precious metals such as ruthenium,[3] rhodium,[4] and iridium[5] have been developed for the *N*-alkylation of amines with alcohols. However, in terms of sustainability, developing catalytic systems based on highly abundant, less toxic, and less expensive metals in this transformation would be highly desirable since this combination of alcohols with earth-abundant nonprecious metals contributes to the preservation of fossil resources and noble metals. In this respect, significant progress in *N*-alkylation reactions of amines with alcohols mediated by first-row transition metals[6] such as Fe,[7] Co,[8] Cu,[9] Ni,[10] and Mn catalysts has been made. Especially, the development of Mn-catalyzed *N*-alkylation of amines with alcohols via a BH/HA strategy[11] is extremely attractive because manganese is the third most abundant transition metal within the Earth's crust and has important functions for the metabolism and development of humans in biology. In 2016, Beller and co-workers reported the first manganese-catalyzed alkylation of amines using a molecular-defined manganese pincer complex **Mn-1** (Scheme 1a).[12] Subsequently, the *N*-methylation of various amines with methanol using a different manganese PNP-pincer complex **Mn-2** (Scheme 1a) was demonstrated successfully by the same research group.[13] Additionally, the selective *N*-methylation of

Scheme 1. Manganese-Catalyzed *N*-Alkylation of Amines with Alcohols

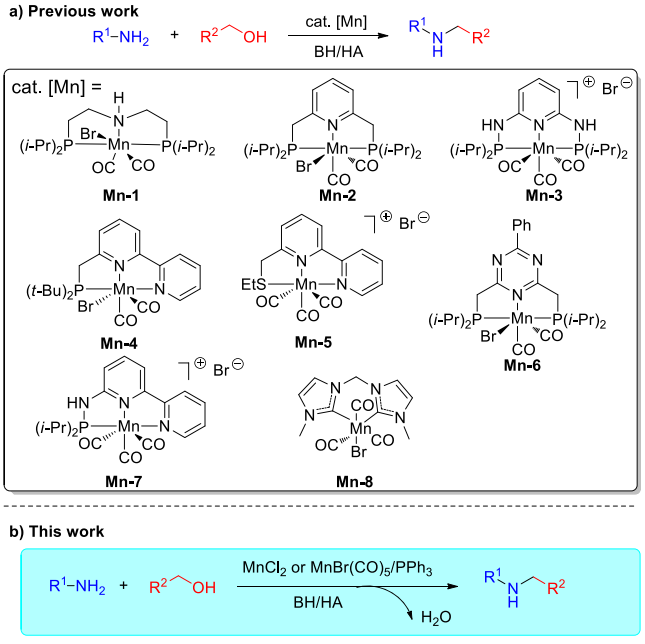


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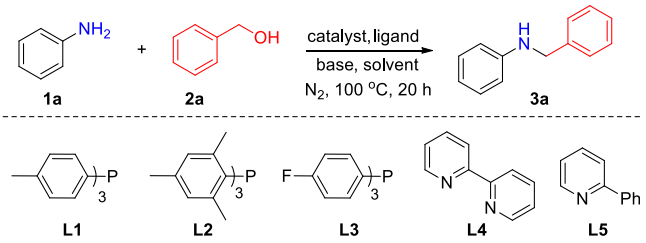
Table 1. Optimization of Reaction Conditions[a]



entry	catalyst	ligand	base	solvent	yield[b]
1	$MnCl_2·4H_2O$	PPh_3	KO*t*-Bu	PhMe	28%
2	$MnCl_2$	PPh_3	KO*t*-Bu	PhMe	79%
3	$MnBr_2$	PPh_3	KO*t*-Bu	PhMe	40%
4	$Mn(OAc)_2$	PPh_3	KO*t*-Bu	PhMe	32%
5	$Mn(acac)_2$	PPh_3	KO*t*-Bu	PhMe	27%
6		PPh_3	KO*t*-Bu	PhMe	trace
7	$MnCl_2$	PPh_3		PhMe	trace
8	$MnCl_2$		KO*t*-Bu	PhMe	34%
9	$MnCl_2$	PEt_3	KO*t*-Bu	PhMe	45%
10	$MnCl_2$	PCy_3	KO*t*-Bu	PhMe	trace
11	$MnCl_2$	**L1**	KO*t*-Bu	PhMe	51%
12	$MnCl_2$	**L2**	KO*t*-Bu	PhMe	59%
13	$MnCl_2$	**L3**	KO*t*-Bu	PhMe	19%
14	$MnCl_2$	$PCy_3·HBF_4$	KO*t*-Bu	PhMe	23%
15	$MnCl_2$	$P(t\text{-Bu})_3·HBF_4$	KO*t*-Bu	PhMe	22%
16	$MnCl_2$	**L4**	KO*t*-Bu	PhMe	22%
17	$MnCl_2$	**L5**	KO*t*-Bu	PhMe	8%
18	$MnCl_2$	PPh_3	NaO*t*-Bu	PhMe	32%
19	$MnCl_2$	PPh_3	K_3PO_4	PhMe	31%
20	$MnCl_2$	PPh_3	NaOAc	PhMe	trace
21[c]	$MnCl_2$	PPh_3	KO*t*-Bu	PhMe	82%
22[c]	$MnCl_2$	PPh_3	KO*t*-Bu	*m*-xylene	57%
23[c]	$MnCl_2$	PPh_3	KO*t*-Bu	mesitylene	62%
24[c]	$MnCl_2$	PPh_3	KO*t*-Bu	DMF	16%
25[c]	$MnCl_2$	PPh_3	KO*t*-Bu	NMP	trace

[a]Reactions were performed on a 1 mmol scale with a 10 mol % catalyst, 20 mol % ligand, 1.2 equiv of base, 1.2 equiv of benzyl alcohol, and 2 mL of solvent at 100 °C in an oil bath under a nitrogen atmosphere for 20 h. [b]Isolated yields are given. [c]The reaction was performed at 130 °C in an oil bath.

aniline derivatives with methanol could also be performed in good-to-excellent yields in the presence of a cationic manganese pincer complex **Mn-3** (Scheme 1a).[14] Of late, the coupling of hydrazine with alcohols catalyzed by a manganese pincer complex **Mn-4** (Scheme 1a) was revealed by Milstein and co-workers for the synthesis of *N*-substituted hydrazones.[15] Moreover, a tridentate NNS ligand-based manganese(I) complex **Mn-5** (Scheme 1a) was synthesized and used to catalyze the reaction of 1,2-diaminobenzenes with alcohols to prepare 1,2-disubstituted benzimidazoles.[16] Very recently, a few molecular-defined manganese complexes **Mn-6**,[17] **Mn-7**,[18] and **Mn-8**[19] (Scheme 1a) were developed and introduced successively for the *N*-alkylation of anilines with alcohols. Despite enormous progress, which has been made in this very young field of research, from a practical point of view, the development of the simple, inexpensive, nontoxic, and commercially available manganese catalysts such as $MnCl_2$ for C−N coupling reactions via BH/HA strategy is still highly desirable since the previously reported molecular-defined manganese(I) complexes were synthesized in multiple steps and are normally sensitive to air and moisture. Recently, Kaur and co-workers reported the synthesis of aldimines via dehydrogenative coupling of amines and alcohols using $MnCl_2$ and terpyridine as a catalytic system.[20] Herein, we demonstrate a new catalytic system including an inexpensive, nontoxic, commercially available $MnCl_2$ or $MnBr(CO)_5$ as the metal salt and triphenylphosphine as a ligand for the efficient alkylation of amines with alcohols (Scheme 1b).

RESULTS AND DISCUSSION

In an exploration of the optimum conditions, *N*-alkylation of aniline with benzyl alcohol to form *N*-benzylaniline (**3a**) was selected as a benchmark reaction. The results are summarized in Table 1, and isolated yields after purification by liquid−liquid extraction and column chromatograph are reported. Initially, five commercially available manganese precatalysts were investigated in the *N*-alkylation of aniline with benzyl alcohol (Table 1, entries 1−5). Notably, a combination of 10 mol % $MnCl_2$, 20 mol % PPh_3, and 1.2 mmol of *t*-BuOK at 100 °C in an oil bath in toluene within 20 h (Figure S1 in the Supporting Information) resulted in the formation of *N*-benzylaniline (**3a**) with 79% isolated yield (Table 1, entry 2). A series of control experiments were conducted to test the necessity of the manganese catalyst, ligand, and base. In the absence of any one of the key reaction components, only trace amount of the expected product **3a** was observed (Table 1, entries 6−7), or the

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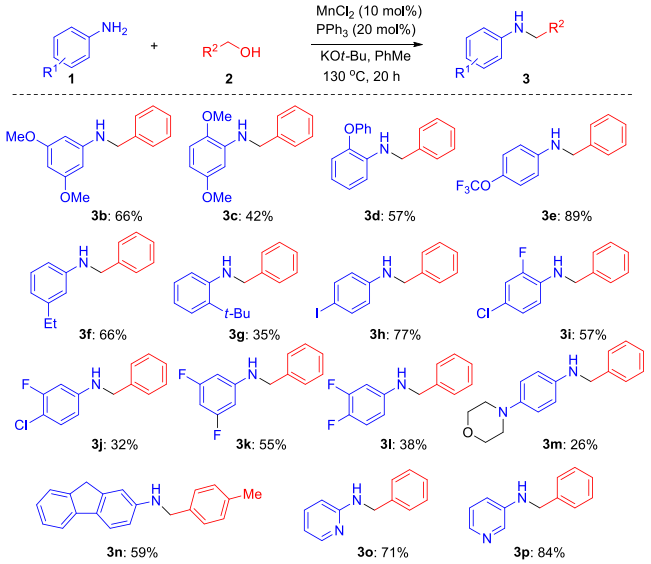
yield of **3a** was very low (Table 1, entry 8). The screening of a variety of phosphine and nitrogen ligands with various electronic and steric natures indicated that the use of PPh_3 as the ligand was beneficial (Table 1, entries 9−17). In addition, potassium *tert*-butoxide was found to be a more effective base than *t*-BuONa, K_3PO_4, or NaOAc (Table 1, entries 18−20). When the reaction temperature was increased to 130 °C, a higher yield of **3a** was given (Table 1, entry 21). The replacement of toluene with *m*-xylene, mesitylene, or polar solvents such as *N*,*N*-dimethylformamide (DMF) and *N*-methyl pyrrolidone (NMP) did not improve the product yield (Table 1, entries 22−25).

Having established the optimized reaction conditions, a number of amines and alcohols were evaluated to determine the substrate generality and limitations of this transformation. First, we tested a variety of substituted aniline derivatives using benzyl alcohol as the alkylating reagent (Scheme 2). It was observed

Scheme 2. Scope of Amines[a,b]

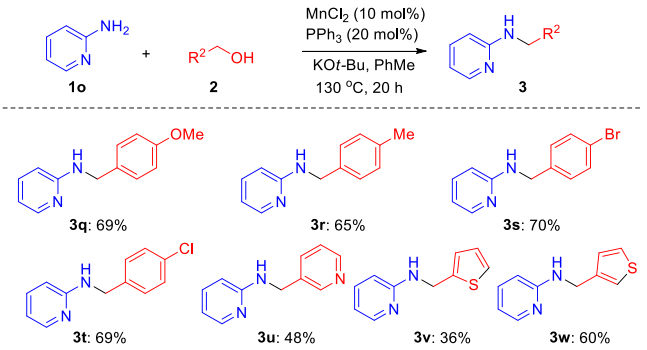


[a]Reactions were performed on a 1 mmol scale with 10 mol % $MnCl_2$, 20 mol % PPh_3, 1.2 equiv of KO*t*-Bu, 1.2 equiv of benzyl alcohol, and 2 mL of toluene at 130 °C in an oil bath under a nitrogen atmosphere for 20 h. [b]Isolated yields are given.

that electron-donating functionalities such as methoxy, phenoxy, trifluoromethoxy, ethyl, and *t*-butyl substituents on the aryl ring of aniline are well-tolerated and afforded the expected alkylated anilines **3b**−**3g** in 35−89% yields. It is worth mentioning that sterically hindered 2,4-dimethoxy, *o*-phenoxy, and 2-(*tert*-butyl)aniline smoothly underwent monoalkylation reaction with benzyl alcohol to afford the desired secondary amines **3c**, **3d**, and **3g**. Furthermore, anilines bearing electron-withdrawing substituents were selectively alkylated to provide monoalkylated anilines **3h**−**3l**, albeit in reduced yields. Under the identical conditions, employing 4-morpholinoaniline furnished the desired product **3m**, which is an important building block for pharmaceuticals. Similarly, the treatment of 2-aminofluorene with *p*-tolyl-methanol led to **3n** in a moderate yield (59%). Notably, selective alkylation of heteroaromatic amines proceeded well, furnishing the secondary amines **3o** and **3p** in 71 and 84% yields, respectively. Unfortunately, under the standard conditions, the reaction of benzylamines, secondary amines, and aliphatic amines with benzyl alcohol did not furnish the desired products, and only a small amount of imine was formed.

We next explored the scope of various primary alcohols with pyridin-2-amine (Scheme 3). Substrates bearing both electron-

Scheme 3. Scope of Alcohols[a,b]

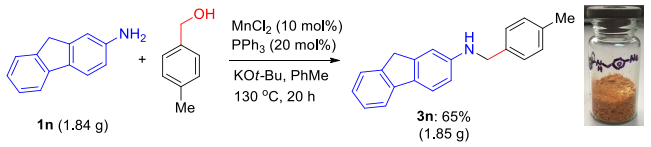


[a]Reactions were performed on a 1 mmol scale with 10 mol % $MnCl_2$, 20 mol % PPh_3, 1.2 equiv of KO*t*-Bu, 1.2 equiv of alcohol, and 2 mL of toluene at 130 °C in an oil bath under a nitrogen atmosphere for 20 h. [b]Isolated yields are given.

withdrawing and electron-donating substituents on the aryl ring of benzyl alcohols were converted smoothly to the corresponding secondary amines **3q**−**3t** in moderate-to-good yields. Interestingly, $MnCl_2$-catalyzed *N*-alkylation protocol is applicable for heterocyclic alcohols. Under the optimal conditions, pyridin-3-yl-methanol, thiophen-2-yl-methanol, and thiophen-3-yl-methanol smoothly underwent *N*-alkylation with pyridin-2-amine, leading to the expected products **3u**−**3w** in 36−60% isolated yields.

To probe the synthetic practicality of the catalytic system, a gram-scale (10 mmol) reaction with 2-aminofluorene and *p*-tolyl-methanol was performed, and the target product **3n** was obtained in 65% yield (Scheme 4).

Scheme 4. Gram-Scale Reaction



Although $MnCl_2$-catalyzed *N*-alkylation of amines with alcohols showed the general applicability, the application of more challenging alkyl alcohols and aniline derivatives bearing cyano, ester, carbonyl, and amide functionalities was not successful. However, when commercially available $MnBr(CO)_5$ replaced $MnCl_2$, the catalytic system gave more promising results (Scheme 5). For instance, the reaction of 2,5-dimethoxyaniline (1 mmol) with benzyl alcohol (1.2 mmol) in the presence of 10 mol % $MnBr(CO)_5$, 20 mol % PPh_3, and 1.2 mmol of *t*-BuOK at 130 °C in an oil bath in toluene within 20 h provided the desired secondary amine **3c** in 92% high yield (42% yield when using $MnCl_2$) irrespective of the sterically hindered *o*-methoxy substituent. Similarly, the use of $MnBr(CO)_5$ in the *N*-alkylation of pyridin-2-amine with thiophen-2-yl-methanol led to the expected products **3v** in a higher yield (62%). Gratifyingly, aniline bearing a cyano substituent was successfully alkylated with *p*-tolyl-methanol to generate the corresponding *N*-alkylated derivative **3x** in 33% yield, while no product formation was detected when the reaction was performed in the presence of $MnCl_2$. To our delight,

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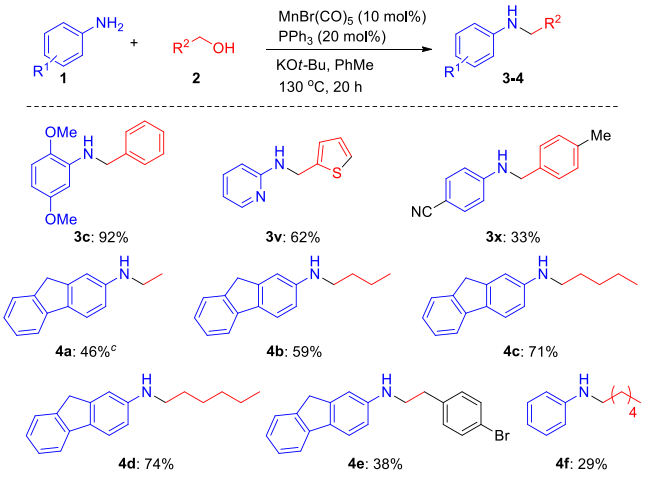
Scheme 5. $MnBr(CO)_5$-Catalyzed *N*-Alkylation of Amines[a,b]

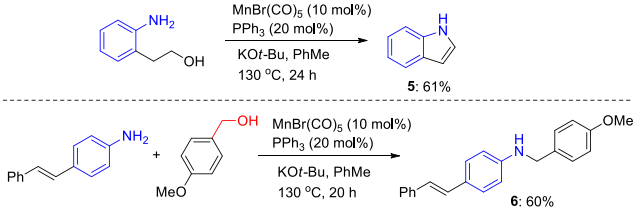


[a]Reactions were performed on a 1 mmol scale with 10 mol % $MnBr(CO)_5$, 20 mol % PPh_3, 1.2 equiv of KO*t*-Bu, 1.2 equiv of alcohol, and 2 mL of toluene at 130 °C in an oil bath under a nitrogen atmosphere for 20 h. [b]Isolated yields are given. [c]An amount of 4 equiv of ethanol was used.

employment of $MnBr(CO)_5$ allowed for an efficient *N*-alkylation of 2-aminofluorene with different alkyl alcohols such as ethanol, butanol, pentanol, and hexanol, affording monosubstituted aniline derivatives **4a**−**4d** in 46−74% isolated yields. It should be noted that long (C_5, C_6)-chain-containing aliphatic alcohols were more reactive in this transformation than short (C_2, C_4)-chain-containing aliphatic alcohols. Unfortunately, under the standard *N*-alkylation conditions, any desired product was not observed when methanol was utilized as an alkylating reagent. Moreover, the reaction of functionalized aliphatic alcohol proceeded smoothly and provided the desired product **4e** in 38% yield. The reaction of hexan-1-ol with aniline was also explored, and the expected product **4f** was afforded in 29% yield. Unfortunately, the sensitive functional groups such as ester, nitro, and hydroxy groups could not be tolerated in $MnBr(CO)_5$-catalyzed *N*-alkylation reaction.

To demonstrate the synthetic potential of this method, the intramolecular cyclization of 2-(2-aminophenyl)ethanol via a tandem borrowing hydrogen/intramolecular cyclization was carried out under identical conditions and led to indole in 61% isolated yield (Scheme 6). The synthetic utility of the catalytic

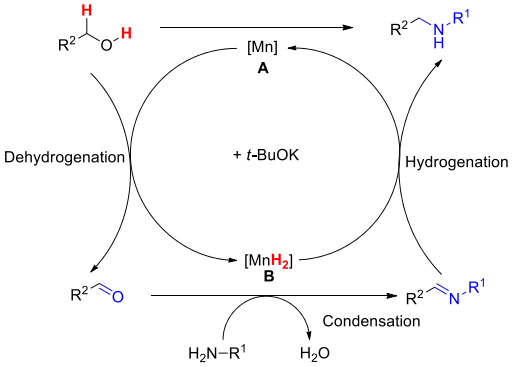
Scheme 6. Synthesis of Indole and Resveratrol-Derived Amine



protocol was also demonstrated for the synthesis of resveratrol-derived amine known to be active for Alzheimer's disease.[21] Under identical conditions, the *N*-alkylation of 4-aminostilbene bearing a vinyl group with (4-methoxyphenyl)methanol proceeded smoothly and furnished the *N*-alkylated derivative **6** in 60% isolated yield.

According to previous reports,[11] a plausible mechanism for Mn-catalyzed *N*-alkylation of amines with alcohols is proposed (Scheme 7). An initial dehydrogenation of alcohol via an

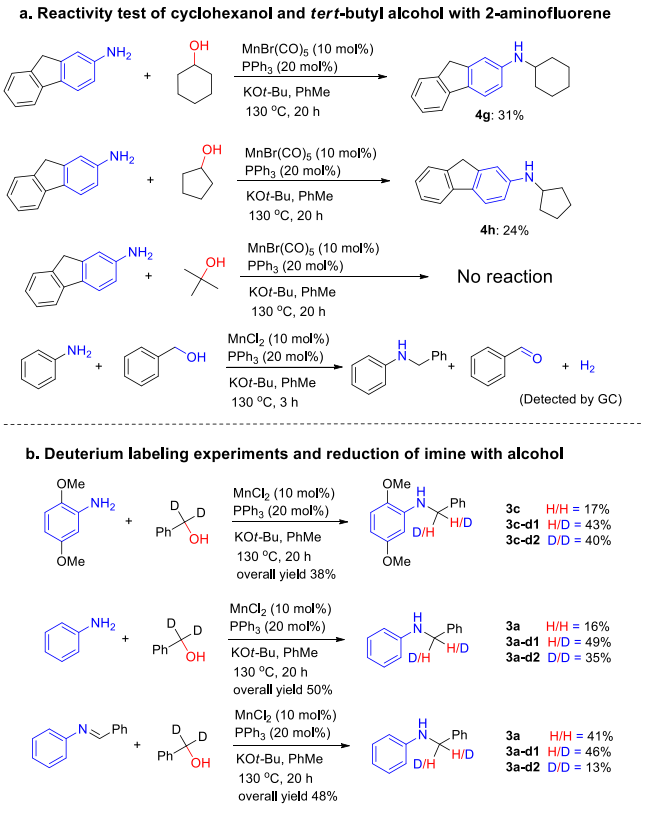
Scheme 7. Plausible Mechanism for Mn-Catalyzed *N*-Alkylation of Amines with Alcohols



acceptor-less dehydrogenative pathway leads to the corresponding aldehyde, and the manganese complex **A** is simultaneously converted to manganese hydride complex **B**. Then, the formed aldehyde condenses with a free amine to provide an imine intermediate, accompanying with the formation of a water molecule. With the base *t*-BuOK, the manganese complex **A** is regenerated in the final step by the hydrogenation of imine with the hydrogen equivalent liberated in the alcohol oxidation step to give the *N*-alkylated amine.

To understand the nature of the proposed mechanism, additional experiments and deuterium labeling experiments were performed (Scheme 8). When secondary alcohols such as

Scheme 8. Preliminary Mechanistic Studies



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cyclohexanol and cyclopentanol were used to react with 2-aminofluorene under the optimal conditions, the expected *N*-cyclohexyl-9*H*-fluoren-2-amine (**4g**) and *N*-cyclopentyl-9*H*-fluoren-2-amine (**4h**) were obtained in 31 and 24% yields, respectively, in the presence of $MnBr(CO)_5$. Additionally, when *tert*-butanol was tested for the *N*-alkylation of 2-aminofluorene, as expected, no product formation was detected. When the reaction mixture containing aniline and benzyl alcohol in the presence of 10 mol % $MnCl_2$, 20 mol % PPh_3, and 1.2 equiv of KO*t*-Bu was heated at 130 °C in an oil bath for 3 h, benzaldehyde was observed, and H_2 was detected (Figure S2) by GC analysis of the reaction headspace (Scheme 8a). These results are consistent with a pathway involving initial alcohol dehydrogenation and support the hydrogen borrowing mechanism. Furthermore, the reaction of amines and imine with deuterated benzyl alcohol was investigated. Under standard reaction conditions, the treatment of 2,5-dimethoxyaniline with isotopically enriched deuterated benzyl alcohol led to fully deuterated product **3c-d2** along with **3c** and **3c-d1** in ratio 40, 17, and 43% respectively, which was determined by ^{1}H NMR and HRMS. Similarly, the desired product **3a-d1**, along with **3a-d2** and **3a**, was obtained in ratio 49, 35, and 16%, respectively. In addition, the reduction of *N*-benzylideneaniline with isotopically enriched deuterated benzyl alcohol gave the expected product **3a-d1**, along with **3a-d2** and **3a**, was obtained in ratio 46, 13, and 41%, respectively (Scheme 8b). Based on these preliminary mechanistic studies, it can be proven that the present catalytic reaction proceeds via borrowing hydrogen or hydrogen auto-transfer process.

CONCLUSIONS

In conclusion, we have revealed a new catalytic system including $MnCl_2$ or $MnBr(CO)_5$ as the metal salt and triphenylphosphine as a ligand for the *N*-alkylation of amines with alcohols. This catalytic system based on acceptor-less dehygrogenation concept is practical and operationally simple because it uses an inexpensive, nontoxic, and commercially available manganese catalyst and much simpler ligand, avoiding prior preparation of the molecular-defined manganese(I) catalyst. A variety of aromatic, heteroaromatic, and aliphatic secondary amines were synthesized in moderate-to-high yields by using this protocol. Moreover, this protocol can be scalable to the gram level and is suitable for synthesizing heterocycles such as indole and resveratrol-derived amines known to be active for Alzheimer's disease. The preliminary mechanistic studies indicated that the present catalytic reaction proceeds via borrowing hydrogen or a hydrogen auto-transfer process. Further studies regarding the mechanistic pathway and future scope of this catalyst system are under way.

EXPERIMENTAL SECTION

General Information. All reactions were carried out under a nitrogen atmosphere in flame-dried glassware. Syringes, which were used to transfer anhydrous solvents or reagents, were purged with nitrogen prior to use. Toluene was continuously refluxed and freshly distilled from sodium benzophenone ketyl under nitrogen. Yields refer to isolated yields of compounds estimated to be >95% pure as determined by ^{1}H NMR (25 °C) and capillary-GC. NMR spectra were recorded on solutions in deuterated chloroform ($CDCl_3$) with residual chloroform (δ7.25 ppm for ^{1}H NMR and δ77.0 ppm for ^{13}C NMR). Abbreviations for signal coupling are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet, br, broad. ESI-QTOF-MS measurements were performed in the positive ion mode (m/z 50−2000 range). Column chromatographical purifications were performed using SiO_2 (200−300 mesh ASTM) from Branch of Qingdao Haiyang Chemical Co., Ltd. if not indicated otherwise.

Typical Procedure (TP1) for $MnCl_2$-Catalyzed *N*-Alkylation Reaction of Amines with Alcohols. To a clean, oven-dried, screw cap reaction tube were added $MnCl_2$ (0.1 mmol, 10 mol %), PPh_3 (0.2 mmol, 20 mol %), alcohol (1.2 mmol), amine (1 mmol), *t*-BuOK (1.2 mmol), and toluene (2 mL) under a nitrogen atmosphere. The reaction mixture was stirred at 130 °C in an oil bath for 20 h. Then, the reaction mixture was diluted with water (5 mL) and extracted with EtOAc (3 × 10 mL). The resultant organic layer was dried over anhydrous $MgSO_4$, and the solvent was evaporated under reduced pressure. The crude mixture was purified by silica gel column chromatography using petroleum ether/EtOAc as the eluting system.

Typical Procedure (TP2) for $MnBr(CO)_5$-Catalyzed *N*-Alkylation Reaction of Amines with Alcohols. To a clean, oven-dried, screw cap reaction tube were added $MnBr(CO)_5$ (0.1 mmol, 10 mol %), PPh_3 (0.2 mmol, 20 mol %), alcohol (1.2 mmol), amine (1 mmol), *t*-BuOK (1.2 mmol), and toluene (2 mL) under a nitrogen atmosphere. The reaction mixture was stirred at 130 °C in an oil bath for 20 h. Then, the reaction mixture was diluted with water (5 mL) and extracted with EtOAc (3 × 10 mL). The resultant organic layer was dried over anhydrous $MgSO_4$, and the solvent was evaporated under reduced pressure. The crude mixture was purified by silica gel column chromatography using petroleum ether/EtOAc as the eluting system.

*N-Benzylaniline (**3a**).* According to **TP1**, the reaction of aniline (93 mg, 1 mmol) with benzyl alcohol (130 mg, 1.2 mmol) afforded the desired product **3a** as a colorless oil (150 mg, 82%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.31 (m, 4 H), 7.28 (m, 1 H), 7.17 (t, J = 7.7 Hz, 2 H), 6.71 (t, J = 7.3 Hz, 1 H), 6.63 (d, J = 8.0 Hz, 2 H), 4.31 (s, 2 H), 4.00 (s, 1 H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 148.1, 139.4, 129.2, 128.6, 127.5, 127.2, 117.5, 112.8, 48.3; IR (diamond-ATR, neat) 3417, 3024, 1601, 1324, 1266, 1179, 747, 694 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{13}H_{14}N$ [M + H]$^+$ 184.1126; found 184.1124; R_f 0.59 (petroleum ether/EtOAc, 50/1).

*N-Benzyl-3,5-dimethoxyaniline (**3b**).* According to **TP1**, the reaction of 3,5-dimethoxyaniline (153 mg, 1 mmol) with benzyl alcohol (130 mg, 1.2 mmol) afforded the desired product **3b** as a colorless oil (161 mg, 66%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42−7.29 (m, 5 H), 5.95 (s, 1 H), 5.87 (s, 2 H), 4.31 (s, 2 H), 4.12 (s, 1 H), 3.75 (s, 6 H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 161.6, 150.0, 139.2, 128.5, 127.4, 127.1, 91.7, 89.8, 55.0, 48.2; IR (diamond-ATR, neat) 3407, 2933, 2839, 1591, 1451, 1200, 1149, 1068, 809, 735 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{15}H_{18}NO_2$ [M + H]$^+$ 244.1338, found 244.1337; R_f 0.37 (petroleum ether/EtOAc, 30/1).

*N-Benzyl-2,5-dimethoxyaniline (**3c**).* According to **TP1**, the reaction of 2,5-dimethoxyaniline (153 mg, 1 mmol) with benzyl alcohol (130 mg, 1.2 mmol) afforded the desired product **3c** as a colorless oil (101 mg, 42%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.30 (m, 4 H), 7.27−7.22 (m, 1 H), 6.67 (d, J = 8.6 Hz, 1 H), 6.21 (d, J = 2.8 Hz, 1 H), 6.15 (dd, J = 8.6, 2.9 Hz, 1 H), 4.68 (s, 1 H), 4.32 (s, 2 H), 3.80 (s, 3 H), 3.71 (s, 3 H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 154.7, 141.5, 139.3, 139.2, 128.6, 127.5, 127.1, 109.9, 98.9, 98.3, 56.0, 55. 5, 47.9; IR (diamond-ATR, neat) 3421, 2831, 1602, 1516, 1452, 1215, 1167, 1023, 698 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{15}H_{18}NO_2$ [M + H]$^+$ 244.1338, found 244.1334; R_f 0.32 (petroleum ether/EtOAc, 30/1).

*N-Benzyl-2-phenoxyaniline (**3d**).* According to **TP1**, the reaction of 2-phenoxyaniline (185 mg, 1 mmol) with benzyl alcohol (130 mg, 1.2 mmol) afforded the desired product **3d** as a yellow solid (157 mg, 57%): mp 77−79 °C (dichloromethane/petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33−7.12 (m, 7 H), 7.06−6.89 (m, 4 H), 6.83 (d, J = 7.9 Hz, 1 H), 6.67 (d, J = 8.0 Hz, 1 H), 6.61 (t, J = 7.6 Hz, 1 H), 4.61 (s, 1 H), 4.33 (s, 2 H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 157.5, 142.9, 140.3, 139.3, 129.6, 128.5, 127.2, 127.1, 124.9, 122.7, 119.2, 117.4, 116.9, 111.7, 47.7; IR (diamond-ATR, neat) 3413, 2927, 1583, 1509, 1437, 1214, 747, 689 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{19}H_{18}NO$ [M + H]$^+$ 276.1388, found 276.1383; R_f 0.45 (petroleum ether/EtOAc, 50/1).

*N-Benzyl-4-(trifluoromethoxy)aniline (**3e**).* According to **TP1**, the reaction of 4-(trifluoromethoxy)aniline (177 mg, 1 mmol) with benzyl alcohol (130 mg, 1.2 mmol) afforded the desired product **3e** as a

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colorless oil (238 mg, 89%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.23 (m, 5 H), 7.01 (d, J = 8.5 Hz, 2 H), 6.55 (d, J = 8.8 Hz, 2 H), 4.28 (s, 2 H), 4.07 (s, 1 H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 146.9, 140.5 (q, J = 2.2 Hz), 138.9, 128.7, 127.4, 127.3, 122.4, 120.7 (q, J = 255.3 Hz), 113.0, 48.4; IR (diamond-ATR, neat) 3428, 3065, 1615, 1514, 1249, 1198, 1151, 815, 742, 696 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{14}H_{13}F_3NO$ [M + H]$^+$ 268.0949, found 268.0944; R_f 0.35 (petroleum ether/EtOAc, 50/1).

*N-Benzyl-3-ethylaniline (**3f**).* According to **TP1**, the reaction of 3-ethylaniline (121 mg, 1 mmol) with benzyl alcohol (130 mg, 1.2 mmol) afforded the desired product **3f** as a colorless oil (139 mg, 66%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.25 (m, 5 H), 7.09 (t, J = 7.7 Hz, 1 H), 6.58 (d, J = 7.5 Hz, 1 H), 6.53−6.42 (m, 2 H), 4.32 (s, 2 H), 3.96 (s, 1 H), 2.56 (q, J = 7.6 Hz, 2 H), 1.20 (t, J = 7.6 Hz, 3 H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 148.3, 145.4, 139.5, 129.2, 128.6, 127.6, 127.2, 117.3, 112.5, 110.1, 48.4, 29.0, 15.5; IR (diamond-ATR, neat) 3312, 2962, 1604, 1435, 1175, 1118, 720, 696, 541 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{15}H_{18}N$ [M + H]$^+$ 212.1439, found 212.1434; R_f 0.33 (petroleum ether/EtOAc, 50/1).

*N-Benzyl-2-(tert-butyl)aniline (**3g**).* According to **TP1**, the reaction of 2-(*tert*-butyl)aniline (149 mg, 1 mmol) with benzyl alcohol (130 mg, 1.2 mmol) afforded the desired product **3g** as a colorless oil (84 mg, 35%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42−7.25 (m, 6 H), 7.14−7.05 (m, 1 H), 6.77−6.59 (m, 2 H), 4.40 (s, 2 H), 4.27 (s, 1 H), 1.43 (s, 9 H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 146.1, 139.6, 133.2, 128.7, 127.5, 127.2, 126.2, 126.1, 117.2, 111.9, 48.8, 34.2, 29.9; IR (diamond-ATR, neat) 2923, 1599, 1507, 1445, 1259, 1056, 743, 696 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{17}H_{22}N$ [M + H]$^+$ 240.1752, found 240.1746; R_f 0.68 (petroleum ether/EtOAc, 50/1).

*N-Benzyl-4-iodoaniline (**3h**).* According to **TP1**, the reaction of 4-iodoaniline (219 mg, 1 mmol) with benzyl alcohol (130 mg, 1.2 mmol) afforded the desired product **3h** as a pale yellow solid (238 mg, 77%): mp 54−56 °C (dichloromethane/petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, J = 8.5 Hz, 2 H), 7.38−7.27 (m, 5 H), 6.42 (d, J = 8.5 Hz, 2 H), 4.30 (s, 2 H), 4.09 (s, 1 H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 147.6, 138.8, 137.7, 128.7, 127.3, 127.3, 115.0, 78.1, 48.0; IR (diamond-ATR, neat) 3408, 2832, 1507, 1435, 1118, 723, 694 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{13}H_{13}IN$ [M + H]$^+$ 310.0093, found 310.0084; R_f 0.27 (petroleum ether/EtOAc, 50/1).

*N-Benzyl-4-chloro-2-fluoroaniline (**3i**).* According to **TP1**, the reaction of 4-chloro-2-fluoroaniline (146 mg, 1 mmol) with benzyl alcohol (130 mg, 1.2 mmol) afforded the desired product **3i** as a colorless oil (134 mg, 57%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.32 (m, 4 H), 7.31−7.26 (m, 1 H), 7.00 (d, J = 11.4 Hz, 1 H), 6.92 (d, J = 8.6 Hz, 1 H), 6.56 (t, J = 8.9 Hz, 1 H), 4.35 (d, J = 4.8 Hz, 2 H), 4.30 (s, 1 H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 150.9 (d, J = 242 Hz), 138.4, 135.3 (d, J = 12 Hz), 128.8, 127.5, 127.3, 124.5 (d, J = 4 Hz), 120.9 (d, J = 10 Hz), 115.2 (d, J = 22 Hz), 112.7 (d, J = 4 Hz), 47.8; IR (diamond-ATR, neat) 3433, 2925, 1618, 1509, 1338, 1266, 1196, 1128, 891, 856, 799, 696 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{13}H_{12}ClFN$ [M + H]$^+$ 236.0642, found 236.0640; R_f 0.52 (petroleum ether/EtOAc, 50/1).

*N-Benzyl-4-chloro-3-fluoroaniline (**3j**).* According to **TP1**, the reaction of 4-chloro-3-fluoroaniline (146 mg, 1 mmol) with benzyl alcohol (130 mg, 1.2 mmol) afforded the desired product **3j** as a colorless oil (75 mg, 32%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41−7.24 (m, 5 H), 7.11 (t, J = 8.5 Hz, 1 H), 6.36 (ddd, J = 18.9, 10.1, 2.6 Hz, 2 H), 4.29 (s, 2 H), 4.18 (s, 1 H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.8 (d, J = 245.3 Hz), 148.3 (d, J = 9.9 Hz), 138.3, 130.6 (d, J = 1.7 Hz), 128.8, 127.5, 127.3, 109.4 (d, J = 2.7 Hz), 108.1 (d, J = 18.0 Hz), 100.6 (d, J = 24.8 Hz), 48.2; IR (diamond-ATR, neat) 3425, 2924, 1613, 1496, 1334, 1180, 825, 696 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{13}H_{12}ClFN$ [M + H]$^+$ 236.0642, found 236.0635; R_f 0.19 (petroleum ether/EtOAc, 50/1).

*N-Benzyl-3,5-difluoroaniline (**3k**).* According to **TP1**, the reaction of 3,5-difluoroaniline (129 mg, 1 mmol) with benzyl alcohol (130 mg, 1.2 mmol) afforded the desired product **3k** as a colorless oil (121 mg, 55%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.26 (m, 5 H), 6.20−6.06 (m, 3 H), 4.29 (s, 2 H), 4.28 (s, 1 H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 164.1 (dd, J = 243.9, 15.8 Hz), 150.3 (t, J = 13.2 Hz), 138.2, 128.8, 127.6, 127.4, 95.5 (dd, J = 12.0, 8.4 Hz), 92.5 (t, J = 26.4 Hz), 48.0; IR (diamond-ATR, neat) 3427, 3029, 1632, 1591, 1484, 1171, 1109, 978, 817, 696, 541 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{13}H_{12}F_2N$ [M + H]$^+$ 220.0938, found 220.0928; R_f 0.39 (petroleum ether/EtOAc, 50/1).

*N-Benzyl-3,4-difluoroaniline (**3l**).* According to **TP1**, the reaction of 3,4-difluoroaniline (129 mg, 1 mmol) with benzyl alcohol (130 mg, 1.2 mmol) afforded the desired product **3l** as a colorless oil (83 mg, 38%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42−7.25 (m, 5 H), 6.93 (q, J = 9.3 Hz, 1 H), 6.39 (ddd, J = 12.7, 6.7, 2.8 Hz, 1 H), 6.28 (dd, J = 8.6, 3.9 Hz, 1 H), 4.26 (s, 2 H), 4.01 (s, 1 H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 150.9 (dd, J = 244.9, 13.4 Hz), 145.1 (dd, J = 8.6, 2.0 Hz), 143.1 (dd, J = 236.5, 12.9 Hz), 138.6, 128.7, 127.5, 127.4, 117.45 (dd, J = 18.0, 1.9 Hz), 107.9 (dd, J = 5.5, 3.1 Hz), 101.4 (d, J = 20.8 Hz), 48.6; IR (diamond-ATR, neat) 3424, 2922, 1614, 1510, 1215, 1170, 776, 696 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{13}H_{12}F_2N$ [M + H]$^+$ 220.0938, found 220.0934; R_f 0.26 (petroleum ether/EtOAc, 50/1).

*N-Benzyl-4-morpholinoaniline (**3m**).* According to **TP1**, the reaction of 4-morpholinoaniline (178 mg, 1 mmol) with benzyl alcohol (130 mg, 1.2 mmol) afforded the desired product **3m** as a yellow solid (70 mg, 26%): mp 65−67 °C (dichloromethane/petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.25 (m, 5 H), 6.83 (d, J = 8.4 Hz, 2 H), 6.62 (d, J = 8.4 Hz, 2 H), 4.29 (s, 2 H), 3.84 (t, J = 4.7 Hz, 4 H), 3.01 (t, J = 4.7 Hz, 4 H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 143.7, 142.8, 139.7, 128.6, 127.5, 127.1, 118.4, 113.9, 67.1, 51.2, 49.0; IR (diamond-ATR, neat) 3309, 2919, 1516, 1449, 1226, 1107, 919, 824, 740 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{17}H_{21}N_2O$ [M + H]$^+$ 269.1654, found 269.1654; R_f 0.21 (petroleum ether/EtOAc, 5/1).

*N-(4-Methylbenzyl)-9H-fluoren-2-amine (**3n**).* According to **TP1**, the reaction of 9*H*-fluoren-2-amine (181 mg, 1 mmol) with *p*-tolylmethanol (149 mg, 1.2 mmol) afforded the desired product **3n** as a yellow solid (168 mg, 59%): mp 152−153 °C (dichloromethane/petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 7.6 Hz, 1 H), 7.52 (d, J = 8.0 Hz, 1 H), 7.31−7.25 (m, 1 H), 7.17−7.08 (m, 6 H), 6.67 (dd, J = 8.0, 2.1 Hz, 1 H), 6.52 (s, 1 H), 4.11 (t, J = 7.6 Hz, 1 H), 3.64 (s, 2 H), 3.03 (d, J = 7.6 Hz, 2 H), 2.37 (s, 3 H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 148.9, 146.1, 145.6, 141.2, 136.9, 135.7, 131.9, 129.4, 128.9, 126.9, 124.9, 124.6, 120.5, 118.4, 114.2, 111.8, 48.6, 39.8, 21.1; IR (diamond-ATR, neat) 3314, 2918, 1617, 1508, 1455, 1267, 804, 734 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{21}H_{20}N$ [M + H]$^+$ 286.1596, found 286.1596; R_f 0.34 (petroleum ether/EtOAc, 5/1).

*N-Benzylpyridin-2-amine (**3o**).* According to **TP1**, the reaction of pyridin-2-amine (94 mg, 1 mmol) with benzyl alcohol (130 mg, 1.2 mmol) afforded the desired product **3o** as a white solid (131 mg, 71%): mp 152−154 °C (dichloromethane/petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (dd, J = 5.1, 1.9 Hz, 1 H), 7.42−7.24 (m, 6 H), 6.58 (dd, J = 7.1, 5.1 Hz, 1 H), 6.36 (d, J = 8.4 Hz, 1 H), 4.92 (s, 1 H), 4.50 (d, J = 5.8 Hz, 2 H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.6, 148.2, 139.2, 137.4, 128.6, 127.4, 127.2, 113.1, 106.8, 46.3; IR (diamond-ATR, neat) 3207, 1575, 1521, 1437, 1291, 1072, 747, 696, 517 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{12}H_{13}N_2$ [M + H]$^+$ 185.1079, found 185.1072; R_f 0.28 (petroleum ether/EtOAc, 5/1).

*N-Benzylpyridin-3-amine (**3p**).* According to **TP1**, the reaction of pyridin-3-amine (94 mg, 1 mmol) with benzyl alcohol (130 mg, 1.2 mmol) afforded the desired product **3p** as a pale yellow solid (155 mg, 84%): mp 84−85 °C (dichloromethane/petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1 H), 7.96 (d, J = 4.6 Hz, 1 H), 7.40−7.22 (m, 5 H), 7.05 (dd, J = 8.4, 4.5 Hz, 1 H), 6.86 (d, J = 7.9 Hz, 1 H), 4.33 (s, 2 H), 4.14 (s, 1 H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 144.0, 138.9, 138.5, 136.2, 128.8, 127.5, 127.4, 123.7, 118.6, 47.9; IR (diamond-ATR, neat) 3258, 2923, 1577, 1523, 1484, 1301, 1243, 1119, 795, 698, 541 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{12}H_{13}N_2$ [M + H]$^+$ 185.1079, found 185.1073; R_f 0.43 (petroleum ether/EtOAc, 50/1).

*N-(4-Methoxybenzyl)pyridin-2-amine (**3q**).* According to **TP1**, the reaction of pyridin-2-amine (94 mg, 1 mmol) with (4-methoxyphenyl)-methanol (166 mg, 1.2 mmol) afforded the desired product **3q** as a white solid (148 mg, 69%): mp 126−127 °C (dichloromethane/petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, J = 4.8 Hz, 1 H), 7.39 (t, J = 7.7 Hz, 1 H), 7.27 (d, J = 8.3 Hz, 2 H), 6.86 (d, J = 8.3 Hz, 2 H), 6.60−6.53 (m, 1 H), 6.36 (d, J = 8.4 Hz, 1 H), 4.79 (s, 1 H), 4.42 (d, J = 5.6 Hz, 2 H), 3.79 (s, 3 H); ^{13}C{^{1}H} NMR (101 MHz,

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$CDCl_3$) δ 158.9, 158.6, 148.2, 137.4, 131.1, 128.7, 114.0, 113.1, 106.8, 55.3, 45.8; IR (diamond-ATR, neat) 3219, 2931, 1575, 1507, 1437, 1226, 1031, 817, 769, 521 cm^{-1}; HRMS (ESI^+) calcd for $C_{13}H_{15}N_2O$ $[M + H]^+$ 215.1184, found 215.1179; R_f 0.21 (petroleum ether/EtOAc, 5/1).

*N-(4-Methylbenzyl)pyridin-2-amine (**3r**).* According to **TP1**, the reaction of pyridin-2-amine (94 mg, 1 mmol) with *p*-tolyl-methanol (147 mg, 1.2 mmol) afforded the desired product **3r** as a white solid (129 mg, 65%): mp 193−195 °C (dichloromethane/petroleum ether); ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 4.5 Hz, 1 H), 7.35 (ddd, J = 8.6, 7.2, 1.9 Hz, 1 H), 7.21 (d, J = 7.6 Hz, 2 H), 7.10 (d, J = 7.6 Hz, 2 H), 6.54 (dd, J = 7.2, 5.1 Hz, 1 H), 6.32 (d, J = 8.3 Hz, 1 H), 4.84 (s, 1 H), 4.41 (d, J = 5.5 Hz, 2 H), 2.30 (s, 3 H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 158.7, 148.2, 137.4, 136.8, 136.1, 129.3, 127.4, 113.1, 106.7, 46.1, 21.1; IR (diamond-ATR, neat) 3217, 2919, 1575, 1521, 1437, 1332, 1155, 805, 764, 517 cm^{-1}; HRMS (ESI^+) calcd for $C_{13}H_{15}N_2$ $[M + H]^+$ 199.1235, found 199.1230; R_f 0.27 (petroleum ether/EtOAc, 5/1).

*N-(4-Bromobenzyl)pyridin-2-amine (**3s**).* According to **TP1**, the reaction of pyridin-2-amine (94 mg, 1 mmol) with (4-bromophenyl)-methanol (224 mg, 1.2 mmol) afforded the desired product **3s** as a white solid (184 mg, 70%): mp 99−100 °C (dichloromethane/petroleum ether); ^1H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 4.3 Hz, 1 H), 7.48−7.33 (m, 3 H), 7.22 (d, J = 8.1 Hz, 2 H), 6.59 (t, J = 6.1 Hz, 1 H), 6.34 (d, J = 8.4 Hz, 1 H), 4.87 (s, 1 H), 4.46 (d, J = 6.0 Hz, 2 H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 158.4, 148.2, 138.4, 137.5, 131.7, 129.0, 120.9, 113.4, 106.9, 45.6; IR (diamond-ATR, neat) 3217, 2976, 1575, 1523, 1439, 1329, 1155, 1011, 769, 515 cm^{-1}; HRMS (ESI^+) calcd for $C_{12}H_{12}BrN_2$ $[M + H]^+$ 263.0184, found 263.0179; R_f 0.23 (petroleum ether/EtOAc, 5/1).

*N-(4-Chlorobenzyl)pyridin-2-amine (**3t**).* According to **TP1**, the reaction of pyridin-2-amine (94 mg, 1 mmol) with (4-chlorophenyl)-methanol (171 mg, 1.2 mmol) afforded the desired product **3t** as a white solid (151 mg, 69%): mp 102−103 °C (dichloromethane/petroleum ether); ^1H NMR (400 MHz, $CDCl_3$) δ 8.09 (dd, J = 5.1, 2.0 Hz, 1 H), 7.39 (ddd, J = 8.8, 7.1, 1.9 Hz, 1 H), 7.30−7.26 (m, 4 H), 6.59 (dd, J = 7.2, 5.1 Hz, 1 H), 6.34 (d, J = 8.4 Hz, 1 H), 4.93 (s, 1 H), 4.48 (d, J = 5.9 Hz, 2 H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 158.4, 148.2, 137.8, 137.5, 132.9, 128.7, 128.6, 113.4, 106.9, 45.5; IR (diamond-ATR, neat) 3215, 2927, 1574, 1439, 1328, 1157, 1081, 769, 688, 515 cm^{-1}; HRMS (ESI^+) calcd for $C_{12}H_{12}ClN_2$ $[M + H]^+$ 219.0689, found 219.0685; R_f 0.24 (petroleum ether/EtOAc, 5/1).

*N-(Pyridin-3-yl-methyl)pyridin-2-amine (**3u**).* According to **TP1**, the reaction of pyridin-2-amine (94 mg, 1 mmol) with pyridin-3-yl-methanol (131 mg, 1.2 mmol) afforded the desired product **3u** as a colorless oil (89 mg, 48%): ^1H NMR (400 MHz, $CDCl_3$) δ 8.60 (s, 1 H), 8.49 (d, J = 4.6 Hz, 1 H), 8.08 (d, J = 5.1 Hz, 1 H), 7.67 (d, J = 7.7 Hz, 1 H), 7.39 (dt, J = 10.8, 5.0 Hz, 1 H), 7.22 (dd, J = 8.1, 4.3 Hz, 1 H), 6.59 (dd, J = 8.1, 5.1 Hz, 1 H), 6.37 (d, J = 8.1 Hz, 1 H), 4.96 (d, J = 32.3 Hz, 1 H), 4.54 (s, 2 H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 158.2, 149.1, 148.6, 148.1, 137.5, 135.1, 134.9, 123.5, 113.5, 107.2, 43.6; IR (diamond-ATR, neat) 3266, 3024, 2921, 1603, 1487, 1420, 1293, 769, 712 cm^{-1}; HRMS (ESI^+) calcd for $C_{11}H_{12}N_3$ $[M + H]^+$ 186.1031, found 186.1030; R_f 0.33 (petroleum ether/EtOAc, 2/1).

*N-(Thiophen-2-yl-methyl)pyridin-2-amine (**3v**).* According to **TP1**, the reaction of pyridin-2-amine (94 mg, 1 mmol) with thiophen-2-yl-methanol (137 mg, 1.2 mmol) afforded the desired product **3v** as a yellow solid (68 mg, 36%): mp 156−158 °C (dichloromethane/petroleum ether); ^1H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, J = 0.8 Hz, 1 H), 7.41 (t, J = 7.7 Hz, 1 H), 7.19 (d, J = 5.0 Hz, 1 H), 7.04−6.90 (m, 2 H), 6.64−6.56 (m, 1 H), 6.42 (d, J = 8.4 Hz, 1 H), 4.90 (s, 1 H), 4.69 (d, J = 5.7 Hz, 2 H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 158.1, 148.1, 142.6, 137.4, 126.8, 125.1, 124.6, 113.5, 107.3, 41.2; IR (diamond-ATR, neat) 3207, 2850, 1575, 1524, 1454, 1293, 1511, 770, 697, 524 cm^{-1}; HRMS (ESI^+) calcd for $C_{10}H_{11}N_2S$ $[M + H]^+$ 191.0643, found 191.0641; R_f 0.56 (petroleum ether/EtOAc, 2/1).

*N-(Thiophen-3-yl-methyl)pyridin-2-amine (**3w**).* According to **TP1**, the reaction of pyridin-2-amine (94 mg, 1 mmol) with thiophen-3-yl-methanol (137 mg, 1.2 mmol) afforded the desired product **3w** as a yellow solid (114 mg, 60%): mp 91−93 °C (dichloromethane/petroleum ether); ^1H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, J = 5.0 Hz, 1 H), 7.44−7.37 (m, 1 H), 7.29 (dd, J = 5.0, 3.0 Hz, 1 H), 7.17 (d, J = 2.9 Hz, 1 H), 7.06 (d, J = 5.0 Hz, 1 H), 6.59 (dd, J = 7.0, 5.1 Hz, 1 H), 6.39 (d, J = 8.4 Hz, 1 H), 4.81 (s, 1 H), 4.50 (d, J = 5.7 Hz, 2 H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 158.5, 148.2, 140.2, 137.4, 127.1, 126.2, 121.6, 113.2, 106.9, 41.8; IR (diamond-ATR, neat) 3198, 2925, 1575, 1507, 1436, 1148, 766, 687 cm^{-1}; HRMS (ESI^+) calcd for $C_{10}H_{11}N_2S$ $[M + H]^+$ 191.0643, found 191.0639; R_f 0.55 (petroleum ether/EtOAc, 2/1).

*N-Benzyl-2,5-dimethoxyaniline (**3c**).* According to **TP2**, $MnBr(CO)_5$-catalyzed *N*-alkylation of 2,5-dimethoxyaniline (153 mg, 1 mmol) with benzyl alcohol (130 mg, 1.2 mmol) afforded the desired product **3c** as a colorless oil (224 mg, 92%).

*N-(Thiophen-2-yl-methyl)pyridin-2-amine (**3v**).* According to **TP2**, $MnBr(CO)_5$-catalyzed *N*-alkylation of pyridin-2-amine (94 mg, 1 mmol) with thiophen-2-yl-methanol (137 mg, 1.2 mmol) afforded the desired product **3v** as a yellow solid (118 mg, 62%).

*4-((4-Methylbenzyl)amino)benzonitrile (**3x**).* According to **TP2**, $MnBr(CO)_5$-catalyzed *N*-alkylation of 4-aminobenzonitrile (118 mg, 1 mmol) with *p*-tolyl-methanol (147 mg, 1.2 mmol) afforded the desired product **3x** as a pale yellow solid (73 mg, 33%): mp 234−236 °C (dichloromethane/petroleum ether); ^1H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J = 8.5 Hz, 2 H), 7.21 (d, J = 7.9 Hz, 2 H), 7.16 (d, J = 7.9 Hz, 2 H), 6.57 (d, J = 8.5 Hz, 2 H), 4.54 (s, 1 H), 4.32 (d, J = 5.4 Hz, 2 H), 2.34 (s, 3 H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 151.1, 137.4, 134.7, 133.7, 129.5, 127.3, 120.4, 112.4, 99.0, 47.3, 21.1; IR (diamond-ATR, neat) 3400, 2919, 2209, 1601, 1511, 1338, 1175, 836, 807, 543 cm^{-1}; HRMS (ESI^+) calcd for $C_{15}H_{15}N_2$ $[M + H]^+$ 223.1235, found 223.1225; R_f 0.36 (petroleum ether/EtOAc, 5/1).

*N-Ethyl-9H-fluoren-2-amine (**4a**).* According to **TP2**, $MnBr(CO)_5$-catalyzed *N*-alkylation of 9*H*-fluoren-2-amine (181 mg, 1 mmol) with ethanol (185 mg, 4 mmol) afforded the desired product **4a** as a pale yellow oil (97 mg, 46%): ^1H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 7.5 Hz, 1 H), 7.53 (d, J = 8.0 Hz, 1 H), 7.44 (d, J = 7.4 Hz, 1 H), 7.30 (t, J = 7.4 Hz, 1 H), 7.20 (td, J = 7.4, 1.2 Hz, 1 H), 6.84 (s, 1 H), 6.69 (dd, J = 8.1, 2.1 Hz, 1 H), 3.87 (t, J = 5.6 Hz, 1 H), 3.74 (s, 2 H), 2.05 (td, J = 7.5, 5.7 Hz, 2 H), 0.72 (t, J = 7.4 Hz, 3 H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 149.1, 146.2, 145.8, 141.8, 132.6, 126.7, 125.1, 124.0, 120.5, 118.4, 114.0, 111.2, 48.3, 25.8, 9.6; IR (diamond-ATR, neat) 3363, 2923, 1614, 1453, 1276, 1126, 819, 766, 735 cm^{-1}; HRMS (ESI^+) calcd for $C_{15}H_{16}N$ $[M + H]^+$ 210.1283, found 210.1276; R_f 0.51 (petroleum ether/EtOAc, 5/1).

*N-Butyl-9H-fluoren-2-amine (**4b**).* According to **TP2**, $MnBr(CO)_5$-catalyzed *N*-alkylation of 9*H*-fluoren-2-amine (181 mg, 1 mmol) with butan-1-ol (89 mg, 1.2 mmol) afforded the desired product **4b** as a pale yellow oil (141 mg, 59%): ^1H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 7.5 Hz, 1 H), 7.52 (d, J = 8.0 Hz, 1 H), 7.43 (d, J = 7.5 Hz, 1 H), 7.29 (t, J = 7.5 Hz, 1 H), 7.19 (t, J = 7.4 Hz, 1 H), 6.84 (s, 1 H), 6.68 (dd, J = 8.1, 2.1 Hz, 1 H), 3.87 (t, J = 5.9 Hz, 1 H), 3.73 (s, 2 H), 2.01−1.90 (m, 2 H), 1.34−1.22 (m, 2 H), 1.21−1.10 (m, 2 H), 0.83 (t, J = 7.2 Hz, 3 H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 149.5, 146.7, 145.8, 141.6, 132.4, 126.7, 125.1, 124.0, 120.5, 118.4, 114.0, 111.2, 47.3, 32.9, 27.7, 23.0, 13.9; IR (diamond-ATR, neat) 3370, 2926, 1615, 1454, 1269, 818, 765, 737 cm^{-1}; HRMS (ESI^+) calcd for $C_{17}H_{20}N$ $[M + H]^+$ 238.1596, found 238.1590; R_f 0.52 (petroleum ether/EtOAc, 5/1).

*N-Pentyl-9H-fluoren-2-amine (**4c**).* According to **TP2**, $MnBr(CO)_5$-catalyzed *N*-alkylation of 9*H*-fluoren-2-amine (181 mg, 1 mmol) with pentan-1-ol (106 mg, 1.2 mmol) afforded the desired product **4c** as a pale yellow oil (178 mg, 71%): ^1H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 7.5 Hz, 1 H), 7.53 (d, J = 8.0 Hz, 1 H), 7.44 (d, J = 7.5 Hz, 1 H), 7.30 (t, J = 7.5 Hz, 1 H), 7.19 (t, J = 7.4 Hz, 1 H), 6.84 (s, 1 H), 6.69 (dd, J = 8.1, 2.1 Hz, 1 H), 3.87 (t, J = 6.0 Hz, 1 H), 3.74 (s, 2 H), 2.02−1.89 (m, 2 H), 1.31−1.13 (m, 6 H), 0.84 (t, J = 6.6 Hz, 3 H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 149.5, 146.7, 145.7, 141.5, 132.4, 126.7, 125.1, 124.0, 120.5, 118.4, 113.9, 111.2, 47.3, 33.2, 32.2, 25.2, 22.5, 14.1; IR (diamond-ATR, neat) 3372, 2925, 1614, 1455, 1274, 1128, 817, 727 cm^{-1}; HRMS (ESI^+) calcd for $C_{18}H_{22}N$ $[M + H]^+$ 252.1752, found 252.1753; R_f 0.52 (petroleum ether/EtOAc, 5/1).

*N-Hexyl-9H-fluoren-2-amine (**4d**).* According to **TP2**, $MnBr(CO)_5$-catalyzed *N*-alkylation of 9*H*-fluoren-2-amine (181 mg, 1

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mmol) with hexan-1-ol (123 mg, 1.2 mmol) afforded the desired product **4d** as a pale yellow oil (198 mg, 74%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 7.6 Hz, 1 H), 7.52 (d, J = 8.0 Hz, 1 H), 7.43 (d, J = 7.4 Hz, 1 H), 7.29 (t, J = 7.5 Hz, 1 H), 7.19 (t, J = 7.4 Hz, 1 H), 6.83 (s, 1 H), 6.68 (d, J = 8.0 Hz, 1 H), 3.87 (t, J = 6.0 Hz, 1 H), 3.73 (s, 2 H), 2.02−1.89 (m, 2 H), 1.30−1.14 (m, 8 H), 0.85 (t, J = 6.5 Hz, 3 H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 149.6, 146.7, 145.8, 141.5, 132.4, 126.7, 125.1, 124.0, 120.5, 118.4, 114.0, 111.2, 47.3, 33.3, 31.7, 29.7, 25.6, 22.6, 14.0; IR (diamond-ATR, neat) 3369, 2925, 1616, 1455, 1272, 819, 766, 737 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{19}H_{24}N$ [M + H]$^+$ 266.1909, found 266.1910; R_f 0.52 (petroleum ether/EtOAc, 5/1).

*N-(4-Bromophenethyl)-9H-fluoren-2-amine (**4e**).* According to **TP2**, $MnBr(CO)_5$-catalyzed *N*-alkylation of 9*H*-fluoren-2-amine (181 mg, 1 mmol) with 2-(4-bromophenyl)ethanol (241 mg, 1.2 mmol) afforded the desired product **4e** as a yellow solid (138 mg, 38%): mp 132−134 °C (dichloromethane/petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 7.2 Hz, 1 H), 7.54 (d, J = 8.0 Hz, 1 H), 7.45 (d, J = 7.4 Hz, 1 H), 7.39−7.26 (m, 3 H), 7.21 (t, J = 7.4 Hz, 1 H), 6.94 (d, J = 8.0 Hz, 2 H), 6.83 (s, 1 H), 6.71 (dd, J = 8.1, 2.1 Hz, 1 H), 3.97 (s, 1 H), 3.76 (s, 2 H), 2.39−2.17 (m, 4 H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 148.6, 145.9, 145.7, 141.8, 141.4, 132.5, 131.2, 130.0, 127.0, 125.3, 123.9, 120.7, 119.3, 118.6, 114.2, 110.9, 46.9, 34.6, 30.6; IR (diamond-ATR, neat) 3309, 2916, 2321, 1616, 1558, 1456, 1007, 819, 737 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{21}H_{19}BrN$ [M + H]$^+$ 364.0701, found 364.0696; R_f 0.34 (petroleum ether/EtOAc, 5/1).

*N-Hexylaniline (**4f**).* According to **TP2**, $MnBr(CO)_5$-catalyzed *N*-alkylation of aniline (93 mg, 1 mmol) with hexan-1-ol (123 mg, 1.2 mmol) afforded the desired product **4f** as a colorless oil (48 mg, 29%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21−7.13 (m, 2 H), 6.68 (t, J = 7.3 Hz, 1 H), 6.60 (d, J = 7.6 Hz, 2 H), 3.58 (s, 1 H), 3.10 (t, J = 7.1 Hz, 2 H), 1.61 (p, J = 7.1 Hz, 2 H), 1.45−1.24 (m, 6 H), 0.90 (t, J = 6.7 Hz, 3 H).); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 148.6, 129.2, 117.1, 112.7, 44.0, 31.7, 29.6, 26.9, 22.7, 14.1; IR (diamond-ATR, neat) 3408, 2925, 1601, 1505, 745, 689 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{12}H_{20}N$ [M + H]$^+$ 178.1596, found 178.1589; R_f 0.50 (petroleum ether/EtOAc, 50/1).

*N-Cyclohexyl-9H-fluoren-2-amine (**4g**).* According to **TP2**, $MnBr(CO)_5$-catalyzed *N*-alkylation of 9*H*-fluoren-2-amine (181 mg, 1 mmol) with cyclohexanol (121 mg, 1.2 mmol) afforded the desired product **4g** as a pale yellow oil (80 mg, 31%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 7.6 Hz, 1 H), 7.50 (d, J = 8.0 Hz, 1 H), 7.46 (d, J = 7.5 Hz, 1 H), 7.28 (t, J = 7.6 Hz, 1 H), 7.17 (t, J = 7.5 Hz, 1 H), 6.87 (d, J = 2.2 Hz, 1 H), 6.68 (dd, J = 8.1, 2.1 Hz, 1 H), 3.77 (s, 1 H), 3.73 (s, 2 H), 2.14−2.03 (m, 1 H), 1.71−1.57 (m, 3 H), 1.51−1.40 (m, 2 H), 1.22−1.14 (m, 3 H), 1.12−1.03 (m, 2 H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 148.4, 145.6, 145.5, 142.1, 132.9, 126.7, 124.9, 124.6, 120.3, 118.2, 113.9, 111.9, 53.4, 43.3, 29.8, 29.4, 27.0, 26.9, 26.5; IR (diamond-ATR, neat) 3372, 2921, 1608, 1449, 1285, 817, 769, 734 cm^{-1}; HRMS (ESI$^+$) ($C_{19}H_{22}N$ [M + H]$^+$ 264.1752, found 264.1759; R_f 0.54 (petroleum ether/EtOAc, 10/1).

*N-Cyclopentyl-9H-fluoren-2-amine (**4h**).* According to **TP2**, $MnBr(CO)_5$-catalyzed *N*-alkylation of 9*H*-fluoren-2-amine (363 mg, 2 mmol) with cyclopentanol (202 mg, 2.4 mmol) afforded the desired product **4h** as a pale yellow oil (124 mg, 24%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 7.6 Hz, 1 H), 7.50 (dd, J = 9.2, 7.6 Hz, 2 H), 7.29 (t, J = 7.4 Hz, 1 H), 7.16 (td, J = 7.5, 1.2 Hz, 1 H), 6.90 (d, J = 2.1 Hz, 1 H), 6.69 (dd, J = 8.1, 2.2 Hz, 1 H), 3.92 (d, J = 5.5 Hz, 1 H), 3.72 (s, 2 H), 2.41−2.30 (m, 1 H), 1.81−1.69 (m, 2 H), 1.58−1.26 (m, 6 H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 149.0, 146.1, 145.6, 141.8, 132.7, 126.8, 124.9, 124.9, 120.4, 118.4, 114.1, 112.2, 50.9, 44.5, 30.0, 29.8, 25.2, 25.2; IR (diamond-ATR, neat) 3371, 2948, 1612, 1451, 1272, 819, 764, 735 cm^{-1}; HRMS (ESI$^+$) ($C_{18}H_{20}N$ [M + H]$^+$ 250.1596, found 250.1588; R_f 0.20 (petroleum ether/EtOAc, 10/1).

*Synthesis of Indole (**5**).* To a clean, oven-dried, screw cap reaction tube were added $MnBr(CO)_5$ (28 mg, 0.1 mmol), PPh_3 (52 mg, 0.2 mmol), 2-(2-aminophenyl)ethanol (141 mg, 1 mmol), *t*-BuOK (135 mg, 1.2 mmol), and toluene (2 mL) under a nitrogen atmosphere. The reaction mixture was stirred at 130 °C in an oil bath for 20 h. Then, the reaction mixture was diluted with water (5 mL) and extracted with EtOAc (3 × 10 mL). The combined organic phases were washed with brine and dried over magnesium sulfate. The solvent was removed by rotary evaporation, and purification by flash column chromatography on silica gel using petroleum ether/ethyl acetate as an eluent gave the expected product **5** as a white crystal (71 mg, 61%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 1 H), 7.64 (d, J = 7.8 Hz, 1 H), 7.31 (d, J = 8.1 Hz, 1 H), 7.18 (t, J = 7.5 Hz, 1 H), 7.15−7.07 (m, 2 H), 6.53 (s, 1 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 135.7, 127.7, 124.1, 121.9, 120.7, 119.7, 111.0, 102.5.

*Synthesis of Resveratrol-Derived Amine **6**.* To a clean, oven-dried, screw cap reaction tube were added $MnBr(CO)_5$ (28 mg, 0.1 mmol), PPh_3 (52 mg, 0.2 mmol), (4-methoxyphenyl)methanol (166 mg, 1.2 mmol), 4-styrylaniline (195 mg, 1 mmol), *t*-BuOK (135 mg, 1.2 mmol), and toluene (2 mL) under a nitrogen atmosphere. The reaction mixture was stirred at 130 °C in an oil bath for 20 h. Then, the reaction mixture was diluted with water (5 mL) and extracted with EtOAc (3 × 10 mL). The combined organic phases were washed with brine and dried over magnesium sulfate. The solvent was removed by rotary evaporation, and purification by flash column chromatography on silica gel using petroleum ether/ethyl acetate as an eluent gave the expected product **6** as a yellow solid (192 mg, 60%): mp 151−153 °C (dichloromethane/petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 7.7 Hz, 2 H), 7.38−7.27 (m, 6 H), 7.24−7.18 (m, 1 H), 7.04 (d, J = 16.3 Hz, 1 H), 6.94−6.86 (m, 3 H), 6.63 (d, J = 8.1 Hz, 2 H), 4.29 (s, 2 H), 4.08 (s, 1 H), 3.81 (s, 3 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 158.9, 147.8, 138.1, 131.1, 128.8, 128.7, 128.5, 127.7, 126.9, 126.7, 125.9, 124.5, 114.0, 112.9, 55.3, 47.6; IR (diamond-ATR, neat) 3392, 2920, 1605, 1511, 1244, 1029, 811, 693 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{22}H_{22}NO$ [M + H]$^+$ 316.1701, found 316.1693; R_f 0.51 (petroleum ether/EtOAc, 5/1).

*Gram-Scale Procedure for the Synthesis of N-(4-Methylbenzyl)-9H-fluoren-2-amine (**3n**).* To a clean, oven-dried, screw cap reaction tube were added $MnCl_2$ (130 mg, 1 mmol), PPh_3 (520 mg, 2 mmol), *p*-tolyl-methanol (1.49 g, 12 mmol), 9*H*-fluoren-2-amine (1.81 g, 10 mmol), *t*-BuOK (1.35 g, 12 mmol), and toluene (20 mL) under a nitrogen atmosphere. The reaction mixture was stirred at 130 °C in an oil bath for 20 h. Then, the reaction mixture was diluted with water (20 mL) and extracted with EtOAc (3 × 40 mL). The combined organic phases were washed with brine and dried over magnesium sulfate. The solvent was removed by rotary evaporation, and purification by flash column chromatography on silica gel using petroleum ether/ethyl acetate as an eluent gave the expected product **3n** as a yellow solid (1.85 g, 65%).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02407.

Experimental procedures, characterization data, deuterium labelling experiments, and ^{1}H and ^{13}C NMR spectra for all products (PDF)

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Notes

The authors declare no competing financial interest.

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