Supporting Information

Efficient and Versatile Catalytic Systems for N-Methylation of Primary Amines with Methanol Catalyzed by N-Heterocyclic Carbene Complexes of Iridium

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5. $^1$H NMR and $^{13}$C($^1$H) NMR spectra of the isolated compounds ............ S7
1. X-ray structure analysis of the complex 1c:
Diffraction data for 1c were obtained with a Rigaku RAXIS RAPID instrument. Reflection data were corrected for Lorentz and polarization effects. Empirical absorption corrections were applied. The structure of 1c was solved by direct method (SIR92)[1] and refined anisotropically for non-hydrogen atoms by full-matrix least-squares calculations. Atomic scattering factors and anomalous dispersion terms were taken from the literature.[2] Hydrogen atoms were located on the idealized positions. The calculations were performed using the program system CrystalStructure.[3,4] ORTEP drawing of 1c is shown in Figure S1. CCDC-1826433 contains the supplementary crystallographic data of 1c. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Selected X-ray crystallographic data for 1c: C_{19}H_{31}Cl_2IrN_2, M_w = 550.59 g/mol, orange-red block, crystal size 0.35 x 0.25 x 0.05 mm, data collection temperature 173 K, monoclinic, space group P2_1/m (#11), a = 7.1953(6) Å, b = 17.004(2) Å, c = 8.4624(6) Å, β = 101.541(3) °, V = 1014.4(2) Å³, Z = 2, D_{calc} = 1.802 g/cm³, μ(Mo-Kα) = 6.8659 mm⁻¹, empirical absorption correction (T_{min} = 0.243 / T_{max} = 0.709), 2θ_{max} = 54.8 °, 9891 measured reflections, 2382 independent reflections (R_{int} = 0.1156), 132 parameters, R = 0.0412 (I>2.00σ(I)), R_w = 0.0490 (all reflections), GOF = 1.030.

![ORTEP drawing of 1c with 50% thermal probability ellipsoids. Hydrogen atoms are omitted for clarity.](image)
2. Discussions on the reaction pathways mentioned in Scheme 1:
The N-methylation reaction using methanol as a methylating agent would proceed through the following elementary steps: (i) conversion of methanol into formaldehyde based on catalytic hydrogen transfer oxidation process, (ii) nucleophilic attack of amine to formaldehyde, (iii) elimination of water to afford imine or iminium ion (in the case of the formation of iminium ion, assistance of proton would be necessary), and (iv) catalytic transfer hydrogenation of imine or iminium ion to give N-methylated or N,N-dimethylated product (Scheme S1).

![Scheme S1](image)

Scheme S1 Plausible mechanism for the N-methylation using methanol catalyzed by iridium complex.

As mentioned in the Scheme 1 in the main manuscript, here we discuss on the pathways of the three types of the N-methylation reactions.

(1) N,N-Dimethylation of aliphatic primary amines:
In this case (reaction conditions shown in Table 2), because of high nucleophilicity of aliphatic amines, the formation of imines and iminium ions would proceed relatively faster even at lower reaction temperatures than the formation of formaldehyde from methanol. Thus, the rate determining step of the reaction would be the catalytic dehydrogenation of methanol, which might proceed mediated by cyclometalated species such as A. Therefore, iridium catalyst bearing an NHC ligand with isopropyl groups on the nitrogen atoms, such as 1c, 2c, 3c, and 4c was indispensable for this type of reaction at lower temperatures. In order to confirm this hypothesis, the reaction of complex 1c with an excess amount
of base (NaOMe, 2.1 eq) was conducted (eq S1). This reaction surely gave cyclometalated hydrido species A; however, A was too unstable for characterization in detail. Thus, derivation into chloro complex A’ was performed in CHCl₃, which resulted in the formation of single crystal of A’ (X-ray structure analysis of A’ was performed), providing the evidence of cyclometalation process. Although similar reactions starting with methyl complex 1a and ethyl complex 1b were also conducted, cyclometalated complexes corresponding to A or A’ could not be obtained. On the basis of these results, we conclude that isopropyl groups in NHC ligand were important for high catalytic performance for the N,N-dimethylation of aliphatic primary amines at low temperature.

Complex A’ (mixture of two diastereomers): ¹H NMR (500 MHz, CDCl₃) δ = 6.88 (d, J = 3 Hz, 1H, CH=CH, minor isomer), 6.86 (d, J = 2 Hz, 1H and 1H, CH=CH, major and minor isomers), 6.80 (d, J = 2 Hz, 1H, CH=CH, major isomer), 4.90 (m, 1H, CH, major isomer), 4.84 (m, 1H, CH, minor isomer), 4.33 (m, 1H, CH, minor isomer), 3.86 (m, 1H, CH, major isomer), 3.20 (m, 1H, CH, minor isomer), 2.69 (t, J = 10 Hz, 1H, CH, major isomer), 2.54 (m, 1H, CH, major isomer), 2.21 (m, 1H, CH, minor isomer), 1.78 (s, 15H, C₅(CH₃)₅, major isomer), 1.77 (s, 15H, C₅(CH₃)₅, minor isomer), 1.53 (d, J = 7 Hz, 3H and 3H, CH₃, major and minor isomers), 1.52 (d, J = 7 Hz, 3H, CH₃, major isomer), 1.48 (d, J = 7 Hz, 3H, CH₃, major isomer), 1.43 (d, J = 7 Hz, 3H, CH₃, minor isomer), 1.18 (d, J = 7 Hz, 3H, CH₃, minor isomer).

¹³C {¹H} NMR (126 MHz, CDCl₃) δ = 162.4 (s, Clr, major isomer), 161.7 (s, Clr, minor isomer), 117.2 (s, CH=CH, minor isomer), 117.0 (s, CH=CH, major isomer), 116.2 (s, CH=CH, minor isomer), 115.7 (s, CH=CH, major isomer), 88.4 (s, C₅(CH₃)₅, minor isomer), 88.1 (s, C₅(CH₃)₅, major isomer), 59.9 (s, CH, major isomer), 58.7 (s, CH, minor isomer), 52.0 (s, CH, minor isomer), 51.5 (s, CH, major isomer), 25.7 (s, CH₃, major isomer), 25.5 (s, CH₃, minor isomer), 25.0 (s, CH₃, minor isomer), 23.5 (s, CH₃, major isomer), 23.2 (s, CH₃, minor isomer), 22.4 (s, CH₃, major isomer), 22.2 (s, CH₂Ir, major isomer), 18.7 (s, CH₂Ir, minor isomer), 9.8 (s, C₅(CH₃)₅, minor isomer), 9.7 (s, C₅(CH₃)₅, major isomer).

Anal. Calcd for C₁₉H₃₀N₂Ir: C, 44.39; H, 5.88; N, 5.45. Found: C, 43.90; H, 5.70; N, 5.37.

(2) N-Monomethylation of aromatic primary amines:
In this case (reaction conditions shown in Table 4), relatively stable conjugated aromatic imines are formed as an intermediate. Thus, the rate determining step of the reaction would be catalytic transfer hydrogenation of imines. Also in these cases, because the reaction was carried out under basic conditions (in the presence of K₂CO₃) and nucleophilicity of aromatic amines are low, formation of iminium ions were suppressed. Thus, selective N-monomethylation would proceed under the conditions shown in Table 4.
(3) *N,N*-Dimethylation of aromatic primary amines:
In this case (reaction conditions shown in Table 5), the reactions are carried out under neutral conditions (in the absence of base). Thus, the generation of an iminium ion would be relatively easy compared to the above case (2) under basic conditions. Additionally, in this case, NHC ligand having small methyl groups on nitrogen atoms is employed. Therefore, coordination sphere of iridium atom are not so crowded. With these situations, *N,N*-dimethylation must be well proceeded.

3. X-ray structure analysis of the complex A':
Diffraction data for A' were obtained with a Rigaku RAXIS RAPID instrument. Reflection data were corrected for Lorentz and polarization effects. Empirical absorption corrections were applied. The structure of A' was solved by direct method (SIR92)[1] and refined anisotropically for non-hydrogen atoms by full-matrix least-squares calculations. Atomic scattering factors and anomalous dispersion terms were taken from the literature.[2] Hydrogen atoms were located on the idealized positions. The calculations were performed using the program system CrystalStructure.[3,4] ORTEP drawing of A' is shown in Figure S2. CCDC-1854939 contains the supplementary crystallographic data of A'. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Selected X-ray crystallographic data for A': C₁₉H₃₀ClIrN₂, *M*_w = 514.13 g/mol, yellow block, crystal size 0.30 x 0.10 x 0.10 mm, data collection temperature 173 K, orthorhombic, space group *Pbcn* (#60), *a* = 23.1827(10) Å, *b* = 11.9895(5) Å, *c* = 14.2696(7) Å, *V* = 3966.2(3) Å³, *Z* = 8, *D*_calc = 1.722 g/cm³, μ(Mo-Kα) = 6.8874 mm⁻¹, empirical absorption correction (*T*_min = 0.250 / *T*_max = 0.502), 2θ_max = 54.9 °, 54216 measured reflections, 4521 independent reflections (*R*_int = 0.0555), 261 parameters, *R* = 0.0605 (*I*>2.00σ(*I*)), *R*_w = 0.0871 (all reflections), GOF = 1.242.

![ORTEP drawing of A' with 50% thermal probability ellipsoids. Hydrogen atoms are omitted for clarity.](image)
4. References:


5) We have attempted to prepare the Cp*Ir-NHC catalyst having more bulky tBu or adamantyl groups on nitrogen atoms. However, it has not been successful so far.
5. $^1$H NMR and $^{13}$C-$^1$H NMR spectra of the isolated compounds:

$^1$H NMR

$N,N$-dimethylcycloheptanamine

Table 2, Entry 2

$^{13}$C-$^1$H NMR

$N,N$-dimethylcycloheptanamine

Table 2, Entry 2
$^1$H NMR

$N,N$-dimethylcyclooctanamine
Table 2, Entry 3

$^{13}$C{$^1$H} NMR

$N,N$-dimethylcyclooctanamine
Table 2, Entry 3
$^1\text{H NMR}$

$N,N$-dimethyladamantan-1-amine
Table 2, Entry 4

$^{13}\text{C}^{(1}\text{H})$ NMR

$N,N$-dimethyladamantan-1-amine
Table 2, Entry 4
$^1$H NMR

$N,N$-dimethyloctan-1-amine
Table 2, Entry 6

$^{13}$C$_{\{^1\text{H}\}}$ NMR

$N,N$-dimethyloctan-1-amine
Table 2, Entry 6
$^{1}H$ NMR

$N,N$-dimethyloctan-2-amine
Table 2, Entry 7

$^{13}C\{^{1}H\}$ NMR

$N,N$-dimethyloctan-2-amine
Table 2, Entry 7
$^1$H NMR

$N, N$-dimethyl(2-methylphenyl)methanamine

Table 2, Entry 9

$^{13}$C{$^1$H} NMR

$N, N$-dimethyl(2-methylphenyl)methanamine

Table 2, Entry 9
**1H NMR**

N,N-dimethyl(3-methylphenyl)methanamine  
Table 2, Entry 10

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**13C{1H} NMR**

N,N-dimethyl(3-methylphenyl)methanamine  
Table 2, Entry 10

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S13
$^{1}H$ NMR

$N,N$-dimethyl(4-methylphenyl)methanamine
Table 2, Entry 11

$^{13}C\{^1H\}$ NMR

$N,N$-dimethyl(4-methylphenyl)methanamine
Table 2, Entry 11
$^1$H NMR

$N,N$-dimethyl(4-methoxyphenyl)methanamine
Table 2, Entry 12

$^{13}$C{$^1$H} NMR

$N,N$-dimethyl(4-methoxyphenyl)methanamine
Table 2, Entry 12
$^1$H NMR

$N,N$-dimethyl(2-chlorophenyl)methanamine

Table 2, Entry 13

$^{13}$C{$^1$H} NMR

$N,N$-dimethyl(2-chlorophenyl)methanamine

Table 2, Entry 13
$^1$H NMR

$N,N$-dimethyl(3-chlorophenyl)methanamine
Table 2, Entry 14

$^{13}$C{$^1$H} NMR

$N,N$-dimethyl(3-chlorophenyl)methanamine
Table 2, Entry 14
$^1$H NMR

$N,N$-dimethyl(4-chlorophenyl)methanamine
Table 2, Entry 15

$^{13}$C{$^1$H} NMR

$N,N$-dimethyl(4-chlorophenyl)methanamine
Table 2, Entry 15
$^1$H NMR

$N,N$-dimethyl(4-cyanophenyl)methanamine
Table 2, Entry 16

$^{13}$C{$^1$H} NMR

$N,N$-dimethyl(4-cyanophenyl)methanamine
Table 2, Entry 16
$^1$H NMR

$N,N$-dimethyl(4-trifluoromethylphenyl)methanamine

Table 2, Entry 17

$^{13}$C$^{1}$H NMR

$N,N$-dimethyl(4-trifluoromethylphenyl)methanamine

Table 2, Entry 17
$^1$H NMR

$N,N$-dimethyl-1-phenylethan-1-amine

Table 2, Entry 18

$^{13}$C{$^1$H} NMR

$N,N$-dimethyl-1-phenylethan-1-amine

Table 2, Entry 18
$^1$H NMR

$N,N$-dimethyl-1-((4-methoxyphenyl)ethan-1-amine
Table 2, Entry 19

$^{13}$C$^{1}$H NMR

$N,N$-dimethyl-1-((4-methoxyphenyl)ethan-1-amine
Table 2, Entry 19
$^1$H NMR

$N,N$-dimethyl-1-(4-chlorophenyl)ethan-1-amine
Table 2, Entry 20

$^{13}$C$^1$H NMR

$N,N$-dimethyl-1-(4-chlorophenyl)ethan-1-amine
Table 2, Entry 20
N-methylaniline

Table 4
$^{1}H$ NMR

$N$-methyl-$m$-toluidine

Table 4

$^{13}C\{^{1}H\}$ NMR

$N$-methyl-$m$-toluidine

Table 4
$^1$H NMR

$^1$H NMR

$^{13}$C{$^1$H} NMR

$^{13}$C{$^1$H} NMR

$N$-methyl-$p$-toluidine

Table 4
$^1$H NMR

N-methyl-4-methoxyaniline
Table 4

$^{13}$C($^1$H) NMR

N-methyl-4-methoxyaniline
Table 4
$^1$H NMR

$^1$H NMR

N-methyl-3-chloroaniline
Table 4

$^{13}$C{$^1$H} NMR

$^{13}$C{$^1$H} NMR

N-methyl-3-chloroaniline
Table 4
$^1$H NMR

$N$-methyl-4-chloroaniline

Table 4

$^{13}$C$\{^1$H$\}$ NMR

$N$-methyl-4-chloroaniline

Table 4
$^1$H NMR

N-methyl-4-bromoaniline
Table 4

$^{13}$C\{$^1$H\} NMR

N-methyl-4-bromoaniline
Table 4
$^{1}H$ NMR

N-methyl-3-nitroaniline

Table 4

$^{13}C\{^{1}H\}$ NMR

N-methyl-3-nitroaniline

Table 4
$^{1}$H NMR

$N$-methyl-$4$-nitroaniline
Table 4

$^{13}$C{$^{1}$H}$ NMR

$N$-methyl-$4$-nitroaniline
Table 4
$^1$H NMR

N-methyl-4-cyanoaniline

Table 4

$^{13}$C($^1$H) NMR

N-methyl-4-cyanoaniline

Table 4
$^1$H NMR

$^1$H NMR

$^1$H NMR

$^13$C{$^1$H} NMR

$^13$C{$^1$H} NMR

$^13$C{$^1$H} NMR

$N$-[4-(methylamino)phenyl]acetamide

Table 4

$N$-[4-(methylamino)phenyl]acetamide

Table 4

$N$-[4-(methylamino)phenyl]acetamide

Table 4

$N$-[4-(methylamino)phenyl]acetamide

Table 4
$^1$H NMR

$N$-methylpyridin-2-amine

Table 4

$^{13}$C$^1$H NMR

$N$-methylpyridin-2-amine

Table 4
$^{1}H$ NMR

$N$-methylpyridin-3-amine
Table 4

$^{13}C\{^1H\}$ NMR

$N$-methylpyridin-3-amine
Table 4
$^{1}H$ NMR

N-methylpyridin-4-amine
Table 4

$^{13}C\{{}^{1}H\}$ NMR

N-methylpyridin-4-amine
Table 4
$^1$H NMR

$N$-methylpyrazin-2-amine  
Table 4

$^{13}$C{$^1$H} NMR  

$N$-methylpyrazin-2-amine  
Table 4
$^1$H NMR

N-methylnaphthalen-1-amine

Table 4

$^{13}$C{$^1$H} NMR

N-methylnaphthalen-1-amine

Table 4
$^1$H NMR

$^1$H NMR

$^{13}$C\{$^1$H\} NMR

$^{13}$C\{$^1$H\} NMR

N-methylisoquinolin-4-amine

Table 4

N-methylisoquinolin-4-amine

Table 4
$^{1}H$ NMR

$N,N$-dimethylaniline

Table 5

$^{13}C^{1}H$ NMR

$N,N$-dimethylaniline

Table 5
$^1$H NMR

$N,N$-dimethyl-$o$-toluidine

Table 5

$^{13}$C$^1$H NMR

$N,N$-dimethyl-$o$-toluidine

Table 5
$^1$H NMR

$N,N$-dimethyl-$m$-toluidine

Table 5

$^{13}$C{$^1$H} NMR

$N,N$-dimethyl-$m$-toluidine

Table 5
$^{1}H$ NMR

$N,N$-dimethyl-$p$-toluidine

Table 5

$^{13}C\{^1H\}$ NMR

$N,N$-dimethyl-$p$-toluidine

Table 5
$^1$H NMR

$N,N$-dimethyl-4-methoxyaniline

Table 5

$^{13}$C{${}^1$H} NMR

$N,N$-dimethyl-4-methoxyaniline

Table 5
$\text{N,N-dimethyl-4-hydroxyaniline}

\text{Table 5}$

$\text{1H NMR}$

$\text{13C}^{1\text{H}} \text{ NMR}$
**$^{1}H$ NMR**

$N,N$-dimethyl-3-chloroaniline

Table 5

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**$^{13}C$\{1$H$\} NMR**

$N,N$-dimethyl-3-chloroaniline

Table 5
$^1$H NMR

$N,N$-dimethyl-4-chloroaniline

Table 5

$^{13}$C{$^1$H} NMR

$N,N$-dimethyl-4-chloroaniline

Table 5
$^1$H NMR

$N,N$-dimethyl-3-nitroaniline

Table 5

$^{13}$C{$^1$H} NMR

$N,N$-dimethyl-3-nitroaniline

Table 5
$^{1}H$ NMR

$N,N$-[4-(dimethylamino)phenyl]acetamide
Table 5

$^{13}C\{^1H\}$ NMR

$N,N$-[4-(dimethylamino)phenyl]acetamide
Table 5
$^1$H NMR

$N,N$-dimethylnaphthalen-1-amine

Table 5

$^{13}$C$^1$H NMR

$N,N$-dimethylnaphthalen-1-amine

Table 5