Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information for

Ruthenium-catalyzed selective imine synthesis from nitriles and secondary alcohols under hydrogen acceptor- and base-free conditions

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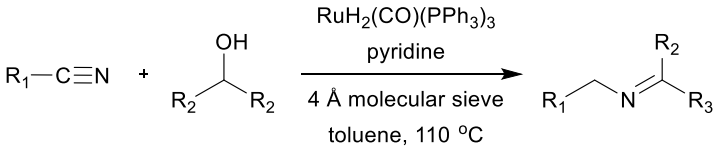
Content

1. Experimental section

General information

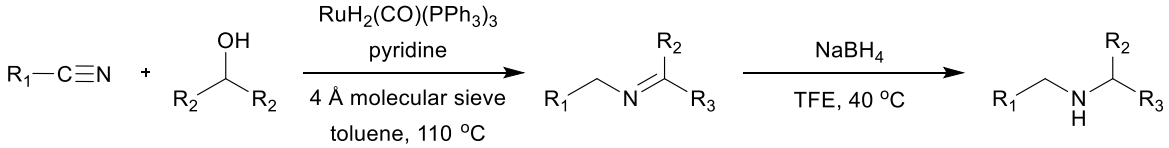
Unless otherwise noted, all reactions were carried out using standard Schlenk techniques or in an argon-filled glove box. All anhydrous solvents were purchased from commercial suppliers and degassed with dry argon before usage. Deuterated solvents were purchased from Cambridge Isotope Laboratories, Inc. NMR spectra were recorded in $CDCl_3$ or benezene-d_6 using Bruker DPX300, AMX400, Agilent 400-MR, JEOL ECA400, or JEOL ECA400SL spectrometer, and TMS (tetramethylsilane) was used as a reference. Chemical shifts were reported in ppm and coupling constant in Hz. GC analysis was carried out with 7980A GC system from Agilent Technologies, equipped with an HP-5 column and FID detector. $RuH_2(CO)(PPh_3)_3$,[1] NHC precursors,[2] $RuH_2(CO)(PPh_3)_2$(I*i*Pr),[3] and other metal reagents were prepared by literature procedures or purchased from Strem Chemicals, Inc.

General procedure for imine synthesis from nitrile and alcohol



Inside an argon-filled glove box, $RuH_2(CO)(PPh_3)_3$ (46 mg, 0.05 mmol), nitrile (0.50 mmol), alcohol (2.5 mmol), pyridine (8.1 μL, 0.10 mmol), 4 Å Molecular sieve (200 mg), and toluene (0.6 mL) were added to an oven-dried 4 mL vial equipped with septum screw cap. Then, the overall reaction media was stirred at 110 ℃ for 1-12 h before being cooled down to room temperature. Crude mixture was filtered through Celite pad and washed with dichloromethane, and all the volatiles were removed under vacuum.

General procedure for imine hydrogenation



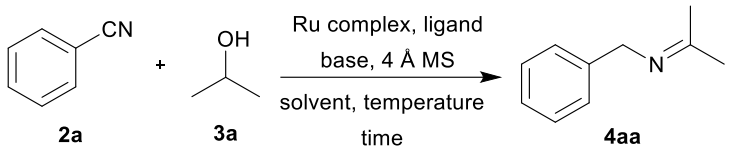
After imine synthesis from above procedure, concentrated mixture was dissolved in 2,2,2-

trifluoroethanol (TFE, 2.0 mL). Sodium borohydride ($NaBH_4$, 28 mg, 0.75 mmol) was added and stirred at 40 ℃ for 1-3 h. After completion of the reaction, the mixture was filtered through Celite pad and washed with dichloromethane. All the volatiles were removed under vacuum. Purification of the crude product was performed by flash chromatography (Eluent: dichloromethane and methanol) to afford the corresponding product.

GC analysis for reaction intermediate detection

$RuH_2(CO)(PPh_3)_3$ (46 mg, 0.05 mmol), benzonitrile (51.6 μL, 0.50 mmol), 2-propanol (191.4 μL, 2.5 mmol), pyridine (8.1 μL, 0.10 mmol), 4 Å Molecular sieve (200 mg), and toluene (0.6 mL) were added to an oven-dried 4 mL vial equipped with septum screw cap inside an argon-filled glove box. Dodecane (56.8 μL, 0.25 mmol) as an internal standard was added to the reaction mixture. Then, the overall reaction medias were stirred at 110 ℃ for 2 min, 5 min, 10 min, 15 min, 20 min, 30 min, 45 min, and 60 min, respectively, before being cooled to room temperature. Each sample was diluted with dichloromethane, and filtered with Celite, and analyzed with GC (Scheme 2).

Table S1 Screening of catalysts for imine synthesis[a]



2a **3a** **4aa**

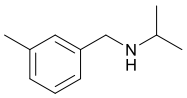
Entry	Ru complex	Ligand (mol%)	Base (mol%)	Solvent (℃)	Time (h)	Yield (%)[b]
1	Shvo's catalyst[c]	-	-	Toluene (110)	18	0
2	Ru-MACHO-BH[d]	-	-	Toluene (110)	18	29
3	$Ru_3(CO)_{12}$	I*i*Pr[e] (5)	NaH (20)	Toluene (110)	18	0
4	$RuHCl(CO)(PPh_3)_3$	I*i*Pr (5)	NaH (20)	Toluene (110)	18	35
5	$RuH_2(PPh_3)_4$	I*i*Pr (5)	NaH (20)	Toluene (110)	18	37
6	$RuH_2(CO)(PPh_3)_3$	I*i*Pr (5)	NaH (20)	Toluene (110)	18	60
7	$RuH_2(CO)(PPh_3)_3$	IMe[f]	NaH (20)	Toluene (110)	18	22
8	$RuH_2(CO)(PPh_3)_3$	IPr[g]	NaH (20)	Toluene (110)	18	27
9	$RuH_2(CO)(PPh_3)_3$	ICy[h]	NaH (20)	Toluene (110)	18	35
10	$RuH_2(CO)(PPh_3)_3$	-	NaH (20)	Toluene (110)	18	27
11	$RuH_2(CO)(PPh_3)_3$	-	NaH (10)	Toluene (110)	18	34
12	$RuH_2(CO)(PPh_3)_3$	-	-	Toluene (110)	18	61
13[i]	$RuH_2(CO)(PPh_3)_3$	-	-	Toluene (110)	18	45
14	$RuH_2(CO)(PPh_3)_3$	-	-	Toluene (100)	18	59
15	$RuH_2(CO)(PPh_3)_3$	-	-	Toluene (120)	18	40
16	$RuH_2(CO)$(I*i*Pr)$(PPh_3)_3$	-	-	Toluene (110)	18	60
17	$RuH_2(CO)(PPh_3)_3$	-	-	Anisole (110)	18	60
18	$RuH_2(CO)(PPh_3)_3$	-	-	CPME (110)[j]	18	55
19	$RuH_2(CO)(PPh_3)_3$			2-propanol (110)	18	27
20	$RuH_2(CO)(PPh_3)_3$	P(*t*Bu)$_3$[k] (5)	-	Toluene (110)	18	73
21	$RuH_2(CO)(PPh_3)_3$	JohnPhos[l] (5)	-	Toluene (110)	18	76
22	$RuH_2(CO)(PPh_3)_3$	CH_3CN (20)	-	Toluene (110)	18	65
23	$RuH_2(CO)(PPh_3)_3$	Pyridine (20)	-	Toluene (110)	18	74
24	$RuH_2(CO)(PPh_3)_3$	Pyridine (10)	-	Toluene (110)	18	57
25	$RuH_2(CO)(PPh_3)_3$	Pyridine (40)	-	Toluene (110)	18	59
26[m]	$RuH_2(CO)(PPh_3)_3$	Pyridine (20)	-	Toluene (110)	18	82
27	$RuH_2(CO)$(I*i*Pr)$(PPh_3)_2$	Pyridine (20)	-	Toluene (110)	18	60
28[n]	$RuH_2(CO)(PPh_3)_3$	Pyridine (20)	-	Toluene (110)	1	84

[a]Reaction conditions: **2a** (0.5 mmol, 1.0 equiv.), **3a** (5 equiv.), Ru complex (5 mol%), ligand, base, 4 Å molecular sieve (200 mg), solvent (0.6 ml), temperature, time. [b]Determined by GC using dodecane as the internal standard. [c]1-Hydroxytetraphenyl-cyclopentadienyl(tetraphenyl-2,4-cyclopentadien-1-one)-μ-hydrotetracarbonyldiruthenium(II). [d]Carbonylhydrido(tetrahydroborato)[bis(2-diphenylphosphinoethyl)-amino]ruthenium(II). [e]1,3-diisopropylimidazolium bromide. [f]1,3-dimethylimidazolium iodide. [g]1,3-(2,6-(diisopropyl)phenylimidazolium chloride. [h]1,3-dicyclohexylimidazolium chloride. [i]Without 4 Å molecular sieve. [j]cyclopentyl methy ether. [k]tri-*tert*-butyl-phosphine. [l](2-Biphenyl)di-*tert*-butylphosphine. [m]10 equiv. of 2-propanol was used. [n]10 mol% of catalyst was used.

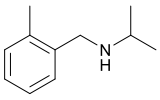
2. Characterization data

Characterization of imines: The reaction was performed in 0.50 mmol scale. All reported compounds, **4aa**,[4] **4ba**,[5] **4ja**,[6] **4ka**[7], **4ab**,[8] **4ad**,[9] **4ae**,[10] **4af**,[10] **4ag**,[11] **4ah**,[12] **4ai**,[12] **4aj**,[13] **4ak**[12] were identified by spectral comparison with literature data or with analogous literature data.

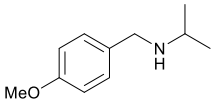
Characterization of newly reported imines, 4ca, **4da**, **4ea**, **4fa**, **4ga**, **4ha**, **4ia**, **4la, 4ac:** corresponding reduced amine form was provided by imine reduction with $NaBH_4$.



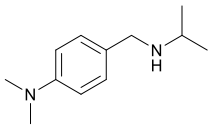
***N*-(3-methylbenzyl)propan-2-amine (4ca):** yellow oil (61.3 mg, 0.375 mmol, 75%); ^{1}H NMR ($CDCl_3$) δ= 1.11 (d, *J*=6.2 Hz, 6H), 2.34 (s, 3H), 2.87 (septet, *J*=6.2 Hz, 1H), 3.75 (s, 2H), 7.05 (d, *J*=7.5 Hz, 1H), 7.11 (d, *J*=7.5 Hz, 1H), 7.15 (s, 1H), 7.20-7.23 (t, *J*=7.5 Hz, 1H). NH was not detected; ^{13}C NMR ($CDCl_3$) δ=138.3, 132.3, 129.2, 128.5, 127.9, 125.5, 51.5, 48.3, 22.8, 21.5; HRMS(ESI) calcd for $C_{11}H_{17}N_1$:163.1361. Found: 163.1360.



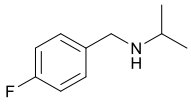
***N*-(2-methylbenzyl)propan-2-amine (4da):**[14] yellow oil (59.8 mg, 0.366 mmol, 73%); ^{1}H NMR ($CDCl_3$) δ= 1.14 (d, *J*=6.2 Hz, 6H), 2.06 (bs, 1H), 2.38 (s, 3H), 2.92 (septet, *J*=6.3 Hz, 1H), 3.78 (s, 2H), 7.16-7.19 (m, 3H), 7.32-7.34 (m, 1H).



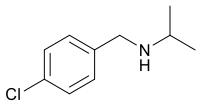
***N*-(4-methoxybenzyl)propan-2-amine (4ea)**:[15] yellow oil (72.0 mg, 0.402 mmol, 80%); ^{1}H NMR ($CDCl_3$) δ= 1.08 (d, *J*=6.2 Hz, 6H), 1.36 (bs, 1H), 2.84 (septet, *J*=6.2 Hz, 1H), 3.71 (s, 2H), 3.78 (s, 3H), 6.84 (d, *J*=8.5 Hz, 2H), 7.22 (d, *J*=8.5 Hz, 2H).



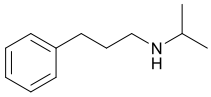
N-((isopropylamino)methyl)-N,N-dimethylaniline (4fa): white crystal (74.4 mg, 0.387 mmol, 77%); ^{1}H NMR ($CDCl_3$) δ= 1.21 (d, *J*=6.5 Hz, 6H), 2.90 (s, 6H), 2.90-3.01 (m, 1H), 3.74 (s, 2H), 6.68 (d, *J*=8.7 Hz, 2H), 7.28 (d, *J*=8.7 Hz, 2H). NH was not detected. ^{13}C NMR ($CDCl_3$) δ= 150.4, 130.2, 124.1, 112.7, 49.6, 48.0, 40.7, 21.4; HRMS(ESI) calcd for $C_{12}H_{20}N_2$: 192.1626. Found: 192.1623.



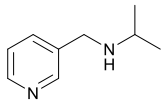
N-(4-fluorobenzyl)propan-2-amine (4ga):[16] yellow oil (51.9 mg, 0.310 mmol, 62%); ^{1}H NMR ($CDCl_3$) δ= 1.11 (d, *J*=6.2 Hz, 6H), 2.87 (septet, *J*=6.3 Hz, 1H), 3.78 (s, 2H), 6.99-7.05 (m, 2H), 7.29-7.34 (m, 2H).



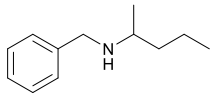
N-(4-chlorobenzyl)propan-2-amine (4ha):[15] yellow solid (60.5 mg, 0.329 mmol, 66%); ^{1}H NMR ($CDCl_3$) δ= 1.08 (d, *J*=6.3 Hz, 6H), 1.33 (bs, 1H), 2.83 (septet, *J*=6.2 Hz, 1H), 3.75 (s, 2H), 7.24-7.29 (m, 4H).



N-isopropyl-3-phenylpropan-1-amine (4ia):[17] white crystal (60.9 mg, 0.344 mmol, 69%); ^{1}H NMR ($CDCl_3$) δ= 1.04 (d, *J*=6.0 Hz, 6H), 1.79-1.83 (m, 2H), 2.26-2.67 (m, 4H), 2.77 (septet, *J*=6.4 Hz, 1H), 7.18-7.29 (m, 5H).



N-(pyridine-3-ylmethyl)propan-2-amine (4la):[18] yellow oil (60.1 mg, 0.400 mmol, 80%); ^{1}H NMR ($CDCl_3$) δ= 1.09 (d, *J*=6.2 Hz, 6H), 1.46 (bs, 1H), 2.85 (septet, *J*=6.3 Hz, 1H), 3.80 (s, 2H), 7.23-7.27 (m, 1H), 7.66 (d, *J*=7.5 Hz, 1H), 8.49 (d, *J*=4.8 Hz, 1H), 8.56 (s, 1H).



N-benzylpentan-2-amine (4ac):[19] yellow oil (62.9 mg, 0.355 mmol, 71%); ^{1}H NMR ($CDCl_3$) δ= 0.89-0.91 (t, *J*=7.0 Hz, 3H), 1.09 (d, *J*=6.4 Hz, 3H), 1.32-1.50 (m, 4H), 1.75 (bs, 1H), 2.70 (heptet, *J*=6.3 Hz, 1H), 3.74 (d, *J*=13.1 Hz, 1H), 3.83 (d, *J*=13.1 Hz, 1H), 7.24-7.33 (m, 5H).

3. Reference

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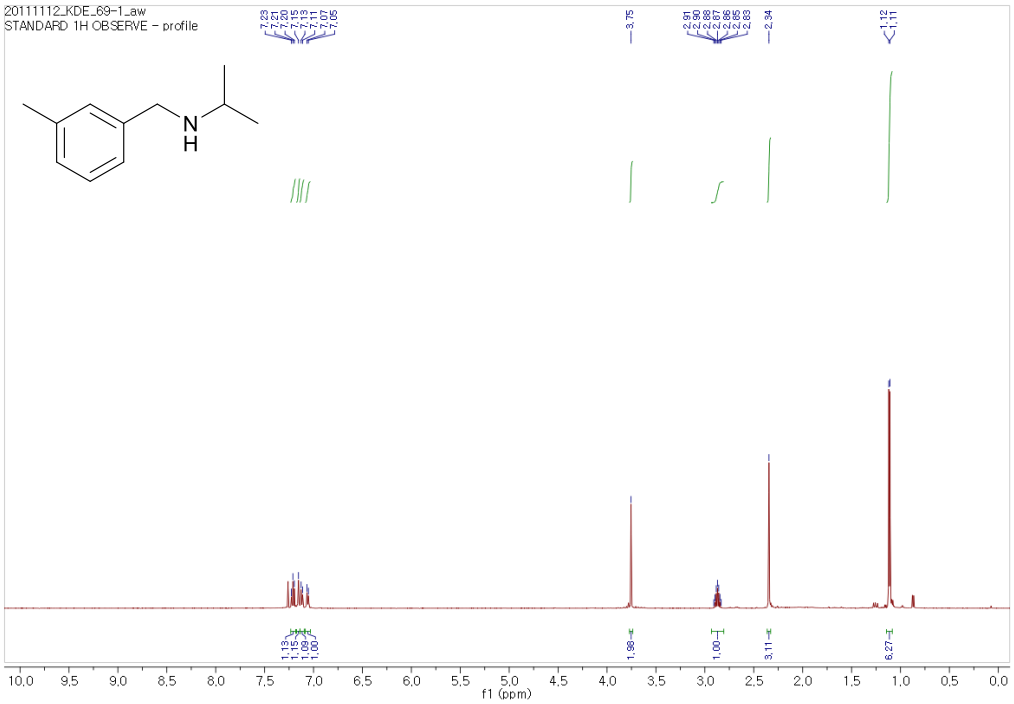
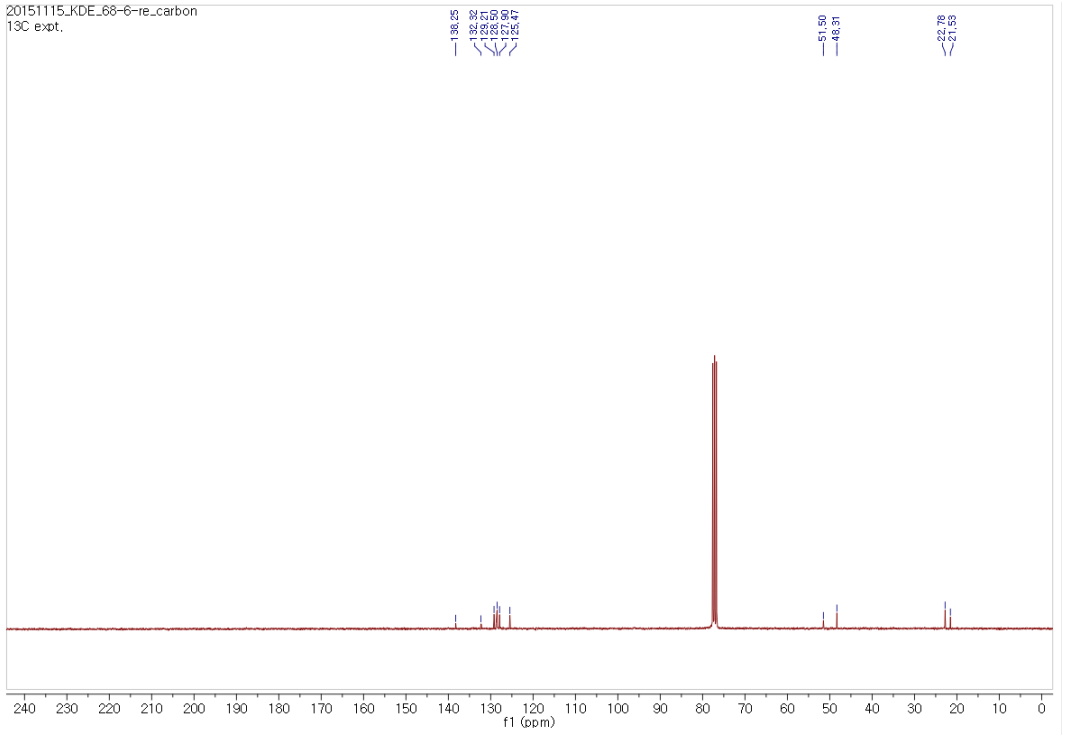
4. NMR spectra

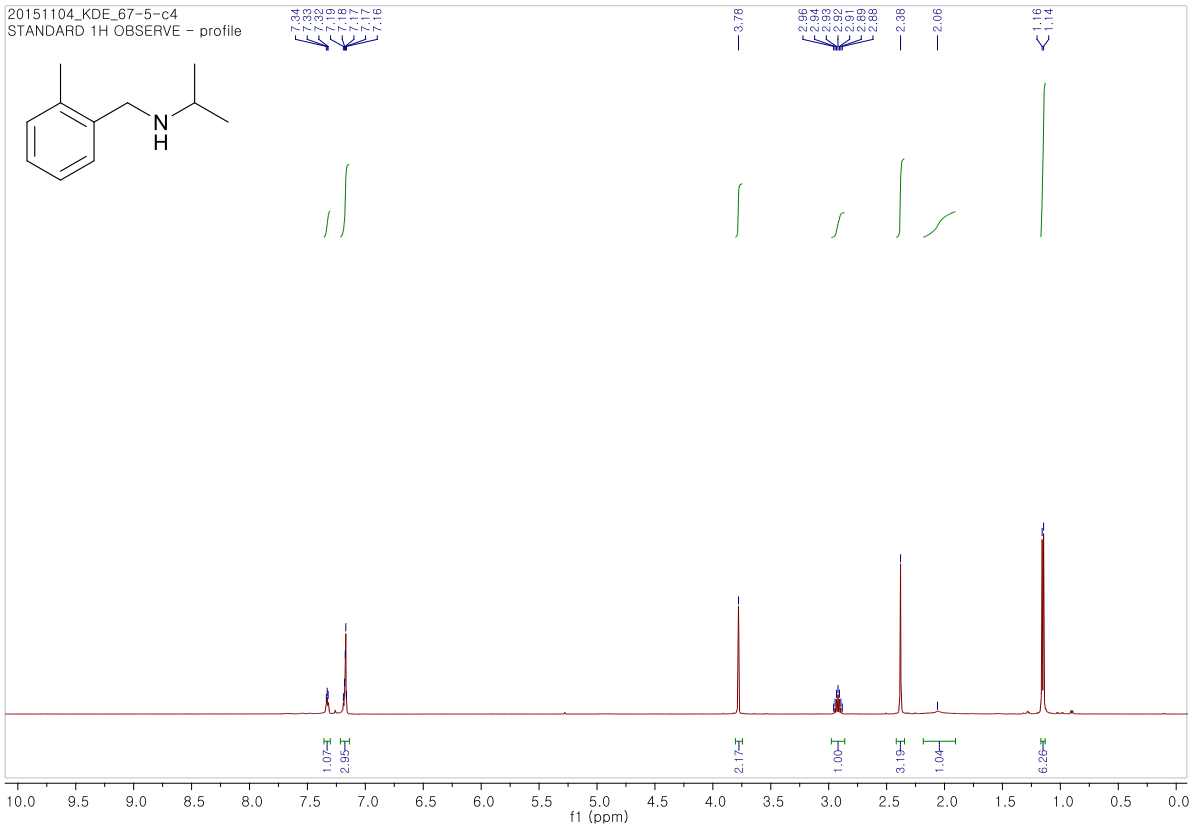
^{1}H NMR (**4ca**) ($CDCl_3$)



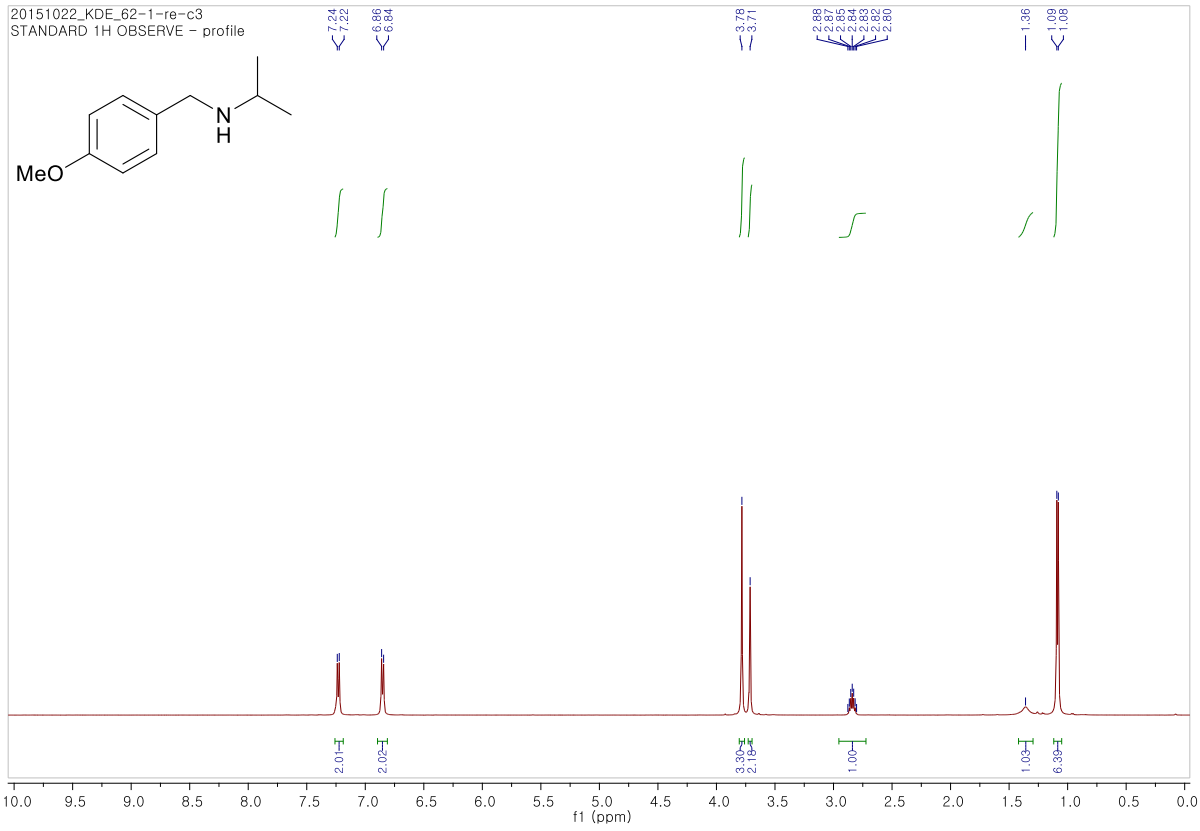
^{13}C NMR (**4ca**) ($CDCl_3$)



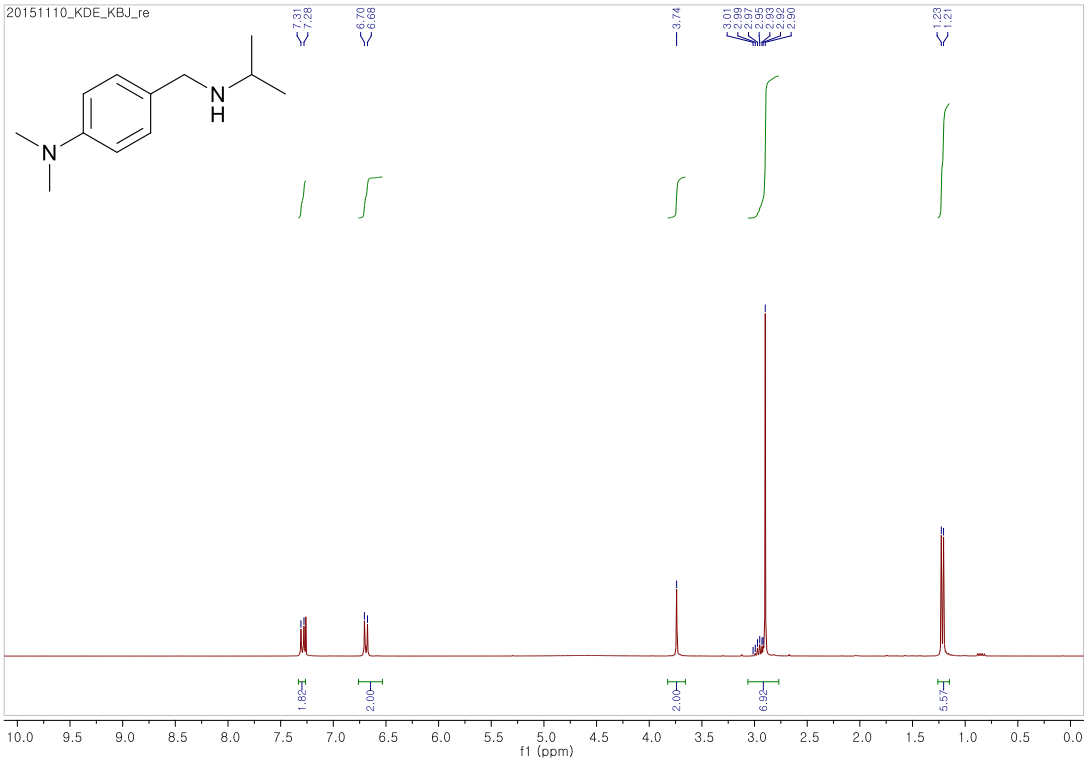
^{1}H NMR (**4da**) ($CDCl_3$)



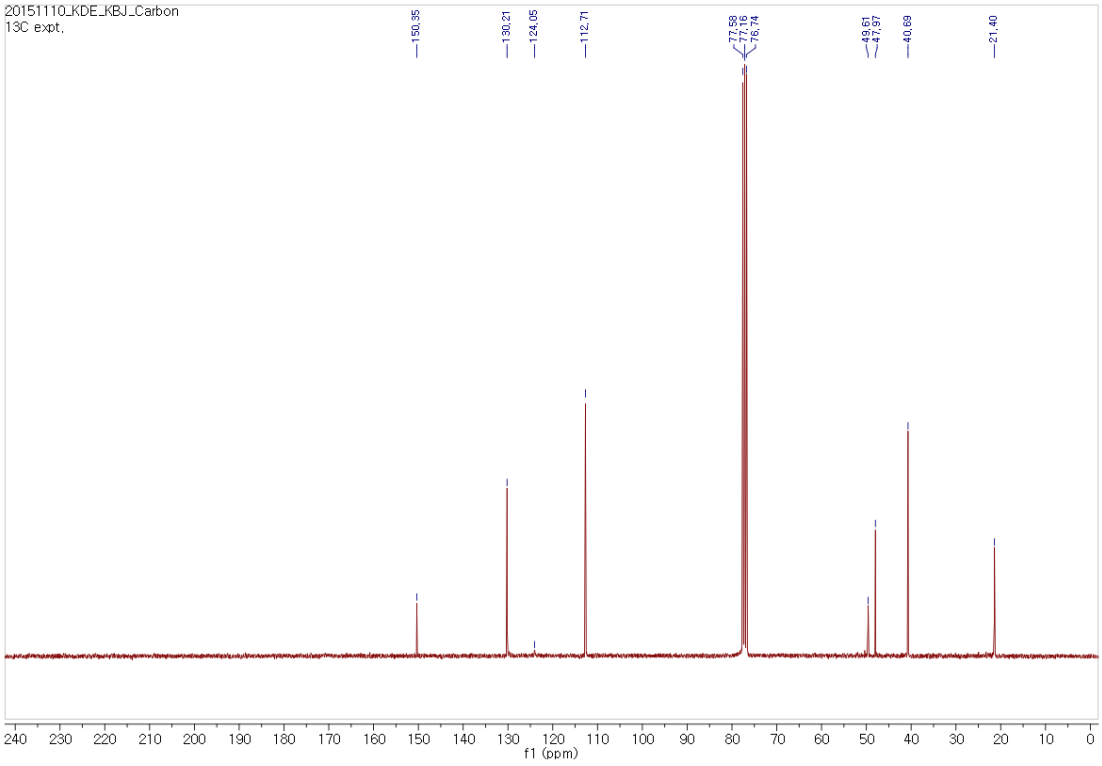
^{1}H NMR (**4ea**) ($CDCl_3$)



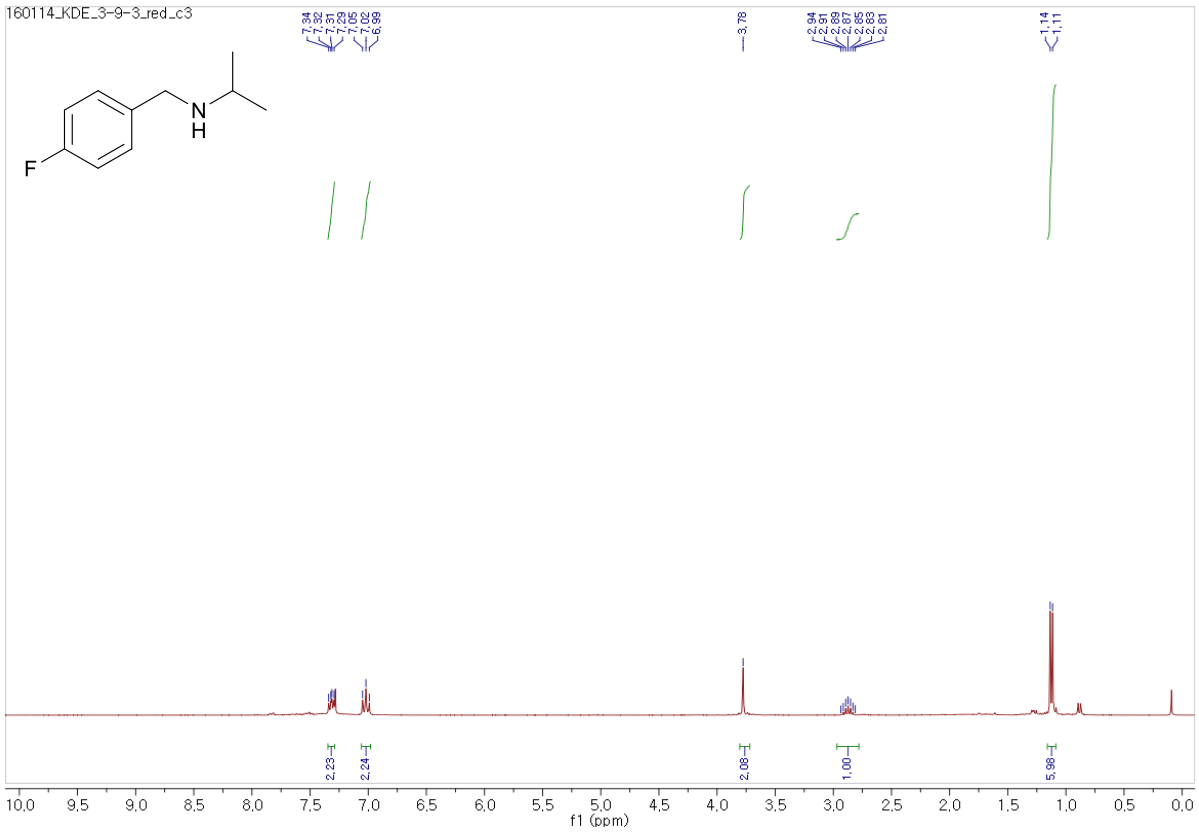
^{1}H NMR (**4fa**) ($CDCl_3$)



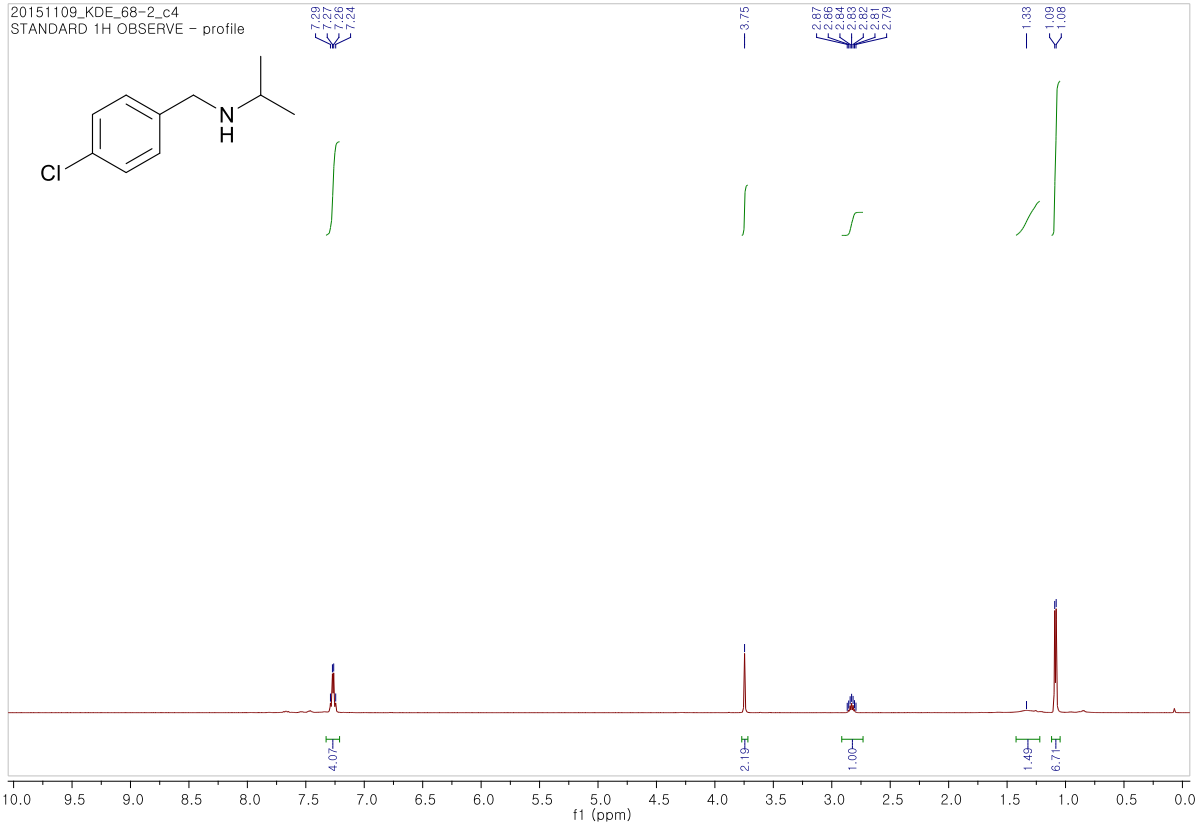
^{13}C NMR (**4fa**) ($CDCl_3$)



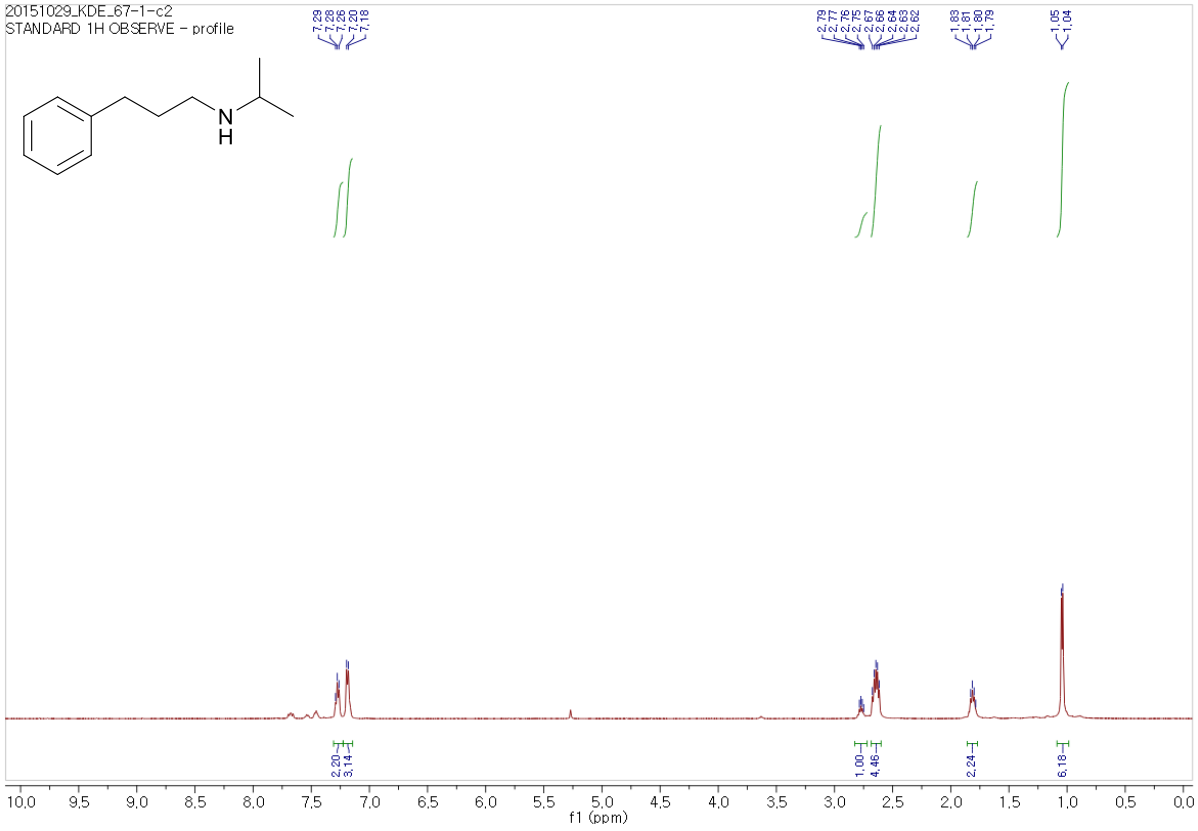
^{1}H NMR (**4ga**) ($CDCl_3$)



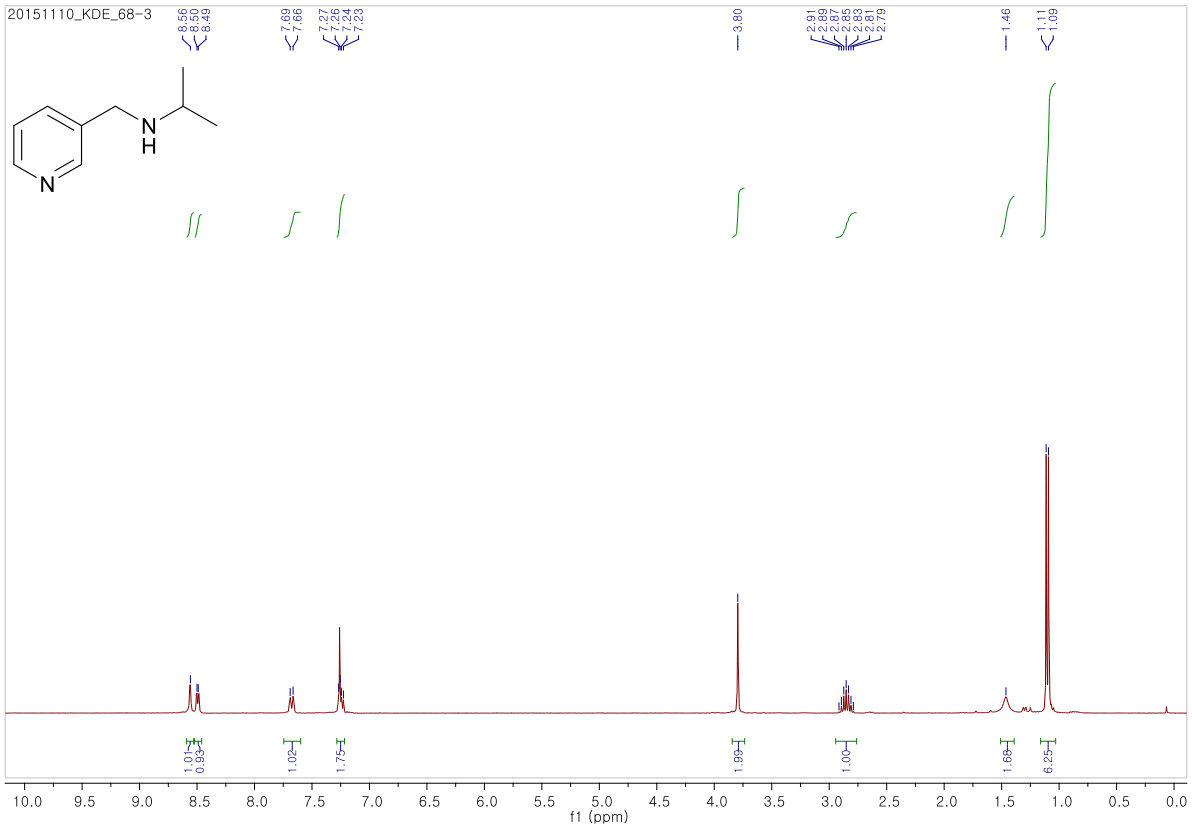
^{1}H NMR (**4ha**) ($CDCl_3$)



^{1}H NMR (**4ia**) ($CDCl_3$)



^{1}H NMR (**4la**) ($CDCl_3$)



^{1}H NMR (**4ac**) ($CDCl_3$)