Supplementary Information

Hydrogenation of Amides Catalyzed by Combined Catalytic System of Ru Complex with Zinc Salt

Yusuke Kita, Takafumi Higuchi, Kazushi Mashima*
Department of Chemistry, Graduate School of Engineering Science, Osaka University
and CREST, JST, Toyonaka, Osaka 560-8531, Japan
mashima@chem.es.osaka-u.ac.jp

Contents

General information S2
Physical measurements S2
General procedure for the catalytic hydrogenation of amides S2
Synthetic procedure of complexes S3
Optimization studies S4
Mechanistic studies S6
Spectral Data S9
$^1$H and $^{13}$C NMR spectra of products S17
General information

All manipulations involving air- and moisture-sensitive compounds were carried out under an argon atmosphere by using of standard vacuum line and Schlenk tube techniques. 1PrOH and Pr2O were distilled under an argon atmosphere from the calcium hydride. Alternatively, toluene, THF, MeCN and hexane were dried and deoxygenated by using Grubbs column (Glass Counter Solvent Dispending System, Nikko Hansen & Co, Ltd.). 1,4-Dioxane was distilled over sodium benzophenone ketyl under an argon atmosphere. Amide substrates were synthesized by standard condensation reaction of acyl chlorides and amines. Zn(OCOCF3)2O was prepared according to literature procedure.1 All other reagents were purchased at the highest commercial quality and used without further purification. Flash column chromatography was performed using silica gel 60 (0.040–0.063 mm, 230–400 mesh ASTM). Hydrogenation was conducted with TAIATSU stainless autoclave.

Physical measurements

1H NMR (300 MHz, 400 MHz), 13C NMR (75MHz, 100 MHz), 19F NMR (376 MHz) and 31P NMR (160 MHz) spectra were measured on Varian Unity Inova-300 and Bruker Avance III-400 spectrometers in 5 mm NMR tubes. All 1H NMR chemical shifts were reported in ppm relative to the residual solvent protons in chloroform-d1 at δ 7.26, benzene-d6 at δ 7.16, dichloromethane-d2 at δ 5.32 and 1,4-dioxane-d8 at δ 3.53. All 13C NMR chemical shifts were reported in ppm relative to carbon resonance in chloroform-d1 at δ 77.16 and dichloromethane-d2 at δ 53.84. All 19F NMR chemical shifts were reported in ppm relative to an external reference of α,α,α-trifluorotoluene at δ -63.9. 31P NMR chemical shifts were recorded in ppm (δ) relative to 85% H3PO4 as an external standard at δ 0.00. GC analyses were recorded on a Shimadzu GC-2014 gas chromatograph with J&W Scientific DB-5 column. Mass spectra were obtained on Bruker Daltonics MicroTOF. IR spectra were recorded on a JASCO FT/IR-230 spectrometer. X-ray crystallographic studies were performed on Rigaku R-AXIS RAPID imaging plate area detector or Rigaku AFC7R/Mercury CCD detector with graphite-monochromated Mo Kα radiation (λ = 0.71075). The elemental analysis was recorded by Perkin-Elmer 2400 at the Faculty of Engineering Science, Osaka University. All melting point were recorded on BUCHI melting point M-565. Elemental analyses were recorded by using Perkin-Elmer 2400 at the Faculty of Engineering Science, Osaka University.

General procedure for the catalytic hydrogenation of amides

A glass tube was charged appropriate amide (1.0 mmol), RuCl2(L1)2 (0.020 mmol), KO2Bu (0.20 mmol) and Zn(OCOCF3)2 (0.040 mmol). The glass tube was placed in an autoclave after three cycles of evacuation/argon backfilling, 1,4-dioxane (3.0 mL) was added to from the inlet, the mixture was charged with H2, and then the hydrogen pressure was increased to 3.0 MPa. The
reaction mixture was stirred at 100 °C for 18 h. The mixture was cooled to r.t. After release of H₂, dodecane was added to the mixture. The yield was determined by GC analysis.

**Synthetic procedure of complexes**

- **Synthesis of \([\text{RuCl}_2(\text{L1})_2]^2\)**

\[
\begin{array}{c}
\text{Ru}([\text{PPh}_3]_2\text{Cl}_2) \\
\text{Ph}_2\text{P}-\text{NH}_2 \\
\text{L1} \\
toluene, 100 °C, 6 h
\end{array}
\rightarrow
\begin{array}{c}
\text{H}_2 \\
\text{Cl} \\
\text{H}_2 \\
\text{N} \\
\text{P} \\
\text{Ph}_2\text{Cl} \\
\text{Ph}_2
\end{array}
\]

\[
\text{Ru}([\text{PPh}_3]_2\text{Cl}_2) \stackrel{\text{Ph}_2\text{P}-\text{NH}_2}{\text{L1}} \rightarrow \text{Ru}([\text{PPh}_3]_2\text{Cl}_2)
\]

84% yield

\[\text{Ph}_2\text{PCH}_2\text{CH}_2\text{NH}_2 \ (\text{L1}, 0.50 \text{ mmol}), \ [\text{RuCl}_2(\text{PPh}_3)_3] \ (0.25 \text{ mmol}) \text{ and toluene (5.0 mL) were added to a schlenk tube equipped with a magnetic stir bar. The mixture was then heated at 100 °C for 6 h. The yellow suspension that resulted was allowed to cool to r.t. before collecting the precipitate by filtration. The precipitate was then washed with 10.0 mL portions of toluene three times. The yellow solid was then dried in vacuo. Yield 133 mg (84%). NMR spectra were described in reference 2.}\]

- **Synthesis of \([\text{Ru(dppp)}_2]\text{Cl}_2^3\)**

\[
\begin{array}{c}
\text{RuCl}_2(\text{PPh}_3)_3 \\
\text{Ph}_2\text{P}-\text{PPh}_2 \\
st\text{dppp (2.1 equiv.)} \\
hexane (50 mL) \\
\text{reflux, 2 h}
\end{array}
\rightarrow
\begin{array}{c}
\text{[Ru(dppp)}_2\text{Cl}_2
\end{array}
\]

A suspension of [RuCl₂(PPh₃)₃] (500 mg, 0.52 mmol, 1.0 equiv) and Ph₂P(CH₂)₃PPh₂ (dppp, 442 mg, 1.07 mmol, 2.1 equiv) in hexane (50 mL) was refluxed for 2 h. The black suspension gradually became pale orange. The product was filtered off while hot, washed with hot hexane, and dried in vacuo. Yield 502 mg (97%). NMR spectra were described in reference 3.

- **Synthesis of \([\text{Ru(dppp)}(\text{dpen})]\text{Cl}_2^3\)**

(±)-1,2-diphenylethylenediamine (dpen, 116 mg, 0.55 mmol, 1.1 equiv) was dissolved in 10 mL of CH₂Cl₂ and the solution was added dropwise to a stirred solution of [Ru(dppp)₂]Cl₂ (500 mg, 0.50 mmol, 1.0 equiv) in 10 mL of CH₂Cl₂ within 10 min. The mixture was stirred for 2 days at room temperature while the color changed from brown to reddish brown. After removal of any turbidity by filtration, the volume of solution was concentrated to about 5 mL under reduced pressure. Addition of 40 mL of Et₂O caused precipitation of a yellow solid, which was filtered and dried in
NMR spectra were described in reference 3.

**Optimization studies**

We screened a variety of conditions such as additive (Table S1), base (Table S2), catalyst (Table S3), solvent (Table S4), hydrogen pressure, concentration, and temperature (Table S5).

**Table S1 Screening of additive**

```
<table>
<thead>
<tr>
<th>entry</th>
<th>additive</th>
<th>yield (%)</th>
<th>entry</th>
<th>additive</th>
<th>yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>LiCl</td>
<td>72</td>
<td>9</td>
<td>CuCl</td>
<td>68</td>
</tr>
<tr>
<td>2</td>
<td>NaCl</td>
<td>57</td>
<td>10</td>
<td>CuCl₂</td>
<td>35</td>
</tr>
<tr>
<td>3</td>
<td>CrCl₂</td>
<td>63</td>
<td>11</td>
<td>ZnCl₂</td>
<td>73</td>
</tr>
<tr>
<td>4</td>
<td>CrCl₃(THF)₃</td>
<td>68</td>
<td>12</td>
<td>PdCl₂</td>
<td>54</td>
</tr>
<tr>
<td>5</td>
<td>MnCl₂</td>
<td>67</td>
<td>13</td>
<td>AgCl</td>
<td>62</td>
</tr>
<tr>
<td>6</td>
<td>FeCl₂</td>
<td>72</td>
<td>14</td>
<td>InCl₃</td>
<td>70</td>
</tr>
<tr>
<td>7</td>
<td>FeCl₃</td>
<td>69</td>
<td>15</td>
<td>CeCl₃</td>
<td>71</td>
</tr>
<tr>
<td>8</td>
<td>NiCl₂</td>
<td>39</td>
<td>16</td>
<td>PtCl₂</td>
<td>45</td>
</tr>
</tbody>
</table>
```

\(^{a}\) The yield was determined by GC analysis with dodecane as an internal standard.

**Table S2 Screening of base**

```
<table>
<thead>
<tr>
<th>entry</th>
<th>base</th>
<th>yield (%)</th>
<th>entry</th>
<th>base</th>
<th>yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NaOMe</td>
<td>74</td>
<td>4</td>
<td>NaOtBu</td>
<td>79</td>
</tr>
<tr>
<td>2</td>
<td>KOMe</td>
<td>77</td>
<td>5</td>
<td>KOTBu</td>
<td>80</td>
</tr>
<tr>
<td>3</td>
<td>K₂CO₃</td>
<td>n.d.</td>
<td>6</td>
<td>DBU</td>
<td>n.d.</td>
</tr>
</tbody>
</table>
```

\(^{a}\) The yield was determined by GC analysis with dodecane as an internal standard.
Table S3 Screening of catalyst

<table>
<thead>
<tr>
<th>entry</th>
<th>Ru complex</th>
<th>yield(^a) (%)</th>
<th>entry</th>
<th>Ru complex</th>
<th>yield(^a) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>RuCl(_2)(L1)(_2)</td>
<td>92</td>
<td>3</td>
<td>RuCl(_2)(dppp)(dpen)</td>
<td>n.d.</td>
</tr>
<tr>
<td>2</td>
<td>RuCl(_2)(L2)(_2)</td>
<td>n.d.</td>
<td>4</td>
<td>Ru(<em>3)(CO)(</em>{12})</td>
<td>n.d.</td>
</tr>
</tbody>
</table>

\(^a\) The yield was determined by GC analysis with dodecane as an internal standard. \(L2 = Bu_2PCH_2CH_2NH_2\)

Table S4 Screening of solvent

<table>
<thead>
<tr>
<th>entry</th>
<th>solvent</th>
<th>yield(^a) (%)</th>
<th>entry</th>
<th>solvent</th>
<th>yield(^a) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1(^{Pr})OH</td>
<td>80</td>
<td>5</td>
<td>toluene</td>
<td>85</td>
</tr>
<tr>
<td>2</td>
<td>THF</td>
<td>87</td>
<td>6</td>
<td>hexane</td>
<td>33</td>
</tr>
<tr>
<td>3</td>
<td>1(^{Pr}_2)O</td>
<td>85</td>
<td>7</td>
<td>MeCN</td>
<td>n.d.</td>
</tr>
<tr>
<td>4</td>
<td>1,4-dioxane</td>
<td>92</td>
<td>8</td>
<td>DCE</td>
<td>n.d.</td>
</tr>
</tbody>
</table>

\(^a\) The yield was determined by GC analysis with dodecane as an internal standard.
Table S5 Optimization study

<table>
<thead>
<tr>
<th>entry</th>
<th>KO'Bu (mol%)</th>
<th>Zn(TFA)₂ (mol%)</th>
<th>H₂ (MPa)</th>
<th>1,4-dioxane (mL)</th>
<th>temp. (°C)</th>
<th>yielda (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50</td>
<td>5.0</td>
<td>3.0</td>
<td>5.0</td>
<td>120</td>
<td>92</td>
</tr>
<tr>
<td>2</td>
<td>50</td>
<td>5.0</td>
<td>3.0</td>
<td>5.0</td>
<td>100</td>
<td>83</td>
</tr>
<tr>
<td>3</td>
<td>50</td>
<td>5.0</td>
<td>3.0</td>
<td>5.0</td>
<td>80</td>
<td>37</td>
</tr>
<tr>
<td>4</td>
<td>50</td>
<td>5.0</td>
<td>3.0</td>
<td>3.0</td>
<td>100</td>
<td>90</td>
</tr>
<tr>
<td>5</td>
<td>50</td>
<td>5.0</td>
<td>3.0</td>
<td>3.0</td>
<td>80</td>
<td>55</td>
</tr>
<tr>
<td>6</td>
<td>50</td>
<td>5.0</td>
<td>3.0</td>
<td>2.0</td>
<td>100</td>
<td>84</td>
</tr>
<tr>
<td>7</td>
<td>50</td>
<td>5.0</td>
<td>3.0</td>
<td>1.0</td>
<td>100</td>
<td>83</td>
</tr>
<tr>
<td>8</td>
<td>20</td>
<td>5.0</td>
<td>3.0</td>
<td>3.0</td>
<td>100</td>
<td>87</td>
</tr>
<tr>
<td>9</td>
<td>10</td>
<td>5.0</td>
<td>3.0</td>
<td>3.0</td>
<td>100</td>
<td>n.d.</td>
</tr>
<tr>
<td>10</td>
<td>20</td>
<td>10.0</td>
<td>3.0</td>
<td>3.0</td>
<td>100</td>
<td>n.d.</td>
</tr>
<tr>
<td>11</td>
<td>20</td>
<td>2.0</td>
<td>3.0</td>
<td>3.0</td>
<td>100</td>
<td>95</td>
</tr>
<tr>
<td>12</td>
<td>20</td>
<td>2.0</td>
<td>2.0</td>
<td>3.0</td>
<td>100</td>
<td>80</td>
</tr>
<tr>
<td>13</td>
<td>20</td>
<td>2.0</td>
<td>1.0</td>
<td>3.0</td>
<td>100</td>
<td>56</td>
</tr>
<tr>
<td>14</td>
<td>20</td>
<td>0.0</td>
<td>3.0</td>
<td>3.0</td>
<td>100</td>
<td>74</td>
</tr>
<tr>
<td>15</td>
<td>20</td>
<td>2.0</td>
<td>3.0</td>
<td>3.0</td>
<td>100</td>
<td>n.d.</td>
</tr>
</tbody>
</table>

* The yield was determined by GC analysis with dodecane as an internal standard. b Without [RuCl₂(L1)₂].

Mechanistic studies

We measured $^{31}$P{³¹H}NMR of a mixture of [RuCl₂(L1)₂] (0.010 mmol), KO'Bu (0.020 mmol) and Zn(OCOCF₃)₂ (0.020 mmol) in 1,4-dioxane-d₈ (0.50 mL). New singlet peaks were appeared at 62.3 and 62.6 ppm (Figure S1). Then, the mixture was heated at 100 °C for 3h. The intensity of the peak at 62.6 ppm was increased compared with that of 62.3 ppm. One of them could be assigned to [Ru(OCOCF₃)₂(L1)₂] after the isolation by the extraction by toluene and subsequent filtration (see below).
**Figure S1** $^{31}\text{P} [^{1}\text{H}]$ NMR spectra of NMR experiments. a) Ruthenium catalyst precursor only, b) isolated $[\text{Ru(OOCF}_3^2\text{)(L1)}_2]$, c) a solution of $[\text{RuCl}_2(L1)_2]$, KO'Bu, and Zn(OOCF$_3$)$_2$ after 5 min mixing at room temperature, d) a solution of $[\text{RuCl}_2(L1)_2]$, KO'Bu, and Zn(OOCF$_3$)$_2$ after heating at 100 °C, 3 h.

**Synthesis of $[\text{Ru(OOCF}_3^2\text{)(L1)}_2] (4)$**

$$[\text{RuCl}_2(L1)_2] + \text{Zn(OOCF}_3^2] \xrightarrow{\text{KO'Bu, 1,4-dioxane (0.02 M)}} [\text{Ru(OOCF}_3^2\text{)(L1)}_2]$$

A mixture of RuCl$_2$(L1)$_2$ (126.1 mg, 0.20 mmol), Zn(OOCF$_3$)$_2$ (116.6 mg, 0.40 mmol) and KO'Bu (44.9 mg, 0.40 mmol) in 1,4-dioxane (10 mL) was stirred at 100 °C for 18 h under an argon atmosphere. After 1,4-dioxane was removed *in vacuo*, the residue was extracted by toluene and filtrated by celite under an argon atmosphere. The filtrate was concentrated *in vacuo* and Ru(OOCF$_3$)$_2$(L1)$_2$ (4) was obtained as yellow solid. Yield 97.0 mg (77%). Crystals suitable for X-ray diffraction were grown by vapor diffusion of *n*-hexane into a saturated 1,4-dioxane solution.

Mp 140 °C (dec.); IR (KBr, ν/cm$^{-1}$) 3314 w, 3060 w, 1678 s, 1434 m, 1197 s, 1136 m, 1100 m, 693 m; $^{1}$H NMR (400 MHz, CD$_2$Cl$_2$, 30 °C) δ 2.6-2.7 (m, 4H, methylene), 3.1-3.2 (m, 4H, methylene), 5.41 (br s, 4H, NH$_2$), 7.0-7.4 (m, 20H, Ar); $^{13}$C NMR (100 MHz, CD$_2$Cl$_2$, 30 °C) δ 33.8 (d, $J_{C-P}$ = 14 Hz), 33.9 (d, $J_{C-P}$ = 12 Hz), 113.7 (q, $J_{C-F}$ = 291 Hz), 128.16 (d, $J_{C-P}$ = 5 Hz), 128.21 (d, $J_{C-P}$ = 4 Hz), 129.8, 133.40 (d, $J_{C-P}$ = 5 Hz), 133.45 (d, $J_{C-P}$ = 5 Hz), 135.3 (d, $J_{C-P}$ = 15 Hz), 135.5 (d, $J_{C-P}$ = 19 Hz), 135.7 (d, $J_{C-P}$ = 19 Hz), 135.9 (d, $J_{C-P}$ = 15 Hz), 166.5 (q, $J_{C-F}$ = 36 Hz); $^{19}$F NMR (376 MHz, CD$_2$Cl$_2$, 30 °C) δ −75.6; $^{31}$P NMR (162 MHz, CD$_2$Cl$_2$, 30 °C) δ 62.0; MS (ESI) m/z 673
([M-OCOCF₃⁺]); HRMS (ESI) m/z calcd. for C₃₀H₃₂F₃N₂O₂P₂Ru 673.0935 ([M-OCOCF₃⁺]) found 673.0959. Anal. Calcd for C₃₂H₃₂F₆N₂O₄P₂Ru: C, 48.92; H, 4.11; N, 3.57. Found: C, 48.34; H, 3.89; N, 3.46.

**Figure S2** Molecular structure of 4. All hydrogen atoms are omitted for clarity.

**Table S5** Crystal data and data collection parameters.

<table>
<thead>
<tr>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>empirical formula</td>
</tr>
<tr>
<td>formula weight</td>
</tr>
<tr>
<td>crystal system</td>
</tr>
<tr>
<td>space group</td>
</tr>
<tr>
<td>a, Å</td>
</tr>
<tr>
<td>b, Å</td>
</tr>
<tr>
<td>c, Å</td>
</tr>
<tr>
<td>α, deg.</td>
</tr>
<tr>
<td>β, deg.</td>
</tr>
<tr>
<td>γ, deg.</td>
</tr>
<tr>
<td>V, Å³</td>
</tr>
<tr>
<td>Z</td>
</tr>
</tbody>
</table>

S8
<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dcalcd, g/cm⁻³</td>
<td>1.570</td>
</tr>
<tr>
<td>μ [Mo-Kα], mm⁻¹</td>
<td>0.641</td>
</tr>
<tr>
<td>T, K</td>
<td>113(2)</td>
</tr>
<tr>
<td>crystal size, mm</td>
<td>0.14 x 0.11 x 0.06</td>
</tr>
<tr>
<td>θ range for data collection (deg.)</td>
<td>3.04 to 24.15</td>
</tr>
<tr>
<td>no. of reflections measured</td>
<td>15791</td>
</tr>
<tr>
<td>unique data (Rint)</td>
<td>7288 (0.1124)</td>
</tr>
<tr>
<td>data / restraints / parameters</td>
<td>5059 / 0 / 352</td>
</tr>
<tr>
<td>R1 (I &gt; 2.0σ(I))</td>
<td>0.1234</td>
</tr>
<tr>
<td>wR2 (I &gt; 2.0σ(I))</td>
<td>0.3060</td>
</tr>
<tr>
<td>R1 (all data)</td>
<td>0.1648</td>
</tr>
<tr>
<td>wR2 (all data)</td>
<td>0.3475</td>
</tr>
<tr>
<td>GOF on F²</td>
<td>1.131</td>
</tr>
<tr>
<td>Δρ, e Å⁻³</td>
<td>2.30, -1.18</td>
</tr>
</tbody>
</table>

a) \( R1 = (\Sigma|Fo| - |Fc|)/(|Fo|) \)  
b) \( wR2 = [(\Sigma w(Fo^2-Fe^2)^2)/(|Fo|^4)]^{1/2} \)

**Spectral Data**

**1a**: N-methylbenzamide  CAS: 88070-48-8

![Structure of 1a](image)

White solid; \(^1^H\) NMR (400 MHz, CDCl₃, 30 °C) δ 3.01 (d, \( J = 4.9 \) Hz, 3H, \( CH_3 \)), 6.20 (br s, 1H, NH), 7.4-7.5 (m, 3H, Ar), 7.7-7.8 (m, 2H, Ar); \(^{13}\)C NMR (100 MHz, CDCl₃, 30 °C) δ 26.9, 127.0, 128.6, 131.4, 134.7, 168.4.

**1b**: N-methyl-4-(trifluoromethyl)benzamide  CAS: 65017-76-7

![Structure of 1b](image)

White solid; \(^1^H\) NMR (400 MHz, CDCl₃, 30 °C) δ 3.04 (d, \( J = 4.8 \) Hz, 3H, \( CH_3 \)), 6.17 (br s, 1H, NH), 7.70 (d, \( J = 8.0 \) Hz, 2H, Ar), 7.87 (d, \( J = 8.0 \), 2H, Ar); \(^{13}\)C NMR (100 MHz, CDCl₃, 30 °C) δ 27.1, 123.8 (q, \( J_{CF} = 273 \) Hz), 125.7 (q, \( J_{CF} = 4 \) Hz), 127.5, 133.3 (q, \( J_{CF} = 33 \) Hz), 138.0, 167.2; \(^{19}\)F NMR (376 MHz, CDCl₃, 30 °C) δ -63.0.
1c: 4-fluoro-N-methylbenzamide    CAS: 701-49-5

[Image of 4-fluoro-N-methylbenzamide]

White solid; $^1$H NMR (400 MHz, CDCl$_3$, 30 °C) δ 3.00 (d, $J = 4.8$ Hz, 3H, CH$_3$), 6.20 (br s, 1H, NH), 7.09 (dd, $J = 8.6$, 8.0 Hz, 2H, Ar), 7.7-7.8 (m, 2H, Ar); $^{13}$C NMR (100 MHz, CDCl$_3$, 30 °C) δ 27.0, 115.7 (d, $J_{CF} = 22$ Hz), 129.3 (d, $J_{CF} = 9$ Hz), 131.0 (d, $J_{CF} = 3$ Hz), 164.8 (d, $J_{CF} = 252$ Hz), 167.3; $^{19}$F NMR (376 MHz, CDCl$_3$, 30 °C) δ -108.5.

1d: 4-methoxy-N-methylbenzamide    CAS: 3400-22-4

[Image of 4-methoxy-N-methylbenzamide]

White solid; $^1$H NMR (400 MHz, CDCl$_3$, 30 °C) δ 2.99 (d, $J = 4.9$ Hz, 3H, CH$_3$), 3.84 (s, 3H, OCH$_3$), 6.07 (br s, 1H, NH), 6.91 (d, $J = 8.8$ Hz, 2H, Ar), 7.72 (d, $J = 8.8$ Hz, 2H, Ar); $^{13}$C NMR (100 MHz, CDCl$_3$, 30 °C) δ 26.9, 55.5, 113.8, 127.1, 128.8, 162.2, 167.9.

1e: 4-(dimethylamino)-N-methylbenzamide    CAS: 21176-94-3

[Image of 4-(dimethylamino)-N-methylbenzamide]

White solid; $^1$H NMR (400 MHz, CDCl$_3$, 30 °C) δ 2.99 (d, $J = 4.8$ Hz, 3H, CH$_3$), 3.01 (s, 6H, N(CH$_3$)$_2$), 5.96 (br s, 1H, NH), 6.67 (d, $J = 8.8$ Hz, 2H, Ar), 7.66 (d, $J = 8.8$ Hz, 2H, Ar); $^{13}$C NMR (100 MHz, CDCl$_3$, 30 °C) δ 26.7, 40.2, 111.2, 121.7, 121.7, 128.4, 152.4, 168.3.

1f: 2-fluoro-N-methylbenzamide    CAS: 52833-63-3

[Image of 2-fluoro-N-methylbenzamide]

White solid; $^1$H NMR (400 MHz, CDCl$_3$, 30 °C) δ 3.04 (d, $J = 4.8$ Hz, 3H, CH$_3$), 6.75 (br s, 1H, NH), 7.11 (dd, $J = 8.3$, 8.3 Hz, 1H, Ar), 7.2-7.3 (m, 1H, Ar), 7.4-7.5 (m, 1H, Ar), 8.11 (ddd, $J = 7.9$, 7.9, 1.6 Hz, 1H, Ar); $^{13}$C NMR (100 MHz, CDCl$_3$, 30 °C) δ 26.9, 116.1 (d, $J_{CF} = 25$ Hz), 121.2 (d, $J_{CF} = 12$ Hz), 124.9 (d, $J_{CF} = 3$ Hz), 132.2 (d, $J_{CF} = 2$ Hz), 133.3 (d, $J_{CF} = 9$ Hz), 160.8 (d, $J_{CF} = 247$ Hz).
164.1; $^{19}$F NMR (376MHz, CDCl$_3$, 30 °C) $\delta$ -114.1.

1g: 2-methoxy-N-methylbenzamide CAS: 3400-35-9

![Structure](image)

White solid; $^1$H NMR (400 MHz, CDCl$_3$, 30 °C) $\delta$ 3.00 (d, $J = 4.8$ Hz, 3H, $CH_3$), 3.94 (s, 3H, OCH$_3$), 5.96 (br s, 1H, NH), 6.67 (d, $J = 8.8$ Hz, 2H, Ar), 7.66 (d, $J = 8.8$ Hz, 2H, Ar); $^{13}$C NMR (100 MHz, CDCl$_3$, 30 °C) $\delta$ 26.7, 40.2, 111.2, 121.7, 121.7, 128.4, 152.4, 168.3.

1h: N,1-dimethyl-1H-indole-3-carboxamide CAS: 85729-23-3

![Structure](image)

White solid; $^1$H NMR (400 MHz, CDCl$_3$, 30 °C) $\delta$ 3.07 (d, $J = 4.8$ Hz, 3H, $CH_3$), 3.81 (s, 3H, NCH$_3$), 5.99 (br s, 1H, NH), 7.2-7.4 (m, 3H, Ar), 7.66 (s, 1H, Ar), 7.97 (d, $J = 7.6$ Hz, 1H, Ar); $^{13}$C NMR (100 MHz, CDCl$_3$, 30 °C) $\delta$ 26.4, 33.2, 110.0, 111.0, 120.4, 121.4, 122.5, 125.6, 132.1, 137.3, 166.1.

1i: N-methylhexanamide CAS: 3418-05-1

![Structure](image)

Colorless liquid; $^1$H NMR (400 MHz, CDCl$_3$, 30 °C) $\delta$ 0.85 (t, $J = 7.0$ Hz, 3H, $CH_3$), 1.2-1.3 (m, 4H, methylene), 1.5-1.6 (m, 2H, methylene), 2.13 (t, $J = 7.8$ Hz, 2H, $CH_2CO$), 2.76 (d, $J = 4.8$ Hz, 3H, NHCH$_3$), 5.90 (br s, 1H, NH); $^{13}$C NMR (100 MHz, CDCl$_3$, 30 °C) $\delta$ 13.9, 22.4, 25.5, 26.1, 31.5, 36.5, 174.3.

1j: N-methylcyclohexanecarboxamide CAS: 6830-84-8

![Structure](image)

White solid; $^1$H NMR (400 MHz, CDCl$_3$, 30 °C) $\delta$ 1.2-2.1 (m, 11H, methylene, methine), 2.79 (d, $J = 4.6$ Hz, 3H, $CH_3$), 5.53 (br s, 1H, NH); $^{13}$C NMR (100 MHz, CDCl$_3$, 30 °C) $\delta$ 25.9, 26.2, 45.6, 176.9.

1k: N,N-dimethylbenzamide CAS: 611-74-5
White solid; $^1$H NMR (400 MHz, CDCl$_3$, 30 ºC) δ 2.97 (s, 3H, $CH_3$), 3.08 (s, 3H, $CH_3$), 7.3-7.4 (m, 5H, Ar); $^{13}$C NMR (100 MHz, CDCl$_3$, 30 ºC) δ 35.3, 39.6, 127.1, 128.4, 129.5, 136.5, 171.6.

II: N-phenylbenzamide   CAS: 93-98-1

White solid; $^1$H NMR (400 MHz, CDCl$_3$, 30 ºC) δ 7.1-7.2 (m, 1H, Ar), 7.1-7.2 (m, 1H, Ar), 7.3-7.4 (m, 2H, Ar), 7.4-7.6 (m, 3H, Ar), 7.6-7.7 (m, 1H, Ar), 7.8-7.9 (m, 2H, Ar), 7.92 (br s, 1H, NH); $^{13}$C NMR (100 MHz, CDCl$_3$, 30 ºC) δ 120.4, 124.7, 127.2, 128.9, 129.2, 131.9, 135.2, 138.1, 165.9.

Im: N-propylbenzamide   CAS: 10546-70-0

White solid; $^1$H NMR (400 MHz, CDCl$_3$, 30 ºC) δ 0.99 (t, $J = 7.5$ Hz, 3H, CH$_2$CH$_3$), 1.6-1.7 (m, 2H, CH$_2$CH$_3$), 3.4-3.5 (m, 2H, NHCH$_2$), 6.17 (br s, 1H, NH), 7.4-7.5 (m, 3H, Ar), 7.7-7.8 (m, 2H, Ar); $^{13}$C NMR (100 MHz, CDCl$_3$, 30 ºC) δ 11.4, 22.9, 41.8, 126.8, 128.5, 131.3, 134.9, 167.5.

In: N-cyclohexylbenzamide   CAS: 1759-68-8

White solid; $^1$H NMR (400 MHz, CDCl$_3$, 30 ºC) δ 1.1-1.2 (m, 3H, methylene), 1.4-1.5 (m, 2H, methylene), 1.6-1.8 (m, 3H, methylene), 2.0-2.1 (m, 2H, methylene), 3.9-4.0 (m, 1H, NHCH), 5.96 (br s, 1H, NH), 7.4-7.5 (m, 3H, Ar), 7.7-7.8 (m, 2H, Ar); $^{13}$C NMR (100 MHz, CDCl$_3$, 30 ºC) δ 24.9, 25.6, 33.2, 48.7, 126.8, 128.5, 131.2, 135.2, 166.6.

Io: Benzamide   CAS: 55-21-0
White solid; $^1$H NMR (400 MHz, CDCl$_3$, 30 °C) δ 6.21 (br s, 2H, NH$_2$), 7.4-7.5 (m, 2H, Ar), 7.5-7.6 (m, 1H, Ar), 7.8-7.9 (m, 2H, Ar); $^{13}$C NMR (100 MHz, CDCl$_3$, 30 °C) δ 127.5, 128.7, 132.1, 133.5, 169.8.

2a: Benzyl alcohol   CAS:100-51-6

Colorless liquid; $^1$H NMR (400 MHz, CDCl$_3$, 30 °C) δ 1.79 (br s, OH), 4.69 (s, 1H, PhCH$_2$), 7.3-7.4 (m, 5H, Ar); $^{13}$C NMR (100 MHz, CDCl$_3$, 30 °C) δ 65.1, 127.0, 127.6, 128.5, 141.0.

2b: (4-(trifluoromethyl)phenyl)methanol   CAS: 349-95-1 air sensitive

Colorless liquid; $^1$H NMR (400 MHz, CDCl$_3$, 30 °C) δ 3.01 (br s, 1H, OH), 4.67 (s, 2H, ArCH$_2$), 7.40 (d, $J = 8.1$ Hz, 2H, Ar), 7.58 (d, $J = 8.1$ Hz, 2H, Ar); $^{13}$C NMR (100 MHz, CDCl$_3$, 30 °C) δ 64.3, 124.3 (q, $J_{C-F} = 272$ Hz), 125.5 (q, $J_{C-F} = 4$ Hz), 126.9, 129.9 (q, $J_{C-F} = 32$ Hz), 144.8; $^{19}$F NMR (376 MHz, CDCl$_3$, 30 °C) δ -62.6.

2c: (4-fluorophenyl)methanol   CAS: 459-56-3

Colorless liquid; $^1$H NMR (400 MHz, CD$_2$Cl$_2$, 30 °C) δ 1.95 (br s, 1H, OH), 4.63 (s, 2H, ArCH$_2$), 7.05 (dd, $J = 8.8$, 8.5 Hz, 2H, Ar), 7.3-7.4 (m, 2H, Ar); $^{13}$C NMR (100 MHz, CD$_2$Cl$_2$, 30 °C) δ 64.8, 115.6 (d, $J_{C-F} = 21$ Hz), 129.1 (d, $J_{C-F} = 8$ Hz), 137.6 (d, $J_{C-F} = 3$ Hz), 162.7 (d, $J_{C-F} = 244$ Hz); $^{19}$F NMR (376 MHz, CDCl$_3$, 30 °C) δ -116.1.

2d: 4-methoxybenzylalcohol   CAS: 105-13-5

Colorless liquid; $^1$H NMR (400 MHz, CDCl$_3$, 30 °C) δ 1.67 (br s, 1H, OH), 3.81 (s, 3H, OCH$_3$), 4.61
(s, 2H, ArCH$_2$), 6.89 (d, $J = 8.6$ Hz, 2H, Ar), 7.29 (d, $J = 8.6$ Hz, 2H, Ar); $^{13}$C NMR (100 MHz, CDCl$_3$, 30 ºC) δ 55.4, 65.2, 114.1, 128.8, 133.3, 159.4.

1e: (4-(dimethylamino)phenyl)methanol  CAS: 1703-46-4

[Chemical structure]

Colorless liquid; $^1$H NMR (400 MHz, CDCl$_3$, 30 ºC) δ 2.93 (s, 6H, N(CH$_3$)$_2$), 4.52 (s, 2H, ArCH$_2$), 6.6-6.7 (m, 2H, Ar), 7.1-7.2 (m, 2H, Ar); $^{13}$C NMR (100 MHz, CDCl$_3$, 30 ºC) δ 40.8, 65.4, 112.9, 128.7, 129.5, 150.9.

2f: (2-fluorophenyl)methanol  CAS: 446-51-5

[Chemical structure]

Colorless liquid; $^1$H NMR (400 MHz, CDCl$_3$, 30 ºC) δ 1.78 (br s, 1H, OH), 4.77 (s, 2H, ArCH$_2$OH), 7.0-7.1 (m, 1H, Ar), 7.1-7.2 (m, 1H, Ar), 7.2-7.3 (m, 1H, Ar), 7.4-7.5 (m, 1.6 Hz, 1H, Ar); $^{13}$C NMR (100 MHz, CDCl$_3$, 30 ºC) δ 59.3, 115.3 (d, $J_{CF} = 21$ Hz), 124.3 (d, $J_{CF} = 3$ Hz), 127.9 (d, $J_{CF} = 15$ Hz), 129.4 (d, $J_{CF} = 4$ Hz), 129.4 (d, $J_{CF} = 9$ Hz), 160.7 (d, $J_{CF} = 246$ Hz); $^{19}$F NMR (376MHz, CDCl$_3$, 30 ºC) δ -119.8.

2g: (2-methoxyphenyl)methanol  CAS: 612-16-8

[Chemical structure]

Colorless liquid; $^1$H NMR (400 MHz, CD$_2$Cl$_2$, 30 ºC) δ 2.52 (t, $J = 6.0$ Hz, 1H, OH), 3.86 (s, 3H, OCH$_3$), 4.65 (d, $J = 6.0$ Hz, 2H, ArCH$_2$), 6.9-7.0 (m, 2H, Ar), 7.2-7.3 (m, 2H, Ar); $^{13}$C NMR (100 MHz, CD$_2$Cl$_2$, 30 ºC) δ 55.6, 61.9, 110.6, 120.9, 128.8, 129.1, 129.9, 157.9.

2h: (1-methylindolin-3-yl)methanol  CAS: 795275-62-6

[Chemical structure]

Yellow oil; $^1$H NMR (400 MHz, CDCl$_3$, 30 ºC) δ 2.76 (s, 3H, NCH$_3$), 3.2-3.3 (m, 1H, ArCH$_2$CH$_2$), 3.4-3.5 (m, 2H, N(CH$_3$)CH$_2$), 3.7-3.8 (m, 2H, OHCH$_2$CH), 6.49 (d, 2H, $J = 7.6$ Hz, Ar), 6.69 (ddd, $J = 7.4$, 7.4, 0.9 Hz, 1H, Ar), 7.1-7.2 (m, 2H, Ar); $^{13}$C NMR (100 MHz, CDCl$_3$, 30 ºC) δ 36.0, 43.6,
58.9, 64.8, 107.5, 117.9, 124.2, 128.4, 130.1, 153.7.

2i: 1-hexanol CAS: 111-27-3

\[ \text{Colorless liquid; } ^1H \text{ NMR (400 MHz, CDCl}_3, 30 ^\circ \text{C}) \delta 0.89 (t, J = 6.2 \text{ Hz, } 1\text{H, CH}_3), 1.2-1.4 \text{ (m, 7H, methylene, O}_H), 1.5-1.6 \text{ (m, 2H, CH}_2\text{CH}_2\text{OH), 3.63 (t, J = 6.6 \text{ Hz, 2H, CH}_2\text{OH); } ^{13}\text{C NMR (100 MHz, CDCl}_3, 30 ^\circ \text{C}) \delta 14.1, 22.8, 25.6, 31.8, 32.9, 63.2.} \]

2j: cyclohexylmethanol CAS: 100-49-2

\[ \text{Colorless liquid; } ^1H \text{ NMR (400 MHz, CDCl}_3, 30 ^\circ \text{C}) \delta 0.9-1.8 \text{ (m, 12H, methylene, methane, O}_H), 3.43 (d, J = 6.3 \text{ Hz, 2H, CH}_2\text{OH); } ^{13}\text{C NMR (100 MHz, CDCl}_3, 30 ^\circ \text{C}) \delta 26.0, 26.7, 29.7, 40.7, 68.9.} \]

2p: 6-aminohexan-1-ol CAS: 4048-33-3

\[ \text{Colorless liquid; } ^1H \text{ NMR (400 MHz, CDCl}_3, 30 ^\circ \text{C}) \delta 1.3-1.6 \text{ (m, 11H, methylene, OH, NH}_2), 2.69 (t, J = 6.8 \text{ Hz, 2H, CH}_2\text{NH}_2), 3.63 (t, J = 6.6 \text{ Hz, 2H, CH}_2\text{OH); } ^{13}\text{C NMR (100 MHz, CDCl}_3, 30 ^\circ \text{C}) \delta 25.7, 26.7, 32.8, 33.6, 42.0, 62.2.} \]

2q: 5-aminohexan-1-ol CAS: 2508-29-4

\[ \text{Colorless liquid; } ^1H \text{ NMR (400 MHz, CDCl}_3, 30 ^\circ \text{C}) \delta 1.3-1.6 \text{ (m, 9H, methylene, OH, NH}_2), 2.71 (t, J = 6.6 \text{ Hz, 2H, CH}_2\text{NH}_2), 3.65 (t, J = 6.5 \text{ Hz, 2H, CH}_2\text{OH); } ^{13}\text{C NMR (100 MHz, CDCl}_3, 30 ^\circ \text{C}) \delta 23.1, 32.5, 33.2, 41.9, 61.8.} \]

3q: piperidine CAS: 110-89-4

\[ \text{Colorless liquid; } ^1H \text{ NMR (400 MHz, CDCl}_3, 30 ^\circ \text{C}) \delta 1.4-1.5 \text{ (m, 7H, methylene, NH), 2.7-2.8 (m, 4H, CH}_2\text{NHCH}_2), 13^\text{C NMR (100 MHz, CDCl}_3, 30 ^\circ \text{C}) \delta 25.0, 27.1, 47.3.} \]

References
$^1$H and $^{13}$C NMR spectra of products

![NMR spectra of product 2a](image)