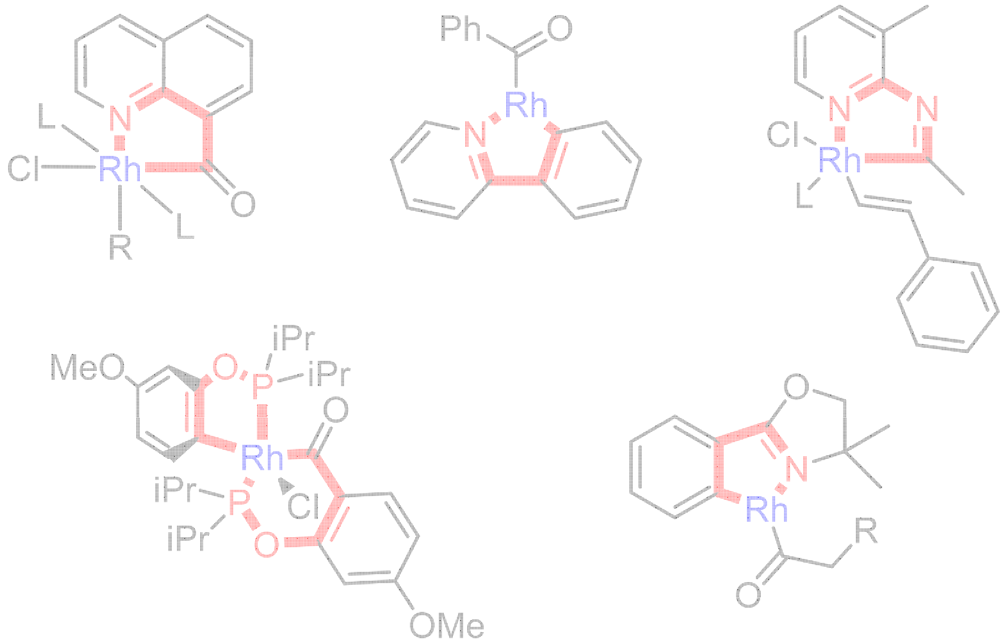
# Directed Cleavage of Unstrained Carbon-Carbon Bond

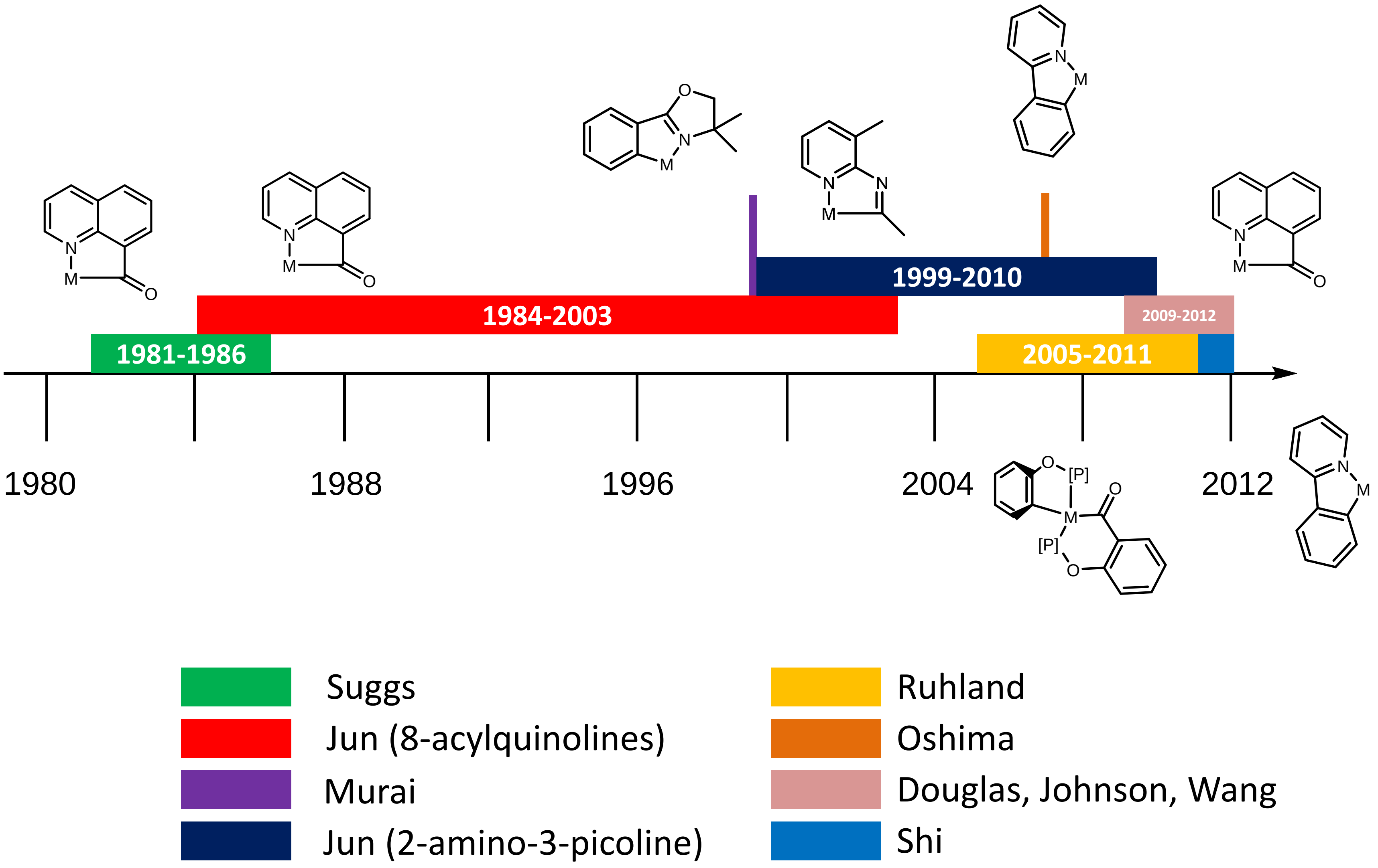



*Penghao Chen*

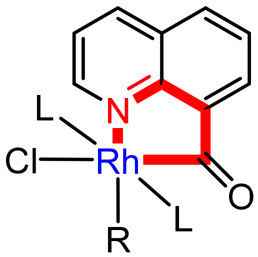
*Dong Group Seminar*

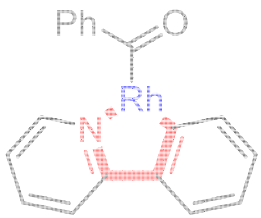

*November, 5th, 2014*

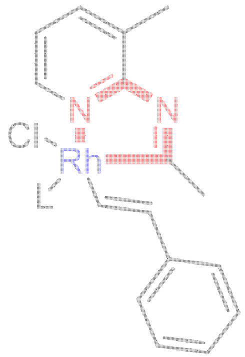
# Time-line of Directing Moieties

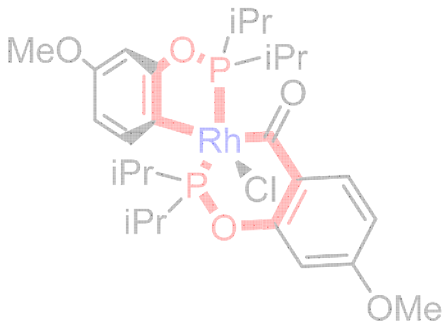


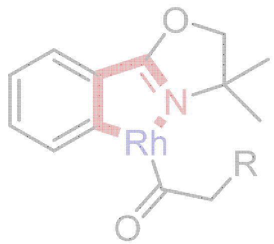
# 8-Acylquinolines



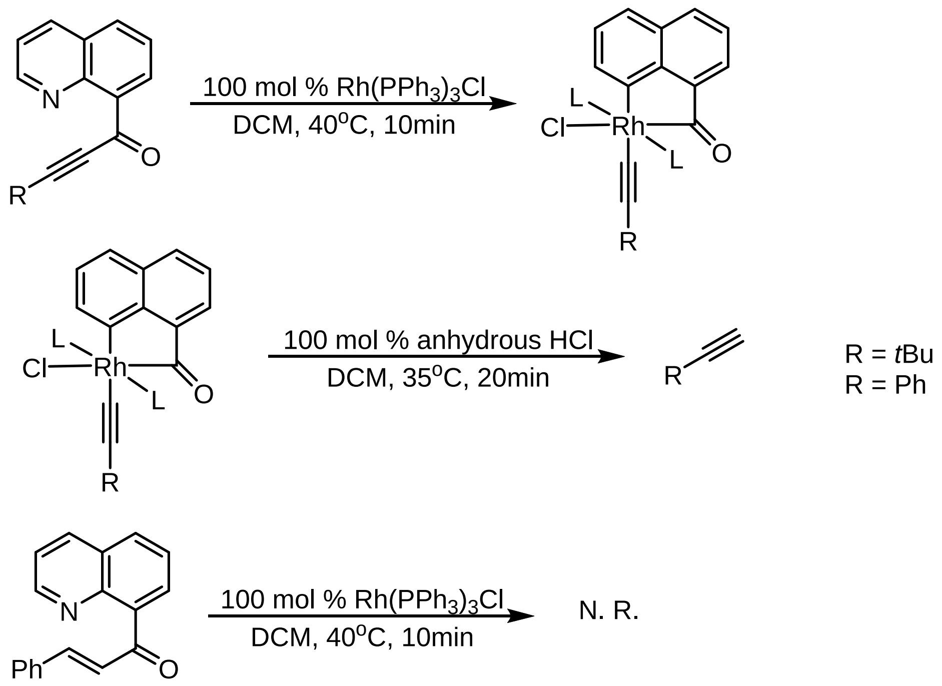



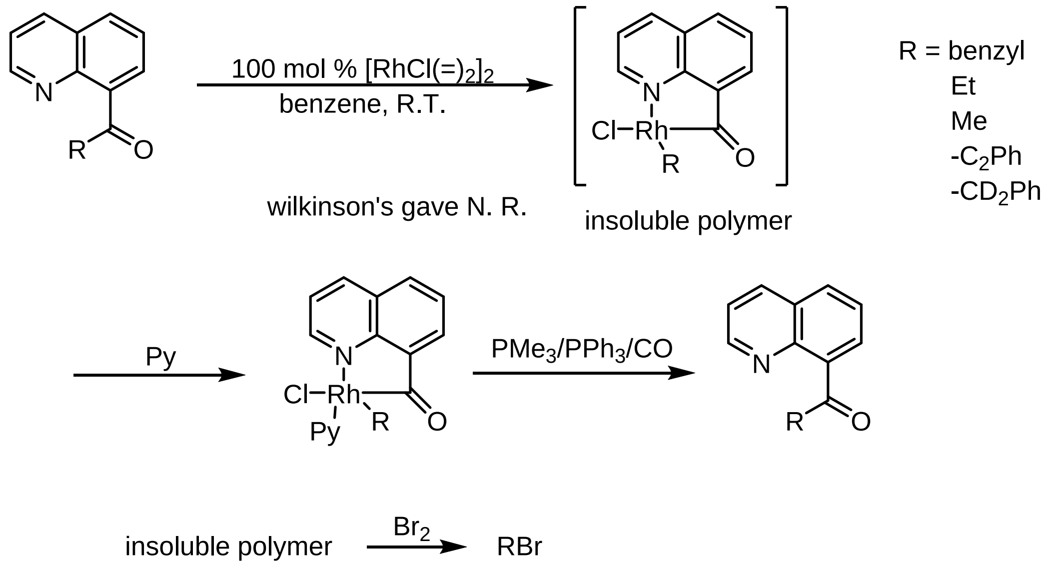



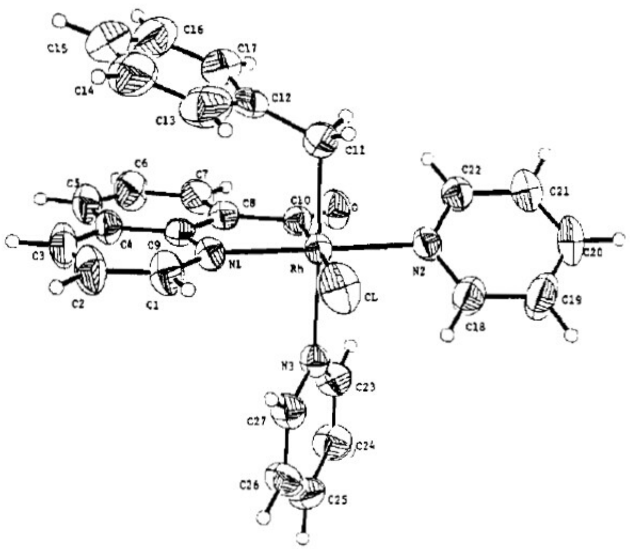
# 8-Acylquinolines




J. Williams Suggs, Sherman D. Cox, *J. Organomet. Chem.* **1981**, *122*, 199

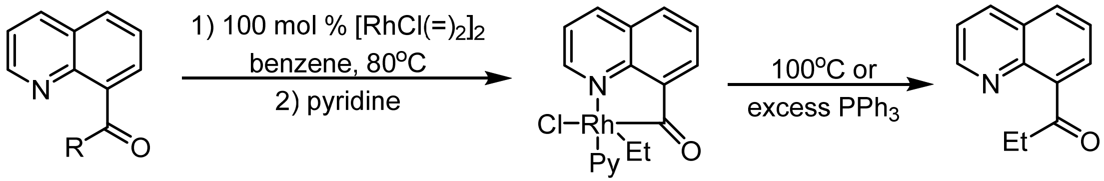
# 8-Acylquinolines



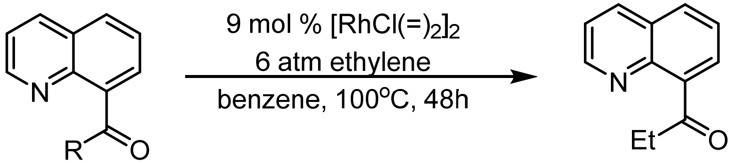
J. William Suggs, Chul-Ho Jun, *J. Am. Chem. Soc.* **1984**, *106*, 3054

# 8-Acylquinolines




>90%

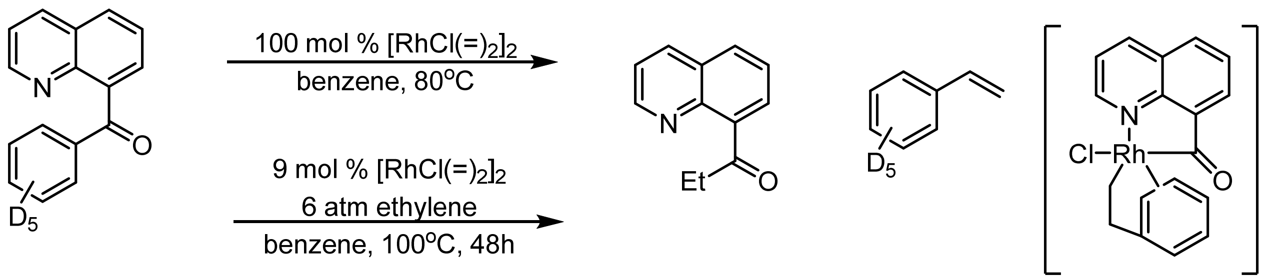
R = *n*Bu, -CH(Me)Ph, -C(Me)$_2$Ph, Cy    in $C_6D_6$, corresponding alkene can be seen




61%, brsm 100%
(678% based on Rh)
First catalytic reaction!
Only ethylene works

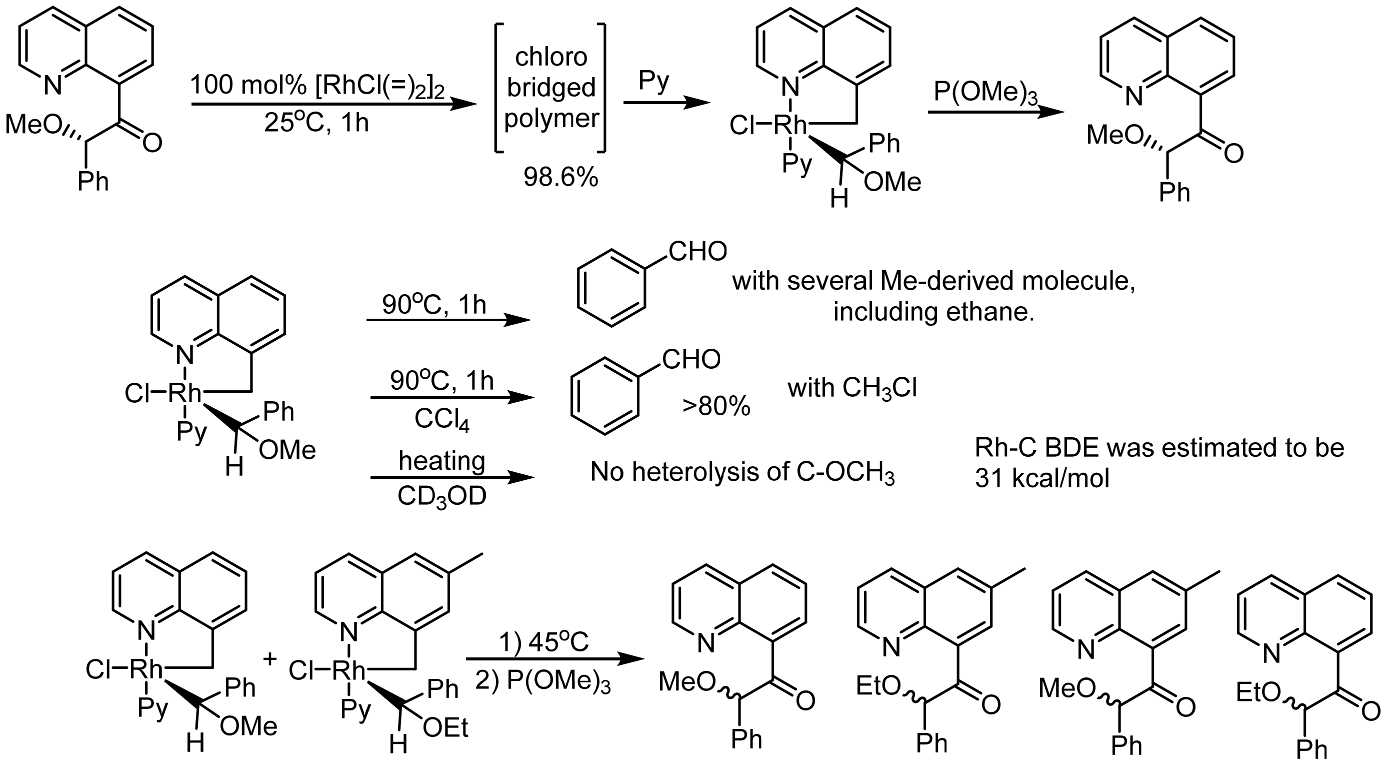
10 mol % TM
6 atm ethylene
100$^o$C, 12h

for [Rh(COD)Cl]$_2$, [Ir(COD)Cl]$_2$ and wilkinson's
N. R. when using Pd(PPh$_3$)$_4$, Pt(PPh$_3$)$_4$, Pd(OAc)$_2$
RuCl$_2$(PPh$_3$)$_3$, and CpRh(=)$_2$



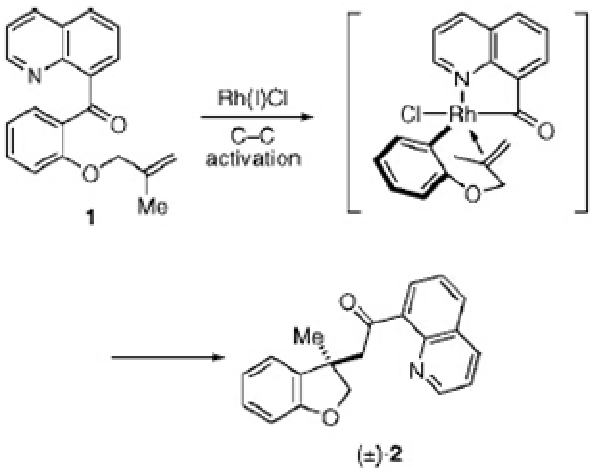

J. William Suggs, Chul-Ho Jun *J. Chem. Soc., Chem. Commun.* **1985**, *107*, 5546

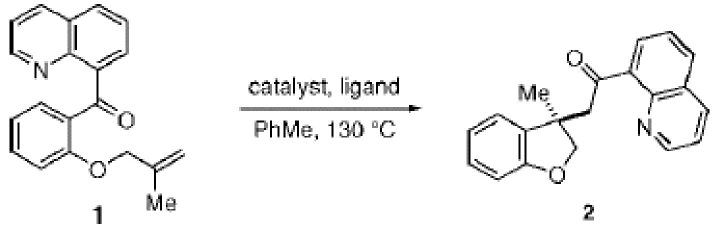
# 8-Acylquinolines




J. Williams Suggs, Chul-Ho Jun, *J. Am. Chem. Soc.* **1986**, *108*, 4679

# 8-Acylquinolines



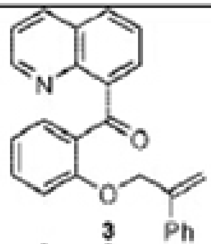
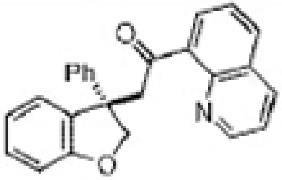
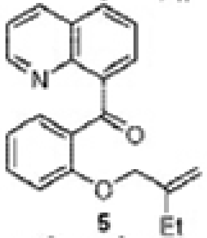
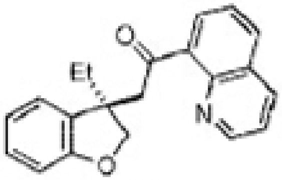
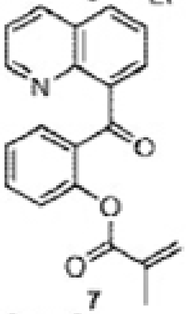
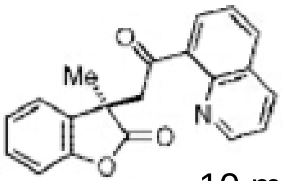
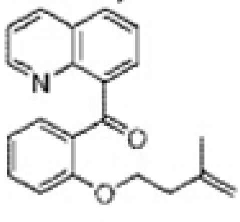
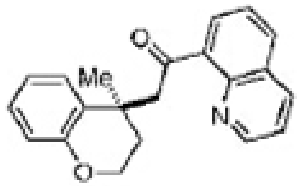




| entry | catalyst | mol % | $L_n$ | yield **2** (%) |
|---|---|---|---|---|
| 1 | $\{RhCl(C_2H_4)_2\}_2$ | 5 | none | 95 |
| 2 | $Rh(OTf)(COD)_2$ | 5 | none | 62 |
| 3 | $RhCl(PPh_3)_3$ | 10 | none | 96 |
| 4 | $RhCl(PPh_3)_3$ | 2 | none | 90[a] |
| 5 | $\{RhCl(C_2H_4)_2\}_2$ | 5 | $PCy_3$ | 62 |
| 6 | $\{RhCl(C_2H_4)_2\}_2$ | 5 | $PMe_3$ | 53 |
| 7 | $Rh(OTf)(COD)_2$ | 5 | $PMe_3$ | 72 |
| 8 | $Rh(OTf)(COD)_2$ | 5 | BINAP | $<5$[b] |
| 9 | $Pd_2dba_3$ | 5 | none | 0 |
| 10 | $Ni(COD)_2$ | 5 | none | 0 |
| 11 | $Pd_2dba_3$ | 5 | $PPh_3$ | 0[a,c] |
| 12 | $Ni(COD)_2$ | 5 | $PPh_3$ | 0 |

[a] As determined using $^1H$ NMR spectroscopy after 48 h. [b] The major product resulted from alkene isomerization to an enol ether. [c] Cleavage of the allyl ether to the corresponding phenol was the major product.

Ashley M. Dreis, Christopher J. Douglas *J. Am. Chem. Soc.* **2009**, *131*, 412

# 8-Acylquinolines

| entry | substrate | cond. | product | % yield[a] |
|---|---|---|---|---|
| 1 |  3 | A |  4 | 94 |
| 2 |  5 | A |  6 | 82 |
| 3 |  7 | A |  8 | 80[b] |
| 4 |  9 | A |  10 | 81 |

10 mol % hydroquinone added

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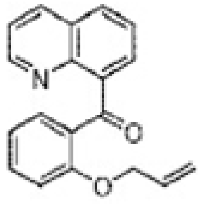
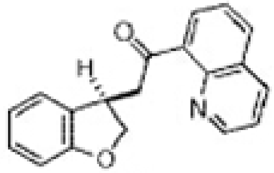
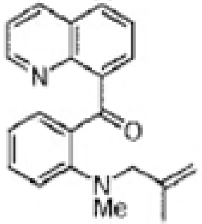
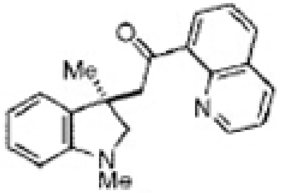
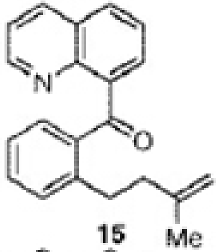
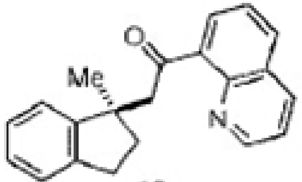
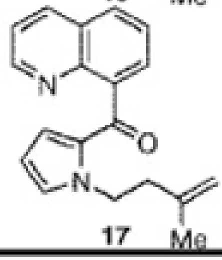
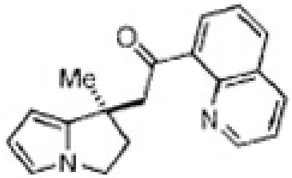
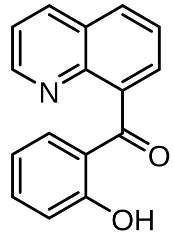
# 8-Acylquinolines

| | | | | |
|---|---|---|---|---|
| 5 |  11 | B |  12 | 25 |
| 6 |  13 | C |  14 | 75 |
| 7 |  15 | A |  16 | 93 |
| 8 |  17 | A |  18 | 63 |



[a] Isolated yield after chromatography with $SiO_2$. [b] Reaction stopped after 24 h. [c] Condition A: 5 mol% $\{RhCl(C_2H_4)_2\}_2$, PhMe, 130 °C, 48 h. Condition B: 5 mol% $Rh(OTf)(COD)_2$, PhMe, 130 °C, 24 h. Condition C: 10 mol% $RhCl(PPh_3)_3$, PhMe, 130 °C, 24 h.

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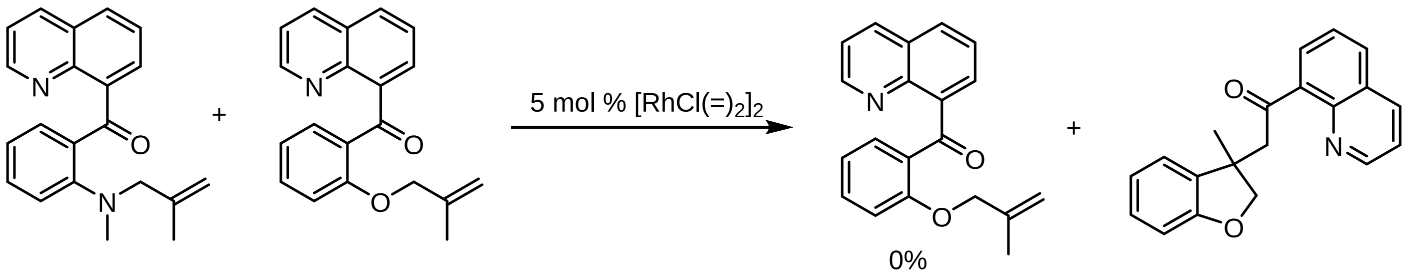
# 8-Acylquinolines

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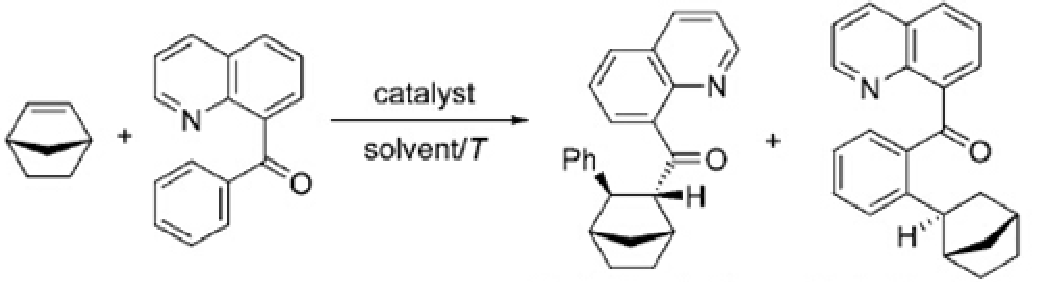
# 8-Acylquinolines




5 9: C–C activation 10: C–H activation

| Entry | Catalyst[b] | Solvent | *T* | Yield, **9/10**[a] |
|---|---|---|---|---|
| 1 | $[Rh(PPh_3)_3]Cl$ | $PhCH_3$ | 130 °C | > 10%, – |
| 2 | $[\{RhCl(C_2H_4)_2\}_2]$[c] | $PhCH_3$ | 130 °C | **79%, 0:1** |
| 3 | $[\{RhCl(C_2H_4)_2\}_2]$[c] | $CH_3CN$ | 100 °C | 35%, ≈1:20 |
| 4 | $[Rh(cod)_2]BF_4$ | $PhCH_3$ | 130 °C | 38%, 1:6 |
| 5 | $[Rh(cod)_2]OTf$ | $PhCH_3$ | 130 °C | 56%, 4:5 |
| 6 | $[Rh(cod)_2]OTf$ | $PhCF_3$ | 130 °C | 44%, 1:5 |
| 7 | $[Rh(cod)_2]OTf$ | $(CH_2Cl)_2$ | 130 °C | 62%, 1:7 |
| 8 | $[Rh(cod)_2]OTf$ | $CH_3CN$ | 100 °C | 41%, 5:3 |
| 9 | $[Rh(cod)_2]OTf$ | THF | 100 °C | **50%, 1:0** |
| 10 | $[Rh(cod)_2]OTf$ | THF[d] | 100 °C | 20%, 1:0 |
| 11 | $[Rh(cod)_2]OTf$ | THF[e] | 100 °C | 12%, 1:0 |

[a] Yields and ratios by $^1H$ NMR spectroscopy with an internal standard. [b] Catalyst loading 10 mol% unless otherwise noted. [c] 5 mol% catalyst used. [d] With 20 mol% $PPh_3$. [e] With 20 mol% $P(tBu)_3$. The values in bold show the most selective reactions. cod = 1,5-cyclooctadiene, THF = tetrahydrofuran, OTf = trifluoromethane sulfonate.

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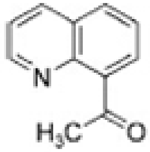
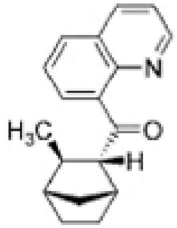
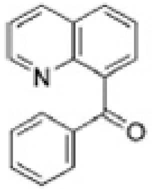
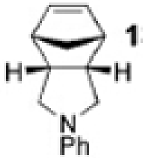
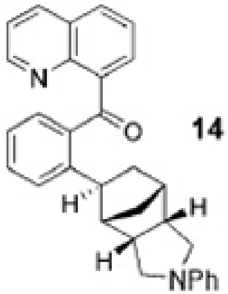
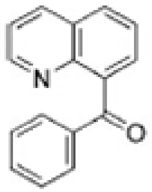
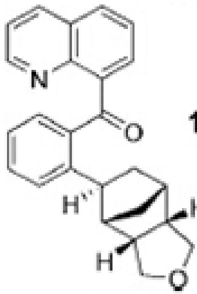
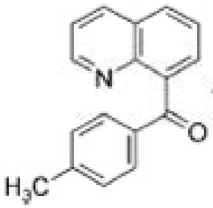
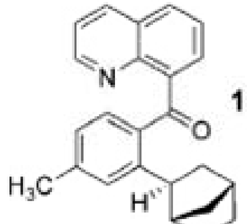
# 8-Acylquinolines

| Quinoline | Alkene | Cond.[a] | Products | Yield[b] |
|---|---|---|---|---|
|  **11** |  | A |  **12** | 39 % (60 %) |
|  **5** |  **13** | A |  **14** | 44 % (65 %) |
|  **5** |  **15** | A |  **16** | 41 % (60 %) |
|  **17** |  | A |  **18** | 44 % (64 %) |

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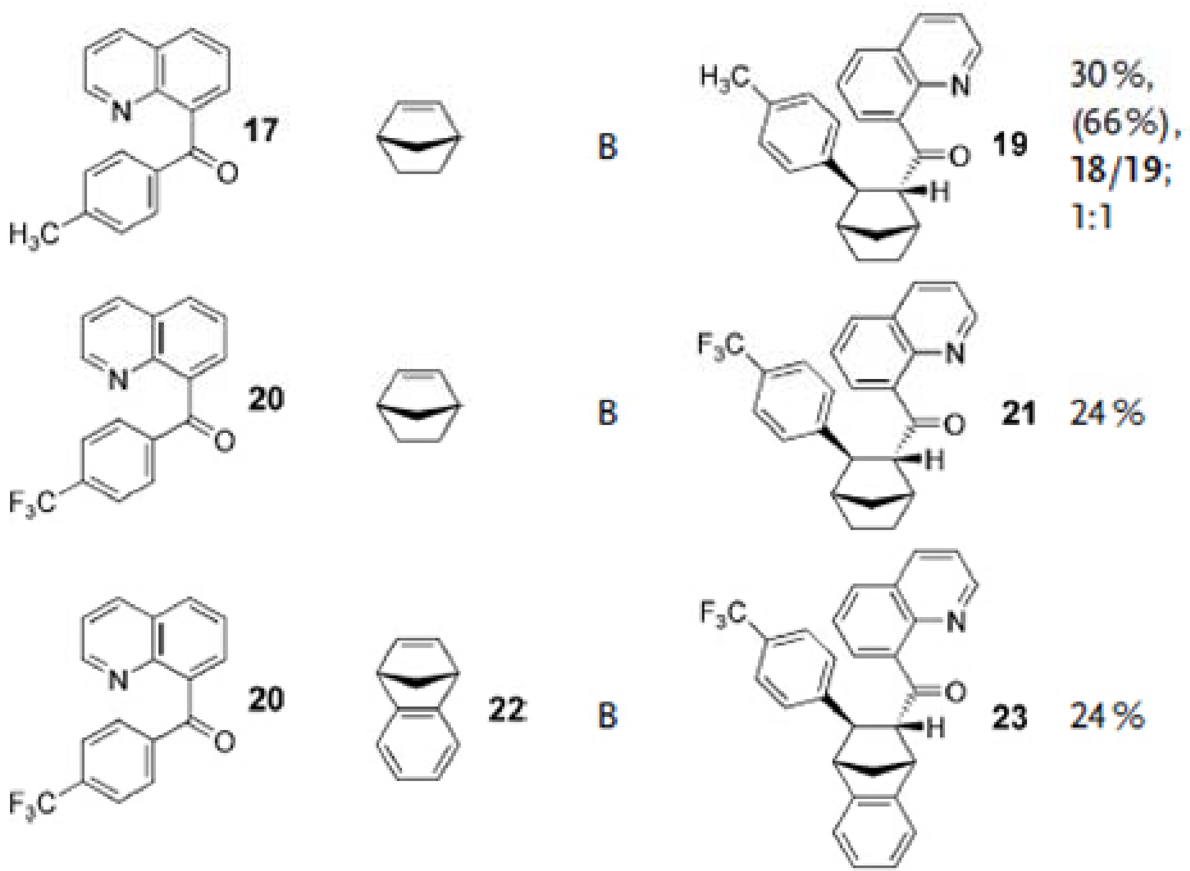
# 8-Acylquinolines




[a] Conditions A: $[\{RhCl(C_2H_4)_2\}_2]$ (5 mol%), $PhCH_3$, 130 °C, 24 h. Conditions B: $[Rh(cod)_2]OTf$ (10 mol%), THF, 100 °C, 24 h. [b] Yields after chromatography, (%) yields based on recovered starting material.

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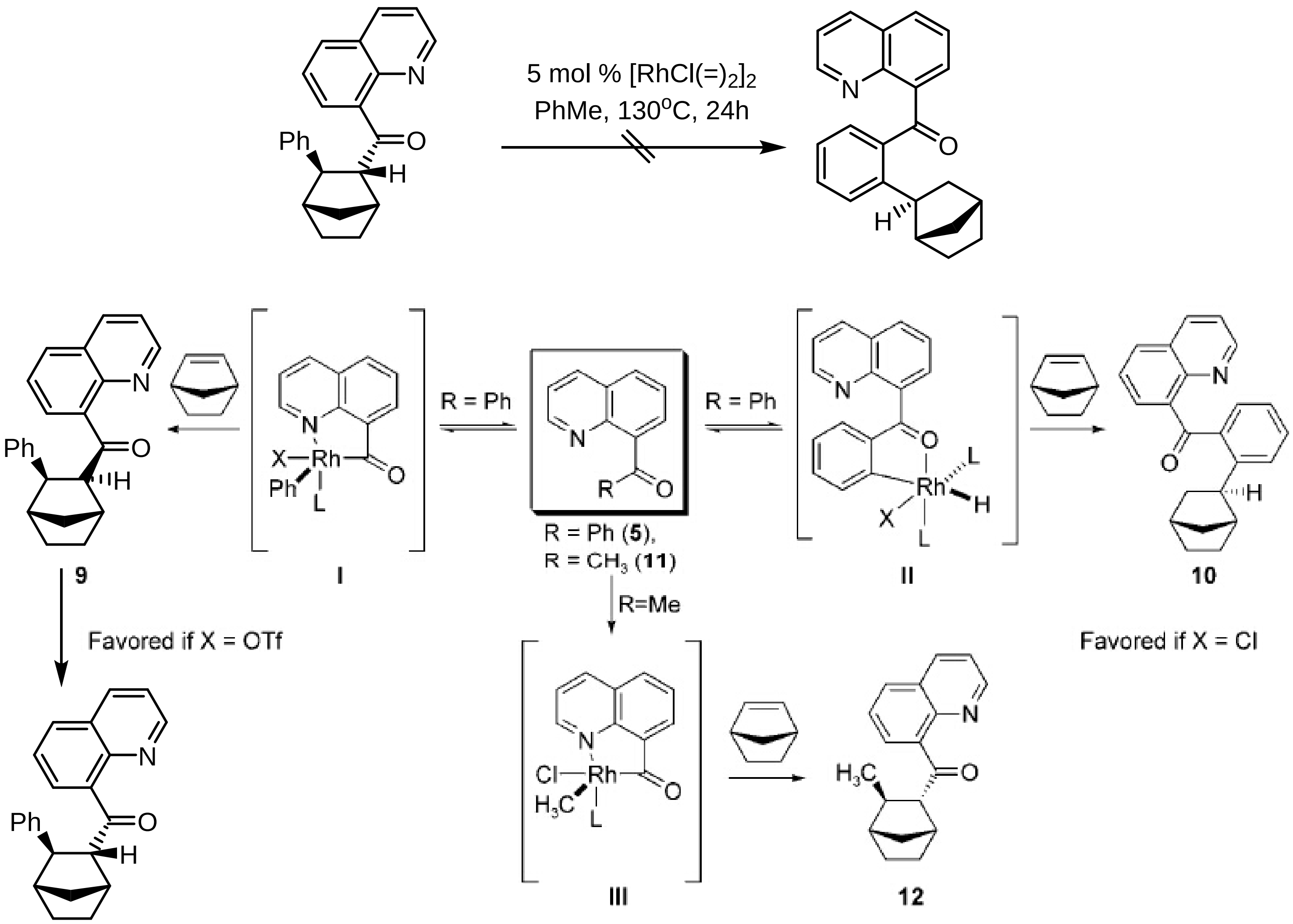
# 8-Acylquinolines

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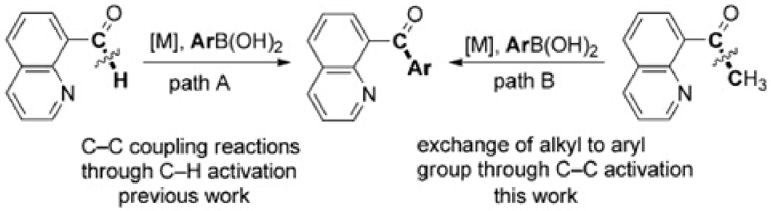
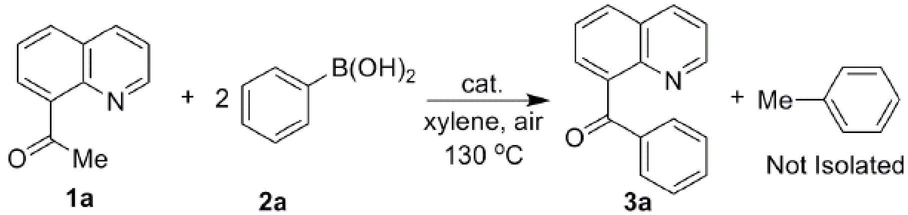
# 8-Acylquinolines




| Entry | Catalyst | Additive | Base | Yield (%)[b] |
|---|---|---|---|---|
| 1 | $(Ph_3P)_3RhCl$ | — | — | 13 |
| 2 | $(Ph_3P)_3RhCl$ | — | $K_2CO_3$ | 23 |
| 3 | $(Ph_3P)_3RhCl$ | — | $Cs_2CO_3$ | 18 |
| 4 | $(Ph_3P)_3RhCl$ | — | $Et_3N$ | <10 |
| 5 | $(Ph_3P)_3RhCl$ | — | $C_5H_5N$ | <10 |
| 6 | $(Ph_3P)_3RhCl$ | — | $K_3PO_4$ | 20 |
| 7 | $(Ph_3P)_3RhCl$ | CuI | $K_2CO_3$ | 93 |
| 8 | $(Ph_3P)_3RhCl$ | CuI | $Cs_2CO_3$ | 55 |
| 9 | $(Ph_3P)_3RhCl$ | CuI | $K_3PO_4$ | 71 |
| 10 | $[Cp^*RhCl_2]_2$ | CuI | $K_2CO_3$ | 51 |
| 11 | $RhCl_3.3H_2O$ | CuI | $K_2CO_3$ | 47 |
| 12 | $[Rh(COD)Cl]_2$ | CuI | $K_2CO_3$ | 53 |
| 13 | $[RhCl(C_2H_4)_2]_2$ | CuI | $K_2CO_3$ | 32 |
| 14 | $Rh(C_5H_5)(C_8H_{12})$ | CuI | $K_2CO_3$ | 26 |
| 15 | $Rh(C_5H_5)(PPh_3)_2$ | CuI | $K_2CO_3$ | 38 |
| 16 | $Pd(OAc)_2$ | CuI | $K_2CO_3$ | no reaction |
| 17 | $Pd(PPh_3)_4$ | CuI | $K_2CO_3$ | no reaction |
| 18 | $Ru(PPh_3)_3Cl_2$ | CuI | $K_2CO_3$ | < 5% |
| 19 | $[Ru(COD)Cl_2]_2$ | CuI | $K_2CO_3$ | < 5% |

[a] Reaction conditions: 1a (0.10 mmol), 2a (0.25 mmol), catalyst (10.0 mol %), CuI (0.20 mmol), base (0.20 mmol), xylene (0.50 mL), 130 °C, 18 h, in the air; [b] Isolated yields.

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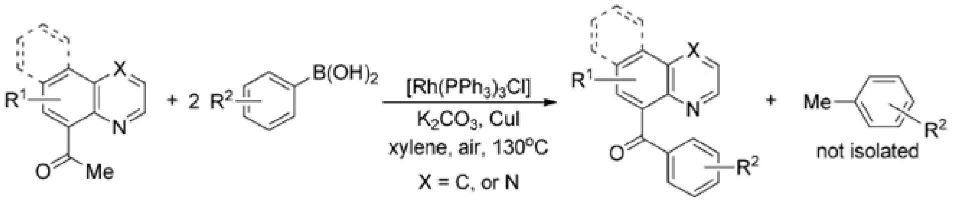
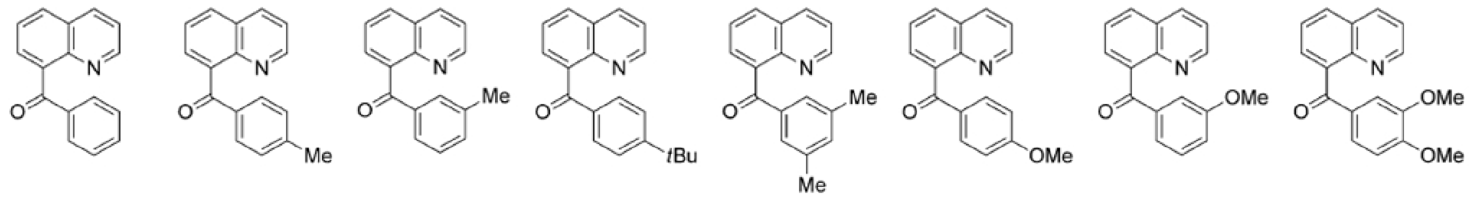
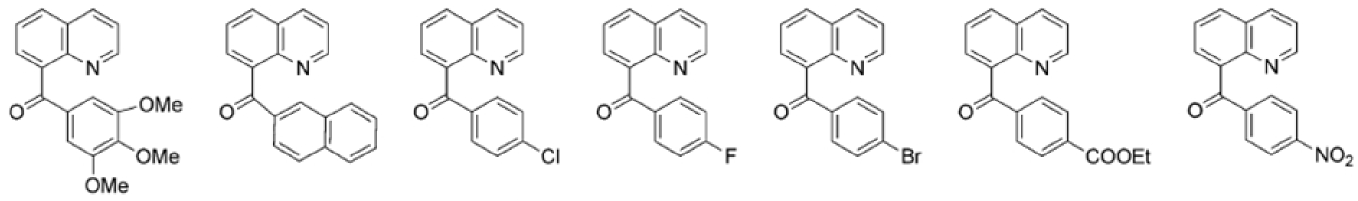
# 8-Acylquinolines

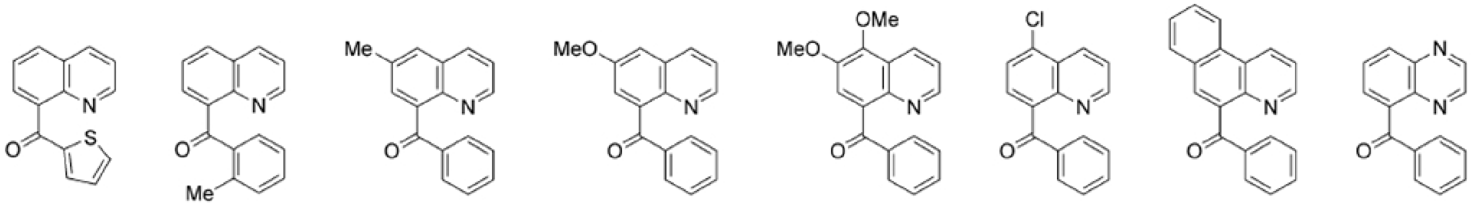



**3a** (93%); (59%)[b,c] **3b** (85%)[d] **3c** (76%)[d] **3d** (83%) **3e** (90%)[d] **3f** (87%) **3g** (85%) **3h** (74%)




**3i** (51%) **3j** (94%)[e] **3k** (83%)[e] **3l** (57%) **3m** (47%) **3n** (57%) **3o** (35%)




**3p** (0%) **3q** (0%) **3r** (69%)[c] **3s** (65%)[c] **3t** (75%)[c] **3u** (81%)[c] **3v** (57%)[c] **3w** (89%)[c]

[a] Reaction conditions: 1-(quinolin-8-yl)ethanone (0.10 mmol), substituted phenylboronic acid (0.25 mmol), CuI (0.20 mmol), $K_2CO_3$ (0.20 mmol), $[Rh(PPh_3)_3Cl]$ (0.01 mmol, 10.0 mol%), xylene (0.5 mL), 130 °C, under air, 48 h; yields of isolated products are given based on **1a**. [b] Sodium tetraphenylborate was used as the substrate. [c] 18 h. [d] 36 h. [e] 24 h.

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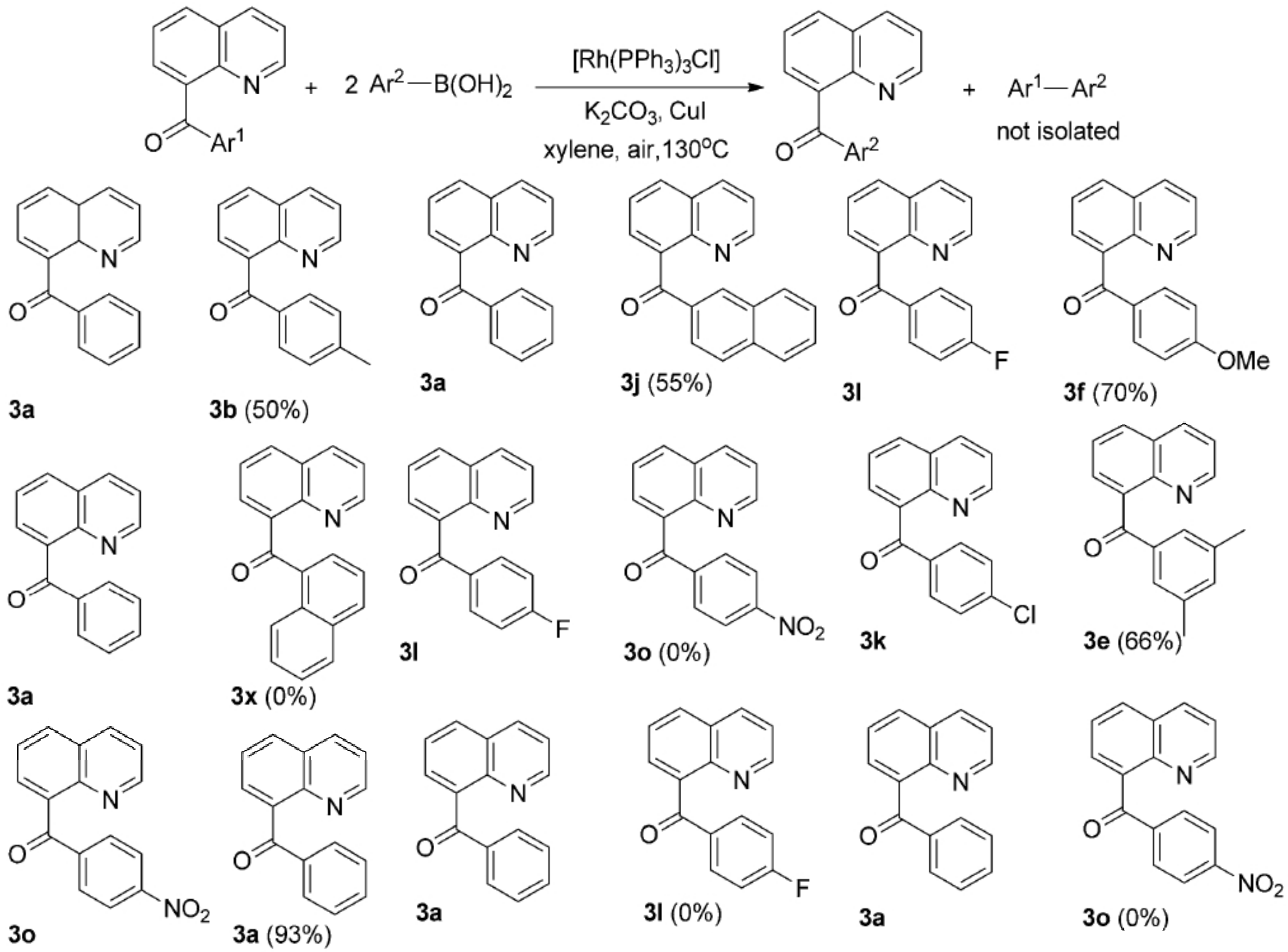
# 8-Acylquinolines

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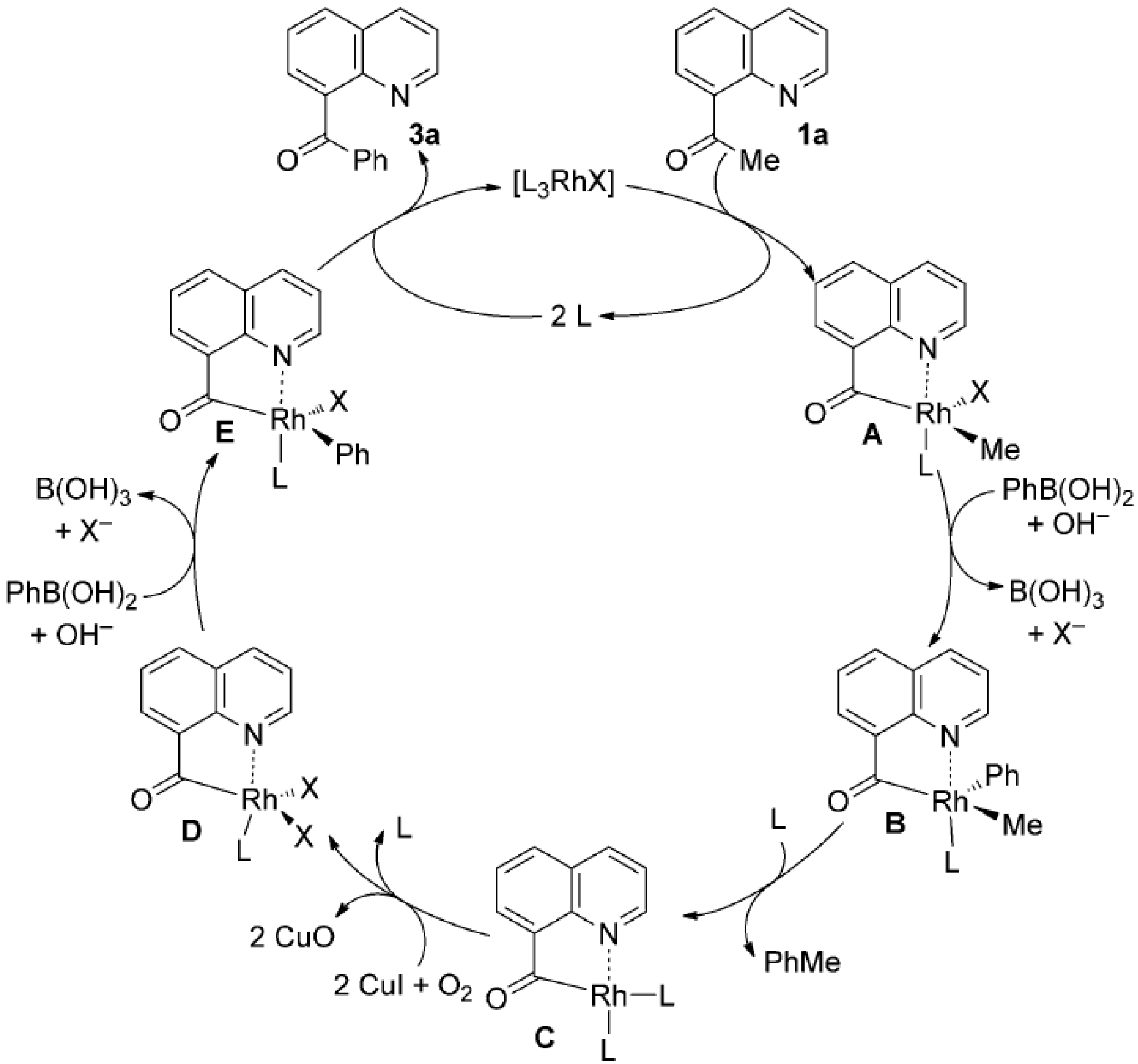
# 8-Acylquinolines

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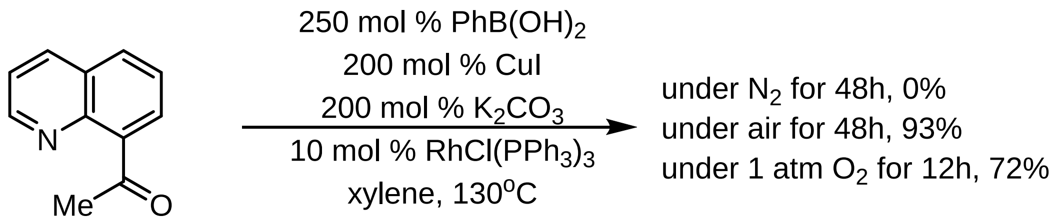
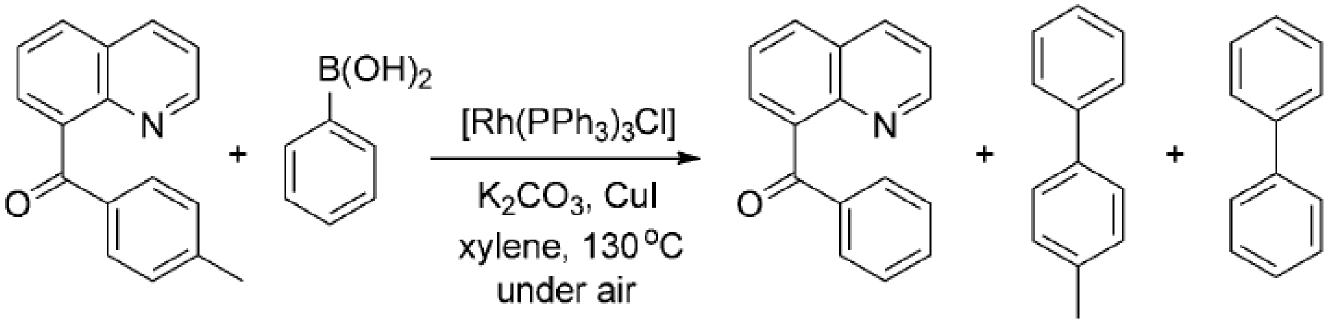
# 8-Acylquinolines




**3b** **2a** **3a** **3ba** **2aa**

molar ratio of **3a** : **3ba** = 1 : 0.9

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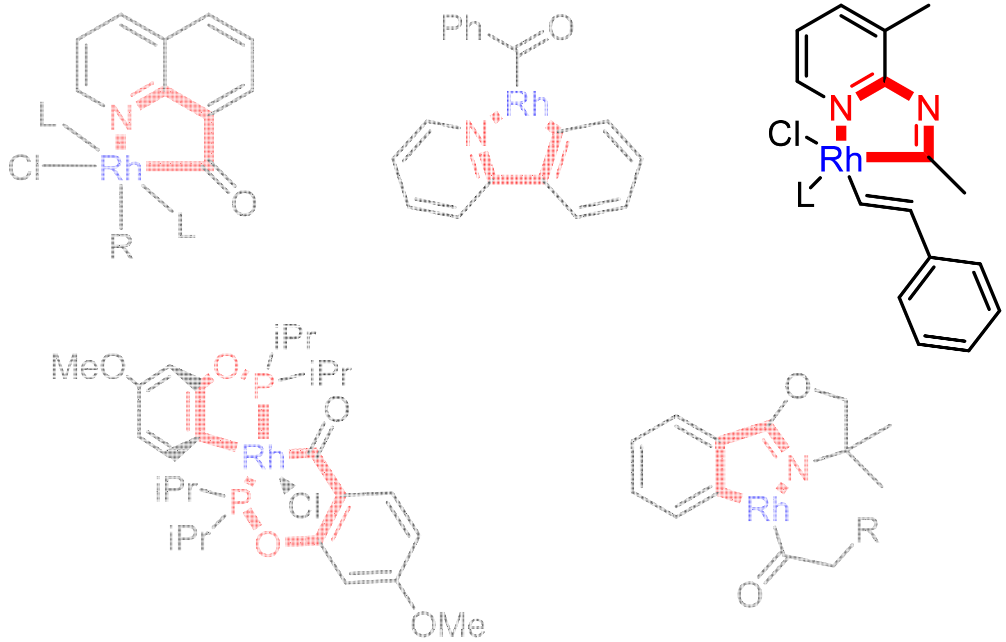
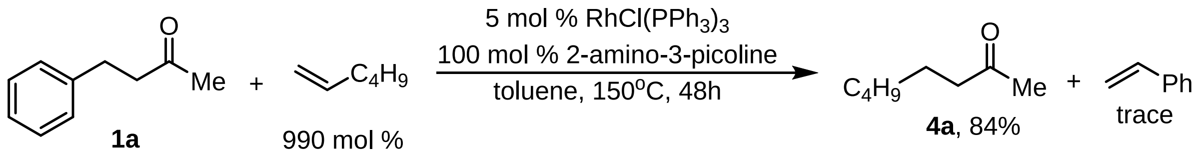
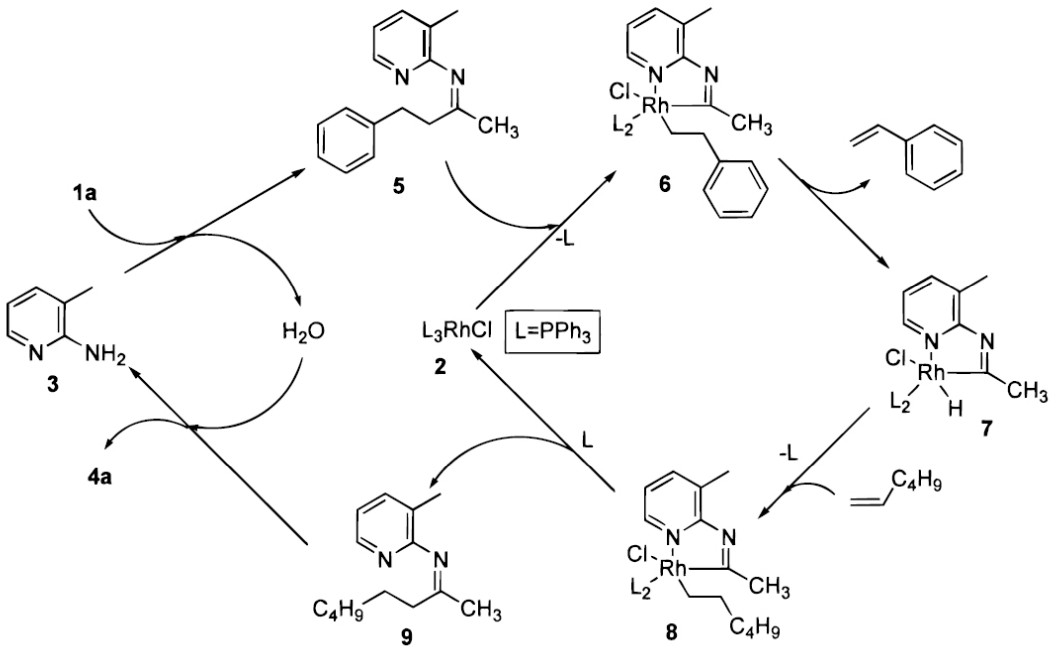
# 2-Amino-3-picoline

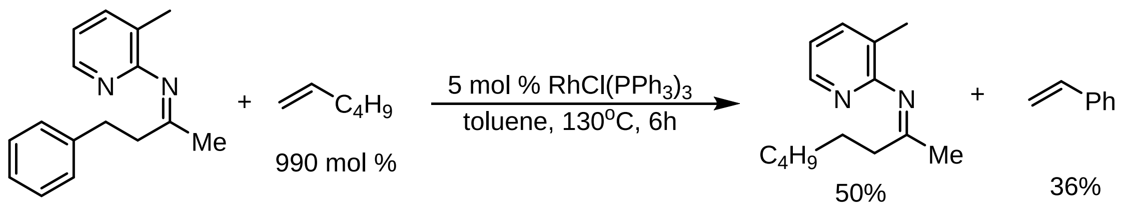


# 2-Amino-3-picoline



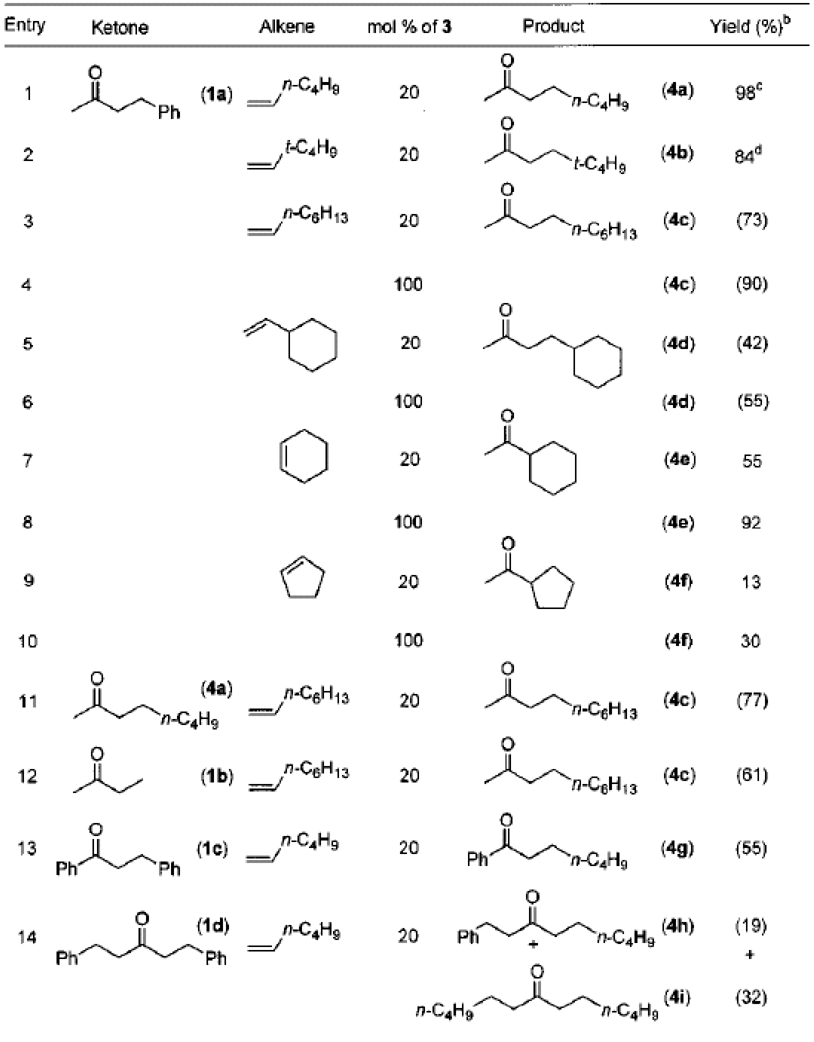

with no 2-amino-3-picoline, no **4a** formed, and **1a** completely recovered



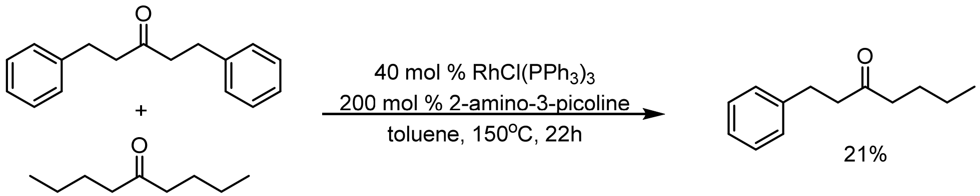

Chul-Ho Jun, Hyuk Lee, *J. Am. Chem. Soc.* **1999**, *121*, 880

# 2-Amino-3-picoline



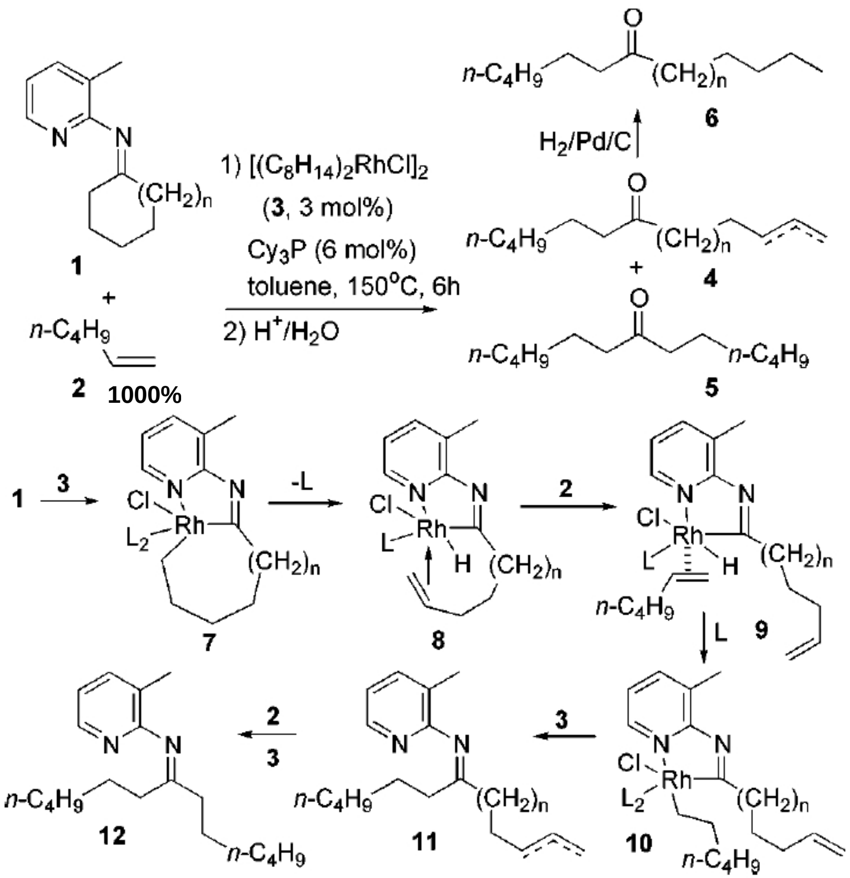
| Entry | Ketone | Alkene | mol % of **3** | Product | Yield (%)[b] |
|---|---|---|---|---|---|
| 1 | Ph (**1a**) | $n$-$C_4H_9$ | 20 | $n$-$C_4H_9$ (**4a**) | 98[c] |
| 2 | | $t$-$C_4H_9$ | 20 | $t$-$C_4H_9$ (**4b**) | 84[d] |
| 3 | | $n$-$C_6H_{13}$ | 20 | $n$-$C_6H_{13}$ (**4c**) | (73) |
| 4 | | | 100 | (**4c**) | (90) |
| 5 | | | 20 | (**4d**) | (42) |
| 6 | | | 100 | (**4d**) | (55) |
| 7 | | | 20 | (**4e**) | 55 |
| 8 | | | 100 | (**4e**) | 92 |
| 9 | | | 20 | (**4f**) | 13 |
| 10 | | | 100 | (**4f**) | 30 |
| 11 | $n$-$C_4H_9$ (**4a**) | $n$-$C_6H_{13}$ | 20 | $n$-$C_6H_{13}$ (**4c**) | (77) |
| 12 | (**1b**) | $n$-$C_6H_{13}$ | 20 | $n$-$C_6H_{13}$ (**4c**) | (61) |
| 13 | Ph, Ph (**1c**) | $n$-$C_4H_9$ | 20 | Ph, $n$-$C_4H_9$ (**4g**) | (55) |
| 14 | Ph, Ph (**1d**) | $n$-$C_4H_9$ | 20 | Ph, $n$-$C_4H_9$ (**4h**) + $n$-$C_4H_9$, $n$-$C_4H_9$ (**4i**) | (19) + (32) |

[a] Reaction of ketone (**1**) and alkene (**1**/alkene = 1/10) was carried out at 150 °C for 48 h under 10 mol % of $(PPh_3)_3RhCl$ (**2**) and 2-amino-3-picoline (**3**) except entry 2. [b] The yields of products were determined by gas chromatography detector (GCD), and isolated yields are shown in parentheses. [c] The ratio of **1a** and 1-hexene is 1/15. [d] Reaction of **1a** and 3,3-dimethyl-1-butene (**1a**/3,3-dimethyl-1-butene = 1/15) was carried out at 150 °C for 48 h under 5 mol % of **2** and 20 mol % of **3**.




Chul-Ho Jun, Hyuk Lee, *J. Am. Chem. Soc.* **1999**, *121*, 880

# 2-Amino-3-picoline

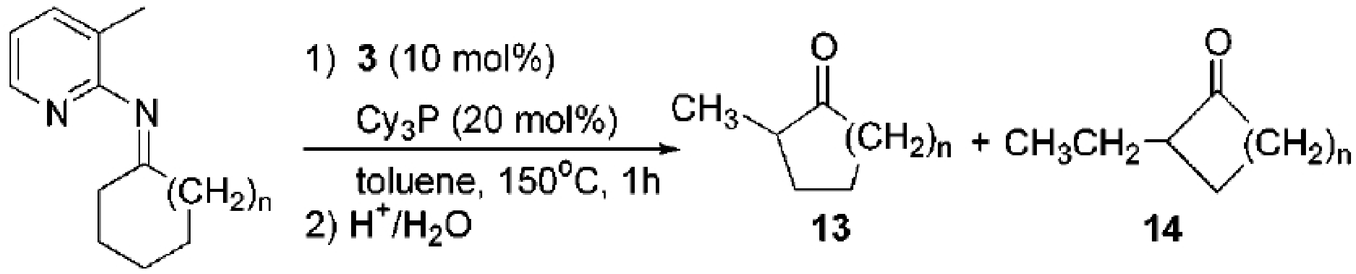



| entry | reactant **1** ($n$) | product(s) | ratio of **4**:**5** (ter:int of **4**)[a] | overall yield,[b] % |
|---|---|---|---|---|
| 1 | **1a** ($n = 0$) | **5** | 0:100 | 9 |
| 2 | **1b** ($n = 1$) | **5** | 0:100 | 5 |
| 3 | **1c** ($n = 2$) | **4c** + **5** | 23:77 (52:48) | 76 |
| 4 | **1d** ($n = 3$) | **4d** + **5** | 39:61 (13:87) | 89 |
| 5 | **1e** ($n = 5$) | **4e** + **5** | 38:62 (15:85) | 83 |
| 6 | **1f** ($n = 7$) | **4f** + **5** | 39:61 (22:78) | 86 |
| 7 | **1g** ($n = 10$) | **4g** + **5** | 37:63 (16:84) | 79 |

[a] The ratio of terminal olefin and internal olefin of **4** was determined by GCD. [b] Yields are determined by GCD.

Chul-Ho Jun, Hyuk Lee, Sung-Gon Lim, *J. Am. Chem. Soc.* **2001**, *123*, 751

# 2-Amino-3-picoline

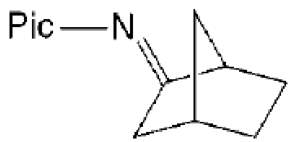



13

14

| entry | reactant **1** (*n*) | products | ratio of **13**:**14** | overall yield,[a] % |
|---|---|---|---|---|
| 1 | **1a** (*n* = 0) | | | 0 |
| 2 | **1b** (*n* = 1) | **13b** | 100:0 | 21 |
| 3 | **1c** (*n* = 2) | **13c** +**14c** | 76:24 | 82 |
| 4 | **1d** (*n* = 3) | **13d** + **14d** | 33:67 | 12 |
| 5 | **1h** (*n* = 4) | | | 0 |

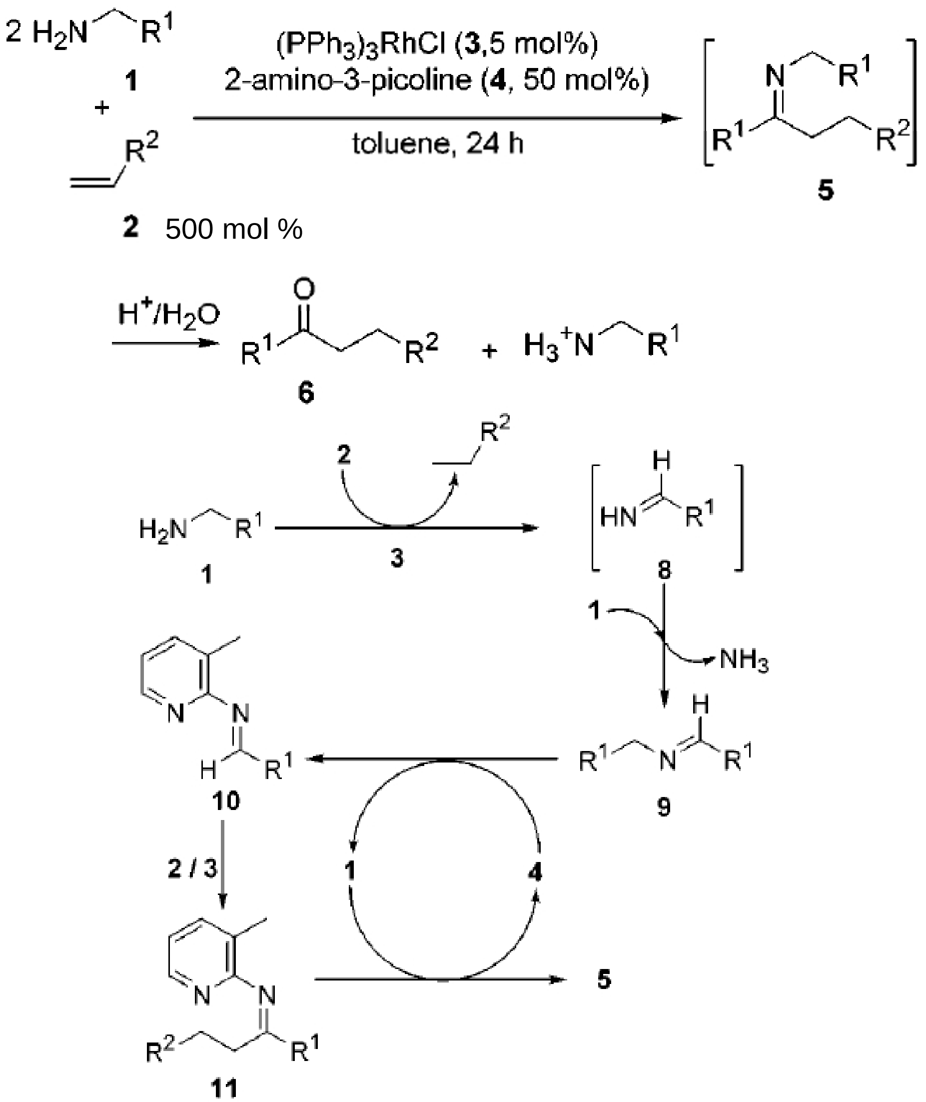
[a] Yields and the ratio of **13** and **14** were determined by GCD.




**20**

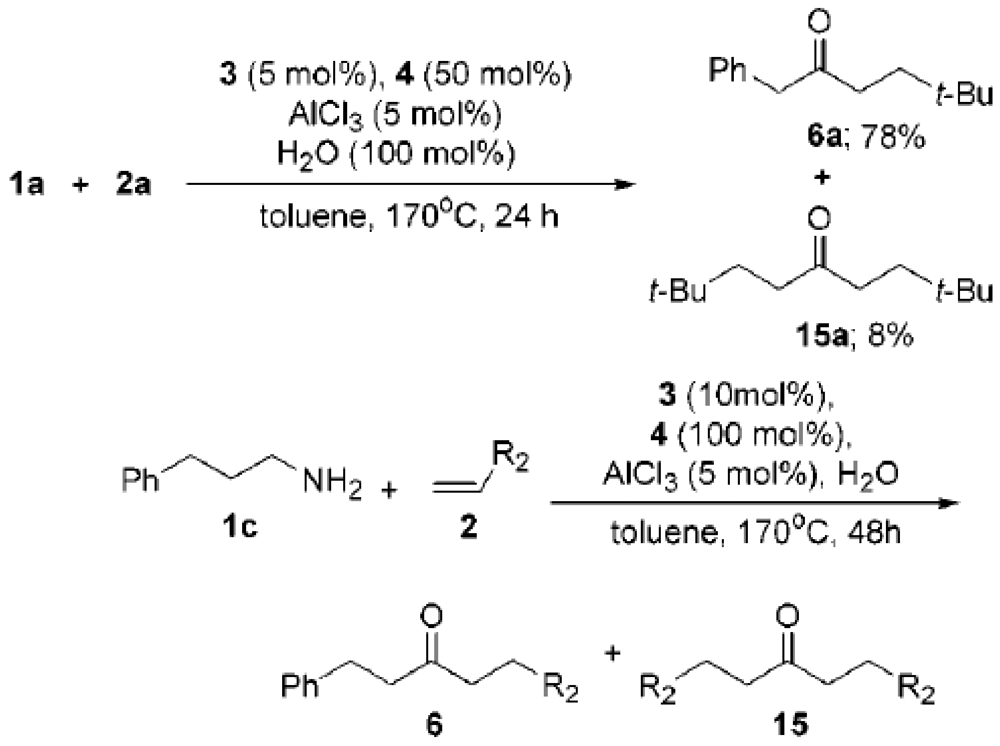
Chul-Ho Jun, Hyuk Lee, Sung-Gon Lim, *J. Am. Chem. Soc.* **2001**, *123*, 751

# 2-Amino-3-picoline




Chul-Ho Jun, Kwan-Yong Chung, Jun-Bae Hong, *Org. Lett.* **2001**, *3*, 785

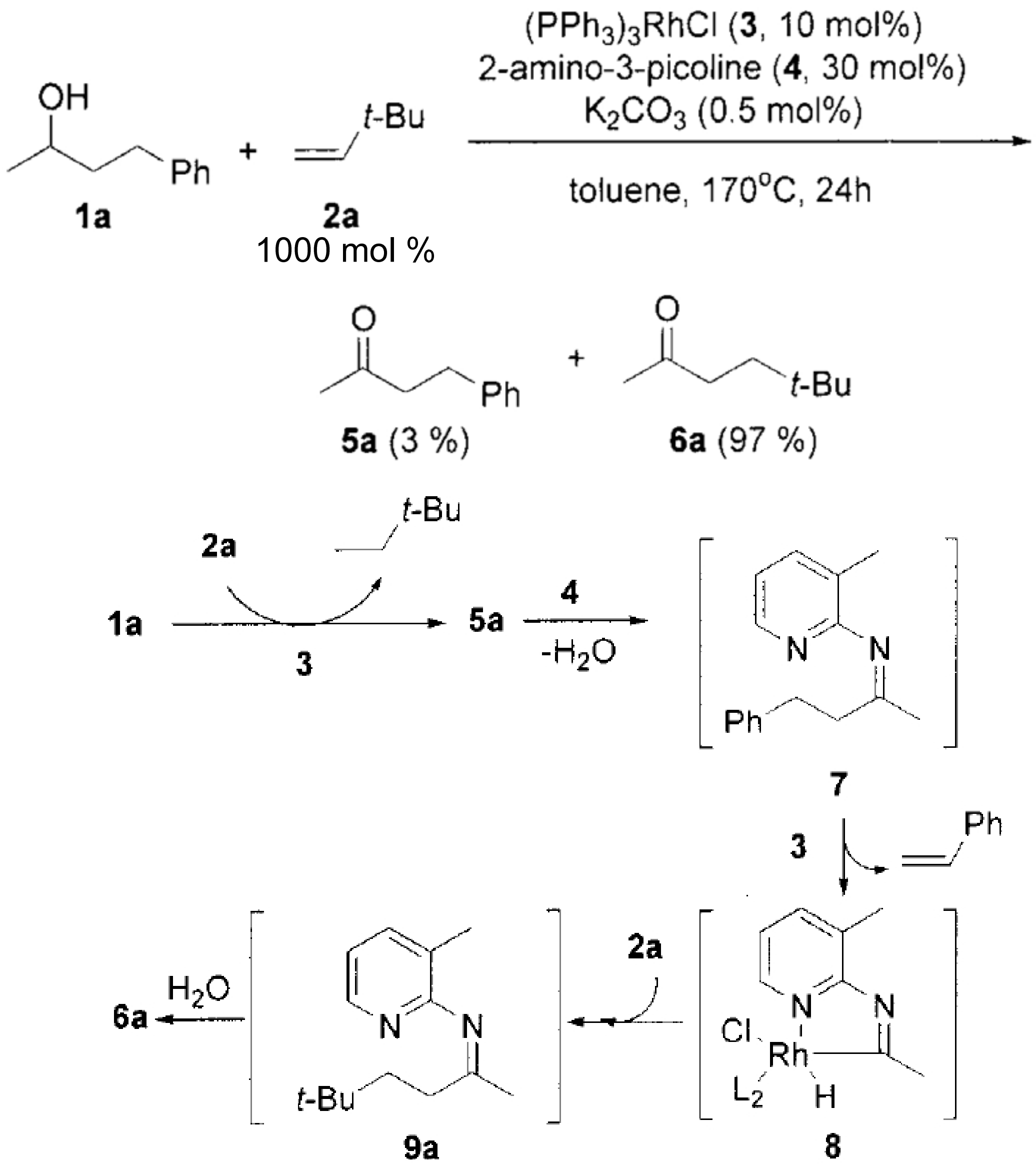
# 2-Amino-3-picoline




| $R_2$ (**2**) | ratio of **6** / **15** | total yield (%) |
|---|---|---|
| *t*-$C_4H_9$ (**2a**) | 50 (**6i**) / 50 (**15a**) | 97 |
| *n*-$C_3H_7$ (**2b**) | 59 (**6j**) / 41 (**15b**) | 88 |
| *n*-$C_6H_{13}$ (**2c**) | 40 (**6k**) / 60 (**15c**) | 81 |
| *n*-$C_8H_{17}$ (**2d**) | 36 (**6l**) / 64 (**15d**) | 77 |
| Cy (**2e**) | 48 (**6m**) / 52 (**15e**) | 73 |

Chul-Ho Jun, Kwan-Yong Chung, Jun-Bae Hong, *Org. Lett.* **2001**, *3*, 785

# 2-Amino-3-picoline




Chul-Ho Jun, Dae-Yon Lee, Yeon-Hee Kim, Hyuk Lee, *Organometallics*, **2001**, *20*, 2928

# 2-Amino-3-picoline

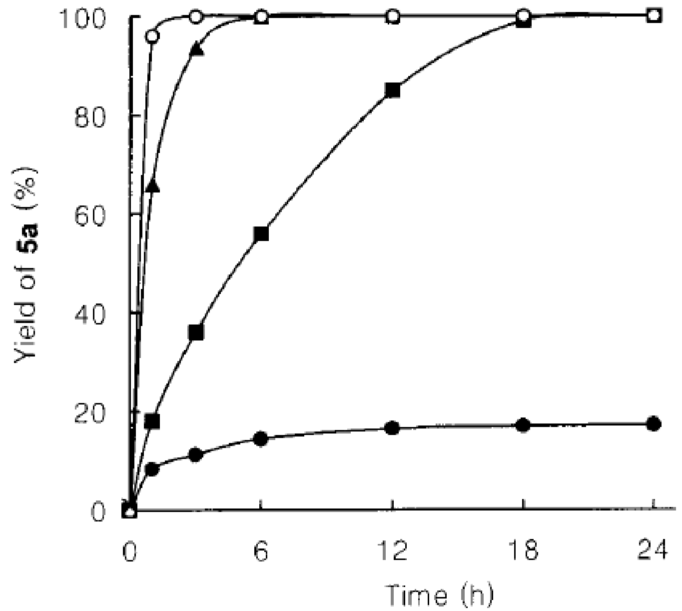



**Figure 1.** Effect of $K_2CO_3$ in the oxidation of **1a** to **5a**. The reactions of **1a** were carried out at 170 °C in the presence of **2a** (**1a**:**2a** = 1:10) and **3** (10 mol %) with 0 mol % (●), 0.5 mol % (■), 2 mol % (▲), and 5 mol % (○) of $K_2CO_3$.

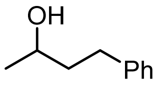
**5a** + **2a** → **6a** (**3** (10 mol%), **4** (30 mol%); toluene, 170°C, 24h)

| | |
|---|---|
| without $K_2CO_3$ | 97 % |
| 0.5 mol% $K_2CO_3$ | 95 % |
| 2.0 mol% $K_2CO_3$ | 60 % |

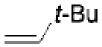
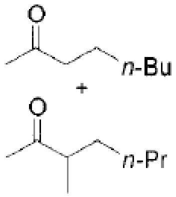
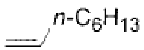
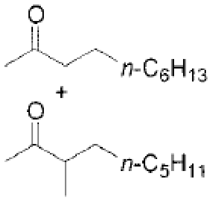
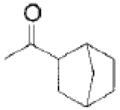
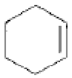
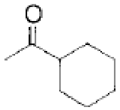
among $K_2CO_3$, $Na_2CO_3$, $Cs_2CO_3$, $NaHCO_3$, KOH, NaOH, $K_2CO_3$ was most effective

Chul-Ho Jun, Dae-Yon Lee, Yeon-Hee Kim, Hyuk Lee, *Organometallics*, **2001**, *20*, 2928

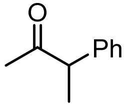
# 2-Amino-3-picoline




**1a**

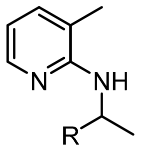
| Entry | Alkenes (2) | | Product(s) (6) | | Yield (%)[b] |
|---|---|---|---|---|---|
| 1 |  | (**2a**) | (**6a**) | | 86[c] |
| 2[d] |  | (**2b**) |  | (**6b**)<br>(**6c**) | 79<br>(**6b**/**6c** =95/5)[e] |
| 3[d] | 2-Hexene | (**2c**) | (**6b**) + (**6c**) | | 64<br>(**6b**/**6c** =94/6)[e] |
| 4[d] |  | (**2d**) |  | (**6d**)<br>(**6e**) | (72)<br>(**6d**/**6e** =95/5)[e] |
| 5 |  | (**2e**) | <br>(*exo*/*endo*=73/27)[f] | (**6f**) | (73) |
| 6[d,g] |  | (**2f**) |  | (**6g**) | 51 |

[a] The reaction of **1a** and **2** (**1a**:**2** = 1:10) was carried out at 170 °C for 24 h under **3** (10 mol %), **4** (30 mol %), and $K_2CO_3$ (0.5 mol %) in toluene. [b] The yield of product was determined by GC, and isolated yields are shown in parentheses. **1a** was fully converted into ketones, except for entry 6. [c] The reaction time was 18 h. [d] A small amount (~2%) of **10** was detected by GC. [e] Determined by GC. [f] Determined by $^1$H NMR. [g] 3% of **1a** was left. 13% of **11a** and 5% of **11b** were detected.

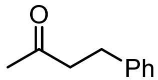



| entry | alkene 2 | yield of 5a (%)[b] |
|---|---|---|
| 1 | **2a** | 85 |
| 2 | **2b** | 57 |
| 3 | **2c** | 52 |
| 4 | **2d** | 56 |
| 5 | **2e** | 53 |
| 6 | **2f** | 13 |

[a] The reaction of **1a** and **2** (**1a**:**2** = 1:10) was carried out at 170 °C for 12 h under **3** (10 mol %) and $K_2CO_3$ (0.5 mol %) in toluene. [b] GC yields.




R = PhEt-
Cy-




**5a**

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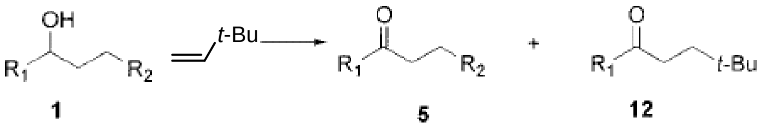
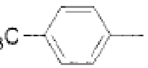
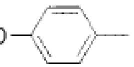
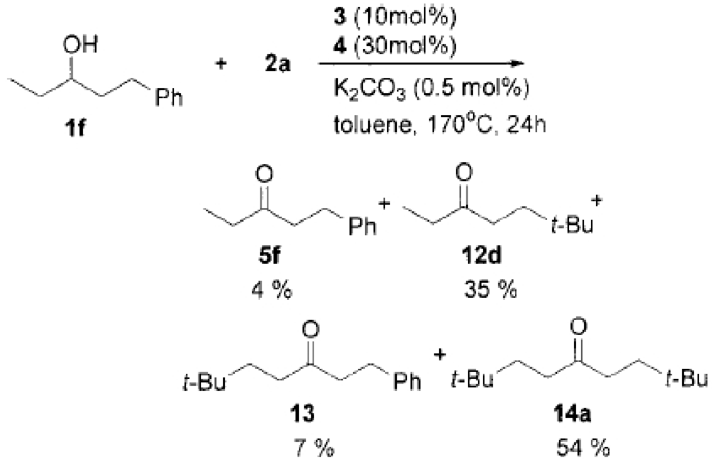
# 2-Amino-3-picoline



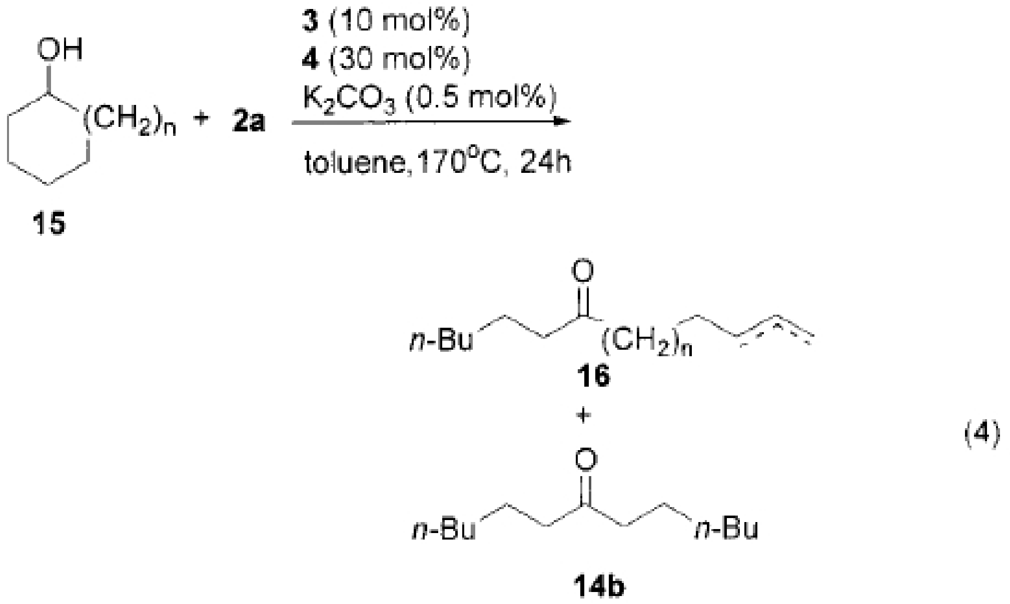

| Entry | Alcohol (1) | | | Products (Isolated Yield, %) | |
|---|---|---|---|---|---|
| | $R_1$ | $R_2$ | | 5 | 12 |
| 1 | Ph- | H- | (**1b**) | **5b** (53) | **12a** (43) |
| 2 | Ph- | Ph- | (**1c**) | **5c** (30) | **12a** (68) |
| 3 | $F_3C$  | Ph- | (**1d**) | **5d** (21) | **12b** (73) |
| 4[b] | MeO  | Ph- | (**1e**) | **5e** (42) | **12c** (46) |

[a] The reaction of **1** and **2a** (**1**:**2a** = 1:10) was carried out at 170 °C for 24 h under **3** (10 mol %), **4** (30 mol %), and $K_2CO_3$ (0.5 mol %) in toluene. [b] Dehydration of **1e** occurred to give a mixture of 3-phenyl-1-(4-methoxyphenyl)propene and 3-(4-methoxyphenyl)-1-phenylpropene in 7% yield (detected by GC).




Chul-Ho Jun, Dae-Yon Lee, Yeon-Hee Kim, Hyuk Lee, *Organometallics*, **2001**, *20*, 2928

# 2-Amino-3-picoline




| | overall yield | ratio of **16**/**14b** (ter. / int. of **16**) |
|---|---|---|
| **15a** (n=1) | <1 % | **16a**(n=1)/**14b**= 0 / 100 |
| **15b** (n=2) | 29 % | **16b**(n=2)/**14b**=14 / 86 (56:44) |
| **15c** (n=3) | 68 % | **16c**(n=3)/**14b**=38 / 62 (34:66) |
| **15d** (n=7) | 75 % | **16d**(n=4)/**14b**=47 / 53 (47:53) |

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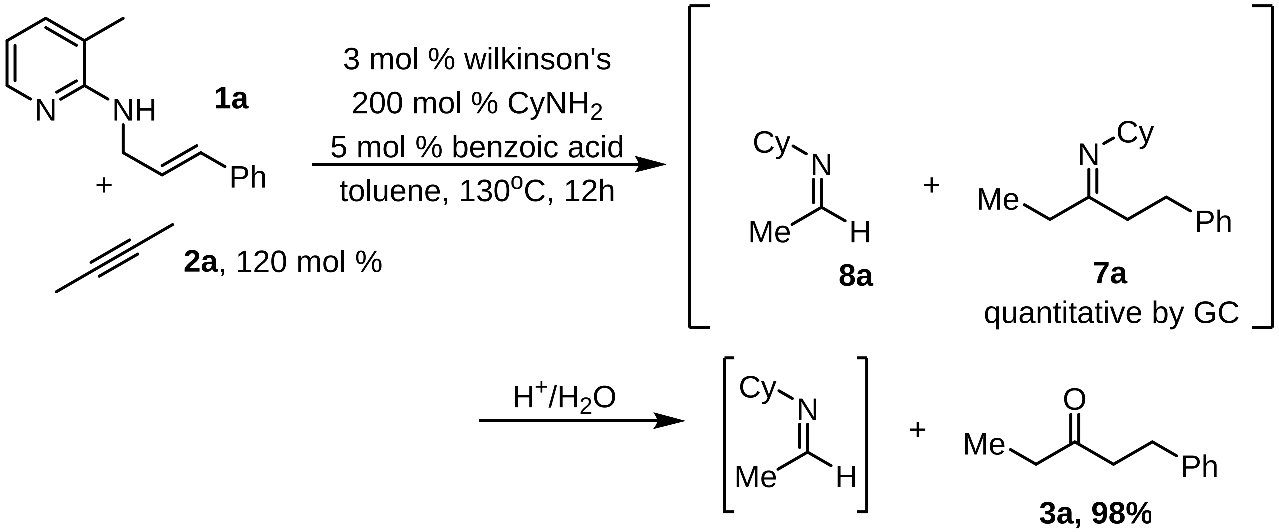
# 2-Amino-3-picoline



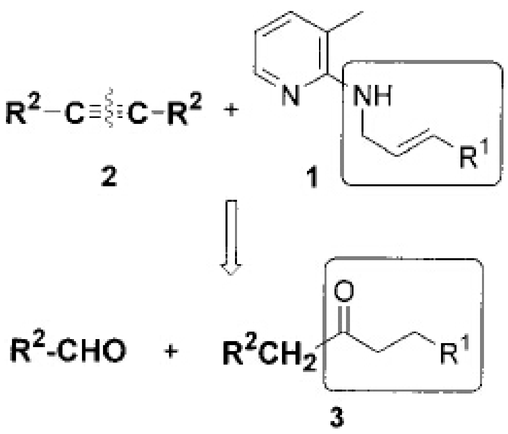



**Table 1.** The C−C triple bond cleavage of alkynes

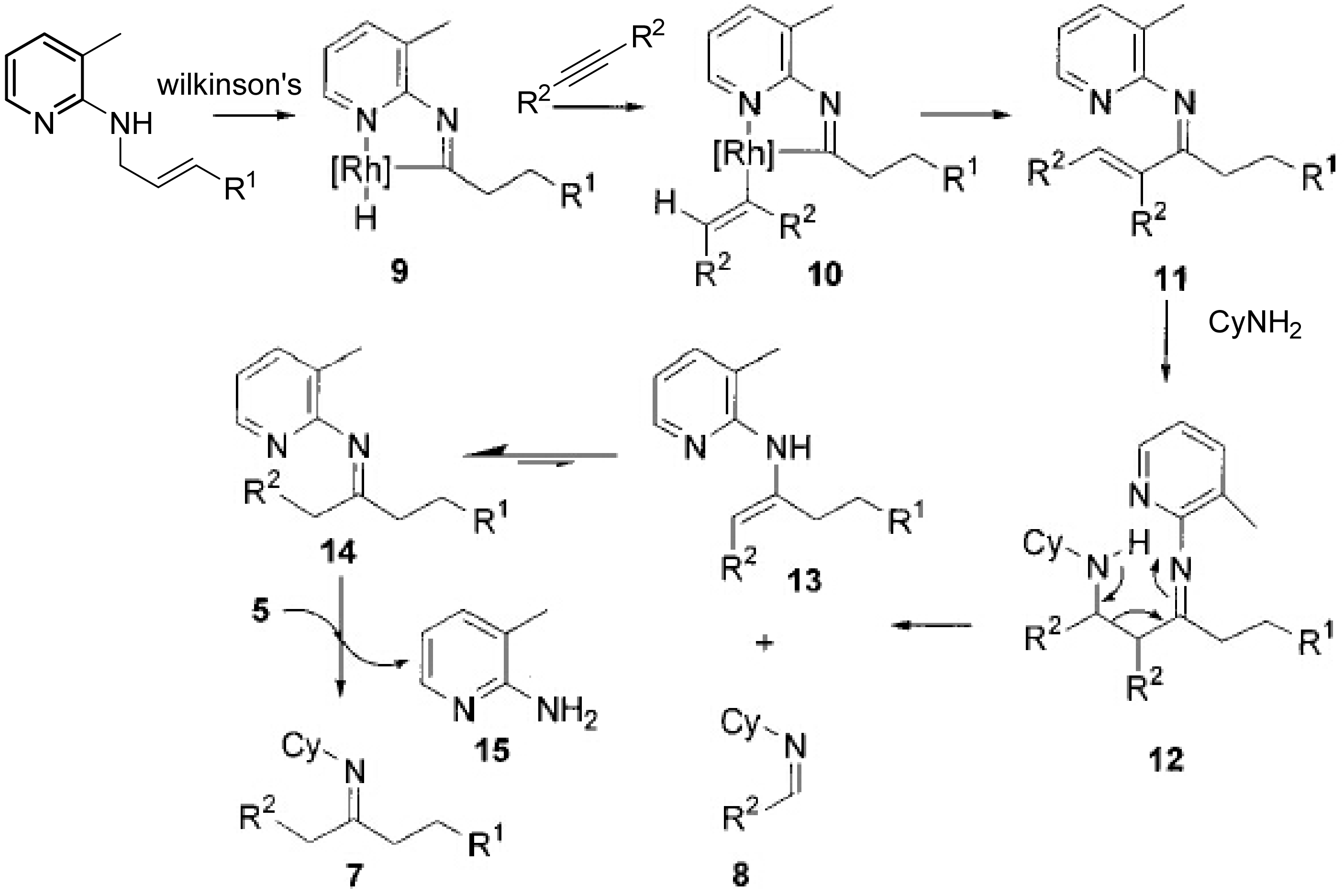
| entry | allylamine (**1**) | alkyne (**2**) | isolated yield (%) |
|---|---|---|---|
| 1 | **1a** ($R^1$ = Ph) | **2a** ($R^2$ = $CH_3$) | 98 (**3a**) |
| 2 | **1a** ($R^1$ = Ph) | **2b** ($R^2$ = *n*-$C_3H_7$) | 84 (**3b**) |
| 3 | **1a** ($R^1$ = Ph) | **2c** ($R^2$ = *n*-$C_2H_5$) | 93 (**3c**) |
| 4 | **1a** ($R^1$ = Ph) | **2d** ($R^2$ = *n*-$C_5H_{11}$) | 91 (**3d**) |
| 5 | **1a** ($R^1$ = Ph) | **2e** ($R^2$ = Ph) | 98[a] (**3e**) |
| 6 | **1b** ($R^1$ = $CH_3$) | **2b** ($R^2$ = *n*-$C_3H_7$) | 80[b] (**3f**) |
| 7 | **1b** ($R^1$ = $CH_3$) | **2e** ($R^2$ = Ph) | 94[a] (**3g**) |
| 8 | **1c** ($R^1$ = H) | **2e** ($R^2$ = Ph) | 92[a] (**3h**) |

[a] The reaction was carried out with **6**. [b] GC yield.

terminal alkyne
N. R.

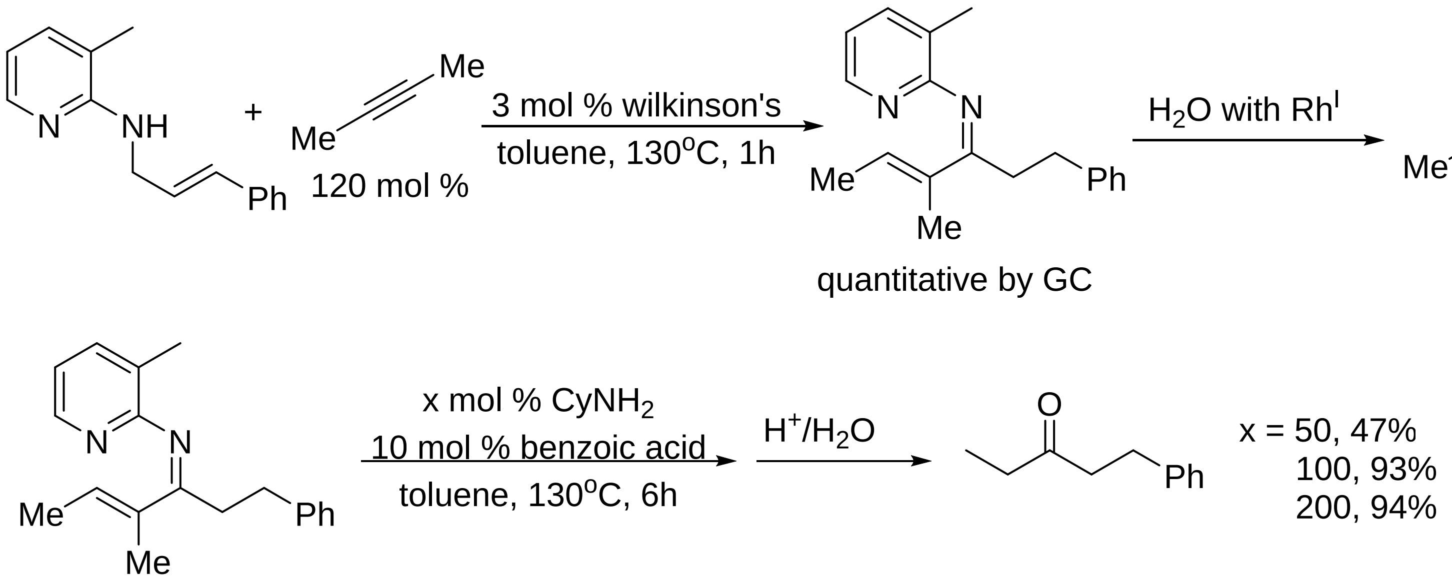
Chul-Ho Jun *et al. J. Am. Chem. Soc.* **2001**, *123*, 8600

# 2-Amino-3-picoline




Chul-Ho Jun *et al. J. Am. Chem. Soc.* **2001**, *123*, 8600

# 2-Amino-3-picoline




Chul-Ho Jun *et al. J. Am. Chem. Soc.* **2001**, *123*, 8600

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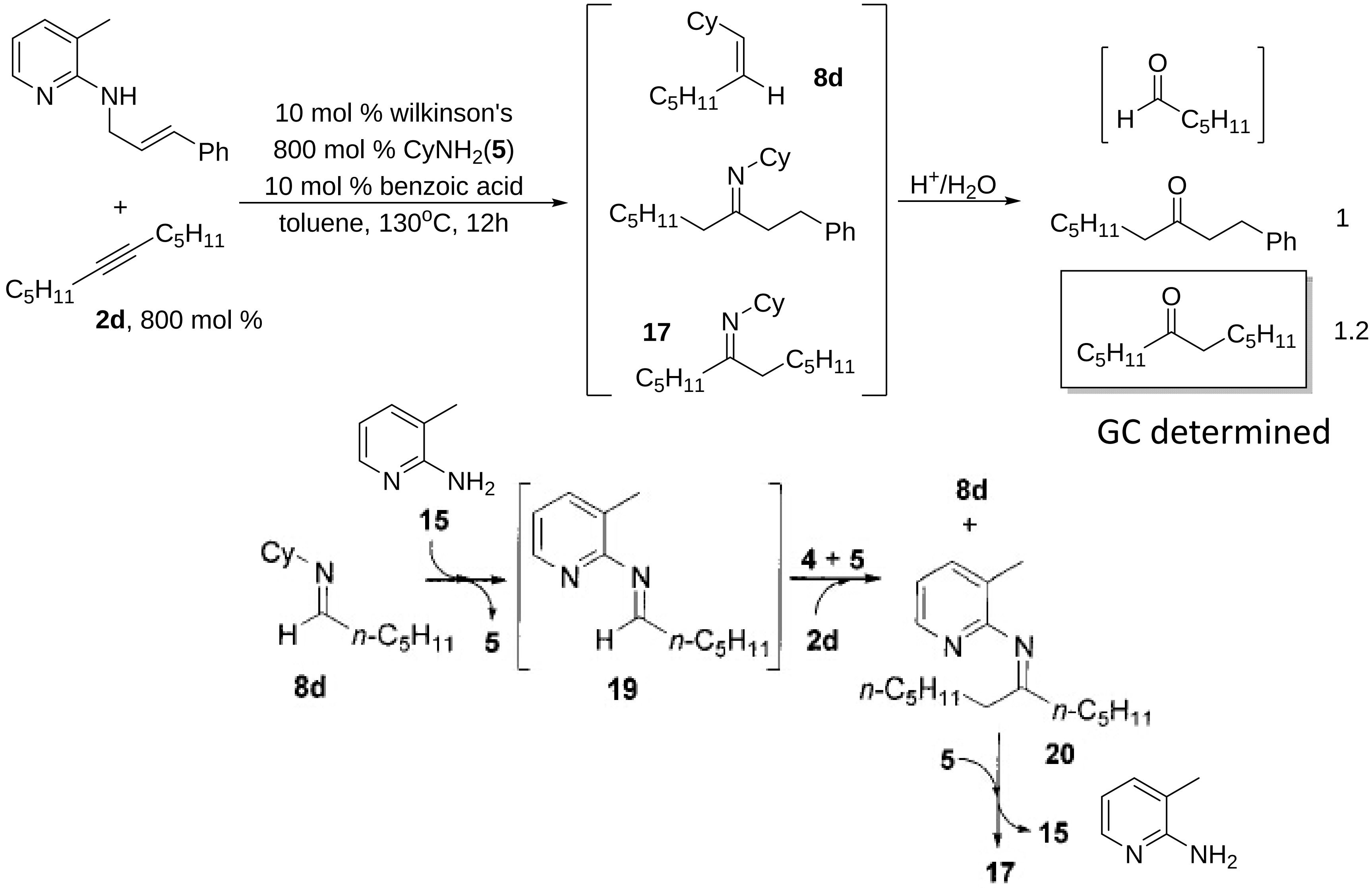


Chul-Ho Jun *et al. J. Am. Chem. Soc.* **2001**, *123*, 8600

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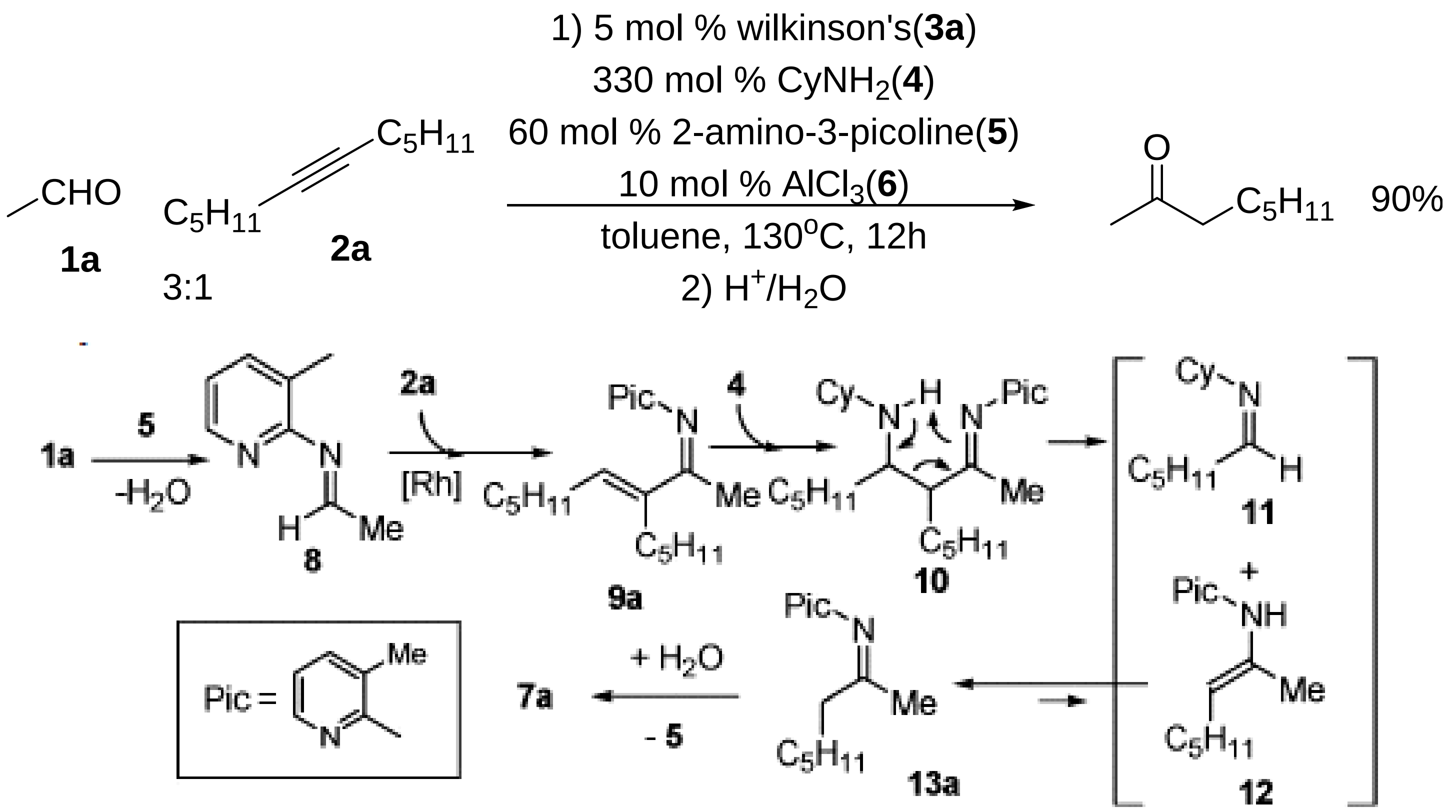
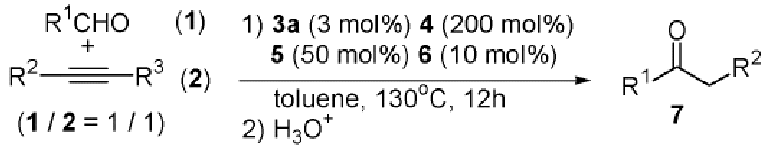


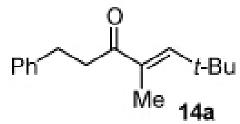

Chul-Ho Jun *et al. J. Am. Chem. Soc.* **2003**, *125*, 6372

# 2-Amino-3-picoline



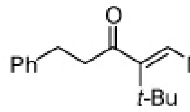

| entry | $R^1$ (1) | $R^2$, $R^3$ (2) | isolated yield of product (7, 7′) |
|---|---|---|---|
| 1 | $PhCH_2CH_2$ (**1b**) | $R^2 = R^3 =$ Me (**2b**) | 90% (**7b**) |
| 2 | | $R^2 = R^3 =$ Et (**2c**) | 91% (**7c**) |
| 3 | | $R^2 = R^3 =$ Pr (**2d**) | 94% (**7d**) |
| 4[a] | | $R^2 =$ Me, $R^3 =$ *t*-Bu (**2e**) | 33% (**7b**) |
| 5 | $C_5H_{11}$ (**1c**) | (**2d**) | 91% (**7e**) |
| 6 | $PhCH_2$ (**1d**) | (**2b**) | 82% (**7f**) |
| 7[b] | *p*-$MeOC_6H_4$ (**1e**) | (**2b**) | 54% (**7g**) |

[a] A parent α,β-unsaturated ketone **14a** remained unreacted (47% yield). [b] The unreacted starting material was detected in 35% GC yield. 100 mol % of **5** was used.




**14a**

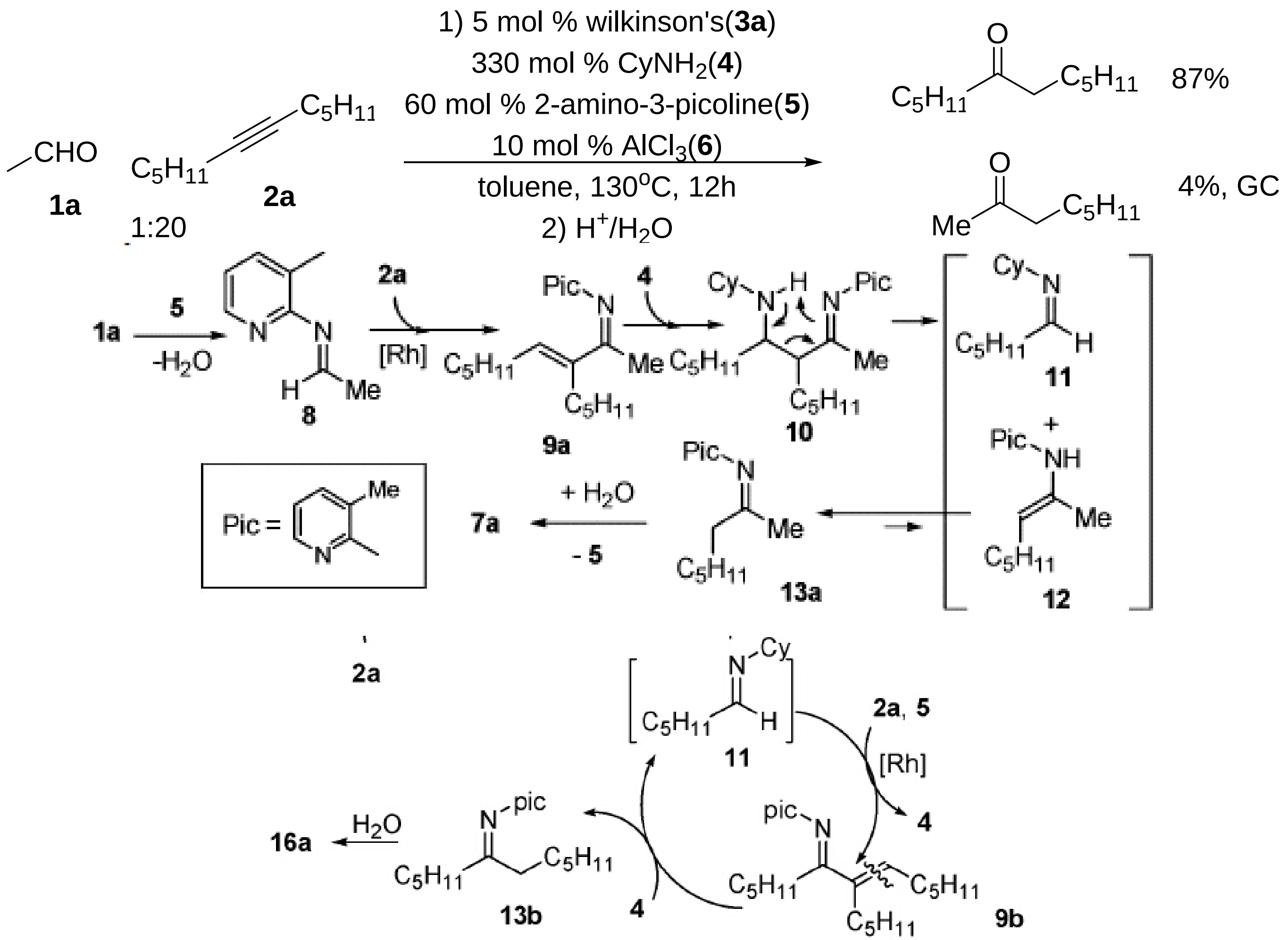
47%




**14b** (not observed)

Chul-Ho Jun *et al. J. Am. Chem. Soc.* **2003**, *125*, 6372

# 2-Amino-3-picoline




Chul-Ho Jun *et al. J. Am. Chem. Soc.* **2003**, *125*, 6372

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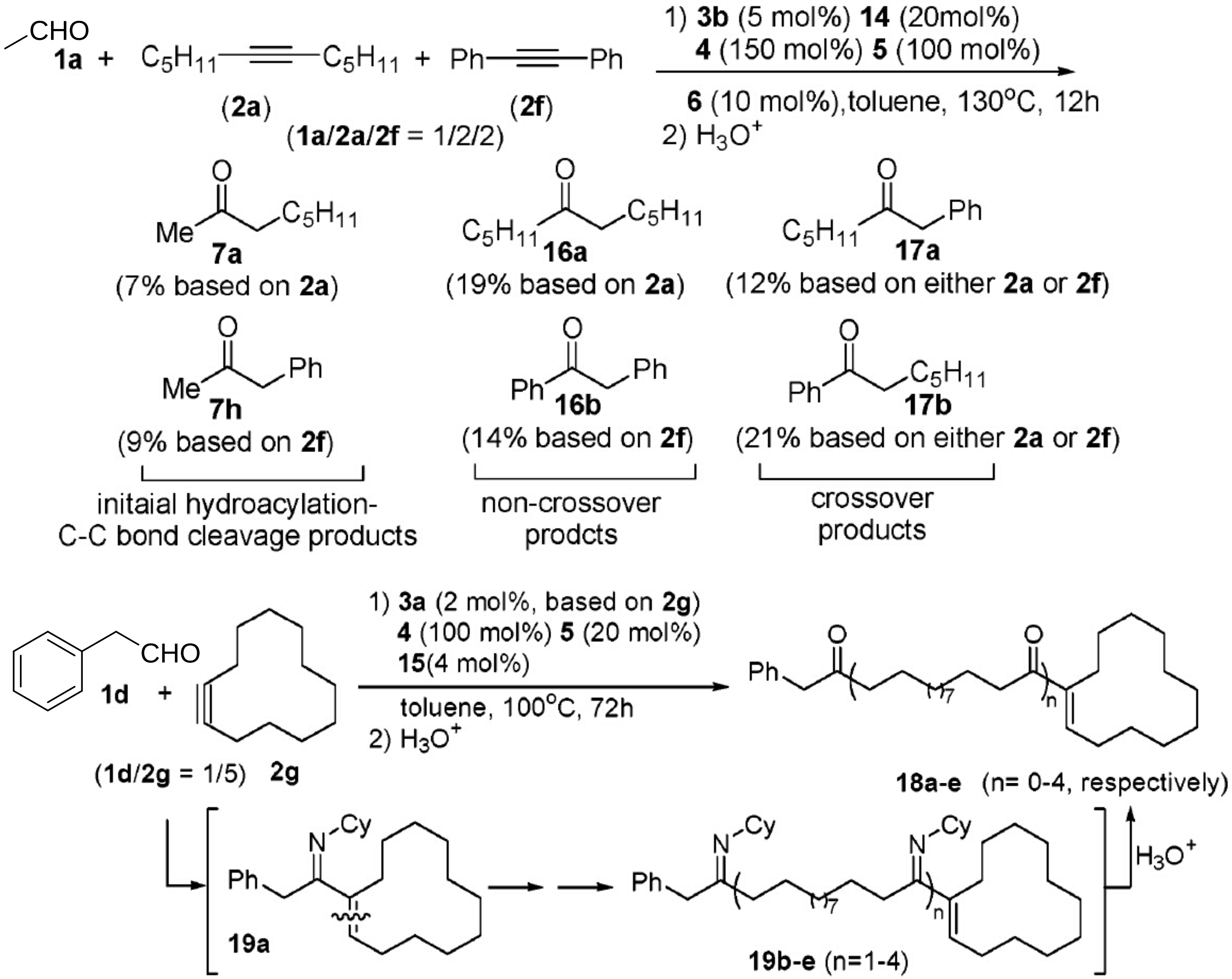


Chul-Ho Jun *et al. J. Am. Chem. Soc.* **2003**, *125*, 6372

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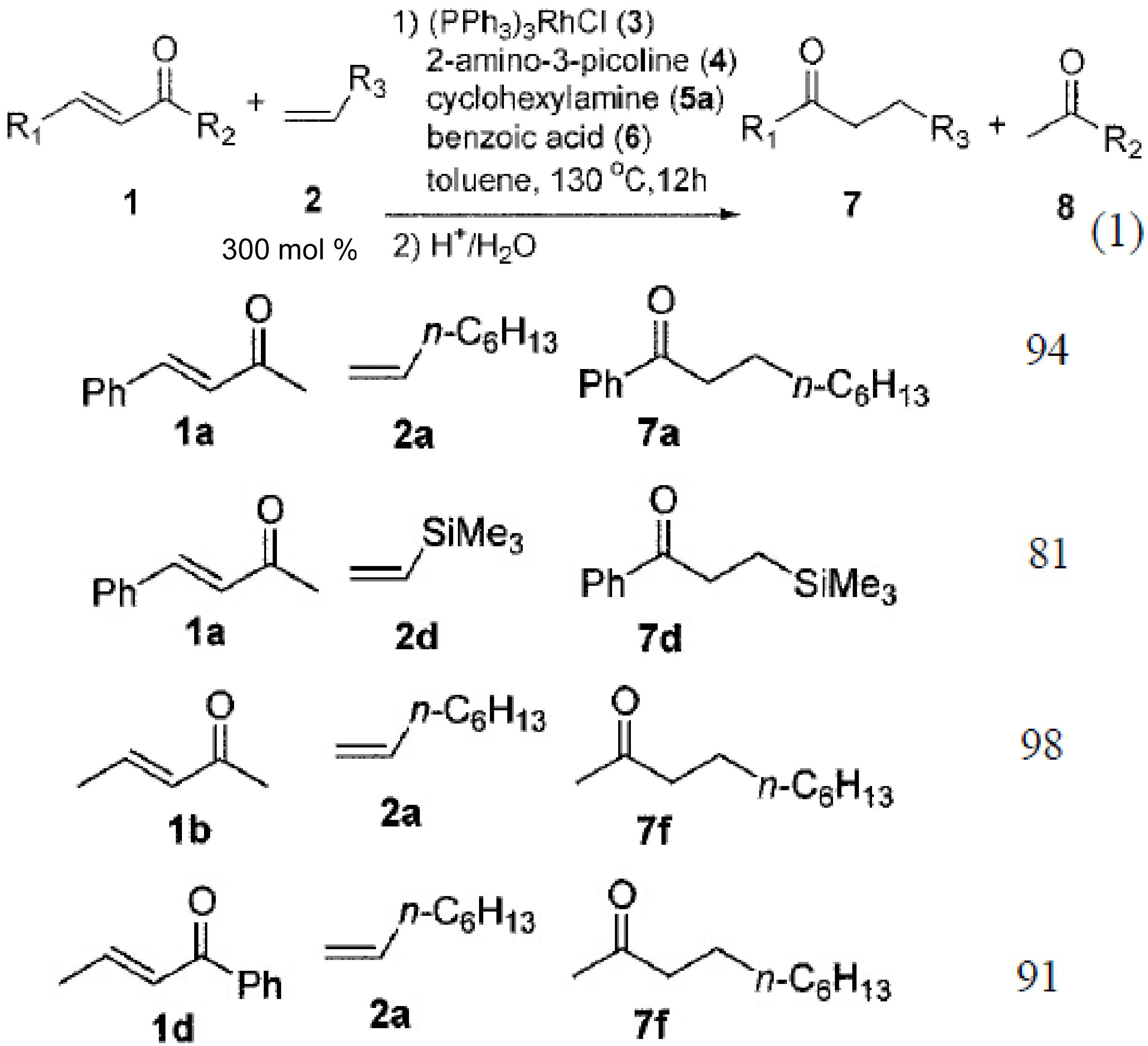
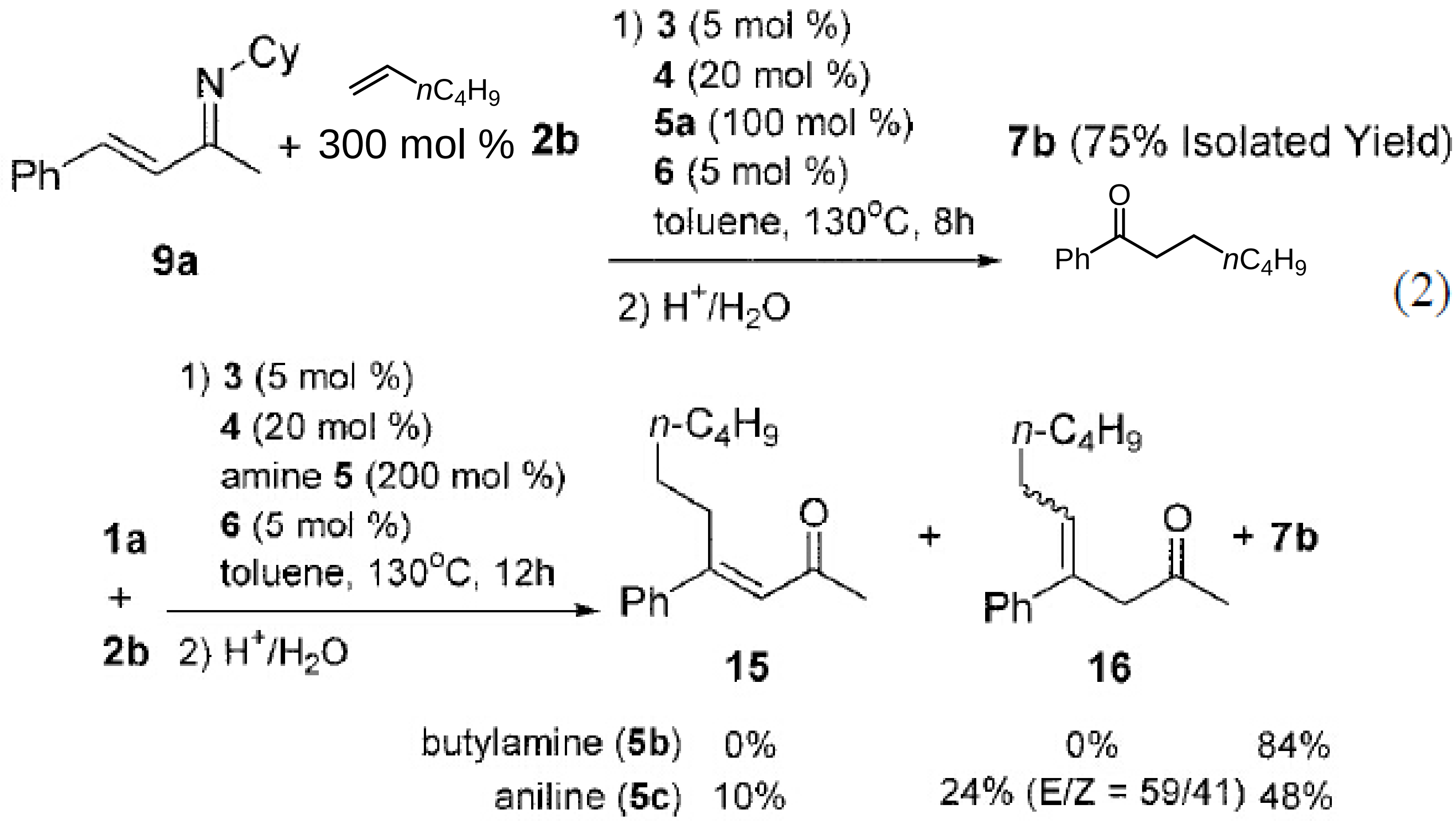



Sung-Gon Lim, Chul-Ho Jun, *Bull. Korean Chem. Soc.* **2004**, *25*, 1623

# 2-Amino-3-picoline




Sung-Gon Lim, Chul-Ho Jun, *Bull. Korean Chem. Soc.* **2004**, *25*, 1623

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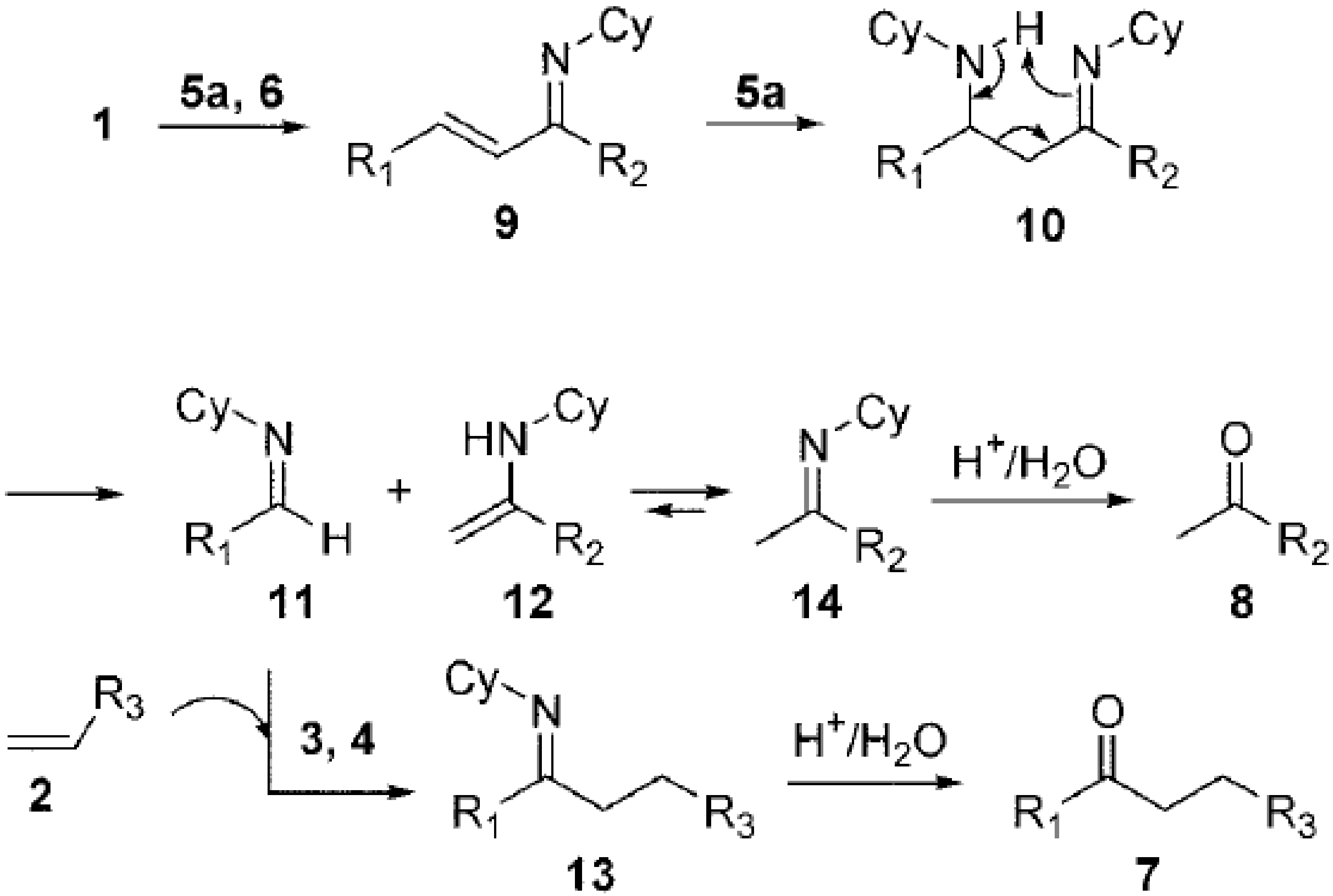
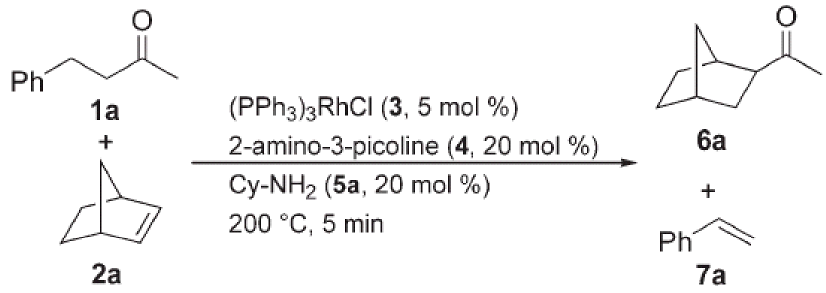


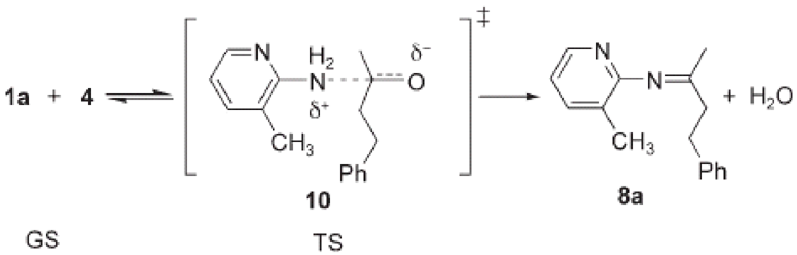

Sung-Gon Lim, Chul-Ho Jun, *Bull. Korean Chem. Soc.* **2004**, *25*, 1623

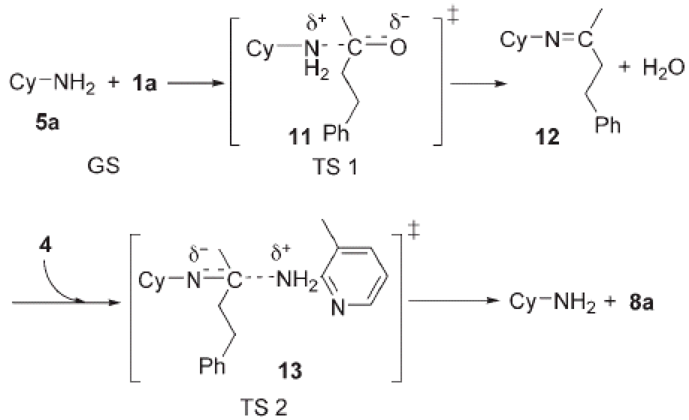
# 2-Amino-3-picoline




| Entry | Cy-$NH_2$ | Activation mode | Yield[a] of 6a (7a) |
|---|---|---|---|
| 1 | none | Δ | 9% (8%) |
| 2 | none | MW | 44% (40%) |
| 3 | 20 mol % | Δ | 16% (14%) |
| 4 | 20 mol % | MW | 85% (84%) |

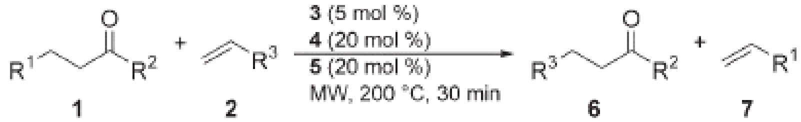
[a] Yield was determined by GC and the ratio of *exo/endo*-**6a** was *ca.* 7/3




Chul-Ho Jun *et. al. Adv. Synth. Catal.* **2006**, *348*, 55

# 2-Amino-3-picoline

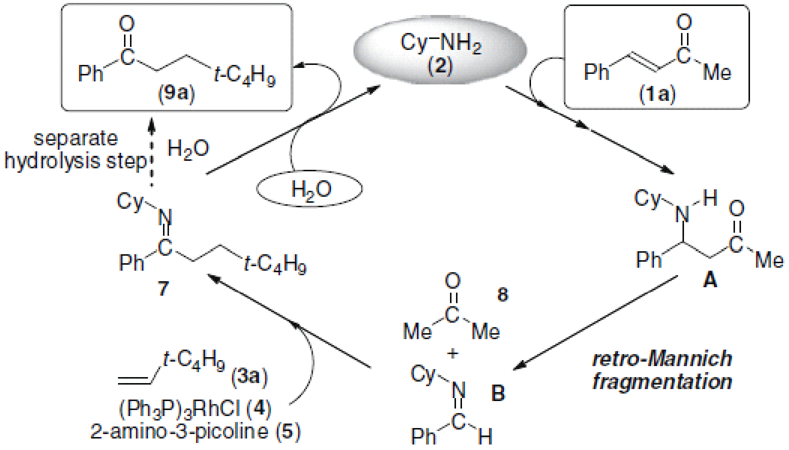


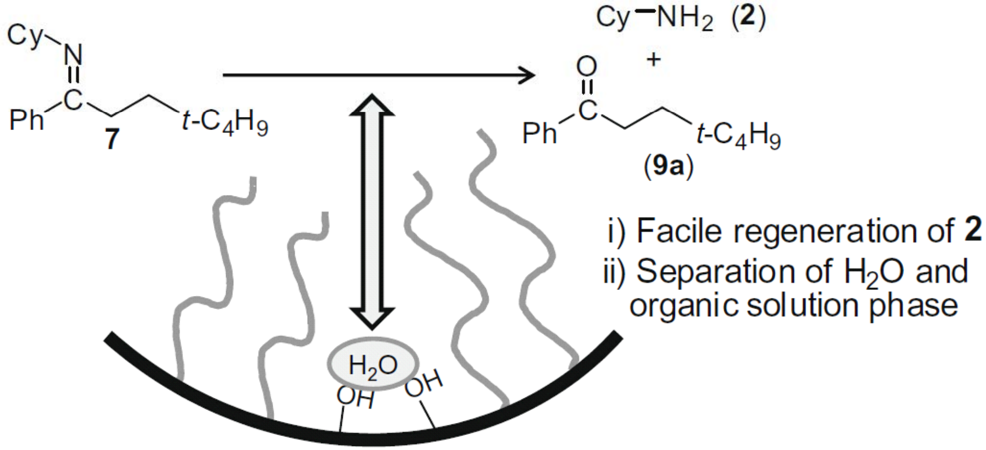

| Entry | 1 (Ketone) | 2 (Olefin) | 6 (Product) | Yield [%][a] |
|---|---|---|---|---|
| 1 | 1a | 2a | 6a | 100% (*exo/endo* = 72/28)[b] |
| 2 | 1b | 2a | 6a | 98% |
| 3 | 1c | 2a | 6a | 98% |
| 4[c] | 1a | 2b | 6b | 93% (76%) |
| 5[c] | 1a | 2c | 6c | 71% (52%) |
| 6[c] | 1a | 2d | 6d | 80% (79%) |
| 7[c] | 1a | 2e | 6e | 64% (67%) |

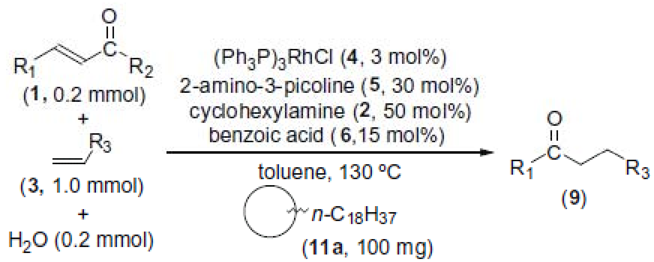
[a] GC yield based on **1** and values in parenthesis are isolated yields.
[b] The ratio was determined by $^1H$ NMR.
[c] 7 equivs. of olefin were used under 100 mol % **4**, 15 mol % **5**, and 10 mol% benzoic acid.

Chul-Ho Jun *et. al. Adv. Synth. Catal.* **2006**, *348*, 55

# 2-Amino-3-picoline



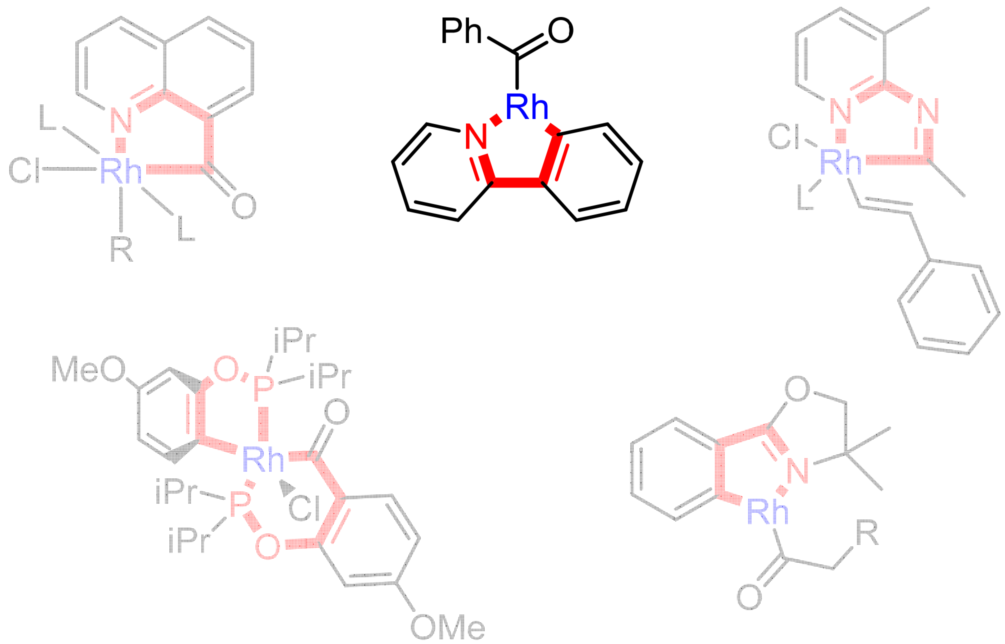




| Entry | α,β-Unsaturated ketone (1) ($R_1$, $R_2$) | Olefin (3) ($R_3$) | Rxn time | Yield of 9[a] (%) | Yield of 9 without using 11a[a] (%) |
|---|---|---|---|---|---|
| 1 | Ph, Me (**1a**) | $n$-$C_4H_9$ (**3b**) | 4 h | 89(98) (**9b**) | 41(51) |
| 2 | | $n$-$C_6H_{13}$ (**3c**) | | 85(98) (**9c**) | 47(56) |
| 3 | | $c$-$C_6H_{12}$ (**3d**) | | 77(80) (**9d**) | 25(33) |
| 4 | | $C_6H_5$ (**3e**) | | 83(95) (**9e**) | 54(58) |
| 5 | | $SiMe_3$ (**3f**) | | 89(99) (**9f**) | 30(45) |
| 6 | | $SiEt_3$ (**3g**) | | 88(97) (**9g**) | 17(33) |
| 7 | Me, Me (**1b**) | **3a** | 45 min | (82) (**9h**) | (44) |
| 8 | Ph, Ph (**1c**) | **3a** | 14 h | 85(89) (**9a**) | 51(61) |

[a] Isolated yield. The yields in parentheses are determined by GC.

Dong Hun Lee, Eun-Ae Jo, Jung-Woo Park, Chul-Ho Jun *Tetrahedron Lett.* **2010**, *51*, 160

# *Pyridine*



Ph
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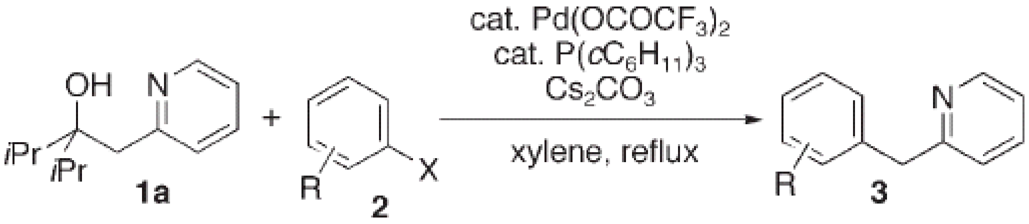
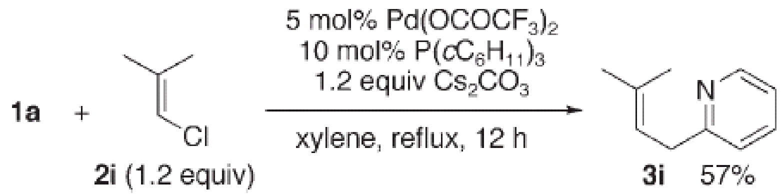
# Pyridine

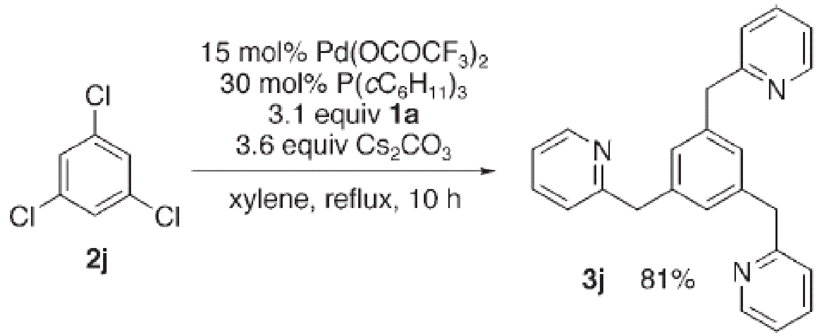



| Entry | R | X | 2 | 3 | Yield[b] [%] |
|---|---|---|---|---|---|
| 1 | H | Cl | **2a** | **3a** | 88 |
| 2 | 4-$CF_3$ | Cl | **2b** | **3b** | 89 |
| 3 | 4-COOEt | Cl | **2c** | **3c** | 80 |
| 4 | 4-CN | Cl | **2d** | **3d** | 70 |
| 5 | 4-OMe | Cl | **2e** | **3e** | 90 |
| 6 | 2-Me | Cl | **2f** | **3f** | 79 |
| 7 | 4-$CH_2$=CH | Cl | **2g** | **3g** | 81 |
| 8 | 2-chloropyridine | | **2h** | **3h** | 50 (63) |
| 9 | H | Cl | **2a** | **3a** | 85[c] |
| 10 | H | Br | **2a-Br** | **3a** | 80[c] |
| 11 | H | I | **2a-I** | **3a** | 88[c] |
| 12 | H | I | **2a-I** | **3a** | 80[c,d] |

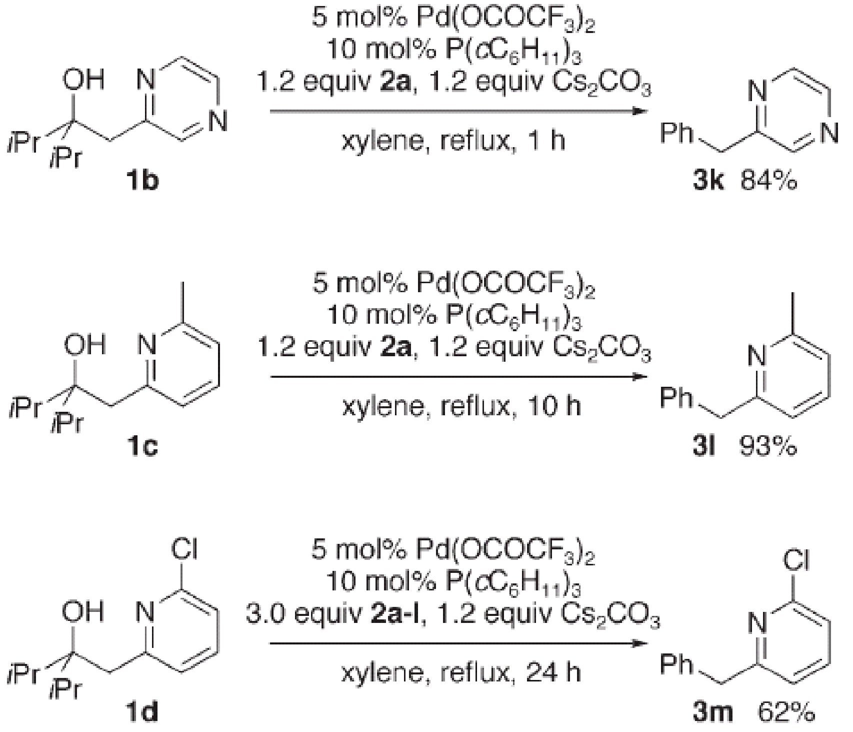
[a] A mixture of **1a** (0.8 mmol), **2** (1.2 equiv), $Pd(OCOCF_3)_2$ (5 mol%), $P(cC_6H_{11})_3$ (10 mol%), and $Cs_2CO_3$ (1.2 equiv) was heated at reflux in xylene (0.5 M) for 1.5–10 h. [b] Yield of isolated product. The yield determined by $^1$H NMR spectroscopy is given in parentheses. [c] Performed in refluxing toluene. [d] $PPh_3$ was used instead of $P(cC_6H_{11})_3$.

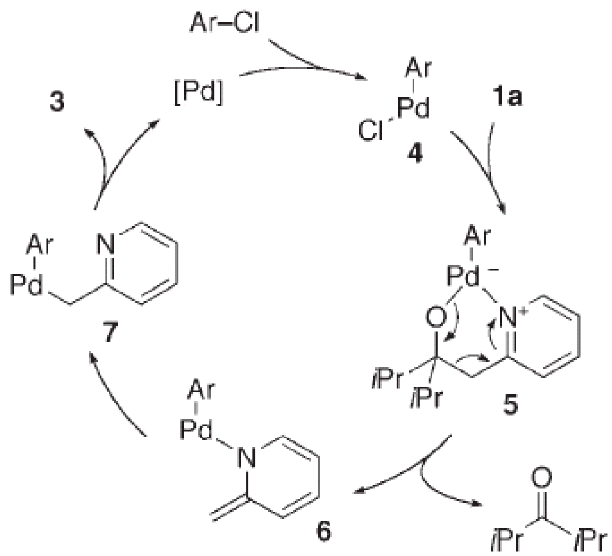
Takashi Niwa, Hideki Yorimitsu, Koichiro Oshima,
*Angew. Chem. Int. Ed.* **2007**, *46*, 2643

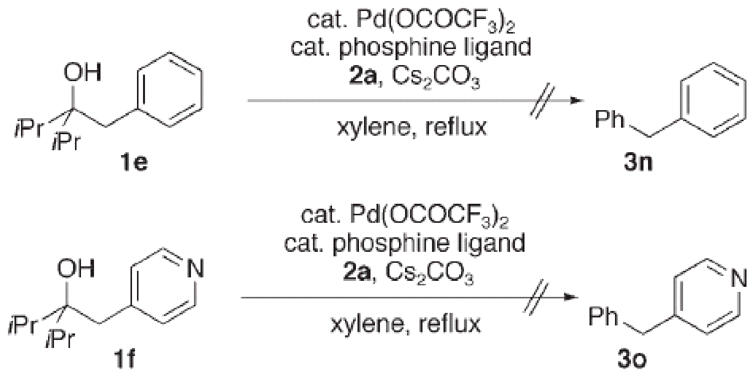


# Pyridine

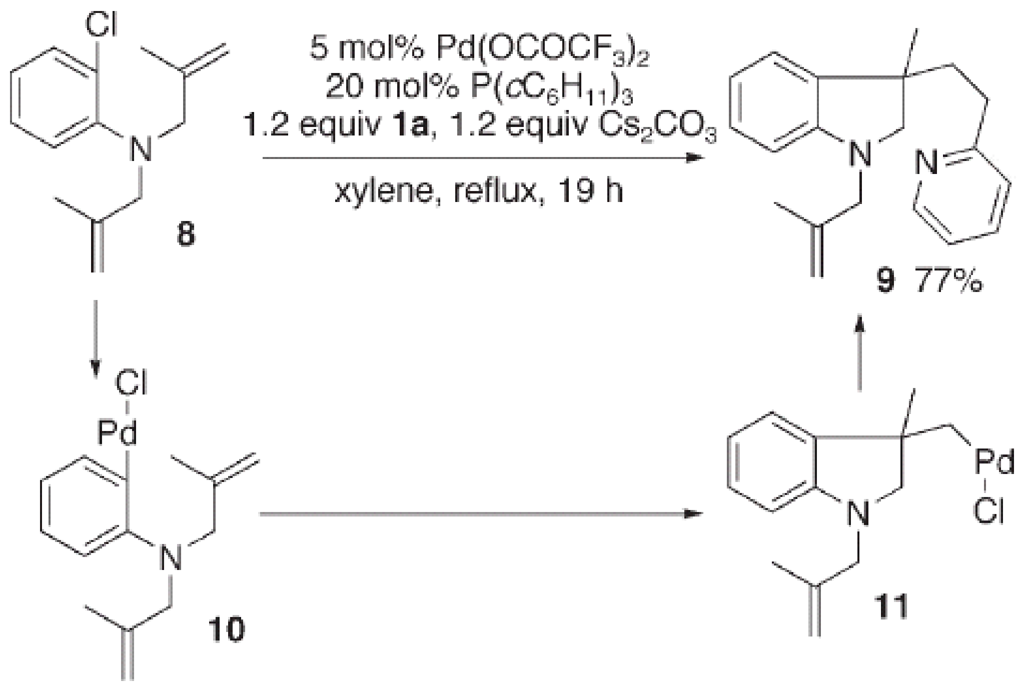


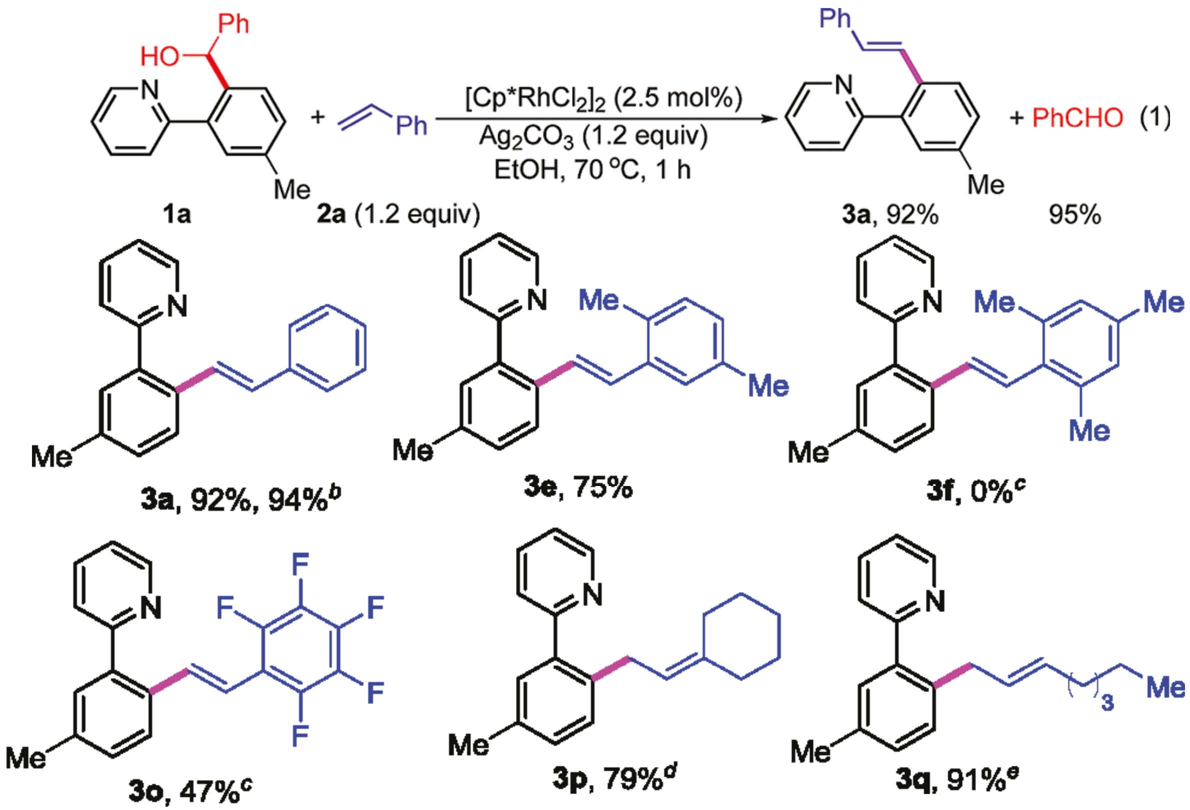

Takashi Niwa, Hideki Yorimitsu, Koichiro Oshima, *Angew. Chem. Int. Ed.* **2007**, *46*, 2643

# Pyridine




Takashi Niwa, Hideki Yorimitsu, Koichiro Oshima, *Angew. Chem. Int. Ed.* **2007**, *46*, 2643

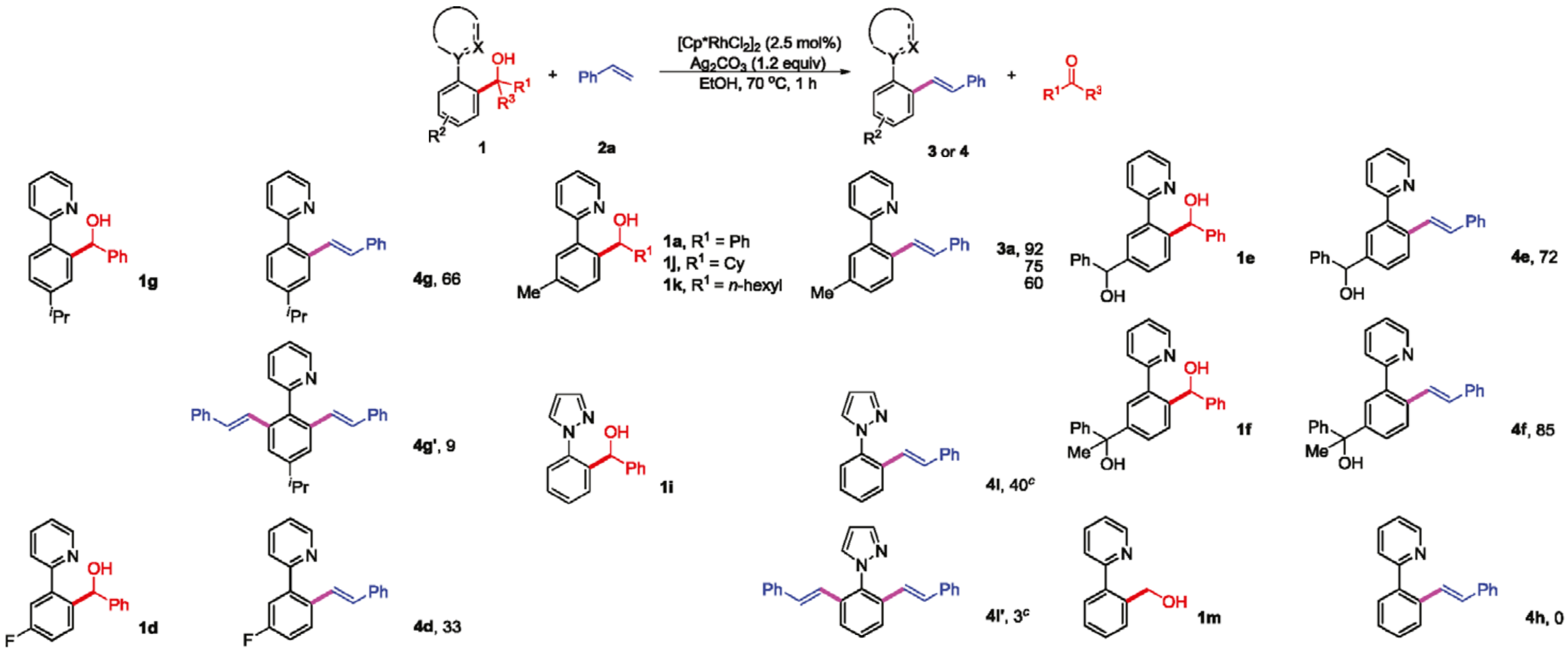
# Pyridine




[a] Reactions conducted with 0.25 mmol of alcohol substrate 1a, 2.5 mol % of $[Cp^*RhCl_2]_2$ as catalyst, 1.2 equiv of alkene, 1.2 equiv of $Ag_2CO_3$, and 1.0 mL of EtOH as solvent unless otherwise noted; isolated yields are given. [b] Reaction performed on 1.0 mmol scale. [c] Reaction ran for 3 h. [d] Reaction ran for 12 h. [e] $E/Z$ = 6.7:1.

Hu Li, Yang Li, Xi-Sha Zhang, Kang Chen, Xin Wang, Zhang-Jie Shi
*J. Am. Chem. Soc.* **2011**, *133*, 15244

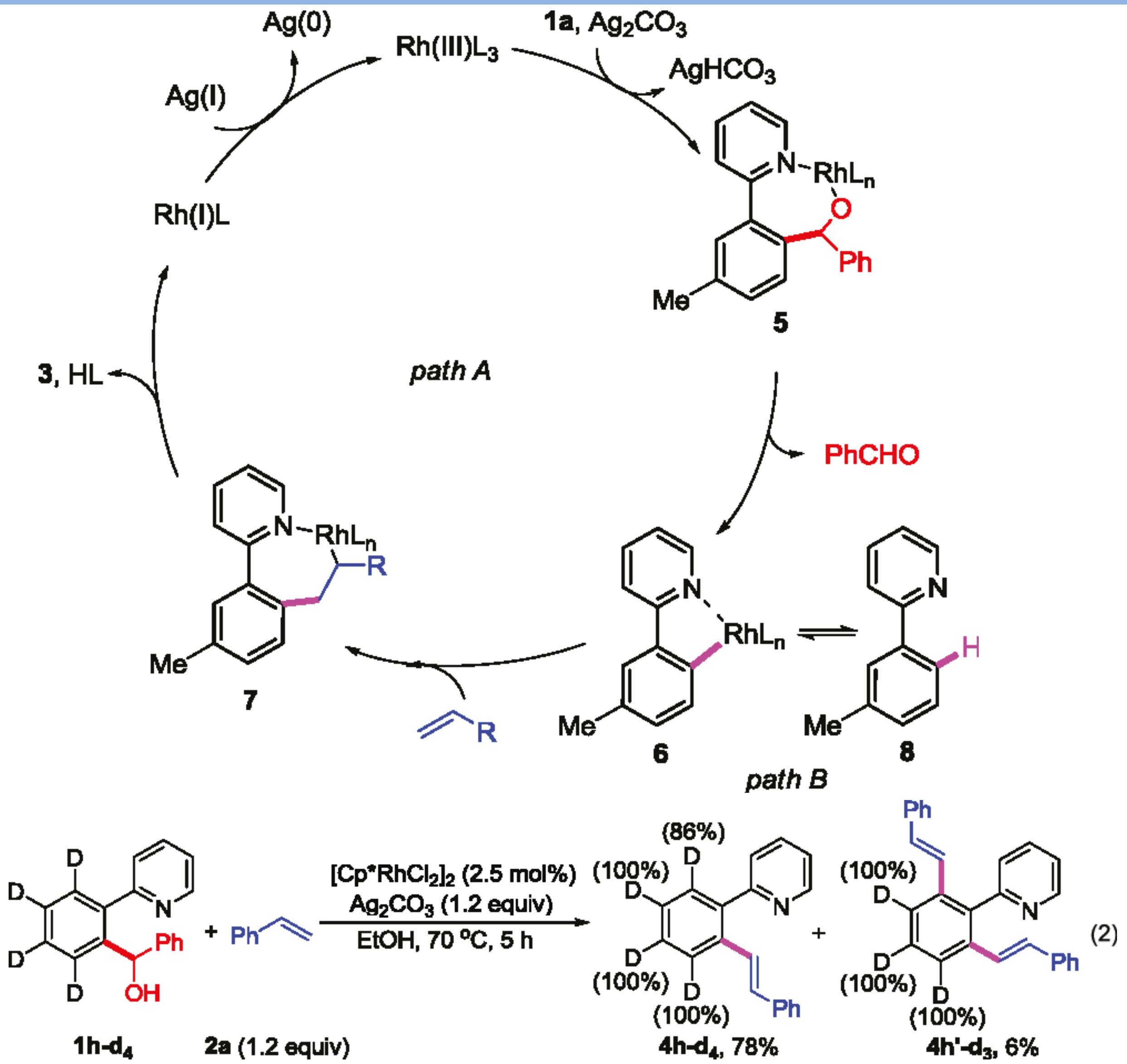
# Pyridine




a Reactions conducted with 0.25mmol of alcohol substrate 1, 2.5 mol % of [Cp*RhCl2]2 as catalyst, 1.2 equiv of styrene, 1.2 equiv of Ag2CO3, and 1.0mL of EtOH as solvent unless otherwise noted. Isolated yields are given. b 3.0 equiv each of styrene and Ag2CO3 were used. c Reaction ran for 5 h. d Reaction ran for 4 h.

Hu Li, Yang Li, Xi-Sha Zhang, Kang Chen, Xin Wang, Zhang-Jie Shi
*J. Am. Chem. Soc.* **2011**, *133*, 15244

# Pyridine

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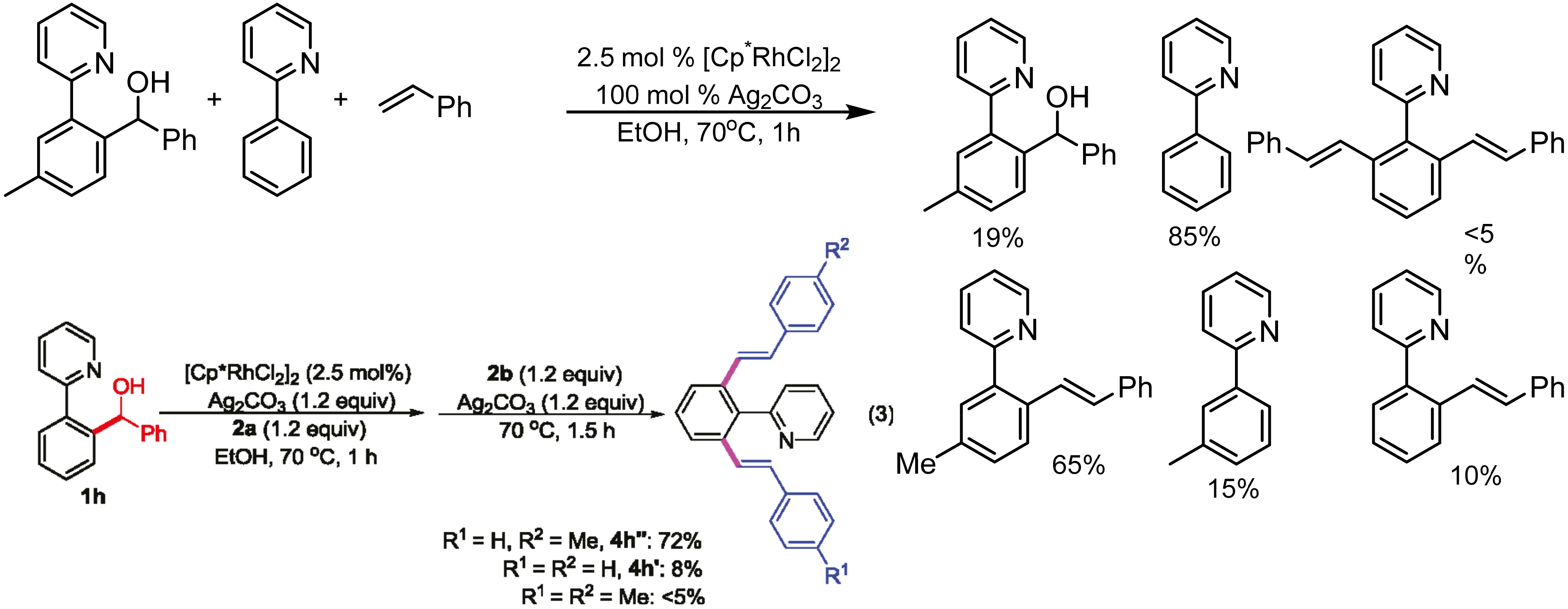


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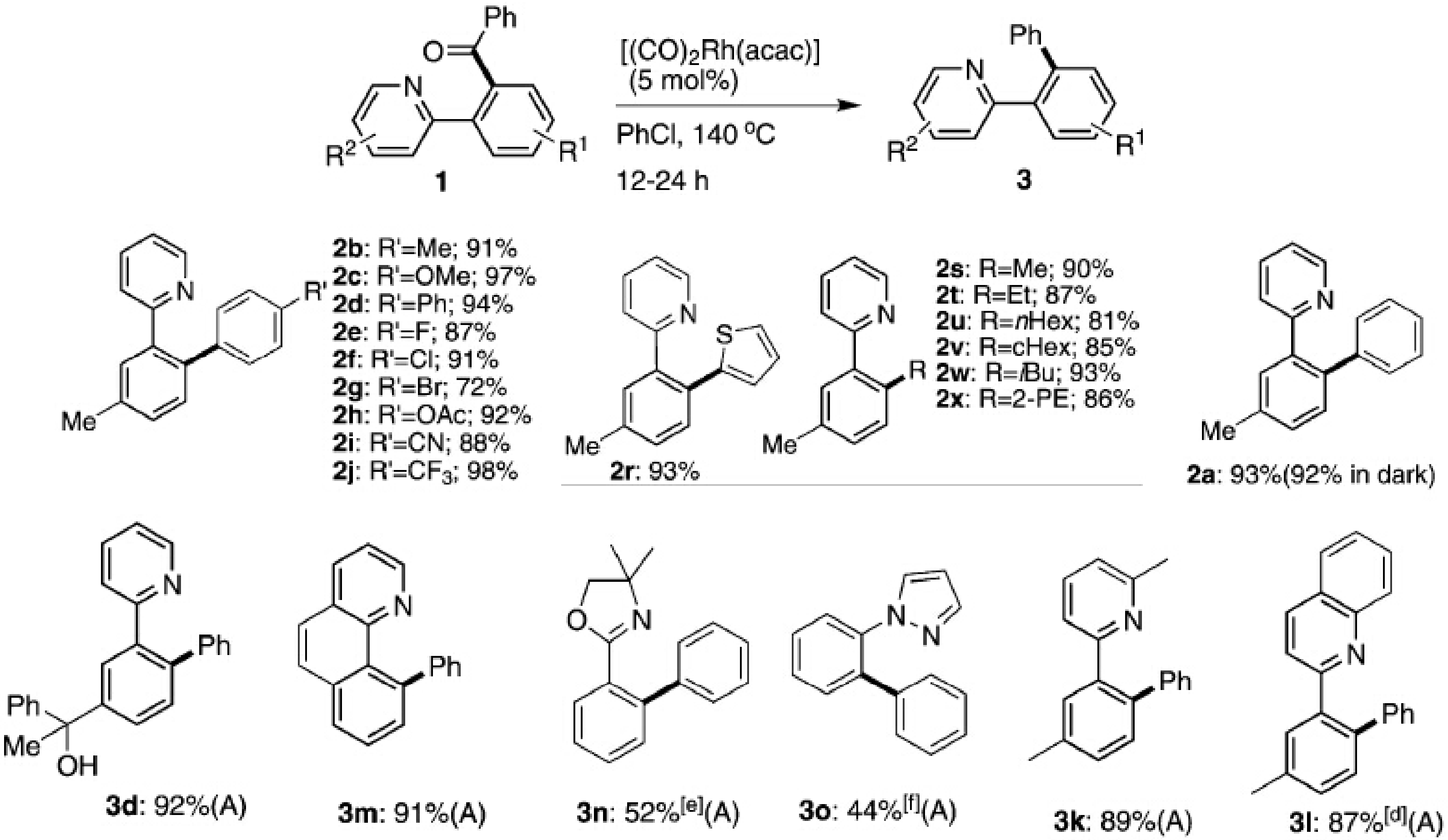
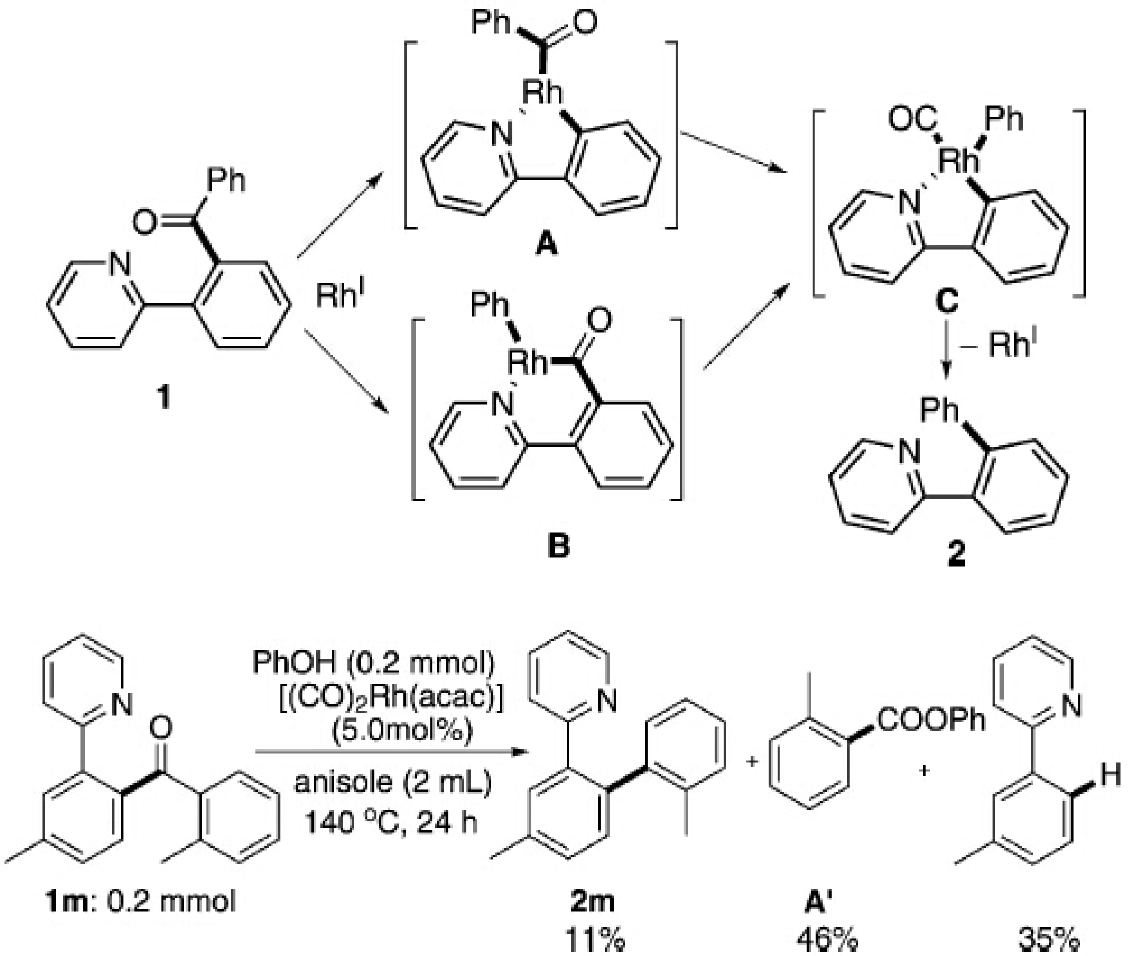
*J. Am. Chem. Soc.* **2011**, *133*, 15244

# Pyridine



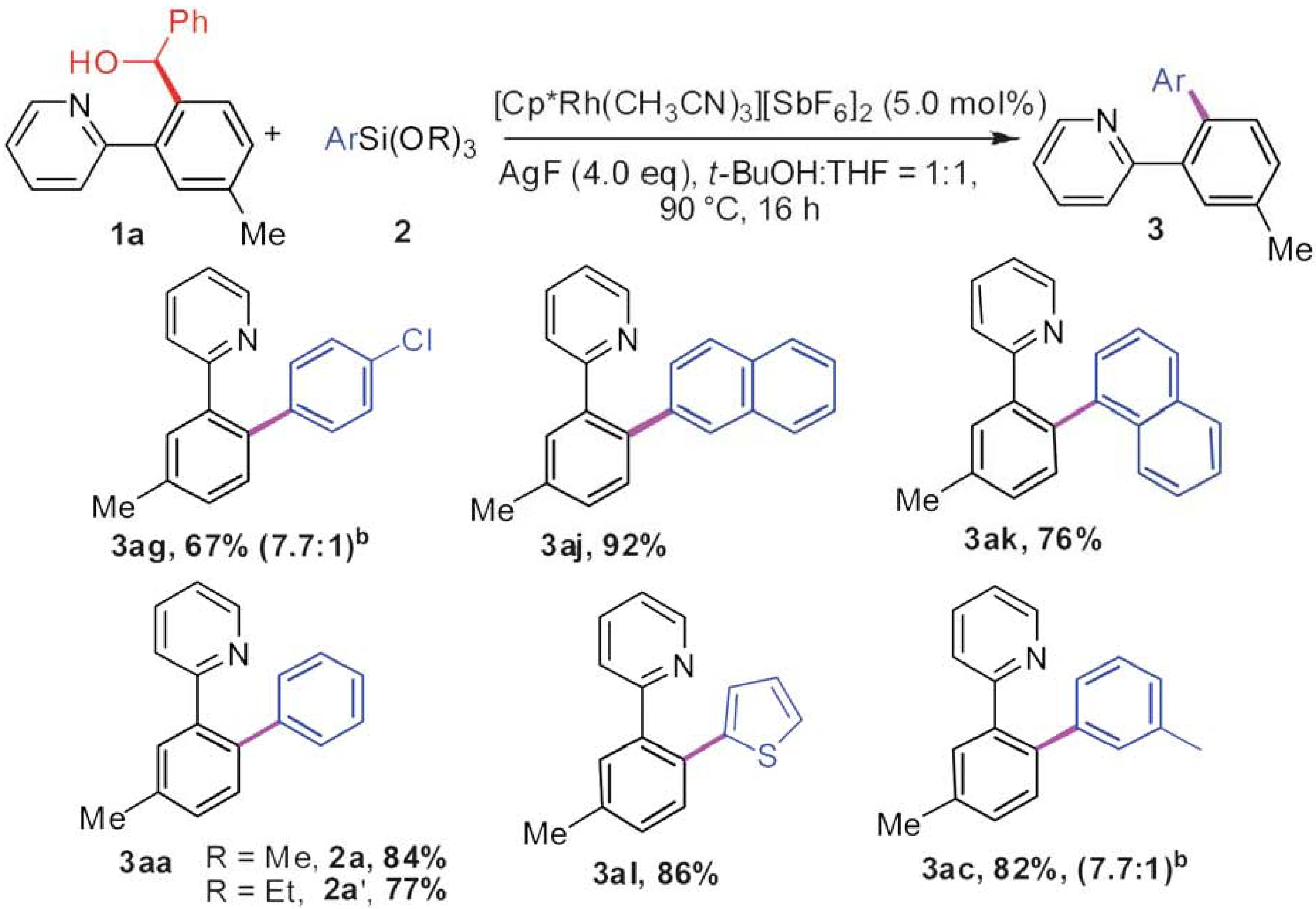

Zhang-Jie Shi *et. al.*, *Angew. Chem. Int. Ed.* **2012**, *51*, 2690

# Pyridine



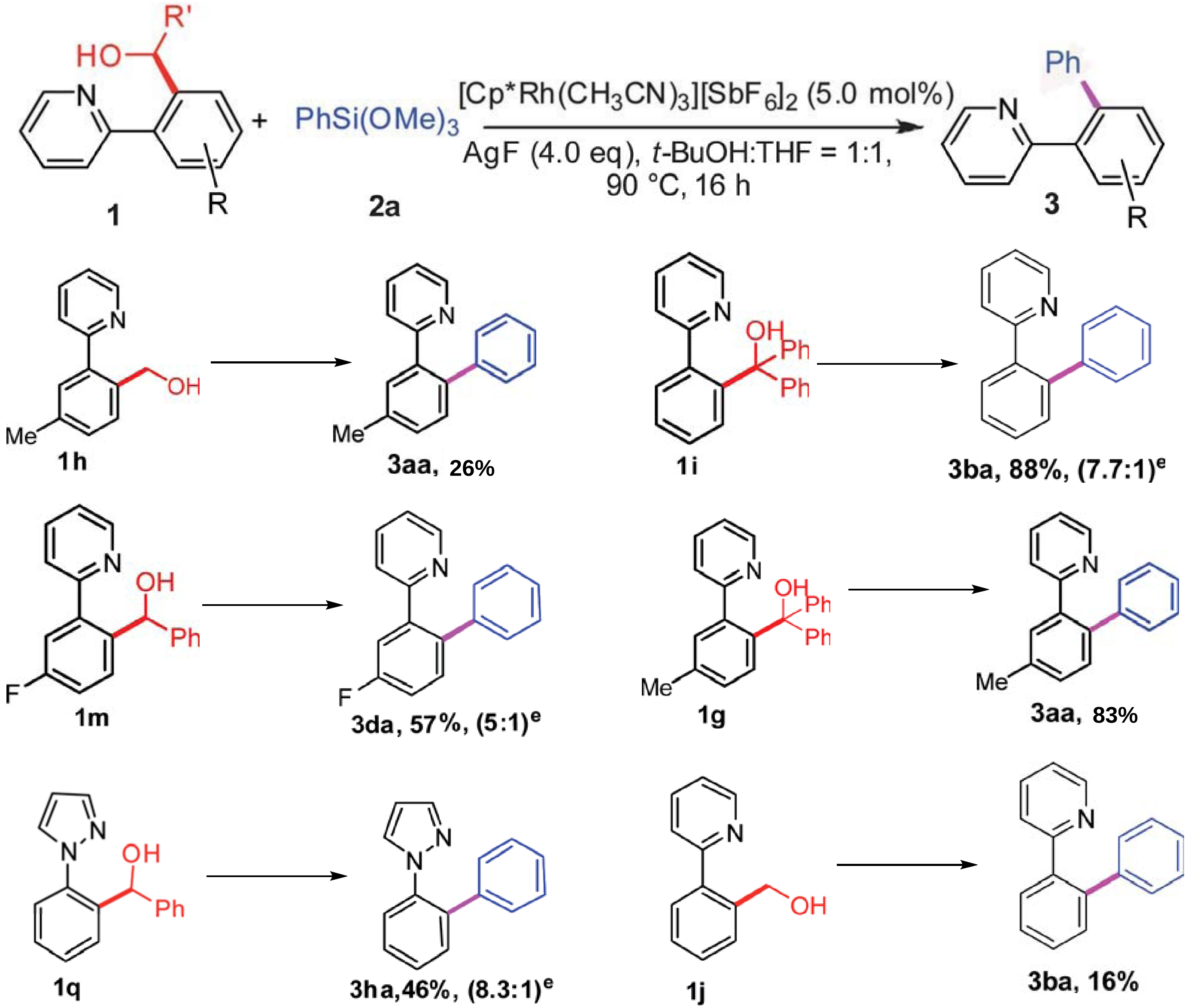

Zhang-Jie Shi *et. al.*, *Angew. Chem. Int. Ed.* **2012**, *51*, 2690

# Pyridine



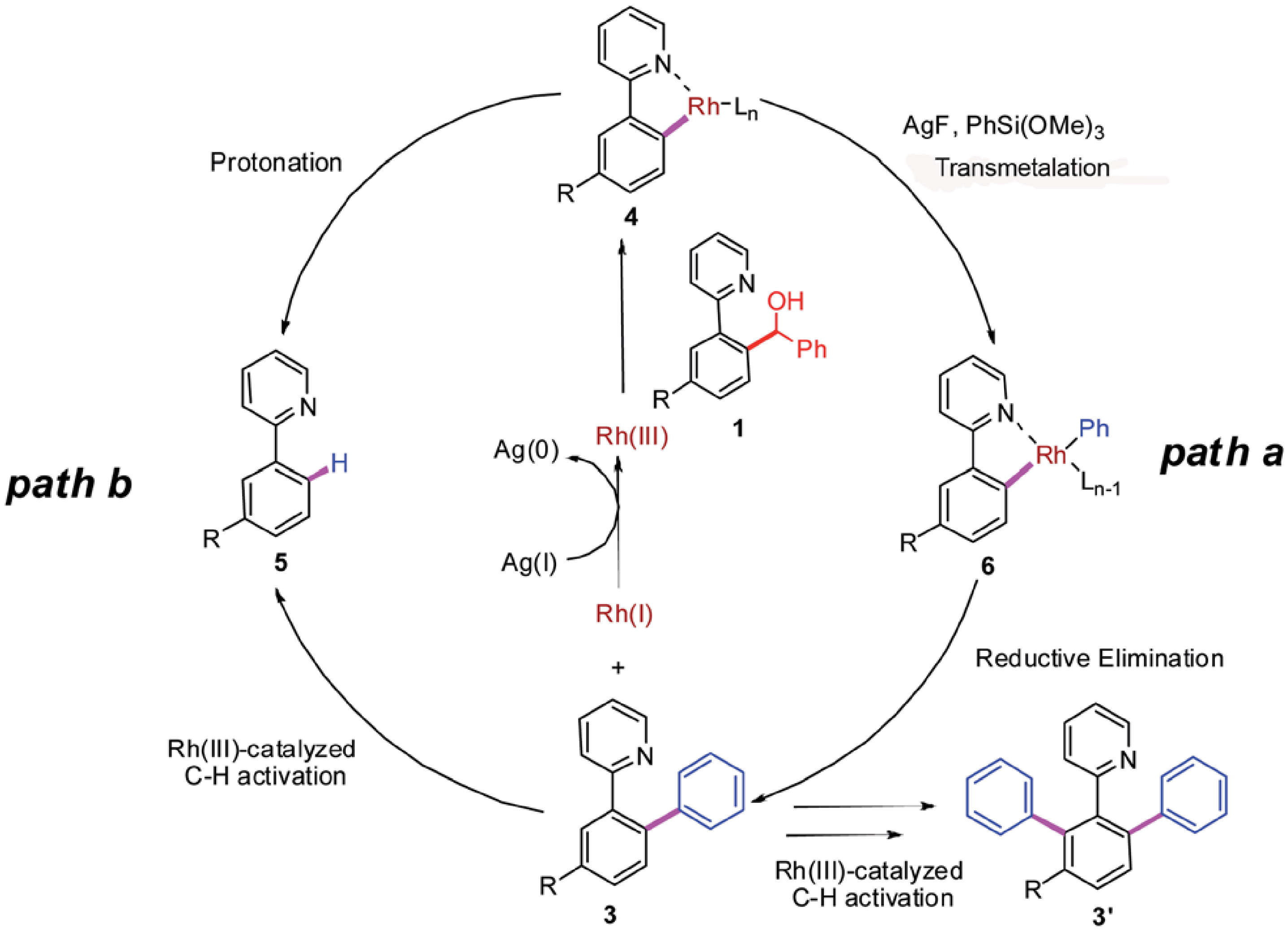

Zhang-Jie Shi, *Chem. Sci.* **2012**, *3*, 1645

# Pyridine



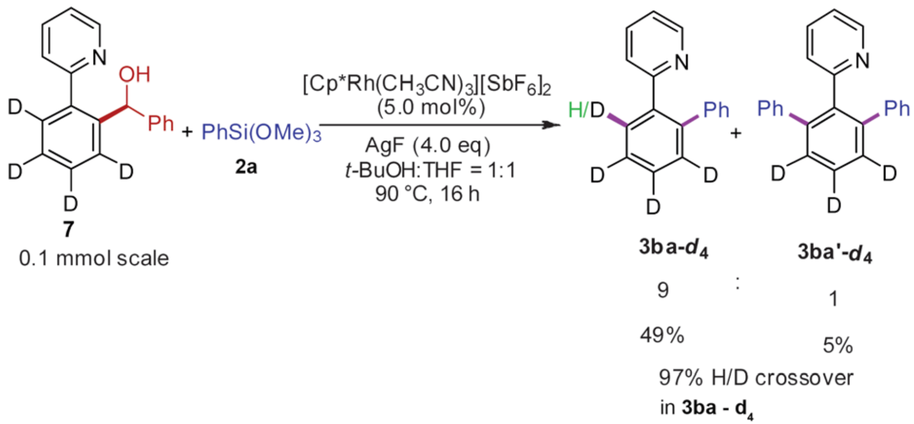

Zhang-Jie Shi, *Chem. Sci.* **2012**, *3*, 1645

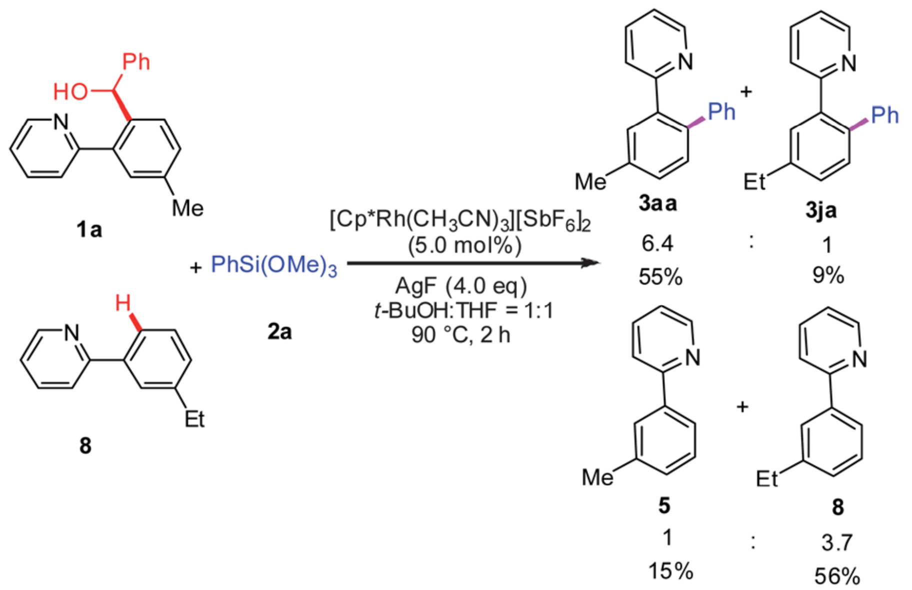
# Pyridine

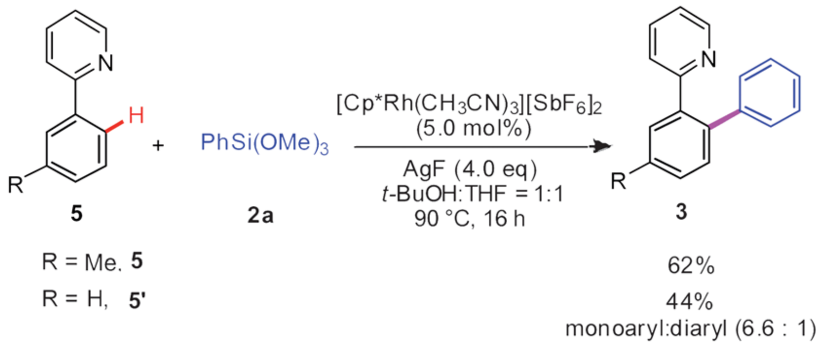



Zhang-Jie Shi, *Chem. Sci.* **2012**, *3*, 1645

# Pyridine

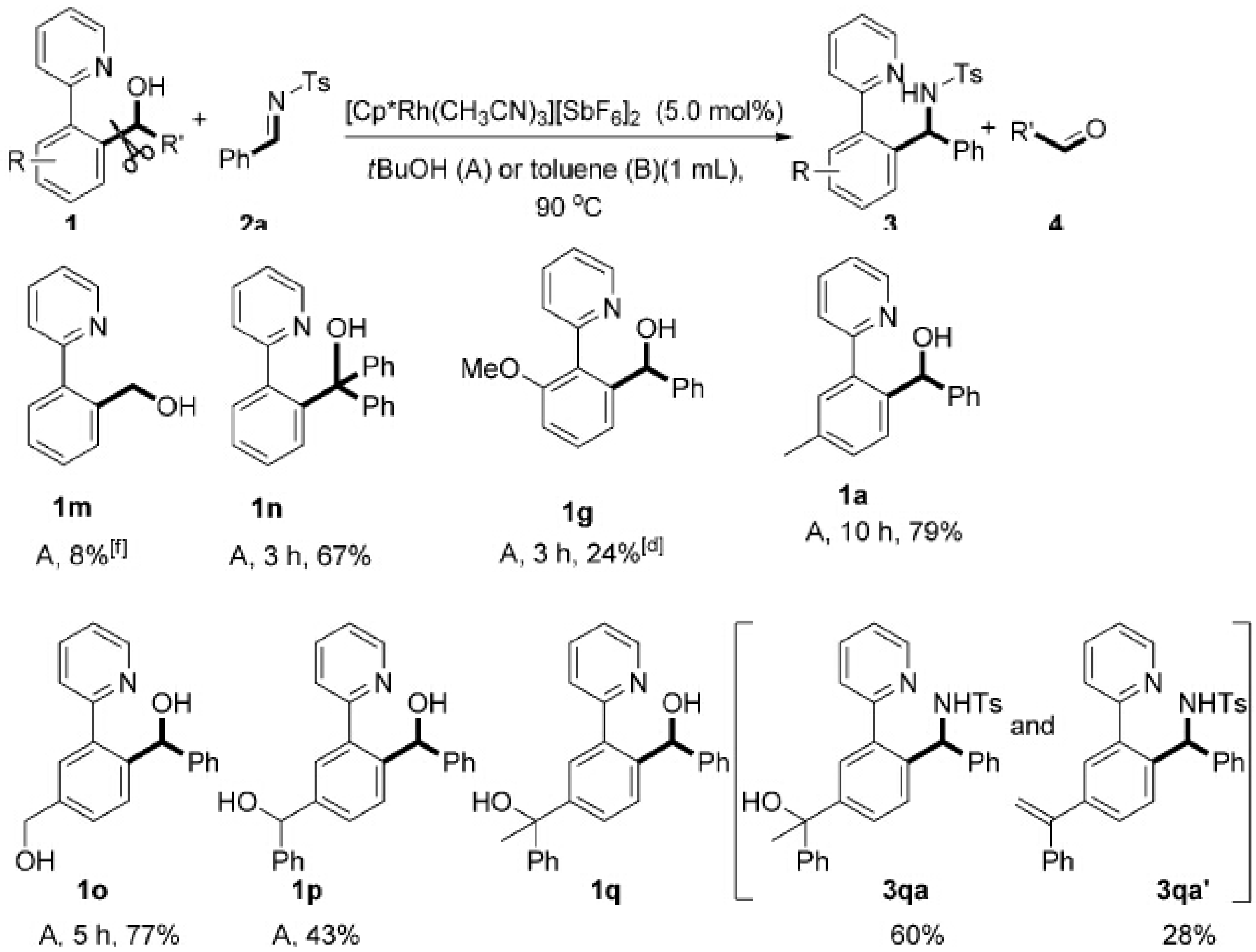


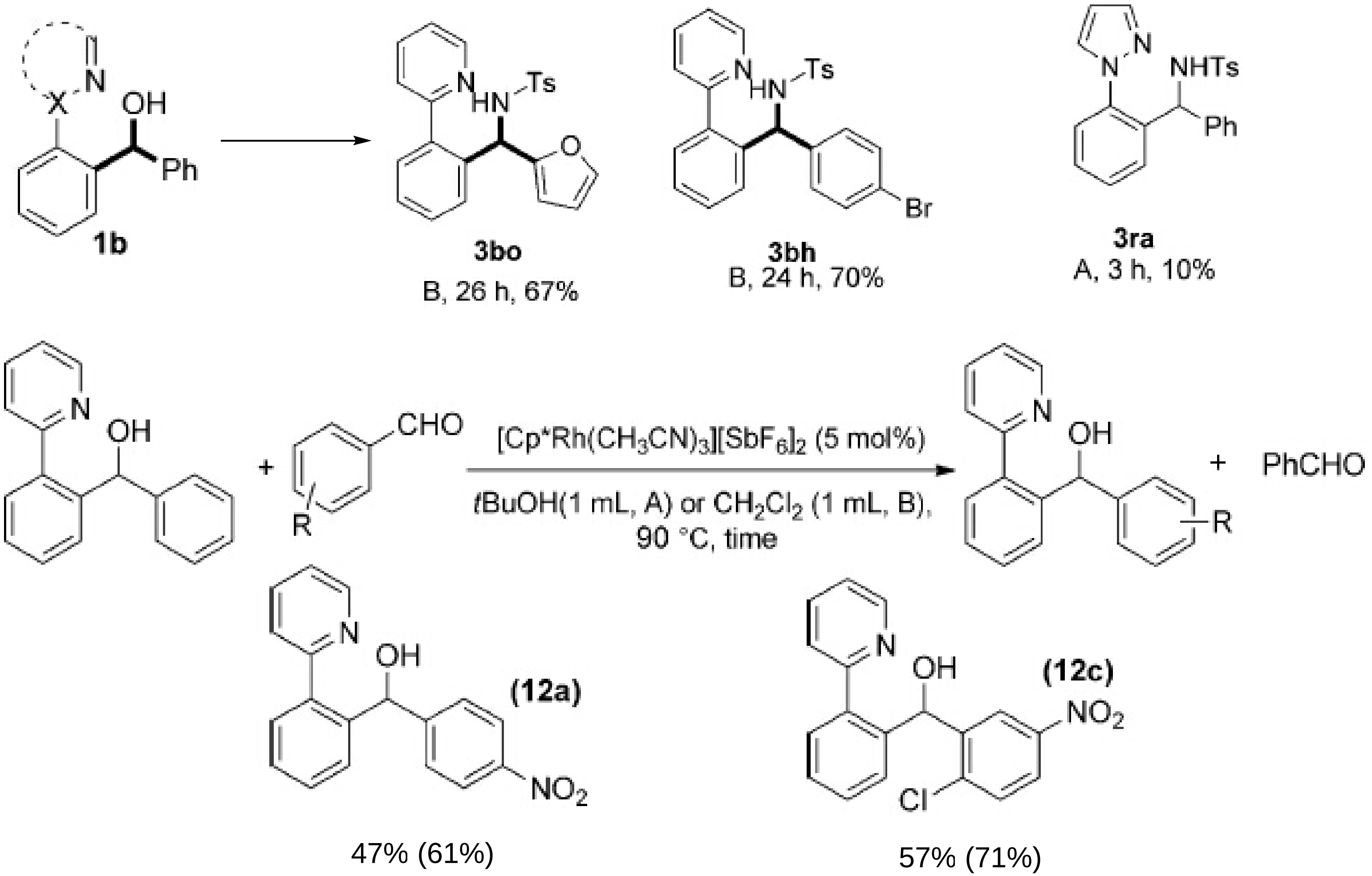

Zhang-Jie Shi, *Chem. Sci.* **2012**, *3*, 1645

# *Pyridine*



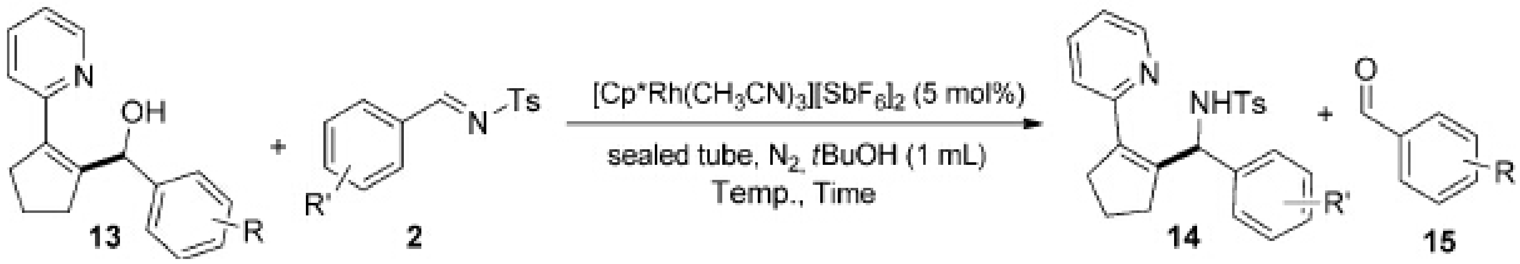

Zhang-Jie Shi, *Chem. Eur. J.* **2012**, *18*, 16214

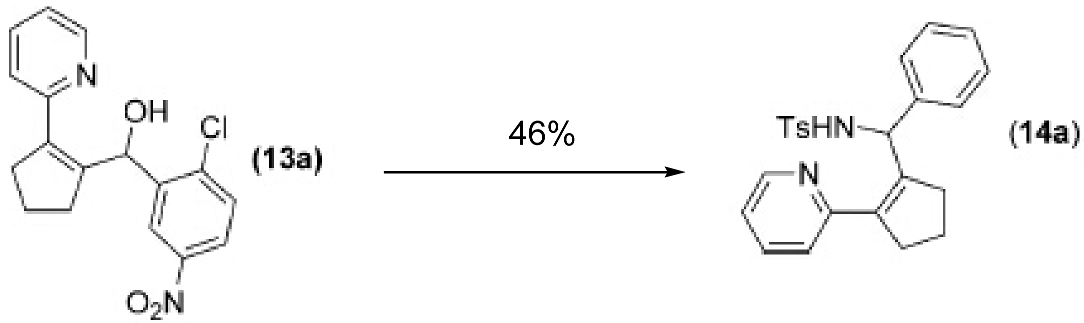
# *Pyridine*




Zhang-Jie Shi, *Chem. Eur. J.* **2012**, *18*, 16214

# Pyridine

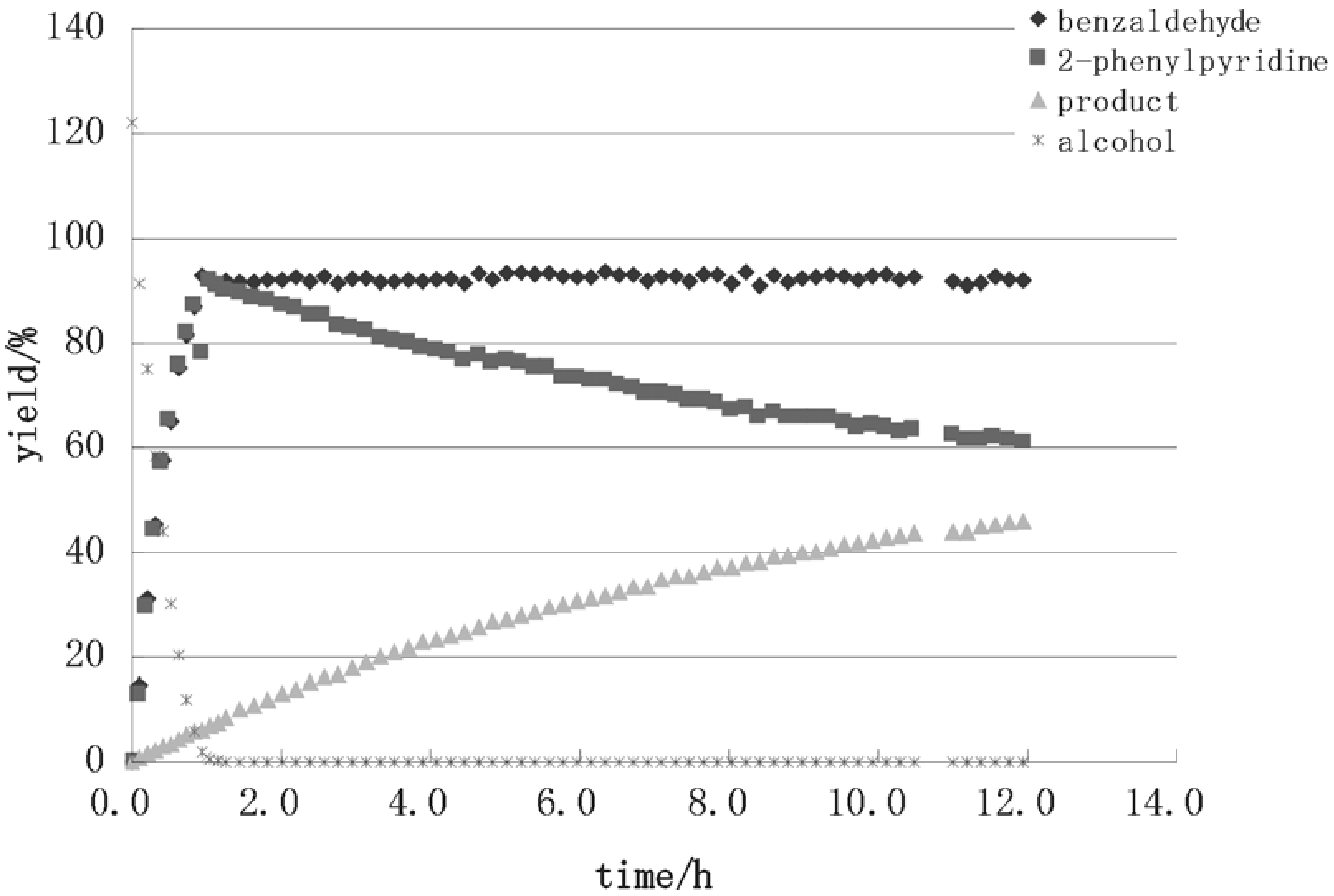




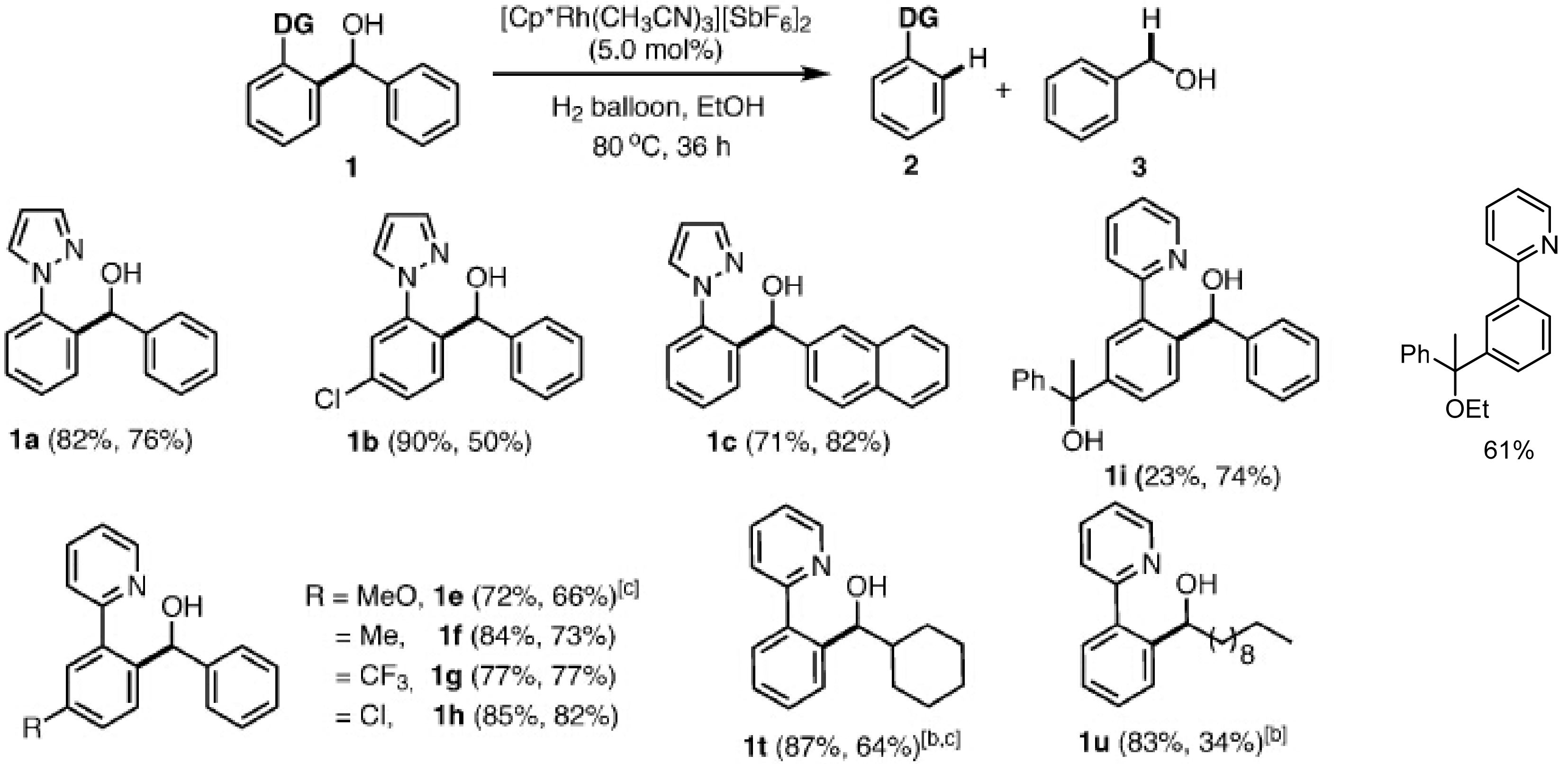
Zhang-Jie Shi, *Chem. Eur. J.* **2012**, *18*, 16214

# Pyridine




Zhang-Jie Shi, *Chem. Eur. J.* **2012**, *18*, 16214

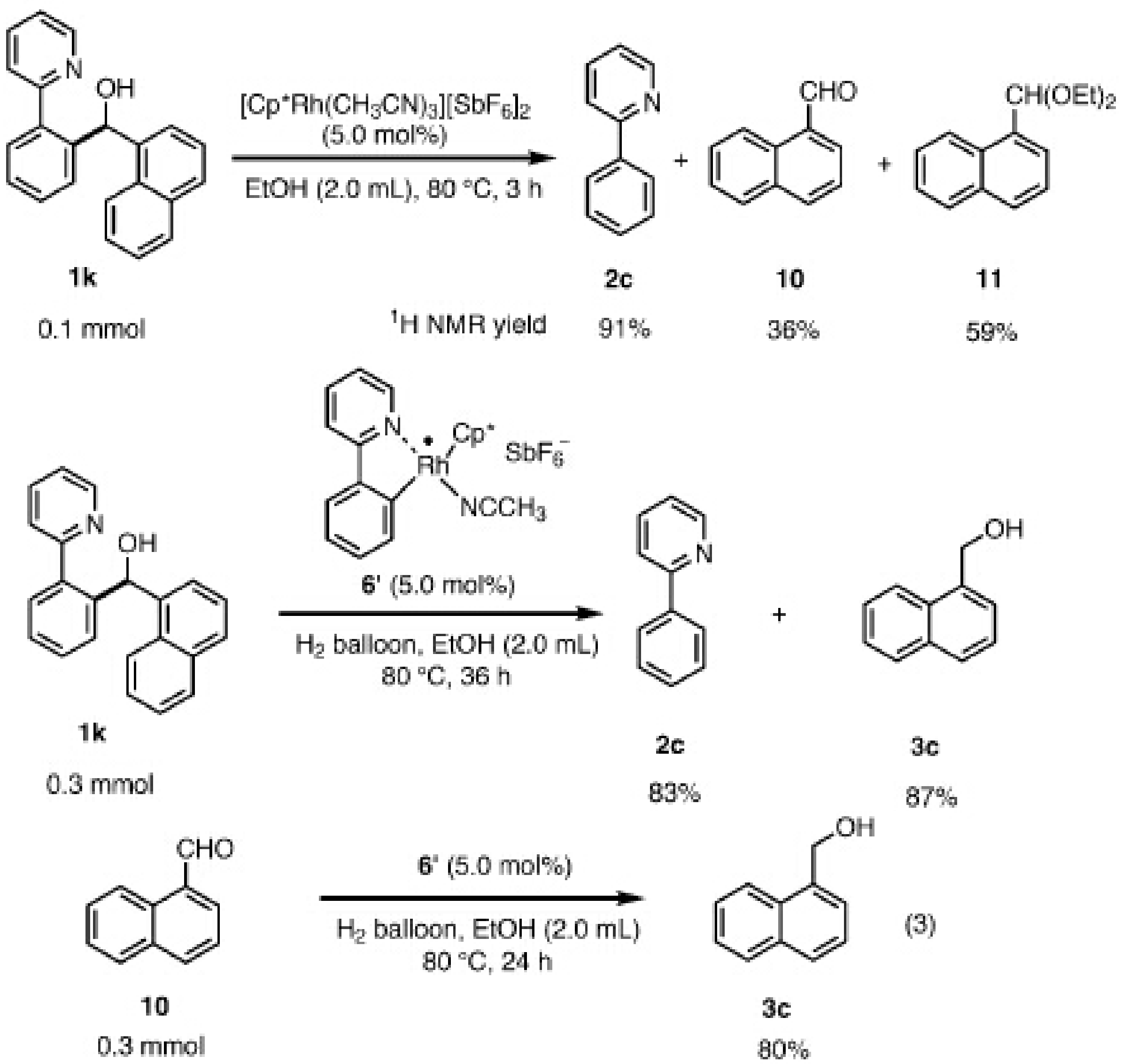
# Pyridine




*Scheme 2.* Substrate scope of 1,1- biarylmethanols for C—C bond reductive cleavage. The yields given in brackets refer to products **2** and **3**, respectively. [a] Alcohol **1** (0.3 mmol), $[Cp^*Rh(CH_3CN)_3][SbF_6]_2$ (0.015 mmol), EtOH (2.0 mL), $H_2$ balloon, 80 °C, 36 h. [b] 48 h. [c] Yield determined by $^1H$ NMR spectroscopy using benzyl methyl ether as the internal standard.

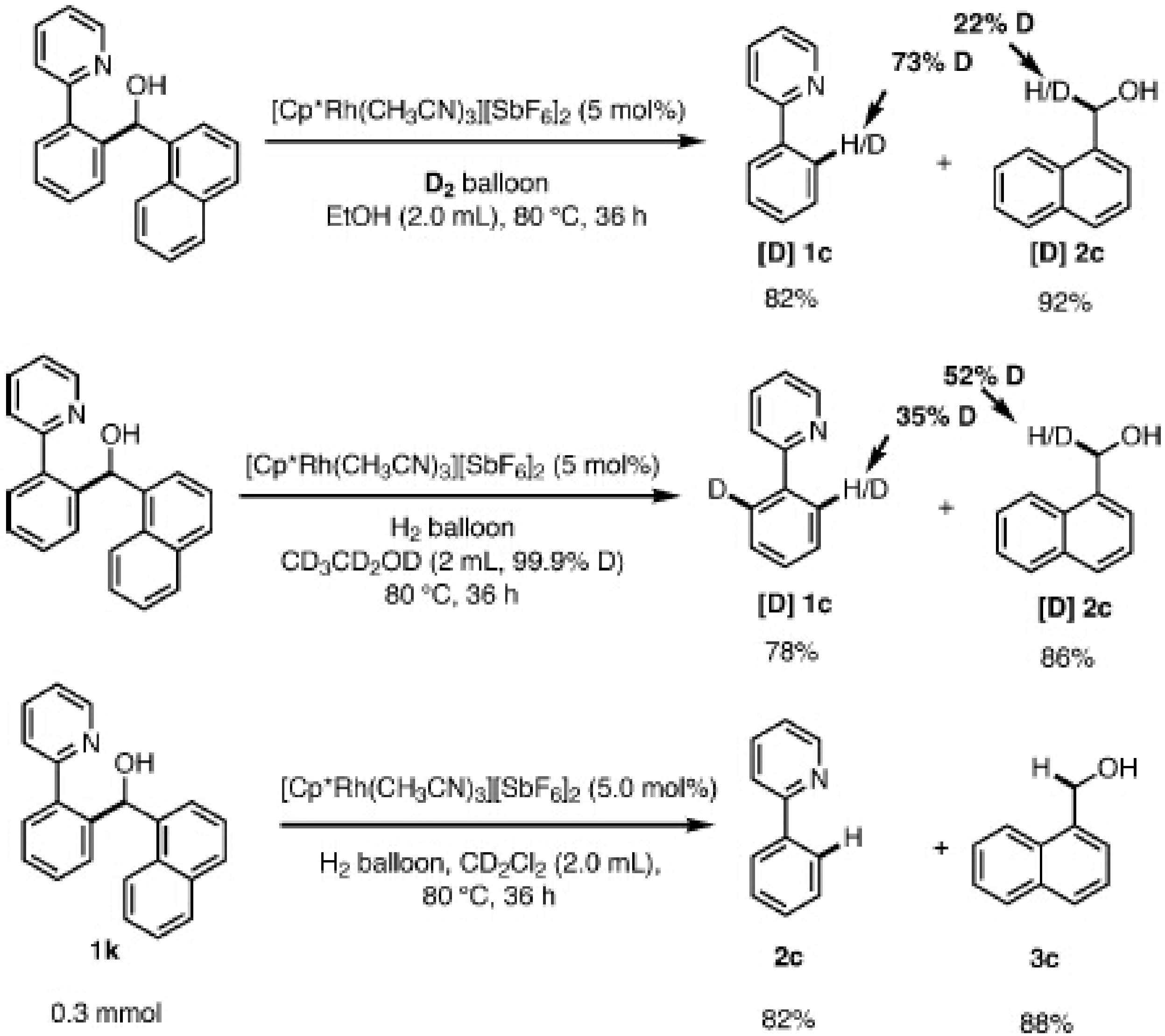
Zhang-Jie Shi *et. al. Angew Chem. Int. Ed.* **2012**, *51*, 9851

# Pyridine




Zhang-Jie Shi *et. al. Angew Chem. Int. Ed.* **2012**, *51*, 9851

# Pyridine




Zhang-Jie Shi *et. al. Angew Chem. Int. Ed.* **2012**, *51*, 9851

# Pyridine

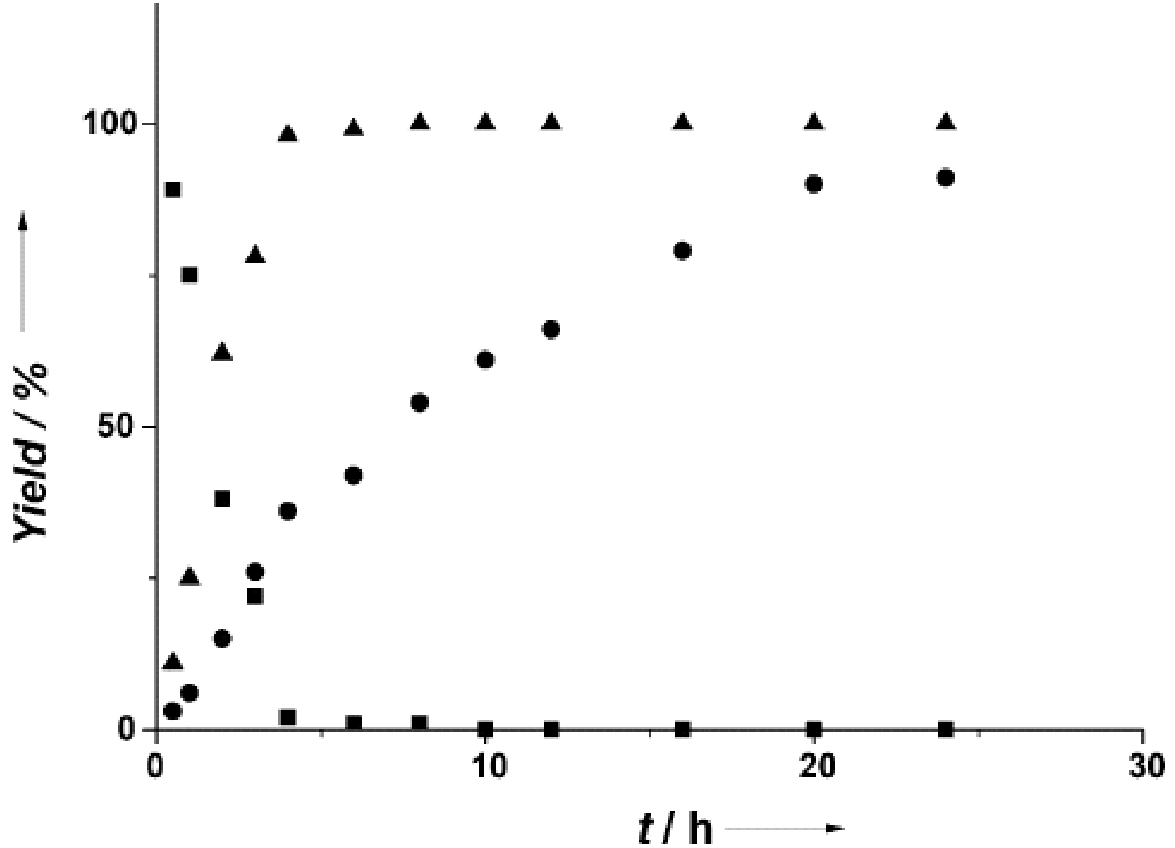
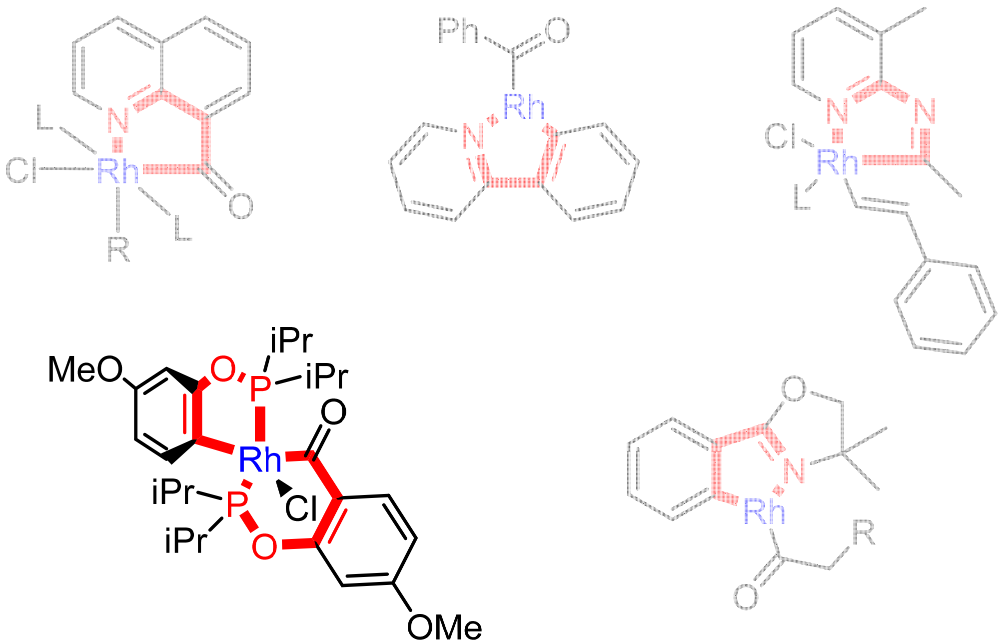


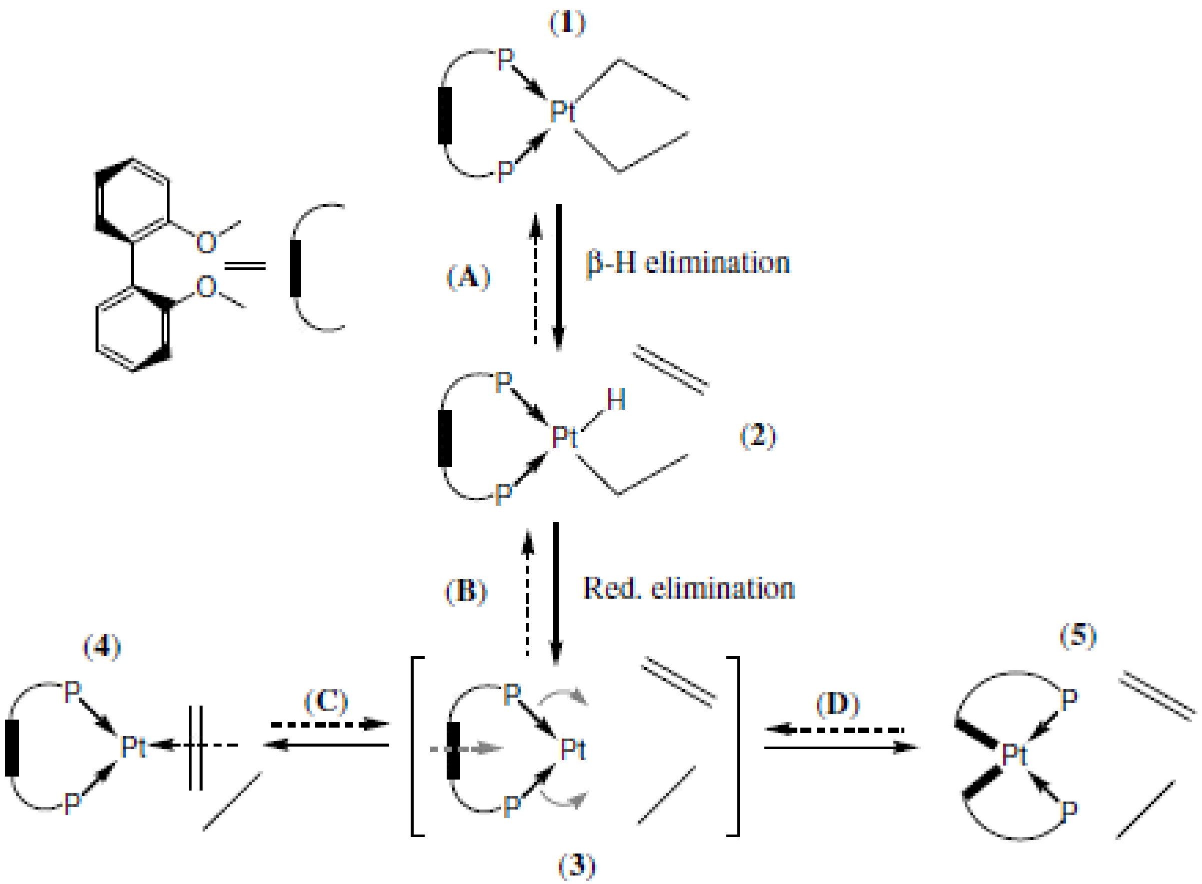

*Figure 1.* Reductive cleavage of **1k** (■) and the formation of **2c** (▲) and **3c** (●) as monitored by [1]H NMR spectroscopy. Reaction conditions: **1k** (0.1 mmol), $[Cp^{*}Rh(CH_3CN)_3][SbF_6]_2$ (0.005 mmol), EtOH (1.0 mL), $H_2$ balloon, 80 °C.

Zhang-Jie Shi *et. al. Angew Chem. Int. Ed.* **2012**, *51*, 9851

# Phosphinite

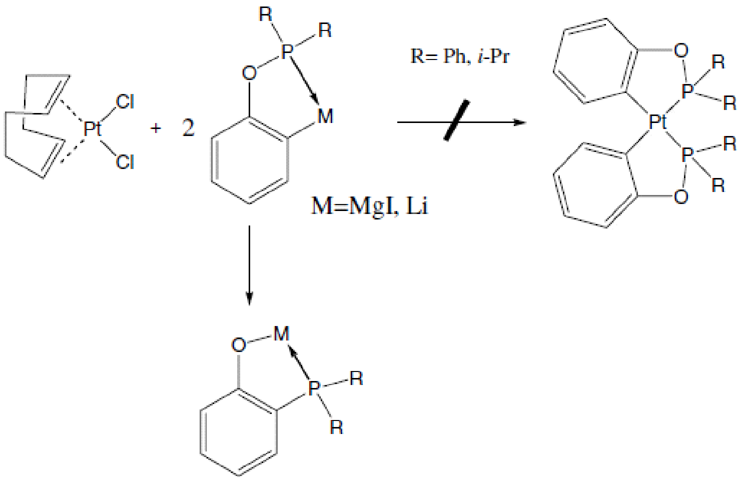


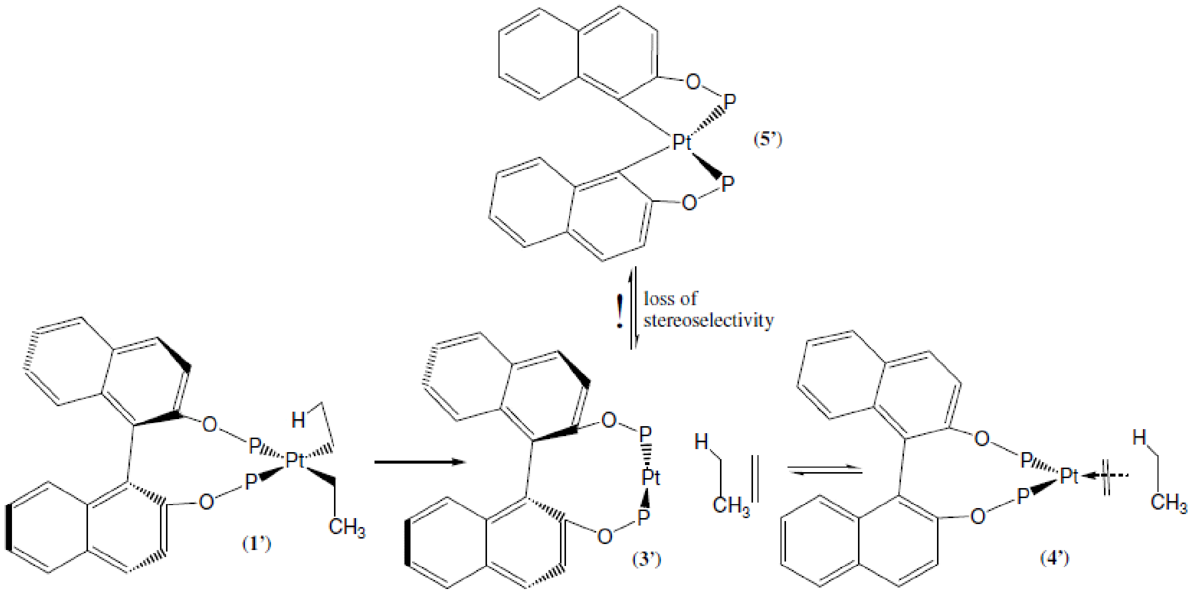
# Phosphinite




Klaus Ruhland, *et. al.* *J. Organomet. Chem.* **2005**, *690*, 5215

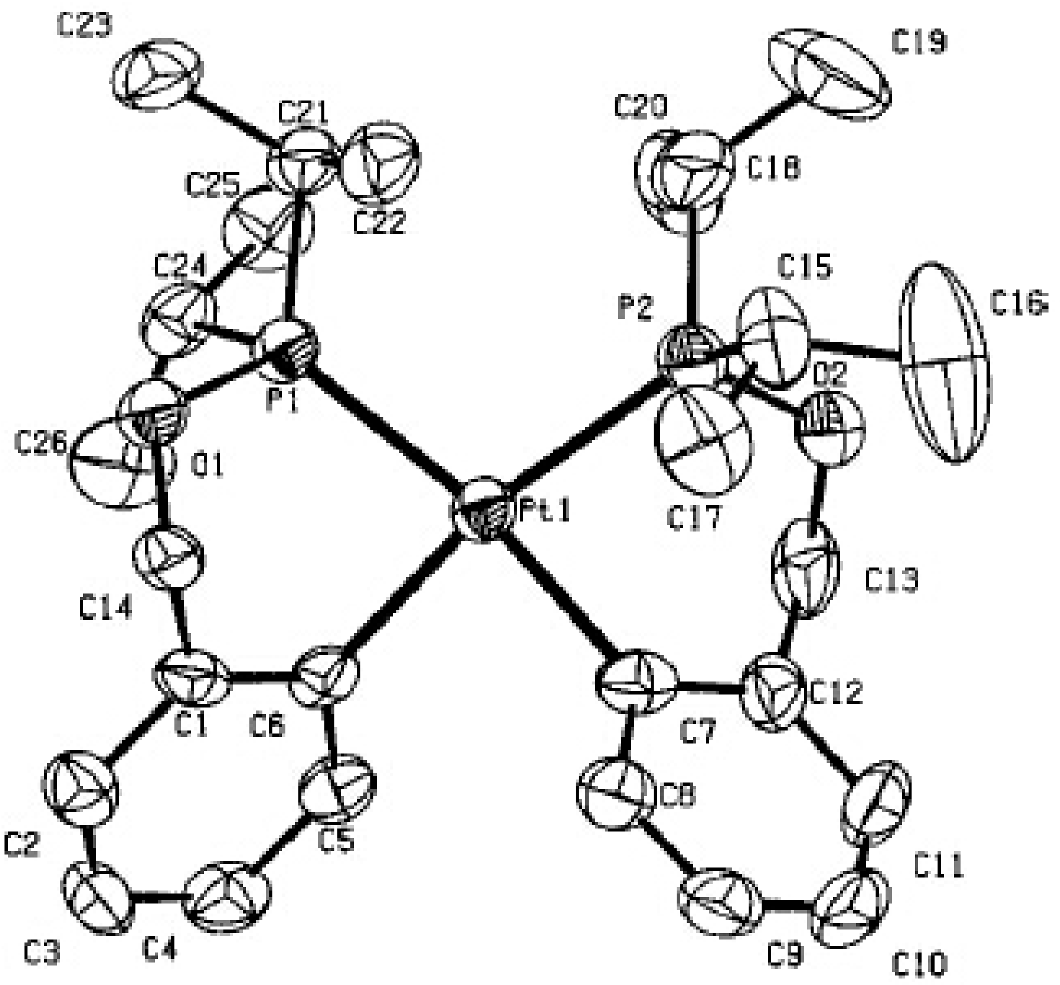
# Phosphinite



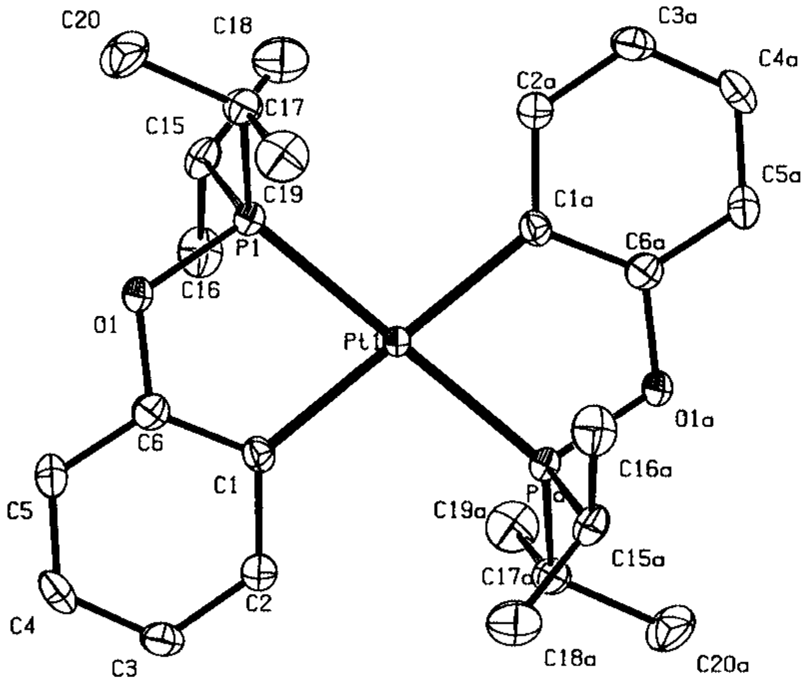

Klaus Ruhland, *et. al.* *J. Organomet. Chem.* **2005**, *690*, 5215

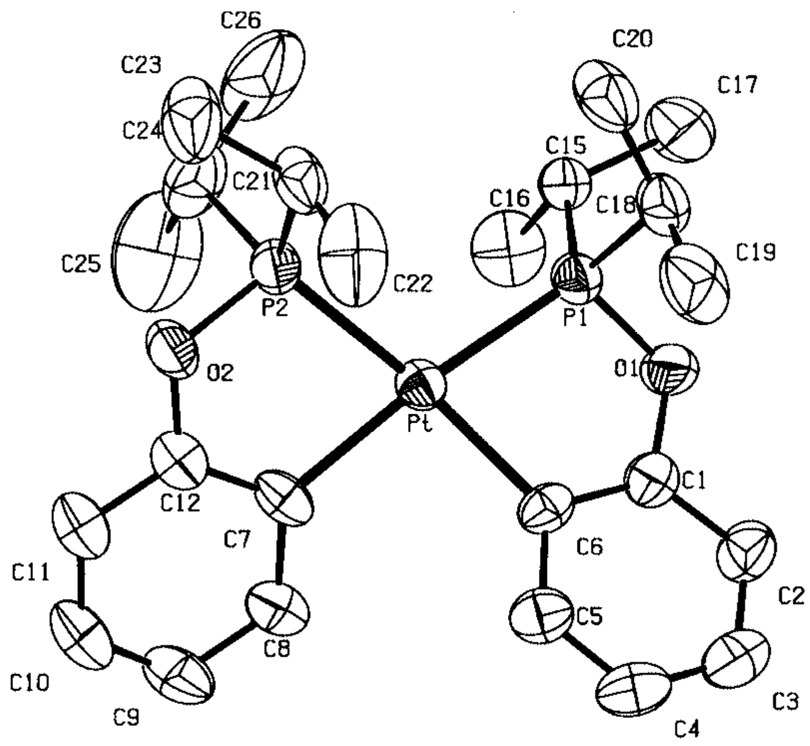
# Phosphinite




Klaus Ruhland, *et. al. Eur. J. Inorg. Chem.* **2007**, 944

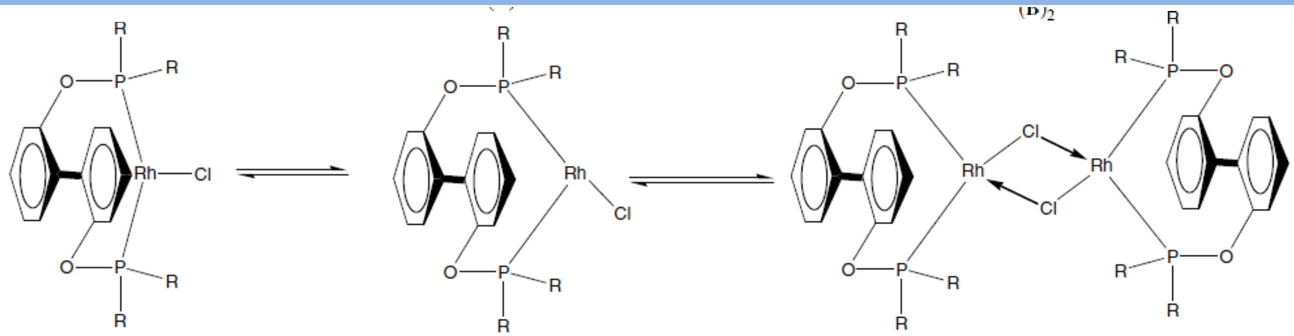
# Phosphinite

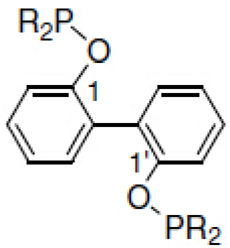


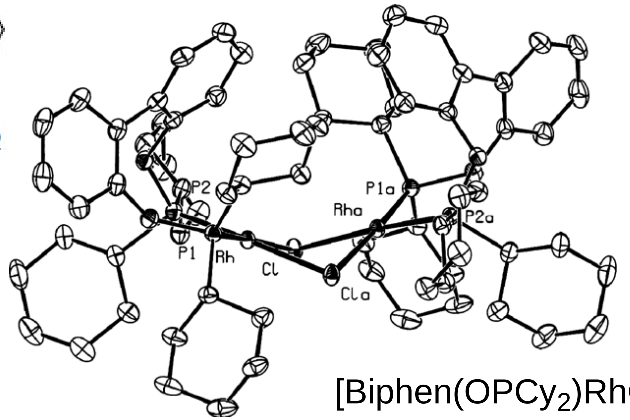




Klaus Ruhland, *et. al. Eur. J. Inorg. Chem.* **2007**, 944

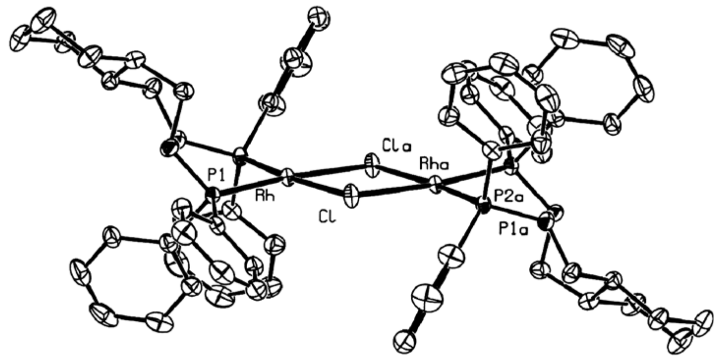
# Phosphinite



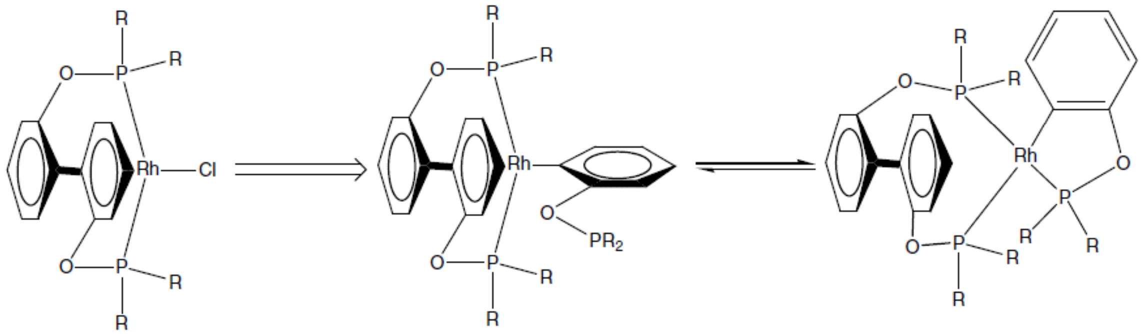




[Biphen(OPCy$_2$)RhCl]$_2$



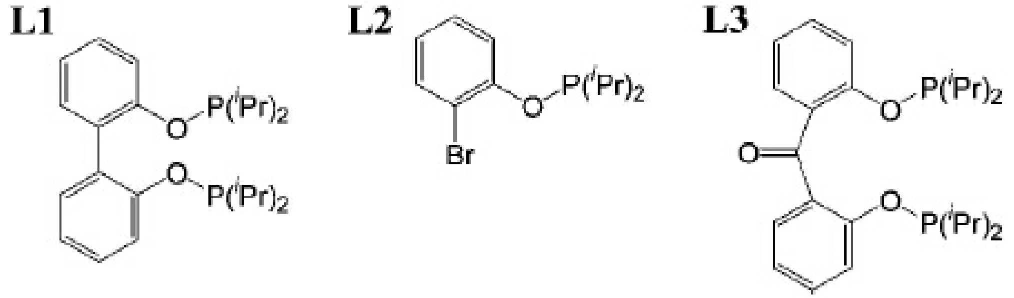
[Cy-1,2-CH$_2$(OPPh$_2$)RhCl]$_2$

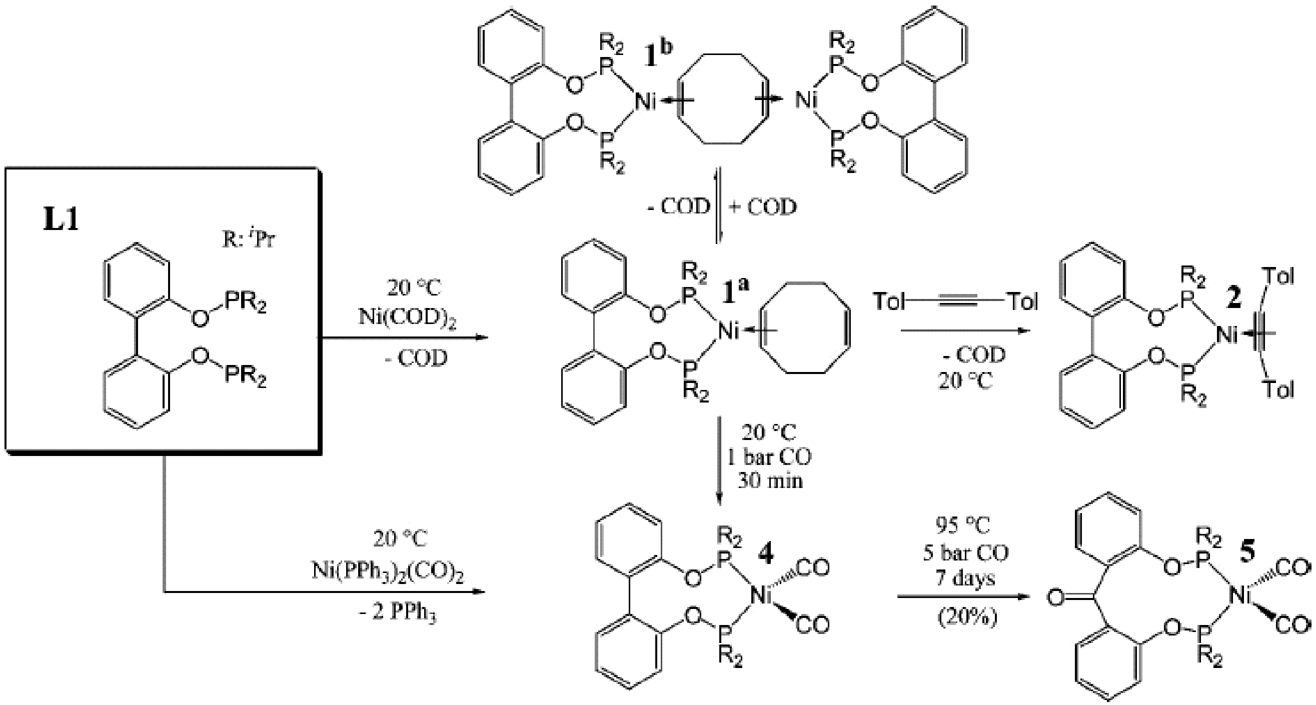


DFT study indicated the energy barrier for the cleavage of the bridging C-C single bond is about 30 kcal/mol

Klaus Ruhland *et. al. J. Organomet. Chem.* **2008**, *693*, 874

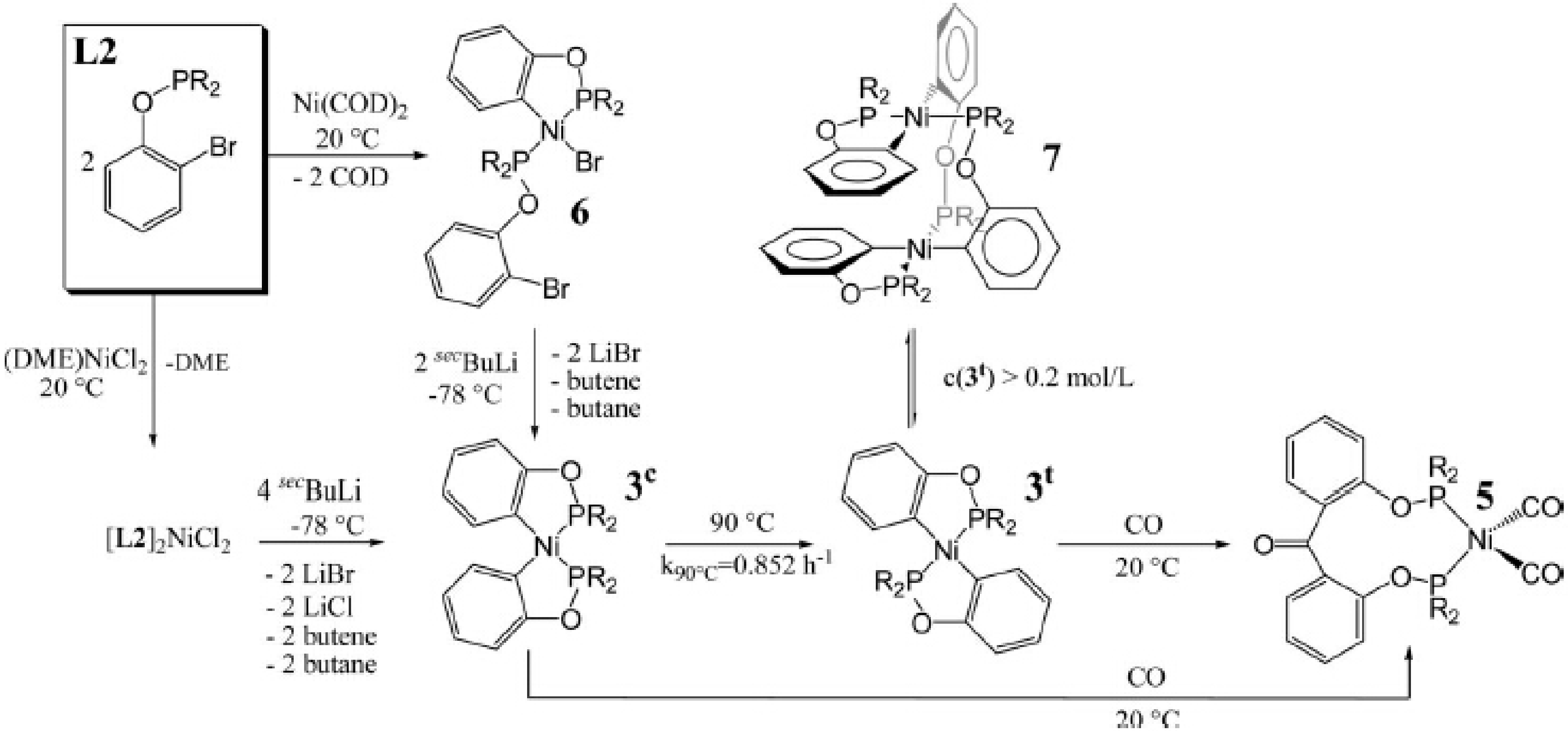
# *Phosphinite Breaking-Through!!*



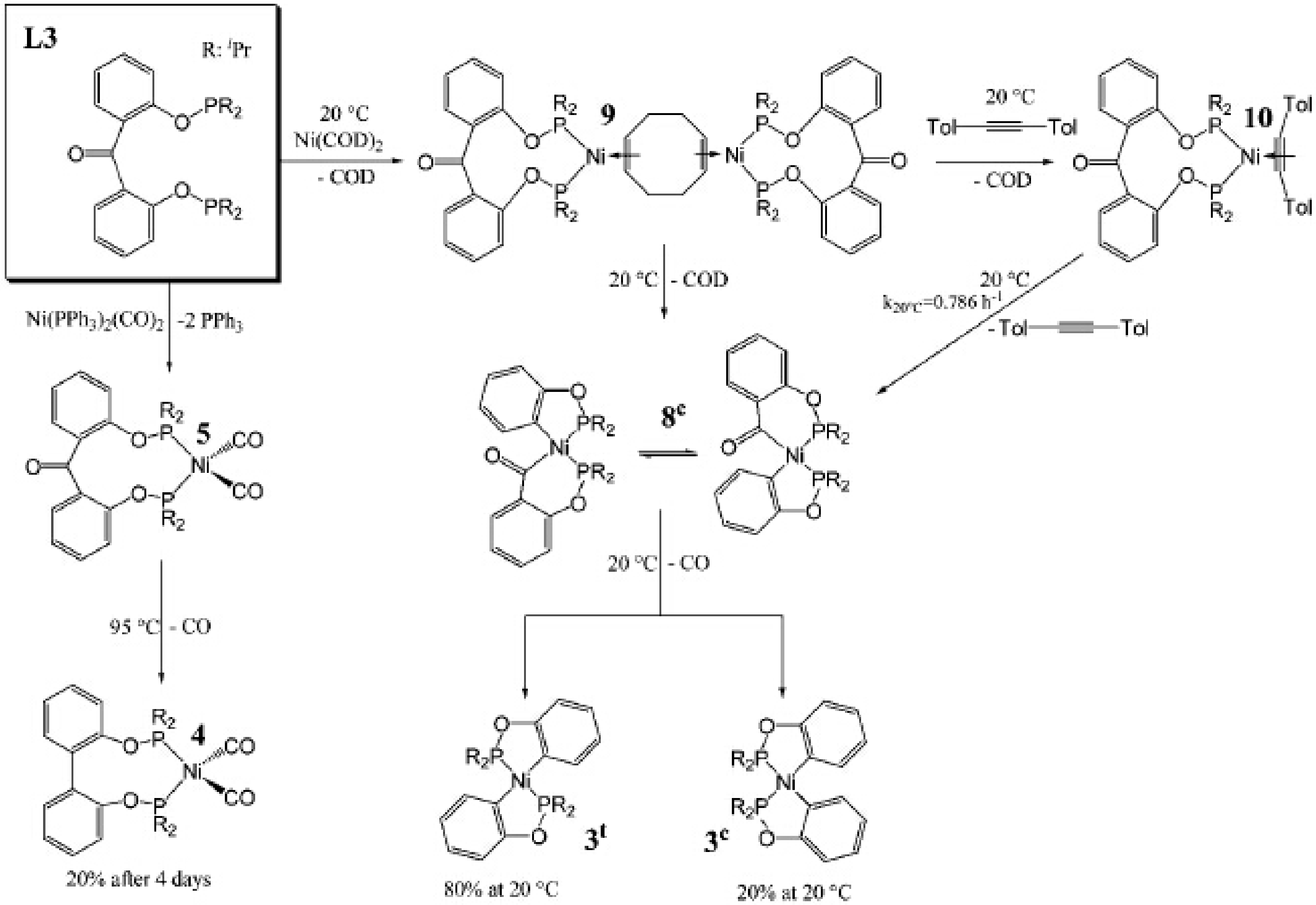

Klaus Ruhland, *Organometallic*, **2008**, *27*, 3482

# Phosphinite



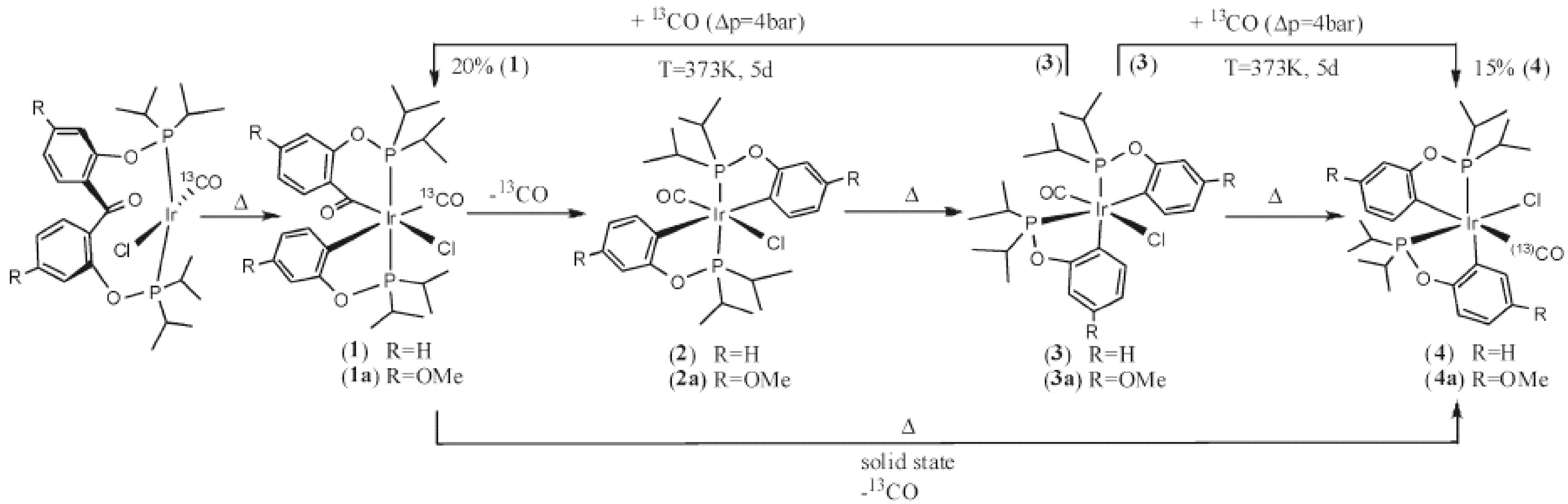

Klaus Ruhland, *Organometallic*, **2008**, *27*, 3482

# Phosphinite



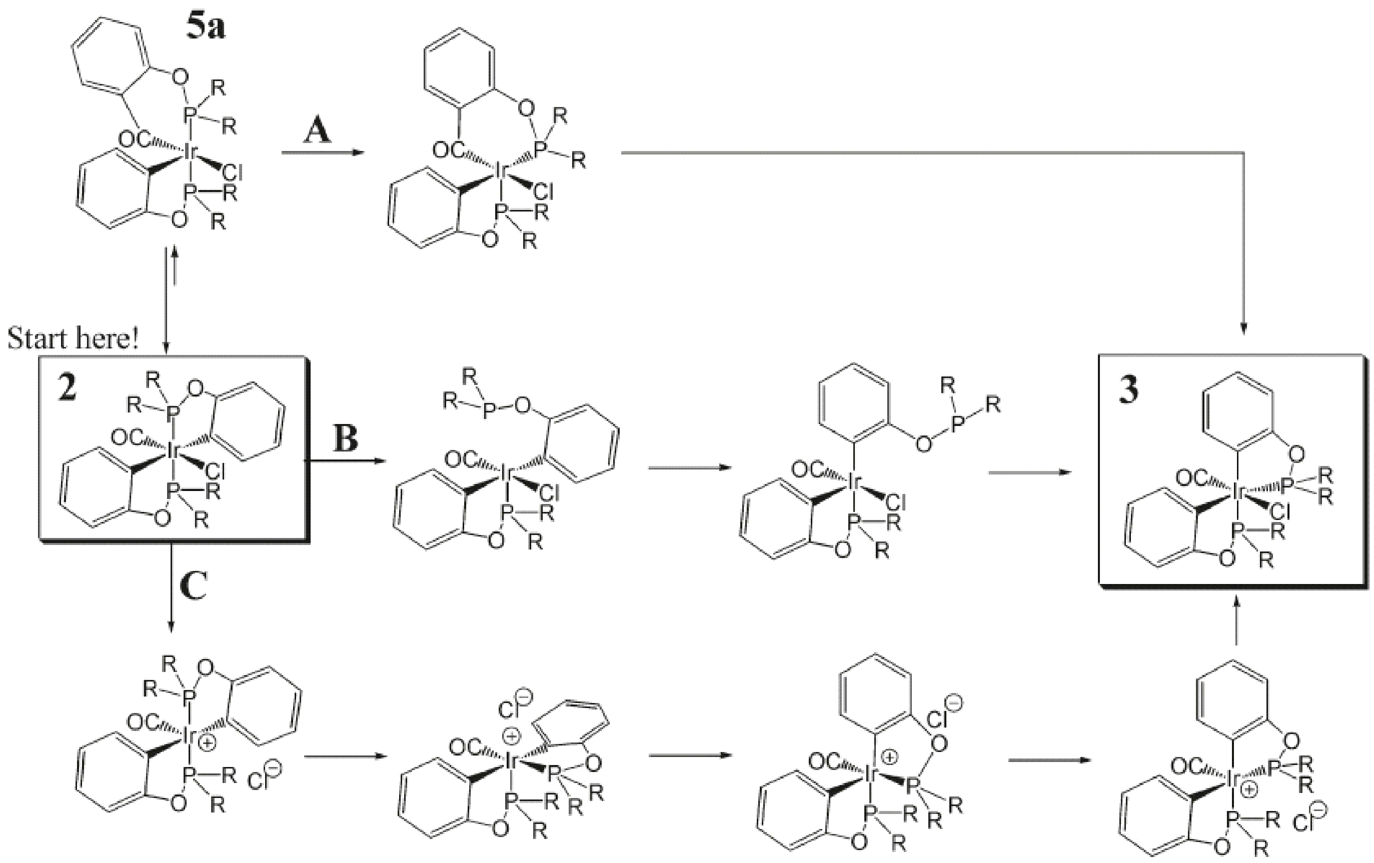

Klaus Ruhland, *Organometallic*, **2008**, *27*, 3482

# Phosphinite



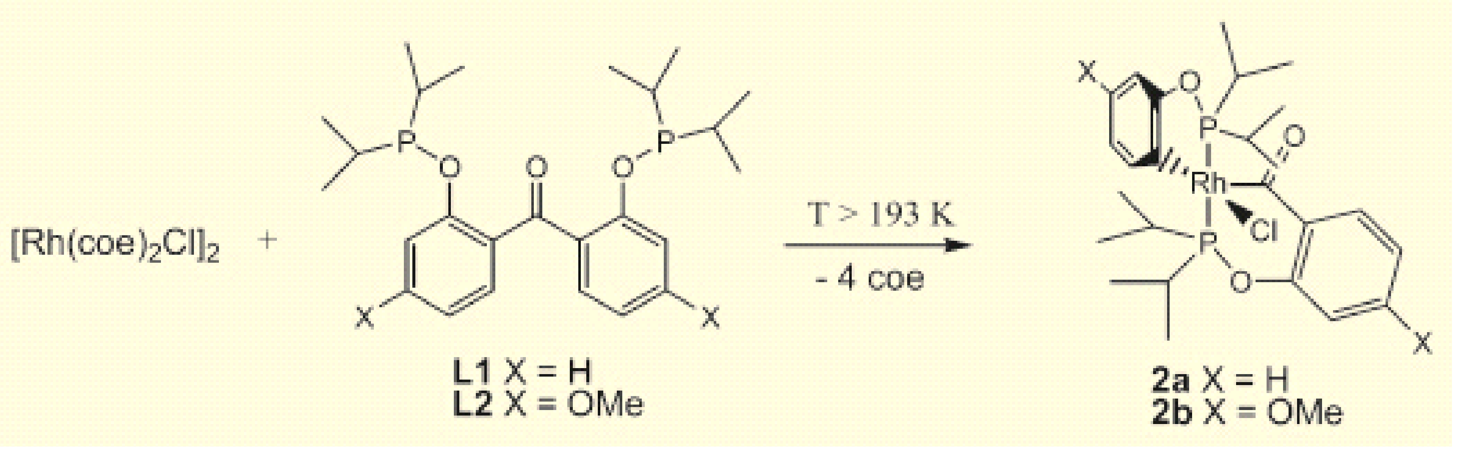

Klaus Ruhland, *Organometallic*, **2011**, *30*, 171

# Phosphinite



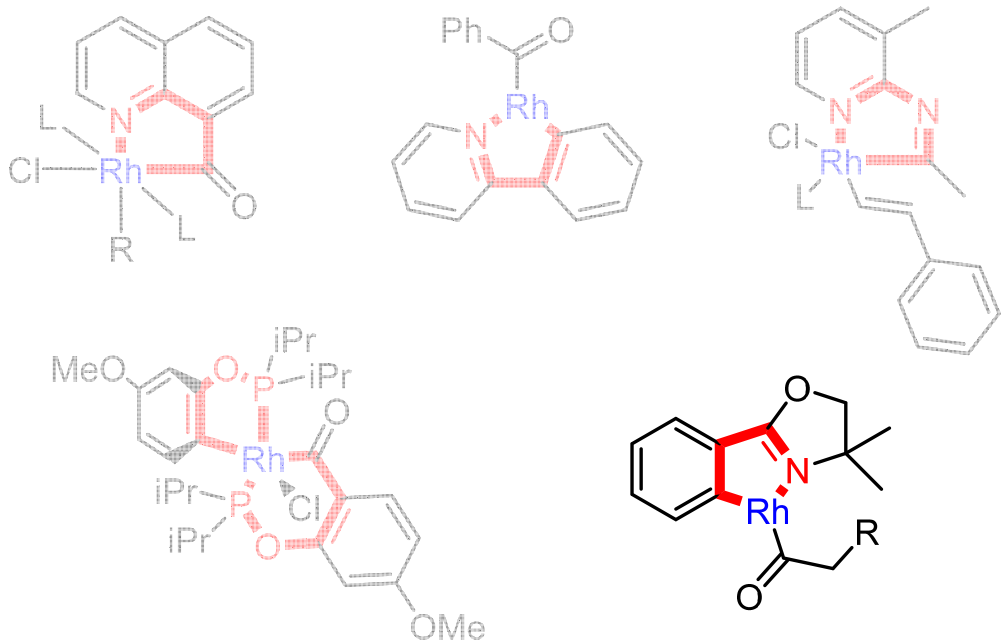

Klaus Ruhland, *Organometallic*, **2011**, *30*, 171

# Phosphinite

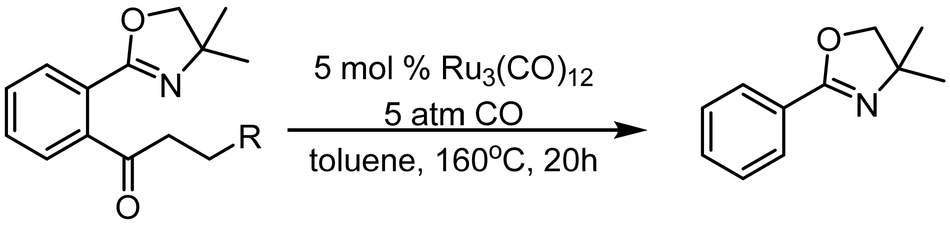


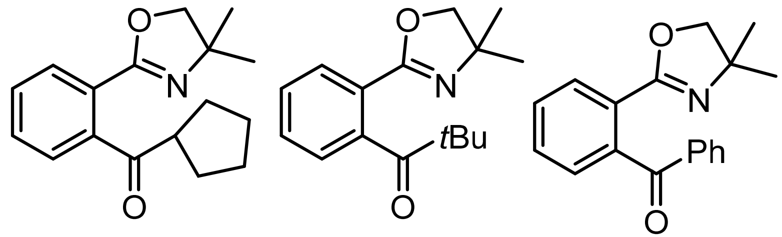

Klaus Ruhland, *Organometallic*, **2011**, *30*, 4039

# *Miscellaneous*

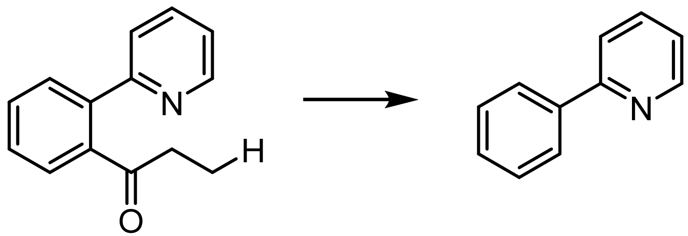


# Miscellaneous

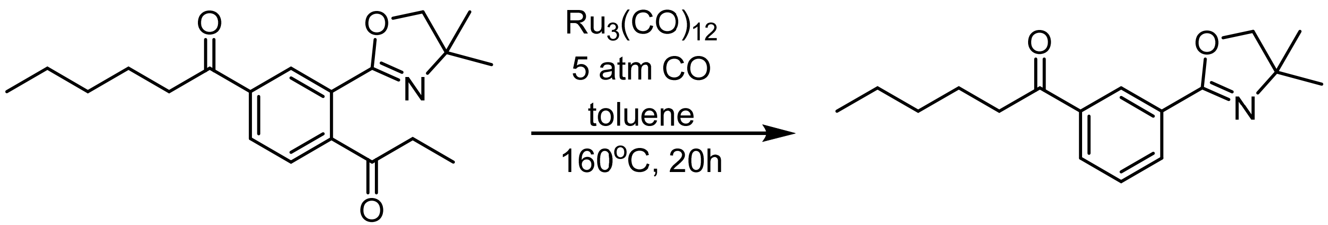



| | | |
|---|---|---|
| **a**: | R = H | 62% (83% brsm) $N_2$, 135$^o$C |
| a: | R = H | 86% |
| **b**: | R = Pr | 96% |
| **c**: | R = TMS | 94% |
| **d**: | R = tetradecyl | 89% (hexadecenes 77%) |



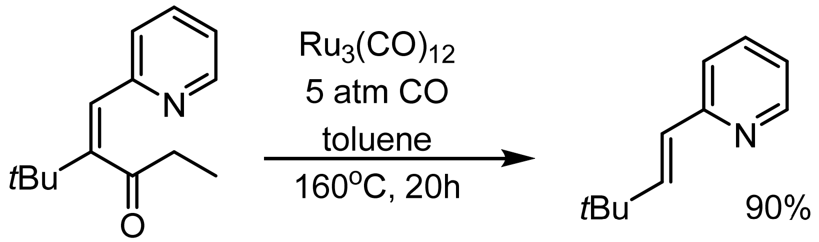

81%

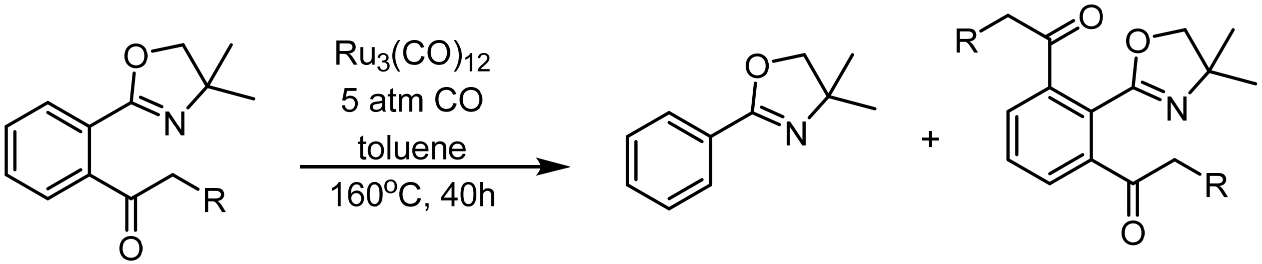


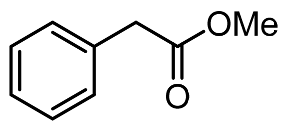

85%

Naoto Chatani, Yutaka Ie, Fumitoshi Kakiuchi, Shinji Murai, *J. Am. Chem. Soc.* **1999**, *121*, 8645

# Miscellaneous



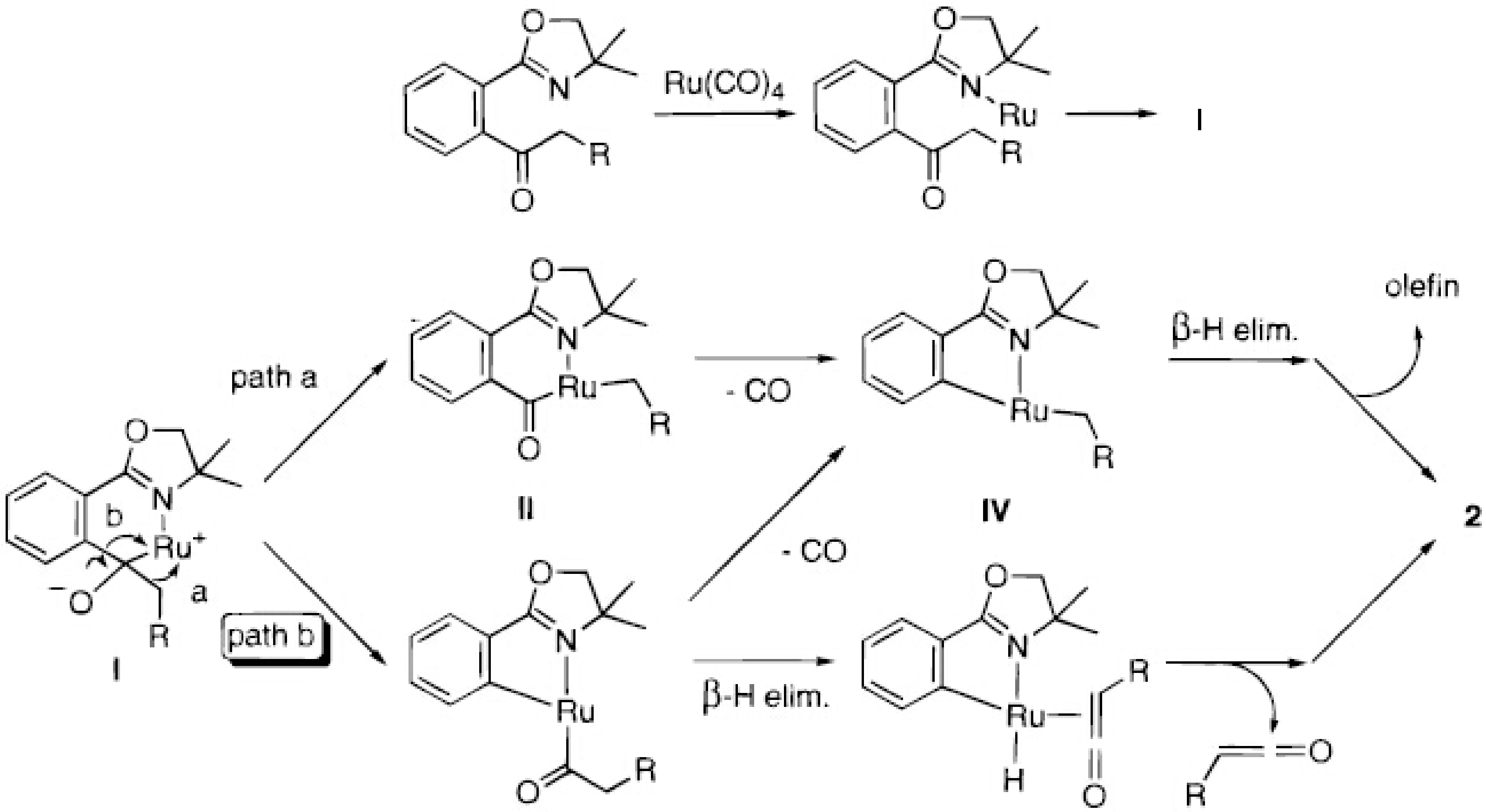




| | | | | |
|---|---|---|---|---|
| **a**: | R = H | 81% | 0% | |
| **b**: | R = Ph | 86% | 0% | |
| | R = Ph (MeOH) | 73% | 0% | 31%  |
| **c**: | R = *t*Bu | 34% | 10% | |



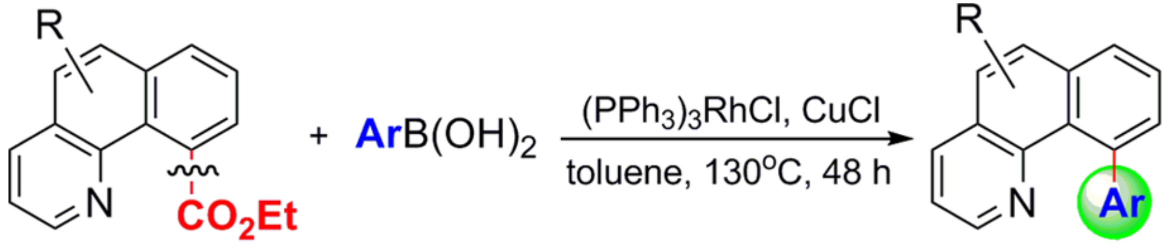

Naoto Chatani, Yutaka Ie, Fumitoshi Kakiuchi, Shinji Murai, *J. Am. Chem. Soc.* **1999**, *121*, 8645

# Miscellaneous

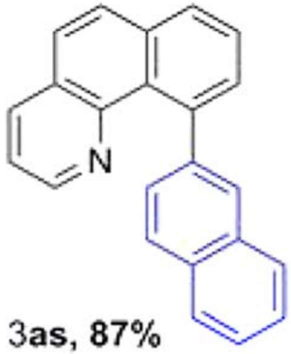



Naoto Chatani, Yutaka Ie, Fumitoshi Kakiuchi, Shinji Murai, *J. Am. Chem. Soc.* **1999**, *121*, 8645

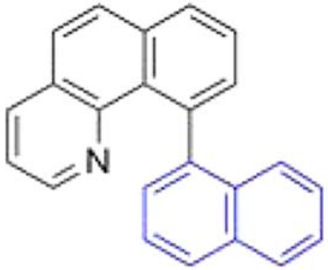
# *Miscellaneous*



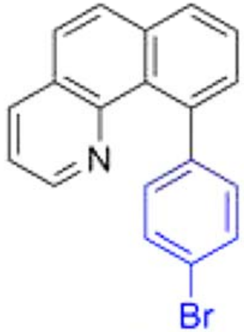

47%-97% Yield



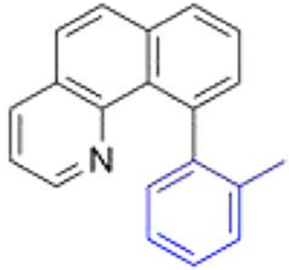

3as, 87%



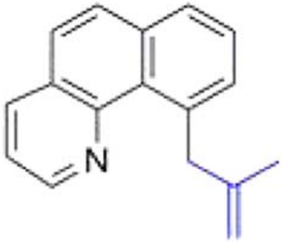

3at, 0%



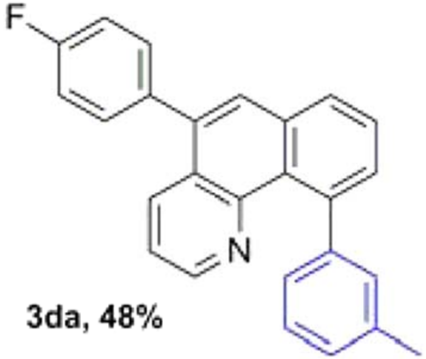

3aq, 59%



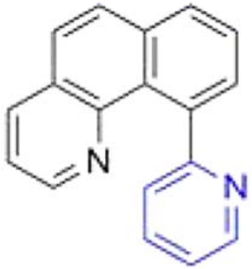

3ab, 38%




3av, 0%



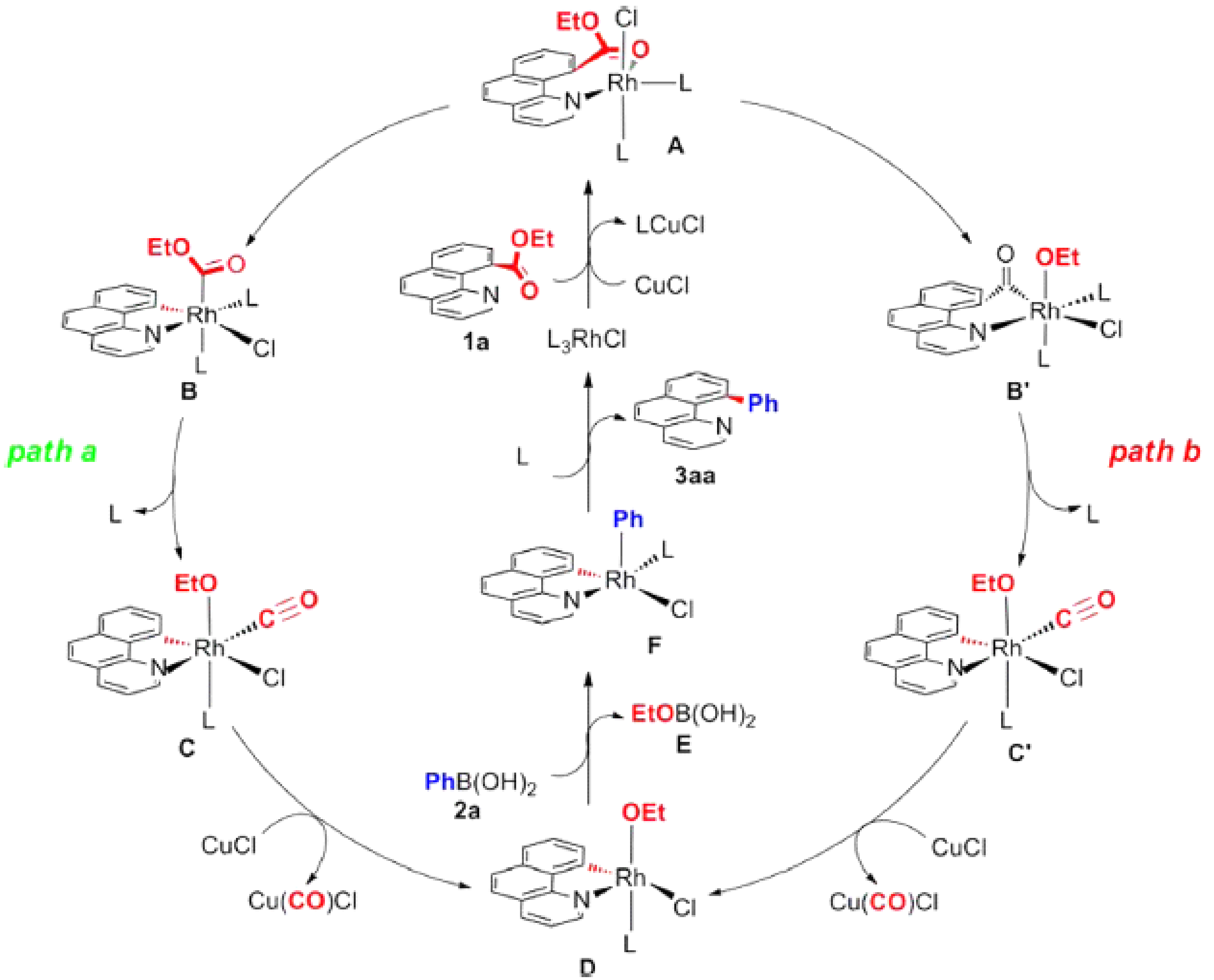

3da, 48%




3au, 0%

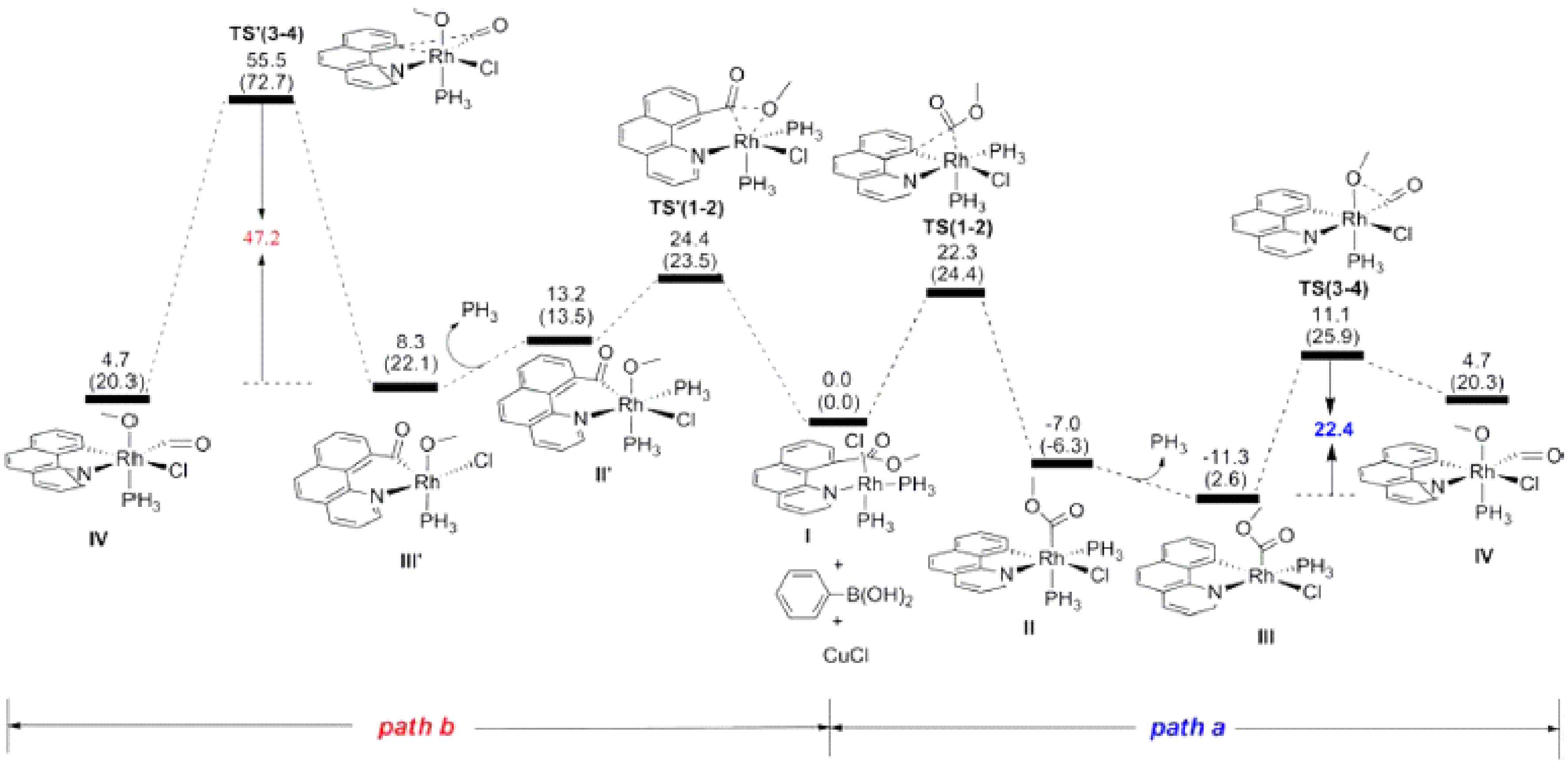
Jingjing Wang, Bowen Liu, Haitao Zhao, Jianhui Wang, *Organometallics* **2012**, *31*, 8598

# Miscellaneous




Jingjing Wang, Bowen Liu, Haitao Zhao, Jianhui Wang, *Organometallics* **2012**, *31*, 8598

# Miscellaneous



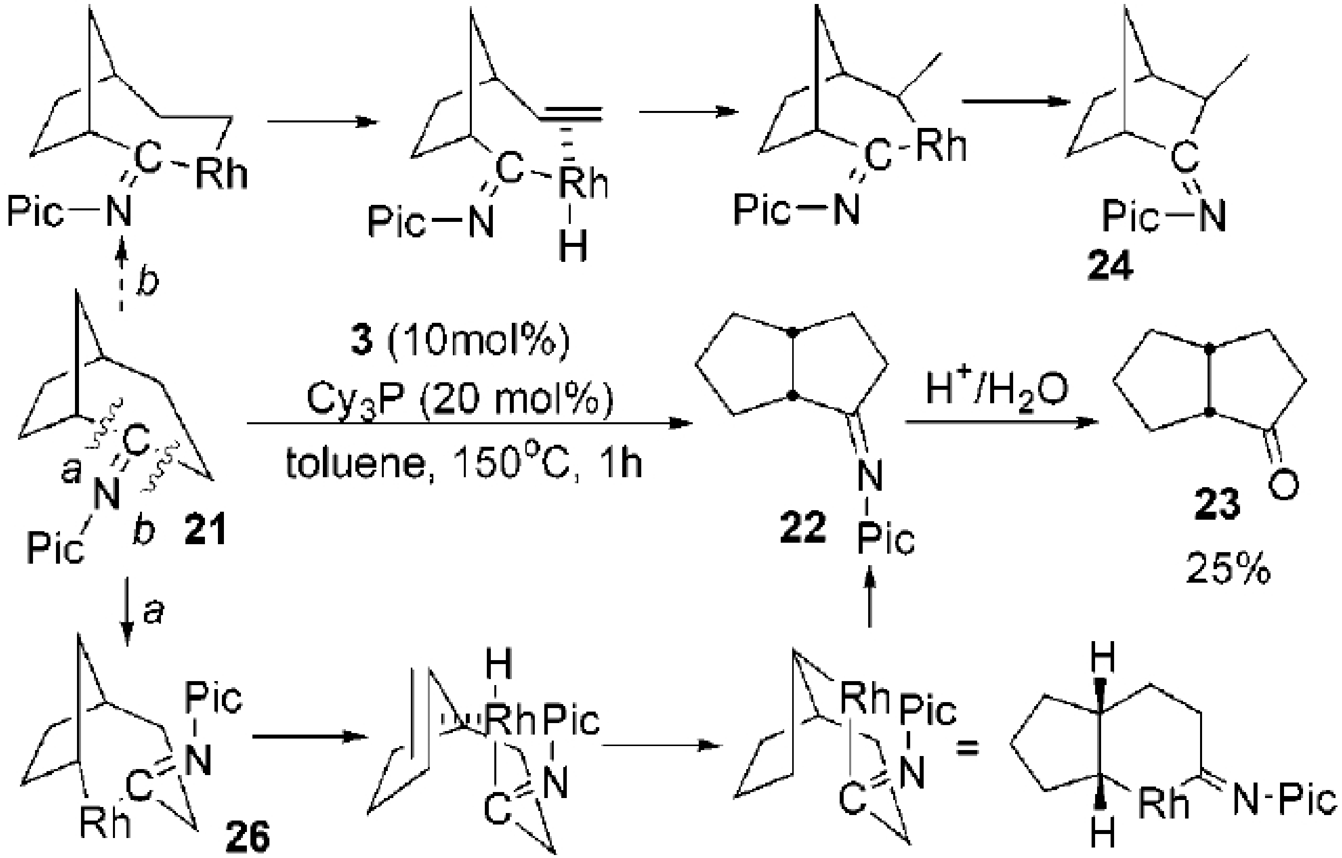

Jingjing Wang, Bowen Liu, Haitao Zhao, Jianhui Wang, *Organometallics* **2012**, *31*, 8598

# *Summary*

- *Milstein's work not included*
- *Stable Intermediate*
- *Compatible with various reactions*
- *Competition with C-H activation can be controlled*
- *β-H elimination usually very fast*
- *Removable directing groups and more target C-C bonds undeveloped*

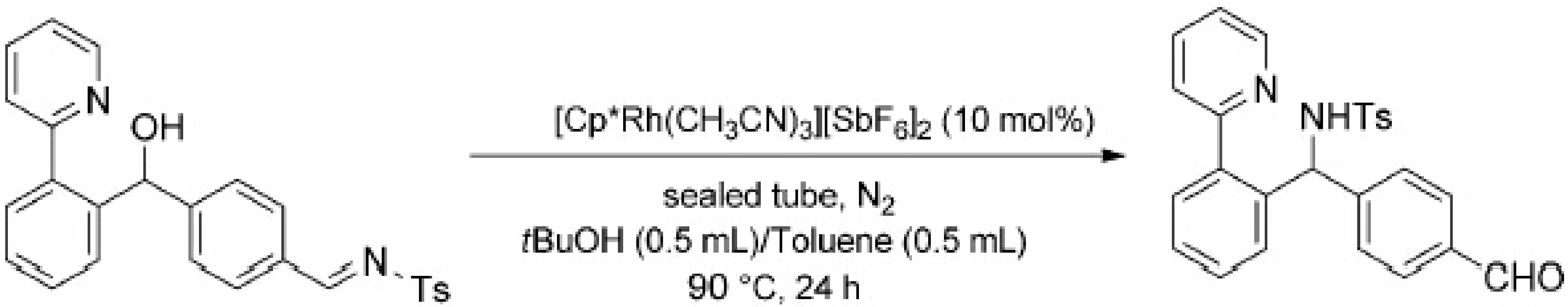
# Acknowledge

# Answer



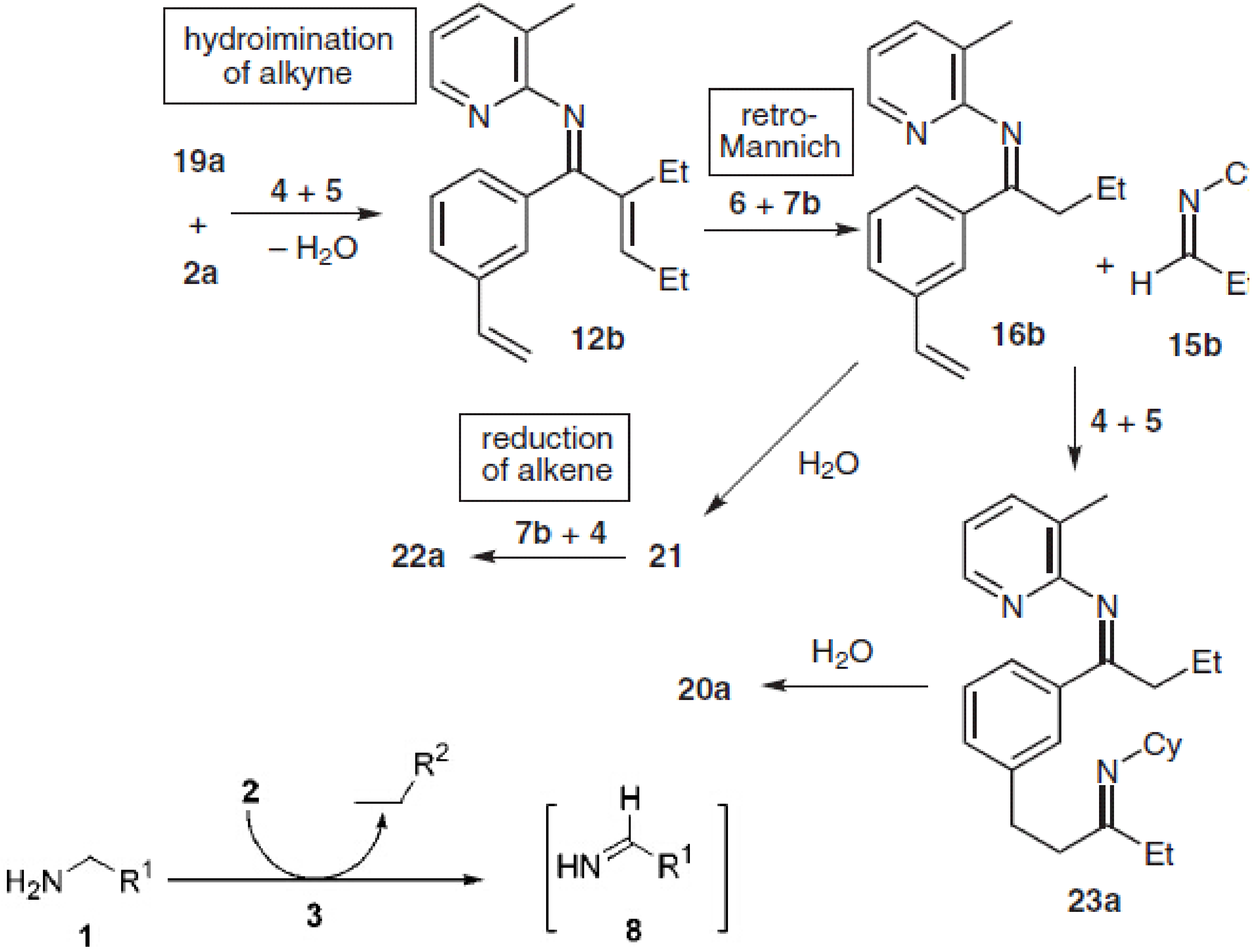
C
Rh
Pic
N
b
C
Rh
H
Pic
N
C
Rh
Pic
N
C
Pic
N
24
3 (10mol%)
Cy3P (20 mol%)
toluene, 150°C, 1h
H+/H2O
C
a
N
Pic
b
21
22
N
Pic
23
O
25%
a
Pic
N
C
Rh
26
H
RhPic
N
C
Rh
Pic
N
C
=
H
H
Rh
N-Pic

# Answer



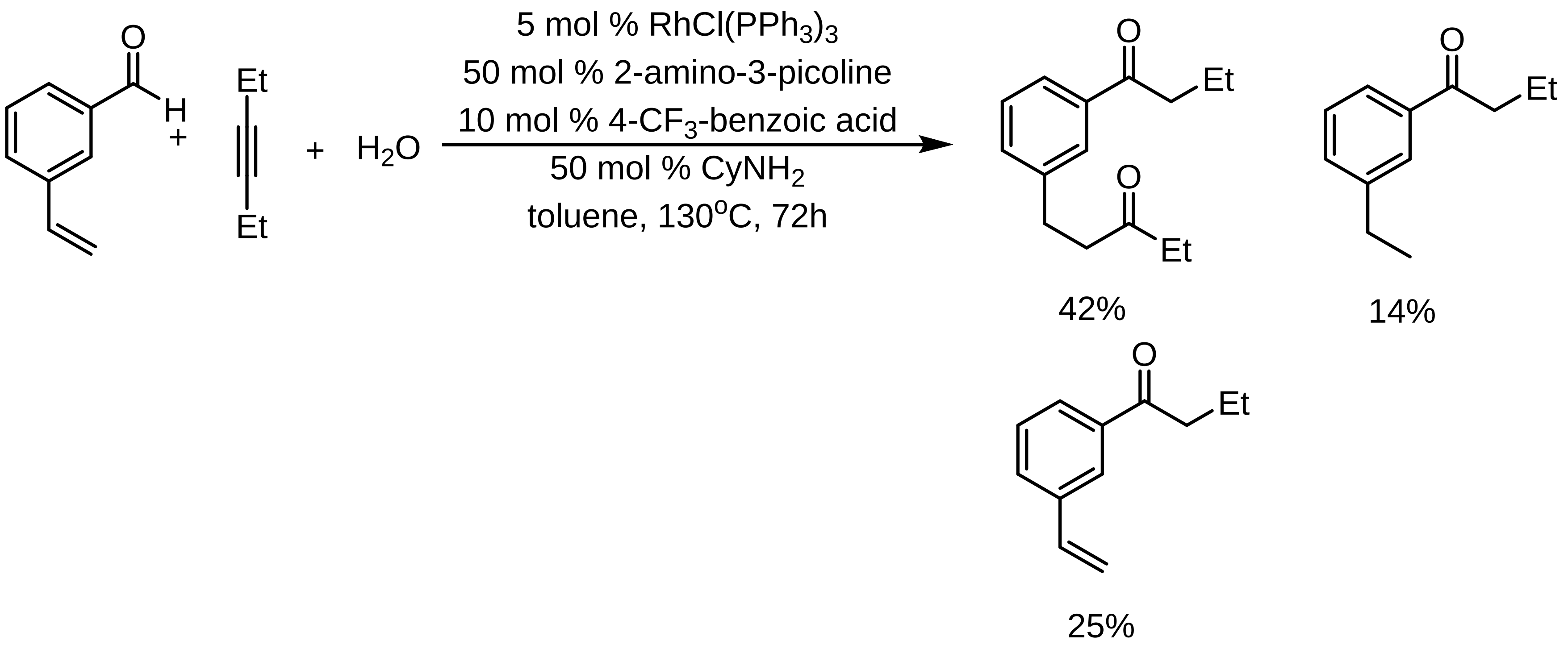
N
OH
N
Ts
[Cp*Rh(CH3CN)3][SbF6]2 (10 mol%)
sealed tube, N2
tBuOH (0.5 mL)/Toluene (0.5 mL)
90 °C, 24 h
N
NHTs
CHO

# Answer



hydroimination of alkyne
19a
+
2a
4 + 5
– H2O
N
N
Et
Et
12b
retro-Mannich
6 + 7b
N
N
Et
+
N
C
H
E
16b
15b
4 + 5
H2O
reduction of alkene
7b + 4
22a
21
N
N
Et
N
Cy
Et
23a
H2O
20a
H2N
R1
1
2
R2
3
H
HN
R1
8

# Answer



O
H
+
Et
Et
+
H2O
5 mol % RhCl(PPh3)3
50 mol % 2-amino-3-picoline
10 mol % 4-CF3-benzoic acid
50 mol % CyNH2
toluene, 130oC, 72h
O
Et
O
Et
42%
O
Et
14%
O
Et
25%