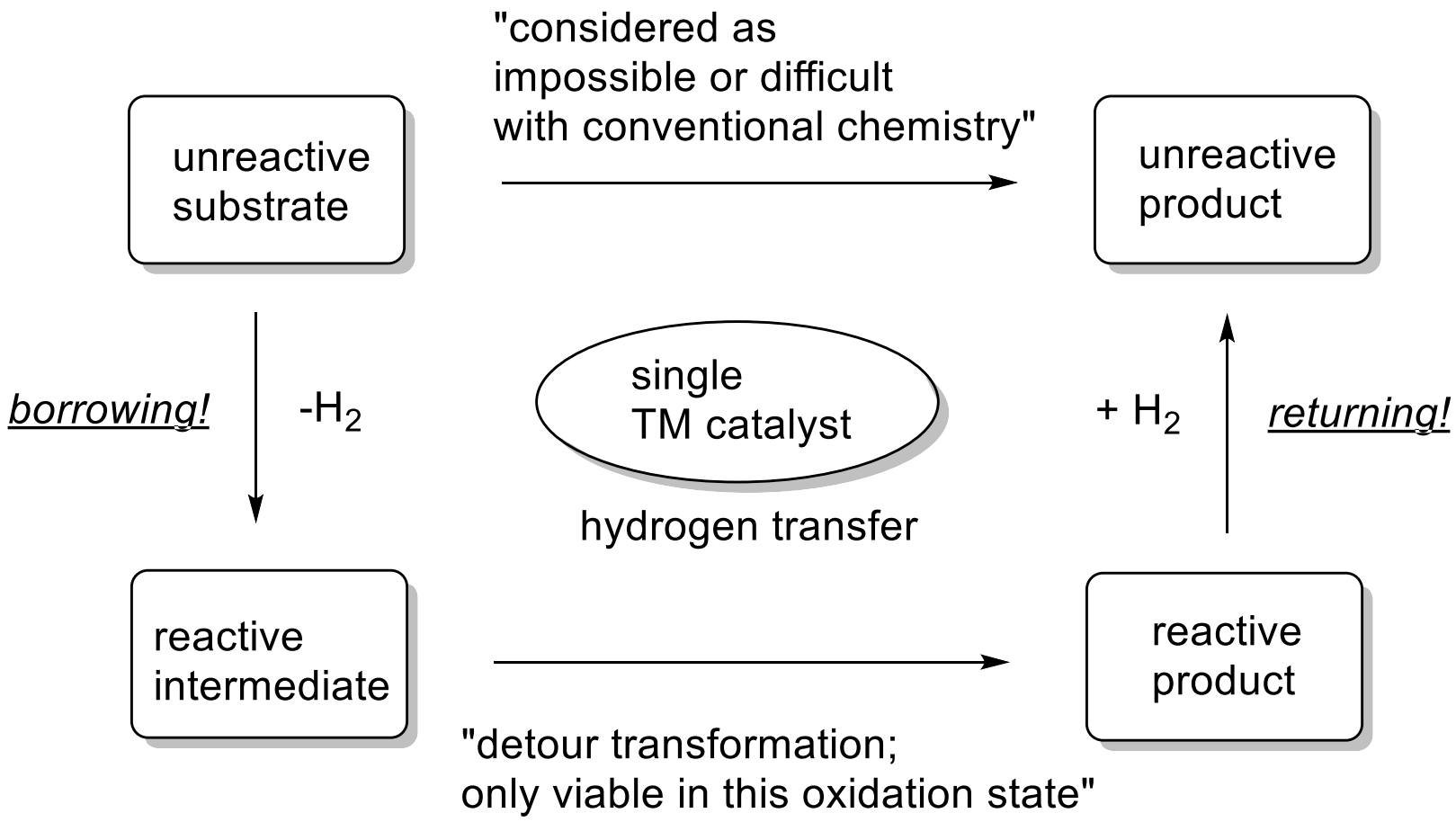
Borrowing H_2
Never ending chemistry??

Literature Talk, 2015, May. 5

Hee Nam Lim

Borrowing H_2; Concept?



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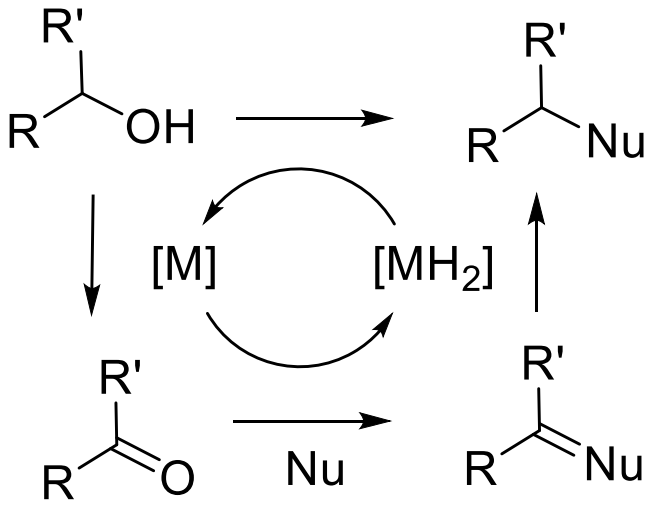
2. Amine Activation – Shim, Porzi, Beller,…

3. Alkane Activation – Brookhart, Goldman, Jensen, saito,….

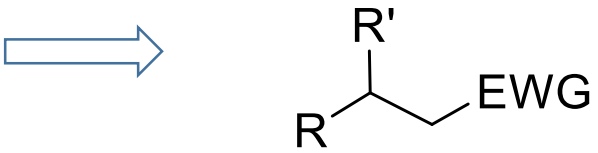
REVIEWS

Dobereiner and Crabtree – *Chem. Rev*. **2010**, *110*, 681-703.
Nixon, Whittlesey, and Williams – *Dalton Trans*., **2009**, 753-762.
Ketcham, Shin, Montgomery, Krische – *ACIE* **2014**, *53*, 9142-9150.
Guillena, Ramon, and Yus- *Chem. Rev*. **2010**, *110*, 1611-1641.
Obora and Ishii *Synlett* **2011**, 30-51.

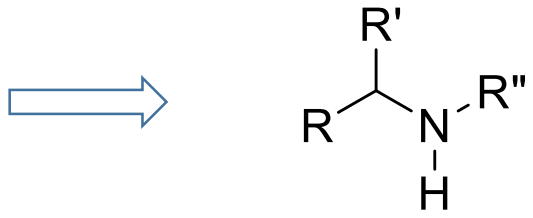
1. Alcohol Activation



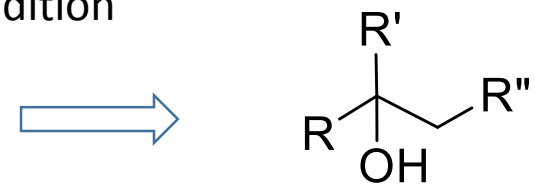
Homologation; Aldol, Wittig, ….. (C-C bond)



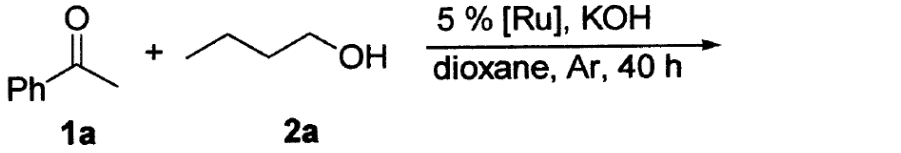
Amination (C-N bond)

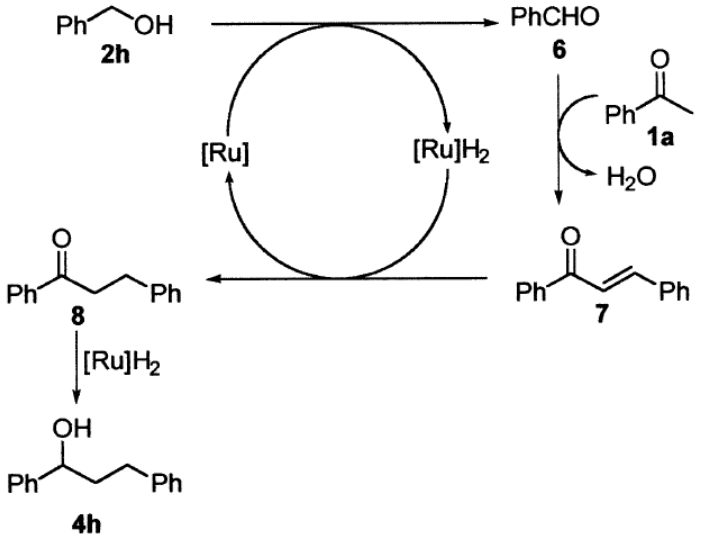


In-situ M-R addition

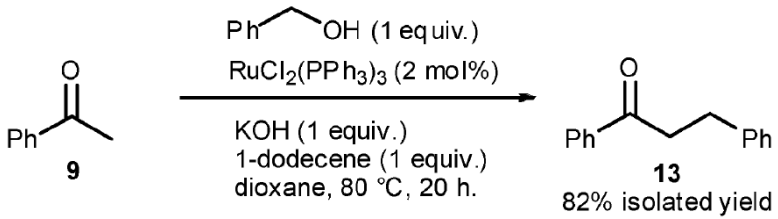


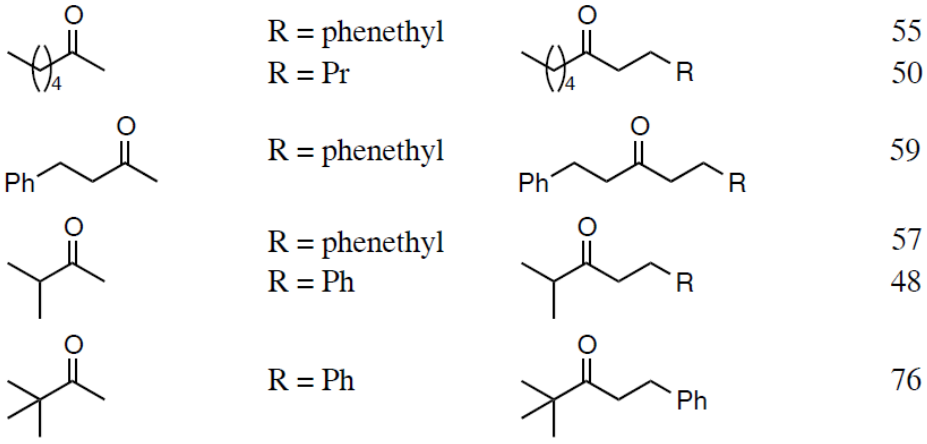
1. Alcohol Activation; ketone alkylation





Shim et al. *JOC*, **2001**, *66*, 9020.





Shim et al. *Tetrahedron Lett*. **2002**, *43*, 7987-7989.

1. Alcohol Activation; Ishii's selective reduction

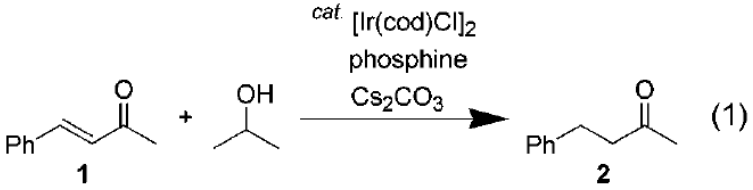
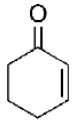
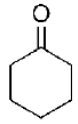
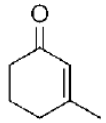
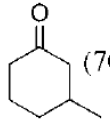
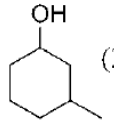
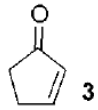
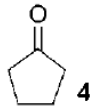
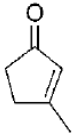
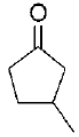
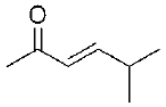
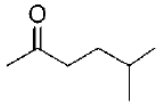
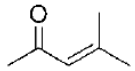
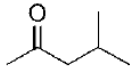
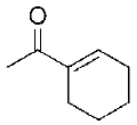
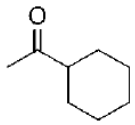
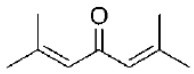
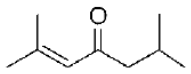
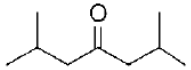
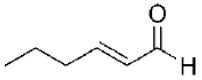
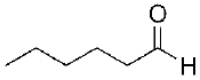
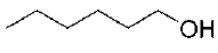


Table 1. Transfer Hydrogenation of 4-Phenyl-3-buten-2-one (1) to 4-Phenylbutan-2-one (2) Catalyzed by $[Ir(cod)Cl]_2$ under Selected Conditions[a]

entry	phosphine	base	convn (%)	yield (%)
1[b]	PCy_3	Cs_2CO_3	76	58
2[b]	PPh_3	Cs_2CO_3	99	37[c]
3	dppe	Cs_2CO_3	89	88
4	dppp	Cs_2CO_3	93	93
5	dppb	Cs_2CO_3	93	87
6			2	1
7	dppp		31	20
8		Cs_2CO_3	42	35
9	dppp	Na_2CO_3	58	52
10	dppp	Et_3N	25	20

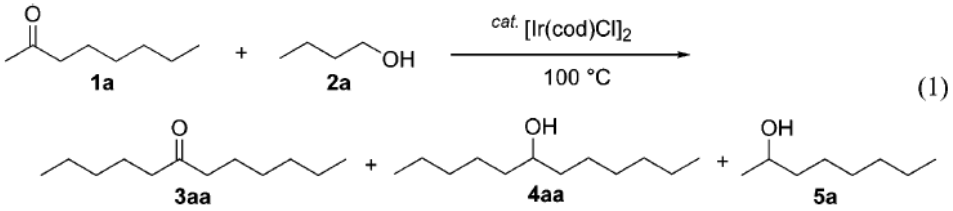
[a] Compound **1** (0.5 mmol) was allowed to react with 2-propanol (5 mmol) in the presence of a catalytic amount of $[Ir(cod)Cl]_2$ (2 mol %), phosphine (2 mol %), and base (2 mol %) in toluene (0.5 mL) at 80 °C for 4 h. [b] Phosphine (4 mol %) was used. [c] 4-Phenyl-2-butanol (60%) was also obtained.

entry	substrate	conv. (%)	product (selectivity/%)
1		99	 (98)
2[b]		91	 (70)  (25)
3[b]	 **3**	96	 **4** (94)
4[c,d]		79	 (96)
5		99	 (95)
6[d]		90	 (98)
7[c,d]		78	 (96)
8[c,e]		68	 (74)
			 (26)
9		75	 (70)
			 (7)

Ishii et al. *JOC* **2001**, *66*, 4710.

1. Alcohol Activation; ketone alkylation

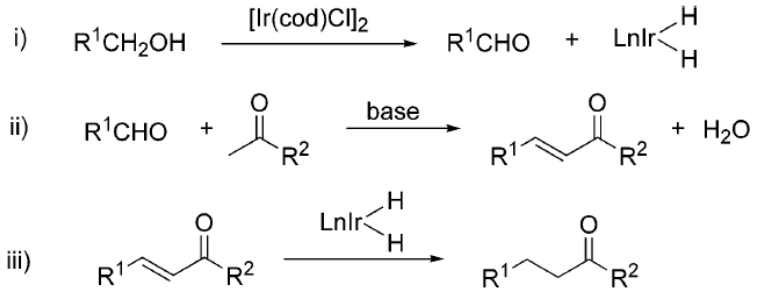
neat



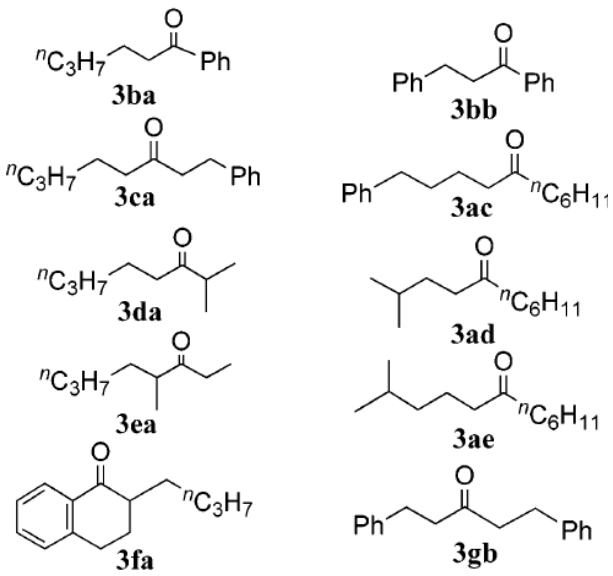
run	ligand	base	conv. (%)[b]	product (%)[c] 3aa	4aa	5a
1	PPh_3	KOH	96	80	2	7
2	PPh_3		3	n.d.	n.d.	1
3	PPh_3	CsOH	97	80	3	8
4	PPh_3	NaOH	98	79	trace	8
5	PPh_3	K_2CO_3	2	1	n.d.	2
6	PPh_3	NEt_3	2	n.d.	n.d.	2
7	PPh_3	$Ba(OH)_2$	44	27	1	15
8	PBu_3	KOH	84	63	2	16
9	PCy_3	KOH	82	48	2	15
10[d]	dppe	KOH	85	28	2	26
11[d]	dppp	KOH	92	23	3	27
12	$P(OPh)_3$	KOH	7	2		5
13[e]	PPh_3	KOH	94	81	3	6
14[f]	PPh_3	KOH	90	76	1	7
15[g]	PPh_3	KOH	80	68	1	5

[a] **1a** (2 mmol) was reacted with **2a** (4 mmol) in the presence of $[Ir(cod)Cl]_2$ (0.02 mmol), base (0.2 mmol), and ligand (0.08 mmol) at 100 °C for 4 h without solvent. [b] Conversion of **1a**. [c] Based on **1a** used. [d] Ligand (0.04 mmol) was used. [e] At 110 °C. [f] At 90 °C. [g] **2a** (2 mmol) was used.

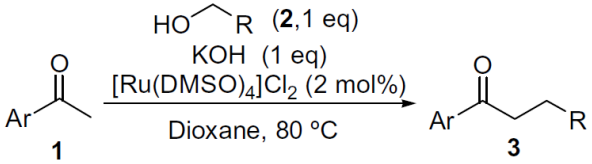
Ishii et al. *JACS* **2004**, *126*, 72



scope

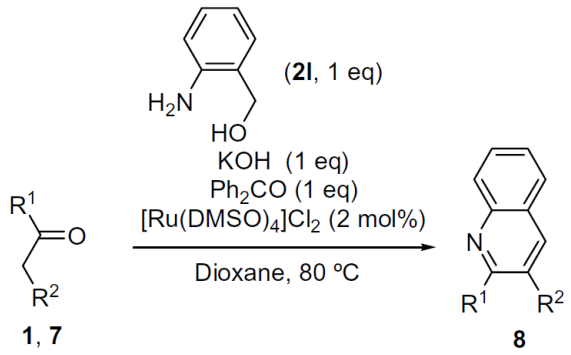


1. Alcohol Activation; ketone alkylation



Entry	Ketone **3**			
	No.	Ar	R	% Yield[a]
1	**a**	Ph	Ph	72
2	**b**	Ph	2-BrC_6H_4	93
3	**c**	Ph	3-$BnOC_6H_4$	86
4	**d**	4-MeC_6H_4	4-$MeOC_6H_4$	93
5	**e**	4-MeC_6H_4	4-ClC_6H_4	85
6	**f**	4-MeC_6H_4	2-ClC_6H_4	92
7	**g**	4-MeC_6H_4	3,4-$(MeO)_2C_6H_4$	69
8	**h**	4-$(F_3C)C_6H_4$	Ph	89[b]
9	**i**	2-$C_{10}H_8$	Ph	87
10	**j**	2-Thiophene	Ph	45
11	**k**	2-Thiophene	2-BrC_6H_4	41

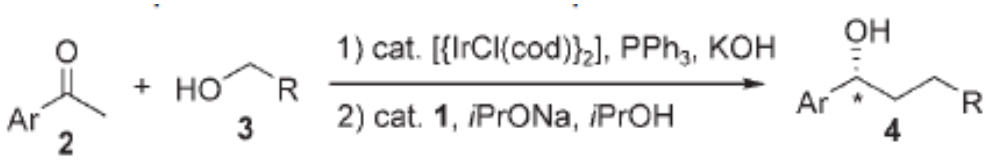
[a] Isolated yields after column chromatography (silica gel: hexane/ethyl acetate).
[b] Yield of the related alcohol when the reaction was performed using 2 equiv of benzyl alcohol.



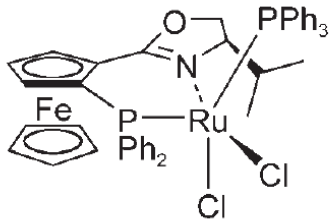
Entry	Quinoline **8**			
	No.	R^1	R^2	% Yield[a]
1	**a**	$-(CH_2)_4-$		88
2	**b**	Ph	H	94
3	**c**	Ph	Me	81
4	**d**	Ph	Et	67
5	**e**	4-MeC_6H_4	H	96
6	**f**	2-Furan	H	89
7	**g**	2-Thiophene	H	96

Yus et al. *TL* **2006**, *62*, 8988.

1. Alcohol Activation; ketone alkylation; in-situ hydrogenation



Entry	2, Ar	3, R	Product	Yield [%][b]	*ee* [%][c]
1	**2a**, Ph	**3a**, *n*Pr	**4aa**	75	94 (*R*)[d]
2	**2b**, 4-MeC_6H_4	**3a**, *n*Pr	**4ba**	72	98
3	**2c**, 3-MeC_6H_4	**3a**, *n*Pr	**4ca**	77	96
4	**2d**, 2-MeC_6H_4	**3a**, *n*Pr	**4da**	52	97
5	**2e**, 4-$MeOC_6H_4$	**3a**, *n*Pr	**4ea**	57	97 (*R*)[d]
6	**2f**, 4-ClC_6H_4	**3a**, *n*Pr	**4fa**	58	88
7	**2g**, 4-FC_6H_4	**3a**, *n*Pr	**4ga**	15	95
8	**2a**, Ph	**3b**, *i*Pr	**4ab**	51	96 (*R*)[d]
9	**2a**, Ph	**3c**, *n*Bu	**4ac**	77	93 (*R*)[d]
10	**2a**, Ph	**3d**, CH_2CHMe_2	**4ad**	79	96
11	**2a**, Ph	**3e**, Ph	**4ae**	0	–

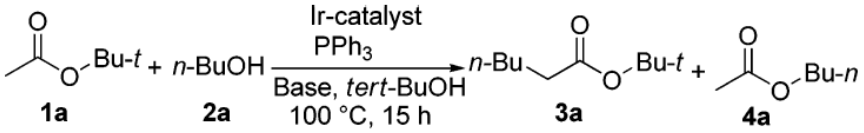


$[RuCl_2(PPh_3)(ip\text{-}foxap)]$ (**1**)

Nishibayashi et al.
ACIE **2006**, 45, 3819-3822.

one pot two step procedure
1 itself didn't produce high ee.

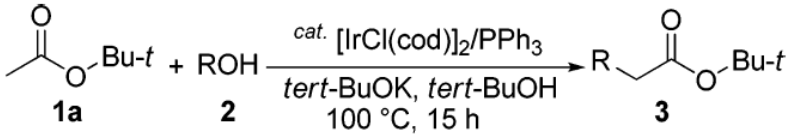
1. Alcohol Activation; ester alkylation



1a **2a** **3a** **4a**

entry	Ir catalyst	base	yield (%)[b] 3a	4a
1	$[IrCl(cod)]_2$	*tert*-BuOK	74 (62)	n.d.[c]
2	$[IrCl(coe)_2]_2$	*tert*-BuOK	60	2
3[d]	[Ir(acac)(cod)]	*tert*-BuOK	68	n.d.[c]
4	$[Cp^*IrCl_2]_2$	*tert*-BuOK	5	38
5[d]	$IrCl_3 \cdot 3H_2O$	*tert*-BuOK	n.d.[c]	51
6	$[IrCl(cod)]_2$	NaH	55	10
7	$[IrCl(cod)]_2$	NaOEt	9	59
8	$[IrCl(cod)]_2$	KOH	n.d.[c]	8
9	$[IrCl(cod)]_2$	Na_2CO_3	n.d.[c]	n.d.[c]
10[e]	$[IrCl(cod)]_2$	*tert*-BuOK	65	8
11[f]	$[IrCl(cod)]_2$	*tert*-BuOK	32	43
12[g]	$[IrCl(cod)]_2$	*tert*-BuOK	8	79
13[h]	$[IrCl(cod)]_2$	*tert*-BuOK	27	18
14[i]	$[IrCl(cod)]_2$	*tert*-BuOK	36	15
15[j]	$[IrCl(cod)]_2$	*tert*-BuOK	34	12
16[k]	$[IrCl(cod)]_2$	*tert*-BuOK	n.d.[c]	74

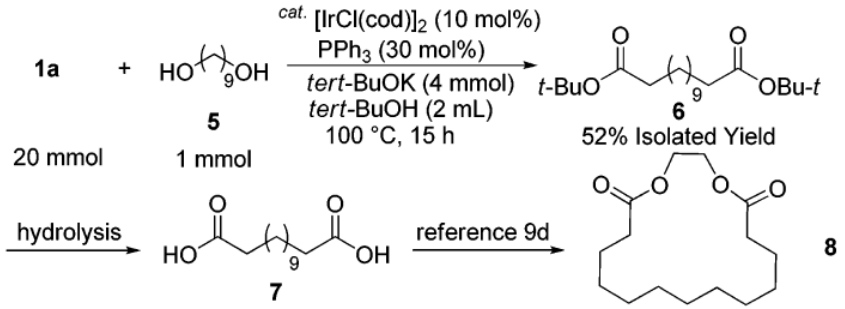
[a] Conditions: **1a** (10 mmol) was allowed to react with **2a** (1 mmol) in the presence of Ir catalyst (0.05 mmol), PPh_3 (0.15 mmol), and base (2 mmol) in *tert*-BuOH (1 mL) at 100 °C for 15 h. [b] GC yields based on the amount of **2a** used. Values in parentheses are isolated yields. [c] Not detected by GC. [d] Ir catalyst (0.10 mmol) was used. [e] *tert*-BuOK (1.5 mmol) was used. [f] *tert*-BuOK (1.0 mmol) was used. [g] *tert*-BuOK (0.5 mmol) was used. [h] Reaction was performed without solvent. [i] *n*-Octane (1 mL) was used as the solvent. [j] Toluene (1 mL) was used as the solvent. [k] DMSO (1 mL) was used as the solvent.



1a **2** **3**

entry	R	2	product	yield (%)[b]
1	$n\text{-}C_6H_{13}$	**2b**	**3b**	78 (75)
2	$n\text{-}C_8H_{17}$	**2c**	**3c**	79 (78)
3	$(CH_3)_2CH(CH_2)_2$	**2d**	**3d**	80 (71)
4	$cyclo\text{-}C_6H_{11}CH_2$	**2e**	**3e**	95(89)
5	$PhCH_2$	**2f**	**3f**	89 (82)
6	$p\text{-}CH_3C_6H_4CH_2$	**2g**	**3g**	75 (64)
7	$p\text{-}CH_3OC_6H_4CH_2$	**2h**	**3h**	75 (69)
8	$p\text{-}CF_3C_6H_4CH_2$	**2i**	**3i**	71 (67)
9	$p\text{-}ClC_6H_4CH_2$	**2j**	**3j**	70 (67)
10	$Ph(CH_2)_3$	**2k**	**3k**	75 (72)
11	2-$NaphCH_2$	**2l**	**3l**	78 (68)

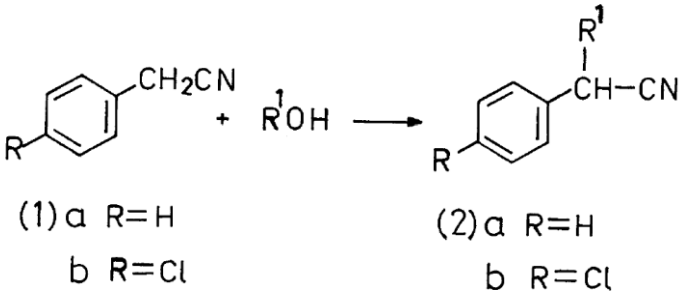
Scheme 1. Synthesis of Ethylene Brassylate (**8**) (Musk T) from **6**



Ishii et al. *JACS* **2010**, *132*, 2536

1. Alcohol Activation; nitrile alkylation

in boling EtOH
Cat (5 mol%)
NaC_2O_3 (110 mol%)



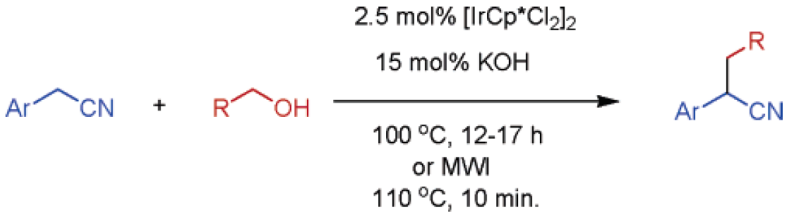
(1) a R=H
b R=Cl

(2) a R=H
b R=Cl

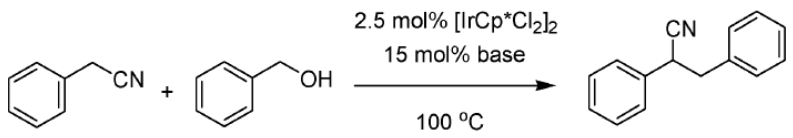
Grigg et al *TL* **1981**, *22*, 4107.

Table 1. Catalytic ethylation of (1a)

Catalyst[b]	Time (h)	Yield (%) of (2a; R^1 = Et)[c]
$RuH_2(PPh_3)_4$	11	78
$RuH_2(PPh_3)_4$	24	92
$RhH(PPh_3)_4$	48	75
$RhCl_3.3H_2O$-PPh_3[d]	48	86
$RhCl(PPh_3)_3$	96	75
$IrCl_3$-PPh_3[d]	48	9



Grigg et al *JOC* **2006**, *71*, 8023.

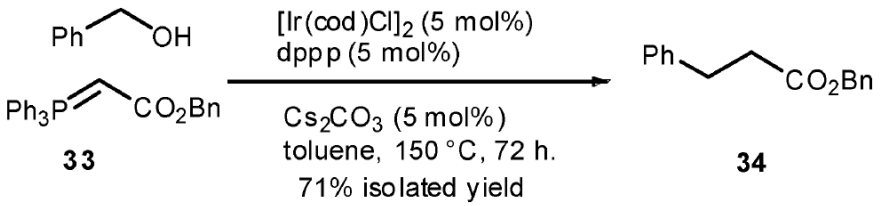


1a **2a** **3a**

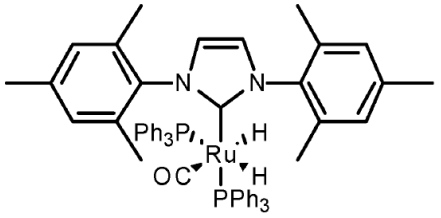
entry	base	**3a** (%)[b]
1	K_2CO_3	<10
2	Cs_2CO_3	<10
3	KO^{t}Bu	<10
4	NaOH	84
5	**KOH**	**>99**
6	CsOH	95
7	Et_3N	0
8	DABCO	0

[a] **1a** (1 mmol) was reacted with **2a** (3 mmol) under the influence of $[Cp^*IrCl_2]_2$ (2.5 mol %) and base (15 mol %) at 100 °C for 13 h. [b] Conversion estimated by ^{1}H NMR spectroscopy based on **1a**.

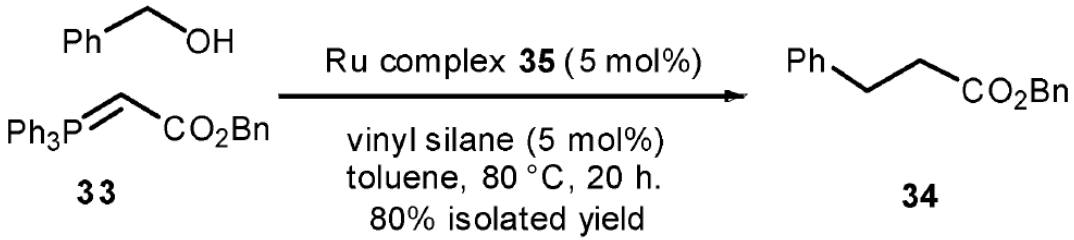
1. Alcohol Activation; homologation followed by hydrogenation



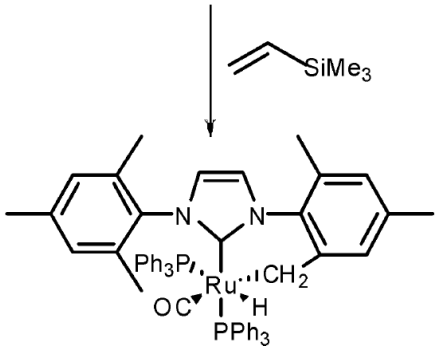
Williams et al. AdvSynCat **2006**, *347*, 591.



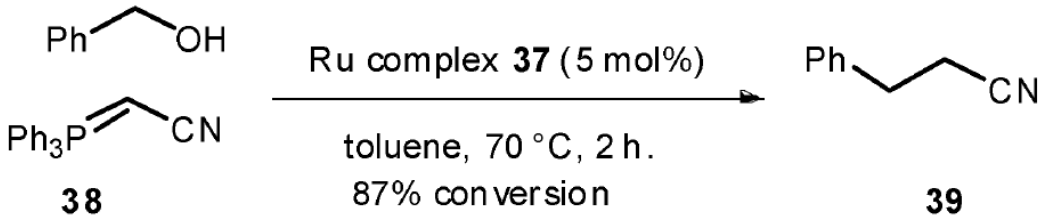
35



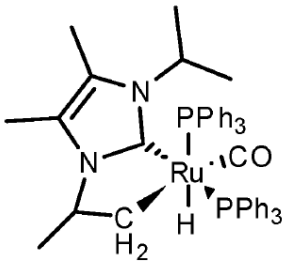
Williams et al. ChemComm **2004**,90.



36



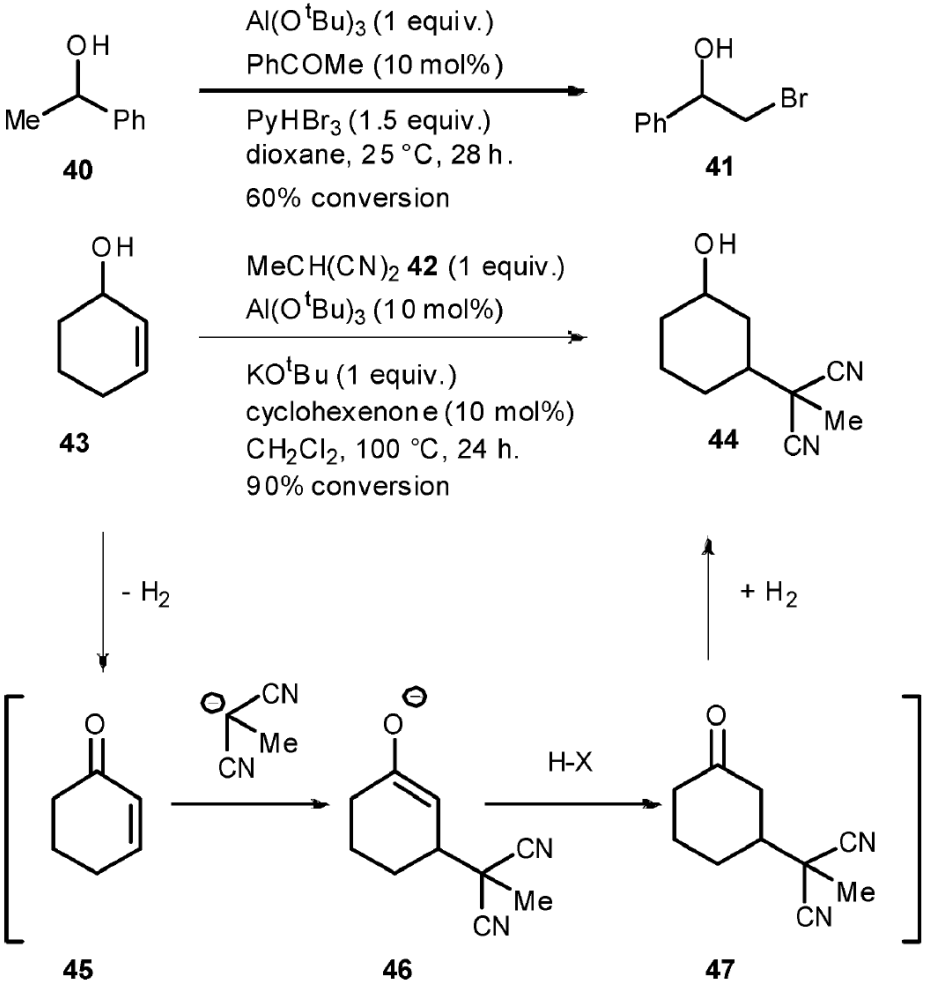
Williams et al. *JACS* **2007**, *129*, 1987.



37

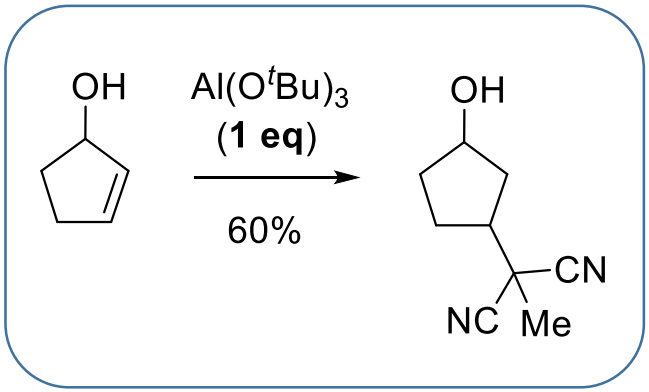
most reactive

1. Alcohol Activation; alcohol β-bromination and Michael addition

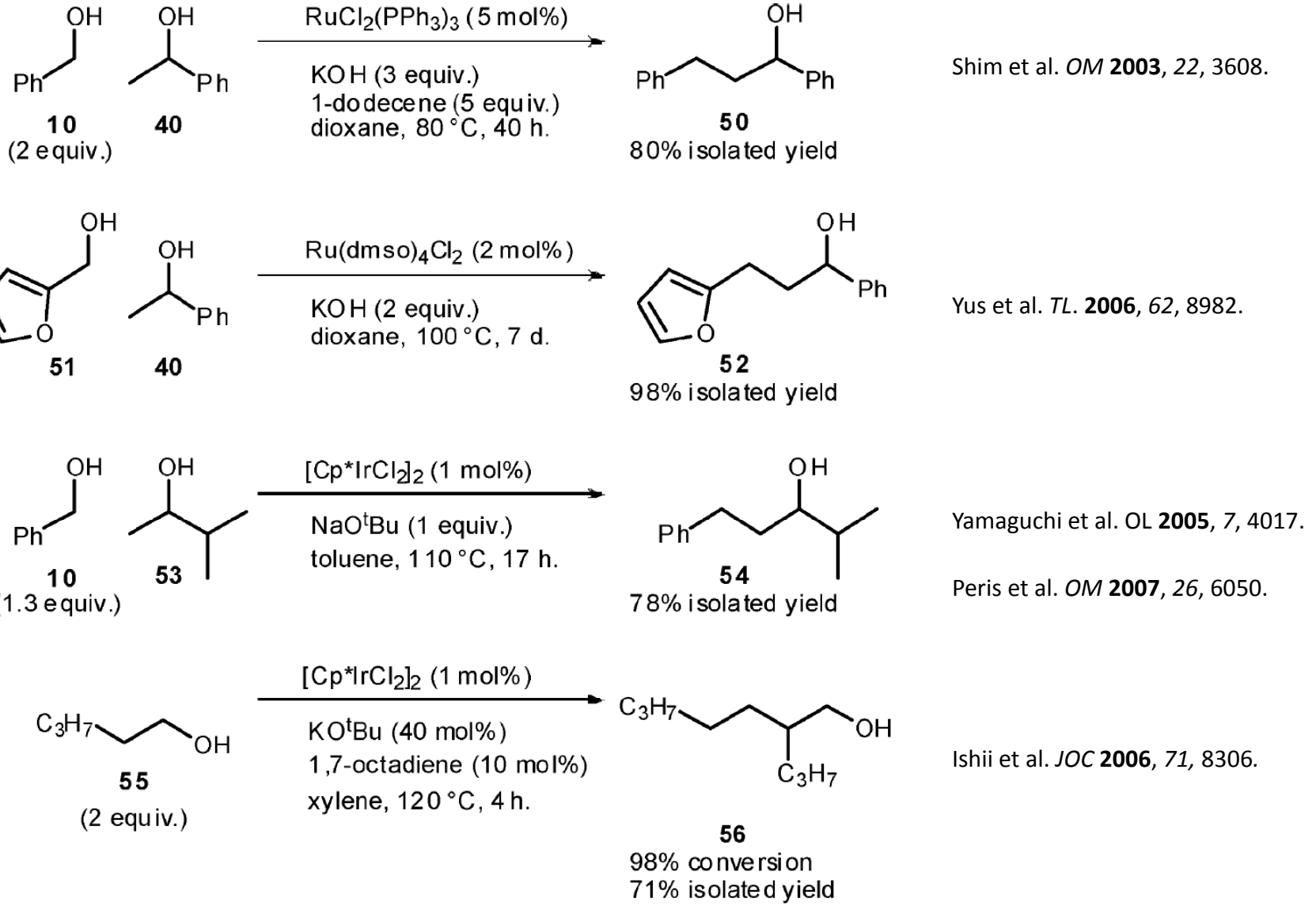


β-bromination; (modest yield)
Williams et al. *Synlett* **2003**, 124.

γ-alkylation product from allylic alcohol
Williams et al. *ACIE* **2001**, *40*, 4475.



1. Alcohol Activation; alcohol β-alkylation



Shim et al. *OM* **2003**, *22*, 3608.

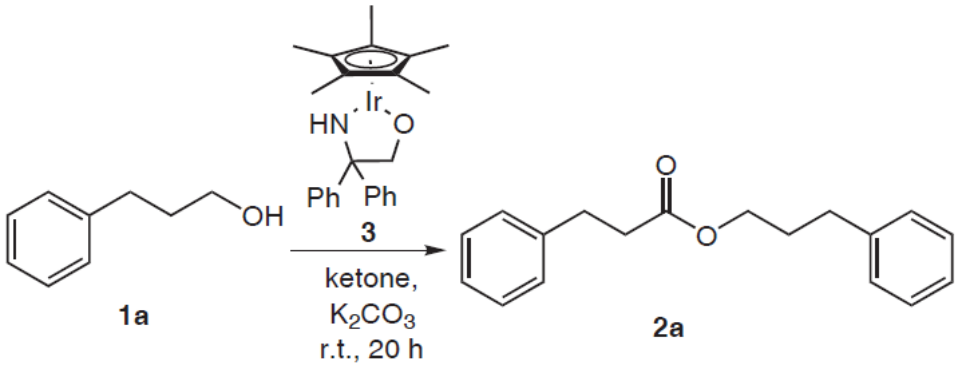
Yus et al. *TL*. **2006**, *62*, 8982.

Yamaguchi et al. OL **2005**, *7*, 4017.

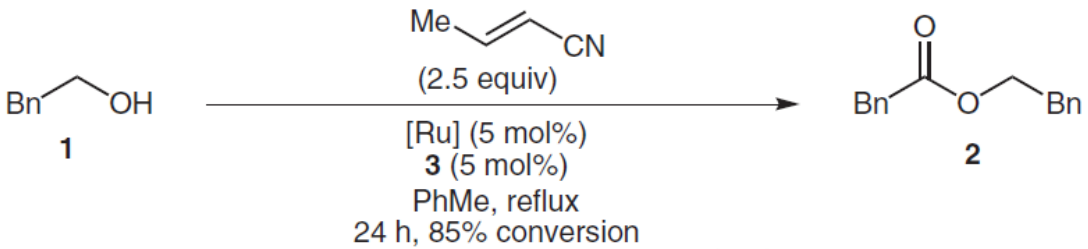
Peris et al. *OM* **2007**, *26*, 6050.

Ishii et al. *JOC* **2006**, *71,* 8306.

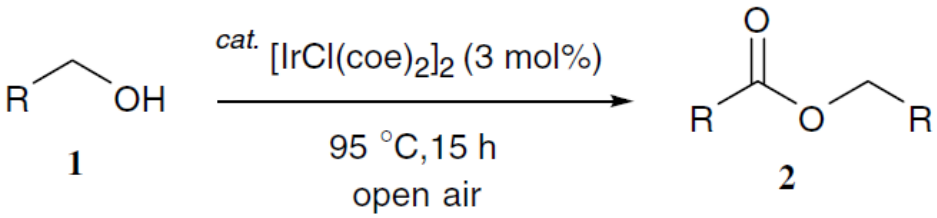
1. Alcohol Activation; oxidative esterification



Suzuki et al. *Synlett* **2005**, 1453..

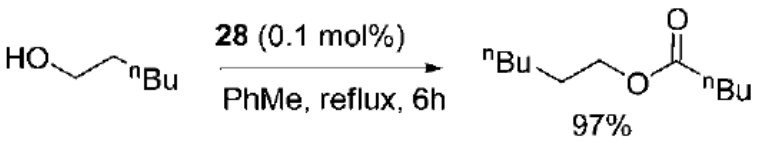


Williams et al. *Synthesis* **2009**, 1578.



Ishii et al. TL **2006**, 47, 9199.

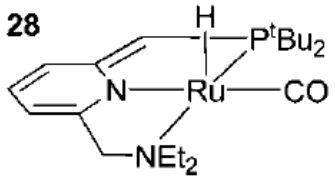
1. Alcohol Activation; oxidative esterification



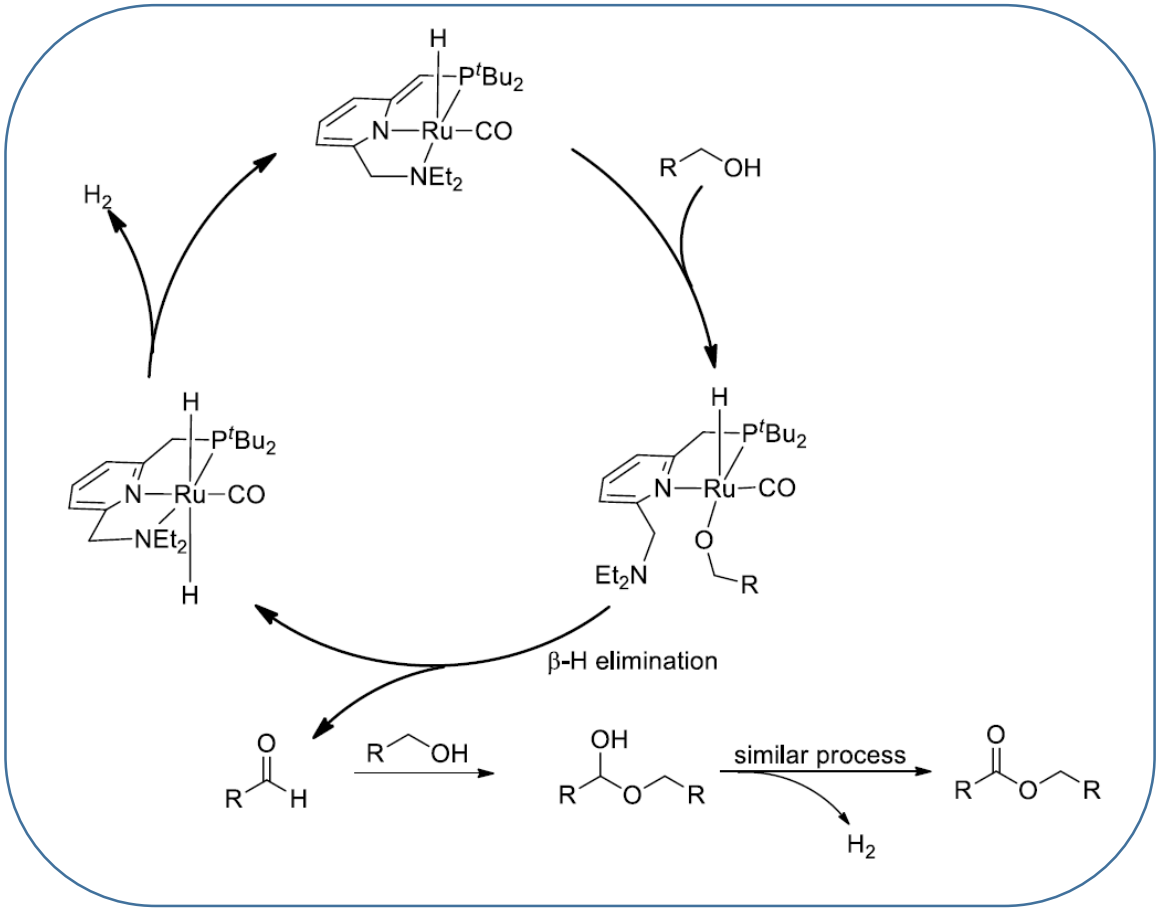
No base

No H_2 acceptor

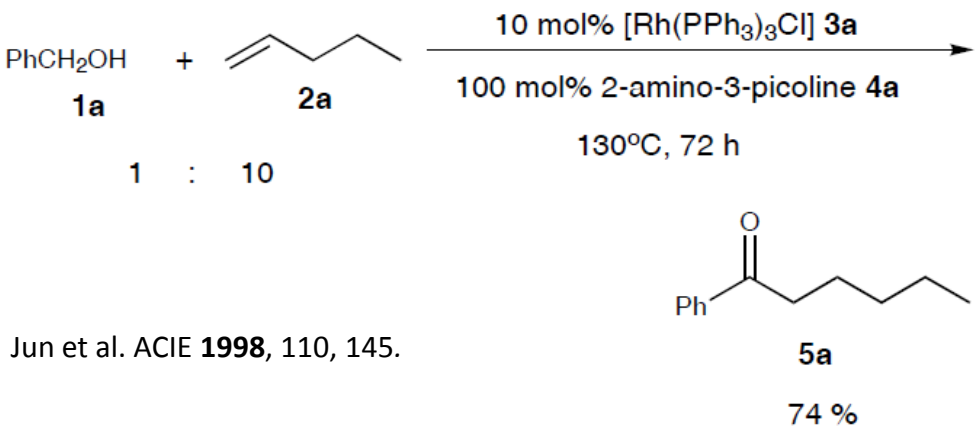
Milstein et al. JACS **2005**, 127, 10840.



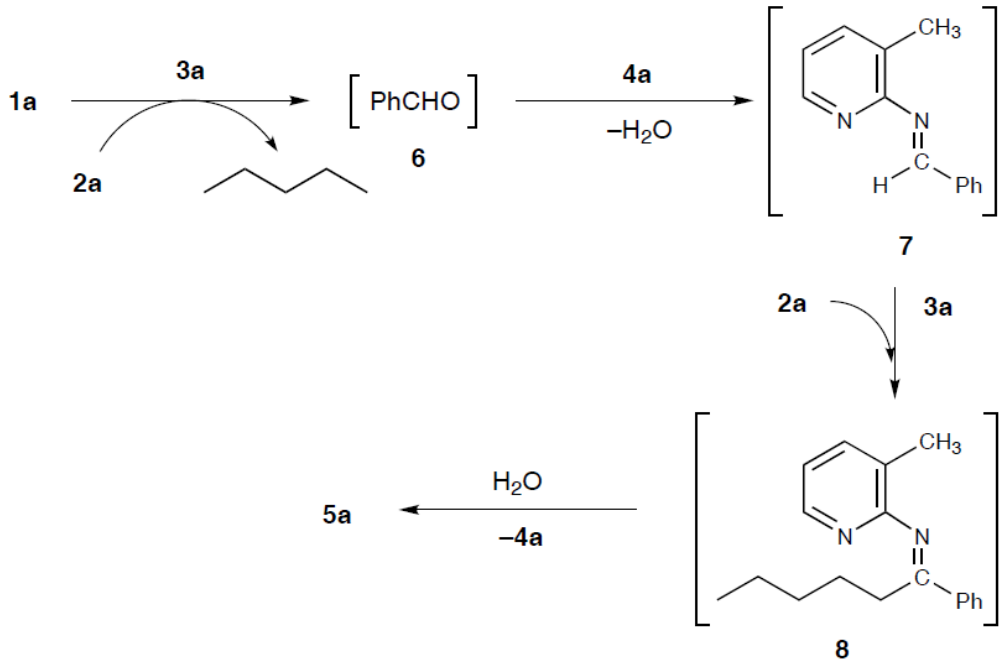
proposed mechansm



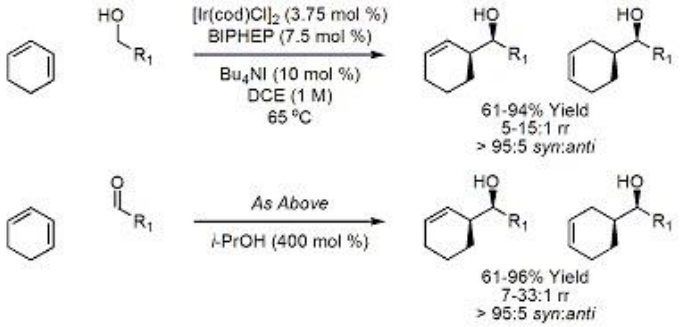
1. Alcohol Activation; dehydrogenative hydroacylation



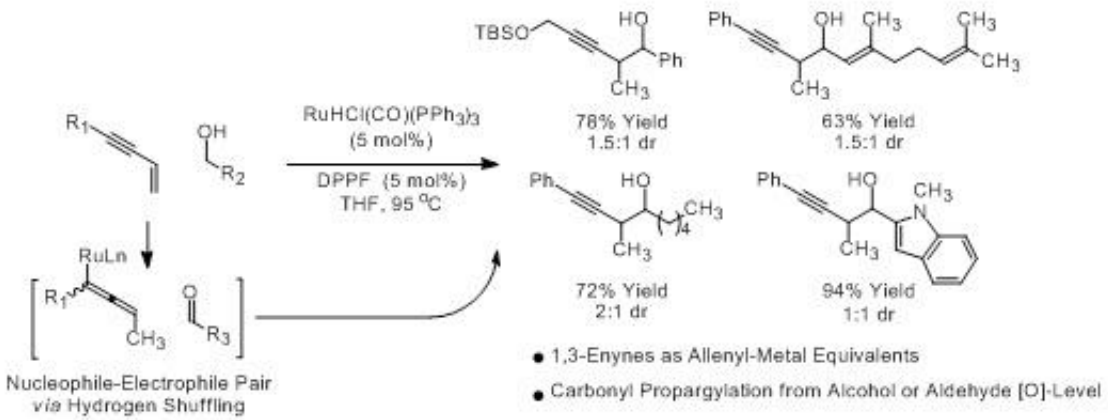
Jun et al. ACIE **1998**, 110, 145.



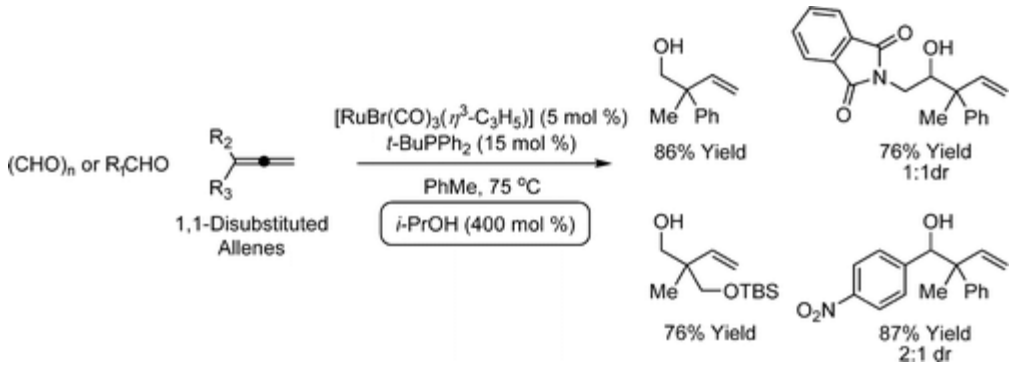
1. Alcohol Activation; alcohol α-alkylation using activated olefin (very early examples)



Krische et al. *OL* **2008***, 10,* 1033.

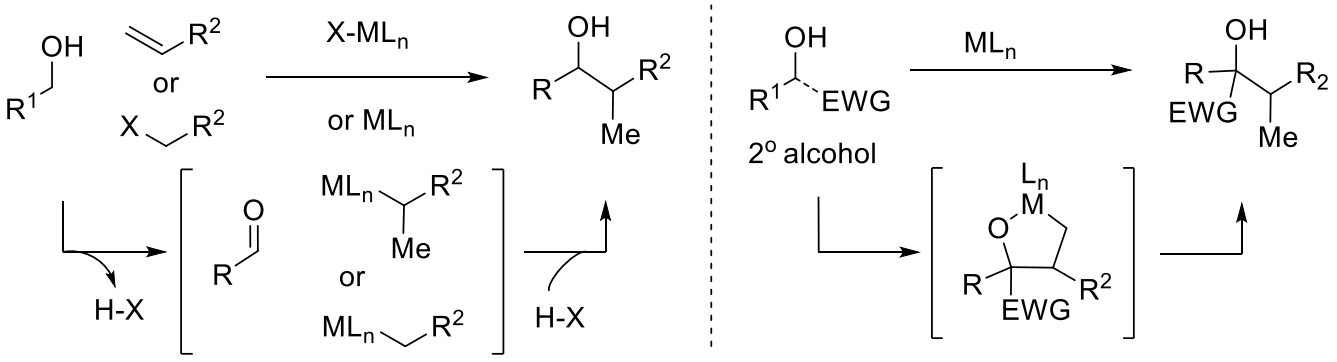


Krische et al. *ACIE*. **2008**, *47*, 5220.



Krische et al. *OL* **2008**, *10*, 2705.

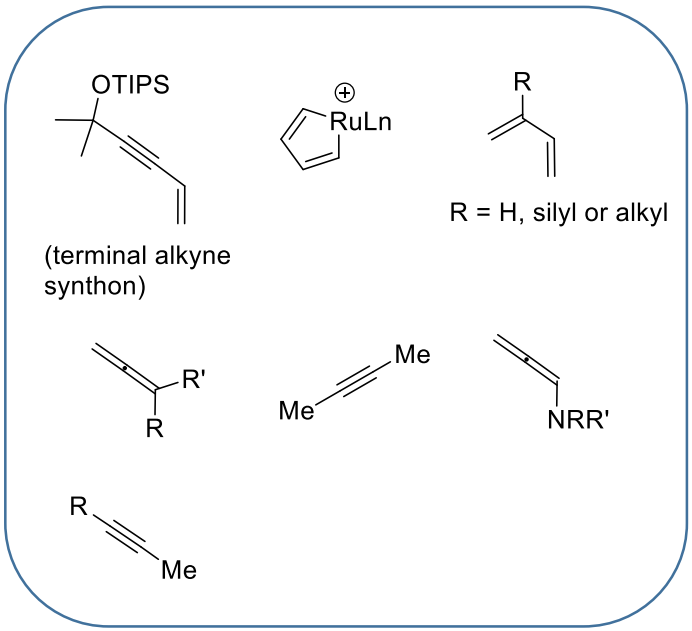
1. Alcohol Activation; What Prof. Krische has done….; addition of activated olefin to the carbonyl

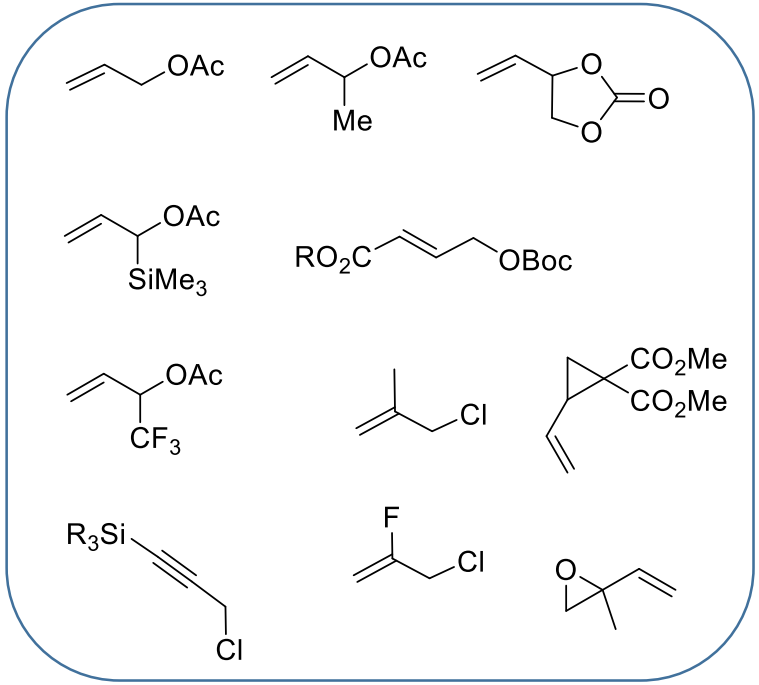


M-H receptors

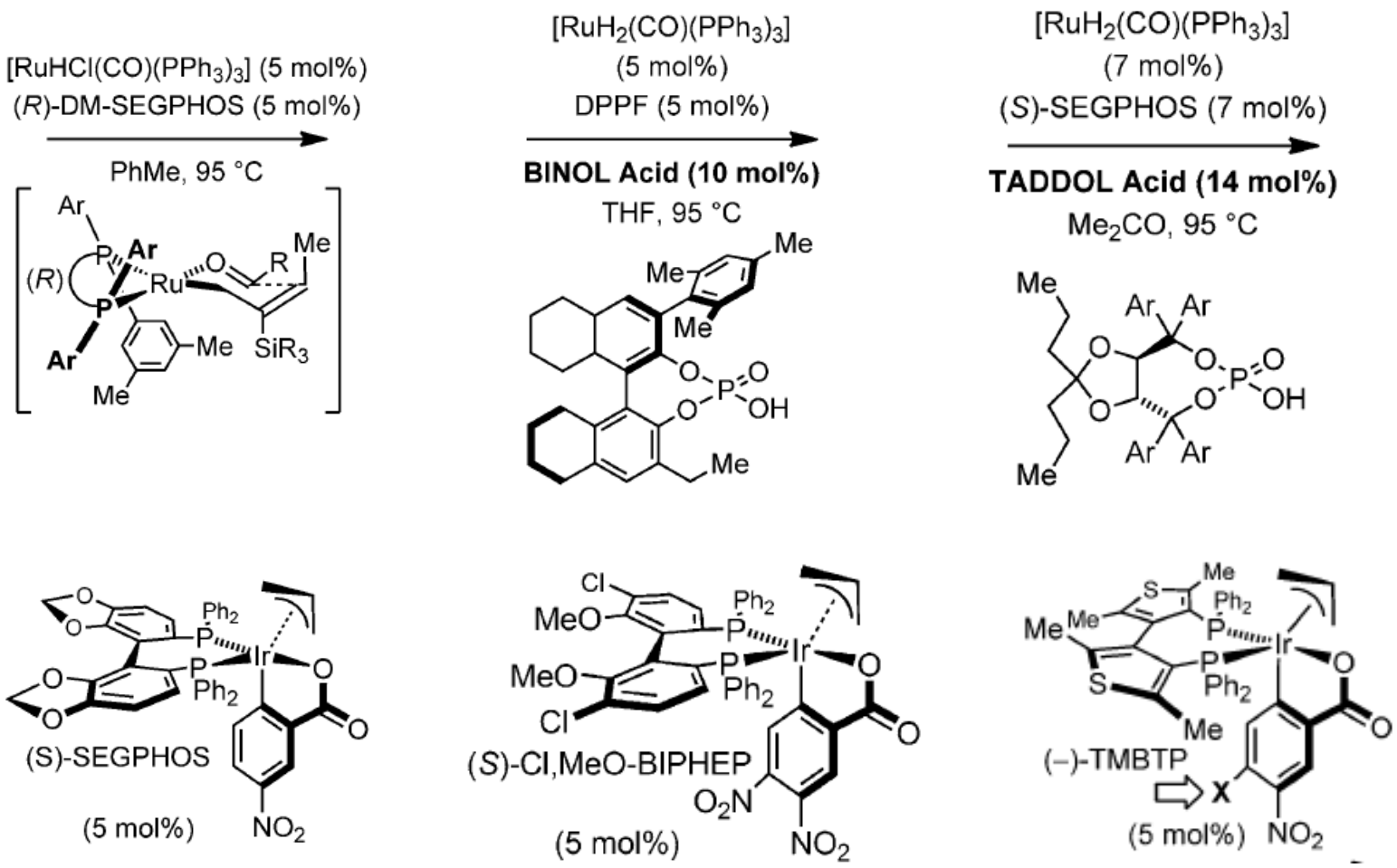
Krische et al. ACIE **2014**, *53*, 9142.

Allyl-species





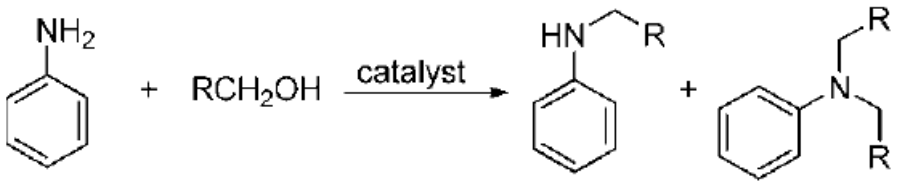
1. Alcohol Activation; What Prof. Krische has done….; addition of activated olefin to the carbonyl



etc…….

Krische et al. ACIE **2014**, *53*, 9142.

1. Alcohol Activation; alcohol amination by metal oxide (heterogenous)



1a **2** **3** **4**

entry	catalyst	R	T (°C)	no.	yield (%)	no.	yield (%)
1	SiO_2	H	362	**3a**	20	**4a**	25
2	SiO_2	Me	385	**3b**	47	**4b**	13
3	SiO_2	Et	385	**3c**	37	**4c**	12
4	SiO_2	Pr	400	**3d**	27	**4d**	9
5	SiO_2	Me	400	**3b**	28	**4b**	5
6	$V_2O_5-SiO_2$	Me	400	**3b**	66	**4b**	15
7	Al_2O_3[a]	H	400	**3a**	32	**4a**	50
8	γ-Al_2O_3	H	400	**3a**	15	**4a**	2
9	γ-Al_2O_3	H	375	**3a**	24	**4a**	18
10	γ-Al_2O_3	H	200	**3a**	41	**4a**	5

[a] Prepared from $Al(OPr^i)_3$.

Brown et al. *JACS* **1924**, *46*, 1836.

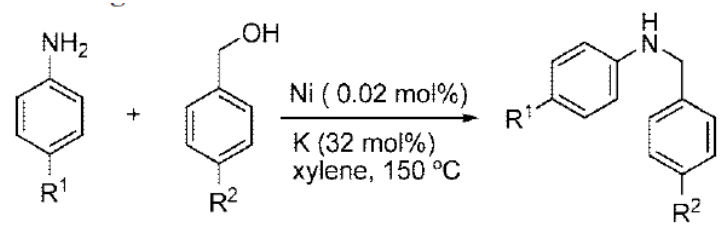
Prasad et al. *JCS ChemComm* **1992**, *1204*.

Arata et al. *BCSJ* **1991**, 64, 2605.

Zhu et al. *Appl. Catal. A.* **1996**, 134, 53.

GAS PHASE

1. Alcohol Activation; alcohol amination by metal oxide (heterogenous)

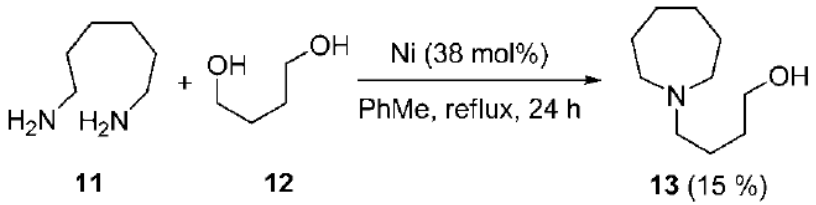


1 **6** **7**

entry	R^1	R^2	no.	yield (%)
1	H	H	**7a**	89
2	H	Cl	**7b**	78
3	H	Me	**7c**	89
4	H	MeO	**7d**	84
5	Cl	H	**7e**	87
6	Me	H	**7f**	93
7	MeO	H	**7g**	88

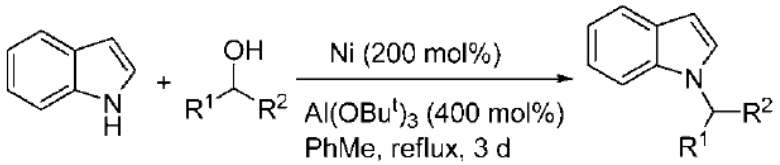
Ni particle from NiO

Frazza et al. *JACS* **1954**, *76*, 6174.



11 **12** **13** (15 %)

Daasch et al. *JOC* **1958**, *23*, 1352.



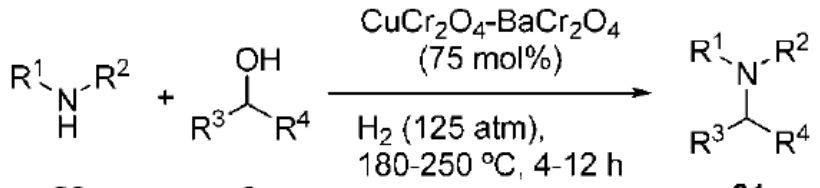
8a **9** **10**

entry	R^1	R^2	no.	yield (%)
1	Me	Me	**10a**	90
2	Me	Et	**10b**	94
3	$(CH_2)_5$		**10c**	70

Nicoletti et al. *Synthesis*, **1977**, 335.

1. Alcohol Activation; alcohol amination by metal oxide (heterogenous)

Simple Cu or Cu-oxide easily lost catalytic activity probably due to reduction.



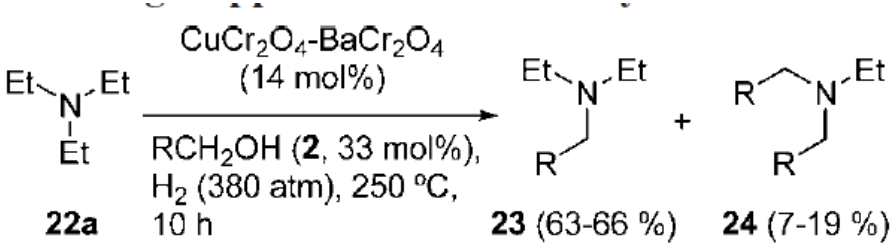
20 **9** **21**

entry	R^1	R^2	R^3	R^4	no.	yield (%)
1	$CH_3(CH_2)_4$	H	Me	H	**21a**	39
2	$CH_3(CH_2)_4$	H	Me	Me	**21b**	43
3	$CH_3(CH_2)_4$	H	Et	H	**21c**	15
4	$(CH_2)_5$		Me	H	**21d**	31
5	$(CH_2)_5$		Me	Me	**21e**	46
6	$(CH_2)_5$		$(CH_2)_5$		**21f**	59
7	PhCHMe	Me	Me	H	**21g**	67
8	Bu^iCHMe	H	Et	H	**21h**	61

Ba- stabilize Cu complex

Cr- increase the metal surface area

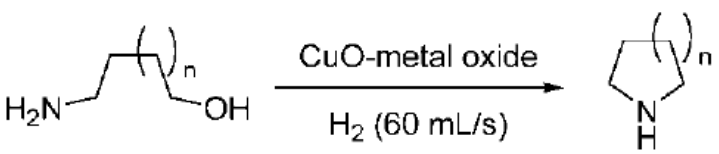
Holowchak et al. *JACS* **1934**, *56*, 153.
Holowchak et al. *JACS* **1934**, *56*, 153.



22a **23** (63-66 %) **24** (7-19 %)

Adkins et al. *JACS* **1939**, *61*, 3499.

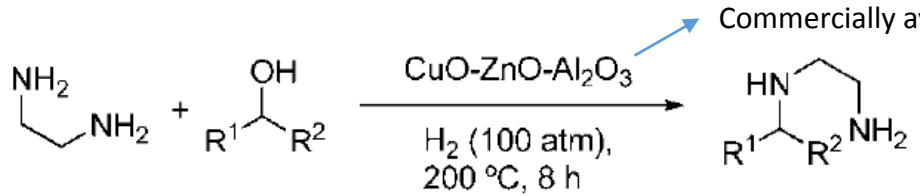
1. Alcohol Activation; alcohol amination by metal oxide (heterogenous)



29 **30**

entry	metal oxide (solvent)	*n*	*T* (°C)	no.	yield (%)[a]
1	γ-Al_2O_3	1	200	**30a**	90
2	γ-Al_2O_3(MeOH)	1	225	**30a**	45 (13)
3	MgO (MeOH)	1	225	**30a**	62 (38)
4	γ-Al_2O_3	2	210	**30b**	75
5	γ-Al_2O_3(MeOH)	2	225	**30b**	89 (10)
6	MgO (MeOH)	2	225	**30b**	62 (37)
7	γ-Al_2O_3	3	225	**30c**	95
8	MgO (MeOH)	3	225	**30c**	84 (13)

Schmitt et al. *JOC* **1981**, *46*, 754.

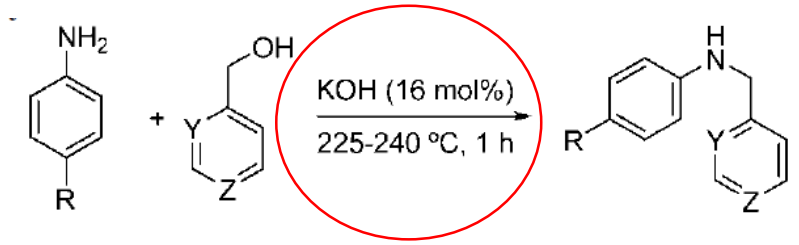


31 **9** **32**

entry	R^1	R^2	no	yield (%)
1	H	H	**32a**	21
2	Me	H	**32b**	50
3	Ph	H	**32c**	45
4	$(CH_2)_5$		**32d**	73

Ogawa et al. *Cat. Comm.* **2004**, *5*, 291.

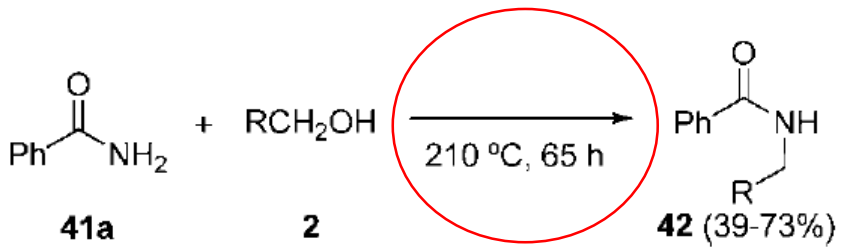
1. Alcohol Activation; alcohol amination w/o Transition metal



1 **39** **40**

entry	R	Y	Z	no.	yield (%)
1	H	N	CH	**40a**	63
2	Me	N	CH	**40b**	50
3	MeO	N	CH	**40c**	71
4	EtO	N	CH	**40d**	68
5	H_2N	N	CH	**40e**	73
6	EtO	CH	N	**40f**	60

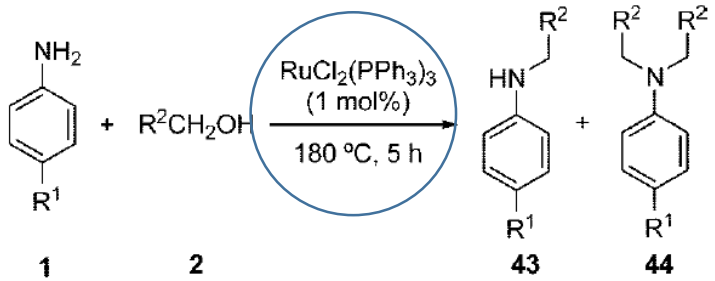
Miyano et al. *Chem. Pharm. Bull.* **1965**, *13*, 1135.



41a **2** **42** (39-73%)

Reid. *Am. Chem. J.*. **1911**, *45*, 38.

1. Alcohol Activation; primary alcohol amination

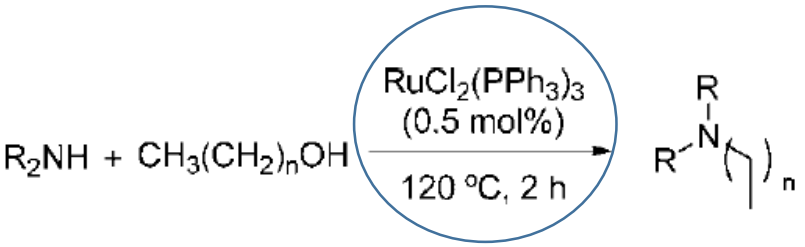


1 2 43 44

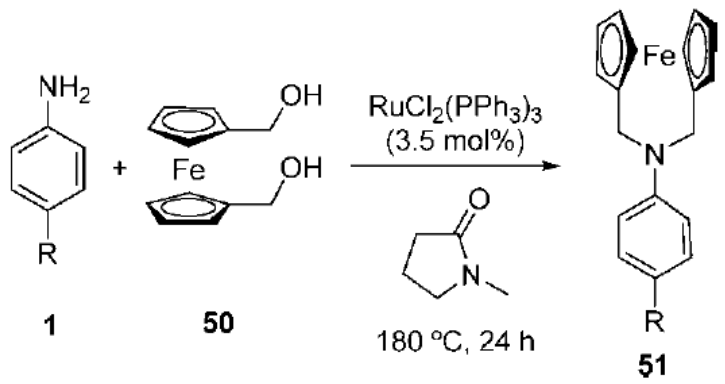
entry	R^1	R^2	no.	yield (%)	no.	yield (%)
1	H	Me	**43a**	13	**44a**	74
2	H	Et	**43b**	10	**44b**	88
3	H	Pr^n	**43c**	15	**44c**	79
4	MeO	Pr^n	**43d**	7	**44d**	91
5	Me	Pr^n	**43e**	15	**44e**	85
6[a]	H	Pr^n	**43c**	79	**44c**	6
7[a]	MeO	Pr^n	**43d**	99	**44d**	

[a] 1:1 ratio of compounds **1/2**.

Porzi et al. JOMC **1982,** *235*, 93.

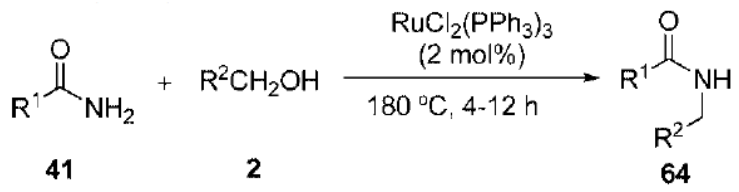


Aliphatic amine; Roundhill et al. Inorg. Chem. **1989,** *28*, 4562.



1 50 51

Yamamoto et al. JOMC. **1999,** *584*, 213.

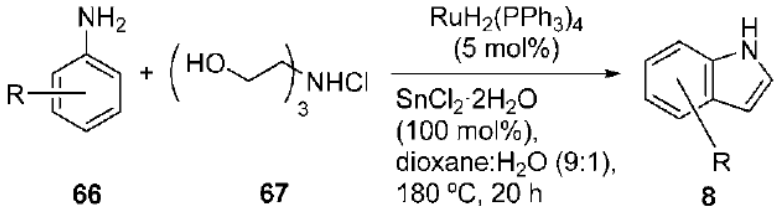


41 2 64

entry	R^1	R^2	no.	yield (%)
1	Me	Me	**64a**	43
2	Me	$CH_3(CH_2)_6$	**64b**	24
3	Ph	$CH_3(CH_2)_6$	**64c**	74
4	$PhCH_2$	Me	**64d**	15
5	Pr^n	$CH_3(CH_2)_6$	**64e**	28

Watanabe et al. BCSJ. **1983,** *56*, 2647.

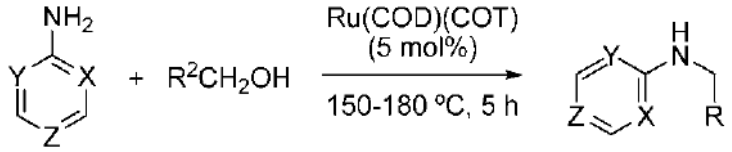
1. Alcohol Activation; primary alcohol amination



66 67 8

entry	no.	R	yield (%)
1	**8a**	H	85
2	**8h**	5-Cl	31
3	**8i**	5-Me	68
4	**8e**	5-MeO	80
5	**8j**	4,7-$(MeO)_2$	21

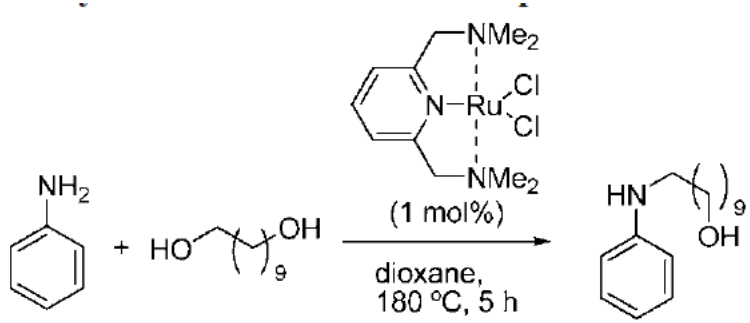
Watanabe et al. BCSJ. **1987,** *60*, 3456.



33 2 68

entry	Z	Y	X	R	no.	yield (%)
1	CH	CH	CH	Me	**68a**	3
2	CH	CH	CH	Me	**68a**	27[a]
3	CH	N	CH	Me	**68b**	79
4	N	CH	CH	Me	**68c**	70
5	CH	N	N	Me	**68d**	37
6	N	CH	CH	H	**68e**	67
7	N	CH	CH	Et	**68f**	82
8	N	CH	CH	Ph	**68g**	45

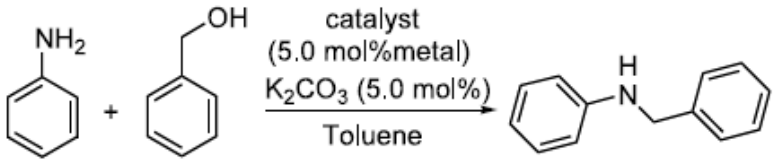
Mitsudo et al. JOC. **1996,** *61*, 4214.



1a 70 **71** (70 %)

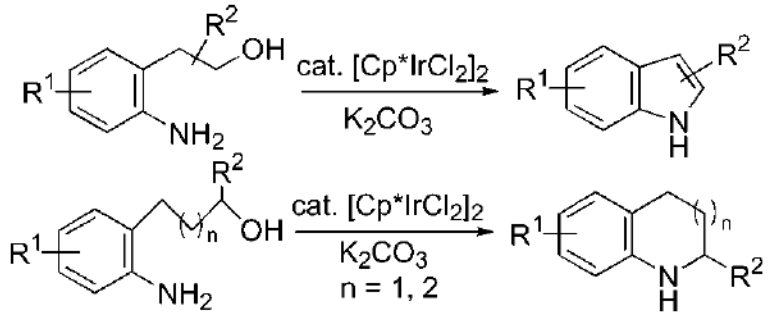
von Koten et al. JOC. **1998,** *63*, 4282.

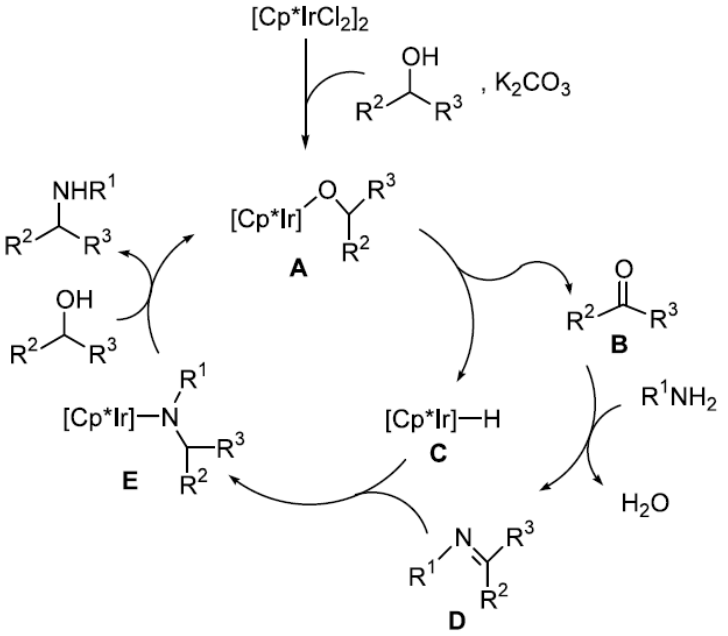
1. Alcohol Activation; primary alcohol amination



Entry	Catalyst	Temp. (°C)	Time (h)	Yield (%)[b]
1	$[Cp^*IrCl_2]_2$	110	17	100
2[c]	$[Cp^*IrCl_2]_2$	110	17	30
3	$[Cp^*IrCl_2]_2$	90	17	52
4	$[Cp^*IrCl_2]_2$	90	40	81
5	$[Cp^*IrHCl]_2$	110	17	55
6	$[IrCl(cod)]_2$	110	17	3
7	$[Cp^*RhCl_2]_2$	110	17	43

[a] The reaction was carried out with aniline (1.0 mmol), benzyl alcohol (1.0 mmol), catalyst (5.0 mol%metal), and K_2CO_3 (0.050 mmol) in toluene (0.5 mL).
[b] Determined by GC.
[c] The reaction was carried out without K_2CO_3.





Yamaguchi et al. TL **2003,** *44*, 2687.

Yamaguchi et al. OL **2002,** *4*, 2691.

1. Alcohol Activation; primary alcohol amination

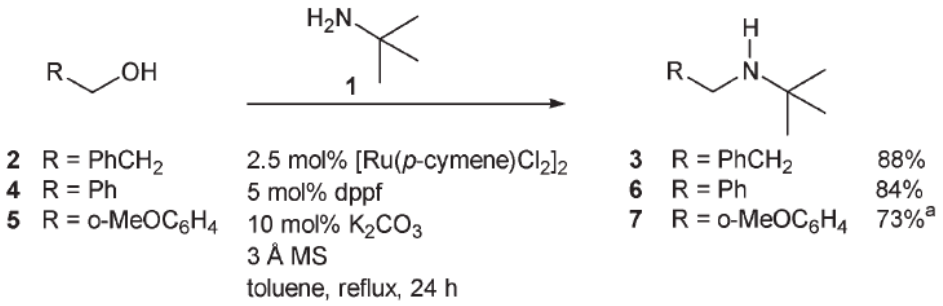
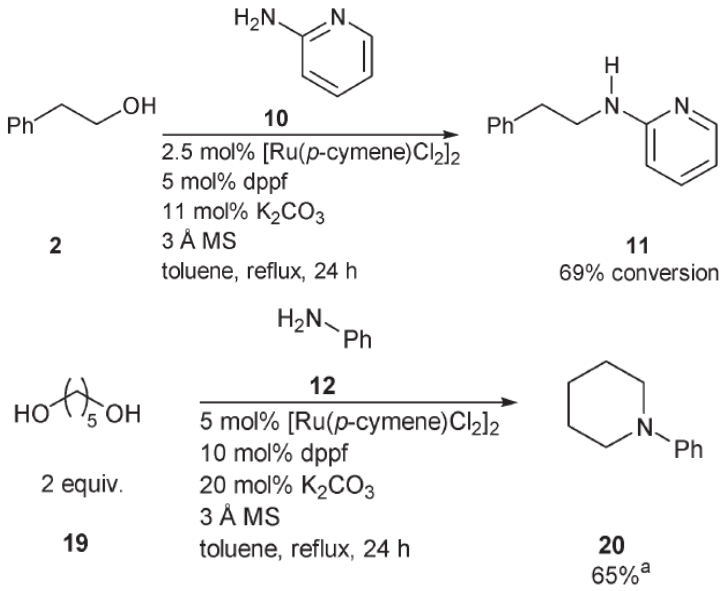


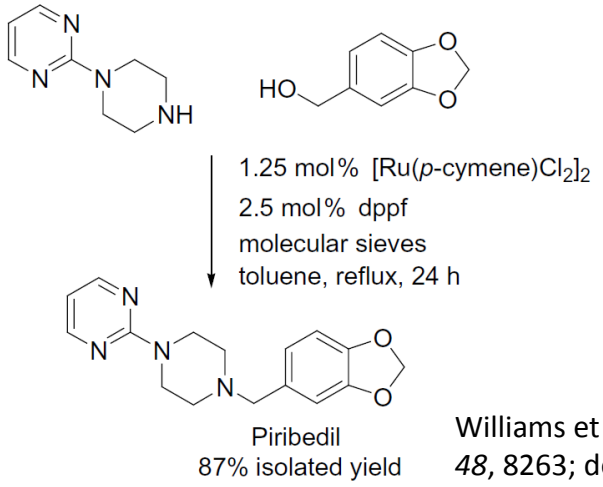
Table 1 Catalyst/ligand evaluation for formation of amine **3**[a]

Catalyst (5 mol% in Ru)	Ligand (5 mol%)	Unreacted alcohol **2** (%)	Amine **3** (%)	Ester[b] (%)
$Ru(CO)(PPh_3)_3H_2$	dppf	74	0	26
$Ru(PPh_3)_3Cl_2$	dppf	65	35	0
$[Ru(p\text{-cymene})Cl_2]_2$	none	92	0	8
$[Ru(p\text{-cymene})Cl_2]_2$	PCy_3 (10 mol%)	90	0	10
$[Ru(p\text{-cymene})Cl_2]_2$	PPh_3 (10 mol%)	54	36	10
$[Ru(p\text{-cymene})Cl_2]_2$	Xantphos	0	39	61
$[Ru(p\text{-cymene})Cl_2]_2$	rac-BINAP	12	35	53
$[Ru(p\text{-cymene})Cl_2]_2$	2,2′-Bipyridine	99	0	1
$[Ru(p\text{-cymene})Cl_2]_2$	dippf	0	80	20
$[Ru(p\text{-cymene})Cl_2]_2$	dppe	80	20	0
$[Ru(p\text{-cymene})Cl_2]_2$	dppp	42	52	6
$[Ru(p\text{-cymene})Cl_2]_2$	dppf	0	100	0
$[Ru(benzene)Cl_2]_2$	dppf	5	88	7
none	dppf	100	0	0

[a] Alcohol : amine (1 : 1), 10 mol% K_2CO_3, 3 Å molecular sieves, toluene, 110 °C, 24 h. Conversions are based on alcohol. Conversion to ester (two alcohols) is given by the amount of alcohol consumed to form it. [b] $PhCH_2CO_2CH_2CH_2Ph$.



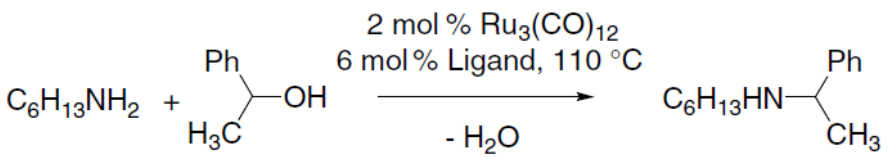
Williams et al. ChemComm **2007,** 725.



Williams et al. TL **2007**, *48*, 8263; dopamine agonist

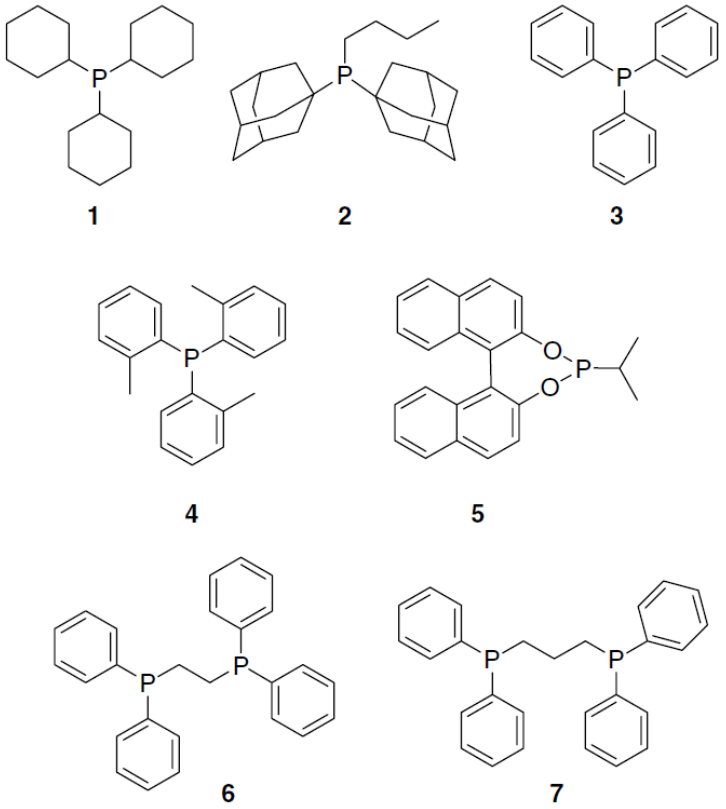
1. Alcohol Activation; secondary alcohol amination

most reactive [Ru]-based cat.



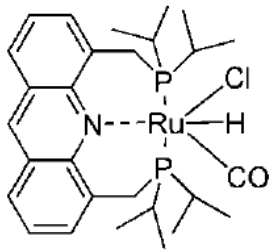
Entry	Ligand	Conversion (%)	Yield (%)
1	None	100	74
2	**1**	100	59
3	**2**	**100**	**90**
4	**3**	81	47
5	**4**	**100**	**97**
6	**5**	56	33
7	**6**	85	30
8	**7**	82	34

[a] Reaction conditions: 2 mmol *n*-hexylamine, 10 mmol 1-phenylethanol, 0.04 mmol $Ru_3(CO)_{12}$, 0.12 mmol monodentate ligand (or 0.06 mmol bidentate ligand), 110 °C, 24 h, conversion and yield were determined by GC analysis with hexadecane as the internal standard.



Beller et al. TL **2006,** *47*, 8881.

1. Alcohol Activation; primary alcohol amination

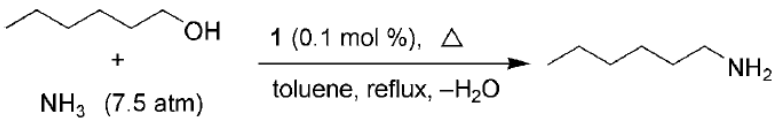


$NH_3 + RCH_2OH \xrightarrow[\text{PhMe , reflux, 12-25 h}]{\text{(0.1 mol\%)}} H_2NCH_2R$

(7.5 atm)

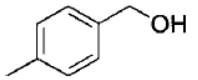
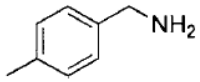
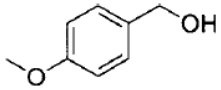
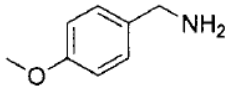
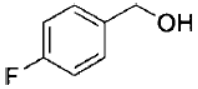
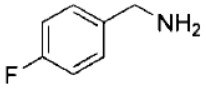
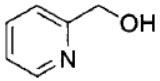
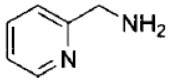
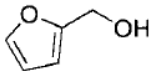
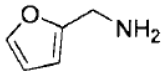
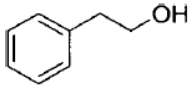
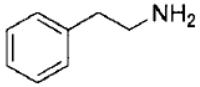
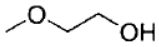
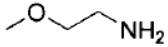
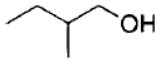
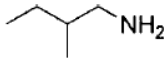
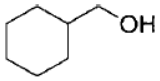
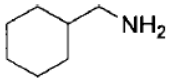
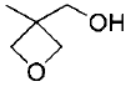
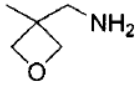
Milstein et al. ACIE. **2008,** *47*, 3367.

model compound



15 h : hexylamine (63%), dihexylamine (3%)
24 h : hexylamine (58%), dihexylamine (18%)

$RCH_2OH + NH_3 \xrightarrow[\text{Toluene, Reflux, } -H_2O]{\text{1 (0.1 mol \%), } \triangle} RCH_2NH_2 + RCH{=}NCH_2R$

Entry	RCH_2OH	*t* [h]	Conv.	RCH_2NH_2	Yield [%][c]
1		12	100		83 (70)
2		14	100		78
3		24	100		91
4		30	100		96
5		12	100		94.8
6[b]		20	97		61 [34.6][d]
7		32	100		68.8
8		12	100		94.5
9[b]		18	93		67.7 (61)
10		25	95.5		82 (73)
11		25	96.4		90 (84)

major byproduct – imine

1. Alcohol Activation; primary alcohol amination

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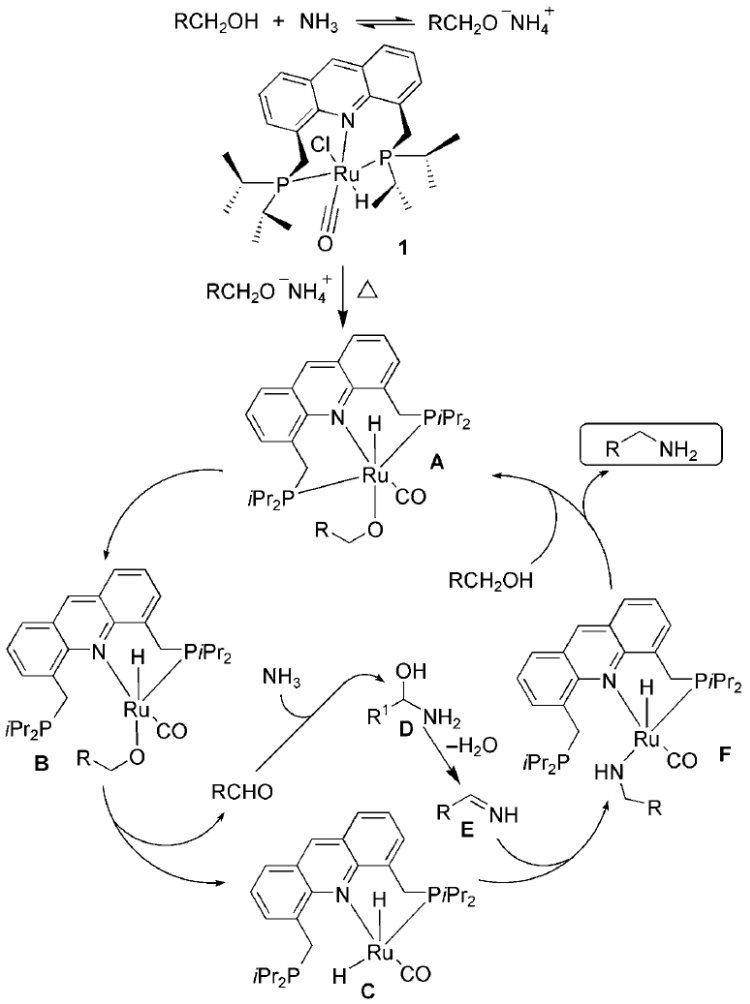
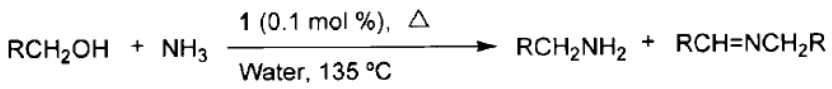
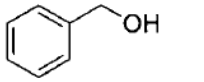
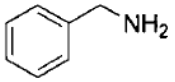
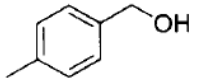
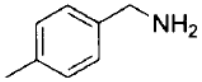
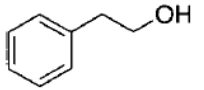
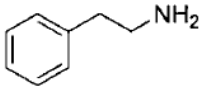
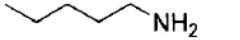


In Water; help hydrolysis imine

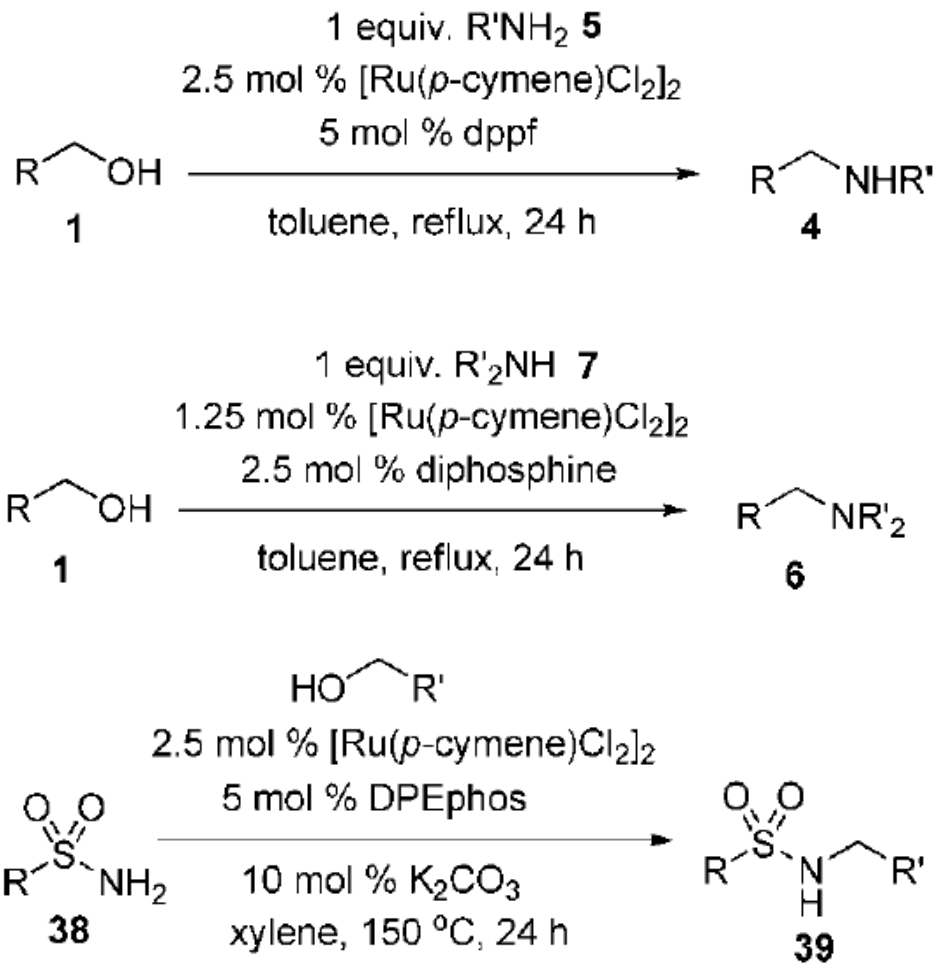


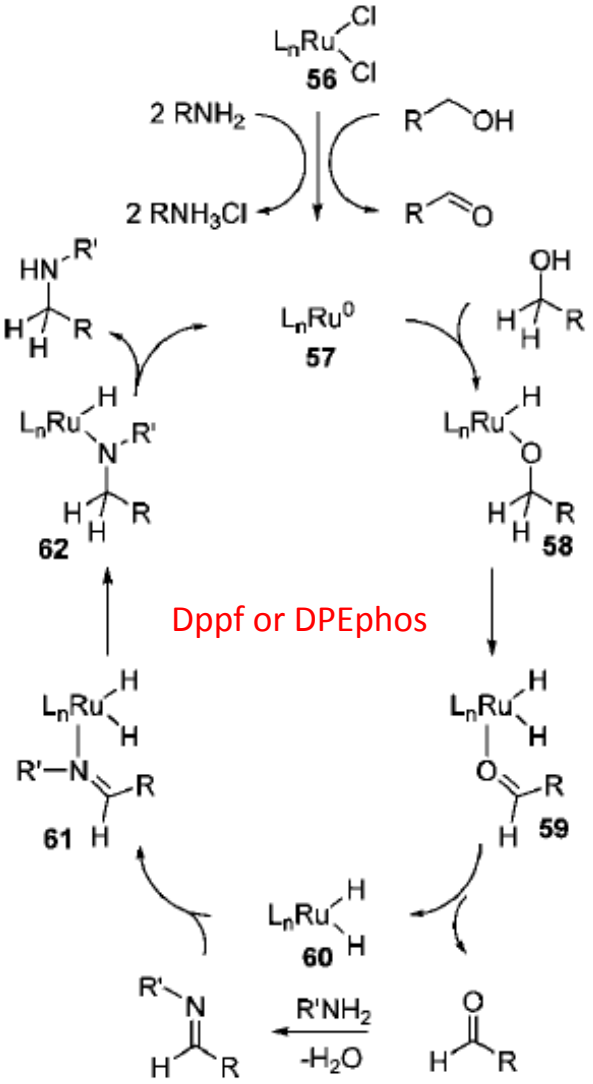
Entry	RCH_2OH	*t* [h]	Conv.	RCH_2NH_2	Yield [%][b]
1		18	100		95.4 (86)
2		18	100		91.7
3		36	100		80.4[c]
4		24	92.4		54.8[d]
5[e]		28	89.4		74.3
6[f]		30	99		79.7
7[f]		30	98.7		70.0

[a] Complex **1** (0.01 mmol), alcohol (10 mmol), ammonia (7.5 atm), and water (3 mL) were heated at reflux in a Fischer–Porter reactor.[23] Conversion of alcohols and yield of products were analyzed by GC; yield of isolated product in parenthesis. [b] Corresponding imine was the major byproduct in entries 1–3; corresponding acid was the byproduct in entries 5–7. [c] Corresponding acids were found in aqueous layer. [d] Hexamide was found in aqueous layer. [e] Mixture of 2 mL water and 2 mL toluene was used as solvent. [f] Mixture of 1 mL water and 2 mL dioxane was used as solvent.

byproduct – amide, acid

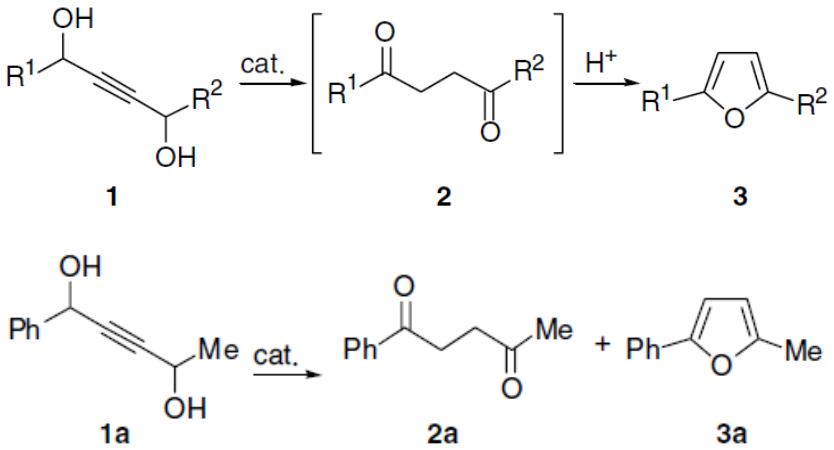
1. Alcohol Activation; primary alcohol amination





Williams et al. JACS. **2009,** *131*, 1766.

1. Alcohol Activation; synthesis of heterocyclic compounds



Scheme 2. Formation of diketone and furan.

Table 1. Preliminary catalyst screen[a]

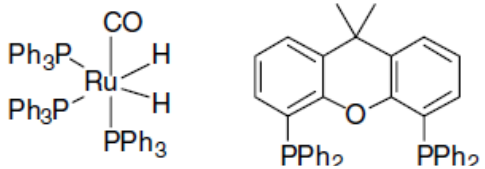
Catalyst	Temperature/time	Conv.[b]	2a/3a[b]
$[Ir(COD)Cl]_2$/dppp[c]	110/42	83	57:31
$[IrCp^*Cl_2]_2$/dppp[d]	110/42	95	87:8
$[RhCp^*Cl_2]_2$/dppp[d]	110/42	22	22:0
$Rh(PPh_3)_3(CO)H$/dppp	110/42	37	14:22
Grubbs[e]	80/24	38	28:10
$[Ru(p\text{-cymene})Cl_2]_2$/dppf[d]	80/24	56	36:20
$Ru(PPh_3)_3(CO)H_2$	80/24	21	21:0

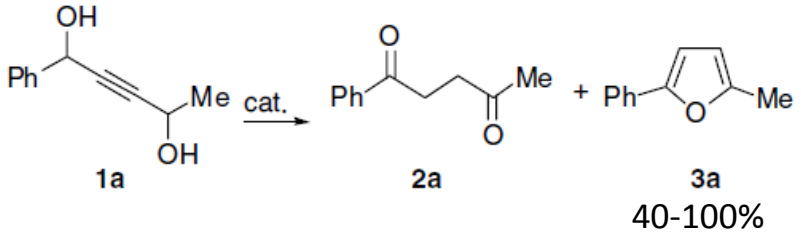
[a] Reaction conditions: Alkyne diol (1 mmol) was dissolved in PhMe (1 mL) in the presence of the catalyst (5 mol % Ir or Ru) and ligand (5 mol %) and heated.
[b] Determined by ^1H NMR analysis.
[c] Cs_2CO_3 (5 mol %) added.
[d] Cs_2CO_3 (10 mol %) added.
[e] Grubbs' first generation metathesis catalyst; $Ru(PCy_3)_2Cl_2(=CHPh)$.

Table 2. Ligand screen using $Ru(PPh_3)_3(CO)H_2$[a]

Ligand	2a[b] (%)	3a[b] (%)	Conv.[b] (%)
None	21	0	21
PCy_3	15	1	16
Dppp	0	0	0
Dppf	21	0	21
Xantphos	56	12	68
Xantphos[c]	18	63	81

[a] Reaction conditions: Alkyne diol (1 mmol) was dissolved in PhMe (1 mL) in the presence of the $[Ru(PPh_3)_3(CO)H_2]$ catalyst (5 mol %) and ligand (5 mol %) and heated to 80 °C for 24 h.
[b] Analysed by ^1H NMR.
[c] Reaction with addition of 5 mol % of AcOH.

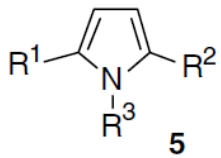




40-100%

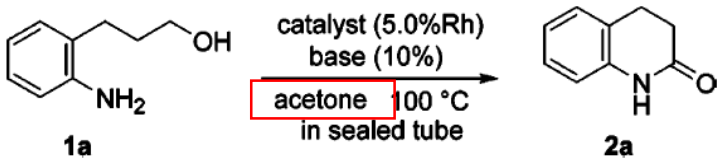
Williams et al. TL **2007,** 48, 5111.

Williams et al. TL **2007,** 48, 5115. →



5

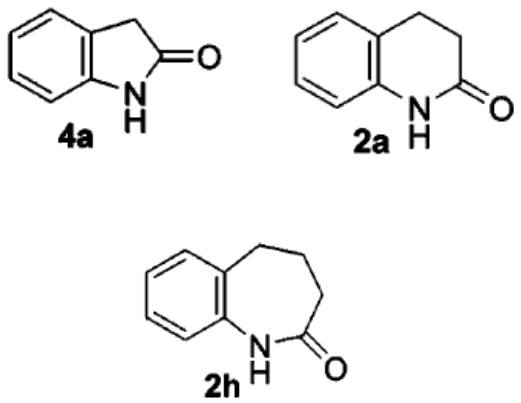
1. Alcohol Activation; intramolecular amidation

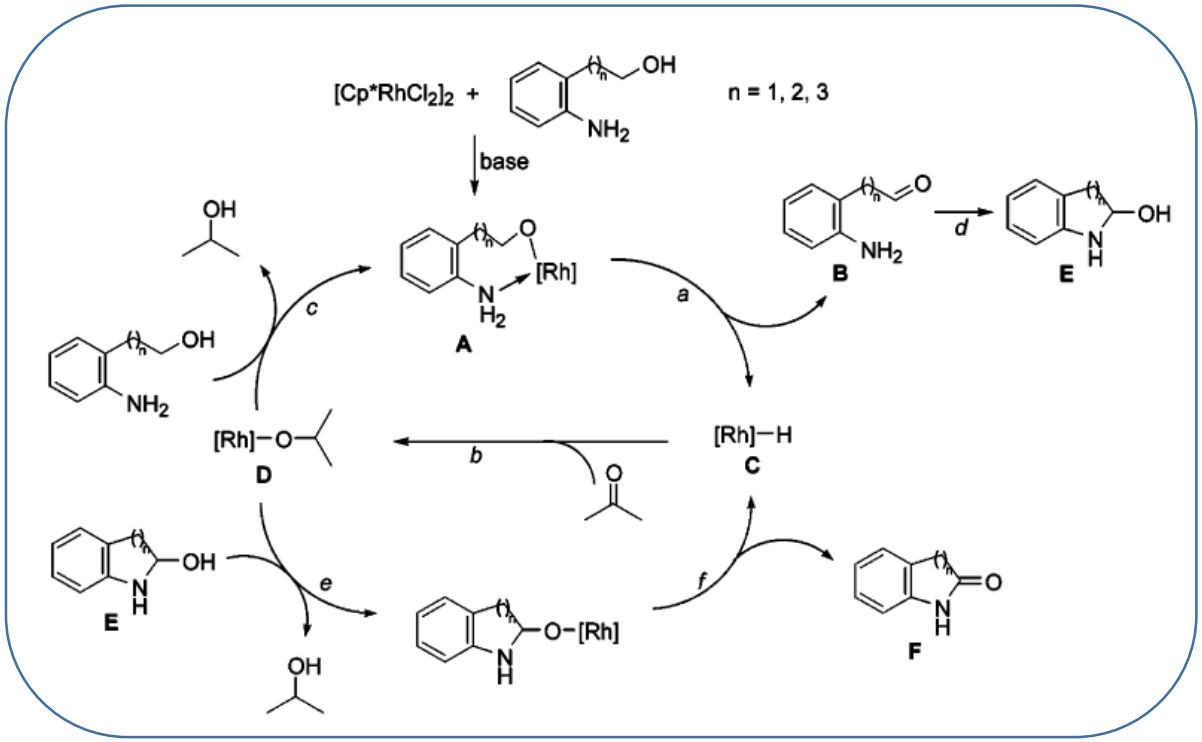


Fujita et al. OL. **2004,** *6*, 2785.

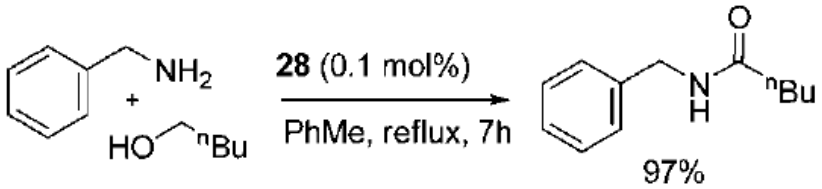
1	$[Cp^*RhCl_2]_2$	K_2CO_3	81
2[c]	$[Cp^*RhCl_2]_2$	K_2CO_3	62
3[d]	$[Cp^*RhCl_2]_2$	K_2CO_3	72
4[e]	$[Cp^*RhCl_2]_2$	K_2CO_3	f
5	$Cp^*Rh(OAc)_2 \cdot H_2O$	K_2CO_3	28
6	$RhCl(PPh_3)_3$	K_2CO_3	43
7	$[RhCl(CO)_2]_2$	K_2CO_3	0
8	$[Cp^*RhCl_2]_2$	Na_2CO_3	46
9	$[Cp^*RhCl_2]_2$	Et_3N	0

[a] Reaction was carried out in a heavy-walled glass reactor at 100 °C for 20 h with **1a** (0.50 mmol), catalyst (5.0% Rh), and base (10%) in acetone (12.5 mL). [b] Determined by GC. [c] Reaction temperature was 80 °C. [d] Amount of acetone was 6.3 mL. [e] Reaction was carried out in toluene (12.5 mL) instead of acetone. [f] 1,2,3,4-Tetrahydroquinoline (32%) was isolated in addition to a small amount of **2a** (ca. 5%).

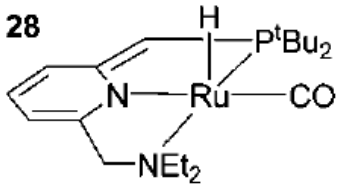


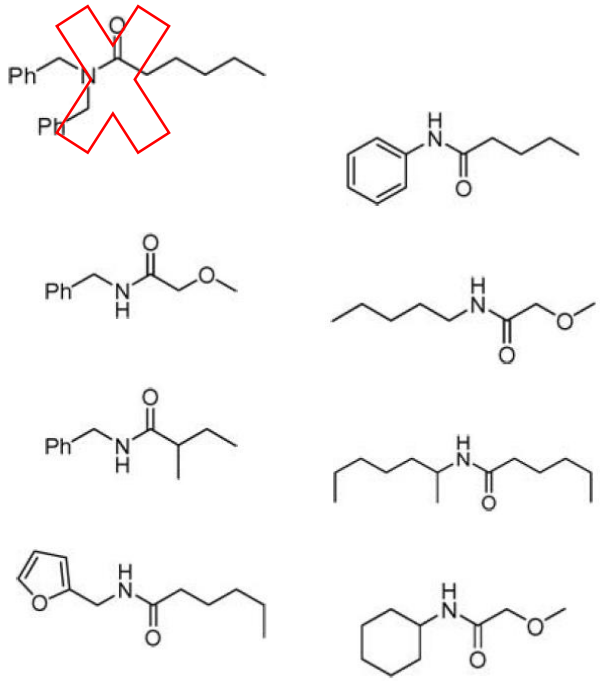


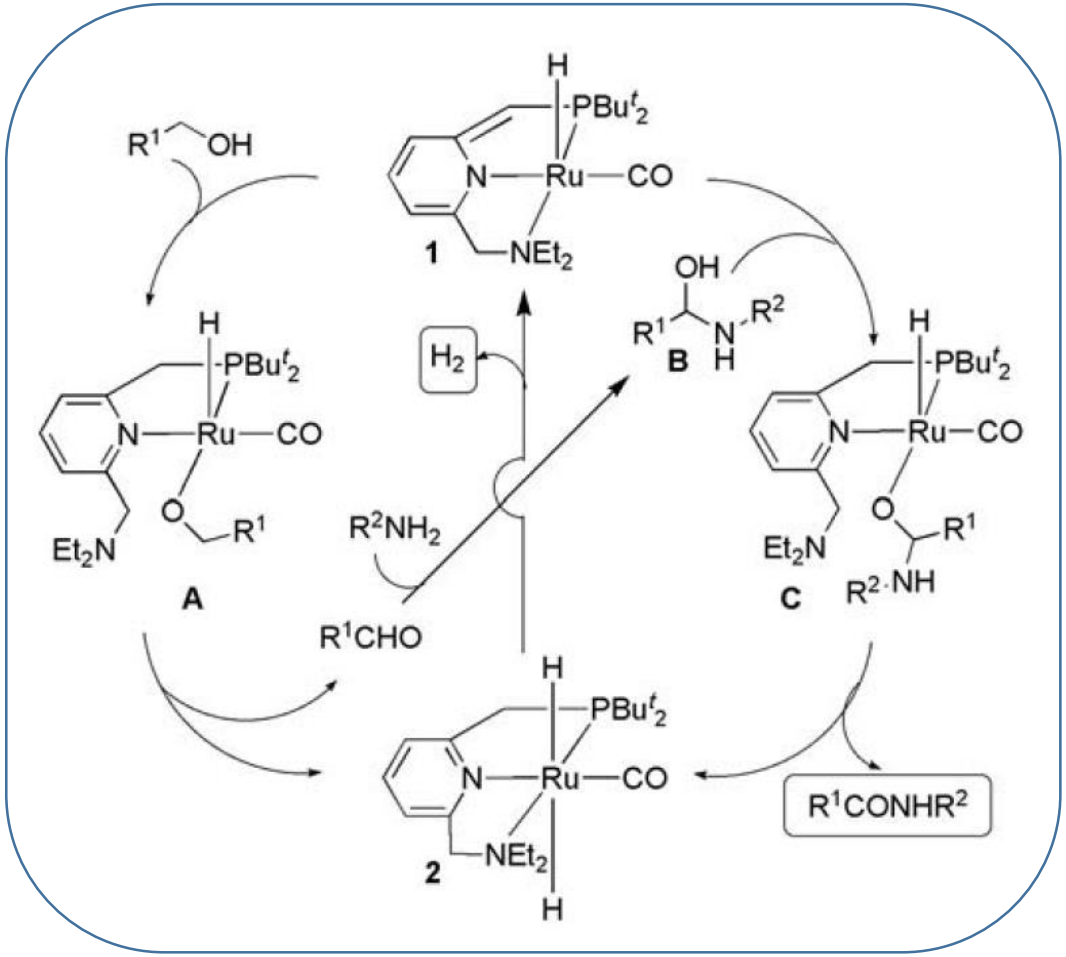
1. Alcohol Activation; dehydrogenative amidation



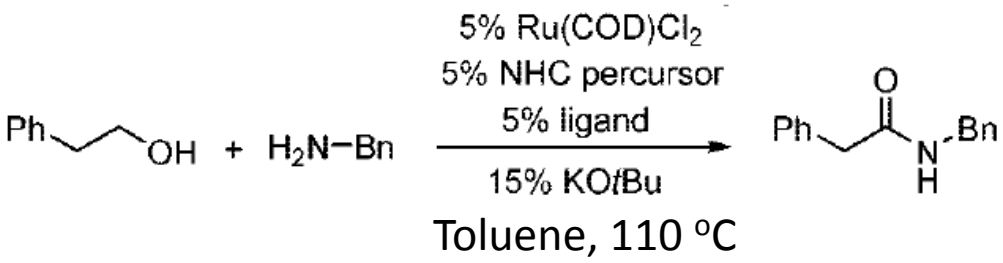
Milstein et al. *Science* **2007,** *317*, 790.





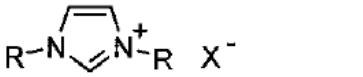


1. Alcohol Activation; primary alcohol amidation

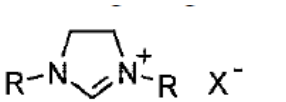


During searching a new condition for the alcohol amination, the unexpected amide formation was found with NHC.

Madsen et al. JACS. **2008,** *130*, 17672.



A: R = Mes, X = Cl
B: R = *t*Bu, X = BF_4
C: R = Cy, X = BF_4
D: R = *i*Pr, X = Cl
E: R = Me, X = $(MeO)_2PO_2$

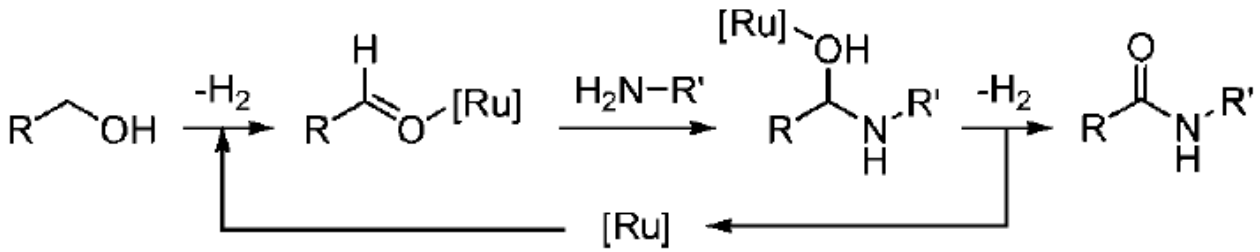


F: R = Mes, X = BF_4
G: R = *t*Bu, X = BF_4
H: R = *i*Pr, X = BF_4

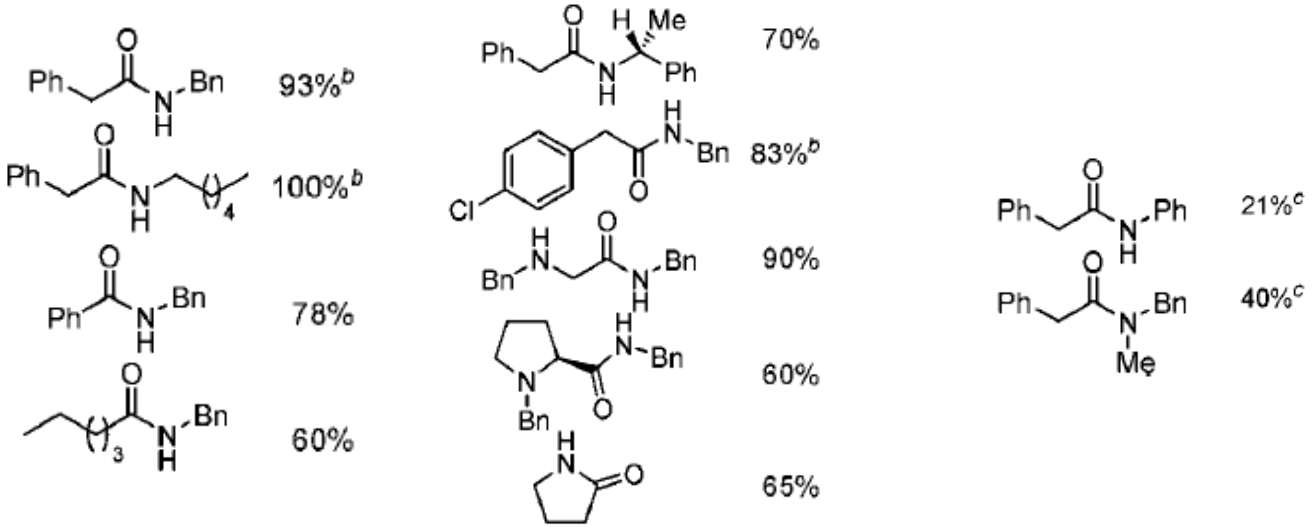
PPh_3	PCy_2Ph
$P(o\text{-tol})_3$	$PCy_2(o\text{-biphenyl})$
PCy_3	$PtBu_2(o\text{-biphenyl})$
$PtBu_3$	$PCyp_3$
$PnBu_3$	$PCyp_3 \cdot HBF_4$

w/o PR_3, no reaction
w/ bidentate, no reaction

1. Alcohol Activation; primary alcohol amidation

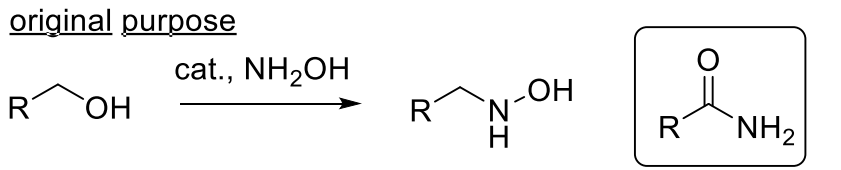


Madsen et al. JACS. **2008,** *130*, 17672.

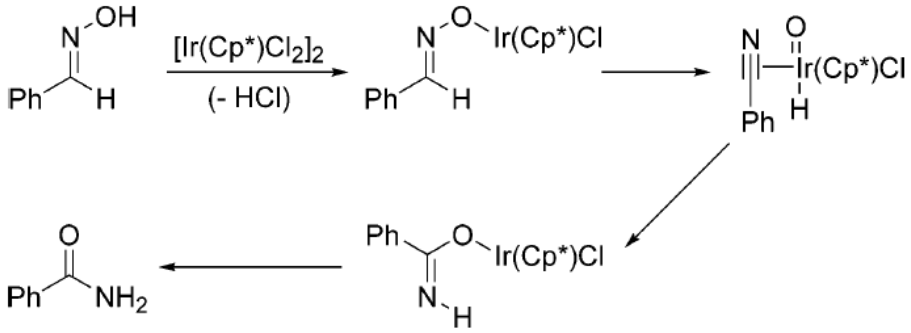


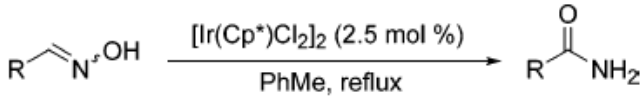
[a] Isolated yield. [b] $Ru(COD)Cl_2$ (2%), ligands (2%), and base (8%). [c] In mesitylene at 163 °C.

1. Alcohol Activation; primary alcohol amidation



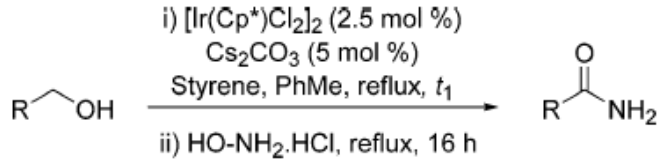
Williams et al. OL. **2007,** *9,* 73.





entry[a]	R[b]	t (h)	yield (%)[c]
1	*Z*-Ph	6	91
2	*E*-Ph	6	92
3	*Z*-(4-MeO)C_6H_4	6	90
4	*E*-(4-MeO)C_6H_4	6	92
5	(2,4-Cl)C_6H_3	8	88
6	(4-O_2N)C_6H_4	8	85
7	C_3H_7	4	97
8	C_6H_5CH=CH	4	94
9	2-furyl	12	82
10[d]	3-pyridyl	16	78

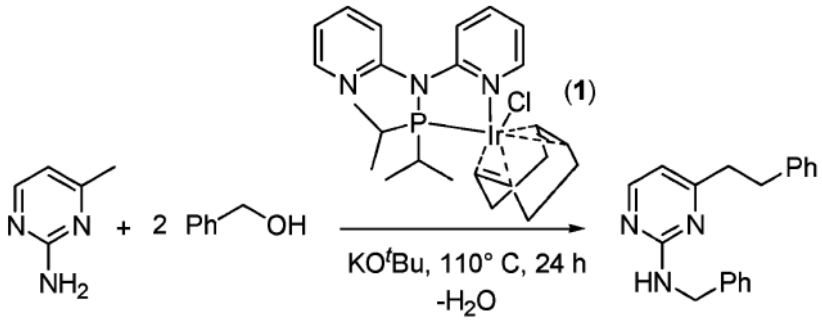
[a] Conditions: oxime (1.0 mmol), $[Ir(Cp^*)Cl_2]_2$ (2.5 mol %), PhMe (2 cm^3); 111 °C. [b] Unless specified, oximes are commercially available as mixed *E*/*Z* isomers. [c] Isolated yields after recrystallization or column chromatography. [d] DMF as solvent; 111 °C.



entry[a]	R	t_1 (h)	yield (%)[b]
1	Ph	24	87
2	(4-Me)C_6H_4	24	90
3	(4-F)C_6H_4	24	84
4	(4-Br)C_6H_4	30	79
5	(4-Cl)C_6H_4	30	83
6	(4-MeO)C_6H_4	24	91
7	(4-BnO)C_6H_4	24	90
8	(4-O_2N)C_6H_4	36	48
9	(4-F_3C)C_6H_4	36	56

[a] Conditions: alcohol (1.0 mmol), $[Ir(Cp^*)Cl_2]_2$ (2.5 mol %), PhMe (2 nL); 111 °C. [b] Isolated yields after recrystallization or column chromatography.

1. Alcohol Activation; C-H activation



Kempe et al. JACS. **2010,** *132*, 924.

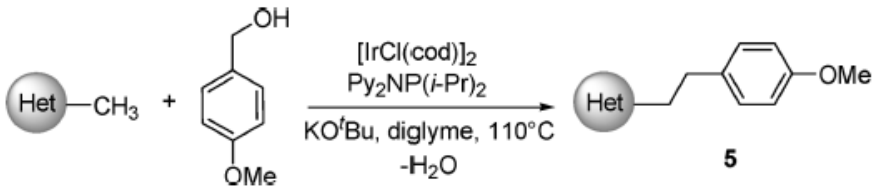
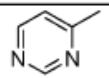
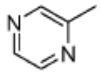
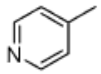
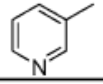
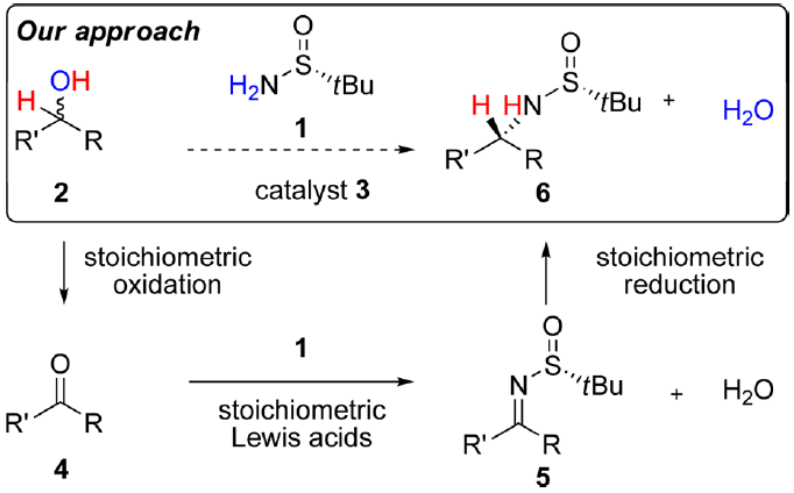


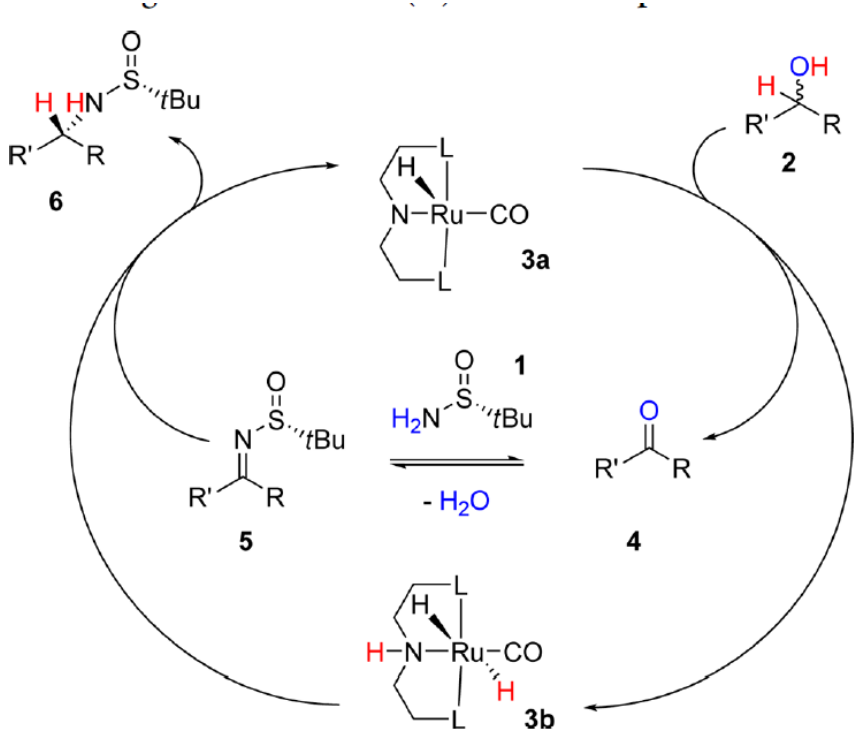
Table 1. Ligand Screening[a]

Entry	Ligand	TON	Yield[b]
1	PPh_3	137	41
2	$Py_2NP(i\text{-}Pr)_2$	243	73
3	$Ph_2PC_3H_6PPh_2$	97	29
4	2,2′-bipyridine	200	60
5	1,3-bis(2,6-dimethylphenyl)-4,5-dihydroimidazole	0	0
6	1,3-bis(2,6-diisopropylphenyl)imidazole	0	0
7	none (COD)	227	68

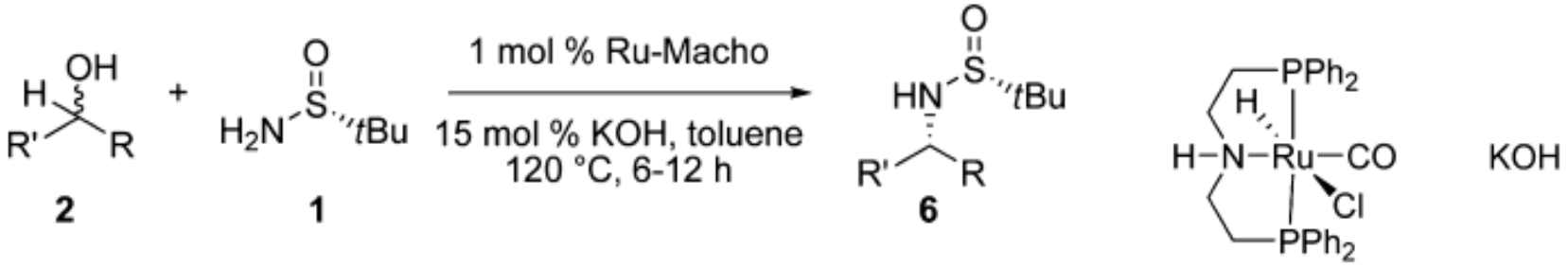
Entry	Cat. Load. [mol% Ir]	(Hetero)arom. educt	Prod.	TON	Yield[b]
1	5.0		**5a**	14	71
2	5.0		**5b**	15	74
3	5.0		**5c**	8	38
4	5.0		**5d**	7	33
5	5.0		**5e**	9	45
6	5.0		---	0	0

1. Alcohol Activation; asymmetric alcohol amination



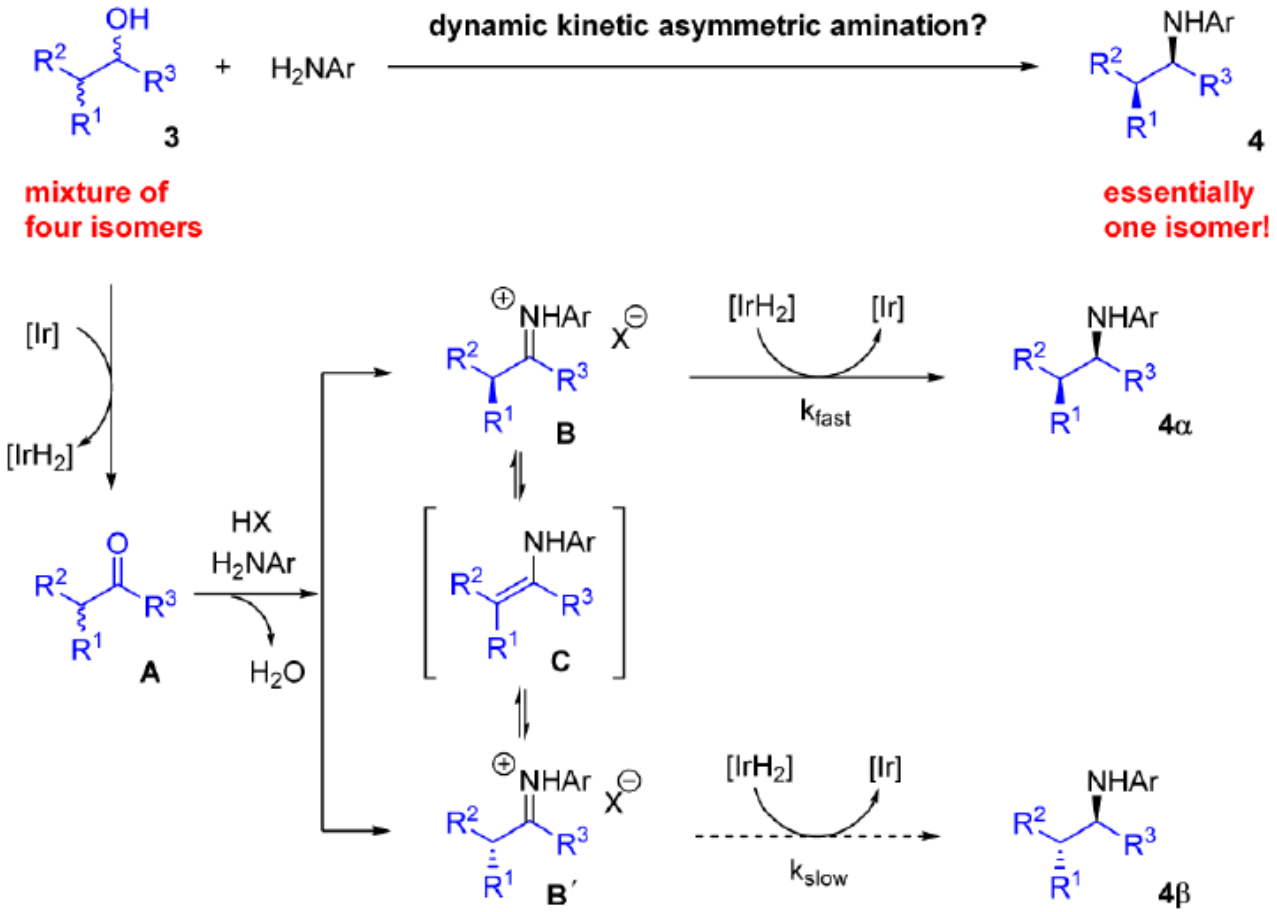


Dong and Guan et al. JACS. **2014,** *136*, 12548.



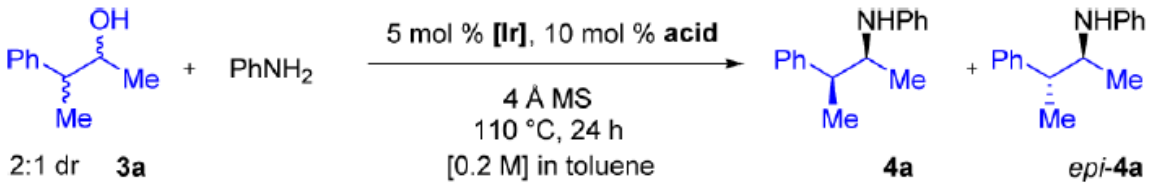
Still limited to symmetric alcohols and benzyl alcohols, aliphatic alcohols – not suitable

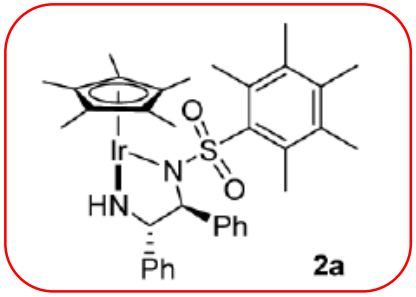
1. Alcohol Activation; asymmetric alcohol amination



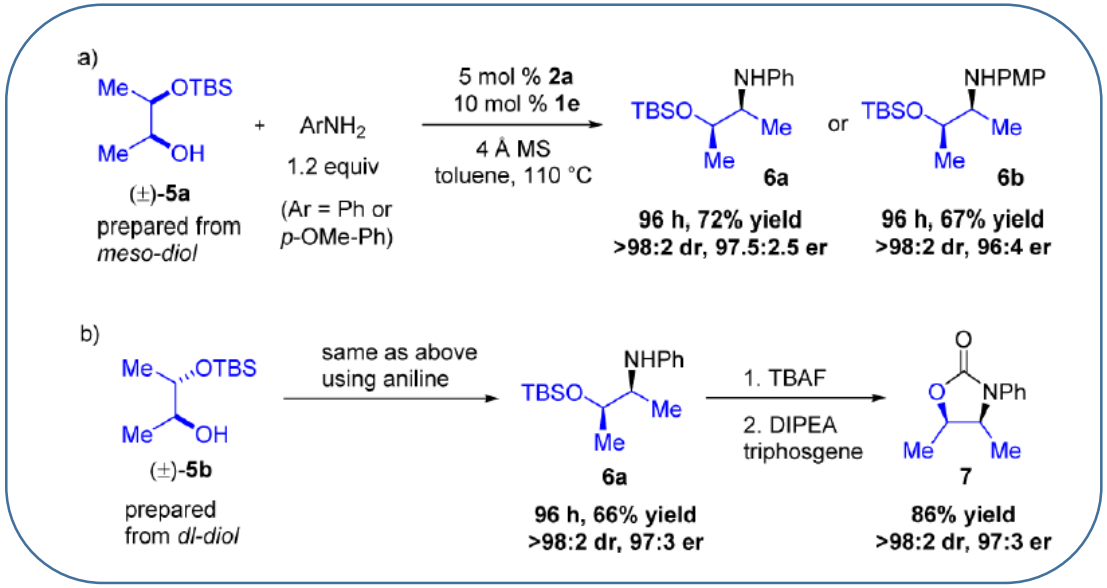
Zhao et al. JACS. **2015,** *137*, 4944.

1. Alcohol Activation; asymmetric alcohol amination

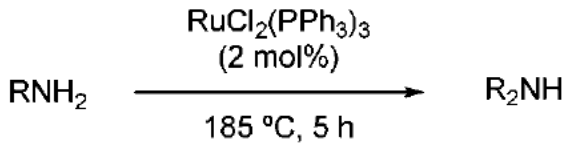




Zhao et al. JACS. **2015,** *137*, 4944.



2. Amine Activation; transimination

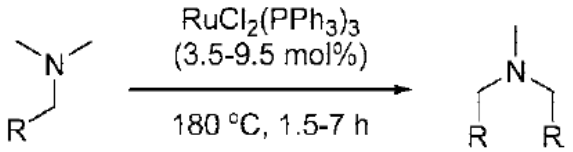


80 **47**

entry	R	no.	yield (%)
1	Pr^i	**47i**	72[a]
2	Bu^n	**47j**	96
3	$CH_3(CH_2)_5$	**47g**	98
4	$CH_3(CH_2)_{11}$	**47k**	99
5	$PhCH_2$	**47l**	99
6	$(CH_2)_5CH$	**47h**	90

[a] THF used as solvent.

Porzi et al. JOMC **1981,** *208*, 249.



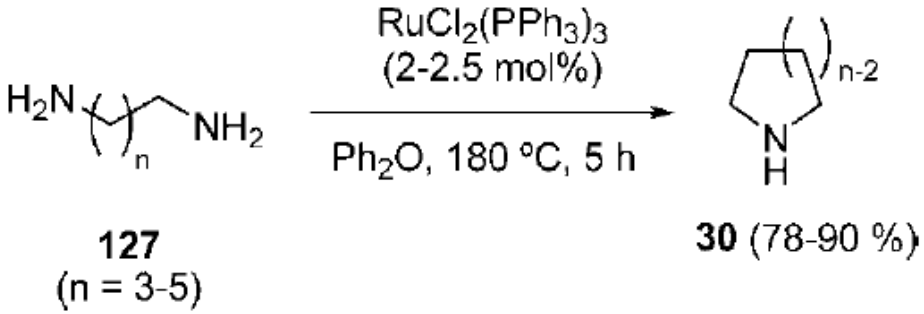
26 **46**

entry	R	no.	yield (%)
1	Pr^n	**46a**	68[a]
2	$CH_3(CH_2)_4$	**46b**	80[a]
3	$CH_3(CH_2)_7$	**46c**	78
4	Ph	**46d**	90

[a] Reaction performed using THF as solvent.

Porzi et al. JOMC **1982,** *231*, C31.

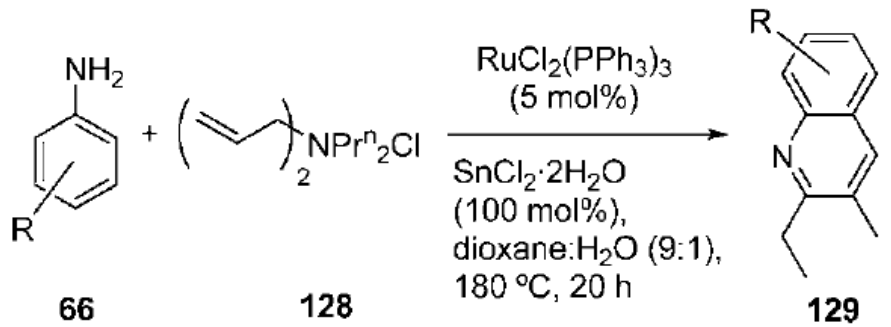
2. Amine Activation; transimination



127
(n = 3-5)

30 (78-90 %)

Porzi et al. JOC **1981,** *46*, 1759.

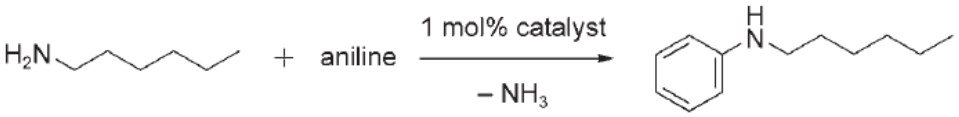


66 **128** **129**

entry	no.	R	yield (%)
1	**129a**	H	57
2	**129b**	6-Cl	34
3	**129c**	6-MeCO	63
4	**129d**	6-Me	64
5	**129e**	6-MeO	58
6	**129f**	7-MeO	50
7	**129g**	8-Me	45

Shim et al. Tetrahedron **2000,** *56*, 7747.

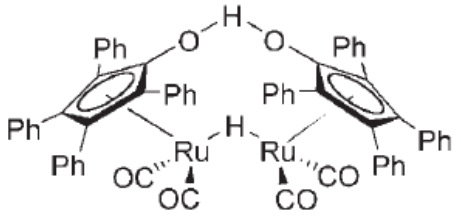
2. Amine Activation; transamination; more challenging than alcohol



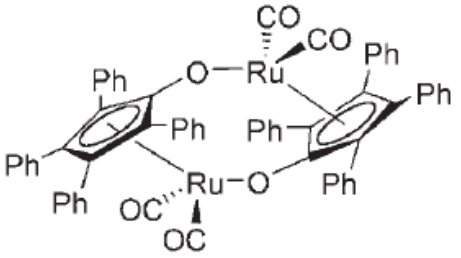
Entry	Catalyst	Yield [%][b]
1	–	–
2	[{Ru[(+)-binap](Cl)}$_2$]	–
3	[Ru(Cl)$_2$(bipy$_2$]·2 H$_2$O	–
4	[RuCO(H)$_2$(PPh$_3$)$_3$]	2
5	[Ru(Cl)$_2$(PPh$_3$)$_3$]	5
6	[{Ru(Cl)(cod)}$_2$]	–
7	[RuCp$_2$]	–
8	[{RuCp*Cl$_2$}$_x$]	–
9	[RuCp*(cod)Cl]	–
10	[{Ru(p-cymene)(Cl)$_2$}$_2$][c]	14
11	[{Ru(p-cymene)(Cl)$_2$}$_2$]/TsDPEN[d]	–
12	[{Ru(p-cymene)(Cl)$_2$}$_2$]/dppf[d]	9
13	[Ru$_3$(CO)$_{12}$]	–
14	[Ru$_3$(CO)$_{12}$]/cataCXium PCy	–
15	Shvo (**1**)	94
16	Shvo–H$_2$ (**2**)	70

[a] Reaction conditions: 1 mol% catalyst relative to *n*-hexylamine, 2 mmol *n*-hexylamine, 4 mmol aniline, 150°C, 24 h. [b] Conversion and yield were determined by GC with hexadecane as internal standard. Conversions and yields are based on the conversion of *n*-hexylamine and *N*-hexylaniline. [c] 4 mol% K_2CO_3. [d] 2 mol% ligand, 4 mol% K_2CO_3, 4-Å

Beller et al. ACIE **2007,** *46*, 8291.

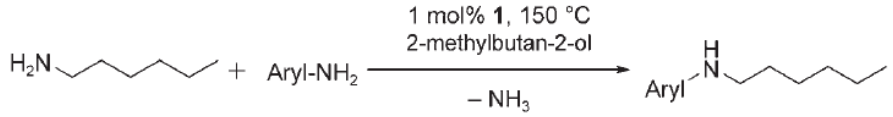


1

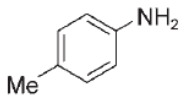
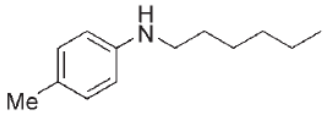
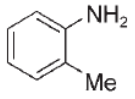
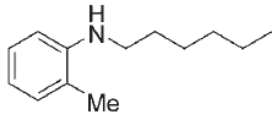
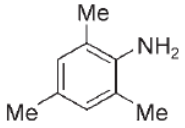
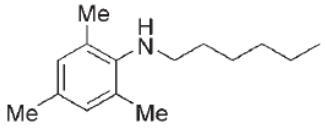
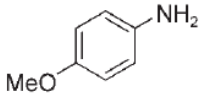
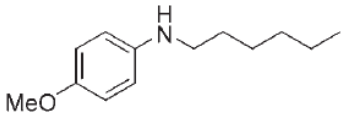
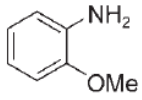
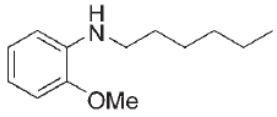
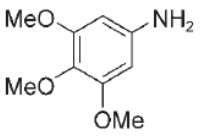
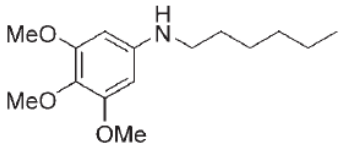
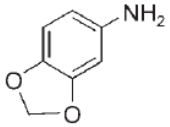
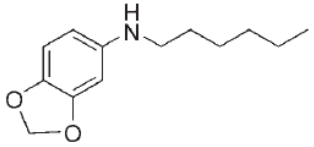
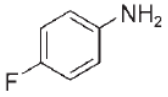
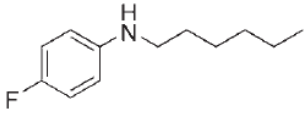
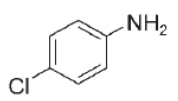
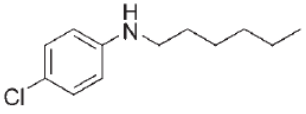
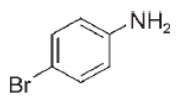
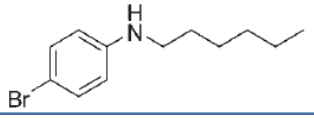
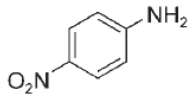
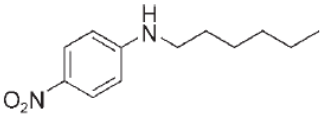
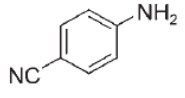
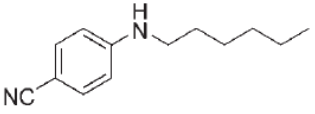
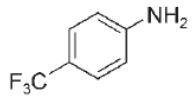
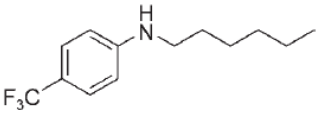
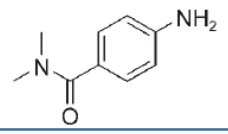
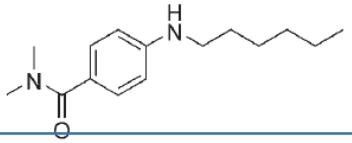
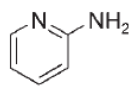
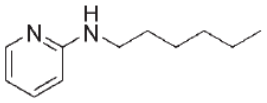
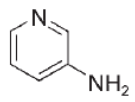
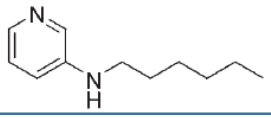


2

2. Amine Activation; transimination

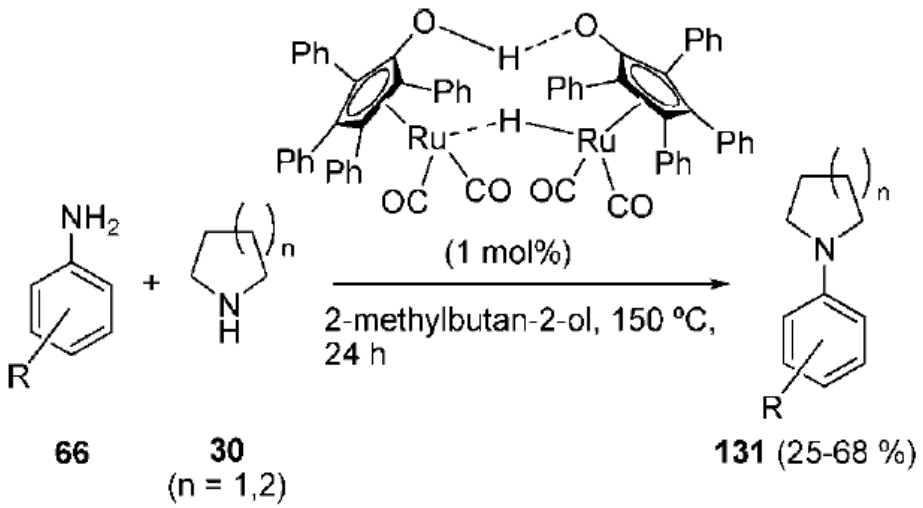


Beller et al. ACIE **2007,** *46*, 8291.

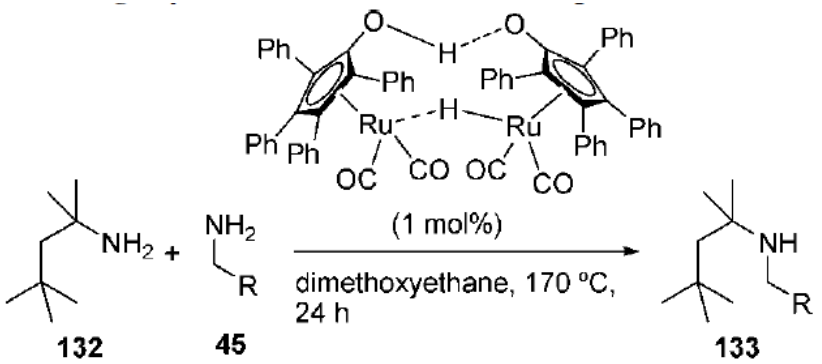
Entry	Aniline	Product	Yield [%][b]
1			98
2			93
3			34
4			98
5			97
6			97
7			86
8			99
9			97
10			94
11			20
12			76
13			95
14			83
15			96
16			77

[a] Reaction conditions: 1 mol % Shvo catalyst **1** relative to *n*-hexylamine, 2 mmol *n*-hexylamine, 4 mmol aryl amine, 2-methylbutan-2-ol, 24 h, 150 °C. [b] Yields of isolated product are based on *n*-hexylamine.

2. Amine Activation; double transimination



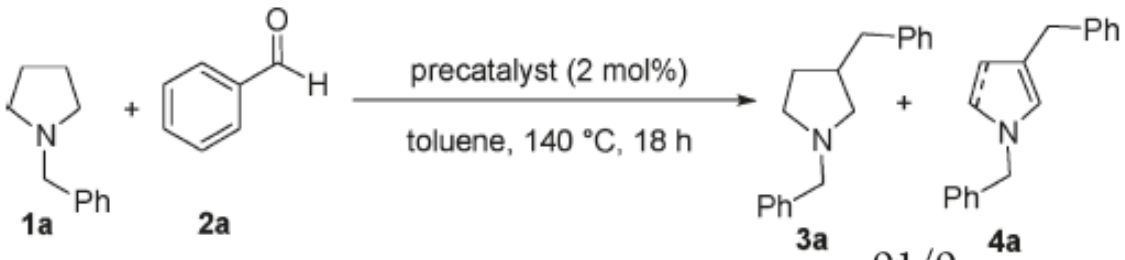
Beller et al. ChemComm **2008,** *3199*.



entry	R	no.	yield (%)
1	Ph	**133a**	58
2	4-$MeOC_6H_4$	**133b**	89
3	$PhCH_2$	**133c**	75
4	$CH_3(CH_2)_6$	**133d**	90

Beller et al. TL **2008,** *49*, 5142.

2. Amine Activation



91/9

89(82)

$[RuCl_2(p\text{-cymene})]_2$

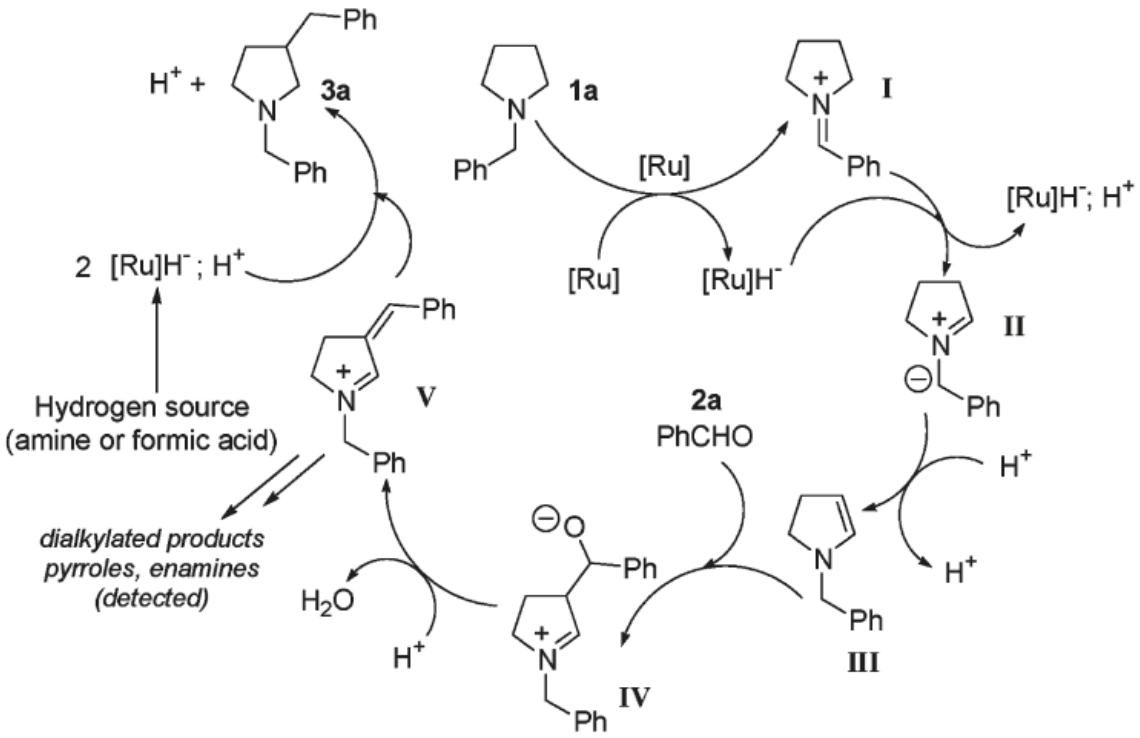
$[RuCl_2(p\text{-cymene})]_2$

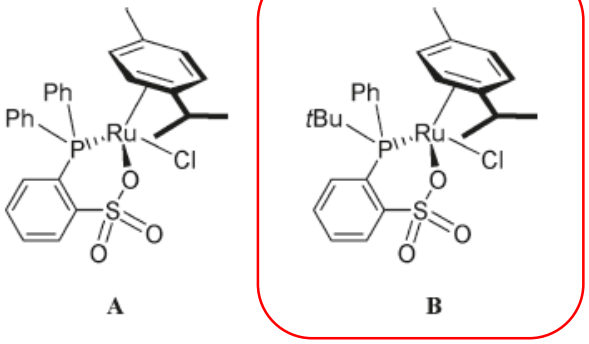
$[RuCl_2(COD)]n$

$Ru_3(CO)_{12}$

Shvo's cat.

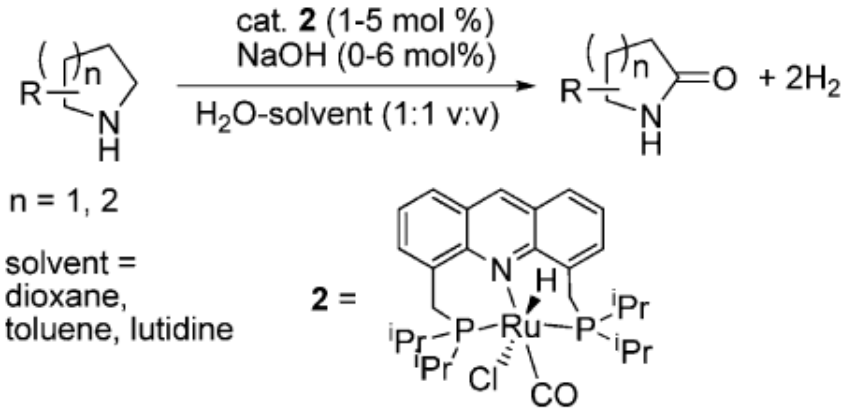
$[Ru(p\text{-cymene})Cl_2]_2$ + dppf



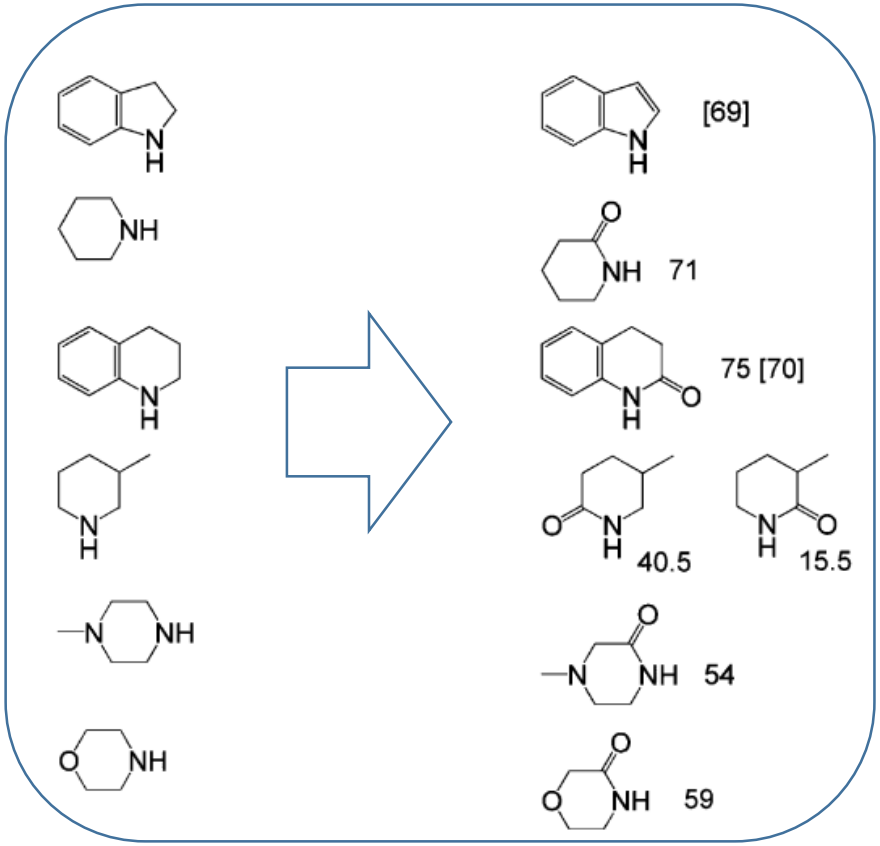


Bruneau et al. JACS **2011,** 133, 10340.

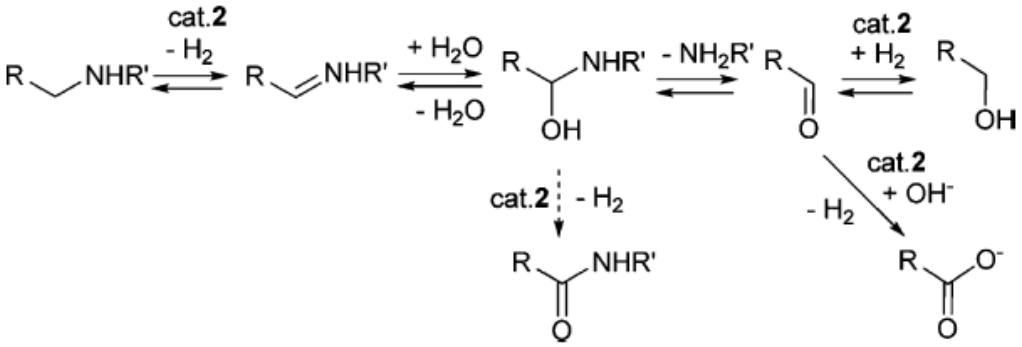
2. Amine Activation



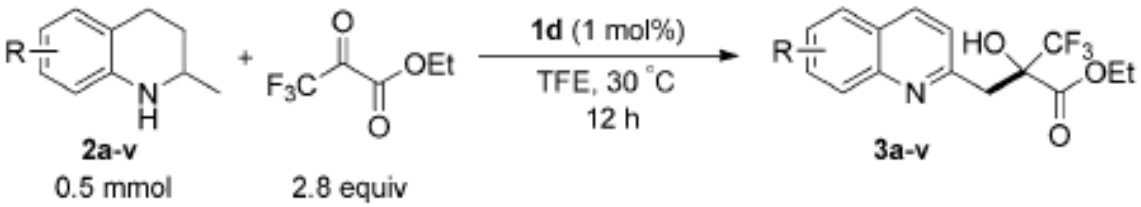
Milstein et al. *JACS* **2014**, *136*, 2998.

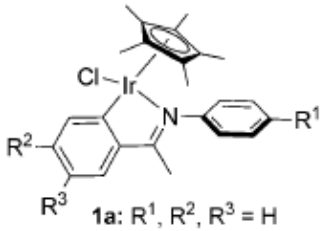


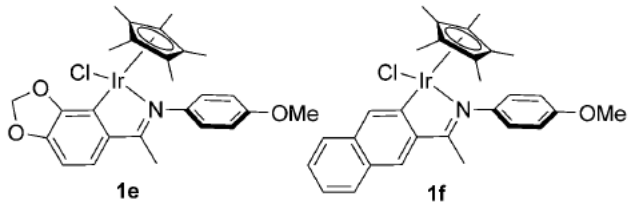
proposed mechanism

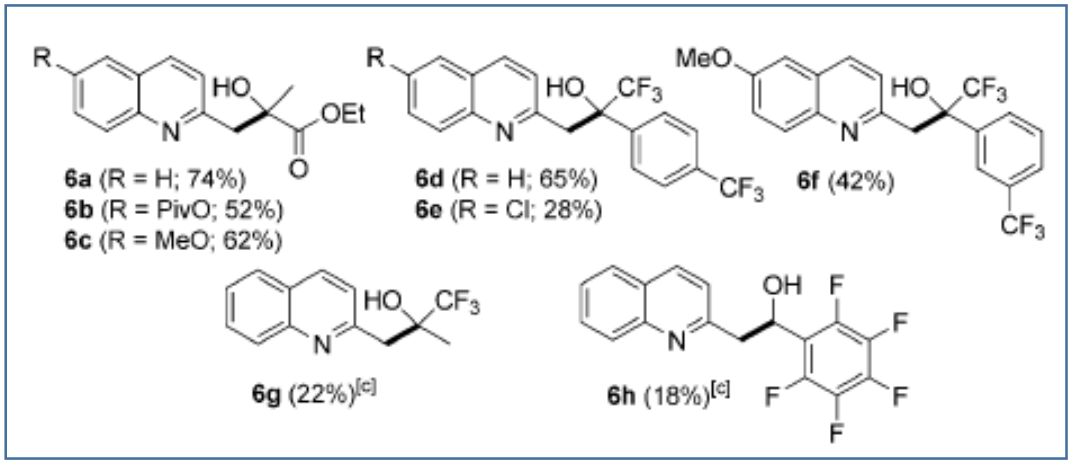


2. Amine Activation









Xiao et al. *ACIE* **2015**, 54, 5223.

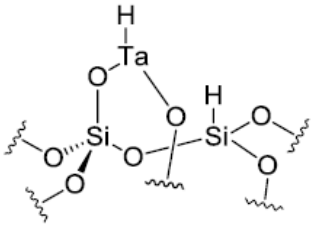
3. Alkane Activation; alkane dehydrogenation

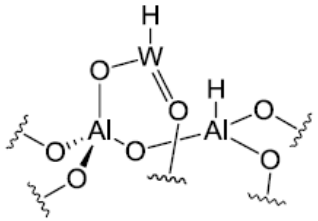
1) Heterogeneous Alkane activation

0.5 %Pt-Li/Al_2O_3
2% WO_3/SiO_2
399 °C, 62.2 atm.

alkanes

Burnett and Hughes





Basset

2) An early homogeneous examples of alkane dehydrogenation by C-H activation

hv, $[Ir(H_2(acetone)_2(PPh_3)_2]BF_4$

Crabtree et al. *JACS* **1979**, 101, 7738.

hv, $[Cp(PMe_3)IrH_2]$

Bergman et al. *JACS* **1982**, *104*, 352.

80 °C, $(PR_3)_2ReH_7$

Felkin et al. *JCS.ChemComm* **1983**, 788.

hv, $[Ir(H_2(O_2CCF3)(PR_3)_2]$

Crabtree et al. *JACS* **1987**, 109, 8025.

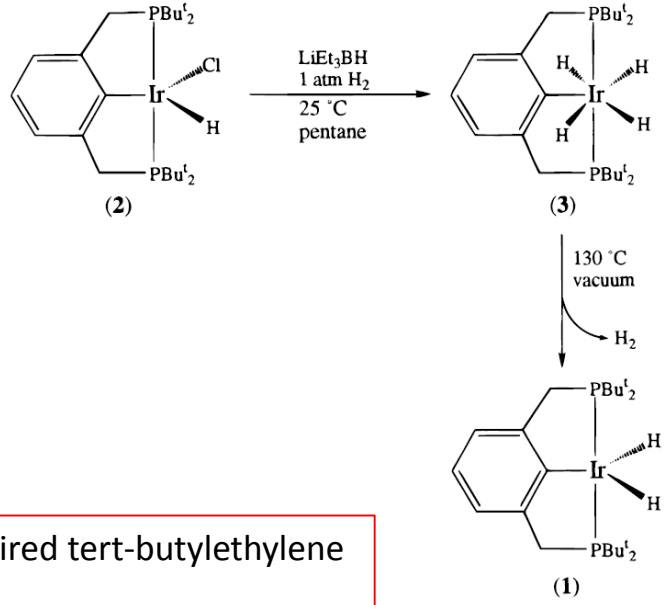
hv, $[Rh(PR_3)_2(CO)Cl]$

(TON>100), still require H_2 acceptors w/ H_2

Goldman et al. *JACS* **1989**, 111, 7088.;
Saito et al. JCSChemComm **1988**, 161.

low turnover number and low stability

3. Alkane Activation; alkane dehydrogenation



Kaska and Jensen et al. *JACS* **1997**, *119*, 840.

TON up to 1000

Not required H_2, but still required tert-butylethylene as hydrogen acceptor

substrate	time (h)	T (°C)	products (mol/mol of **1**)	dehydrogenated/hydrogenated C−C bonds
cyclohexane	1	150	cyclohexene (44) benzene (54), tba (211)	0.98
cyclohexane	0.5	200	cyclohexene (86) benzene (77), tba (310)	1.02
methylcyclohexane	1	150	methylcyclohexenes: 1 (8), 3 (20), 4 (41) toluene (11), tba (105)	0.97
methylcyclohexane	1	200	methylcyclohexenes: 1 (27), 3 (39), 4 (70) toluene (54), tba (310)	0.96
methylcyclohexane	120	150	methylcyclohexenes: 1 (67), 3 (13), 4 (25) toluene (65), tba (310)	0.97
decalin	72	150	octahydronaphthalenes (24) tetrahydronaphthalene (8) naphthalene (4), tba (71)	0.96
decalin	1	200	octahydronaphthalenes (69) tetrahydronaphthalene (16) naphthalene (7), tba (159)	0.96

3. Alkane Activation; alkane dehydrogenation

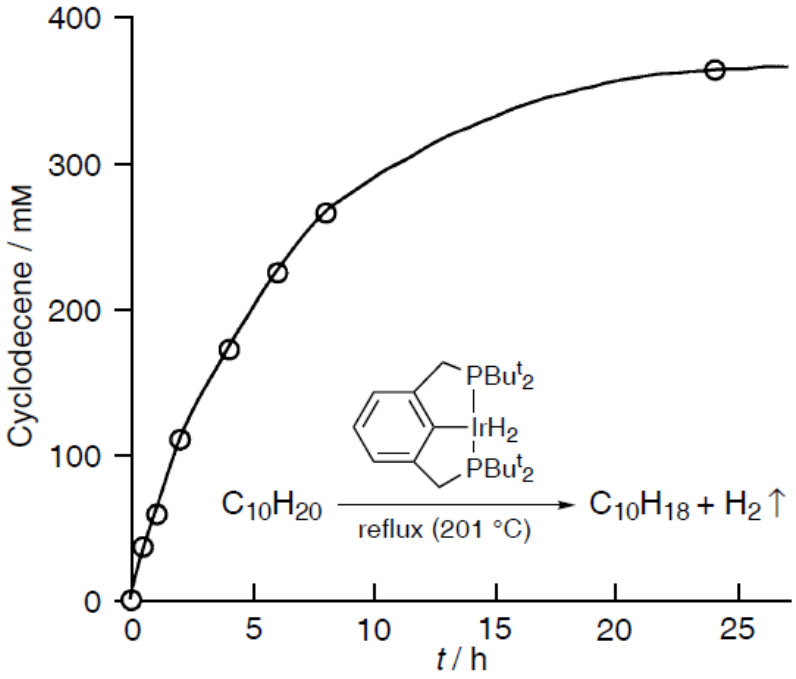


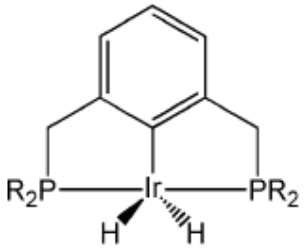
Fig. 1 Cyclodecene formation (total, *ca.* 3 : 1 *cis*:*trans*) *vs.* time; (PCP)IrH$_2$ in refluxing cyclodecane (1.0 mM, 201 °C)

w/o H_2 acceptor

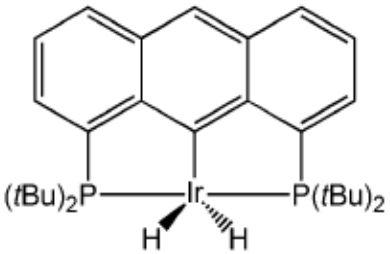
Kaska, Jensen and Goldman et al. *ChemComm* **1997**, 2273.

TON up to 360

maximum build-up of olefin inhibits further catalsis

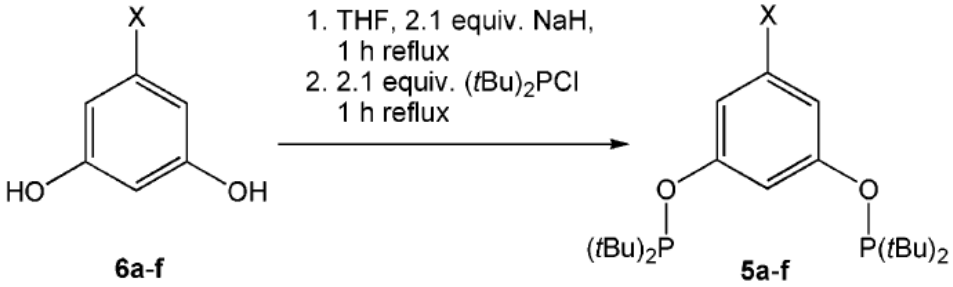


R = *t*Bu (**1**)
R = *i*Pr (**2**)



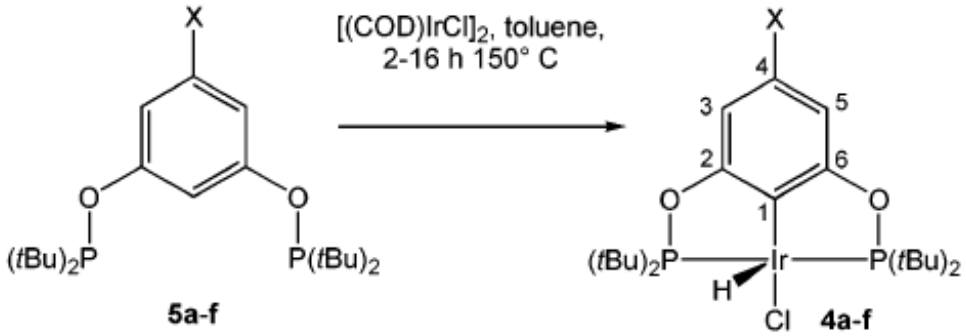
(**3**)

3. Alkane Activation; alkane dehydrogenation



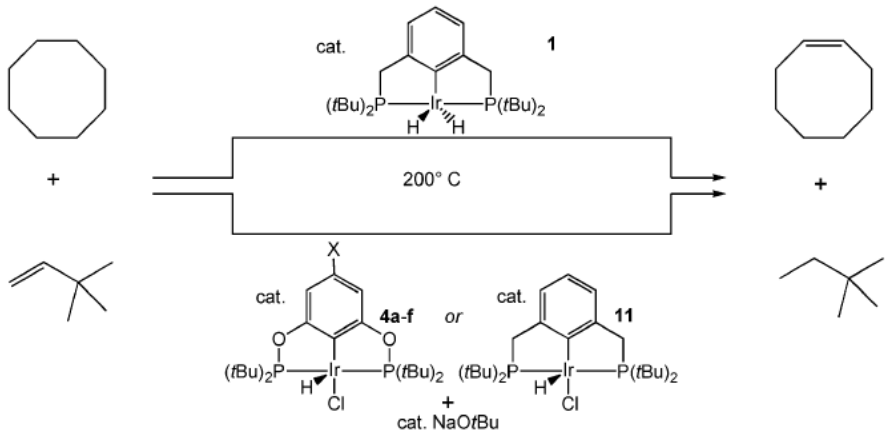
	X	5 [%][a]
5a	MeO	82
5b	Me	87
5c	H	93
5d	F	96
5e	C_6F_5	91
5f	Ar^F	90

[a]NMR purity ca. 95%



Brookhart et al. JACS **2004**, 126, 1804.

3. Alkane Activation; alkane dehydrogenation

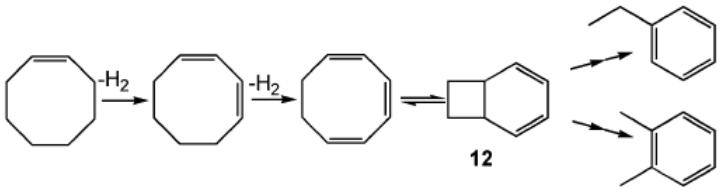


Brookhart et al. JACS **2004**, 126, 1804.

Table 1. TONs for the Transfer Dehydrogenation of COA and TBE Catalyzed by **4a**–**f** and **11** Plus NaO*t*Bu Obtained at 200 °C and the COE:1,3-COD Product Ratio[a]

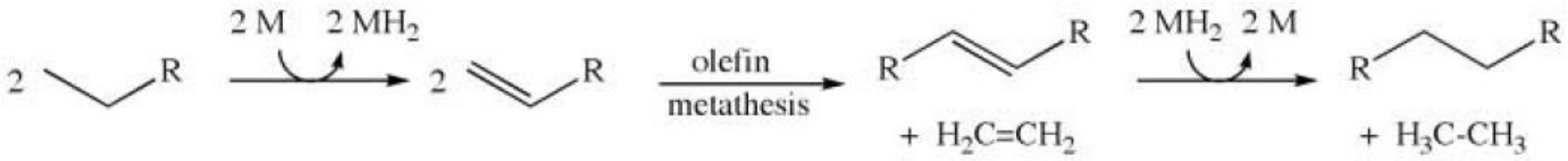
	4 (*p*-X=)						
	a MeO	**b** Me	**c** H	**d** F	**e** C_6F_5	**f** Ar^F	**11** H
8 min	806	811	922	840	1150	1162	156
(COE/COD)[b]	(100/0)	(100/0)	(99/1)	(99/1)	(94/6)	(94/6)	(100/0)
31 min	1226	1087	1194	1108	1401	1424	198
(COE/COD)[b]	(93/7)	(95/5)	(93/7)	(93/7)	(90/10)	(89/11)	(100/0)
178 min	1564	1356	1514	1380	1699	1735	216
(COE/COD)[b]	(86/14)	(87/13)	(86/14)	(85/15)	(83/17)	(82/18)	(100/0)
918 min	1674	1413	1512	1465	1863	1893	212
(COE/COD)[b]	(83/17)	(87/13)	(86/14)	(85/15)	(80/20)	(79/21)	(100/0)
2398 min	1904	1484	1583	1530	2041	2070	227
(COE/COD)[b]	(81/19)	(86/14)	(84/16)	(84/16)	(78/22)	(76/24)	(100/0)
6170 min	2017	1488	1609	1605	2175	2186	230
(COE/COD)[b]	(78/22)	(86/14)	(83/17)	(83/17)	(75/25)	(75/25)	(100/0)
20 305 min	2047	1485	1603	1633	2170	2210	230
(COE/COD)[b]	(78/22)	(85/15)	(83/17)	(82/18)	(75/25)	(75/25)	(100/0)

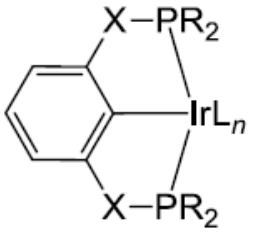
byproducts



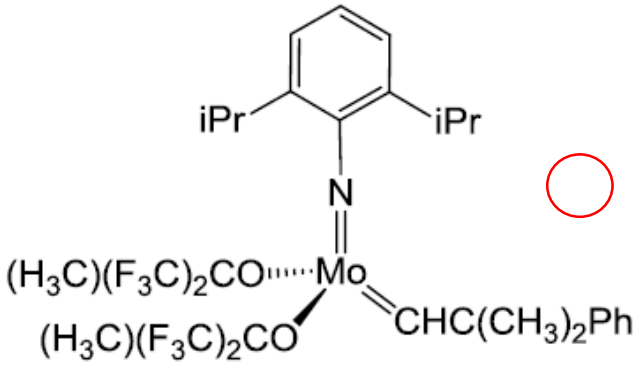
3. Alkane Activation; alkane metathesis

Tandem catalysis

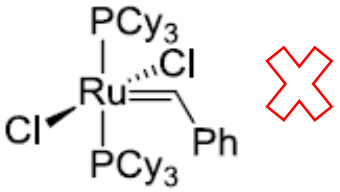




R=tBu, iPr
X=CH_2, O
L_n=H_2, H_4, C_2H_4

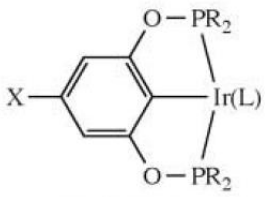


Developed by Goldman and Brookhart



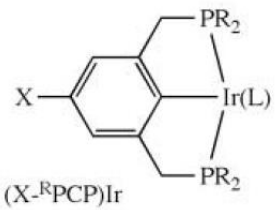
Goldman and Brookhart Science**, 2006**, *312*, 257.

3. Alkane Activation; alkane metathesis



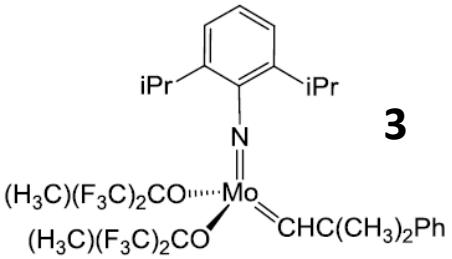
(X-^{R}POCOP)Ir

1: R = *t*-Bu, X = H
L = C_2H_4, H_2



(X-^{R}PCP)Ir

2a: R = *t*-Bu, X = H
2b: R = *i*-Pr, X = OMe
L = H_2 and/or H_4



3

(7.6M)

1 (10 mM), **3** (16 mM)

C2-C15+

(0.75M) + 6 h

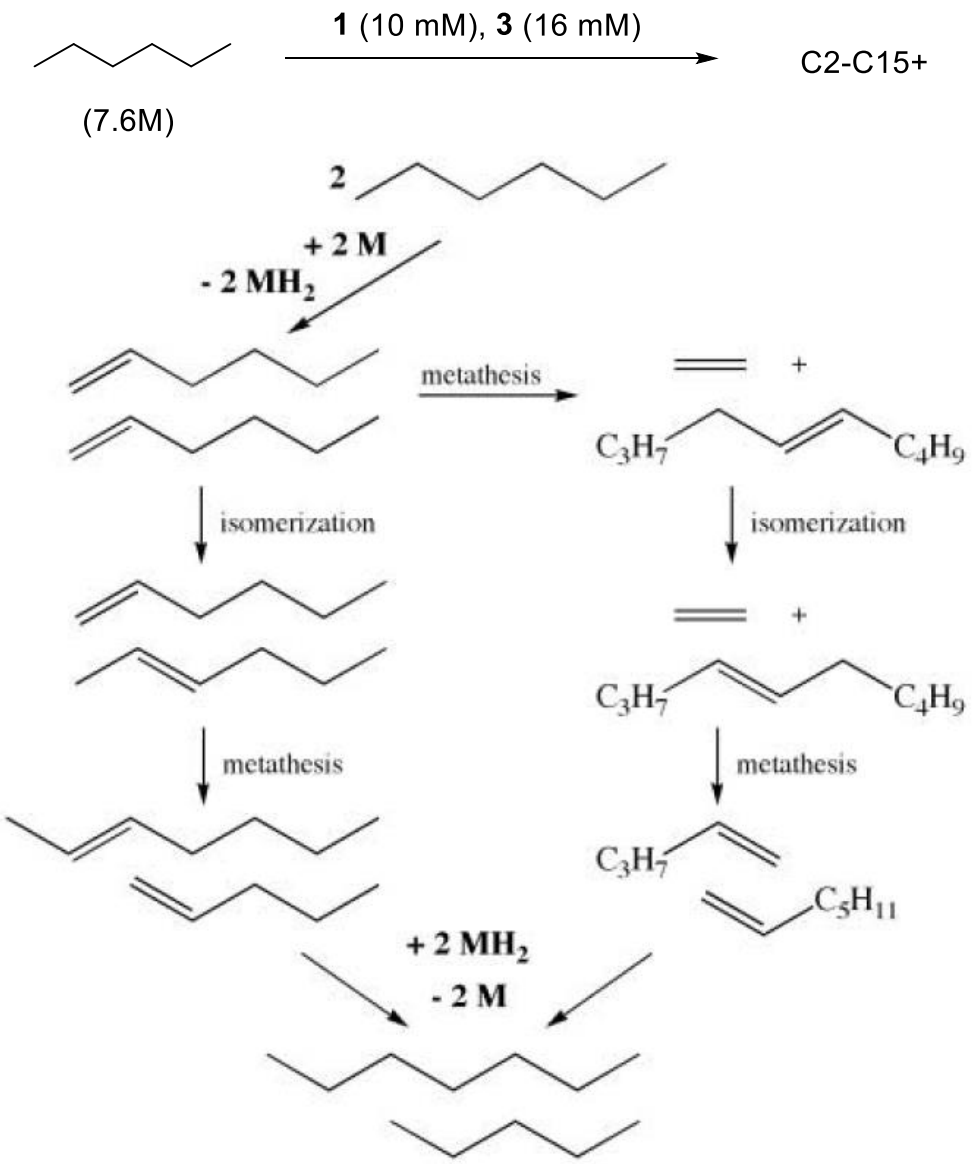
(1.57M) + 4 d, then adding fresh Schrock cat.

(2.81M) + 5 d

Entry	Ir catalyst	[TBE] (mM)	Temp. (°C)	Time	Product concentration (mM) C_2	C_3	C_4	C_5	C_7	C_8	C_9	C_{10}	C_{11}	C_{12}	C_{13}	C_{14}	$C_{>15}$	Total product (M)
1	**1**-C_2H_4	0	125	6 hours	123		105	183	131	73	70	47	10	4	2	1	0.3	0.75
				24 hours	233		191	319	234	133	122	81	22	9	5	2	1	1.35
				2 days	261		215	362	265	147	138	89	25	11	6	3	1	1.52
				4 days	264		218	372	276	154	146	95	26	12	6	3	1	1.57
Added additional **3** (8 mM)																		
				5 days	502		436	721	420	239	223	153	56	30	18	10	5	2.81
2	**1**-H_2	20	125	1 day	458		345	547	258	151	139	95	29	13	6	3	2	2.05
3	**2a**-H_2*	20	125	23 hours	(131)	176	127	306	155	37	49	232	18	4	4	10	2	1.25
Added additional **3** (6.4 mM)																		
				46 hours	(189)	255	193	399	208	61	81	343	31	9	9	22	7	1.81

Goldman and Brookhart Science**, 2006**, *312*, 257.

3. Alkane Activation; alkane metathesis



Goldman and Brookhart Science**, 2006**, *312*, 257.

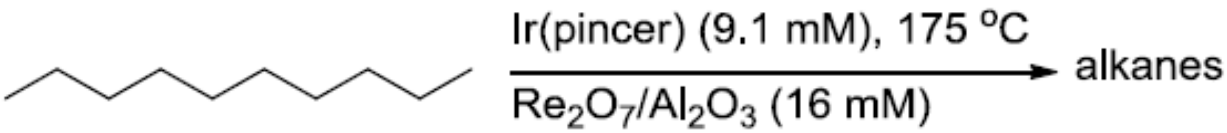
3. Alkane Activation; alkane metathesis

Alkane cross metathesis reaction of **C6 and C20**

Table 2. Concentrations of C_2 to C_{38} *n*-alkane products resulting from the metathesis of *n*-hexane (4.36 M) and eicosane (*n*-$C_{20}H_{42}$; 1.09 M) by **1**-C_2H_4 (7.14 mM) and **3** (11.43 mM) at 125°C.

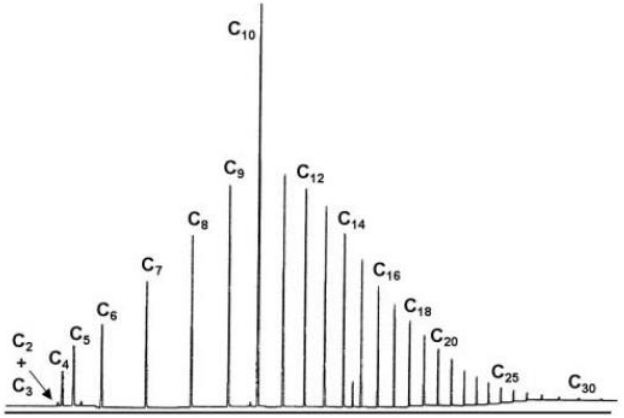
Time	Product concentration (M)						Total product
	C_{2-5}	C_{7-10}	C_{11-14}	C_{15-19}	C_{21-24}	C_{25-38}	
1 day	0.44	0.36	0.24	0.31	0.14	0.066	1.56
6 days	0.56	0.64	0.31	0.27	0.12	0.070	1.97

Compatibility of Ir-pincer with heterogeneous catalyst



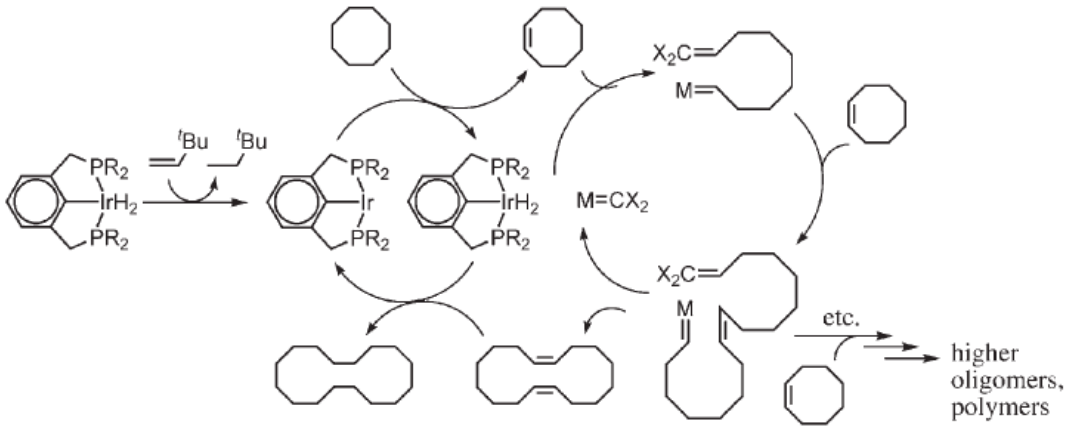
(heterogeneous olefin metathesis catalyst)
thermally stable

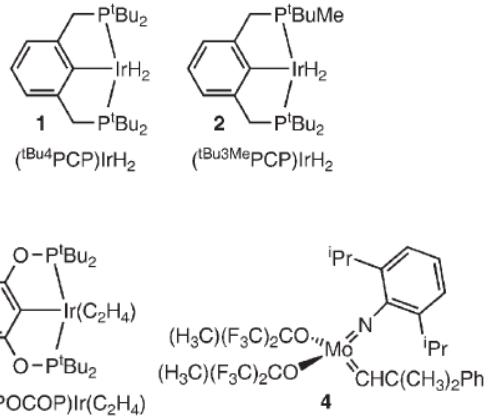
Observed GC trace



Goldman and Brookhart Science**, 2006**, *312*, 257.

3. Alkane Activation; alkane metathesis





			Cycloalkanes (% by weight)												
Cat.	TBE/mM	Time/h	C_6	C_7	C_8	C_{15}	C_{16}	C_{17}	C_{24}	C_{32}	C_{33}	C_{40}	Sum C_{6-40} prod.	Insol. %	% Conv. C_8
1[c]	10	24	0.0	1.3	**79**	0.0	0.7	0.3	0.3	0.2	0.1	0.1	3.8	7.8	21
1[c]	10	72	0.2	2.7	**61**	0.1	1.9	0.6	0.7	0.4	0.2	0.2	7.8	16	39
1[c]	20	24	0.1	2.7	**73**	0.1	0.7	0.4	0.3	0.1	0.1	0.1	5.3	11	27
1[c]	20	72	0.3	4.0	**47**	0.1	3.2	0.7	1.2	0.5	0.2	0.3	11.5	29	53
1[c]	100	24	0.3	5.3	**45**	0.1	0.7	0.4	0.3	0.1	0.1	0.1	8.2	32	55
1[c]	100	72	0.5	5.6	**43**	0.1	1.3	0.4	0.6	0.2	0.1	0.1	9.9	33	57
2[d]	20	6	0.1	0.2	**41**	0.0	14	0.3	9.4	4.6	0.1	2.2	32	4.0	59
2[d]	20	12	0.1	0.3	**20**	0.0	14	0.3	10	5.6	0.2	2.7	34	10	80
3[e]	20	24	0.0	0.3	**42**	0.0	15	0.2	10	4.0	0.1	1.2	37	5.6	58

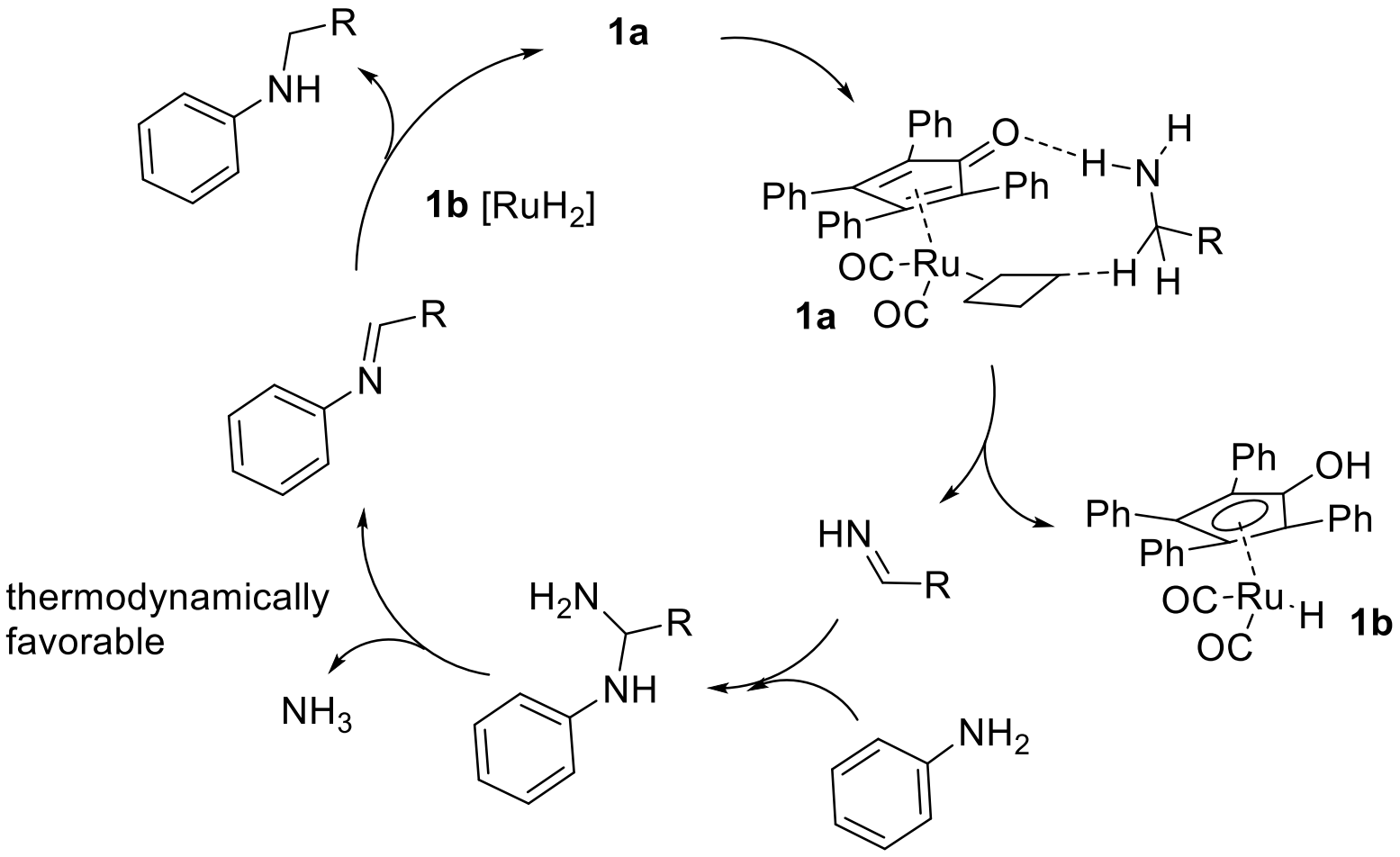
[a] Heating beyond times given did not afford significant additional product. Other ring sizes, formed in lesser amounts, are described in the ESI. [b] Insol. = material insoluble in toluene at ambient temperature. [c] C_8H_{16} (0.75 mL, 625 mg); **1** (4.4 mg; 10 mM); **4** (3.7 mg; 6.5 mM). [d] C_8H_{16} (0.75 mL, 625 mg); **2** (4.2 mg; 10 mM); **4** (3.7 mg; 6.5 mM). [e] C_8H_{16} (1.5 mL, 1.25 g); **3** (14.0 mg; 15 mM); **4** (11.5 mg; 10 mM).

major component of insoluble material – PE (Mw = 49,600, Mn = 29,700, PDI = 1.67)

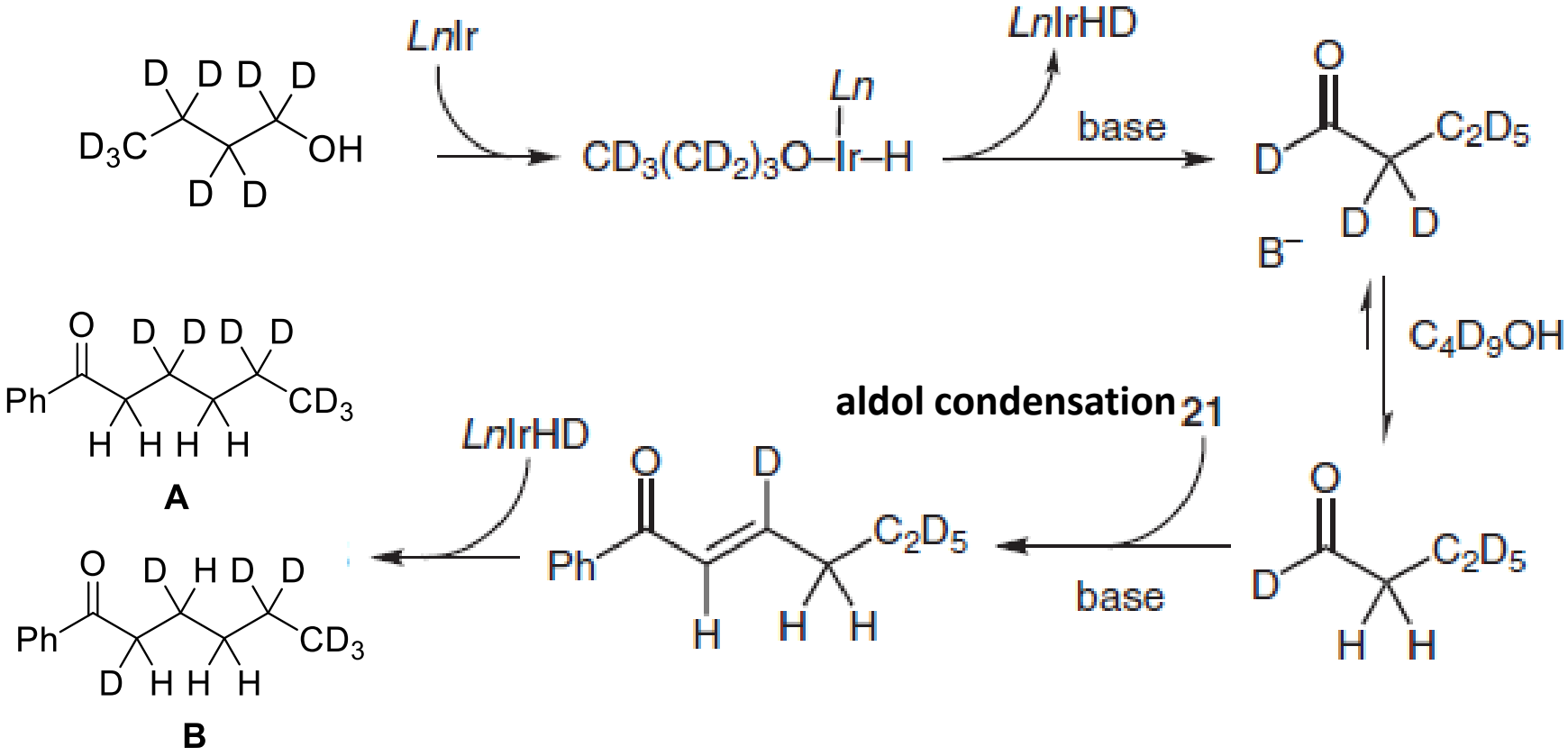
Goldman and Brookhart *ChemComm*, **2008**, 253.


Thank You!
Q&A
You have Questions
We have Answers

Quiz 1.

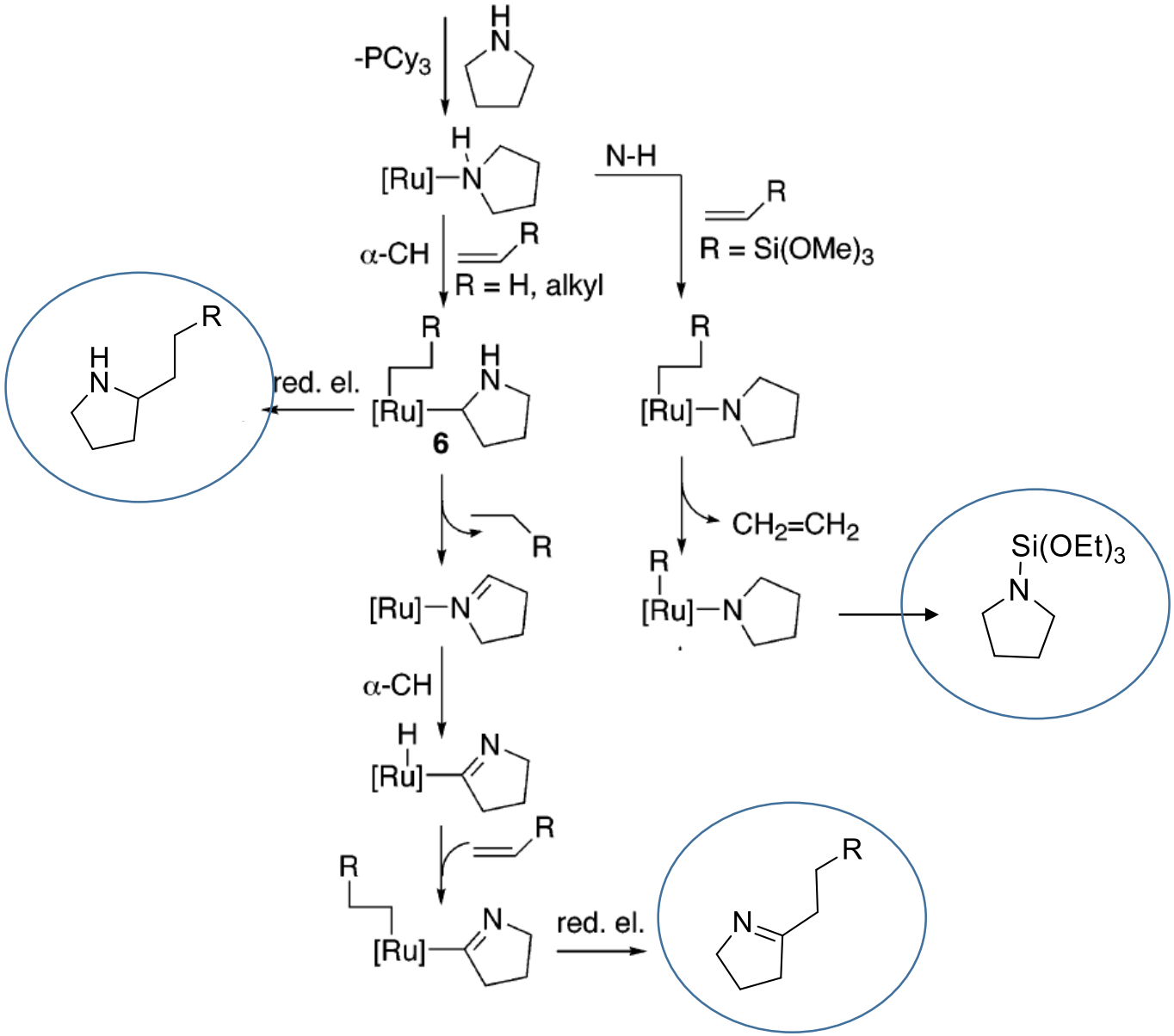


Quiz 2.



major product A was derived from α-deuterium proton exchange by H_2O or excess alcohols.

Quiz 3.


-PCy3
[Ru]
α-CH
R = H, alkyl
N-H
R = Si(OMe)3
red. el.
6
CH2=CH2
Si(OEt)3
α-CH
red. el.

1. Alcohol Activation; vinyl ether synthesis

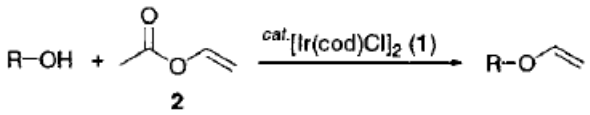


Table 1. Reaction of **3** with **2** to **4** Catalyzed by **1**[a]

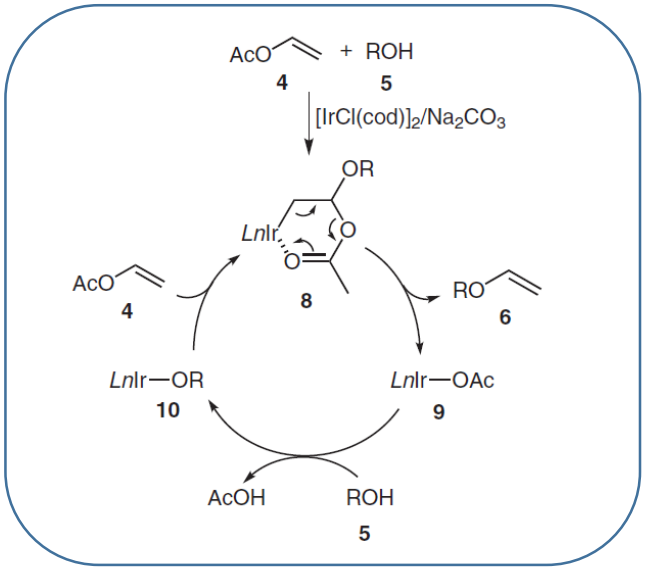
run	additive	(mmol)	conv./%	yield/%[b]
1	Na_2CO_3	(0.6)	100	quantitative
2[c]	Na_2CO_3	(0.3)	100	82
3[c]	Na_2CO_3	(0.01)	86	67
4[c]	none		3	1
5	NaOAc	(0.6)	100	82
6	$NaHCO_3$	(1.2)	99	93
7	K_2CO_3	(0.6)	39	3
8	Cs_2CO_3	(0.6)	30	6
9	pyridine	(1.2)	2	1
10[d]	Na_2CO_3	(0.6)	98	96
11[e]	Na_2CO_3	(0.6)	85	84
12[f]	Na_2CO_3	(0.6)	98	97

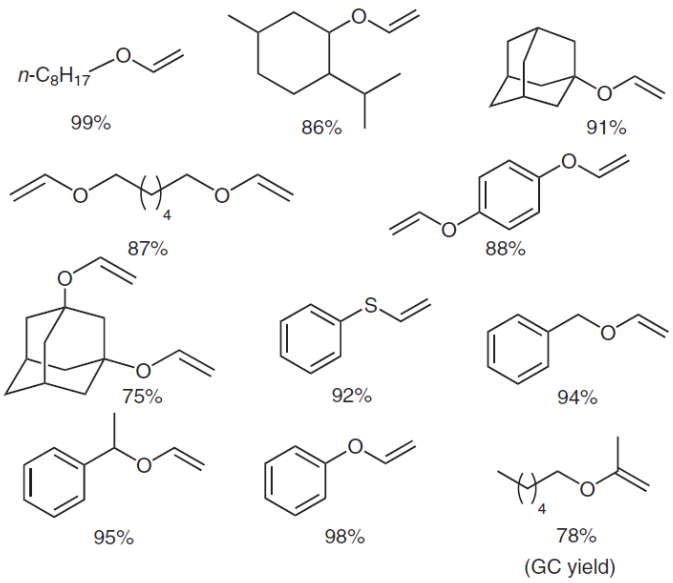
[a] **3** (1 mmol) was allowed to react with **2** (2 mmol) in the presence of **1** (0.01 mmol) in toluene (1 mL) at 100 °C for 2 h under Ar. [b] GC yield. [c] **2** (5 mmol) was used. [d] 90 °C, 3 h. [e] 1,4-Dioxane (1 mL) was used as a solvent. [f] Vinyl benzoate (1 mmol) was used instead of **2**.

Table 2. Reaction of **3** with **2** to **4** Catalyzed by Several Transition Metal Complexes[a]

run	catalyst	conv./%	yield/%[b]
1	**1**	100	quantitative
2	$[Ir(cod)_2]^+BF_4$-	72	70
3	$[Ir(cod)(CH_3CN)]^+BF_4^-$	98	90
4	$IrCl(CO)(PPh_3)_2$	no reaction	
5	$[RhCl(cod)]_2$	28	3[c]
6	$RuCl_2(cod)$	4	4
7	$PtCl_2(cod)$	9	1
8	$Pd(OAc)_2/PPh_3$	no reaction	

[a] Reaction was run as shown in Table 1 *a*. [b] GC yield. [c] *n*-Octyl acetate (25%) was produced.





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