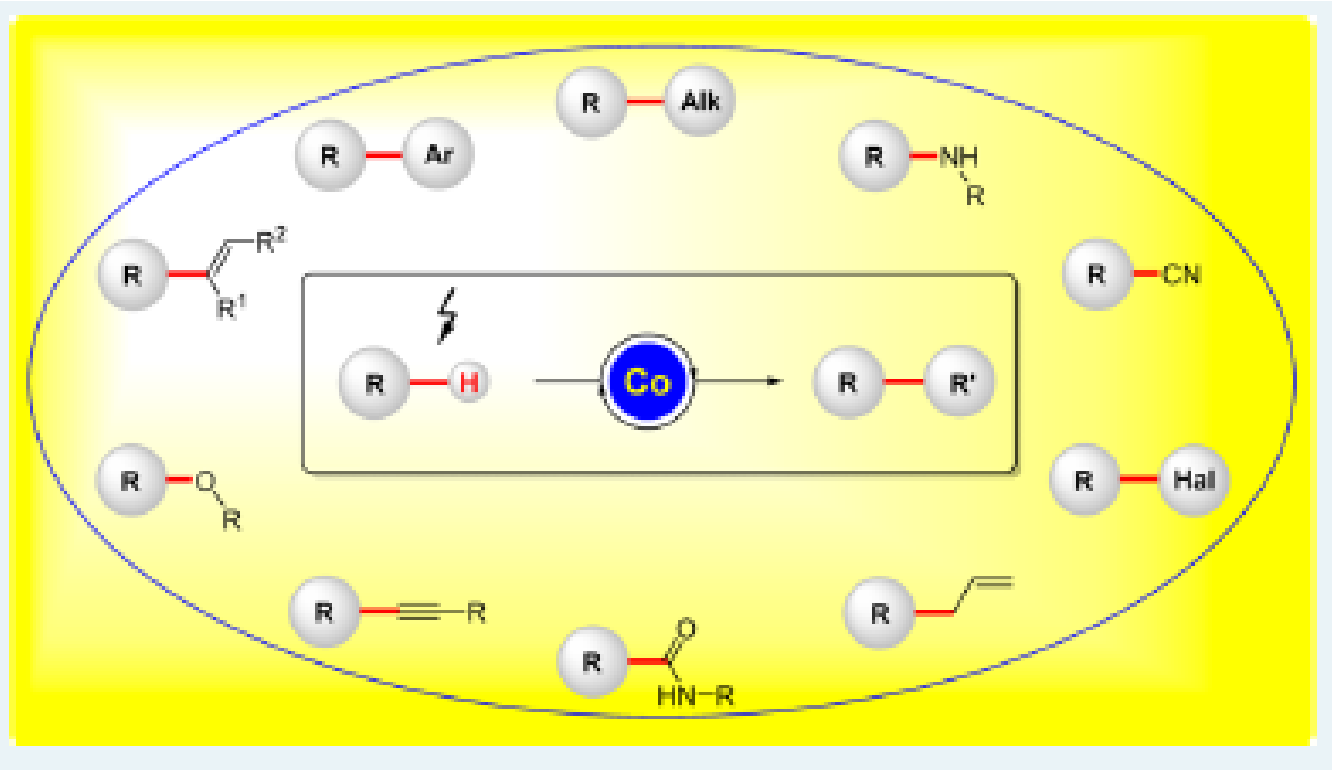
DUDOGNON Yohan - 04 07 2016

Cooperative Lewis Acid/Cp*Co^{III} Catalyzed C-H Bond Activation for the Synthesis of Isoquinolin-3-ones

Ju Hyun Kim, Steffen Greßies and Frank Glorius, *Angew. Chem. Int. Ed.* **2016**, *55*, 1

Towards the use of earth-abundant metals for C-H activation



Ackermann and al. *ACS Catal.* 2016, *6*, 498

Cobalt as **environmental** and **economical friendly alternative** to second-row TM such as Pd, Ru and Rh

Latest devellopments: Cheng and al. *Angew. Chem. Int. Ed.* 2016, *128*, 1876; Ellman and al. *J. Am. Chem. Soc.* 2015, *137*, 490; Chang and al. *Angew. Chem. Int. Ed.* 2015, *54*, 14103; Ackermann and al. *Angew. Chem. Int. Ed.* 2015, *54*, 3635; Ackermann and al. *J. Org. Chem.* 2014, *79*, 8948.

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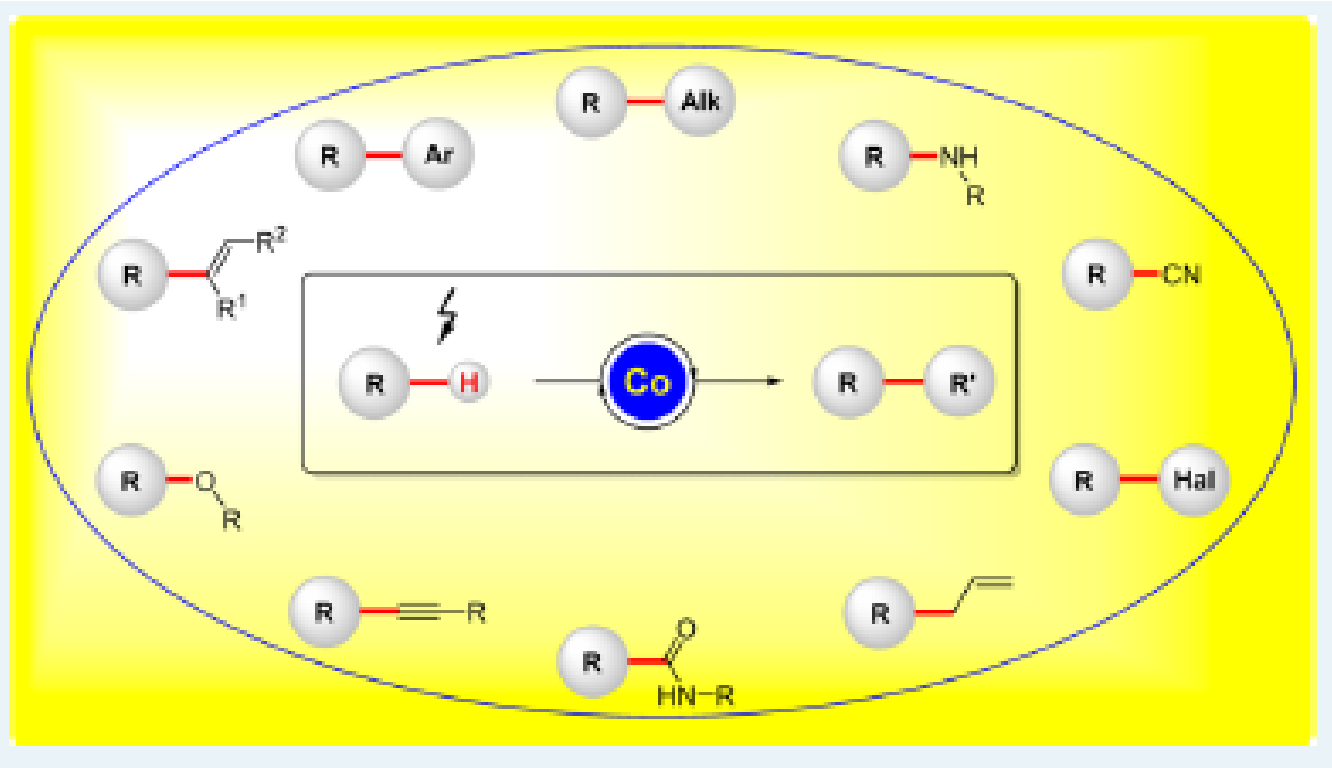

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Remarkable progress in Co-cat. C-H activation in the last 3 years

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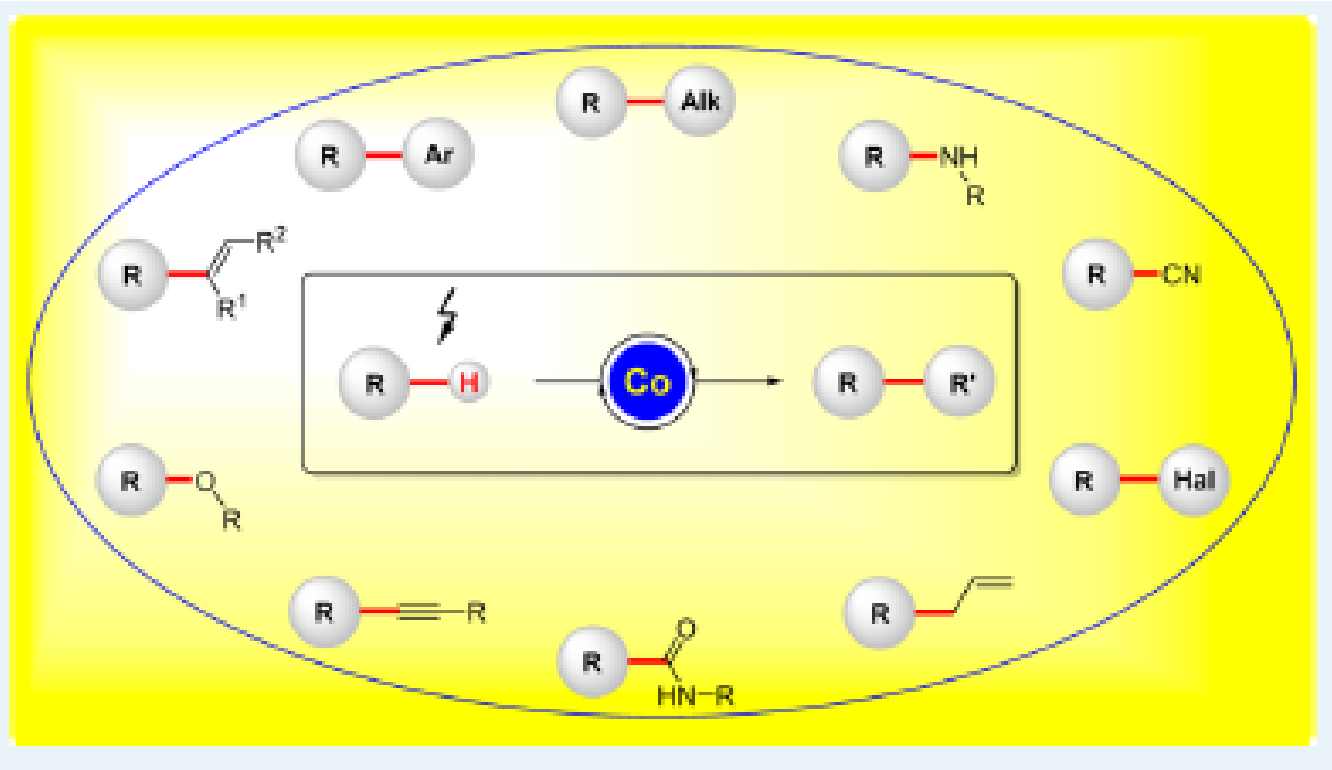

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Cobalt as **environmental** and **economical friendly alternative** to second-row TM such as Pd, Ru and Rh

Remarkable progress in Co-cat. C-H activation in the last 3 years

Remaining challenges:

Improve catalyst turnover
Broaden substrate scope
Develop better directing groups

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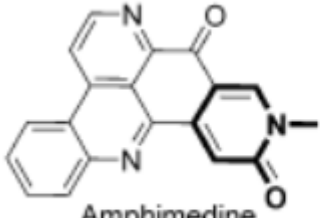
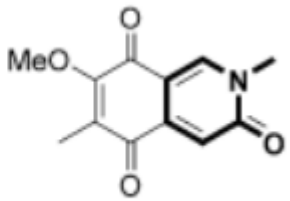
Isoquinoline-3-ones, a product of interest



Amphimedine



Mimosamycin

Isoquinolin-3-ones, prevalent motif in a wide variety of natural and biologically active compounds

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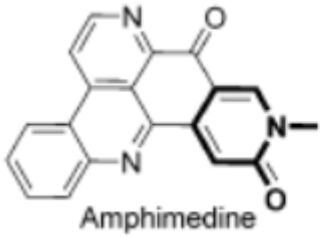

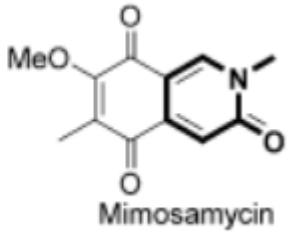

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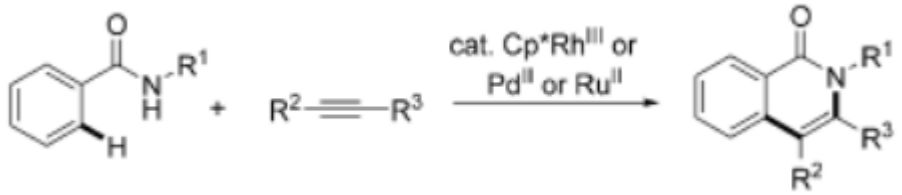
Isoquinolin-1-one



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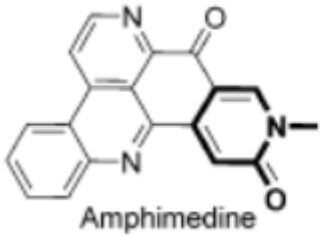

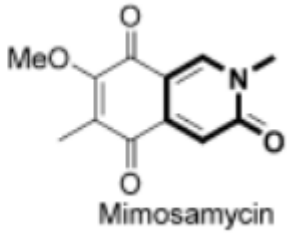

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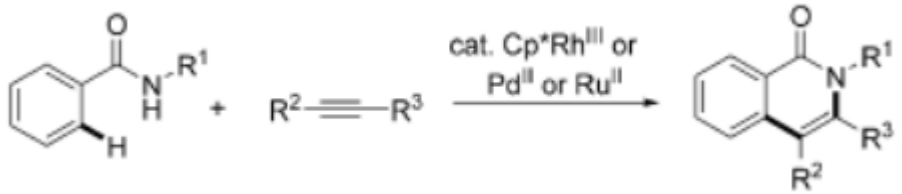

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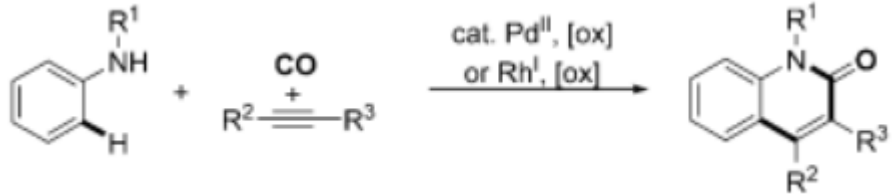

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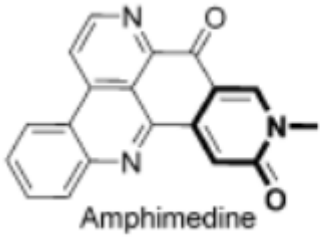

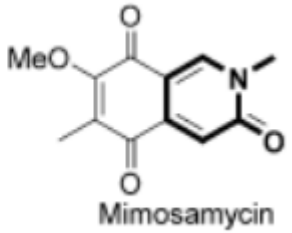

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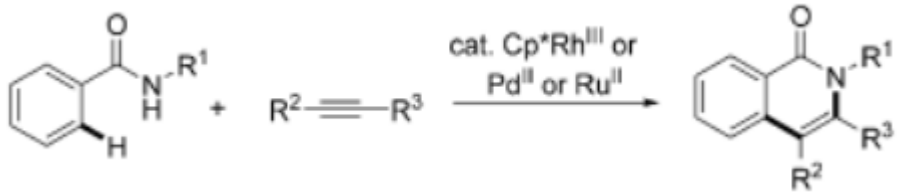

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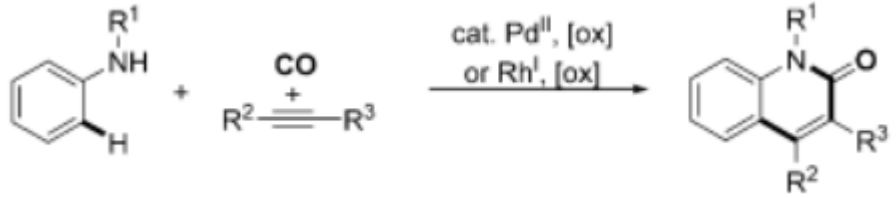

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No efficient catalytic general method
For Isoquinolin-3-one synthesis

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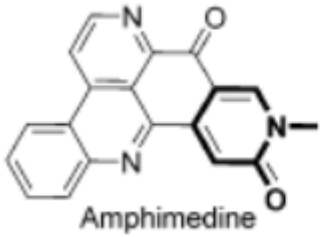

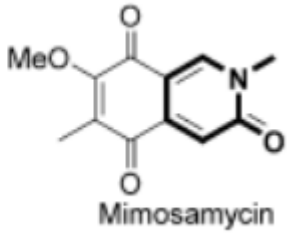

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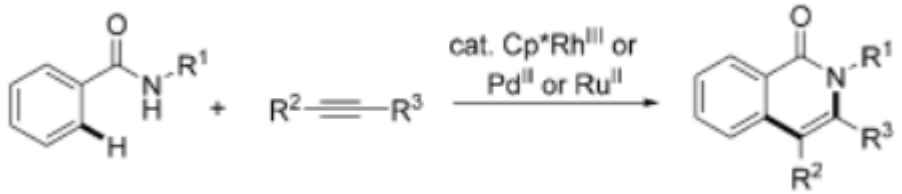

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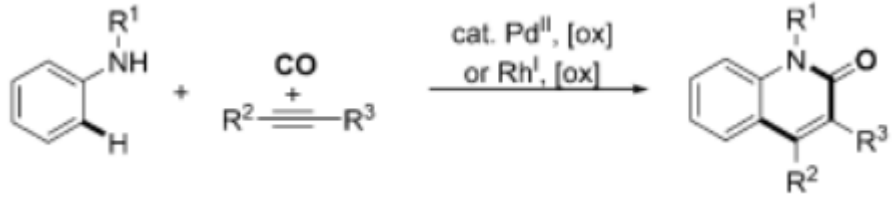

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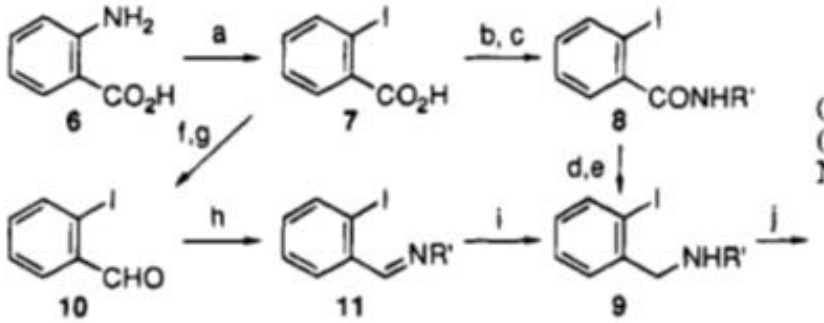
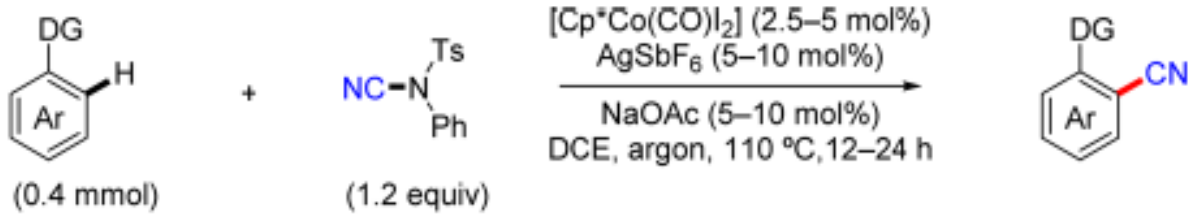


[a] Key: (a) $NaNO_2$, HCl, KI (70%); (b) $SOCl_2$; (c) $R'NH_2$ (85%); (d) $POCl_3$; (e) $NaBH_4$, HCl (60–70%); (f) $BF_3{\cdot}OEt_2$, $NaBH_4$ (90%); (g) PDC (80%); (h) $R'NH_2$ (100%); (i) $NaBH_4$ (60–80%); (j) $NCCH_2CO_2H$, $(EtO)_2P(O)CN$, Et_3N (77–95%).

Suzuki and al. *J. Org. Chem.* **1994**, *59*, 6116.

Glorius' group insight on Co-cat. C-H activation



J. Am. Chem. Soc. **2014**, *136*, 17722.

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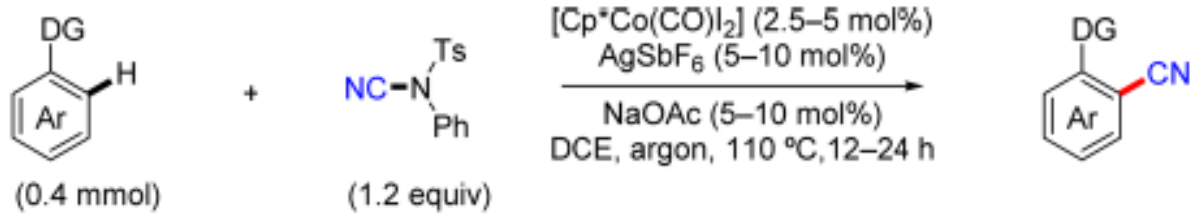

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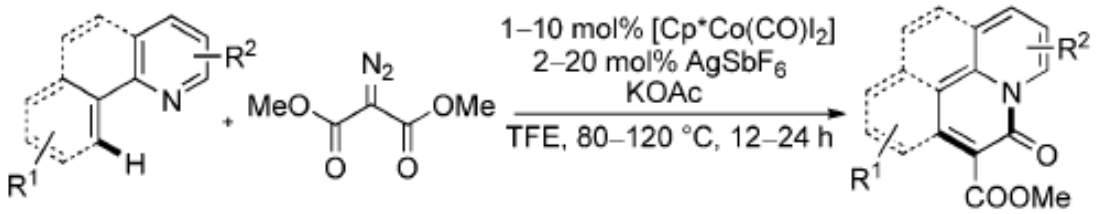

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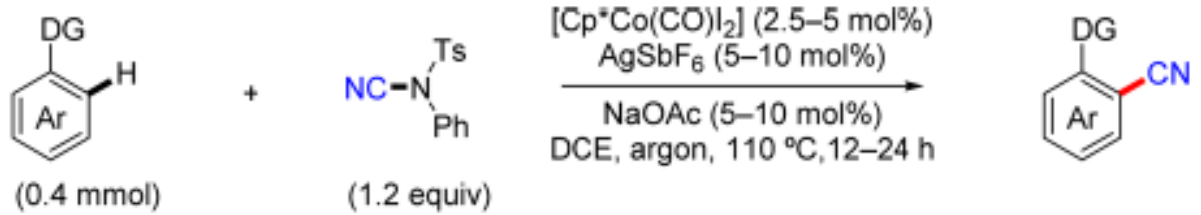

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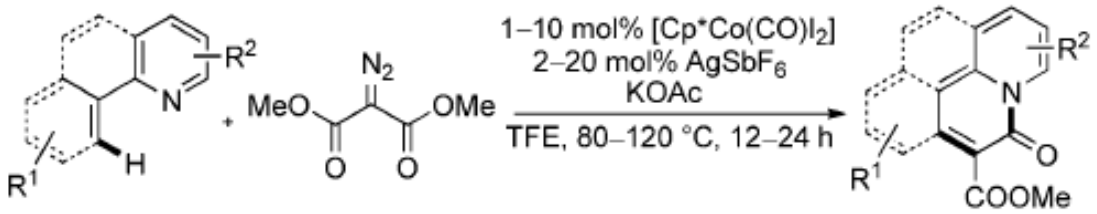

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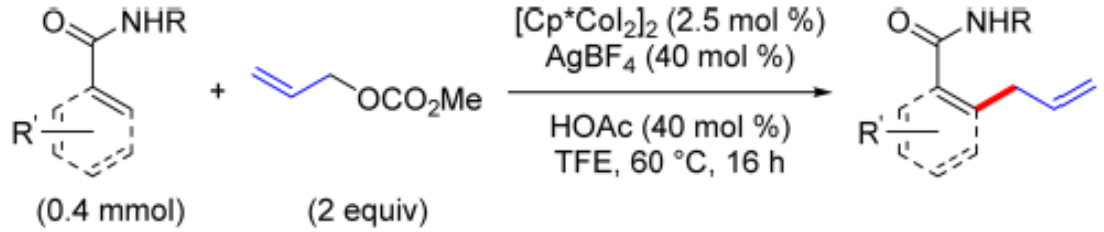

Org. Lett. **2015**, *17*, 3714.

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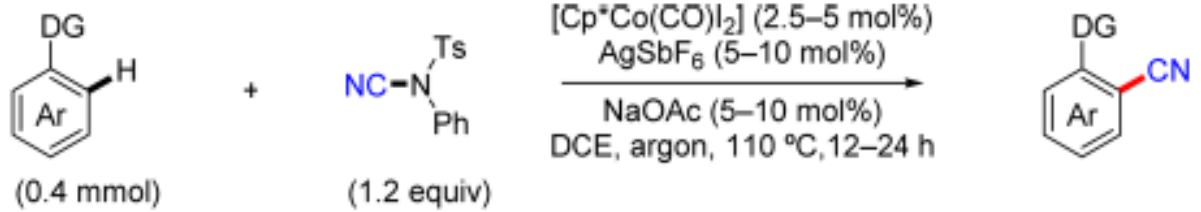

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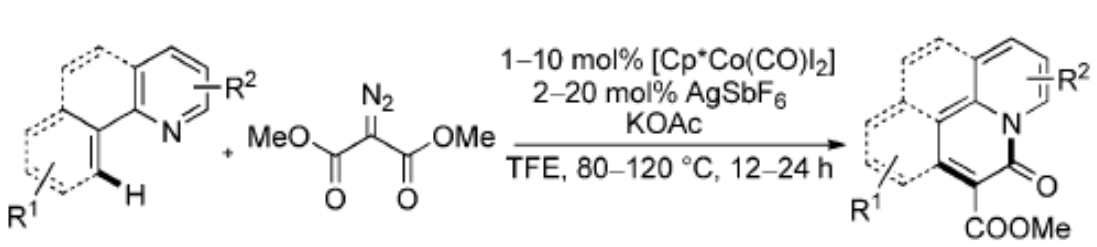

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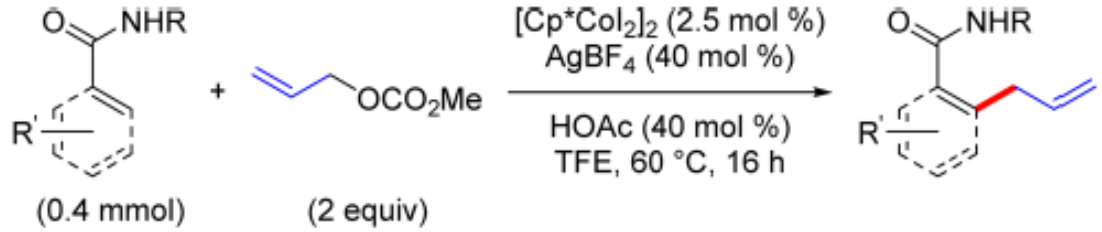

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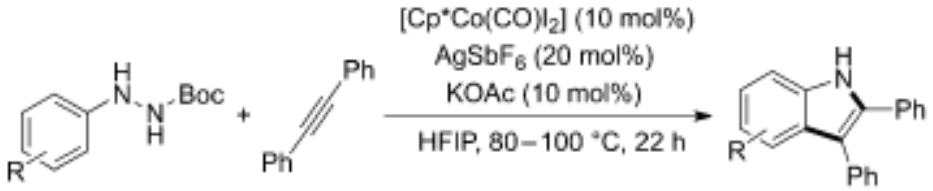

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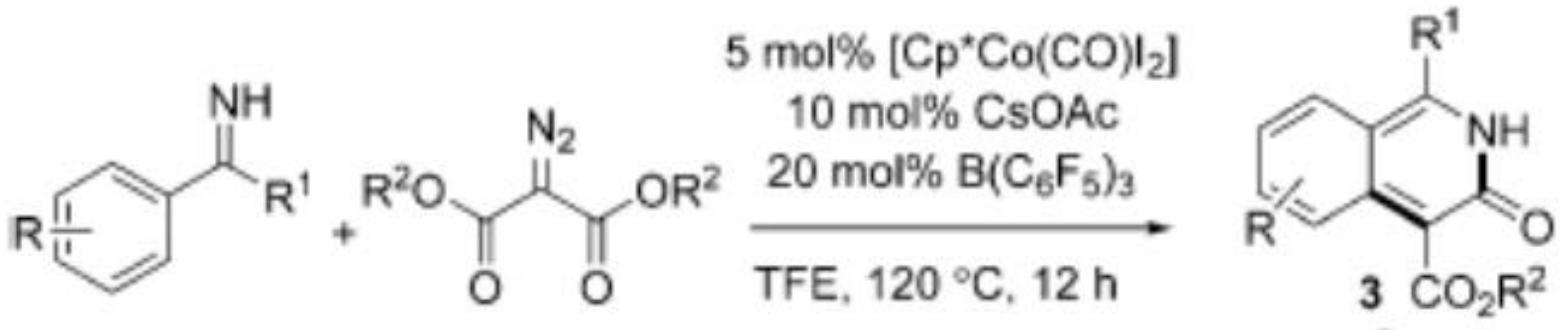

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First **synthetic method towards isoquinoline-3-ones** through C-H bond activation

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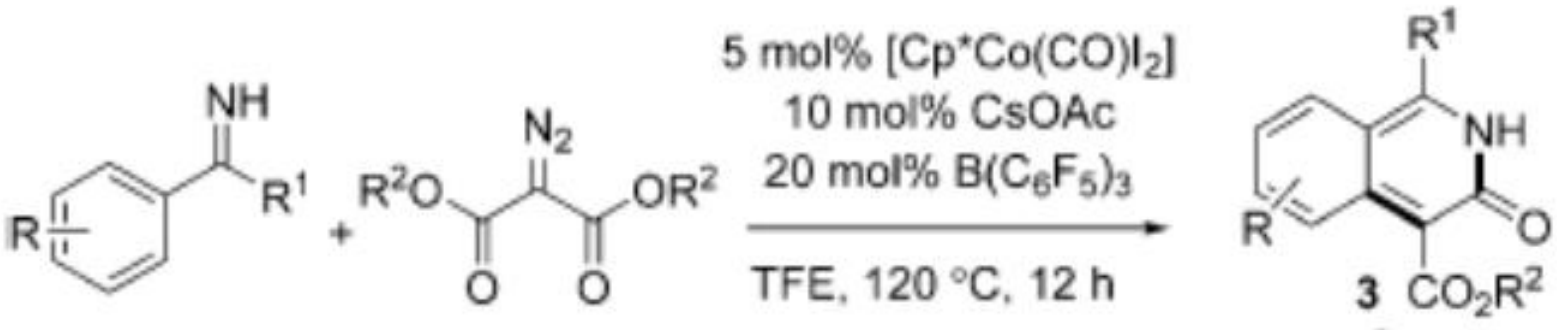

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NH imines as the most atom-economic directing group
No prefunctionalization or additional deprotection

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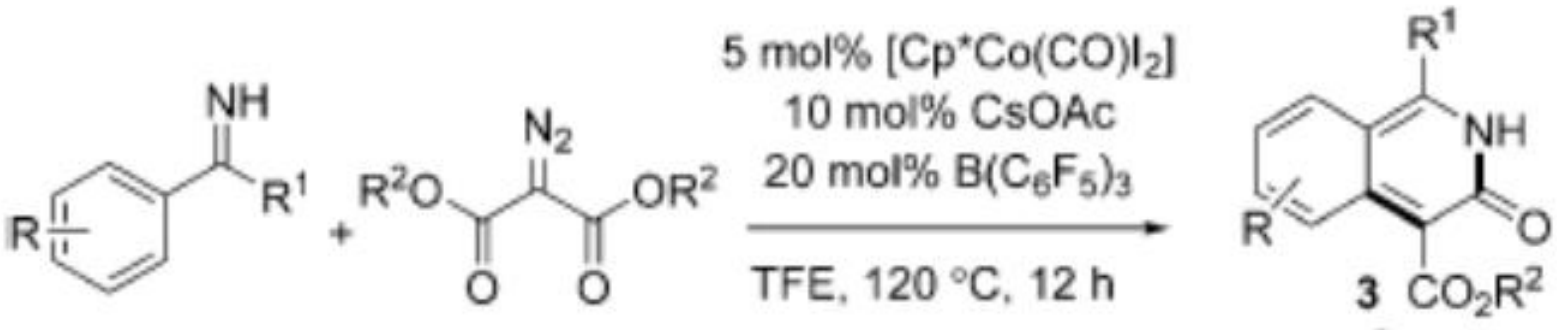

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No prefunctionalization or additional deprotection

Problems:
Imines are easily hydrolyzed
Can undergo nucleophilic addition
Possible side reactions with the metal
Imine/enamine tautomerization may alter the chelation abillity

Condition screening

Entry	Catalyst (mol%)	[Ag] (mol%)	additive (mol%)	Solvent	Yield (%)[b]
9	[Cp*Co(CO)I$_2$] (5)	AgSbF$_6$ (10)	—	TFE	(7)[d]
17[e]	[Cp*Co(CO)I$_2$] (5)	AgSbF$_6$ (10)	CsOAc (10)	TFE	33
18	[Cp*Co(CO)I$_2$] (5)	AgSbF$_6$ (10)	CsOAc (10), Zn(OTf)$_2$ (20)	TFE	37
19	[Cp*Co(CO)I$_2$] (5)	AgSbF$_6$ (10)	CsOAc (10), Sc(OTf)$_2$ (20)	TFE	39
20	[Cp*Co(CO)I$_2$] (5)	AgSbF$_6$ (10)	CsOAc (10), Cu(OAc)$_2$ (20)	TFE	<10
21	[Cp*Co(CO)I$_2$] (5)	AgSbF$_6$ (10)	CsOAc (10), BF_3OEt_2 (20)	TFE	66
22	[Cp*Co(CO)I$_2$] (5)	AgSbF$_6$ (10)	CsOAc (10), BF_3OEt_2 (60)	TFE	80
23	**[Cp*Co(CO)I$_2$] (5)**	**AgSbF$_6$ (10)**	**CsOAc (10), B(C$_6$F$_5$)$_3$(20)**	**TFE**	**82**
24	**[Cp*Co(CO)I$_2$] (5)**	**—**	**CsOAc (10), B(C$_6$F$_5$)$_3$(20)**	**TFE**	**80**
26	[Cp*Co(CO)I$_2$] (5)	—	CsOAc (10), B(C$_6$F$_5$)$_3$(10)	MeOH	(40)
27	[Cp*Co(CO)I$_2$] (5)	—	CsOAc (10), B(C$_6$F$_5$)$_3$(10)	AcOH	n.r.
28	[Co(acac)$_3$]	—	CsOAc (10), B(C$_6$F$_5$)$_3$(20)	TFE	(<5)[d]
29	[Cp*Co(C$_6$H$_6$)][B(C(5)$_6$F$_5$)$_4$]$_2$ (5)	—	—	TFE	46
30	[Cp*Co(C$_6$H$_6$)][B(C(5)$_6$F$_5$)$_4$]$_2$ (5)	—	CsOAc (10)	TFE	69

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Entry	Catalyst (mol%)	[Ag] (mol%)	additive (mol%)	Solvent	Yield (%)[b]
9	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	—	TFE	(7)[d]
17[e]	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	CsOAc (10)	TFE	33
18	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	CsOAc (10), $Zn(OTf)_2$ (20)	TFE	37
19	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	CsOAc (10), $Sc(OTf)_2$ (20)	TFE	39
20	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	CsOAc (10), $Cu(OAc)_2$ (20)	TFE	<10
21	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	CsOAc (10), BF_3OEt_2 (20)	TFE	66
22	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	CsOAc (10), BF_3OEt_2 (60)	TFE	80
23	**$[Cp^*Co(CO)I_2]$ (5)**	**$AgSbF_6$ (10)**	**CsOAc (10), $B(C_6F_5)_3$(20)**	**TFE**	**82**
24	**$[Cp^*Co(CO)I_2]$ (5)**	**—**	**CsOAc (10), $B(C_6F_5)_3$(20)**	**TFE**	**80**
26	$[Cp^*Co(CO)I_2]$ (5)	—	CsOAc (10), $B(C_6F_5)_3$(10)	MeOH	(40)
27	$[Cp^*Co(CO)I_2]$ (5)	—	CsOAc (10), $B(C_6F_5)_3$(10)	AcOH	n.r.
28	$[Co(acac)_3]$	—	CsOAc (10), $B(C_6F_5)_3$(20)	TFE	(<5)[d]
29	$[Cp^*Co(C_6H_6)][B(C(5)_6F_5)_4]_2$ (5)	—	—	TFE	46
30	$[Cp^*Co(C_6H_6)][B(C(5)_6F_5)_4]_2$ (5)	—	CsOAc (10)	TFE	69

A base increased the yield

Condition screening

Entry	Catalyst (mol%)	[Ag] (mol%)	additive (mol%)	Solvent	Yield (%)[b]
9	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	—	TFE	(7)[d]
17[e]	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	CsOAc (10)	TFE	33
18	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	CsOAc (10), $Zn(OTf)_2$ (20)	TFE	37
19	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	CsOAc (10), $Sc(OTf)_2$ (20)	TFE	39
20	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	CsOAc (10), $Cu(OAc)_2$ (20)	TFE	<10
21	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	CsOAc (10), BF_3OEt_2 (20)	TFE	66
22	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	CsOAc (10), BF_3OEt_2 (60)	TFE	80
23	**$[Cp^*Co(CO)I_2]$ (5)**	**$AgSbF_6$ (10)**	**CsOAc (10), $B(C_6F_5)_3$(20)**	**TFE**	**82**
24	**$[Cp^*Co(CO)I_2]$ (5)**	**—**	**CsOAc (10), $B(C_6F_5)_3$(20)**	**TFE**	**80**
26	$[Cp^*Co(CO)I_2]$ (5)	—	CsOAc (10), $B(C_6F_5)_3$(10)	MeOH	(40)
27	$[Cp^*Co(CO)I_2]$ (5)	—	CsOAc (10), $B(C_6F_5)_3$(10)	AcOH	n.r.
28	$[Co(acac)_3]$	—	CsOAc (10), $B(C_6F_5)_3$(20)	TFE	(<5)[d]
29	$[Cp^*Co(C_6H_6)][B(C(5)_6F_5)_4]_2$ (5)	—	—	TFE	46
30	$[Cp^*Co(C_6H_6)][B(C(5)_6F_5)_4]_2$ (5)	—	CsOAc (10)	TFE	69

A base increased the yield

$B(C_6F_5)_3$ is the best Lewis acid

Condition screening

Entry	Catalyst (mol%)	[Ag] (mol%)	additive (mol%)	Solvent	Yield (%)[b]
9	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	—	TFE	(7)[d]
17[e]	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	CsOAc (10)	TFE	33
18	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	CsOAc (10), $Zn(OTf)_2$ (20)	TFE	37
19	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	CsOAc (10), $Sc(OTf)_2$ (20)	TFE	39
20	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	CsOAc (10), $Cu(OAc)_2$ (20)	TFE	<10
21	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	CsOAc (10), BF_3OEt_2 (20)	TFE	66
22	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	CsOAc (10), BF_3OEt_2 (60)	TFE	80
23	**$[Cp^*Co(CO)I_2]$ (5)**	**$AgSbF_6$ (10)**	**CsOAc (10), $B(C_6F_5)_3$(20)**	**TFE**	**82**
24	**$[Cp^*Co(CO)I_2]$ (5)**	**—**	**CsOAc (10), $B(C_6F_5)_3$(20)**	**TFE**	**80**
26	$[Cp^*Co(CO)I_2]$ (5)	—	CsOAc (10), $B(C_6F_5)_3$(10)	MeOH	(40)
27	$[Cp^*Co(CO)I_2]$ (5)	—	CsOAc (10), $B(C_6F_5)_3$(10)	AcOH	n.r.
28	$[Co(acac)_3]$	—	CsOAc (10), $B(C_6F_5)_3$(20)	TFE	(<5)[d]
29	$[Cp^*Co(C_6H_6)][B(C(5)_6F_5)_4]_2$ (5)	—	—	TFE	46
30	$[Cp^*Co(C_6H_6)][B(C(5)_6F_5)_4]_2$ (5)	—	CsOAc (10)	TFE	69

A base increased the yield

$B(C_6F_5)_3$ is the best Lewis acid

$AgSbF_6$ is actually not necessary

Condition screening

Entry	Catalyst (mol%)	[Ag] (mol%)	additive (mol%)	Solvent	Yield (%)[b]
9	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	—	TFE	(7)[d]
17[e]	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	CsOAc (10)	TFE	33
18	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	CsOAc (10), $Zn(OTf)_2$ (20)	TFE	37
19	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	CsOAc (10), $Sc(OTf)_2$ (20)	TFE	39
20	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	CsOAc (10), $Cu(OAc)_2$ (20)	TFE	<10
21	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	CsOAc (10), BF_3OEt_2 (20)	TFE	66
22	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	CsOAc (10), BF_3OEt_2 (60)	TFE	80
23	**$[Cp^*Co(CO)I_2]$ (5)**	**$AgSbF_6$ (10)**	**CsOAc (10), $B(C_6F_5)_3$(20)**	**TFE**	**82**
24	**$[Cp^*Co(CO)I_2]$ (5)**	**—**	**CsOAc (10), $B(C_6F_5)_3$(20)**	**TFE**	**80**
26	$[Cp^*Co(CO)I_2]$ (5)	—	CsOAc (10), $B(C_6F_5)_3$(10)	MeOH	(40)
27	$[Cp^*Co(CO)I_2]$ (5)	—	CsOAc (10), $B(C_6F_5)_3$(10)	AcOH	n.r.
28	$[Co(acac)_3]$	—	CsOAc (10), $B(C_6F_5)_3$(20)	TFE	(<5)[d]
29	$[Cp^*Co(C_6H_6)][B(C(5)_6F_5)_4]_2$ (5)	—	—	TFE	46
30	$[Cp^*Co(C_6H_6)][B(C(5)_6F_5)_4]_2$ (5)	—	CsOAc (10)	TFE	69

A base increased the yield

$B(C_6F_5)_3$ is the best Lewis acid

$AgSbF_6$ is actually not necessary

TFE is the best solvent

Condition screening

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9	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	—	TFE	(7)[d]
17[e]	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	CsOAc (10)	TFE	33
18	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	CsOAc (10), $Zn(OTf)_2$ (20)	TFE	37
19	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	CsOAc (10), $Sc(OTf)_2$ (20)	TFE	39
20	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	CsOAc (10), $Cu(OAc)_2$ (20)	TFE	<10
21	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	CsOAc (10), BF_3OEt_2 (20)	TFE	66
22	$[Cp^*Co(CO)I_2]$ (5)	$AgSbF_6$ (10)	CsOAc (10), BF_3OEt_2 (60)	TFE	80
23	**$[Cp^*Co(CO)I_2]$ (5)**	**$AgSbF_6$ (10)**	**CsOAc (10), $B(C_6F_5)_3$(20)**	**TFE**	**82**
24	**$[Cp^*Co(CO)I_2]$ (5)**	—	**CsOAc (10), $B(C_6F_5)_3$(20)**	**TFE**	**80**
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27	$[Cp^*Co(CO)I_2]$ (5)	—	CsOAc (10), $B(C_6F_5)_3$(10)	AcOH	n.r.
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29	$[Cp^*Co(C_6H_6)][B(C(5)_6F_5)_4]_2$ (5)	—	—	TFE	46
30	$[Cp^*Co(C_6H_6)][B(C(5)_6F_5)_4]_2$ (5)	—	CsOAc (10)	TFE	69

A base increased the yield

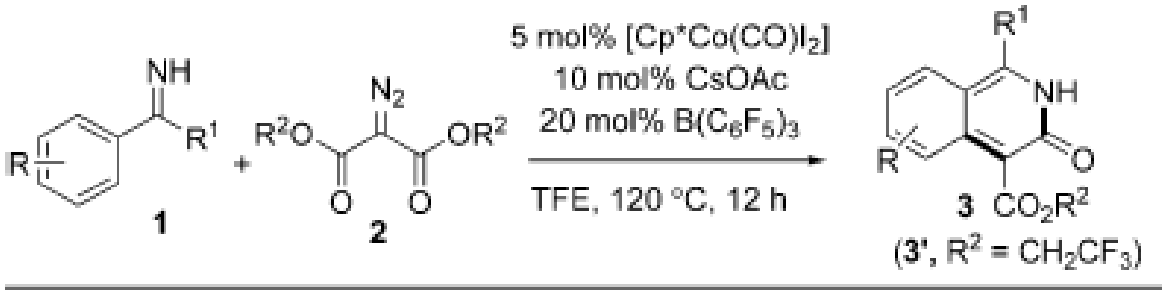
$B(C_6F_5)_3$ is the best Lewis acid

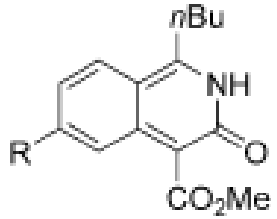
$AgSbF_6$ is actually not necessary

TFE is the best solvent

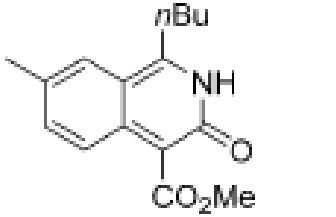
$[Cp^*Co(CO)I_2]$ is the best catalyst

Reaction scope - imines and diazo

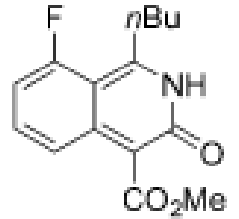




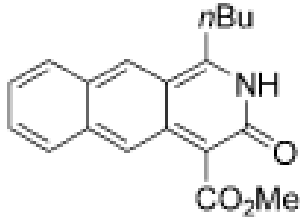
R = H, 80% (**3a/3a'** = 89:11)
R = CH_3, 80% (**3b/3b'** = 89:11)
R = OCH_3, 79% (**3c/3c'** = 91:9)
R = NMe_2, 93% (**3d/3d'** = 75:25)
R = Cl, 77% (**3e/3e'** = 92:8)
R = CF_3, 70% (**3f/3f'** = 86:14)



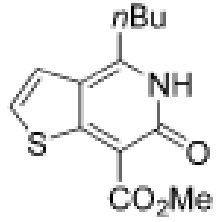
81% (**3g/3g'** = 89:11)



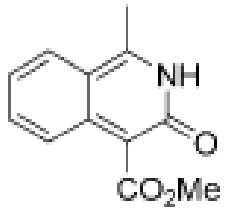
63% (**3h/3h'** = 70:30)



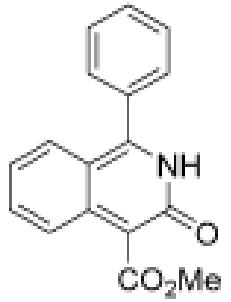
81% (**3i/3i'** = 89:11)



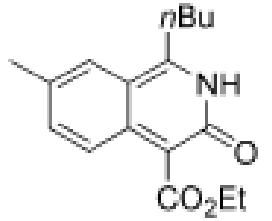
79% (**3j/3j'** = 95:5)



57% (**3k/3k'** = 75:25)



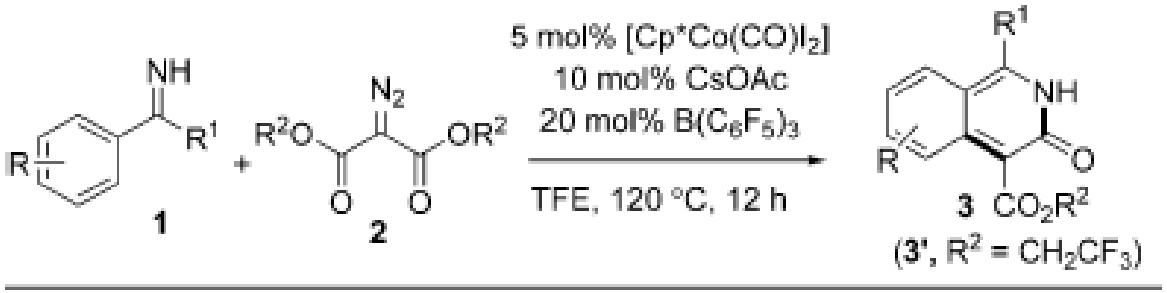
99% (**3l/3l'** = 93:7)

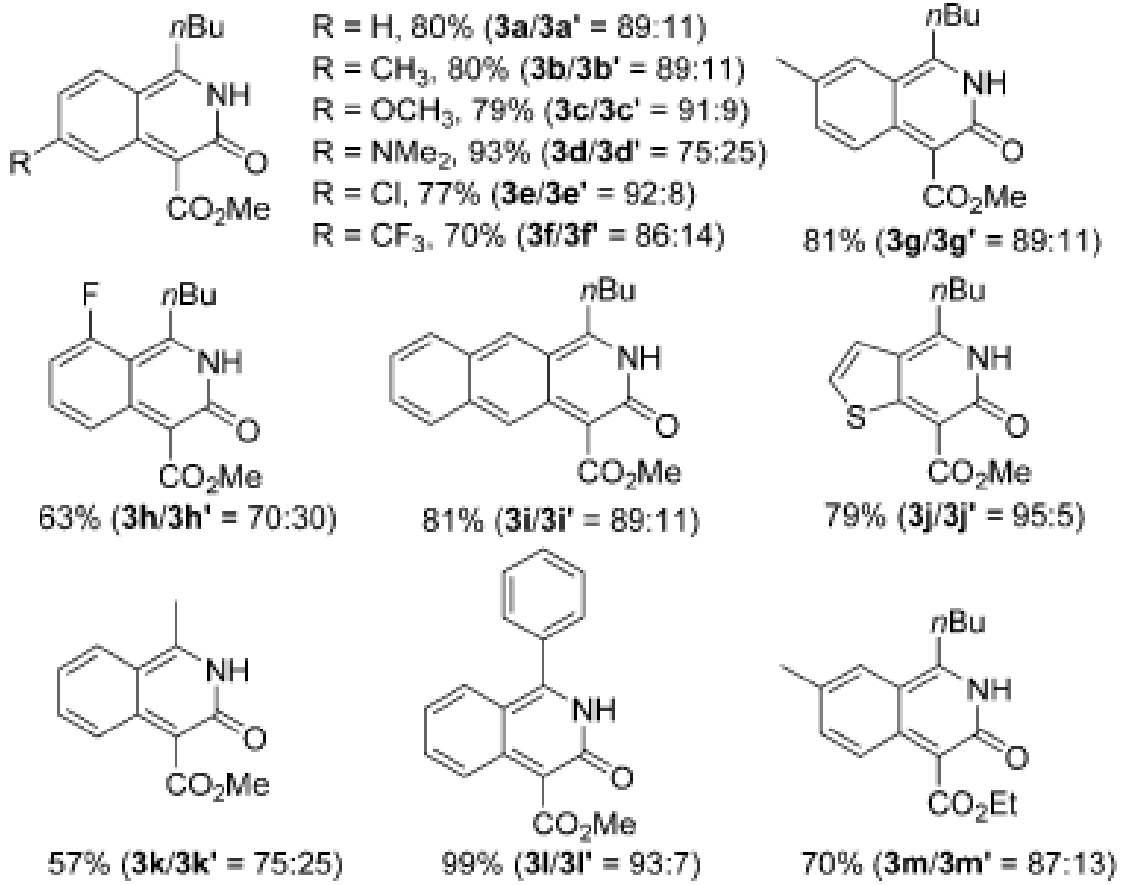


70% (**3m/3m'** = 87:13)

Separable mix between **product** and the **trans-esterified** one

Reaction scope - imines and diazo

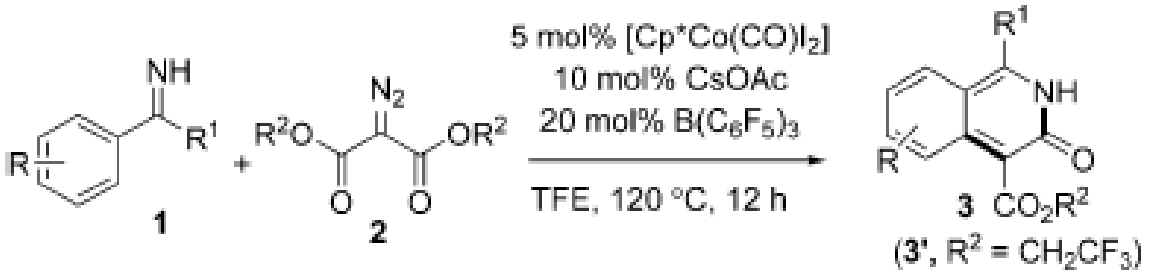


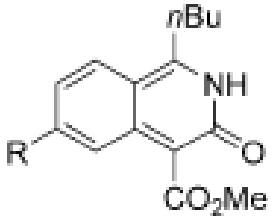


Separable mix between **product** and the **trans-esterified** one

EDG and **EWG** are **tolerated** on the aryl moiety

Reaction scope - imines and diazo





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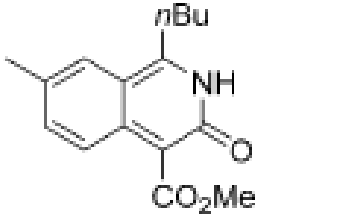

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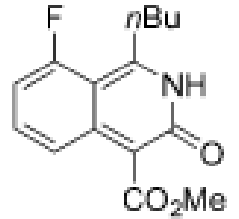

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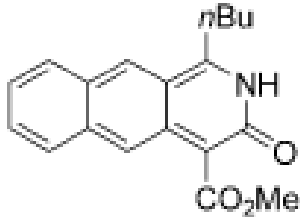
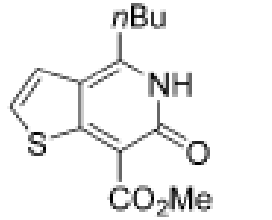


81% (**3i/3i'** = 89:11)



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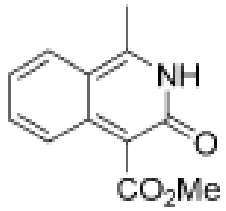

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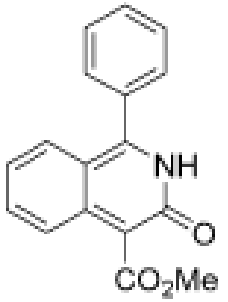
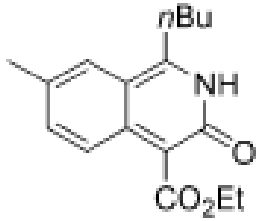


99% (**3l/3l'** = 93:7)



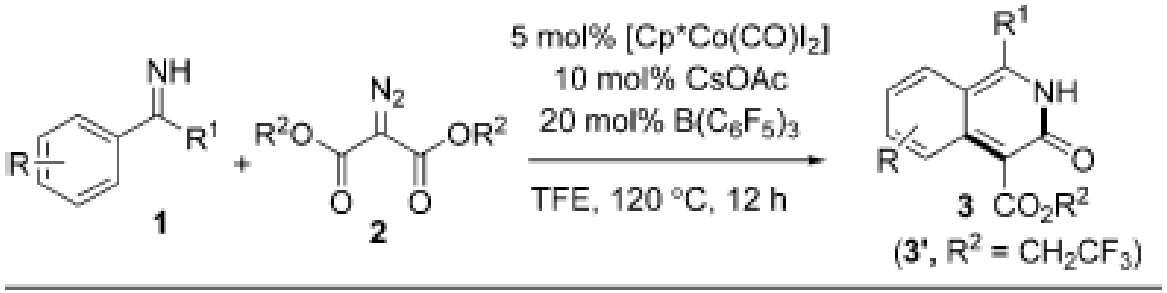
70% (**3m/3m'** = 87:13)

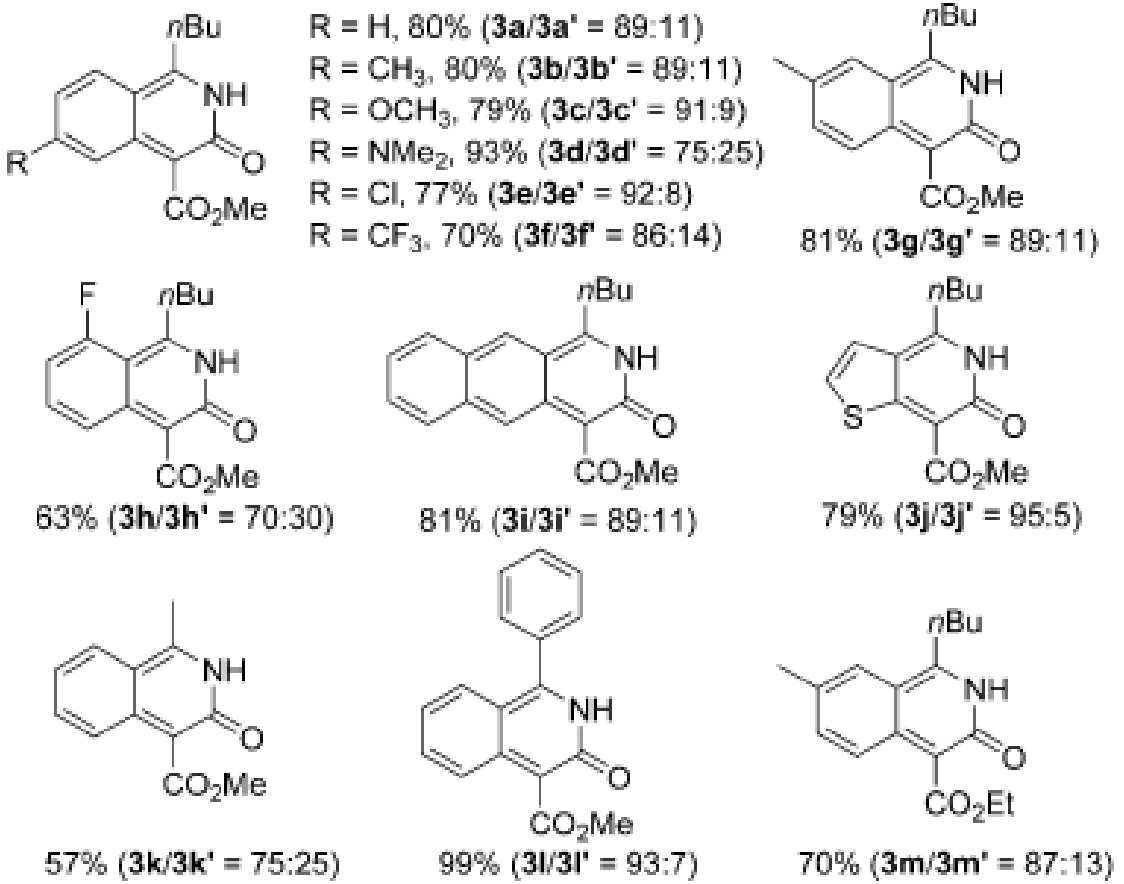
Separable mix between **product** and the **trans-esterified** one

EDG and **EWG** are **tolerated** on the aryl moiety

Regioselectivity when R is in ***ortho*** and ***meta*** positions

Reaction scope - imines and diazo





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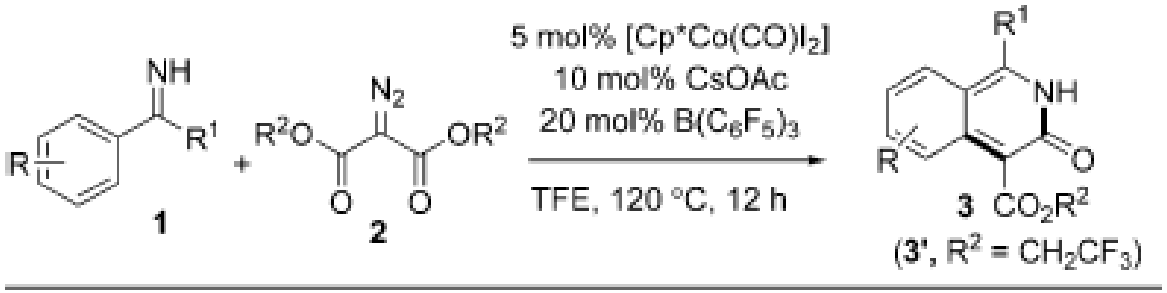
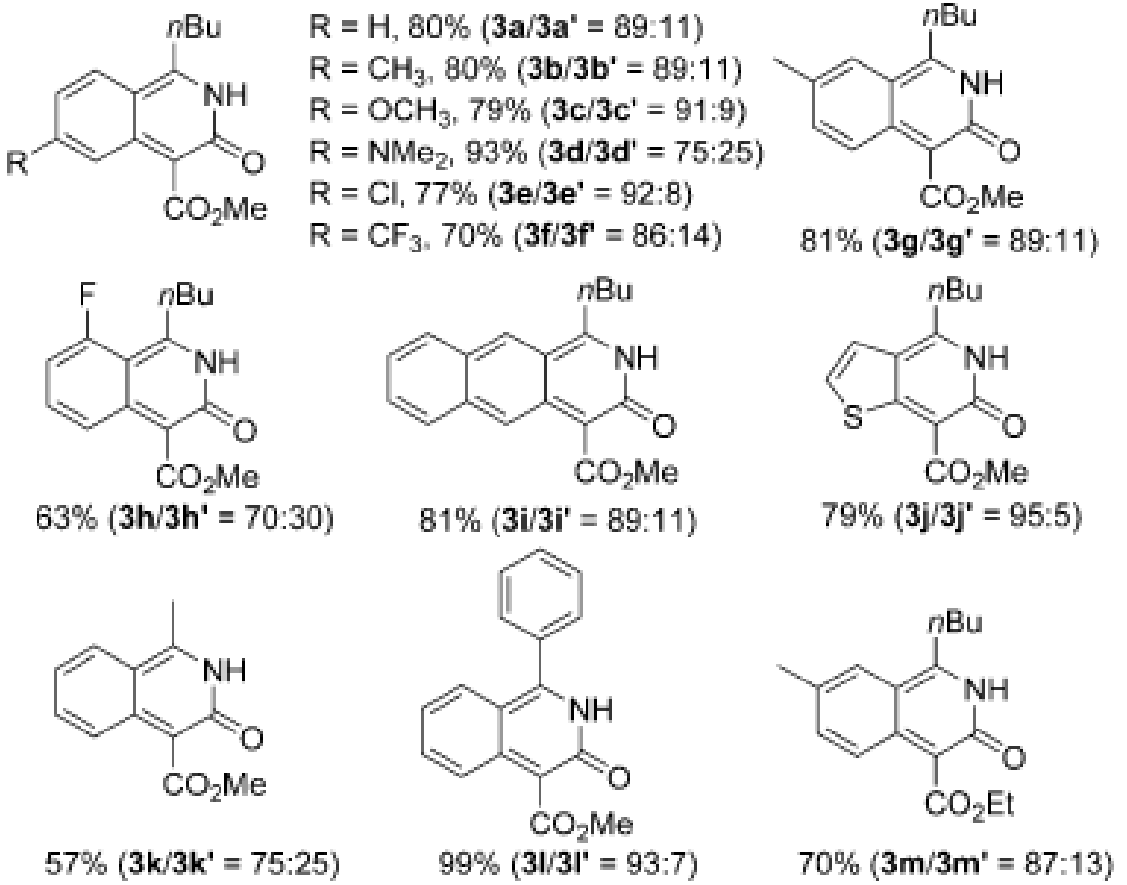
Regioselectivity when R is in ***ortho*** and ***meta*** positions

« **Variation of R_1 and diazo** compound had **little effect** on the reaction efficiency «

Reaction scope - imines and diazo





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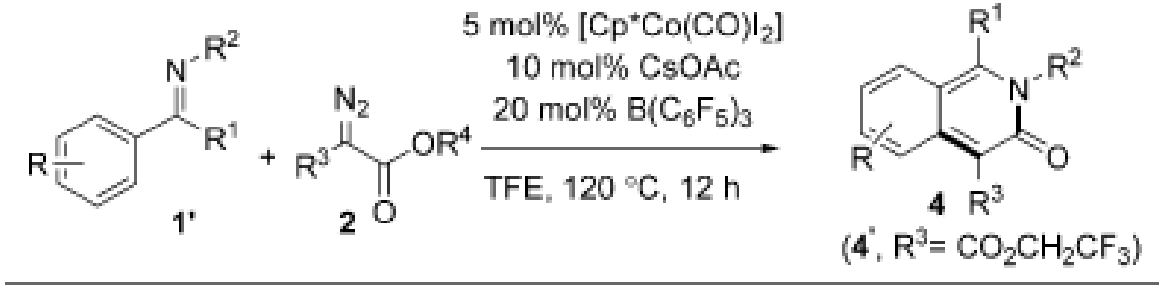
EDG and **EWG** are **tolerated** on the aryl moiety

Regioselectivity when R is in ***ortho*** and ***meta*** positions

« **Variation of R_1 and diazo** compound had **little effect** on the reaction efficiency «

Is it **really the case** ?

Reaction scope - N-substituted imines and diazo



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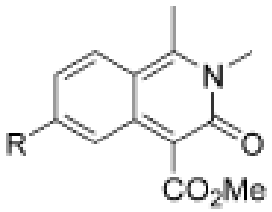

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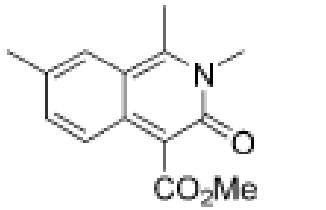

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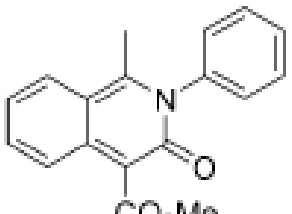

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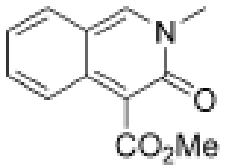

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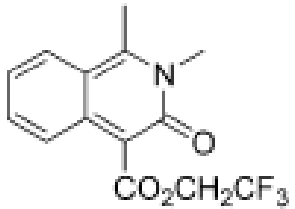

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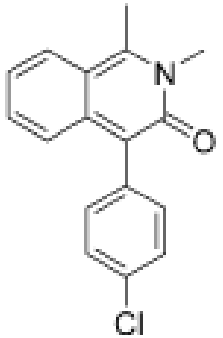

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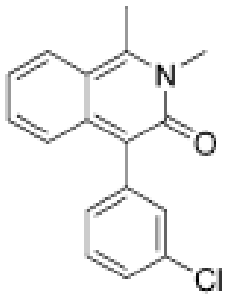

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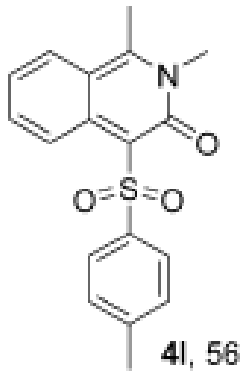

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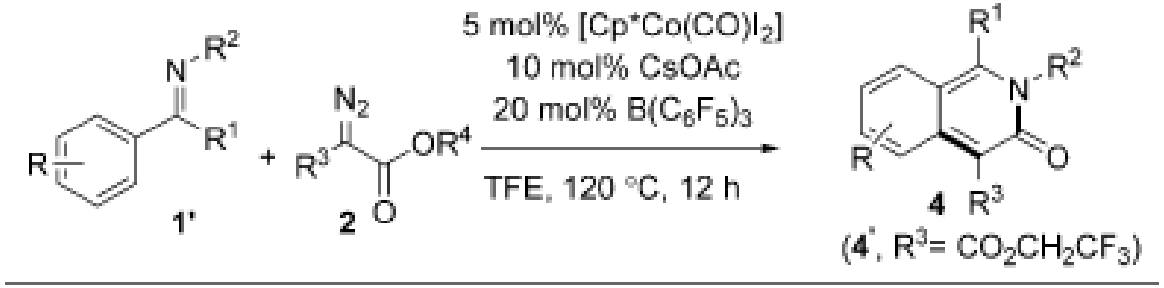

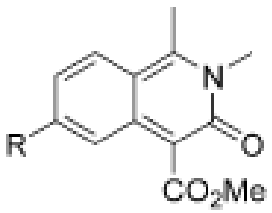

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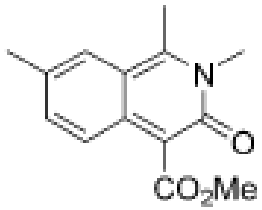

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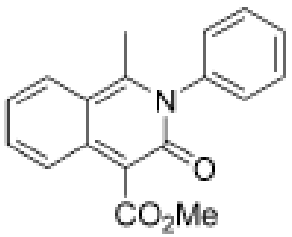

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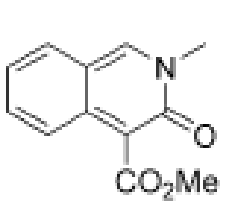

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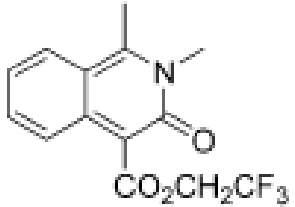

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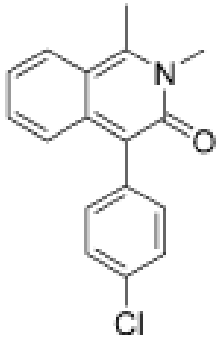

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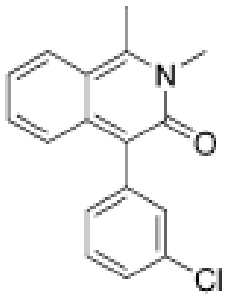

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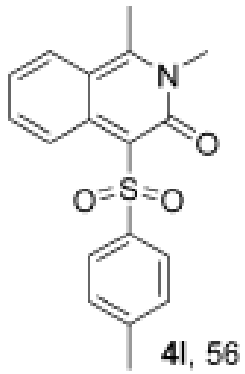

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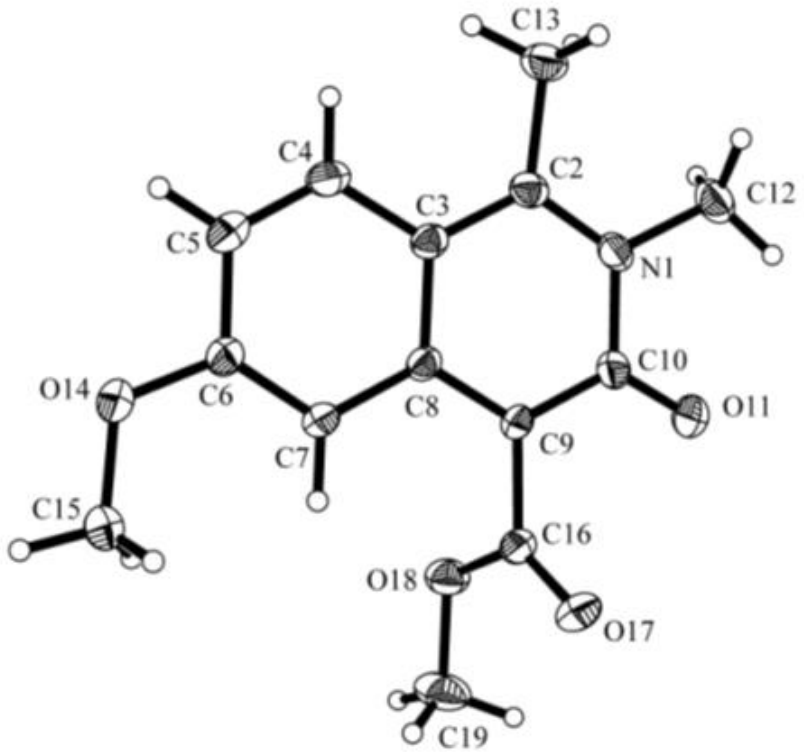

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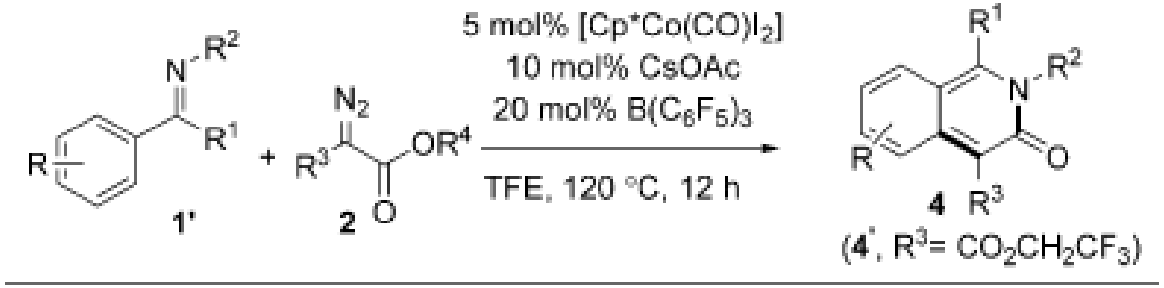

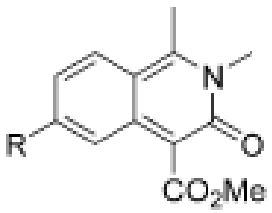

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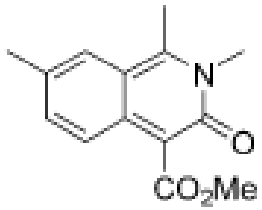

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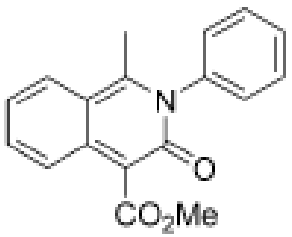

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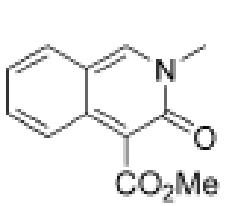

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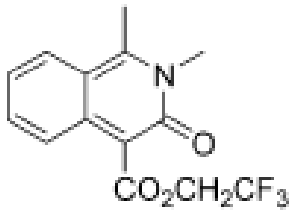

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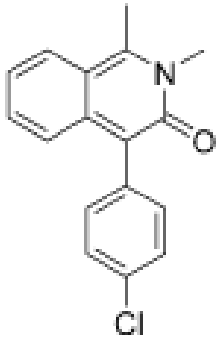

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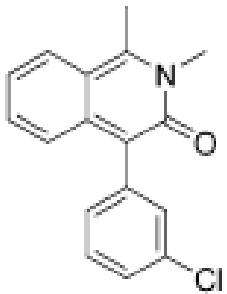

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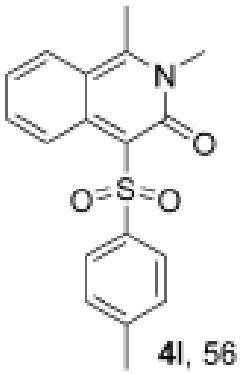

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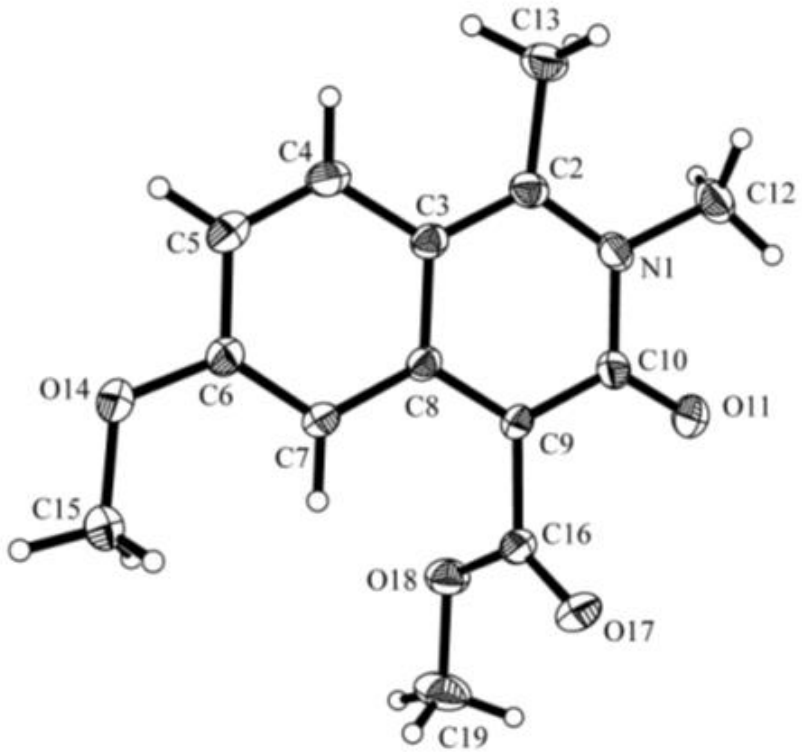
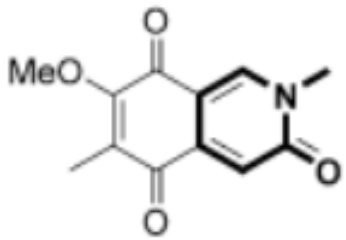
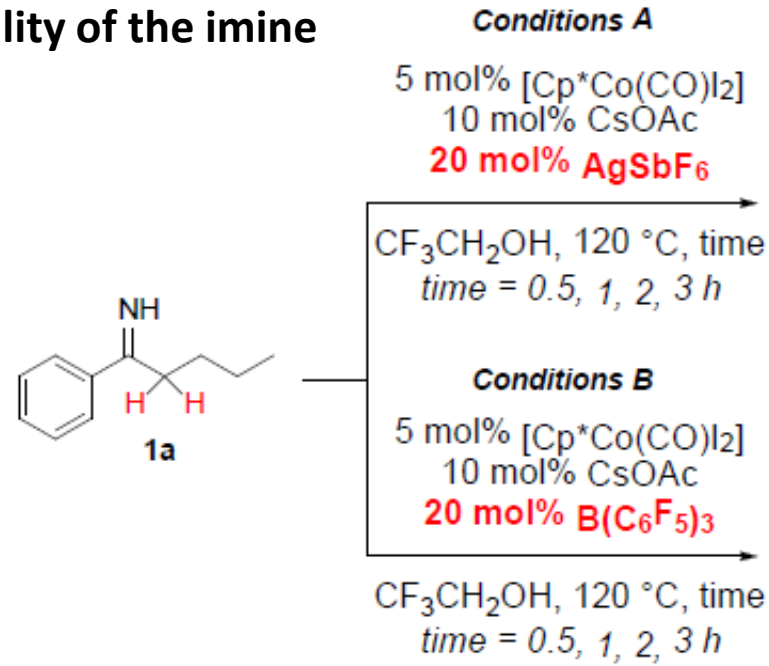


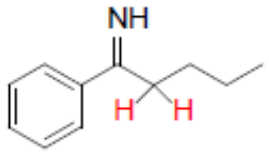
4h important scaffold of **natural compounds**



Reaction study

Stability of the imine





Remaining amount of **1a**

Entry	Time (hours)	Remaining **1 a** Conditions **A**	Conditions **B**
1	0.5	50%	**77%**
2	1	38%	**73%**
3	2	<10%	**67%**
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Study of the decomposition without diazo:

Decomposition over time
Slower decomposition with $B(C_6F_5)_3$ than $AgSbF_6$

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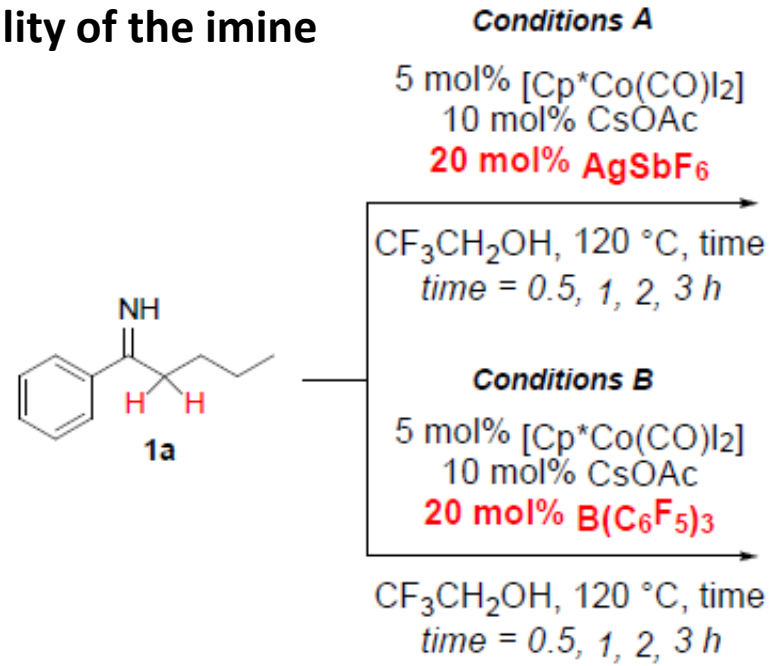

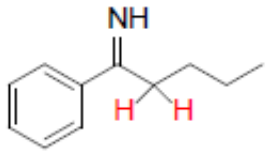

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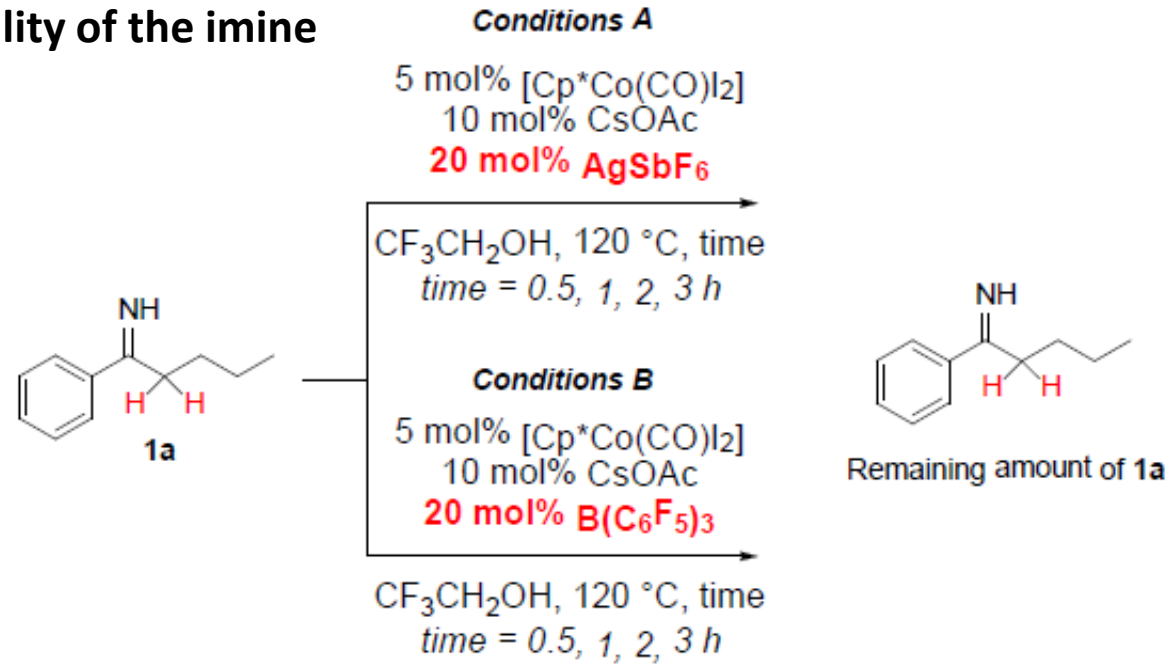

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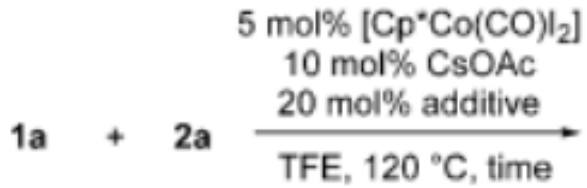


(1)

time	10 min	20 min	40 min	80 min
with $B(C_6F_5)_3$/yield[a]	**15%**	**32%**	**38%**	**43%**
with $AgSbF_6$/yield[a]	9 %	16 %	18 %	27 %

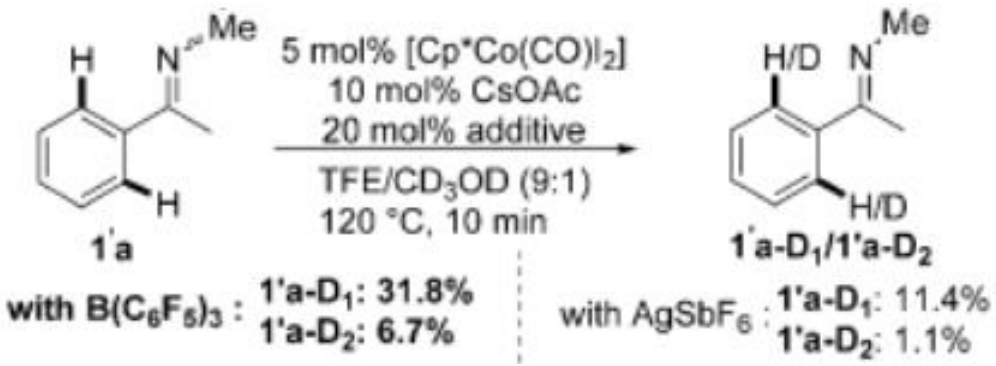
[a] ^{1}H NMR yield

Significant Rate enhancement with $B(C_6F_5)_3$

High reactivity and **role of $B(C_6F_5)_3$** of are **still ambiguous**

Reaction study

Deuterium incorporation



Better deuterium incorporation with $B(C_6F_5)_3$ than $AgSbF_6$
32% under optimized conditions

C-H activation is **reversible**

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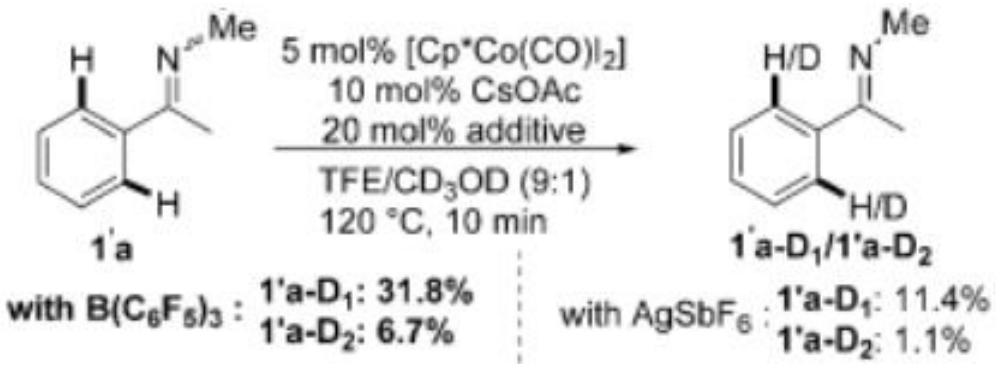

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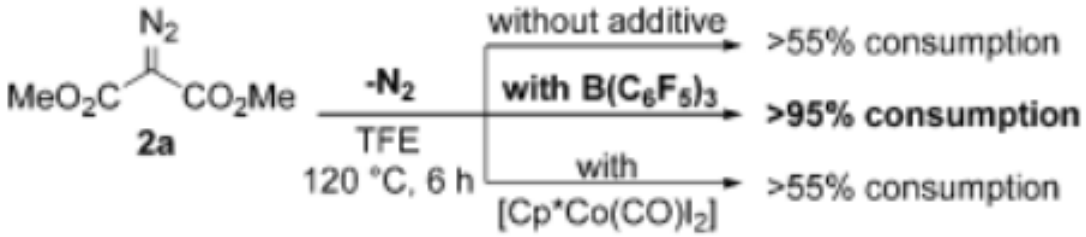
Diazo decomposition

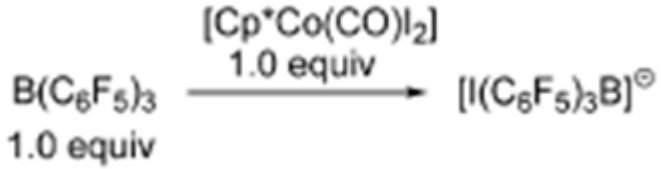


Decomposition of **diazo compound / Formation** of the **carbene**

Accelerated with **$B(C_6F_5)_3$**

Reaction study

Abstraction of iodide from the Co cat.



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Iodide abstraction from the Co cat.
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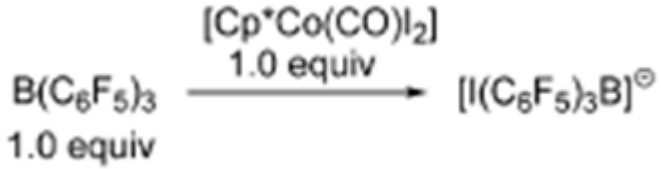

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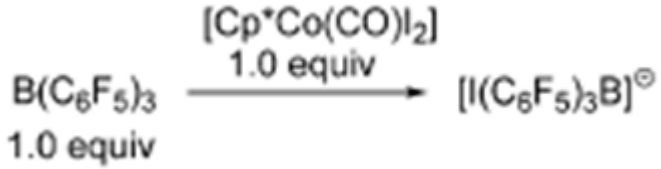

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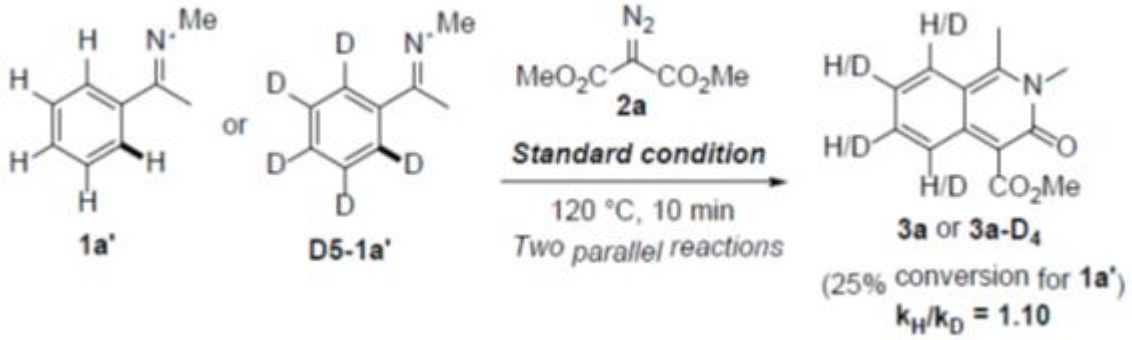

k_H / k_D = 1.1

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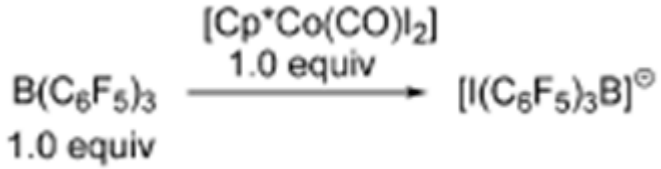

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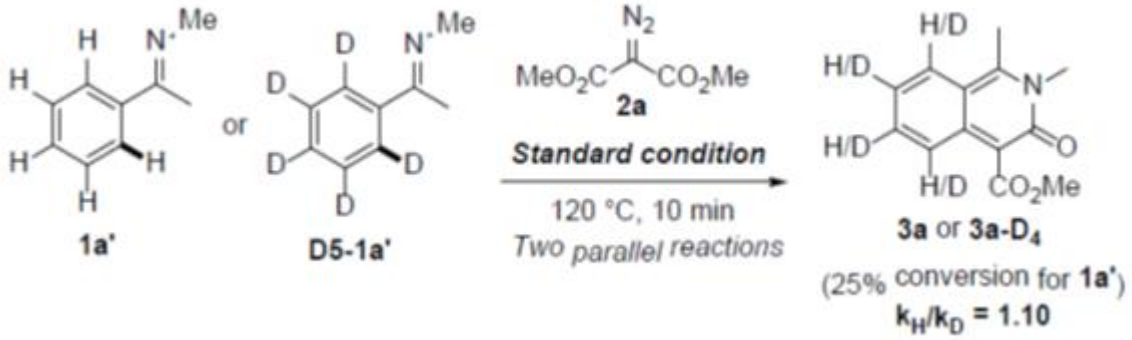
Kinetic isotopic effects

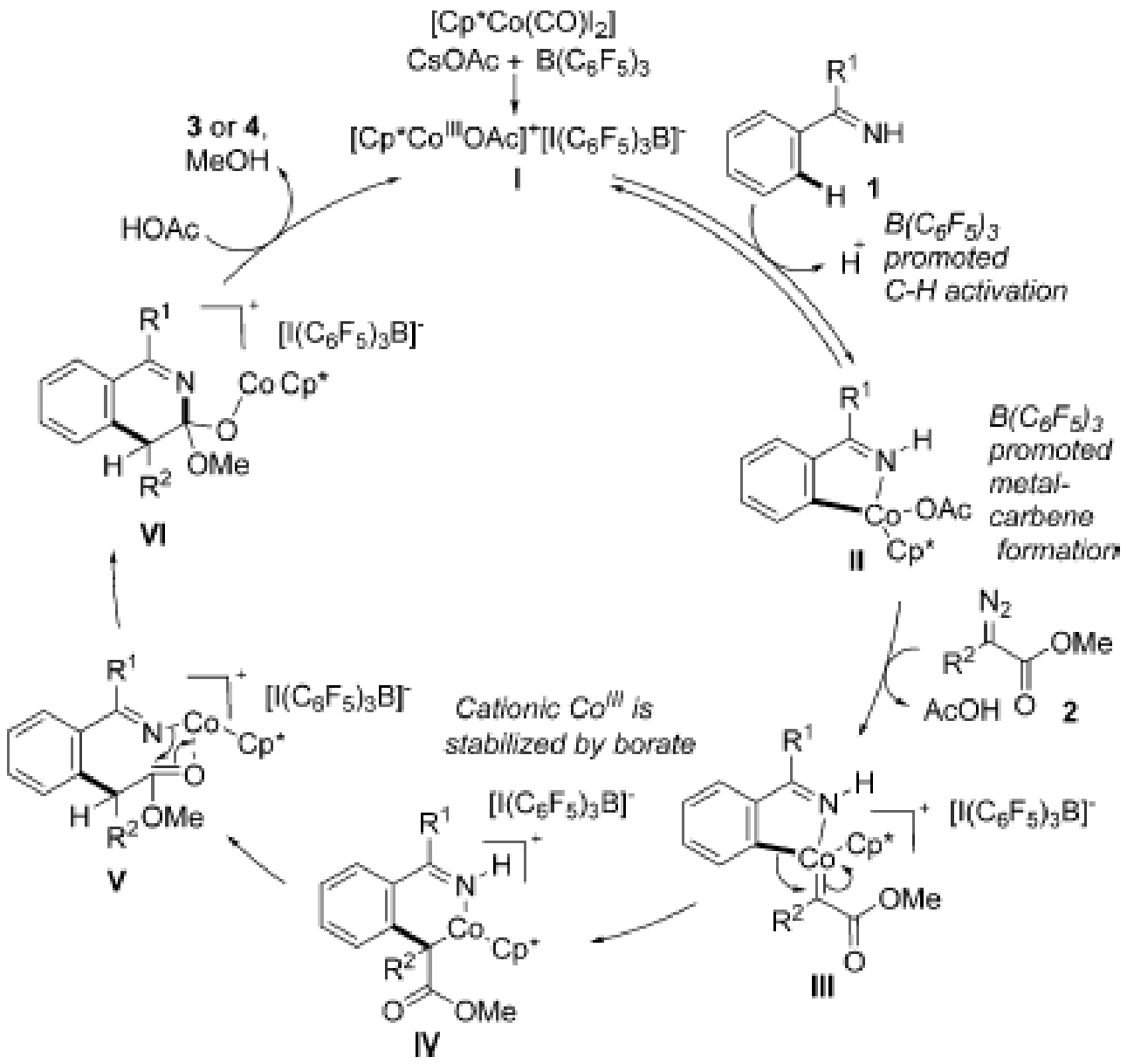


k_H / k_D = 1.1

Conclusion: CH bond cleavage is likely not the **rate determining step**

Mechanism

1) **Active cationic Co^{III}** is generated



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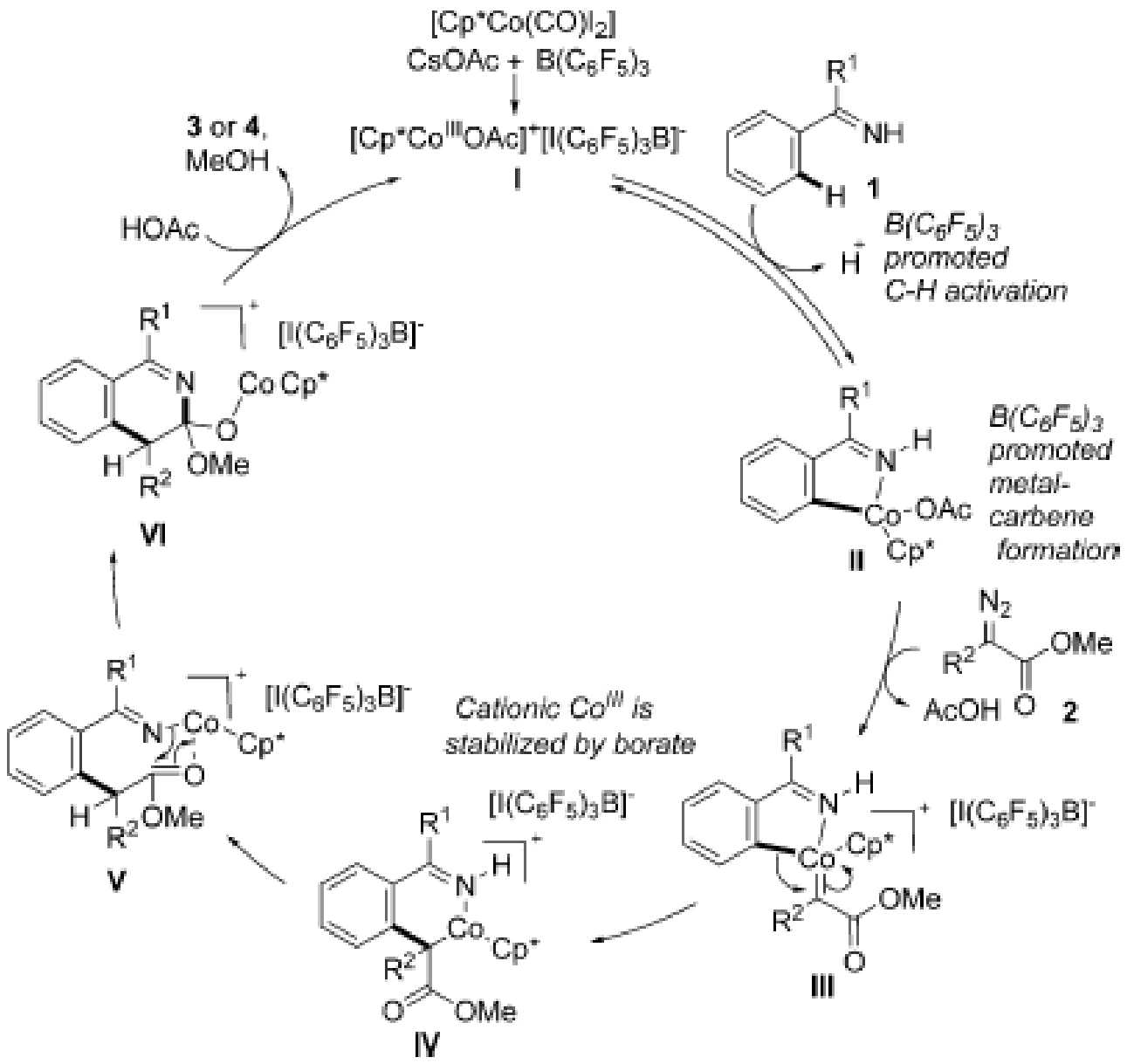

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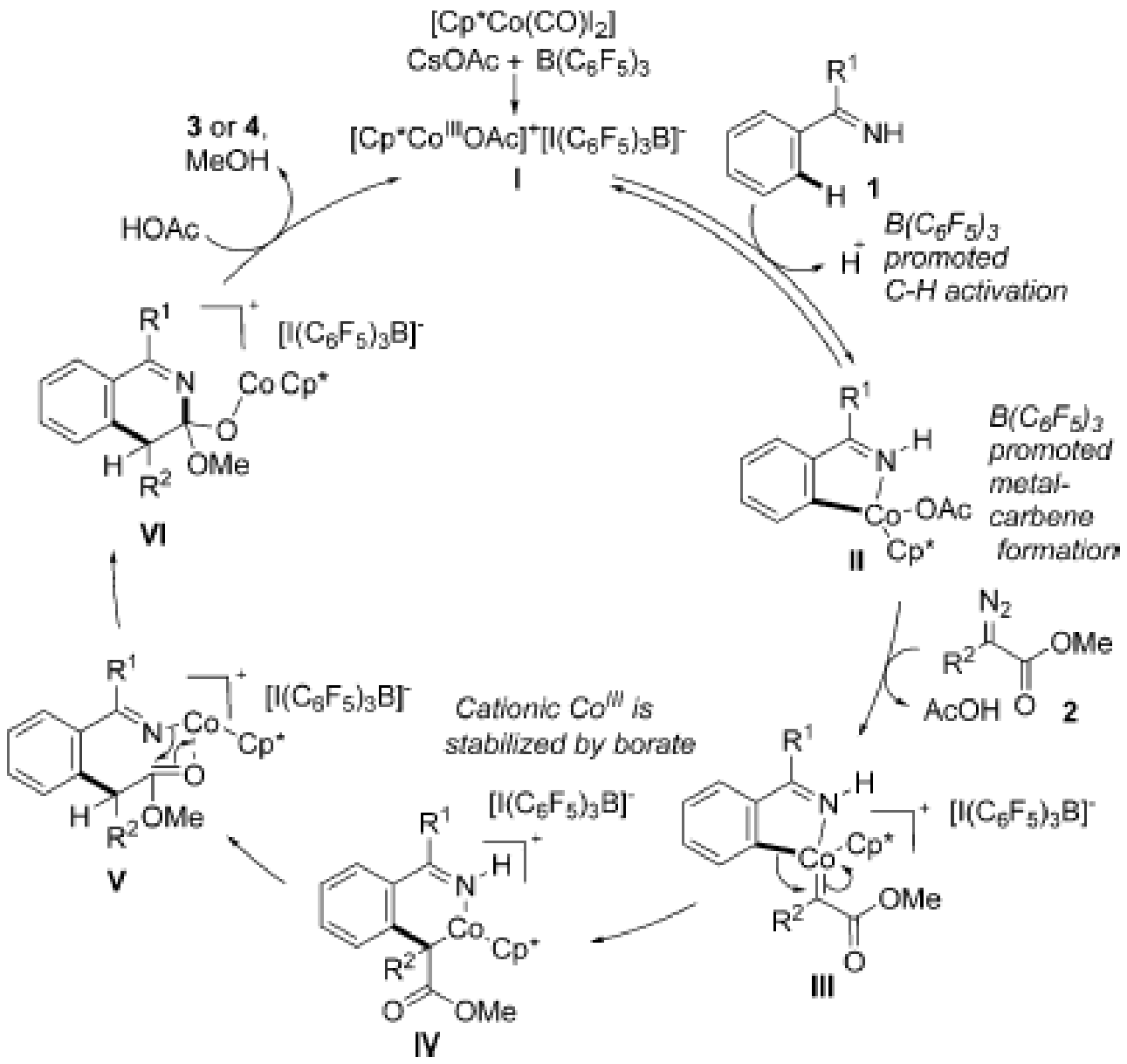

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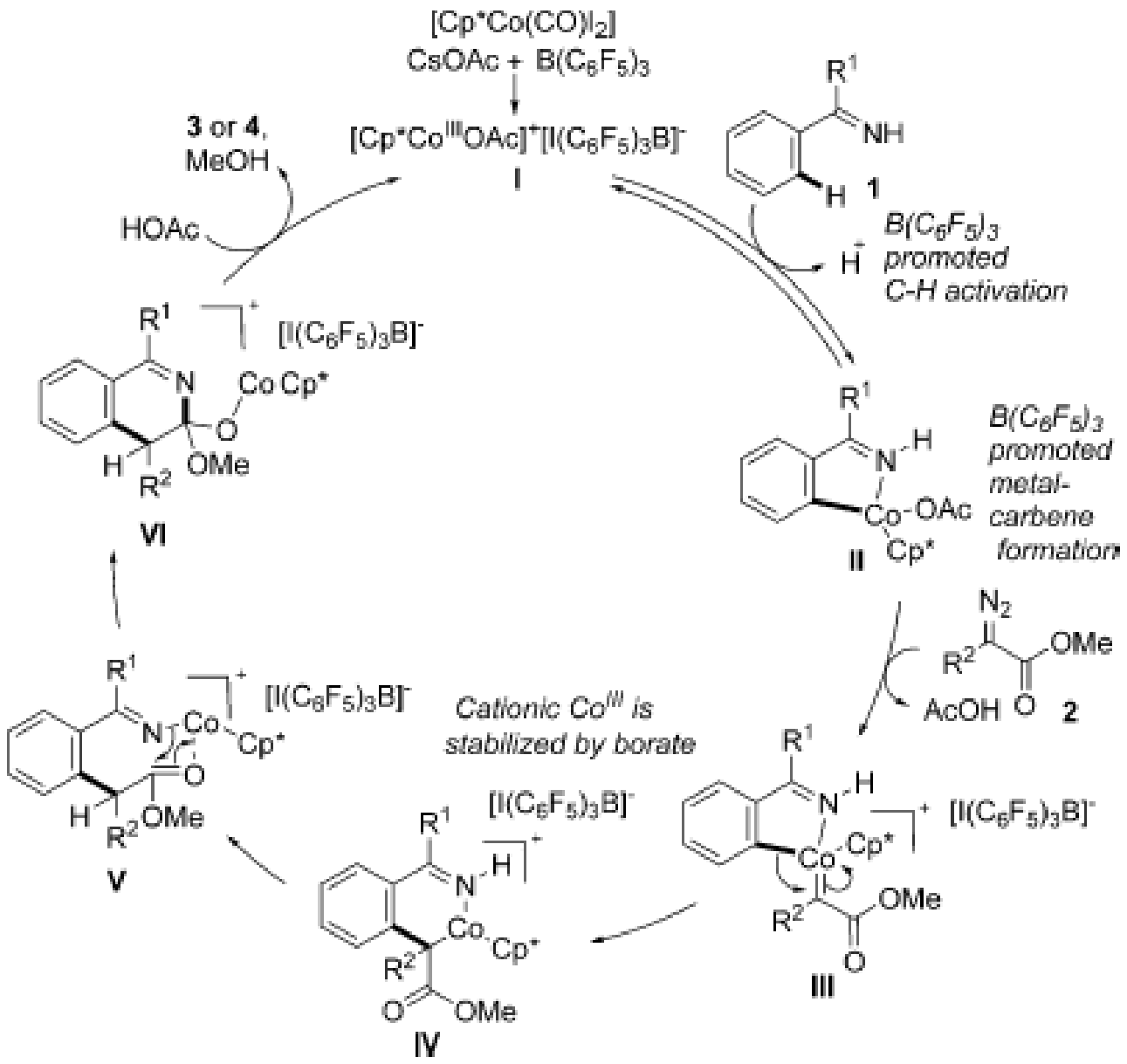

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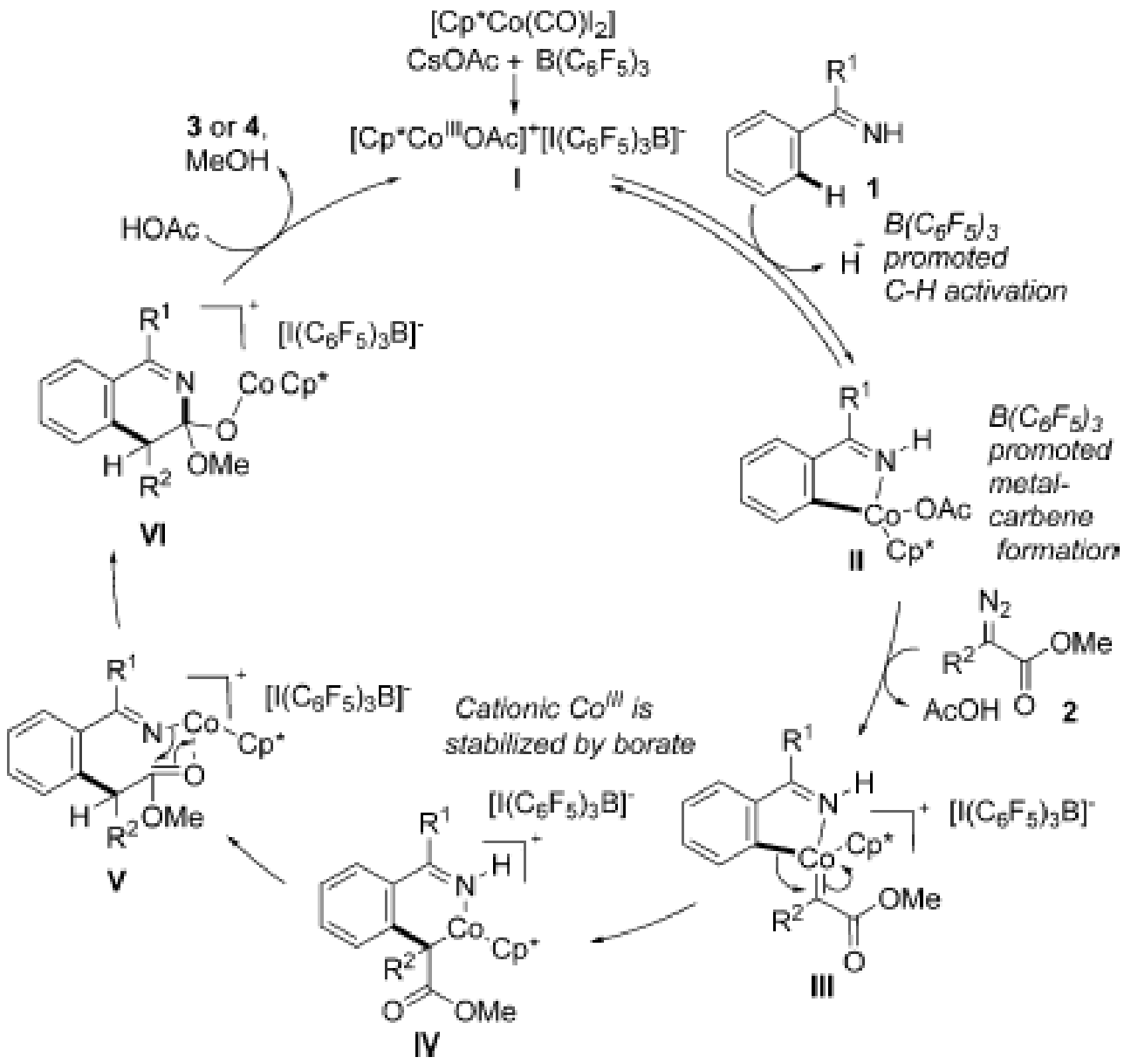

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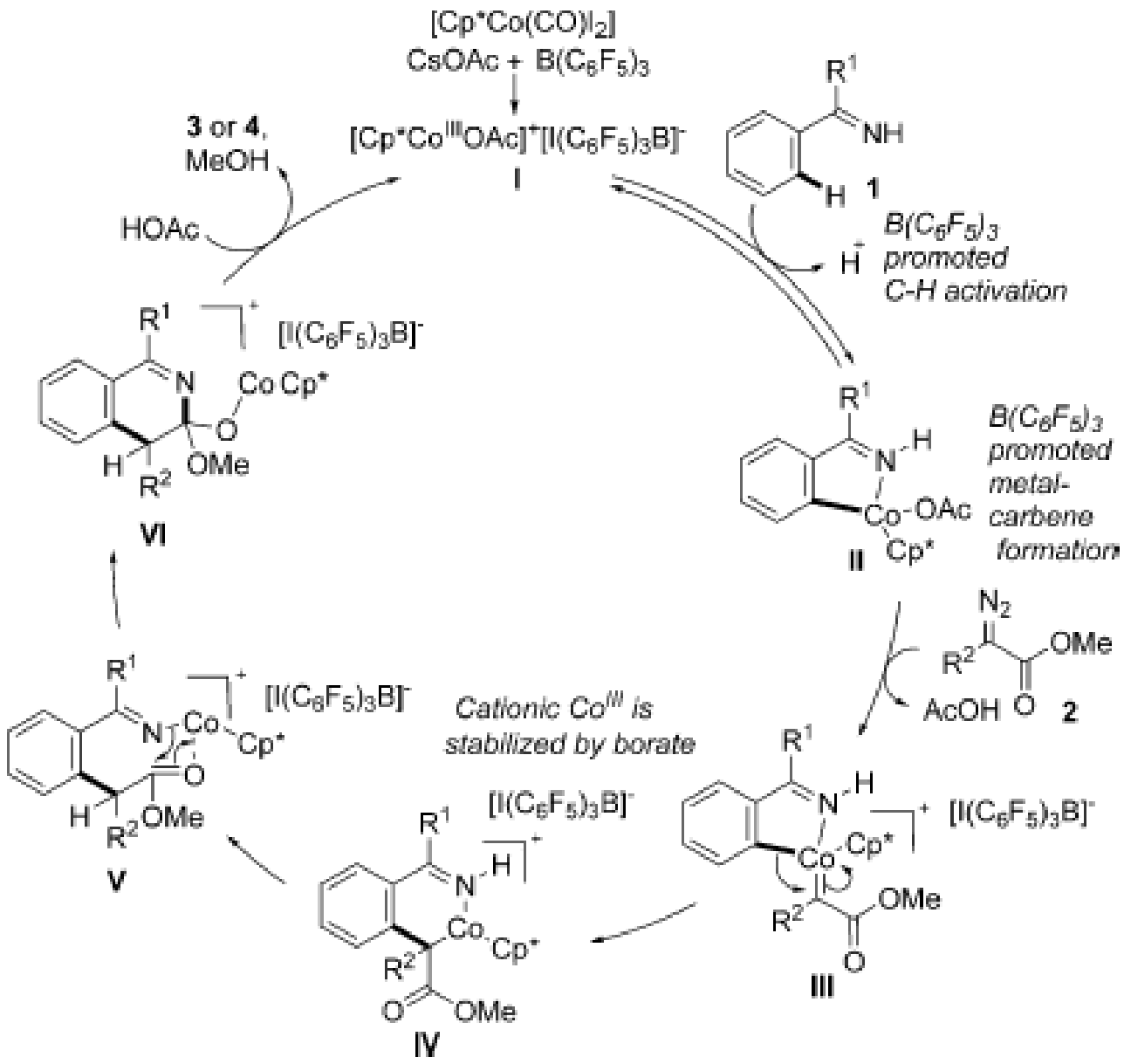

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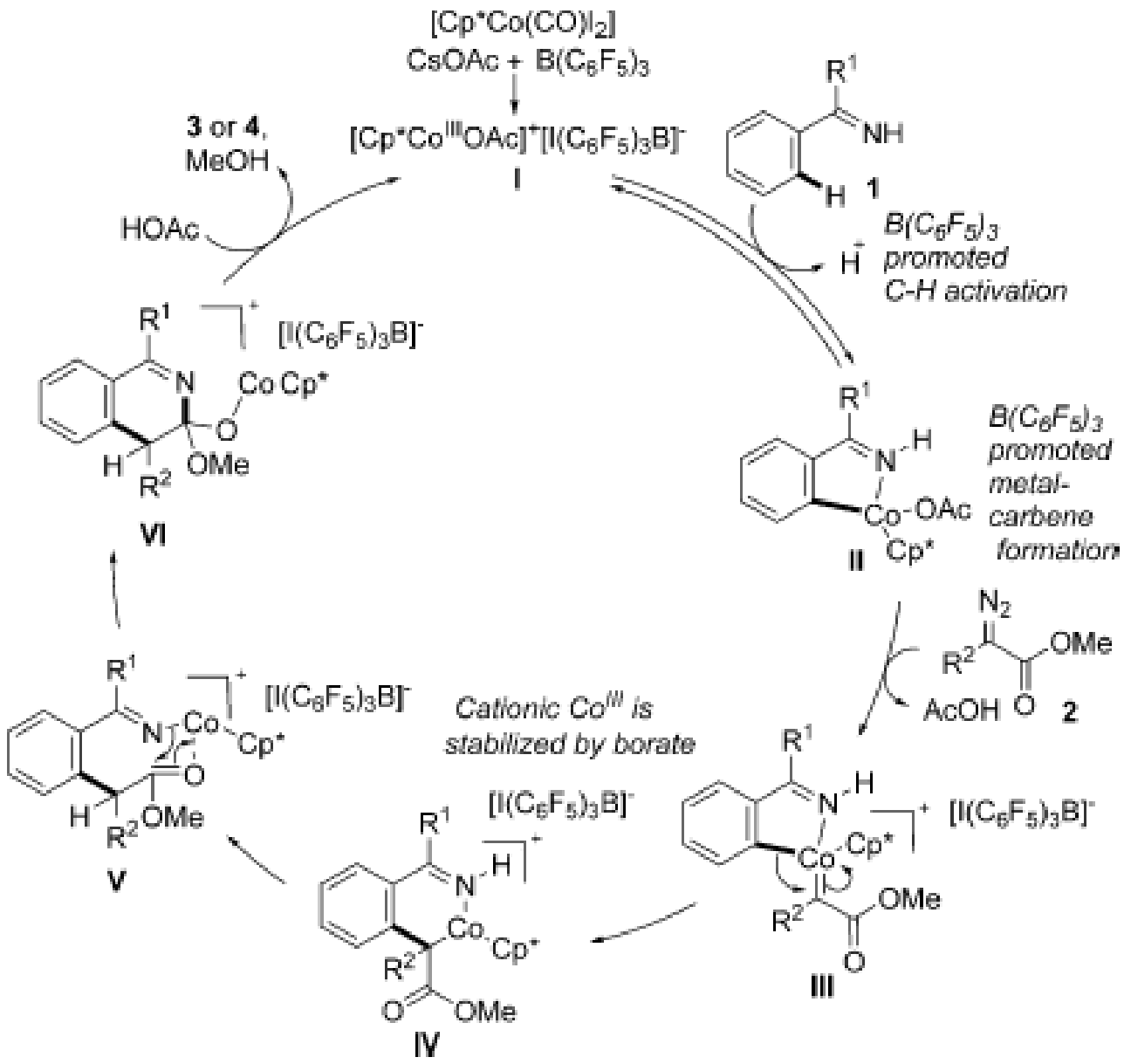
7) **Elimination of the methoxy** and **proton transfert**



Conclusion

Development of a **Co^{III} catalyzed C-H activation** of **imines** with diazo compounds

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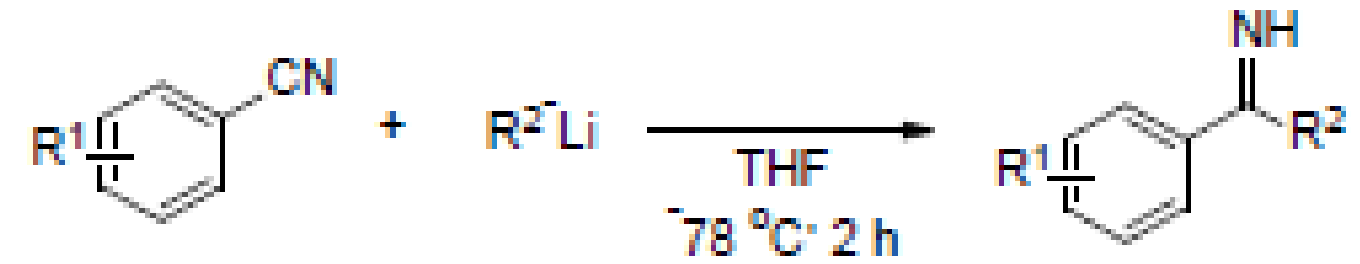
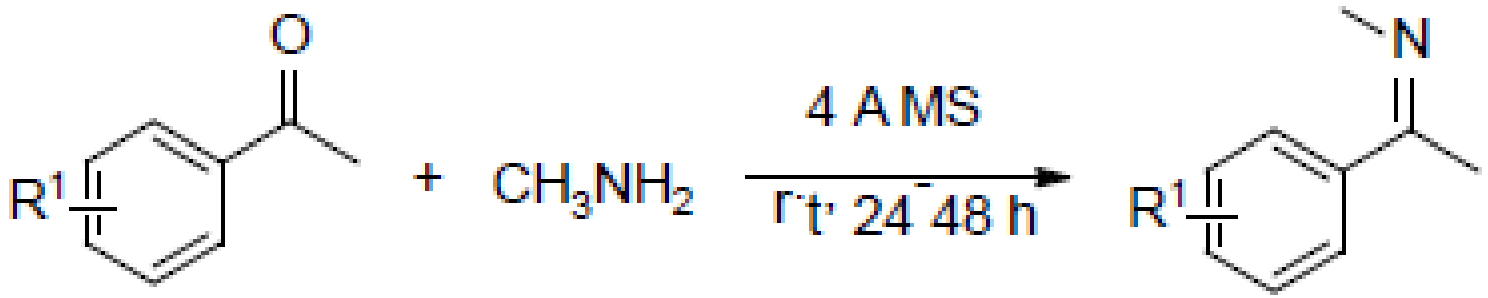
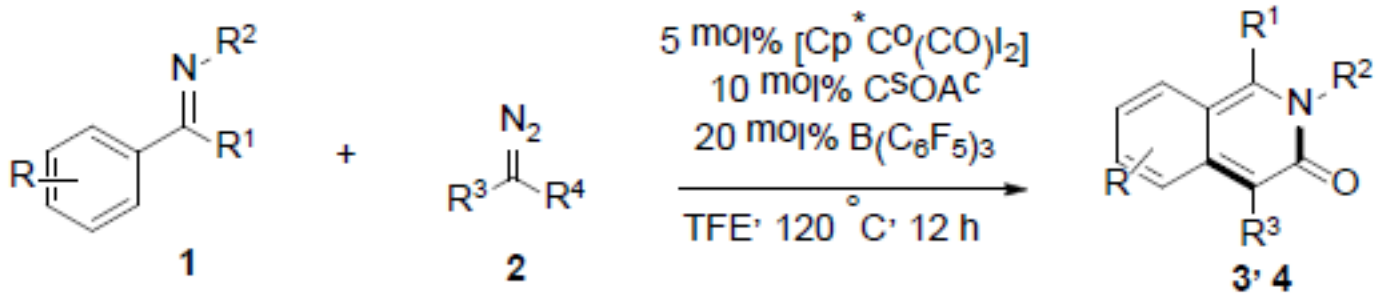
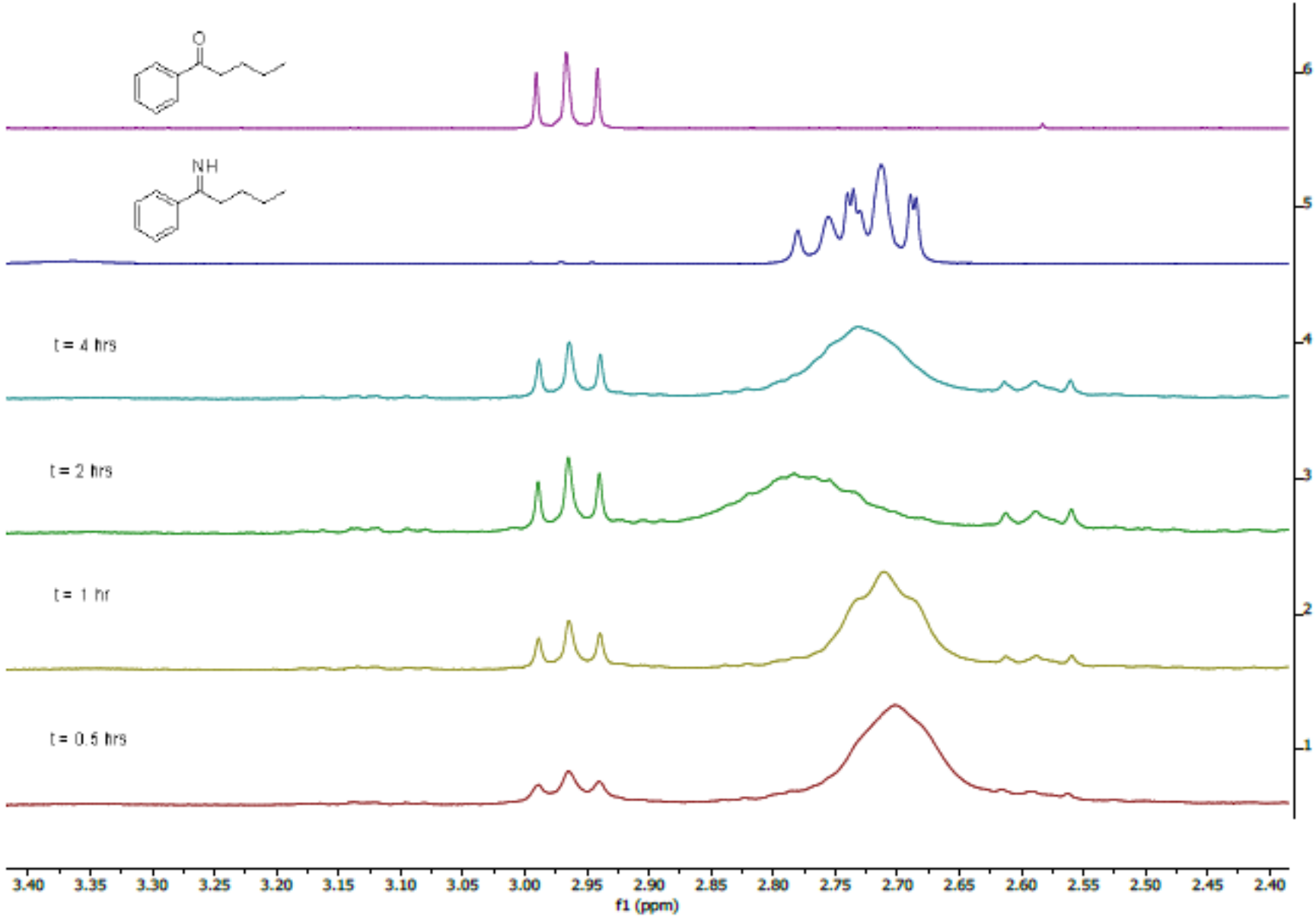
This **newly developed** Co^{III}/ $B(C_6F_5)_3$ cooperative catalytic system could **allow new transformations**


CN
R1
+
R2Li
THF
-78 °C, 2 h
NH
R2
R1


O
R1
+
CH3NH2
4 A MS
rt, 24-48 h
N
R1



An oven dried screw-capped vial was evacuated and flushed with argon three times and then evacuated and transferred to the glovebox. Tris(pentafluorophenyl)borane (0.04 mmol, 5.0 mol%) and cesium acetate (0.02 mmol, 10.0 mol%) were added. The vial was transferred to the fume hood and connected to the argon atmosphere. [Cp*Co(CO)I_2] (0.01 mmol, 5.0 mol%), imines **1** (0.2 mmol, 1.0 equiv), diazo compounds **2** (0.3 mmol, 1.5 eq.) and degassed anhydrous TFE (1.0 mL) were added under an argon atmosphere. The resulting mixture was sealed with a Teflon-lined cap and stirred at 120 °C for 12 h.


O
NH
t = 4 hrs
t = 2 hrs
t = 1 hr
t = 0.5 hrs
6
5
4
3
2
1
3.40 3.35 3.30 3.25 3.20 3.15 3.10 3.05 3.00 2.95 2.90 2.85 2.80 2.75 2.70 2.65 2.60 2.55 2.50 2.45 2.40
f1 (ppm)