Literature Report

Silver-Catalyzed Substrate Controlled C-N Formation Reactions of Triflic Amides

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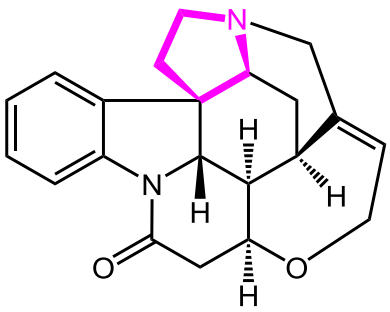
Date : 2015-12-15

Shi, Z.-J. *et al*.
J. Am. Chem. Soc. **2015**, *137*, 14586.

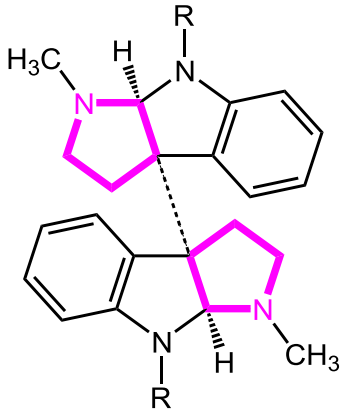
Peking University

Contents

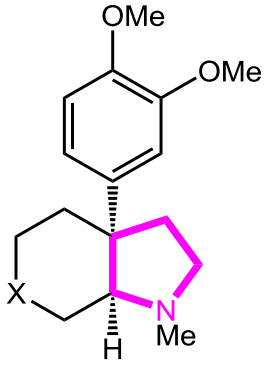
Pyrroline Structural Active Compounds



Strychnine



R = H, (+)-Chimonanthine
R = Me, (+)-Folicanthine



X = CO, (-)-Mesembrine
X = CH_2, Mesembrane

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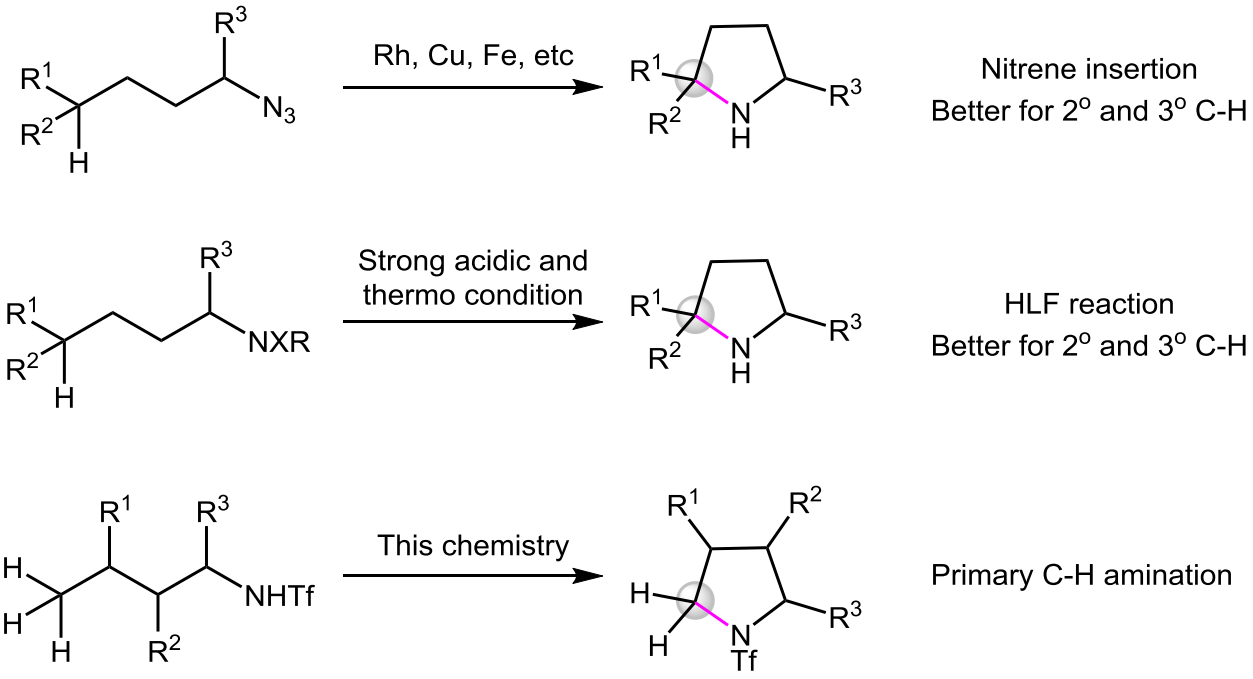
Synthetic Methods To Pyrroline Architectures



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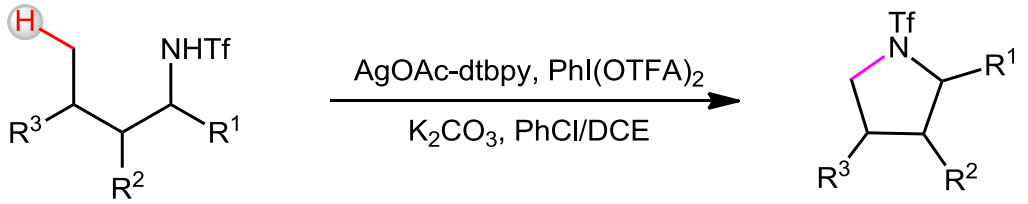
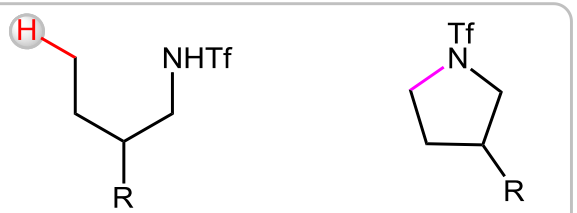
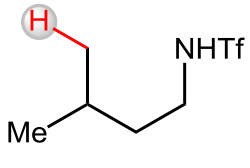
Direct Amination of Unacivated C-H Bonds



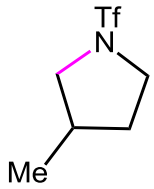


1a (R = Me)
1b (R = Et)

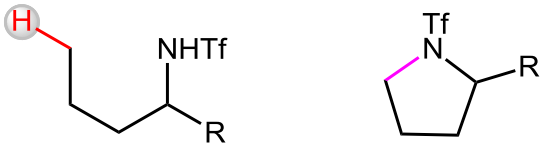
2a 70%
2b 66%



1f

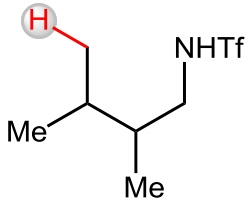


2f 52%

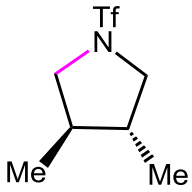


1c (R = Me)
1d (R = ^{n}Pr)
1e (R = Ph)

2c 57%
2d 43%
2e 25%

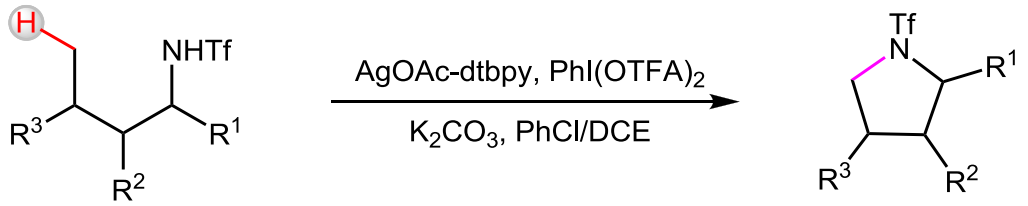


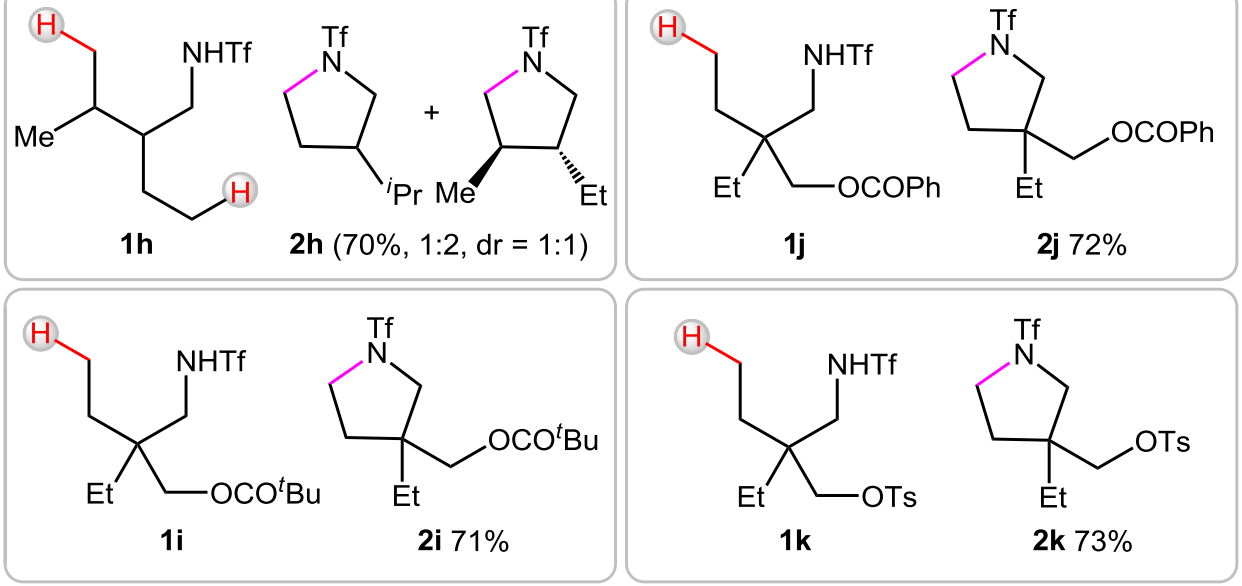
1g



2g, 66%, dr = 86/14

Direct Amination of Unacivated C-H Bonds





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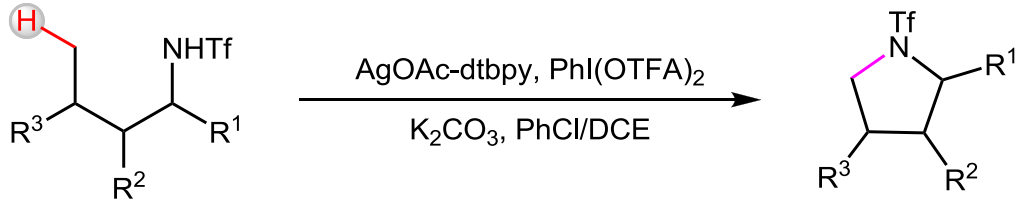
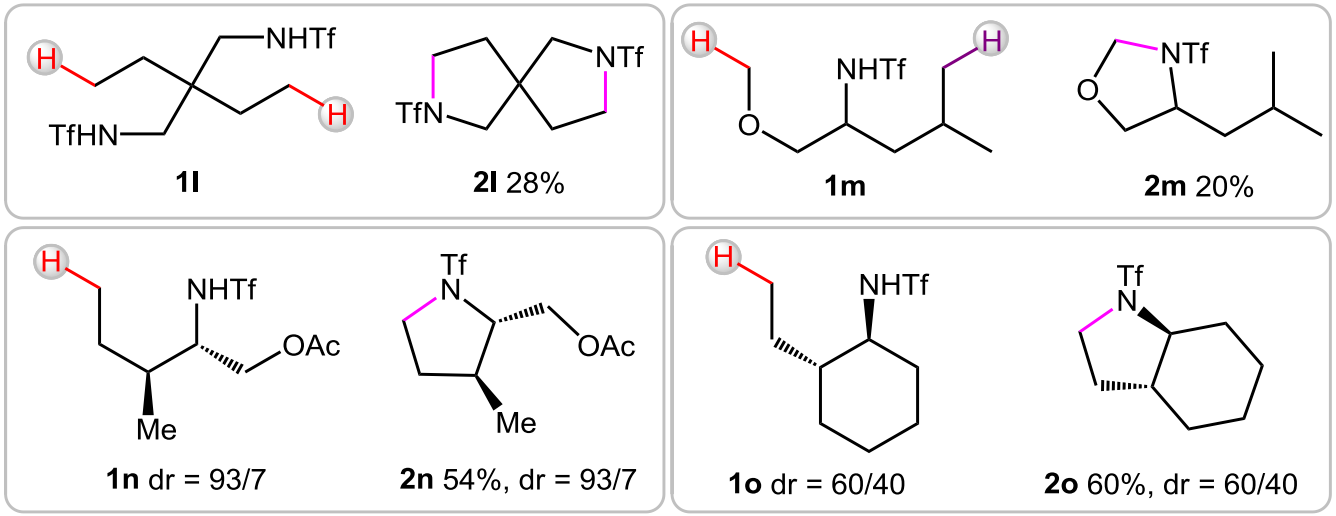
Direct Amination of Unacivated C-H Bonds





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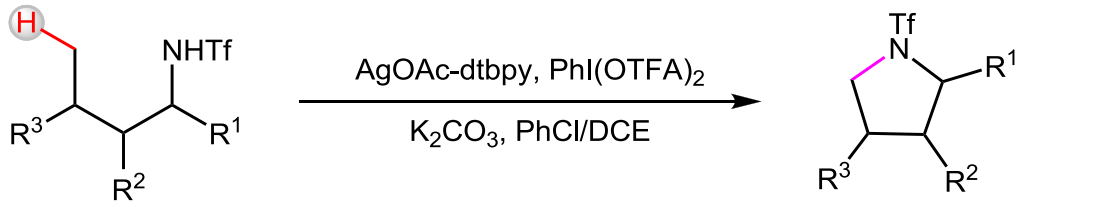
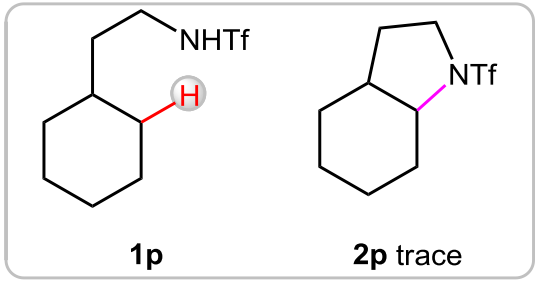
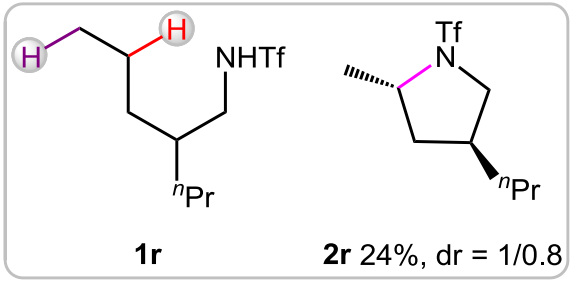
Direct Amination of Unacivated C-H Bonds

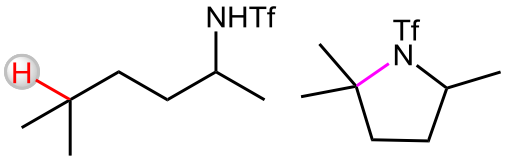




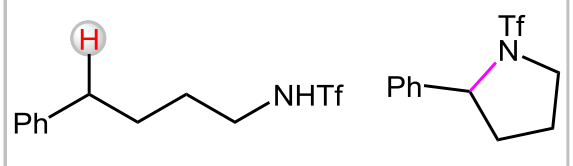
1p **2p** trace



1r **2r** 24%, dr = 1/0.8



1q **2q** trace



1s **2s** 65%

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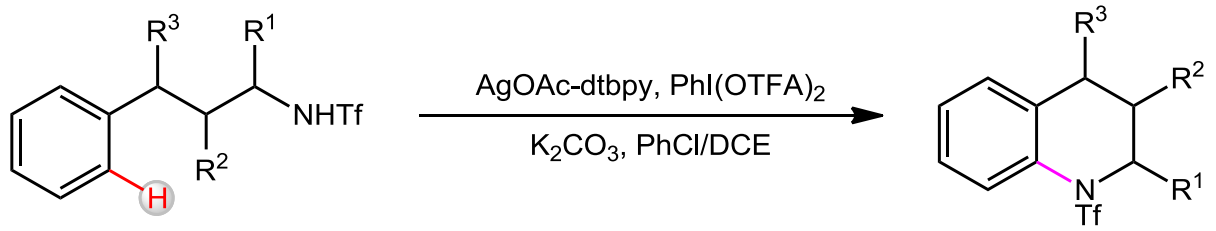
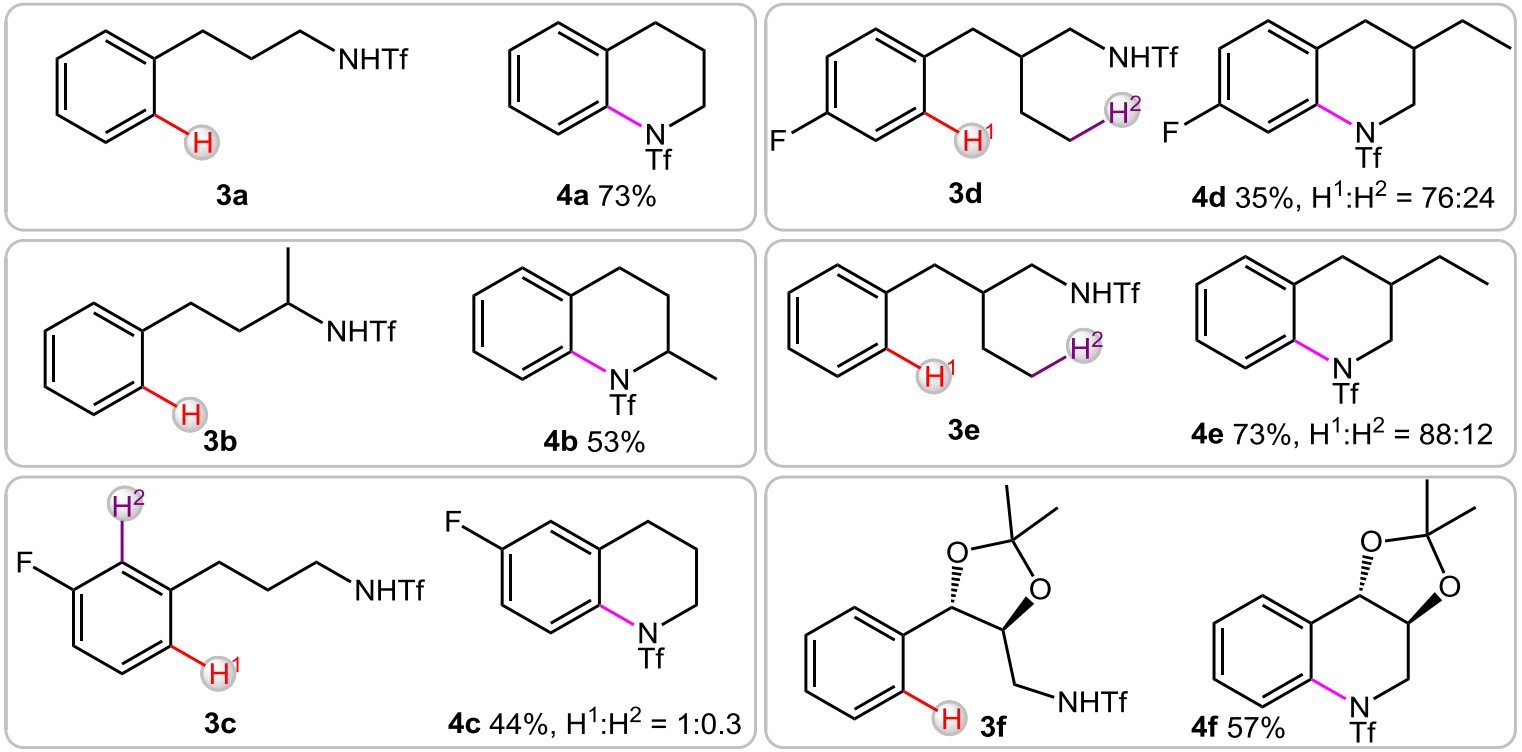
Direct Amination of Aromatic C-H Bonds





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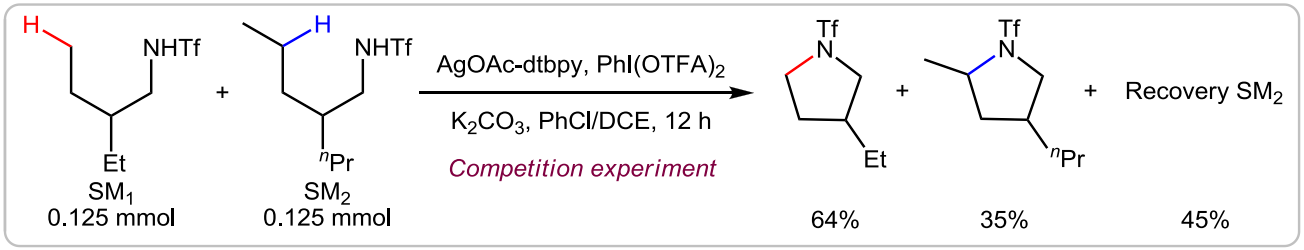
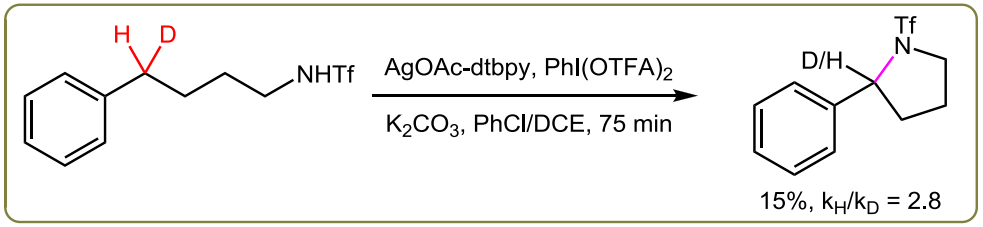
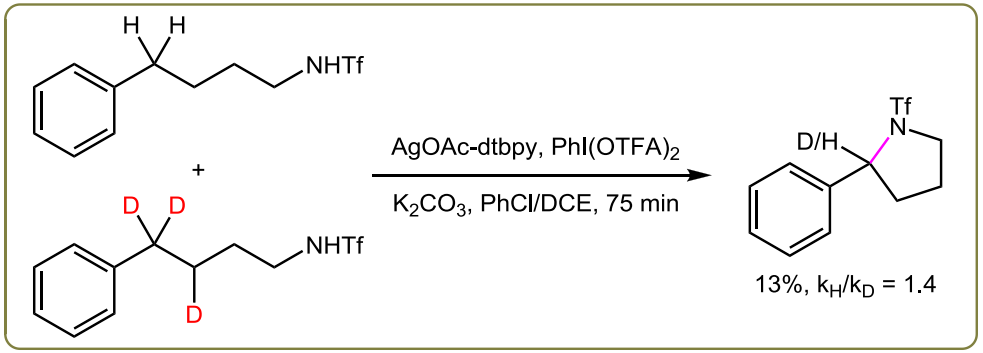
Competition Experiment and KIE





Kinetic Isotope Effect



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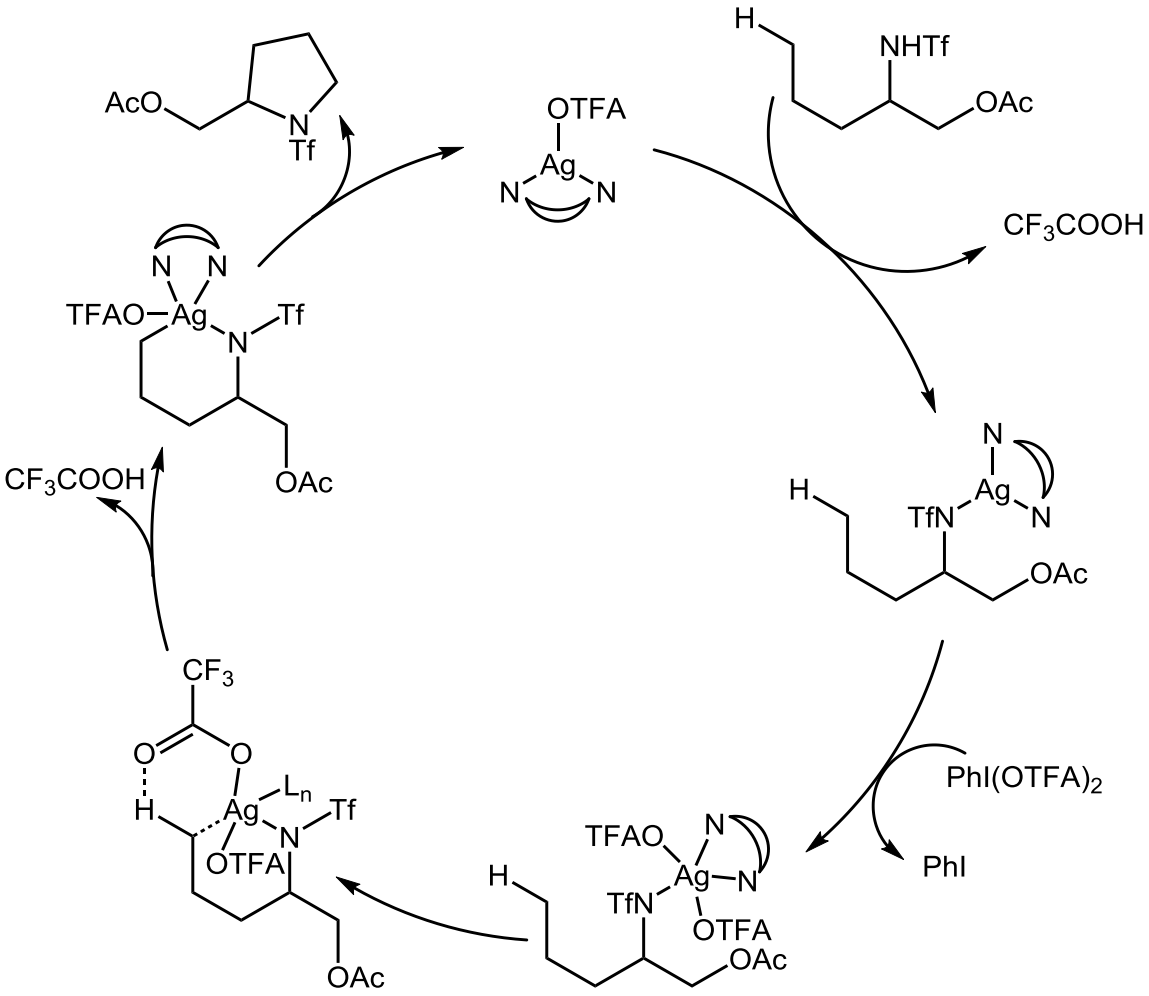
Proposed Catalytic Cycle



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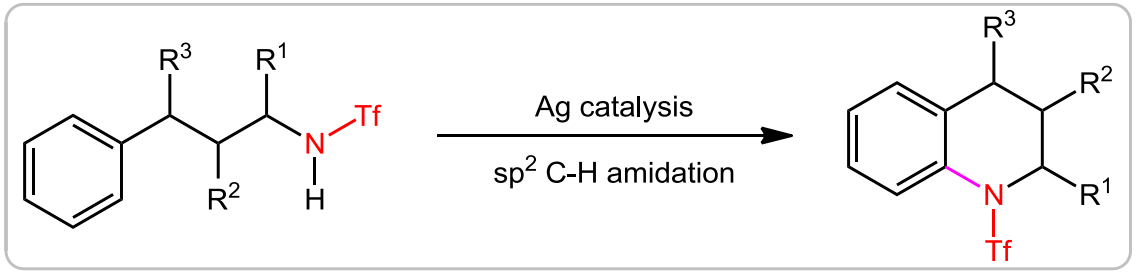
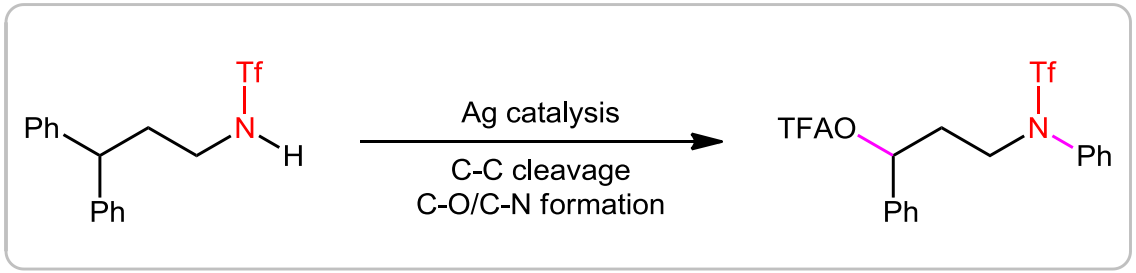
Different Chemistry of Triflic Amides

Previous work



Discovery



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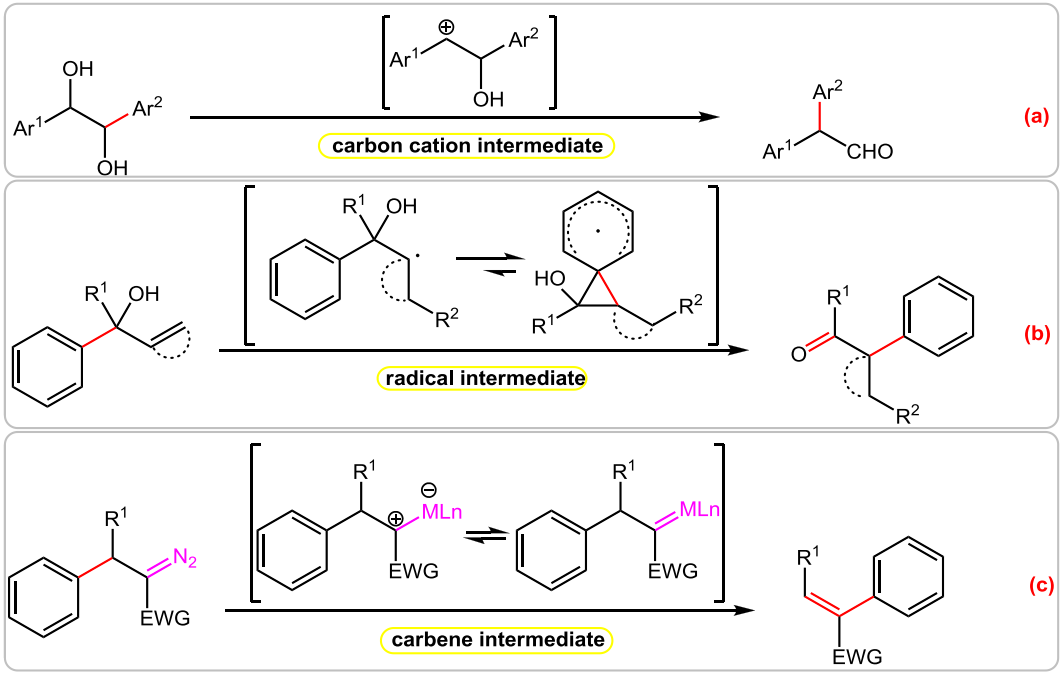
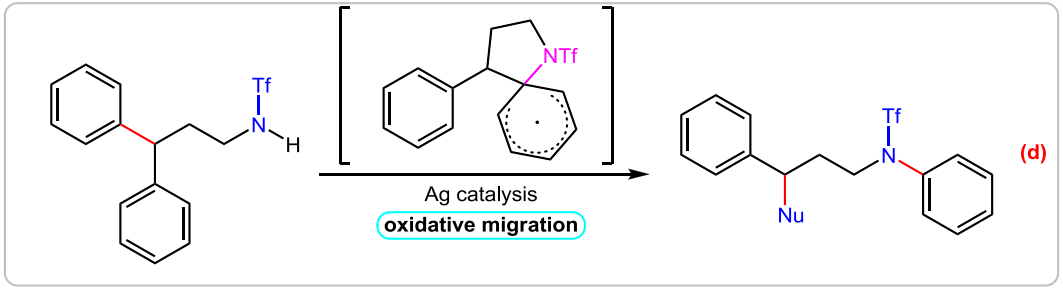
Long-Distance Aryl Migration

Previous Aryl Migration from Vicinal Carbon to Carbon



This work: Aryl Migration from Carbon Center to Nitrogen Center



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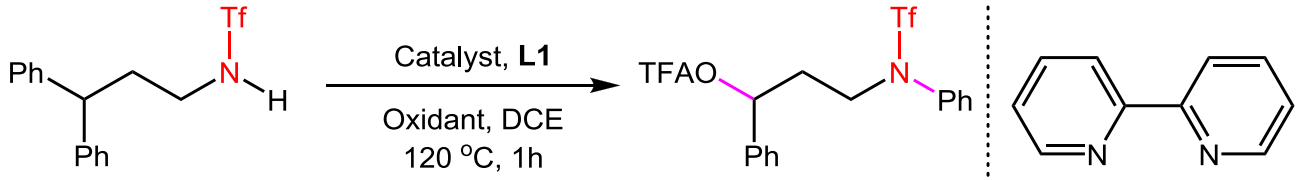
Optimization of Reaction Conditions



1a **2a** **L1**

Entry[a]	Catalyst	Oxidant	Yield (%)[b]
1	AgOAc	-	0
2	AgOAc	Oxone	0
3	AgOAc	$PhI(OAc)_2$	0
4	AgOAc	$K_2S_2O_8$	0
5	AgOAc	$PhI(OTFA)_2$	31
6	$Pd(OAc)_2$	$PhI(OTFA)_2$	Trace
7	CuOAc	$PhI(OTFA)_2$	0
8	AuCl	$PhI(OTFA)_2$	0
9	Ag_2O	$PhI(OTFA)_2$	29
10	$AgNO_3$	$PhI(OTFA)_2$	17
11	Ag_2CO_3	$PhI(OTFA)_2$	28

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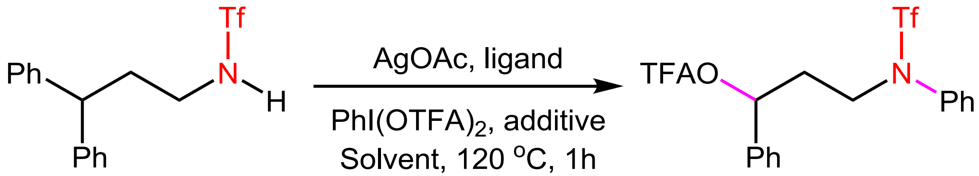
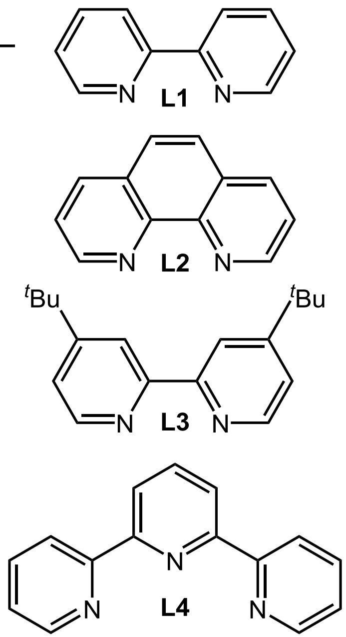
Optimization of Reaction Conditions



Entry[a]	Ligand	Additive	Solvent	Yield (%)[b]
12	**L2**	-	DCE	37
13	**L3**	-	DCE	38
14	**L4**	-	DCE	21
15	**L3**	Cs_2CO_3	DCE	12
16	**L3**	KO*t*Bu	DCE	36
17	**L3**	Li_2CO_3	DCE	60
18	**L3**	K_2CO_3	DCE	65
19	**L3**	K_2CO_3	DCE/PhCl	75



[a] Reaction condtions: substrate (0.1 mmol), catalyst (20 mol%), ligand (20 mol%), oxidant (2.0 equiv.), additive (2.0 equiv.), DCE (2.0 mL), 120 °C, 1 h. [b] The yield was determined by ^{1}H NMR of the crude reaction mixture with CH_2Br_2 as internal standard.

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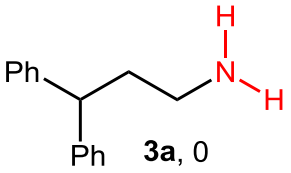
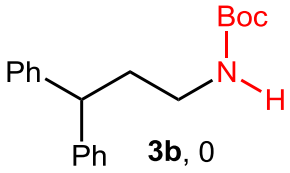
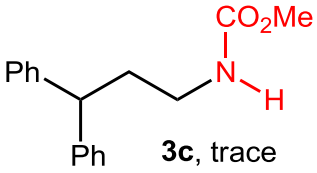
Evaluating Different Amides



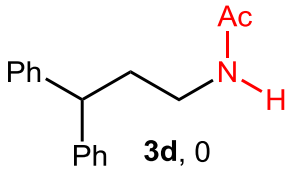
3a, 0



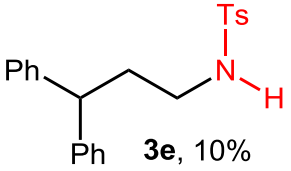
3b, 0



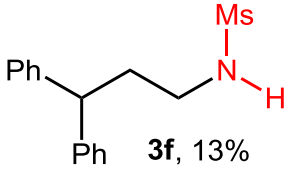
3c, trace



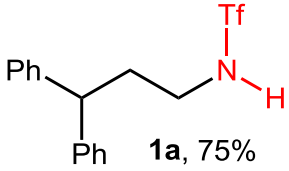
3d, 0



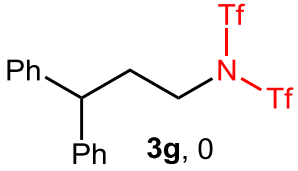
3e, 10%



3f, 13%



1a, 75%



3g, 0

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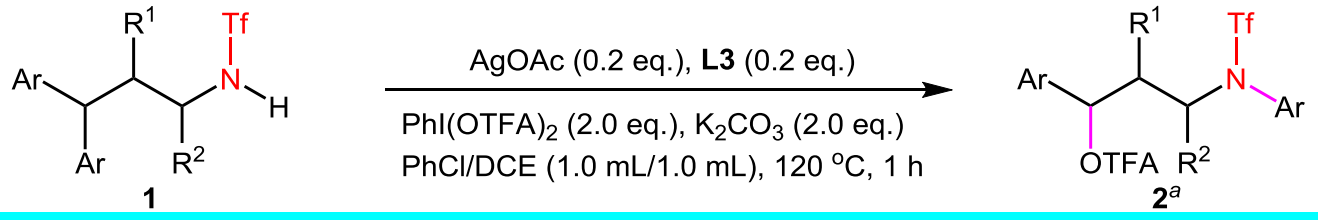
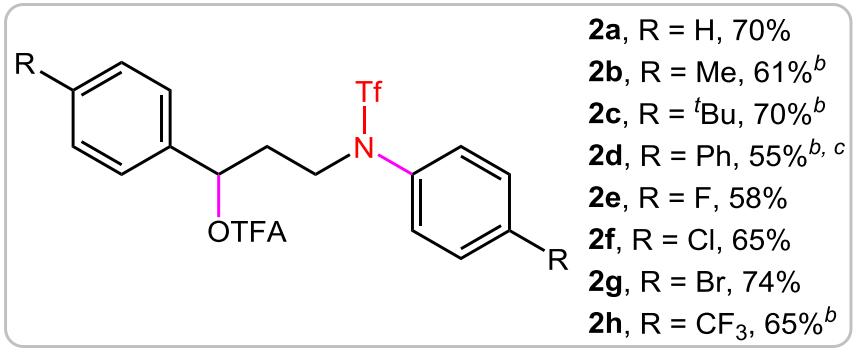
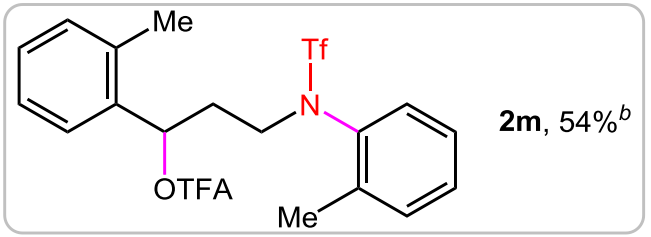
Ag-Catalyzed Aryl Migration

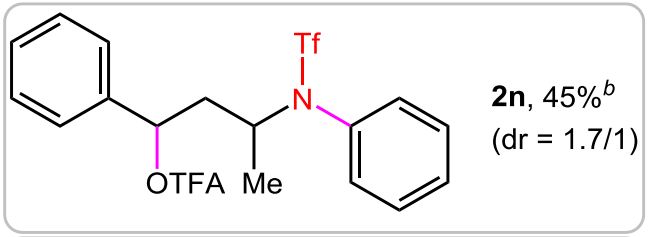




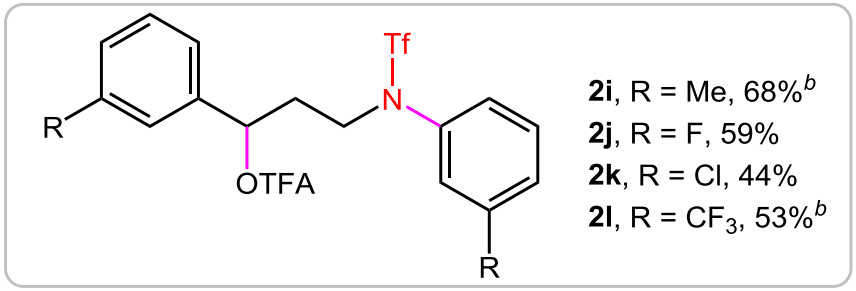
2a, R = H, 70%
2b, R = Me, 61%[b]
2c, R = ^{t}Bu, 70%[b]
2d, R = Ph, 55%[b, c]
2e, R = F, 58%
2f, R = Cl, 65%
2g, R = Br, 74%
2h, R = CF_3, 65%[b]



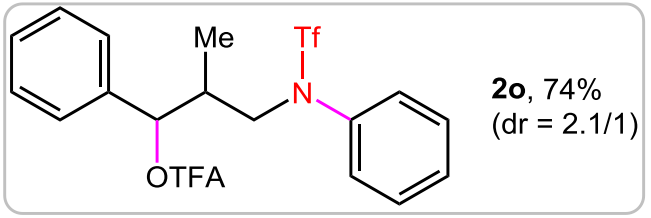
2m, 54%[b]



2n, 45%[b]
(dr = 1.7/1)



2i, R = Me, 68%[b]
2j, R = F, 59%
2k, R = Cl, 44%
2l, R = CF_3, 53%[b]



2o, 74%
(dr = 2.1/1)

[a] Yields of isolated products. [b] Yields of isolated corresponding alcoholysis products, which were easily formed upon purification by flash column chromatography (silica gel). [c] 120 °C, 10 h.

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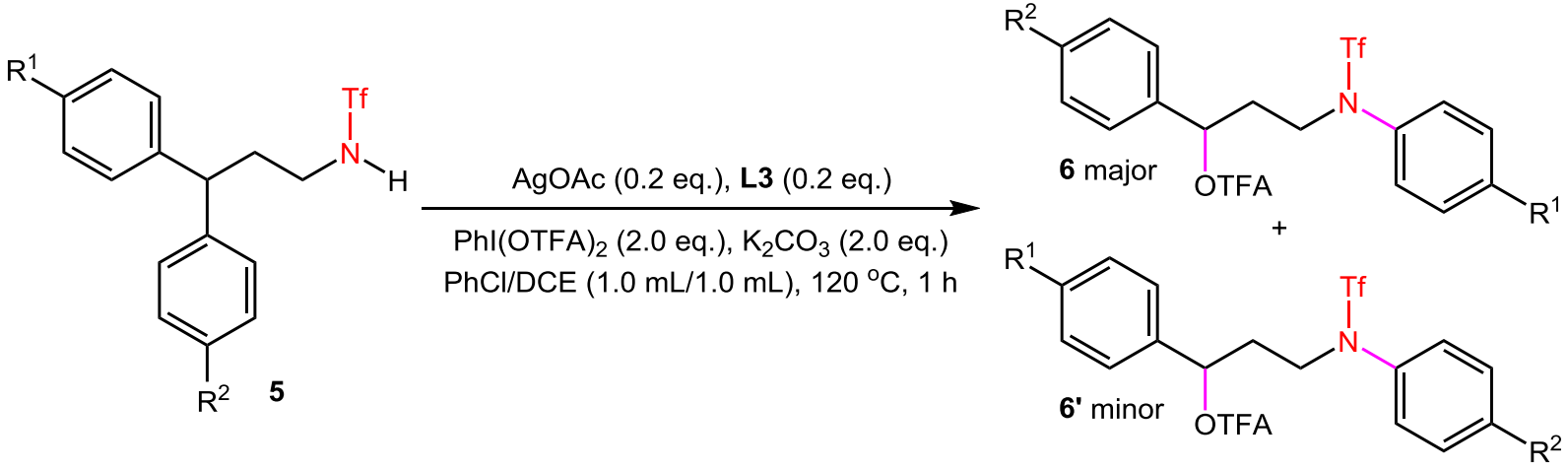
Ag-Catalyzed Aryl Migration



Entry	Substrate	R^1	R^2	Major migrating group	Yield (%)	Ratio (%)[c]
1	**5a**	H	Cl	Ph	65[a]	1.4/1
2	**5b**	H	CF_3	Ph	49[a, b]	5.9/1
3	**5c**	Me	CF_3	4-MeC_6H_4	58[a, b]	25/1
4	**5d**	^{t}Bu	CF_3	4-^{t}BuC_6H_4	51[b]	-
5	**5e**	^{t}Bu	Cl	4-^{t}BuC_6H_4	71[a, b]	3.4/1
6	**5f**	^{t}Bu	H	4-^{t}BuC_6H_4	74[a]	4.5/1

[a] Total yields of two isomers. [b] Yields of isolated corresponding alcoholysis products, which were easily formed upon purification by flash column chromatography (silica gel). [c] The ratio of the isomers was determined by ^1H or ^{19}F NMR of the crude reaction mixture.

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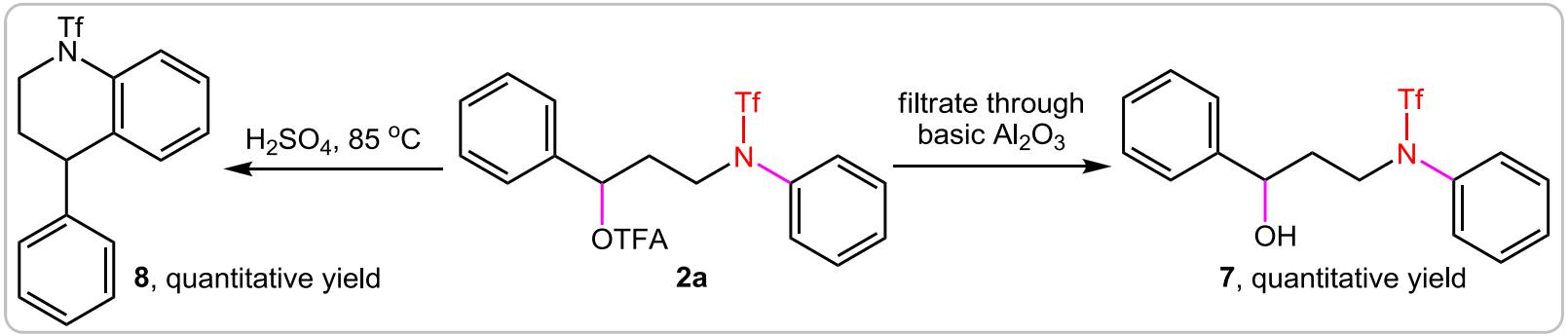
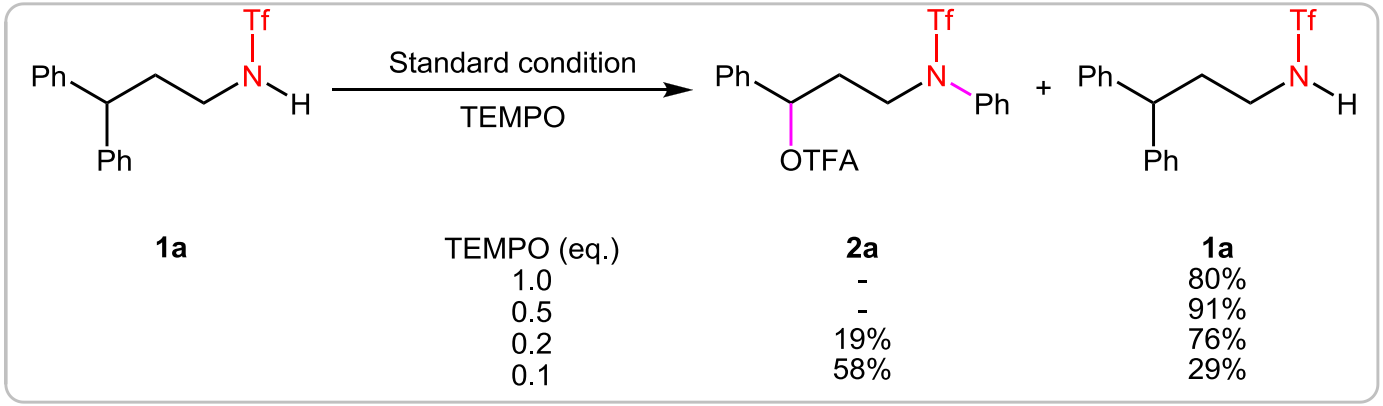
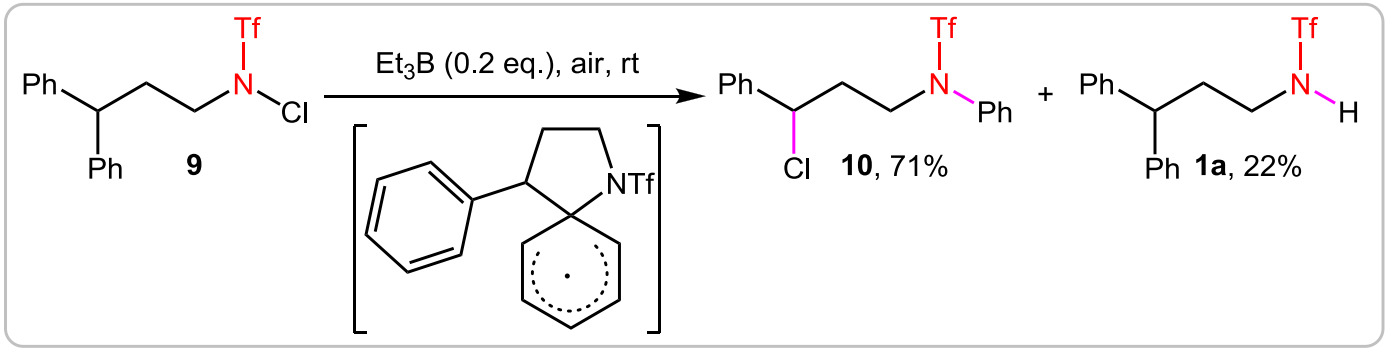
Alcoholysis and Cyclization and Control Experiments





TEMPO (eq.)	2a	1a
1.0	-	80%
0.5	-	91%
0.2	19%	76%
0.1	58%	29%



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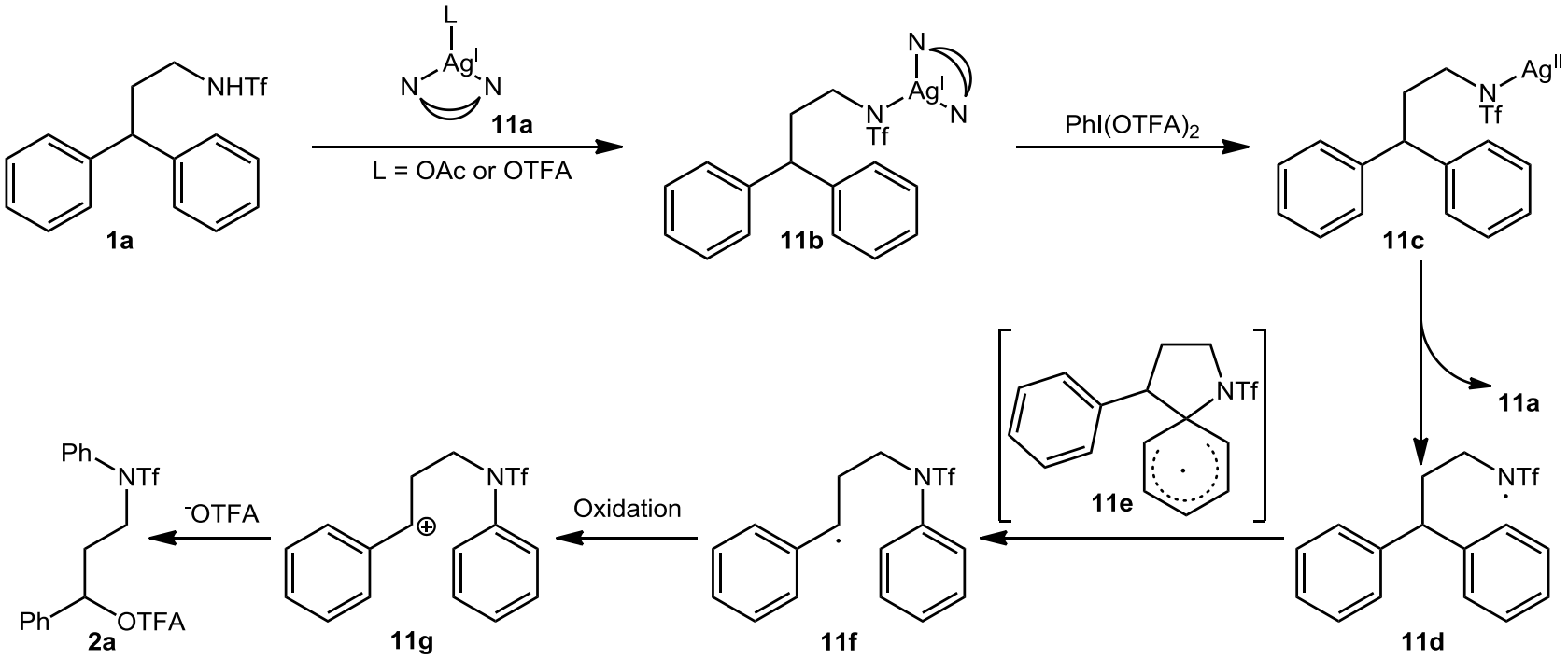
Proposed Mechanism



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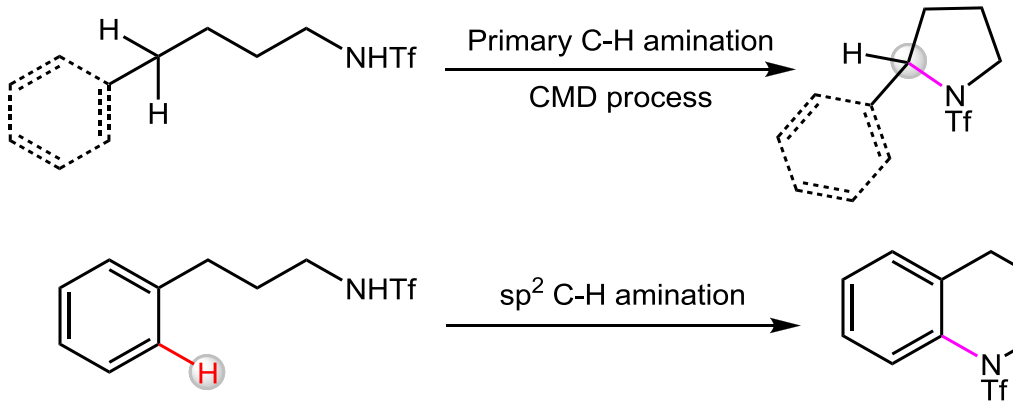
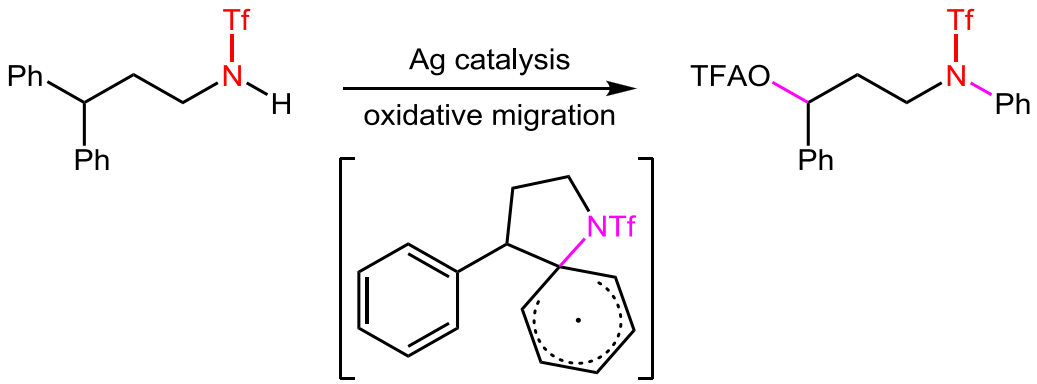
Summary





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Selective C−C bond activation/cleavage has attracted much attention in recent years. Not only is it one of the most challenging themes in fundamental organic chemistry, but it also represents a powerful, straightforward, and atom-economic strategy for constructing new organic compounds through a completely new pathway based on reorganization of the skeletons of easily available compounds, differentiating it from conventional organic syntheses. During the past few decades, many achievements in transition-metal-catalyzed C−C cleavage have been made, starting from strained and unstrained compounds. In the absence of transition metal catalysts, C−C could be cleaved and transformed through radical and cationic intermediates. Among different strategies to approach direct C−C cleavage of unstrained molecules, the migration of carbon-based groups is common and important to facilitate the C−C cleavage and new C−C formation.

In summary, we have developed a novel silver-catalyzed long-distance aryl migration of *γ,γ*-disubstituted triflic amides through C−C bond cleavage, accompanied by the formation of new C−O/C−N bonds. More electron-rich aryl groups showed better performance than electron-deficient aryl motifs during the migration. The migration products were easily converted to *γ*-hydroxy amines and tetrahydroquinoline derivatives under mild conditions. According to the control experiments, this transformation was proposed to proceed through a silver-promoted radical pathway. Studies to clearly understand the mechanism and explore the potential applications are underway.