A Mild, Ferrocene-Catalyzed C−H Imidation of (Hetero)Arenes

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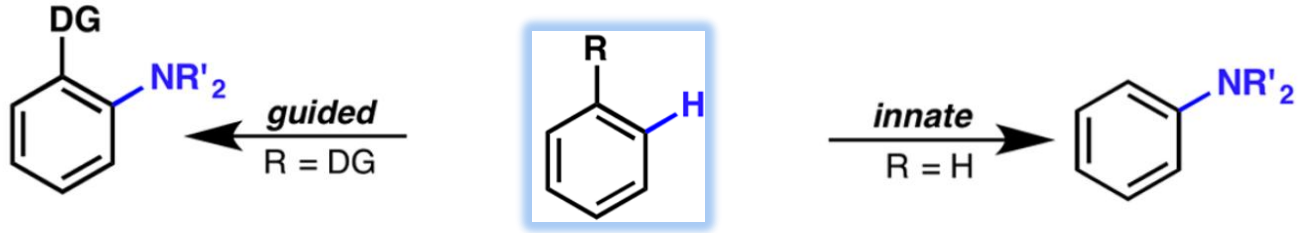
Diana Castillo
14/04/2014

Methods for intermolecular C(sp^2)-H amination



External reagent or directing group

Metal complexation

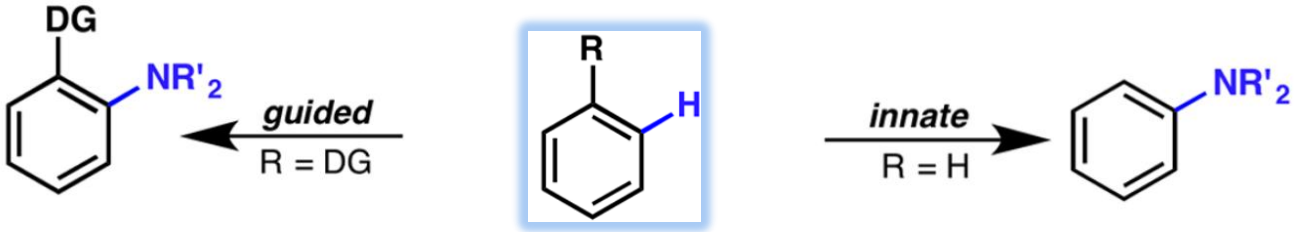
Steric bias of the reagent

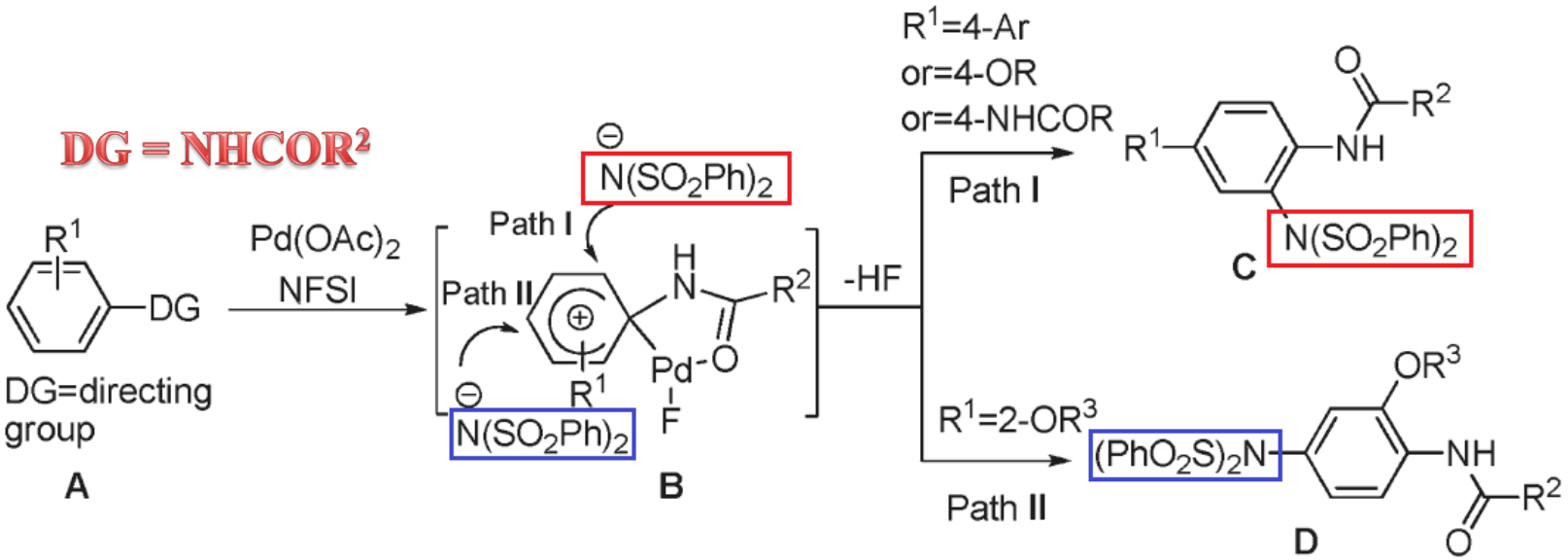
Natural reactivity patterns

Absence of external directing forces

Sun, K.; Li, Y.; Xiong, T.; Zhang, J.; Zhang, Q. *J. Am. Chem. Soc.* **2011**, 133, 1694.

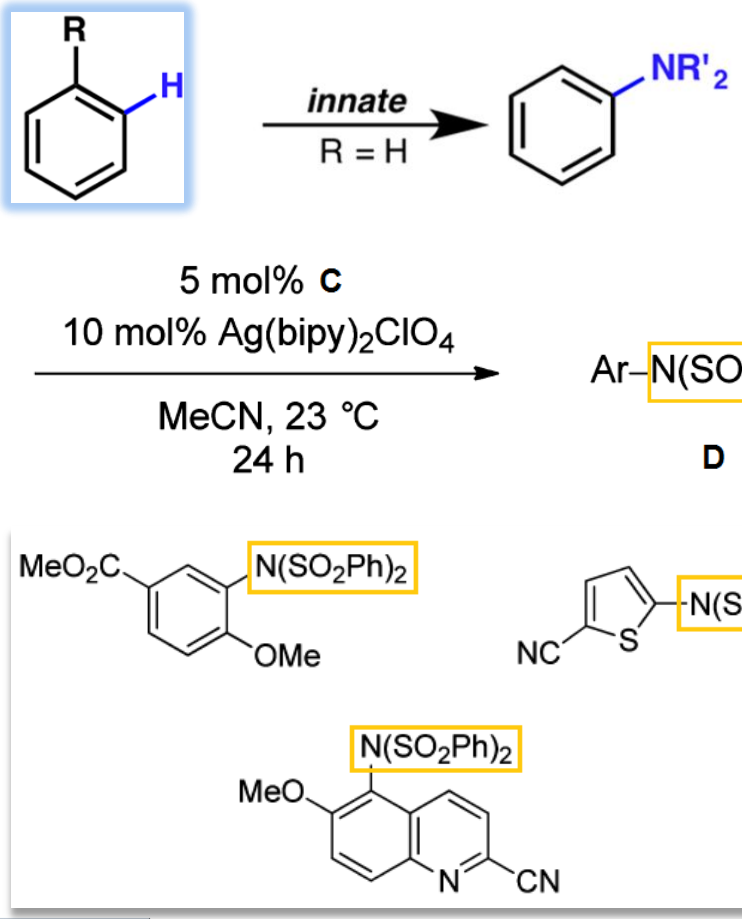
Methods for intermolecular C(sp²)-H amination





NFSI = *N*-fluorobenzenesulfonimide

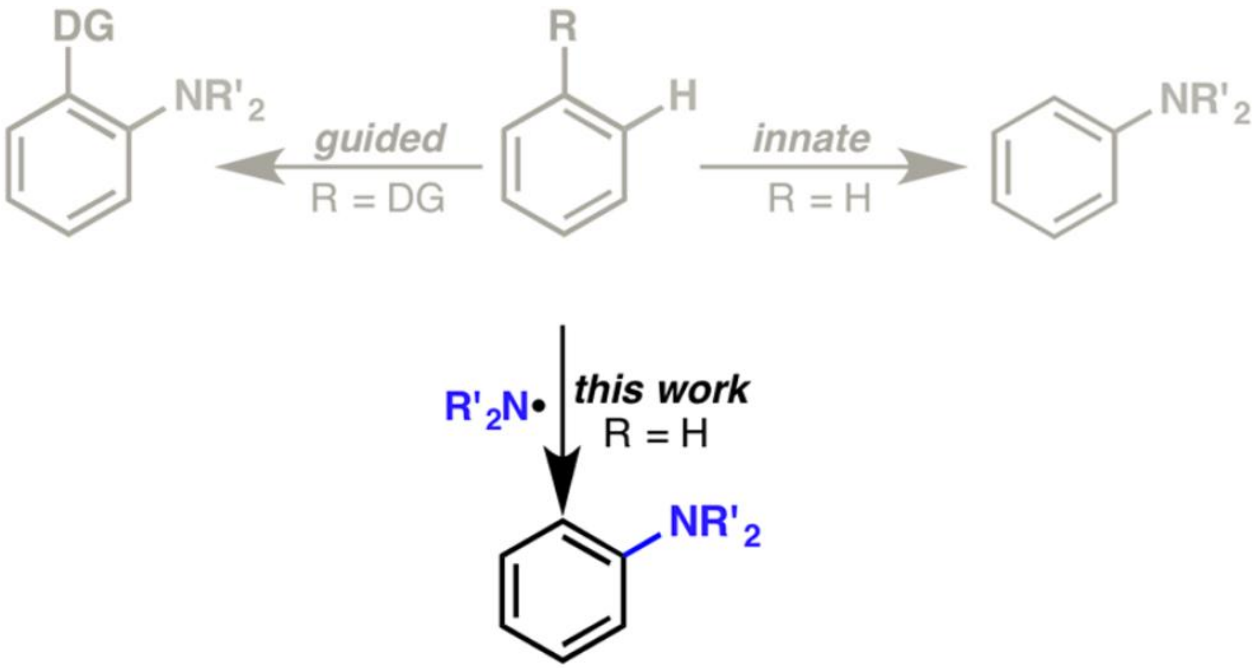
Sun, K.; Li, Y.; Xiong, T.; Zhang, J.; Zhang, Q. *J. Am. Chem. Soc.* **2011**, 133, 1694.



Not require coordinating directing groups

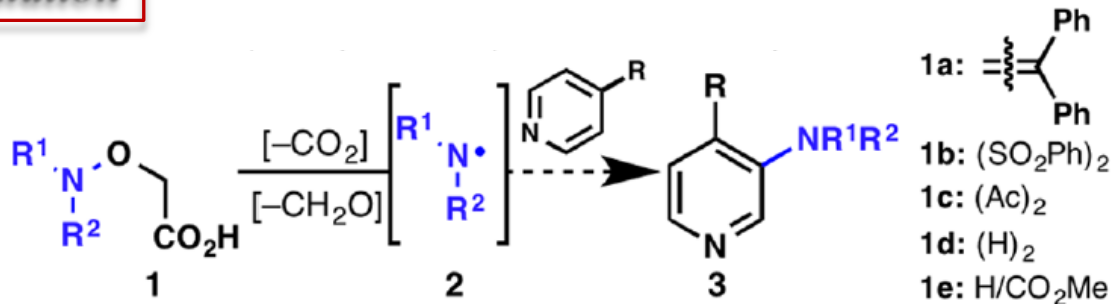
Without the formation of conventional organometallic intermediates

Boursalian, G. B.; Ngai, M.-Y.; Hojczyk, K. N.; Ritter, T. *J. Am. Chem. Soc.* **2013**, 135, 13278.


DG
NR'2
guided
R = DG
R
H
innate
R = H
NR'2
R'2N•
this work
R = H
NR'2

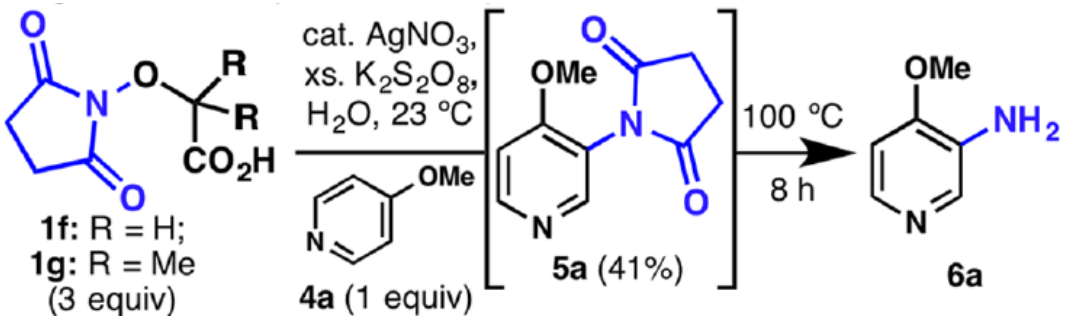
Preliminary studies towards radical-based C-H amination

First approximation



- Propensity of *N*-radicals to hydrogen abstraction
- Degradation

Second approximation



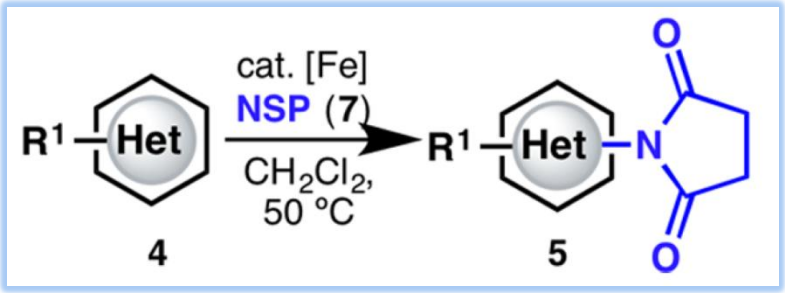
Electron-rich substrates

Decomposition

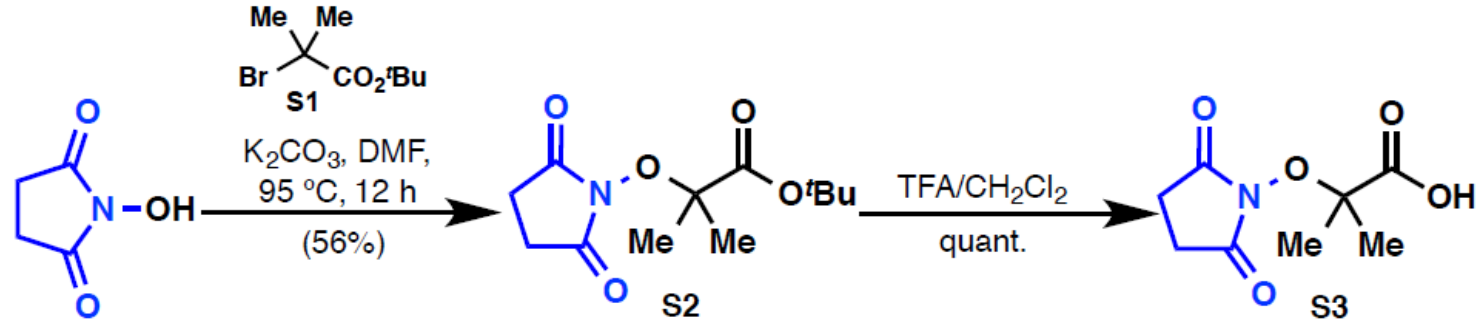
Design → $R'_2N^{\bullet}$ → *decarboxylation/deformylation*

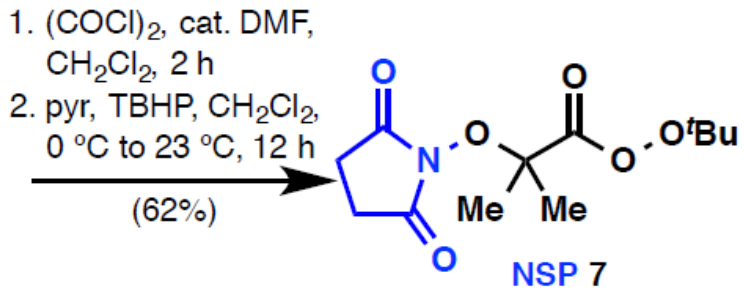
Forrester, A. R.; Gill, M.; Meyer, C. J.; Sadd, J. S.; Thomson, R. H. *J. Chem. Soc., Chem. Commun.* **1975**, 291.

C–H Imidation of (Hetero)Arenes



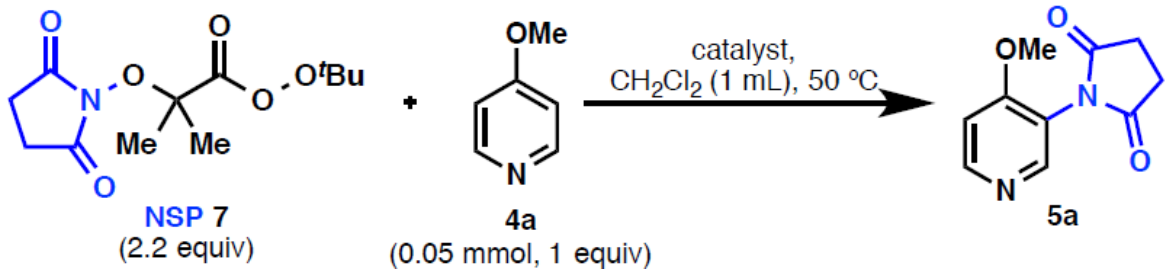
Preparation of NSP (N-succinimidyl perester) 7





Reaction condition optimization

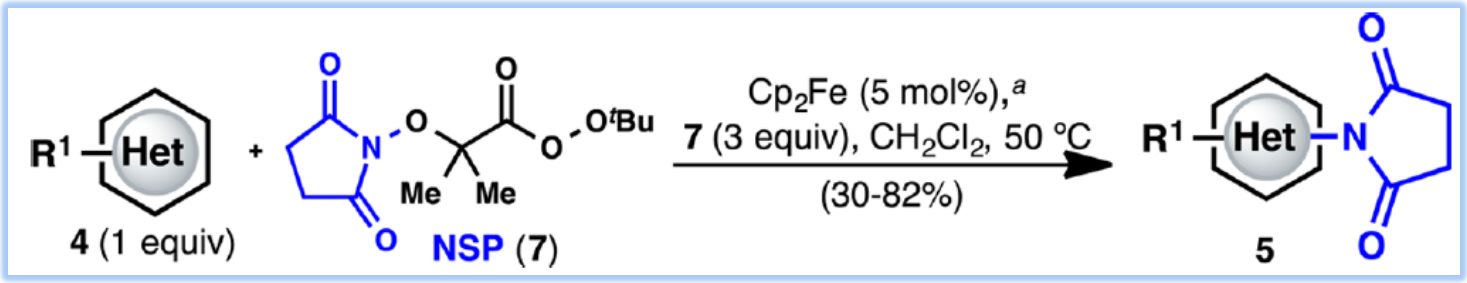
Table 1. Catalyst screening for reaction of NSP **7** with 4-methoxypyridine (**4a**).

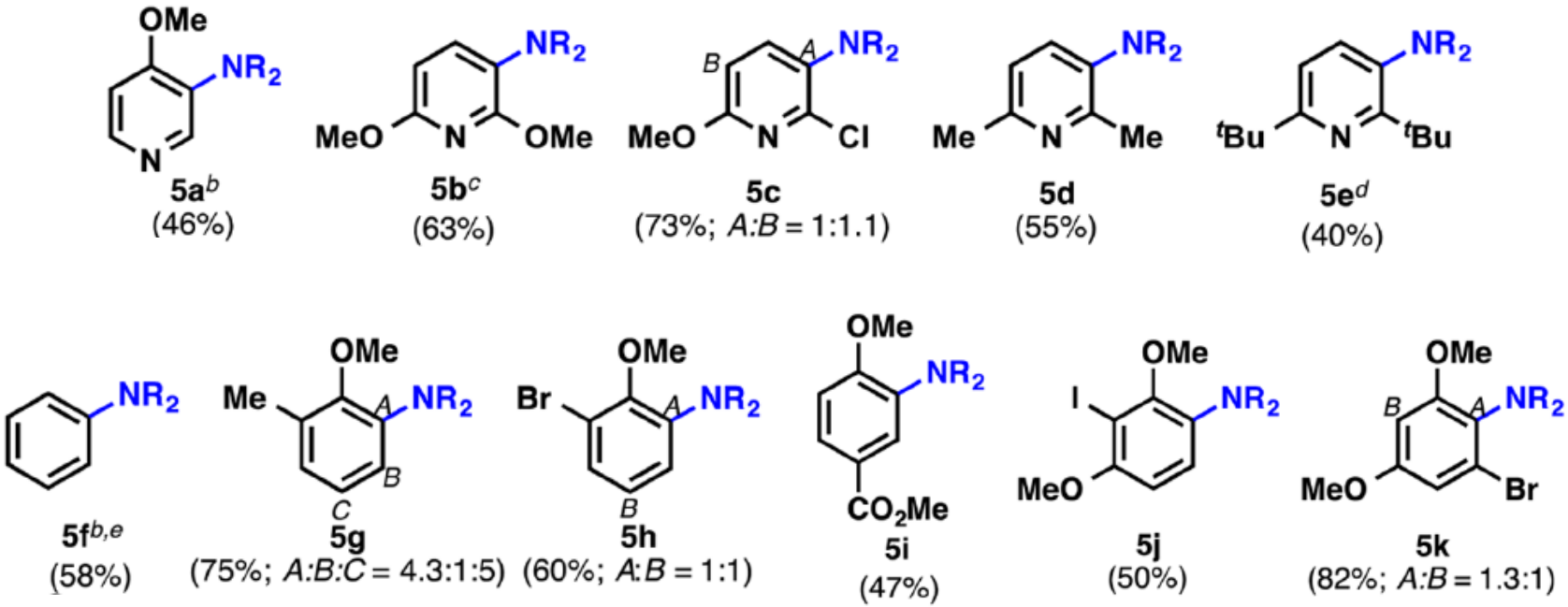


Entry	Catalyst	(mol%)	Yield (%)[a]	Entry	Catalyst[a]	(mol%)	Yield (%)[a]
1	**none**	-	7	8	**Cp_2Fe**	5	52
2	**CuCl**	20	13	9	**$FeSO_4$**	10	24
3	**CuI**	20	14	10	**$FeCl_3$**	10	15
4	**CuBr**	20	14	11	**$Fe(acac)_3$**	10	23
5	**CuCN**	20	18	12	**$Fe(OAc)_2$**	10	25
6	**$Cu(OTf)_2$**	10	26	13	**$Co(acac)_3$**	10	21
7	**CuF_2**	10	14	14	**$Mn(acac)_2$**	10	23

[a]Yield is based on NMR comparison.

Table 2. Substrate Scope of Ferrocene-Catalyzed C−H Imidation of (Hetero)Arenes **4**





[a]Cp_2Fe (5 mol%), (hetero)arene 4 (0.2 mmol), NSP (**7**) (3 equiv), CH_2Cl_2 (0.05 M), 50 °C, 2−7 h; isolated yields reported. [b]NSP (**7**) (4 equiv) was used. [c] NSP (7) (2.75 equiv) was used. [d]NSP (**7**) (5 equiv) was used. [e]Cp_2Fe (10 mol%) was used.

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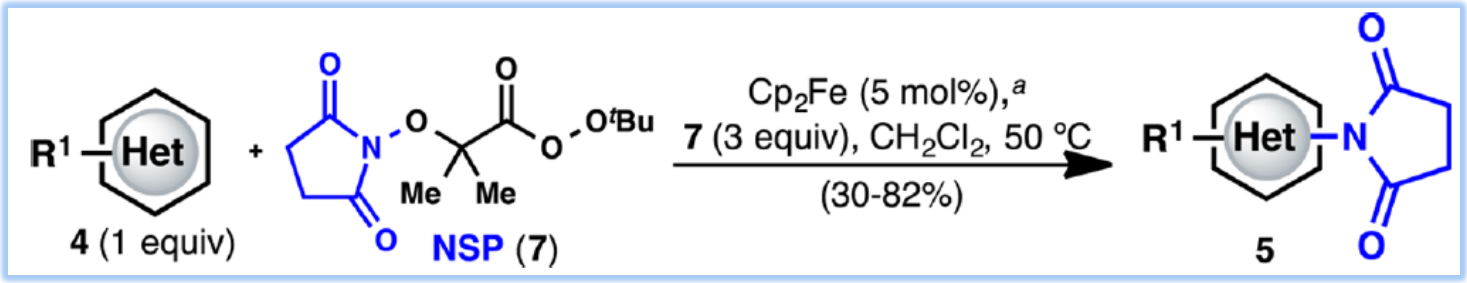

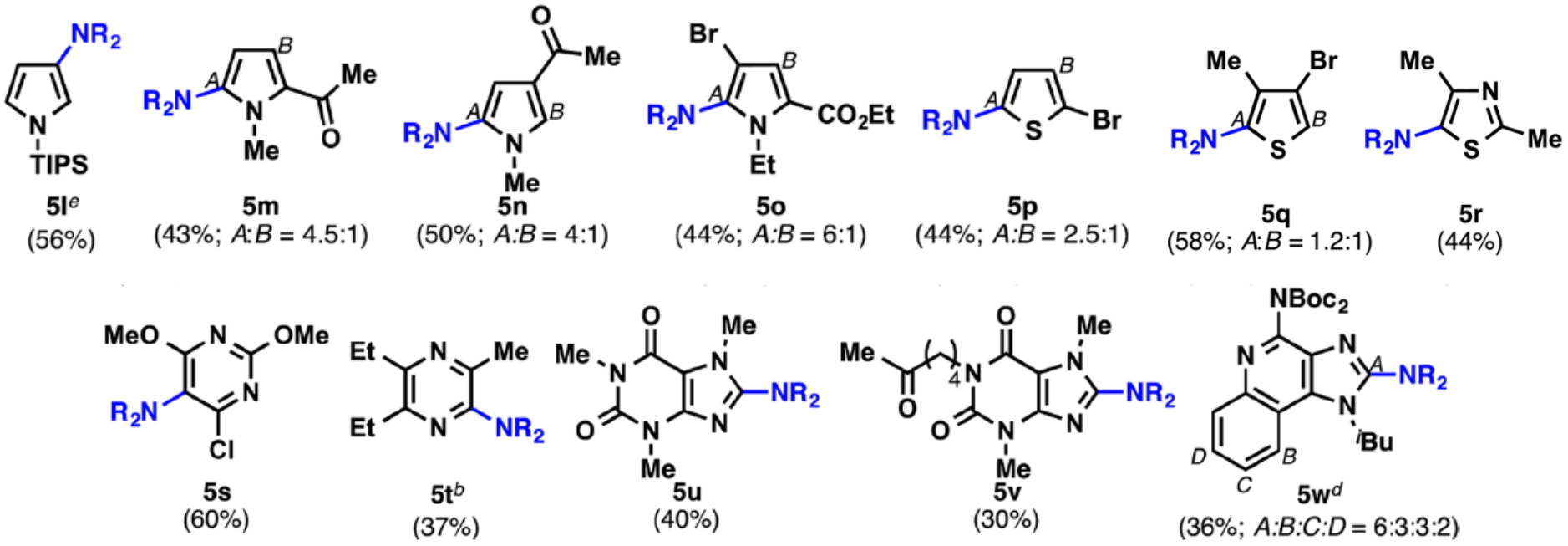

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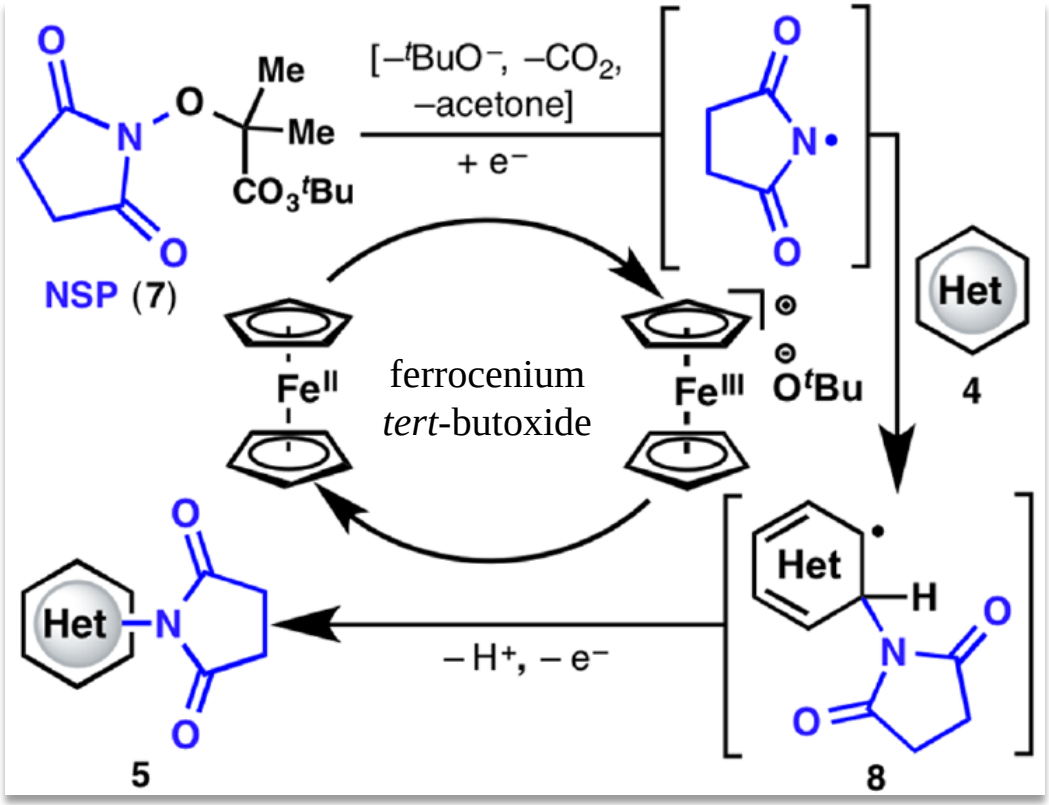
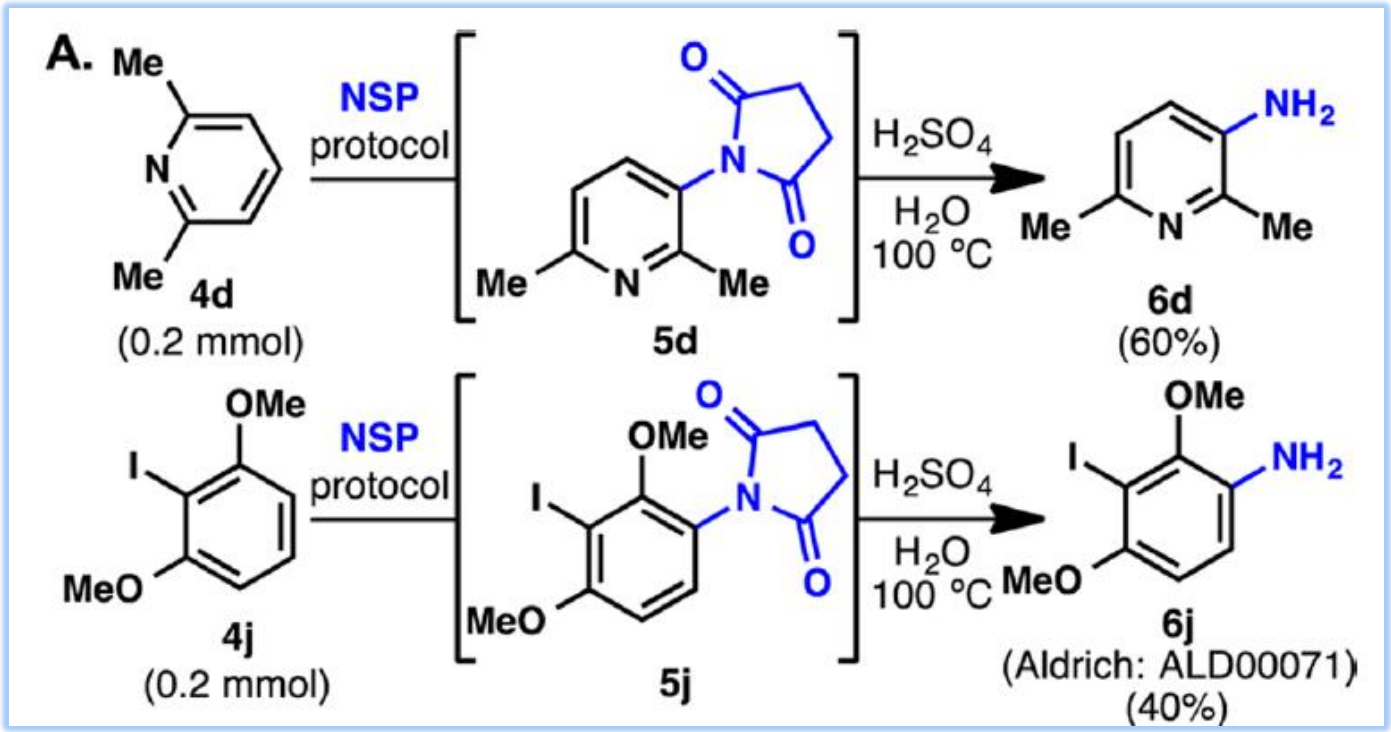
Proposed mechanism

single-electron tranfer from Cp_2Fe to NSP
O-O bond cleavage



one-electron oxidation
and deprotonation

One-pot C−H imidation/deprotection of 4d and 4j



CONCLUSION

A simple method for direct C−H imidation is reported using a new perester-based self-immolating reagent and a base-metal catalyst.

The scope of the reaction is broad, the conditions are extremely mild, and the reaction is tolerant of oxidizable and acid labile functionality, multiple heteroatoms, and aryl iodides.

The succinimide products obtained can be easily deprotected in to reveal the corresponding anilines directly.