Amide N–C Bond Activation: A Graphical Overview of Acyl and Decarbonylative Coupling

Chengwei Liu *[a,b]
Michal Szostak *[b]

[a] Department of Chemistry, Shanghai University, 99 Shangda Road, Shanghai 200444, P. R. of China
chengwei_liu@shu.edu.cn
[b] Department of Chemistry, Rutgers University, 73 Warren Street, Newark, NJ 07102, USA
michal.szostak@rutgers.edu

Received: 13.01.2023
Accepted after revision: 14.02.2023
Published online: 14.02.2023 (Accepted Manuscript), 06.03.2023 (Version of Record)
DOI: 10.1055/a-2035-6733; Art ID: so-2023-01-0006-GR

Abstract This Graphical Review provides an overview of amide bond activation achieved by selective oxidative addition of the N–C(O) acyl bond to transition metals and nucleophilic acyl addition, resulting in acyl and decarbonylative coupling, together with key mechanistic details pertaining to amide bond distortion underlying this reactivity manifold.

Key words C–N activation, amide bond activation, acyl coupling, decarbonylative coupling, acyl addition, catalysis

The importance of amide bonds is undeniable. The amide bond is the fundamental linkage of life in peptides and proteins. Due to its special dipolar character, amides are indispensable in pharmaceuticals, pesticides, and polymers. At present, more than 50% of drug candidates contain amide bonds. Remarkably, reactions of amides are the most common type of reactions used in current medicinal chemistry.

Typical planar amides feature strong amidic resonance, $n_N \rightarrow \pi^*_{C=O}$ conjugation (15–20 kcal/mol), which renders amide bond cleavage extremely difficult. However, the amide bond can be sterically twisted or electronically activated by functionalizing the nitrogen atom of the amide bond. In this way, the amide bond resonance can be significantly decreased or diverted onto the activating group, thus enabling highly selective activation of N–C(O) amide bonds.

Recent years have seen an explosion of amide bond activation methods. Although the concept of amide bond twisting and the concurrent decrease of amidic resonance in bridged lactams was proposed as early as the 1930s, it was not until 2015 that generic acyclic twisted amides were used for the first time as cross-coupling partners in selective N–C(O) bond activation, thus effectively serving as surrogates for acyl and aryl halides and pseudohalides in transition-metal catalysis.

Amide bond activation can be categorized as acyl coupling and decarbonylative coupling. This reactivity is triggered by selective oxidative addition of the N–C(O) acyl bond to a transition metal, leading to either direct transmetalation or CO de-insertion. Furthermore, the successful use of amides as acyl halide equivalents in transition-metal catalysis spearheaded the development of an array of highly selective methods for nucleophilic acyl addition to amide bonds, resulting in an alternative disconnection to acyl products. In many cases, the direct nucleophilic acyl addition shows advantages over transition-metal-catalyzed variants; however, it should be noted that these manifolds are broadly complementary.

This Graphical Review provides an overview of the key studies in amide bond activation covering the period of 2015 to 2022. The goal of this Graphical Review is to provide a summary of the reactions developed and the manifolds established in the main areas of amide bond activation, including acyl and decarbonylative coupling as well as acyl nucleophilic addition, while highlighting the underlying mechanisms and amides that are critical to this reactivity manifold. Throughout the review we have attempted to cite the seminal reports and precedents. However, the reader should note that due to the format of this review and the large number of contributions, the review is not comprehensive.

Throughout the review, the reactions are categorized by the type of mechanism. An important aspect that the reader should pay special attention to is the role of specific amides that participate in each reaction manifold. In general, sterically twisted or electronically activated amides can be prepared (1) from carboxylic acids or their derivatives, or (2) from generic 1° or 2° amides. Both methods are valuable in terms of the synthetic advantages of amide bonds in cross-coupling and acyl addition chemistry. However, for derivatization of biomolecules and late-stage functionalization of pharmaceuticals, only amides that can be generically prepared from 1° or 2° amides are useful. We hope that this Graphical Review will stimulate further progress in this tremendously important field of chemistry.

Biographical Sketches

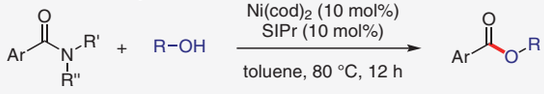
Chengwei Liu received his Ph.D. from Rutgers University with Prof. Michal Szostak in 2020. He conducted his postdoctoral research at the University of Oxford with Prof. Stephen P. Fletcher from 2020 to 2021. He was subsequently an assistant professor at Nanjing University of Information Science and Technology from 2021 to 2022. In the summer of 2022, he joined the faculty at Shanghai University, where he started his independent career and was promoted to full professor in 2022. His research group is focused on amide bond activation, C–O bond activation, C–S bond activation, and lanthanide organometallic chemistry.

Michal Szostak received his Ph.D. from the University of Kansas in 2009. He carried out postdoctoral research at Princeton University and the University of Manchester. In 2014, he joined the faculty at Rutgers University, where he is currently Professor of Chemistry. His research group developed the concept of acyclic twisted amide bond activation. In 2022, he edited the book '*Amide Bond Activation: Concepts and Reactions*'. His current research is focused on the development of new synthetic methodology based on transition-metal catalysis, amide bond activation, NHC ligands, inert bond activation, and applications to the synthesis of biologically active molecules. He is the author of over 240 publications.

Notable features:
- New concept
- Bench-stable electrophiles
- Non-toxic

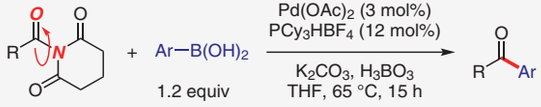
(1a) Szostak, *Amide Bond Activation: Concepts and Reactions*, 2022.

Seminal discovery

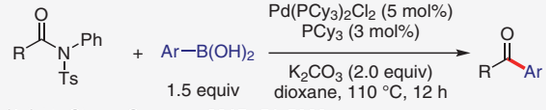


(1b) Hie, *Nature* **2015**, *524*, 79.

- *First correlation between amide bond distortion and reactivity*



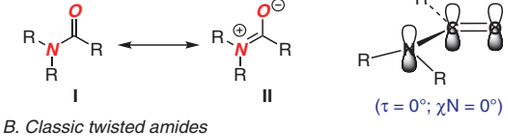
(1c) Meng, *Org. Lett.* **2015**, *17*, 4364.



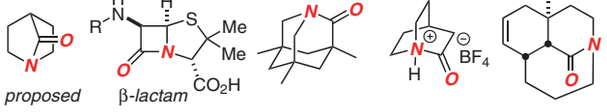
(1d) Li, *Chem. Commun.* **2015**, *51*, 5089.

Concept was first introduced: C–N bond activation of twisted amides

A. Amide bond resonance

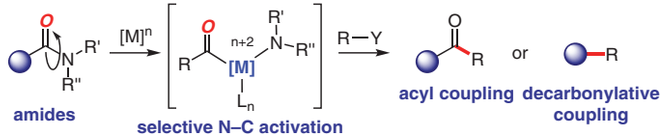


B. Classic twisted amides

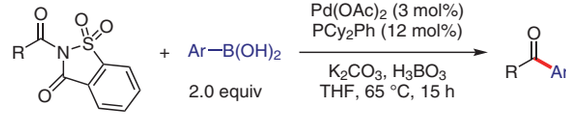


proposed	β-*lactam*			
1938	1941	1998	2006	2005
Lukes	Woodward	Kirby	Stoltz	Aubé
		perpendicularly twisted (τ = 90°, χN = 60°)		medium bridged (τ = 50°; χN = 35°)

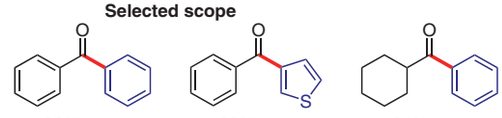
C. Twisted amides in cross-coupling reactions



Pd-catalyzed acyl Suzuki–Miyaura coupling of *N*-acylsaccharins



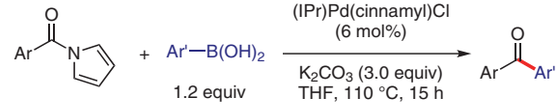
Selected scope



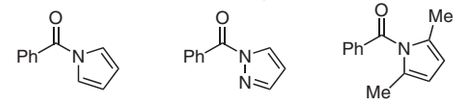
80% yield 86% yield 91% yield

(1t) Liu, *Org. Lett.* **2016**, *18*, 4194.

Pd-catalyzed Suzuki coupling of *N*-acyl pyrroles and pyrazoles



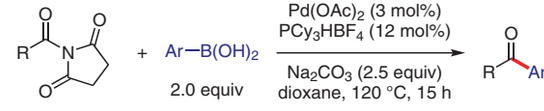
Selected amides *when Ar' = 4-Me-C6H4*



81% yield 66% yield 79% yield

(1u) Meng, *Org. Lett.* **2017**, *19*, 3596.

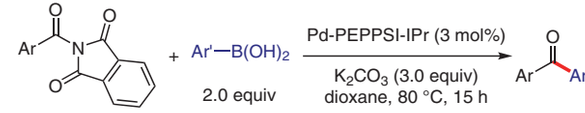
Pd-catalyzed acyl Suzuki–Miyaura reaction of *N*-acylsuccinimides



(1v) Osumi, *Org. Biomol. Chem.* **2017**, *15*, 8867.

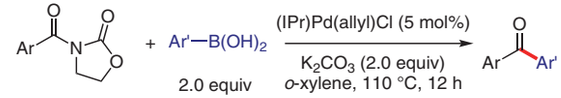
Further reading
Reviews on twisted amide bond activation:
(1e) Szostak, *Chem. Rev.* **2013**, *113*, 5701.
(1f) Meng, *Chem. Rev.* **2021**, *121*, 12746.
(1g) Meng, *Synlett* **2016**, *27*, 2530.
(1h) Liu, *Chem. Eur. J.* **2017**, *23*, 7157.
(1i) Meng, *Eur. J. Org. Chem.* **2018**, 2352.
(1j) Takise, *Chem. Soc. Rev.* **2017**, *46*, 5864.
(1k) Kaiser, *Chem. Soc. Rev.* **2018**, *47*, 7899.
(1l) Dander, *ACS Catal.* **2017**, *7*, 1413.
(1m) Adachi, *Tetrahedron Lett.* **2018**, *59*, 1147.
(1n) Guo, *Chem. Eur. J.* **2018**, *24*, 7794.
(1o) Bourne-Branchu, *Chem. Eur. J.* **2019**, *25*, 2663.
(1p) Chaudhari, *Chem. Asian J.* **2019**, *14*, 76.
(1q) Li, *Trends Chem.* **2020**, *2*, 914.
(1r) Gao, *J. Org. Chem.* **2022**, in press, DOI: 10.1021/acs.joc.2c01094.
(1s) Feng, *Angew. Chem. Int. Ed.* **2022**, *61*, e202212213.

Pd-catalyzed acyl Suzuki–Miyaura reaction of *N*-acylphthalimides



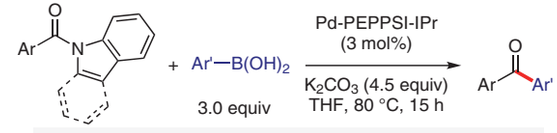
(1w) Rahman, *Catalysts* **2019**, *9*, 129.

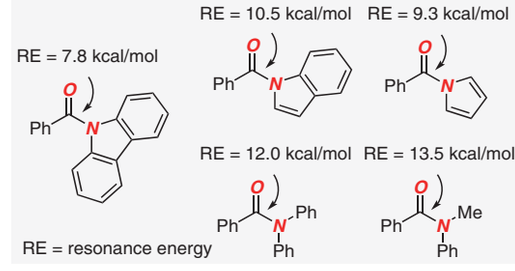
Pd-catalyzed acyl Suzuki–Miyaura reaction of *N*-acyloxazolidinones



(1x) Jian, *Eur. J. Org. Chem.* **2020**, 4176.

Pd-catalyzed acyl arylation of *N*-acylcarbazoles and *N*-acylindoles



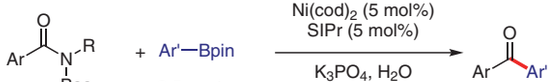


(1y) Buchspies, *Org. Lett.* **2020**, *22*, 4703.

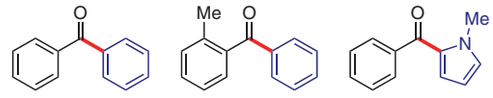
Further reading
Other selected contributions:
(1z) Meng, *Org. Biomol. Chem.* **2016**, *14*, 5690.
(1aa) Wu, *Adv. Synth. Catal.* **2016**, *358*, 3876.
(1ab) Cui, *Tetrahedron Lett.* **2017**, *58*, 3819.
(1ac) Wang, *J. Organomet. Chem.* **2018**, *877*, 80.
(1ad) Liu, *Org. Lett.* **2019**, *21*, 7976.
(1ae) Rahman, *J. Org. Chem.* **2020**, *85*, 5475.
(1af) Ma, *Adv. Synth. Catal.* **2020**, *362*, 1887.
(1ag) Luo, *Org. Process Res. Dev.* **2018**, *22*, 1188.
(1ah) Wang, *Org. Process Res. Dev.* **2020**, *24*, 1043.
(1ai) Rahman, *J. Org. Chem.* **2021**, *86*, 10455.

Figure 1 Amide bond activation: concept and discoveries[1]

Nickel-catalyzed acyl Suzuki–Miyaura reaction of amides



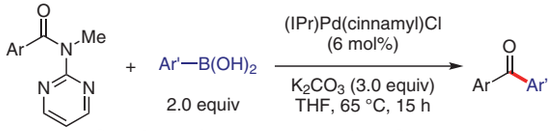
Selected scope



96% yield 51% yield 96% yield

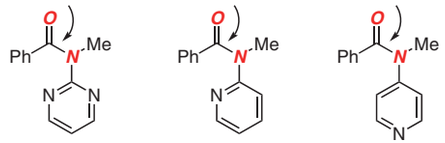
(2a) Weires, *Nat. Chem.* **2016**, *8*, 75.

Pd-catalyzed Suzuki coupling of *N*-methylamino pyrimidyl amides



Selected amides *when Ar' = 4-Me-C6H4*

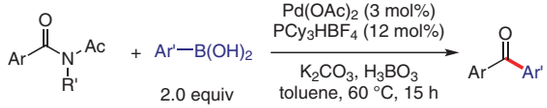
RE = 6.7 kcal/mol RE = 8.8 kcal/mol RE = 10.7 kcal/mol



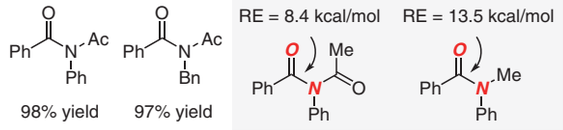
85% yield 30% yield <5% yield

(2b) Meng, *Org. Lett.* **2017**, *19*, 4656. RE = resonance energy

Pd-catalyzed acyl Suzuki–Miyaura coupling of *N*-acetylamides



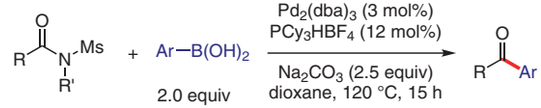
Selected amides *when Ar' = 4-Me-C6H4* RE = resonance energy



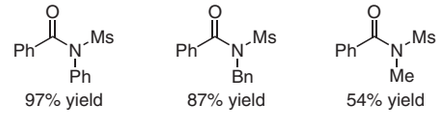
98% yield 97% yield RE = 8.4 kcal/mol RE = 13.5 kcal/mol

(2c) Liu, *ACS Catal.* **2018**, *8*, 9131.

Pd-catalyzed acyl Suzuki–Miyaura coupling of *N*-mesylamides



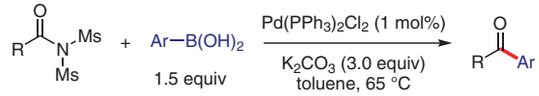
Selected amides *when Ar = 4-Me-C6H4*



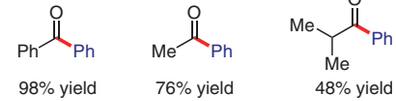
97% yield 87% yield 54% yield

(2d) Liu, *Org. Lett.* **2017**, *19*, 1434.

Pd-catalyzed acyl Suzuki–Miyaura coupling of *N,N*-di-Ms amides



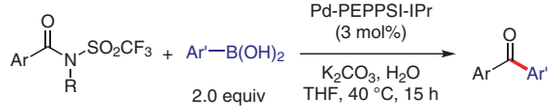
Selected scope



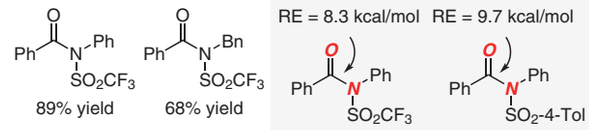
98% yield 76% yield 48% yield

(2e) Lim, *Eur. J. Org. Chem.* **2018**, 5717.

Pd-catalyzed acyl Suzuki–Miyaura coupling of *N*-sulfonyl amides



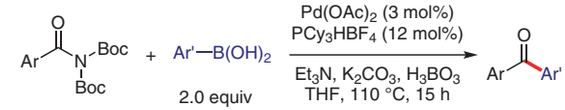
Selected amides *when Ar' = 4-Me-C6H4* RE = resonance energy

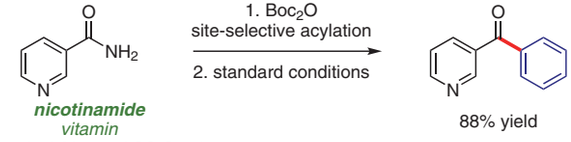


89% yield 68% yield RE = 8.3 kcal/mol RE = 9.7 kcal/mol

(2f) Shi, *Org. Lett.* **2019**, *21*, 1253.

Pd-catalyzed acyl Suzuki–Miyaura coupling of primary amides

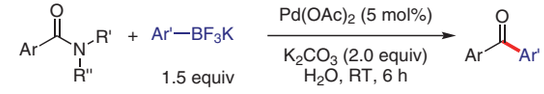




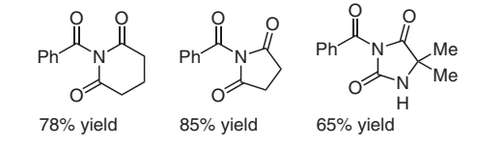
88% yield

(2g) Meng, *ACS Catal.* **2016**, *6*, 7335.

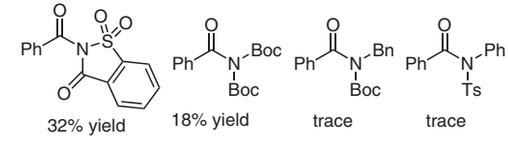
Green method for acyl Suzuki–Miyaura reactions of amides



Selected amides *when Ar' = Ph*



78% yield 85% yield 65% yield



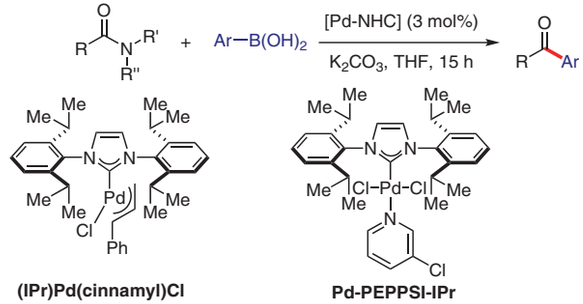
32% yield 18% yield trace trace

(2h) Zhang, *Eur. J. Org. Chem.* **2020**, 1620.

Further reading

Other selected contributions:
(2i) Li, *J. Organomet. Chem.* **2015**, *794*, 136.
(2j) Szostak, *J. Org. Chem.* **2016**, *81*, 8091.
(2k) Pace, *Chem. Eur. J.* **2016**, *22*, 14494.
(2l) Pace, *Chem. Commun.* **2019**, *55*, 4423.
(2m) Szostak, *J. Org. Chem.* **2017**, *82*, 6373.
(2n) Meng, *J. Am. Chem. Soc.* **2018**, *140*, 727.
(2o) Szostak, *Org. Lett.* **2018**, *20*, 1342.
(2p) Szostak, *J. Org. Chem.* **2018**, *83*, 14676.
(2q) Ielo, *Chem. Eur. J.* **2020**, *26*, 16246.
(2r) Liu, *Org. Lett.* **2018**, *20*, 7771.
(2s) Boit, *ACS Catal.* **2018**, *8*, 1003.
(2t) Mai, *Eur. J. Org. Chem.* **2019**, 7814.
(2u) Mehta, *Org. Lett.* **2020**, *22*, 1.
(2v) Shi, *Tetrahedron Lett.* **2020**, *61*, 152140.
(2w) Wang, *ACS Catal.* **2022**, *12*, 2426.
(2x) Zhang, *Angew. Chem. Int. Ed.* **2022**, *61*, e202114146.
(2y) Li, *Chem. Eur. J.* **2021**, *27*, 2699.

Figure 2 Transition-metal-catalyzed acyl Suzuki–Miyaura coupling of amides[2]

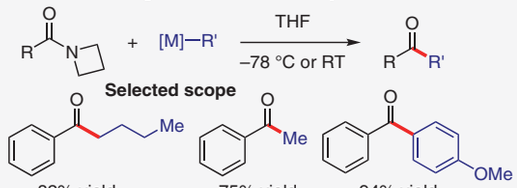


(3a) Lei, *ACS Catal.* **2017**, *7*, 1960. (3b) Lei, *J. Org. Chem.* **2017**, *82*, 6638. (3c) Lei, *Chem. Sci.* **2017**, *8*, 6525.

Further reading
Review on Pd/NHC-catalyzed C–N activation:
(3d) Shi, *Acc. Chem. Res.* **2018**, *51*, 2589.

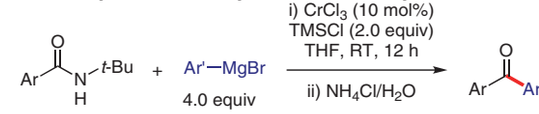
Other examples on Pd/NHC-catalyzed C–N activation:
(3e) Lei, *Org. Lett.* **2017**, *19*, 6510.
(3f) Lei, *Adv. Synth. Catal.* **2019**, *361*, 5654.
(3g) Li, *ChemCatChem* **2018**, *10*, 3096.
(3h) Shi, *Chem. Commun.* **2017**, *53*, 10584.
(3i) Zhou, *Org. Lett.* **2019**, *21*, 3304.
(3j) Li, *Catal. Sci. Technol.* **2020**, *10*, 710.
(3k) Buchspies, *Catalysts* **2020**, *10*, 372.
(3l) Zhou, *iScience* **2020**, *23*, 101377.
(3m) Lei, *Synthesis* **2021**, *53*, 682.
(3n) Lei, *ACS Sustainable Chem. Eng.* **2021**, *9*, 552.
(3o) Lei, *ACS Sustainable Chem. Eng.* **2021**, *9*, 14937.
(3p) Buchspies, *Molecules* **2021**, *26*, 188.

Addition of organometallics to *N*-acylazetidines



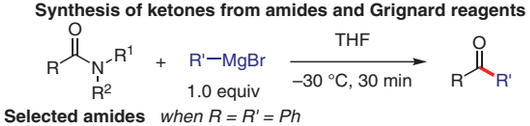
(3y) Liu, *Org. Lett.* **2016**, *18*, 2375.

Cr-catalyzed Kumada arylation of secondary amides



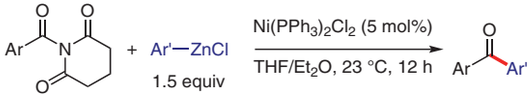
(3z) Chen, *ACS Catal.* **2018**, *8*, 5864.

Synthesis of ketones from amides and Grignard reagents



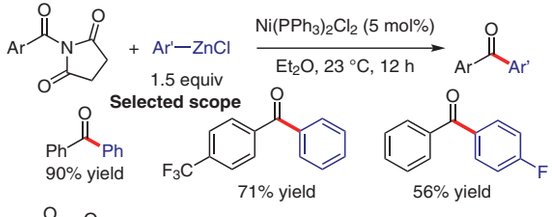
(3aa) Sureshbabu, *J. Org. Chem.* **2019**, *84*, 11823.

Ni-catalyzed acyl Negishi reaction of *N*-acyl glutarimides



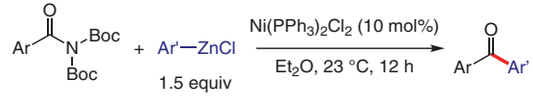
(3q) Shi, *Chem. Eur. J.* **2016**, *22*, 10420.

Ni-catalyzed acyl Negishi reaction of *N*-acylsuccinimides



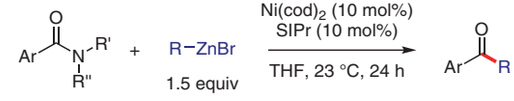
(3r) Shi, *Synthesis* **2017**, *49*, 3602.

Ni-catalyzed acyl Negishi reaction of primary amides

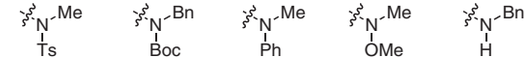


(3s) Shi, *Org. Lett.* **2016**, *18*, 5872.

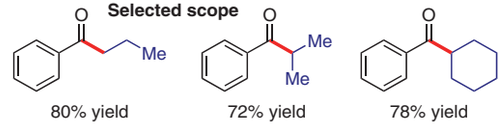
Nickel-catalyzed alkylation of amides



Selected amides *when Ar = 2-Np, R = CH2Ph*

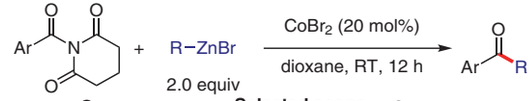


Selected scope

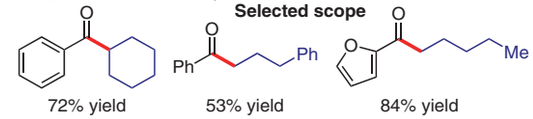


(3t) Simmons, *ACS Catal.* **2016**, *6*, 3176.

Co-catalyzed acyl Negishi reaction of *N*-acyl glutarimides



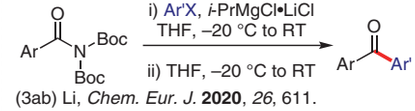
Selected scope



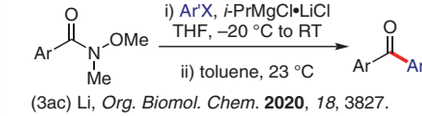
(3u) Dorval, *Org. Lett.* **2022**, *24*, 2778.

Other examples of ketone synthesis from amides with metal reagents:
(3v) Dorval, *Adv. Synth. Catal.* **2019**, *361*, 1777.
(3w) Bao, *Commun. Chem.* **2021**, *4*, 138.
(3x) Kim, *Tetrahedron Lett.* **2022**, *111*, 154201.

Synthesis of ketones from amides and Grignard reagents



(3ab) Li, *Chem. Eur. J.* **2020**, *26*, 611.



(3ac) Li, *Org. Biomol. Chem.* **2020**, *18*, 3827.

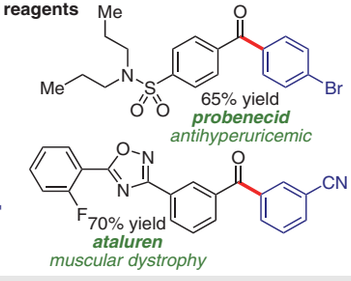


Figure 3 Synthesis of ketones via transition-metal catalysis and metal-free conditions[3]

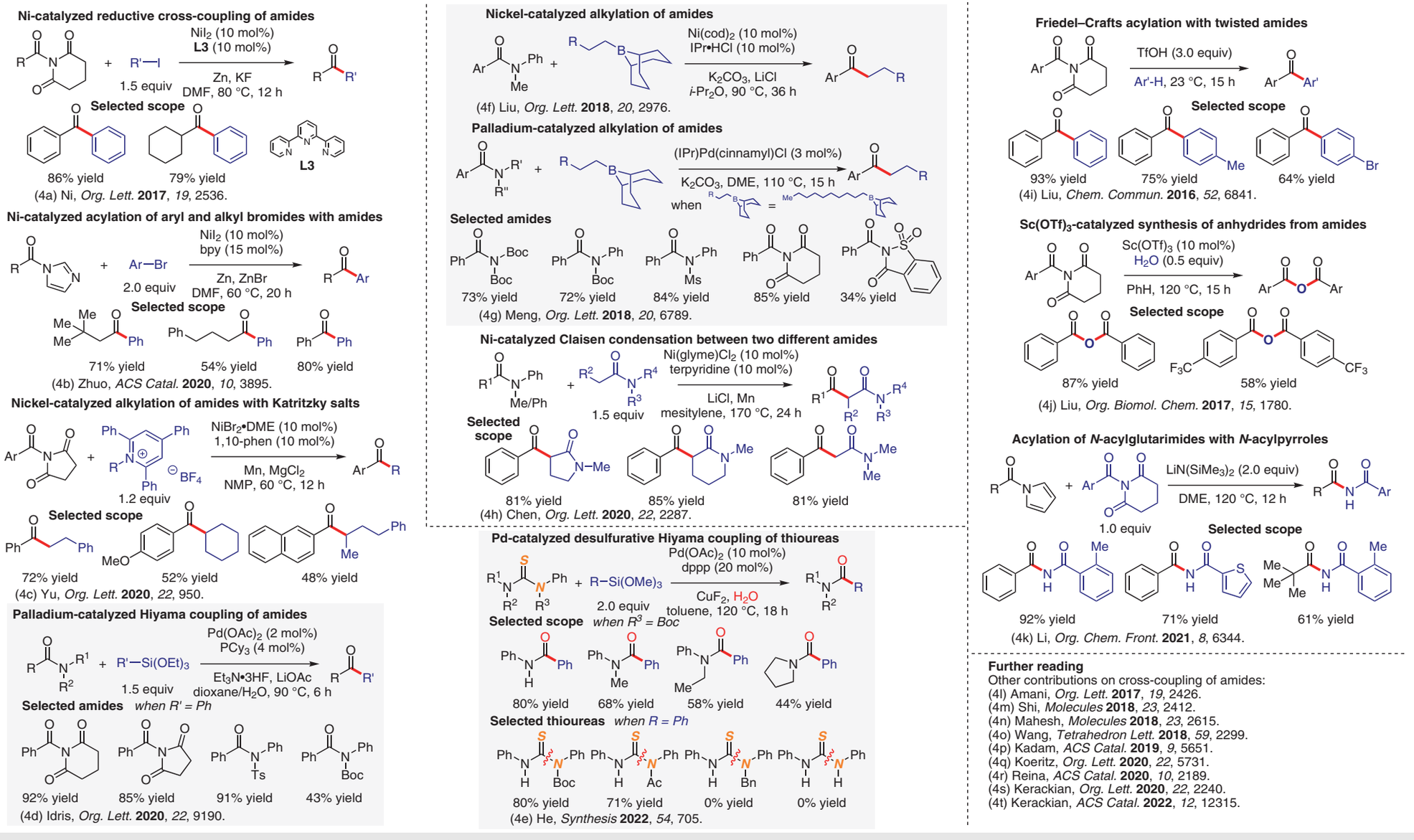
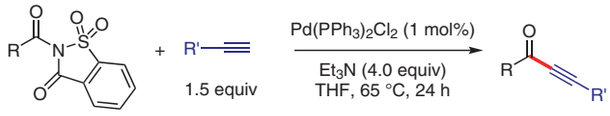
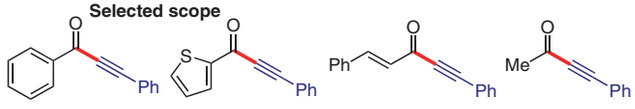


Figure 4 Amides as acylating reagents in various synthetic methodologies[4]

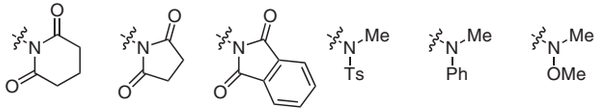
Pd-catalyzed Sonogashira coupling of *N*-acylsaccharins



Selected scope

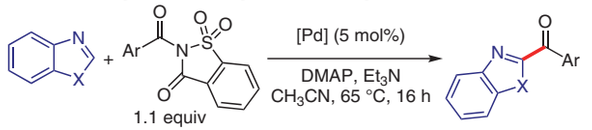


Selected amides *when R = Ph, R′ = Ph*

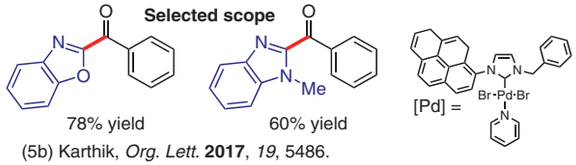


(5a) Cui, *Chem. Commun.* **2016**, *52*, 12076.

Pd/NHC-catalyzed heteroarylation of *N*-acylsaccharins

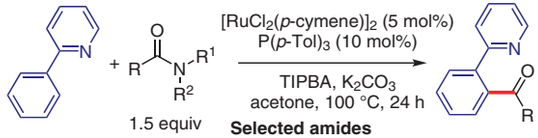


Selected scope

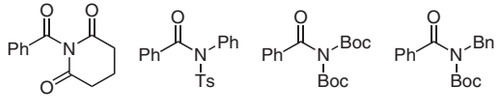


(5b) Karthik, *Org. Lett.* **2017**, *19*, 5486.

Ru-catalyzed aromatic acylation using amides

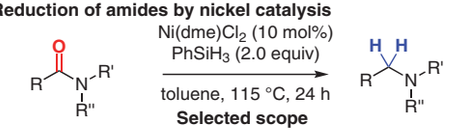


Selected amides

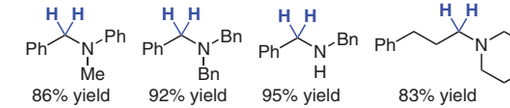


(5c) Li, *Org. Lett.* **2021**, *23*, 2521.

Reduction of amides by nickel catalysis

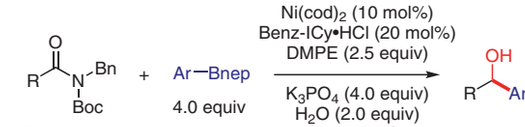


Selected scope

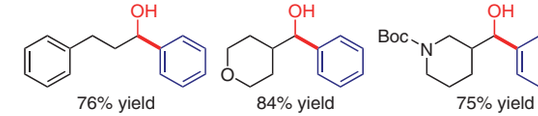


(5d) Simmons, *Org. Lett.* **2017**, *19*, 1910.
(5e) Simmons, *Org. Synth.* **2019**, *96*, 436.

Reductive arylation of amides via nickel catalysis

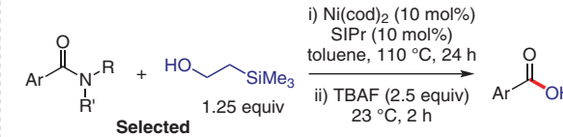


Selected scope

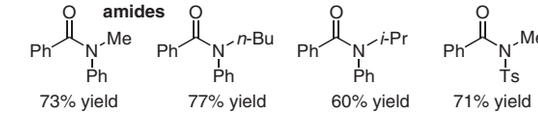


(5f) Boit, *Angew. Chem. Int. Ed.* **2021**, *60*, 2472.
(5g) Dander, *Commun. Chem.* **2019**, *2*, 82.

Ni-catalyzed conversion of amides into carboxylic acids

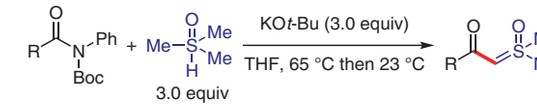


Selected amides



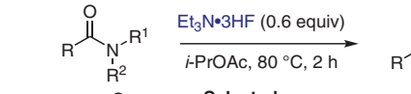
(5h) Knapp, *Org. Lett.* **2020**, *22*, 2833.
(5i) Bulger, *Org. Synth.* **2022**, *99*, 305.

Ni-catalyzed reductive cross-coupling of amides

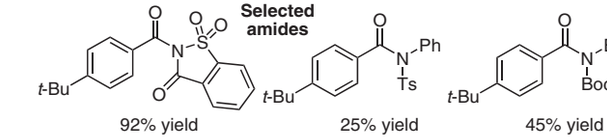


(5j) Rahman, *Org. Lett.* **2021**, *23*, 4818.

Synthesis of acyl fluorides via fluorination of amides

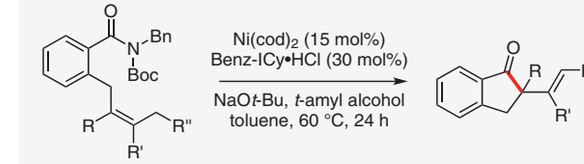


Selected amides



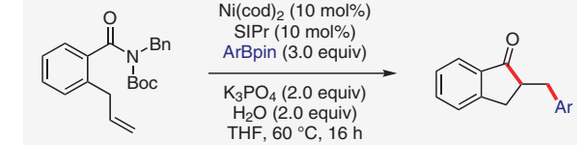
(5k) Idris, *Adv. Synth. Catal.* **2022**, *364*, 2449.

Nickel-catalyzed cyclization of amides



(5l) Medina, *Angew. Chem. Int. Ed.* **2017**, *56*, 6567.

Nickel-catalyzed cyclization of amides



(5m) Walker, *J. Am. Chem. Soc.* **2017**, *139*, 10228.

Further reading

Other contributions on the synthesis of benzoxazoles from amides:
(5n) Luo, *Adv. Synth. Catal.* **2019**, *361*, 4117.

Other contributions on the reduction of amides:
(5o) Azeez, *Org. Biomol. Chem.* **2022**, *20*, 2048.

Other contributions on computational studies for amides:
(5p) Liu, *J. Org. Chem.* **2016**, *81*, 11686.
(5q) Chu, *J. Org. Chem.* **2018**, *83*, 5009.
(5r) Wang, *Chem. Commun.* **2019**, *55*, 11330.

Selected scope

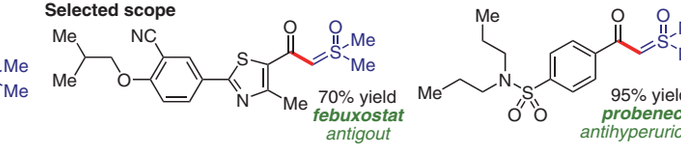
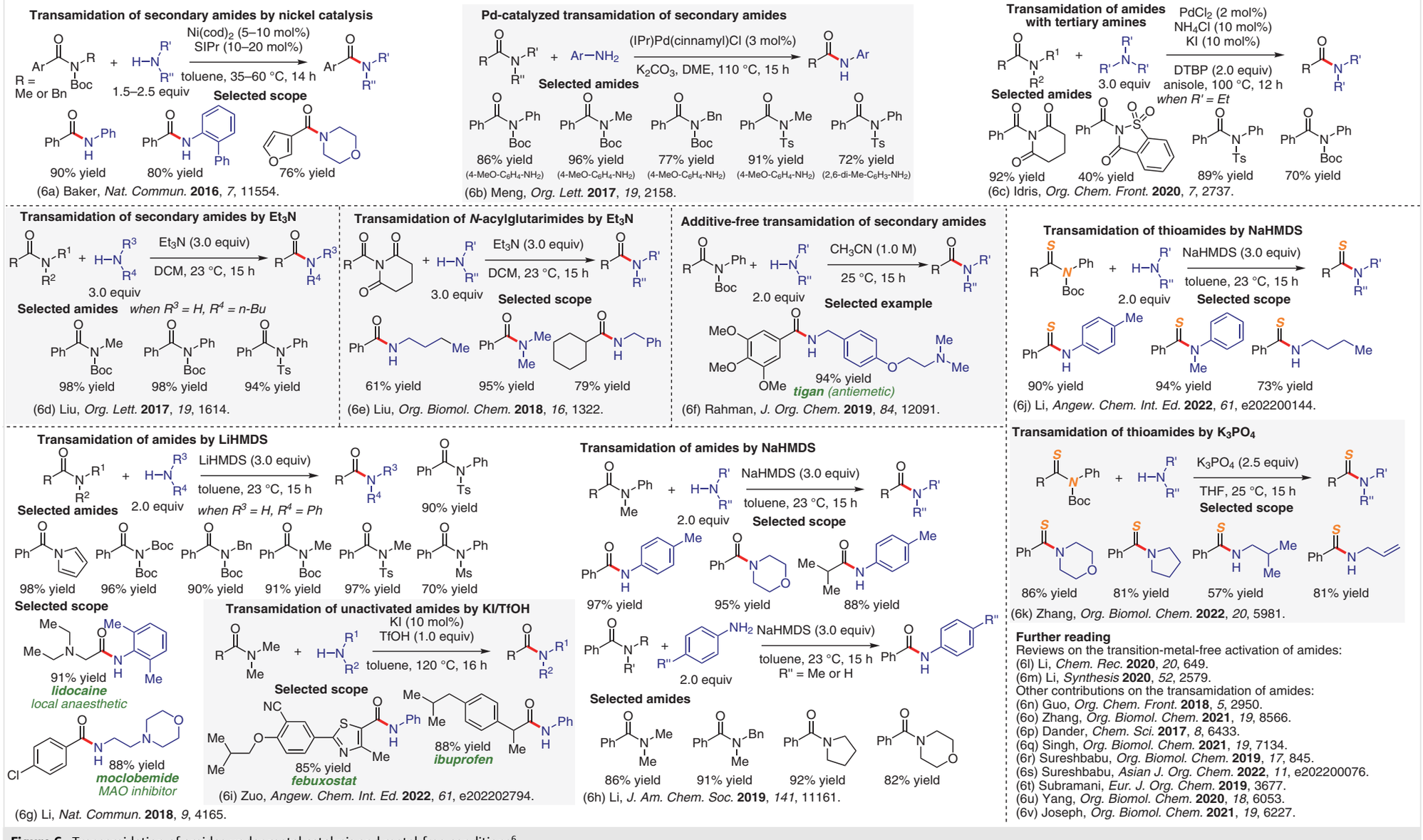


Figure 5 Cross-coupling of amides with versatile partners[5]

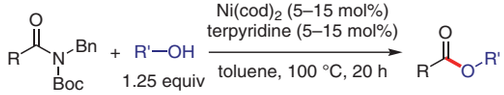


Further reading

Reviews on the transition-metal-free activation of amides:
(6l) Li, *Chem. Rec.* **2020**, *20*, 649.
(6m) Li, *Synthesis* **2020**, *52*, 2579.
Other contributions on the transamidation of amides:
(6n) Guo, *Org. Chem. Front.* **2018**, *5*, 2950.
(6o) Zhang, *Org. Biomol. Chem.* **2021**, *19*, 8566.
(6p) Dander, *Chem. Sci.* **2017**, *8*, 6433.
(6q) Singh, *Org. Biomol. Chem.* **2021**, *19*, 7134.
(6r) Sureshbabu, *Org. Biomol. Chem.* **2019**, *17*, 845.
(6s) Sureshbabu, *Asian J. Org. Chem.* **2022**, *11*, e202200076.
(6t) Subramani, *Eur. J. Org. Chem.* **2019**, 3677.
(6u) Yang, *Org. Biomol. Chem.* **2020**, *18*, 6053.
(6v) Joseph, *Org. Biomol. Chem.* **2021**, *19*, 6227.

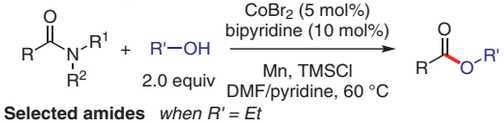
Figure 6 Transamidation of amides under metal catalysis and metal-free conditions[6]

Nickel-catalyzed esterification of secondary amides

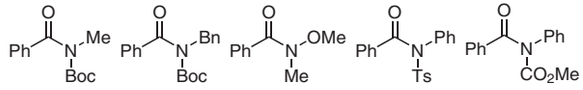


(7a) Hie, *Angew. Chem. Int. Ed.* **2016**, *55*, 15129.

Cobalt-catalyzed esterification of amides

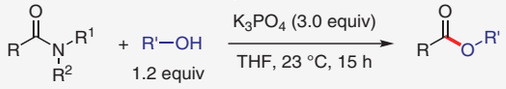


Selected amides *when R' = Et*

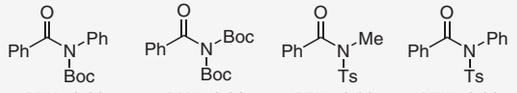


(7b) Bourne-Branchu, *Chem. Eur. J.* **2017**, *23*, 10043.

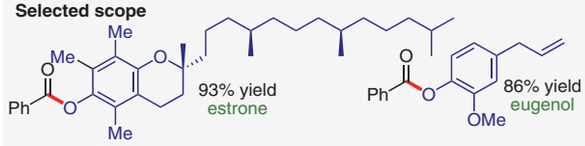
Esterification of amides by K_3PO_4



Selected amides *when R' = Ph*

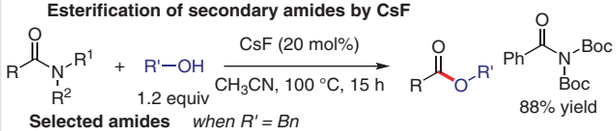


Selected scope

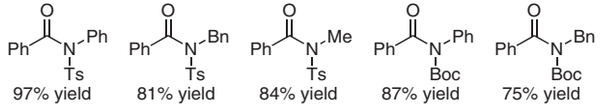


(7c) Li, *Org. Lett.* **2018**, *20*, 5622.

Esterification of secondary amides by CsF

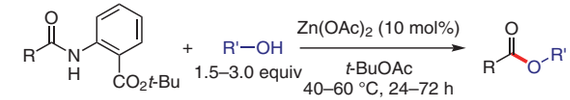


Selected amides *when R' = Bn*

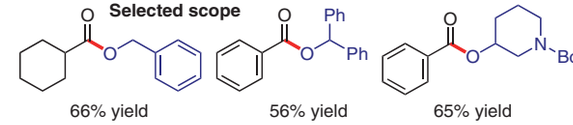


(7d) Wu, *Chem. Eur. J.* **2018**, *24*, 3444.

Zn-catalyzed esterification of secondary amides

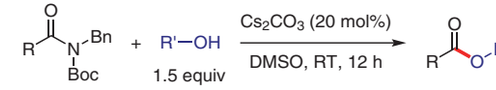


Selected scope



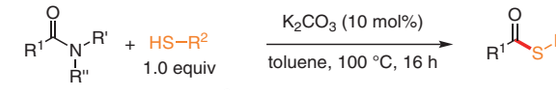
(7e) Wybon, *ACS Catal.* **2018**, *8*, 203.

Esterification of secondary amides by Cs_2CO_3

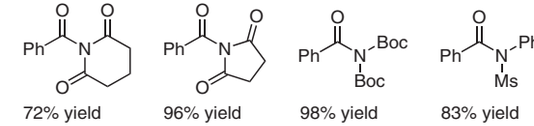


(7f) Ye, *Org. Lett.* **2019**, *21*, 6888.

Pd-catalyzed transamidation of secondary amides

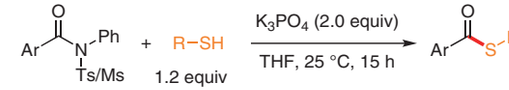


Selected amides *when R^2 = 4-Me-C_6H_4*

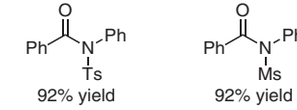


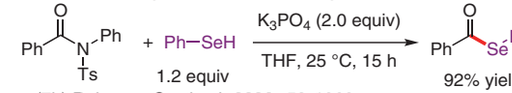
(7g) Wang, *New J. Chem.* **2019**, *43*, 9384.

Thioesterification and selenoesterification of amides by K_3PO_4



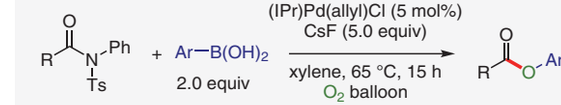
Selected amides *when R = Ph*



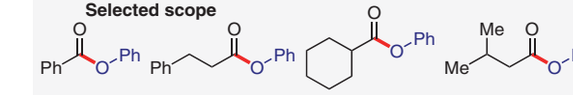


(7h) Rahman, *Synthesis* **2020**, *52*, 1060.

Pd-catalyzed aerobic oxidative coupling of amides

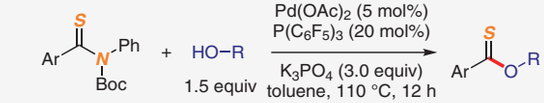


Selected scope

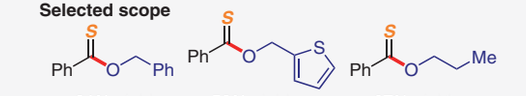


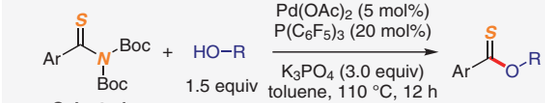
(7i) Li, *Eur. J. Org. Chem.* **2019**, 4357.

Pd-catalyzed thionoesterification of thioamides

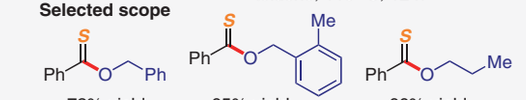


Selected scope





Selected scope



(7j) Liu, *Org. Biomol. Chem.* **2022**, *20*, 1532.

Further reading

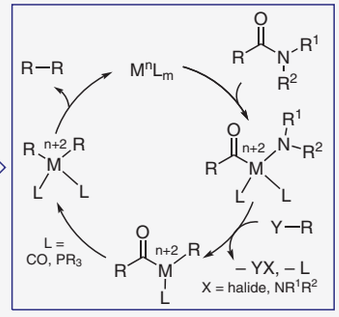
Other contributions on the esterification of amides:
(7k) Weires, *ACS Catal.* **2017**, *7*, 4381.
(7l) Dander, *J. Chem. Educ.* **2019**, *96*, 776.
(7m) Nagae, *Chem. Sci.* **2019**, *10*, 2860.

Figure 7 Esterification of amides via metal catalysis and metal-free conditions[7]

Notable features

- New concept
- Bench-stable electrophiles
- Non-toxic

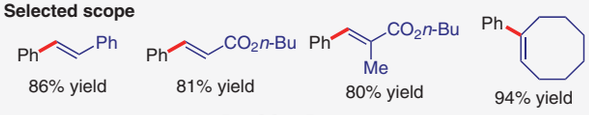
Reaction mechanism for the decarbonylative coupling of amides



First example of the decarbonylative coupling of amides:

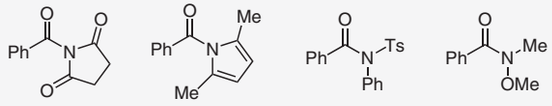
Pd-catalyzed decarbonylative Heck reaction of amides

Selected scope



86% yield | 81% yield | 80% yield | 94% yield

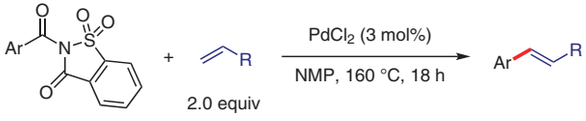
Selected amides *when R = CO_2n-Bu*



<5% yield | <5% yield | <5% yield | <5% yield

(8a) Meng, *Angew. Chem. Int. Ed.* **2015**, *54*, 14518.

Pd-catalyzed decarbonylative Heck reaction of *N*-acylsaccharins



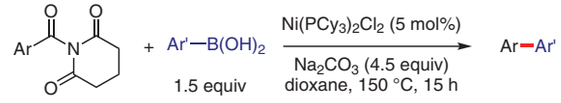
(8b) Liu, *J. Org. Chem.* **2016**, *81*, 12023.

Further reading

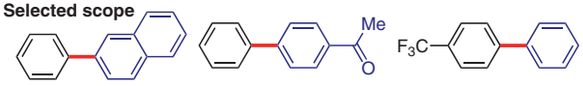
Reviews on the decarbonylative coupling of amides:
(8c) Liu, *Org. Biomol. Chem.* **2018**, *16*, 7998.

Computational studies on decarbonylative coupling of amides:
(8d) Ji, *J. Am. Chem. Soc.* **2017**, *139*, 15522.
(8e) Tong, *Chem. Commun.* **2020**, *56*, 113.
(8f) Li, *J. Org. Chem.* **2020**, *85*, 833.

Ni-catalyzed decarbonylative Suzuki coupling of amides

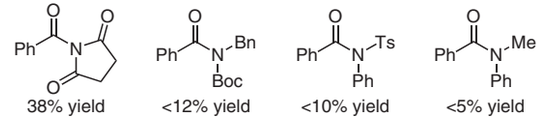


Selected scope



83% yield | 77% yield | 74% yield

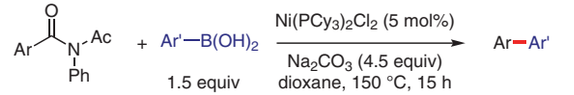
Selected amides *when Ar' = 2-Np*



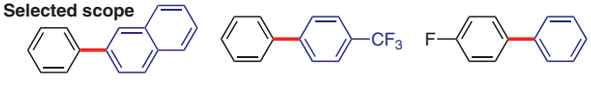
38% yield | <12% yield | <10% yield | <5% yield

(8g) Shi, *Angew. Chem. Int. Ed.* **2016**, *55*, 6959.

Ni-catalyzed decarbonylative Suzuki coupling of *N*-acetylamides



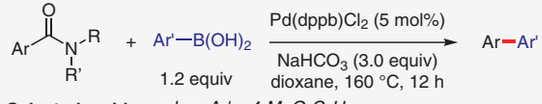
Selected scope



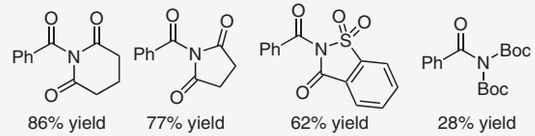
72% yield | 69% yield | 56% yield

(2c) Liu, *ACS Catal.* **2018**, *8*, 9131.

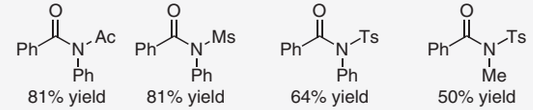
Pd-catalyzed decarbonylative Suzuki coupling of amides



Selected amides *when Ar' = 4-MeO-C_6H_4*



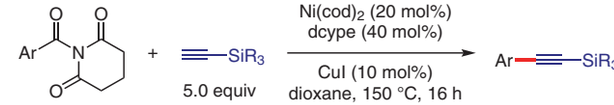
86% yield | 77% yield | 62% yield | 28% yield



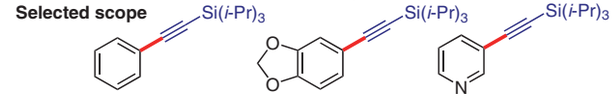
81% yield | 81% yield | 64% yield | 50% yield

(8h) Zhou, *Chem. Sci.* **2019**, *10*, 9865.

Ni-catalyzed decarbonylative alkynylation of amides



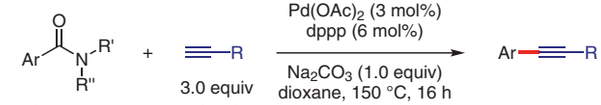
Selected scope



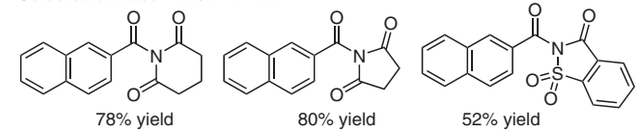
87% yield | 72% yield | 96% yield

(8j) Srimontree, *Org. Lett.* **2017**, *19*, 3091.

Pd-catalyzed decarbonylative alkynylation of amides



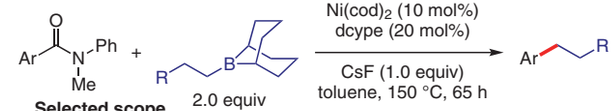
Selected amides *when R = Ph*



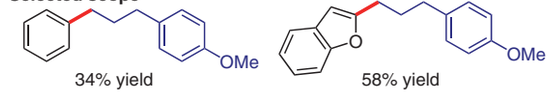
78% yield | 80% yield | 52% yield

(8k) Liu, *Org. Lett.* **2018**, *20*, 2741.

Ni-catalyzed decarbonylative alkylation of amides



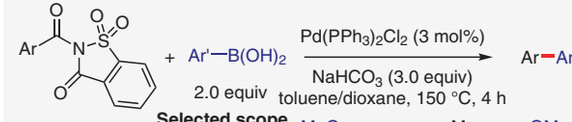
Selected scope



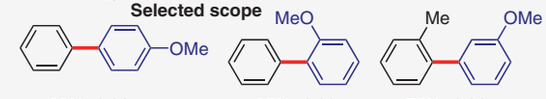
34% yield | 58% yield

(8l) Chatupheeraphat, *J. Am. Chem. Soc.* **2018**, *140*, 3724.

Pd-catalyzed decarbonylative Suzuki coupling of amides



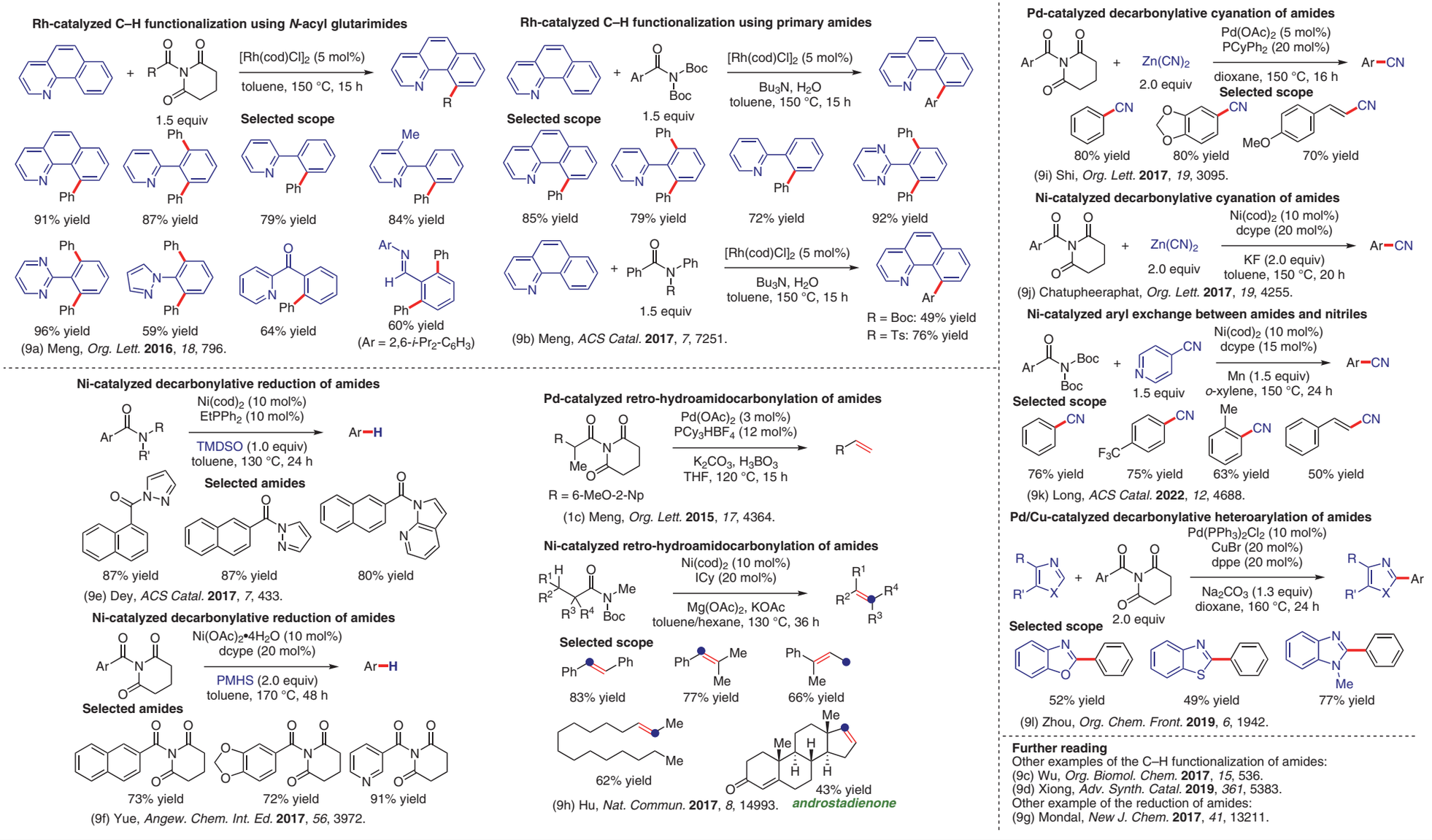
Selected scope



88% yield | 65% yield | 75% yield

(8i) Luo, *J. Org. Chem.* **2019**, *84*, 10559.

Figure 8 Decarbonylative cross-coupling of amides: discoveries and mechanism[8]



Further reading

Other examples of the C–H functionalization of amides:
(9c) Wu, *Org. Biomol. Chem.* **2017**, *15*, 536.
(9d) Xiong, *Adv. Synth. Catal.* **2019**, *361*, 5383.
Other example of the reduction of amides:
(9g) Mondal, *New J. Chem.* **2017**, *41*, 13211.

Figure 9 Decarbonylative cross-coupling of amides: construction of carbon–carbon and carbon–hydrogen bonds[9]

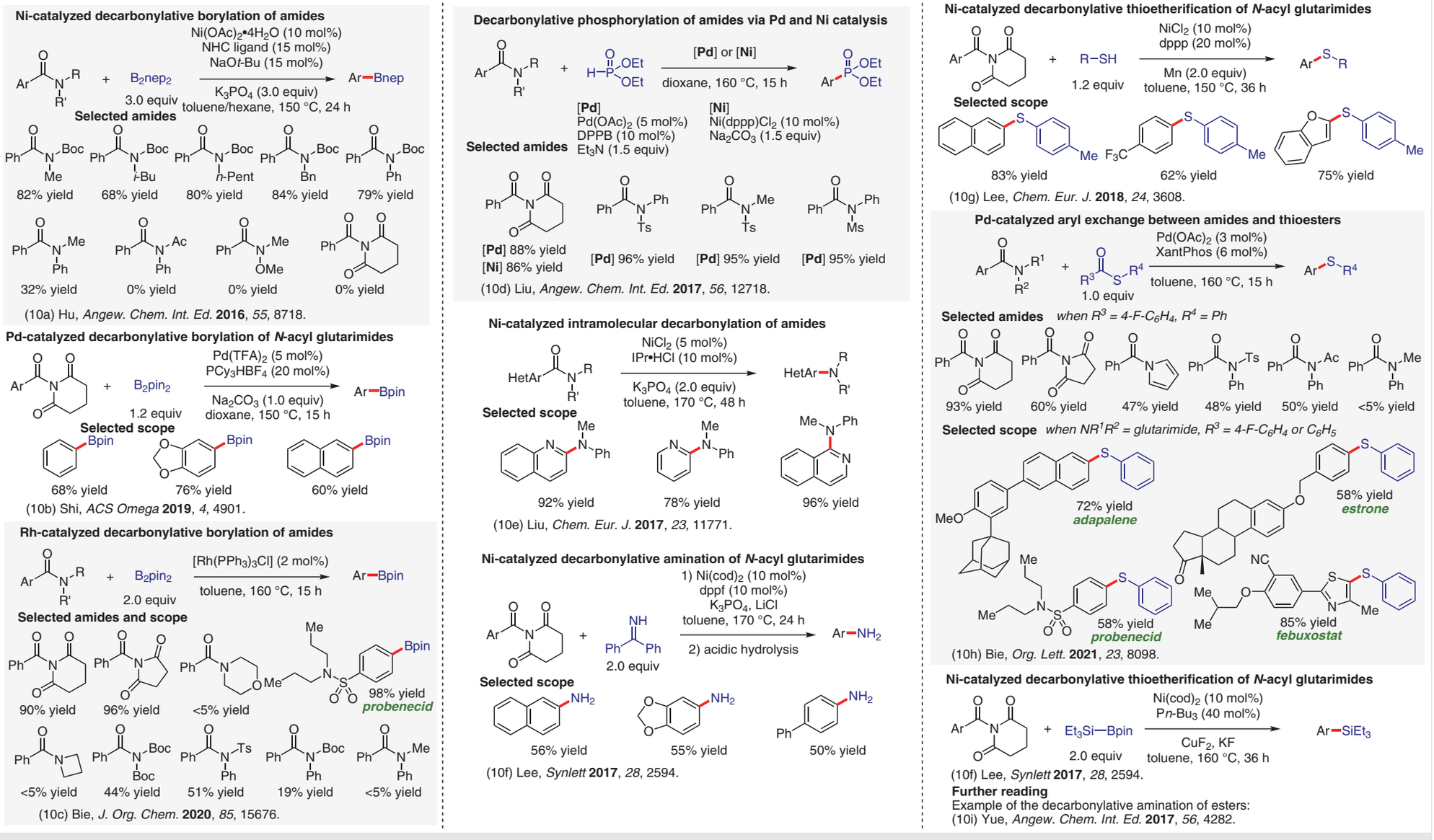


Figure 10 Decarbonylative cross-coupling of amides: construction of carbon–heteroatom bonds[10,11]

Conflict of Interest

The authors declare no conflict of interest.

Funding Information

We thank the National Science Foundation (NSF) (CAREER CHE-1650766), the National Institutes of Health (NIH) (R35GM133326), Rutgers University, the Overseas High-Level Talents Fund of Shanghai, and Shanghai University for generous support.

Acknowledgment

We thank the current and former members of the Szostak group who have contributed to establishing the concept of amide bond activation.

References

(1) (a) *Amide Bond Activation: Concepts and Reactions*; Szostak, M., Ed.; Wiley-VCH: Weinheim, **2022**. (b) Hie, L.; Fine Nathel, N. F.; Shah, T. K.; Baker, E. L.; Hong, X.; Yang, Y. F.; Liu, P.; Houk, K. N.; Garg, N. K. *Nature* **2015**, *524*, 79. (c) Meng, G.; Szostak, M. *Org. Lett.* **2015**, *17*, 4364. (d) Li, X.; Zou, G. *Chem. Commun.* **2015**, *51*, 5089. (e) Szostak, M.; Aube, J. *Chem. Rev.* **2013**, *113*, 5701. (f) Meng, G.; Zhang, J.; Szostak, M. *Chem. Rev.* **2021**, *121*, 12746. (g) Meng, G.; Shi, S.; Szostak, M. *Synlett* **2016**, *27*, 2530. (h) Liu, C.; Szostak, M. *Chem. Eur. J.* **2017**, *23*, 7157. (i) Meng, G.; Szostak, M. *Eur. J. Org. Chem.* **2018**, 2352. (j) Takise, R.; Muto, K.; Yamaguchi, J. *Chem. Soc. Rev.* **2017**, *46*, 5864. (k) Kaiser, D.; Bauer, A.; Lemmerer, M.; Maulide, N. *Chem. Soc. Rev.* **2018**, *47*, 7899. (l) Dander, J. E.; Garg, N. K. *ACS Catal.* **2017**, *7*, 1413. (m) Adachi, S.; Kumagai, N.; Shibasaki, M. *Tetrahedron Lett.* **2018**, *59*, 1147. (n) Guo, L.; Rueping, M. *Chem. Eur. J.* **2018**, *24*, 7794. (o) Bourne-Branchu, Y.; Gosmini, C.; Danoun, G. *Chem. Eur. J.* **2019**, *25*, 2663. (p) Chaudhari, M. B.; Gnanaprakasam, B. *Chem. Asian J.* **2019**, *14*, 76. (q) Li, G.; Ma, S.; Szostak, M. *Trends Chem.* **2020**, *2*, 914. (r) Gao, P.; Rahman, M. M.; Zamalloa, A.; Feliciano, J.; Szostak, M. *J. Org. Chem.* **2023**, *88*, in press; 10.1021/acs.joc.2c01094. (s) Feng, M.; Zhang, H.; Maulide, N. *Angew. Chem. Int. Ed.* **2022**, *61*, e202212213. (t) Liu, C.; Meng, G.; Liu, Y.; Liu, R.; Lalancette, R.; Szostak, R.; Szostak, M. *Org. Lett.* **2016**, *18*, 4194. (u) Meng, G.; Szostak, R.; Szostak, M. *Org. Lett.* **2017**, *19*, 3596. (v) Osumi, Y.; Liu, C.; Szostak, M. *Org. Biomol. Chem.* **2017**, *15*, 8867. (w) Rahman, M. M.; Buchspies, J.; Szostak, M. *Catalysts* **2019**, *9*, 129. (x) Jian, J.; He, Z.; Zhang, Y.; Liu, T.; Liu, L.; Wang, Z.; Wang, H.; Wang, S.; Zeng, Z. *Eur. J. Org. Chem.* **2020**, 4176. (y) Buchspies, J.; Rahman, M. M.; Szostak, R.; Szostak, M. *Org. Lett.* **2020**, *22*, 4703. (z) Meng, G.; Szostak, M. *Org. Biomol. Chem.* **2016**, *14*, 5690. (aa) Wu, H.; Li, Y.; Cui, M.; Jian, J.; Zeng, Z. *Adv. Synth. Catal.* **2016**, *358*, 3876. (ab) Cui, M.; Chen, Z.; Liu, T.; Wang, H.; Zeng, Z. *Tetrahedron Lett.* **2017**, *58*, 3819. (ac) Wang, T.; Guo, J.; Wang, H.; Guo, H.; Jia, D.; Zhang, W.; Liu, L. *J. Organomet. Chem.* **2018**, *877*, 80. (ad) Liu, C.; Lalancette, R.; Szostak, R.; Szostak, M. *Org. Lett.* **2019**, *21*, 7976. (ae) Rahman, M. M.; Liu, C.; Bisz, E.; Dziuk, B.; Lalancette, R.; Wang, Q.; Chen, H.; Szostak, R.; Szostak, M. *J. Org. Chem.* **2020**, *85*, 5475. (af) Ma, S.; Zhou, T.; Li, G.; Szostak, M. *Adv. Synth. Catal.* **2020**, *362*, 1887. (ag) Luo, Z.; Liu, T.; Guo, W.; Wang, Z.; Huang, J.; Zhu, Y.; Zeng, Z. *Org. Process Res. Dev.* **2018**, *22*, 1188. (ah) Wang, C. A.; Liu, C.; Szostak, M. *Org. Process Res. Dev.* **2020**, *24*, 1043. (ai) Rahman, M. M.; Pyle, D. J.; Bisz, E.; Dziuk, B.; Ejsmont, K.; Lalancette, R.; Wang, Q.; Chen, H.; Szostak, R.; Szostak, M. *J. Org. Chem.* **2021**, *86*, 10455.

(2) (a) Weires, N. A.; Baker, E. L.; Garg, N. K. *Nat. Chem.* **2016**, *8*, 75. (b) Meng, G.; Lalancette, R.; Szostak, R.; Szostak, M. *Org. Lett.* **2017**, *19*, 4656. (c) Liu, C.; Li, G.; Shi, S.; Meng, G.; Lalancette, R.; Szostak, R.; Szostak, M. *ACS Catal.* **2018**, *8*, 9131. (d) Liu, C.; Liu, Y.; Liu, R.; Lalancette, R.; Szostak, R.; Szostak, M. *Org. Lett.* **2017**, *19*, 1434. (e) Lim, M.; Kim, H.; Ban, J.; Son, J.; Lee, J. K.; Min, S. J.; Lee, S. U.; Rhee, H. *Eur. J. Org. Chem.* **2018**, 5717. (f) Shi, S.; Lalancette, R.; Szostak, R.; Szostak, M. *Org. Lett.* **2019**, *21*, 1253. (g) Meng, G.; Shi, S.; Szostak, M. *ACS Catal.* **2016**, *6*, 7335. (h) Zhang, Y.; Wang, Z.; Tang, Z.; Luo, Z.; Wu, H.; Liu, T.; Zhu, Y.; Zeng, Z. *Eur. J. Org. Chem.* **2020**, 1620. (i) Li, X.; Zou, G. *J. Organomet. Chem.* **2015**, *794*, 136. (j) Szostak, R.; Shi, S.; Meng, G.; Lalancette, R.; Szostak, M. *J. Org. Chem.* **2016**, *81*, 8091. (k) Pace, V.; Holzer, W.; Meng, G.; Shi, S.; Lalancette, R.; Szostak, R.; Szostak, M. *Chem. Eur. J.* **2016**, *22*, 14494. (l) Pace, V.; Holzer, W.; Ielo, L.; Shi, S.; Meng, G.; Hanna, M.; Szostak, R.; Szostak, M. *Chem. Commun.* **2019**, *55*, 4423. (m) Szostak, R.; Meng, G.; Szostak, M. *J. Org. Chem.* **2017**, *82*, 6373. (n) Meng, G.; Shi, S.; Lalancette, R.; Szostak, R.; Szostak, M. *J. Am. Chem. Soc.* **2018**, *140*, 727. (o) Szostak, R.; Szostak, M. *Org. Lett.* **2018**, *20*, 1342. (p) Szostak, R.; Liu, C.; Lalancette, R.; Szostak, M. *J. Org. Chem.* **2018**, *83*, 14676. (q) Ielo, L.; Pace, V.; Holzer, W.; Rahman, M. M.; Meng, G.; Szostak, R.; Szostak, M. *Chem. Eur. J.* **2020**, *26*, 16246. (r) Liu, C.; Shi, S.; Liu, Y.; Liu, R.; Lalancette, R.; Szostak, R.; Szostak, M. *Org. Lett.* **2018**, *20*, 7771. (s) Boit, T. B.; Weires, N. A.; Kim, J.; Garg, N. K. *ACS Catal.* **2018**, *8*, 1003. (t) Mai, W. P.; Liu, Y.; Sui, H. D.; Xiao, Y. M.; Mao, P.; Lu, K. *Eur. J. Org. Chem.* **2019**, 7814. (u) Mehta, M. M.; Boit, T. B.; Dander, J. E.; Garg, N. K. *Org. Lett.* **2020**, *22*, 1. (v) Shi, W.; Sun, G.; Zou, G. *Tetrahedron Lett.* **2020**, *61*, 152140. (w) Wang, C. A.; Rahman, M. M.; Bisz, E.; Dziuk, B.; Szostak, R.; Szostak, M. *ACS Catal.* **2022**, *12*, 2426. (x) Zhang, J.; Zhang, P.; Shao, L.; Wang, R.; Ma, Y.; Szostak, M. *Angew. Chem. Int. Ed.* **2022**, *61*, e202114146. (y) Li, C. X.; Ning, Q.; Zhao, W.; Cao, H. J.; Wang, Y. P.; Yan, H.; Lu, C. S.; Liang, Y. *Chem. Eur. J.* **2021**, *27*, 2699.

(3) (a) Lei, P.; Meng, G.; Szostak, M. *ACS Catal.* **2017**, *7*, 1960. (b) Lei, P.; Meng, G.; Ling, Y.; An, J.; Szostak, M. *J. Org. Chem.* **2017**, *82*, 6638. (c) Lei, P.; Meng, G.; Shi, S.; Ling, Y.; An, J.; Szostak, R.; Szostak, M. *Chem. Sci.* **2017**, *8*, 6525. (d) Shi, S.; Nolan, S. P.; Szostak, M. *Acc. Chem. Res.* **2018**, *51*, 2589. (e) Lei, P.; Meng, G.; Ling, Y.; An, J.; Nolan, S. P.; Szostak, M. *Org. Lett.* **2017**, *19*, 6510. (f) Lei, P.; Ling, Y.; An, J.; Nolan, S. P.; Szostak, M. *Adv. Synth. Catal.* **2019**, *361*, 5654. (g) Li, G.; Lei, P.; Szostak, M.; Casals-Cruanas, E.; Poater, A.; Cavallo, L.; Nolan, S. P. *ChemCatChem* **2018**, *10*, 3096. (h) Shi, S.; Szostak, M. *Chem. Commun.* **2017**, *53*, 10584. (i) Zhou, T.; Li, G.; Nolan, S. P.; Szostak, M. *Org. Lett.* **2019**, *21*, 3304. (j) Li, G.; Zhou, T.; Poater, A.; Cavallo, L.; Nolan, S. P.; Szostak, M. *Catal. Sci. Technol.* **2020**, *10*, 710. (k) Buchspies, J.; Rahman, M. M.; Szostak, M. *Catalysts* **2020**, *10*, 372. (l) Zhou, T.; Ma, S.; Nahra, F.; Obled, A. M. C.; Poater, A.; Cavallo, L.; Cazin, C. S. J.; Nolan, S. P.; Szostak, M. *iScience* **2020**, *23*, 101377. (m) Lei, P.; Li, G.; Ling, Y.; An, J.; Nolan, S. P.; Szostak, M. *Synthesis* **2021**, *53*, 682. (n) Lei, P.; Mu, Y.; Wang, Y.; Wang, Y.; Ma, Z.; Feng, J.; Liu, X.; Szostak, M. *ACS Sustainable Chem. Eng.* **2021**, *9*, 552. (o) Lei, P.; Wang, Y.; Mu, Y.; Wang, Y.; Ma, Z.; Feng, J.; Liu, X.; Szostak, M. *ACS Sustainable Chem. Eng.* **2021**, *9*, 14937. (p) Buchspies, J.; Rahman, M. M.; Szostak, M. *Molecules* **2021**, *26*, 188. (q) Shi, S.; Szostak, M. *Chem. Eur. J.* **2016**, *22*, 10420. (r) Shi, S.; Szostak, M. *Synthesis* **2017**, *49*, 3602. (s) Shi, S.; Szostak, M. *Org. Lett.* **2016**, *18*, 5872. (t) Simmons, B. J.; Weires, N. A.; Dander, J. E.; Garg, N. K. *ACS Catal.* **2016**, *6*, 3176. (u) Dorval, C.; Stetsiuk, O.; Gaillard, S.; Dubois, E.; Gosmini, C.; Danoun, G. *Org. Lett.* **2022**, *24*, 2778. (v) Dorval, C.; Dubois, E.; Bourne-Branchu, Y.; Gosmini, C.; Danoun, G. *Adv. Synth. Catal.* **2019**, *361*, 1777. (w) Bao, C. C.; Du, H. Z.; Luo, Y. L.; Guan, B. T. *Commun. Chem.* **2021**, *4*, 138. (x) Kim, J.; Park, M. S.; Lee, S.; Song, K. H. *Tetrahedron Lett.* **2022**, *111*, 154201. (y) Liu, C.; Achtenhagen, M.; Szostak, M. *Org. Lett.* **2016**, *18*, 2375. (z) Chen, C.; Liu, P.; Luo, M.; Zeng, X. *ACS Catal.* **2018**, *8*, 5864. (aa) Sureshbabu, P.; Azeez, S.; Muniyappan, N.; Sabiah, S.; Kandasamy, J. *J. Org. Chem.* **2019**, *84*, 11823. (ab) Li, G.; Szostak, M. *Chem. Eur. J.* **2020**, *26*, 611. (ac) Li, G.; Szostak, M. *Org. Biomol. Chem.* **2020**, *18*, 3827.

(4) (a) Ni, S.; Zhang, W.; Mei, H.; Han, J.; Pan, Y. *Org. Lett.* **2017**, *19*, 2536. (b) Zhuo, J.; Zhang, Y.; Li, Z.; Li, C. *ACS Catal.* **2020**, *10*, 3895. (c) Yu, C. G.; Matsuo, Y. *Org. Lett.* **2020**, *22*, 950. (d) Idris, M. A.; Lee, S. *Org. Lett.* **2020**, *22*, 9190. (e) He, Z.; Yan, C.; Zhang, M.; Irfan, M.; Wang, Z.; Zeng, Z. *Synthesis* **2022**, *54*, 705. (f) Liu, X.; Hsiao, C. C.; Guo, L.; Rueping, M. *Org. Lett.* **2018**, *20*, 2976. (g) Meng, G.; Szostak, M. *Org. Lett.* **2018**, *20*,

6789. (h) Chen, J.; Xu, M.; Yu, S.; Xia, Y.; Lee, S. *Org. Lett.* **2020**, *22*, 2287. (i) Liu, Y.; Meng, G.; Liu, R.; Szostak, M. *Chem. Commun.* **2016**, *52*, 6841. (j) Liu, Y.; Liu, R.; Szostak, M. *Org. Biomol. Chem.* **2017**, *15*, 1780. (k) Li, J.; Yao, J.; Chen, L.; Zou, D.; Walsh, P. J.; Liang, G. *Org. Chem. Front.* **2021**, *8*, 6344. (l) Amani, J.; Alam, R.; Badir, S.; Molander, G. A. *Org. Lett.* **2017**, *19*, 2426. (m) Shi, W.; Zou, G. *Molecules* **2018**, *23*, 2412. (n) Mahesh, S.; Tang, K. C.; Raj, M. *Molecules* **2018**, *23*, 2615. (o) Wang, C.; Huang, L.; Wang, F.; Zou, G. *Tetrahedron Lett.* **2018**, *59*, 2299. (p) Kadam, A. A.; Metz, T. L.; Qian, Y.; Stanley, L. M. *ACS Catal.* **2019**, *9*, 5651. (q) Koeritz, M. T.; Burgett, R. W.; Kadam, A. A.; Stanley, L. M. *Org. Lett.* **2020**, *22*, 5731. (r) Reina, A.; Krachko, T.; Onida, K.; Bouyssi, D.; Jeanneau, E.; Monteiro, N.; Amgoune, A. *ACS Catal.* **2020**, *10*, 2189. (s) Kerackian, T.; Reina, A.; Bouyssi, D.; Monteiro, N.; Amgoune, A. *Org. Lett.* **2020**, *22*, 2240. (t) Kerackian, T.; Bouyssi, D.; Pilet, G.; Medebielle, M.; Monteiro, N.; Vantourout, J. C.; Amgoune, A. *ACS Catal.* **2022**, *12*, 12315.

(5) (a) Cui, M.; Wu, H.; Jian, J.; Wang, H.; Liu, C.; Daniel, S.; Zeng, Z. *Chem. Commun.* **2016**, *52*, 12076. (b) Karthik, S.; Gandhi, T. *Org. Lett.* **2017**, *19*, 5486. (c) Li, W.; Zhang, S.; Feng, X.; Yu, X.; Yamamoto, Y.; Bao, M. *Org. Lett.* **2021**, *23*, 2521. (d) Simmons, B. J.; Hoffmann, M.; Hwang, J.; Jackl, M. K.; Garg, N. K. *Org. Lett.* **2017**, *19*, 1910. (e) Simmons, B. J.; Ramirez, M.; Garg, N. K. *Org. Synth.* **2019**, *96*, 436. (f) Boit, T. B.; Mehta, M. M.; Kim, J.; Baker, E. L.; Garg, N. K. *Angew. Chem. Int. Ed.* **2021**, *60*, 2472. (g) Dander, J. E.; Giroud, M.; Racine, S.; Darzi, E. R.; Alvizo, O.; Entwistle, D.; Garg, N. K. *Commun. Chem.* **2019**, *2*, 82. (h) Knapp, R. R.; Bulger, A. S.; Garg, N. K. *Org. Lett.* **2020**, *22*, 2833. (i) Bulger, A. S.; Witkowski, D. C.; Garg, N. K. *Org. Synth.* **2022**, *99*, 305. (j) Rahman, M. M.; Szostak, M. *Org. Lett.* **2021**, *23*, 4818. (k) Idris, M. A.; Song, K. H.; Lee, S. *Adv. Synth. Catal.* **2022**, *364*, 2449. (l) Medina, J. M.; Moreno, J.; Racine, S.; Du, S.; Garg, N. K. *Angew. Chem. Int. Ed.* **2017**, *56*, 6567. (m) Walker, J. A.; Vickerman, K. L.; Humke, J. N.; Stanley, L. M. *J. Am. Chem. Soc.* **2017**, *139*, 10228. (n) Luo, Z.; Wu, H.; Li, Y.; Chen, Y.; Nie, J.; Lu, S.; Zhu, Y.; Zeng, Z. *Adv. Synth. Catal.* **2019**, *361*, 4117. (o) Azeez, S.; Sureshbabu, P.; Sabiah, S.; Kandasamy, J. *Org. Biomol. Chem.* **2022**, *20*, 2048. (p) Liu, L. L.; Chen, P.; Sun, Y.; Wu, Y.; Chen, S.; Zhu, J.; Zhao, Y. *J. Org. Chem.* **2016**, *81*, 11686. (q) Chu, C. Q.; Dang, L. *J. Org. Chem.* **2018**, *83*, 5009. (r) Wang, H.; Zhang, S. Q.; Hong, X. *Chem. Commun.* **2019**, *55*, 11330.

(6) (a) Baker, E. L.; Yamano, M. M.; Zhou, Y.; Anthony, S. M.; Garg, N. K. *Nat. Commun.* **2016**, *7*, 11554. (b) Meng, G.; Lei, P.; Szostak, M. *Org. Lett.* **2017**, *19*, 2158. (c) Idris, M. A.; Lee, S. *Org. Chem. Front.* **2020**, *7*, 2737. (d) Liu, Y.; Shi, S.; Achtenhagen, M.; Liu, R.; Szostak, M. *Org. Lett.* **2017**, *19*, 1614. (e) Liu, Y.; Achtenhagen, M.; Liu, R.; Szostak, M. *Org. Biomol. Chem.* **2018**, *16*, 1322. (f) Rahman, M. M.; Li, G.; Szostak, M. *J. Org. Chem.* **2019**, *84*, 12091. (g) Li, G.; Szostak, M. *Nat. Commun.* **2018**, *9*, 4165. (h) Li, G.; Ji, C. L.; Hong, X.; Szostak, M. *J. Am. Chem. Soc.* **2019**, *141*, 11161. (i) Zuo, D.; Wang, Q.; Liu, L.; Huang, T.; Szostak, M.; Chen, T. *Angew. Chem. Int. Ed.* **2022**, *61*, e202202794. (j) Li, G.; Xing, Y.; Zhao, H.; Zhang, J.; Hong, X.; Szostak, M. *Angew. Chem. Int. Ed.* **2022**, *61*, e202200144. (k) Zhang, J.; Zhao, H.; Li, G.; Zhu, X.; Shang, L.; He, Y.; Liu, X.; Ma, Y.; Szostak, M. *Org. Biomol. Chem.* **2022**, *20*, 5981. (l) Li, G.; Szostak, M. *Chem. Rec.* **2020**, *20*, 649. (m) Li, G.; Szostak, M. *Synthesis* **2020**, *52*, 2579. (n) Guo, W.; Huang, J.; Wu, H.; Liu, T.; Luo, Z.; Jian, J.; Zeng, Z. *Org. Chem. Front.* **2018**, *5*, 2950. (o) Zhang, Y.; Ye, X.; Liu, S.; Chen, W.; Majeed, I.; Liu, T.; Zhu, Y.; Zeng, Z. *Org. Biomol. Chem.* **2021**, *19*, 8566. (p) Dander, J. E.; Baker, E. L.; Garg, N. K. *Chem. Sci.* **2017**, *8*, 6433. (q) Singh, S.; Popuri, S.; Junaid, Q. M.; Sabiah, S.; Kandasamy, J. *Org. Biomol. Chem.* **2021**, *19*, 7134. (r) Sureshbabu, P.; Azeez, S.; Chaudhary, P.; Kandasamy, J. *Org. Biomol. Chem.* **2019**, *17*, 845. (s) Sureshbabu, P.; Azeez, S.; Pattanaik, K.; Sabiah, S.; Kandasamy, J. *Asian J. Org. Chem.* **2022**, *11*, e202200076. (t) Subramani, M.; Rajendran, S. K. *Eur. J. Org. Chem.* **2019**, 3677. (u) Yang, D.; Shin, T.; Kim, H.; Lee, S. *Org. Biomol. Chem.* **2020**, *18*, 6053. (v) Joseph, D.; Park, M. S.; Lee, S. *Org. Biomol. Chem.* **2021**, *19*, 6227.

(7) (a) Hie, L.; Baker, E. L.; Anthony, S. M.; Desrosiers, J. N.; Senanayake, C.; Garg, N. K. *Angew. Chem. Int. Ed.* **2016**, *55*, 15129. (b) Bourne-Branchu, Y.; Gosmini, C.; Danoun, G. *Chem. Eur. J.* **2017**, *23*, 10043. (c) Li, G.; Lei, P.; Szostak, M. *Org. Lett.* **2018**, *20*, 5622. (d) Wu, H.; Guo, W.; Daniel, S.; Li, Y.; Liu, C.; Zeng, Z. *Chem. Eur. J.* **2018**, *24*, 3444. (e) Wybon, C. C. D.; Mensch, C.; Hollanders, C.; Gadais, C.; Herrebout, W. A.; Ballet, S.; Maes, B. U. W. *ACS Catal.* **2018**, *8*, 203. (f) Ye, D.; Liu, Z.; Chen, H.; Sessler, J. L.; Lei, C. *Org. Lett.* **2019**, *21*, 6888. (g) Wang, Q.; Liu, L.; Dong, J.; Tian, Z.; Chen, T. *New J. Chem.* **2019**, *43*, 9384. (h) Rahman, M. M.; Li, G.; Szostak, M. *Synthesis* **2020**, *52*, 1060. (i) Li, Y.; Wu, H.; Zeng, Z. *Eur. J. Org. Chem.* **2019**, 4357. (j) Liu, Y.; Mo, X.; Majeed, I.; Zhang, M.; Wang, H.; Zeng, Z. *Org. Biomol. Chem.* **2022**, *20*, 1532. (k) Weires, N. A.; Caspi, D. D.; Garg, N. K. *ACS Catal.* **2017**, *7*, 4381. (l) Dander, J. E.; Morrill, L. A.; Nguyen, M. M.; Chen, S.; Garg, N. K. *J. Chem. Educ.* **2019**, *96*, 776. (m) Nagae, H.; Hirai, T.; Kato, D.; Soma, S.; Akebi, S. Y.; Mashima, K. *Chem. Sci.* **2019**, *10*, 2860.

(8) (a) Meng, G.; Szostak, M. *Angew. Chem. Int. Ed.* **2015**, *54*, 14518. (b) Liu, C.; Meng, G.; Szostak, M. *J. Org. Chem.* **2016**, *81*, 12023. (c) Liu, C.; Szostak, M. *Org. Biomol. Chem.* **2018**, *16*, 7998. (d) Ji, C. L.; Hong, X. *J. Am. Chem. Soc.* **2017**, *139*, 15522. (e) Tong, W. Y.; Ly, T. D.; Zhao, T. T.; Wu, Y. B.; Wang, X. *Chem. Commun.* **2020**, *56*, 113. (f) Li, R.; Xu, H.; Zhao, N.; Jin, X.; Dang, Y. *J. Org. Chem.* **2020**, *85*, 833. (g) Shi, S.; Meng, G.; Szostak, M. *Angew. Chem. Int. Ed.* **2016**, *55*, 6959. (h) Zhou, T.; Ji, C. L.; Hong, X.; Szostak, M. *Chem. Sci.* **2019**, *10*, 9865. (i) Luo, Z.; Xiong, L.; Liu, T.; Zhang, Y.; Lu, S.; Chen, Y.; Guo, W.; Zhu, Y.; Zeng, Z. *J. Org. Chem.* **2019**, *84*, 10559. (j) Srimontree, W.; Chatupheeraphat, A.; Liao, H. H.; Rueping, M. *Org. Lett.* **2017**, *19*, 3091. (k) Liu, L.; Zhou, D.; Liu, M.; Zhou, Y.; Chen, T. *Org. Lett.* **2018**, *20*, 2741. (l) Chatupheeraphat, A.; Liao, H. H.; Srimontree, W.; Guo, L.; Minenkov, Y.; Poater, A.; Cavallo, L.; Rueping, M. *J. Am. Chem. Soc.* **2018**, *140*, 3724.

(9) (a) Meng, G.; Szostak, M. *Org. Lett.* **2016**, *18*, 796. (b) Meng, G.; Szostak, M. *ACS Catal.* **2017**, *7*, 7251. (c) Wu, H.; Liu, T.; Cui, M.; Li, Y.; Jian, J.; Wang, H.; Zeng, Z. *Org. Biomol. Chem.* **2017**, *15*, 536. (d) Xiong, L.; Deng, R.; Liu, T.; Luo, Z.; Wang, Z.; Zhu, X. F.; Wang, H.; Zeng, Z. *Adv. Synth. Catal.* **2019**, *361*, 5383. (e) Dey, A.; Sasmal, S.; Seth, K.; Lahiri, G. K.; Maiti, D. *ACS Catal.* **2017**, *7*, 433. (f) Yue, H.; Guo, L.; Lee, S. C.; Liu, X.; Rueping, M. *Angew. Chem. Int. Ed.* **2017**, *56*, 3972. (g) Mondal, M.; Bharali, P. *New J. Chem.* **2017**, *41*, 13211. (h) Hu, J.; Wang, M.; Pu, X.; Shi, Z. *Nat. Commun.* **2017**, *8*, 14993. (i) Shi, S.; Szostak, M. *Org. Lett.* **2017**, *19*, 3095. (j) Chatupheeraphat, A.; Liao, H. H.; Lee, S. C.; Rueping, M. *Org. Lett.* **2017**, *19*, 4255. (k) Long, Y.; Zheng, Y.; Xia, Y.; Qu, L.; Yang, Y.; Xiang, H.; Zhou, X. *ACS Catal.* **2022**, *12*, 4688. (l) Zhou, P. X.; Shi, S.; Wang, J.; Zhang, Y.; Li, C.; Ge, C. *Org. Chem. Front.* **2019**, *6*, 1942.

(10) (a) Hu, J.; Zhao, Y.; Liu, J.; Zhang, Y.; Shi, Z. *Angew. Chem. Int. Ed.* **2016**, *55*, 8718. (b) Shi, S.; Szostak, M. *ACS Omega* **2019**, *4*, 4901. (c) Bie, F.; Liu, X.; Shi, Y.; Cao, H.; Han, Y.; Szostak, M.; Liu, C. *J. Org. Chem.* **2020**, *85*, 15676. (d) Liu, C.; Szostak, M. *Angew. Chem. Int. Ed.* **2017**, *56*, 12718. (e) Liu, X.; Yue, H.; Jia, J.; Guo, L.; Rueping, M. *Chem. Eur. J.* **2017**, *23*, 11771. (f) Lee, S. C.; Guo, L.; Yue, H.; Liao, H. H.; Rueping, M. *Synlett* **2017**, *28*, 2594. (g) Lee, S. C.; Liao, H. H.; Chatupheeraphat, A.; Rueping, M. *Chem. Eur. J.* **2018**, *24*, 3608. (h) Bie, F.; Liu, X.; Cao, H.; Shi, Y.; Zhou, T.; Szostak, M.; Liu, C. *Org. Lett.* **2021**, *23*, 8098. (i) Yue, H.; Guo, L.; Liao, H. H.; Cai, Y.; Zhu, C.; Rueping, M. *Angew. Chem. Int. Ed.* **2017**, *56*, 4282.

(11) For additional information, see: (a) Long, Y.; Su, Z.; Zheng, Y.; He, S.; Zhong, J.; Xiang, H.; Zhou, X. *ACS Catal.* **2020**, *10*, 3398. (b) Ito, Y.; Nakatani, S.; Shiraki, R.; Kodama, T.; Tobisu, M. *J. Am. Chem. Soc.* **2022**, *144*, 662. (c) Zhang, Z. B.; Ji, C. L.; Yang, C.; Chen, J.; Hong, X.; Xia, J. B. *Org. Lett.* **2019**, *21*, 1226. (d) Gao, P.; Szostak, M. *Org. Lett.* **2020**, *22*, 6010. (e) Zhang, Z. B.; Yang, Y.; Yu, Z. X.; Xia, J. B. *ACS Catal.* **2020**, *10*, 5419. (f) Min, K. H.; Iqbal, N.; Cho, E. J. *Org. Lett.* **2022**, *24*, 989. (g) Hollanders, C.; Renders, E.; Gadais, C.; Masullo, D.; Van Raemdonck, L.; Wybon, C. C. D.; Martin, C.; Herrebout, W. A.; Maes, B. U. W.; Ballet, S. *ACS Catal.* **2020**, *10*, 4280. (h) Lee, G. S.; Won, J.; Choi, S.; Baik, M.-H.; Hong, S. H. *Angew. Chem. Int. Ed.* **2020**, *59*, 16933. (i) Sun, W.; Wang, L.; Hu, Y.; Wu, X.; Xia, C.; Liu, C. *Nat. Commun.* **2020**, *11*, 3113. (j) Chen, J.; Joseph, D.; Xia, Y.; Lee, S. *J. Org. Chem.* **2021**, *86*, 5943. (k) Joseph, D.; Lee, S. *Org. Lett.* **2022**, *24*, 6186. (l) Xu, Y.; Wang, B.; Jiang, J.; Yu, H.; Fu, Y. *J. Org. Chem.* **2019**, *84*, 9474. (m) Xie, P. P.; Qin, Z. X.; Zhang, S. Q.; Hong, X. *ChemCatChem* **2021**, *13*, 3536. (n) Tomasini, M.; Zhang, J.; Zhao, H.; Besalu, E.; Falivene, L.; Caporaso, L.; Szostak, M.; Poater, A. *Chem. Commun.* **2022**, *58*, 9950.