Gregory C. Fu

Kik Prapapongpan

2024/04/02

http://fugroup.caltech.edu/current-members.html

Education

1984 – 1985: Undergraduate student, MIT

Advisor: Prof. K. B. Sharpless

1985 – 1991: Graduate Student, Harvard University

Advisor: Prof. D. A. Evans

1991 – 1993: Postdoctoral Fellow, Caltech

Advisor: Prof. R. H. Grubbs

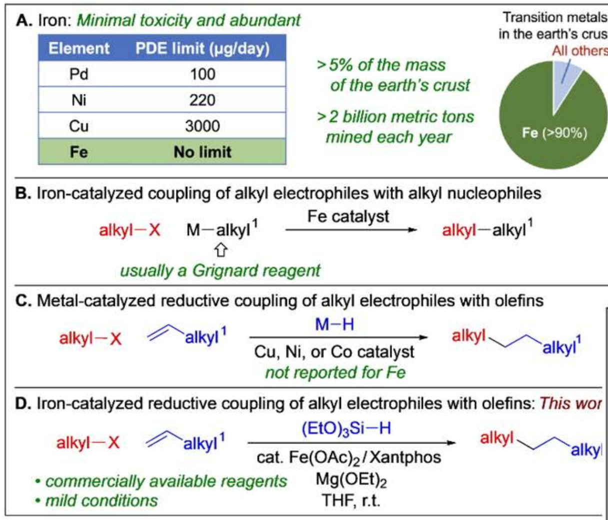
Career

1993 – 1998: Assistant Professor of Chemistry, MIT
1998 – 1999: Associate Professor of Chemistry, MIT
1999 – 2007: Professor of Chemistry, MIT
2007 – 2012: Firmenich Professor of Chemistry, MIT
2012 – 2016: Altair Professor of Chemistry, Caltech
2016 – present: Norman Chandler Professor of Chemistry, Caltech

Award

2018	Herbert C. Brown Award, *American Chemical Society*
2015	Associated Students of the California Institute of Technology (ASCIT) Teaching Award
2015	Yamada-Koga Prize
2014	Member, *National Academy of Sciences*
2013	Alexander von Humboldt Research Fellow
2012	Award for Creative Work in Synthetic Organic Chemistry, *American Chemical Society*
2007	Fellow, *American Academy of Arts and Sciences*
2007	Catalysis Science Award, *Mitsui Chemicals*
2006	Mukaiyama Award, *Society of Synthetic Organic Chemistry of Japan*
2004	Elias J. Corey Award, *American Chemical Society*
2001	Springer Award in Organometallic Chemistry
2000	School of Science Undergraduate Teaching Prize, *Massachusetts Institute of Technology*
2000	Chan Memorial Award in Organic Chemistry
1998	Arthur C. Cope Scholar Award, *American Chemical Society*
1997	Camille Dreyfus Teacher-Scholar Award
1997	Alfred P. Sloan Research Fellow
1996	Lilly Grantee Award, *Eli Lilly*
1996	Cottrell Scholar Award, *Research Corporation*
1995	American Cancer Society Junior Faculty Research Award
1994	National Science Foundation Young Investigator Award
1993	Camille and Henry Dreyfus Foundation New Faculty Award

Iron-Catalyzed Reductive Cross-Coupling of Alkyl Electrophiles with Olefins



A. Iron: *Minimal toxicity and abundant*

Element	PDE limit (µg/day)
Pd	100
Ni	220
Cu	3000
Fe	**No limit**

>5% of the mass of the earth's crust

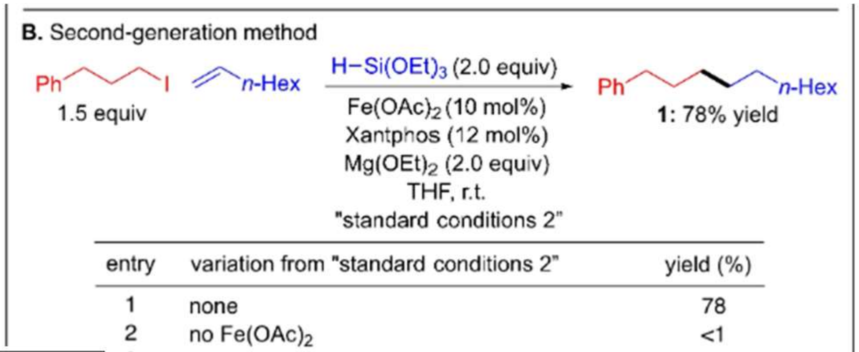
>2 billion metric tons mined each year

B. Iron-catalyzed coupling of alkyl electrophiles with alkyl nucleophiles

C. Metal-catalyzed reductive coupling of alkyl electrophiles with olefins

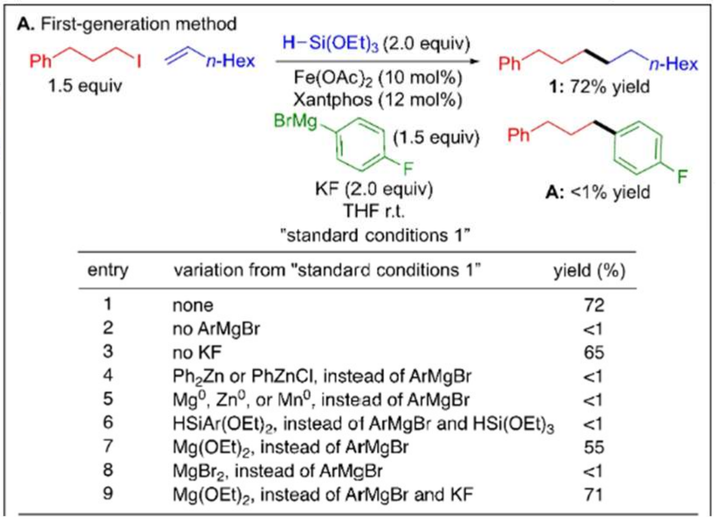
D. Iron-catalyzed reductive coupling of alkyl electrophiles with olefins: *This wor*

- *commercially available reagents*
- *mild conditions*



B. Second-generation method

entry	variation from "standard conditions 2"	yield (%)
1	none	78
2	no $Fe(OAc)_2$	<1
3	no Xantphos	2
4	no $Mg(OEt)_2$	<1
5	$Fe(OAc)_2$ (5 mol%), Xantphos (6 mol%)	63
6	alkyl bromide, instead of alkyl iodide	67
7	0.1 equiv of water added	64
8	0.5 mL of air added via syringe to the headspace	71

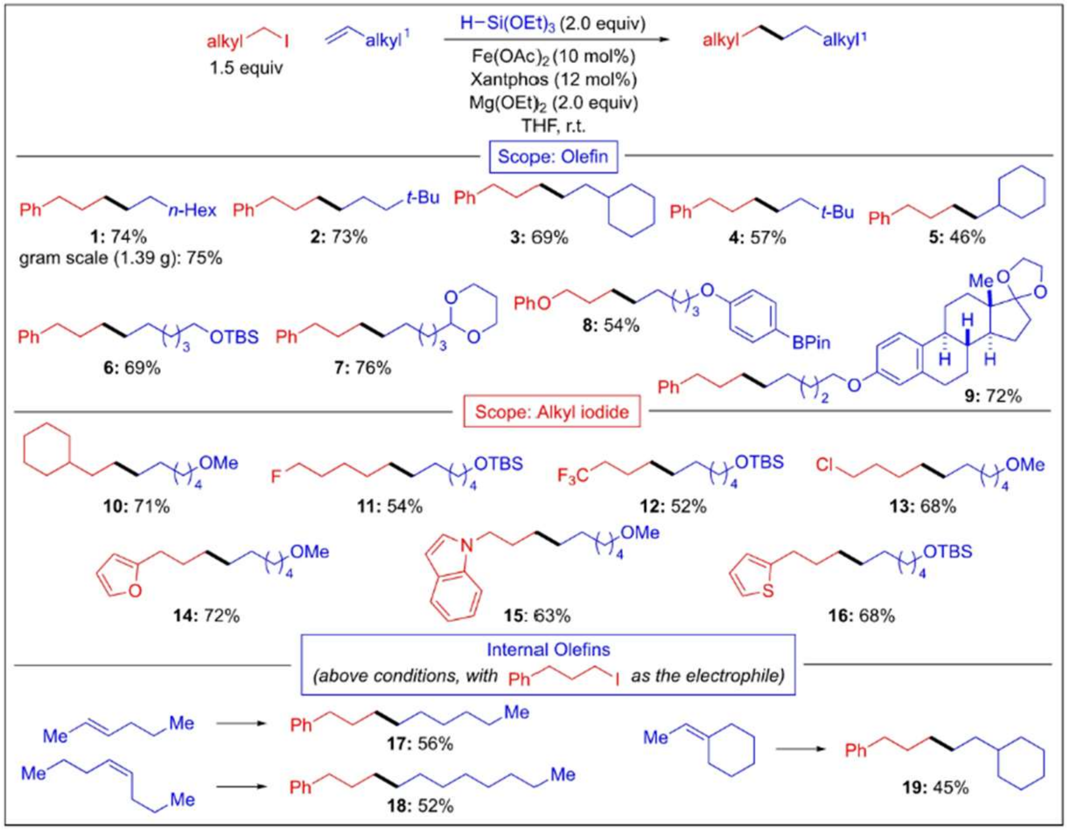


A. First-generation method

entry	variation from "standard conditions 1"	yield (%)
1	none	72
2	no ArMgBr	<1
3	no KF	65
4	Ph_2Zn or PhZnCl, instead of ArMgBr	<1
5	Mg^0, Zn^0, or Mn^0, instead of ArMgBr	<1
6	$HSiAr(OEt)_2$, instead of ArMgBr and $HSi(OEt)_3$	<1
7	$Mg(OEt)_2$, instead of ArMgBr	55
8	$MgBr_2$, instead of ArMgBr	<1
9	$Mg(OEt)_2$, instead of ArMgBr and KF	71

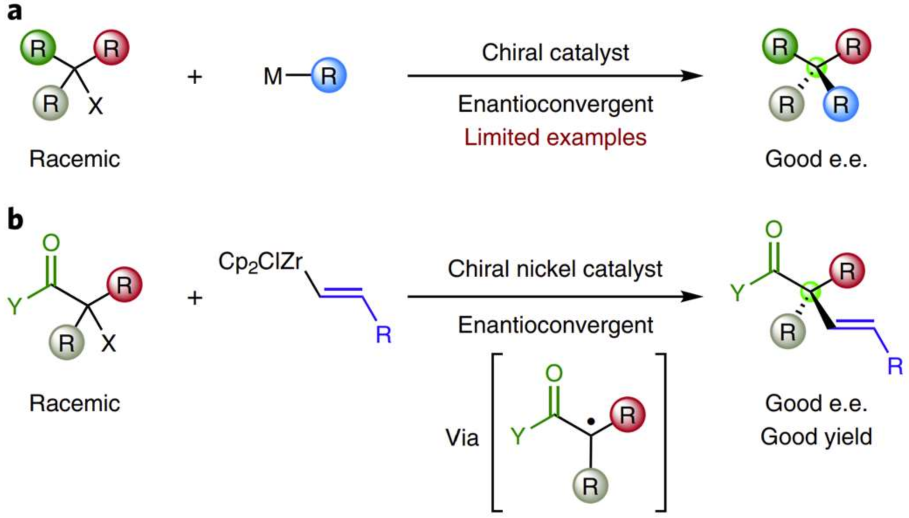
Angew. Chem.Int. Ed.2023,62, e2023066

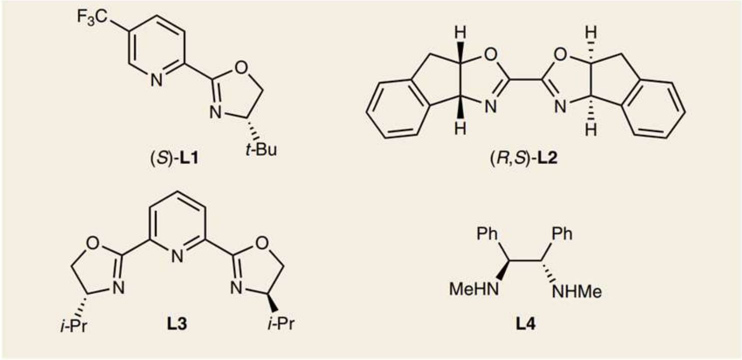
Iron-Catalyzed Reductive Cross-Coupling of Alkyl Electrophiles with Olefins



Angew. Chem.Int. Ed.2023,62, e2023066

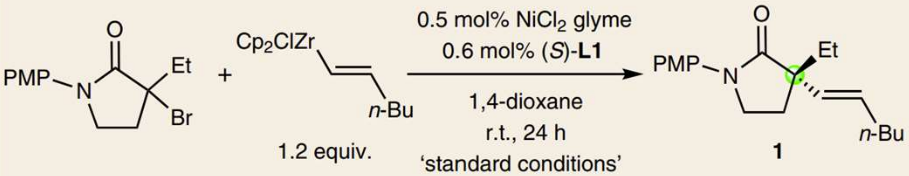
Quaternary stereocenters via catalytic enantioconvergent nucleophilic substitution reactions of tertiary alkyl halides (Ni-catalyzed reaction)





Nat. Chem. **2021**, *13*, 236–242.

Table 1 | Effect of reaction parameters on the nickel-catalysed enantioconvergent substitution reaction of a tertiary cyclic electrophile



Entry	Variation from 'standard conditions'	Yield (%)	e.e. (%)
1	None	88	98
2	No $NiCl_2$ glyme	<1	–
3	No **L1**	20	–
4	**L2**, instead of **L1**	36	27
5	**L3**, instead of **L1**	<1	–
6	**L4**, instead of **L1**	5	<5
7	1.0, instead of 1.2 equiv. of the Zr reagent	78	98
8	12 h, instead of 24 h	82	98
9	0.05 equiv. of H_2O added	76	98
10	1 ml of air, added via syringe	78	98
11	0.10 mol% $NiCl_2$ glyme, 0.12 mol% **L1**	43	98
12	0.10 mol% $NiCl_2$ glyme, 0.12 mol% **L1**, 5 days	76	98
13	0.025 mol% $NiCl_2$ glyme, 0.030 mol% **L1**, 5 days	41	98
14	α-Cl, instead of α-Br, electrophile	4	98

Quaternary stereocenters via catalytic enantioconvergent nucleophilic substitution reactions of tertiary alkyl halides (Ni-catalyzed reaction)

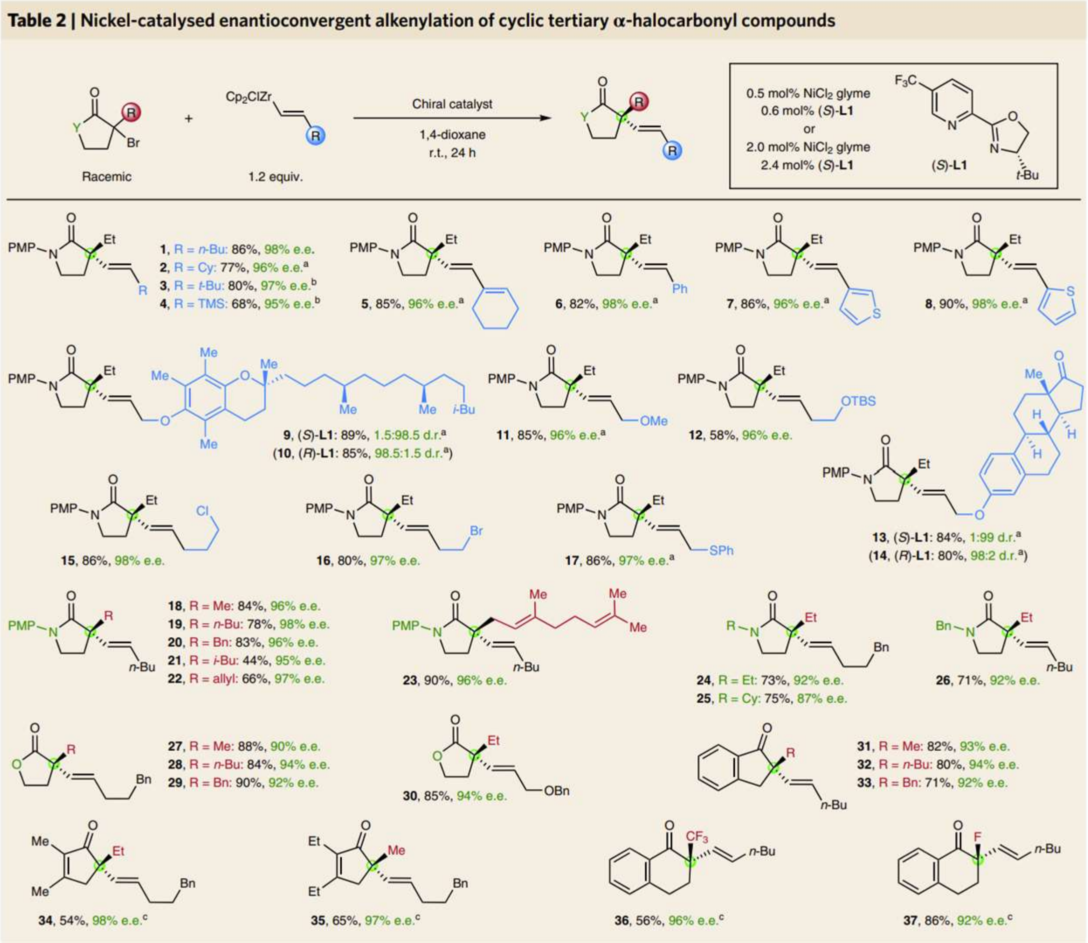


Table 2 | Nickel-catalysed enantioconvergent alkenylation of cyclic tertiary α-halocarbonyl compounds

Nat. Chem. **2021**, *13*, 236–242.

Quaternary stereocenters via catalytic enantioconvergent nucleophilic substitution reactions of tertiary alkyl halides (Ni-catalyzed reaction)

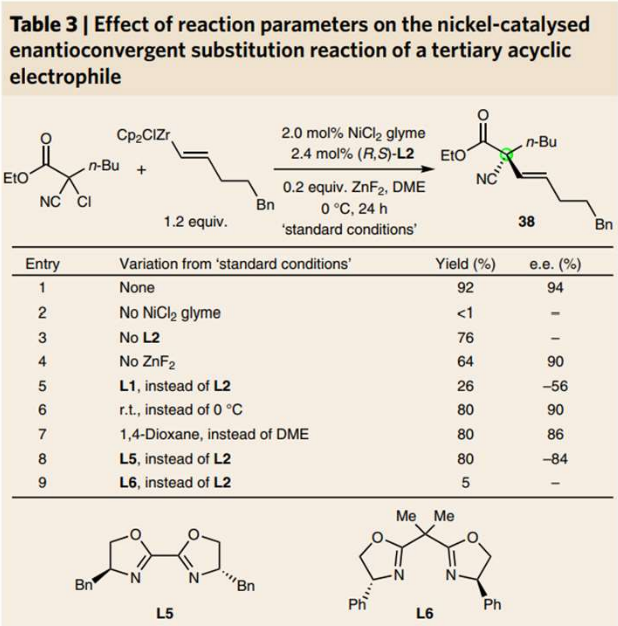


Table 3 | Effect of reaction parameters on the nickel-catalysed enantioconvergent substitution reaction of a tertiary acyclic electrophile

Entry	Variation from 'standard conditions'	Yield (%)	e.e. (%)
1	None	92	94
2	No NiCl$_2$ glyme	<1	–
3	No **L2**	76	–
4	No ZnF$_2$	64	90
5	**L1**, instead of **L2**	26	−56
6	r.t., instead of 0 °C	80	90
7	1,4-Dioxane, instead of DME	80	86
8	**L5**, instead of **L2**	80	−84
9	**L6**, instead of **L2**	5	–

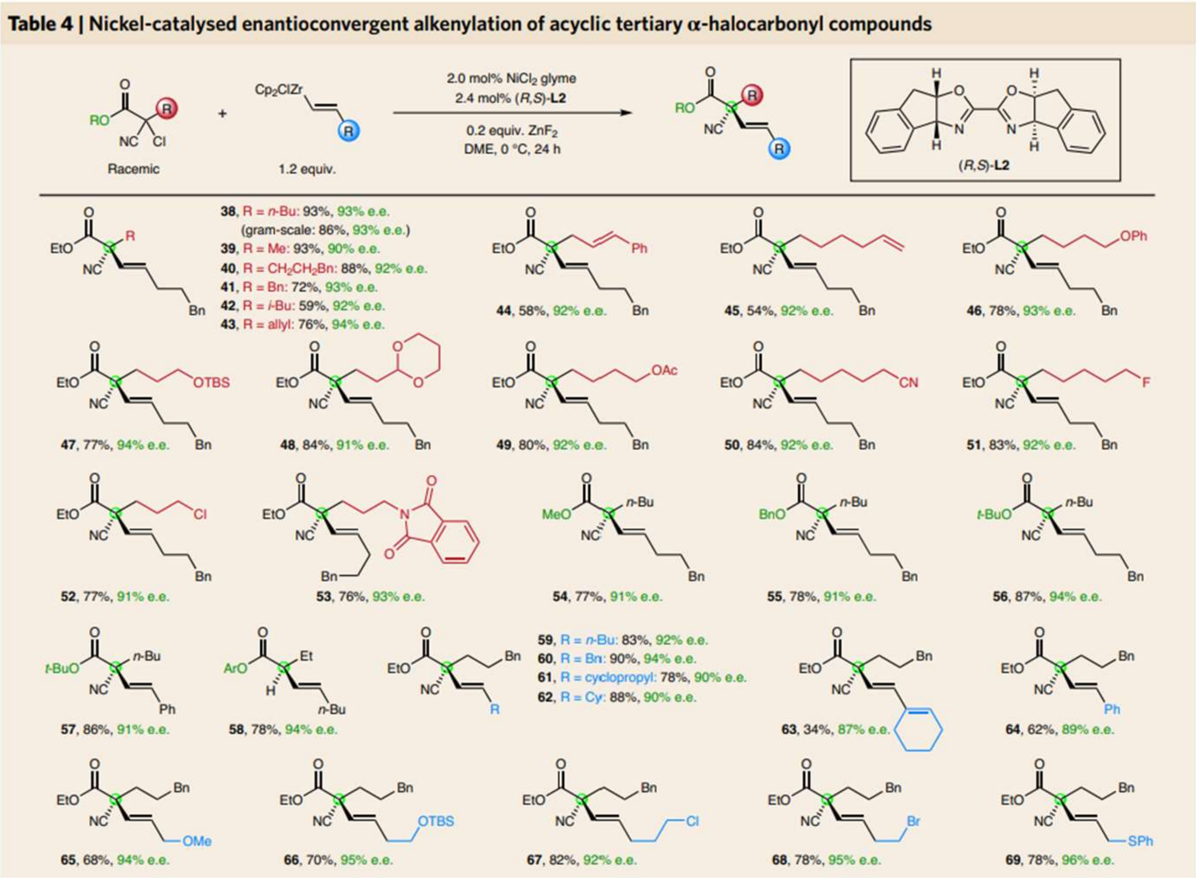


Table 4 | Nickel-catalysed enantioconvergent alkenylation of acyclic tertiary α-halocarbonyl compounds

38, R = n-Bu: 93%, 93% e.e.
(gram-scale: 86%, 93% e.e.)
39, R = Me: 93%, 90% e.e.
40, R = CH$_2$CH$_2$Bn: 88%, 92% e.e.
41, R = Bn: 72%, 93% e.e.
42, R = i-Bu: 59%, 92% e.e.
43, R = allyl: 76%, 94% e.e.

44, 58%, 92% e.e.

45, 54%, 92% e.e.

46, 78%, 93% e.e.

47, 77%, 94% e.e.

48, 84%, 91% e.e.

49, 80%, 92% e.e.

50, 84%, 92% e.e.

51, 83%, 92% e.e.

52, 77%, 91% e.e.

53, 76%, 93% e.e.

54, 77%, 91% e.e.

55, 78%, 91% e.e.

56, 87%, 94% e.e.

57, 86%, 91% e.e.

58, 78%, 94% e.e.

59, R = n-Bu: 83%, 92% e.e.
60, R = Bn: 90%, 94% e.e.
61, R = cyclopropyl: 78%, 90% e.e.
62, R = Cy: 88%, 90% e.e.

63, 34%, 87% e.e.

64, 62%, 89% e.e.

65, 68%, 94% e.e.

66, 70%, 95% e.e.

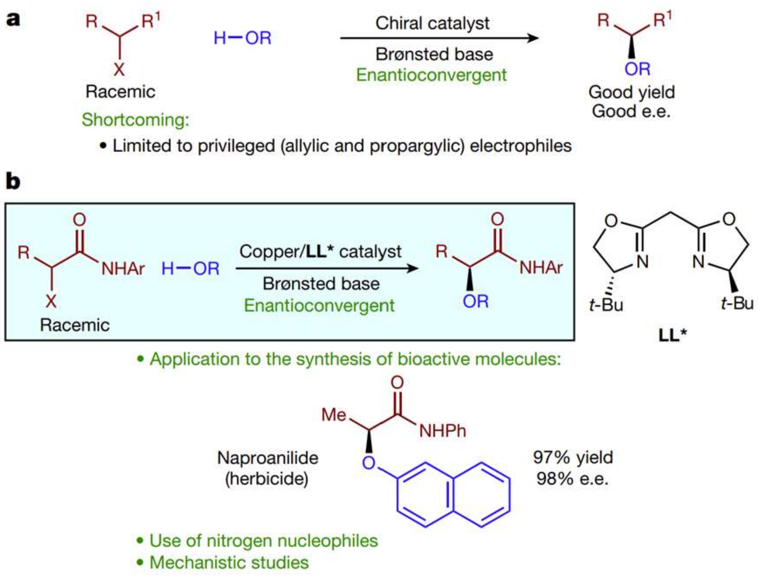
67, 82%, 92% e.e.

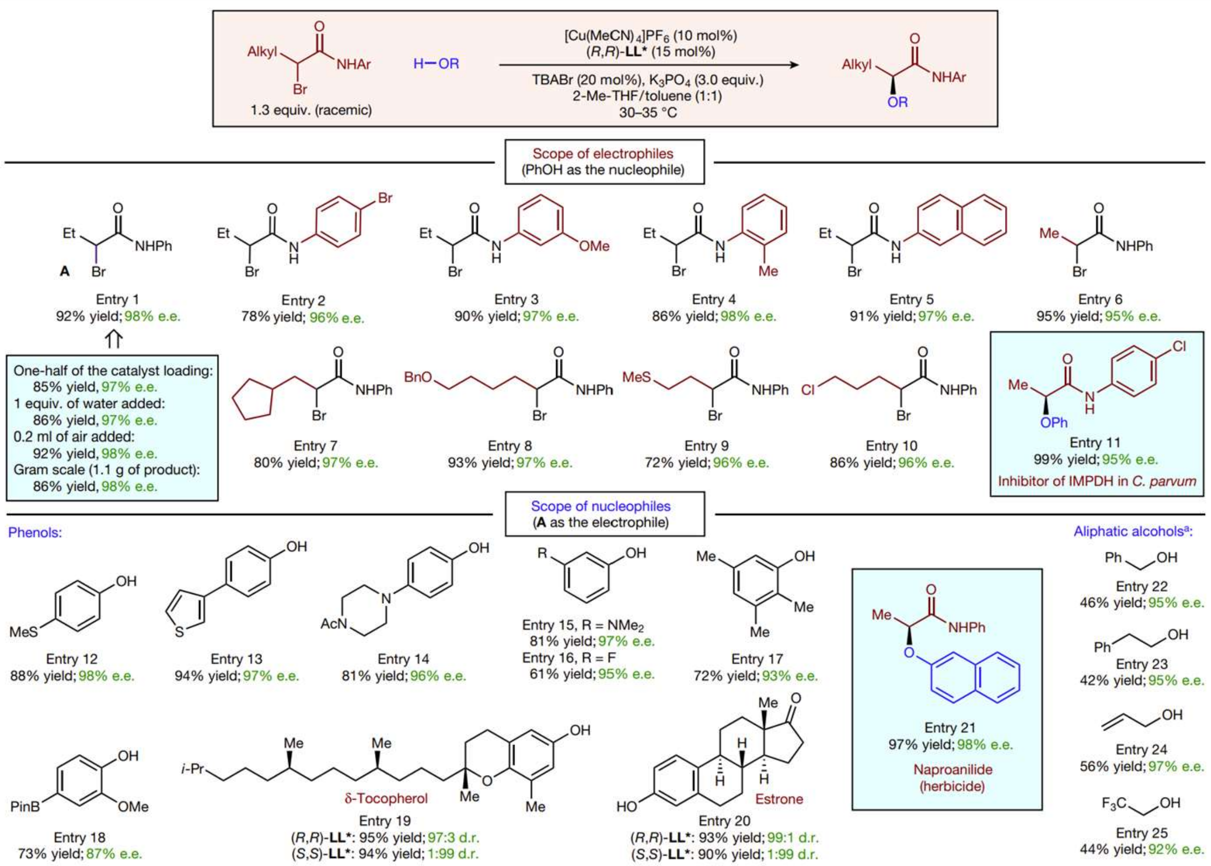
68, 78%, 95% e.e.

69, 78%, 96% e.e.

Nat. Chem. **2021**, *13*, 236–242.

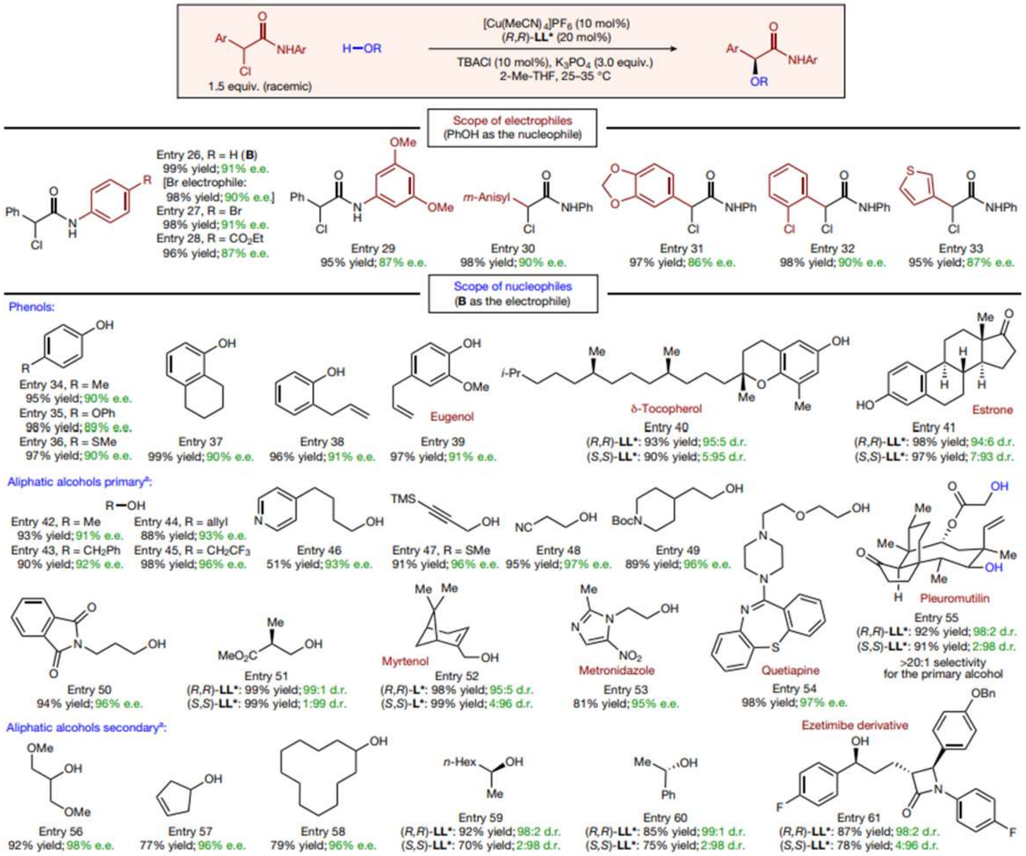
Copper-catalyzed enantioconvergent alkylation of oxygen nucleophiles

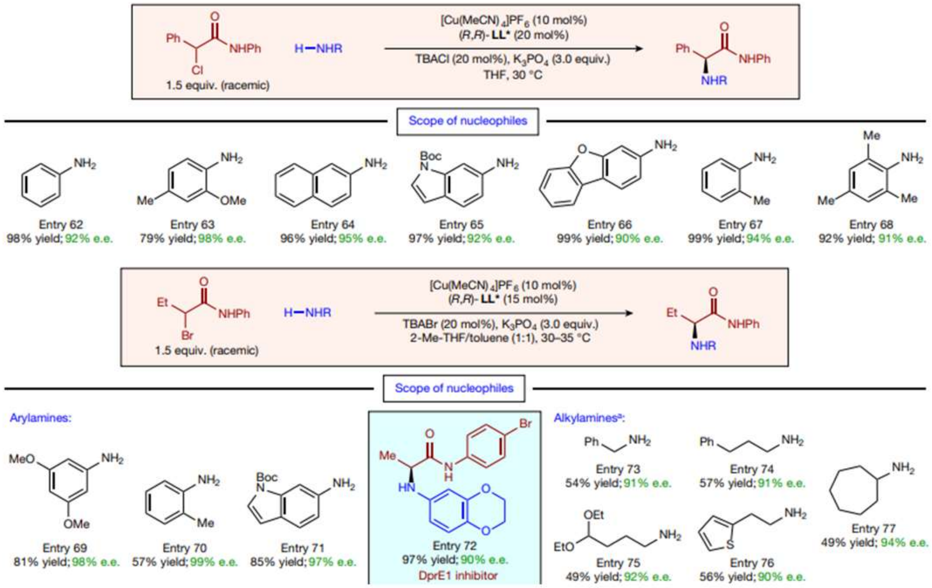




Nature **2023**, *618*, 301–307.

Copper-catalyzed enantioconvergent alkylation of oxygen nucleophiles





Nature **2023**, *618*, 301–307.