Reactions Catalyzed by Nickel Utilizing Chelation Assistance

Reporter: Liang Lu
Supervior: Jing Zhao

Naoto Chatani
茶谷 直人
Osaka University

Naoto Chatani studied chemistry at Osaka University and received his PhD in 1984 under the guidance of Profs. Noboru Sonoda and Shinji Murai. He then joined the Institute of Scientific and Industrial Research at Osaka University as an Assistant Professor in the group of Prof. Terukiyo Hanafusa. After postdoctoral studies with Prof. Scott E. Denmark at the University of Illinois, Urbana-Champaign, he returned to Osaka University (Prof. Shinji Murai's group), and became Associate Professor in 1992 and Professor in 2003. His research interests center on the area of catalysis.

Research overview

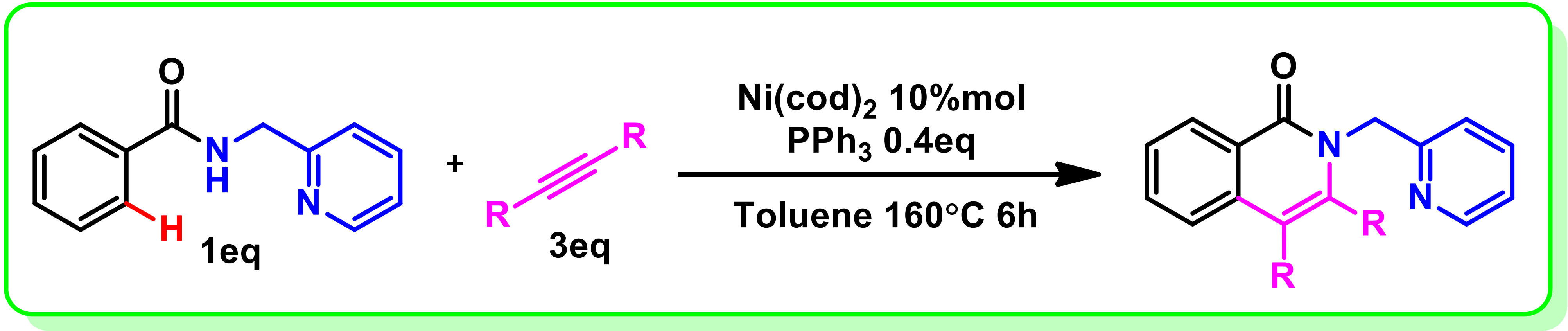
- **Catalysis through the Activation of Unreactive Bonds, such as C-H, C-C, C-F, and C-O Bonds**
- **New Synthetic Methodologies through an Efficient Capture of Reactive Intermediates**
- **Catalytic Cycloaddition**

JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
COMMUNICATION
pubs.acs.org/JACS

Nickel-Catalyzed Chelation-Assisted Transformations Involving Ortho C—H Bond Activation: Regioselective Oxidative Cycloaddition of Aromatic Amides to Alkynes

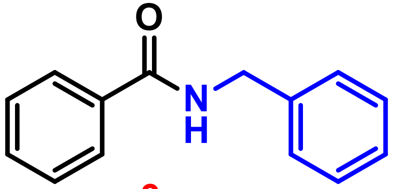
Hirotaka Shiota, Yusuke Ano, Yoshinori Aihara, Yoshiya Fukumoto, and Naoto Chatani*

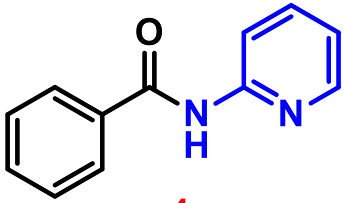
Department of Applied Chemistry, Faculty of Engineering, Osaka University, Suita, Osaka 565-0871, Japan

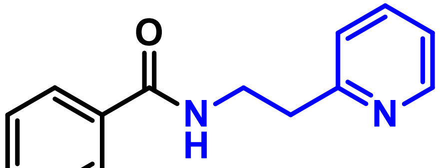


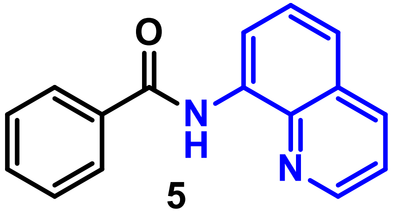
J. Am. Chem. Soc. 2011, 133, 14952–14955

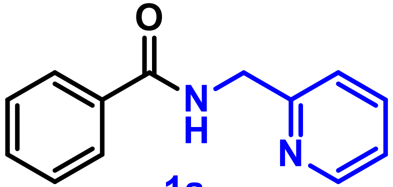
Effect of the directing group


3


4


6


5


1a

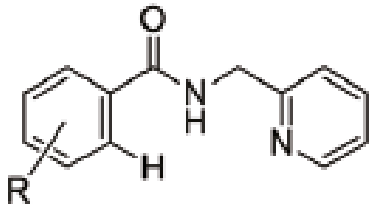
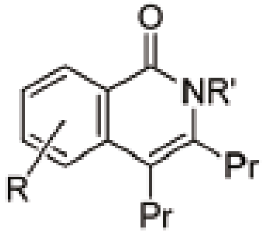
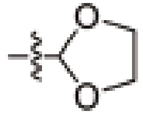
The corresponding benzyl amide 3 and the one-carbon-shorter amide 4 did not react with 4-octyne under the standard conditions.

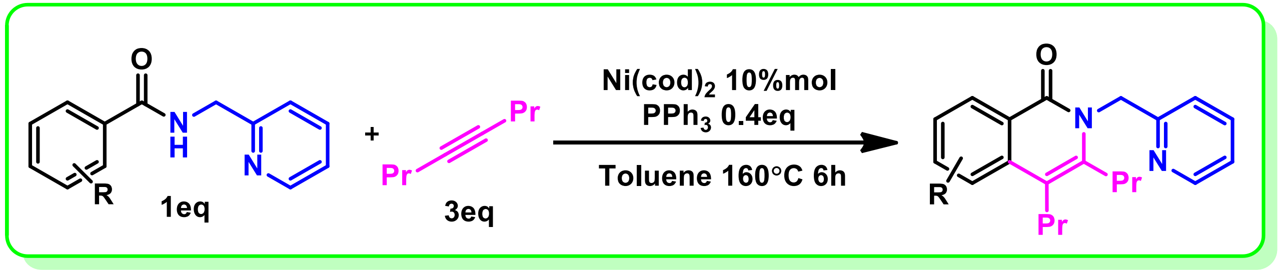
However, the reaction of the one-carbon-longer amide 6 with 4-octyne under the standard conditions gave isoquinolone derivative in 66% yield along with 15% recovery of 6.

Among the directing groups examined, 2-pyridinylmethylamine gave the best results.

J. Am. Chem. Soc. 2011, 133, 14952–14955

Ni-Catalyzed Reactions of Aromatic Amides with 4-Octyne

amide	product
	
R = H (**1a**)	**2a** 86%
R = 4-CH_3 (**1b**)	**2b** 84%
R = 4-OCH_3 (**1c**)	**2c** 73%
R = 4-NMe_2 (**1d**)	**2d** 69%
R = 4-CF_3 (**1e**)	**2e** 91%
R = 4-Ac (**1f**)	**2f** 85%
R = 4-CN (**1g**)	**2g** 83%
R = 4-  (**1h**)	**2h** 87%
R = 4-Ph (**1i**)	**2i** 87%
R = 2-Ph (**1j**)	**2j** 52%

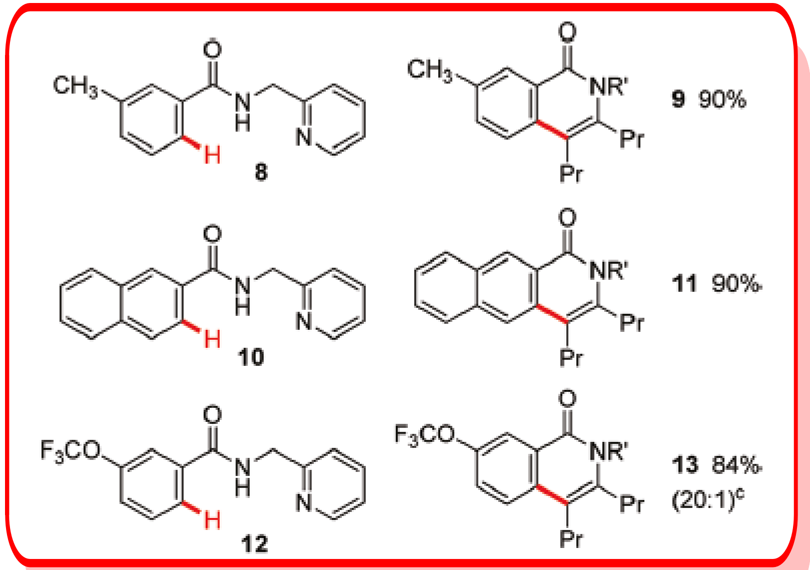


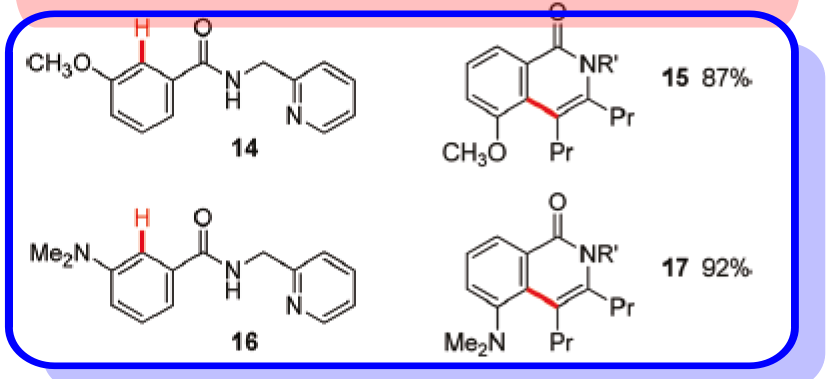
Various functional groups, such as methoxy, amino, trifluoromethyl, acetyl, cyano, and acetal groups, were tolerated under the reaction conditions.

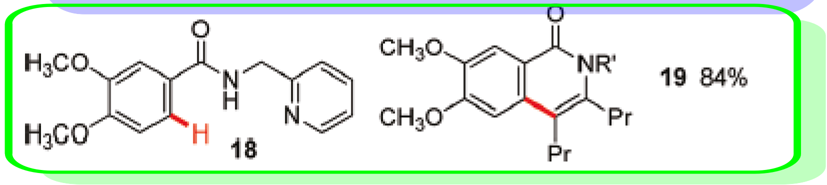
Substrates with an electron-donating group were slightly less reactive than those with an electron-withdrawing group.

J. Am. Chem. Soc. 2011, 133, 14952–14955

Ni-Catalyzed Reactions of Aromatic Amides with 4-Octyne







A single regioisomer through selective cleavage of the less-hindered C-H bond.

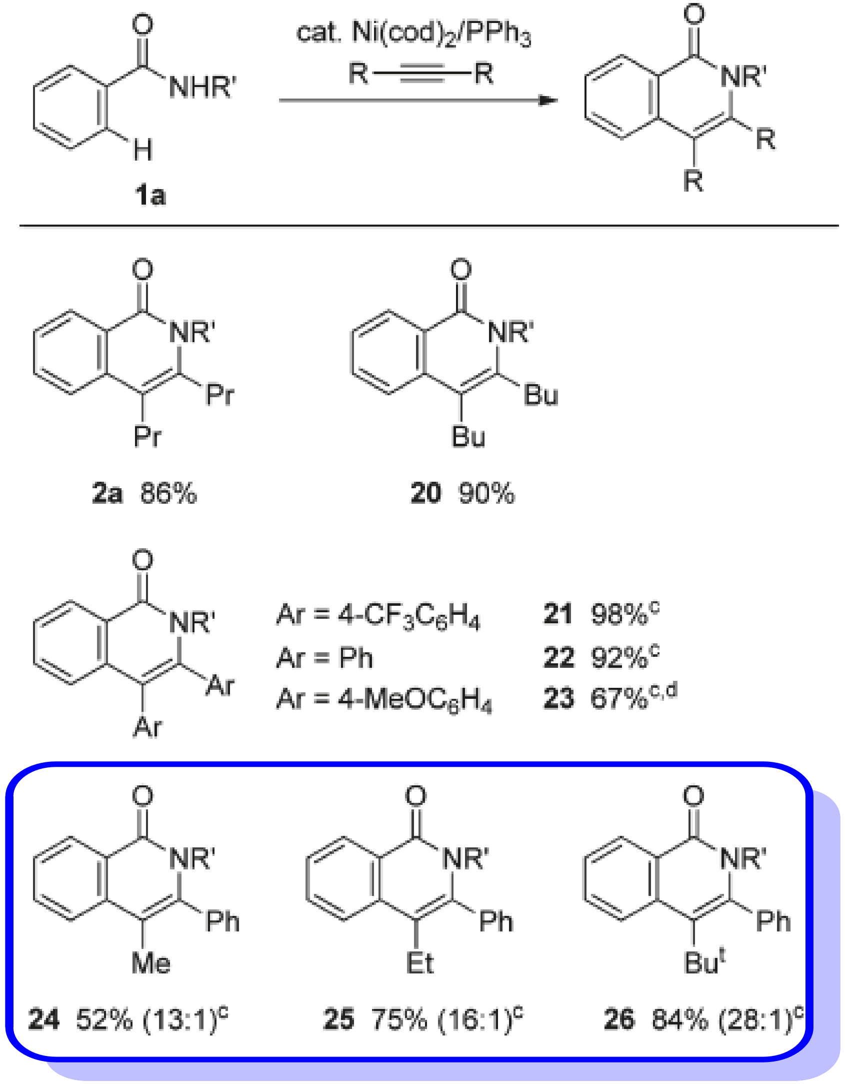
In sharp contrast, in the case of m-methoxy- and m-dimethylamino-substituted substrates , the more-hindered C-H bond was cleaved.

However, the reaction took place at the less-hindered C-H bond in the reaction of 3,4-dimethoxy-substituted substrate.

These results suggest that steric effects are a dominant factor for this type of reaction but that the electronic nature of the substituents also can have a significant effect on the regioselectivity of the reaction if they have a lone pair of electrons.

J. Am. Chem. Soc. 2011, 133, 14952–14955

Ni-Catalyzed Reactions of Amide 1a with Internal Alkynes

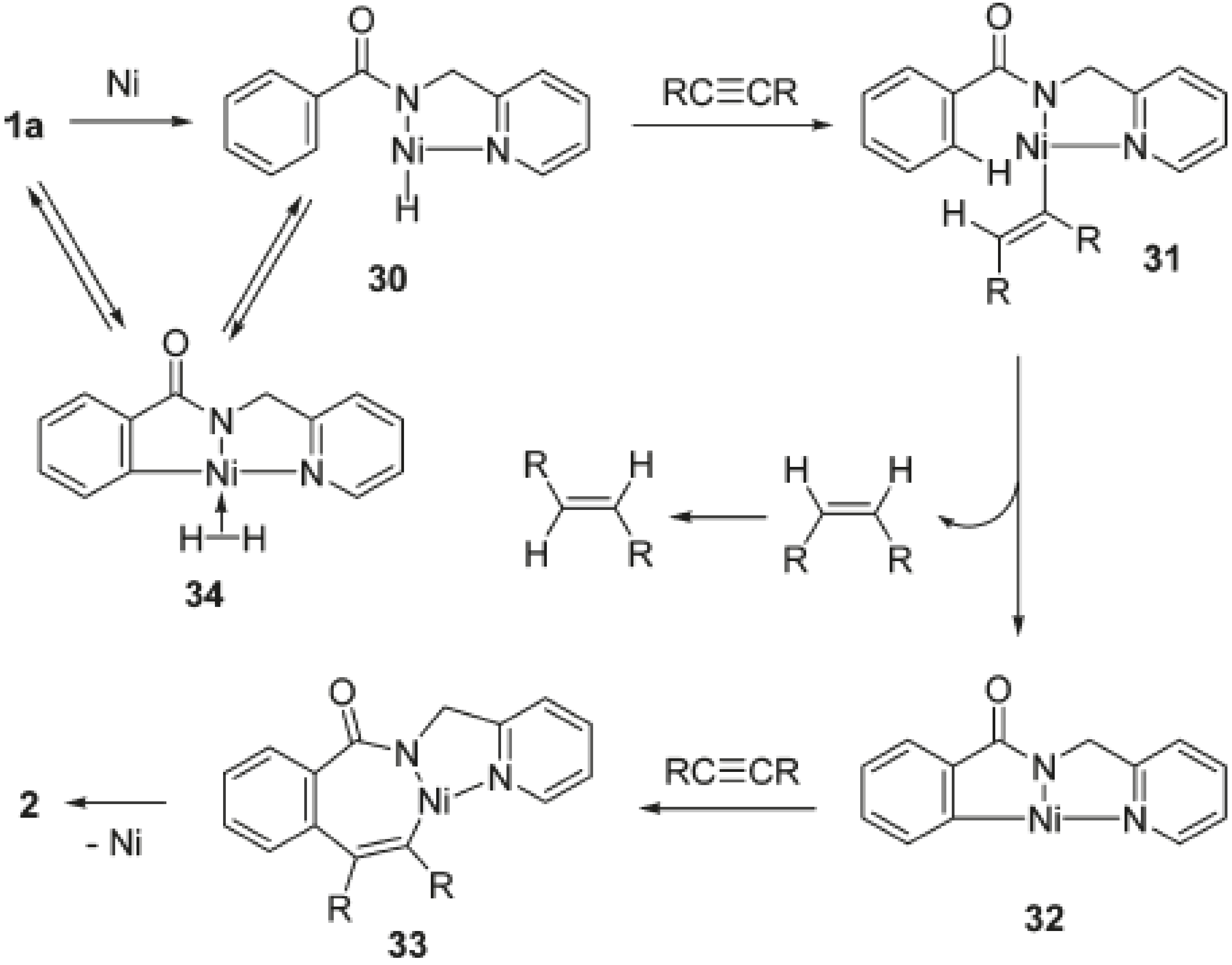


Unsymmetrical alkynes regioselectively gave the corresponding isoquinolones having the aryl group attached at the carbon adjacent to the nitrogen atom.

Thus, the presence of an electron-donating group resulted in a slightly increased regioselectivity.

J. Am. Chem. Soc. 2011, 133, 14952–14955

Proposed Mechanism



J. Am. Chem. Soc. 2011, 133, 14952–14955

Summary

A new catalytic system that takes advantage of chelation assistanceby a 2-pyridinylmethylamine moiety.

The first example of the Ni-catalyzed transformation of *ortho* C-H bonds utilizing chelation assistance has been achieved.

It is significant that even less expensive nickel complexes can be used as catalysts for the reaction.

JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

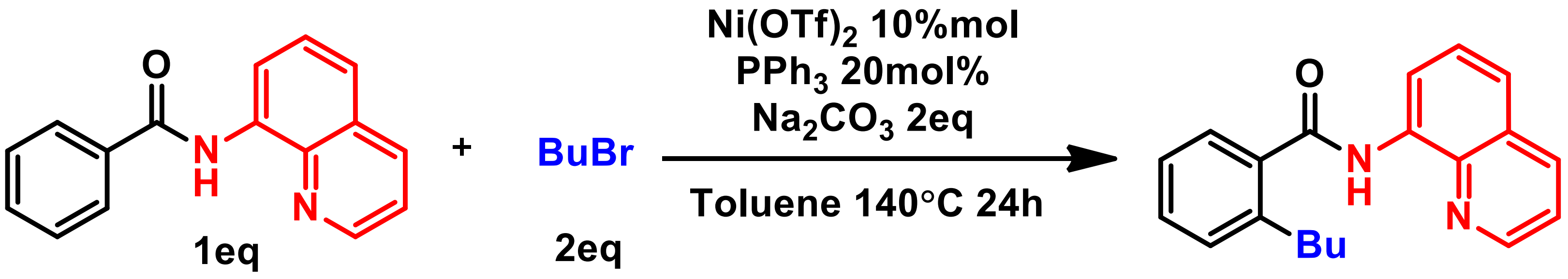
Communication

pubs.acs.org/JACS

Nickel-Catalyzed Direct Alkylation of C–H Bonds in Benzamides and Acrylamides with Functionalized Alkyl Halides via Bidentate-Chelation Assistance

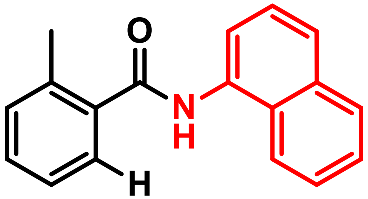
Yoshinori Aihara and Naoto Chatani*

Department of Applied Chemistry, Faculty of Engineering, Osaka University, Suita, Osaka 565-0871, Japan

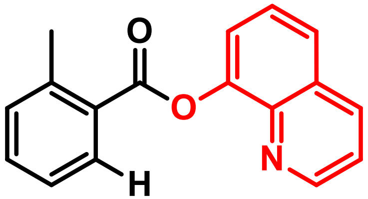


J. Am. Chem. Soc. 2013, 135, 5308–5311

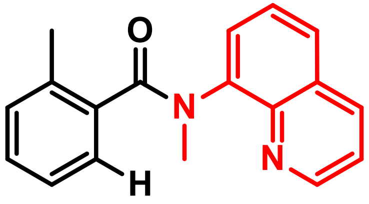
Effect of the directing group



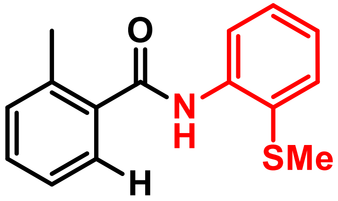
0%



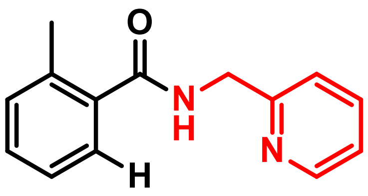
0%



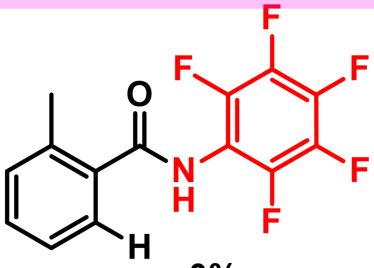
0%



25%



16%



0%

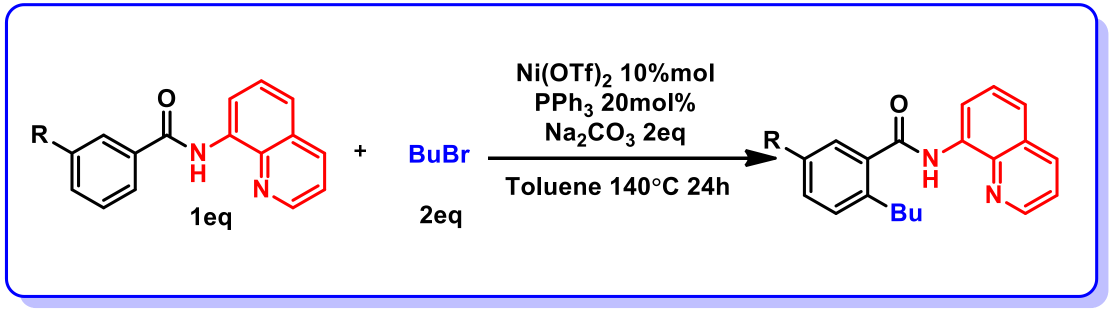
Indicating that coordination in an N,N′ fashion by the 8-aminoquinolinemoiety is essential for the reaction to proceed.

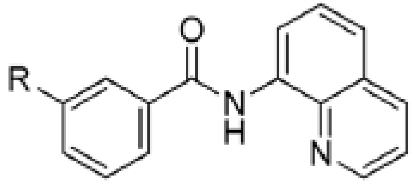
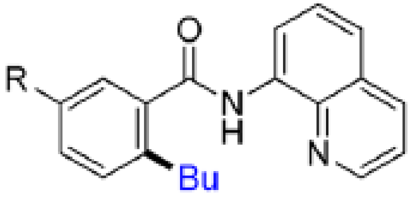
Indicating that the presence of a proton on the amide nitrogen is required for the reaction to proceed, although NH is not included in the product at first sight.

The reaction appears to be more efficient with the 8-aminoquinoline motif.

J. Am. Chem. Soc. 2013, 135, 5308−5311

Butylation of C–H Bonds in Aromatic Amides



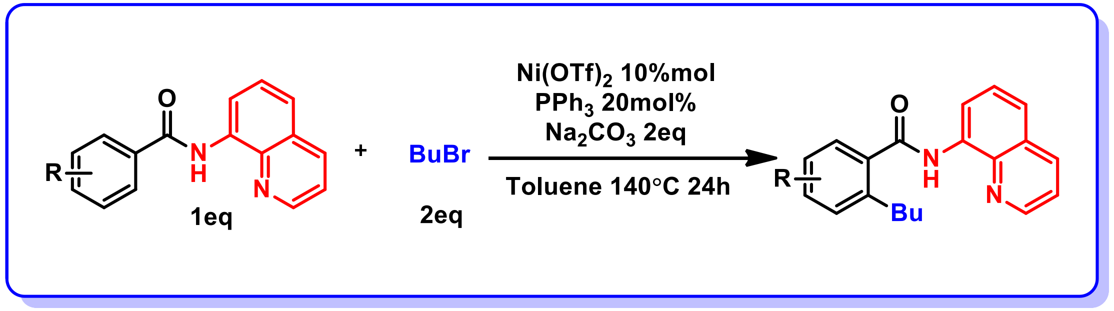
amide	product[b]	
		
R = OMe (**1b**)	**2b**	74% (89%)[c]
OCH$_2$Ph (**1c**)	**2c**	72% (85%)[c]
OSiMe$_2$Bu^t (**1d**)	**2d**	75%
Me (**1e**)	**2e**	92%[d]
Ph (**1f**)	**2f**	81%[d]
Cl (**1g**)	**2g**	92%[e]
I (**1h**)	**2h**	68%[e]
C(O)CH$_3$ (**1i**)	**2i**	75%[d]
CF$_3$ (**1j**)	**2j**	95%[d]

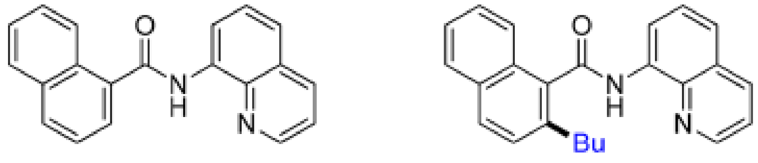
A variety of functional groups were tolerated in the reaction.

The reaction of meta-substituted substrates resulted in **selective alkylation exclusively at the less hindered C–H bond**, irrespective of the electronic nature of the substituent, indicating that the **regioselectivity of the reaction is controlled by the steric nature of the substituent groups.**

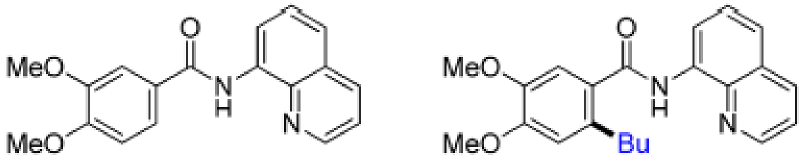
J. Am. Chem. Soc. 2013, 135, 5308–5311

Butylation of C–H Bonds in Aromatic Amides

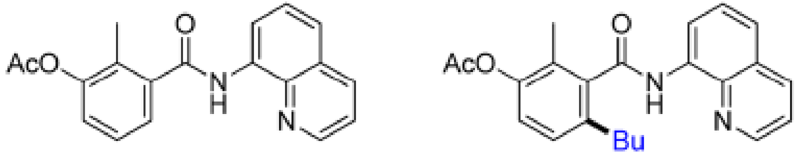




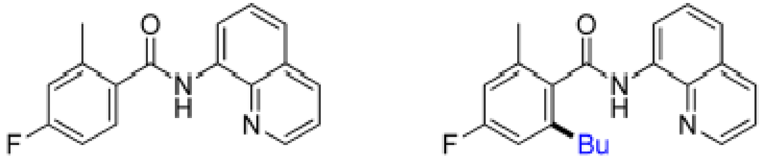
9 79%[d]



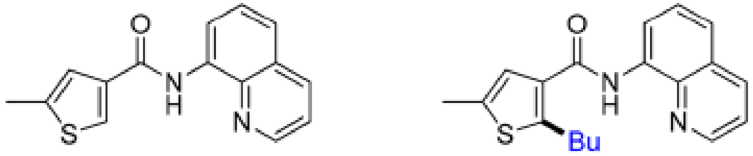
10 92%



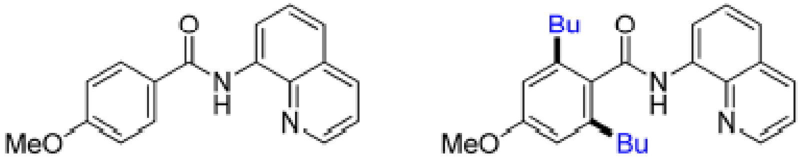
11 52%



12 87%



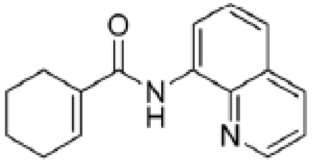
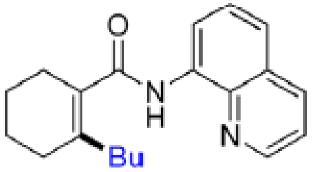
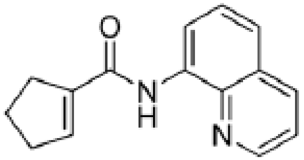
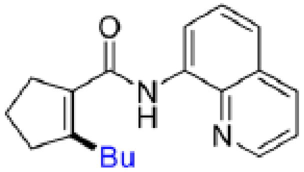
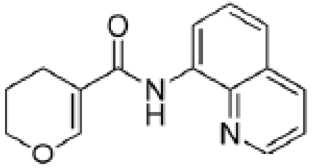
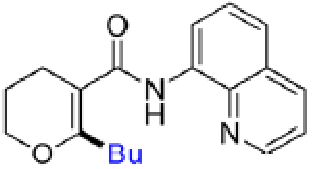
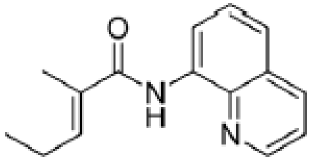
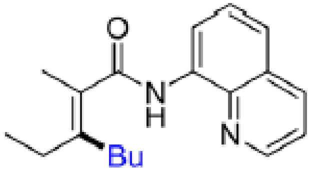
13 50%

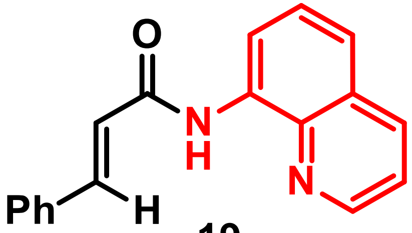


14 88%[d,f]

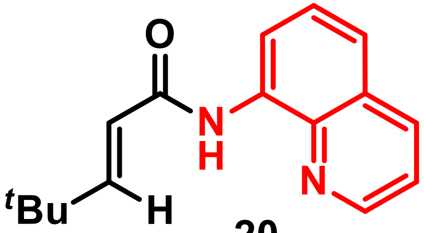
J. Am. Chem. Soc. 2013, 135, 5308–5311

Butylation of C–H Bonds in α,β-Unsaturated Amides

amide	product[b]
	 **15** 81%
	 **16** 67%
	 **17** 72%
	 **18** 54% (E:Z = 85:15)



19



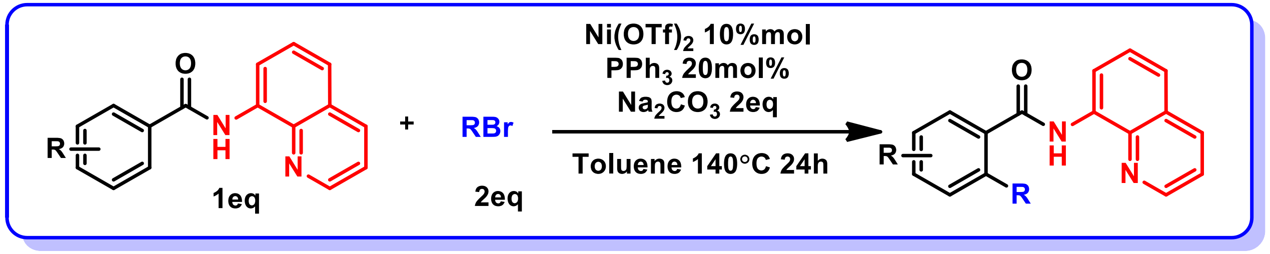
20

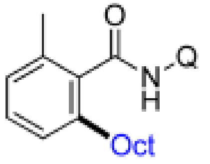
This alkylation reaction was also applicable to α,β-unsaturated amides

However, the reaction was limited to trisubstituted α,β-unsaturated amides, suggesting that the presence of a substituent at the α-carbon is an important factor in terms of the reactivity of the substrate.

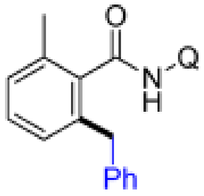
J. Am. Chem. Soc. 2013, 135, 5308−5311

Alkylation of C–H Bonds in Aromatic Amides with Functionalized Alkyl Halides

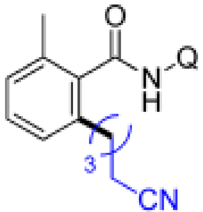




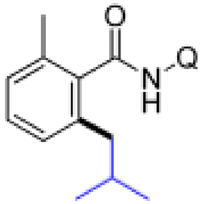
21 Oct—I 88%
Oct—Br 92%
Oct—Cl 0% (88%)



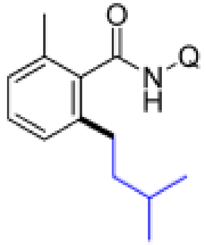
22 74%



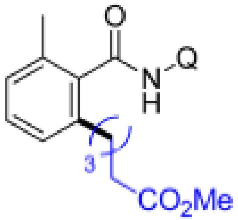
23 77%



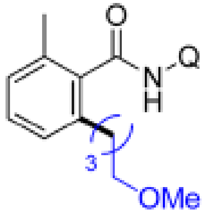
27 trace (44%)



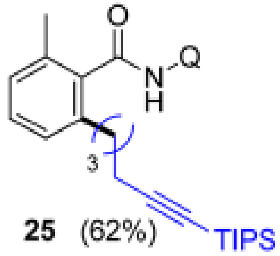
28 47% (81%)



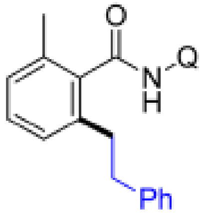
29 60% (76%)



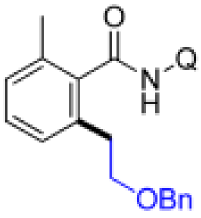
24 91%



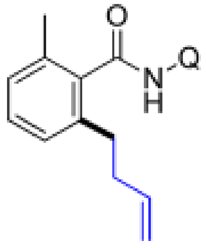
25 (62%)



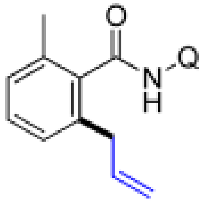
26 trace (61%)



30 35% (70%)



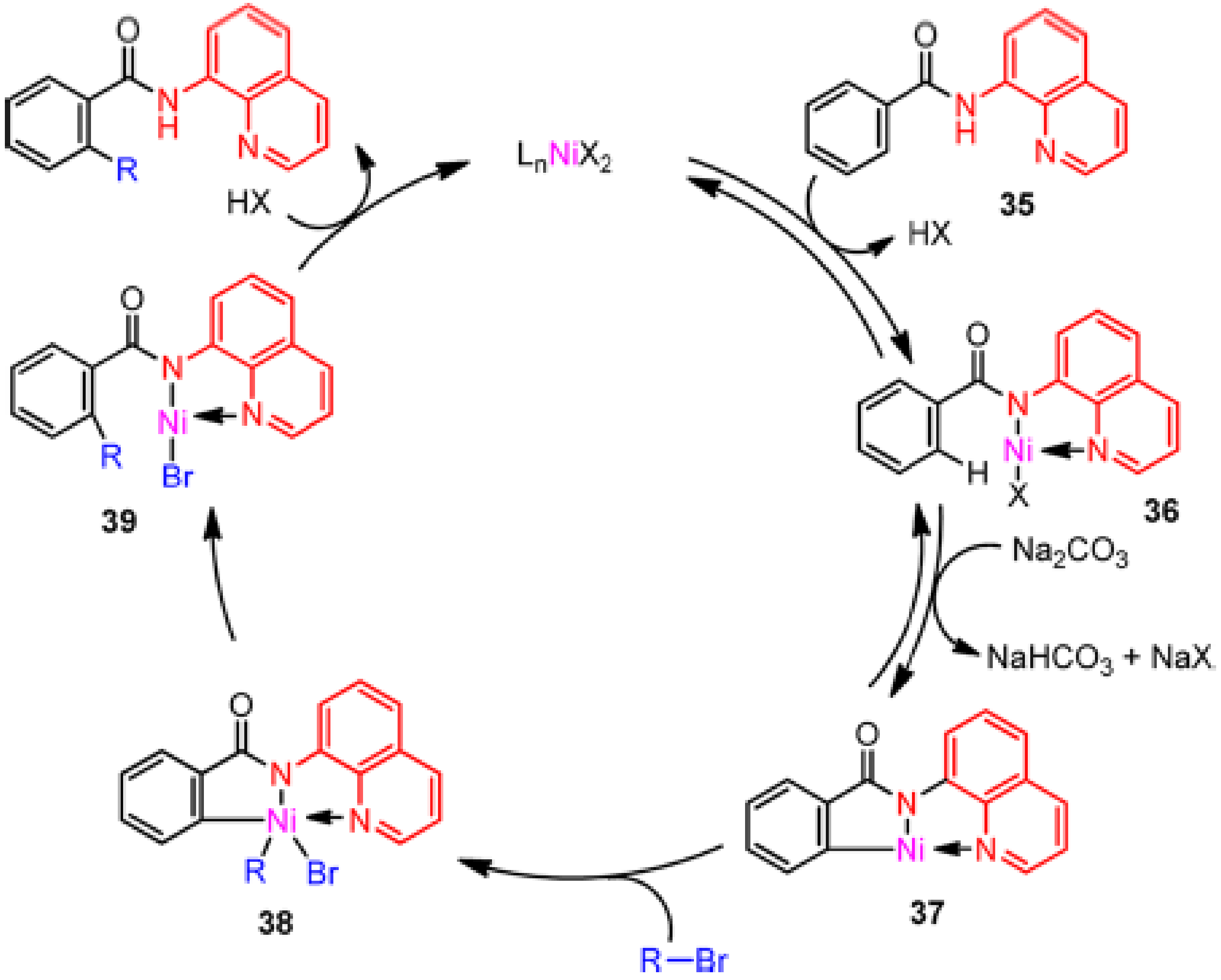
31 72% (92%)



32 83%

J. Am. Chem. Soc. 2013, 135, 5308–5311

Proposed Mechanism



J. Am. Chem. Soc. 2013, 135, 5308–5311

Summary

A new catalytic system that takes advantage of chelation assistance by an 8-aminoquinoline moiety.

The first example of Ni catalyzed *ortho* alkylation of benzamides and acrylamide derivatives with unactivated alkyl halides in which C−H bonds are cleaved.

This alkylation reaction was also applicable to α,β-unsaturated amides.

The reaction proceeds in a highly selective manner at the less hindered C−H bond in the reaction of meta-substituted aromatic amides.

Thank you for your listening