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Nickel-Catalyzed Direct Arylation of C(sp^3)–H Bonds in Aliphatic Amides via Bidentate-Chelation Assistance

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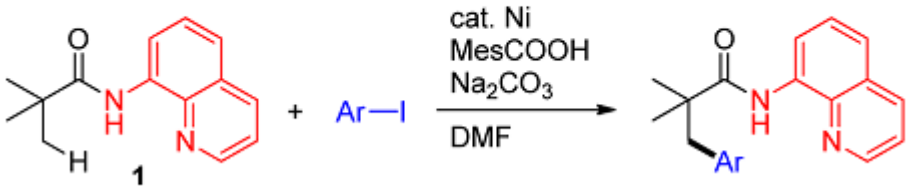
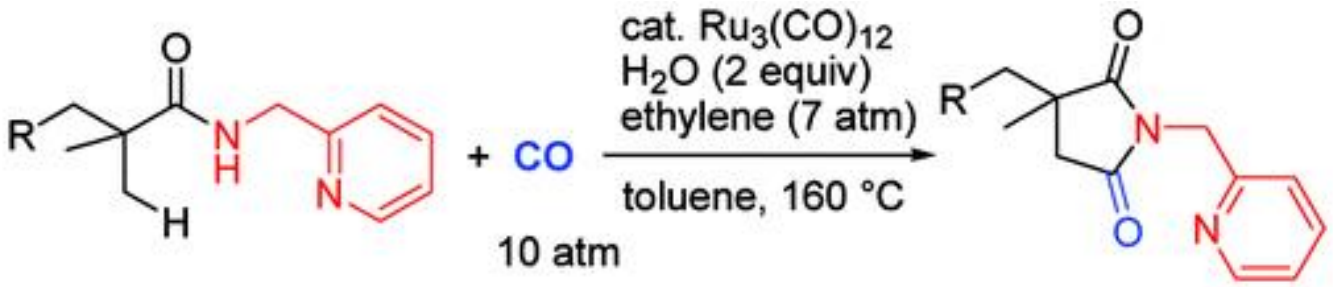
Supporting Information

Scheme 1. Nickel-Catalyzed Direct Arylation of C(sp^3)–H Bonds in Aliphatic Amides

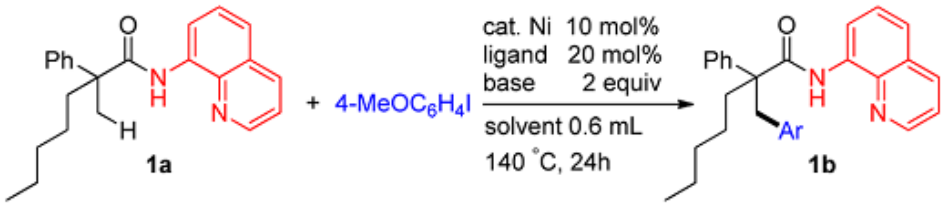


Zhang, S.-Y.; Li, Q.; He, G.; Nack, W. A.; Chen, G. *J. Am. Chem. Soc*.**2013**, *135*, 12135.



Hasegawa, N.; Charra, V.; Inoue, S.; Fukumoto, Y.; Chatani, N. *J. Am. Chem. Soc*. **2011**, *133*, 8070

Table 1. Optimaization of the Nickel-Catalyzed Direct Arylation of Aliphatic Amide 1a with 4-iodoanisole[a]



entry	catalyst	ligand	base	solvent	yield (**1b**/**1a**)[b] (%)/(%)
1	$Ni(OTf)_2$	none	Na_2CO_3	DMA	40/44
2	$Ni(OTf)_2$	PhCOOH	Na_2CO_3	DMA	70/22
3	$Ni(OTf)_2$	2-PhC_6H_4COOH	Na_2CO_3	DMA	72/24
4	$Ni(OTf)_2$	MesCOOH	Na_2CO_3	DMA	82 (78) /17
5	$Ni(OTf)_2$	2,6-$^iPr_2C_6H_3COOH$	Na_2CO_3	DMA	74/23
6	$Ni(OTf)_2$	2,6-$Ph_2C_6H_3COOH$	Na_2CO_3	DMA	81/21
7	$Ni(OTf)_2$	1-AdCOOH	Na_2CO_3	DMA	72/27
8	$Ni(OTf)_2$	MesCOOH	Li_2CO_3	DMA	49/35
9	$Ni(OTf)_2$	MesCOOH	$NaHCO_3$	DMA	14/72
10	$Ni(OTf)_2$	MesCOOH	K_2CO_3	DMA	0/103
11	$Ni(OTf)_2$	MesCOOH	Cs_2CO_3	DMA	57/42
12	$Ni(OTf)_2$	MesCOOH	Na_2CO_3	DMF	88 (83)/12
13	$Ni(OTf)_2$	MesCOOH	Na_2CO_3	toluene	59/38
15	$Ni(OTf)_2$	MesCOOH	Na_2CO_3	AcOH	0/99
16	$NiCI_2$	MesCOOH	Na_2CO_3	DMF	81/10
17	$Ni(OAc)_2$	MesCOOH	Na_2CO_3	DMF	81/10
18	$Ni(cod)_2$	MesCOOH	Na_2CO_3	DMF	79/ 10

[a]Reaction conditions: amide **1a** (0.3 mmol), 4-iodoanisole (0.6 mmol), catalyst (0.03 mmol), ligand (0.06 mmol), base (0.6 mmol) in solven mL) at 140 °C for 24 h. [b]NMR yields. The number in parentheses is the isolated yield.

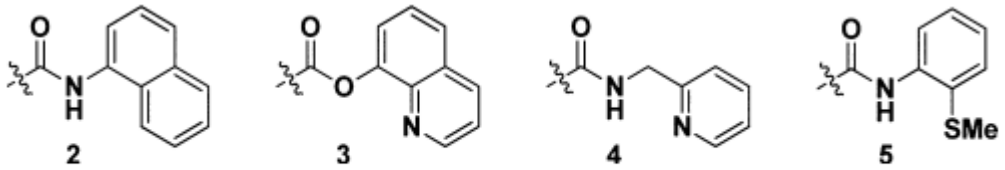
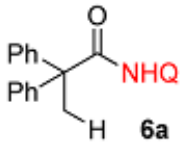
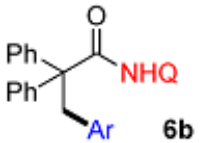
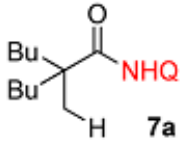
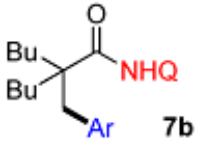
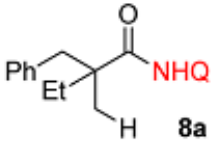
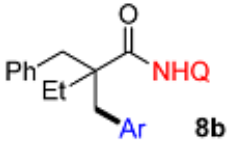
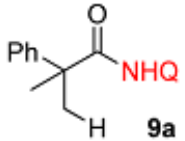
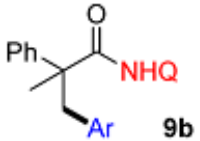
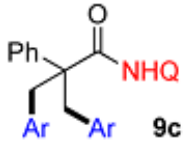
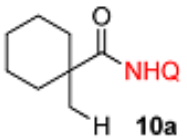


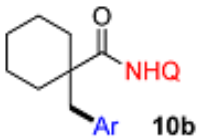
Figure 1. Ineffective directing groups.

Table 2. Nickel-Catalyzed Direct Arylation of Aliphatic Amides with Aryliodides[a]

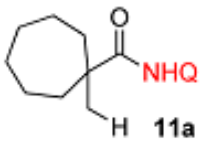
substrate	products[b]		
 **6a**	 **6b**	72% (10%)	Ar = *p*-MeOC$_6$H$_4$
 **7a**	 **7b**	50% (32%)	
 **8a**	 **8b**	56% (31%)	
 **9a**	 **9b**	29%	 **9c** 54% (6%)



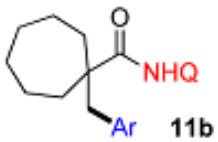
10a



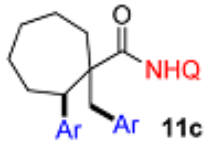
10b 61% (26%)



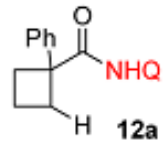
11a



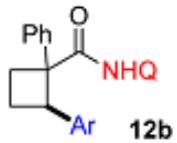
11b 41%



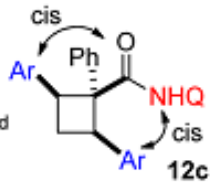
11c 33%[c]



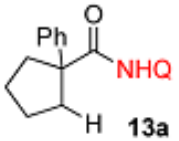
12a



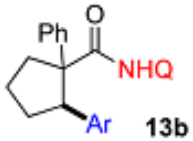
12b 50%[c] 12%[c,d]



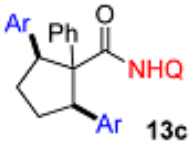
12c 33% (15%) 62% (0%)[d]



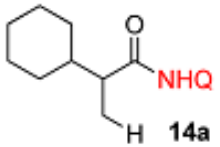
13a



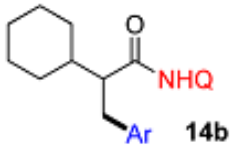
13b 41%[c] 42%[c,d]



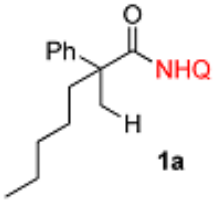
13c 8% (40%)[c] 18% (14%)[c,d]



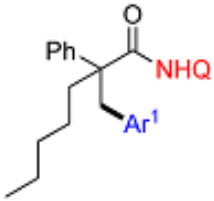
14a



14b 30% (40%)

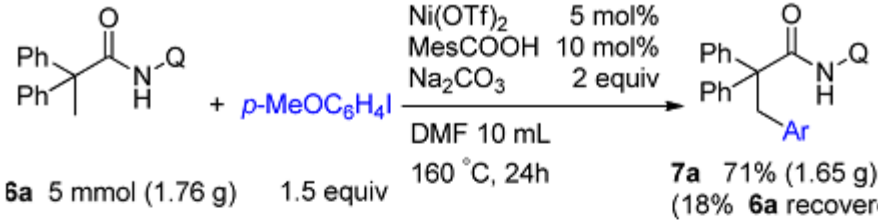


1a

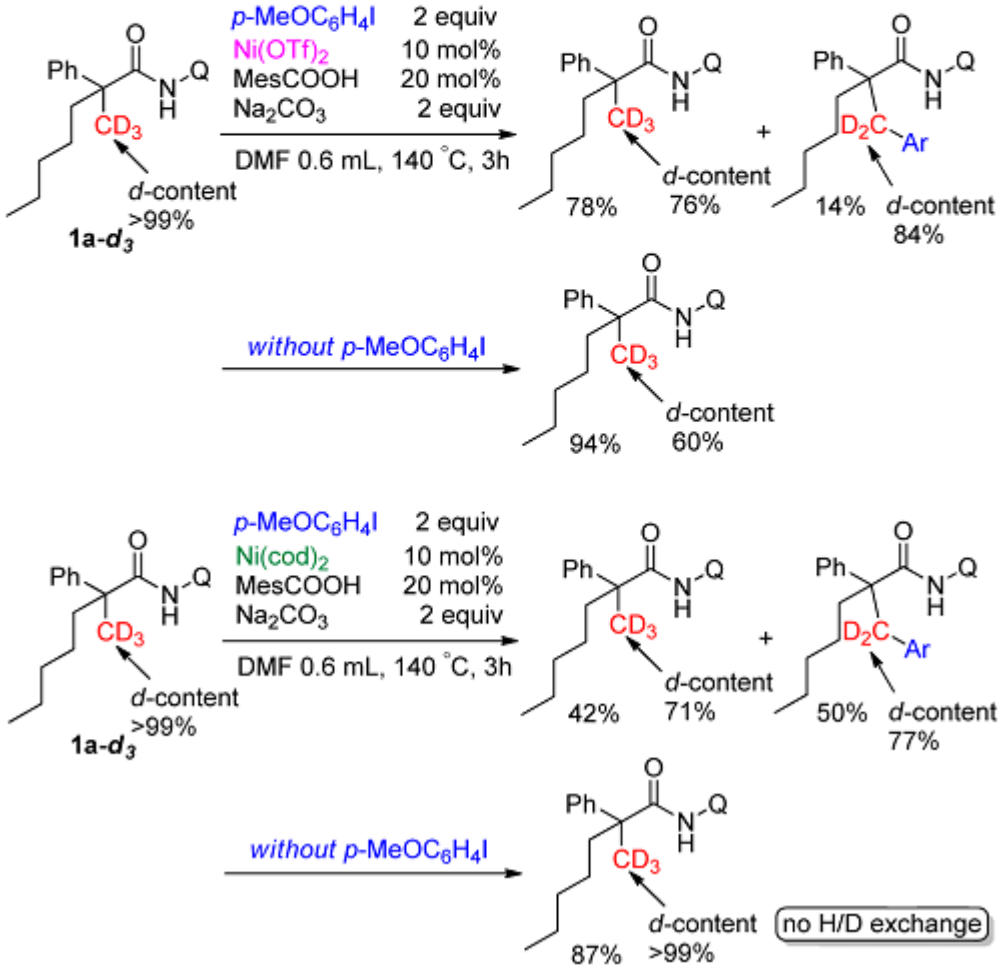


Ar^1	=	*p*-CF_3 **1c**	49% (22%)[e]
	=	*p*-CO_2Me **1d**	44% (19%)
	=	*p*-Ac **1e**	66% (15%)
	=	*p*-I **1f**	61% (trace)[e]
	=	*p*-Cl **1g**	60% (12%)[e]
	=	*p*-Me **1h**	76% (13%)[e]
	=	*p*-NH_2 **1j**	68% (10%)
	=	*p*-NMe_2 **1k**	75% (12%)
	=	*p*-OMe **1b**	83% (12%)
	=	*o*-Me **1l**	0% (99%)
	=	5-indole **1m**	75% (11%)
	=	2-thiophene **1n**	60% (trace)

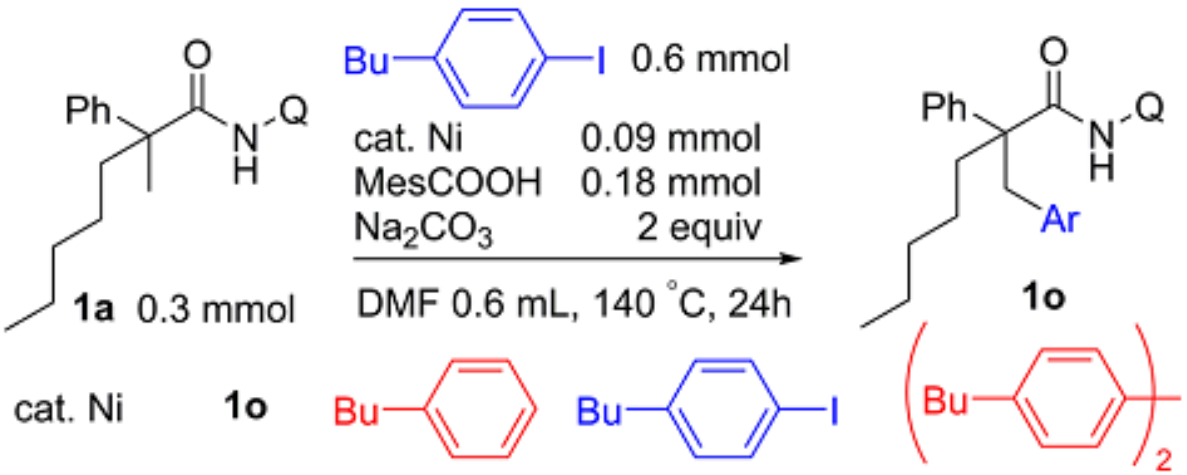
Scheme 2. Large-Scale Reaction of 6a



Scheme 3. Deuterium-Labeling Experiments



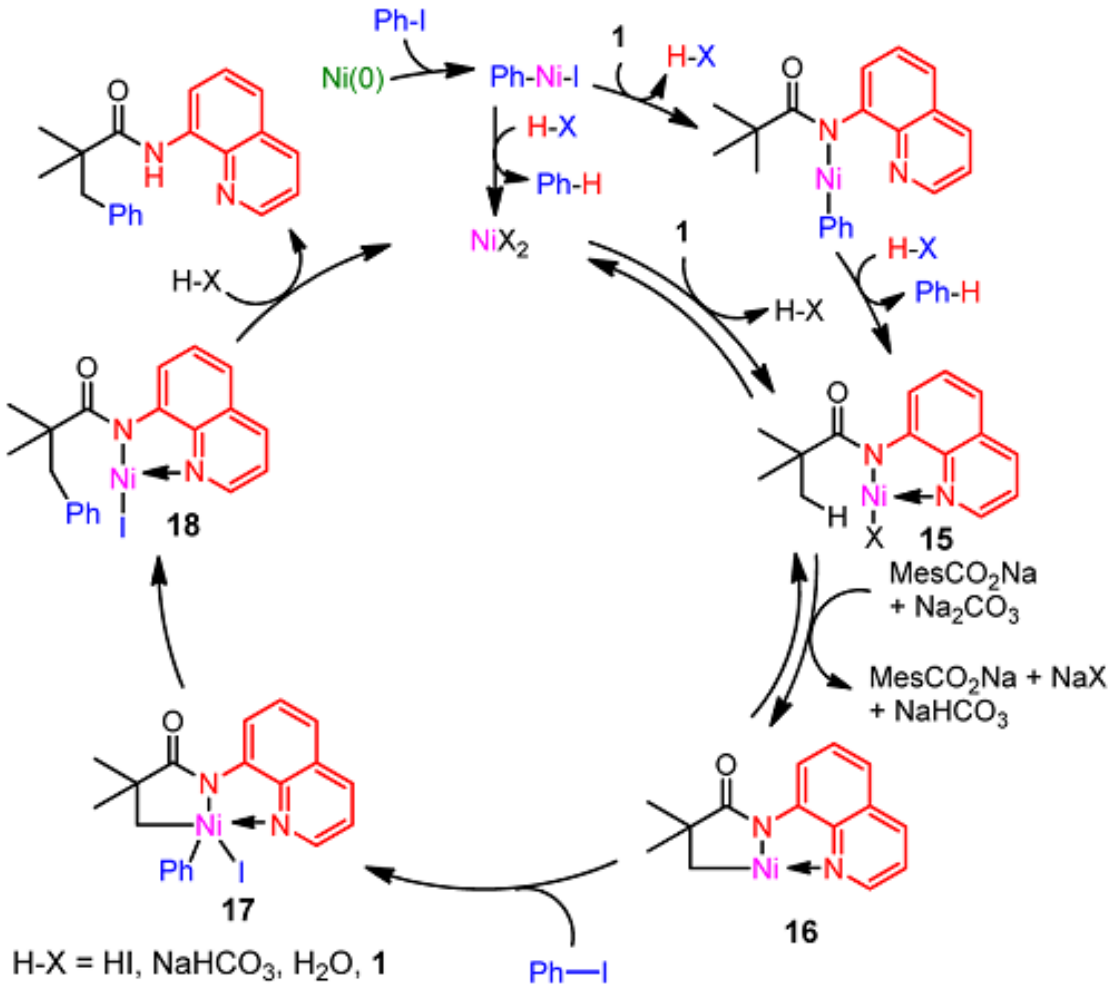
Scheme 4. Product Distribution



$Ni(cod)_2$	0.20 mmol 67%/**1a** (32%)	0.077 mmol 86%/Ni(0)	0.20 mmol	not observed
$Ni(OTf)_2$	0.195 mmol 65%/**1a** (36%)	trace	0.37 mmol	not observed

The number in parentheses is the yield of the recovered **1a**.

Scheme 5. Proposed Mechanism



Thanks!