

Ni-Catalyzed Direct Reductive Amidation via C–O Bond Cleavage

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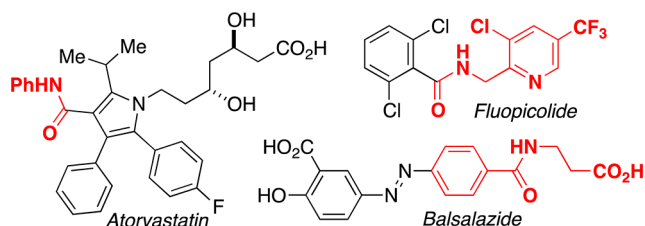
S Supporting Information

ABSTRACT: A novel Ni-catalyzed reductive amidation of C(sp²)–O and C(sp³)–O electrophiles with isocyanates is described. This umpolung reaction allows for an unconventional preparation of benzamides using simple starting materials and easy-to-handle Ni catalysts.

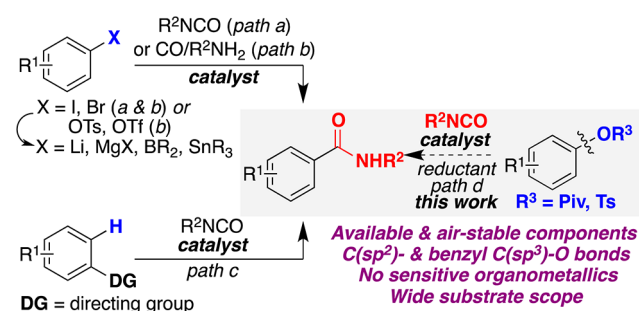
Within a few years, C–O electrophiles have emerged as powerful and environmentally friendly alternatives to the use of organic halides in the arena of cross-coupling.¹ Among their advantages are the low toxicity, ready availability, and natural abundance of phenols together with their unique pivotal role in organic synthesis, making them particularly attractive for further applications. Despite formidable advances, these processes are primarily restricted to the use of nucleophilic entities such as boronic acids, organozincs, or Grignard reagents.^{2,3} Recently, catalytic reductive processes of organic halides with other electrophilic partners have received considerable attention.^{4–6} These methods represent a formal umpolung or a polarity inversion strategy, employing unconventional substrate combinations while avoiding the use of well-defined and stoichiometric organometallic reagents, thus changing the logic in chemical reactivity and increasing our ever-growing synthetic toolkit. Strikingly, *metal-catalyzed reductive events employing aryl C–O electrophiles are relatively scarce*.^{7,8} This might be due to the proclivity of C–O electrophiles to undesired pathways and site-selectivity issues with multiple C–O reaction sites, giving the notion that the use of aryl C–O electrophiles in catalytic reductive protocols constitutes a notorious difficult challenge. The discovery of new reactivity within this field would be a highly desirable goal of utmost synthetic importance.

Benzamides are key structural units in a wide variety of compounds that display important biological properties, such as Atorvastatin, Fluopicolide, and Balsalazide, among others (Scheme 1).⁹ Recently, metal-catalyzed amidation protocols using well-defined and stoichiometric organometallic species

Scheme 1. Biological Significance of Benzamides



Scheme 2. Catalytic Cross-Coupling Routes to Benzamides

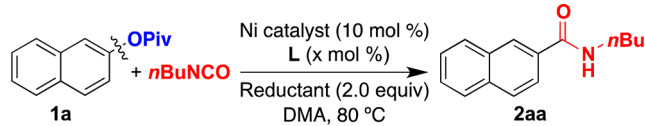


(Scheme 2, path a),¹⁰ carbonylation methods using CO¹¹ or CO surrogates¹² (path b), or C–H functionalization techniques promoted by suitable *ortho*-directing groups (path c)¹³ have shown to be viable synthetic alternatives to classical methods for preparing such privileged motifs.^{14,15} We envisioned that benzamides would be within reach by a reductive event using C–O electrophiles and isocyanates, thus providing a unique opportunity to improve the efficiency and applicability of C–O electrophiles while offering an innovative bond disconnection not apparent at first sight (path d).¹⁶ As part of our interest in C–O bond activation,¹⁷ we report herein the discovery of a novel catalytic protocol that deals with such challenge, exploiting a previously unrecognized opportunity in the field of C–O bond cleavage. The method is characterized by its wide scope and excellent chemoselectivity profile, including challenging substrate combinations. Likewise, the use of readily available and air-stable compounds represents an additional benefit from a practical standpoint.

We began our investigations by examining the reactivity of **1a** with *n*-butyl isocyanate using Ni precatalysts (Table 1), and the effects of all reaction parameters were systematically examined.¹⁸ As for other catalytic reductive processes,^{4–7} we anticipated that the nature of the ligand would play a critical role for success. As shown in entries 1–5, this was indeed the case: while dppf provided promising results in DMA with Mn as reducing agent (entry 1), the use of other related ligands was rather unsatisfactory, not affording even traces of **2aa** and invariably resulting in 2-naphthol or reduced naphthalene (entries 2–5).¹⁸ Interestingly, the replacement of Mn by Zn under otherwise identical reaction conditions significantly improved the yield of **2aa** (entry 6).¹⁹ Although different Ni sources could be utilized (entries 6–11), the best results were

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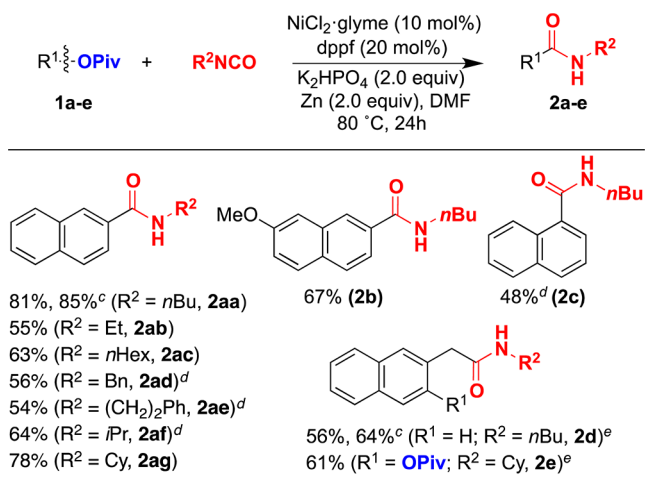
Table 1. Optimization of the Reaction Conditions^a

entry	Ni catalyst	L (x mol%)	reductant	yield 2aa (%) ^b
1	NiCl ₂ (dppf)	dppf (10)	Mn	18
2	NiCl ₂ (dppp)	dppp (10)	Mn	0
3	NiCl ₂ (PMe ₃) ₂	PMe ₃ (10)	Mn	0
4	NiCl ₂ (PPh ₃) ₂	PPh ₃ (10)	Mn	0
5	NiBr ₂ (bpy) ₂	bpy (10)	Mn	0
6	NiCl ₂ (dppf)	dppf (10)	Zn	38
7	Ni(acac) ₂	dppf (20)	Zn	28
8	Ni(OTf) ₂	dppf (20)	Zn	21
9	NiBr ₂ ·glyme	dppf (20)	Zn	46
10	NiBr ₂ ·H ₂ O	dppf (20)	Zn	42
11	NiCl ₂ ·glyme	dppf (20)	Zn	55
12	NiCl ₂ ·glyme	dppf (10)	Zn	4
13 ^{c,d}	NiCl ₂ ·glyme	dppf (20)	Zn	70 ^f
14 ^{d,e}	NiCl ₂ ·glyme	dppf (20)	Zn	81 ^f

^aReaction conditions: **1a** (0.50 mmol), *n*BuNCO (2.0 equiv), [Ni] (10 mol%), L (x mol%), reductant (2.0 equiv), DMA (0.25 M) at 80 °C for 24 h. ^bHPLC yield using anisole as internal standard. ^cK₂HPO₄ (1.0 equiv) was added. ^dDMF as solvent. ^eK₂HPO₄ (2.0 equiv) was added. ^fIsolated yield.

accomplished using NiCl₂·glyme (entry 11). Intriguingly, the inclusion of K₂HPO₄ in anhydrous DMF had a dramatic effect on reactivity, providing **2aa** in 81% isolated yield while minimizing undesired reaction pathways such as formation of carbamate or isocyanurates by trimerization of *n*BuNCO (entry 14). To put these results into perspective, control experiments revealed that NiCl₂·glyme, dppf, and Zn were absolutely required to promote the reductive coupling event.¹⁸

Encouraged by our initial results, we sought to examine the preparative scope and generality of our Ni-catalyzed reductive amidation event using naphthyl pivalates as substrates (Table 2).²⁰ As shown for **2aa**–**2ag**, moderate to good yields were obtained regardless of the substitution pattern on the

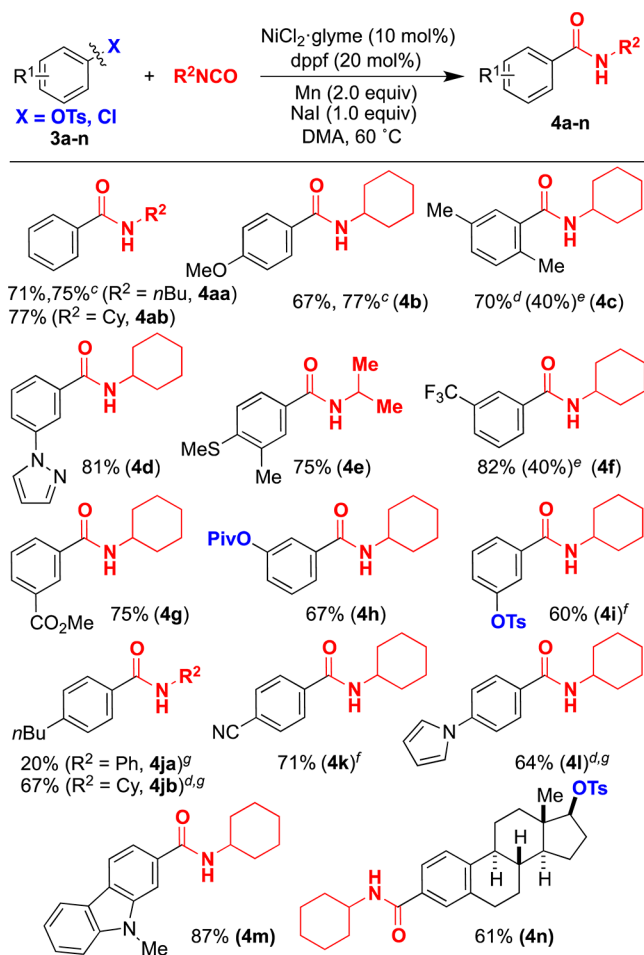
Table 2. Catalytic Reductive Amidation of Pivalates^{a,b}

^aReaction conditions as for Table 1, entry 14. ^bIsolated yields, average of at least two independent runs. ^c2.50 mmol scale. ^d90 °C. ^eMn (2.0 equiv) at rt.

isocyanate motif. Gratifyingly, minor modifications on the reaction conditions allowed for effecting the Ni-catalyzed reductive amidation of benzylic C(sp³)–O bonds at room temperature (**2d**, **2e**). Of significant interest is the successful preparation of **2e**; in this particular case, we found that the reductive amidation event occurred exclusively at the C(sp³)–O motif by leaving the proximal C(sp²)–O bond intact, an observation that is in line with the higher propensity of benzylic positions toward oxidative addition.^{21,22} As for many other C–OPiv bond-cleavage processes,²³ however, we found that our protocol was restricted to the use of π -extended systems, an observation that is tentatively attributed to the intermediacy of η^2 -arene or Meisenheimer-type complexes.²⁴

Challenged by the limitation to π -extended systems, we envisioned a further extension of the scope of this novel method to accommodate simple phenyl derivatives. We hypothesized that the use of slightly more activated C–O electrophiles such as aryl tosylates would be ideal for our purposes.²⁵ Owing to their higher reactivity, however, we anticipated a certain degree of undesired dimerization events using aryl tosylates. Indeed, this turned out to be the case for most of the ligands analyzed,¹⁸ while the use of 2,2'-bipyridine provided homocoupling products quantitatively, the use of dppf as the ligand was found to be critical to effect the rather challenging amidation of phenyl derivatives in high yields at 60 °C. Interestingly, the inclusion of NaI as additive totally suppressed the competitive dimerization event, an observation that is in line with other reports recently described in the literature.²⁶ Under these reaction conditions, a wide variety of substituted phenyl tosylates smoothly underwent the desired reductive amidation process (Table 3). Control experiments in the absence of NaI clearly confirmed its beneficial effect on reactivity (**4c**, **4f**). The chemoselectivity profile is nicely illustrated by the fact that ethers (**4b**), thioethers (**4e**), ester (**4g**), nitriles (**4k**), pivalates (**4h**), and tosylates (**4i**, **4n**) were perfectly accommodated. Of remarkable interest is the selectivity pattern observed for **4h** and **4i**, thus leaving ample opportunities for manipulation via common cross-coupling techniques. As shown for **4c**, the reaction was not hampered by the presence of nitrogen-containing heterocycles such as pyrazole (**4d**), pyrrole (**4l**), and carbazole (**4m**) posed no problems, delivering the corresponding amides in good to excellent yields. Even more instructive was the successful preparation of **4n**, evidencing the selectivity profile among different C–OTs bonds as well as the practical utility of our method for late-stage modification of biologically relevant compounds. It is worth noting that the catalytic reductive amidation of aryl chlorides (**4ja**, **4jb**, **4k**, and **4l**), particularly challenging substrates in the cross-coupling arena,²⁷ could be conducted at room temperature under otherwise identical reaction conditions, an observation that clearly highlights the robustness and generality of our protocol.^{28,29}

Although a detailed mechanistic picture requires further studies, several experiments were performed to gain insights into the reaction mechanism. We found that the catalytic reductive coupling of **1a**, **3a**, and **3k** was completely inhibited by the addition of TEMPO.¹⁸ While such observation might indicate that single electron transfer processes come into play, care must be taken when generalizing this, as other radical scavengers such as BHT or galvinoxyl followed an opposite reactivity pattern.¹⁸ Interestingly, we found no reaction of **1a** or **3a** when replacing *n*-butyl isocyanate with butyraldehyde or

Table 3. Reductive Amidation of ArOTs and ArCl^{a,b}

^aReaction conditions: ArOTs (0.50 mmol), R²NCO (1.0 mmol), NiCl₂·glyme (10 mol%), dppf (20 mol%), NaI (1.0 equiv), Mn (2.0 equiv), DMA (0.25 M) at 60 °C for 24 h. ^bIsolated yields, average of at least two independent runs. ^c2.50 mmol scale. ^d48 h reaction time. ^eIn the absence of NaI. ^fMn (1.20 equiv). ^gReaction performed at rt using ArCl as substrate.

ethyl glyoxalate, thus leaving some doubt about the intermediacy of *in situ* generated organozinc or organomanganese species, respectively. At present, we tentatively believe the reaction is triggered by Mn- or Zn-assisted reduction of Ni(II) to Ni(0) followed by oxidative addition into the corresponding C–O bond.³⁰ Subsequently, isocyanate insertion and a final transmetalation with Mn (Zn) would regenerate the active Ni(0) species with concomitant formation of the corresponding zinc (manganese) amide that upon hydrolytic workup would deliver the expected product.^{31,32}

In summary, we have described an unprecedented Ni-catalyzed reductive amidation of C–O electrophiles with isocyanates. This protocol constitutes a practical, user-friendly, and operationally simple strategy for the assembly of a wide range of synthetically relevant benzamides. This formal umpolung reaction complements existing methodologies based on functional group manipulation, directing group methodologies, or the use of well-defined and air-sensitive organometallics. Further mechanistic studies and other related reductive coupling events are currently underway in our laboratories.

■ ASSOCIATED CONTENT

📄 Supporting Information

Experimental procedures and spectral data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

- (1) Recent reviews (a) Tehetena, M.; Garg, N. K. *Org. Process Res. Dev.* **2013**, *17*, 29. (b) Yamaguchi, J.; Muto, K.; Itami, K. *Eur. J. Org. Chem.* **2013**, 19. (c) Correa, A.; Cornella, J.; Martin, R. *Angew. Chem., Int. Ed.* **2013**, *52*, 1878. (d) Rosen, B. M.; Quasdorf, K. W.; Wilkson, D. A.; Zhang, N.; Resmerita, A.-M.; Garg, N. K.; Percec, B. *Chem. Rev.* **2011**, *111*, 1346. (e) Yu, D.-G.; Li, B.-J.; Shi, Z.-J. *Acc. Chem. Res.* **2010**, *43*, 1486.
- (2) Selected C–C bond-forming processes via C–O bond cleavage: (a) Ramgren, S. D.; Hie, L.; Ye, Y.; Garg, N. K. *Org. Lett.* **2013**, *15*, 3950. (b) Amaike, K.; Muto, K.; Yamaguchi, J.; Itami, K. *J. Am. Chem. Soc.* **2012**, *135*, 14573. (c) Leowanawat, P.; Zhang, N.; Percec, V. *J. Org. Chem.* **2012**, *77*, 1018 and references cited therein.
- (3) Selected C–heteroatom bond-forming processes via C–O bond cleavage: (a) Zarate, C.; Martin, R. *J. Am. Chem. Soc.* **2014**, *136*, 2236. (b) Ramgren, S. D.; Silberstein, A. L.; Yang, Y.; Garg, N. K. *Angew. Chem., Int. Ed.* **2011**, *50*, 2171. (c) Huang, K.; Yu, D.-G.; Zheng, S.-F.; Wu, Z.-H.; Shi, Z.-J. *Chem.—Eur. J.* **2011**, *17*, 786. (d) Shimasaki, T.; Tobisu, M.; Chatani, N. *Angew. Chem., Int. Ed.* **2010**, *49*, 2929.
- (4) Selected catalytic reductive couplings not employing organic halides as coupling partners: (a) Montgomery, J.; Sormunen, G. J. *Top. Curr. Chem.* **2007**, *279*, 1. (b) Montgomery, J. *Angew. Chem., Int. Ed.* **2004**, *49*, 3890. (c) Moslin, R. M.; Miller-Moslin, K.; Jamison, T. F. *Chem. Commun.* **2007**, 4441. (d) Jeganmohan, M.; Cheng, C. H. *Chem.—Eur. J.* **2008**, *14*, 10876.
- (5) Selected recent examples of catalytic reductive coupling events of organic halides: (a) Shrestha, R.; Dorn, S. C. M.; Weix, D. J. *J. Am. Chem. Soc.* **2013**, *135*, 751. (b) Peng, Y.; Luo, L.; Yan, C.-S.; Zhang, J.-J.; Wang, Y.-W. *J. Org. Chem.* **2013**, *78*, 10960. (c) Cherney, A. H.; Kadunce, N. T.; Reisman, S. E. *J. Am. Chem. Soc.* **2013**, *135*, 7442. (d) Everson, D. A.; Jones, B. A.; Weix, D. J. *J. Am. Chem. Soc.* **2012**, *134*, 6146. (e) Wang, S.; Qian, Q.; Gong, H. *Org. Lett.* **2012**, *12*, 3352. (f) Wu, F.; Lu, W.; Qian, Q.; Ren, Q.; Gong, H. *Org. Lett.* **2012**, *14*, 3044.
- (6) Recent catalytic reductive couplings of aryl halides with CO₂: (a) León, T.; Correa, A.; Martin, R. *J. Am. Chem. Soc.* **2013**, *135*, 1221. (b) Tran-Vu, H.; Daugulis, O. *ACS Catal.* **2013**, *3*, 2417. (c) Fujihara, T.; Nogi, K.; Xu, T.; Terao, J.; Tsuji, Y. *J. Am. Chem. Soc.* **2012**, *134*, 9106. (d) Correa, A.; Martin, R. *J. Am. Chem. Soc.* **2009**, *131*, 15974.
- (7) Remarkable exceptions using aryl and benzyl C–O electrophiles in reductive couplings: (a) Correa, A.; León, T.; Martin, R. *J. Am. Chem. Soc.* **2014**, *136*, 1062. (b) Kotsuki, H.; Datta, P. K.; Suenaga, H. *Synthesis* **1996**, 470. (c) Ref 6c.
- (8) For the use of related activated allyl C–O electrophiles in reductive cleavage events, see: (a) Tan, Z.; Wang, X.; Zang, Z.; Qian, Q.; Deng, W.; Gong, H. *Chem. Commun.* **2014**, *50*, 3827. (b) Anka-Lufford, L. L.; Prinsell, M. R.; Weix, D. J. *J. Org. Chem.* **2012**, *77*, 9989.

- (9) (a) Pattabiraman, V. R.; Bode, J. W. *Nature* **2011**, *480*, 471. (b) Arthur, G. *The Amide Linkage: Selected Structural Aspects in Chemistry, Biochemistry, and Materials Science*; Wiley-Interscience: New York, 2000.
- (10) Selected examples: (a) Lygin, A. V.; de Meijere, A. *Org. Lett.* **2009**, *11*, 389. (b) Kianmehr, E.; Rajabi, A.; Ghanbari, M. *Tetrahedron Lett.* **2009**, *50*, 1687. (c) Chorell, E.; Das, P.; Almqvist, F. *J. Org. Chem.* **2007**, *72*, 4917. (d) Miura, T.; Takahashi, Y.; Murakami, M. *Chem. Commun.* **2007**, 3577. (e) Koike, T.; Takahashi, M.; Arai, N.; Mori, A. *Chem. Lett.* **2004**, 1364. (f) Christophersen, C.; Begtrup, M.; Ebdrup, S.; Petersen, H.; Vedsø, P. *J. Org. Chem.* **2003**, *68*, 9513.
- (11) Reviews: (a) Brennfürher, A.; Neumann, H.; Beller, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 4114. (b) Li, Y.; Xue, D.; Wang, C.; Liu, Z.; Xiao, J. *Chem. Commun.* **2012**, *48*, 1320.
- (12) Examples: (a) Odell, L. R.; Sävmarker, J.; Larhed, M. *Tetrahedron Lett.* **2008**, *49*, 6115. (b) Larhed, M.; Wannberg, J. In *Modern Carbonylation Methods*; Kollar, L., Ed.; Wiley-VCH: Weinheim, 2008; p 93.
- (13) Selected examples: (a) Shin, K.; Ryu, J.; Chang, S. *Org. Lett.* **2014**, *16*, 2022. (b) Zhou, B.; Hou, W.; Yang, Y.; Li, Y. *Chem.—Eur. J.* **2013**, *19*, 4701. (c) Muralirajan, K.; Parthasarathy, K.; Cheng, C.-H. *Org. Lett.* **2012**, *14*, 4262. (d) Hesp, K. D.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2011**, *133*, 11430.
- (14) Classical synthetic methods en route to benzamides: (a) El-Faham, A.; Albericio, F. *Chem. Rev.* **2011**, *111*, 6557. (b) Valeur, E.; Bradley, M. *Chem. Soc. Rev.* **2009**, *38*, 606.
- (15) Alternative oxidative catalytic amidation of alcohols or amines: (a) De Sarkar, S.; Studer, A. *Org. Lett.* **2010**, *12*, 1992. (b) Yoo, W.-J.; Li, C.-J. *J. Am. Chem. Soc.* **2006**, *128*, 13064. (c) Gunanathan, C.; Ben-David, Y.; Milstein, D. *Science* **2007**, *317*, 790. (d) Nordstrøm, L. U.; Vogt, H.; Madsen, R. *J. Am. Chem. Soc.* **2008**, *130*, 17672. For other amidation methods, see: (e) Naredla, R. R.; Klumpp, D. A. *Tetrahedron Lett.* **2012**, *53*, 4779. (f) López, B.; Rodriguez, A.; Santos, D.; Albert, J.; Ariza, X.; Garcia, J.; Granell, J. *Chem. Commun.* **2011**, 47, 1054. (g) Orito, K.; Horibata, A.; Nakamura, T.; Ushito, H.; Nagasaki, H.; Yuguchi, M.; Yamashita, S.; Tokuda, M. *J. Am. Chem. Soc.* **2004**, *126*, 14342.
- (16) Reductive cleavage of organic halides with isocyanates: Hsieh, J.-C.; Cheng, C.-H. *Chem. Commun.* **2005**, 4554.
- (17) (a) Cornella, J.; Martin, R. *Org. Lett.* **2013**, *15*, 6298. (b) Cornella, J.; Gómez-Bengoia, E.; Martin, R. *J. Am. Chem. Soc.* **2013**, *135*, 1997. (c) Álvarez-Bercedo, P.; Martin, R. *J. Am. Chem. Soc.* **2010**, *132*, 17352. (d) See refs 3a and 7a.
- (18) See Supporting Information for more details. The optimal Ni:L ratio was found to be 1:2; little conversion was observed at lower Ni:L ratio and lower catalyst loading. In all cases, reduced arenes and free alcohols were observed as byproducts.
- (19) The difference in reactivity when using Zn and Mn is in analogy with recent literature data on reductive coupling events. See, for example, refs 5, 6a, and 6c.
- (20) The use of other related C(sp²)-O electrophiles such as naphthyl acetates, carbamates, or benzoates provided amide **2a** in comparatively much lower yields. See ref 18.
- (21) The higher reactivity of benzylic C(sp³)-O bonds is illustrated by the observation that a mixture of **1a** and **1d** (1:1 ratio) with cyclohexyl isocyanate at rt using Mn as reductant resulted in **2ag** and **2dg** (1:10 ratio). This result is in agreement with the higher reactivity of benzylic over aromatic moieties in related reductive coupling events. See for example, refs 6a and 7a.
- (22) Competitive reduced arene was found in the reaction mixture.
- (23) Selected C-O activation events limited to the use of π -extended systems: (a) Wisniewska, H. M.; Swift, E. C.; Jarvo, E. R. *J. Am. Chem. Soc.* **2013**, *135*, 9083. (b) Taylor, B. L.; Harris, M. R.; Jarvo, E. R. *Angew. Chem., Int. Ed.* **2012**, *51*, 7790. (c) Taylor, B. L. H.; Swift, E. C.; Waetzig, J. D.; Jarvo, E. R. *J. Am. Chem. Soc.* **2011**, *133*, 389. (d) Yu, D.-G.; Shi, Z.-J. *Angew. Chem., Int. Ed.* **2011**, *50*, 7097. (e) Yu, D.-G.; Li, B.-J.; Zheng, S.-F.; Guan, B.-T.; Wang, B.-Q.; Shi, Z.-J. *Angew. Chem., Int. Ed.* **2010**, *49*, 4566.
- (24) See, for example: (a) Tobisu, M.; Shimasaki, T.; Chatani, N. *Angew. Chem., Int. Ed.* **2008**, *47*, 4866. (b) Ref 7a. (c) Ref 17b. (d) Brauer, D. J.; Krueger, C. *Inorg. Chem.* **1977**, *16*, 884. (e) Chatt, J.; Duncanson, L. A.; Venanzi, L. M. *J. Chem. Soc.* **1955**, 4456.
- (25) A comparative study of a variety of activated C(sp²)-O electrophiles led us to identify aryl tosylates as the most suitable electrophiles; other groups such as aryl triflates or sulfamates were found much less efficient in our reductive amidation protocol. See ref 18.
- (26) The use of NaI and other iodide sources as additives has been found to be beneficial in Ni-catalyzed reductive coupling reactions: (a) Prinsell, M. R.; Everson, D. A.; Weix, D. J. *Chem. Commun.* **2010**, 5743. (b) Iyoda, M.; Otsuka, H.; Sato, K.; Nisato, N.; Oda, M. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 80. (c) Iyoda, M.; Sakaitini, M.; Otsuka, H.; Oda, M. *Chem. Lett.* **1985**, 127. (d) Piber, M.; Jensen, A. E.; Rottländer, M.; Knochel, P. *Org. Lett.* **1999**, *1*, 1323. (e) Ref 5d.
- (27) Reviews dealing with cross-coupling reactions of aryl chlorides: (a) Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 4176. (b) Grushin, V. V.; Alper, H. *Chem. Rev.* **1994**, *94*, 1047.
- (28) These results are in sharp contrast with the use of aryl iodides or bromides for similar purposes at high temperatures; see ref 16.
- (29) Aryl isocyanates could not be utilized as coupling partners in catalytic reductive amidation processes with either aryl pivalates or tosylates. In all cases analyzed, we found considerable amounts of isocyanurates via trimerization of the aryl isocyanate. Such trimerization is well-documented in the presence of zerovalent metal complexes: (a) Paul, F.; Moulin, S.; Piechaczyk, O.; Le Floch, P.; Osborn, J. A. *J. Am. Chem. Soc.* **2007**, *129*, 7294. (b) Foley, S. R.; Yap, G. P.; Richeson, D. S. *Organometallics* **1999**, *18*, 4700. (c) Tang, J.-S.; Verkade, J. G. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 896. Similarly, isocyanates bearing tosyl or silyl groups could not be utilized.
- (30) Muto, K.; Yamaguchi, J.; Lei, A.; Itami, K. *J. Am. Chem. Soc.* **2013**, *135*, 16384.
- (31) While not entirely conclusive, such a scenario was supported by the fact that chloro(1-naphthyl)(dppf)nickel(II) was catalytically competent as reaction intermediate under the optimized reaction conditions.
- (32) The available data, however, do not allow us to rigorously rule out Ni(I) intermediates via single electron transfer processes or comproportionation events. For some references in this regard: (a) Goldup, S. M.; Leigh, D. A.; McBurney, R. T.; McGonigal, P. R.; Plant, A. *Chem. Sci.* **2010**, *1*, 383. (b) Refs 5a, 6a, 6c, 7a, 17b, and 26a. (c) Velian, A.; Lin, S.; Miller, A. J. M.; Day, M. W.; Agapie, T. *J. Am. Chem. Soc.* **2010**, *132*, 6296. (d) Jones, G. D.; Martin, J. L.; McFarland, C.; Allen, O. R.; Hall, R. E.; Haley, A. D.; Brandon, R. J.; Konovalova, T.; Desrochers, P. J.; Pulay, P.; Vacic, D. A. *J. Am. Chem. Soc.* **2006**, *128*, 13175.