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Synthesis of Seven-Membered Benzolactones by Nickel-Catalyzed C–H Coupling of Benzamides with Oxetanes

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Dedication ((optional))

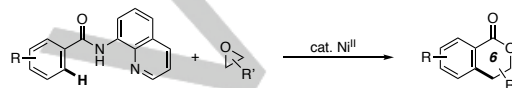
Abstract: A NiCl₂(PEt₃)₂-catalyzed regioselective C–H coupling of 8-aminoquinoline-derived benzamides with oxetanes has been developed. The reaction proceeds with concomitant removal of the 8-aminoquinoline auxiliary to directly form the corresponding seven-membered benzolactones, which frequently occur in natural products and bioactive molecules. Additionally, no stereochemical erosion is observed during the course of the reaction, and the use of enantioenriched and substituted oxetane thus provides a new avenue to the optically active benzolactone.

Oxetane constitutes an important class of cyclic ethers in organic synthetic chemistry and polymer synthesis. Owing to its high strain energy,^[1] it can undergo a variety of ring-opening reactions with highly reactive organometallic reagents and heteroatom nucleophiles in the presence or absence of Brønsted and Lewis acid promoters to form the corresponding three-carbon homologated, oxygenated products and/or polyethers.^[2] However, redox-active transition-metal-catalyzed coupling reactions with oxetane are relatively limited, compared to a three-membered analogue, epoxide, probably because of slightly less distortion energy (oxetane: 107 kJ mol⁻¹ vs. epoxide: 114 kJ mol⁻¹).^[1] As an early work, Murai and coworkers developed the rhodium-catalyzed silylformylation of oxetanes with hydrosilanes and carbon monoxide.^[3] Gansäuer also reported the titanocene-catalyzed ring-opening reductive dimerization to provide 1,6-hexanediols.^[4] Recently, some research groups developed unique coupling reactions of oxetanes, including the rhodium-catalyzed carbene insertion,^[5] gold-nanoparticle-catalyzed silaboration,^[6] and iron-catalyzed oxidative C–H coupling,^[7] but synthetic utility of oxetanes under transition-metal catalysis still remains underdeveloped.

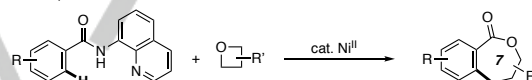
Meanwhile, our research group recently reported the nickel-catalyzed C–H coupling reaction^[8] of benzamides with epoxides (Scheme 1a).^[9,10] The reaction was promoted by the N,N-doubly coordinated aminoquinoline auxiliary, which was originally developed by Daugulis,^[11] and the corresponding six-membered benzolactones were directly obtained with the concomitant removal of aminoquinoline directing group. During our continuing interest in this chemistry, we next envisioned the C–H coupling reaction with oxetanes. Herein, we report a nickel-catalyzed coupling reaction of quinoline amides with oxetanes

via the N,N-double chelation-assisted C–H cleavage (Scheme 1b). As observed in our previous work with epoxides,^[9a] a successive ring-closing reaction occurred^[12] to directly deliver the corresponding seven-membered benzolactones of prevalent medium-sized ring system found in natural products and bioactive molecules.^[13]

a) Ni-catalyzed C–H coupling of benzamides with epoxides leading to six-membered benzolactones (previous work)



b) Ni-catalyzed C–H coupling of benzamides with oxetanes leading to seven-membered benzolactones (this work)



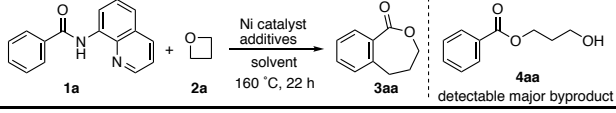
Scheme 1. Nickel-catalyzed C–H couplings of quinoline benzamides with epoxides (a) and oxetanes (b).

We selected benzamide **1a** and parent oxetane (**2a**) as model substrates and started optimization studies (Table 1). In an early experiment, treatment of **1a** with **2a** (4.0 equiv) and 20 mol% NiCl₂(PCy₃)₂ in diglyme at 160 °C (our previous optimal conditions^[9a]) afforded the seven-membered benzolactone **3aa** in 30% ¹H NMR yield (entry 1). Subsequent brief screening of nickel catalysts revealed that NiCl₂(PEt₃)₂ showed better performance (entries 2–4). Solvent and concentration effects were also critical: DMF further increased the yield to 56% yield, particularly under higher concentration (entries 5 and 6), whereas the reaction in other solvents including NMP, DMSO, and toluene was almost sluggish (entries 7–9). On the other hand, an additional survey of phosphine ligands combined with the NiCl₂·glyme salt in the DMF solvent provided no improvement of the yield (entries 10–14). The use of nickel(0) catalyst, Ni(cod)₂, also gave almost no conversion (entry 15). The higher nickel catalyst loading (30 mol%) slightly improved the yield (entry 16); however, at this point we found the formation of the ester **4aa** as the major byproduct (≈30%), which apparently suggests occurrence of the ring-opening side reaction of oxetane (**2a**) with contaminated water. Thus, we tested the addition of several dehydrating agents (entries 17–20). Pleasingly, 3Å MS effectively suppressed the byproduct **4aa** to furnish **3aa** in 74% isolated yield (entry 20) with good reproducibility. Finally, with the Et₃N additive (20 mol%), the targeted benzolactone **3aa** was isolated in slightly higher yield of 78% (entry 21). Additional observations worth noting are that other organic bases such as 1,4-diazabicyclo[2.2.2]octane (DABCO) and 4-dimethylaminopyridine (DMAP) were detrimental (data not shown); the aminoquinoline auxiliary was indispensable, and other monodentately and bidentately coordinating amide substrates showed sluggish reactivity under the present conditions. Unfortunately, both long reaction time

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and high reaction temperature were necessary for good conversion and reproducibility.

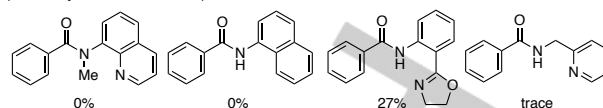
Table 1. Optimization studies for nickel-catalyzed C–H coupling of benzamide **1a** with oxetane (**2a**) for the synthesis of seven-membered benzolactone **3aa**.^[a]



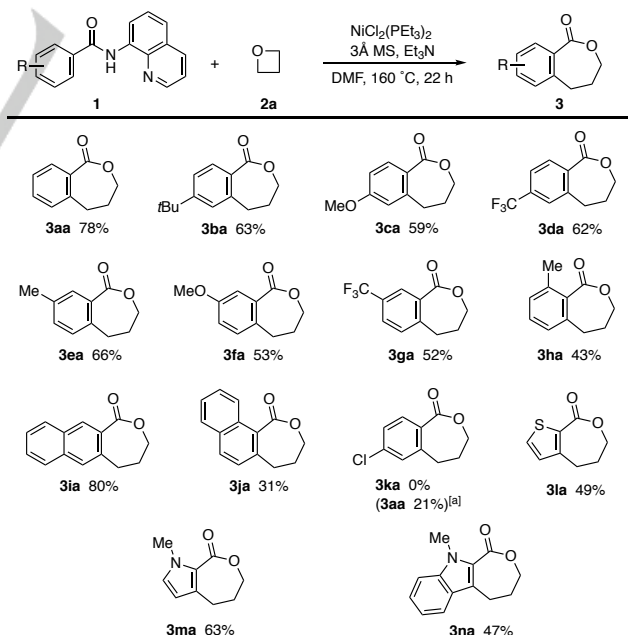
Entry	Ni cat. (loading [mol%])	Additives	Solvent [mL]	Yield [%] ^[b]
1	NiCl ₂ (PCy ₃) ₂ (20)	none	diglyme (1.0)	30
2	NiCl ₂ (PEt ₃) ₂ (20)	none	diglyme (1.0)	36
3	NiCl ₂ ·glyme (20)	none	diglyme (1.0)	25
4	Ni(acac) ₂ (20)	none	diglyme (1.0)	0
5	NiCl ₂ (PEt ₃) ₂ (20)	none	DMF (1.0)	33
6	NiCl ₂ (PEt ₃) ₂ (20)	none	DMF (0.5)	56
7	NiCl ₂ (PEt ₃) ₂ (20)	none	NMP (1.0)	8
8	NiCl ₂ (PEt ₃) ₂ (20)	none	DMSO (1.0)	0
9	NiCl ₂ (PEt ₃) ₂ (20)	none	toluene (1.0)	0
10	NiCl ₂ ·glyme (20) dppbz (20)	none	DMF (0.5)	30
11	NiCl ₂ ·glyme (20) dppe (20)	none	DMF (0.5)	9
12	NiCl ₂ ·glyme (20) PPh ₃ (40)	none	DMF (0.5)	30
13	NiCl ₂ ·glyme (20) PBu ₃ (40)	none	DMF (0.5)	8
14	NiCl ₂ ·glyme (20) P(tBu) ₃ (40)	none	DMF (0.5)	26
15	Ni(cod) ₂ (20)	none	DMF (0.5)	trace
16	NiCl ₂ (PEt ₃) ₂ (30)	none	DMF (0.5)	59
17	NiCl ₂ (PEt ₃) ₂ (30)	Na ₂ SO ₄	DMF (0.5)	41
18	NiCl ₂ (PEt ₃) ₂ (30)	MgSO ₄	DMF (0.5)	39
19	NiCl ₂ (PEt ₃) ₂ (30)	4Å MS	DMF (0.5)	56–68 ^[c]
20	NiCl ₂ (PEt ₃) ₂ (30)	3Å MS	DMF (0.5)	(74)
21	NiCl ₂ (PEt ₃) ₂ (30)	3Å MS Et ₃ N ^[d]	DMF (0.5)	(78)

[a] Conditions: **1a** (0.20 mmol), **2a** (0.80 mmol), Ni cat., additives, solvent, 160 °C, 22 h, N₂. [b] Estimated by ¹H NMR with triphenylmethane as an internal standard. Yields of isolated material in parentheses. [c] Poor reproducibility. [d] 20 mol% of Et₃N. Abbreviations: acac = acetylacetonate, cod = 1,5-cyclooctadiene, DMF = *N,N*-dimethylformamide, DMSO = dimethylsulfoxide, dppbz = 1,2-bis(diphenylphosphino)benzene, dppe = 1,2-bis(diphenylphosphino)ethane, NMP = *N*-methylpyrrolidone.

substrates with lower or no reactivity under conditions in entry 6 (¹H NMR yield of **3aa** is shown)

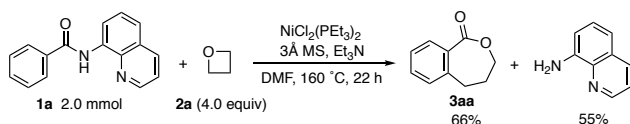


With good conditions in hand (entry 21 in Table 1), we investigated the scope and limitations of benzamide substrates **1** with the parent oxetane (**2a**; Scheme 2). The nickel catalyst was equally compatible with electron-neutral, -donating, and withdrawing groups (*t*Bu, MeO, CF₃) at the *para* position to form the corresponding benzolactones **3ba–da** in good yields. In the case of *meta*-substituted benzamides, the reaction occurred selectively at the more sterically accessible C–H bond, regardless of the electronic nature of substituents (**3ea–ga**). Albeit with somewhat lower efficiency, the substitution at the *ortho* position was also tolerated (**3ha**). Higher fused naphthalene derivatives **1i** and **1j** could also be employed: the 2-naphthalenecarboxamide was coupled with **2a** at the sterically less hindered C3 position to form the corresponding tricyclic system **3ia** in 80% yield, whereas the 1-naphthyl isomer showed lower reactivity (**3ja**, 31%) probably due to steric factors similar to the result of **3ha**. Unfortunately, the reaction of chloro-substituted benzamide **1k** was sluggish, and only the protodechlorinated product **3aa** was observed (not **3ka**); however, the unsuccessful result gave information about the oxidation state of active nickel species (vide infra). Additional advantage is accommodation of some heteroaromatics. Thiophene-, pyrrole-, and indole-derived carboxamides underwent the C–H coupling-cyclization cascade to deliver **3la–na** in synthetically acceptable yields.^[14]



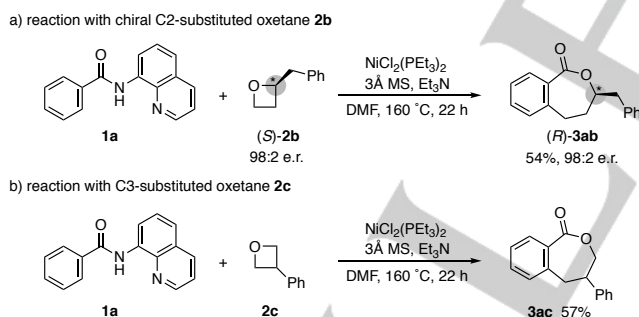
Scheme 2. Nickel-catalyzed C–H coupling of various benzamides **1** with oxetane (**2a**). Conditions: **1** (0.20 mmol), **2a** (0.80 mmol), NiCl₂(PEt₃)₂ (0.060 mmol), Et₃N (0.040 mmol), 3Å MS (100 mg), DMF (0.50 mL), 160 °C, 22 h, N₂. Yields of isolated products are given. [a] Only the protodechlorinated product **3aa** was formed.

An additional feature of this nickel catalysis is the spontaneous removal and successful recycling of directing group (Scheme 3). The model reaction of **1a** with **2a** could also be performed on a 2.0 mmol scale, and the desired **3aa** was isolated in 66% yield along with 55% recovery of 8-aminoquinoline auxiliary; the result deserves some attention from synthetic point of view, because the removal of such a bidentate directing group often requires tedious and additional experimental operations.^[12]



Scheme 3. Reaction on 2.0 mmol scale.

The scope and limitation of oxetanes **2** was then briefly surveyed. In the reaction with the C2-substituted oxetane (*S*)-**2b**, the more sterically accessible C4–O bond was selectively cleaved to form the benzolactone (*R*)-**3ab** as the sole regioisomer (Scheme 4a). Additionally, its chirality was successfully transferred without erosion of enantiomeric excess, thus providing a new route to chiral seven-membered benzolactones from relatively easily prepared enantioenriched oxetanes. The C3-substituted oxetane **2c** was also coupled with **1a**, and the corresponding **3ac** was obtained in 57% yield (Scheme 4b). On the other hand, unsuccessful oxetanes included 2,2- and 3,3-disubstituted oxetanes. In the former case, the ring-opening isomerization predominantly occurred to form the corresponding homoallylic alcohol, whereas the latter substrates resulted in no conversion probably because of steric factors (data not shown).



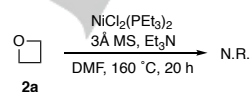
Scheme 4. Nickel-catalyzed C–H coupling of benzamide **1a** with some substituted oxetanes **2**. For conditions, see the caption of Scheme 2.

To get some insight into the reaction mechanism, we implemented the following control experiments. In the absence of the benzamide **1**, the parent oxetane (**2a**) gave no detectable amount of ring-opening side products (Scheme 5a). Additionally, the reaction of **1a** with 3-chloropropanol (**5**), which is the most conceivable ring-opening side product promoted by the NiCl₂ salt, resulted in no conversion (Scheme 5b). These outcomes suggest that the oxetane itself is directly coupled with **1a**. Deuterium-labeling experiments with [D₅]-**1a** were also performed (Scheme 5c). In the presence and absence of oxetane (**2a**), significant *ortho*-H/D scrambling occurred even at

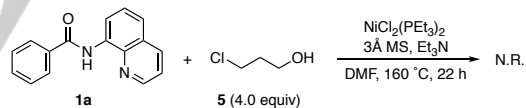
an early stage of the reaction, thus indicating that the C–H cleavage process is facile and not the rate-limiting step.^[15]

Based on the above findings, we are tempted to propose that the reaction mechanism of **1a** with **2a** is as shown in Scheme 6. First, the nickel(II) precatalyst NiCl₂(PEt₃)₂ is believed to be reduced to nickel(I) species **6**.^[16] The observed incompatibility with the ArCl moiety (Scheme 2, **3ka**) can support the intermediacy of nickel at the lower oxidation state. Although the exact reductant remains to be elucidated, the benzamide substrate or PEt₃ can be a good candidate.^[17] The coordination of benzamide **1a** (**6** to **7**) is followed by *N,N*-bidentate coordination-assisted reversible C–H cleavage to form the nickelacycle **8**. The chelated nickel complex **8** then undergoes oxidative addition with **2a** (**8** to **9**), and subsequent reductive elimination generates the C–H alkylated intermediate **10**. Acceleration of the aforementioned and somewhat challenging oxidative addition of oxetane can be an additional role of PEt₃ ligand. Upon protonolysis with HCl, the corresponding alcohol **11** is liberated along with regeneration of the starting nickel **6**. Final intramolecular alcoholysis delivers the observed seven-membered benzolactone **3aa** and free 8-aminoquinoline. The role of Et₃N additive is unclear at this stage, but it can work as a proton shuttle in the catalytic cycle. The cyclization event can also be accelerated by the nickel catalyst. The NiCl₂(PEt₃)₂ catalyst successfully converted the independently prepared **11ha** to the lactone **3ha**, whereas no reaction occurred in the absence of any nickel catalyst (Scheme 7).^[18]

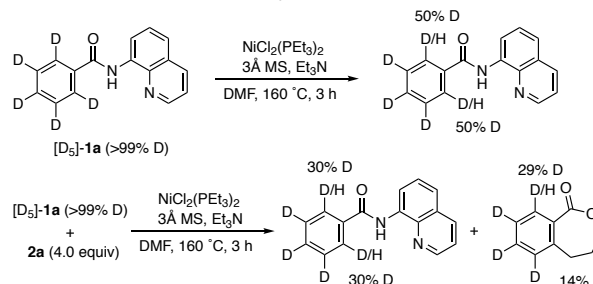
a) reaction of oxetane (**2a**) without benzamide **1**



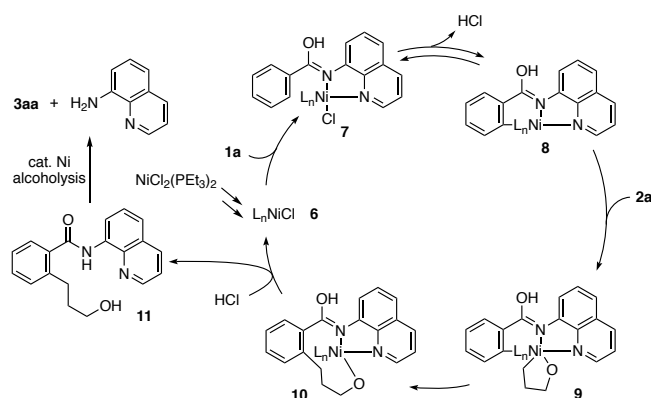
b) reaction of **1a** with 3-chloropropanol (**5**) instead of oxetane (**2a**)



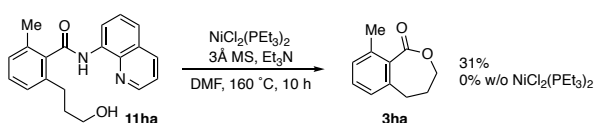
c) deuterium-labeling experiments with [D₅]-**1a**



Scheme 5. Control experiments. N.R. = no reaction.



Scheme 6. Plausible mechanism. L = ligand.



Scheme 7. Effects of nickel catalyst in intramolecular alcoholysis.

In conclusion, we have developed a nickel-catalyzed C–H coupling of 8-aminoquinoline-derived benzamides with oxetanes. The reaction occurs with the spontaneous removal of the 8-aminoquinoline bidentate auxiliary to form the corresponding seven-membered benzolactones directly. The present nickel catalysis can provide a new avenue to such medium-sized lactones of frequent occurrence in bioactive molecules and natural products. Additionally, this is one of the limited successful applications of oxetanes under the redox-active transition-metal catalysis. Further improvement of catalyst turnover, expansion of substrate scope, and development of related C–H coupling with other strained heterocycles are under investigation in our laboratory.

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Conflict of Interest

The authors declare no conflict of interest.

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- [1] a) A.S. Pell, G. Pilcher, *Trans. Faraday Soc.* **1965**, *61*, 71; b) H. Sakurai, *J. Photopolym. Sci. Technol.* **2000**, *13*, 119.
- [2] a) S. Ahmad, M. Yousaf, A. Mansha, N. Rasool, A. F. Zahoor, F. Hafeez, S. M. A. Rizvi, *Synth. Commun.* **2016**, *46*, 1397; b) S. Minegishi, S. Tsuchida, M. Sasaki, A. Kameyama, H. Kudo, T. Nishikubo, *J. Polym. Sci. Part A: Polym. Chem.* **2002**, *40*, 3835.
- [3] Y. Fukumoto, S. Yamaguchi, N. Chatani, S. Murai, *J. Organomet. Chem.* **1995**, *489*, 215.
- [4] A. Gansäuer, N. Ndene, T. Lauterbach, J. Justicia, I. Winkler, C. Mück-Lichtenfeld, S. Grimme, *Tetrahedron* **2008**, *64*, 11839.
- [5] A. Guarnieri-Ibáñez, F. Medina, C. Besnard, S. L. Kidd, D. R. Spring, J. Lacour, *Chem. Sci.* **2017**, *8*, 5713.
- [6] E. Vasilikogiannaki, A. Louka, M. Stratakis, *Organometallics* **2016**, *35*, 3895.
- [7] Z. An, L. Zhao, M. Wu, J. Ni, Z. Qi, G. Yu, R. Yan, *Chem. Commun.* **2017**, *53*, 11572.
- [8] Recent selected reviews on the metal-promoted C–H functionalization, see: a) F. Kakiuchi, T. Kochi, *Synthesis* **2008**, *2008*, 3013; b) L. Ackermann, R. Vicente, A. R. Kapdi, *Angew. Chem. Int. Ed.* **2009**, *48*, 9792; *Angew. Chem.* **2009**, *121*, 9976; c) T. W. Lyons, M. S. Sanford, *Chem. Rev.* **2010**, *110*, 1147; d) T. Satoh, M. Miura, *Chem. Eur. J.* **2010**, *16*, 11212; e) C. Liu, H. Zhang, W. Shi, A. Lei, *Chem. Rev.* **2011**, *111*, 1780; f) J. Yamaguchi, A. D. Yamaguchi, K. Itami, *Angew. Chem. Int. Ed.* **2012**, *51*, 8960; *Angew. Chem.* **2012**, *124*, 9092; g) K. Hirano, M. Miura, *Chem. Lett.* **2015**, *44*, 868; h) V. P. Boyarskiy, D. S. Ryabukhin, N. A. Bokach, A. V. Vasilyev, *Chem. Rev.* **2016**, *116*, 5894; i) F. Wang, S. Yu, X. Li, *Chem. Soc. Rev.* **2016**, *45*, 6462; j) R.-Y. Zhu, M. E. Farmer, Y.-Q. Chen, J.-Q. Yu, *Angew. Chem. Int. Ed.* **2016**, *55*, 10578; *Angew. Chem.* **2016**, *128*, 10734; k) M. Gulías, J. L. Mascareñas, *Angew. Chem. Int. Ed.* **2016**, *55*, 11000; *Angew. Chem.* **2016**, *128*, 11164; l) L. Ping, D. S. Chung, J. Bouffard, S. Li, *Chem. Soc. Rev.* **2017**, *46*, 4299; m) M. T. Mihai, G. R. Genov, R. J. Phipps, *Chem. Soc. Rev.* **2018**, *47*, 149; n) J. C. K. Chu, T. Rovis, *Angew. Chem. Int. Ed.* **2018**, *57*, 62; *Angew. Chem.* **2018**, *130*, 64; o) C. Sambiagio, D. Schönbauer, R. Blicke, T. Dao-Huy, G. Pototschnig, P. Schaaf, T. Wiesinger, M. F. Zia, J. Wencel-Delord, T. Besset, B. U. W. Maes, M. Schnürch, *Chem. Soc. Rev.* **2018**, *47*, 6603.
- [9] a) S. Xu, K. Takamatsu, K. Hirano, M. Miura, *Angew. Chem. Int. Ed.* **2018**, *57*, 11797; *Angew. Chem.* **2018**, *130*, 11971. For related Pd-catalyzed C–H couplings with epoxides, see: b) Z. Wang, Y. Kuninobu, M. Kanai, *J. Am. Chem. Soc.* **2015**, *137*, 6140; c) G. Cheng, T.-J. Li, J.-Q. Yu, *J. Am. Chem. Soc.* **2015**, *137*, 10950; d) R. Li, G. Dong, *Angew. Chem. Int. Ed.* **2018**, *57*, 1697; *Angew. Chem.* **2018**, *130*, 1713.
- [10] For selected seminal work and reviews on nickel-catalyzed C–H couplings with the assistance of aminoquinoline *N,N*-double coordination, see: a) H. Shiota, Y. Ano, Y. Aihara, Y. Fukumoto, N. Chatani, *J. Am. Chem. Soc.* **2011**, *133*, 14952; b) Y. Aihara, N. Chatani, *J. Am. Chem. Soc.* **2013**, *135*, 5308; c) Y. Aihara, N. Chatani, *J. Am. Chem. Soc.* **2014**, *136*, 898; d) L. C. M. Castro, N. Chatani, *Chem. Lett.* **2015**, *44*, 410.
- [11] Pioneering work: a) V. Z. Zaitsev, D. Shabashov, O. Daugulis, *J. Am. Chem. Soc.* **2005**, *127*, 13154. Selected reviews: b) M. Corbet, F. De Campo, *Angew. Chem. Int. Ed.* **2013**, *52*, 9896; *Angew. Chem.* **2013**, *125*, 10080; c) G. Rouquet, N. Chatani, *Angew. Chem. Int. Ed.* **2013**, *52*, 11726; *Angew. Chem.* **2013**, *125*, 11942; d) N. Chatani, *Top. Organomet. Chem.* **2016**, *56*, 19; e) J. Liu, G. Chen, Z. Tan, *Adv. Synth. Catal.* **2016**, *358*, 1174; f) Y. Kommagalla, N. Chatani, *Coord. Chem. Rev.* **2017**, *350*, 117.
- [12] For limited successful examples of C–H couplings with concomitant removal of bidentate directing groups, see: a) K. Takamatsu, K. Hirano, M. Miura, *Org. Lett.* **2015**, *17*, 4066; b) T. Uemura, T. Igarashi, M. Noguchi, K. Shibata, N. Chatani, *Chem. Lett.* **2015**, *44*, 621; c) P. Gandeepan, P. Rajamalli, C.-H. Cheng, *Angew. Chem. Int. Ed.* **2016**, *55*, 4308; *Angew. Chem.* **2016**, *128*, 4380; d) C. Yamamoto, K. Takamatsu, K. Hirano, M. Miura, *J. Org. Chem.* **2017**, *82*, 9112; e) J. Liu, J. Zou, J. Yao, G. Chen, *Adv. Synth. Catal.* **2018**, *360*, 659.

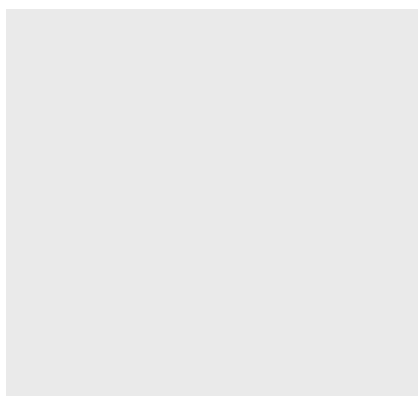
- [13] Selected examples: a) H. Fujimoto, M. Inagaki, Y. Satoh, E. Yoshida, M. Yamazaki, *Chem. Pharm. Bull.* **1996**, *44*, 1090; b) S. Miethbauer, W. Günther, K.-U. Schmidtke, I. Heiser, S. Gräfe, B. Gitter, B. Liebermann, *J. Nat. Prod.* **2008**, *71*, 1371; c) A. H. Aly, R. Edrada-Ebel, I. D. Indriani, V. Wray, W. E. G. Müller, F. Totzke, U. Zirrgiebel, C. Schächtele, M. H. G. Kubbutat, W. H. Lin, P. Proksch, R. Ebel, *J. Nat. Prod.* **2008**, *71*, 972; d) H.-J. Yan, X.-M. Li, C.-S. Li, B.-G. Wang, *Helv. Chim. Acta* **2012**, *95*, 163; e) Y.-J. Jiang, D.-S. Zhang, H.-J. Zhang, J.-Q. Li, W.-J. Ding, C.-D. Xu, Z.-J. Ma, *J. Nat. Prod.* **2018**, *81*, 2120.
- [14] Unfortunately, attempts to apply aliphatic amides such as pivalamide remained unsuccessful under the present conditions.
- [15] The source of H might still be contaminated water. We confirmed the partial deuterium incorporation (22% D) at the ortho position of **1a** when a mixture of **1a**, D₂O (1.0 equiv), and nickel catalyst was simply heated in DMF.
- [16] For examples of nickel(I) species in other cross-coupling reactions, see: a) G. D. Jones, J. L. Martin, C. McFarland, O. R. Allen, R. E. Hall, A. D. Haley, R. J. Brandon, T. Konovalova, P. J. Desrochers, P. Pulay, D. A. Vivic, *J. Am. Chem. Soc.* **2006**, *128*, 13175; b) J. Breitenfeld, J. Ruiz, M. D. Wodrich, X. Hu, *J. Am. Chem. Soc.* **2013**, *135*, 12004; c) N. D. Schley, G. C. Fu, *J. Am. Chem. Soc.* **2014**, *136*, 16588; d) R. A. Jagtap, C. P. Vinod, B. Punji, *ACS Catal.* **2019**, *9*, 431.
- [17] In particular, phosphorus (III) compounds were believed to reduce Ni^{II} salts to them of lower oxidation state at high reaction temperature; a) T. M. Balthazor, R. C. Grabiak, *J. Org. Chem.* **1980**, *45*, 5425; b) Y.-L. Zhao, G.-J. Wu, Y. Li, L.-X. Gao, F.-S. Han, *Chem. Eur. J.* **2012**, *18*, 9622.
- [18] Ohshima reported the related nickel(II)-catalyzed alcoholysis of 8-aminoquinoline amides. T. Deguchi, H.-L. Xin, H. Morimoto, T. Ohshima, *ACS Catal.* **2017**, *7*, 3157. The yield of **3ha** was lower than that observed in Scheme 2, which suggests another lactonization pathway, such as the direct conversion of Ni-associated intermediate **10** to the benzolactone **3aa** (Scheme 6).

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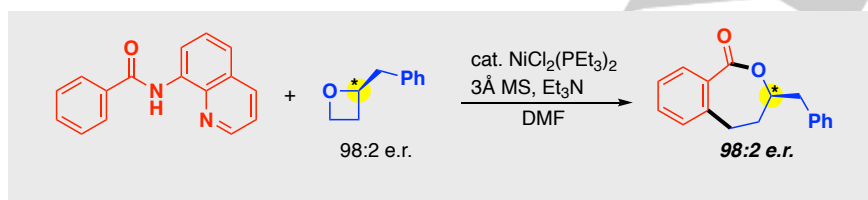
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Synthesis of Seven-Membered Benzolactones by Nickel-Catalyzed C–H Coupling of Benzamides with Oxetanes

Breaking the fourth wall: A $\text{NiCl}_2(\text{PEt}_3)_2$ -catalyzed regioselective C–H coupling of 8-aminoquinoline-derived benzamides with oxetanes has been developed. The reaction proceeds with concomitant removals of the 8-aminoquinoline auxiliary to directly form the corresponding seven-membered benzolactones, which frequently occur in natural products and bioactive molecules. Additionally, the use of enantioenriched and substituted oxetane provides a new avenue to the optically active benzolactone.