

Precise Control of the Site-Selectivity in Ruthenium-Catalyzed C-H Bond Amidations by Cyclic Amides as Powerful Directing Groups

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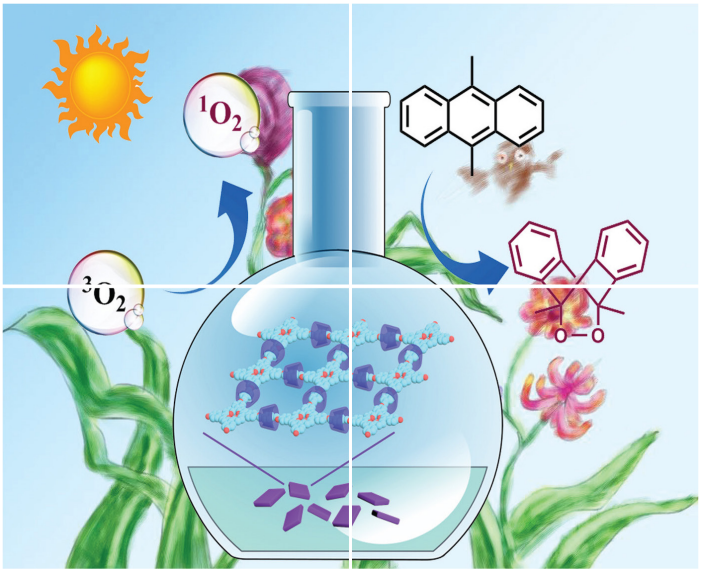
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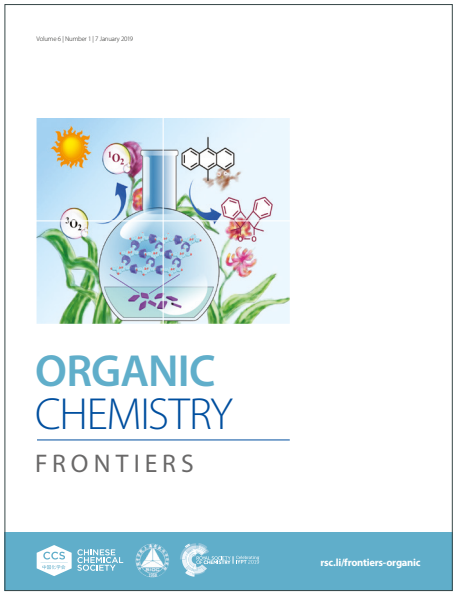
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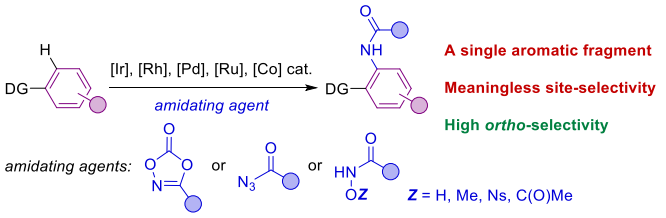
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Selective C-H functionalizations aiming at the formation of new C-N bonds is of paramount importance in the context of step- and atom-economy methodologies in organic synthesis. Although the implementation of noble metal catalysts is prevalent, more benign cobalt pre-catalysts have recently appeared promising. However, they sometimes feature selectivity issues that limits its applicability in late-stage functionalization. Herein, we report on a highly reactive ruthenium-based catalytic system displaying excellent levels of mono-, regio- and site-selectivity exploiting a series of biologically-relevant cyclic amides as weak directing groups. The use of dioxazolone derivatives as the amidating reagent overcomes the issues encountered in the use of unstable azide derivatives for such transformations and it enables to perform these reactions under very mild reaction conditions (air, 40 ºC). Moreover, a combination of deuteration experiments and a comparative study with different types of directing groups highlight the relevance of weak amide directing groups for enabling formation of six-membered cycloruthenate intermediates in key elementary steps of the catalytic cycle. In addition, DFT computational calculations were carried out for the first time for studying ruthenium-catalyzed C-N bond-forming processes via C-H activation assisted by weak directing groups, thereby elucidating the origin of the regio- and site-selectivity.

Introduction

The selective formation of C-heteroatom bonds is a fundamental transformation with direct consequences in the streaming synthesis of highly elaborated molecules with important applications ranging from pharmacology to materials sciences.[1] In this context, C-N bond-forming processes are significantly relevant as they can be targeted in a sustainable manner using transition metal complexes as homogeneous catalysts.[2] Since the pioneering discoveries of the Ullmann coupling with copper catalysts[3] to the most recent Buchwald-Hartwig aminations with palladium ones,[4] these and analogous transformations have completely revolutionized the way of conceiving organic synthesis.[5] However, most of these protocols require the use of pre-activated starting materials which impose synthetic limitations together with undesired over-stoichiometric formation of hazardous by-products.[3-5] Consequently, new promising approaches based on transition metal-catalyzed C-H bond functionalizations have appeared in the last decades for amination reactions that can directly be performed on low functionalized starting materials.[6] In this scenario, the selectivity is typically controlled by the presence of a directing group (DG) nearby the C-H bond desired to be functionalized.[7] Therefore, this leads typically to *ortho*-selectivity for aromatic C-H bond aminations[7] although few cases of remote, *meta*- and *para*-C-H bond aminations have been reported.[8]



Scheme 1 General case of a transition metal-catalyzed C-H bond amidation on aromatic scaffolds. DG = directing groups.

From the many known C-N bond-forming reactions, transition metal-catalyzed *ortho*-C-H amidation ones are particularly interesting given the ubiquitous nature of amide bonds.[9,10] Catalysts based on Ir, Rh, Pd, Ru or Co are of choice due to their high reactivity[11] and amidating agents derived from dioxazolone are preferred instead of azides because of their benchmark stability.[12] Taken this into account, it appears that all reports from the literature dealing with transition metal-catalyzed C-H bond amidations focused exclusively on substrates containing only one aromatic C-H bond available for reaction (Scheme 1).[7,11,12] However, for implementation in late-stage functionalization for instance, the methodologies may

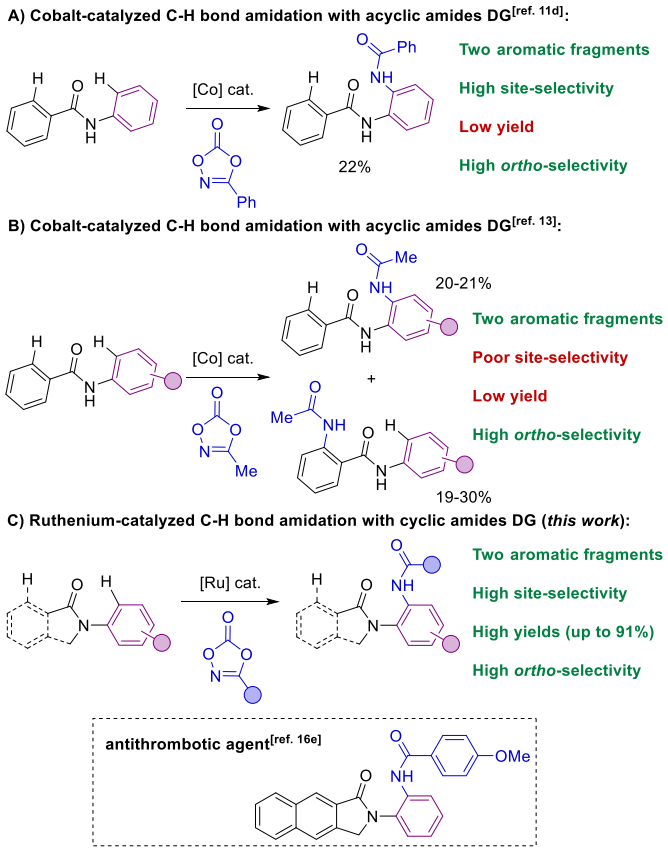
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consider also the compatibility with other aromatic C-H bonds prone to react. Unfortunately, the site-selectivity of aromatic C-H bond amidation reactions have been rarely studied to date with low levels of selectivity so far reported. In a first study in 2017, Chang and co-workers demonstrated for a single example (*N*-phenylbenzamide) that a C-H bond amidation could be site-selective with a cobalt catalyst and unproductive with a ruthenium catalyst, albeit with a modest yield (Scheme 2A).[11d] Later, Whiteoak and co-workers showed, as it could be expected, that a statistical mixture of amidated products is obtained using a cobalt catalyst with the assistance of an acyclic amide directing group in yields not exceeding 30% (Scheme 2B).[13]



Scheme 2 Transition metal-catalyzed C-H bond amidations on aromatic scaffolds using amides as directing groups: state-of-the-art (A and B) *versus* present work (C).

These examples undoubtedly show the difficulty to reach site-selective C-H bond amidations in the presence of multiple aromatic fragments. Herein, we show that both regio- and site-selectivity is achieved when using cyclic amides as directing groups in the presence of two aromatic sites prone to react by means of a ruthenium catalyst that additionally displays a large functional group tolerance (Scheme 2C). We found that *ortho*-C-H bond amidations selectively took place in the *N*-aryl fragment rather than in the *C*(O)-aryl site. Control experiments, preliminary mechanistic studies and thorough DFT calculations unambiguously support that cyclic amides enable formation of catalytically productive six-membered ruthenacycles as unique intermediates[14] as it was evoked but never demonstrated in C-O and C-C bond forming reactions.[15] It is worthy to note that cyclic amides, such as the isoindolinones employed in this study, are prevalent motifs encountered in several daily-life chemicals (Scheme 2C, framed),[16] thereby the presented methodology paves the way towards the use of ruthenium catalysts in C-H bond late-stage functionalization strategies.[17] An in-depth comparative study with other type of common directing groups is presented indicating the suitability of weak amide directing groups over the more coordinating ones, such as pyridines, for ruthenium-catalyzed C-H bond amidations. In addition, cyclic amides were found to outperform acyclic ones as directing groups for this relevant transformation.

Results and discussion

Our initial efforts started by using *N*-arylisoindolinone (**1a**) as the model substrate for the optimization of the C-H bond amidation reaction with 3-phenyl-1,4,2-dioxazol-5-one (**2a**) as the amidating agent in the presence of $[RuCl_2(p\text{-cymene})]_2$ as the pre-catalyst. After screening a number of parameters (Table 1 and Table S1 in the Supporting Information), we found suitable reaction conditions that afforded exclusively the amide derivative **3a**, in which the C-H bond amidation occurred in the hydrogen atom Ha (*ortho* position with respect to the nitrogen atom). The C-H bond functionalization taking place at the other possible hydrogen atom Hb was not observed (Table 1). The reaction conditions consist of 5 mol% of $[RuCl_2(p\text{-cymene})]_2$, $AgSbF_6$ as a chloride scavenger, PivOH as additive in 2,2,2-trifluoroethanol (TFE) as the solvent at 40 °C under air atmosphere during 24 hours (Table 1, entry 1). In this way, **3a** was obtained in 80% isolated yield. Control experiments indicated the need of both the chloride scavenger $AgSbF_6$ and the ruthenium pre-catalyst (Table 1, entries 2-3). Additives influenced in a different manner the reactivity and selectivity of the C-H bond amidation reaction. Among the different protic additives evaluated, PivOH was found to be the most suitable one (Table 1, entries 4-7). Screening other solvents such as 1,2-dichloroethane (DCE), 1,4-dioxane and tetrahydrofuran (THF) was detrimental to the catalysis compared to TFE (Table 1, entries 8-10). Lowering the loading of the amidating agent **2a** to 1.2 equivalents, afforded the corresponding amidated product **3a** in a modest 60% yield (Table 1, entry 11). Gratifyingly, we found that the reaction was also operating when decreasing the temperature to room temperature, leading to 70% yield of **3a** in a reaction conducted at an ambient temperature of 25 °C (Table 1, entry 12). Swapping the ruthenium pre-catalyst for a cobalt complex largely used in C-H bond amidations[13] did not afford any product so far (Table 1, entry 13). The use of tosyl azide (TsN_3), which is a well-known nitrene source,[7] as amidating agent led to traces of the corresponding *N*-tosylated product analogue of **3a** (NHTs instead of NHCOPh, Table 1, entry 14). Overall, these findings highlight the suitability of ruthenium

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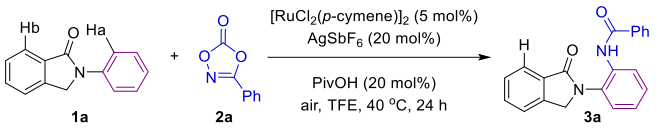
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catalysts over the more expensive iridium, palladium or rhodium ones,[18] as well as dioxazolone **2a** as ideal and safe partner for this type of transformation.

Table 1 Optimization of the site-selective ruthenium-catalyzed *ortho*-C-H bond amidation of **1a** with dioxazolone **2a**.[a]



Entry	Deviation from above conditions	**3a** (%)[b]
1	none	82 (80)[c]
2	no $[RuCl_2(p\text{-cymene})]_2$	0
3	no $AgSbF_6$	0
4	no PivOH	73
5	AcOH instead of PivOH	76
6	$AdCO_2H$ instead of PivOH	79
7	H_2O instead of PivOH	54
8	DCE instead of TFE	65
9	1,4-dioxane instead of TFE	0
10[d]	THF instead of TFE	19
11	1.2 equiv. of **2a**	60
12	25 °C instead of 40 °C	70
13	$Cp^*Co(CO)I_2$ instead of $[RuCl_2(p\text{-cymene})]_2$	0
14[e]	TsN_3 instead of **2a**	traces

[a] Reaction conditions: **1a** (0.1 mmol), **2a** (0.15 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $AgSbF_6$ (20 mol%), PivOH (0.02 mmol, 0.2 equiv.), TFE (0.5 mL), 40 °C, 20 h, air. [b] Determined by ^1H NMR spectroscopy against dibromomethane as an internal standard. [c] Isolated yield shown in parentheses after purification by column chromatography. [d] Reaction performed without PivOH. [e] The product for this reaction is expected to bear a NHTs in place of a NHCOPh fragment in **3a**.

After reaction optimization (Table 1, entry 1), the scope of the catalysis was evaluated with different synthetically useful functional groups at different positions in both compound **1** as well as the dioxazolone partner **2** (Table 2). *para*-Substitution patterns in the *N*-phenyl ring with electron-donating groups, such as methyl and methoxy, were tolerated for the catalysis yielding the corresponding *ortho*-amidated products **3b** and **3c** in 76% and 83% yields, respectively. In addition, X-ray diffraction studies performed on single crystals of **3c** (Table 2) established without ambiguity the site- and regio-selectivity observed in this C-H bond amidation reaction.[19] Similarly, introducing electron-withdrawing groups in the *para*-position such as fluoro and ester groups was also tolerated by the catalysis and afforded the corresponding *ortho*-amidated products **3d** and **3e** in 45% and 66% isolated yields, respectively. Notably, although ester groups have been identified as suitable directing groups in several ruthenium-catalyzed C-H bond activations,[20] in the case of **3e**, it is the cyclic amide group (and not the ester group) which dictates the exclusive site-selectivity observed in the C-H bond amidation. Other halide groups such as chloro and bromo were compatible leading to products **3f** and **3g** in 62% and 73% yields, which is relevant for further derivatization sequences by cross-coupling chemistry.[21] Methyl- and methoxy-substituted isoindolinones in *meta* position of the *N*-phenyl ring afforded the *ortho*-amidated products **3h** and **3i** in 81% and 90% yield, respectively, in a selective manner, without any functionalization occurring in the other *ortho*-C-H bond positions. Analogously, the catalysis was found compatible with a significant number of functional groups attached to the dioxazolone core. For instance, aryl-substituted dioxazolone de-rivatives bearing either electron-donating or electron-withdrawing groups at *para* position such as methyl, *tert*-butyl, trifluoromethyl and chloro reacted smoothly with **1a** affording the corresponding *ortho*-C-H bond amidated products **3j**-**3m** in an excellent range of 83-92% isolated yields. Electron deficient substituents on the aryl-substituted dioxazolone such as 3-Cl was also tolerated under the developed catalysis leading to the amidated product **3n** in a remarkable 91% yield, which makes the halide site available for post-functionalization.[21] Multisubstituted groups on the dioxazolones partner were also employed in this catalysis as shown in the successful synthesis of compound **3o** in 66% yield that contains two chloride substitutents at both *meta* positons. Additionally, the reaction was also compatible with a very bulky polycyclic aromatic hydrocarbon fragment such as 1-naphthalene substituted dioxazolone leading to **3p** in 38% yield. Interestingly, heteroaromatic-containing amidating agents can also be employed. In the case of furan-containing dioxazolone, the corresponding product (**3q**) was obtained in 32% yield. However, the more coordinating thiophene one inhibited the catalysis. Gratifyingly, further exploration of the scope of this C-H bond amidation reaction revealed that the aliphatic-substituted dioxazolones were also reactive. For instance, methyl-, *tert*-butyl- and *n*-heptyl-substituted dioxazolones led to the *ortho*-C-H bond amidated products **3r**, **3s** and **3t** in 80%, 76% and 80% yields, respectively.

Overall, a panel of more than twenty different functional groups in different positions around both reagents **1** and **2** were tolerated with no products resulting from other site- and/or re-gio-selectivity. The absence of bis-*ortho*-amidated products might be rationalized by a plausible intramolecular hydrogen bonding between the NH group from the amide and the carbonyl group from the directing group that forbids the second *ortho*-C-H bond amidation.[22] We additionally noted that the catalysis was sensitive to the steric hindrance found in the coupling partners as evidenced in the lack of reactivity observed for the *ortho*-tolyl derivative from **1** and the *ortho*-chloro-containing aryl-substituted dioxazolone derived from **2**, respectively.[23] Further limitations were encountered when using hydroxyl- or cyano-substituted coupling partners.[24]

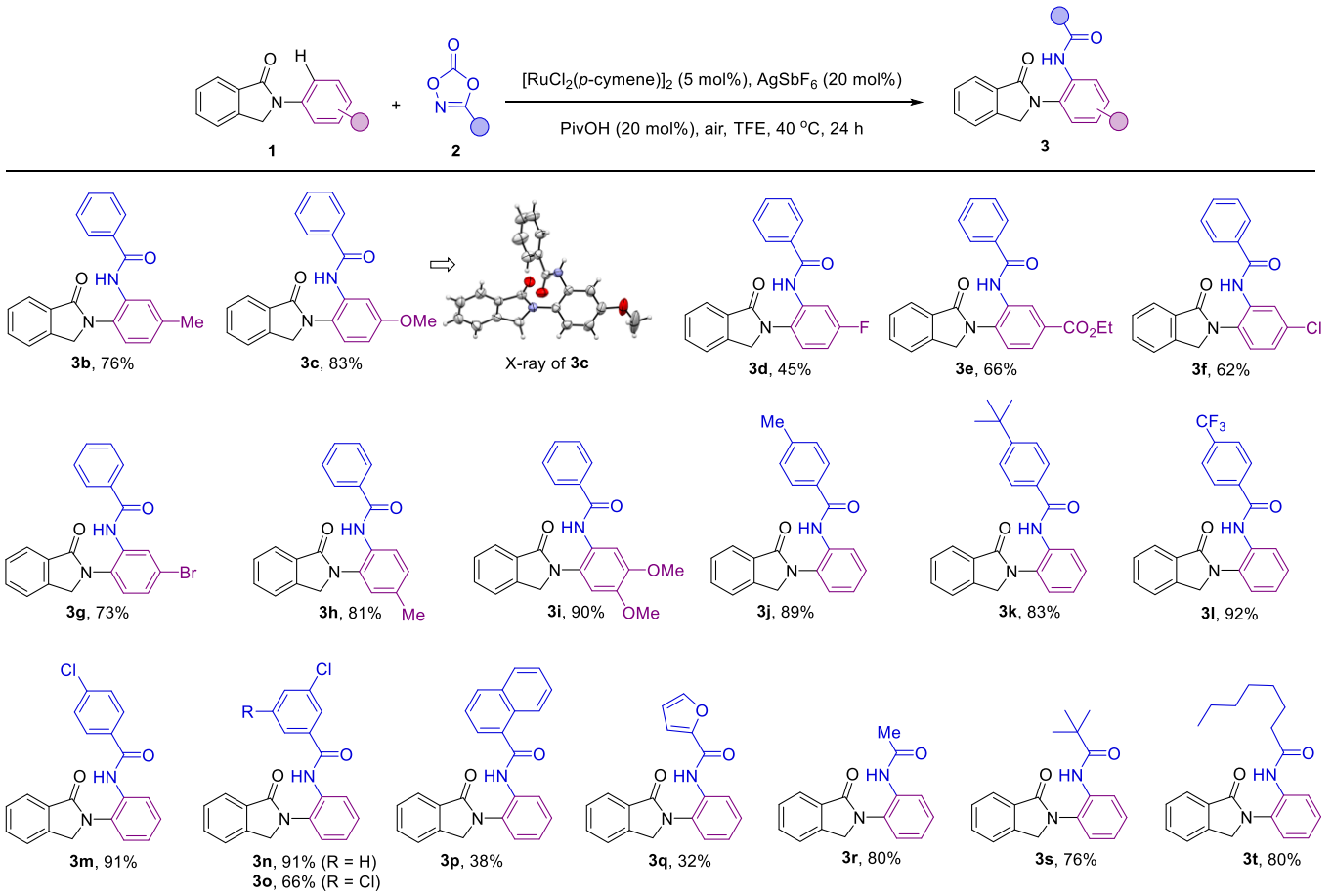
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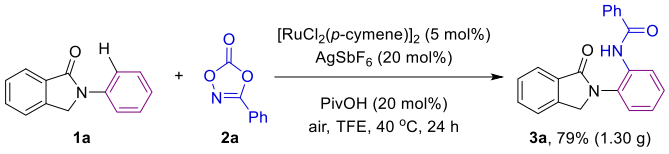
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Table 2 Evaluation of the scope for the ruthenium-catalyzed *ortho*-C-H bond amidation of both **1** and dioxazolone **2**.[a,b]



[a] Reaction conditions: **1** (0.3 mmol), **2** (0.45 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $AgSbF_6$ (20 mol%), PivOH (0.06 mmol, 0.2 equiv.), TFE (1.5 mL), 40 °C, 20 h, air. [b] Isolated yield by column chromatography.

Importantly, the reaction was scalable and the same excellent results of yield and selectivity were obtained when conducting the ruthenium catalyzed C-H bond amidation at gram scale starting with 5 mmol of **1a** leading to *ca.* 1.30 g of product **3a**, thus showing the robustness of the methodology (Scheme 3).



Scheme 3 Scale-up reaction for the ruthenium-catalyzed *ortho*-C-H bond amidation.

For comparison purposes, the catalysis was applied to other substrates featuring cyclic amides as potential directing groups in view to address the versatility of this transformation (Scheme 4). Using pyrrolidone, the simplest cyclic amide, as the directing group, afforded the corresponding *ortho*-C-H bond amidated product **4** in 60% yield (Scheme 4). Note that the synthesis of **4** applying this methodology is more sustainable and efficient compared to previous examples in the literature,[25] that required long and tedious reaction sequences using hazardous rea-gents that have so far limited their exploitation. Interestingly, a remarkable difference of reactivity was encountered exploiting acyclic amide directing groups. Indeed, whilst acetanilide still afforded the corresponding *ortho*-amidated product **5** in 51% yield, no reactivity was observed for the *N*-methylated version nor for benzanilide as the substrates (Scheme 4). Analogously, a complete absence of reactivity was encountered with *N*-phenylphthalimide, which features a cyclic imide as a potential directing group, as well as with the more strongly coordinating 2-pyridyl directing group (Scheme 4), which is rather counterintuitive considering previous contributions.[26]

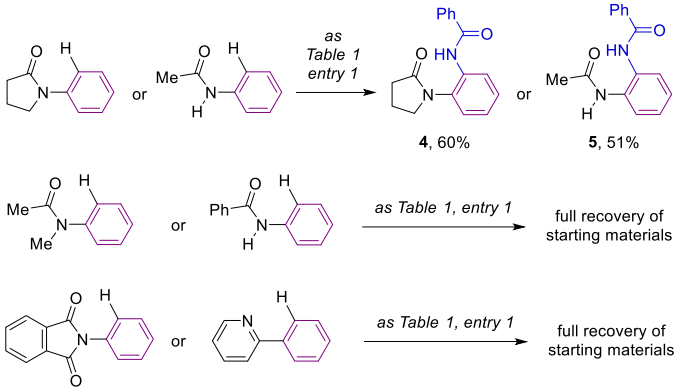
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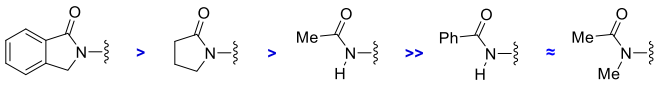
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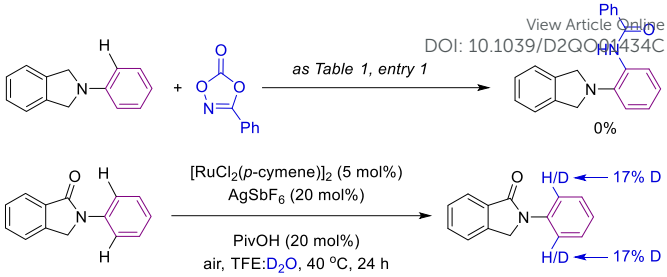
Scheme 4 Evaluation of the catalysis with different types of relevant directing groups.

Consequently, the reported ruthenium-catalyzed transformation appears to need a compromise between the geometry, the steric and electronic parameters as well as the coordinating ability of the directing groups. Furthermore, these findings establish that the directing ability of cyclic amides outperforms that of acyclic amides following a clear trend as shown in Scheme 5.



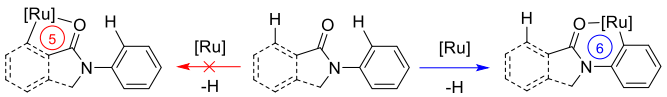
Scheme 5 Order of efficiency for amides as directing groups in ruthenium-catalyzed *ortho*-C-H bond amidations.

After having demonstrated the enhanced efficiency of cyclic amides as superior directing groups in ruthenium-catalyzed aromatic C-H bond amidations, we performed several experiments to better understand the mechanism operating in the catalysis (Scheme 6). Firstly, we verified the necessity of the carbonyl group by attempting a catalytic reaction using a carbonyl-free substrate such as isoindoline (Scheme 6, top). In this case, no C-H bond functionalization was detected, indirectly demonstrating the importance of the carbonyl group to assist the catalysis likely *via* coordination to ruthenium.[14,15] In addition, deuteration experiments were performed under the catalytic conditions but in the absence of the amidating partner **2** with a mixture of solvents TFE:D_2O (Scheme 6, bottom). In these conditions, 17% deuteration incorporation was observed in the *ortho*-C-H bonds of the phenyl ring attached to the nitrogen atom with no deuteration observed elsewhere in the molecule (Scheme 6, bottom).



Scheme 6 Control experiment in the absence of a carbonyl directing group (top) and a deuteration experiment (bottom).

The overall above-described findings strongly suggest that the cyclic amides prefer to accommodate six-membered ruthenacycle species within the catalytic cycle over the commonly found five-membered ones for C-N bond forming reactions *via* C-H bond activation (Scheme 7). This may account for the observed regio- and site-selectivity observed in the catalysis.



Scheme 7 Mechanistic consideration highlighting stabilization of six-membered ruthenacycles over five-membered ones in the key C-H bond activation event.

Due to the difficulty on obtaining reproducible data for kinetic studies ascribed to solubility issues and the unsuccessful attempts to detect reaction intermediates, we turned our attention to further unveil the precise reaction mechanism by DFT computational calculations at the M06-D3/Def2TZVP~sdd(smd)//BP86-D3/Def2SVP level of theory (Fig. 1).[24] In order to keep the whole reaction pathway in the same cationic level, the preactivation started from the cationic intermediate **I0**, derived from the [$RuCl_2$(*p*-cymene)]$_2$, after releasing the chlorides by means of the reagent $AgSbF_6$ (a known halide scavenger). As such, SbF_6^- is considered the weak coordinating anion throughout the whole catalytic cycle. In the next intermediate **I0'** the anionic SbF_6^- ligand is substituted by the $PivO^-$ anion that comes from the other reagent, PivOH, with $HSbF_6$ release. This step is thermodynamically unfavoured by 13.1 kcal/mol, although the formation of complex **I0'** is essential to stabilize the intermediate **I0"** by 10.7 kcal/mol after the combination of **I0'** with substrate **1a**. From **I0"** there are two potential aryl C-H activations to explore: from the phenyl on the nitrogen, or the aryl ring annulated to the five-membered ring.[27] Our simulations show energy barriers of 18.3 and 20.3 kcal/mol, respectively. Besides to the 2 kcal/mol of difference, the C-H bond activation of the aryl ring leads to a worsening of 9.7 kcal/mol for the resulting intermediate **I'** as compared to **I**, as is illustrated in the catalytic cycle in Fig. 1 (red pathway). The resulting ruthenacycle intermediate with assistance of the cyclic amide as the directing group has literature precedents.[7,11-13]

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In the catalytically productive pathway (Fig. 1, blue pathway), species **I** coordinates to dioxazolone forming species **II** followed by extrusion of CO_2, overcoming an energy barrier of 13.4 kcal/mol, giving rise to the formation of Ru^{IV}-imido species **III**. The migratory insertion of imido species **III**, with the C-N bond formation associated, leads to the generation of ruthenacycle **IV**, with a low energy barrier of only 8.4 kcal/mol. To close the catalytic cycle, the protodemetalation of species **IV** occurs with a new molecule of substrate **1**, which is in excess in the reaction mixture compared to the catalyst. This step could also be performed with $HSbF_6$ or PivOH furnishing the amidated product, as well. However, instead of the regeneration of the active ruthenium catalyst **I**, the process would end up in intermediates **I0** or **I0'**, respectively.

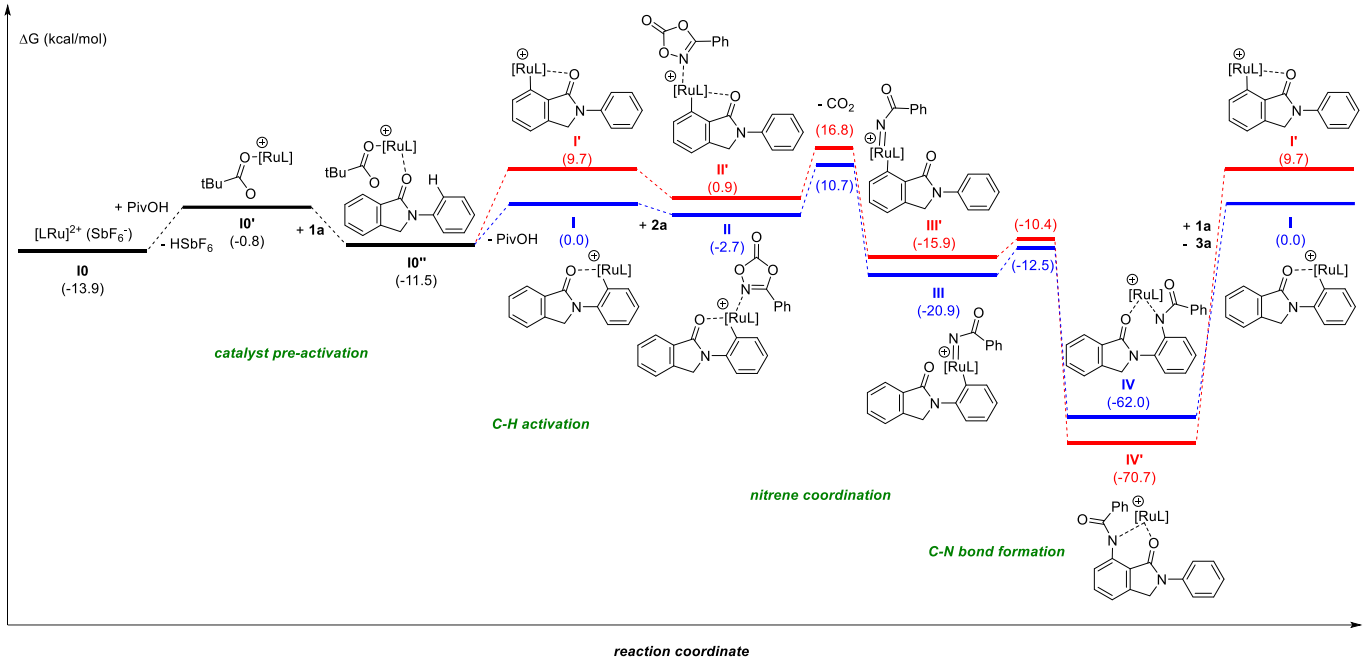


Fig. 1 Computed Gibbs energy reaction profile in kcal/mol (in brackets) of the ruthenium-catalyzed *ortho*-C-H bond amidation with cyclic amides as weak directing groups. L = *p*-cymene. Black pathway = catalyst pre-activation, red color = disfavoured pathway, blue color = favoured pathway.

The most difficult step in the pre-activation sequence is the C-H bond activation that leads to the ruthenacycle, either **I** or **I'** selectively (Fig. 1). On the other hand, the rate determining step (rds) of the catalytic pathway corresponds to the transition state **II**-to-**III**. Considering the catalytic cycle for an elusive C-H bond activation at the aryl ring annulated to the five-membered ring of the substrate **1** (red pathway, Fig. 1), the corresponding transition state **II**-to-**III** is 6.1 kcal/mol higher in energy compared to the C-H bond activation at the phenyl ring linked to the nitrogen atom in **1** (blue pathway, Fig. 1). Thus, it confirms the selectivity towards the reaction profile with **I** as the catalytic active species. The reason is not steric, but it is related with the fact that **I** forms a rather stable 6-membered ruthenacycle whereas **I'** has a 5-membered ruthenacycle (Fig. 2). In addition, in the transition state the pivalate ligand forms a less strained interaction to remove the proton, and actually the distances in the transition state leading to **I** are closer to an agostic interaction, with a more activated aryl C-H bond (by nearly 0.1 Å).

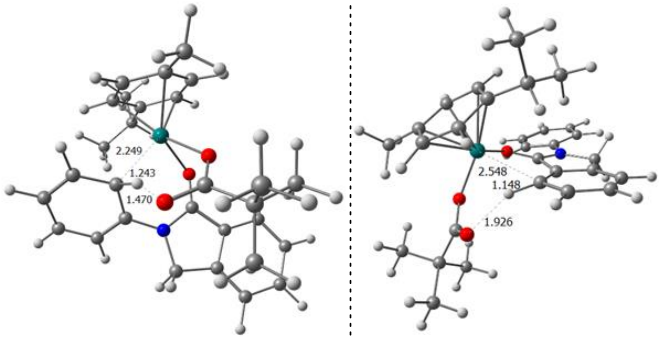


Fig. 2 Transition states **I0''** → **I** (left) and **I0''** → **I'** (right) with selected distances given in Å.

For the sake of consistency and validate mainly the rds, we explored all the possibilities considering the intermediates in the preactivation and the two substrates. Interestingly, from intermediate **I0'** the coordination of the dioxazolone before **1** is omitted since the kinetic cost of the CO_2 release increases by 5.3 kcal/mol (Fig. 3). Such findings strongly contrast with the initial elementary steps of the reaction mechanism associated to the ruthenium-catalyzed C-H bond amidation with azides, in which the ruthenium-nitrene species are postulated to form before the C-H bond activation step in the substrate.[28]

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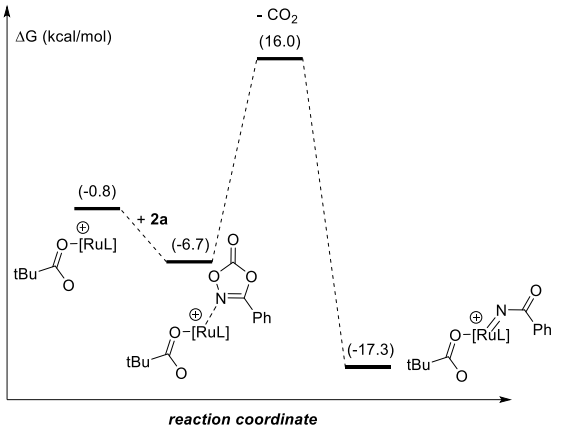


Fig. 3 Reaction profile of the extrusion of CO_2 with the coordination of dioxazolone in **I0'**. Relative Gibbs energies relative to **I** (in kcal/mol). L = *p*-cymene.

To further check the importance of the different anions we performed additional analyses with the initial $[RuCl_2(p\text{-cymene})]_2$. The stability of this dimer is not relevant as its cleavage only requires 1.1 kcal/mol. The substitution of one or both chlorides by SbF_6^- is affordable, consuming only 3.1 and 2.8 kcal/mol, respectively. Moreover, for the reaction profile described in Fig. 1, the counter anion SbF_6^-, that would neutralize the system, was omitted assuming that it does not affect significantly. Preliminary calculations show that the counter anion destabilizes intermediates **I** and **II** by 4.1 and 0.5 kcal/mol, respectively.

Conclusions

In summary, we have developed efficient site-selective C-H bond amidation reactions to form unprecedented C-N bonds exploiting the directing group ability of cyclic amides *via* six-membered ruthenacycles formation. A simple ruthenium(II) pre-catalyst and safe amidating agent have been employed leading to a versatile catalytic system compatible with a large number of synthetically useful functional groups (more than 20 examples). This *"close to room temperature"* methodology offers a convenient route to access *ortho*-amidated cyclic amides, that might be potentially relevant in medicinal chemistry.[16] This study also shows the subtlety associated to C-H bond amidations because in the present case ruthenium outperforms cobalt as catalyst and dioxazolone outperforms tosylazide as amidating agents, respectively, which is somehow unexpected as regards of precedents in the literature.[6-13,28] Moreover, this contribution establishes that cyclic amides are more powerful directing groups than acylic ones or other coordinating groups such as imides and pyridines, at least for ruthenium-catalyzed C-H bond amidations. In addition, we provide the first mechanistic considerations of ruthenium-catalyzed C-H bond aminations supported by in-depth DFT calculations. Although the rate-determining step is the extrusion of CO_2 in order to form ruthenium species coordinated to both the substrate and the nitrene group, the site-selective step is determined by the strong destabilization associated to the formation of a five-membered ruthenacycle over a six-membered one. In conclusion, further research directed to new carbon-heteroatom bond forming pro-cess via ruthenium-catalyzed C-H bond functionalization strategies should provide appealing methodologies for direct implementation into organic synthesis.

Experimental

General procedure for the ruthenium-catalyzed C-H bond amidation. A suspension of substrate **1** (0.3 mmol, 1.0 equiv.), dioxazolone **2** (0.45 mmol, 1.5 equiv.), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $AgSbF_6$ (20 mol%), and PivOH (0.06 mmol, 0.2 equiv.) in anhydrous TFE (1.5 mL) was stirred at 40 °C for 20 hours under air. At ambient temperature, then the solvent was evaporated in vacuo, and the resulting crude reaction mixture was purified by flash column chromatography to afford the corresponding product **3**-**5** as analytically pure solids.

Computational Details. All the DFT static calculations were performed with the Gausian16 set of programs,[29] using the BP86 functional of Becke and Perdew,[30-32] together with the Grimme D3 correction term to the electronic energy.[33] The electronic configuration of the molecular systems was described with the double-ζ basis set with polarization of Ahlrichs for main-group atoms (Def2SVP keyword in Gaussian),[34] whereas for ruthenium the small−core quasi−relativistic Stuttgart/Dresden effective core potential, with an associated valence basis set (standard SDD keywords in Gaussian09) were employed.[35-37] The geometry optimizations were performed without symmetry constraints, with analytical frequency calculations for the characterization of the located stationary points. These frequencies were used to calculate unscaled zero-point energies (ZPEs) as well as thermal corrections and entropy effects at 298.15 K. Energies were obtained by single-point calculations on the optimized geometries with the M06 functional,[38] with the Grimme D3 correction term,[33] and the Def2TZVP basis set.[39] The reported Gibbs energies in this work contain electronic energies obtained at the M06-D3/Def2TZVP~sdd level of theory corrected with zero-point energies, thermal corrections and entropy effects evaluated at 298.15 K, achieved at the BP86-D3/Def2SVP~sdd level plus a solvation contribute evaluated by means of the SMD continuum solvation model based on the quantum mechanical charge density of the solute interacting with a continuum description of the solvent (2,2,2-trifluoroethanol, TFE).[40]

Conflicts of interest

There are no conflicts to declare.

Author contributions

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Y-C. Y., Q.-L. L. and X.-T. Z. performed all synthesis, product characterization and catalysis. S. P.-P., M. S. and A. B. performed DFT computational calculations. T. R. performed X-ray diffraction studies. Y.-C. Y. and R. G.-D. conceptualized and directed the study. All authors contributed to manuscript writing.

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