

# Ruthenium-catalyzed *ortho*-C–H bond alkylation of aromatic amides with $\alpha,\beta$ -unsaturated ketones *via* bidentate-chelation assistance†‡

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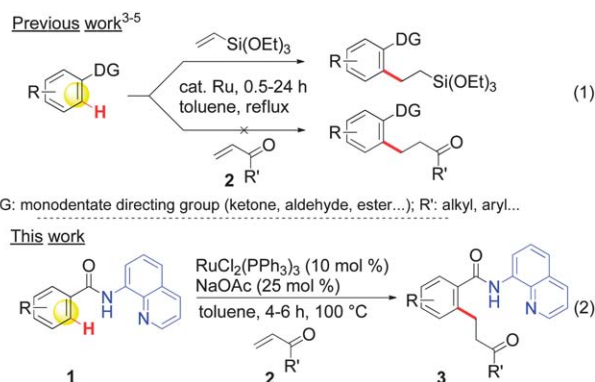
A new chelation assisted reaction using a removable 8-aminoquinoline bidentate directing group that permits the ruthenium-catalyzed *ortho*-C–H bond alkylation of aromatic amides with various  $\alpha,\beta$ -unsaturated ketones under straightforward conditions has been developed. This methodology represents the first efficient utilization of enones in the *ortho* directed ruthenium-catalyzed addition of C–H bonds to C–C double bonds. The reaction offers a broad scope and a high functional group tolerance.

## Introduction

The successful development of new transition metal-catalyzed reactions for the formation of C–C bonds represents a crucial and long-standing challenge in synthetic organic chemistry.<sup>1</sup> Among the many strategies available, catalytic C–H bond activation has recently emerged as one of the most promising and powerful methods for the construction of C–C bond frameworks.<sup>2</sup> This statement was beautifully illustrated in 1993, when Murai published a report on the ruthenium-catalyzed *ortho*-C–H bond alkylation of aromatic ketones with olefins *via* a chelation assisted strategy. The reaction permits the direct and selective transformation of a C–H bond into a C–C bond through the addition to an olefin.<sup>3</sup> This reaction can be considered to constitute an ideal pathway in terms of step and atom economy for the formation of C–C bonds and was rapidly expanded to other aromatic substrates.<sup>4</sup> Advances were subsequently reported by Darses and Genet *et al.*<sup>5</sup> through the development of an *in situ*-generated active catalyst prepared from [RuCl<sub>2</sub>(*p*-cymene)]<sub>2</sub>, which can be regarded as more flexible and practical than the ruthenium species (Ru<sub>3</sub>(CO)<sub>12</sub>, RuH<sub>2</sub>(PPh<sub>3</sub>)<sub>4</sub>, RuH<sub>2</sub>(CO)(PPh<sub>3</sub>)<sub>3</sub>...) traditionally used in these types of reactions. However, most olefin-bearing functional groups still remain unusable in these processes,<sup>6</sup> and this severely limits the scope of this fundamental transformation in synthesis by virtue of the fact that some of the more important families of acceptors, such as  $\alpha,\beta$ -unsaturated acceptors, cannot be used (eqn (1), Scheme 1). A few alternatives to address this issue have begun to appear in

the literature,<sup>7</sup> but, although promising, these methods are rather rare, limited in scope and require the use of expensive rhodium<sup>7a,c,d</sup> or rhenium<sup>7b</sup> catalysts. The search for new ruthenium-based catalytic systems to fulfil this ambition remains challenging and no alternatives have been reported so far, despite the strong appeal of this metal.<sup>8</sup>

In a first approach, we hypothesized that the lack of reactivity of a large range of olefins in the ruthenium-catalyzed reactions reported by Murai *et al.*<sup>4,6</sup> may be due to the inappropriate nature of the monodentate directing groups used. Bidentate-type directing groups have recently emerged as a new tool in exploring reactions that have not been achieved with conventional monodentate directing groups through the publications of Daugulis *et al.*,<sup>9</sup> which were followed by others,<sup>10</sup> including some from our laboratory.<sup>11</sup> We have, thus, anticipated that bidentate directing groups could open new horizons for expanding the scope of the ruthenium-catalyzed *ortho*-C–H bond alkylation of aromatic substrates.<sup>12</sup> Herein, in support of our hypothesis, we report on a new chelation assisted strategy in which a removable 8-aminoquinoline bidentate directing group



**Scheme 1** *ortho*-C–H bond alkylation of aromatic substrates with  $\alpha,\beta$ -unsaturated ketones: monodentate vs. bidentate directing groups.

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† Dedicated to Professor Irina Petrovna Beletskaya for her contribution to metal-catalyzed reactions.

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is used<sup>9b</sup> (as in **1**, Scheme 1) that allows the first ruthenium-catalyzed *ortho*-C–H bond alkylation of aromatic amides *via* 1,4-addition to various  $\alpha,\beta$ -unsaturated ketones under straightforward reaction conditions by using attractive  $\text{RuCl}_2(\text{PPh}_3)_3$  or  $[\text{RuCl}_2(p\text{-cymene})]_2$  catalysts (eqn (2), Scheme 1).<sup>13</sup>

## Results and discussion

### Preliminary studies

We initiated our studies by examining the feasibility of the ruthenium-catalyzed *ortho*-C–H bond alkylation of amide **1a** with methyl vinyl ketone (MVK **2a**) (Table 1). Our efforts were initially rewarded, when it was found that, when  $\text{Ru}_3(\text{CO})_{12}$  was used, the expected product **3aa** was produced in 6% yield, but the cyclic **4aa** was also produced in 6% yield (entry 3). The formation of **4aa** could be attributed to a competitive  $\beta$ -hydride elimination that produces the alkenylated amide **5aa**,<sup>14</sup> which immediately undergoes an intramolecular Michael reaction. Our attempts to improve the yields in this reaction were fruitless and we finally abandoned further experiments using this catalyst.

$[\text{RuCl}_2(p\text{-cymene})]_2$  then, attracted our attention when we noticed its ability to cleanly produce **3aa** as the exclusive product but in a poor yield (entry 4). To our delight, the yield of **3aa** was improved when the system of Darses and Genet *et al.* (entry 5) was applied.<sup>5a</sup> In part inspired by the success of carboxylate-assisted metal-catalyzed C–H functionalization reactions,<sup>15</sup> we discovered that optimum efficiency could be achieved by replacing sodium formate with sodium acetate (entry 6). Interestingly, neither **5aa** nor **4aa** were obtained under these conditions, while Ackermann, Dixneuf and others, reported that Ru(II) catalysts are powerful catalysts in Fujiwara–

Moritani type reactions with  $\alpha,\beta$ -unsaturated acceptors.<sup>2r,16</sup> Furthermore, it was not necessary to use triphenylphosphine for a successful reaction in the case of *o*-substituted amides (entry 7).<sup>17a</sup> After further investigations of the scope, the combination  $\text{RuCl}_2(\text{PPh}_3)_3/\text{NaOAc}$  (entry 8) provided more satisfactory results and, thus, was chosen to develop our methodology.<sup>17b</sup> Other metalated carboxylate bases were effective but they failed to provide better results<sup>17b</sup> and, contrary to all expectations, some organic bases, such as  $\text{Et}_3\text{N}$  (entry 9), were found to be reactive. The crucial role of the bidentate structure was then highlighted, thanks to a survey of different directing groups (Fig. 1) and the reaction appears to be specific to the 8-aminoquinoline motif.

### Scope and limitation

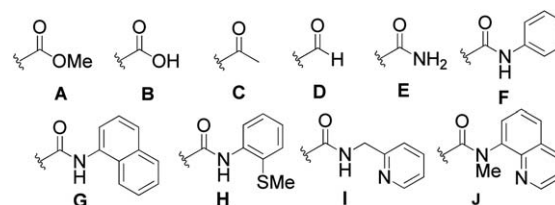
With optimized conditions in hand, the scope of the reaction was expanded to some representative amides. *o*-Substituted amides were initially examined (Table 2, entries 1–5) and high yields were obtained with *o*-phenyl (**1b**) or *o*-CF<sub>3</sub> groups (**1c**). Difficulties were encountered in the cases of *o*-methoxy (**1d**) and *o*-fluorine (**1e**) groups, which afforded lower yields. Longer reaction times or higher temperatures failed to improve these results. It has been observed in the literature that, in the same configuration, cleavage of the C–O bond may occur<sup>5c,18</sup> and that *o*-fluorine can affect reactivity.<sup>5c</sup> However, these groups are more easily tolerated in our system and no reduced compound **3fa** or **1f** corresponding to the cleavage of the C–O bond were detected. In the case of *p*-substituted amides (entries 6–9), the formation of di-alkylated amides **6** was preferred. We were unable to avoid the formation of compound **6**, even when the amount of **2a** used (entry 6a) or the reaction times were reduced and finally decided to optimize the formation of compound **6** by using 3 equivalents of **2a**. In this manner, **6** was consistently obtained in quantitative yields, while the formation of the di-alkylated product was not absolutely predominant in previous studies.<sup>5,6,18</sup>

A series of more delicate *m*-substituted amides were investigated next (Table 3). In this arrangement, a second C–H activation leading to **6** is, also, likely to occur. Indeed, the *m*-methyl amide **1j** gave the desired **3ja** as the major product, but **6ja** was also isolated (entry 1a). The formation of **6ja** could be slightly minimized by using the bulky base NaOPiv (entry 1b). In the case of the *m*-phenyl (**1k**) and *m*-trifluoromethyl (**1l**), the alkylation took place exclusively at the less sterically demanding position, affording **3ka** and **3la** in high yields (entries 2 and 3). In contrast, in the case of an *m*-methoxy group (entry 4a) the formation of **6ma** was strongly facilitated. Moreover, the mono-alkylation product was obtained as a 3 : 1 mixture of regioisomers **3ma** and

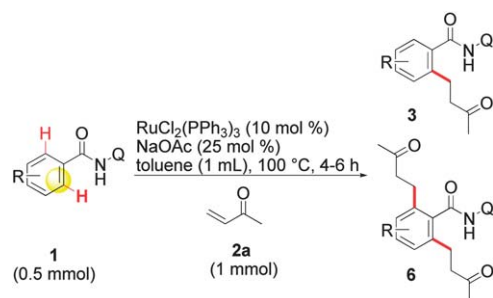
**Table 1** Selected examples of reaction optimization<sup>17b</sup>

Entry	Catalyst <sup>a</sup>	Additive	<b>3aa</b> <sup>b</sup> (%)
1	$\text{RuH}_2(\text{CO})(\text{PPh}_3)_3$	—	0 (98)
2	$\text{RuH}_2(\text{PPh}_3)_4$	—	0 (95)
3	$\text{Ru}_3(\text{CO})_{12}$	—	6 (68) <sup>c</sup>
4	$[\text{RuCl}_2(p\text{-cymene})]_2$	—	10 (84)
5	$[\text{RuCl}_2(p\text{-cymene})]_2$	$\text{NaHCO}_2/\text{PPh}_3$ <sup>d</sup>	50 (43)
6	$[\text{RuCl}_2(p\text{-cymene})]_2$	$\text{NaOAc}/\text{PPh}_3$ <sup>d</sup>	90 (0)
7	$[\text{RuCl}_2(p\text{-cymene})]_2$	$\text{NaOAc}$	91 (0)
8	$\text{RuCl}_2(\text{PPh}_3)_3$	$\text{NaOAc}$	94 (0)
9	$\text{RuCl}_2(\text{PPh}_3)_3$	$\text{Et}_3\text{N}$	54 (32)

<sup>a</sup> 5 mol% of  $[\text{RuCl}_2(p\text{-cymene})]_2$  was used. <sup>b</sup> Numbers in parentheses are recovered **1a**. <sup>c</sup> 6% of **4aa** was isolated. <sup>d</sup> 30 mol% of  $\text{PPh}_3$ .



**Fig. 1** Ineffective directing groups.

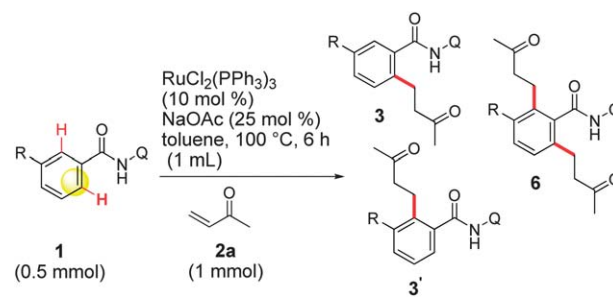
**Table 2** Alkylation of *o*- and *p*-substituted amides with MVK 2a

Entry	<i>t</i> (h)	<b>1</b> , R	<b>3</b> <sup>a</sup> (%)	<b>6</b> (%)
1	4	<b>1a</b> , 2-Me	<b>3aa</b> , 94	—
2	4	<b>1b</b> , 2-Ph	<b>3ba</b> , 91 (<5)	—
3	4	<b>1c</b> , 2-CF <sub>3</sub>	<b>3ca</b> , 98	—
4 <sup>b</sup>	4	<b>1d</b> , 2-OMe	<b>3da</b> , 63 (23)	—
5	4	<b>1e</b> , 2-F	<b>3ea</b> , 60 (25)	—
6a <sup>c</sup>	4	<b>1f</b> , 4-H	<b>3fa</b> , 43 (31)	<b>6fa</b> , 21
6b <sup>d</sup>	4	<b>1f</b> , 4-H	<b>3fa</b> , 0	<b>6fa</b> , 96
7 <sup>d</sup>	6	<b>1g</b> , 4-Me	<b>3ga</b> , 0	<b>6ga</b> , 98
8 <sup>d</sup>	6	<b>1h</b> , 4-CO <sub>2</sub> Me	<b>3ha</b> , 0	<b>6ha</b> , 97
9 <sup>d,e</sup>	6	<b>1i</b> , 4-OMe	<b>3ia</b> , 0	<b>6ia</b> , 97

<sup>a</sup> Numbers in parentheses are recovered **1**. <sup>b</sup>  $[\text{RuCl}_2(p\text{-cymene})]_2$  (5 mol %) was used. <sup>c</sup> MVK **2a**: 1 equiv. <sup>d</sup> MVK **2a**: 3 equiv. <sup>e</sup> 1 mmol scale.

**3'ma**. However, the formation of **6ma** may cloud the real value of this ratio and it was not possible to reverse this by using NaOPiv (entry 4b). This effect can be overcome by protecting the oxygen with a trifluoromethyl group (entry 5a),<sup>11d,18</sup> affording **3na** in a good yield without a trace of the regioisomer **3'na**. In addition, only a very small amount of **6na** was isolated when the reaction was carried out in the presence of NaOPiv (entry 5b). This reverse of the regioselectivity was not observed with an *m*-dimethylamino group (entry 6),<sup>18</sup> therefore, only **3oa** was isolated. The reaction offers a high tolerance to halogen atoms (entries 7–10), even the delicate iodide **1p** survived in our reaction conditions. In general terms, without regard to the fluorine-containing **1s**, the yield of **6** increases as the size of the halogen substituent decreases but, once again, it can be lowered by using NaOPiv. In the special case of the fluorine-containing **1s** (entries 10a and b), the regioselectivity of the alkylation was completely reversed, as evidenced by the exclusive formation of **3'sa**, irrespective of the base used. The effects that control this reactivity and the ratio of **3**, **3'** and **6**, are not well defined, as of this writing. Nonetheless, the results for *m*-substituted amides appear to be in line with those reported in the literature for the same type of reactions.<sup>5c,18</sup> It is entirely possible that a second complexation of the metal by the lone pair of electrons on the *m*-substituent could direct the activation to the most substituted side. A greater stabilization of the oxidative-addition intermediate, thanks to an additional coordination to the metal, can also explain this reactivity.

This concise overview was then expanded by testing a series of polysubstituted amides (Scheme 2). A wide range of original molecular frameworks were amenable for use. We also noted an ease of access to bulky C–H bonds (**8aa** and **8ba**), as well as the

**Table 3** Alkylation of *m*-substituted amides with MVK 2a

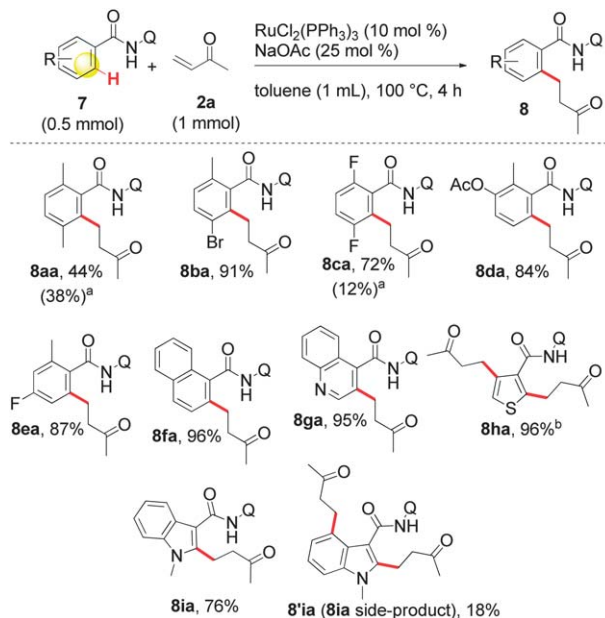
Entry	<b>1</b> , R	<b>3</b> <sup>a</sup> (%)	<b>6</b> (%)
1a	<b>1j</b> , Me	<b>3ja</b> , 77	<b>6ja</b> , 17
1b <sup>b</sup>	<b>1j</b> , Me	<b>3ja</b> , 84 (6)	<b>6ja</b> , 8
2	<b>1k</b> , Ph	<b>3ka</b> , 91	<b>6ka</b> , 0
3	<b>1l</b> , CF <sub>3</sub>	<b>3la</b> , 98	<b>6la</b> , 0
4a	<b>1m</b> , OMe	<b>3ma</b> , 30 <sup>c</sup>	<b>6ma</b> , 35
4b <sup>b</sup>	<b>1m</b> , OMe	42 <sup>c</sup>	<b>6ma</b> , 43
5a	<b>1n</b> , OCF <sub>3</sub>	<b>3na</b> , 63 (14)	<b>6na</b> , 18
5b <sup>b</sup>	<b>1n</b> , OCF <sub>3</sub>	<b>3na</b> , 70 (10)	<b>6na</b> , 8
6	<b>1o</b> , NMe <sub>2</sub>	<b>3oa</b> , 61(22)	<b>6oa</b> , 0
7a	<b>1p</b> , I	<b>3pa</b> , 52	<b>6pa</b> , 21
7b <sup>b</sup>	<b>1p</b> , I	<b>3pa</b> , 58	<b>6pa</b> , 13
8a	<b>1q</b> , Br	<b>3qa</b> , 35	<b>6qa</b> , 54
8b <sup>b</sup>	<b>1q</b> , Br	<b>3qa</b> , 65	<b>6qa</b> , 24
9a	<b>1r</b> , Cl	<b>3ra</b> , 22	<b>6ra</b> , 70
9b <sup>b</sup>	<b>1r</b> , Cl	<b>3ra</b> , 43	<b>6ra</b> , 38
10a	<b>1s</b> , F	<b>3'sa</b> , 24	<b>6sa</b> , 44
10b <sup>b</sup>	<b>1s</b> , F	<b>3'sa</b> , 29	<b>6sa</b> , 61

<sup>a</sup> Numbers in parentheses are recovered **1**. <sup>b</sup> NaOPiv (25 mol %) as base. <sup>c</sup> Isolated as a mixture of **3ma** and **3'ma** (NMR ratio **3ma** : **3'ma** = 3 : 1).

possibility of using heteroaromatic substrates. Interestingly the indole core furnished a di-alkylated by-product **8'ia**.

The second part of our work consisted in varying the nature of the acceptor molecules (Table 4). The reactivities of aliphatic enones **2b** and **2c** were very close to that of MVK **2a** when examined in a reaction with amide **1a** and the final products **3ab** and **3ac** were produced in very good yields. However, more sterically hindered double bonds proved to be more reluctant. For example, high temperatures were necessary (140 °C, entry 3a vs. 3b) to totally consume **1a** if **2d** was used. As expected, bulkier internal double bonds **2e** and **2f** are more resilient and the alkylation proceeded with moderate efficacy at a temperature of 140 °C. The more electron poor aromatic **1c** provided similar results when it was reacted with **2e**. Under the same conditions, olefins that were non-conjugated with a C=O bond (styrene, *n*-hexene) failed to react with **1a**. This suggests that the C=O bond plays an important role in the reaction mechanism.

Phenyl vinyl ketone (PVK, **2g**) and some derivatives of PVK were then considered (Table 5). From a general point of view, as the acceptors become more electrophilic, the yields of product **3** decrease. In this respect, the more electron-rich **2h** and **2i** afforded **3ah** and **3ai** in good yields, whereas enones bearing an electron-withdrawing group (**2j–m**) yielded **3aj** and **3ak** in moderate yields and **3al** and **3am** in low yields. We also noted

**Table 4** Scope of various  $\alpha,\beta$ -unsaturated ketones

Entry	1, R	2	3 <sup>a</sup> (%)
1	<b>1a</b> , 2-Me	<b>2b</b>	<b>3ab</b> , 93
2	<b>1a</b> , 2-Me	<b>2c</b>	<b>3ac</b> , 88
3a	<b>1a</b> , 2-Me	<b>2d</b>	<b>3ad</b> , 37 (58)
3b			<b>3ad</b> , 94 <sup>b</sup>
4	<b>1a</b> , 2-Me	<b>2e</b>	<b>3ae</b> , 58 (37) <sup>b</sup>
5	<b>1c</b> , 3-CF <sub>3</sub>	<b>2e</b>	<b>3ce</b> , 46 (42) <sup>b</sup>
6	<b>1a</b> , 2-Me	<b>2f</b>	<b>3af</b> , 16 (75) <sup>b</sup>

<sup>a</sup> Numbers in parentheses are recovered **1a**. <sup>b</sup> At 140 °C.

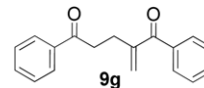
that when reacted with PVK, the more electron deficient amide **1c** (entry 2) provided better results than **1a**. PVK derivatives offered a singular reactivity, in that we were able to isolate a side-product (as **9g** derived from **2g**) in a yield of around 20%. The side-product **9g**, arising from the self-condensation of **2g**, may be formed *via* a Rauhut–Currier reaction (Morita–Baylis–

**Table 5** Scope of PVK derivatives

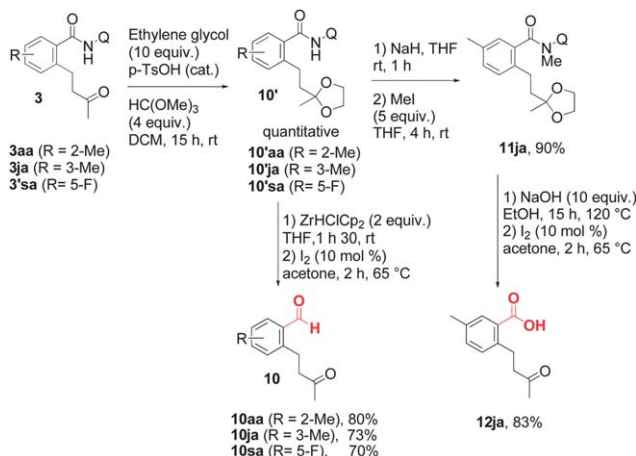
Entry	1, R	2	3 <sup>a,b,c</sup> (%)
1	<b>1a</b> , 2-Me	<b>2g</b>	<b>3ag</b> , 71 (22)
2	<b>1c</b> , 3-CF <sub>3</sub>	<b>2g</b>	<b>3cg</b> , 88
3	<b>1a</b> , 2-Me	<b>2h</b>	<b>3ah</b> , 78 (16)
4	<b>1a</b> , 2-Me	<b>2i</b>	<b>3ai</b> , 81 (12)
5	<b>1a</b> , 2-Me	<b>2j</b>	<b>3aj</b> , 61 (35)
6	<b>1a</b> , 2-Me	<b>2k</b>	<b>3ak</b> , 51 (32)
7	<b>1a</b> , 2-Me	<b>2l</b>	<b>3al</b> , 31 (60)
8	<b>1a</b> , 2-Me	<b>2m</b>	<b>3am</b> , 14 (60)

<sup>a</sup> Numbers in parentheses are recovered **1**. <sup>b</sup> **3ah–m** were isolated by HPLC. <sup>c</sup> Longer reaction times or higher temperatures did not improve the yields.

Hillman analogous), which is known to afford these types of adducts from  $\alpha,\beta$ -unsaturated ketones.<sup>19</sup> Nucleophilic species that are present in the reaction medium can react with **2g** and thus initiate this background process.



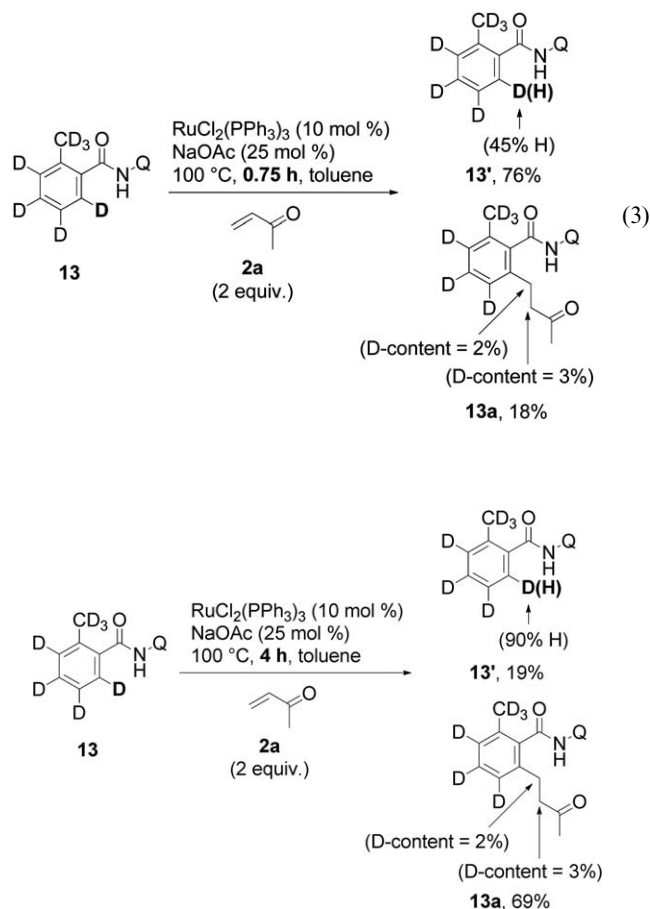
The potential of the present methodology was expanded through the facile conversion of the amide moiety into a variety of different useful functional groups.<sup>9–11</sup> For example, to illustrate this statement, the use of Schwartz's reagent allowed the formation of aldehydes **10** from amides **3** under mild conditions (Scheme 3), even with the bulky amide **3aa**. Under these conditions, the prior protection of the ketone was required to achieve good yields. The carboxylic acid can also be obtained *via* basic hydrolysis of the *N*-methylated amide (Scheme 3).<sup>9e</sup>



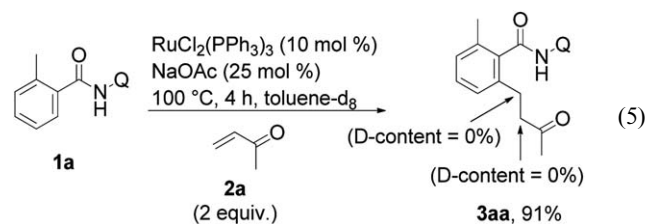
**Scheme 3** Cleavage of the 8-aminoquinoline directing group.

### Mechanistic investigation

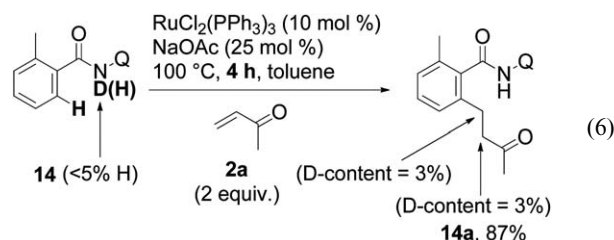
In the last stage of our study, some aspects of the mechanism of the reaction were investigated. When the reaction was run with isotopically labeled substrates **13**, a fast H/D scrambling was detected, indicating that C–H bond cleavage is not likely the rate determining step and is thus reversible in nature (eqn (3) and (4)). Contrary to our expectations, no clear evidence for the incorporation of deuterium into product **13a** was found. This left some doubts about the origin of the incorporated hydrogen.



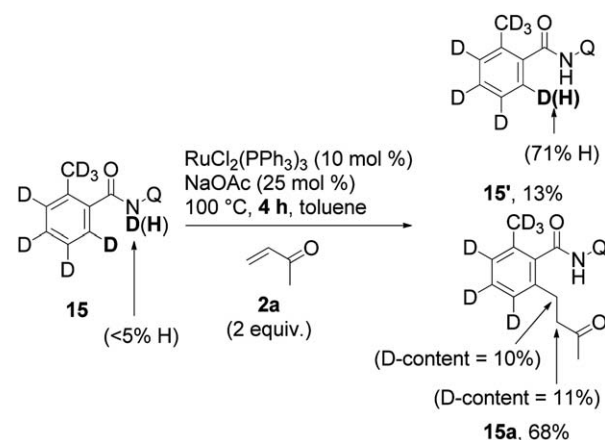
No trace of deuterium incorporation was detected when the reaction was performed in toluene-d<sub>8</sub> with amide **1a** (eqn (5)).



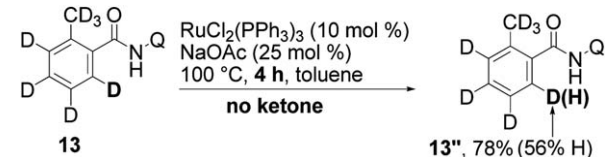
We then investigated whether the hydrogen of the N–H bond may act as a source of hydrogen. When substrate **14** was employed, a poor deuterium incorporation was observed (eqn (6)).



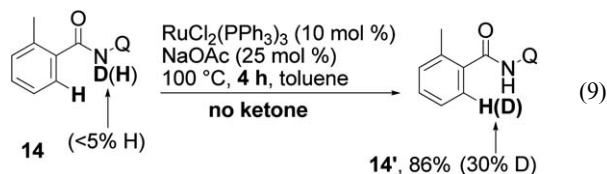
Then the reaction was performed with deuterium-containing substrate **15** (eqn (7)). A larger incorporation of deuterium into the final product was finally observed, compared with eqn (4). Incorporation of hydrogen into the recovered starting material (**15'**) was also observed as in eqn (4), but not to the same degree.<sup>20</sup>



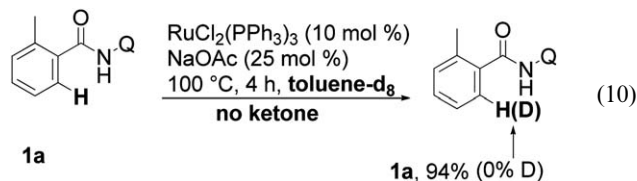
When the reaction was carried out in absence of acceptor **2a** (eqn (8)), H/D exchange was detected. It therefore appears that the cleavage of the C–H bond can take place, even in absence of the acceptor.



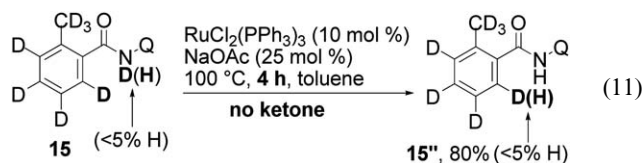
Interestingly, when the same reaction was carried out with substrate **14**, 30% of deuterium incorporation at the *ortho* position of the amide was found (eqn (9)). It appears that cleavage of the N–H bond likely occurs in the mechanism.



The solvent did not have any impact on these processes, as evidenced by the total absence of deuterium incorporation when the reaction was run in toluene- $d_8$  (eqn (10)).



Almost no hydrogen incorporation took place when the reaction was carried out with **15** (eqn (11)), confirming that hydrogen incorporation in eqn (8) was the result of an exchange with the hydrogen of the N–H bond.



**Table 6** Competition experiments

Entry	<b>1</b> <sub>A</sub> , R <sub>1</sub>	<b>1</b> <sub>B</sub> , R <sub>2</sub>	<b>3</b> <sub>A</sub> <sup>a</sup> (%)	<b>3</b> <sub>B</sub> <sup>a</sup> (%)
1	<b>1l</b> , CF <sub>3</sub>	<b>1j</b> , Me	<b>3la</b> , 80	<b>3ja</b> , <6
2	<b>1k</b> , Ph	<b>1j</b> , Me	<b>3ka</b> , 59	<b>3ja</b> , 14
3	<b>1l</b> , CF <sub>3</sub>	<b>1m</b> , OMe	<b>3la</b> , 81	<b>3ma</b> , <6
4	<b>1l</b> , CF <sub>3</sub>	<b>1o</b> , NMe <sub>2</sub>	<b>3la</b> , 71	<b>3oa</b> , <6
5	<b>1o</b> , NMe <sub>2</sub>	<b>1j</b> , Me	<b>3oa</b> , 24	<b>3ja</b> , 34

<sup>a</sup> Yields were estimated from <sup>1</sup>H NMR spectra.

Competition experiments intended to shed light on electronic effects (Table 6) tend to support the view that the reaction is facilitated by an electron-deficient ring. However, our attempts to rationalize electronic effects through a Hammett plot were unsuccessful and a very bad correlation was obtained. This suggests that substituent effects are not governed by the Hammett equation and, thus, the reactivity is likely ruled by a subtle combination of electronic, steric and coordination effects.

The original mechanism of the chelation-assisted ruthenium-catalyzed *ortho* alkylation of aromatic substrates with olefins, suggested by Murai and co-workers,<sup>4,6</sup> involves the formation of a key ruthenium-hydride intermediate *via* activation of the C–H bond. Reversible insertion of the olefin into the Ru–H bond (hydrometalation type mechanism), followed by a reductive elimination of the alkyl group,<sup>21</sup> leads to the formation of the expected C–C bond. As things stand, we cannot assert definitively that such a mechanism occurs in the present reaction, despite that some similarities are observed. In particular, the involvement of a ruthenium-hydride species still has to be clarified. It appears too soon to draw any conclusions concerning the nature of the mechanism and more investigations are currently being pursued.

## Conclusion

In summary, the ability of an 8-aminoquinoline bidentate directing group in promoting a new ruthenium-catalyzed C–H bond *ortho* alkylation of aromatic amides with various  $\alpha,\beta$ -unsaturated ketones under straightforward reaction conditions is reported. This methodology highlights the fact that bidentate directing groups can be used as an efficient tool for achieving transformations that proceed with difficulty when conventional methods are used and represents the first utilization of a family of  $\alpha,\beta$ -unsaturated acceptors in the “*ortho* directed ruthenium-catalyzed addition of C–H bonds to C–C double bonds”. Thus, a new way to expand the scope of the ruthenium-catalyzed transformations initiated by Murai *et al.* 20 years ago has been achieved.<sup>3,22</sup> It is also noteworthy that no ruthenium-catalyzed C–H bond alkylation of secondary benzamides with olefins *via* chelation assistance by using an amide directing group has been reported to date.<sup>23</sup> Furthermore, the attractiveness and flexibility of the catalyst systems used, open numerous perspectives for the further development of this strategy. The present method offers a high functional group tolerance, provides fast and economical access to very interesting and functionalizable molecular backbones, and is enhanced by the potential transformation of the amide moiety to various functional groups. The mechanism of the reaction remains unclear and more investigations into this aspect of the reaction are currently in progress. Extensions of the methodology are also currently being pursued in our laboratory and will be reported in due course.

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