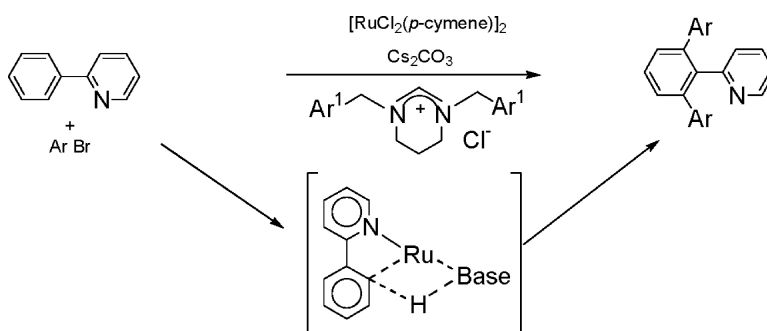## Communication

Direct Arylation of Arene C−H Bonds by Cooperative Action of NHCarbene−Ruthenium(II) Catalyst and Carbonate via Proton Abstraction Mechanism

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Direct Arylation of Arene C−H Bonds by Cooperative Action of NHCarbene−Ruthenium(II) Catalyst and Carbonate via Proton Abstraction Mechanism

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Metal-catalyzed cross-coupling reactions constitute the most useful method for C−C bond formation and the access to diaryls and heterocycles, via the coupling of an organic halide with a variety of organometallics.[1] The search for C−H bond activation[2] has allowed discovery of alternative routes to C−C bond formation via catalytic economical functionalization of sp[2] C−H bonds.[3−6] Direct arylation of functional arenes and heterocycles can now be performed especially with Pd[7] and Rh[8] based catalysts. Ruthenium-(0) catalysts are contributing to this field by initial insertion of Ru-(0) species into C−H bonds.[4,9] Alternatively, some ruthenium(II−IV) catalysts, containing phosphines,[10] phosphine oxides,[11] or N-methylpyrrolidone,[12] recently promoted the direct arylation of arenes and heterocycles; however, the mechanism has not been elucidated and an electrophilic substitution by a Ru(IV) species[10] is still questionable. In contrast, it is established that ruthenium(II) complexes, under mild conditions, allow orthometalation of functional arenes with [RuCl₂(arene)]₂ and a base.[13] Consequently, a ruthenium(II) C−H bond functionalization via an orthometalation process[10d] should be also considered.

We have addressed this problem by studying the arylation of 2-pyridylbenzene, in the presence of new NHC−ruthenium(II) catalysts and a base. We now report that the in situ generation of catalysts, from [RuCl₂(p-cymene)]₂ and a pyrimidinium or benzimidazolium salt in the presence of Cs₂CO₃, selectively promotes the diarylation of 2-pyridylbenzene with arylbromides (eq 1), and that DFT calculations performed on the system RuCl₂(NHC)(2-pyridylbenzene) support an ortho proton abstraction by the cooperative actions of both the carbonate and the ruthenium(II) center.
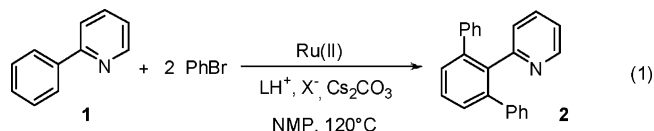

The catalytic system was explored on the basis of (i) the formation of NHC−ruthenium(II) complexes on reaction of [RuCl₂-(p-cymene)]₂ with imidazolinium salts and Cs₂CO₃[14] and (ii) the coordination of carbonate on its reaction with RuCl₂(NHC)(arene) complexes.[15] The diphenylation of 2-pyridylbenzene 1 with PhBr was evaluated with catalysts prepared from 0.05 mmol of mononuclear metal source, 0.10 mmol of pyrimidinium salt LH⁺X⁻ 3b, and an excess of Cs₂CO₃ under Table 1 conditions. [RuCl₂(nbd)]ₙ and [RuCl₂(p-cymene)]₂ led to complete conversion of 1 into product 2, isolated in 77 and 88% yields, respectively (eq 1, Figure 1).

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Table 1. Influence of 1,3-Dinitrogen Salts LH⁺X⁻ **3−5** on Diphenylation of **1**[a]

entry	LH⁺Cl⁻	2 (yield[b])	entry	LH⁺Cl⁻	2 (yield[b])
1	**4**	71	5	**5a**	88
2	**3a**	89	6	**5b**	58
3	**3b**	88	7	**5c**	79
4	**3c**	84	8	**5d**	81

[a] Conditions: 1 mmol of **1** and 2.2 mmol of PhBr were added to a mixture of [RuCl₂(p-cymene)]₂ (0.025 mmol), 0.10 mmol of salt LH⁺Cl⁻ (**3−5**), 3 mmol of Cs₂CO₃ in 2 mL of NMP (N-methylpyrrolidone), 20 h at 120 °C. [b] Isolated yield %.
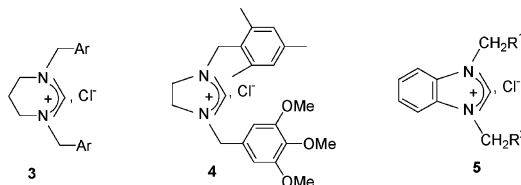
3: Ar = 3,4,5-(MeO)₃C₆H₂- (**3a**) ; 2,4,6-(MeO)₃C₆H₂- (**3b**) ; 2,4,6-Me₃C₆H₂- (**3c**)
5: R¹,R² = **5a**: 3,4,5-(MeO)₃C₆H₂-; **5b** :CH₂OMe, Mes ; **5c** :CH₂OMe ; **5d** : CH₂NEt₂;

**Figure 1.** 1,3-Dinitrogen salts LH⁺X⁻ **3−5** as NHC precursors.

Table 2. Influence of the Bromoarenes p-Y−C₆H₄Br

p-Y−C₆H₄Br	yield[b] of **6−9**	**3a**	**3b**	**3c**	**5c**
p-NC−C₆H₄Br	**6**	75	77	56	51
p-MeCO−C₆H₄Br	**7**	88	82	76	70
p-MeO−C₆H₄Br	**8**	84	87	60	66
p-Me−C₆H₄Br	**9**	87	91	80	71

[a] Conditions: as in Table 1 during 10 h at 120 °C. [b] Isolated yields.

[RuCl₂(p-cymene)]₂ was used to reveal the influence of salts **3−5** as the NHC precursor. The results in Table 1 show that the pyrimidinium salts **3** and the benzimidazolium salts **5** give complete conversion of **1** and good isolated yields of **2**.

To gather information on the mechanism and to explore the scope of ortho arylation, the influence of arylbromide p-Y−C₆H₄Br has been evaluated, but only during 10 h at 120 °C to allow better comparison. The ortho-diarylated products **6−9** were obtained in good yields (eq 2, Table 2).
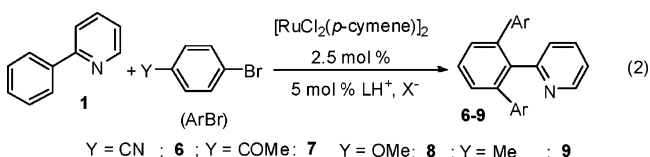
Y = CN : **6** ; Y = COMe: **7** Y = OMe: **8** ; Y = Me : **9**

The results show that the arylbromides containing a para electron-donating group lead to similar yields of **8** and **9** as those with the
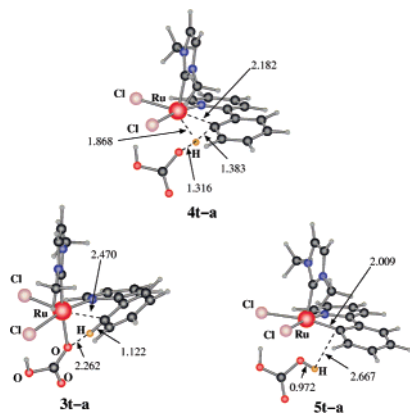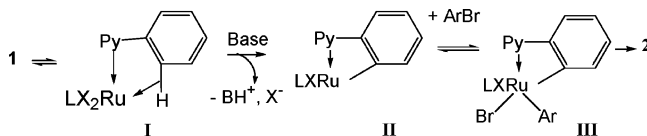
Figure 2. B3LYP-optimized structures for complexes **3t-a**, **4t-a**, and **5t-a**. Selected distances are indicated in Å.

Scheme 1. Possible Orthometalation Intermediates

electron-withdrawing ones leading to **6** and **7**. This absence of discrimination by various arylbromides does not support an arene electrophilic substitution process.

In contrast, as 2-pyridylbenzene with [RuCl₂(arene)]₂ easily leads to orthometalation,[13] a plausible mechanism via an initial ortho-metalation-like process is presented in Scheme 1 (L = NHC). The intermediate **II** is expected to undergo PhBr reversible oxidative addition to give **III**, that is able to release the arylation product **2** by reductive elimination. The less intuitive aspect is the critical cleavage of the C−H bond. In principle, two mechanisms can be postulated, the C−H oxidative addition producing a Ru(IV) intermediate with a hydride ligand, or a direct proton abstraction[16,17] from the phenyl by the base. We studied the process computationally through DFT calculations[18] on the system [Ru(IMe)(Cl)₂(2-pyridylbenzene)] (**1t**) (IMe = *N,N′*-dimethylimidazolylidene), corresponding to **I**, plus HCO₃⁻.[19] The system **1t** has several isomers, all of them producing similar energy profiles. Only the most stable one, labeled **1t-a**, will be discussed here, and the optimized structures for the other isomers are collected in the Supporting Information.

Complex **1t-a** presents an important agostic distortion, with an ortho C−H distance of 1.179 Å. However, oxidative addition from this species is disfavored, and the associated octahedral complex with a hydride ligand **2t-a** has a relative energy of 28.2 kcal/mol, quite high above **1t-a**. Both complexes are shown in the Supporting Information. In contrast, the proton abstraction mechanism is much easier. The introduction of HCO₃⁻ in the system results in its coordination to ruthenium and the formation of an adduct, **3t-a**, 22.9 kcal/mol below the separated fragments. This adduct evolves to product **5t-a**, with a Ru−phenyl bond, through transition state **4t-a**. The transformation from **3t-a** to **5t-a** is exothermic by 13.7 kcal/mol, and the barrier is 13.9 kcal/mol. This low barrier indicates a strong preference for the proton abstraction mechanism, even when considering the weak HCO₃⁻ base.

The structures for species **3t-a**, **4t-a**, and **5t-a** are shown in Figure 2. It is worth noticing that the hydrogen atom being transferred is practically halfway between carbon (C−H distance, 1.383 Å) and oxygen (O−H distance, 1.316 Å) in the transition state. In contrast, the Ru−C bond is almost formed in the transition state **4t-a**: the Ru−C distance is 2.182 Å, whereas it is 2.009 Å in **5t-a**. The Ru−H

distance of 1.868 Å is similar to that obtained in previous studies of C−H activation by σ-bond metathesis.[20] The role of the metal and the formation of the Ru−C are critical in favoring the otherwise unexpected deprotonation of a phenyl group by a relatively weak base.

The above results show that more aryl and heterocyclic C−H bond functionalizations should be possible with catalysts offering, via metal/base cooperative proton abstraction, an easy initial orthometalation path.

Supporting Information Available: Computational details, Cartesian coordinates, and absolute energies for all computed structures. This material is available free of charge via the Internet at http://pubs.acs.org.

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