Ruthenium-Catalyzed Reductive Cleavage of Unstrained Aryl─Aryl Bonds: Reaction Development and Mechanistic Study

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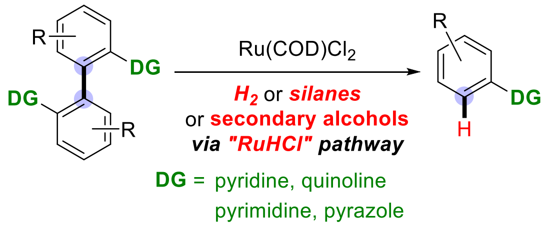
Abstract

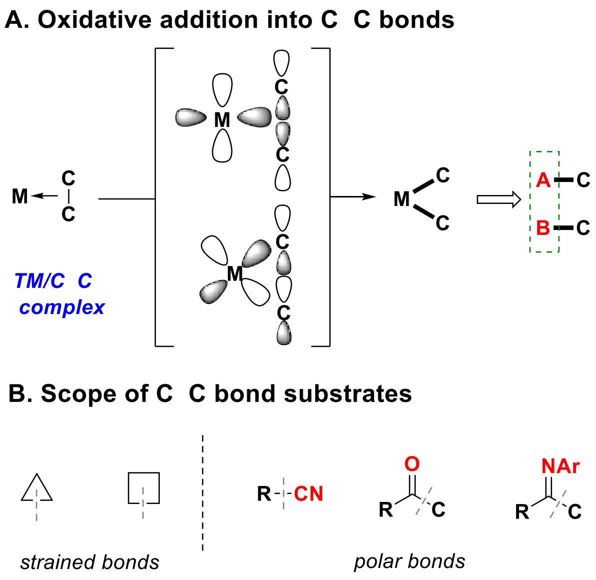
Cleavage of carbon−carbon bonds has been found in important industrial processes, e.g. petroleum cracking, and has inspired development of numerous synthetic methods. However, non-polar unstrained C(aryl)−C(aryl) bonds remain one of the toughest bonds to be activated. As a study of a fundamental reaction mode, here a full story is described about our development of a Ru-catalyzed reductive cleavage of unstrained C(aryl)−C(aryl) bonds. A wide range of biaryl compounds that contain DGs at 2,2' positions can serve as effective substrates to undergo reductive C−C cleavage. Various heterocycles, such as pyridine, quinoline, pyrimidine and pyrazole, can be employed as DGs. Besides hydrogen gas, other reagents, such as Hantzsch ester, silanes and alcohols, can be employed as terminal reductants. The reaction is neutral and free of oxidants, thus a number of functional groups are tolerated. Notably, a one-pot C−C activation/C−C coupling has been realized. Computational and experimental mechanistic studies indicate that the reaction involves a ruthenium(II) monohydride-mediated C(aryl)−C(aryl) activation, which could inspire development other transformations based on this reaction mode.



Introduction

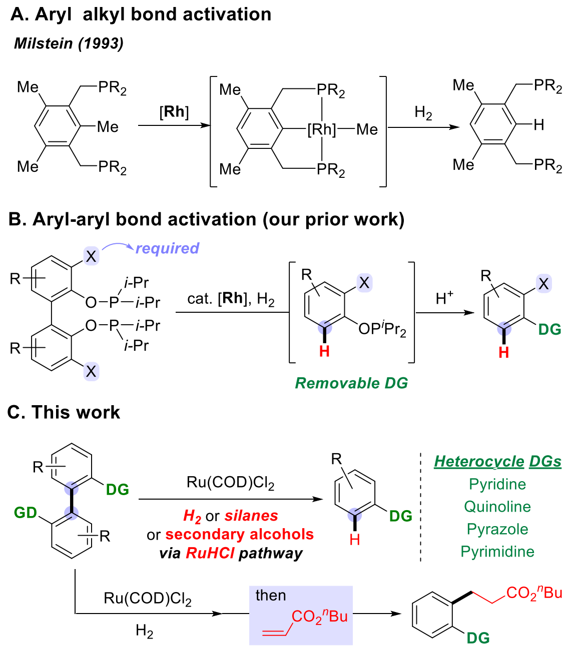
Oxidative addition of a transition metal (TM) into a carbon−carbon (C−C) bond represents an important means of activating C−C bonds, which has led to development of numerous synthetically valuable methods.[i] This process converts one relatively inert C−C bond into two more reactive C−TM bonds that can undergo further transformations, affording dual functionalization of both carbon terminuses (Scheme 1A).[ii] To date, a number of catalytic C−C cleavage/functionalization methods have been developed based on such a mode of activation. However, the scope of C−C bonds that can undergo oxidative addition with

TMs is still narrow (Scheme 1B). The major class of suitable substrates contains a three or four-membered ring, in which strain release becomes the main driving force for the C–C cleavage.[iii] On the other hand, more polar C–C bonds, such as C–CN,[iv] C–carbonyl and C–iminyl bonds in less strained substrates,[v] can also be activated by low valent TMs due to favorable interactions between the low-lying π* orbital in these moieties and TM's filled d orbitals, which promotes forming the requisite C–C/TM σ complex.



Scheme 1. C–C Bond Activation via Oxidative Addition

In contrast, TM insertion into non-polar and unstrained C–C bonds has been extremely rare. In 1993, Milstein and co-workers reported a phosphine-directed activation of an aryl–alkyl bond in a pincer-type substrate, which was driven by forming a two-five-membered-fused rhodacycle (Scheme 2A).[vi] The catalytic transformation was also developed a few years later by the same group.[vii] Recently, Kakiuchi and coworkers developed a novel Rh-catalyzed cleavage of unstained aryl-allyl bonds, albeit through a β-carbon elimination mechanism.[viii] Activation of unstrained aryl–aryl bonds has been elusive[ix] until our recent work (Scheme 2B).[x] The C(aryl)–C(aryl) bonds in 2,2'-biphenols were catalytically cleaved with hydrogen gas using a rhodium catalyst and phosphinite directing groups (DGs). Despite this promising initial result, our understanding of the activation of unstrained aryl–aryl bonds is still limited, and a number of questions remain to be addressed. For example, can other types of DGs, besides those strongly coordinative phosphorus-based ones, be used in the C(aryl)–C(aryl) bond activation? Can other TMs besides expensive rhodium be employed as the catalyst? Can other reagents besides hydrogen gas react with the C–C cleavage intermediate? Answers to these questions could be important for expanding the substrate scope and reaction varieties of this transformation. In this full article, we describe a detailed development of a ruthenium-catalyzed reductive cleavage of unstrained C(aryl)–C(aryl) bonds and the mechanistic study of this reaction (Scheme 2C). Nitrogen-based heterocycles were found to be excellent DGs and, besides hydrogen gas, secondary alcohols and silanes could also be employed as the reductant for this transformation.

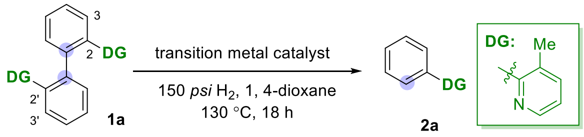


Scheme 2. Activation of Non-polar Unstrained C−C Bonds

Result and Discussion

Pyridine and related heterocycles have been frequently employed as DGs in catalytic C−H activation reactions.[xi] They have also been used in C−C activation of ketones.[xii] Thus, the 2,2'-(3-methylpyrdinyl) substituted biphenyl (**1a**) was chosen as the initial substrate. Using $[Rh(C_2H_4)Cl]_2$, $[Rh(COD)Cl]_2$ or $Rh(COD)_2NTf_2$ as the catalyst, trace or no desired product was observed (Table 1, entries 1-3). However, adding NaI as the additive, 39% yield of the desired C−C cleavage product was obtained (Table 1, entry 4). This result showed the feasibility of using pyridine as DGs for C(aryl)−C(aryl) bond activation, though the exact role of NaI is unclear. Note that using the pyridine DG, substitution at the 3,3' positions is not required. This motivated us to examine other readily available TM complexes as precatalysts for this transformation. While the Ni(0), Co(0), and Ir(I) complexes gave no desired cleavage product (entries 5-7), Ru(II) dichloride complexes nevertheless exhibited remarkable reactivity (entries 11-18). $RuCl_3 \cdot xH_2O$ showed moderate reactivity (entry 10), but $Ru_3(CO)_{12}$[xiii]$_{12b}$ and Cp*Ru(COD)Cl were not reactive. Among various Ru complexes examined, $Ru(COD)Cl_2$ was found to be most efficient (entry 14). Besides 1,4-dioxane, other solvents, such as toluene and THF, were also suitable for this transformation (entries 15 and 16).

Table 1. Selected Optimization Study for the Hydrogenation Condition

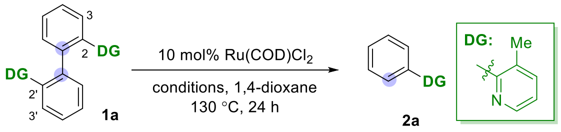


Entry[a]	Conditions	Yield[b]
1	10 mol% $[Rh(C_2H_4)Cl]_2$	trace
2	10 mol% $[Rh(COD)Cl]_2$	n.d.
3	10 mol% $[Rh(COD)Cl]_2$+100 mol% NaI	39%
4	20 mol% $Rh(COD)_2NTf_2$	n.d.
5	20 mol% $Ni(COD)_2$	n.d.
6	10 mol% $Co_2(CO)_8$	n.d.
7	10 mol% $[Ir(COD)Cl_2]_2$	n.d.
8	6.7 mol% $Ru_3(CO)_{12}$	n.d.
9	20 mol% Cp*Ru(COD)Cl	n.d.
10[c]	20 mol% $RuCl_3 \bullet xH_2O$	26%
11	10 mol% [Ru(*p*-cymeme)Cl_2]$_2$	50%
12	10 mol% [Ru(*p*-cymeme)I_2]$_2$	66%
13	20 mol% $Ru(COD)Cl_2$	89%
14	10 mol% $Ru(COD)Cl_2$	89%(83%)
15	10 mol% $Ru(COD)Cl_2$, Tol. as solvent	88%
16	10 mol% $Ru(COD)Cl_2$, THF as solvent	77%

[a] Reaction conditions: **1a** (0.1 mmol), 20 mol% monomer or 10 mol% dimer or 6.7 mol% trimer of metal catalyst, 1,4-dioxane (0.075 M), 130 °C, 18 h, Q-tube filled with 150 psi H_2 gas. [b] Unless otherwise noted, the yields were determined by ^1H NMR using 1,1,2,2-tetrachloroethane as internal standard; n.d. = not detected; the yield in parentheses is isolated yield. [c] The catalyst loading was based on the formula of $RuCl_3$.

Alternative reductants besides H_2 gas were then sought, which, if successful, could provide a more convenient way to operate this C−C cleavage reaction (**Table 2**). To our delight, a variety of mild reductants was found reactive under this Ru-catalyzed condition, and afforded the desired product. For example, potassium formate salt and Hantzsch ester gave 9% and 58% yields of product **2a**, respectively (entries 2 and 3). Diverse secondary alcohols could also serve as a hydride source through a transfer hydrogenation process (entries 4-8). Among all the alcohols tested, cyclopentanol proved to most efficient (entry 8), though an excess amount was needed for a higher conversion (entries 9-13). 84% yield was achieved using 50 equiv of cyclopentanol with toluene as solvent. In addition, a combination of silane and water (1:1) was found to be an excellent reductant (entries 14-18).[xiv] An optimal result (a 85% yield) was obtained when using 5.0 equiv of diphenylmethylsilane with 5.0 equiv of H_2O (entry 18).

Table 2. Screening for Alternative Reductants[a]

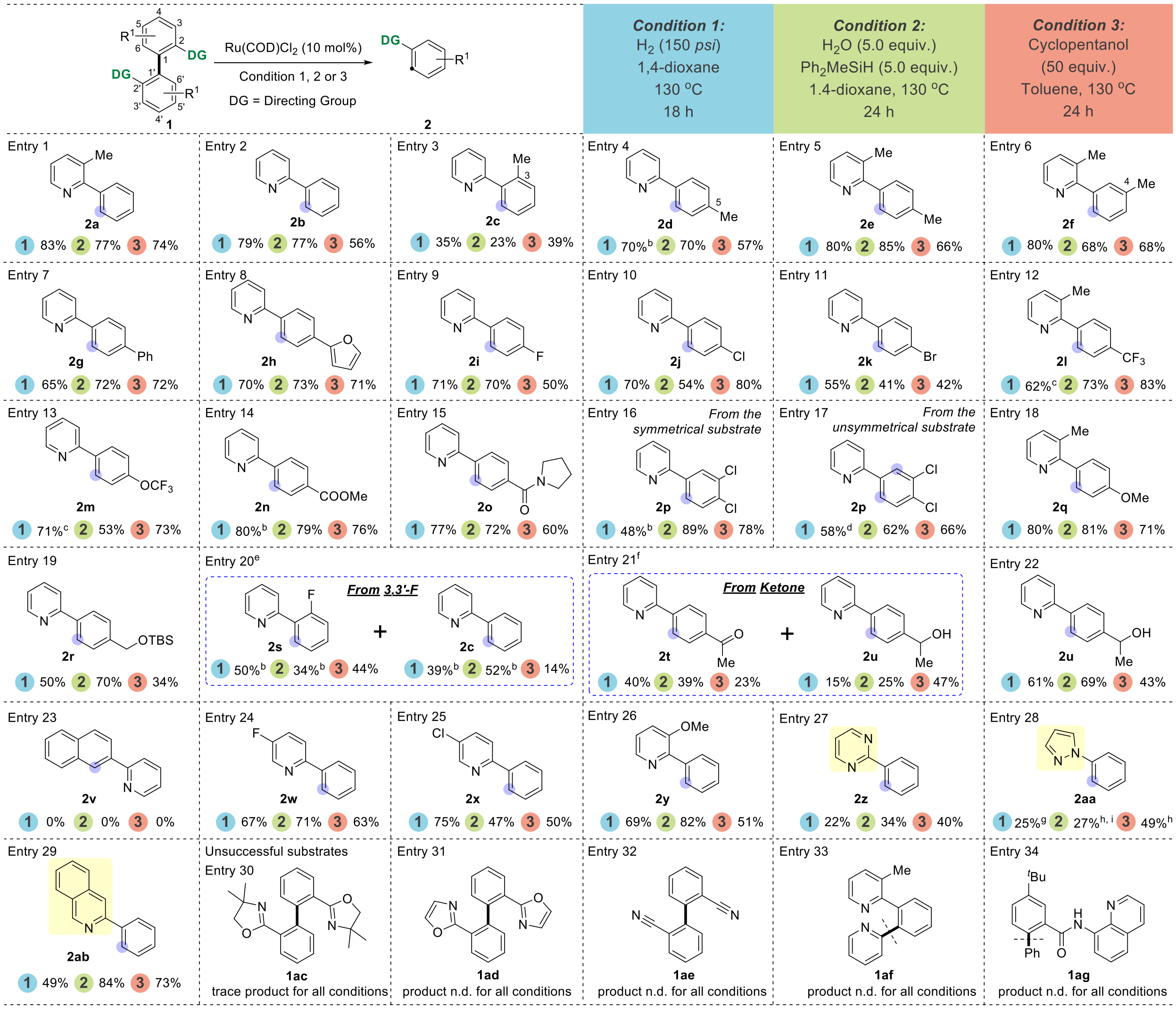


Entry[a]	Conditions	Yield[b]
1	10 *equiv.* $HCOONH_4$	n.d.
2	10 *equiv.* HCOOK	9%
3	10 *equiv.* Hantzsch ester	58%
4	10 *equiv.* diphenylmethanol	20%
5[c]	2-propanol	11%
6[c]	2-butanol	22%
7[c]	3-pentanol	47%
8[c]	cyclopentanol	70%
9	50 *equiv.* cyclopentanol	66%
10	30 *equiv.* cyclopentanol	62%
11	10 *equiv.* cyclopentanol	51%
12	50 *equiv.* cyclopentanol, Tol as solvent	84% (81%)
13	50 *equiv.* cyclopentanol, THF as solvent	46%
14	10 *equiv.* $(TMS)_3SiH$ + 10 *equiv.* H_2O	12%
15	10 *equiv.* Et_3SiH + 10 *equiv.* H_2O	28%
16	10 *equiv.* $PhMe_2SiH$ + 10 *equiv.* H_2O	42%
17	10 *equiv.* Ph_2MeSiH + 10 *equiv.* H_2O	80%
18	5 *equiv.* Ph_2MeSiH + 5 *equiv.* H_2O	85% (78%)

[a] Reaction condition: **1a** (0.1 mmol), 10 mol% Ru(COD)Cl$_2$, 1,4-dioxane or other solvents (1.0 mL), 130 °C, 24 h, sealed vial. [b] Unless otherwise noted, the yields were determined by ^{1}H NMR using 1,1,2,2-tetrachloroethane as internal standard; n.d. = not detected; the yields in parentheses are isolated yields. [c] The indicated alcohols were used as solvent.

With three high yielding conditions in hand, the substrate scope was investigated next (Table 3). First, besides 3-methylpyrdine, simple pyridine can also serve as an effective DG (entry 2). Substitutions on the arene at 3, 4 or 5 positions were all tolerated (entries 3-6), and the yield was lower for the 3,3'-substiutted substrates likely due to the steric hindrance (**2c**). In addition, phenyl and furyl-substituted substrates (**2g** and **2h**) showed good reactivity. A range of functionalization groups, such as fluoride (**2i**), chloride (**2j** and **2p**), bromide (**2k**), trifluoromethyl (**2l**), OCF$_3$ (**2m**), ester (**2n**), amide (**2o**), OMe (**2q**) and silyl ether (**2r**) were found compatible. Interestingly, when a fluorine substituent is *ortho* to the DG (entry 20), partial C−F bond activation/cleavage product was obtained;[xv] for comparison, fluorine substitutions at other positions (**2i** and **2w**) were intact. When a ketone moiety is present (entry 21), partial reduction to the corresponding alcohol was observed, particularly under the transfer hydrogenation conditions. Unsurprisingly, alcohol moieties (**2u**) were tolerated. Unfortunately, the bulkier binaphthyl-derived substrate was not reactive (entry 23). Regarding the scope of DGs, substituted pyridines with various electronic properties exhibited similar reactivity (entries 24-26). Gratifyingly, other heteroarenes, including pyrimidine (entry 28), 5-membered pyrazole (entry 29) and quinoline (entry 27), were found as competent DGs. More labile oxazoline (**1ac**), oxazole (**1ad**) and nitrile (**1ae**) were ineffective. Finally, attempts to cleave an aryl−pyridyl bond or use a mono bidentate DG were unfruitful at this stage (entries 33 and 34).

Table 3. The Substrate Scope [a]



	Condition 1: H_2 (150 *psi*) 1,4-dioxane 130 °C 18 h	Condition 2: H_2O (5.0 equiv.) Ph_2MeSiH (5.0 equiv.) 1.4-dioxane, 130 °C 24 h	Condition 3: Cyclopentanol (50 equiv.) Toluene, 130 °C 24 h
Entry 1, **2a**	83%	77%	74%
Entry 2, **2b**	79%	77%	56%
Entry 3, **2c**	35%	23%	39%
Entry 4, **2d**	70%[b]	70%	57%
Entry 5, **2e**	80%	85%	66%
Entry 6, **2f**	80%	68%	68%
Entry 7, **2g**	65%	72%	72%
Entry 8, **2h**	70%	73%	71%
Entry 9, **2i**	71%	70%	50%
Entry 10, **2j**	70%	54%	80%
Entry 11, **2k**	55%	41%	42%
Entry 12, **2l**	62%[c]	73%	83%
Entry 13, **2m**	71%[c]	53%	73%
Entry 14, **2n**	80%[b]	79%	76%
Entry 15, **2o**	77%	72%	60%
Entry 16, From the symmetrical substrate, **2p**	48%[b]	89%	78%
Entry 17, From the unsymmetrical substrate, **2p**	58%[d]	62%	66%
Entry 18, **2q**	80%	81%	71%
Entry 19, **2r**	50%	70%	34%
Entry 20[e], From 3,3'-F, **2s**	50%[b]	34%[b]	44%
Entry 20[e], From 3,3'-F, **2c**	39%[b]	52%[b]	14%
Entry 21[f], From Ketone, **2t**	40%	39%	23%
Entry 21[f], From Ketone, **2u**	15%	25%	47%
Entry 22, **2u**	61%	69%	43%
Entry 23, **2v**	0%	0%	0%
Entry 24, **2w**	67%	71%	63%
Entry 25, **2x**	75%	47%	50%
Entry 26, **2y**	69%	82%	51%
Entry 27, **2z**	22%	34%	40%
Entry 28, **2aa**	25%[g]	27%[h, i]	49%[h]
Entry 29, **2ab**	49%	84%	73%

Unsuccessful substrates

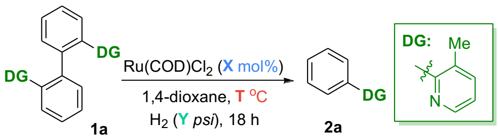
Entry 30, **1ac**	trace product for all conditions
Entry 31, **1ad**	product n.d. for all conditions
Entry 32, **1ae**	product n.d. for all conditions
Entry 33, **1af**	product n.d. for all conditions
Entry 34, **1ag**	product n.d. for all conditions

[a] Condition 1: **1** (0.1-0.2 mmol), Ru(COD)Cl_2 (10 mol %), 1,4-dioxane (0.075 M), 130 °C, 18 h, Q-tube filled with 150 psi H_2 gas; Condition 2: **1** (0.1-0.2 mmol), Ru(COD)Cl_2 (10 mol %), 5.0 equiv of Ph_2MeSiH, 5.0 equiv of H_2O, 1,4-dioxane (1.0 mL/0.1 mmol **1**), 130 °C, 24 h, sealed vial; (3) **1** (0.1-0.2 mmol), Ru(COD)Cl_2 (10 mol %), 50 equiv of cyclopentanol, toluene (1.0 mL/0.1 mmol **1**), 130 °C, 24 h, sealed vial. All yields are isolation yields. [b] Reaction time was 6 h. [c] Reaction time was 3 h. [d] Reaction time was 11 h. [e] The total yields are isolation yields, and the ratio of the two products were determined by ^1H NMR. [f] The two products were both observed and isolated from the reaction system. [g] Ru(COD)Cl_2 (20 mol %), 160 °C. [h] Ru(COD)Cl_2 (20 mol %), 150 °C. [i] $(EtO)_3SiH$ (5.0 equiv) was used instead of Ph_2MeSiH. n.d. = not detected.

The limits of the catalyst loading and reaction temperature under the hydrogenation condition was then examined (Table 4). Reducing the Ru loading from 10 mol% to 2.5 mol% only marginally affected the yield (entry 1, Table 4); further lowering the catalyst loading to 1 mol% still afforded 55% yield of the product (entry 2, Table 4). It was surprising that, at a lower temperature (110 °C), a higher yield (90%) was obtained (entry 4, Table 4). Further decreasing the temperature to 70 °C still showed moderate reactivity (entries

4-6, Table 4). The hydrogen pressure would be further reduced to 70 psi without affecting the reaction efficiency (entries 7 and 8, Table 4). A lower yield was obtained when 30 psi of hydrogen was used (entry 9, Table 4).

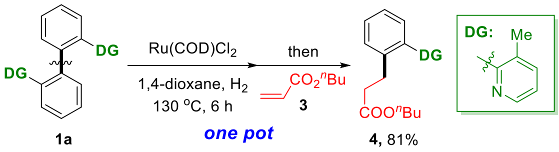
Table 4. Exploring the limits of hydrogenolysis of the C(aryl)–C(aryl) Bonds



Entry[a]	X (mol%)	T (°C)	Y (*psi*)	Yield[b]
1[c]	2.5	130	150	80%
2[d]	1.0	130	150	55%
3[e]	10	130	150	83%
4	10	110	150	90%
5	10	90	150	59%
6	10	70	150	33%
7	10	130	110	90%
8	10	130	70	89%
9	10	130	30	65%

[a]Conditions:**1a** (0.2 mmol), Ru(COD)Cl$_2$, 1,4-dioxane (*C*cat = 0.0075 M), 18 h, Q-tube filled with H$_2$ gas. [b]Isolated yield. [c]0.4 mmol **1a** was used. [d]1.0 mmol **1a** was used. [e]0.1 mmol **1a** was used.

In addition, a one-pot C–C activation/C–C formation approach has also been established (Eq 2). After the hydrogenation of the aryl–aryl bond, the ruthenium catalyst was found to remain reactive. Subsequent addition of acrylate allowed for mono *ortho* alkylation of the C–C cleavage product in a high yield.[xvi] This result shows the potential to couple aryl–aryl bond activation with subsequent functionalization using a single catalyst.



(2)

Mechanistic Studies

The mechanism of the Ru-catalyzed aryl–aryl bond activation was explored using a combination of computational and experimental efforts. Three possible reaction pathways are proposed (Figure 1). **Path a** involves insertion of a Ru(II) dichloride species ("RuCl$_2$") into the aryl–aryl bond to give a Ru(IV) intermediate, which then undergoes hydrogenolysis to give the monomer product. **Path b** is initiated by a Ru(II) monohydride monochloride species ("RuHCl"), generated via mono-hydrogenation from the ruthenium dichloride precursor.[xvii] Oxidative addition of the "RuHCl" into the aryl–aryl bond followed by C–H reductive elimination affords one monomer product, and the resulting ruthenium aryl intermediate then reacts with H$_2$ to deliver the other monomer product and regenerate the "RuHCl" catalyst. **Path c** is based on a Ru(II) dihydride ("RuH$_2$") species, generated from double hydrogenation of the "RuCl$_2$" precursor.[xviii] Similarly, insertion of the RuH$_2$ intermediate into the aryl–aryl bond, followed by double C–H reductive elimination, should afford two monomer products. The resulting Ru(0) can then react with H_2 to regenerate the “RuH_2” species (for a discussion of an alternative Ru(0)-initiated pathway, see the Supporting Information).

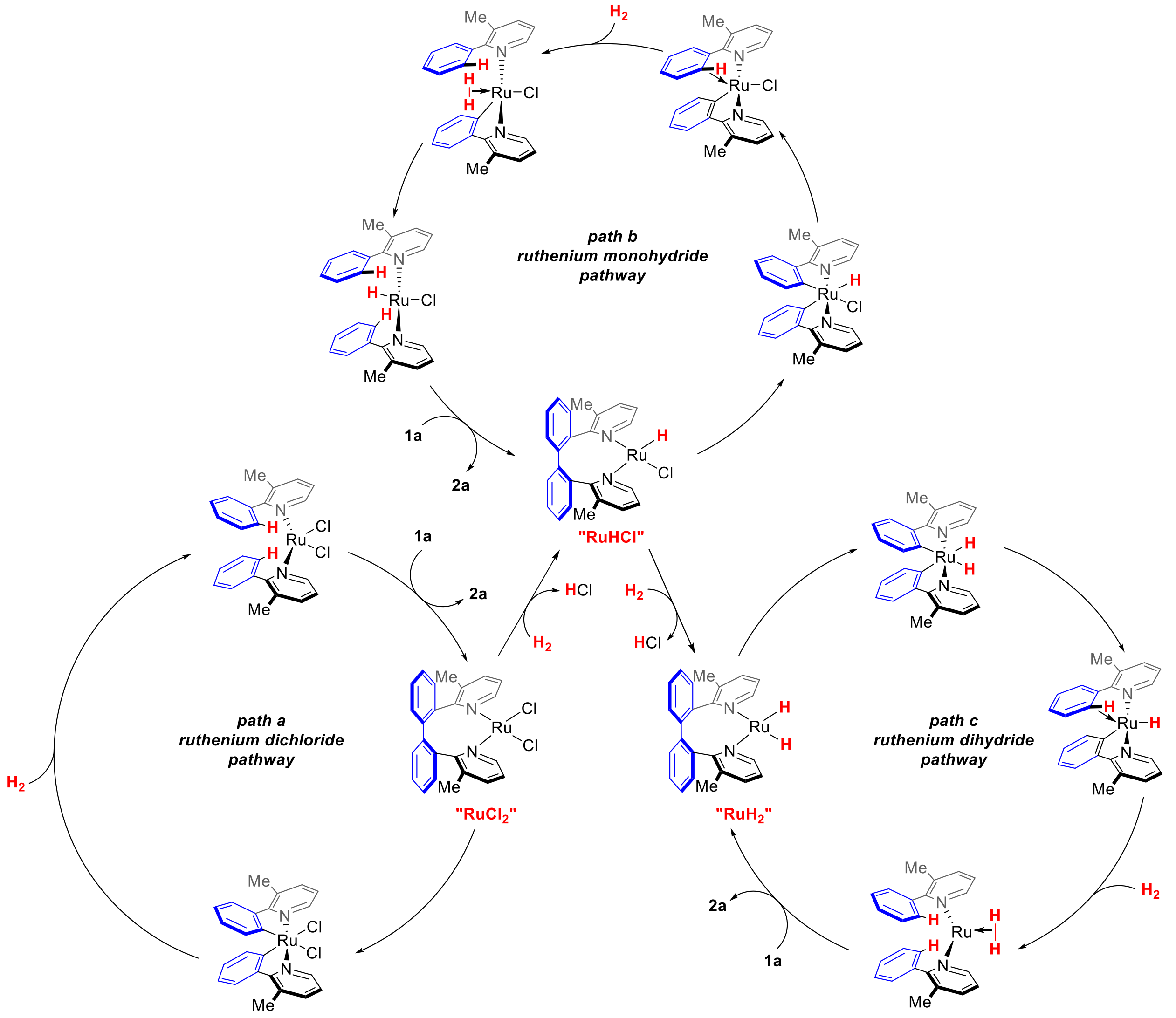


Figure 1. Proposed possible reaction pathways.

To differentiate the three possible pathways, density functional theory (DFT) calculations were performed. It was found that the RuHCl pathway (**path b**) was the most favorable. The computed energy profile in Figure 2 shows that RuHCl complex **5b** is the active catalyst species in the catalytic cycle, which is formed from the endothermic reaction of $RuCl_2$ species **5a** with H_2 via **TS1** with a barrier of 21.3 kcal/mol. In both **5a** and **5b**, the two pyridine DGs adopt a *trans* geometry. This places the target aryl–aryl bond in closer proximity to the Ru, which is evidenced by the much shorter Ru···C distances of 2.3-2.6 Å in **5a** and **5b** than those (3.8-4.0 Å) in the structures with the two pyridine DGs *cis* to each other (see Figure S1 in the Supporting Information). This agostic C–C/Ru coordination leads to a low barrier of 12.2 kcal/mol for the subsequent C(aryl)–C(aryl) oxidative addition transition state **TS2b** with respect to **5b**. The overall activation free energy of **TS2b** is 24.5 kcal/mol with respect to the resting state **5a**. In contrast, the experimentally observed low reactivity of bi-aryl substrates with only one pyridine substituent (e.g. **1af**) can be attributed to the lack of the agostic C–C coordination with the Ru (see Figure S2 for detailed computational results). The necessity of two DGs for the C(aryl)–C(aryl) bond cleavage has also been demonstrated in the catalytic activation of the C(aryl)–C(aryl) bonds of 2,2′-biphenols by installing phosphinites as DGs in our prior study.[x] After the C–C cleavage step, the ensuing C–H reductive elimination (**TS3**) and σ-bond metathesis with H_2 (**TS4**) both occur with low barriers, leading to two monomer products (**2a**) and regenerating the "RuHCl" catalyst (**5b**).

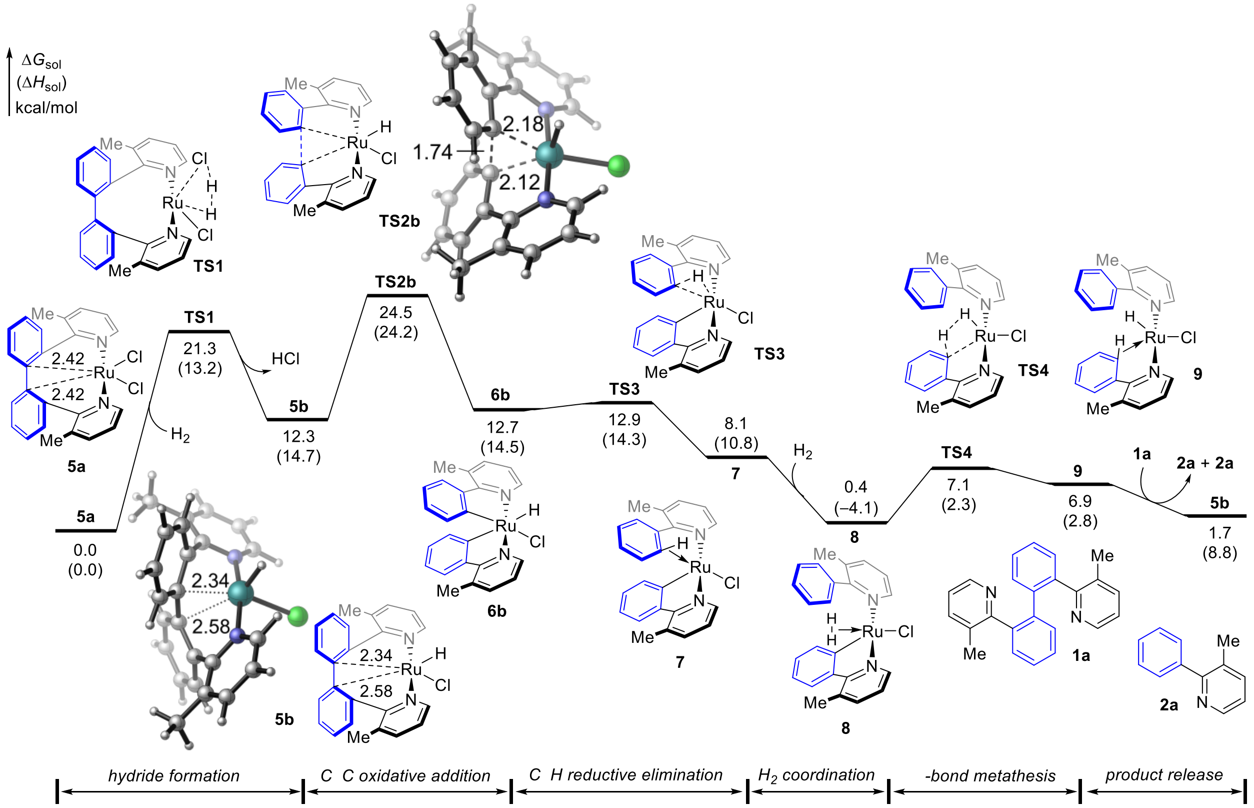


Figure 2. DFT-computed reaction energy profile of the C(aryl)−C(aryl) bond activation of substrate **1a** catalyzed by a Ru monohydride monochloride catalyst (path b).

The possibility of the "$RuCl_2$" and "RuH_2" pathways are also considered and the key results are summarized in Figure 3. In the "RuCl2" pathway (path a, Figure 3A), although the oxidative addition of C(aryl)–C(aryl) (**TS2a**) requires a relatively low barrier of 20.8 kcal/mol with respect to the "$RuCl_2$" species **5a**, the resulting octahedral Ru intermediate **6a** is coordinatively saturated and thus incapable of binding with H_2 and undergoing hydrogenolysis of the Ru–C(aryl) bonds. The transition state **TS5** for H_2 cleavage has a barrier of 28.6 kcal/mol, even higher than that of the C(aryl)–C(aryl) cleavage (**TS2b**) in the "RuHCl" pathways (Figure 2). Our calculations indicated several other possible pathways of **6a** reacting with H_2, including via dissociation of one of the pyridine DGs or one chloride ligand,[xix] all require high barriers (see details in the Supporting Information, Figure S3). Figure 3B shows that the formation of the RuH_2 complex **5c** from **5a** is endergonic by 34.8 kcal/mol. This results in a highly disfavored C(aryl)–C(aryl) oxidative addition transition state **TS2c** ($\Delta G^{\ddagger}$ = 53.0 kcal/mol with respect to **5a**) via the ruthenium dihydride complex (see details in Figure S4). Taken together, these computational results indicate that the $RuCl_2$ and RuH_2 pathways are both disfavored. In addition, our DFT calculations show that although the reductive elimination of RuH_2 (**5c**) to form a Ru(0) species is energetically feasible, the Ru(0) pathway requires very high activation barriers for the C(aryl)–C(aryl) oxidative addition and the further hydrogenolysis steps (see details in Figure S5). Therefore, the DFT calculations suggested the RuHCl pathway (**path b**, Figure 1) is the most feasible.

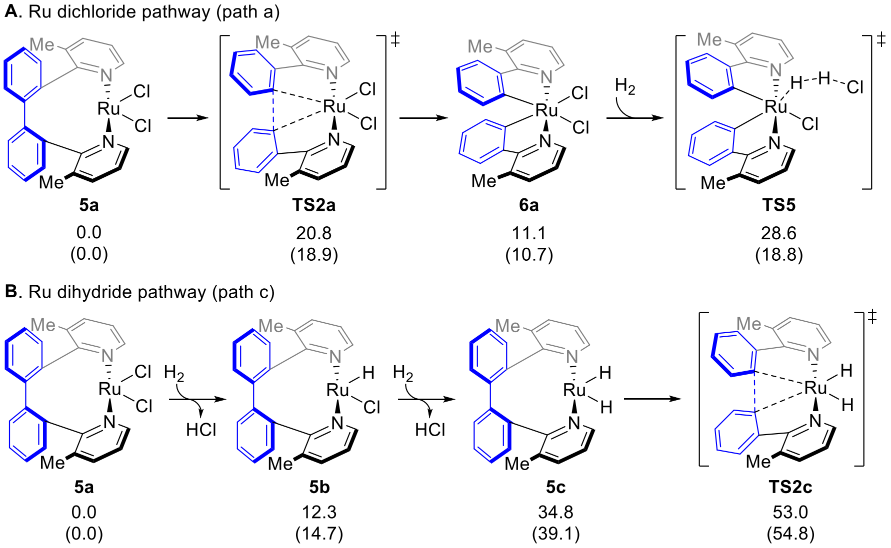


Figure 3. DFT computed pathways for the C(aryl)−C(aryl) bond activation of substrate **1a** catalyzed by Ru dichloride and Ru dihydride catalysts. Gibbs free energies and enthalpies (in parentheses) are in kcal/mol with respect to the $RuCl_2$ complex **5a**.

To validate the computational results that favor the RuHCl pathway, the following experiments were conducted. First, Ryabov and Lagadec reported synthesis of a Ru(II) biaryl bispyridyl complex, which shows an interesting η^4 coordination mode between two arene π bonds and the Ru center (Figure 4).[xx] Such a coordination structure suggests that in our system an agnostic interaction between the C(aryl)−C(aryl) bond and the Ru center can possibly happen. Second, the corresponding substrate-$RuCl_2$ complex was prepared from $[Ru(C_6H_6)Cl_2]_2$ (Scheme 3). The X-ray crystal structure shows that the metal center exhibits octahedral geometry and the two pyridine DGs adopt *cis* spatial relationship (Eq 3). In addition, a ruthenium monohydride monochloride complex **15** was synthesized and subjected to the reaction with substrate **1a** in the absence of hydrogen gas (Eq 4).[xxi] To our delight, 60% yield of the desired monomer product was obtained in 60% yield based on the hydride on the Ru. For comparison, the analogous ruthenium dihydride complex[xxii] gave only trace product via LC-MS analysis under the same reaction conditions (Eq 5). These results are consistent with the DFT condition, suggesting that the RuHCl pathway is more feasible than the RuH_2 pathway.

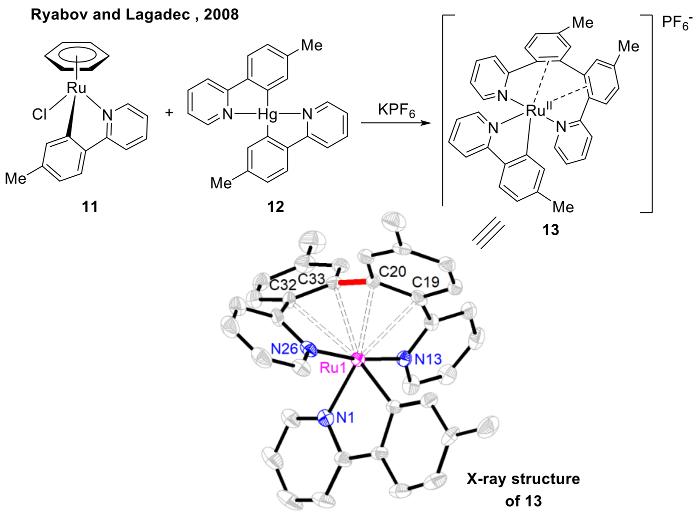
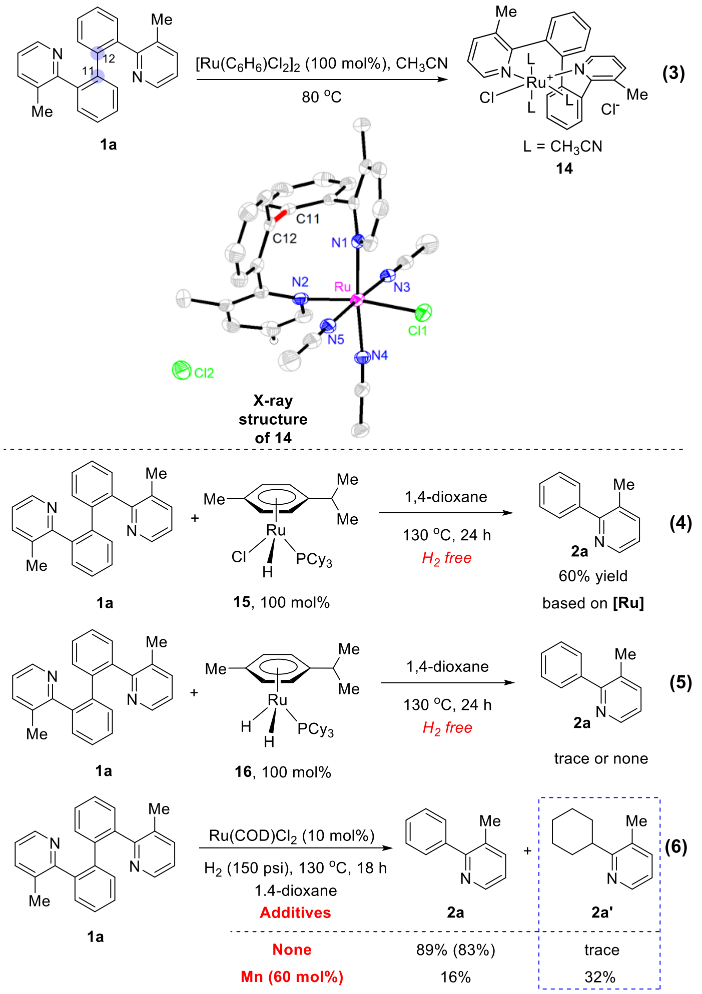


Figure 4. η^4 Coordination Between the Aryl-Aryl Bond and the Ruthenium Center.



Scheme 3. Preliminary mechanistic study.

To further examine the possibility of the Ru(0)-initiated pathway, a control experiment was run with 60 mol% of Mn added to the reaction, as Mn metal is known to be capable of reducing Ru(II) to Ru(0) facilely (Eq. 6).[xxiii] To our surprise, the reaction with Mn not only gave a lower overall yield on the C−C cleavage products, but also generated a significant amount of arene hydrogenation product (**2a’**). It is intriguing that the neutral benzene ring is selectively reduced instead of the more electron-deficient pyridine ring, which indicating a directed hydrogenation likely by a Ru(0) catalyst.[xxiv] For comparison, such over-reduction product was almost not observed under the standard reaction conditions. This experiment suggests that the Ru(0) is unlikely to be the actual catalyst for the activation of the C(aryl)−C(aryl) bonds.

Conclusion

In summary, to explore a fundamental reaction mode, we have conducted a detailed study of an unusual Ru-catalyzed activation of unstrained C(aryl)−C(aryl) bonds. The reaction limits and substrate scopes have been carefully examined. Besides hydrogen gas, a number of other reagents, such as Hantzsch ester, silanes and alcohols, have also been found effective to serve as terminal reductants for the reductive cleavage. Various heterocycles, such as pyridine, quinoline, pyrimidine and pyrazole, can be employed as DGs. In addition, a number of functional groups are compatible under the reaction conditions. Moreover, a one-pot C−C activation/C−C coupling has been realized. Finally, the reaction mechanism has been investigated through collaborative efforts between DFT calculations and experiments. The involvement of a ruthenium(II) monohydride-mediated C(aryl)−C(aryl) activation should have broad implications beyond this work. The knowledge obtained in this study should improve our understanding on activating strong, non-polar and unstrained chemical bonds. Efforts on expanding the reaction mode to non-reductive processes are ongoing in our laboratories.

ASSOCIATED CONTENT

Text, figures, tables, and CIF files giving experimental procedures, kinetics data, and crystallographic information. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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