Catalysis Science & Technology

Accepted Manuscript

ROYAL SOCIETY OF CHEMISTRY

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Journal name

ARTICLE

Mechanistic Insight into Ruthenium Catalysed *Meta*-Sulfonation of 2-Phenylpyridine

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

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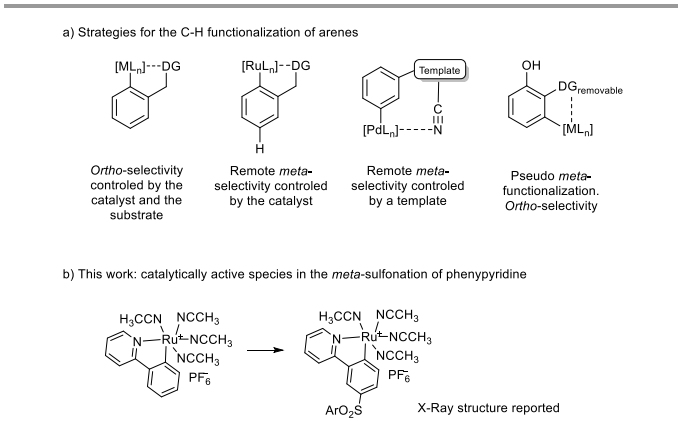
The catalytic *meta*-functionalization of arenes has emerged as important synthetic methodology in the last decade. We report herein structural and mechanistic studies of the *meta*-sulfonation of phenylpyridine using ruthenium complexes. Furthermore, we disclose that the catalytically active species does not require the presence of a η^6-arene ligand. Furthermore, the novel cycloruthenated phenylpyridine complex tosylated at the *para* position to the metal has been isolated and fully characterised. Protodemetallation studies suggest that a concerted C-H activation-demetallation process may be involved. Overall, this study provides fundamental insight into the *meta*-sulfonation phenylpyridine reaction pathway and uncovers new reaction intermediates that will guide the design of new catalytic systems for remote *meta*-functionalization.

Introduction

The functionalization of arenes catalysed by a metal complex *via* C-H activation has attracted great attention in the last decade.[1,2] This transformation requires the presence of a directing group (DG) that coordinates to the metal centre to facilitate the C-H activation at the *ortho* position to form a metallacycle. Once the metallacycle is formed the introduction of a functional group can be achieved at the *ortho*[1,2] and *meta* positions.[3] The *ortho*-functionalization of arenes has been widely studied and there are many transformations reported in the literature such as arylations,[4] alkylations,[5] olefinations[6] and amidations[7,2a] among others.[1,2] Despite the great achievements in this area, the direct introduction of a functional group at the *meta* position remains a challenge. We reported the first example of catalytic *meta*-functionalization by remote electronic activation using ruthenium catalysis.[8,9] This important switch of regioselectivity in the sulfonation of phenylpyridines from the *ortho*[10] to the *meta* position was realised by changing the catalyst from Pd(II) to Ru(II). The innovative template assisted direct *meta*-C–H bond activation first reported by Yu *et al.* involves the use of a removable tethered directing group capable of coordinating to the catalyst and directing it to the *meta* position.[11] Other strategies involve transient mediators such as a carboxylic acid[12] or norbornene[13] that direct *ortho* but reveal *meta*-arylated products after their removal (Scheme 1a).

Recently, new examples of *meta* selective catalytic C-H functionalization controlled by the catalyst have been achieved using secondary[14] or tertiary[15,16] alkyl halides and bromination reagents.[17]



Scheme 1

To account for the switch in regioselectivity in the *meta*-sulfonation, we hypothesized that the chelating group facilitates the formation of a stable Ru-C$_{aryl}$ σ-bond that induces a strong *para* directing effect.[8] Although the σ-activation of aromatics has been studied for a range of stoichiometric processes such as electrophilic halogenation,[18] acylation,[19] and nitration,[18b,18c,20] a catalytic σ-activation process invokes a novel mechanistic pathway for C-H functionalization processes.[15] Recent studies have revealed that the *meta*-functionalization of arenes *via* cycloruthenated complexes may follow a radical pathway.[14,15,16]

Herein, we present mechanistic studies to establish important steps and intermediates in the *meta*-sulfonation of phenylpyridines. We also demonstrate that the presence of a *p*-cymene ligand is not essential for catalytic turnover. Moreover, this is the first time that the cycloruthenated tosylpyridine complex has been isolated and fully characterised confirming the σ-activation pathway in the catalytic *meta*-sulfonation

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† Electronic Supplementary Information (ESI) available: Experimental data and full spectroscopic data for all organic compounds and ruthenium complexes. See DOI: 10.1039/x0xx00000x

process (Scheme 1b). This study provides fundamental insight into the reaction pathway and contributes to the broader understanding needed to design future catalytic processes for *meta*-selective C-H functionalization.

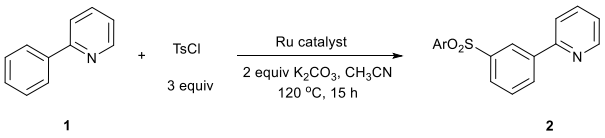
Results and discussion

The catalytic species. The C-H activation step of heteroarenes is crucial for further functionalization at the *ortho* position[21] and has been thoroughly investigated.[22] Recent studies carried out by Dixneuf and Jutand have revealed that C-H activation is an autocatalytic process which goes through a S_E3 mechanism when [Ru(O_2CR)(*p*-cymene)] complexes are employed.[23,24] In contrast, DFT calculations carried out by Dixneuf and Maseras postulated that the C-H activation with Ru(II)-NHC complexes goes through a concerted metalation-deprotonation (CMD) mechanism.[25]

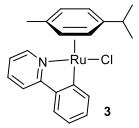
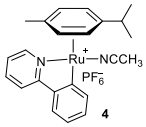
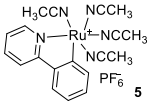
Intrigued by the nature of the active species involved in the catalytic cycle for *meta*-functionalization, a number of ruthenium complexes were synthesised. Based on previous studies in which ruthenium cyclometallated complexes were shown to be key intermediates, complexes **3**, **4** and **5** were initially investigated (Table 1).[23,24,26] As we have previously reported, complex **3** selectively delivered the sulfonated phenylpyridine in good yield.[8] Preformed cationic complex **4** was also found to perform competitively. Remarkably, Ru(II) complex **5** with no *p*-cymene coordinated was also catalytically competent. This is in contrast to the work of Jutand *et al*. who showed that this ligand was essential for catalytic turnover in *ortho* arylation reactions catalysed by Ru(II).[24] It is worth noting that *ortho* arylations employing Ru(III) and Ru(IV) complexes did not require the presence *p*-cymene ligand to achieve high reaction conversions.[27]

In order to observe the evolution of the ruthenium intermediates during the catalytic process, a series of reactions were followed by *in situ* ^{1}H-NMR. [$RuCl_2$(*p*-cymene)]$_2$ as well as complexes **3** and **4** were employed as the precatalysts. When [$RuCl_2$(*p*-cymene)]$_2$ was used, it was converted into cyclometalled complex **4** within 40 min at 393 K (Figure 1). The presence of a new doublet at 9.22 ppm (J = 5.82 Hz, H12) along with two doublets at 0.95 ppm and 0.92 ppm (J = 6.92 Hz, H17, H18) confirmed the formation of complex **4**. A new doublet at 1.23 ppm (J = 6.93 Hz, H17, H18) was also observed and assigned to free *p*-cymene (**6**). After 2 h, signals from complex **4** and free *p*-cymene (**6**) were also identified along with characteristic signals from the tosylated phenylpyridine (**2**). After 4 h, only traces of ruthenium complex **4** remained with a significant increase in the signals corresponding to free *p*-cymene. The fact that complex **4** was detected along with the formation of the final product indicates that the Ru(II) species **4** is not involved in the catalytic cycle. Additionally, the increase of the signals of the free *p*-cymene together with the formation of the final product suggests that the active catalytic species does not contain *p*-cymene as ligand. Similar behaviour was observed when complex **3** was employed. In this case, in the initial stages of the reaction the characteristic signals of **3** appeared at 9.32 ppm (d, J = 5.79 Hz, H12), 0.92 ppm and 0.82 ppm (d, J = 6.92, H17, H18).

Table 1 Catalytic sulfonation using Ru(II) complexes potentially involved in the reaction



1 2

Entry	Catalyst loading (mol%)	Ru Catalyst	Yield (%)[a]
1	5	[$RuCl_2$(*p*-cymene)]	50
2	10	 3	52
3	10	 4	53
4	10	 5	50

a) Isolated yields.

After 40 min at 393 K these signals disappeared to give new peaks which were assigned to complex **4** and free *p*-cymene (Figure S2, see ESI$^+$). When the reaction was performed with complex **4**, no changes in the ruthenium complex were observed after 1 h at 393 K (Figure S3, see ESI$^+$). These results were consistent with previous observations.

In order to know whether the chloride anion was involved in a coordination-discoordination equilibrium, complex **4** was treated with 15 equivalents of KCl in CD_3CN and heated at 363 K overnight. Changes in the ^{1}H-NMR splitting pattern showed the formation of **5** along with the dissociation of the *p*-cymene, but no evidence for the formation of **3** was detected. This experiment supported the fact that when the chloride dissociates from the metal centre it is very unlikely to re-coordinate under these reaction conditions (Figure S4, see ESI$^+$). In recent work published by Dixneuf and Jutand,[22] the attempt to isolate [Ru(OAc)(PhPy)(*p*-cymene)] by flash chromatography using a chloroform as eluent failed and gave **3** instead, showing that chloride is a better ligand for the Ru(II) centre than acetate. Although under Dixneuf conditions the re-coordination of the chloride was evident, the ruthenium species detected by ^{1}H-NMR in our experiment confirms that the ruthenium precatalyst does not contain chloride as ligand.

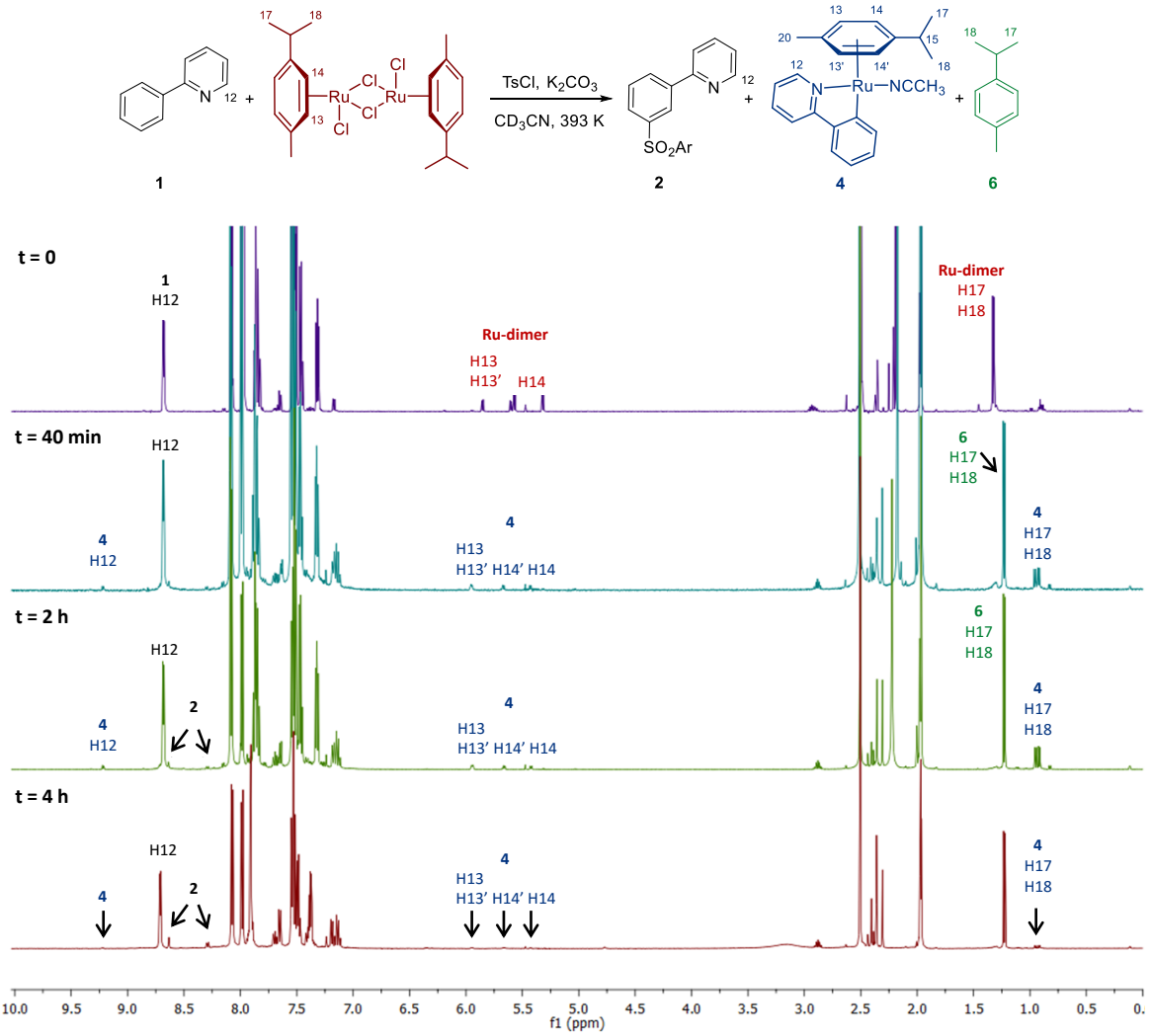


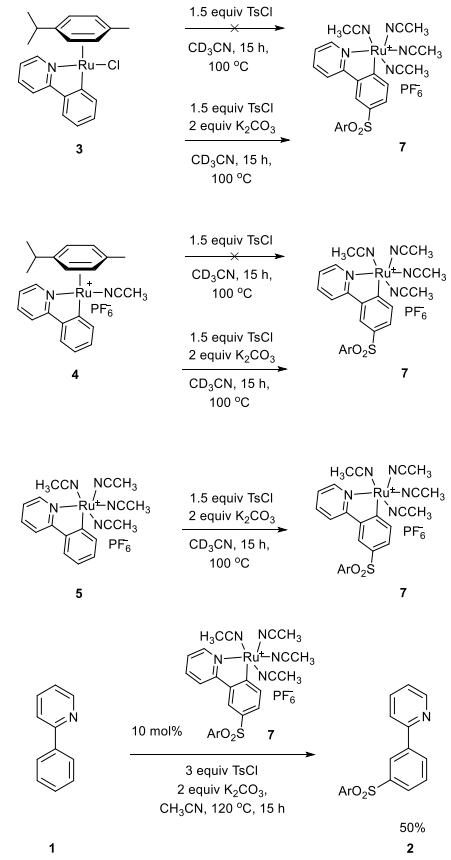
Figure 1 ^{1}H NMR *meta*-sulfonation of phenylpyridine using $[RuCl_2(p\text{-cymene})]_2$

Tosylation step. The tosylation step was also subjected to investigation. The cycloruthenated complex **3** was placed in a NMR tube and treated with 1.5 equivalents of *p*-toluenesulfonyl chloride (TsCl) in CD_3CN at 373 K (Scheme 2). Interestingly, after heating the reaction overnight only the formation of **5** was observed. Taking into account that during the tosylation step a proton has to be abstracted, the presence of a base would favour the substitution. Thus, complex **3** was treated with TsCl and 2 equivalents of K_2CO_3. When the NMR tube was heated at 373 K the dissociation of the *p*-cymene ligand started taking place and, after 2 h the formation of a new complex was observed.

The appearance of a new doublet at 8.92 ppm with a coupling constant of 5.5 Hz and a new doublet at 8.14 ppm with a small coupling constant of 1.8 Hz prompted us to think that the formation of the cycloruthenated tosylpyridine complex **7** was occurring. An analogous stoichiometric experiment was also performed on complex **4** and similar reactivity to **3** was observed (Scheme 2). The treatment of **4** with TsCl afforded complex **5** with concomitant dissociation of the *p*-cymene. Subsequent addition of K_2CO_3 was also necessary to detect the formation of the new ruthenium complex observed previously.

To prove that this new ruthenium complex was indeed **7**, the tosylation on **5** was carried out under the same reaction conditions. After purification of the reaction mixture and full spectroscopic and X-ray analysis of the product, compound **7** was unequivocally assigned to the tosylated phenylpyridine complex with the tosyl group located at the *para* position to the Ru(II) (Figure 2). In light of these results, it could be confirmed that the *meta*-tosylation reaction proceeds by the activation of the *para* position to the Ru(II). This evidence corroborates the

role of Ru(II) acting as a *para* directing group.[28] Finally, complex **7** was also used as precatalyst in the sulfonation reaction.



Scheme 2

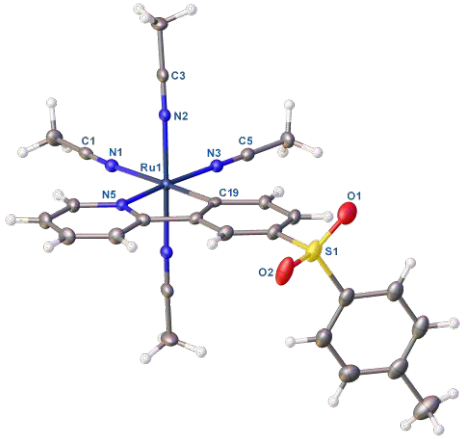


Figure 2 Single crystal X-ray structure of the cation in complex **7**.[29] Ellipsoids are represented at 30% of probability.

Gratifyingly, it was found to be catalytically active, indicating the likelihood of sulfonated complexes involved in the catalytic cycle (Scheme 2). Interestingly, it has recently been demonstrated that similar ruthenium complexes such as $[Ru(^tBuCN)_6][BF_4]_2$ can catalyse the C-H arylation of fluoroarenes and arenes with directing groups.[30]

Dissociation of *p*-cymene. In all previous experiments it was impossible to detect the tosylated Ru(II) complex with the *p*-cymene coordinated. This indicated that the dissociation of the *p*-cymene is faster than the tosylation reaction under stoichiometric conditions.

At this point, we decided to investigate the nature of the *p*-cymene dissociation. In order to study the stability of the cyclometallated Ru complex **3**, a NMR tube was charged with **3** in CD_3CN. The sample was heated at 343 K for one hour, showing no modification of the splitting pattern. Then, 1.5 equivalents of tosyl chloride were added and the sample was kept at 343 K. After 24 min the dissociation of *p*-cymene was observed showing that TsCl promotes the dissociation of the *p*-cymene ligand. The mechanism of this process is still uncertain. However, it is worth noting that the dissociation of *p*-cymene can be accomplished by a thermal process but longer reaction times are required.[31]

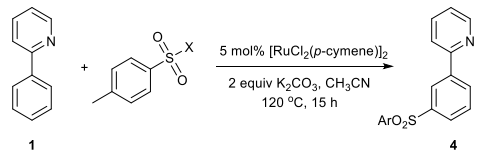
Nature of the *meta*-functionalization. Having confirmed that sulfonation occurs at the *para* position to the newly installed C-Ru bond, we became intrigued by the nature of this process. We had previously proposed that cyclometallation increases the electron density of the aromatic ring, activating it for S_EAr type reactivity. However, recent studies have shown the likelihood of a radical mechanism in *meta*-selective alkylation reactions.[14,15,16]

In order to investigate a possible the S_EAr pathway, the effect of various sulfonating reagents were subjected to study (Table 2). Sulfonating reagents more susceptible to react with nucleophiles such as tosylimidazole, TsOBt and *p*-toluenesulfonic anhydride were employed in this transformation. Analysis of the crude reaction mixture did not show any evidence for the formation of **2** indicating that a simple S_EAr pathway was doubtful.

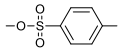
We also noted that the use of the radical scavenger TEMPO caused a detrimental effect on the reaction conversions (see ESI†). Other mechanistic studies carried out on *meta*-functionalization catalysed by ruthenium have also shown inhibition when TEMPO was employed as radical scavenger.[14,15] In this context, we have previously proposed a mechanism involving a distinct Ru(II)/Ru(III)Cl redox cycle whereby a Ru(II) species can cause homolytic cleavage of a C-X bond to generate reactive radical species. Upon site selective addition to the aromatic substrate, the newly formed Ru(III)Cl species can reoxidise the resulting cyclohexadienyl radical intermediate.

This proposal was independently supported by Ackermann in analogous *meta*-selective alkylation reactions.[16] It is therefore possible that the *meta*-selective sulfonation reaction follows analogous reactivity. This is supported by the precedence for the generation of sulfonyl radicals throughout the literature, including those promoted by ruthenium complexes.[32]

Table 2 Effect of various sulfonating reagents on the *meta*-sulfonation[a]



1 4

Entry	X	Yield (%)[b]
1	Cl	50
2		0
3		0
4		0

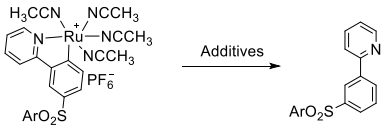
a) Reaction conditions: 2-phenylpyridine (1.0 mmol), sulfonating reagent (3.0 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%), CH_3CN (3 mL), 120 °C, 15 h. b) Isolated yield.

Protodemetallation. The protodemetallation of the cyclometallated ruthenium tosylphenylpyridine is the process responsible of the release of the product with the concomitant regeneration of the catalyst. Precedent in the literature has hypothesized that the proton coming from the C-H activation is involved in the demetallation step.[22] The demetallation of product **2** from complex **7** was subjected to study (Table 3). Since $KHCO_3$ is generated during the reaction we thought that this was a plausible proton source. Thus, complex **7** was treated with 10 equivalents of $KHCO_3$ in CD_3CN. However after heating the mixture at 393 K overnight the release of **2** was not detected (Table 3, entry 1). A number of other acid sources were tested in the same manner yet none resulted in the release of product **2** (Table 3, entries 2-4), nor did the addition of 1 equivalent of phenylpyridine (Table 3, entry 5).

Treatment of **7** with *p*-toluenesulfonic acid (*p*-TSA) afforded a new product. The spectroscopic analysis revealed that the carbon (Ru-C) was no longer coordinated to the Ru(II), but the nitrogen from the pyridyl unit was still coordinated (Figure S7, see ESI†). In order to study the influence of TsCl and phenylpyridine on the reaction turnover, complex **7** was treated with 4.5 equivalents of TsCl. After heating the reaction mixture at 363 K overnight, 23% of the demetallated tosyl phenylpyridine was observed (Table 3, entry 7). A parallel experiment was carried out using 10 equivalents of phenylpyridine and 26% of the final product was detected (Table 3, entry 8). These results demonstrated that both TsCl and phenylpyridine[16] are important in facilitating the demetallation process and that $KHCO_3$ does not play a significant role. A concerted C-H activation-demetallation step cannot be ruled out which would also explain the formation of dimers as by-products during the reaction.[33,34]

Deuterium labelled experiments. In order to determine the C-H bonds involved in kinetically relevant steps, deuterium labelled experiments were performed. Competitive reaction of **[D$_5$]-1** and **[D$_0$]-1** showed a kinetic preference to react with unlabelled **[D$_0$]-1** (Scheme 3a) similar to that demonstrated in previous studies.[8,14] In order to ascertain whether it was the *ortho* or *meta* C-H protons causing this effect, **[D$_2$]-1** and **[D$_3$]-1** were studied. A competitive reaction between **[D$_2$]-1** and **1** was carried out and the mixed product fraction was analysed. This revealed a product ratio of almost 1:1 of the deuterated and non-deuterated **2** when the H2 protons were considered. This is consistent with no kinetically relevant *ortho* C-H bond cleavage. Comparison of H2 and H6 in **[D$_n$]-2** showed a different ratio of deuterium incorporation. This may reflect the involvement of **2** in a reversible C-H activation reaction[35] which could cause this proton enrichment at the less hindered position. In contrast, the competitive reaction between **[D$_3$]-1** and **1** showed a higher percentage of the non-labelled product indicating a clear isotopic effect (Scheme 3c).

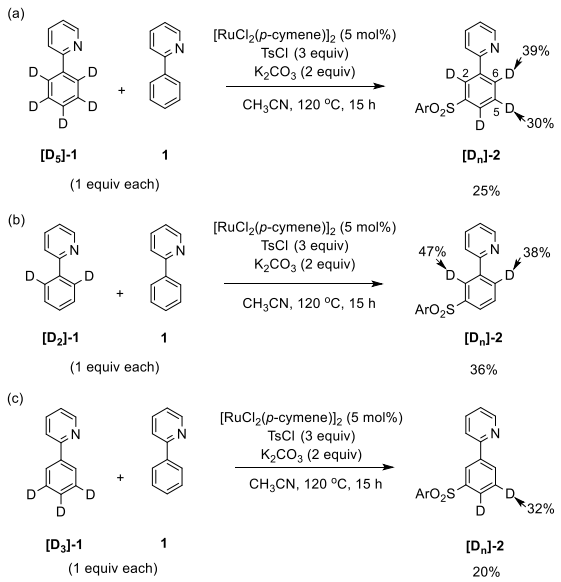
Table 3 Study of the protodemetallation of the TsPhPy from the metal centre.



7 2

Entry	Additives	2 (%)
1	10 equiv $KHCO_3$	--
2	1 equiv $MesCO_2H$ 2 equiv K_2CO_3	--
3	1.5 equiv $MesCO_2H$	--
4	10 equiv $MesCO_2H$	--
5	1 equiv PhPy 2 equiv K_2CO_3	--
6	1.5 equiv *p*-TSA	--[a]
7	4.5 equiv TsCl 2 equiv K_2CO_3	23
8	10 equiv PhPy 2 equiv K_2CO_3	26

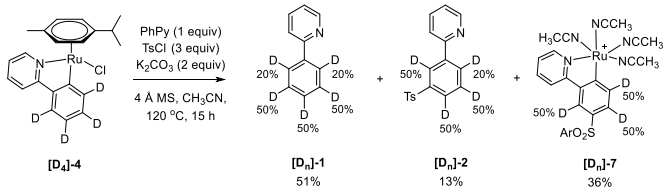
a) Demetallation of the sulfone was observed but the pyridyl moiety was still coordinated to the Ru. b) 1.5 equivalents of tosyl chloride were added for the formation of the sulfone. The reaction was performed at 363 K in an NMR tube.



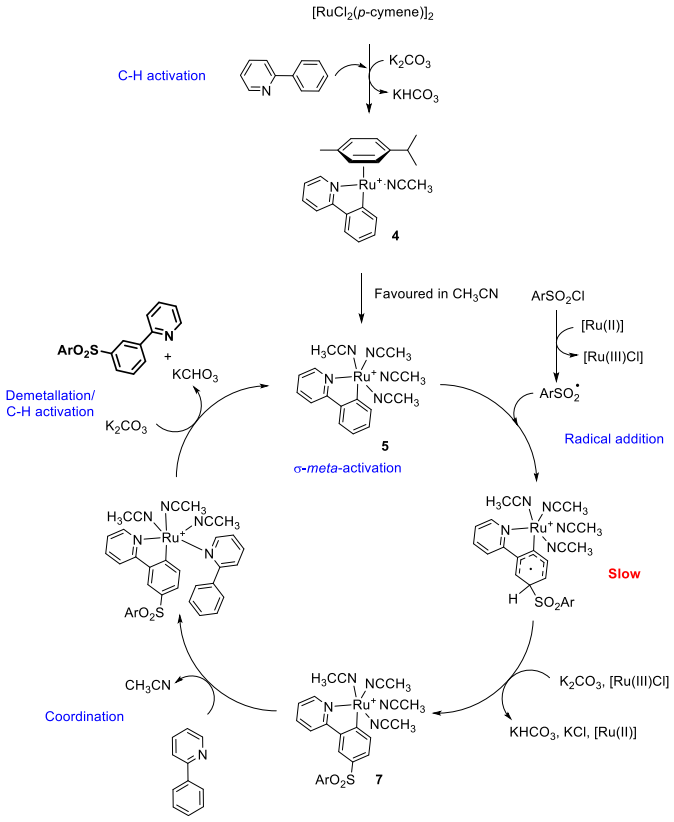
Scheme 3 Studies with isotopically labelled compounds

Single Turnover Experiment. To provide further insight into the mechanism of catalyst turnover, a stoichiometric experiment was performed using an isotopically labelled ruthenium complex **[D$_4$]-4** and unlabelled 2-phenylpyridine. The deuterium incorporation of the resulting organic and inorganic components was then analysed by ^{1}H-NMR (Scheme 4). In recovered fractions **[D$_n$]-1**, **[D$_n$]-2** and **[D$_n$]-7**, 50% deuteration was observed at the *meta* and *para* positions to the pyridine ring. These results indicate that **1** and the labelled phenylpyridine ligand exchange multiple times before a slower tosylation step. Analysis of the *ortho* positions in **[D$_n$]-1** and **[D$_n$]-2** also revealed proton enrichment at the less hindered positions. This evidence supports the fact that tosylphenylpyridine is also involved in a reversible C-H activation.

We propose that the catalytic cycle starts by the breaking of the dimer followed by C-H activation of phenylpyridine with concomitant dissociation of the chloride to give complex **4**. Once complex **4** is formed, the presence of CH_3CN favours the dissociation of the *p*-cymene ligand generating **5** which is the active Ru(II) species involved in the catalytic cycle. This cycloruthenated species **5** activates the phenyl ring from the phenylpyridine towards a radical addition of tosyl chloride at the *para* position. The tosylation step has been determined as a kinetically relevant step.



Scheme 4 Single turnover experiment with isotopically labelled ruthenium complex **[D$_4$]-4**.



Scheme 5 Proposed catalytic cycle

The demetallation step has been proved to be promoted by the presence of TsCl and phenylpyridine. The latter is believed to proceed through a concerted C-H activation-demetallation process (Scheme 5).

Conclusions

The mechanism of the *meta*-sulfonation catalysed by Ru(II) complexes has been subjected to study. This is the first time in which the *meta*-sulfonylated Ru(II) complex **7** has been isolated and fully characterized. This proves that this new catalytic C-H functionalization goes unequivocally *via* the activation of the *para* position to the Ru(II) complex. It has also been demonstrated that complexes **5** and **7** are the active catalytic species which has been shown to be inactive in other catalytic processes. This study reveals that the presence of a *p*-cymene ligand is not crucial for the *meta*-sulfonation of phenylpyridines and it is postulated that the *meta*-sulfonation follows a radical mechanism.

Experimental

General Considerations

All chemicals used were reagent grade and used as supplied unless otherwise specified. HPLC grade acetonitrile (CH_3CN),

and diethyl ether were dried using a solvent purification system (PS-400-7®). ^{1}H and ^{13}C NMR spectra were recorded on Bruker, AV 300, AV 400 or AV 500 spectrometers spectrometer in CD_3CN as solvent, with chemical shifts (δ) were referenced internally to residual protic solvent signal for CD_3CN (1.94 ppm ^{1}H (q), 1.39 ppm ^{13}C (sep)). 2D correlation spectra (gCOSY, gHSQC, gHMBC) were recorded to fully characterise the non-reported ruthenium complexes. Multiplicities are presented as: singlet (s), broad singlet (br s), doublet (d), apparent doublet (app d), doublet of doublets (dd), doublet of doublet of doublets (ddd), triplet (t), triplet of doublets (td), doublet doublet doublet of doublets (dddd), triplet of triplets (tt), quartet (q), quintet (quint.), and multiplet (m). Coupling constants, (*J*) were expressed in Hertz (Hz).

ESI MS were run on an Agilent® 1200 Series LC/MSD. Elemental analysis (C, H, N, S) was run in London Metropolitan University. Analytical thin layer chromatography (TLC) was performed on Merck® silica gel 60 F254 glass or aluminium plates. Organic compounds were visualized by UV (254 nm) irradiation. Flash column chromatography was carried out using forced flow or by gravity of the indicated solvent on Fluka® silica gel 60 (230-400 mesh) or on Acros® neutral aluminium oxide (50-200 μm, 60 Å). All complexes were synthesised using standard Schlenck techniques under nitrogen atmosphere. The precursor catalyst $[RuCl_2(p\text{-cymene})]_2$ was purchased from Strem Chemicals and used without further purification. $[RuCl(PhPy)(p\text{-cymene})]$,[23,26] $[Ru(PhPy)(p\text{-cymene})(CH_3CN)]PF_6$,[23] $[Ru(PhPy)(CH_3CN)_4]PF_6$,[23] D^5-2-phenylpyridine[36] and D^3-2-phenylpyridine[14], 1H-benzo[d][1,2,3]triazol-1-yl 4-methylbenzenesulfonate[37] and 1-tosyl-1*H*-imidazole[38] were prepared according literature methods.

Experimental procedures for the NMR experiments, full characterisation data for all new compounds and crystallographic data (CIF) can be found in the supporting information.

Preparation of $[Ru(TsPhPy)(CH_3CN)_4]PF_6$ (7). A dried Schlenck tube under argon was charged with molecular sieves 4 Å, complex **5** (0.1 g, 0.18 mmol) and dry CH_3CN (1.8 mL). Then, *p*-toluenesulfonyl chloride (67 mg, 0.35 mmol) and oven-dried K_2CO_3 (61 mg, 0.44 mmol) were added. After stirring the reaction mixture overnight at 120 °C, the reaction crude was purified through oven-dried neutral alumina (Al_2O_3) and eluted with CH_3CN. The solution was concentrated under reduced pressure and precipitated with diethyl ether. After filtration and drying, complex **7** was obtained as green solid (66 mg, 52%). Crystals of **7** were grown by vapour diffusion using CH_3CN–Et_2O. ^{1}H NMR (500 MHz, CD_3CN) δ 8.92 (d, *J* = 5.5 Hz, 1H), 8.22 (d, *J* = 8.0 Hz, 1H), 8.14 (d, *J* = 1.8 Hz, 1H), 8.04 (d, *J* = 8.1 Hz, 1H), 7.88 (d, *J* = 8.3 Hz, 2H), 7.81 (td, *J* = 8.0, 1.5 Hz, 1H), 7.49 (dd, *J* = 8.0, 1.9 Hz, 1H), 7.37 (d, *J* = 8.2 Hz, 2H), 7.25 (t, *J* = 6.5 Hz, 1H), 2.50 (s, 3H, CH_3CN), 2.38 (s, 3H), 2.14 (s, 16H, CH_3CN), 1.97 (s, 5H, CH_3CN), 1.96 (s, 3H, CH_3CN). ^{13}C NMR (126 MHz, CD_3CN) δ 201.76, 167.73, 153.96, 149.45, 145.40, 141.64, 140.55, 137.92, 135.27, 131.35, 128.44, 125.52, 123.74, 121.56, 120.02, 118.69, 21.89, 4.75 (CH_3CN), 4.50 (CH_3CN). HRMS-ESI Calcd for $C_{24}H_{23}N_4O_2RuS$: 533.0585 $[M\text{-}CH_3CN]^+$. Found 533.0573. Anal. Calcd for $C_{26}H_{26}F_6N_5O_2PRuS$: C, 43.46; H, 3.65; N, 9.75; Found: C, 43.35; H, 3.75; N, 9.67.

Catalytic reactions. To a nitrogen-purged ampule, $[RuCl_2(p\text{-cymene})]_2$ (21 mg, 5 mol%), $[RuCl(PhPy)(p\text{-cymene})]$ (30 mg, 10 mol%) or $[Ru(PhPy)(p\text{-cymene})(CH_3CN)]PF_6$ (40 mg, 10 mol%) was dissolved in dry CH_3CN (4 mL). Then, phenylpyridine (0.1 mL, 0.70 mmol), K_2CO_3 (0.193 g, 1.4 mmol) and tosyl chloride (0.4 g, 2.1 mmol) were added and the reaction mixture was heated at 120 °C in an oil bath overnight. The reaction crude was filtered over celite using EtOAc as eluent and the resulting mixture was purified by flash chromatography (from 20% EtOAc/hexane to 40% EtOAc) affording **2** as yellowish solid (0.11 g, 50%).

General procedure for the competitive experiments. To a nitrogen-purged ampule, $[RuCl_2(p\text{-cymene})]_2$ (11 mg, 5 mol%) was dissolved in dry CD_3CN (4 mL). Then, phenylpyridine (50 μL, 0.35 mmol), **[D_5]-1** (56 mg, 0.35 mmol), **[D_2]-1** (51 mg, 0.35 mmol) or **[D_3]-1** (55 mg, 0.35 mmol) along with K_2CO_3 (97 mg, 0.7 mmol) and tosyl chloride (0.2 g, 1 mmol) were added. The reaction mixture was heated at 120 °C in an oil bath. The reaction mixture was filtered through a pad of celite and the crude was purified by flash chromatography on silica gel (from 20% EtOAc:hexane to 40% EtOAc).

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29 **Crystal Data** for compound **7**: $C_{30}H_{36}F_6N_5O_3PRuS$, M = 792.74 g mol^{-1}, triclinic, space group P-1 (no. 2), a = 8.2870(1), b = 8.4860(1), c = 25.3050(5) Å, α = 95.062(1), β = 92.854(1), γ = 97.449(1)°, U = 1754.25(5) Å^3, Z = 2, T = 150 K, μ(MoKα) = 0.622 mm^{-1}, D_c = 1.501 g cm^{-3}, 29703 reflections measured (7.162° ≤ 2θ ≤ 55.304°), 7976 unique (R_{int} = 0.0668) which were used in all calculations. The final R1 was 0.0439 ($I > 2\sigma(I)$) and wR2 was 0.0883 (all data). CCDC 1479685 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
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Graphical Abstract

Mechanistic Insight into Ruthenium Catalysed *Meta*-Sulfonation of 2-Phenylpyridine

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The mechanism of the ruthenium catalysed *meta*-sulfonation has been studied and a novel cycloruthenated phenylpyridine complex tosylated at the *para* position to the metal has been structurally characterised.