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Ruthenium-Catalyzed Hydroarylation of Methylenecyclopropanes through C–H Bond Cleavage: Scope and Mechanism

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Abstract: Intermolecular hydroarylation reactions of highly strained methylenecyclopropanes 2-phenylmethylenecyclopropane (**1**), 2,2-diphenylmethylenecyclopropane (**2**), methylenespiropentane (**3**), bicyclopropylidene (**4**), (dicyclopropylmethylene)cyclopropane (**5**), and benzhydrylidenecyclopropane (**6**) through C–H bond functionalization of 2-phenylpyridine (**7a**) and other arenes with directing groups were studied. The reaction was very sensitive to the substitution on the methylenecyclopropanes. Although these transformations involved (cyclopropylcarbinyl)–metal intermediates, substrates **1** and **4** furnished anti-Markovnikov hydroarylation products with complete conservation of all cyclopropane rings in 11–93% yield, whereas starting materials **3** and **5** were inert toward hydroarylation. Methylenecyclopropane **6** formed the products of formal hydroarylation reactions of the longest distal C–C bond in the methylenecyclopropane moiety in high yield, and hydrocarbon **2** afforded mixtures of hydroarylated products in low yields with a predominance of compounds that retained the cyclopropane unit. As byproducts, Diels–Alder cycloadducts and self-reorganization products were obtained in several cases from substrates **1**–**3** and **5**. The structures of the most important new products have been unambiguously determined by X-ray diffraction analyses. On the basis of the results of hydroarylation experiments with isotopically labeled **7a**-[D_5], a plausible mechanistic rationale and a catalytic cycle for these unusual ruthenium-catalyzed hydroarylation reactions have been proposed. Arene-tethered ruthenium–phosphane complex **53**, either isolated from the reaction mixture or independently prepared, did not show any catalytic activity.

Keywords: homogeneous catalysis · C–H activation · hydroarylation · methylenecyclopropanes · ruthenium

Introduction

Transition-metal-catalyzed reactions are indispensable tools in modern synthetic chemistry.[1] Particularly, transition-metal-catalyzed additions of arenes onto C–C multiple bonds, namely, hydroarylation reactions, have received considerable attention as an ecologically and economically friendly approach to the direct functionalization[2] of aromatic C–H bonds. Consequently, a number of valuable protocols for intermolecular hydroarylation reactions of alkenes, alkynes, and allenes have been developed,[3] with ruthenium-catalyzed[4] directed[5] C–H bond functionalization among the most powerful strategies.[6,7]

The chemistry of highly strained methylenecyclopropanes[8] continues to be fascinating because their enhanced reactivities allow fundamental concepts in organic chemistry to be probed and enable the development of novel synthetic methodologies. Thus, metal-mediated or -catalyzed reactions of methylenecyclopropanes have been studied extensively.[9] Notably, these transformations proceeded almost exclusively through the opening of at least one cyclopropane ring,[10] whereas the formation of cyclopropane-containing compounds was observed as a side reaction only. Recently, we have developed the first protocol for intermolecular hydroarylation reactions of highly strained methylenecyclopropanes through C–H bond functionalization[11,12] under ruthenium catalysis.[13] Surprisingly, these reactions occurred with complete conservation of all the cyclopropane rings. Such a formation of functionalized cyclopropane derivatives is unique and important from the viewpoint of both transition-metal catalysis and organic synthesis. To elucidate the synthetic versatility of this transformation and probe the influence of the steric and electronic factors in the arene and methylenecyclopropane substrates, we performed, and report herein, detailed synthetic and mechanistic studies on atom-economical hydroarylation reactions of differently substituted methylenecyclopropanes **1**–**6** through ruthenium-catalyzed C–H bond functionalization of arenes **7**–**11** with various directing groups (Figure 1).

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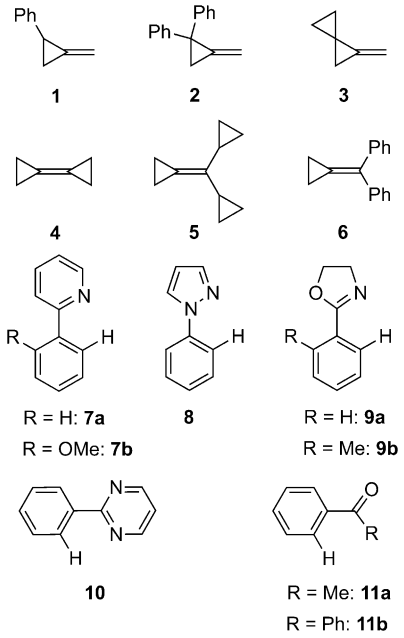
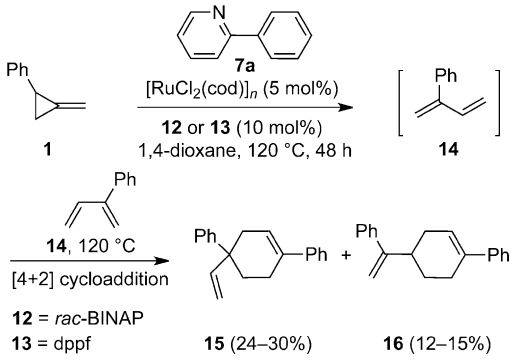


Figure 1. Substituted methylenecyclopropanes **1**–**6** used in hydroarylation reactions through ruthenium-catalyzed C–H functionalization of arenes **7**–**11**.



Scheme 1. Competitive ring-opening reaction of **1** followed by a Diels–Alder [4+2] cycloaddition. BINAP = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl, cod = *cis*-1,4-cyclooctadiene, dppf = 1,1′-bis(diphenylphosphino)ferrocene.

Results and Discussion

Hydroarylation reactions of 2-phenylmethylenecyclopropane (1): Although metal-catalyzed reactions of methylenecyclopropanes have been studied exhaustibly, their hydroarylation reactions through the C–H bond functionalization of arenes have never been probed before. Based on previous reports,[9] one would expect any of the known[14] skeletal reorganization of a cyclopropane moiety to proceed in these transformations as well. Indeed, at the outset of our studies, catalytic amounts of $[\{RhCl(cod)\}_2]$ and PPh_3 quantitatively yielded ring opening of 2-phenylmethylenecyclopropane (**1**) into a buta-1,3-diene derivative—presumably through initial hydroruthenation of the C=C bond with subsequent elimination of the cyclopropane β-carbon atom and final β-hydrogen elimination[15]—followed by polymerization, even at 50 °C. Upon testing hydroarylation reactions of substrate **1** with pyridine **7a** and by employing $[\{RuCl_2(cod)\}_n]$ as the precatalyst modified with a representative set of commonly used ligands,[11] application of triarylphosphanes as *rac*-BINAP (**12**) or 1,2-bis(diphenylphosphino)ethane (dppe; **13**) as ligands resulted only in the formation of undesired products **15** and **16** due to Diels–Alder [4+2] cycloaddition reactions of the intermediate 2-phenylbuta-1,4-diene (**14**; Scheme 1). Furthermore, starting material **7a** was reisolated in virtually quantitative yield.

On the contrary, more selective catalysis was achieved under otherwise identical reaction conditions, when more the sterically hindered ligands P(*o*-biphenyl)(*t*Bu)$_2$ (JohnPhos; **17**) or dicyclohexyl-(2′,4′,6′-triisopropylbiphenyl-2-yl)-phosphane (X-Phos; **18**)[16] were employed in the hydroarylation of **1** with phenylpyridine **7a**, thus giving rise to new product **19a**, with phosphane X-Phos (**18**)[16] being superior.

Detailed NMR spectroscopic studies proved the structure of the newly formed product to be 2-{[2-(*cis*-2-phenylcyclopropyl)methyl]phenyl}pyridine (**19a**; Table 1, entries 1–3). Remarkably, the anti-Markovnikov addition of arene **7a** occurred with complete conservation of the three-membered ring, thus yielding cyclopropane derivate **19a** highly selectively. Such reactivity is rather unusual for methylenecyclopropanes under transition-metal catalysis.[9,10]

With an active and selective catalyst in hand, we studied its application to the challenging hydroarylation of **1** through C–H bond functionalization on arenes **7**–**11** (Table 1). Under the optimized reaction conditions, substrate **7b** was converted into the corresponding *cis*-adducts **19b** in even greater yield (78%) with excellent chemo- and site-selectivity (Table 1, entry 4). Analogous hydroarylation reactions with arenes **8**–**11**, which possess different directing groups, appeared to be less efficient (Table 1, entries 5–10). Interestingly, hydroarylation products were also not formed in the attempted reaction of substrate **1** with acetophenone (**11a**) under recently reported reaction conditions.[7a] Yet, it is important to note that all of the isolated hydroarylation products **19a**, **19b**, **20**, and **21b** contained a conserved cyclopropane moiety. In spite of the fact that no special kinetic measurements were performed, it should be mentioned that the attempted hydroarylation of **1** with **7a** with 2.5 mol% of the ruthenium precatalyst or upon heating for 20 hours only resulted in the formation of **19a** in 28 and 25% yield, respectively (Table 1, entry 11). This outcome can be interpreted in favor of a first-order reaction with respect to [Ru].

For the pyridine **19b**, *cis* substitution on a cyclopropane ring and the conservation of the ring during C–H bond functionalization were unambiguously established by X-ray diffraction analysis of its *para*-toluenesulfonate **19b**·*p*-TsOH (Figure 2).

Substitution on the cyclopropane ring: Incorporation of a second phenyl group into the phenylmethylenecyclopropane moiety resulted in a drastic decrease of its reactivity toward

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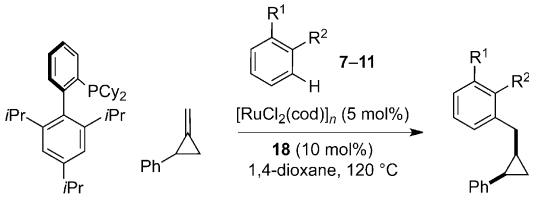
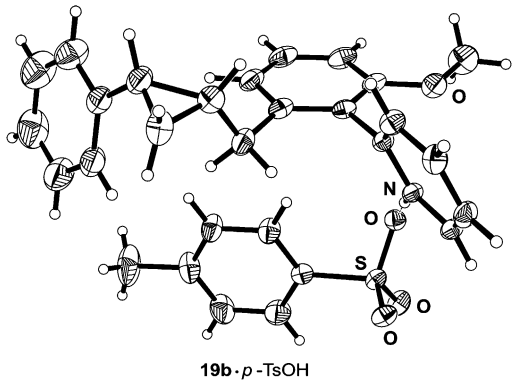
Table 1. Ruthenium-catalyzed hydroarylation reactions of methylenecyclopropane **1** with arenes **7–11**.[a]



18 **1** **19–22**

Entry	Arene	R^1	R^2	Product	Yield of arene [%]	Yield of products **19–22** [%]
1[b]	**7a**	H		**19a**	53	46
2	**7a**	H		**19a**	39	53
3[c]	**7a**	H		**19a**	40	54
4	**7b**	OMe		**19b**	18	78
5	**8**	H		**20**	75	19
6	**9a**	H		**21a**	96	–
7	**9b**	Me		**21b**	63	29
8	**10**	H		**22**	90	< 5
9	**11a**	H		–	95	–
10	**11b**	H		–	97	–
11	**7a**	H		**19a**	65 64	28[d] 25[e]

[a] Reaction conditions: **1** (3 equiv),[17–20] **7–11** (1–2 mmol), [{$RuCl_2$(cod)}$_n$] (5 mol%), **18** (10 mol%), 1,4-dioxane (3 mL), 120 °C, 48 h. [b] P(*o*-biphenyl)(*t*Bu)$_2$ (**17**) as the ligand. [c] *N*-methylpyrrolidone (3 mL) as the solvent. [d] 2.5 mol% of [{$RuCl_2$(cod)}$_n$]. [e] Reaction time 20 h.



19b·*p*-TsOH

Figure 2. Molecular structure of pyridine *para*-toluenesulfonate **19b**·*p*-TsOH in the crystal.

hydroarylation and partially changed the mode of reactivity (Scheme 2). Thus, along with the formation of products that retained the cyclopropane moiety (i.e., **23a**,**b**) in low yields and three unidentified minor hydroarylation products, traces of pyridine **24a** were also observed. This latter compound corresponds to formal hydroarylation of the distal C–C bond (with respect to the methylene group) of the cyclopropane fragment in **2**. Moreover, the product of the ruthenium-catalyzed self-reorganization of **2**, namely, 2-methylene-1-phenylindane (**25**), was formed as a major component of the reaction mixture.

Spirocyclopropanation of a cyclopropane moiety caused inertness of methylenespiropentane **3** in hydroarylation reactions under the optimized reaction conditions. In this case, the ruthenium complex only initiated the rearrangement of substrate **3** into triene **26** by initial hydroruthenation of the C=C bond followed by elimination of the cyclopropane β-carbon atom and final β-hydride elimination.[21] A [4+2] cycloaddition reaction of intermediate **26** afforded tetraene **27** in moderate yield (Scheme 2). The relative reactivity of methylenecyclopropanes **2** and **3** highlights the importance of steric factors in the hydroarylation reactions. Hence, presumably, at least one side of the cyclopropane plane should be available for an approach by the bulky ruthenium complex.

Substitution at the methylene moiety: Replacement of a methylene group in methylenecyclopropane with a cyclopropylidene moiety results in an increased efficiency within the ruthenium-catalyzed hydroarylation reactions, but does not influence the mode of reactivity. This behavior was demonstrated in hydroarylation reactions of highly strained bicyclopropylidene (**4**)[22] with arenes **7–11** under identical reaction conditions. As in the case of methylenecyclopropane **1**, no reactions of substrates **9a**, **11a**, and **11b** were observed. However, compounds **7a**, **7b**, **8**, **9b**, and **10** demonstrated improved results (Table 2). Thus, under the optimized reaction conditions, **7a** was quantitatively converted into a mixture of mono- and dialkylated pyridines **28a** and **29**, which were isolated in 33 and 60% yield, respectively, whereas **28b** was obtained from **7b** in an improved yield of the isolated product.

Importantly, X-ray diffraction analyses of these newly formed products **28a**, **28b**, **29**, and **31b** (the latter as its *para*-toluenesulfonate species) revealed that all three-membered rings were conserved during the C–H bond functionalization reactions (Figure 3).[23] The bicyclopropyl fragments in molecules **28a**, **28b**, **29**, and **31b** do not contain any abnormal bonds and all the compounds adopted typical[8a] *gauche* (*synclinal*) conformations with the torsion angle ϕ C(Ph)-C(Cp)-C(Cp)-H, which describes the mutual orientation of two adjacent cyclopropane rings, in the range 51.6–59.3°. Short intramolecular C-H···N (C-H···O in **31b**) contacts between tertiary hydrogen atoms of bicyclopropyl moieties and nitrogen or oxygen atoms of the heterocycles were found in all four molecules (H···O: 2.543 in **28a**, 2.716 in **28b**, 2.447 and 2.704 in **29**, and 2.489 Å in **31b**). These distances might be regarded as weak hydrogen bonds. The conformations of the molecules in the crystals must result in each case from energetic compromises between these hydro-

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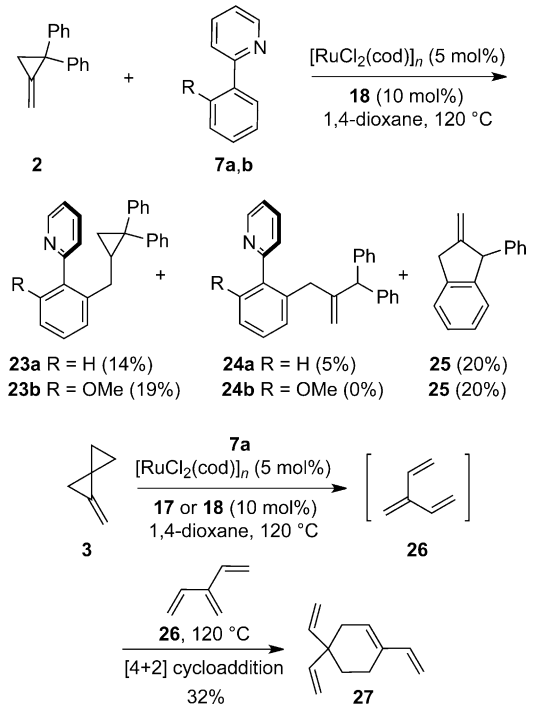
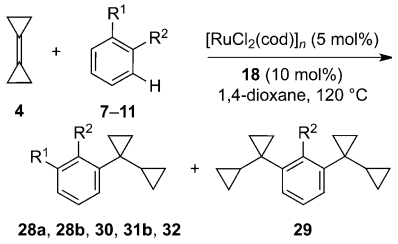


Scheme 2. Ruthenium-catalyzed hydroarylation reactions of substrates **2**

Table 2. Ruthenium-catalyzed hydroarylation reactions of bicyclopropylidene **4** with arenes **7**–**11**.[a]



Entry	Arene	R^1	R^2	Products	Yield of arene [%]	Yield of products [%]
1	**7a**	H		**28a** **29**	0	33 60
2[b]	**7a**	H		**28a** **29**	9	65 28
3	**7b**	OMe		**28b**	0	85
4	**8**	H		**30**	65	21
5	**9a**	H		–	95	0
6	**9b**	Me		**31b**	54	40
7	**10**	H		**32**	82	11
8	**11a**	H		–	97	–
9	**11b**	H		–	96	–

[a] Reaction conditions: **4** (3 equiv), **7**–**11** (1–2 mmol), [{$RuCl_2$(cod)}$_n$] (5 mol%), **18** (10 mol%), 1,4-dioxane (3 mL), 120 °C, 48 h. [b] Compound **17** (10 mol%) as the ligand.

gen bonding, conjugation effects, and intramolecular van der Waals interactions between hydrogen atoms and crystal-packing effects.

Thus, the angles between the planes of the pyridine and benzene moieties in the more sterically congested compounds **28b** (79.4) and **29** (71.7°) are higher than those angles in **28a**, with one bicyclopropyl fragment (55.1°). This finding holds true for the angles between the planes of the benzene ring and the adjacent three-membered ring of the bicyclopropyl core in **28b** (122.6°), **29** (123.8 and 120.3°), and **28a** (118.4°). Broadening of signals of the methylene carbon atoms in the ^{13}C NMR spectrum of **29** (see below) indicates an increased rotation barrier for the bicyclopropyl moieties in solution as well. In all four structures, the molecules are linked by C-H···π interactions, and the shortest C-H···C distances are 2.764, 2.941, 2.779, and 2.615 Å in **28a**, **28b**, **29**, and **31b**, respectively. Interestingly, no stacking π···π interactions were observed in structures **28a**, **28b**, and **29**, and such contacts between the benzene rings of the adjacent molecules are present only in **31b**, probably due to replacement of the pyridine ring by the less-bulky dihydrooxazole ring.

Surprisingly, replacement of a methylene group in methylenecyclopropane with a dicyclopropylmethylene fragment completely inhibited hydroarylation under ruthenium catalysis in methylenecyclopropane **5**.[24] In contrast, diphenylation of a methylene moiety, as in benzhydrylidenecyclopropane (**6**), increased the reactivity of the methylenecyclopropane moiety, but drastically changed the mode of reaction. Hence, in each case the major products **33** and **35** correspond to formal hydroarylation reactions of the longest[22a] distal C–C bond in cyclopropane in **6** (Scheme 3). This outcome indicates that the mechanisms of hydroarylation reactions of alkenes **1** and **4** and of benzhydrylidenecyclopropane (**6**) are different at the rate-limiting step, likely because of the delocalizing effects of the bulky phenyl substituents in the latter case.

X-ray crystal analysis of these newly formed pyridines **33a**, **33b**, and **35** (the latter as its *para*-toluenesulfonate) confirmed their structures as products with an unusual type of ring opening[12] from starting material **6** (Figure 4).

As side products of the transformation of substrate **6**, significant amounts of 4-phenyl-1,2-dihydronaphthalene (**36**) and traces of 4-chloro-1,1-diphenyl-but-1-ene (**37**) were isolated (Scheme 3). Presumably, intermediate **34**, initially formed by hydroruthenation of the C=C bond in **6**, is prone to elimination of the cyclopropane β-carbon atom to give intermediate **38**. The latter can either undergo intramolecular C–H insertion[15b,g] with the neighboring phenyl ring followed by elimination or direct elimination of the ruthenium atom to afford product **37**.

Mechanistic rationale for ruthenium-catalyzed hydroarylation reactions of methylenecyclopropanes: Because the high selectivity of our novel ruthenium catalyst enabled C–H bond functionalization to occur with either an unprecedented retention of the cyclopropane moiety or, in rare cases,

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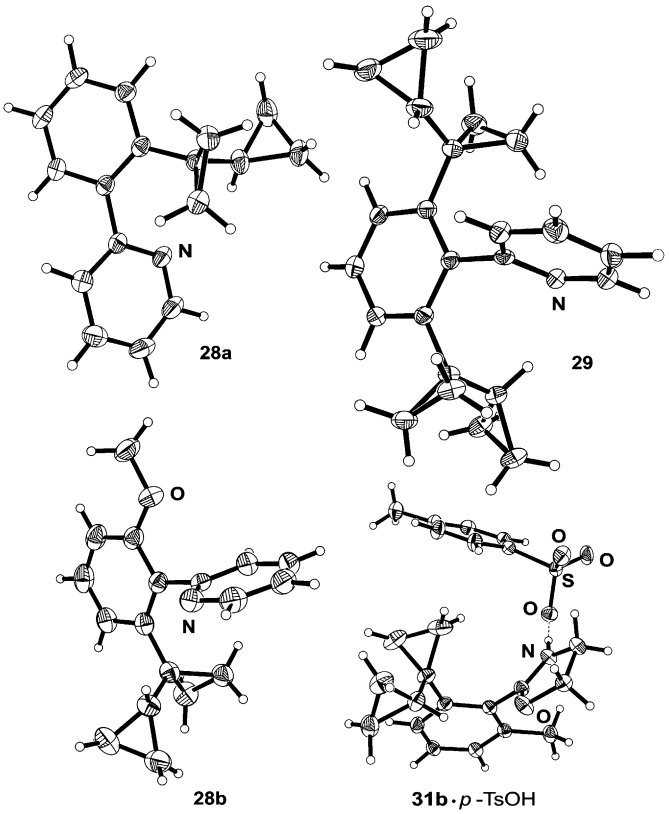
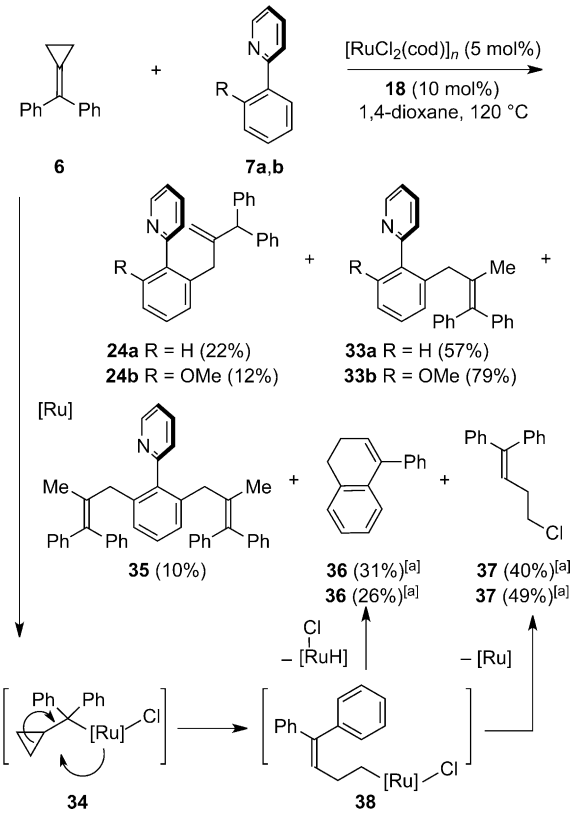


Figure 3. Molecular structures of pyridines **28a**, **28b**, **29**, and oxazoline *para*-toluenesulfonate **31b**·*p*-TsOH according to X-ray crystal studies.[23]

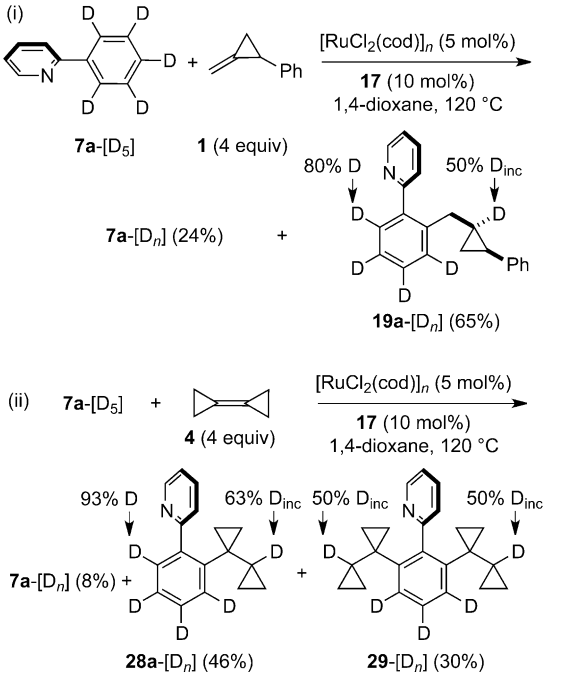


Scheme 3. Ruthenium-catalyzed hydroarylation reactions of substrates **6** with arenes **7a** and **7b**. [a] Yields based on [{$RuCl_2(cod)$}$_n$].

with complete opening of the cyclopropane ring, we became interested in testing its working mode. Indeed, the efficiency of these reactions did correlate neither with the basicity of the directing group (pK_a = 5.37, 1.28, and 14.18 for pyridine, pyrimidine, and 1*H*-pyrazole, respectively)[25] nor with the known first ionization energies of the alkenes (9.10, 8.93, and 8.25 eV for **3**–**5**, respectively).[26] To shed light on the mechanism of these hydroarylation reactions, we subjected deuterium-labeled pyridine **7a**-[D_5] to the optimized reaction conditions for the hydroarylation of alkenes **1**, **4**, and **6** (Schemes 4 and 5). Ratios of [D_3]/[D_5] isotopomers for the adducts were obtained by ^{1}H NMR spectroscopic and mass-spectrometric (ESI) analysis (see the Supporting Information).

Interestingly, deuterium incorporation into the cyclopropane moiety of products **19**-[D_n], **28**-[D_n], **29**-[D_n], **24**-[D_n], and **35**-[D_n] was only 50, 63, 50, 65, and 61%, respectively. Moreover, the recovered starting material revealed a regioselective deuterium/proton exchange in the *ortho* position of pyridine **7a**-[D_5],[27] and the content of incorporated hydrogen (23–90%) into [D_3]/[D_5] isotopomers depended mainly on the reaction time (see the Supporting Information).

Notably, hydroarylation of alkenes **1**, **4**, and **6** with pyridine **7a**-[D_5] highlighted a regioselective deuterium/proton exchange as well, thus indicating that C–H bond metalation is not rate limiting (Schemes 4 and 5). When using DMF-



Scheme 4. Ruthenium-catalyzed hydroarylation of alkenes **1** and **4** with pyridine **7a**-[D_5] (D_{inc} = ^{2}H incorporation).

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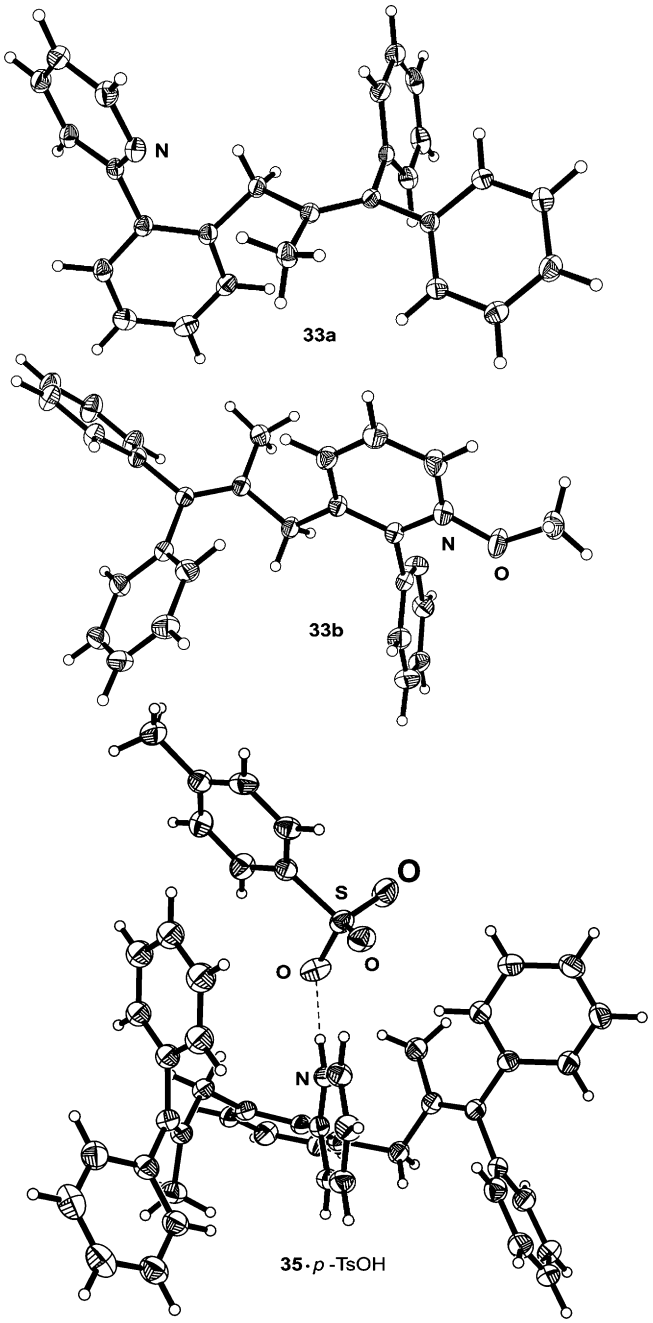
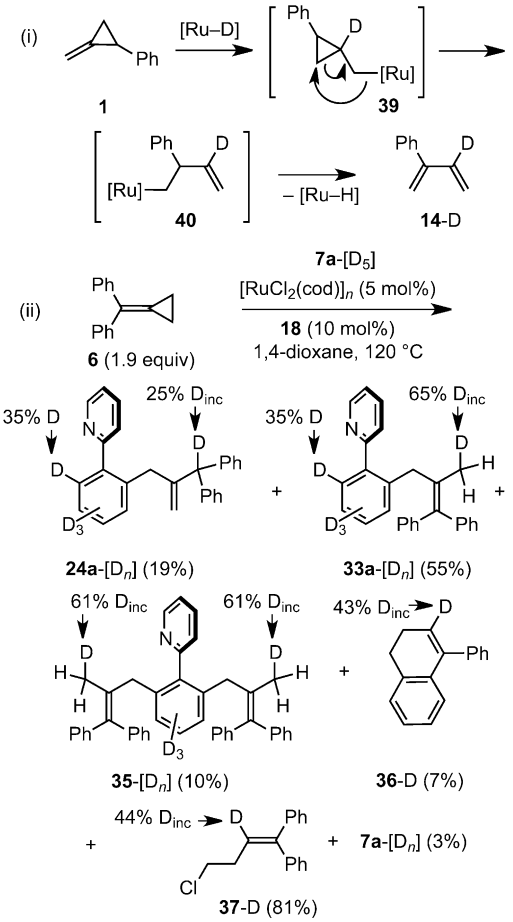


Figure 4. Molecular structures of pyridine **33a**, **33b**, and pyridine *para*-toluenesulfonate **35**·*p*-TsOH according to X-ray crystal studies.[23]

[D_7] as the solvent, the proton/deuterium exchange was not observed for pyridines **7a** and **19** under otherwise identical reaction conditions. Most likely, in the deuterium/proton exchange reactions, starting materials **1**, **4**, and **6**, respectively, served as proton donors. Thus, ruthenium-catalyzed reorganization (Schemes 3 and 5) through initial hydroruthenation of the C=C bond in **1** and **6** followed by elimination of the cyclopropane β-carbon atom and final β-hydride elimination from intermediates **38** and **40**[15] replaced [RuD] with the [RuH] species.



Scheme 5. Ruthenium-catalyzed hydroarylation of alkene **6** with pyridine **7a**-[D_5].

In our first attempt to prove this hypothesis, the reaction of substrates **1** and **7a**-[D_5] with dppf (**13**) as the ligand resulted in isolation of Diels–Alder adducts **15** and **16** (Scheme 1), which did not contain any deuterium, and recovery of **7a**-[D_5] demonstrated a deuterium/proton exchange of less than 5%.

From the reaction mixture obtained from substrate **7a**-[D_5] and methylenespiropentane **3** (Scheme 2), 1,4,4-trivinylcyclohexene (**27**-D) was isolated, which did contain deuterium at the methyne positions of the double bonds according to the ^{1}H NMR and mass spectra (see Supporting Information). Fortunately, formation of the deuterium-labeled 4-phenyl-1,2-dihydronaphthalene (**36**-D_n) and of 4-chloro-1,1-diphenyl-but-1-ene (**37**-D_n) (Scheme 5) undoubtedly demonstrated the alkenes to be the proton donors in deuterium/proton exchange reactions.

Based on our mechanistic studies, we propose the following mechanistic rationalization depicted in Schemes 6 and 7. Coordination of the catalytically competent ruthenium complex **41** initiates the rapid and reversible C–H bond metalation, thus providing ruthenacycle **43**. Subsequently, cyclometalated complex **43** adds to a double bond or, alternatively, to a distal bond of methylenecyclopropane **44** to yield inter-

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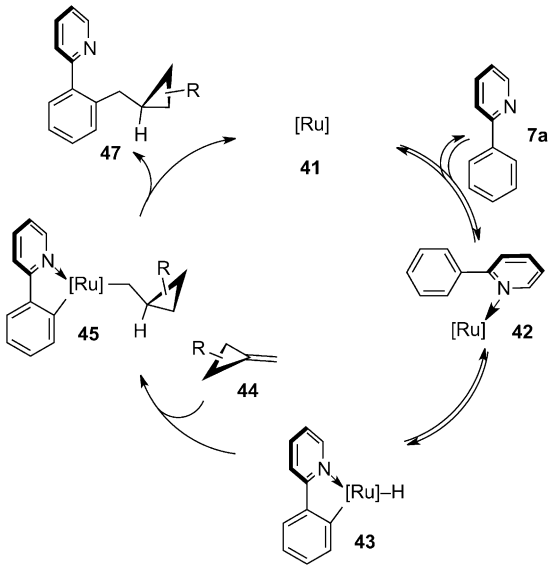
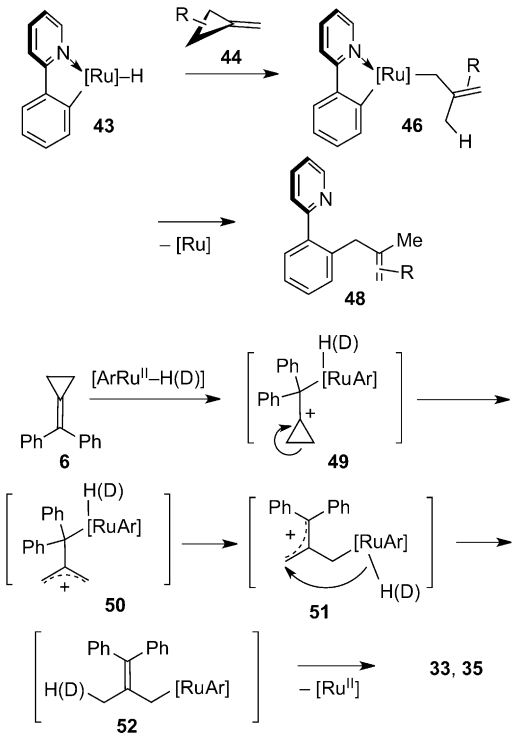


Scheme 6. Proposed catalytic cycle for Ruthenium-catalyzed hydroarylation reactions of methylenecyclopropanes **44** with the conservation of the three-membered ring.



Scheme 7. Proposed mechanistic rationalization for Ruthenium-catalyzed hydroarylation reactions of methylenecyclopropanes **44** with cyclopropane ring opening.

mediates **45** (Scheme 6) or **46** (Scheme 7), respectively. Reductive elimination of the latter compound affords products **47** or **48**, respectively, thereby regenerating the catalytically active species **41**. In the case of intermediate **45**, the rate of the final reductive elimination in the catalytic cycle is at least of the order as the rate observed for the well-known, very fast rearrangement of (cyclopropylmethyl)–metal to homoallyl–metal.[9e,15,28] The latter reorganization, along with a subsequent β-hydride elimination, results in the formation of buta-1,3-dienes as byproducts according to mechanism discussed above (Scheme 5i), which accounts for the observed deuterium/proton exchange reactions with **7a**-[D_5] as the substrate. The detailed mechanism of the hydroruthenation of a distal bond in methylenecyclopropanes can only be speculated on. However, by taking into account the unusual type of ring opening and distribution of the deuterium label, it is most likely that this transformation proceeds in several steps with the participation of cyclopropyl cationic intermediates (Scheme 7). These latter species undergo ring-opening reactions to form allylic cations almost without energetic barriers and are typical reactions for methylenecyclopropanes,[26b,29] for example, chloropalladation reactions.[30] According to this process, two phenyl groups in **6** promote a stepwise addition of [RuH] species onto a double bond of **6** with an initial formation of the half-opened or closed[29a] carbocation **49**, which rearranges to intermediate **50** and then to the more-stable carbocation **51**. Hydride transfer in this latter compound followed by reductive elimination of **52** furnishes products of the type **33** or **35**. Hydride transfer to the benzhydrilic position in **52** and reductive elimination can afford compounds of the type **24**. However, by taking into consideration the low deuterium content in **24**-[D_n], formation of the latter can better be explained through isomerization of **33** through addition/elimination of [RuH] ([RuD]) intermediates.

The exact structure of the catalytically competent ruthenium complex **41** demands further elucidation. The high selectivity obtained with monophosphane biphenyl ligands **17** and **18** could probably be explained by the formation of arene-tethered ruthenium–phosphane complexes. A number of such complexes has previously been synthesized.[31] Indeed, in several hydroarylation reactions, traces of air- and moisture-stable ruthenium complexes have been isolated (see the Experimental Section), and X-ray diffraction analysis revealed the structure of dichloro[η^6:η^1-dicyclohexyl-(2′,4′,6′-triisopropylbiphenyl-2-yl)phosphane]ruthenium(II) (**53**; Figure 5).

Complex **53** has also been prepared independently from [{$RuCl_2$(cod)}$_n$] and X-Phos in virtually quantitative yield by adapting a modified reported procedure,[32] and X-ray diffraction analysis confirmed the structure of **53a**. Unfortunately, complex **53** did not demonstrate catalytic activity in our hydroarylation reactions. Heating a solution of **4** in $CDCl_3$ in the presence of **53a** (5 mol%, 70 °C, 96 h) also caused no reorganization of **4**.[33]

Conclusions

We have developed the first protocol for intermolecular hydroarylation reactions of highly strained methylenecyclopropanes through C–H bond functionalization. Notably, this re-

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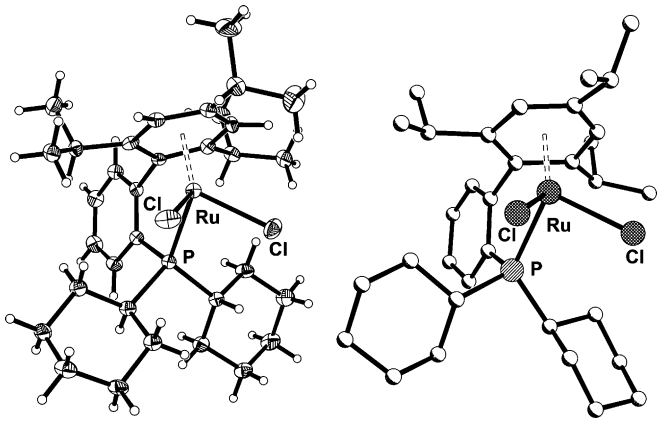

Figure 5. Molecular structure of **53** according to X-ray crystal studies.[23] ORTEP (left) and ball-and-stick (right) presentations.

action is very sensitive to the substitution pattern on methylenecyclopropane. Although these transformations involved (cyclopropylcarbinyl)–metal intermediates, in most cases these hydroarylation reactions resulted in complete retention of the cyclopropane moieties in the products. Even minor steric hindrance on the cyclopropane fragment, however, drastically decreased the yields of the hydroarylation products. This unique reactivity pattern is a strong testament to the mild reaction conditions of ruthenium-catalyzed C–H bond functionalization. In several rare cases, however, an unusual mode of ring opening of the cyclopropane moiety, which corresponds to formal hydroarylation reactions of the longest distal C–C bond in cyclopropane fragment, was observed.

Acknowledgements

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[24] This result is unexpected in view of an attempted reaction in the presence of H_2O (1 equiv) under otherwise identical reaction conditions; tricyclopropylmethanol was isolated in 43% yield (see the Supporting Information) through the ruthenium-catalyzed hydratation of **5** with retention of all three cyclopropane rings.

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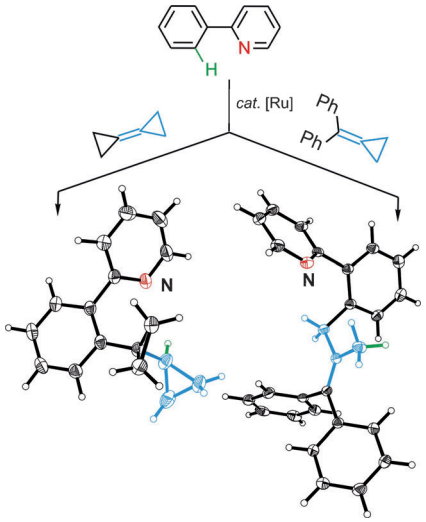
A highly chemo- and site-selective ruthenium catalyst has achieved intermolecular hydroarylation reactions of methylenecyclopropanes (see scheme) through chelation assistance. The C–H bond functionalization of 2-phenylpyridine and other arenes with directing groups has been studied. Furthermore, a plausible mechanistic rationale and a catalytic cycle for these unusual ruthenium-catalyzed hydroarylation reactions are proposed.



Catalytic Hydroarylation

L. Ackermann, S. I. Kozhushkov, D. S. Yufit* ..... ▮▮▮▮–▮▮▮▮

Ruthenium-Catalyzed Hydroarylation of Methylenecyclopropanes through C–H Bond Cleavage: Scope and Mechanism

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