Soft Ruthenium and Hard Brønsted Acid Combined Catalyst for Efficient Cleavage of Allyloxy Bonds. Application to Protecting Group Chemistry.

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ABSTRACT

We show that a monocationic CpRu(II) complex of quinaldic acid (QAH) and a monocationic CpRu(IV)(-allyl)QA complex catalyze efficient cleavage of the allyloxy bond in allyl ethers, allyl esters, allyl carbonates, and allyl carbamates in methanol without the need for additional nucleophiles. The only co-product is volatile allyl methyl ether, enhancing operational simplicity during isolation of the deprotected alcohols, acids, and amines. This clean and high-performance catalytic system should contribute to protecting group chemistry during the multistep synthesis of pharmaceutically important natural products. Full details of this system, including the mechanism, are reported.

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1. Introduction

Protecting groups (PGs) are the unsung heroes or heroines of chemistry. This detail is barely acknowledged in the retrosynthetic analysis of complicated natural and unnatural products, but it would not be too strong to say that accomplishing total synthesis is impossible without PGs, even in the 21st century with its variety of highly sophisticated synthetic methods.¹ **Fig. 1** illustrates the general process for the protection of a function, **A**, in the conversion of **B** to **Z**. As is standard, **A** is first protected by a PG (red circle), and then the function **B** is subjected to a series of target reactions. Finally, **A** is deprotected by the action of reagents (black sphere) to give the desired product together with the co-product. High stability of the PG under various reaction conditions, as well as facile and chemoselective removal of the PG on demand, is essential. Furthermore, easy separation of the excess reagent and accompanying co-product from the desired product is also required. These requirements become even more stringent during the synthesis of polar biomolecular compounds such as peptides, nucleotides, and polysaccharides.

Among more than a thousand PGs invented so far, we have revisited the allyl (All) group for protecting an alcohol as an allyl ether, which has a structure as simple as that of an acetyl group and has higher stability toward both acidic and basic conditions. This chemical stability, however, often causes difficulty in

Fig. 1. Protecting group (PG) chemistry and the utility of allyl PG for alcohols in organic synthesis. i) Protection. ii) Target function transformation from **B** to **Z**. iii) Deprotection. Red circle: protecting group. Black sphere: reagent for deprotection. Black sphere in red circle: co-product.

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deprotection or deallylation under mild conditions. As shown in **Fig. 1a**, the most popular approach to deprotection is Corey's method.² $\text{RhCl}(\text{P}(\text{C}_6\text{H}_5)_3)_3$ catalyzes a 1,3-hydrogen shift of the allyl ether to the corresponding alkenyl ether, which is then either hydrolyzed under acidic conditions or oxidatively cleaved. $[\text{Ir}(\text{P}(\text{C}_6\text{H}_5)_2(\text{CH}_3))_2(\text{cod})]\text{PF}_6$ reported by van Boom in 1980 shows higher catalytic performance.³ The types of one-step deprotection shown in **Fig. 1b** and **Fig. 1c** are simple, and many methods have been invented on the basis of Tsuji's Pd-allyl chemistry,⁴ Ni-allyl chemistry,⁵ and Os-catalyzed oxidative cleavage.⁶

A major disadvantage common to all of these methods is that an excess amount of acids, bases, oxidizing reagents, or reducing reagents is required, complicating the reaction system. The ideal approach would clearly be the "No additive, One step," process shown in **Fig. 1b**, but such a catalytic system has not been attained. We therefore aimed to develop an optimal process that performs direct cleavage of the allyl ether under very mild conditions, and ultimately attained a monocationic CpRu(II) complex of quinaldic acid (QAH) and a monocationic CpRu(IV) (-allyl)QA complex. The present article describes full details of the screening results establishing CpRu⁺/QAH-catalyzed deallylation/allylation⁷ and a mechanistic study of this process.

2. Results and discussion

2.1. Catalyst design concept

We previously established a leading concept for the design of a molecular catalyst, "intramolecular metathesis-type donor-acceptor bifunctional catalyst" (Intramol-MDACat), via the detailed mechanistic study of catalytic asymmetric 1,2-addition of diorganozincs to aldehydes.⁸ This concept realized a new type of asymmetric reaction including reduction,⁹ 1,4-addition of diorganozincs to enones,¹⁰ and others.¹¹ Furthermore, the Intramol-MDACat concept has been extended to "Intermol-MDACat" and to a "soft transition metal/hard Brønsted acid-combined catalyst" to achieve the efficient asymmetric hydrogenation of α -keto esters.¹²

With this approach in mind, we designed a concept catalyst for allyloxy bond cleavage on the basis of a "intramolecular redox-mediated donor-acceptor bifunctional catalyst" (Intramol-RDACat), as shown in **Fig. 2**. Here, the central transition metal $\text{M}(n)$ is coordinated by $\text{L}_s\text{-L}_h\text{H}$ (L_s , soft ligating atom; L_h , hard ligating atom) and a monoanionic and highly electron-donative η^5 -cyclopentadienyl (Cp) ligand, endowing the M complex with a soft coordination site and a hydrogen-bond donor site. In this soft M/hard H^+ combined system, the hard oxygen atom of an allyl ether substrate would interact with H^+ , while the soft C=C double bond would coordinate to M as a π -ligand. Enhancement of the electrophilicity or acceptability of the allyl moiety synergistically cooperates with the high nucleophilicity or donicity of the CpM(n) moiety, thereby facilitating movement of the substrate/catalyst complex to a $\delta^+ \text{---} \delta^- \text{---} \delta^+ \text{---} \delta^-$ charge-alternating transition state involving M(n) oxidation. Such stabilization of the transition state would result in easy generation of the corresponding π -allyl CpM($n+2$) moiety. In addition, introduction of Cp and the bidentate property of $\text{L}_s\text{-L}_h\text{H}$ should prevent self-aggregation of the catalyst, which often causes catalyst deactivation. Lastly, if the π -allyl complex can react with CH_3OH , which could be used as a possible solvent, the CpM($\text{L}_s\text{-L}_h\text{H}$) catalyst would be regenerated alongside liberation of the deprotected alcohols and allyl methyl ether (CH_3OAll) as the co-product, which could be easily removed simply by

evaporation. This concept catalyst would be applicable to allyl esters, allyl carbonates, and allyl carbamates.

Fig. 2. Concept catalyst designed on the basis of "intramolecular redox-mediated donor-acceptor bifunctional catalyst (Intramol-RDACat)." L_s : soft ligating atom. L_h : hard ligating atom.

2.2. Screening of $\text{L}_s\text{-L}_h\text{H}$ ligands

Initially, the central metal was selected as Ru(II) in $[\text{RuCp}(\text{CH}_3\text{CN})_3]\text{PF}_6$ (**1**) on the basis of our finding in 2002 that $[\text{RuCp}(\text{P}(\text{C}_6\text{H}_5)_3)(\text{CH}_3\text{CN})_2]\text{PF}_6$ prepared from **1** and $\text{P}(\text{C}_6\text{H}_5)_3$ catalyzes the allyloxy bond cleavage of allyl esters.¹³ The catalyst screening was combinatorially conducted by using the customized automated synthesizer Chemspeed,¹⁴⁻¹⁵ which has five reaction blocks each containing 16 reaction vessels, and can be used under an inert Ar atmosphere. Forty-eight commercially available ligands L1–L48 (except for L36), used in a combination of L_s (sp^3P , sp^2N , sp^3N , and others) with L_hH (COOH , OH , NH_2 , and no proton), were screened simultaneously under the following ideal conditions for alcohol deprotection: $[\text{C}_6\text{H}_5\text{-CH}_2\text{CH}_2\text{OCH}_2\text{CH=CH}_2$ ($\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{OAll}$ (**2**))] = 100 mM; [**1**] = 1 mM; [$\text{L}_s\text{-L}_h\text{H}$] = 1 mM; solvent, CH_3OH ; 30 °C; 3 h. The Chemspeed system automatically mixed the CH_3OH solutions of the $\text{L}_s\text{-L}_h\text{H}$ ligands, **1**, and $\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{OAll}$ (**2**) in the reaction vessels, and sampled the reaction mixtures in a programed way. GC analysis was used to determine the yields of deprotected alcohol **3** and 1,3-hydrogen shift side product **4** (column, DB-WAX (0.25 mm x 15 m) as follows: temp., 50 °C + 10 °C/min; t_R , 6.0 min (**2**), 4.0 min (**3**), and 4.5 min (**4**)). **Fig. 3** shows the results. 2-Pyridinecarboxylic acid (PAH; PA indicates 2-pyridinecarboxylate) quantitatively afforded **3**. 8-Hydroxyl quinoline derivatives also showed some acceleration effect. Sulfides and azoles showed almost no reactivity, and phosphines tended to isomerize the allyl group to the corresponding alkenyl ether **4**.

As shown in **Table 1**, the ligand structure–reactivity relationship was further investigated by shortening the reaction time to 1 h using the particularly highly reactive PAH as the starting point (entry 1). Neither pyridine nor benzoic acid, nor a 1:1 mixture of pyridine and benzoic acid showed an acceleration effect (entries 2–4). No reaction proceeded when the location of COOH in PAH was changed from C(2) to C(3) or C(4) (entries 5 and 6) or when H^+ was removed from PAH as PANa (sodium 2-picolinate) or PACH_3 (methyl 2-picolinate) (entries 7 and 8). Replacement of the carboxyl group with a hydroxymethyl or aminomethyl group also resulted in no reaction, although a proton is located in the same position as the carboxyl group (entries 9 and 10). Quinoline-8-carboxylic acid, in which the sp^2N atom and H^+ are located in a 1,6 manner rather than the 1,5 manner of PAH, showed no reactivity (entry 11). The presence of an electron-withdrawing substituent at the C(4) position of the pyridine ring of PAH tended to increase the reactivity with values of 27% (4- CH_3O), 39% (4-H), 50% (4-Cl), 54% (4- CF_3), and 59% (4- NO_2) (entries 1 and 12–15). Introduction of $\text{PO}(\text{OH})_2$ ($\text{p}K_a$ ca. 1.5) instead of COOH ($\text{p}K_a$ ca. 5.4) in PAH enhanced the reactivity; however, further increasing the acidity by replacing COOH with SO_3H ($\text{p}K_a$ ca. –3) resulted in deceleration (entries

Fig. 3. Screening of L_s - L_h H under ideal conditions of $[2] = 100$ mM; $[1] = 1$ mM; $[L_s-L_hH] = 1$ mM; CH_3OH ; 30 °C; 3 h. The x-coordinate shows the functional group of L_h moiety. "None" indicates no functional group. The y-coordinate corresponds to L_s moiety such as sulfide, azole, amine, pyridine, and phosphine. The vertical axis shows the % yields of the products (light blue-colored bar for the desired phenylethyl alcohol (**3**), and the purple bar for the undesired 1,3-hydrogen shift product (**4**). The structures of efficient ligands were drawn in the graph. For the structures of other ligands, see Experimentals. The numbers 1–48 in the graph correspond to L1–L48.

16 and 17) (*vide infra*). Fusion of a benzene ring at C(3)/C(4) or C(4)/C(5) of PAH led to deceleration, while the most impressive enhancement in reactivity was attained with quinaldic acid (QAH, 2-quinolinecarboxylic acid; QA indicates 2-quinolinecarboxy-late), in which a benzene ring is fused at C(5) and C(6) of PAH (entries 18–20); in this case, the reaction was completed within 1 h. The results in **Table 1** clearly indicate

Table 1. Ligand structure-reactivity relationship in the deallylation of $C_6H_5CH_2CH_2OAl$ (**2**) to $C_6H_5CH_2CH_2OH$ (**3**) using $[RuCp(CH_3CN)_3]PF_6$ (**1**)^a

Entry	Ligand	Yield % ^b	Entry	Ligand	Yield % ^b
1		39 (80)	11 ^c		0
2 ^c		0	12		27 (70)
3 ^c		0	13		50 (91)
4 ^c		0	14		54 (95)
5 ^c		0	15		59 (96)
6 ^c		0	16		63 (92)
7 ^c		0	17		24 (31)
8 ^c		0	18		97 (99)
9 ^c		0	19		18 (48)
10 ^c		0	20		12 (43)

^aConditions: $[2] = 500$ mM; $[1] = [ligand] = 1$ mM; solvent, CH_3OH ; temperature, 30 °C; 1 h.

^bValues in parentheses are obtained after 3 h.

^c $[2] = 100$ mM.

the importance of i) a synergetic effect between the sp^2N atom and the adjacent COOH group, producing a five-membered chelating ring with the monocationic CpRu(II) catalyst precursor;

Table 2. Optimization of deallylation conditions using QAH/[RuCp(CH₃CN)₃]PF₆ (**1**), [RuCp(³-C₃H₅)(QA)]PF₆ (**5**), or PAH/CpM precursors

Entry	Metal Precursor	Ligand	1 , mM	S/C	Solvent	Time, h	Yield % ^b
1	[CpRu(CH ₃ CN) ₃]PF ₆	QAH	100	100	CH ₃ OH	0.5	>99
2	[CpRu(CH ₃ CN) ₃]PF ₆	QAH	500	500	CH ₃ OH	3	99
3	[CpRu(CH ₃ CN) ₃]PF ₆	QAH	1000	1000	CH ₃ OH	3	98
4	[CpRu(³ -C ₃ H ₅)(QA)]PF ₆	—	3000	10000	CH ₃ OH	24	99
5	[CpRu(CH ₃ CN) ₃]PF ₆	QAH	100	100	C ₂ H ₅ OH	2	99
6	[CpRu(CH ₃ CN) ₃]PF ₆	QAH	100	100	<i>i</i> -C ₃ H ₇ OH	3	98
7	[CpRu(CH ₃ CN) ₃]PF ₆	QAH	100	100	<i>t</i> -C ₄ H ₉ OH	13	82
8	[CpRu(CH ₃ CN) ₃]PF ₆	QAH	100	100	1:1 CH ₃ OH–H ₂ O	6	99
9	[CpRu(CH ₃ CN) ₃]PF ₆	QAH	100	100	1:1 CH ₃ OH–DMF	6	99
10	[CpRu(CH ₃ CN) ₃]PF ₆	QAH	100	100	1:1 CH ₃ OH–THF	0.5	99
11	[CpRu(CH ₃ CN) ₃]PF ₆	QAH	100	100	1:1 CH ₃ OH–CH ₂ Cl ₂	0.5	99
12	[CpRu(CH ₃ CN) ₃]PF ₆	QAH	100	100	1:1 CH ₃ OH–CH ₃ CN	3	18
13	[MoCp(CO) ₃] ₂	PAH	100	100	CH ₃ OH	3	0
14	[WCp(CO) ₃] ₂	PAH	100	100	CH ₃ OH	3	0
15	[FeCp(CO) ₃] ₂	PAH	100	100	CH ₃ OH	3	0
16	RhCp(cod)	PAH	100	100	CH ₃ OH	3	0
17	IrCp(cod)	PAH	100	100	CH ₃ OH	3	0

^aUnless specified otherwise, all of reactions were carried out at 30 °C.^bGC analysis.^c2-g scale.^dUnder a reduced pressure of 200 mmHg.^eThe pressure of the reaction system was reduced to ca. 200 mmHg for 5 min every 2 h.

ii) the acidity of the proton; and iii) the molecular orbital coefficient of the ligand (see Mechanism).

2.3. Optimization

Table 2 showed the results of optimization of the standard reaction (**2** → **3**) using QAH and **1**, and other Cp metal precursors. The QAH/**1**-combined system was highly reactive, completing the reaction within 30 min (entry 1). Even with a substrate/catalyst (S/C) ratio of 500, deprotection was achieved in 3 h (entry 2). Under a slightly reduced pressure (200 mmHg), the S/C ratio could be increased to 1000 (entry 3). Further enhancement in the reactivity was realized by using a ³-allyl complex, [RuCp(³-C₃H₅)(QA)]PF₆ (**5**), which was quantitatively prepared as a pale yellow solid from **1**, QAH, and allyl alcohol (AlOH) in an exact 1:1:1 ratio (**1** and QAH, acetone, rt, <5 min; addition of AlOH, rt, 15 min; concentration of the mixture to 1/10 volume).^{7c} The complex **5** is air- and moisture-stable, which increases operational simplicity. Even with a 0.01 mol% of **5** (S/C = 10000), the reaction could be completed at 30 °C in 24 h by reducing the pressure to ca. 200 mmHg at 2-h intervals (entry 4). Removal of the co-product allyl methyl ether (CH₃OAlI) would force the equilibrium toward the desired product side. In addition to CH₃OH, C₂H₅OH and *i*-C₃H₇OH could be used as solvents, whereas *t*-C₄H₉OH gave a lower yield (entries 5–7). Reactivity was maintained in CH₃OH containing H₂O, DMF, THF, or CH₂Cl₂ as a co-solvent. Using CH₃CN as a co-solvent significantly retarded the reaction (entries 8–12). Although our investigations of the central metal were limited, CpMo, CpW, CpFe, CpRh, and CpIr precursors—which are known to form ³-allyl complexes—were not effective under the standard conditions using PAH (entries 13–17).

Fig. 4. Quantitative removal of allyl group from various allyl ethers at 30 °C for 3 h in CH₃OH with S/C ratio of 500 unless specified otherwise. ^aS/C = 100. ^bS/C = 100 and 0.5 h. All = CH₂CH=CH₂. Bz = COC₆H₅. Bn = CH₂C₆H₅. MOM = CH₂OCH₃. TBDPS = Si(*t*-C₄H₉)(C₆H₅)₂.

2.4. Generality

Fig. 4 summarizes the generality of the CpRu/QAH-catalyzed deprotection of alcohols from allyl ethers.^{7a–7c} Primary, secondary, and tertiary alkanols, and phenol were quantitatively deprotected. No Claisen rearrangement occurred with allyl phenyl ether. Both allyl 4-pentenyl ether and allyl 4-pentynyl ether were quantitatively converted to the corresponding alcohol without, respectively, isomerization of the terminal olefin to an internal olefin or inhibition from the terminally alkyne. Benzoate, benzyl ether, methoxymethyl ether, and *tert*-butyldiphenylsilyl ether were not affected at all, realizing selective removal of allyl group.

As shown in **Fig. 5**, the present catalytic allyloxy bond cleaver could be used for allyl esters including carbonates, carboxylates, and phosphates.^{7c} Allyloxy carbonyl (AOC)-protected alcohols showed much higher reactivity than other esters: a turnover number of one million was attained by continuous removal of

a allyl carbonate ([sub] = 500 mM) **b allyl carboxylate** ([sub] = 100 mM) **c allyl carbamate** ([sub] = [TfOH] = 100 mM) **e**

Fig. 5. Quantitative removal of allyl group from various allyl esters at 30 °C in CH₃OH with S/C ratio of 500 unless specified otherwise. The value is the reaction time. **f** 10-g scale. **d** 9 days with S/C ratio of 1.0 x 10⁶. **e** iPrOH instead of CH₃OH. **c** 500 mM. **b** S/C = 100. **a** 88% yield.

volatile CH₃OAll. For diallyl carbonates, only less substituted allyl groups were selectively removed. Amines protected as an *N*-AOC group were efficiently deprotected in the presence of a 1-mol amount of CF₃SO₃H to give the corresponding ammonium salt without any *N*-allylated side product.^{7d} The effectiveness of isolation could be amplified by salt formation. A 1-mol amount of Nafion (SO₃H equivalent), CH₃SO₃H, and 12 M aqueous HCl could be used, whereas a 10-mol amount of CH₃COOH was required for efficient cleavage.

The “*No additive-One step*” allyl cleaver functions smoothly without requiring an excess amount of reducing reagents, acids, bases, or oxidizing reagents, which often complicate the process of isolating the products. Therefore, the CpRu/QAH-combined catalyst can be applied to peptide synthesis and to the final deprotection stage in the synthesis of polar biomolecular compounds. Some examples are shown in **Fig. 6**. Highly multifunctionalized molecules, such as *N*-Fmoc-(*S*)-Glu(OAll)-OtBu, *N*-Fmoc-(*S*)-Phe-(*S*)-Glu(OAll)-OtBu, *N*-Fmoc-(*S*)-Ser(OAll)-(*S*)-Phe-OtBu, 2'-OAll uridine, *N*-AOC-(*S*)-Pro-OtBu, and *N*-AOC-(*S*)-Pro-(*S*)-Pro-Gly-OtBu, were quantitatively deallylated without affecting the *t*Bu ester or Fmoc groups and without loss of reactivity, even in the presence of a highly coordinative peptide linkage.^{7a,7d,7e} An RNA-related molecule—fully allyl-protected 3,5-U—was also converted in one step to 3,5-U, which was then isolated after (C₂H₅)₃N addition.^{7f} After the

Fig. 6. Application to highly polar molecules. The deprotection yield as well as the conditions are shown below the substrate structure.

deprotection process, a catalyst sometimes ends up as an impurity in the final product. In this regard, a homogeneous catalyst is disadvantageous in comparison to its heterogeneous counterpart. The heterogeneous deallylation catalyst **6** immobilized on micro-size spherical SiO₂ particles containing Fe₃O₄ should be all the more practical because it can operate in alcoholic solvents in the absence of extra additives and the only co-product is volatile CH₃OAll. Products can be easily isolated through a simple deprotection step, followed by magnetic separation of **6**, and an evaporation process. 3,5-U was successfully deprotected by using the heterogeneous version of the catalyst.^{7h}

2.5. Mechanism

2.5.1. NMR study and kinetics

Fig. 7 shows the step-by-step changes in the ^1H -NMR spectrum during the reaction of QAH, $[\text{RuCp}(\text{CH}_3\text{CN})_3]\text{PF}_6$ (**1**), $\text{CH}_2=\text{CHCH}_2\text{OH}$ (**Al**OH), $\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{OAl}$ (**2**), and CH_3OH in acetone- d_6 at 30°C . When a 1-mol amount of **1** was added to a solution of QAH, the six aromatic proton signals of QAH completely and immediately disappeared to generate two new sets of relatively broad signals in a 20:1 ratio (**Fig. 7a** and **7b**). The major set could be plausibly assigned to $[\text{RuCp}(\text{QAH})\text{S}]\text{PF}_6$ (**7**, $\text{S} = \text{CH}_3\text{CN}$ or $(\text{CD}_3)_2\text{CO}$), while the minor one might be due to a species equilibrating with **7**—for example, $[\text{RuCp}(\text{QA})\text{S}]\text{PF}_6$ (**8**)/ HPF_6 or a COOH -dangling complex **9** (for supposed structures, see **Fig. 11**).

Consistent with such a dynamic system, both the major and minor signals were converted to a single set of sharp signals when a 1-mol amount of **2** was introduced (**Fig. 7c**). The new signals could be definitely assigned to the π -allyl complex $[\text{RuCp}(\pi\text{-C}_3\text{H}_5)(\text{QA})]\text{PF}_6$ (**5**), in which the π -allyl ligand takes an *endo* conformation to Cp, as supported by the observation of 2% and 4.5% nOe enhancement between the closely located CpH and the anti-protons H_A and H_A' of the π -allyl group.^{7b} The

Fig. 7. ^1H -NMR behavior in the reaction of QAH with $[\text{RuCp}(\text{CH}_3\text{CN})_3]\text{PF}_6$ (**1**), $\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{OAl}$ (**2**), and CH_3OH (acetone- d_6 , 30°C). (a) Quinaldic acid (QAH) (10 mM). (b) 10 min after addition of 1 mol amount of **1**. (c) 30 min after addition of 1 mol amount of **2**. The structure of QA moiety in the spectrum is omitted. (d) 12 h after addition of 10 mol amounts of **2** and 100 mol amounts of CH_3OH . Blue sphere: $\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{OH}$ (**3**). Red triangle: $\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{OAl}$ (**2**). Green square: CH_3OAl . All = $\text{CH}_2\text{CH}=\text{CH}_2$. The factor of OCH_2 signal intensity of CH_3OAl for **2** was ca. 0.5.

$\text{A}_2\text{B}_2\text{X}$ signal pattern of the π -allyl ligand, rather than A_4X , indicates that the π - π exchange in **5** is slow on the ^1H NMR timescale. Stereoselective generation of *endo*-**5** can be explained by attractive interactions between π -allyl 1,3-p orbitals and Ru d_{xy}^* and between π -allyl 2-p* orbital and Ru d_{z^2} .^{13b, 16}

The spectrum was not changed by the addition of a 1-mol amount of $\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{OAl}$ (**2**) into the solution of **5**. When 10-mol amounts of **2** and 100-mol amounts of CH_3OH were added to **5**, 70% of **2** was consumed after 12 h at 30°C to generate $\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{OH}$ (**3**) and CH_3OAl in a 1:1 ratio (**Fig. 7d**). Here, only the π -allyl complex **5** was observed, showing i) that a π -allyl mechanism is operating; ii) that **5** is in the resting state of the catalytic cycle; and iii) that the rate is determined at the reductive nucleophilic attack of CH_3OH on the π -allyl C(1) or C(3) of **5** (see section 2.5.4).

The ^1H -NMR behavior agreed well with the kinetics shown in **Fig. 8**: the reaction proceeded with a 0th-order dependence on the initial concentration of $\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{OAl}$ (**2**) and with a 1st-order dependence on the initial concentration of the Ru complex **5** during the early stage of 0%–30% conversion of **2**.¹⁵ Because both **2** and CH_3OAl act as an allyl donor, an excess amount of CH_3OH forced the equilibrium $\text{2} + \text{CH}_3\text{OH} \rightleftharpoons \text{3} + \text{CH}_3\text{OAl}$ far to the right side. The 0.25:0.788:0.688:9.31 ratio of **2**, **3**, CH_3OAl , and CH_3OH observed in the ^1H -NMR spectrum (**Fig. 7d**) determined an equilibrium constant K of ca. 0.23, indicating that the **2** + CH_3OH side is preferred over the **3** + CH_3OAl side under the reaction conditions.

Fig. 8. Dependence of the initial rate v_0 (mM/min) on $[\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{OAl}]$ (**2**)₀ and $[[\text{RuCp}(\pi\text{-C}_3\text{H}_5)(\text{QA})]\text{PF}_6]$ (**5**)₀ in the deallylation of **2** in CD_3OD at 30°C . (a) Plot of v_0 as a function of $[\text{2}]_0$ from 300 mM to 1000 mM ($[\text{5}]_0 = 1.00 \text{ mM}$). (b) Plot of v_0 as a function of $[\text{5}]_0$ from 0.500 mM to 2.00 mM ($[\text{2}]_0 = 500 \text{ mM}$).

2.5.2. X-ray crystallographic analysis

The π -allyl complex **5** was air- and moisture-stable and easily crystallized from dichloromethane (yellow, prism, mp 166°C (dec)).^{7b} A series of π -allyl Ru complexes of 4-X-substituted picolinate (4-X-PA, where X = CH_3O , H, Cl, CF_3 , and NO_2) were prepared, and the molecular structures in the crystalline state are shown in **Fig. 9**. In all cases, the π -allyl ligand had a conformation that was *endo* to the Cp group, being consistent with the structure of **5** in solution. The π -allyl C(3)–Ru bond was ca. 5% longer than the C(1)–Ru bond, albeit with a few exceptions. This observation indicates that the rate-determining reductive nucleophilic attack of CH_3OH may occur on the C(3) carbon.

2.5.3. Hammett plots and molecular orbital analysis

The relative reactivity of PAH for 4-X-PAH (X = CH_3O , Cl, CF_3 , and NO_2) was investigated in the Ru-catalyzed deallylation of **2** to **3** under the conditions of $[\text{4-X-PAH}] = [\text{1}] = 1 \text{ mM}$; $[\text{2}] = 500 \text{ mM}$; CH_3OH ; 30°C). As shown in **Fig. 10a**, a stronger electron-withdrawing ability of X led to higher reactivity, but the

Fig. 9. Molecular structures of [RuCp(η^3 -C₃H₅)(QA)]PF₆ (**a**) and [RuCp(η^3 -C₃H₅)(4-X-PA)]PF₆ (**b–f**) in the crystalline state. QAH: quinaldic acid. 4-X-PAH: 4-X-substituted picolinic acid.

degree of rate enhancement was not as significant as expected: 0.7 (CH₃O, -0.28 (value)), 1 (H, 0.00), 1.4 (Cl, 0.22), 1.6 (CF₃, 0.53), and 1.9 (NO₂, 0.81). Hammett plots of $\log(k_X/k_H)$ versus the standard constant for the substituent parameter exhibited two linear free-energy relationships with a ρ value of +0.63 for X = CH₃O, H, and Cl, and +0.20 for X = Cl, CF₃, and NO₂, respectively. The two-line behavior may be rationalized by the balance between two factors: i) the π -accepting ability of the pyridine moiety, and ii) the acidity of the carboxylic acid of 4-X-PAH.¹⁷ In the rate-determining reductive nucleophilic attack of CH₃OH on the π -allyl ligand of [Ru(IV)Cp(η^3 -C₃H₅)(4-X-PA)]PF₆, a ligand with higher π -acceptability and a lower lowest unoccupied molecular orbital (LUMO) level should stabilize the transition state. This view is consistent with the LUMO level/reactivity relationship shown in **Fig. 10b**, and holds even after taking the atomic orbital coefficient (AtOrCo) of the nitrogen atom into consideration. As the AtOrCo/LUMO value decreases, the reactivity increases. π -Expanded QAH, which has a LUMO level 0.6 eV lower than that of PAH (2.12 vs 1.52), shows a reactivity that is 5–10-fold higher than PAH. At the same time, however, a strong electron-withdrawing group with a high ρ value raises the acidity of COOH. The dibasic mono salt [Ru(II)Cp(4-X-PAH)]PF₆ may exist in equilibrium with the neutral complex [Ru(II)Cp(4-X-PA)] and HPF₆. The acidity of COOH in [Ru(II)Cp(4-X-PAH)]PF₆ would be enhanced by coordination of the COOH oxygen atom to the mono cationic central Ru atom, intensifying the acidity of COOH beyond expectation from the general pK_a values of PAH (ca. 5.4) and HPF₆ (ca. -20). An increase in the generation of neutral species

Fig. 10. Relationship between reactivity, LUMO energy level and acidity of 4-X-substituted picolinic acid (4-X-PAH) in deallylation of C₆H₅CH₂CH₂OAlI (**2**) to C₆H₅CH₂CH₂OH (**3**) under the conditions of [2] = 500 mM; [[RuCp(CH₃CN)₃]PF₆ (**1**)] = [4-X-PAH] = 1 mM; CH₃OH; 30 °C. All = CH₂CH=CH₂. (a) Hammett plots of relative reactivity ($\log(k_X/k_H)$) as a function of standard constants. (b) LUMO energy calculated at a 6-31G* level, AtOrCo (atomic orbital coefficient on N), and pK_a (COOH) of 4-X-PAH.

with no Intramol-RDACat ability is likely to lower the catalyst performance of the CpRu(II)⁺/Brønsted acid-combined system. This would explain our observation that replacement of COOH in PAH with highly acidic SO₃H led to low reactivity (**Table 1**, entry 17).

2.5.4. Supposed catalytic cycle

On the basis of the results of the NMR study, kinetics experiments, structural analysis of Ru π -allyl complexes by X-ray diffraction, Hammett plots analysis, and molecular orbital calculation, the catalytic cycle of the present deallylation using the [RuCp(CH₃CN)₃]PF₆ (**1**)/QAH-combined system or [RuCp(η^3 -C₃H₅)(QA)]PF₆ (**5**) was deduced, as shown in **Fig. 11**. First of all, CH₃CN in **1** is easily replaced by QAH to generate a mono cationic complex [RuCp(QAH)S]PF₆ (**7**), which is in equilibrium with both a neutral complex [RuCp(QA)S] (**8**)/HPF₆ and a COOH-dangling species [RuCp(QAH)S₂]PF₆ (**9**). The Ru(II)⁺/H⁺ in [RuCp(QAH)S]PF₆ captures an allyl ether substrate, CH₂=CHCH₂OR, to form the catalyst/substrate complex **10**, in which the hard ether O atom interacts with the hard H⁺ ion, and the soft olefin double bond interacts with the soft Ru atom. The hydrogen bond in **10** enhances the electrophilicity of C(3) and C(1) in CH₂=CHCH₂OR, while the electron donicity or nucleophilicity of the central Ru atom is amplified by coordination of the carboxylate-like O atom, electron-donative sp²N atom, and mono anionic ⁵ Cp ligand. This synergetic effect realizes a charge alternation in H--O--C(1)--C(2)=C(3)--Ru--OCO to reduce the energy level of the transition state. The Intramol-RDACat ability facilitates the oxidative formation of the *endo*- π -allyl complex **5**, liberating a deprotected alcohol. The rate-determining reductive nucleophilic attack of

CH₃OH on the -allyl carbon is made easier by the lower LUMO energy of QAH, generating **11**. The CH₃OAlI is then replaced with the substrate **2**, thereby completing the cycle. All elementary steps are reversible, but the presence of an excess amount of CH₃OH solvent rotates the cycle in a clockwise way. Removal of the volatile co-product by reducing the internal pressure or by purging the reaction mixture with an inert gas would result in an infinite turnover number.

Fig. 11. Supposed catalytic cycle in deprotection of alcohols using CpRu⁺/QAH-combined system. S = CH₃CN, CH₃OH, substrate, product, etc.

3. Conclusion

In summary, the CpRuPF₆-quinaldic acid catalyst described here functions as a highly reactive and chemoselective allyloxy bond cleaver in alcoholic solvents under very mild and essentially additive-free conditions. The only co-product is volatile ether. The efficiency and simplicity of the reaction should further increase the practical utility of allyl groups for the protection of alcohols, esters, and amines, among many other protecting groups in organic synthesis. Furthermore, the validity of our leading concept for designing the molecular catalyst—namely “soft transition metal/hard Brønsted acid-combined catalyst” or “redox-mediated donor-accepter bifunctional catalyst (RDACat)” —has been confirmed by a series of experiments including i) ¹H-NMR spectrometry; ii) X-ray crystallographic analyses of CpRu⁺-allyl complexes of picolinic acid derivatives; iii) Hammett plot analysis; and iv) the relationship between LUMO levels of ligands and reactivity. The present study should stimulate further ideas, not only for the retrosynthetic design of pharmaceutically important natural and unnatural compounds, but also for the continued development of molecular catalysis.¹⁸

4. Experimental

4.1. General

A Chemspeed ASW2000 system was used to screen ligands. Nuclear magnetic resonance (NMR) spectra were recorded on a JEOL JNM-ECA-600 spectrometer. Chemical shifts are expressed in parts per million (ppm) downfield from tetramethylsilane or in ppm relative to CHCl₃ and CHD₂COCD₃ (7.26 and 2.05 in ¹H NMR, and 77.0 and 29.8 in ¹³C NMR). The signal patterns of ¹H NMR are indicated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; and br, broad signal. X-ray crystallographic analysis was conducted on a Rigaku Saturn 70 CCD system, and the structure was solved by direct methods using CrystalStructure crystallographic software. Quantum chemical calculations were performed using the Spartan 10 program implemented on an Apple iMac 3.4 GHz intel core i7. Gas chromatography analyses were performed on a Shimadzu GC-17A instrument. Argon (Ar) gas was purified by passage first through a column of BASF R3-11 catalyst at 80 °C and then through a column of granular calcium sulfate. Solvents for the deallylation and the synthesis of Ru complexes were dried, degassed at reflux temperature in the presence of the following appropriate drying agents (250 mg/100 mL) under an Ar stream for 6 h, and distilled into Schlenk flasks: calcium hydride for *i*PrOH, CH₂Cl₂, CH₃CN and CD₃CN; magnesium for C₂H₅OH, CH₃OH and CD₃OD; sodium for hexane, benzene and benzene-*d*₆; and MS4A for acetone, acetone-*d*₆, (CH₃)₂CDOH and (CD₃)₂CDOD. The solvent was degassed by three freeze-thaw cycles before deallylation. In a similar manner, diethyl ether, THF and THF-*d*₈ were distilled from sodium benzophenone ketyl (3 g/L). CDCl₃ was purchased from Cambridge Isotope Laboratories and purified by alumina column chromatography. It was degassed by three freeze-thaw cycles before use in the ¹H NMR study. All other solvents were obtained commercially and used without further purification unless stated otherwise.

Details for the deallylation procedure, the results of the allyloxy substrates in “section 2.4 on Generality,” and the NMR data of the substrates and deprotected products have been reported in the supporting information of previous short communications.⁷

4.2. Ligand and CpM screening

4.2.1. Materials

Ligands L1–L48 shown in **Fig. 3** were as follows: picolinic acid (PAH, L1), hydroxy(pyridin-2-yl)methanesulfonic acid (L2), quinoline-8-sulfonyl chloride (L3), 1*H*-imidazole-4-carboxylic acid (L4), pyridine-2,6-dicarboxylic acid (L5), 1*H*-benzo[d]imidazole-2-sulfonic acid (L6), pyridin-2-ylmethanol (L7), 2-((dimethylamino)methyl)pyridin-3-ol (L8), (*Z*)-picolinaldehyde oxime (L9), 3*H*-[1,2,3]triazolo[4,5-*b*]pyridin-3-ol (L10), 1*H*-benzo[d][1,2,3]triazol-1-ol (L11), pyridin-2-ol (L12), quinolin-8-ol (L13), 5-chloroquinolin-8-ol (L14), 8-hydroxyquinoline-5-sulfonic acid (L15), 5-nitroquinolin-8-ol (L16), 5-(chloro-λ⁵-azanyl)quinolin-8-ol hydrochloride (L17), 2-(benzo[d]oxazol-2-yl)phenol (L18), pyridin-2-ylmethanamine (L19), picolinamide (L20), [2,2':6',2''-terpyridin]-4'(1'*H*)-one (L21), 2-(pyridin-2-yl)-1*H*-benzo[d]imidazole (L22), 6-ethoxybenzo[d]thiazole-2-sulfonamide (L23), 1*H*-pyrazole-1-carboximidamide hydrochloride (L24), 2,2'-bipyridine (L25), pyridine (L26), glycine (L27), (*S*)-2-amino-3,3-dimethylbutanoic acid (L28), proline (L29), piperidine-2-carboxylic acid (L30), piperazine-2-carboxylic acid hydrochloride (L31), 1*H*-indole-2-carboxylic acid (L32), 1*H*-pyrrole-2-carboxylic acid (L33), dimethylglycine (L34), methyl-*L*-proline (L35), 2-(diphenyl-

phosphanyl)acetic acid (L36), 2-(diphenylphosphanyl)benzoic acid (L37), 2-(diphenylphosphanyl)ethan-1-ol (L38), 2-(diphenylphosphanyl)ethan-1-amine (L39), triphenylphosphane (L40), tricyclohexylphosphane (L41), (2-methoxyethyl)diphenylphosphane (L42), 2-(diphenylphosphanyl)-*N,N*-dimethylethan-1-amine (L43), 2-(4-oxo-2-thioxothiazolidin-3-yl)acetic acid (L44), thianthren-1-ylboronic acid (L45), 2-(thiophen-2-yl)acetic acid (L46), benzo[*b*]thiophen-2-ylboronic acid (L47), and furan-2-carboxylic acid (L48). Except for L36, all ligands were commercially purchased and used without further purification. L36 was synthesized according to a previously reported method.¹⁹

The ligands shown in **Table 1** were as follows: benzoic acid, nicotinic acid, isonicotinic acid, sodium picolinate, methyl picolinate, quinoline-8-carboxylic acid, 4-methoxypicolinic acid (4-CH₃O-PAH), 4-chloropicolinic acid (4-Cl-PAH), 4-(trifluoromethyl)picolinic acid (4-CF₃-PAH), 4-nitropicolinic acid (4-NO₂-PAH), pyridin-2-ylphosphonic acid (PyPO(OH)₂), pyridine-2-sulfonic acid (PySO₃H), isoquinoline-1-carboxylic acid, isoquinoline-3-carboxylic acid, quinoline-2-carboxylic acid (QAH). Except for PySO₃H, all ligands were commercially purchased and used without further purification. PySO₃H was prepared by a previously reported method.²⁰

[RuCp(CH₃CN)₃]PF₆ (**1**), [MoCp(CO)₃]₂, [WCp(CO)₃]₂, [FeCp(CO)₃]₂, RhCp(cod), and IrCp(cod) were commercially purchased. Commercial 2-propen-1-ol (AlOH) and synthetic (2-allyloxyethyl)benzene (C₆H₅CH₂CH₂OAll (**2**))²¹ were purified by distillation and stored in a Schlenk flask under Ar.

4.2.2. Ligand screening in Fig. 3

The Chemspeed ASW2000 (single syringe) system was customized for use under an inert atmosphere (see Supplementary Data), and Chemspeed-G735 software was used to program the screening. Five sets of reaction blocks, each containing 16 glass vials, were heated at 120 °C for 30 min under a reduced pressure of 200 mmHg. To each of 48 vials, ligands L1-L48 (each 5.00 mol) were manually added within a glovebox, and the temperature of the five reaction blocks was adjusted to 30 °C. A 10.0 mM stock solution of [RuCp(CH₃CN)₃]PF₆ (**1**) in CH₃OH (30 mL), and three 111 mM stock solutions of C₆H₅CH₂CH₂OAll (**2**) (80 mL x 3) were prepared in four 100-mL vials in a storage tray. A 500- L aliquot of solution **1** (5.00 mol) was first added to each 20-mL reaction vessel, and then the single syringe needle was subjected to a 20-sec outside/inside rinse with CH₃OH. Next, a 4.50-mL aliquot of solution **2** (500 mol) was added to each of the vessels. All other reactions (L2-L48) were prepared in this way, taking ca. 1 h. After being shaken at 30 °C for 3 h from the start point of the first reaction (L1), the glovebox-type hood was opened, and a 200 L aliquot of the reaction mixture (L1) was placed in a 5-mL vial of a sampling tray, and the syringe was cleaned by a 20-sec outside/inside rinse with CH₃OH. The sample was manually frozen by using liquid N₂. All other samples, which were consecutively transferred from the corresponding reaction vessels every 75 sec, were frozen. Gas chromatography analyses of the samples were performed on Shimadzu GC-14B and GC-17A instruments with the following conditions: capillary column, J&W Scientific DB-WAX (0.25 mm x 15 m); column temperature, 50–250 °C; rate of temperature increase, 10 °C/min; *t*_R 4.0 min (**2**) and 6.0 min (**3**).

4.2.3. Ligand optimization in Tables 1 and 2

All reactions were carried out under Ar atmosphere by using a general Schlenk technique. Schlenk flasks were dried at ca. 250 °C by using a heat gun under reduced pressure, and a Teflon-

coated magnetic bar was used to stir the reaction mixture. The typical procedure is represented by the reaction of entry 1 in **Table 1**: [RuCp(CH₃CN)₃]PF₆ (**1**) (1.60 mg, 3.69 μmol) and CH₃OH (0.330 mL) were placed in a 20-mL Schlenk tube under Ar stream. A 100 mM solution of PAH (0.0370 mL, 37.0 μmol) in CH₃OH was added to the mixture. After standing for 30 min at rt, the reddish brown solution was transferred into a 20-mL Schlenk tube equipped with a Young's tap containing C₆H₅CH₂CH₂OAll (**2**) (300 mg, 1.85 mmol) and CH₃OH (3.00 mL). The yellow solution was stirred for 1 h at 30 °C. GC analysis (conditions as above) was used to determine the yield of C₆H₅CH₂CH₂OH (**3**). Instead of **1** and PAH, other CpM precursors and ligands were used.

4.3. NMR experiments

A dry and Ar-filled 5-mm Young-type NMR tube was charged with a 200-mM (CD₃)₂CO solution of QAH (0.500 mL, 100 mol), and subjected to ¹H-NMR analysis at 30 °C (**Fig. 7a**). After degassing the mixture by two freeze/thaw cycles, a 200-mM (CD₃)₂CO solution of [RuCp(CH₃CN)₃]PF₆ (**1**) (0.500 mL, 100 mol) was added to the NMR tube under Ar atmosphere. After 10 min at 30 °C, the ¹H-NMR spectrum was recorded (**Fig. 7b**), and then a 500-mM (CD₃)₂CO solution of C₆H₅CH₂CH₂OAll (**2**) (0.200 mL, 100 mol) was added. After 30 min at 30 °C, the ¹H-NMR spectrum was recorded (**Fig. 7c**), and then **2** (162 mg, 1.00 mmol) and CH₃OH (405 L, 320 mg, 10.0 mmol) were added. After 12 h at 30 °C, the final ¹H-NMR spectrum was recorded (**Fig. 7d**). In a separate experiment, a 1:1 mixture of the deprotected alcohol, C₆H₅CH₂CH₂OH (**3**), and the co-product, CH₃OAll, showed OCH₂ signals in a ca. 1:0.5 ratio.

4.4. Kinetic experiments

The allyl ether substrate C₆H₅CH₂CH₂OAll (**2**) and air- and moisture-stable [RuCp(³-C₃H₅)(QA)]PF₆ (**5**) were used for the kinetic study. Three stock solutions of **2** in CD₃OD at 333 mM (S-I), 556 mM (S-II), and 1.11 M (S-III), and three stock solutions of **5** in CD₃OD at 5.00 mM (C-I), 10.0 mM (C-II), and 20.0 mM (C-III) were prepared in advance, and degassed by three freeze/thaw cycles. Five dried and Ar-filled 5-mm Young-type NMR tubes were charged, respectively, with S-I (900 L, 300 mol **2**), three lots of S-II (900 L, 500 mol **2**), and S-III (900 L, 1.00 mmol **2**), and then immersed in a dry ice/CH₃OH bath. To these tubes were added, C-I (100 L, 0.500 mol **5**), three lots of C-II (100 L, 1.00 mol), and C-III (100 L, 2.00 mol). Each of the five cooled S-I/C-II, S-II/C-II, S-III/C-II, S-II/C-I, S-II/C-II combined systems was measured by ¹H-NMR with the probe temperature adjusted to 30 °C. FID was sampled every 5 min for 3 h. The signal intensity at 3.77 (2H, t, *J* = 7.57 Hz, C₆H₅CH₂CH₂OH (**3**)) was plotted over time, and the rate was determined in the 0%–30% conversion range.¹⁵ In the early reaction stage, logarithmic plotting afforded high linearity to determine the following initial rates: 12.2 mM/min (S-I/C-II), 12.4 mM/min (S-II/C-II), 12.6 mM/min (S-III/C-II), 8.32 mM/min (S-II/C-I), and 26.3 mM/min (S-II/C-II).

4.5. Preparation of metal complexes and X-ray crystallographic analysis

4.5.1. [RuCp(³-C₃H₅)(4-CH₃O-PA)]PF₆

A dry and Ar-filled 10-mL Schlenk flask was charged with [RuCp(CH₃CN)₃]PF₆ (**1**) (3.21 mg, 73.9 μmol), 4-CH₃O-PAH (11.3 mg, 73.8 μmol), and (CH₃)₂CO (7.0 mL) at rt. After the resulting yellow solution was stirred at rt for 5 min, a 200-mM (CH₃)₂CO solution of AlOH (369 L, 73.7 μmol) was introduced to the Schlenk flask. The resulting purple solution was cannulated into a 5-mL tube placed in a 20-mL Schlenk

flask, and hexane (3.0 mL) was added to the Schlenk flask outside the 5-mL tube. After sealing the system by using a silicone-greased glass stopper, the whole system was kept at 5 °C for 12 h to generate yellow prismatic crystals (32.0 mg, 63.5 mol, 86% yield): ^1H NMR ($(\text{CD}_3)_2\text{CO}$) 4.09 (s, 3H, OCH_3), 4.23 (dd, $J = 6.54$, 2.75 Hz, 1H, CH_{syn}), 4.39 (dd, $J = 6.20$, 2.75 Hz, 1H, CH_{syn}), 4.46 (d, $J = 11.02$ Hz, 1H, CH_{anti}), 4.60 (d, $J = 11.02$ Hz, 1H, CH_{anti}), 4.86 (dddd, $J = 11.02$, 11.02, 6.20, 6.20 Hz, 1H, $\text{CH}_{\text{center}}$), 6.36 (s, 5H, Cp), 7.40 (dd, $J = 6.54$, 2.75 Hz, 1H, C(5)H), 7.45 (d, $J = 2.75$ Hz, 1H, C(3)H), 8.81 (d, $J = 6.89$ Hz, 1H, C(6)H); ^{13}C NMR ($(\text{CD}_3)_2\text{CO}$) 57.7, 66.3, 68.4, 97.1, 101.8, 114.2, 116.7, 152.4, 158.4, 170.8, 171.1; HRMS (ESI) m/z : calcd for $\text{C}_{15}\text{H}_{16}\text{NO}_3\text{Ru} [\text{M}-\text{PF}_6]^+$, 360.0174; found, 360.0174; mp 186 °C (decomposed).

Crystallographic data for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk). $[\text{RuCp}(\text{}^3\text{-C}_3\text{H}_5)(4\text{-CH}_3\text{O-PA})]\text{PF}_6$ is available as supplementary publication no. CCDC 1052811. Crystals of $[\text{RuCp}(\text{}^3\text{-C}_3\text{H}_5)(\text{PA})]\text{PF}_6$, $[\text{RuCp}(\text{}^3\text{-C}_3\text{H}_5)(4\text{-Cl-PA})]\text{PF}_6$, $[\text{RuCp}(\text{}^3\text{-C}_3\text{H}_5)(4\text{-CF}_3\text{-PA})]\text{PF}_6$, and $[\text{RuCp}(\text{}^3\text{-C}_3\text{H}_5)(4\text{-NO}_2\text{-PA})]\text{PF}_6$ were prepared in the same way.

4.5.2. $[\text{RuCp}(\text{}^3\text{-C}_3\text{H}_5)(\text{PA})]\text{PF}_6$

Conditions: $[\text{RuCp}(\text{CH}_3\text{CN})_3]\text{PF}_6$ (**1**) (32.0 mg, 73.7 mol), PAH (9.01 mg, 73.2 mol), $(\text{CH}_3)_2\text{CO}$ (7.00 mL), a 200-mM $(\text{CH}_3)_2\text{CO}$ solution of AlOH (369 L, 73.7 mol). $[\text{RuCp}(\text{}^3\text{-C}_3\text{H}_5)(\text{PA})]\text{PF}_6$ (31.3 mg, 66.0 mol, 90% yield) as yellow prismatic crystals: ^1H NMR ($(\text{CD}_3)_2\text{CO}$) 4.27 (dd, $J = 6.54$, 2.75 Hz, 1H, CH_{syn}), 4.45 (dd, $J = 6.20$, 2.75 Hz, 1H, CH_{syn}), 4.50 (d, $J = 11.02$ Hz, CH_{anti}), 4.66 (d, $J = 10.33$ Hz, 1H, CH_{anti}), 4.94 (dddd, $J = 11.02$, 11.02, 6.20, 6.20 Hz, 1H, $\text{CH}_{\text{center}}$), 6.39 (s, 5H, Cp), 7.89 (dd, $J = 6.89$, 6.20 Hz, C(5)H), 7.99 (d, $J = 8.26$ Hz, 1H, C(3)H), 8.35 (dd, $J = 7.57$, 7.57 Hz, 1H, C(4)H), 9.08 (d, $J = 5.51$ Hz, 1H, C(6)H); ^{13}C NMR ($(\text{CD}_3)_2\text{CO}$) 66.4, 69.3, 97.4, 101.9, 128.9, 130.5, 142.9, 151.0, 158.2, 171.3; HRMS (ESI) m/z : calcd for $\text{C}_{14}\text{H}_{14}\text{NO}_2\text{Ru} [\text{M}-\text{PF}_6]^+$, 330.0068; found, 330.0090; mp 210 °C (decomposed). Crystallographic data no. CCDC 1052813.

4.5.3. $[\text{RuCp}(\text{}^3\text{-C}_3\text{H}_5)(4\text{-Cl-PA})]\text{PF}_6$

Conditions: $[\text{RuCp}(\text{CH}_3\text{CN})_3]\text{PF}_6$ (**1**) (32.2 mg, 74.1 mol), 4-Cl-PAH (11.6 mg, 73.7 mol), $(\text{CH}_3)_2\text{CO}$ (7.0 mL), a 200-mM $(\text{CH}_3)_2\text{CO}$ solution of AlOH (369 L, 73.7 mol). $[\text{RuCp}(\text{}^3\text{-C}_3\text{H}_5)(4\text{-Cl-PA})]\text{PF}_6$ (37.5 mg, 60.1 mol, 82% yield) as yellow prismatic crystals: ^1H NMR ($(\text{CD}_3)_2\text{CO}$) 4.29 (dd, $J = 6.89$, 2.75 Hz, 1H, CH_{syn}), 4.48 (dd, $J = 6.20$, 2.75 Hz, 1H, CH_{syn}), 4.52 (d, $J = 11.02$ Hz, 1H, CH_{anti}), 4.69 (d, $J = 11.02$ Hz, 1H, CH_{anti}), 5.02 (dddd, $J = 11.02$, 11.02, 6.89, 6.20 Hz, 1H, $\text{CH}_{\text{center}}$), 6.41 (s, 5H, Cp), 7.96 (d, $J = 2.75$ Hz, 1H, C(3)H), 8.00 (dd, $J = 6.20$, 2.75 Hz, 1H, C(5)H), 9.05 (d, $J = 6.20$ Hz, 1H, C(6)H); ^{13}C NMR ($(\text{CD}_3)_2\text{CO}$) 66.6, 69.6, 97.4, 102.1, 128.7, 130.4, 150.7, 152.2, 158.8, 170.3; HRMS (ESI) m/z : calcd for $\text{C}_{14}\text{H}_{13}\text{ClNO}_2\text{Ru} [\text{M}-\text{PF}_6]^+$, 363.9678; found, 363.9703; mp 216 °C (decomposed). Crystallographic data no. CCDC 1052810.

4.5.4. $[\text{RuCp}(\text{}^3\text{-C}_3\text{H}_5)(4\text{-CF}_3\text{-PA})]\text{PF}_6$

Conditions: $[\text{RuCp}(\text{CH}_3\text{CN})_3]\text{PF}_6$ (**1**) (32.1 mg, 73.9 mol), 4-CF₃-PAH (14.1 mg, 73.8 mol), $(\text{CH}_3)_2\text{CO}$ (7.0 mL), a 200-mM $(\text{CH}_3)_2\text{CO}$ solution of AlOH (369 L, 73.7 mol). $[\text{RuCp}(\text{}^3\text{-C}_3\text{H}_5)(4\text{-CF}_3\text{-PA})]\text{PF}_6$ (30.1 mg, 55.6 mol, 75% yield) as yellow prismatic crystals: ^1H NMR ($(\text{CD}_3)_2\text{CO}$) 4.34 (dd, $J = 6.46$, 2.75 Hz, 1H, CH_{syn}), 4.53 (dd, $J = 5.93$, 2.75 Hz, 1H, CH_{syn}), 4.56 (d, $J = 11.02$ Hz, 1H, CH_{anti}), 4.75 (d, $J = 11.02$ Hz, 1H, CH_{anti}),

5.07 (dddd, $J = 11.02$, 11.02, 6.89, 6.20 Hz, 1H, $\text{CH}_{\text{center}}$), 6.43 (s, 5H, Cp), 8.15 (d, $J = 2.07$ Hz, 1H, C(3)H), 8.23 (dd, $J = 5.51$, 2.07 Hz, 1H, C(5)H), 9.40 (d, $J = 6.20$ Hz, 1H, C(6)H); ^{13}C NMR ($(\text{CD}_3)_2\text{CO}$) 66.7, 70.2, 97.5, 102.2, 124.2, 126.1, 142.9 (q, $J = 141.4$ Hz), 152.9 (2C), 160.0, 170.2; HRMS (ESI) m/z : calcd for $\text{C}_{15}\text{H}_{13}\text{F}_3\text{NO}_2\text{Ru} [\text{M}-\text{PF}_6]^+$, 397.9942; found, 397.9968; mp 182 °C (decomposed). Crystallographic data no. CCDC 1052809.

4.5.5. $[\text{RuCp}(\text{}^3\text{-C}_3\text{H}_5)(4\text{-NO}_2\text{-PA})]\text{PF}_6$

Conditions: $[\text{RuCp}(\text{CH}_3\text{CN})_3]\text{PF}_6$ (**1**) (32.0 mg, 73.7 mol), 4-NO₂-PAH (12.4 mg, 73.8 mol), $(\text{CH}_3)_2\text{CO}$ (7.0 mL), a 200-mM $(\text{CH}_3)_2\text{CO}$ solution of AlOH (369 L, 73.7 mol). $[\text{RuCp}(\text{}^3\text{-C}_3\text{H}_5)(4\text{-NO}_2\text{-PA})]\text{PF}_6$ (22.2 mg, 42.8 mol, 58% yield) as yellow prismatic crystals: ^1H NMR ($(\text{CD}_3)_2\text{CO}$) 4.37 (dd, $J = 6.54$, 2.75 Hz, 1H, CH_{syn}), 4.55 (dd, $J = 6.20$, 2.75 Hz, 1H, CH_{syn}), 4.60 (d, $J = 11.02$ Hz, 1H, CH_{anti}), 4.78 (d, $J = 11.02$ Hz, 1H, CH_{anti}), 5.09 (dddd, $J = 11.71$, 11.02, 6.89, 6.20 Hz, 1H, $\text{CH}_{\text{center}}$), 6.46 (s, 5H, Cp), 8.43 (d, $J = 2.75$ Hz, 1H, C(3)H), 8.56 (dd, $J = 6.20$, 2.75 Hz, 1H, C(5)H), 9.53 (d, $J = 6.20$ Hz, 1H, C(6)H); ^{13}C NMR ($(\text{CD}_3)_2\text{CO}$) 66.8, 70.7, 97.6, 102.4, 121.0, 122.9, 154.3, 157.8, 161.1, 169.8; HRMS (ESI) m/z : calcd for $\text{C}_{14}\text{H}_{13}\text{N}_2\text{O}_4\text{Ru} [\text{M}-\text{PF}_6]^+$, 374.9919; found, 374.9933; mp 172 °C (decomposed). Crystallographic data no. CCDC 1052812.

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Soft Ruthenium and Hard Brønsted Acid Combined Catalyst for Efficient Cleavage of Allyloxy Bonds. Application to Protecting Group Chemistry.

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