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Chemical Communication

EDGE ARTICLE

Rh(III)-Catalyzed Relay Carbenoid Functionalization of Aromatic C-H Bonds: Access to π-Conjugated Fused Heteroarenes†

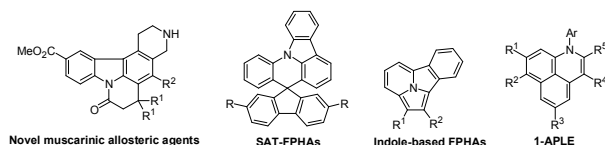Ying Xie, [a, c, ‡] Xun Chen, [a, ‡] Xin Liu, [b] Shi-Jian Su,[*, b] Jianzhang Li, [c] and Wei Zeng[*, a]

A novel Rh(III)-catalyzed relay cross-coupling/cyclization cascade between arylketoimines and diazoesters is described. This transformation provides a concise access to unique π-conjugated 1-azaphenalenes (1-APLEs) *via* a double aryl Csp^2-H bond carbenoid functionalization process. As illustrative examples, the 1-APLE-based π-conjugated molecules which possess low-lying HOMO levels could be converted to promising organic optoelectronic materials.

Introduction

Fused polycyclic heteroarenes (FPHAs) are commonly encountered in natural products, biologically-active molecules and organic functional materials. [1] Among them, π-conjugated hetero atom-fused polycyclic backbones have aroused growing concerns for their potential application in the field of organic photovoltaic and organic field-effect transistor materials. [2] For examples, various nitrogen-containing FPHAs such as indole-based FPHAs, [3] carbazole-based FPHAs, [4] spiro-annulated triarylamine-based FPHAs (SAT-FPHAs) [5] and others [6] have been well evaluated for their optoelectronic applications (Figure 1). However, the material property explorations derive-

Figure 1. Selected Examples of *N*-Fused Polycylic Heteroarenes

Novel muscarinic allosteric agents   SAT-FPHAs   Indole-based FPHAs   1-APLE

d from 1-azaphenalenes (1-APLEs) are rarely reported owning to the restriction of efficient synthetic access to 1-APLE library, even though these compounds are gradually attracting remarkable attention because of their potential material properties. [7] Therefore, the development of concise methods for rapidly assembling 1-APLE derivatives has been an important goal for synthetic chemists.

In the past decade, metal-catalyzed cross-coupling of aryl C-H bonds with carbenoids provides a very powerful tool to form C-X bonds (X = C, N, and O, etc.). In this regards, various directing groups have been successively explored to allow for regioselectively introducing particular single functional group into aryl ring system via C-H activation process. [8] However, in contrast to these moncarbenoid functionalization of Csp^2-H bonds, the double cross-coupling of aryl C-H bonds with carbenoids would possibly provide an attractive and sustainable approach to more complex compounds due to that neither of the two aryl C-H bonds need to be prefunctionalized. Our recent work about the trapping of six-membered metallacycle species which derived from *N*-(2-pyridyl)-ketoimines **A** (Scheme 1a) by unsaturated alkynes [9] and CO, [10] inspired us to successfully realize Rh(III)-catalyzed chelation-assisted intermolecular carbenoid functionalization of Csp^3-H bonds, in which insertion of carbenoids regioselectively occurred at α-imino alkyl Csp^3-H bond instead of phenyl Csp^2-H bonds (Scheme 1a). [11] Owing to the synthetic importance of 1-APLEs, these results stimulated us to further envision that Rh(III) catalysts could doubly activate *C*-imino aryl Csp^2-H bonds employing imine as chelating group once switching the pyridyl group from *N*-(2-pyridyl)-ketoimines **A** to phenyl group (**E**), followed by the cross-coupling with α-acyl diazocarbonyl compounds (**G** and **I**) to furnish multisubstituted 1-APLE deriv-

a) Our Recent Work: Pyridine-directed Rh(III)-catalyzed Csp^3-H functionalization with diazo compounds
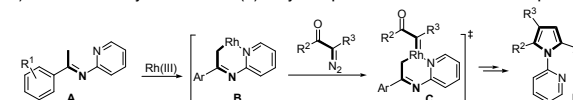
b) This Work: Ketoimine-directed Rh(III)-catalyzed Relay aryl C-H functionalization with diazo compounds
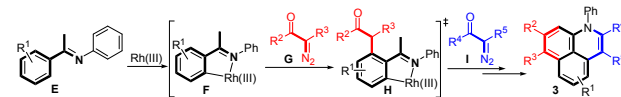
Scheme 1 Rh(III)-Catalyzed C-C Coupling Cascade Involving Imines and Diazo compounds

atives (Scheme 1b). To identify this hypothesis, herein we report a novel Rh(III)-catalyzed relay carbenoid functionalization of aryl C-H bonds to rapidly establish 1-APLE library through a single-step chemical process from basic

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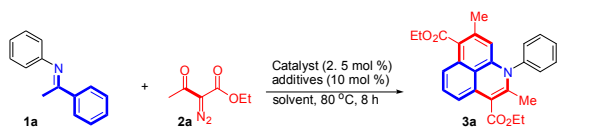† *These authors contributed equally.*

reagents. The existing synthetic methods about 1-APLE derivatives generally suffer from tedious reaction procedure, harsh reaction conditions and poor substrate generality. [12]

Results and discussion

Optimization studies

In the light of the fact that Pd(II), Cu(II) and Ir(III) catalysts, etc could easily react with diazo compounds to generate metal carbene intermediates,[13] our early investigation began with the cross-coupling/cyclization cascade of *N*-phenyl-ketoimine (**1a**) and α-acyldiazoacetate (**2a**) using various catalytic transition-metal salts in the presence of AgBF$_4$ (10 mol %) in 1, 2-dichloroethane (DCE) at 80 °C under Ar atmosphere for 8 h (Table 1, entries 1–8). After an extensive catalyst screening, we soon found catalysts [Cp*IrCl$_2$]$_2$ and [Cp*RhCl$_2$]$_2$ could afford the desired polysubstituted 1-APLE **3a** in 7% and 64% yields (entries 5 and 8), respectively; and (Cp*RhCl$_2$)$_2$ proved to be optimal (entry 8). Subsequently, the investigation of the effect of different silver additives towards the reaction was carried out, it showed that the reaction yield could be moderately increased to 85% by using AgSbF$_6$ as additive (compare entries 8–11 with 12). The further solvent screening demonstrated that DCE belongs to the most suitable solvent for this reaction (compare entries 13–17 with 12). Notably, extending the reaction time or increasing the reaction temperature led to a decreased conversion of **1a** to some degree (entries 18 and 19 vs 12). Finally, changing the ratio of **1a/2a** from 1:3 to 1:1 or 1:2 decreased the reaction yields (entries 20-21), and also no mono-aryl Csp^2-H bond functionalization product was observed.

Table 1. Optimization of Reaction Conditions ^{a}

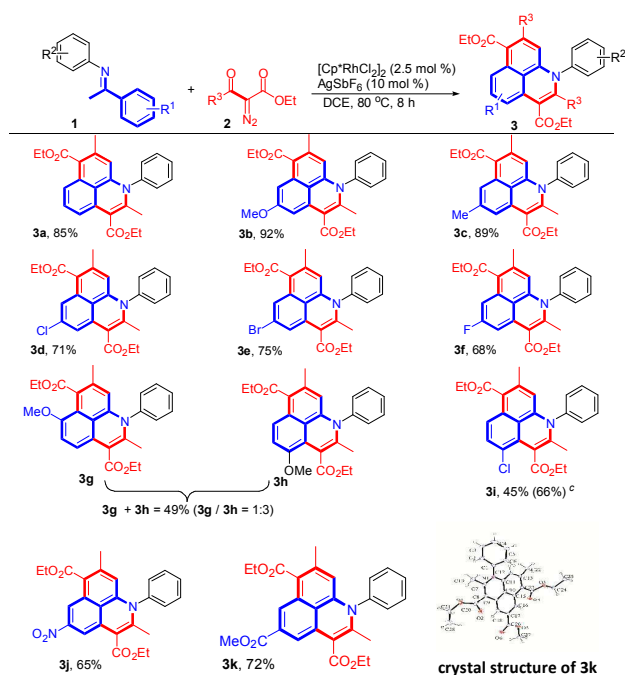| entry	catalysts	additives	solvent	yield (%) ^{b}
1	Pd(OAc)$_2$	AgBF$_4$	DCE	0
2	Cu(OAc)$_2$	AgBF$_4$	DCE	0
3	CuI	AgBF$_4$	DCE	0
4	[Ru(p-cymene)Cl$_2$]	AgBF$_4$	DCE	0
5	[Cp*IrCl$_2$]$_2$	AgBF$_4$	DCE	7
6	RhCl$_3$	AgBF$_4$	DCE	0
7	Rh$_2$(COD)$_2$Cl$_2$	AgBF$_4$	DCE	0
8	[Cp*RhCl$_2$]$_2$	AgBF$_4$	DCE	64
9	[Cp*RhCl$_2$]$_2$	AgClO$_4$	DCE	38
10	[Cp*RhCl$_2$]$_2$	AgNTf$_2$	DCE	81
11	[Cp*RhCl$_2$]$_2$	AgOAc	DCE	69
12	[Cp*RhCl$_2$]$_2$	AgSbF$_6$	DCE	85
13	[Cp*RhCl$_2$]$_2$	AgSbF$_6$	DMF	trace
14	[Cp*RhCl$_2$]$_2$	AgSbF$_6$	THF	58
15	[Cp*RhCl$_2$]$_2$	AgSbF$_6$	toluene	62
16	[Cp*RhCl$_2$]$_2$	AgSbF$_6$	CH$_3$CN	31
17	[Cp*RhCl$_2$]$_2$	AgSbF$_6$	DMSO	26
18	[Cp*RhCl$_2$]$_2$	AgSbF$_6$	DCE	71 ^{c}
19	[Cp*RhCl$_2$]$_2$	AgSbF$_6$	DCE	82 ^{d}
20	[Cp*RhCl$_2$]$_2$	AgSbF$_6$	DCE	24 ^{e}
21	[Cp*RhCl$_2$]$_2$	AgSbF$_6$	DCE	69 ^{f}

^{a} Unless otherwise noted, all the reactions were carried out using ketoimine (**1a**) (0.10 mmol) and diazocompound (**2a**) (0.30 mmol) with metal catalysts (2.5 mol %) in the presence of silver salts additives (10 mol %) in solvent (2.0 mL) at 80 °C for 8 h under Ar in a sealed reaction tube, followed by flash chromatography on SiO$_2$. ^{b} Isolated yield. ^{c} The reaction temperature is 60 °C. ^{d} The reaction temperature is 100 °C. ^{e} The ratio of
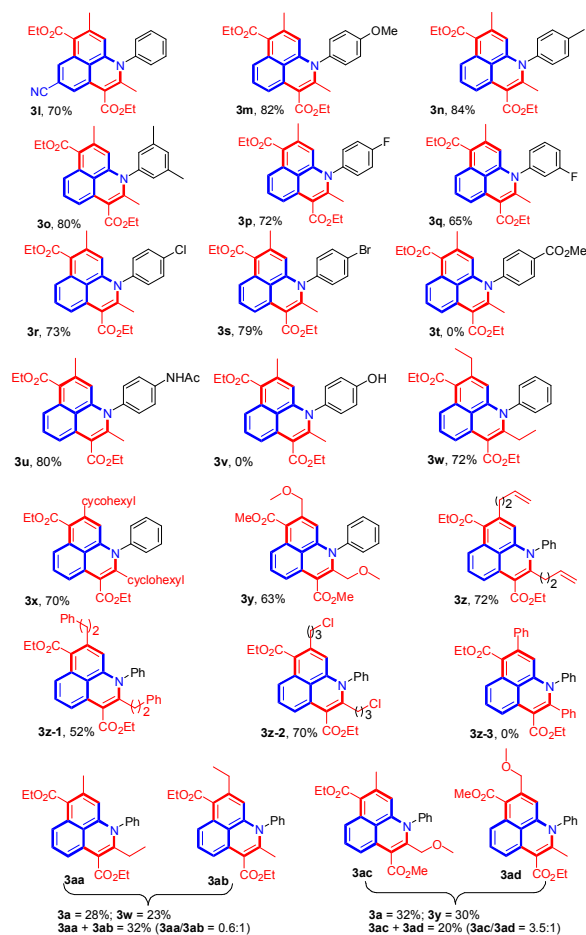
1a/2a is 1:1. ^{f} The ratio of **1a/2a** is 1:2 and the reaction time is 4 h.

Substrate scope

Having established the optimized reaction conditions that enable the relay aryl Csp^2-H bond carbenoid functionalization of **1a** with **2a**, we next investigated its scope with regard to the substituted *N*-phenyl-ketoimines (**1**). As illustrated in Scheme 2, the substitution on the iminobenzene ring (R^1) of **1** showed no significant electronic effects, the ketoimine derivatives with *para*-electron-donating group or halide (4-Me, 4-MeO, 4-Cl, 4-Br, 4-F) on the phenyl ring afforded the 1-APLE derivatives in good to excellent yields (68–92%, **3a**–**3f**), and electron-poor substrates with nitro group, ethoxylcarbonyl group and nitrile group on the phenyl ring could also underwent smoothly conversion to provide 65–72% yields of the desired products **3j**–**3l**. Compared with the *para*-substituted arylketoimines, introducing a methoxy group or chloride to the *meta*-position of the *C*-iminobenzene ring led to poor reaction conversions due to steric hindrance (**3g**–**3i**). Of note, electron-donating group- or halogen-substituted phenylamine moieties gave the 1-APLEs (**3m**–**3s**, **3u**) in 65-82% yields, but electron-poor *N*-(4-ethoxylcarbonyl-substituted phenyl)ketoimine and hydroxyl-containing ketoimine were not allowed for this transformation (**3t** and **3v**), and the starting materials were completely recovered. The scope of the present procedure with regard to diazo compound coupling partners has also been established, and a wide scope of α-alkylacyl substituted diazoacetates with alkoxyl, aryl, alkenyl and halogen groups could easily enable assembling the desried 1-APLEs **3u**–**3z-2** in 52–72% yields. Unfortunately, α-benzoyl substituted diazoacetate was not applicable to this transformation (**3z**–**3**). Finally, the Rh(III)-catalyzed cascade aryl Csp^2-H bond carbenoid functionalization of **1a** (2.0 equiv) with different diazoacetates via one-pot process was performed. As expected, we got the corresponding cross-coupling cyclization products **3aa**–**3ad** in the overall 20–32% yields.[14]

Table 2. Substrate scope ^{a}

3l, 70%

3m, 82%

3n, 84%

3o, 80%

3p, 72%

3q, 65%

3r, 73%

3s, 79%

3t, 0%

3u, 80%

3v, 0%

3w, 72%

3x, 70%

3y, 63%

3z, 72%

3z-1, 52%

3z-2, 70%

3z-3, 0%

3aa

3ab

3ac

3ad

3a = 28%; **3w** = 23%
3aa + **3ab** = 32% (**3aa/3ab** = 0.6:1)

3a = 32%; **3y** = 30%
3ac + **3ad** = 20% (**3ac/3ad** = 3.5:1)

[a] All the reactions were carried out using ketoimines (**1**) (0.10 mmol) and diazocompounds (**2**) (0.3 mmol) with [Cp*RhCl₂]₂ (2.5 mol %) in the presence of AgSbF₆ (10 mol %) in DCE (2.0 mL) at 80 °C for 8 h under Ar in a sealed reaction tube, followed by flash chromatography on SiO₂. [b] Isolated yield. [c] The reaction conversion determined by crude ^{1}H NMR spectrum.

Synthetic application

To evaluate the potentiality of the 1-APLEs as an electron donor in organic photovoltaic devices, we prepared carbazole-(Cz) or 1,5-dithia-s-indacene (BDT)-containing APLE-based π-conjugated organic small molecules **5** (70% yield) and **7** (88% yield) through traditional Pd-catalyzed cross-coupling strategy (Scheme 3). The photophysical properties of these organic small molecules were investigated by UV-vis absorption and photoluminescence spectroscopy. The small molecule **5** shows the absorption ranges from 320 to 380 nm, while the small molecule **7** exhibits the wider absorption ranges from 340 to 430 nm (Figure S1), and the photoluminescence spectra of **5** and **7** show maximum emission peaks at 530 and 520 nm, respectively (Figure S2). The highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) energy levels of these organic small molecules are important parameters in the design of optoelectronic devices.[15] To our delight, the cyclic voltammogram (CV) curves from compounds **5** and **7** demonstrated that their HOMO energy level are up to -5.76 eV and -5.57 eV (Figure S3 and Table S5), respectively. These energy levels were lower-lying compared with the benzothiadiazole-based polymers.[16] Given
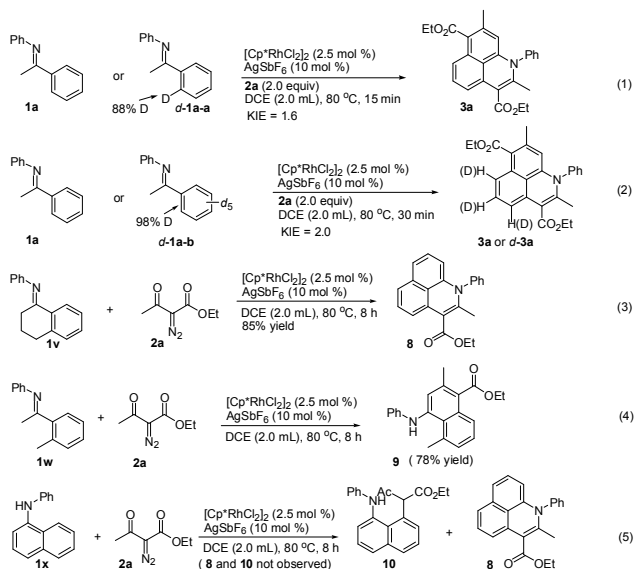
that the low-lying HOMO levels of the small donor molecules are essential to higher open-circuit voltage (Voc) of the organic solar cells (OSCs),[17] so the combination of 1-APLEs and carbazole-(Cz) or 1,5-dithia-s-indacene (BDT) units provided promising precursors with the lower HOMO energy level to assemble high-performance organic optoelectronic materials.

Scheme 3. Product Transformations

4

5 (70% yield) R⁴ = -CH(C₈H₁₇)₂

3e

6

7 (88% yield) R⁵ = -CH₂-CH(CH₂CH₂CH₂CH₃)(CH₂CH₃)
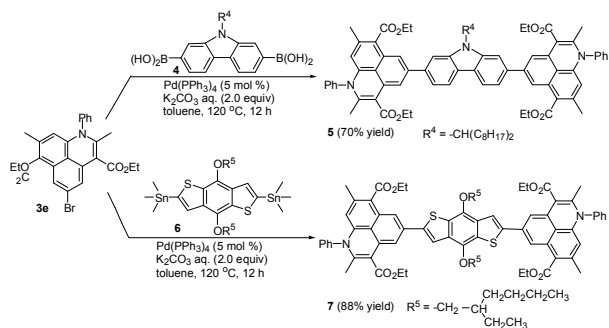
Mechanistic insights

Several control experiments were designed to elucidate the aryl Csp²-H bond carbenoid functionalization process (Scheme 4). First, the parallel kinetic isotope effect from monodeuterat-

1a or 88% D *d*-**1a-a**

[Cp*RhCl₂]₂ (2.5 mol %)
AgSbF₆ (10 mol %)
2a (2.0 equiv)
DCE (2.0 mL), 80 °C, 15 min
KIE = 1.6

3a (1)

1a or 98% D *d*-**1a-b**

[Cp*RhCl₂]₂ (2.5 mol %)
AgSbF₆ (10 mol %)
2a (2.0 equiv)
DCE (2.0 mL), 80 °C, 30 min
KIE = 2.0

3a or *d*-**3a** (2)

1v + **2a**

[Cp*RhCl₂]₂ (2.5 mol %)
AgSbF₆ (10 mol %)
DCE (2.0 mL), 80 °C, 8 h
85% yield

8 (3)

1w + **2a**

[Cp*RhCl₂]₂ (2.5 mol %)
AgSbF₆ (10 mol %)
DCE (2.0 mL), 80 °C, 8 h

9 (78% yield) (4)

1x + **2a**

[Cp*RhCl₂]₂ (2.5 mol %)
AgSbF₆ (10 mol %)
DCE (2.0 mL), 80 °C, 8 h
(**8** and **10** not observed)

10 + **8** (5)

Scheme 4 Preliminary Mechanism Studies

ed ketoimine *d*-**1a-a** (k_H/k_D = 1.6) and its pentadeuterate analogue *d*-**1a-b** (k_H/k_D = 2.0) demonstrated that double aryl Csp²-H bond activations were involved in this transformation (eq. 1 and eq. 2), and the second Csp²-H cleavage is a major contributor to the overall rate of the reaction. [18] Subsequently, when *ortho*-substituted arylcycloketoimine **1v** was subjected to the same reaction system, 1-APLE **8** was obtained in 85% yield (eq. 3). Meanwhile, the *ortho*-methyl ketoimine **1w** afforded the mono-aryl Csp²-H bond functionalization/cyclization arylamine product **9** in 78% yield (eq. 4). On the contrary, employing 2-(*N*-phenyl)naphthalenamine **1x** as starting material could not lead to the formation of 1-APLE **8** and amine product **10** (eq. 5),

these results suggested that the cyclization process would possibly occur after the second ary Csp[2]-H carbenoid functionalization was done, and aryl amine intermediates was also not involved in this transformation.

Based on the aforementioned results, a plausible reaction mechanism is proposed as shown in Scheme 5. Initially, (Cp*RhCl$_2$)$_2$ dedimerizes and produces a rhodacycle intermediate **A** by an imino "nitrogen"-assisted concerted metalation/deprotonation (CMD) process. Subsequently, the coordination of the diazoestate (**2a**) to the rhodium center is followed by the denitrogenation/ migratory insertion/ protonolysis to afford monofuctionalized ketoimine intermediate **D**. In the process herein, given that aryl amine (**1x**) could not lead to ortho-aryl Csp[2]-H bond carbenoid functionalization (see Scheme 4, eq. 5), the possibility of an alternative catalytic pathway **B** was excluded. Finally, the secondary Rh(III)-catalyzed imine-directed Csp[2]-H bond carbenoid functionalization/cyclization cascade of **D** furnished the desired 1-APLE **3a** with release of Rh(III) catalyst.
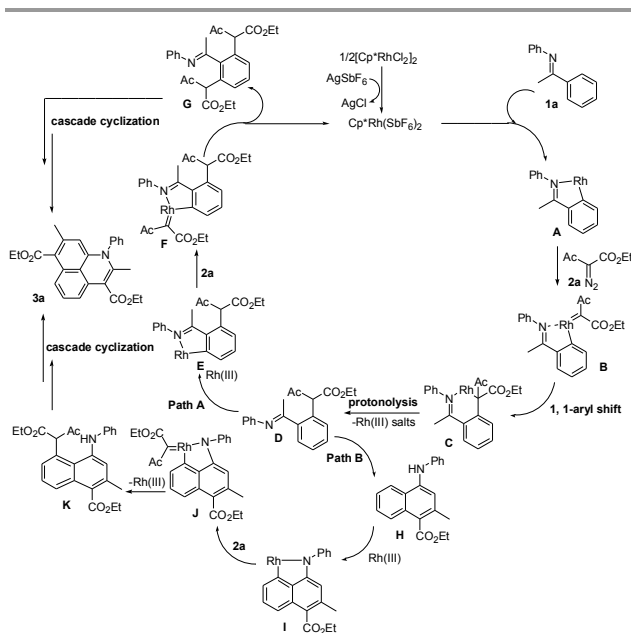
Scheme 5. Possible Mechanism for the Transformation

Conclusions

In conclusion, we have developed a novel Rh(III)-catalyzed relay aryl Csp[2]-H bond carbenoid functionalization between arylketoimines and diazoesters. This reaction can serve as a concise method for rapidly assemblying unique π-conjugated 1-APLEs with wide reactive functional group tolerance. The primary exploration about photovoltaic performance of 1-APLE-based π-conjugated molecules demonstrated that these compounds could be further converted to promising organic optoelectronic materials.

Acknowledgements

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