



Note

Cationic iridium–BINAP complex-catalyzed addition of aryl ketones to alkynes and alkenes via directed C–H bond cleavage

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ABSTRACT

Cationic Ir complex ($[\text{Ir}(\text{cod})_2]\text{BF}_4 + \text{BINAP}$) catalyzed the addition of *ortho*-C–H bonds in aryl ketones to alkynes, which gave alkenylated products in good to high yield. Styrene derivatives were good substrates, and the enantioselective addition to norbornene was also described.

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1. Introduction

The transition metal-catalyzed inactive C–H bond functionalization is an attractive process from both synthetic and atom-economical points of view, because it can eliminate the pre-activation step of substrates and reduce waste by-products [1]. Especially, Murai's report [2a], where *ortho*-C–H bonds in aryl ketones were added to olefins catalyzed by a ruthenium complex, opened a new frontier in highly selective C–H bond activation using directing groups such as carbonyl and imine [2]. In most of these examples, transition metal complexes with monodentate ligands were used and the examples of catalysts with bidentate ligands were few [3].

We previously reported that the cationic Rh-BIPHEP (BIPHEP: 2,2'-bis(diphenylphosphino)-1,1'-biphenyl) complex-catalyzed hydroarylation cyclization of diynes and enynes with aryl ketones [4]. We assumed that the bond cleavage of the *ortho*-C–H bonds in aryl ketones is an initial step of the cyclization [5]. In the course of our mechanistic studies, Rh-BIPHEP was also found to be an active catalyst in the addition of benzophenone to diphenylacetylene, which encouraged us to consider that cationic transition metal-diphosphine complex could catalyze directed C–H bond functionalization. We here disclose that cationic Ir–BINAP complex exhibits

the high catalytic activity in the addition of aryl ketones to alkynes [6]. The additions to several alkenes are also reported.

2. Results and discussion

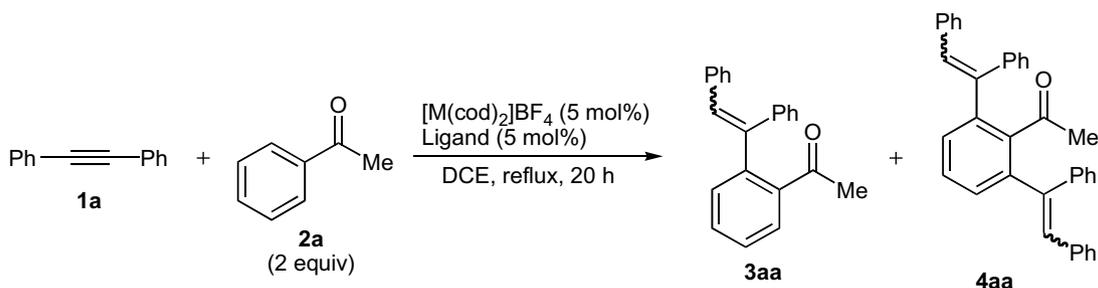
2.1. Optimization of the reaction conditions

We chose diphenylacetylene (**1a**) and acetophenone (**2a**) as model substrates, and examined several Rh and Ir catalysts in refluxed 1,2-dichloroethane (DCE) for 20 h (Table 1). $[\text{Rh}(\text{biphep})]\text{BF}_4$, which was prepared *in situ* from $[\text{Rh}(\text{cod})_2]\text{BF}_4$ and BIPHEP, and pre-treated with hydrogen gas to exclude 1,5-cyclooctadiene (COD), gave a low conversion (entry 1). Notably, the replacement of Rh with Ir dramatically increased the conversion ratio and yield (entry 2). Moreover, the exclusion of COD was found to be unnecessary: $[\text{Ir}(\text{cod})_2]\text{BF}_4$ and BIPHEP gave hydroarylation product **3aa** with high yield along with a small amount of dialkenylated product **4aa** (entry 3). *rac*-BINAP was more effective and product **3aa** was afforded in high yield as a sole stereoisomer (entry 4). In the case of monodentate ligands such as triphenyl and tricyclohexyl phosphines, and other bidentate ones such as 1,2-bis(2,5-dimethylphospholano)benzene (MeDUPHOS), most substrates were recovered and the adducts could not be detected under the same reaction conditions. These results mean that Ir–bidentate biaryl phosphine complex possesses high catalytic activity for the present reaction. Actually, the catalyst loading could be lowered to 1 mol%, which also achieved the high yield (entry 5). We decided to apply the reaction conditions of Entry 4 for further investigation.

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Table 1
Screening of reaction conditions.



| Entry | M | Ligand | Yield of 3aa /% ^a (E/Z) ^b | Yield of 4aa /% ^a |
|-----------------------|-----------|------------------|--|-------------------------------------|
| 1 ^c | Rh | BIPHEP | 22 (15/1) | ND ^d |
| 2 ^c | Ir | BIPHEP | 63 (1/1.8) | ND ^d |
| 3 | Ir | BIPHEP | 74 (7.4/1) | 6 |
| 4 | Ir | rac-BINAP | 83 (75)^e (>20/1) | 15 |
| 5 ^f | Ir | rac-BINAP | 80 (13/1) | 16 |

^a Yield was determined by ¹H NMR integration relative to 1,1,2,2-tetrachloroethane as an internal standard.

^b The stereochemistry of **3aa** was determined by the comparison of ¹H NMR analysis of that of **3ai** in Table 2.

^c 1,5-Cyclooctadiene (cod) in the metal catalyst was excluded prior to the reaction.

^d Not detected.

^e Isolated yield.

^f The catalyst (1 mol%) was loaded.

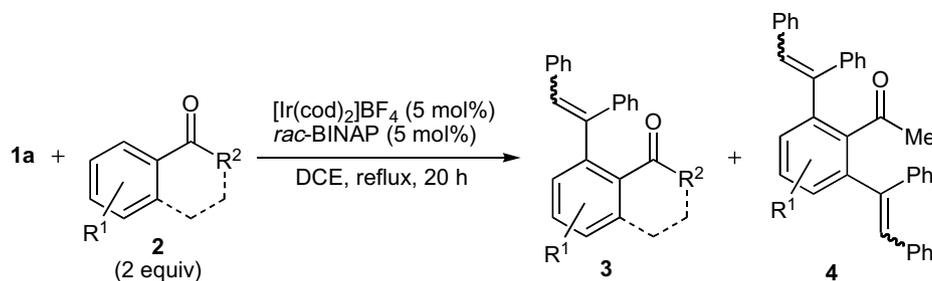
2.2. Examination of several aryl ketones with alkynes

We examined the addition of several aryl ketones to alkyne **1a** (Table 2). Various substituents at the *para* position of acetophenone were tolerable in the present reaction: *p*-methyl, *p*-methoxy, and *p*-trifluoromethyl groups did not retard the reaction and good conversions to mono and dialkenylated products were achieved (entries 1–3). However, substituents at the *ortho* position significantly affected the reactivity: tetralone (**2e**) and *o*-methoxyacetophenone (**2f**) provided the hydroarylatives products in high yields but *o*-trifluoromethylacetophenone (**2g**) did not give detectable

amount of the corresponding adduct (entries 4–6). Benzophenone (**2h**) and *tert*-butyl phenyl ketone (**2i**) were submitted to the reaction and the sole stereoisomers were obtained with high to quantitative yield (entries 7 and 8). The stereochemistry of adducts **3ah** and **3ai** was determined to be *E* by X-ray crystallography [7], which supports that the present reaction would involve carbonyl-directed *ortho*-C-H bond cleavage of aryl ketones and *syn*-addition to diphenylacetylene.

1-Phenyl-2-(trimethylsilyl)acetylene (**1b**) also reacted with ketone **2f**: adduct **3bf** was obtained in moderate yield along with an inseparable isomer Eq. (1) [8,9].

Table 2
Direct addition of *ortho*-C-H bonds of aryl ketones **2** to diphenylacetylene (**1a**).



| Entry | R ¹ | R ² | 2 | Yield of 3 /% ^a (E/Z) ^b | Yield of 4 /% ^c |
|-----------------------|---------------------------|------------------------------------|-----------|--|-----------------------------------|
| 1 | <i>p</i> -Me | Me | 2b | 67 (3ab) (5.8/1) | 26 (4ab) |
| 2 | <i>p</i> -OMe | Me | 2c | 72 (3ac) (>20/1) | 20 (4ac) |
| 3 | <i>p</i> -CF ₃ | Me | 2d | 59 (3ad) (>20/1) | 10 (4ad) |
| 4 | H | -(CH ₂) ₃ - | 2e | Quant. (3ae) (5.4/1) | – |
| 5 | <i>o</i> -OMe | Me | 2f | Quant. (3af) (>20/1) | – |
| 6 | <i>o</i> -CF ₃ | Me | 2g | ND ^d | – |
| 7 ^e | H | Ph | 2h | Quant. (3ah) (>20/1) ^f | ND ^d |
| 8 | H | <i>t</i> -Bu | 2i | 84 (3ai) (>20/1) ^f | ND ^d |

^a Isolated yield.

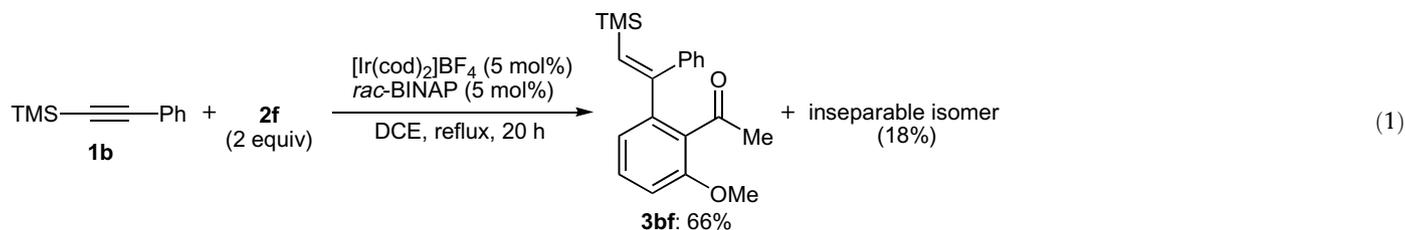
^b The stereochemistry of adduct **3** was determined by the comparison of ¹H NMR analysis of that of **3ai** in Entry 8.

^c Yield was determined by ¹H NMR integration relative to 1,1,2,2-tetrachloroethane as an internal standard.

^d Not detected.

^e The reaction time is 6 h.

^f The stereochemistry was determined to be *E* by X-ray crystallography.



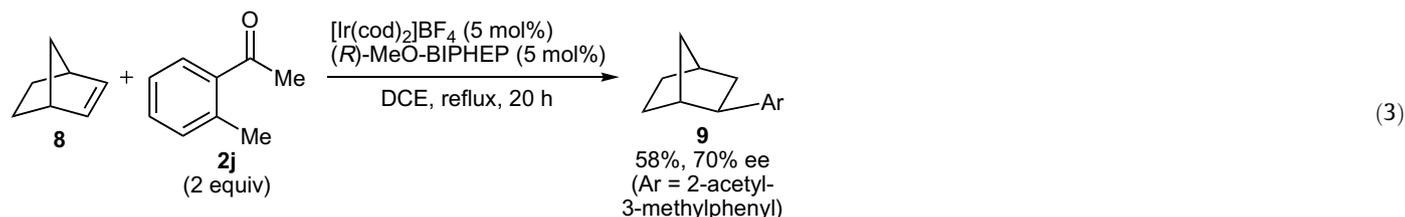
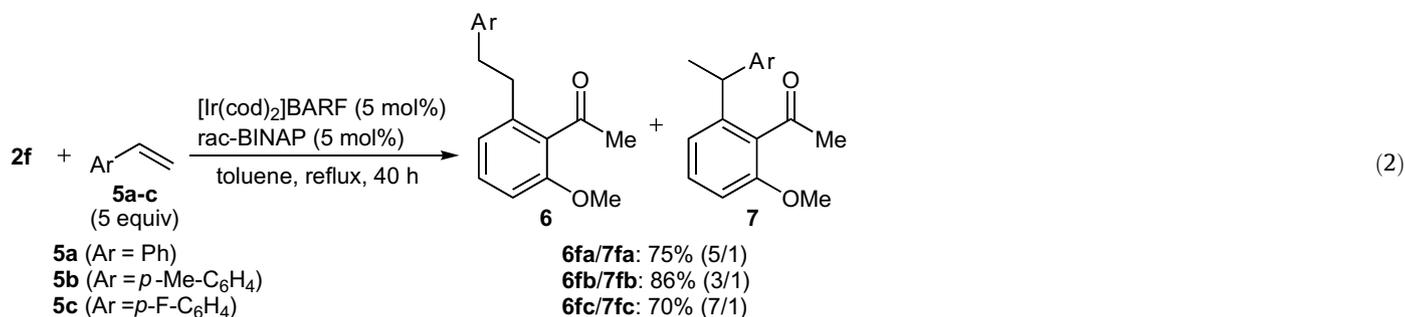
2.3. The hydroarylation to alkenes including an enantioselective reaction

Alkenes were also applicable to the present reactions using the cationic Ir–diphosphine complex. Styrene derivatives gave corresponding adducts with moderate regioselectivity, where tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (BARF) as a counter anion of iridium complex and higher temperature were required to achieve good yields Eq. (2) [10]. Norbornene (**8**) was also found to be a good substrate: the enantioselective addition of *o*-methylacetophenone (**2i**) to norbornene was achieved using (*R*)-MeO-BIPHEP (2,2′-bis(diphenylphosphino)-6,6′-dimethoxy-1,1′-biphenyl) as a chiral ligand Eq. (3) [3a].

ined under an argon atmosphere. IR spectra were recorded with a JASCO FT/IR-4100 spectrometer. NMR spectra were recorded with a JEOL AL-400 and Lambda 500 spectrometer using tetramethylsilane as an internal standard and CDCl_3 as a solvent. High-resolution mass spectra were measured on a JEOL JMS-SX102A with FAB (Fast atomic bombardment) method.

4.2. Typical experimental procedure

Entry 4 in Table 1: Under an atmosphere of argon, $[\text{Ir}(\text{cod})_2]\text{BF}_4$ (2.5 mg, 5 μmol) and *rac*-BINAP (3.1 mg, 5 μmol) were placed in a Schlenk tube. After addition of alkyne **1a** (18.0 mg, 0.1 mmol), aryl ketone **2a** (23 mL, 0.2 mmol), and degassed DCE (0.2 mL), the solu-



3. Conclusion

In summary, we have demonstrated the catalytic activity of cationic iridium–bidentate phosphine complex in carbonyl-directed C–H bond cleavage. Alkenes could be also used and the enantioselective reaction was accomplished in the reaction with norbornene. Further studies on the applications of this catalytic system are in progress.

4. Experimental

4.1. General

Anhydrous 1,2-dichloroethane and toluene are commercially available. They were dried over molecular sieves 4A (MS 4A) and degassed by argon bubbling before use. All reactions were exam-

tion was heated at reflux temperature for 20 h. The resultant mixture was filtered through a silica pad, and dried in vacuo. The crude products were purified by thin-layer chromatography (hexane/AcOEt = 10/1) to give analytically pure **3aa** (75%, *E/Z* = >20/1).

1-(2-(1,2-diphenylvinyl)phenyl)ethanone (**3aa**): ¹H NMR (400 MHz) δ = 2.36 (s, 3H), 6.58 (s, 1H), 7.08–7.49 (m, 14H); ¹³C NMR (125 MHz) δ = 30.0, 127.2, 127.5, 127.7, 127.7, 128.1, 128.3, 129.4, 130.2, 130.7, 130.7, 131.8, 137.0, 139.7, 141.3, 141.7, 143.1, 204.2; IR (acetone) 1689, 762, 708 cm^{-1} ; HRMS (FAB⁺) for M+1 found *m/z* 299.1436, Calc. for C₂₂H₁₉O: 299.1436.

Acknowledgements

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Appendix A. Supplementary material

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.jorganchem.2008.09.065](https://doi.org/10.1016/j.jorganchem.2008.09.065).

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- [7] Deposit No.: CCDC 696130 for **3ai** and CCDC 696131 for **3ah**.
- [8] The inseparable product would be a regio- or stereoisomer of product **3bf** but could not be fully characterized without purification.
- [9] When 3-hexyne was used as an alkyne under the same reactions conditions, only a trace amount of the corresponding adduct was detected.
- [10] When $[\text{Ir}(\text{cod})_2]\text{BF}_4\text{-rac-BINAP}$ was used in refluxed DCE, the reaction of styrene with **2f** gave the product with low yield of 39%.