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AgOTf-Catalyzed Tandem Reaction of Oxabenzonorbornadienes with Arylacetylenes

Yongyun Zhou, Shanshan Liu, Hualei Chen, Jingchao Chen, Weiqing Sun,
Sifeng Li, Qingjing Yang, and Baomin Fan*

*YMU-HKBU Joint Laboratory of Traditional Natural Medicine, Yunnan Minzu University,
Kunming, Yunnan 650500, China*

A tandem isomerization/hydroarylation reaction of oxabenzonorbornadienes and arylacetylenes was realized by using AgOTf as catalyst. 1,1-Diarylethylenes could be easily generated as products in moderate to good yields in this tandem reaction.

Keywords silver, tandem reaction, catalyze, 1,1-diarylethylene, oxabenzonorbornadiene

Introduction

The reactions between oxabenzonorbornadienes and terminal alkynes demonstrate the versatile power of catalysts in organic synthesis. By using different metal complexes as catalysts, tremendous reactive diversities have been achieved for these reactions, with molecules having different structures generated. For example, [2+1],[1,2] [2+2],[3-10] and [2+2+2][11-13] cycloaddition reactions, as well as ring-opening reactions[14] and hydroalkynylation reactions,[15] have been reported for oxabenzonorbornadienes and terminal alkynes with various cyclic compounds as products. Despite of these reported reactions, it is still interesting and desirable to develop new catalytic reactions for oxabenzonorbornadienes and terminal alkynes by employing new catalysts.

Over the past several years, our group had been devoted to studying the transition-metal-catalyzed asymmetric reactions of norbornadiene derivatives, especially those with terminal alkynes. We had established two effective chiral iridium catalysts for the asymmetric hydroalkynylation reaction[16,17] and asymmetric [2+2] cycloaddition reaction[18,19] of norbornadiene derivatives with terminal alkynes respectively. Recently, we had found that the combination of $Pd(OAc)_2$/(*R*)-xyl-Binap and CuOTf could form a high efficient co-catalytic system for the asymmetric ring opening reaction of azabenzonorbornadienes with various terminal alkynes.[20] By fine tuning the catalytic system to be $Pd(OAc)_2$/(*R*)-xylyl-Phanephos and AgOTf, the new catalytic system was proved to be suitable for the same reactions of oxabenzonorbornadienes.[21] Obviously, Lewis acids had played an important role in the catalytic procedures of these reactions. It should be noted that Lewis acids, for example $Fe(OTf)_3$, had also been successfully used as catalyst for the hydroalkynylation reaction of norbornadiene derivatives.[22] For better understanding the effects of Lewis acids in such reactions, it is necessary to explore the catalytic activities of Lewis acids in the reactions between oxabenzonorbornadienes and terminal alkynes. Herein, we report a AgOTf catalyzed tandem isomerization/hydroarylation reaction of oxabenzonorbornadienes and arylacetylenes.

Experimental

General

The reactions and manipulations were performed under an argon atmosphere by using standard Schlenk techniques and a drybox (Mikrouna, Supper 1220/750). Anhydrous toluene, DME (dimethoxyethane), THF (tetrahydrofuran), and dioxane were distilled from sodium benzophenoneketyl prior to use. Anhydrous DCE (1,2-dichloroethane) was distilled from calcium hydride and stored under argon. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker-Avance 400 MHz spectrometer. $CDCl_3$ was used as solvent. Chemical shifts (δ) were reported with tetramethylsilane as an internal standard, and *J* values were reported in Hz. High-resolution mass spectra (HRMS) were obtained on a VG Autospec-3000 spectrometer. Column chromatography was performed using silica gel (200—300 mesh).

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* E-mail: adams.bmf@hotmail.com; Fax: 0086-871-65913103

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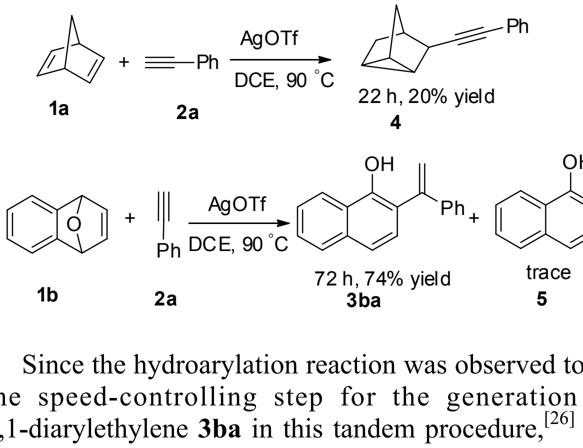
Typical procedure for AgOTf-catalyzed tandem reaction of oxabenzonorbornadiene with terminal alkyne

Under the protection of argon, AgOTf (5.1 mg, 0.02 mmol), oxabenzanorbornadiene (28.8 mg, 0.2 mmol), and 1.0 mL DCE were added to a Schlenk tube. The solution obtained was stirred at room temperature. 10 min later, arylacetylene (44 μL, 0.4 mmol) and 1.0 mL DCE were added, and the Schlenk tube was sealed with a rubber septum and moved to an oil bath. The mixture was stirred at 90 ℃ (bath temperature) until the reaction was complete. After vacuum evaporation of the reaction solvent, the residue was purified by column chromatography on silica gel to yield the 1,1-diarylethylene product.

Results and Discussion

Initially, we selected norbornadiene **1a** to react with phenylacetylene **2a** under the promotion of AgOTf (Scheme 1). After 22 h of heating and stirring, phenylacetylene was completely consumed, and the hydroalkynylation product **4** was isolated in 20% yield. Encouraged by this result, oxabenzonorbornadiene **1b** was employed as a substrate for the reaction. Interestingly, 1,1-diarylethylene **3ba** was generated, along with a small amount of naphthol **5** instead of the expected hydroalkynylation product. It was observed that, under the catalysis of AgOTf, oxabenzonorbornadiene **1b** could be almost quantitatively isomerized to naphthol **5** in a very short time.[23] We also observed that under the same catalytic condition, naphthol **5** could react with phenylacetylene **2a** to generate the hydroarylation product **3ba** in 90% yield in 16 h (Scheme 2). Thus, a silver-catalyzed tandem ring-opening isomerization and hydroarylation procedure for oxabenzonorbornadiene **1b** and phenylacetylene **2a** could be proposed for the generation of 1,1-diarylethylene **3ba**.[24,25]

Scheme 1 AgOTf-catalyzed reactions between norbornadiene or oxabenzonorbornadiene and phenylacetylene



Since the hydroarylation reaction was observed to be the speed-controlling step for the generation of 1,1-diarylethylene **3ba** in this tandem procedure,[26] the catalytic conditions for this step were further examined by using naphthol **5** and phenylacetylene **2a** as standard substrates. First, a series of Lewis acids were screened as catalysts (Table 1). It was observed that $Zn(OTf)_2$ and $Fe(OTf)_2$ were ineffective in this reaction (Entries 2 and 3). $Fe(OTf)_3$ was proved to be a poor catalyst for the transformation, and after 42 h of heating and stirring, **3ba** was obtained in only 17% yield (Entry 4). Both CuOTf and $Cu(OTf)_2$ could catalyze the desired reaction, with the latter showing higher efficiency and producing the hydroarylation product in 85% yield (Entry 6). Changing the anion of the silver salt did not enhance the efficiency of the catalyst (Entries 7 and 8). AgOTf was proved to be the best catalyst for this transformation.

Scheme 2 AgOTf-catalyzed isomerization and hydroarylation reactions

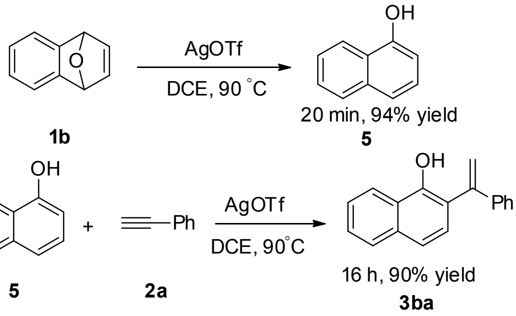
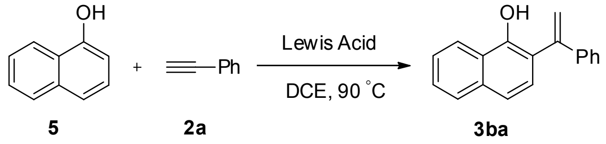


Table 1 Screening of different Lewis acids as catalyst in hydroarylation reaction of naphthol (**5**) and phenylacetylene (**2a**)[a]

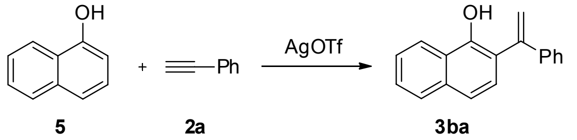


Entry	Metal catalyst	Time/h	Yield[b]/%
1	AgOTf	16	90
2	$Zn(OTf)_2$	24	n. r.
3	$Fe(OTf)_2$	24	n. r.
4	$Fe(OTf)_3$	42	17
5	CuOTf	42	59
6	$Cu(OTf)_2$	28	85
7	$AgSbF_6$	16	<5
8	$AgBF_4$	16	57

[a] Reagents and conditions: naphthol (**5**; 0.2 mmol), phenylacetylene (**2a**; 0.4 mmol), metal salt (10 mol%), DCE (2 mL), reflux. [b] Isolated yield.

Using AgOTf as a catalyst, the solvent and reaction temperature for the hydroarylation reaction of naphthol **5** and phenylacetylene **2a** were further optimized; the results are summarized in Table 2. As shown, DCE was the best solvent because the highest yield was achieved within the shortest reaction time (Entry 5). It was observed that the yield of the product decreased significantly with the decreasing of reaction temperature (Entries 6 and 7). Thus, the optimum reaction conditions for this speed-controlling step could be determined using AgOTf as the catalyst, in DCE solvent and at 90 ℃, which should also be the best condition for the entire tandem reaction.

Table 2 Screening of the solvents and temperature[a]



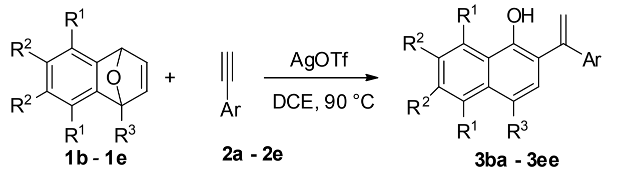
Entry	Solvent	Temperature/℃	Time/h	Yield[b]/%
1	THF	90	23	24
2	Toluene	90	42	71
3	Dioxane	90	42	48
4	DME	90	37	53
5	DCE	90	16	90
6	DCE	70	52	56
7	DCE	50	72	39

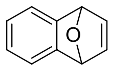
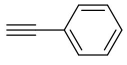
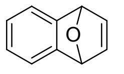
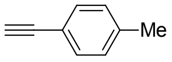
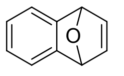
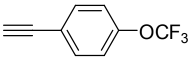
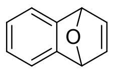
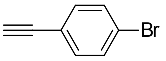
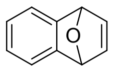
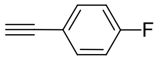
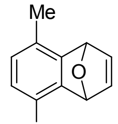
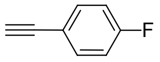
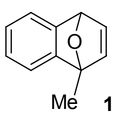
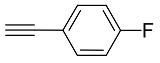
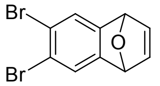
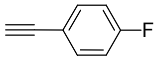
[a] Reagents and conditions: naphthol (**5**; 0.2 mmol), phenylacetylene (**2a**; 0.4 mmol), AgOTf (10 mol%), DCE (2 mL). [b] Isolated yield.

To further probe the generality of this methodology, several substituted oxabenzonorbornadienes and arylacetylenes were used as substrates in this silver-catalyzed tandem reaction system. The results are presented in Table 3, which demonstrate that the electronic properties of the substituents on the phenyl ring had a distinct effect on the yield of the reactions (Entries 1—5). The reaction of oxabenzonorbornadiene and phenyl acetylene afforded the hydroarylation product in good yield (74%) (Entry 1). However, electron-donating groups on the aromatic rings of terminal alkynes resulted in a lower yield (Entry 2). Substituents with electron-withdrawing groups on the aromatic rings of terminal alkynes were well tolerated in this tandem reaction (Entry 3—5). It should be noted that the terminal alkyne with an F group on the aromatic ring afforded the hydroarylation product in good yield (83%) (Entry 5). Several other substituted oxabenzonorbornadiene derivatives were also examined and proved to be suitable substrates (Entry 6—8). In particular, 4-monosubstituted oxabenzonorbornadiene also afforded the corresponding product in 66% yield (Entry 7).

On the basis of literature[23] and our own observations, the proposed mechanism for this novel tandem reaction is shown in Scheme 3. The catalytic cycle is initiated by the coordination of oxabenzonorbornadiene with silver ion to generate the active silver complex **A**, which undergoes ring-opening reaction to afford the silver alkoxide species **B**. Subsequently, intermediate **B** might be in equilibrium with isomer **C** that generates side-product **5** from silver alkoxide **D** by proton elimination and the following cation exchange. However, as reaction time prolonged, the silver alkoxide **D** coordinates with arylacetylene to generate complex **E**, which gives intermediate **F** by nucleophilic addition. Finally, the tandem reaction product **3ba** is obtained by cation exchange.

Table 3 AgOTf-catalyzed tandem isomerization/hydroarylation reaction of oxabenzonorbornadienes and arylacetylenes[a]



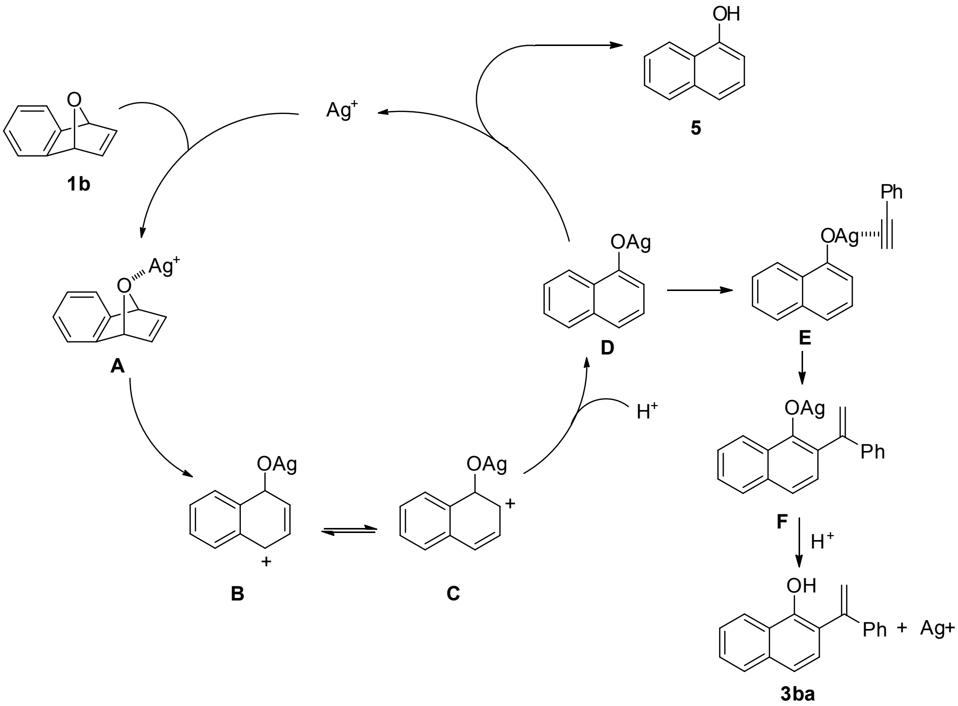
Entry	Oxabenzonorbornadiene	Arylacetylene	Time/h	Yield[b]/%
1	 1b	 2a	72	74
2	 1b	 2b	68	25
3	 1b	 2c	91	48
4	 1b	 2d	72	66
5	 1b	 2e	48	83
6	 1c	 2e	66	62
7	 1d	 2e	67	66
8	 1e	 2e	48	38

[a] Reagents and conditions: oxabenzonorbornadienes (**1b**—**1e**, 0.2 mmol), arylacetylene (**2a**—**2e**, 0.4 mmol), AgOTf (10 mol%), DCE (2 mL). [b] Isolated yield.

Conclusions

In summary, a tandem isomerization/hydroarylation reaction of oxabenzonorbornadienes and arylacetylenes has been developed. 1,1-Diarylethylenes could be generated in yields of up to 83% when using AgOTf as

Scheme 3 Proposed mechanism for AgOTf-catalyzed tandem reaction of oxabenzonorbornadiene with arylacetylene



a catalyst. This reaction provides an attractive method for the facile and economical construction of 1,1-diarylethylenes, which are important motifs in both naturally occurring and biologically active compounds.

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