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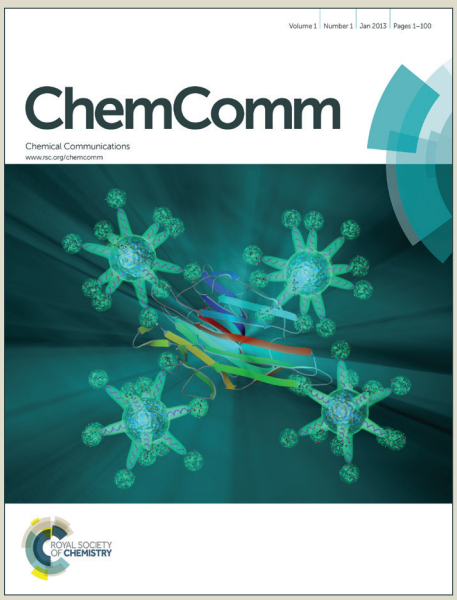

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Preparation of phenanthrenes from *ortho*-amino-biphenyls and alkynes *via* base-promoted homolytic aromatic substitution

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A transition-metal-free phenanthrene synthesis starting from readily accessible *ortho*-amino-biaryls is presented. The biarylamines are *in situ* transformed to the corresponding diazonium salts which upon single electron reduction give the corresponding aryl radicals. Addition to an alkyne and subsequent base promoted homolytic aromatic substitution (BHAS) provide phenanthrenes in moderate to good yields.

Base-promoted homolytic aromatic substitution (BHAS) has recently gained great attention for direct C-H arylation.[1,2] The BHAS reaction can also be incorporated as key step in radical cascade processes. This has been nicely documented by several groups for preparation of phenanthridines starting with 2-isocyanobiphenyls (Figure 1).[3-9] These 2-isocyanobiphenyls are readily accessed from the corresponding 2-aminobiphenyls by formylation and subsequent dehydration. We wondered whether 2-aminobiphenyls can also serve as precursors for preparation of phenanthrenes via a radical cascade comprising a BHAS reaction. Phenanthrenes are important organic compounds which have found application in medicinal chemistry[10] and in materials science.[11] Various methods for their preparation such as [4+2] benzannulation,[12] cycloisomerisation[13] or photocyclization[14] have been reported. In addition, Zhou and co-workers recently introduced a radical approach to phenanthrenes by reacting biaryldiazonium salts as aryl radical precursors with alkynes in the presence of a photoredox catalyst.[15] A similar sequence for phenanthrene synthesis starting with diazonium salts was also disclosed by

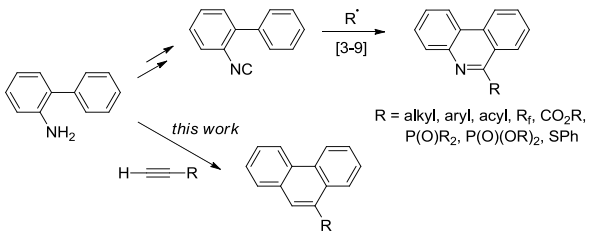

Figure 1 Phenanthridines and phenanthrenes from *ortho*-aminobiphenyl via BHAS reactions.

Zanardi.[16] The scope was limited and yields were moderate but these examples clearly reveal that such a cascade reaction is feasible. However, not all aryldiazonium salts are easily accessible and isolation or storage due to their limited stability is problematic. Herein we report a practical method for preparation of phenanthrenes starting from readily accessible biaryl amines. The biaryl amines are *in situ* transformed to the corresponding diazonium salts which act as radical precursors. In the past, diazonium salts have been successfully used in radical cyclizations[17] and more recently aryldiazonium salt chemistry by using *in situ* generated diazonium salts has found increased attention.[18]

Reaction was optimized by using biaryl amine **1a** as a radical precursor in combination with phenyl acetylene to provide phenanthrene **2a** (Table 1). We used isoamyl nitrite for *in situ* diazonium salt generation, Bu_4NI as a radical initiator and tested various bases. Reactions were conducted under argon atmosphere at 70 °C for 24 h in acetonitrile. Since we aimed at a base-promoted homolytic aromatic substitution process, a challenge was to identify basic conditions for *in situ* diazonium salt generation. Note that in most cases, diazonium salt formation occurs under acidic conditions.[17,18]

The initial experiment was performed by using NaOAc with 3 equiv of phenyl acetylene and phenanthrene **2a** was formed in 22% yield (entry 1). By increasing the amount of radical acceptor

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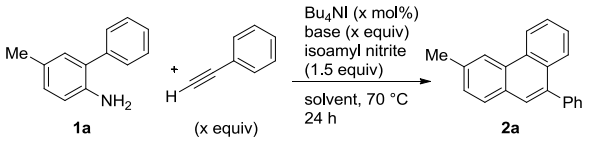
to 5 equiv, isolated yield was improved to 55% (entry 2). However, with 10 equiv of phenyl acetylene a worse result was obtained (entry 3). Increasing initiator loading to 20 mol% resulted in a lower conversion (entry 4) and lowering the amount of NaOAc also afforded a worse result (entry 5). Yield was increased to 62% upon switching the solvent from MeCN to benzotrifluoride (BTF, entry 6).

Table 1 Optimization studies.



entry	HCCPh (equiv)	Bu_4NI (mol%)	base (equiv)	solvent	yield[a] (%)
1	3.0	10	NaOAc (3.0)	MeCN	22
2	5.0	10	NaOAc (3.0)	MeCN	55[b]
3	10.0	10	NaOAc (3.0)	MeCN	34
4	5.0	20	NaOAc (3.0)	MeCN	32
5	5.0	10	NaOAc (1.1)	MeCN	48
6	5.0	10	NaOAc (1.1)	BTF	62
7	5.0	10	CsOAc (1.1)	BTF	46
8	5.0	10	-	BTF	60
9	5.0	10	-	dioxane	14
10	5.0	10	-	BTF	54[c]
11	5.0	10	-	BTF	60[d]
12	**10.0**	**10**	**-**	**BTF**	**78[b]**
13	15.0	10	-	BTF	72
14	10.0	5	-	BTF	66
15	10.0	10	-	BTF	55[e]
16	10.0	-	-	BTF	39

[a]Yield determined by ^{1}H NMR analysis using an internal standard. [b]Isolated yield. [c]With 1 equiv of isoamyl nitrite. [d]With 3 equiv of isoamyl nitrite. [e]*tert*-butyl nitrite instead of isoamyl nitrite was used.

CsOAc as a base provided **2a** in only 46% (entry 7). Interestingly, we found that external base is not needed rendering the overall process even more economic (entry 8). Dioxane was not a suitable solvent (entry 9) and 1.5 equiv of isomamyl nitrite was found to be optimal for that cascade (entries 10 and 11). Yield was further improved to 78% if 10 equiv of radical acceptor is added (entry 12). A further increase of the radical acceptor concentration (15 equiv) or decreasing the initiator loading to 5 mol% did not provide a better result (entries 13, 14). The yield dropped to 55% by using ^{t}BuONO for diazonium salt formation (entry 15). Without any initiator, **2a** was obtained in 39% (entry 16). Initiation likely occurred by traces of transition metals. An experiment under optimized conditions at lager scale (1 mmol) provided **2a** in 68% yield.

Under optimized conditions (Table 1, entry 12) various aminobiphenyls[19] **1b-n** were reacted with phenylacetylene to give the corresponding phenanthrenes **2b-n** in moderate to good yield (Figure 2). Preparation of the biphenyls **1b-n** is described in the Supporting Information. We first investigated the effect of substituent at the arene moiety of the biaryl where the BHAS reaction occurs. Aminobiphenyls carrying electron-donating groups at the *para*-position worked well and phenanthrenes **2c-f** were isolated in 69-85% yield. Electronic effects at the *para*-position are not important since also for systems carrying electron withdrawing groups phenanthrene synthesis worked well (see **2g-k**). Disappointingly, BHAS onto a naphthyl moiety was low yielding (see **2l**). For the *ortho*-F-biphenyl derivative yield was significantly lower (see **2m**) and as expected, the *meta*-congener **1n** reacted with low regioselectivity and both isomers **2n** and **2n'** were formed. The structures of **2c** and **2g** were confirmed by X-ray analysis (see SI).

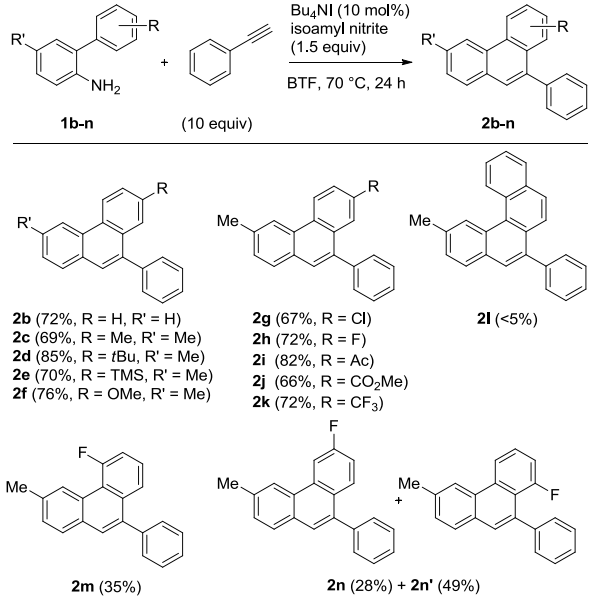


Figure 2 Substrate scope (variation of the aminobiphenyl component)

We next investigated the scope with respect to the alkyne radical acceptor. Electronic effects exerted by the *para*-substituent of the aryl acetylene are weak and phenanthrenes **2o-r** were isolated in 69-80% yield. *Ortho* and *meta*-substituents at the aryl moiety were tolerated (**2s**,**t**), the naphthyl derivative worked well (**2u**) and also 2-pyridyl acetylene provided the targeted product **2v** in good yield.

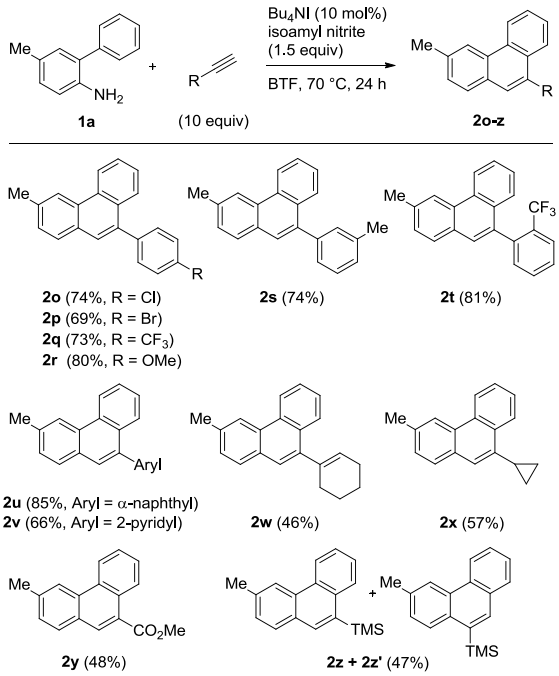


Figure 3 Substrate scope (variation of the alkyne component)

Enyne **1w** was a substrate and also the cyclopropyl derivative **1x** underwent addition/cyclization (see **2x**). For the latter, products derived from cyclopropane ring-opening were not identified. This is likely due to the fact that ring-opening is reversible and the BHAS reaction can only occur on the cyclized vinyl radical. The electron-poor methyl propiolate provided phenanthrene **2y** in 48% yield. If ethynyltrimethylsilane is used as an acceptor, initial addition of the aryl radical was not fully regioselective and the cascade provided the two inseparable regioisomers **2z** and **2z'** in 47% combined yield.

The suggested mechanism for the radical phenanthrene synthesis is presented in Figure 4. The biaryl amine is first converted to the corresponding diazonium salt with isoamyl nitrite. Initiation of the chain occurs by SET reduction of the diazonium salt with Bu_4NI[20] to generate aryl radical **A**.[21] Addition of **A** to the alkyne provides vinyl radical **B** which cyclizes to the arene to give cyclohexadienyl radical **C**. Deprotonation[22] of **C** by the alcoholate derived from isoamyl nitrite generates radical anion **D** which is eventually oxidized to phenanthrene **2**. In this step an electron is formally liberated which then reduces the diazonium salt documenting the role of the electron as a catalyst in this cycle.[23,24]

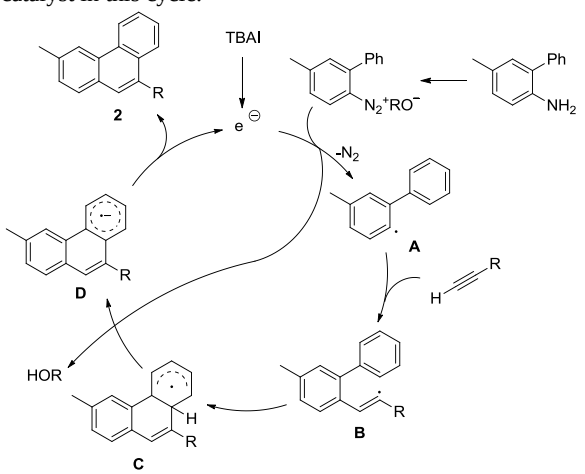


Figure 4 Suggested mechanism

In summary, we have developed a novel method for the preparation of phenanthrenes. Starting materials are readily prepared and reactions are easy to conduct. TBAI is used as a cheap and commercially available chain initiator. Substrate scope is broad and product phenanthrenes are obtained in moderate to good yields.

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