



Gold-catalyzed nucleophilic tandem cyclizations of tetraethynylethene derivatives



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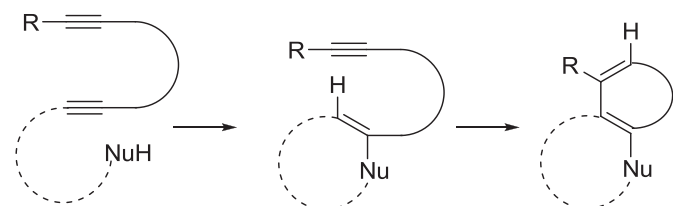
ABSTRACT

Symmetric and non-symmetric tetraethynylethene derivatives possessing nucleophilic groups were synthesized and subjected to gold catalysts. By a fourfold nucleophilic tandem cyclization extended π -systems like carbazolocarbazoles are accessible in high efficiency and in complete atom economy.

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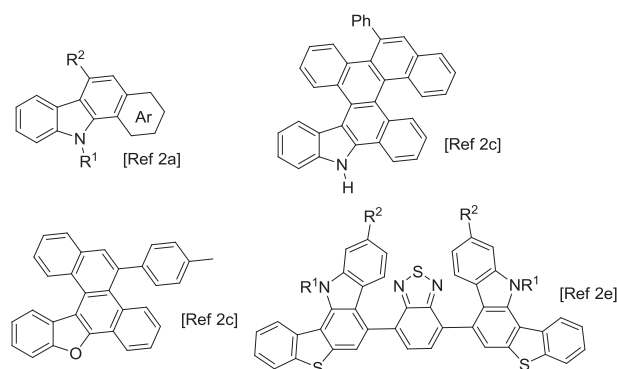
1. Introduction

Diyne or polyynes systems have proven to be extremely useful precursors for transition-metal-catalyzed processes.¹ In particular, conjugated 1,5-diyne systems have attracted considerable attention as these systems offer an entry towards interesting polyaromatic structures that are not easily available via classical synthetic strategies.² Cascade reactions provide an interesting strategic reaction pathway into polyyne systems, and can be initiated by the attack of an inter- or intramolecular nucleophile, which offer fast access to



Scheme 1. General reactivity pattern for gold-catalyzed nucleophilic polyynes cyclizations.

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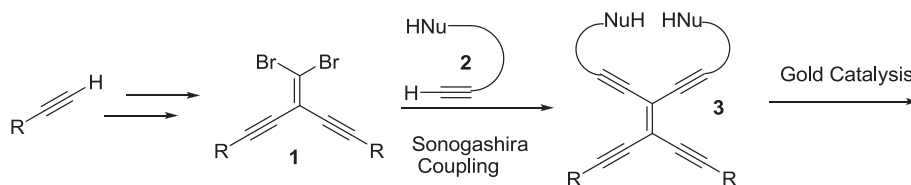


Scheme 2. Representative examples for polyaromatic compounds derived from conjugated 1,5-diyne systems.

diverse diyne or polyyne structures in a complete atom economic fashion (Scheme 1). The target compounds can be obtained without the need for the isolation of intermediates that saves energy and time, and furthermore avoids the generation of waste. Scheme 2 depicts representative examples of interesting polycyclic aromatic systems that are all derived from gold-catalyzed³ tandem processes involving 1,5-diyne systems.

All of the mentioned approaches are based on aromatic backbones as precursors. We envisioned that easily accessible tetraethynylethene derivatives might also serve as suitable precursors for

metal-catalyzed nucleophilic cascade reactions. The use of this non-aromatic scaffold should enable a modular approach towards new polycyclic aromatic systems via a bidirectional synthesis (Scheme 3). This methodology would nicely expand the concept of polyene cyclizations as it would allow the synthesis of interesting targets that cannot be accessed from the common aromatic precursors. Interestingly, despite the frequent use in material chemistry⁴ no reports can be found on transition metal-catalyzed nucleophilic cyclization of tetraethynylethene derivatives. Our studies on the cyclization of these compounds are summarized in this contribution.



Scheme 3. Synthetic approach towards the tetraethynylethene starting materials.

2. Results and discussion

Following the synthetic concept shown in Scheme 3, various starting materials could be prepared starting from commercially available alkynes. The depicted *gem*-dibrominated endiynes **3** were obtained via addition of lithium acetylides to ethylformate followed by oxidation and a Corey Fuchs sequence. Finally, a Sonogashira reaction delivered the starting materials for the gold catalysis.

The conversion of substrate **3a** was used for the catalyst optimization (Table 1). First we tested the NHC-gold(I) complex IPrAuCl in combination with different co-catalysts that were used for the activation of the pre catalyst (entries 1–5). AgNTf₂ (entry 1), AgOTf₂ (entry 3) and AgPF₆ (entry 5) gave the best results. The co-catalysts AgNTf₂ (entry 8) and AgPF₆ (entry 15) alone were catalytically

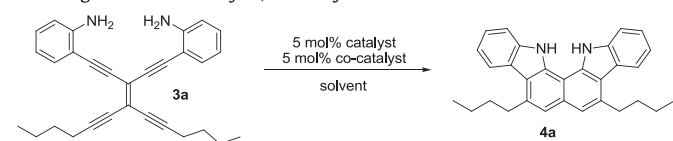
inactive, the same is true for Au(III) (entry 6), isonitrilegold(I) chloride (entry 10), NaAuCl₄ (entry 7) and triphenylphosphine-gold(I) chlorid (entry 11). For these catalysts, only slow decomposition of the starting materials was detected, which most probably is based on the instability of the starting materials at elevated temperatures. In entry 5, it became obvious that AgPF₆ shows only moderate solubility in benzene, which indicates that better yields might be achievable if the catalyst was completely dissolved. Thus the reaction with IPrAuCl/AgPF₆ was conducted in CH₂Cl₂ at room temperature (entry 14) in order to prevent competing degradation pathways of the starting materials. Indeed the

yield was significantly higher under these conditions. AgNTf₂ (entry 12) did not react at room temperature in CH₂Cl₂, and AgSbF₆ also gave a good yield (entry 13), but needed a longer reaction time than AgPF₆.

The obtained carbazole ring system is one of the prominent heterocycles, a structural motif found in many areas of chemistry and different synthetic strategies for that two-fold annellated arene have been developed.⁶ In the context of material science some carbazole derivatives have the potential to possess highly interesting properties.⁷ It is noteworthy that, despite the importance of the carbazole motif, only rare approaches towards the carbazolocarbazole motive (like compound **4a**) can be found in the literature (Fig. 1).⁸

This is probably based on the lack of efficient synthetic strategies, hence new efficient strategies are valuable. Encouraged by this, we focussed on the conversion of different starting materials (Table 2). On a preparative scale the substrate **3a** could indeed be transformed to carbazolocarbazole **4a** in 74% isolated yield (entry 1). Unfortunately, substrate **3b** bearing phenyl instead of alkyl substituents, could not be converted at all (entry 2). Even an intense screening for different reaction conditions/catalysts did not result in any conversion. As a consequence we switched back to alkyl-substituted alkynes as starting materials. These alkyl-substituted substrates were also sensitive to steric bulk; with two *tert*-butyl groups on two of the alkynes (**3c**) only the sterically less hindered alkynes reacted, **5c** was generated. Due to the steric bulk of the *tert*-butyl groups, no further nucleophilic attack of the indole moieties was observed (entry 3). A methyl group in *para*-position of the amino group of the aniline nucleophile significantly lowered the yield (entry 4). On the other hand, a OCF₃-group at the same position gave the best result, 84% of product **4e** could be isolated (entry 5). Acceptors like a cyano group or a pyridine ring, which further reduce the nucleophilicity of the aniline, gave no product (entries 6 and 7). An alkyl alcohol instead of the aniline nucleophile was also tolerated, but for this substrate class a reaction temperature of 80 °C was necessary and the yield was significantly lower (26%, entry 8). Benzylic alcohols were not tolerated and only an unselective reaction was observed and the product mixture could not be separated (entry 9). Sonogashira couplings with 2-ethynylphenol delivered the bis-benzofuran systems **5j**, but no second cyclization was observed in the presence of the palladium catalyst. If a gold catalyst was applied, the desired hydroarylation reaction took place at 80 °C and product **4j** was isolated in 58% yield (entry 10). At 80 °C the alkyne

Table 1
Screening of different catalysts, co-catalysts and solvents with substrate **3a**^a



Entry	Catalyst	Co-Catalyst	Solvent	Temp [°C]	Time [h]	Conv. [%]	Yield [%]
1	IPrAuCl	AgNTf ₂	benzene	80	16	100	51
2	IPrAuCl	AgSbF ₆	benzene	80	16	100	42
3	IPrAuCl	AgOTf ₂	benzene	80	16	100	51
4	IPrAuCl	AgBF ₄	benzene	80	16	100	24
5	IPrAuCl	AgPF ₆	benzene	80	16	100	54 ^b
6	AuCl ₃		benzene	80	16	76	—
7	NaAuCl ₄		benzene	80	24	57	—
8		AgNTf ₂	benzene	80	24	36	—
9	SPhosAuCl	AgNTf ₂	benzene	80	24	47	42
10	^t BuNCAuCl ^c	AgNTf ₂	benzene	80	24	50	—
11	Ph ₃ PAuCl	AgNTf ₂	benzene	80	24	40	2
12	IPrAuCl	AgNTf ₂	CH ₂ Cl ₂	rt	24	20	—
13	IPrAuCl	AgSbF ₆	CH ₂ Cl ₂	rt	24	100	62
14	IPrAuCl	AgPF₆	CH ₂ Cl ₂	rt	6	100	78
15		AgPF ₆	CH ₂ Cl ₂	rt	24	0	0

^a Unless stated otherwise, the reaction of diyne **3a** (20 mg) was carried out with 5 mol% catalyst and 5 mol% co-catalyst in solvent (1.0 mL) in an NMR tube. Conversions and yields were determined after 16 h by ¹H NMR using 1 equiv benzyltrimethylsilane as an internal standard.

^b AgPF₆ is only moderately soluble in benzene.

^c Ref. 5.

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