Gold Catalysis

Gold-Catalyzed Annulation of 1,8-Dialkynylnaphthalenes: Synthesis and Photoelectric Properties of Indenophenalene-Based Derivatives

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Abstract: A simple gold-catalyzed annulation of 1,8-dialkynylnaphthalenes utilizing a cationic gold catalyst was developed. Such a peri-position of two alkynyl substituents has not been studied in gold catalysis before. Depending on the substrate, the reactions either follow a mechanism involving vinyl cation intermediates or involve a dual gold catalysis mechanism which in an initial 6-endo-dig-cyclization generates gold(I) vinylidene intermediates that are able to insert into C–H bonds. Indenophenalene derivatives were obtained in moderate to high yields. In addition, the bidirectional gold-catalyzed annulation of tetratynes provided even larger conjugated π-systems. The optoelectronic properties of the products were also investigated.

Introduction

Over the last two decades, homogeneous gold catalysis[1] has been utilized for the electrophilic activation of alkynes. Gold most commonly acts as a redox-neutral and carbophilic π-acid that activates carbon-carbon multiple bonds towards nucleophilic attack.[2] Alkynes are still the dominating class of substrates, among them diyne systems[3] are very important as starting materials for gold-catalyzed annihilations to extended π-systems. Different from the majority of gold-catalyzed reactions, diyne substrates lead to high-energy intermediates, in the case of two internal alkynes to vinyl cations as intermediates,[4] when at least one terminal alkyn is present, gold vinylidene intermediates[5] are generated. Both types of intermediates are able to insert into non-activated aliphatic C(sp²)–H or aromatic C(sp³)–H bonds. This provides easy access to a diverse set of interesting organic scaffolds,[5, 6] including π-extended structures. Polycyclic aromatic hydrocarbons (PAHs), which might be the largest class of organic molecules, have been intensively investigated, due to their small HOMO–LUMO gaps these highly conjugated systems are promising for applications in the field of organic electronics.[7] Therefore, the development of modular synthetic methods to access polycyclic π-extended conjugated systems is a promising research topic.

1,8-Dialkynyl naphthalene structures are flexible and have been extensively been used as substrates in intramolecular[7] and intermolecular[8] annihilations. Recently Wang’s group reported an iodine-mediated electrophilic poly-cyclization in one step, which provides two different products, probably generated from vinyl cation intermediates or radical intermediates.[7] Additionally, the synthesis of indeno[2,1-alphenalene derivatives by an iodine-mediated electrophilic cyclization of 1,8-dialkynylnaphthalenes was published (Figure 1).[7a, 8] Tobe’s group...
Results and Discussion

The 1,8-diyne 1a was chosen as a model substrate (Table 1). 5 mol% of various gold catalysts with sterically demanding ligands were examined in CDCl₃. Even at room temperature the conversions were fast (2.5 h or less, Table 1, entries 1–5). With the IPr ligand the product 2a was obtained in 94% yield (Table 1, entry 1).[12] With the triphenylphosphine ligand no improvement in the yield was achieved, but the yield was slightly higher than in the case of the electron-poor phosphine ligand (CF₃CH₂O)₃P (94% versus 90%) (Table 1, entries 2 and 3). Despite a complete conversion of all starting material, the SPhos-ligated cationic gold catalyst gave a lower yield (88%, Table 1, entry 4). In C₆D₆ the reaction was completed within 15 min to afford 2a in 96% yield (Table 1, entry 5). (IPr)AuCl gave poor results even after prolonged reaction times (4 h), (Table 1, entry 6), and (IPr*)AuCl/AgSbF₆ delivered 2a in 90% yield (Table 1, entry 7). With a silver(I) catalyst only low yields of 2a were obtained (Table 1, entry 8).

Then we explored the reaction scope under the optimized conditions from Table 1, entry 1. A series of diynes with phenyl groups with various substituents at the aromatic system were synthesized, all diynes provided the corresponding products (2a–2k, Table 2). Electron-donating substituents (Me and OMe) at para- and ortho-positions of the phenyl ring gave yields between 89–95% (2a–2d), while for arene 2e the yield dropped significantly (73%). The structure of 2e at the solid state was confirmed by the single-crystal X-ray structural analysis.[12] Also substrates with fluorine substituents were smoothly converted to the corresponding phenalenones 2f and 2j in 89 and 84% yield, but for 2j heating to 50 °C for 48 h was necessary. The mesitylene-substituted substrate 1g was also converted to the corresponding phenalene 2g in 94% yield via the carbocation rearrangement. Amazingly, product 2h was directly obtained from the general procedure for the Sonogashira-coupling to form 1h, no gold catalyst was needed, the palladium did the conversion; for none of the other substrates this was observed. This probably is induced by the significantly more electron-rich thiophene ring, which allows the palladium species present during the cross coupling to interact with the alkyne units more strongly—unlike in the other substrates, which are dependent on the gold catalyst. Acenaphthene substrates with different substituents (Me and F) at para-position on the phenyl groups were successfully converted to the corresponding phenalenones 2i and 2j in 89 and 84% yield. The reaction of 5,6-diethynylacenaphthene 1k did not give the corresponding phenalene at all.

Then we tested the reactivity of the unsymmetrical diyne 11 to investigate the effect of the mesitylethynyl and 2-benzo[b]-thiopheneethyl substituents (Table 3). First different steric hindered ligands were examined. The reaction of 11 under the...
standard conditions (Table 3, entry 1) through 5 mol % of (IPr)Au(NCMe)SbF₆ in 1,2-dichlororethane (DCE), resulting in azuleno[1,2-a]acenaphthylene 3I (36 %) and phenalene 4I (18 %) as major products due to a 5-exo pathway as well as a small amount of [b]fluorantheno[8,9-d]thiophene 2I (36 %) due to a 6-endo pathway (Scheme 1). The structures of 2I and 4I at the solid state were unambiguously confirmed by X-ray structural analysis (Figure 2). The more sterically hindered gold catalyst (IPr*)AuCl/AgNTf₂ dramatically diminished the formation of the phenalene 2I and improved regioselectivity of products 3I and 4I (Table 3, entry 2). Switching the counter ion from NTf₂⁻ to SbF₆⁻ were able to efficiently produce the compound 4I with less of 3I, but the product 2I was not observed at all (Table 3, entry 3). Changing the solvent to benzene and toluene improved regioselectivity towards 3I (Table 3, entries 4 and 5). Interestingly, when the reaction was conducted with electron-poor ligands, P(OC₆H₄CF₃)₃ and P(C₆F₅)₃ azuleno[1,2-a]acenaphthylene 3I was obtained as a confirmed product (Table 3, entries 6 and 9). Further screening showed that in the present of the bulky phosphate ligand tBuXPhos the reaction proceeded faster and three isomers were obtained in 89 % yield in a ratio of 1:2:2 (Table 3, entry 7). In contrast, neither (IPr)AuCl, (IPr*)AuCl/AgSbF₆, (IPr*)AuCl/AgNTf₂, (IPr)AuCl/AgSbF₆, (IPr*)AuCl/AgSbF₆, or (IPr*)AuCl/AgNTf₂ were able to be isolated.

### Table 2. Scope of the reaction.[a]

| Entry | Cat. | Time [h] | Solvent | Ratio 2I/3I/4I | Yield [%] |
|-------|------|----------|---------|---------------|----------|
| 1     | (IPr)Au(NCMe)SbF₆ | 2.5 | DCE | 2:2:1 | 90 |
| 2     | (IPr*)AuCl/AgNTf₂ | 5 | DCE | 3:4:1 | 92 |
| 3     | (IPr*)AuCl/AgSbF₆ | 5 | DCE | 3:5:1 | 94 |
| 4     | (IPr*)AuCl/AgSbF₆ | 3 | PhH | 3:1:1 | 70 |
| 5     | (IPr*)AuCl/AgSbF₆ | 3 | toluene | 3:1:1 | 70 |
| 6     | (CF₃CH₂O)₃P[AuCl/AgSbF₆ | 3 | DCE | 1:3:2 | 95 |
| 7     | (BuXPhos)[AuCl/AgSbF₆ | 1.5 | DCE | 1:2:2 | 89 |
| 8     | (IPr)AuCl/AgSbF₆ | 1 | DCE | 1:2:2 | 88 |
| 9     | (IPr)AuCl/AgSbF₆ | 4 | DCE | 1:2:5 | 73 |
| 10    | AgSbF₆ | 5 | DCE | ND | ND |
| 11    | (IPr)AuCl | 5 | DCE | ND | ND |

[a] Reaction conditions: 1a (0.05 mmol), catalyst (5 mol %), solvent (CHCl₃ 1 mL), r.t. [b] Product 2h was obtained directly from the palladium-catalyzed coupling, which should have provided 1h. [c] 50 °C.
nor AgSbF$_6$ alone promoted the desired reaction, showing that a cationic gold species is necessary for the annulation (Table 3, entries 10 and 11).

Recently, Zhang’s group [3a] and our group [3b–f, 4a] showed that gold vinylidenes, accessible from an internal and terminal alkyne, are highly reactive intermediates and can efficiently insert into C(sp$^2$)–H bonds or C(sp$^3$)–H bonds. Thus, we next tested our naphthalene-linked diynes systems (1m, 1n) with a dual activation gold catalysts (TDAC[Pf$_6$]) in DCE at 90°C. These were efficiently converted into the targets 5m and 5n in 89 and 97% yields, respectively (Scheme 1). On the other hand, for yet unknown reasons no conversions were observed for the electron-rich substituents (R$_2$ = OMe, tBu) 1o and 1p (Scheme 1).

Next, the bidirectional gold-catalyzed conversion of the 1,4,5,8-tetra-(phenylethynyl)naphthalenes 6a and 6b was explored (Scheme 2). First we tested the standard reaction conditions, when the solution of the tetrayne 6a in DCE was treated with (IPr)Au(NCMe)SbF$_6$ (10 mol%) at 50°C, the two dark purple isomers 7a and 8a were isolated in 32% and 17% yield (Scheme 2). The lack of symmetry of the compound visible from the $^1$H NMR spectra of these products indicated that neither of them are the expected symmetrical products. Interestingly, an unexpected mode of intramolecular cyclization was observed. The expected 6-endo-dig-cyclization proceeded in one side to construct a phenalene moiety, but the unexpected 5-exo-dig-cyclization in the other side occurred to form a fluoroanthene moiety. Regioisomers 7 and 8 were potentially produced via vinyl cation intermediates Va and Vb (Scheme 2). The connectivity of 8a was unambiguously confirmed by single-crystal X-ray diffraction analysis. [12]

In the case of 1,4,5,8-tetakis-(phenylethynyl)naphthalene 6a and 6b, additional mode of distortion to reduce steric repulsion is effect to obtain the unsymmetrical products. According to the X-ray structure of phenylethynylnaphthalene derivatives, [8a] while the structure of diene 1 is involved the expanding mode of distortion in the naphthalene core, in the case of tetrayne 6, both the twisting and expanding modes are observed together with bending of phenylethynyl units, in particular the carbons attached directly to the naphthalene core move away from each other compared to 1. [13]

We used density functional theory (DFT) calculations at the SMD/M06/def2-TZVP//SMD/B3LYP-D3//6-31G(d), SDD(Au) level of theory in DCE to understand the mechanistic details of the bidirectional gold-catalyzed reaction by considering 6c as a model for 6b (Figure 3). This combination of methods and basis sets has been recently confirmed by us to provide results having a better consistency with the experimental data. [14] Accordingly, the reaction commences with coordination of the gold complex to one of the alkyne moieties of 6c in an enediyne fashion with $\Delta G^\ddagger = 3.5$ kcal mol$^{-1}$. The resultant intermediate VI is a branching point for two routes, A 6-endo-dig-cyclization via TS$^{VI\cdot a}$ and a 5-exo-dig-cyclization via TS$^{VI\cdot b}$. The calculations indicate that TS$^{VI\cdot a}$ is lower in energy than TS$^{VI\cdot b}$, implying that in agreement with the experimental finding, the...
cyclization prefers the 6-endo-cyclization mode. Once the first cyclization has occurred, intermediate VII is formed by another cyclization via transition structure TS\textsubscript{VII}, furnishing intermediate VIII. Since TS\textsubscript{VII} lies much lower in energy than TS\textsubscript{VI}-a and intermediate VIII is highly stable with a relative free energy of \(-17.8\), the transformation VI \(\rightarrow\) VII \(\rightarrow\) VIII is not reversible and thus the regioselectivity of the cyclization is determined by the energy difference between TS\textsubscript{VI}-a and TS\textsubscript{VI}-b. Subsequently, the organic molecule IX is produced with \(\Delta G = -66.1\) kcal mol\(^{-1}\) followed by a series of chemical steps from intermediate VII, as shown in Figure 3.

The organic molecule IX has two different sites for coordination of the gold complex. If the gold complex coordinates to IX to give X, the ensuing intermediate then is a bifurcation point for two processes, 6-endo-dig-cyclization via TS\textsubscript{X}-a and 5-exo-dig-cyclization via TS\textsubscript{X}-b. In line with the experimental observations, the calculations support favorability of the 5-exo-dig-cyclization, as evidenced by the finding that TS\textsubscript{X}-b is 3.9 kcal mol\(^{-1}\) lower in energy than TS\textsubscript{X}-a. The same is true if we assume that the cyclization occurs from the other \(\pi\)-complex that is, intermediate XI; similarly, for this case, transition structure of the 5-exo-dig-cyclization (TS\textsubscript{XI}-b) lies 2.1 kcal mol\(^{-1}\) below that of the 6-endo-dig-cyclization (TS\textsubscript{XI}-a), a result which agrees with the regioselectivity observed experimentally. Finally, we want to note that due to the closeness of the relative free energies of TS\textsubscript{X}-b and TS\textsubscript{XI}-b, both the syn- and anti-products are predicted computationally to be produced with a nearly equal amount. This prediction is fully consistent with our experimental observations, the results of which are given in Scheme 2.

The optical properties of phenalenenes 2a–2k were examined by UV/Vis absorption spectroscopy in dichloromethane (Figure 4). In view of maximum absorption wavelengths of 2a, 2f and 2l, they show strong absorption at long wavelength (about 460 nm). Comparison with phenalenenes structures, azulenoacenaphthylene 3l exhibits the distinct broad peak between 500 \(\sim\) 750 nm. The \(\pi\)-extension has a significant effect on the absorption of 7a and 8a (\(\lambda = 510\) and 550 nm). The HOMO and LUMO levels of 2a, 2f, 7a, and 8a were estimated by cyclic voltammetry (Table 4). The HOMO energy level of 2a containing an electron donor group (\(-5.33\) eV) was higher than 2f containing an electron acceptor (\(-5.47\) eV). Based on the compounds 7a and 8a, \(\pi\)-extension with fluoranthene provided lower LUMO levels and smaller HOMO–LUMO energy gaps.

In conclusion, an efficient gold-catalyzed annulation protocol through vinyl cation or \(-\)vinylidene intermediates via a selective shift towards a 6-endo-dig-cyclization mode for the indeno[2,1-a]phenalenenes synthesis was developed. In addition, the bidirectional gold-catalyzed annulation of tetraynes provided even larger conjugated \(\pi\)-systems, the interesting different mode of the first and the second cyclization, leading to unsymmetrical products, was explored by a computational study.

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**Conflict of interest**

The authors declare no conflict of interest.
Figure 3. Calculated mechanism for cyclization of 6c catalyzed by [(IPr)AuNCMe]+. The relative free energies (in red) are given in kcal mol⁻¹.
Keywords: alkenes - annulation - bidirectional synthesis - dual gold catalysis - extended π systems

Figure 4. UV absorption of 2a, 2f, 4a, 7a, and 8a.

Table 4. Cyclic voltammetry data and estimated HOMO and LUMO energies.\(^\text{[a]}\)

| E\(_{\text{on}}\) [V] | E\(_{\text{ox}}\) [V] | E\(_{\text{HOMO}}\) [eV] | E\(_{\text{LUMO}}\) [eV] | E\(_{\text{ip}}\) [eV] |
|----------------|----------------|----------------|----------------|----------------|
| 2a              | 0.53           | -1.93          | -3.33          | -2.87          | 2.46           |
| 2f              | 0.67           | -1.74          | -5.47          | -3.06          | 2.41           |
| 7a              | 0.41           | -1.20          | -5.21          | -3.60          | 1.61           |
| 8a              | 0.54           | -1.16          | -5.34          | -3.64          | 1.70           |

[a] Cyclic voltammetry in CH\(_2\)Cl\(_2\), containing 0.1 M Bu\(_4\)NBF\(_4\). (b) HOMO and LUMO energy levels in eV were approximated using the equation HOMO = (-4.80 + E\(_{\text{on}}\)), and LUMO = (-4.80 + E\(_{\text{ox}}\)).

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[12] Single-crystal X-ray structure analysis: Deposition numbers 2042439 (2e), 2042440 (2l), 2042441 (4l), and 2042442 (8a) contain the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service.

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