Communication

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Fluorenes and Styrenes by Au(I)-Catalyzed Annulation of Enynes and Alkynes

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Metal-catalyzed cycloaddition reactions provide attractive and efficient methods for the synthesis of arenes, although regioselectivity presents a major challenge for intermolecular reactions. The synthesis of polysubstituted benzenes by the [2 + 2 + 2] cyclotrimerization of alkynes has been extensively studied, as has the Pd-catalyzed [4 + 2] cycloaddition of enynes and activated alkynes. We report herein a mechanistically distinct intramolecular annulation of enynes and alkynes to produce multiply substituted arenes (eq 1); styrene or fluorene products can be selectively accessed by judicious choice of reaction conditions.

![Chemical structure](image)

Given the synthetic utility of vinyl cyclopropanes, we anticipated that alkenyl cyclopropanes derived from the cyclopropanation of 1,3-enynes would provide similar opportunities for organic synthesis. In light of our previous work employing propargyl esters as carbene precursors in Au(I)-catalyzed cyclopropanation reactions of olefins, the reaction of 1 with enyne 2 was investigated.

Initially, treatment of 1 and 2 with a cationic phosphinegold(I) complex resulted in a mixture of products, including styrene 3, fluorene 4, and cyclopropane 5 (eq 2). The unexpected products 3 and 4 were intriguing; 3 formally results from a completely regioselective [4 + 2] cross-dimerization of two different enynes, while compounds such as 4 are of interest due to the blue-light emitting properties of polyfluorenes.

Since cyclopropane 5 was obtained exclusively as the trans-diastereomer, we hypothesized that 3 and 4 arose from the cis-diastereomer. Therefore, we were pleased to find that the less reactive AuCl cleanly catalyzed the synthesis of cyclopropane 5 with high cis-diastereoselectivity and complete regioselectivity. With ready access to cis-5, we next investigated its transformation to 3 and 4.

![Chemical structure](image)

Gratifyingly, either compound could be selectively prepared simply by changing the silver salt cocatalyst in conjunction with triarylphosphitegold(I) chloride (Ar = 2,4-di-tert-butylphenyl). Thus, reaction of cis-5 with the Au complex and AgOTf provided 3 in 89% yield, while the reaction with AgSbF 6 under otherwise identical conditions provided 4 in 76% yield (eq 3).

### Table 1. Au(I)-Catalyzed Arene Synthesis: Enyne Scope

<table>
<thead>
<tr>
<th>Entry</th>
<th>Enyne</th>
<th>cp yield</th>
<th>Conditions</th>
<th>Yield</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>84%</td>
<td>10% AgOTf, 5% AgCl, CH2Cl2</td>
<td>79%</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>84%</td>
<td>5% AgSbF 6</td>
<td>79%</td>
<td></td>
</tr>
</tbody>
</table>

* Isolated yields of cis-cyclopropane. Reactions run with 3:1 ratio of enyne. A: 5% AgOTf, 5% (ArO)3PAuCl, CH2Cl2. B: 5% AgSbF 6. C: Isolated yields. D: Ratio of regioisomers. E: Conditions B were not investigated with 58, 61, and 64.

The substrate scope of the two-step, divergent syntheses of fluorenes and styrenes was investigated with other enynes (Table 1). Aryl enynes with a variety of substitution patterns and functional groups were tolerated, demonstrating the power of this method to prepare multiply substituted arenes from simple starting materials (entries 1–13). Moreover, both electron-rich and electron-poor enynes and fluorenes undergo the cyclopropanation and arene syntheses; however, commensurate with the expected nucleophilicities of the aryl group, they demonstrated diametric preferences for styrenes versus fluorene formation (entries 3, 4). Alkyl-substituted enynes are also tolerated in both the cyclopropanation and annulation steps (entries 14–16).

The carbene precursor was also varied (Table 2). The pivalate ester provided the best selectivity in differentiating between the styrene and fluorene pathways (entries 1–3). Dibutyl-substituted fluorene 82 was prepared (entry 6); such hydrophobic solubilizing groups are often found in fluorenes designed for subsequent polymerization. Additionally, the use of unsymmetrical pivaloate 83 readily provided 85 or 86 (entries 7).

A mechanism accounting for the observed products begins with the formation of 5 by intermolecular cyclopropanation of enyne 2
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Supporting Information Available: Experimental procedures and compound characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

References


(4) (a) Rubin, M.; Rubina, M.; Georgy, V. Chem. Rev. 2007, 107, 3117.


(11) Other phosphine catalysts provided lower selectivity. For example, treatment of cis-5 with PPh3AuCl/AgSbF6 resulted in 63% 4 and 34% 3.


(14) Optimization of the one-pot synthesis was produced in lower yield from 4 and 2. See Supporting Information.

(15) 89 was isolated and restructured to the reaction conditions with and without the addition of triarylphosphine gold(I) chloride to afford the expected products, suggesting the possibility for silver or acidic catalysis in the final step. Control experiments indicate that neither AgOTf nor HOTf catalyze the cycloisomerization of 5. See Supporting Information.

(16) Further experiments (see Supporting Information) indicate that 3 readily isomerizes to 4 under strongly acidic conditions. A deuterium-labeling experiment suggested that this is not a major pathway for the formation of 4 under our reaction conditions:

via the gold carbeneid produced from rearrangement of propargyl ester 1. Following coordination of the cationic gold catalyst to the resulting alkene, the pendant olefin can participate in either a 5-endo-dig or 6-endo-dig cyclization (Scheme 1). When tertiary propargyl esters are employed in the gold-catalyzed annulation, the 5-endo-dig cyclization to generate tertiary carboxylation 38 dominates. Subsequent migration of the pivaloyloxy group gives allylic cation 39 that may be further stabilized by delocalization of the charge onto gold. Cyclopentyl opening leads to 89 via a pentadienyl cation, which is most likely converted to 3 and 4 by E1 and S2 mechanisms, respectively.15,16

Use of secondary propargyl pivaloate 90 diverted the reaction pathway toward the 6-endo-dig cyclization and formation of cycloheptatriene 92 (eq 4). Selectivity for the 5-endo-dig pathway could be partially restored using 94, which predominantly provided the fluorene 97, suggesting that, for trisubstituted olefins, electronic factors govern the regioselectivity of the cycloisomerization.

In conclusion, readily available enynes and propargyl esters may be selectively transformed into styrenes or fluorenes under catalyst control via two new Au(I)-catalyzed processes. Synthesized by a rarely investigated, highly selective cycloisomerization of 1,3 enynes, cis-vinyl-alkynyl-cyclopropanes undergo a novel cycloisomerization reaction, the outcome of which may be controlled simply through the choice of catalyst counterion.