**Novel Syntheses of [6,7,n]-Benzazepinone and [6,6,n]-Benzophenanthridinone Derivatives by Rhodium-catalyzed Cyclization of o-(n-Cyanoalkynyl)benzaldehydes**

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Since transition metal catalysis allows simultaneous formation of more than one bond in a single step operation with high selectivity, the exploitation of a model compound for nitrogen-containing polycyclic biologically active natural products has been a worthwhile contribution in synthetic and medicinal chemistry. Intramolecular hydroarylation of acetylenes, carbonylation of 2-alkylbenzylamines, 1-aryl-3-hexen-1,5-dienes initiated by methoxide addition, fluorocarones and nitriles via 1,2-arynes, nitroarylstannanes, radical dearomatization of benzene and hydrothermal reaction of o-phenylaniline, uillamann cross-coupling of 1-bromo-2-nitroarenes and 1,3-dipolar cycloaddition of nonstabilized azomethine ylides and photocycloaddition of phthalimide anion to alkenes have been used to synthesize benzazepinone, phenanthridine and benzophenanthridinone derivatives. However, these synthetic routes are often complicated and limited to only some substrates. Recently, we reported various cycloisomerization reactions with different unsaturated systems catalyzed by Au, Pt, Pd, and Rh. Our continued interest in the synthesis of polycyclic systems prompted us to develop the Rh-catalyzed cyclization of o-alkynylbenzaldehydes having a nitrile tether that produced tricyclic benzazepinones and benzophenanthridine derivatives via [3+2] and [4+2] cycloaddition via pyrylium intermediates as shown in Scheme 1.

An initial study was tested with o-alkynylbenzaldehyde 1a in the presence of various late transition metal catalysts (Table 1). PtCl₄ as a catalyst in refluxing 1,4-dioxane for 12 h converted 1a to give a mixture of products, which were separated by column chromatography to give 2,3-dihydrobenzo[e]cyclopenta[b]azepin-5(1H)-one (3a) in 50% yield along with the hydrated product 2a in 30% yield (entry 1). When this reaction was carried out in dry 1,4-dioxane in the presence of 4 Å molecular sieves, the reaction was dramatically accelerated to give the product 3a in 59% yield still along with 2a in 10% yield (entry 2). We presumed that a trace amount of water in the reaction medium or in solvent might generate a nucelophile which could undergo hydration to the metal-activated triple bond followed by tautomerization to the corresponding ketoaldehyde 2a.

It was observed that gold(III) bromide in 1,2-dichloroethane (EDC) hydrated 1a to afford 2a even at room temperature exclusively (entry 3). This might be understood by the high reactivity of gold catalyst or the poor reactivity of the nitrile group toward the pyrylium intermediate A. We tried the same reaction with different catalysts, such as AuC₅, AuCl(PPh₃) with AgSbF₆ and AgSbF₆ itself, under dry reaction conditions, but led to hydration (entries 4-6). In fact, Zhu et al. reported that o-alkynylbenzaldehydes were hydrated in the presence of gold(III) catalysts and trifluoroacetic acid to afford the corresponding ketoaldehyde. Finally, we found [Rh(COD)Cl] as an optimal catalyst for the present [3+2] cyclization of pyrylium intermediate, generated in situ with alkynopholic metatations, with a pendent nitrile. Thus, when the substrate 1a in the presence of [Rh(COD)Cl] (10 mol%) in dry xylene containing 4 Å molecular sieves was heated at 110 °C for 12 h, the product 3a was isolated in 71% yield along with the ketoaldehyde 2a in 10% yield. With this promising result, we further examined this [3+2] cycloaddition with structural alteration in the tether (eq. 1-2).

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![Scheme 1]

**Table 1. Optimization of intramolecular [3 + 2] cyclization-cycloaddition under various reaction conditions with 1a**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst (mol %)</th>
<th>Solvent</th>
<th>T, °C / h</th>
<th>Products Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PtCl₄ (10)</td>
<td>1,4-Dioxane</td>
<td>100/12</td>
<td>2a, 3a</td>
</tr>
<tr>
<td>2</td>
<td>PtCl₄ (10)</td>
<td>1,4-Dioxane</td>
<td>100/12</td>
<td>4 A MS</td>
</tr>
<tr>
<td>3</td>
<td>AuBr₃ (10)</td>
<td>EDC</td>
<td>RT/12</td>
<td>2a</td>
</tr>
<tr>
<td>4</td>
<td>AuCl (10)</td>
<td>EDC</td>
<td>RT/12</td>
<td>2a</td>
</tr>
<tr>
<td>5</td>
<td>AuCl(PPh₃)(5)</td>
<td>EDC</td>
<td>RT/12</td>
<td>2a</td>
</tr>
<tr>
<td>6</td>
<td>AgSbF₆ (5)</td>
<td>EDC</td>
<td>RT/12</td>
<td>2a</td>
</tr>
<tr>
<td>7</td>
<td>[Rh(cod)Cl] (10)</td>
<td>Xylene</td>
<td>110/12</td>
<td>2a, 3a</td>
</tr>
</tbody>
</table>

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*This paper is dedicated to Professor Sang Chul Shim at Kyungpook National University on the occasion of his honorable retirement.*
Substrate 1b, an one-carbon longer homolog in the tether, underwent the present reaction to afford (4aE,11Z)-3,4-dihydro-1H-dibenzo[b,e]azepin-6(2H)-one (3b) in 69% yield. The same reaction with the substrate 1c, having -NTs group in the tether, also proceeded under the same reaction condition to afford the corresponding product 3c, (3aE,10Z)-2-oxo-1,2-dihydrobenzo[b]pyrrolo[3,4-b]azepin-5(1H)-one in 77% yield. Interestingly, the similar substrate 1d having a gem-diester group required longer time (36 h) for completion: the corresponding [4+2] cycloaddition product 4d, diethyl 1-oxo-1,2-dihydrophenanthridine-3,4(6H)-dicarboxylate, was obtained in 81% yield (eq. 3). It is worth to note that the reaction proceeded smoothly with the substrate 1e, one-carbon homolog of 1d, to give the corresponding product 4e in 65% yield (eq 4).

Both structures of 3a and 4d were confirmed by 2D NMR. We should note that the present method could provide an easy access to [6,6,7]-tricyclic compounds without the gem-diester group and [6,6,6]-tricyclic compounds with the gem-diester group.

Mechanistic speculation was summarized in Scheme 2. The aromatic ring might form the pyrylium intermediate 1 and its resonance form 2, which would undergo either: [3+2] cycloaddition leading to 3 or [4+2] cycloaddition leading to 4. A key factor associated with the chemoselectivity in cycloaddition should be related to group Z but is not recovered yet. This method was applied to aliphatic systems 5a and 5b, where the aldehyde group and the triple bond were conjugated with cycloalkenes. These substrates were reactive toward Rh(I) even at room temperature but seemed to form CI intermediate which would be eliminated followed by protolysis to give the furan derivatives 6a and 6b in almost quantitative yields (eq 5).

In conclusion, we have found a new and atom economical Rh-catalyzed cyclization reaction with o-alkynyl benzaldehydes having a nitrile tether leading to synthetically valuable nitrogen containing polycyclic compounds. Further studies to extend the scope of its synthetic utility and applications are in progress in our laboratory.

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References and Notes