Rhenium-Catalyzed Cyclization via 1,2-Iodine and 1,5-Hydrogen Migration for the Synthesis of 2-Iodo-1H-indenes

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Supporting Information

ABSTRACT: A rhenium complex catalyzed the formation of 2-iodo-1H-indene derivatives through iodine and hydrogen migration of 3-iodopropargyl ethers. The reaction proceeded via generation of 1-iodoalkenylrhenium carbene species by sequential 1,2-iodo and 1,5-hydrogen shifts with readily available precursors under neutral conditions. Insight into the reaction mechanism and the reactivity of the generated alkynecarbene species were also investigated.

Transition metal-catalyzed 1,2-H shift of terminal acetylenes is a powerful and operationally simple method to provide synthetically useful vinylidene species atom-efficiently.¹ Reactivity of the resulting vinylidene species is influenced by substituents adjacent to the generated carbene carbon centers. Therefore, vinylidene formation from alkynes with functional groups, such as SiR₃, GeR₃, SnR₃, SR, SeR, or a halogen group, at the terminus via their 1,2-shift is an efficient and straightforward approach to reactive and functionalized vinylidene species.²³ Among the functional groups, the iodo group is an important coupling partner, and the precursors, iodoalkynes, are attractive class of alkynes having unique reactivity.⁴ Since the seminal report by Iwasawa describing tungsten-catalyzed cycloisomerization leading to 1-iodonaphthalenes via generation of iodovinylidene species,³⁴⁻⁵,¹² 1,2-I shifts have been used in several unique transformations by Fürstner and Hashimi et al. (Scheme 1).³⁹⁻⁶⁰ However, most of the iodoalkynes used in the previous studies were derived from arylacetylenes,⁵⁶⁻⁶⁸ and the activity of catalysts other than tungsten, rhenium, and gold complexes is unknown. Recently, we have reported rhenium-catalyzed anti-Markovnikov addition reaction of carbon nucleophiles to terminal alkynes, which involves the formation of rhenium vinylidene species generated via a 1,2-H shift of the terminal proton of acetylene.⁶¹⁻⁶⁵ We envisioned that rhenium complexes may also serve as promoters for the generation of halogen-substituted vinylidene species via 1,2-halogen shift of haloalkynes.⁶ To investigate the catalytic generation of iodovinylidene species via 1,2-I shift of 1-iodo-2-alkylalkynes derived from aliphatic acetylenes, a propargyl ether I was selected as a precursor in this work. Since the resulting vinylidene species possesses an electrophilic carbene center attached with electron-withdrawing iodo substituents, further conversion into 1-iodoalkenyl carbene species A was hypothesized to occur via sequential 1,5-H shift followed by elimination of an aldehyde (Eq 1).⁹ Although an alkynyl carbene species is widely used for the construction of various heterocycles by cycloadditions and annulations,⁹⁻¹⁰ those that possess an iodo group at the alkynyl or carbene carbon are rare.

The present study began with treatment of benzyl propargyl ether 1a with a catalytic amount of a transition metal complex in 1,4-dioxane (0.10 M) at 80 °C. 2-Iodo-1H-indene 2a was formed with the use of several rhenium catalysts, such as ReBr(CO)₅, ReI(CO)₅, and [ReBr(CO)₅(thf)]₂ (Table 1, entries 1-3). In contrast, other metal complexes, including W(CO)₅(thf), AuCl, and IPrAuNTH₂, which were effective for the generation of iodovinylidene species via 1,2-I shift in a previous study,⁷ did not provide 2a even at higher temperatures due to
competitive decomposition of 1a.\textsuperscript{11} Although a higher temperature (120 °C) is required, 2a was also obtained, albeit in low yield using Re\(_2\)(CO)\(_{10}\) as a catalyst (entry 4). The proper choice of solvents was crucial, and formation of 2a was observed in ethereal solvents, such as THF, CPME, \(4\)Bu\(_2\)O, and DME (entries 5-6).\textsuperscript{12} Substituents on the oxygen atom slightly affected reaction efficiency, and precursors 1aa, 1ab, 1ac, and 1ad containing methoxymethoxy, propoxy, or benzyloxy groups with electron-donating and -withdrawing functional groups were converted to 2a in lower yields compared to those with 1a (entries 7-10).\textsuperscript{13,14}

Table 1. Optimization of reaction conditions

<table>
<thead>
<tr>
<th>Entry</th>
<th>Cat. Re</th>
<th>Solvent</th>
<th>R Substrate</th>
<th>Yield / %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>ReBr(CO)(_5)</td>
<td>Dioxane</td>
<td>Ph 1a</td>
<td>71</td>
</tr>
<tr>
<td>2</td>
<td>Re(CO)(_5)</td>
<td>Dioxane</td>
<td>Ph 1a</td>
<td>70</td>
</tr>
<tr>
<td>3</td>
<td>[ReBr(CO)(_3)(thf)](_2)</td>
<td>Dioxane</td>
<td>Ph 1a</td>
<td>78 (77)</td>
</tr>
<tr>
<td>4*</td>
<td>Re(_2)(CO)(_5)</td>
<td>THF</td>
<td>Ph 1a</td>
<td>22</td>
</tr>
<tr>
<td>5</td>
<td>[ReBr(CO)(_3)(thf)](_2)</td>
<td>CI(_2)CH(_2)CI</td>
<td>Ph 1a</td>
<td>7</td>
</tr>
<tr>
<td>6</td>
<td>[ReBr(CO)(_3)(thf)](_2)</td>
<td>dioxane</td>
<td>OMe 1aa</td>
<td>63</td>
</tr>
<tr>
<td>7</td>
<td>[ReBr(CO)(_3)(thf)](_2)</td>
<td>Dioxane</td>
<td>Et 1ab</td>
<td>68</td>
</tr>
<tr>
<td>8</td>
<td>[ReBr(CO)(_3)(thf)](_2)</td>
<td>Dioxane</td>
<td>4-MeO(_2)C(_6)H(_4) 1ac</td>
<td>71</td>
</tr>
<tr>
<td>9</td>
<td>[ReBr(CO)(_3)(thf)](_2)</td>
<td>Dioxane</td>
<td>4-Br(_2)C(_6)H(_4) 1ad</td>
<td>74</td>
</tr>
</tbody>
</table>

*120 °C for 18 h.

Under the optimized reaction conditions listed in entry 3 of Table 1, the scope and functional group tolerance were investigated briefly with several benzyl propargyl ethers 1 (Figure 1). Functional groups such as methoxy, fluoro, and chloro groups were tolerated to provide the corresponding 2-iodo-1H-indene derivatives 2b, 2c, and 2d, respectively, in good yields. Higher reaction temperatures were necessary for complete conversion of trifluoromethyl group substituted precursor 1e leading to 2e. In this case, transposition of the double bond to yield 2e\(^\circ\) occurred competitively due to the presence of an acidic benzyl proton in the structure of 2e.\textsuperscript{15} The reaction could be applicable to benzyl propargyl ether 1f derived from dibenzosuberone, and indene fused tetracycle 2f was formed in moderate yield. Precursor 1g, which contained a meta-methoxyphenyl group, reacted preferentially at the less sterically hindered position to afford 2g along with its regioisomer 2g\(^\prime\) as a minor product (Eq 2).

A proposed mechanism for the formation of 2-iodo-1H-indenes 2 in the current reaction is shown in Scheme 2. First, alkynyl carbene species A\(^\circ\) was generated via sequential 1,2- and 1,5-H shifts, followed by elimination of benzaldehyde, as shown in Eq 1. A deuterium-labelling experiment using 1a-d confirmed that a 1,5-shift of the deuterium atom from the benzyl group of 1a onto the alkynyl carbon of 2a (Scheme 3a). Furthermore, a parallel reaction of 1a and 1a-d in a separate flask provided a KIE value of 1.08, which suggested that the hydrogen shift of 1a was not involved in the rate-determining step (Scheme 3b). Due to the relatively fast this 1,5-H shift, direct insertion of a vinylidene species into the benzylcyclic C–H bond\textsuperscript{16} leading to 3-iodo-2,5-dihydropyran derivatives did not occur. A crossover experiment using 1a-d and 1e in the same flask provided 2a-d and 2c, and no exchange of the deuterium label was observed (Scheme 3c). Thus, the current 1,5-H shift occurred through an intramolecular process. Because cyclization of 1e, which contained electron-withdrawing trifluoromethyl groups, required higher temperatures, the carbonyl carbon of A\(^\circ\) possessed electrophilic character. Thus, nucleophilic attack of the aryl group on the carbene carbon, followed by subsequent elimination of rhenium species and aromatization, is most plausible for formation of the indene skeletons (Scheme 2).\textsuperscript{16} As an alternate pathway, however, direct insertion of the carbonyl carbon of A\(^\circ\) into a nearby aromatic C–H bond followed by transposition of double bond would also afford 2.

Scheme 2. Proposed reaction mechanism for formation of 2-iodo-1H-indenes 2

The corresponding 2-iodo-1H-indene 2h was also obtained from benzyl propargyl ether 1h containing phenyl and methyl groups at the propargyl position. In this system, the alkenylcarbene intermediate B, having a carbene center situated anti to the phenyl group, was thought to be predominant to B\(^\circ\) due to steric repulsion.\textsuperscript{17} However, formation of 2h in moderate yield suggested that B could be interconverted to B\(^\circ\) via zwitterionic intermediate C (Scheme 4).\textsuperscript{18}

In contrast, iodoallene 3i was obtained in 88% yield when benzyl propargyl ether 1i, which did not possess aryl groups at the propargyl position, was used as a precursor (Scheme 5).\textsuperscript{19} The 1,5-H shift followed by elimination of benzaldehyde occurred very quickly, and products derived from vinylidene...
groups at the propargyl position also revealed that this 1,2-I shift occurred through an intramolecular process (see Eq S1 in SI). The optimized rhenium catalyst, [ReBr(CO)(thf)]₂, was also effective for vinylidene formation from iodoalkynes derived from arylacetylenes. For example, formation of 3-iodo-1H-indene derivative 6 via insertion of C(sp³)−H bond into rhenium vinylidene species proceeded efficiently under the identical conditions (Scheme 6).8

Scheme 6. Rhenium-catalyzed cycloisomerization of iodoalkyne 5 derived from arylacetylene

In conclusion, 3-iodopropargyl ethers were found to be efficient 1-iodoalkenyl carbene generators when using rhenium catalysis under neutral conditions without additional phosphine or nitrogen-based ligands. Iodoalkynes derived from alkylalkynes were applicable as precursors, and the carbene intermediates generated were trapped efficiently through intramolecular cyclization for conversion into 2-iodo-1H-indene derivatives. The mechanistic study revealed that insights into the 1,2-I and 1,5-H shifts as well as the reactivity of the generated alkenylcarbene species. The current results provide novel insights into the reactivity of iodoalkynes, and offer new potential as readily available building blocks.

ASSOCIATED CONTENT
Supporting Information
Experimental procedures, spectroscopic data for all new compounds, and copies of ¹H and ¹³C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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REFERENCES

Attempted synthesis of 2

Effect of other solvents with 2.5 mol% of [ReBr(\text{CO})\text{(thf)}]: at 80 °C for 3 h: Yield of 2a was 12% in toluene, 9% in cyclohexane, 41% in BuO; 63% in CFMe, 43% in DME. 17% in AcOEt, 0% in MeCN or DME. Effect of temperature with 2.5 mol% of [ReBr(\text{CO})\text{(thf)}]: in 1,4-dioxane for 3 h: 68% at 70 °C, 58% at 90 °C. Additives, including amines, phosphines, and MSAA4 failed to improve the yield of 2a.

Conversion of the corresponding bromoalkyne 1(k see SI for the structure) instead of iodoalkyne 1a did not occur at 80 °C. The desired 2-bromo-1H-indene was obtained at 120 °C but in less than 15% yield. For the generation of bromovinylidene species, see ref 2i.

Attempted synthesis of 2-iodo-1-phenyl-1H-inden-3-yl acetate from 1-iodopropargyl acetate 1ae (see SI for the structure) via sequential 1,2-1 and 1,3-acetoxy shifts followed by cyclization provided the complex mixture.

Transposition of the double bond of 2e occurred even at 80 °C to afford a mixture of 2e and 2\text{e}' in the ratio of 67/32. See SI for the structure of 2e*.


Attempted intramolecular trap for alkynylcarbene intermediate B by cyclopropanation with alkenes or insertion into C-H or Si-H bonds did not give the corresponding products.