# Mercuric Triflate Catalyzed Cycloisomerization of Alkynyl-1,3-Cyclohexanedione and Alkynyl-1,3-Cyclopentanedione

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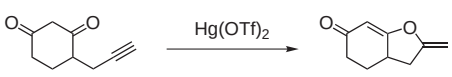
**Abstract:** Mercuric triflate was used to catalyze cycloisomerization of alkynyl-1,3-cyclohexanediones and cyclopentanediones to give fused oxabicyclic systems under mild reaction conditions with high catalytic turnover up to 1000 times.

**Key words:** mercuric triflate, catalytic cycloisomerization, alkynyl-1,3-cyclohexanediones

Alkyne heteroatom cyclization catalyzed by an electrophilic metal complex is a subject of considerable interest in modern synthetic organic chemistry.[1] Although cycloisomerization of alkynyl alcohols, amines, and carboxylic acids has been studied intensively, cyclization of alkynyl ketones has been limited to furan synthesis.[2] We previously reported a 2-methylfuran synthesis[3] by cyclization of 1-alkyn-5-one. The reaction was catalyzed by mercury(II) trifluoromethanesulfonate [mercuric triflate, hereafter $Hg(OTf)_2$], developed in our group as an olefin cyclization agent.[4] Recently, we also reported that $Hg(OTf)_2$ and a $Hg(OTf)_2$-tetramethylurea (hereafter TMU) complex showed highly efficient catalytic activity for the following reactions: 1) hydration of terminal alkynes to give methyl ketones,[5] 2) hydroxylative 1,6-enyne cyclization to give exomethylene five-membered ring products,[6] 3) arylalkyne cyclization leading to dihydronaphthalene derivatives,[7] and 4) biomimetic tandem cyclization yielding polycarbocycles.[8,9] Using a variety of metal complexes Mascarenas and co-workers described cycloisomerization of 4-propargyl-1,3-cyclohexanedione and cyclopentanedione generating dihydropyrane or dihydrofuran.[10] In the present study, we examined cycloisomerization of alkynyl-1,3-cyclohexanediones and cyclopentanediones at ambient temperature using catalytic amounts of $Hg(OTf)_2$. Notably, we observed very high catalytic efficiencies up to 1000 times catalytic turnover in producing fused oxabicyclic products.




1 2

**Scheme 1**

**Table 1** $Hg(OTf)_2$-Catalyzed Cyclization of **1**

| Entry | Catalyst (mol%) | Solvent | Time (min) | Yield (%)[a] |
|---|---|---|---|---|
| 1 | $Hg(OTf)_2$ (1) | $CH_3NO_2$ | 60 | 75 |
| 2 | $Hg(OTf)_2$ (1) | $CH_2Cl_2$ | 40 | 73 |
| 3 | $Hg(OTf)_2$ (1) | $C_6H_6$ | 45 | 81 |
| 4 | $Hg(OTf)_2$ (1) | MeCN | 5 | 87 |
| 5 | $Hg(OTf)_2$ (1) | MeCN | 0.5 | 92 |
| 6 | $Hg(OTf)_2$ (0.1) | MeCN | 20 | 88 |
| 7 | $Hg(OTf)_2$ (0.01) | MeCN | 300 | 0 |
| 8 | $Hg(OTf)_2$·TMU (1) | MeCN | 15 | 91 |
| 9 | $Hg(OTf)_2$·2TMU (1) | MeCN | 20 | 93 |
| 10 | $Hg(OTf)_2$·3TMU (1) | MeCN | 30 | 96 |
| 11 | $Hg(OTf)_2$·3TMU (0.1) | MeCN | 180 | 22 |
| 12 | $Hg(OAc)_2$ (1) | MeCN | 40 | 0 |
| 13 | $Hg(OTFA)_2$ (1) | MeCN | 10 | 93 |
| 14 | $Hg(OTFA)_2$ (0.1) | MeCN | 1200 | 85 |

[a] Isolated yield.

When the alkynyldione **1** was treated with 1 mol% of $Hg(OTf)_2$ in $CH_3NO_2$ at room temperature for 1 hour, the oxabicyclic product **2** was obtained (Scheme 1). Yield of **2** was 75% after column chromatography on silica gel (Table 1, entry 1). Although comparable yields were obtained by using $CH_2Cl_2$ or benzene as the solvent, MeCN afforded an improved yield of 87% yield (entries 2–4). When the reaction of **1** with 1 mol% of $Hg(OTf)_2$ in MeCN was quenched after 30 seconds by addition of $Et_3N$, the yield was 92% (entry 5).[11] Using 0.1 mol% of $Hg(OTf)_2$, an 88% yield of **2** was obtained within an acceptable reaction period (entry 6). $Hg(OTf)_2$·TMU and $Hg(OTf)_2$·2TMU complexes afforded **2** in high yield (entries 8 and 9). However, the highest yield was obtained using $Hg(OTf)_2$·3TMU complex to produce **2** with a 96% yield after a 30 minutes reaction (entry 10), These results suggested that the unstable product **2** was partially decomposed by the reactive $Hg(OTf)_2$. Although $Hg(OAc)_2$ did not catalyze any detectable cycloisomerization (entry 12),

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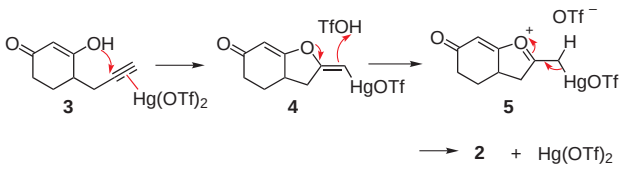
conversion to **2** was achieved using $Hg(OTFA)_2$ (1 mol%) with a 93% yield after 10 minutes in MeCN (entry 13). Increased reactivity of $Hg(OTf)_2$ versus $Hg(OTFA)_2$ is evident when the reactions with 0.1 mol% catalyst are compared. The reaction of **1** with 0.1 mol% of $Hg(OTf)_2$ afforded an 88% yield of **2** after 20 min (entry 6), however, $Hg(OTFA)_2$ required 20 hours to give an 85% yield of **2** (entry 14).

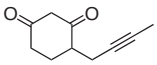
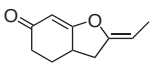
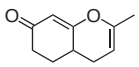
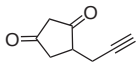
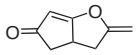
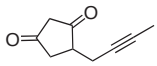
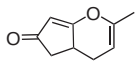
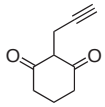
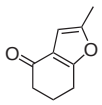
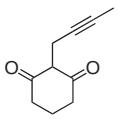
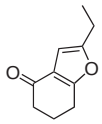
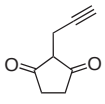
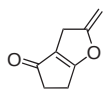
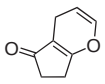
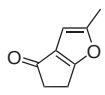
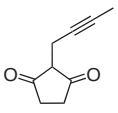
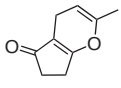
The cycloisomerization catalyzed by $Hg(OTf)_2$ is predicted to proceed as shown in Scheme 2. The reaction is initiated by π-complexation of an alkynyl group with $Hg(OTf)_2$ as seen in **3**. Participation of an enol group leads to vinyl mercury intermediate **4**. Protonation of **4** by in situ generated TfOH leads to oxonium cation **5**. Subsequent demercuration of **5** yields product **2** and regenerates the catalyst $Hg(OTf)_2$.




**Scheme 2**

Next we examined $Hg(OTf)_2$-catalyzed cyclization of various 1,3-diones (Table 2). Dione **6** (a methyl homologue of **1**) was reacted with $Hg(OTf)_2$ (1 mol%) in MeCN at room temperature for 30 minutes. This reaction produced a mixture of *exo*-cyclization product **7** and *endo*-cyclization product **8** in an 88:12 ratio, with a total yield of 84%. Cyclization of **6** was also achieved using 0.1 mol% of $Hg(OTf)_2$ producing **7** and **8** with an 80% total yield (87:13 ratio) after three hours at room temperature.

**Table 2** $Hg(OTf)_2$-Catalyzed Cyclization of 1,3-Dione

| Substrate | $Hg(OTf)_2$ | Product (yield)[a] | | |
|---|---|---|---|---|
|  **6** | 1 mol%, 30 min, 84% (88:12)[b]<br>0.1 mol%, 3 h, 80% (87:13) |  **7** | |  **8** |
|  **9** | 1 mol%, 25 min, 78%<br>0.1 mol%, 3 h, 73% |  **10** | | |
|  **11** | 1 mol%, 5 min, 76% |  **12** | | |
|  **13** | 1 mol%, 20 min |  **14** 90% | | |
|  **15** | 1 mol%, 20 min |  **16** 89% | | |
|  **17** | 1 mol%, 30 min |  **18** 48% |  **19** 8% |  **20** 28% |
|  **21** | 1 mol%, 30 min |  **22** 82% | | |

[a] Isolated yield.
[b] The ratio was determined by $^1H$ NMR.

Reaction of 4-propargyl-1, 3-cyclopentanedione (**9**) with 1 mol% and 0.1 mol% of $Hg(OTf)_2$ generated *exo*-methylene oxabicyclic product **10** with 78% (25 min) and 73% (3 h) yields, respectively. In contrast, methyl homologue **11** was converted to its *endo*-mode cyclization product **12** with a 76% yield using 1 mol% catalyst after only five minutes. Next, we examined the cyclization of 2-propargyl-1,3-cyclohexanedione (**13**) using 1 mol% of $Hg(OTf)_2$ in MeCN at room temperature for five minutes. This reaction gave rise to 2-methylfuran **14** with a 90% yield. Similarly, methyl homologue **15** was converted to 2-ethylfuran **16** with an 89% yield. On the other hand, cyclization of 2-propargyl-1,3-cyclopentanedione (**17**) produced a mixture of *exo*-mode cyclization product **18**, *endo*-mode cyclization product **19**, and 2-methylfuran **20** with 48%, 8%, and 28% yields, respectively. Reaction of the methyl homologue **21** produced exclusively *endo*-mode cyclization product **22** with an 82% yield.

Therefore, $Hg(OTf)_2$-catalyzed cycloisomerization of alkynyl-1,3-cyclohexanediones and cyclopentanediones occurs readily at ambient temperature. In comparison with previous transition-metal-catalyzed procedures,[10] very high catalytic turnovers were achieved.

## Acknowledgment

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## References and Notes

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(11) **Typical Experimental Procedure.**
Tetramethylurea (1.15 mg, 0.0099 mmol) and a stock solution of $Hg(OTf)_2$ in MeCN (0.01 M solution, 330 μL, 0.0033 mmol) were added to a solution of alkynyldione **1** (50 mg, 0.333 mmol) in MeCN (3.3 mL, 0.1 M) at r.t. The solution was stirred for 30 min at r.t., and aq $NaHCO_3$ was added. The mixture was extracted with $CH_2Cl_2$ and dried. Concentrated extract was subjected to a column chromatography on silica gel (hexane–EtOAc, 6:1) to give exclusively the oxabicyclic product **2** (50 mg, 0.333 mmol).