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Mercuric Triflate Catalyzed Hydroxylative Carbocyclization of 1,6-Enynes

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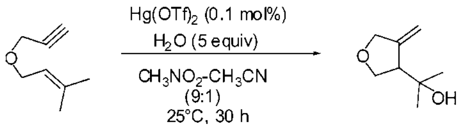
ABSTRACT



Hg(OTf)$_2$ exhibits remarkable catalytic activity for the hydroxylative cyclization of 1,6-enynes. The present procedure should involve a sequence of mercuration of a terminal alkyne, carbocyclization, hydration, and protodemercuration that regenerates the catalyst.

Carbocyclization is an important subject in modern organic synthesis,[1,2] and α,ω-enynes have been employed as the key substrate for transition metal (Pd,[3] Pt,[4] Ru,[5] Rh,[6] Ir,[7] Ti,[8] or Ga[9]) catalyzed alkene-exo mode cyclization. Mercuric salts have also been employed for enyne carbocyclization; however, stoichiometric amounts were used.[10] We have developed mercuric triflate Hg(OTf)$_2$ as a highly efficient olefin cyclization agent,[11] and its complex with an amine or tetramethylurea (TMU) was employed for the synthesis of a variety of polycyclic natural products.[12,13] Recently, we discovered that Hg(OTf)$_2$·(TMU)$_2$ complex exhibits effective catalytic activity for the hydration of terminal alkynes to give

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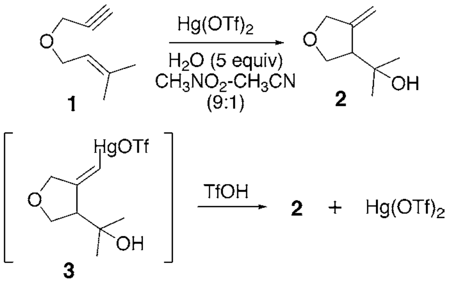
Table 1. $Hg(OTf)_2$-Catalyzed Hydroxylative Cyclization of **1**

entry	$Hg(OTf)_2$ (mol %)	TMU (mol %)	time (h)	yield (%)[a]
	10	0	3	99
2	5	0	6	99
3	1	0	16	99
4	0.1	0	30[b]	99
5	10	10	3	96
6	5	5	5	99
7	1	1	16	98
8	10	20	3	93
9	5	10	6	89
10	1	2	16	93
11[c]			16	0

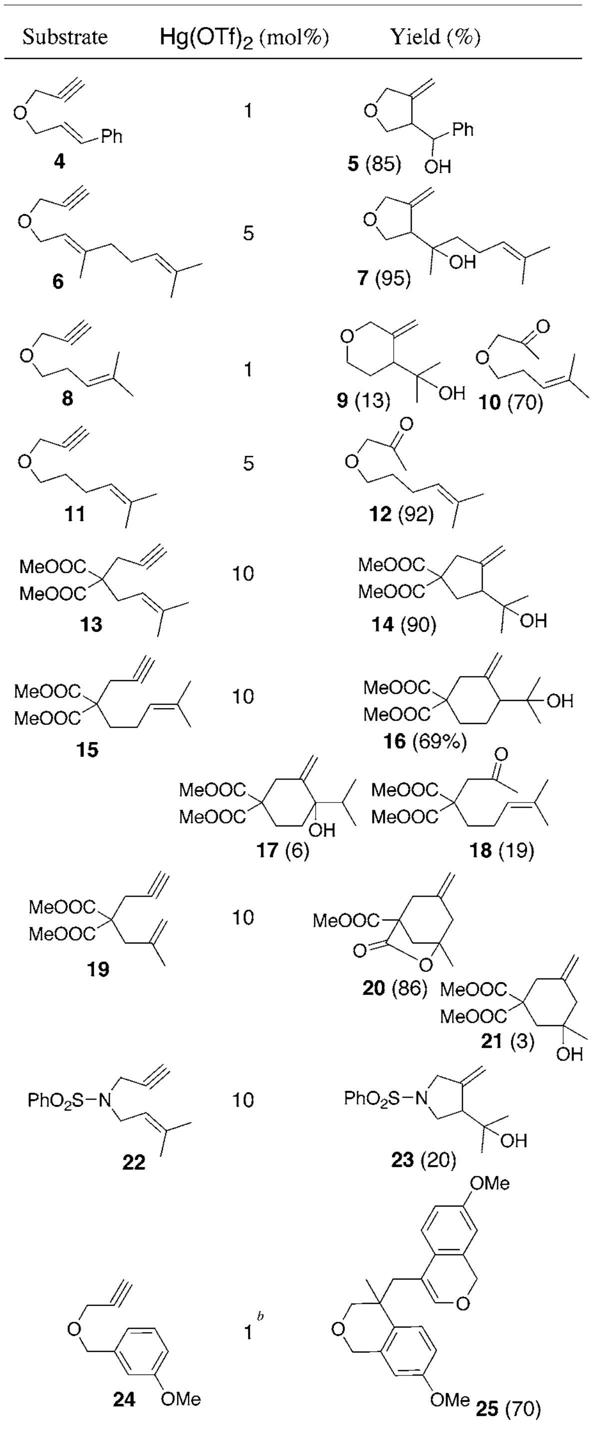
[a] GLC yield using hexadecane as an internal standard. [b] Reaction was carried out on a 0.5 M substrate concentration. [c] Reaction with 10 mol % of TfOH

methyl ketones in excellent yields.[14] The reaction should involve Hg^{2+}-induced hydration of alkyne and subsequent protodemercuration[10c] by TfOH that is generated in situ. Thus, we expected the intervention of a cyclization step prior to the hydration and developed an efficient catalytic process to prepare exomethylene carbocycles. Although the mercuric salt catalyzed cyclization of ω-alkynoic acids affording lactones is reported,[15] to our best knowledge the present protocol is the first mercuric salt catalyzed carbocyclization.



The reaction of prenyl propargyl ether **1** with 10 mol % of $Hg(OTf)_2$ in the presence of 5 equiv of water in CH_3NO_2/CH_3CN (9:1, 0.1 M concentration) at room temperature for 3 h afforded the exomethylene carbinol **2** in quantitative yield (Table 1, entry 1). The reaction should involve the vinyl mercury compound **3** as the intermediate, and the reaction with triflic acid, generated in situ, regenerates mercuric triflate, which establishes the catalytic cycle. A 5 or 1 mol % loading of catalyst was also enough to complete the reaction to give **2** in 99% yield within 5 and 16 h, respectively (entries 2 and 3). Even 0.1 mol % of $Hg(OTf)_2$ afforded **2** quantitatively within 30 h by conducting the reaction at 0.5 M substrate concentration (entry 4). When a 1:1 complex of $Hg(OTf)_2$ and TMU was employed, essentially the same results were obtained (entries 5−7). However, the 1:2 complex afforded slightly lower yields (entries 8−10). Generally $Hg(OTf)_2$ is stable in the presence of H_2O (although it is soluble and hygroscopic);[11b,12b,c,e] however, some people are suspicious about its decomposition to $Hg(OH)_2$ and TfOH and feel that it is probably the TfOH that brings about the reaction. Therefore, a control experiment

Table 2. $Hg(OTf)_2$-Catalyzed Hydroxylative Cyclization[a]



[a] Reaction was carried out in the presence of 5 equiv of H_2O. [b] One equivalent of H_2O was used.

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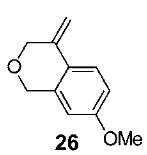
with 10 mol % of TfOH was performed, and it afforded none of the product **2** (entry 11) but an alkylation product (10%) as the only isolable material from a complicated mixture.[16]

The reaction of cinnamyl propargyl ether **4** with 1 mol % of $Hg(OTf)_2$ in the presence of 5 equiv of water in CH_3NO_2/CH_3CN (9:1) at room temperature for 20 h afforded the carbinol **5** as a 16:1 mixture of diastereomers in 85% yield. Treatment of geranyl propargyl ether **6** with 5 mol % of $Hg(OTf)_2$ provided carbinol **7** as a 20:1 mixture in 95% yield. Reaction of the homoprenyl propargyl ether **8** with 1 mol % of $Hg(OTf)_2$, however, afforded six-membered ring ether **9** in only 13% yield, and the major product was the ketone **10** in 70% yield. Bishomoprenyl propargyl ether **11** did not afford any seven-membered ring product, and the ketone **12** was obtained in 92% yield by the reaction using 5 mol % catalyst. Dimethyl malonate derivative **13** afforded the cyclization product **14**; however, it required at least 10 mol % of catalyst to complete the reaction, probably as a result of chelation with the malonate residue. Reaction of **15** with 10 mol % of catalyst afforded the six-membered carbocycle **16** in 69% yield. However, the reaction was not as clean as the others, affording the isomeric carbinol **17** (6%) and the methyl ketone **18** (19%). On the other hand, the reaction of the enyne **19** with 10 mol % catalyst and 2 equiv of water afforded the lactone **20** in 86% yield along with the alcohol **21** (3%). The reaction of sulfonamide derivative **22** and 10 mol % of catalyst afforded the five-membered ring carbinol **23**, albeit in only 20% yield. Methoxybenzyl propargyl ether **24** reacted with 1 mol % $Hg(OTf)_2$ and 1 equiv of water to furnish the dimerization product **25** in 70% yield, probably via acid-catalyzed dimerization of the primary product **26**. Reaction with 5 equiv of water, on the other hand, afforded only the hydrolysis product **27** in 85% yield. Thus, we have developed a novel $Hg(OTf)_2$-catalyzed hydroxylative carbocyclization to construct five-membered ring products in good to excellent yields via mercuration of a terminal alkyne, carbocyclization, hydration, and protodemercuration sequence regenerating the catalyst, $Hg(OTf)_2$. The reaction is mild enough to be applied to a variety of substrates, and particularly, the observation of the equal applicability of the mercuric triflate−TMU complex allows a wider possibility to achieve the reactions of acid-sensitive substrates. The efficiency to construct six-membered rings from 1,7-enynes under $Hg(OTf)_2$-catalysis is an unsolved problem, and we are currently exploring to find suitable conditions.



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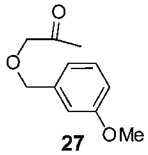

27

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Supporting Information Available: Experimental procedure and NMR data. This material is available free of charge via the Internet at http://pubs.acs.org.

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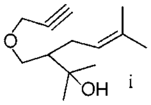
(16) The structure of the alkylation product was deduced from spectral data to be following.



i