ORGANIC LETTERS

2003
Vol. 5, No. 24
4563−4565

Mercuric Triflate–$(TMU)_3$-Catalyzed Cyclization of ω-Arylalkyne Leading to Dihydronaphthalenes

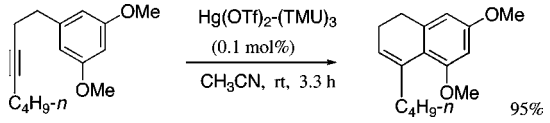
Mugio Nishizawa,* Hiroko Takao, Veejendra K. Yadav,† Hiroshi Imagawa, and Takumichi Sugihara

Faculty of Pharmaceutical Sciences, Tokushima Bunri University, Yamashiro-cho, Tokushima 770-8514, Japan

mugi@ph.bunri-u.ac.jp

Received August 27, 2003

ABSTRACT



Efficient arylyne cyclization catalyzed by the $Hg(OTf)_2$–$(TMU)_3$ complex has been developed. The reaction was carried out at ambient temperature in acetonitrile, and the catalytic cycle reaches up to 1000 turnovers.

Carbocyclization is an important subject of modern organic synthesis.[1] Arylalkyne cyclization catalyzed by transition metal compounds such as Ru complex,[2] $GaCl_3$,[3] and $PtCl_4$[4] affording dihydronaphthalene derivatives, Pd(0)- or $PtCl_2$-catalyzed reaction generating phenanthrenes,[5] $HfCl_4$-catalyzed cyclization of silylarylalkyne,[6] and Pd-catalyzed coumarin synthesis[7] have been intensively studied. Silver and mercuric salts have been employed in stoichiometric amounts to mediate the cyclization of aryl propynyl ethers.[8−10] We have developed mercury(II) trifluoromethanesulfonate, so-called mercuric triflate [hereafter $Hg(OTf)_2$], as a highly efficient olefin cyclization agent[11] and applied it for the synthesis of polycyclic terpenoids.[12] Recently, we found that the $Hg(OTf)_2$ and $Hg(OTf)_2$−tetramethylurea (hereafter TMU) complex showed effective catalytic activity for the

† On leave from Indian Institute of Technology, Kanpur, India, as a JSPS Visiting Scientist.

(1) For reviews on metal-catalyzed carbocyclization, see: (a) Ojima, I.; Tzamarioudaki, M. L. Z.; Donovan, R. J. *Chem. Rev.* **1996**, *96*, 635−662. (b) Negishi, E.; Coperet, C.; Ma, S.; Liou, S.-Y.; Liu, F. *Chem. Rev.* **1996**, *96*, 365−393. (c) Trost, B. M. *Chem. Eur. J.* **1998**, *4*, 2405−2412.

(2) Chatani, N.; Inoue, H.; Ikeda, T.; Murai, S. *J. Org. Chem.* **2000**, *65*, 4913−4918.

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10.1021/ol035622e CCC: $25.00
Published on Web 10/28/2003

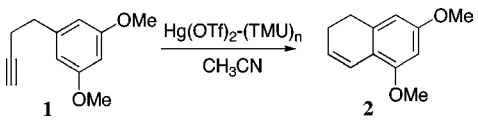
Table 1. $Hg(OTf)_2$-Catalyzed Cyclization of **1**

entry	catalyst	mol %	temp (°C)	time (h)	yield (%)[a] **2**	yield (%)[a] **1**
1	$Hg(OTf)_2$	2	rt	1	7	62
2	$Hg(OCOCF_3)_2$	2	rt	1	4[b]	86[b]
3	$Hg(OAc)_2$	20	rt	24	0	62
4	TfOH	20	rt	12	0	78
5	$Hg(OCOCF_3)_2$−TMU	2	rt	1	3[b]	84[b]
6	$Hg(OTf)_2$−TMU	2	rt	1	58	
7	$Hg(OTf)_2$−TMU	20	−20	2.5	52[c]	
8	$Hg(OTf)_2$−$(TMU)_2$	2	rt	1	83	
9	$Hg(OTf)_2$−$(TMU)_3$	2	rt	0.8	91	
10	$Hg(OTf)_2$−$(TMU)_3$	0.2	rt	12	13	77
11	$Hg(OTf)_2$−$(TMU)_5$	2	rt	12	22[b]	44[b]
12[d]	$Hg(OTf)_2$−$(TMU)_3$	2	rt	12	3[b]	44[b]

[a] Isolated yield after column chromatography. [b] NMR yield using dibromomethane as an internal standard. [c] Organomercuric chloride corresponds to **7** was isolated in 16% yield. [d] Reaction in CH_3NO_2.

hydration of terminal alkynes to give methyl ketones[13] and hydroxylative 1,6-enyne cyclization to give exomethylene five-membered ring products.[14] The reaction should involve a protodemercuration step of the vinylmercury intermediate induced by TfOH that is generated in situ. We describe herein the $Hg(OTf)_2$−$(TMU)_3$-catalyzed practical cyclization of ω-arylalkynes under very mild conditions, affording dihydronaphthalenes in a catalytic cycle with up to 1000 turnovers.[15]

First, we examined the reaction of terminal alkyne **1** with 2 mol % of $Hg(OTf)_2$ in CH_3CN at room temperature for 1 h. A product obtained in 7% yield was analyzed to be dihydronaphthalene derivative **2** (Table 1, entry 1). Although



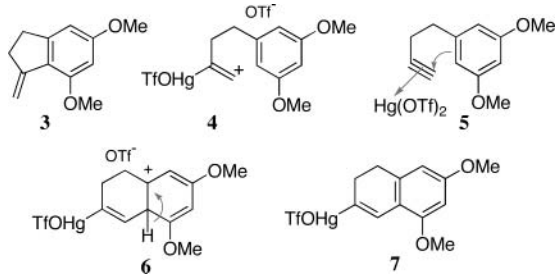
the yield is not satisfactory, we achieved mercuric salt catalyzed arylyne cyclization. $Hg(OCOCF_3)_2$ (2 mol %) also afforded **2** in 4% yield after 1 h (entry 2); however, even in 20 mol % of $Hg(OAc)_2$ or TfOH, it did not give any **2** at all (entries 3 and 4). The reactivity of $Hg(OCOCF_3)_2$−TMU complex was similar to that of $Hg(OCOCF_3)_2$ itself (entry 5); however, the $Hg(OTf)_2$−TMU complex was more reactive than $Hg(OTf)_2$, affording **2** in 58% yield after 1 h (entry 6). Surprisingly, $Hg(OTf)_2$−$(TMU)_2$ complex and furthermore $Hg(OTf)_2$−$(TMU)_3$ complex were more reactive and afforded **2** in 83% and 91% yield, respectively, within 1 h (entries 8 and 9).[16] However, 0.2 mol % of $Hg(OTf)_2$−$(TMU)_3$ was not enough to complete the reaction within an acceptable reaction period (entry 10). The reaction with $Hg(OTf)_2$−$(TMU)_5$ was not clean, and cyclization product **2** was obtained only in 22% yield along with 44% of **1** and unidentified decomposition products (entry 11). The reaction in CH_3NO_2 was sluggish to give **2** in only 3% yield after 12 h by using 2 mol % of catalyst (entry 12), and this solvent effect was in sharp contrast with the hydroxylative cyclization of 1,6-enyne that efficiently took place in CH_3NO_2−CH_3CN (9:1).[14]

Table 2. $Hg(OTf)_2$−$(TMU)_3$-Catalyzed Cyclization of **8**

entry	mol % of $Hg(OTf)_2$−$(TMU)_3$	time (h)	yield (%)[a]
1	2	0.5	93
2	0.2	2.2	94
3	0.1	3.3	95
4	0.05	24	54
5	1[b]	3	
6	1[c]	3	

[a] Isolated yield after column chromatography. [b] Reaction with TfOH. [c] Reaction with $TiCl_4$.

Although the reaction of 1,6-enyne afforded only the exomethylene five-membered ring product,[14] it is particularly noteworthy that the cyclization of **1** took place to afford only the 6-*endo* mode product **2**, and no trace of the 5-*exo* mode product such as **3** was detected. Because the formation of the anti-Markovnikov cation **4** is not likely, we concluded that the cyclization proceeded through a π-complex as shown in **5**. Deprotonation from the cation **6** should afford aromatic intermediate **7**,[10] and the vinyl-Hg bond of **7** is cleaved by the reaction with the in situ formed TfOH to afford **2** and the catalyst $Hg(OTf)_2$. When the reaction with 20 mol % of $Hg(OTf)_2$−TMU was carried out at −20 °C, 16% of the vinylmercuric chloride corresponds to **7** was isolated (entry 7), and thus the protodemercuration should be the rate-limiting step.



Our second substrate was butyl homologue **8**, and again the $Hg(OTf)_2$−$(TMU)_3$ complex exhibited extremely efficient catalytic activity to give only the *endo* mode cyclization product **9** as seen in Table 2. Even 0.1 mol % of the catalyst

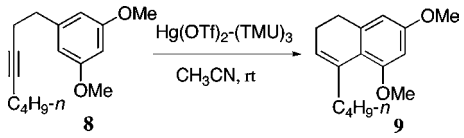
(13) Nishizawa, M.; Skwarczynski, M.; Imagawa, H.; Sugihara, T. *Chem. Lett.* **2002**, 12−13.

(14) Nishizawa, M.; Yadav, V. K.; Skwarczynski, M.; Takao, H.; Imagawa, H.; Sugihara, T. *Org. Lett.* **2003**, *5*, 1609−1611.

(15) The toxicity of mercury has been pointed out elsewhere. Although CH_3HgCl and $(CH_3)_2Hg$ are extremely dangerous, causing serious damage to the central nervous system, most organomercury compounds with higher molecular weight such as phenylmercuric acetate and mercurochrome have been employed as agrochemicals and medicine, respectively, and are not so toxic.

(16) **General Procedure.** To a stirred solution of $Hg(OTf)_2$−$(TMU)_3$ complex, prepared by mixing triflic anhydride and yellow mercuric oxide in CH_3CN at 0 °C and then TMU, was added a solution of an aryl alkyne (1 mmol) in CH_3CN (total 3 mL), and the resulting mixture was stirred at the indicated temperature until all starting material was consumed. After aqueous workup by adding aqueous $NaHCO_3$−NaCl (1:1) solution, the organic extract was dried and concentrated. Column chromatography of the crude material with hexane and ethyl acetate afforded the product.

was enough to produce **9** in 95% yield within 4 h (entry 3); therefore, a catalytic cycle of 1000 turnovers was achieved. Neither TfOH nor $TiCl_4$ (1 mol % each) afforded **9** (entries 5 and 6).



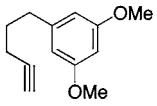
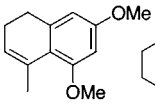
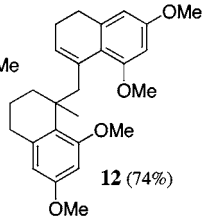
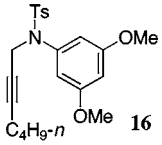
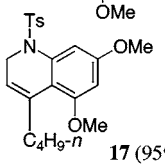
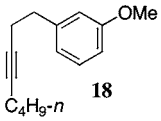
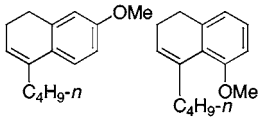
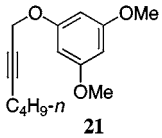
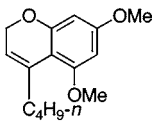
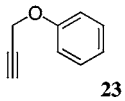
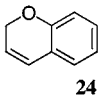
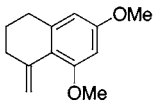
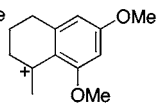
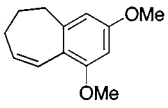
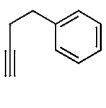
8 **9**

The reaction of the homologous terminal alkyne **10** with 0.2 mol % of $Hg(OTf)_2-(TMU)_3$ afforded the dihydronaphthalene derivative **11** only in 25% yield, and the major product was a dimeric product **12** in 74% yield (Table 3). The dimerization should result from the coupling of primary product **13** and its protonated stable cation **14**. Therefore, the reaction of **10** took place via the 6-*exo* mode cyclization, and no trace of a seven-membered ring product such as **15** was detected. Nitrogen analogue **16** was transformed to *endo* cyclization product **17** in 95% yield on treatment with 0.2 mol % of $Hg(OTf)_2-(TMU)_3$ at room temperature for 18 h. Monomethoxy derivative **18** afforded a mixture of dihydronaphthalenes **19** and **20** in 82% and 18% yields, respectively, on treatment with 2 mol % of $Hg(OTf)_2-(TMU)_3$ at room temperature for 6 h.[17] Although the result of the reaction of aryl propynyl ether **21** at room temperature was poor, a satisfactory result was obtained at low temperature.[4] A reaction with 0.2 mol % of $Hg(OTf)_2-(TMU)_3$ at −20 °C afforded **22** in 96% yield after 7 h. Ru complex- or $GaCl_3$-catalyzed cycloisomerization of *ω*-aryl-1-alkyne reported by Murai and co-workers could not be applied to ether-tethered substrates because they suffered from the cleavage of the carbon−oxygen bond.[2,3] Phenyl propargyl ether **23** afforded **24** in 50% isolated yield by the reaction with 10 mol % of $Hg(OTf)_2-(TMU)_3$ at room temperature for 24 h. The nonactivated aromatic compound **25** did not provide any cyclization product on treatment with 10 mol % of $Hg(OTf)_2-(TMU)_3$ at room temperature for 24 h.

Therefore, we have developed a very mild and efficient protocol to effect *ω*-arylalkyne cyclization to prepare unstable dihydronaphthalene derivatives by using a catalytic amount of the $Hg(OTf)_2-(TMU)_3$ complex.

(17) NMR yield based upon dibromomethane as an internal standard.

Table 3. $Hg(OTf)_2-(TMU)_3$-Catalyzed Cyclization in CH_3CN

Substrate	$Hg(OTf)_2$-$(TMU)_3$ (conditions)	Product (yield, %)
 **10**	0.2 mol% (rt, 2 h)	 **11** (25%)  **12** (74%)
 **16**	0.2 mol% (rt, 18 h)	 **17** (95%)
 **18**	2 mol% (rt, 6 h)	 **19** (82%) **20** (18%)
 **21**	0.2 mol% (-20°C, 7 h)	 **22** (96%)
 **23**	10 mol% (rt, 24 h)	 **24** (50%)
 **13**  **14**  **15**  **25**		

Acknowledgment. This work was supported by a Grant-in-Aid from the Ministry of Education, Culture, Sports, Science, and Technology of Japanese Government.

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

OL035622E