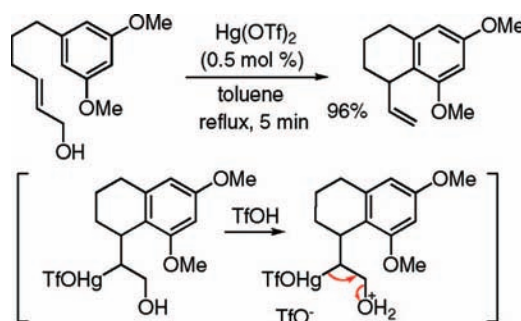


Hg(OTf)₂-Catalyzed Arylene CyclizationKosuke Namba, Hirofumi Yamamoto, Ikuo Sasaki, Kumiko Mori, Hiroshi Imagawa,
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ABSTRACT



Novel Hg(OTf)₂-catalyzed arylene cyclization was achieved with highly efficient catalytic turnover (up to 200 times). The reaction takes place via protonation of allylic hydroxyl group by in situ formed TfOH of an organomercuric intermediate to generate a cationic species. Subsequent smooth demercuration regenerates the catalyst.

Transition metal-catalyzed arylyne cycloisomerizations have been intensively studied and play an important role in modern organic synthesis.^{1,2} In sharp contrast, catalytic arylene cycloisomerization is almost unknown. We reported that Hg(OTf)₂-tristetramethylurea (TMU) complex catalyzes the

efficient cycloisomerization of arylalkyne **1** to give dihydronaphthalene derivative **2** with a catalytic turnover up to 1000 times.³ The reaction involves protonation of the alkenyl mercury intermediate **3** with in situ formed TfOH to generate cation **4**. Subsequent smooth demercuration leads to **2** and the regenerated catalyst.^{4,5} Hg(OTf)₂ was originally developed in 1983 as an efficient olefin cyclization agent,⁶ and the reaction of farnesyl sulfone **5** with 1.2 equiv of

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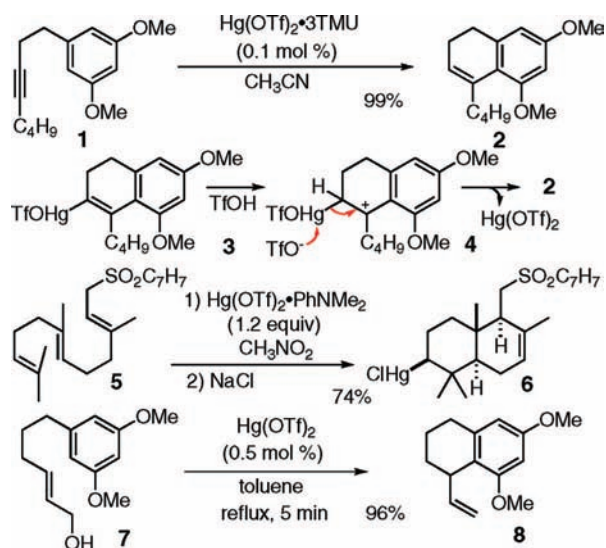
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Hg(OTf)₂•PhNMe₂ afforded bicyclic product **6** in 74% yield.^{6a} Because the latter reaction produces stable organomercuric product **6**, it is essentially a stoichiometric reaction.⁷ To achieve catalytic aryene cyclization, we tried to introduce an oxygen-based functional group into the allylic position for the protonation site, thereby triggering smooth demercuration. We found that the reaction of the (*E*)-6-(3,5-dimethoxyphenyl)-2-hexen-1-ol (**7**) with 0.5 mol % of Hg(OTf)₂ in toluene at reflux temperature for 5 min was sufficient to afford cyclization product **8** in 96% yield. The alkenyl functional group maintained in the product **8** should be useful for further molecular modification such as hydroboration, ozonolysis, and metathesis. Friedel–Crafts type aryl allyl alcohol cyclization was reported using triflic acid as solvent.⁸ Although related Pd-catalyzed aryl halide allyl acetate cyclization⁹ and InCl₃-catalyzed aryl allyl bromide cyclization¹⁰ have been recorded, catalytic turnovers are not very high. Recently Pt-catalyzed aryene cyclization was reported by Widenhoefer and co-workers.¹¹

Scheme 1. Hg(OTf)₂-Induced and Catalyzed Cyclizations



Initially, we examined the reaction of **7** with 1 mol % of Hg(OTf)₂ in acetonitrile at room temperature. However, no reaction products could be detected (Table 1, entry 1). When the mixture was heated to reflux, a slow reaction took place and afforded desired product **8** in 43% yield along with 17% of starting material after 24 h (entry 2). Among the solvents investigated, toluene was found to be the best. Toluene

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Table 1. Catalytic Cyclization of **7**

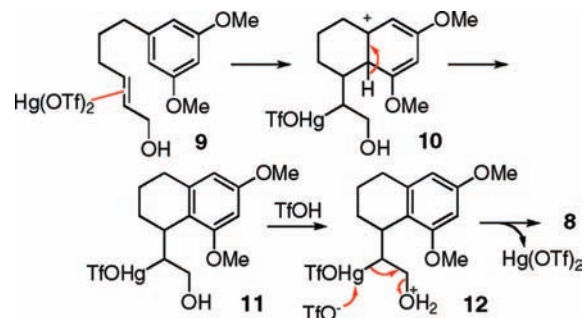
entry	catalyst (mol %)	solvent	temperature	time (h)	yield (%) ^a	
					8	7
1	Hg(OTf) ₂ (1)	CH ₃ CN	rt	24	–	95
2	Hg(OTf) ₂ (1)	CH ₃ CN	reflux	24	43	17
3	Hg(OTf) ₂ (1)	CH ₃ NO ₂	reflux	1.5	82	–
4	Hg(OTf) ₂ (1)	CH ₂ Cl ₂	reflux	24	30	38
5	Hg(OTf) ₂ (1)	(CH ₂ Cl) ₂	reflux	0.5	82	–
6	Hg(OTf) ₂ (1)	C ₆ H ₅ CH ₃	reflux	0.08	84	–
7	Hg(OTf) ₂ (1)	C ₆ H ₅ CH ₃	rt	24	–	74
8	Hg(OTf) ₂ (0.5)	C ₆ H ₅ CH ₃	reflux	0.08	96	–
9	Hg(OTf) ₂ (0.1)	C ₆ H ₅ CH ₃	reflux	24	–	90
10	Hg(OTFA) ₂ (1)	C ₆ H ₅ CH ₃	reflux	24	–	98
11	TfOH (0.5)	C ₆ H ₅ CH ₃	reflux	0.08	60	12

^a Isolated yield.

afforded **8** in 96% yield when 0.5 mol % of Hg(OTf)₂ was used under reflux conditions for 5 min (entry 8). Reaction using 1 mol % catalyst gave 84% yield, probably due to partial decomposition of the product (entry 6). When the reaction in toluene was performed at room temperature no products were formed (entry 7). The yield using 0.1 mol % catalyst was too low to justify further investigation (entry 9). Reactions with Hg(OTFA)₂ as well as triflic acid were also examined under the same conditions. Although 1 mol % of Hg(OTFA)₂ was entirely inert for the reaction (entry 10), 0.5 mol % of TfOH also afforded **8** in 60% yield (entry 11), indicating that the Hg(OTf)₂ is the real catalytic species of our reaction (Scheme 1).

We propose that the reaction is likely to be initiated from a π -complex **9**.^{4,5} Friedel–Crafts type cyclization leads to carbocation **10**, and the organomercuric intermediate **11** is produced by deprotonation. Protonation of the hydroxyl moiety of **11** by in situ generated TfOH leads to oxonium cation **12**. Demercuration regenerates the catalyst Hg(OTf)₂ and affords the product **8** (Scheme 2).

Scheme 2. Possible Reaction Mechanism



We subsequently examined the reaction of *Z*-allyl alcohol **13** with 0.5 mol % of Hg(OTf)₂ in toluene. The same cyclization product **8** was obtained in 95% yield after reflux for 10 min (Table 2). Thus, the geometry of the double bond

Table 2. Hg(OTf)₂-Catalyzed Arylene Cyclization

substrate	conditions	product (yield, %) ^a
	0.5 mol % toluene, reflux 10 min	8 (95%)
	0.5 mol % toluene, reflux 1 h	8 (63%)
	0.5 mol % toluene, reflux 1 h	8 (76%)
	1 mol % toluene, reflux 10 min	17 (71%) 18 (23%)
	1 mol % toluene, reflux 15 min	20 (30%) ^b
	1 mol % toluene, reflux 10 min	22 (90%)
	1 mol % toluene, reflux 5 min	24 (65%) ^b
	1 mol % toluene, reflux 5 min	26 (67%) 27 (25%)
	1 mol % toluene, reflux 5 min	29 (90%)
	1 mol % toluene, reflux 10 h	31 (99%)

^a Isolated yield. ^b NMR yield using CH₂Br₂ as the internal standard.

does not contribute to the reactivity. Reaction of allylic acetate **14** afforded **8** in 63% yield after 1 h reflux in toluene, which is slower than the reaction with alcohol **7** or **13**. The corresponding methoxy derivative **15** also afforded **8** in 76% yield after 1 h reflux in toluene. Reaction of (*E*)-6-(3-methoxyphenyl)-2-hexen-1-ol (**16**) with 1 mol % of

Table 3. Hg(OTf)₂-Catalyzed Arylene Cyclization

substrate	conditions	product (yield, %) ^a
	Hg(OTf) ₂ (1 mol %) toluene, rt, 5 min	33 (67%)
	Hg(OTf) ₂ (1 mol %) various conditions	36 (0%)
	Hg(OTf) ₂ (1 mol %) toluene, rt, 10 min	38 (84%)
	Hg(OTf) ₂ (1 mol %) toluene, rt, 5 min	39 (9%) 41 (67%)

^a Isolated yield.

Hg(OTf)₂ in toluene at reflux for 10 min afforded *p*-cyclization product **17** in 71% yield¹² along with *o*-cyclization product **18** in 23% yield. Although *o*-methoxy substituted hexenol derivative **19** afforded cyclization product **20** in very low yield (30%) along with unidentified complex products, *p*-substituted **21** gave **22** in 90% yield. Nonactivated phenyl-substituted **23** could also be used giving rise to **24** in 65% yield after reflux for 5 min.¹³ Reaction of biphenyl derivative **25** with 1 mol % of Hg(OTf)₂ produced alkenyl substituted dihydrophenanthrene derivatives **26** and **27** in 67 and 25% yield, respectively. Reaction of indole derivative **28** with 1 mol % of Hg(OTf)₂ generated tricyclic indole **29** in 90% yield. Reaction of alternative allylic alcohol

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30 also provided **31** in 99% yield by the reaction with 1 mol % of Hg(OTf)₂ in toluene at reflux temperature for 10 h.

The methoxy group of vinyl methyl ether also could act as a protonation site. Thus, compound **32** (*E/Z* 6:4 mixture) was treated with 1 mol % of Hg(OTf)₂ in toluene. The reaction was completed within 5 min at room temperature, giving rise to dihydronaphthalene **33** in 67% yield along with dimeric product **34** in 24% yield (Table 3).³ *p*-Substituted **35**, however, did not afford any cyclization product at room temperature but afforded hydrolyzed aldehyde at elevated temperature. Reaction of a biphenyl derivative **37** with 1 mol % of Hg(OTf)₂ in toluene at room temperature for 10 min afforded phenanthrene derivative **38** in 84% yield along with 9% of **39**.²¹ Indole derivative **40** was converted to tricyclic product **41** in 67% yield along with dimeric byproducts by the reaction in toluene at room temperature for 5 min.

In conclusion, we achieved novel Hg(OTf)₂-catalyzed arylene cyclization by introducing a protonation site at the

appropriate position to obtain high catalytic turnover. The results described in this paper should enable the creation of new quaternary carbon centers and facilitate the development of catalytic asymmetric cyclization which have been very difficult to accomplish the cyclization initiated from alkyne.¹⁴

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

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(14) Although a variety of chiral auxiliaries were examined for the Hg(OTf)₂-catalyzed enyne cyclization, no trace of chiral induction was detected.