Hg(OAc)₂·0.1Sc(OTf)₃-Catalyzed Cycloisomerization of 2-(4-Pentynyl)furan

Hirofumi Yamamoto, Ikuo Sasaki, Hiroshi Imagawa, and Mugio Nishizawa*

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

mugi@ph.bunri-u.ac.jp

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ABSTRACT



Although the Hg(OTf)₂·3TMU-catalyzed Friedel–Crafts-type reaction of 3-(4-pentynyl)furan afforded the exo cyclization product, the reaction of 2-(4-pentynyl)furan furnished a very low yield. We found a 10:1 mixed reagent of Hg(OAc)₂ and Sc(OTf)₃ showed remarkable catalytic activity for the latter transformation. The actual reacting species is presumed to be Hg(OAc)(OTf), which is efficiently generated in situ by mixing the two reagents.

Transition-metal-catalyzed cycloisomerization of arylalkynes has been intensively studied and has played an important role in modern organic synthesis.¹ Electron-rich arenes react with alkynes in the presence of electrophilic metal halides or Brønsted acids.² We have also reported six-endo cycloisomerization of arylalkynes to give dihydronaphthalene derivatives.³ Intramolecular reaction of furan with alkynes, however, mostly affords phenolic products via Diels–Alder reaction followed by a fragmentation.⁴ Although an endo

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mode Friedel–Crafts-type cyclization of furanoalkynes affording benzofurans has been reported,⁵ exo mode cyclization of alkynyl furans has not been recorded except for one example using PtCl₂ as catalyst, affording a benzofuran derivative.^{4e} Therefore, the Friedel–Crafts-type cycloisomerization of alkynyl furans is an almost unknown area of research, and thus we have investigated the cycloisomerizations of 3-(4-pentynyl)furan (1) and 2-(4-pentynyl)furan (3) by using the reagent that we originated, mercuric triflate [Hg-(OSO₂CF₃)₂, hereafter Hg(OTf)₂].⁶⁻¹³ The latter type of cycloisomerization (3 to 4) is entirely unknown. The reaction

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of 3-(4-pentynyl)furan (1) and 1 mol % of mercuric triflate. 3tetramethylurea (hereafter TMU) complex afforded exo cyclization product 2 in 81% yield. However, the reaction of 2-(4-pentynyl)furan (3) with a variety of modified Hg- $(OTf)_2$ reagents gave a very low yield of 4. We found that a 10:1 mixed reagent of Hg(OAc)₂ and Sc(OTf)₃ showed remarkable catalytic activity for the latter transformation leading to 4. The actual reacting species is presumed to be Hg(OAc)(OTf) efficiently generated in situ by mixing the two reagents. First, we examined the reaction of 3-(4-



pentynyl)furan (1) with 1 mol % of Hg(OTf)₂ in CH₃CN at -20 °C for 3 h, and only a trace amount of 2 was detected along with 25% of starting material and some polymeric materials (Table 1, entry 1). This result suggested the

Table 1. Cycloisomerization of 1 in CH ₃ CN at -20 °C.								
				yield (%) ^a				
entry	catalyst	mol %	time	2	1			
1	Hg(OTf) ₂	1	3 h	tr	25			
2	Hg(OTf) ₂ ·TMU	1	20 min	5	57			
3	Hg(OTf)2.TMU	1	3 h	\mathbf{tr}	52			
4	Hg(OTf)2·2TMU	1	20 min	50	20			
5	Hg(OTf) ₂ ·2TMU	1	3 h	7	16			
6	Hg(OTf) ₂ ·3TMU	1	20 min	81	tr			
7	Hg(OTf) ₂ ·3TMU	1	3 h	5				
8	Hg(OTf) ₂ ·3TMU	0.5	3 h	8	36			
9	Hg(OTf) ₂ ·3TMU	0.1	3 h	10	78			
10	AuCl ₃	1	5 min					
11	$PtCl_2$	1	1 h		96^b			

^a NMR yield using naphthalene as the internal standard. ^b Reactions in acetone at -20 °C for 1 h afforded 2 in 2% yield along with 77% of 1.

existence of some catalyst suicide mechanism, probably by the reaction of $Hg(OTf)_2$ and the product 2. Reaction with Hg(OTf)₂•TMU (1 mol %) for 20 min or 3 h also furnished disappointing results (entries 2 and 3). A 20 min reaction

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with Hg(OTf)₂·2TMU (1 mol %) afforded 2 in 50% yield (NMR yield using naphthalene as the internal standard) along with 20% of starting material; however, prolonged reaction for 3 h resulted in decomposition to give 2 in only 7% yield (entries 4 and 5). The best result was obtained by using Hg-(OTf)₂•3TMU (1 mol %) in CH₃CN at -20 °C for 20 min, affording 2 in 81% yield (entry 6). However, prolonged reaction for 3 h again decreased the yield significantly as the result of some decomposition (entry 7). Neither 0.5 mol % catalyst nor 0.1 mol % catalyst afforded good results (entries 8 and 9). Reaction using AuCl₃ (1 mol %) resulted in complete decomposition of material (entry 10). In contrast, the reaction with $PtCl_2$ (1 mol %) at -25 °C for 1 h resulted in recovery of starting material (entry 11). Thus, not only the starting material 1 but also the product 2 were very sensitive to even mildly acidic conditions.

Next we examined the cycloisomerization of 2-(4-pentynyl)furan (3) by expecting a Friedel-Crafts type product such as 4. As shown in Table 2, transformation of 3 to 4 is

Table 2.	Cycloisomerization	of 3 in CH ₃ CN for 20 min	
			-

		additive		yield (%) ^a	
entry	Hg salt (mol %)	(mol %)	(°C)	4	3
1	$Hg(OTf)_2(1)$		0	8	40
2	Hg(OTf) ₂ ·3TMU (1)		0	17	55
3	Hg(OTf) ₂ ·3TMU (1)		25	36	18
4	Hg(OTf) ₂ ·3TMU (5)		0	30	b
5	Hg(OTf) ₂ ·3TMU (5)	$AgSbF_{6}\left(0.5 ight)$	25	38	
6	$Hg(OTf)_2(5)$	$Sc(OTf)_{3}(0.5)$	25		
7	Hg(OTf) ₂ ·3TMU (5)	$Sc(OTf)_{3}(0.5)$	25	4	61
8	$Hg(OAc)_2(5)$	$AgSbF_{6}\left(0.5 ight)$	25		90
9	$Hg(OAc)_2(5)$	AgOTf(0.5)	25		86
10	$Hg(OAc)_2(5)$	$La(OTf)_3(0.5)$	25	19	60
11	$Hg(OAc)_2(5)$	$Eu(OTf)_3(0.5)$	25	26	60
12	$Hg(OAc)_2(5)$	Yb(OTf)3 (0.5)	25	39	37
13	$Hg(OAc)_2(5)$	$Sc(OTf)_{3}(0.5)$	25	80	
14	$Hg(OAc)_2(5)$	$Sc(OTf)_3(5)$	25	3	b
15	$Hg(OAc)_2(5)$		25		90 ^c
16		$Sc(OTf)_{3}(0.5)$	25		94
17	$Hg(OAc)_2(5)$	TfOH (0.5)	25	66	
18	$Hg(OAc)_2(5)$	TfOH (5)	25		b
19	$PtCl_{2}(5)$		25		d

^a NMR yield using naphthalene as the internal standard. ^b Complex mixture was formed. ^c Small amount of 5 was detected. ^d A 10:1 mixture of phenol 6 and an unidentified product was obtained in 72% yield after 10 h at reflux in acetone.



very difficult even by using Hg(OTf)₂·3TMU complex. A better result was obtained by the reaction of 3 with 1 mol % catalyst in CH₃CN at 25 °C for 20 min, but the yield was still 36% (Table 2, entry 3). Thus, we decided to examine other possibilities. Upon learning of the enyne cycloisomerization catalyzed by a mixed reagent of Au complex and $AgSbF_{6}$ ¹⁴ we tried the reaction of **3** with a 10:1 mixed reagent of Hg(OTf)₂·3TMU and AgSbF₆ in CH₃CN at 25

°C for 20 min and obtained 4 in 38% yield (entry 5). Then we screened a variety of combinations of mercuric salts and additives in a 10:1 ratio. Because no promising results were obtained by using Hg(OTf)₂ or its TMU complex (entries 6 and 7), we switched to $Hg(OAc)_2$. Then, we found the combination of Hg(OAc)₂ and La(OTf)₃ (10:1) affords 4 in 19% yield along with 60% of starting material (entry 10). A 10:1 combination of Hg(OAc)₂ with Eu(OTf)₃ also afforded 4 in 26% yield, and with Yb(OTf)₃ gave a 39% yield of 4 together with significant quantities of starting material 3 (entries 11 and 12). Finally we found that the combination of Hg(OAc)₂ and Sc(OTf)₃ (10:1) gave rise to 4 in 80% yield (entry 13). However, the reaction using a 1:1 mixture of Hg-(OAc)₂ and Sc(OTf)₃ afforded 4 only in 3% yield along with complex polymeric products (entry 14). The reaction with only Hg(OAc)₂ (5 mol %) did not afford 4 at all, and most of the starting material was recovered along with trace amounts of unstable byproduct that is dimeric mercury acetylide 5 (entry 15). Acetylide formation is a catalyst suicide mechanism. Reaction with 0.5 mol % of Sc(OTf)₃ resulted in complete recovery of starting material (entry 16). However, a 10:1 combination of $Hg(OAc)_2$ and TfOH afforded 4 in 66% yield (entry 17), and a 1:1 reagent did not afford 4, instead producing complex mixtures (entry 18). When the reaction of **3** with $PtCl_2$ (5 mol %) in acetone was examined at reflux for 10 h, Diels-Alder and following fragmentation took place to give a 10:1 mixture of phenol 6 and an unidentified product in 72% yield.^{4e,15}

The results suggested the actual reacting species to be Hg-(OAc)(OTf) generated by the reaction of Hg(OAc)₂ and small amounts of Sc(OTf)₃ or TfOH (entries 13 and 17). When Hg(OAc)₂ and an equal amount of either Sc(OTf)₃ or TfOH were mixed, decomposition took place because of the partially formed Hg(OTf)₂ (entries 14 and 18). However, we failed to detect any occurrence of Hg(OAc)(OTf) or Hg-(OTf)₂ by NMR experiment, probably due to too low concentration.

Therefore, we propose that the reaction is likely to be initiated from π -complex 7, cyclized oxonium cation 9 is generated probably via the spirocyclic cation 8, and the cation 9 produces the vinylmercury intermediate 10 by deprotonation. Then, the protonation of 10 by in situ generated TfOH leads to alternative oxonium cation 11 and upon demercuration regenerates the catalyst Hg(OAc)(OTf) and affords the product 4. Probably Hg(OAc)(OTf) is inert against 4. However, as shown in Table 2, Hg(OTf)₂ also reacts with the product 4, generating cation 12. Further reaction of 12 with 4 should lead to complex polymerization products. Occurrence of an sp³-C-Hg bond formed by the deprotonation of polymeric products should be the alternative catalyst suicide mechanism. The procedure was applied to the reaction of 2-methyl-5-(4-pentynyl)furan (13). A reaction with 5 mol % of Hg(OAc)₂·0.1Sc(OTf)₃ in CH₃CN at room temperature for 20 min afforded exo cyclization product 14 in 75% yield (Table 3). Malonate derivative 15 was converted



to **16** in 91% yield. The reaction of 2-methyl-5-(4-nonynyl)furan (**17**) with 5 mol % of Hg(OAc)₂•0.1Sc(OTf)₃ in CH₃-CN required 60 °C and afforded endo cyclized sevenmembered ring product **18** in 75% yield after 17 h. Although the reaction of 2-(4-nonynoyl)furan (**19**) afforded sevenmembered ring product **20** in low yield (44%) even after 24 h reaction at 60 °C, the phenyl-substituted analogues **21** and **23** afforded endo cyclization products **22** (90% yield) and **24** (93% yield), respectively. Reaction of 2-(3-butynyl)-5methyfuran (**25**) with Hg(OAc)₂•0.1Sc(OTf)₃ at 25 °C for

Table 3. Reaction of Alkynyfurans with 5 mol % of $Hg(OAc)_2 \cdot 0.1Sc(OTf)_3$ in CH₃CN.



^a Starting material was recovered in 88% yield.

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24 h resulted in 88% recovery of starting material without forming 26. Elevating the reaction temperature to 60 °C for 24 h led to decomposition. These results suggest that the rearrangement mechanism is from spirocyclic intermediate 8 to 9, since the case of 25 has to generate a spirocyclic four-membered ring intermediate. It must be pointed out that internal alkynyl furans 17, 19, 21, and 23 selectively afforded seven-membered ring products 18, 20, 22, and 24, respec-

tively. The results reflect the stability of **28** over **27**, and the rearrangement to **29** was the only possible path (Scheme 3).

Thus, we have developed a new, mild catalytic system, $Hg(OAc)_2 \cdot 0.1Sc(OTf)_3$, and achieved novel cycloisomerization of very sensitive substrates such as 2-(4-pentynyl)furan and analogues.

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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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