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Hg(OTf)$_2$-catalyzed Cycloisomerization of Aryl- and Hetero-substituted 1,3-Dienes

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We developed Hg(OTf)$_2$-catalyzed Friedel–Crafts-like cycloisomerization of 7-arylhepta-1,3-dienes to give propenyl-substituted tetrahydronaphthalenes in excellent catalytic turnover under very mild conditions. 1,3-Dienyl sulfonamides and 1,3-dienyl alcohols were also efficiently cyclized to afford heterocyclic compounds.

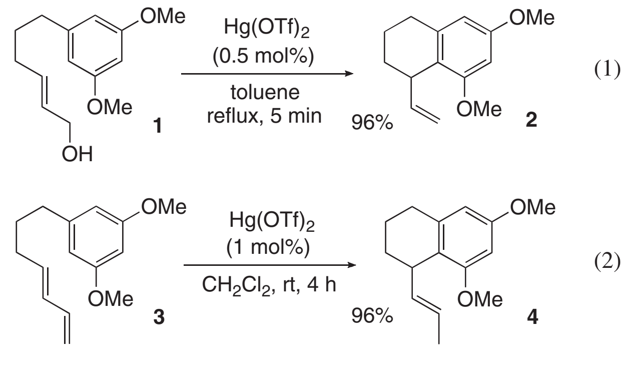
In the last five years Hg(OTf)$_2$ has been increasingly used for metal-catalyzed cycloisomerization of alkynes to generate C–C as well as C–heteroatom bonds.[1] The key step in these catalytic reactions is the protonation of vinylmercury intermediates by TfOH, which is formed in situ.[2] Recently the procedure has been extended to alkene cyclizations by the introduction of an allylic hydroxy moiety as the protonation site to trigger the smooth demercuration step that regenerates the catalyst. For example the reaction of **1** with 0.5 mol % of Hg(OTf)$_2$ in toluene affords **2** in excellent yield (Scheme 1, eq 1). The vinyl functionality maintained in the product will be useful for further molecular modifications such as hydroboration, ozonolysis, and metathesis.[3] Here, we show that Hg(OTf)$_2$-catalyzed cycloisomerization of aryl 1,3-diene **3** affords tetrahydronaphthalene **4** in high catalytic turnover under very mild reaction conditions (eq 2). 1,3-Dienyl sulfonamides as well as 1,3-dienyl alcohols were also found to efficiently react in the presence of a catalytic amount of Hg(OTf)$_2$ to give heterocycles. The Friedel–Crafts-like metal salt-catalyzed cycloisomerization of aryl-substituted 1,3-diene has not yet been reported,[4] although a few catalytic heterocycle syntheses from 1,3-dienes have been described.[5]

First, we examined the reaction of **3** with 1 mol % of Hg(OTf)$_2$ in CH_3CN at room temperature. However, no reaction products were detected (Table 1, Entry 1). After examining a variety of solvents, CH_2Cl_2 was found to be the solvent of choice. Although $(CH_2Cl)_2$ provided **4** in 63% yield, CH_2Cl_2 gave **4** in 96% yield after 4 h at room temperature (Entries 4 and 5). The reaction took place with complete *E*-selectivity even when a mixture of *E*- and *Z*-dienes was employed. Complete reaction was achieved within 24 h using a catalyst loading of 0.5 mol % (Entry 6). By contrast, Hg(OTFA)$_2$ did not afford any product (Entry 7). Although less effective than Hg(OTf)$_2$, TfOH acted as a catalyst to give a cyclic product after 12 h (Entry 8).

Table 1. Hg(OTf)$_2$-catalyzed cycloisomerization of **3**[a]

Entry	Catalyst	Mol %	Solvent	Time/h	Yield/%[b]	
					3	**4**
1	Hg(OTf)$_2$	1	CH_3CN	4	94	—
2	Hg(OTf)$_2$	1	CH_3NO_2	4	93	—
3	Hg(OTf)$_2$	1	$C_6H_5CH_3$	4	98	—
4	Hg(OTf)$_2$	1	$(CH_2Cl)_2$	4	13	63
5	Hg(OTf)$_2$	1	CH_2Cl_2	4	—	96
6	Hg(OTf)$_2$	0.5	CH_2Cl_2	24	—	90
7	Hg(OTFA)$_2$	1	CH_2Cl_2	24	99	0
8	TfOH	1	CH_2Cl_2	12	—	88

[a]Reactions were carried out at room temperature. [b]Isolated yield.



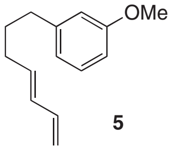
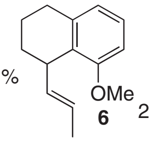
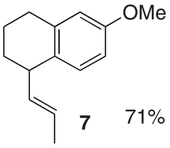
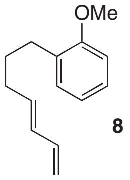
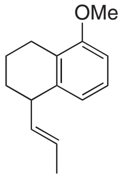
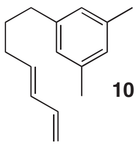
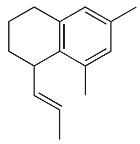
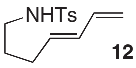
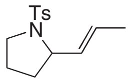
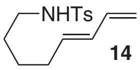
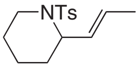
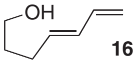
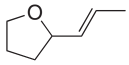
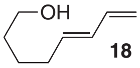
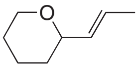
Scheme 1. Hg(OTf)$_2$-catalyzed cyclizations.

Table 2 shows the generality of Hg(OTf)$_2$ using a variety of 1,3-diene derivatives. The reaction of *m*-methoxyphenyl-substituted heptadiene **5** with 1 mol % of Hg(OTf)$_2$ in CH_2Cl_2 for 2 h at room temperature afforded the cyclization product **7** at the *p*-position for the methoxy group in 71% yield along with the *o*-position product **6** in 27% yield. In contrast, the *o*-substituted **8** gave a complex mixture of reaction products that did not include **9**. The *m*-xylene derivative **10** behaved as a suitable precursor to afford **11** in good yield. We then examined heterocyclizations to generate C–N and C–O bonds. The reaction of heptadienyl sulfonamide **12** with 2 mol % of Hg(OTf)$_2$ was completed in 6 h at room temperature. The homolog **14** also afforded the piperidine derivative **15** in excellent yield under the same reaction conditions. The corresponding dienyl alcohols **16**[6] and **18**[7] were found to be less reactive, requiring 8 mol % of Hg(OTf)$_2$ to obtain **17** in 78% and **19** in 92%, respectively.[8]

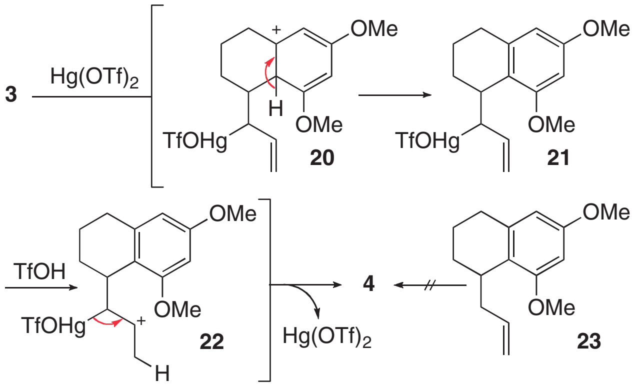
The reaction is likely to be initiated from a mercury–diene complex. Cation **20**, generated by the Friedel–Crafts-like cyclization, produces organomercuric intermediate **21** via deprotonation (Scheme 2). Protonation of the remaining vinyl moiety of **21** by TfOH, which is formed in situ, leads to an alternative cation **22**.

Demercuration of **22** regenerates the catalyst Hg(OTf)$_2$ and forms the product **4**. In order to confirm the mechanism, we prepared the isomeric terminal olefin **23** from 6,8-dimethoxy-3,4-dihydronaphthalen-1(2*H*)-one.[9] When **23** was treated with either 1 mol % of Hg(OTf)$_2$ or TfOH in CH_2Cl_2 at room temperature, no reaction took place even after 24 h. Thus the potential isomerization of the double bond from the terminal position to the internal position could be disregarded. It is now

Table 2. Reactivity of various 1,3-diene derivatives[a]

Substrate	Hg(OTf)$_2$/Time	Product	Yield[b]
 **5**	1 mol% 2 h	 **6** 27% +  **7**	71%
 **8**	1 mol% 24 h	 **9**	0%
 **10**	1 mol% 0.3 h	 **11**	98%
 **12**	2 mol% 6 h	 **13**	89%
 **14**	2 mol% 9 h	 **15**	94%
 **16**	8 mol% 6 h	 **17**	78%
 **18**	8 mol% 6 h	 **19**	92%

[a]Reactions were carried out at room temperature. [b]Isolated yield.



Scheme 2. Possible reaction mechanism.

clear that the reaction of **3** with Hg(OTf)$_2$ was initiated from the internal alkene to generate the intermediate **21**. Protonation of **21** with TfOH to form cation **22** is probably facilitated by the β-cation stabilizing effect of the C–Hg bond (akin to the C–Si bond), although this has not yet been confirmed.

In conclusion, we have achieved a novel Hg(OTf)$_2$-catalyzed aryl-substituted 1,3-diene cyclization in high yield and high catalytic turnover under very mild conditions.[10] Dienyl sulfonamides as well as dienyl alcohols were also found to react, giving rise to heterocycles in efficient catalytic turnover. The present results will help facilitate the synthesis of various alkenyl cyclic products.

References and Notes

† Deceased May 1, 2010.

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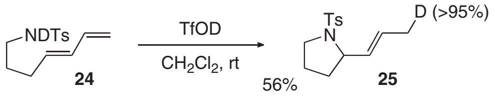
8 In the heterocyclizations of **14**, **16**, and **18**, TfOH was less effective and gave products **15** (51%), **17** (50%), and **19** (52%), respectively. These TfOH-catalyzed reactions are initiated from the protonation of the terminal double bond via the allylic cation. Indeed, this mechanism was confirmed by the reaction of deuterated **24** with TfOD, which gave rise to **25** as the sole product.



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10 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.