Manganese Porphyrin Catalyzed Cycloisomerization of Enynes
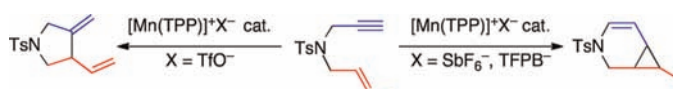
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ABSTRACT

Cycloisomerization of 1,6-enynes to five- or six-membered ring systems is successfully carried out in the presence of a cationic manganese(III) catalyst. The use of a structurally rigid tetradentate porphyrin as the equatorial ligand and a weakly coordinating axial ligand is the key to bringing out the catalytic reactivity of manganese for the reaction. The axial ligand of the catalyst has a marked effect on the product and selectively aids the formation of five- or six-membered cyclic products.

In the past few decades, many transition-metal (Ru, Rh, Ir Pt, and Au) complexes have emerged as powerful catalysts for the cycloisomerization of enynes, a reaction that gives easy access to highly functionalized carbocyclic and heterocyclic compounds in an essentially atom-economical manner.[1] This cycloisomerization is considered to be triggered by activation of the alkyne moiety through coordination to the electrophilic metal complex to afford key intermediates such as vinyl metal and metal alkylidene species. Therefore, taking into account the Lewis acidity of the metal complexes toward π-bonds, we state that higher-valent redox-stable complexes that do not oxidize the substrate are more favorable catalysts for the cycloisomerization than are low-valent metal complexes. In this context, we supposed that a cationic high-valent metalloporphyrin would be an ideal catalyst because the structurally rigid tetradentate porphyrin ligand with a large π-conjugated planar aromatic structure can help in maintaining the high oxidation state of the metal throughout the catalytic process. This characteristic feature of porphyrin ligands can be exploited to reveal the potential catalytic ability of some high-valent transition metals that have not been unexplored for use as catalysts in cycloisomerization.[2] Herein, we report that the cationic manganese(III) porphyrin complex behaves like a precious-metal complex such as a Pt complex and catalyzes the cycloisomerization of enynes to afford cyclic compounds.

[Mn(TPP)]SbF_6 was synthesized by treating [Mn(TPP)]Cl with $AgSbF_6$ in CH_2Cl_2 at ambient temperature for 5 h (Scheme 1).[3] Recrystallization of the resulting [Mn(TPP)]SbF_6 from toluene afforded the [Mn(TPP)]SbF_6(toluene) complex. The X-ray crystal structure analysis at ambient

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(2) For examples of the use of metalloporphyrins in nonoxidative bond formation, see: (a) Suda, K.; Baba, K.; Nakajima, S.-I.; Takanami, T. *Chem. Commun.* **2002**, 2570. (b) Suda, K.; Kikkawa, T.; Nakajima, S.-I.; Takanami, T. *J. Am. Chem. Soc.* **2004**, *126*, 9554. (c) Suda, K.; Baba, K.; Nakajima, S.-I.; Takanami, T. *Tetrahedron Lett.* **1999**, *40*, 7243. (d) Chen, J.; Che, C.-M. *Angew. Chem., Int. Ed.* **2004**, *43*, 4950. (e) Li, Y.; Chan, P. W. H.; Zhu, N.-Y.; Che, C.-M.; Kwong, H.-L. *Organometallics* **2004**, *23*, 54. (f) Schmidt, J. A. R.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2005**, *127*, 11426. (g) Zhou, C.-H.; Chan, P. W. H.; Che, C.-M. *Org. Lett.* **2006**, *8*, 325. (h) Fujiwara, K.; Kurahashi, T.; Matsubara, S. *J. Am. Chem. Soc.* **2012**, *134*, 5512. (i) Morandi, B.; Dolva, A.; Carreira, E. M. *Org. Lett.* **2012**, *14*, 2162.

(3) (a) Williamson, M. M.; Hill, C. L. *Inorg. Chem.* **1987**, *26*, 4155. (b) Munro, O. Q.; Camp, G. L. *Acta Crystallogr., Sect. C* **2003**, *59*, 132. (c) Williamson, M. M.; Hill, C. L. *Inorg. Chem.* **1986**, *25*, 4668. (d) Hill, H. A. O.; Macfarlane, A. J.; Williams, R. J. P. *J. Chem. Soc. A* **1969**, 1704. (e) Reed, C. A.; Kouba, J. K.; Grimes, C. J.; Cheung, S. K. *Inorg. Chem.* **1978**, *17*, 2666. (f) Kirner, J. F.; Reed, C. A.; Scheidt, W. R. *J. Am. Chem. Soc.* **1977**, *99*, 1093.

temperature revealed the short contact distances between the manganese(III) complex and toluene: the $Mn\cdots C1^T$, $Mn\cdots C2^T$, and $Mn\cdots C3^T$ distances were 3.65(6), 3.28(1), and 3.44(4) Å, respectively (Figure 1). These contact distances were significantly shorter than the sum of the van der Waals radii of the manganese and carbon atoms (3.86 Å), indicating the electrophilic interaction between the cationic manganese(III) porphyrin complex and toluene. Thus, we presumed that this type of cationic manganese complex would activate the unsaturated carbon–carbon bonds of the enyne for cycloisomerization.
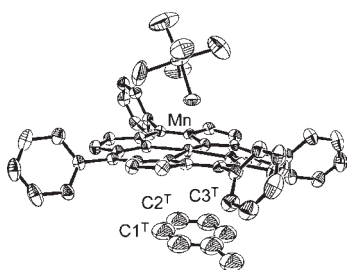
Figure 1. ORTEP drawing of [Mn(TPP)]SbF$_6$(toluene).

Scheme 1. Synthesis of [Mn(TPP)]SbF$_6$ Catalyst
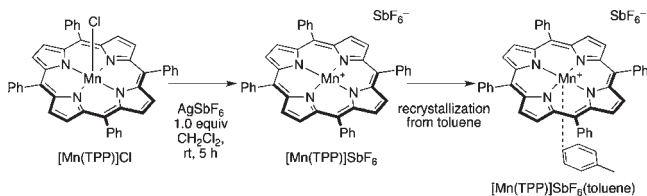
Cycloisomerization of enyne **1a** with [Mn(TPP)]SbF$_6$ (Table 1, entry 1) afforded the cyclopropane-annulated six-membered product **2a** in 61% yield, along with the five-membered product **3a** in 30% yield. Encouraged by this result, we screened the reaction parameters and found that the counteranion had a significant effect on the product selectivity of **2a** and **3a**. In the presence of [Mn(TPP)]BF$_4$ catalyst, **3a** was obtained in 86% yield along with trace amounts of **2a** (5% yield) (entry 2). Further, **3a** was obtained as the sole product in 95% yield when [Mn(TPP)]OTf was employed as the catalyst (entry 3). However, [Mn(TPP)]Cl was inefficient for the reaction, probably because strong coordination with the chloride ion made the manganese center less cationic and less electrophilic (entry 4). Further, the effects of tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (TFPB), which is a weaker coordinating counteranion than are SbF$_6^-$, BF$_4^-$, TfO$^-$, and Cl$^-$, were examined. The reaction carried

(4) Beck, W.; Sünkel, K. *Chem. Rev.* **1988**, *88*, 1405.

out using [Mn(TPP)]TFPB afforded **2a** in 75% isolated yield and **3a** in 21% yield (entry 5).[4] Another manganese catalyst, [Mn(salen)]SbF$_6$, however, showed lower catalytic activity for the cycloisomerization than did the cationic manganese(III) porphyrin complexes (entry 6). The use of AgSbF$_6$ or AgOTf in place of the cationic manganese complex afforded trace amounts of products (entries 7 and 8). The reaction with the [Fe(TPP)]SbF$_6$ catalyst did not afford **2a** or **3a** (entry 9).[2h]

Table 1. Manganese-Catalyzed Cycloisomerization of **1a**[a]

entry	catalyst	yield (%)[b]	
		2a	**3a**
1	[Mn(TPP)]SbF$_6$	61	30
2	[Mn(TPP)]BF$_4$	5	86
3	[Mn(TPP)]OTf	<1	95
4	[Mn(TPP)]Cl	<1	<1
5	[Mn(TPP)]TFPB[c]	75	21
6	[Mn(salen)]SbF$_6$[d]	34	17
7	AgSbF$_6$	7	<1
8	AgOTf	13	14
9	[Fe(TPP)]SbF$_6$	<1	<1

[a] Reactions were carried out using the catalyst (10 mol %) and enyne **1a** (0.2 mmol) in 1.6 mL of xylene at 160 °C for 24 h. [b] Isolated yields based on enyne **1a**. [c] TFPB: tetrakis[3,5-bis(trifluoromethyl)phenyl]borate. [d] [Mn(salen)]SbF$_6$: (*R*,*R*)-(−)-*N*,*N′*-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediaminomanganese(III) hexafluoroantimonate.

In order to demonstrate the scope of this counteranion-dependent manganese-catalyzed cycloisomerization, we carried out the reaction using various enynes **1** (Table 2). The reaction of **1b** with [Mn(TPP)]TFPB afforded **2b** in 67% yield along with **3b** in 21% yield, while the reaction of **1b** with the [Mn(TPP)]OTf catalyst furnished **3b** as the sole product in 96% yield (entry 2). Enyne **1c**, which had a cyclopropyl moiety, reacted with [Mn(TPP)]SbF$_6$ to yield the correspondingly substituted product **2c** in moderate yield (entry 3); the cyclopropyl substituent was well tolerated under the reaction conditions. On the other hand, very low or trace amounts of the cyclic product were obtained in the reaction of **1c** with [Mn(TPP)]TFPB and [Mn(TPP)]OTf. The [Mn(TPP)]OTf-catalyzed reaction of **1d**, **1e**, and **1f** afforded the corresponding five-membered products **3** selectively in high yields, irrespective of the tether groups. In sharp contrast, the product selectivity in the [Mn(TPP)]-TFPB- and [Mn(TPP)]SbF$_6$-catalyzed reactions was largely affected by the tether groups (entries 4–6). For example, **1d**, which had a 2-nitrobenzenesulfonamide (NsN) tether group, underwent cycloisomerization in the presence of [Mn(TPP)]TFPB to give **2d** and **3d** in 71% and 19% yields, respectively (entry 4), but afforded **2d** and **3d** in

Table 2. Manganese-Catalyzed Cycloisomerization of 1[a]

entry	substrate	Mn catalyst	yield (%)[b]	
1	1a	[Mn(TPP)]TFPB	2a: 75	3a: 21
		[Mn(TPP)]SbF$_6$	61	30
		[Mn(TPP)]OTf	<1	95
2	1b	[Mn(TPP)]TFPB	2b: 67	3b: 21
		[Mn(TPP)]SbF$_6$	60	26
		[Mn(TPP)]OTf	<1	96
3	1c	[Mn(TPP)]TFPB	2c: 31[c]	3c: <1
		[Mn(TPP)]SbF$_6$	62	<1
		[Mn(TPP)]OTf	<1	<1
4[d]	1d	[Mn(TPP)]TFPB	2d: 71	3d: 19
		[Mn(TPP)]SbF$_6$	38	36
		[Mn(TPP)]OTf	<1	81
5[e]	1e	[Mn(TPP)]TFPB	2e: 23[c]	3e: 44[c]
		[Mn(TPP)]SbF$_6$	38	60
		[Mn(TPP)]OTf	<1	90
6	1f	[Mn(TPP)]TFPB	2f: <1	3f: 52[c]
		[Mn(TPP)]SbF$_6$	<1	57
		[Mn(TPP)]OTf	<1	90

[a] Reactions were carried out using a Mn catalyst (10 mol %) and enyne 1 (0.2 mmol) in 1.6 mL of xylene at 160 °C for 24 h. [b] Isolated yields. [c] NMR yields. [d] NsN: 2-nitrobenzenesulfonamide. [e] MesSO$_2$N: 2,4,6-trimethylbenzenesulfonamide.

Table 3. Manganese-Catalyzed Cycloisomerization of 1[a]

entry	substrate	Mn catalyst	yield (%)[b]
1	1g	[Mn(TPP)]SbF$_6$	2g: 76
		[Mn(TPP)]OTf	<1
2	1h	[Mn(TPP)]SbF$_6$	2h: 86
		[Mn(TPP)]OTf	<1
3	1i	[Mn(TPP)]SbF$_6$	2i: 74
		[Mn(TPP)]OTf	<1
4	cis-1g	[Mn(TPP)]SbF$_6$	2g: 61
		[Mn(TPP)]OTf	<1

[a] Reactions were carried out using a Mn catalyst (10 mol %) and enyne 1 (0.2 mmol) in 1.6 mL of xylene at 160 °C for 24 h. [b] Isolated yields.
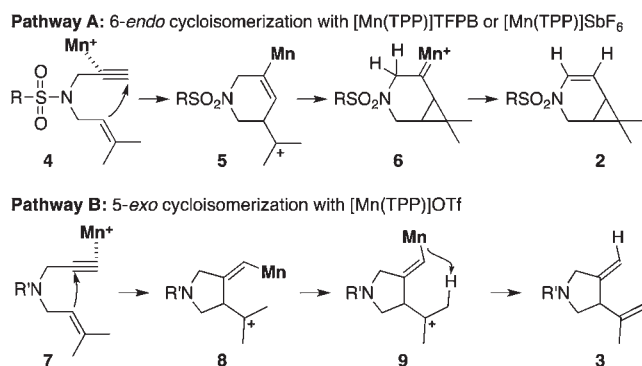
in the presence of [Mn(TPP)]TFPB and [Mn(TPP)]SbF$_6$, and the product yields were 44% and 60%, respectively (entry 5). The reaction of aniline-tethered enyne **1f** selectively furnished **3f**, irrespective of the counteranion of the catalyst (entry 6). These results indicated that the sulfonyl moiety played an important role in the formation of the six-membered cyclic product **2**.[5]

As can be seen in Table 3, the aryl groups on the alkene facilitate the cycloisomerization with [Mn(TPP)]SbF$_6$ to afford the six-membered products **2** selectively (entries 1−3). The structure of **2g** was unambiguously confirmed by X-ray analysis (Supporitng Information). On the other hand, the reaction of the same enynes, **1g**, **1h**, and **1i**, with [Mn(TPP)]OTf afforded neither **2** nor any other cyclic compound, and the enynes were recovered. However, in the presence of [Mn(TPP)]TFPB, the enynes decomposed. The effect of the double bond geometry was evaluated by carrying out the reaction using cis-**1g** (entry 4). The reaction of cis-**1g** with [Mn(TPP)]SbF$_6$ afforded **2g** as the sole product in 61% yield. The same isomer was predominantly formed in the reaction of trans-**1g** with [Mn(TPP)]SbF$_6$, indicating that the reaction is independent of the double bond geometry of the enyne (entries 1 and 4). That is, the [Mn(TPP)]SbF$_6$-catalyzed cycloisomerization probably involved a stepwise reaction pathway via the formation of a cationic intermediate, which induced loss of the double bond geometry.
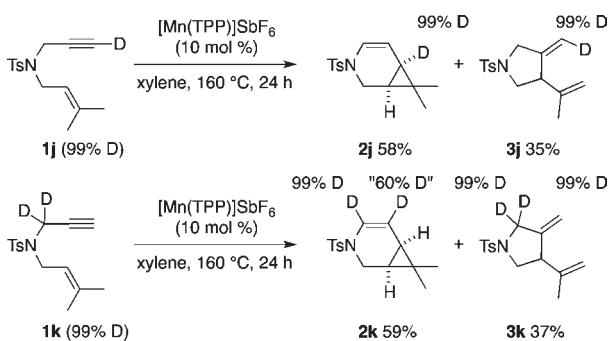
Taking into account the aforementioned data, we proposed the following reaction pathway for the cycloisomerization

almost equal amounts in the presence of [Mn(TPP)]SbF$_6$. Further, the cycloisomerization of **1e**, which had a relatively bulkier amide tether group (2,4,6-trimethylphenyl-sulfonamide (MesSO$_2$N)), afforded **3e** as the major product

(5) Fürstner et al. reported Pt catalyzed cycloisomerization of the same enyne **1** to form cyclopropane-annulated six-membered product **2**. They observed that the formation of **2** takes place only if enynes were tethered with heteroatoms such as nitrogen and oxigen but not with carbon. The manganese-catalyzed cycloisomerization of ether-tethered enyne also resulted in complete consumption of starting enyne; however, we could not obtain any cyclic products probably due to decomposition during the reaction. (a) Fürstner, A.; Stelzer, F.; Szillat, H. *J. Am. Chem. Soc.* **2001**, *123*, 11863. (b) Chatani, N.; Furukawa, N.; Sakurai, H.; Murai, S. *Organometallics* **1996**, *15*, 901 (in ref 21).

of **1** to **2** in the presence of [Mn(TPP)]TFPB or [Mn(TPP)]SbF$_6$ (Scheme 2, pathway A). The reaction would be triggered by coordination of the cationic manganese(III) to the alkyne to afford intermediate **4**, which undergoes 6-*endo* cyclization via nucleophilic addition of the internal olefin to the alkyne to give intermediate **5**. Isomerization of **5** yields the manganese alkylidene complex **6**, and subsequent 1,2-hydride shift yields the expected product **2**. A plausible reaction pathway (pathway B) for the formation of the five-membered product **3** in the presence of [Mn(TPP)]OTf is also outlined in Scheme 2. This mechanism involves the formation of vinyl metal spices **8** via 5-*exo* cyclization initiated by coordination of the cationic manganese(III) to the alkyne moiety. Further reaction with proton shift affords **3**, and the cationic manganese catalyst is regenerated.

Scheme 2. Plausible Reaction Pathways

Pathway A: 6-*endo* cycloisomerization with [Mn(TPP)]TFPB or [Mn(TPP)]SbF$_6$

Pathway B: 5-*exo* cycloisomerization with [Mn(TPP)]OTf

**Scheme 3.** Reaction of Deuterium-Labeled Enynes

The reaction of deuterium-labeled enynes was performed to elucidate the reaction pathways (Scheme 3). The reaction of **1j** with [Mn(TPP)]SbF$_6$ afforded **2j** with 99% deuterium labeling at the six-membered ring and **3j** with 99% deuterium labeling at the olefin. Under the same reaction conditions, the *gem*-dideuterated enyne **1k** afforded *vic*-dideuterated **2k** with 60% deuteration at the C-5 position of the six-membered ring and **3k** with 99% *gem*-deuterium labeling. The incomplete deuteration at

the C-5 position of **2k** could be explained by the competing reaction of the manganese alkylidene intermediate **6** with trace amounts of H$_2$O that might have been present in the reaction mixture. To test the effect of residual H$_2$O on deuteration, we performed an experiment involving the reaction of **1a** in the presence of D$_2$O (Scheme 4). The reaction gave **2a** with 40% deuteration at the same C-5 position of the six-membered ring. The observed data indicate that the conversion of **1** to **2** proceeded via the formation of **6**, which underwent a 1,2-hydogen shift in competition with protonation. On the other hand, the conversion of **1** to **3** did not proceed via the formation of intermediate **6**.

Scheme 4. Cycloisomerization of **1a** in the Presence of D$_2$O
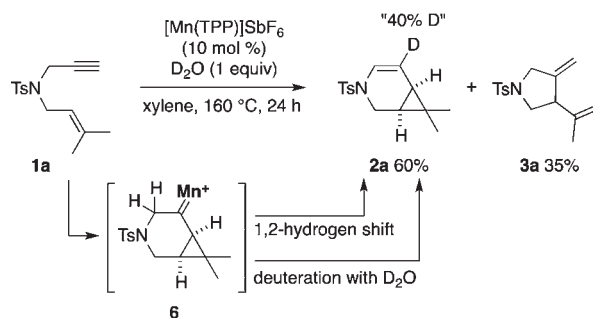
In summary, we have developed manganese-catalyzed cycloisomerization of enynes for the first time. The key to the success of this reaction is the use of a porphyrin ligand along with a weakly coordinating axial counteranion ligand, which makes the manganese center cationic and sufficiently electrophilic to activate a triple bond. Moreover, the counteranion has a considerable effect on the reaction pathway, so that either six- or five-membered ring systems are obtained. Thus, when using the porphyrin template, the Lewis acidity of the cationic manganese, which affects the mode of substrate activation, can be easily controlled by simply changing the axial counteranion ligand.

Supporting Information Available. Experimental procedures including spectroscopic and analytical data of new compounds (PDF). CIF files of [Mn(TPP)] SbF$_6$-(toluene) and **2g**. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.