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An Effective *cis*-β-Octahedral Mn(III) SALPN Catalyst for the Mukaiyama-Isayama Hydration of α,β-Unsaturated Esters†§

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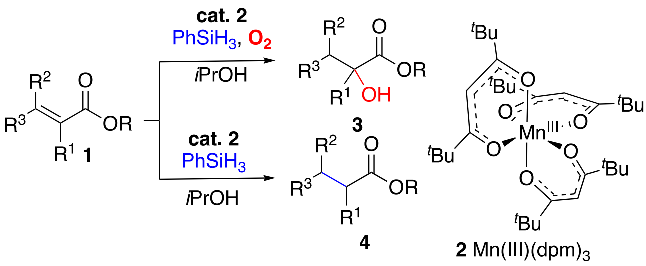
Two *cis*-β-Mn(III)SALPN catalysts were synthesised and tested in the Mukaiyama-Isayama hydration of α,β-unsaturated esters. The Mn(III)EtOSALPN(acac) complex 7 is the most active and catalyses hydration with little or no detectable undesired alkene reduction. This catalyst is superior for alkene hydration compared to the originally reported Mn(dpm)$_3$ catalyst.

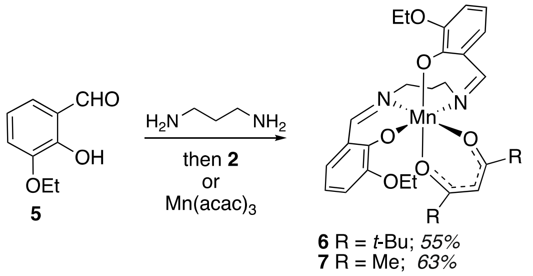
The hydration of polar alkenes using a Co^{II} catalyst, PhSiH$_3$ and dioxygen was reported by Isayama and Mukaiyama in 1989.[1] Further developments included the regioselective direct and predominantly α-hydration of α,β-unsaturated esters (**1**) catalyzed by Mn^{II}(dpm)$_2$ in the presence of PhSiH$_3$ and dioxygen in *i*PrOH to afford α-hydroxy esters (**3**) after reductive workup (Scheme 1).[2] Some 10 years later, this Mn catalysed hydration was reinvestigated by Magnus and co-workers[3,4] and the active catalyst was revealed by analysis by X-ray crystallography to be octahedral complex Mn^{III}(dpm)$_3$ (**2**)[5] and suggested this was the catalyst and not Mn^{II}(dpm)$_2$ as reported as Mn^{II} complexes typically oxidise rapidly to Mn^{III} in air.[6]



Scheme 1: Mukaiyama Hydration of α,β-unsaturated esters

In the absence of oxygen, reduction by hydrogen atom transfer (HAT)[7] and protonation occurs to give saturated esters **4**. On several occasions, we have observed that treatment of unsaturated esters (**1**) with catalyst **2** and PhSiH$_3$ in the presence of O$_2$ gas gave the desired hydration product but also significant amounts of unwanted material arising from reduction through hydrogen atom transfer. We therefore elected to examine an alternative Mn(III) coordination complex that would favor hydration over reduction.

Magnus noted that Jacobsen's catalyst (a *trans*-Mn(salen)X$_2$ complex) did not catalyse the Mukaiyama-Isayama hydration and this also failed in our hands.[4,8] We reasoned that coordination geometry about the metal ion in the catalyst allowing for conformational flexibility was key and elected to investigate *cis*-β-octahedral Mn(III) complexes which features an ethoxySALPN Schiff base ligand,[9] prepared by the condensation of 1,3-diaminopropane with 3-ethoxysalicylaldehyde (5) (Scheme 2). The use of a β-diketone bidentate co-ligand promotes the formation of *cis*-β Mn^{III} complexes. The Schiff base derived from commercially available aldehyde **5** was used to improve solubility of the complex in *i*-PrOH which is the solvent of choice for this alkene hydration.



Scheme 2: Synthesis of *cis*-β-SALPN catalysts **6** and **7**

Reaction of the Schiff base with Mn(III) complex **2** or Mn^{III}(acac)$_3$ in methanol afforded the complexes Mn^{III}SALPN(dpm) **6** and Mn^{III}SALPN(acac) **7** respectively in good yields. Each of these recrystallized from CH$_2$Cl$_2$ to provide crystals that were suitable for analysis by X-ray crystallography.[10] The X-ray structures for

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§In memory of Professor Teruaki Mukaiyama

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6 and **7** (Figure 1) confirm that the Mn(III) complexes possess the cis-β coordination geometry.

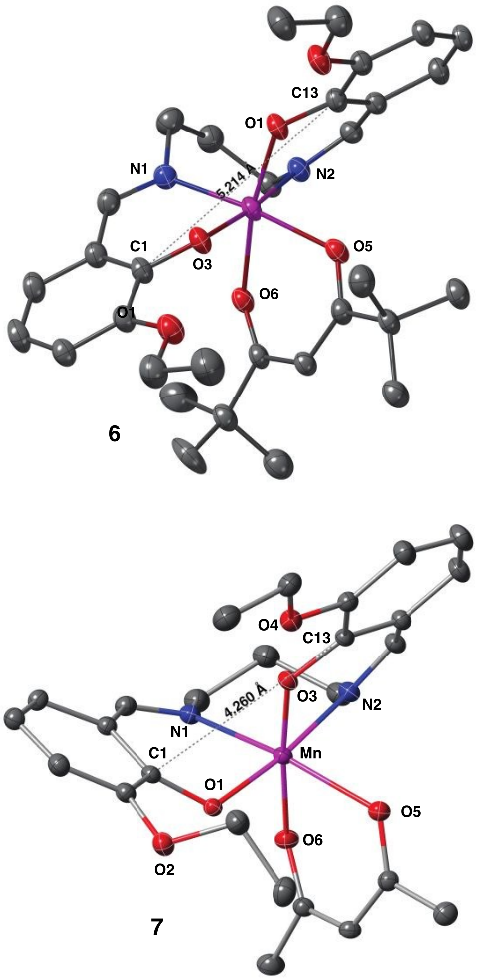
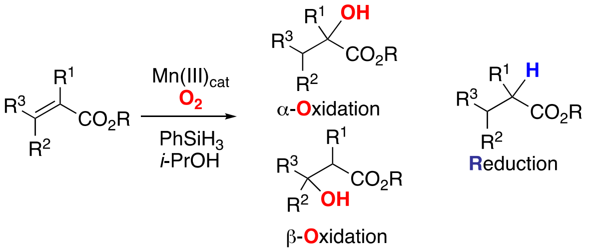


Figure 1: ORTEP representations (40% probability, H atoms omitted) of X-ray crystal structures for Mn(III) complexes **6** and **7**. Selected bond lengths: **6** [O1–Mn1.8685(91), N2–Mn 1.990(102), O3–Mn 1.999(120), O5–Mn 2.038(130), N1–Mn 2.0769(125) O6–Mn 2.1081(118)]; **7** [N1–Mn 2.1836(13), N1–Mn 2.1836(13), N2–Mn 2.0083(14), O1–Mn 1.9155(10) O3–Mn 1.8710(11), O5–Mn 2.1725(12), O6–Mn 2.0171(11)]

The solid-state structures of **6** and **7** differed considerably in the conformation of the SALPN ligand. The distance between aromatic phenolic carbon atoms (C1 and C13, Figure 1) of both rings is almost 1 Å longer in the complex **6** possibly due to the ethoxy substituent on one aromatic ring interacting with the *t*-Bu group of the dpm ligand which forces the rings further apart. The six-membered chelate ring involving the 3-carbon bridge, two nitrogen atoms and the Mn atom adopts a twist boat-like (skew) conformation in **6** whilst this ring is chair-like in complex **7**. In both structures the MnIII is in distorted octahedral environment. The Mn-N and Mn-O bond distances are similar to those found in the X-ray structure of [Mn(SALPN)acac].[11] Both complexes exhibit Jahn-Teller distortions that would be expected for high spin d^4 Mn^{III}.[11] A tetragonal distortion is particularly evident in **7** along the N1-Mn-O5 axis (Mn-N1 = 2.1846(13), Mn-O5 = 2.1725(12)).

We next tested each of the complexes in a Mukaiyama- Isayama hydration reaction of a selection of α,β-unsaturated esters (Scheme 3 and Table 1). Each reaction was also conducted using the standard Mn(dpm)$_3$ catalyst for comparison. All the reactions were carried out in *i*-PrOH solvent with PhSiH$_3$ was used as the hydride source in all cases. Other co-solvents such as CH$_2$Cl$_2$ and the application of the more reactive silane PhSi(O*i*-Pr)H$_2$ as reported by Shenvi[12] offered no significant improvement to the yields or reaction times. We also found that adding P(EtO)$_3$ in order to reduce any peroxides as described in the original procedure[2,3] was not required (suggesting hydroperoxides are not formed in significant amounts) and only complicated purification. It appears that the use of excess silane may also serve to reduce the small amounts of hydroperoxide formed. In addition, the use of *t*-BuOOH as an additive[13] was not necessary as the O$_2$ can effectively oxidise the any Mn(II).



Scheme 3: General hydration reaction

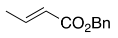
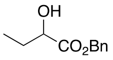
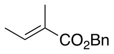
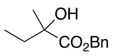
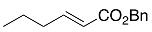
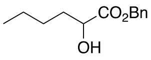
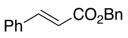
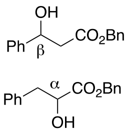
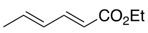
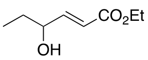
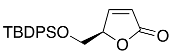
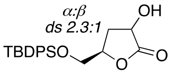
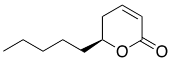
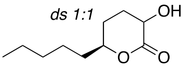
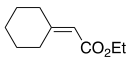
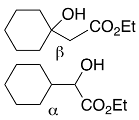
Entry	Substrate	Hydration Product	Yields Cat. 2	Yields Cat. 7
1			[O] 38% [R] 53%	[O] 70% [R] 0%
2			[O] 44% [R] 21%	[O] 67% [R] 0%
3			[O] 51% [R] 30%	[O] 70% [R] 0%
4			[O] 44% 1:3 α:β [R] 0%	[O] 61% 1:30 α:β [R] 0%
5			[O] 0% [R] 0%	[O] 20% [R] 0%
6			[O] 6% [R] 80%	[O] 72% [R] 6%
7			[O] 17% [R] 71%	[O] 68% [R] 6%
8			[O] 69% 3.7:1 α:β [R] 0%	[O] 32% 1:2.6 α:β [R] 0%

Table 1: **[O]**=yield of hydration product; **[R]**=yield of reduction product. All reactions carried out under an O$_2$ balloon with using 20 mol% catalyst, (Except entries 5 and 7, 10 mol% catalyst), rt, 16h.

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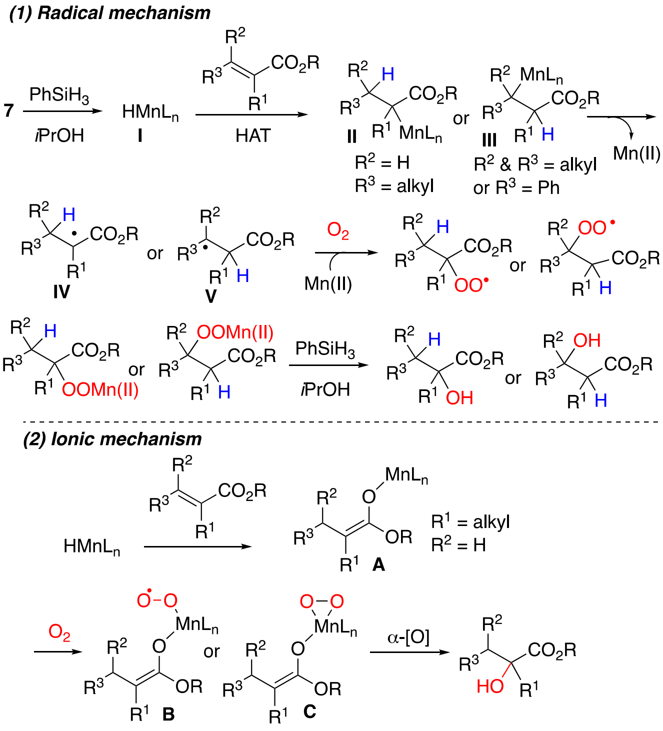
The Mn^{III}(SALPN)(dpm) complex **6** catalysed the hydration of α,β-unsaturated esters but the rate was extremely slow with most reactions failing to go to completion after several days. Pleasingly, the Mn^{III}(SALPN)(acac) complex **7** was more active, catalysing the hydrations in 16 h in most cases with no detectable reduction (HAT). For simple benzyl esters (entries 1-3), the complex **7** was superior to dmp complex **2** in all cases affording good yields of the α-hydration products and no reduction whilst original catalyst **2** gave considerable amounts of reduction products.

Cinammate ester (entry 4) gave mostly the β-hydration product, again with catalyst **7** giving the best yields and high β-selectivity. This result reinforces the suggestion that a radical process is occurring as opposed to the ionic mechanism suggested by Magnus.[3] A stark result was obtained for the $\alpha,\beta,\gamma,\delta$-unsaturated substrate (entry 5) which afforded the γ-hydration product in 20% using catalyst **7** but gave only decomposition with the original catalyst **2**. The alternative synthesis of this hydration product involves multiple steps with comparable overall yields.[14] α,β-Unsaturated lactones were also effectively hydrated with catalyst **7** (entries 6 and 7) providing far superior results to those for catalyst **2**. Some stereoselectivity was observed in the case of the 5-membered lactone (entry 6) and a small amount of reduction was seen with catalyst **7** for for the 6-membered lactone (entry 7). The α-hydroxylactone (entry 6) can also be synthesised by oxidation of the enolate derived from the corresponding saturated lactone however, this involves the use of the toxic oxidant MoOPH.[15] The final entry 8 involving a cyclohexylidene substrate is the only example where the yields using the original catalysts are superior to SALPN catalyst **7**. Interestingly, with both catalysts **2** and **7**, reduction was not observed but β-selectivity was higher for catalyst **7**.

Mukaiyama first suggested that the mechanism of this hydration involves a radical intermediate[2] whilst Magnus proposed an ionic mechanism.[3] More recently, Carreira has shown that hydroazidation and hydrohydrazinations of essentially non-polar olefins catalysed by Mn and Co complexes probably proceed via a free radical or metal-radical pairs as supported by radical clock experiments.[13] In addition, Nojima has suggested that Co(III)-catalyzed triethylsilylperoxidation of alkenes using Et_3SiH as the hydride source proceeds via Co(III)-alkyl or alkylperoxo complex.[16] Our results suggest that a radical intermediate could be involved as some products (entries 4 and 8) appear to be the result of a more stable radical intermediate whilst the other regioisomers might result from ionic type mechanism and two speculative rationales are shown in Scheme 4.

Treatment of the catalysts **7** with $PhSiH_3$ gives the metal hydride **I** which can then add to the polar alkene for form regioisomers **II** and **III**. Loss of Mn(II) follows and either a benzylic or tertiary free radical **V** (R^2 = Ph or $R^2 = R^3$ = alkyl) or α-radical **IV** (R^2 = H; R^3 = alkyl) is formed and then captured by O_2 to give the peroxides formation of metal-peroxy complexes followed reduction provides the hydroxyesters. The steric bulk of the SALPN ligand combined with the conformational flexibility allows for a more stable metal-peroxy intermediate complex without rapid reduction by HAT to the reduced by-product.

The ionic mechanism shown is modified from that proposed by Magnus.[3] Conjugate reduction of the α,β-unsaturated ester affords the Mn enolate **A** which is then oxidised with O_2 to the peroxide **B** or manganeseperoxyenolate **C**. Alternatively, a μ-oxo dimer type complex could be involved as we[17] and others[11] have observed the formation of Mn(IV) μ-oxo complexes from cis-β-Mn(III) complexes. Oxidation of the enolate then gives the α-hydroxyester. In the case of our catalyst **7**, little hydroperoxide appears to form which suggests there is a preference for O-O cleavage rather than O-Mn in this step.[3] In addition, the SAPLN ligand could shield the enolate from protonation retarding formation of the reduction by-product.



Scheme 4: Proposed hydration reaction mechanisms

In conclusion, we have developed a useful catalyst for the Mukaiyama hydration of α,β-unsaturated esters. The catalyst **7** can be easily synthesised from commercial starting materials in a one pot operation. Investigations into further applications of catalyst **7** and related complexes are underway.

Conflicts of interest

There are no conflicts to declare.

Notes and references

1. S. Isayama; T. Mukaiyama *Chem. Lett.* **1989**, *18*, 1071.
2. S. Inoki; K. Kato; S. Isayama; T. Mukaiyama *Chem. Lett.* **1990**, *19*, 1869.
3. P. Magnus; A. Payne; M. Waring; D. Scott; V. Lynch *Tetrahedron Lett.* **2000**, *41*, 9725.
4. P. Magnus; M. J. Waring; D. A. Scott *Tetrahedron Lett.* **2000**, *41*, 9731.

View Article Online
DOI: 10.1039/C9CC03921J

5. G. S. Hammond; D. C. Nonhebel; C.-H. S. Wu *Inorg. Chem.* **1963**, *2*, 73.
6. W. C. Fernelius; B. E. Bryant *Inorg. Synth.* **1957**, *5*, 105.
7. S. W. M. Crossley; C. Obradors; R. M. Martinez; R. A. Shenvi *Chem. Rev.* **2016**, *116*, 8912.
8. For application of the Co varient of Jaconsen's catalyst in H-atom transfer see: S. W. M. Crossley; F. Barabé; R. A. Shenvi *J. Am. Chem. Soc.* **2014**, *136*, 16788.
9. M. Maiti; D. Sadhukhan; S. Thakurta; S. Sen; E. Zangrando; R. J. Butcher; R. C. Deka; S. Mitra *Eur. J. Inorg. Chem.* **2012**, *2013*, 527.
10. Crystallographic data. For **6**: M = 634.65, triclinic, a = 10.2610(16), b = 10.8556(15), c = 14.6929(15), a = 81.588(10)° b = 85.042(10)° g = 85.486(12)° U = 1609.3(4) Å3, T = 130.0 K, space group P-1, Z = 2, (Mo-Kα) =0.460 mm−1, 7657 reflections measured, 7657 unique (refined as a two-component twin). The final wR was 0.0757, CCDC deposit code 1908184. For **7**: M = 607.39, triclinic, a = 7.9107(4), b = 11.7226(7), c = 15.1375(7) a = 85.161(10)° b = 87.054(4)° g = 87.105(4)°, U = 1395.40(13) Å3, T = 130.0 K, space group P-1, Z = 2, (Mo-Kα) =0.708 mm−1, 19556 reflections measured, 12720 unique, (R = 0.0360). The final wR was 0.0522, CCDC deposit code 1908183., In
11. E. J. Larson; V. L. Pecoraro *J. Am. Chem. Soc.* **1991**, *113*, 3810.
12. C. Obradors; R. M. Martinez; R. A. Shenvi *J. Am. Chem. Soc.* **2016**, *138*, 4962.
13. J. Waser; B. Gaspar; H. Nambu; E. M. Carreira *J. Am. Chem. Soc.* **2006**, *128*, 11693.
14. G.-Q. Tian; J. Yang; K. Rosa-Perez *Org. Lett.* **2010**, *12*, 5072.
15. W. Li; J. Gan; D. Ma *Angew. Chem. Int. Ed.* **2009**, *48*, 8891.
16. T. Tokuyasu; S. Kunikawa; A. Masuyama; M. Nojima *Org. Lett.* **2002**, *4*, 3595.
17. D. Loits; S. Bräse; A. J. North; J. M. White; P. S. Donnelly; M. A. Rizzacasa *Eur. J. Inorg. Chem.* **2016**, 3541.