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Selectivity Trends in Olefin Epoxidations Catalyzed by (NNNN)Manganese(+II) Complexes using Trifluoroethanol as the Solvent

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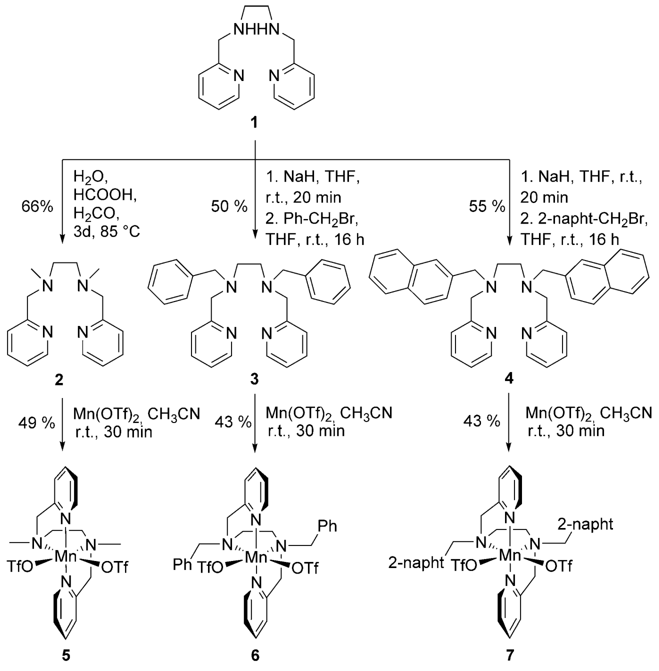
The epoxidation of olefins is certainly one of the most important oxygen-transfer reactions in organic synthesis. The development of both regio- and stereoselective protocols and the search for catalysts that combine high selectivity with abundancy is a topic of current interest. Herein, we report an unexpected odd–even-type selectivity trend in the diastereoselective epoxidation of unfunctionalized aliphatic alkenes by using a non-hem-type Mn catalyst in trifluoroethanol as the solvent.

The identification of parameters that allow selectivities in chemical transformations to be influenced is one of the major challenges in chemistry. Systematic variation of the solvent, temperature, and, if required, pressure often affects the course of a chemical reaction. Furthermore, significant changes in selectivities can be obtained by changing the nature of the specific reagent. Within the past 40 years, the latter strategy has built the basis for the success of transition-metal catalysis in organic chemistry.[1] The interplay of ligand structure and electronic properties of the metal center has been used to direct stereo- but also regioselectivities mostly by using favorable steric interactions. However, in the most successful cases strong and sterically defined coordination of the substrate to the catalytic center is necessary.[2] The selective transformation of unfunctionalized organic molecules such as simple aliphatic olefins lacking any polar coordinating functional group is somewhat less elaborated than the number of successful selective transformations of functionalized organic molecules.[3] The electronic properties of the different isomeric olefins are similar and, hence, not suitable for differentiation. Steric arguments are not as valid as for heavily functionalized starting materials. In this manuscript, we report an unexpected selectivity trend for the oxidation of olefins by using a (NNNN)Mn^{2+} complex and H_2O_2 as a stoichiometric oxidant. First indications for an unusual odd–even-type selectivity were obtained.

Recently, we reported the synthesis of evaluation of a set of (NNNN,P)Ru complexes [NNNN=N,N′-bisbenzyl-*N*,*N*-bis(2-pyrdiylmethyl)ethylenediamine (bep)] as catalysts in hydrogen autotransfer catalysis.[4] Depending on the substitution pattern of the ligand, profound effects on the catalytic turnover in this type of multistep catalysis were observed. Having these ligands in hand and with regard to the seminal contributions on the use of (NNNN)Mn complexes bearing related ligands by the groups of Que, Jr.,[5] White,[6] Costas,[7] Sun,[8] and Bryliakov,[9] we prepared a set of Mn complexes with different N-substitution patterns at the ethylenediamine backbone of the ligand. The ligands were accessible in a straightforward manner and were subsequently transferred into the corresponding paramagnetic Mn^{2+} complexes (Scheme 1). The structures of complexes **5**–**7** were unequivocally assigned by X-ray crystallography.).

Subsequently, the catalytic activity of [Mn(bep)$(OTf)_2$] (**6**) in the epoxidation of *cis*-cyclooctene (**8**) was tested. The literature-reported conditions (CH_3CN/HOAc, H_2O_2) were chosen as a starting point; however, only a slight excess amount of H_2O_2 was used (Table 1). Initial test experiments indicated that fast catalytic decomposition of H_2O_2 took place. Hence, we decided to add both a catalyst and a H_2O_2 solution simultaneously by using a syringe pump. Moderate conversion was observed at −20 °C. Upon increasing the reaction temperature to 0 °C,



Scheme 1. Synthesis of complexes **5**–**7**. napht = naphthyl, OTf = trifluoromethanesulfonate.

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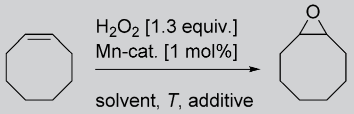
Table 1. Optimization table.[a]



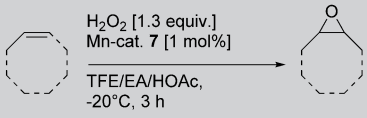
8
1 equiv.

9

Entry	*T* [°C]	Additive	Solvent	Yield[b] [%]
1[c]	−20	HOAc[d]	MeCN	59
2	−20	HOAc[d]	MeCN	83
3	0	HOAc[d]	MeCN	92
4	r.t.	HOAc[d]	MeCN	84
5	−20	none	MeCN	–
6	−20	HOAc[d]	TFE/EA (7:3)	91
7	−20	HOAc[d]	TFE/EA (9:1)	91
8	−20	none	TFE/EA (9:1)	29
9	−20	none	TFE	26

[a] Reaction conditions: all reactions were performed on a 1 mmol scale by using the appropriate solvent (2 mL) at the given temperature for 3 h. Both the catalyst (0.01 mmol, dissolved in 1 mL of the appropriate solvent) and the aqueous H_2O_2 solution (1.3 mmol, 30 wt%) were added simultaneously by means of a syringe pump (0.5 mL h^{-1}). [b] Determined by GC integration by using *n*-dodecane as an internal standard. [c] Only H_2O_2 was added by syringe pump. [d] HOAc (14 equiv.) was employed.

Table 2. Epoxidation of alkenes/cycloalkenes–Effect of the N substituent of the catalyst.[a]



Entry	Product	Yield [%] **5**	**6**	**7**
1	cyclopentene oxide (**10**)	71	83	76
2	cyclohexene oxide (**11**)	74	85	86
3	cycloheptene oxide (**12**)	84	89	95
4	cyclooctene oxide (**9**)	94	91	92
5	1-hexene oxide (**13**)	74	86	84
6	1-heptene oxide (**14**)	74	71	88
7	1-octene oxide (**15**)	71	70	84
8	*trans*-2-octene oxide (**16**)	72	70	67
9	*trans*-3-octene oxide (**17**)	65	66	62
10	*trans*-4-octene oxide (**18**)	71	66	69
11	*cis*-4-octene oxide (**19**)		73	
11	1-nonene oxide (**20**)	76	70	74
12	*trans*-5-decene oxide (**21**)	53	47	53
13	norbornene oxide (**22**)	58	71	72
14	chalcone oxide (**23**)	70	72	71

[a] Reaction conditions: all reactions were performed on a 1 mmol scale by using TFE/EA (9:1, 2 mL) as solvent and HOAc (14 mmol) as additive at −20 °C for 3 h. Both the catalyst (0.01 mmol, dissolved in 1 mL TFE) and the aqueous H_2O_2 solution (1.3 mmol, 30 wt%) were added simultaneously by means of a syringe pump (0.5 mL h^{-1}). Yields were determined by GC integration by using *n*-dodecane as an internal standard. [b] Catalyst was dissolved in MeCN.

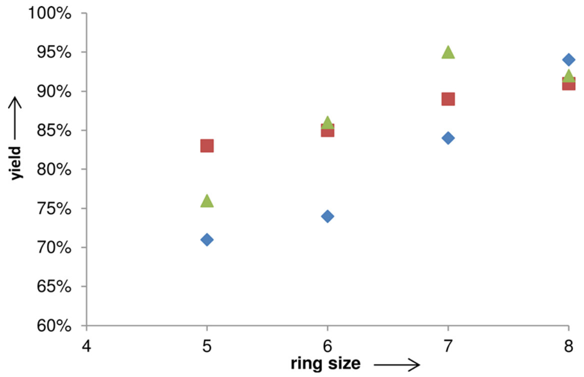


Figure 1.
Epoxidation of cycloalkenes (yield refers to GC yield); ◆ = mep, ■ = bep, ▲ = nep.

almost quantitative conversion and a yield of 91% were obtained (Table 1, entry 2). A further increase in the reaction temperature, however, led to a decrease in the yield (Table 1, entries 3 and 4). At that point, we became interested in the role of the additive, acetic acid (HOAc); by using acetonitrile as the solvent, no conversion was observed in the absence of this additive (Table 1, entry 5). In an attempt to increase the acidity of acetic acid, we replaced acetonitrile with trifluoroethanol (TFE) as the solvent. Given that cyclooctene and TFE are not miscible, a small amount of ethyl acetate (EA) was added. We were delighted to find that the reaction proceeded equally well as it did in acetonitrile (Table 1, entries 6 and 7), but more importantly, the product was isolated in 29% yield in the absence of acetic acid (Table 1, entry 8). To exclude the possible formation of acetic acid through hydrolysis of ethyl acetate that was added as a co-solvent, the reaction was performed in the absence of ethyl acetate. Interestingly, almost identical yields were observed (Table 1, entry 9).

With the optimized conditions in hand, we decided to perform a first comparative screening of the application range. The catalytic system showed good substrate scope in the epoxidation of unfunctionalized olefins (Table 2). Interestingly, although identical reaction conditions were used for all catalysts, the N substituent within the Mn complexes had a strong impact on the yield of this reaction. In general, the reactivities of the complexes with the *N,N*′-phenylmethylene (bep) and *N,N*′-(2-naphthyl)methylene (nep) ligands were significantly higher than that of complex **5** with the *N,N*′-methyl (mep) ligand for small ring sizes (Figure 1). Moreover, [Mn(nep)(OTf)$_2$] (**7**) showed a conversion maximum in the epoxidation of cycloheptene, and the product was isolated in 95% yield by using a substrate/H_2O_2 stoichiometry of 1: 1.3 (Table 2, entry 3; Figure 1). Subsequently, we investigated the reactivity of various 1-alkenes under the standard conditions (Table 2, entries 5–14; Figure 2) and were surprised to find that the effect of the N substituent on the conversion was similar to that observed in the oxidation of cycloalkenes. [Mn(nep)(OTf)$_2$] (**7**) again showed preference for C_7 olefins and gave 1-heptene oxide in 88% yield (Figure 2). In sharp contrast, the corresponding bep and mep complexes gave the product in yields of 74 and 71%, respectively. Furthermore, the use of [Mn(bep)(OTf)$_2$] (**6**) resulted in a significant drop in reactivity upon

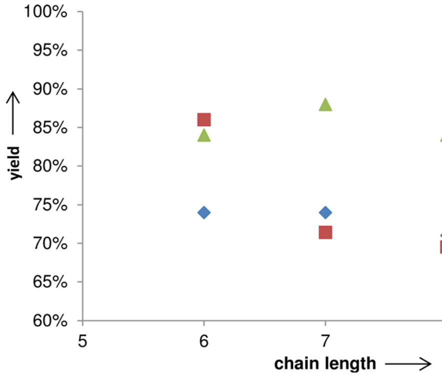


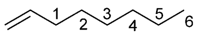
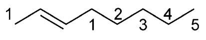
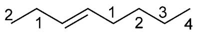
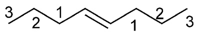
Figure 2.
Epoxidation of 1-alkenes (yield refers to GC yield); ◆ = mep, ■ = bep, ▲ = nep.

moving from 1-hexene to 1-heptene. The mep complex showed significantly lower, but almost constant, reactivity, independent of the chain length of the employed olefin.

As mentioned before, chemoselectivity in the epoxidation of isomeric unfunctionalized olefins is one of the challenges in catalysis. The unexpected "C_7" selectivity in the oxidation of alkenes and cycloalkenes by using catalyst **7** attracted our interest, and we decided to set up competition experiments by treating a 1:1:1:1 mixture of 1-octene/2-octene/3-octene/4-octene with H_2O_2 (2.6 equiv.) under the established conditions in the presence of Mn catalysts **5**–**7** (Table 3).

Again, catalyst **7** showed the most significant discrimination between the four olefins employed. In general, the yield increased upon shifting the π bond from C1 to C2 but dropped significantly for 3-octene. A further shift in the double bond led to a moderate increase in reactivity. Similar, yet not as pronounced, tendencies were observed for catalysts **5** and **6**, and the latter showed sharper discrimination of the isomers than the former. Apparently, the aromatic substituent is somewhat responsible for this wavelike conversion trend. With regard to substitution of the π bond, it appears as if the length of the substituent chain is somewhat responsible for this effect.

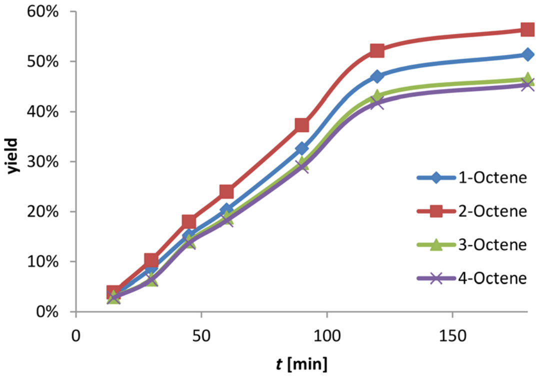
Table 3. Selectivities in olefin epoxidations in competition experiments.[a]

Olefin	Selectivity [%]			
	5	**6**	**7**[b]	**7**[b,c]
	47	41	50	46
	52	47	57	57
	44	31	40	40
	45	37	45	46

[a] Reaction conditions: all reactions were performed with each octane isomer (0.5 mmol) by using TFE/EA (9:1, 2 mL) as solvent and HOAc as additive (14 mmol) at −20 °C for 3 h. Both the catalyst (0.01 mmol, dissolved in 1 mL TFE) and the aqueous H_2O_2 solution (1.3 mmol, 30 wt %) were added simultaneously by means of a syringe pump (0.5 mL h^{-1}). Yields were determined by GC integration by using *n*-dodecane as an internal standard. [b] Catalyst was dissolved in MeCN. [c] The reaction was performed in MeCN instead of a TFE/EA mixture.

A time–conversion analysis for the oxidation of all four octane isomers in one pot with continuous addition of the catalyst and oxidant was performed to check the course of the selectivity over time (Table 4). As can be seen from the time–yield course, the selectivity trends that were observed after full consumption of H_2O_2 are the result of the fact that oxidation of 2-octene is faster than oxidation of 1-octene. The product ratio over time did not change.

Table 4. Time–yield curve for the oxidation of octenes.[a,b]



Olefin	Yield [%]						
	0 min	15 min	30 min	45 min	60 min	90 min	180 min
1-octene	0	3.3	8.6	15.2	20.4	32.6	51.4
2-octene	0	3.9	10.3	18.0	24.0	37.3	56.4
3-octene	0	3.0	6.5	14.0	18.8	29.7	46.5
4-octene	0	2.8	6.4	13.7	18.2	28.9	45.3

[a] Reaction conditions: all reactions were performed with each octane isomer (0.5 mmol) by using TFE/EA (9:1, 2 mL) as solvent and HOAc (14 mmol) as additive at −20 °C for 3 h. Both catalyst **7** (0.01 mmol, dissolved in 1 mL MeCN) and the aqueous H_2O_2 solution (1.3 mmol, 30 wt %) were added simultaneously by means of a syringe pump (0.5 mL h^{-1}). Yields were determined by GC integration by using nitrobenzene as an internal standard. [b] The presented data are the average of two independent competition experiments. Only minor deviations were observed.

Subsequently, we performed similar experiments by using equimolar mixtures of isomeric heptenes and nonenes. The results are shown in Figure 3. To compare the reactivities, we normalized the yields relative to that of 2-heptene as the most reactive substrate. As can be seen from this figure, the reactivity decreases with increasing chain length; however, we attribute this effect mainly to the lower miscibility of nonenes relative to that of heptenes. In each case, "wavetype" conversion was observed with a clear maximum for the epoxidation of 2-alkenes and, less pronounced, for 4-alkenes. Interestingly, it appears as if the chain length of the shorter side chain is somewhat responsible. If the side chain has an odd number, the reactivity increases. In 2-octene and 4-octene, both side chains have an odd number of C atoms, and these olefins show significantly higher selectivity preferences than 2-nonene and 4-nonene, for which only one side chain has an odd number.

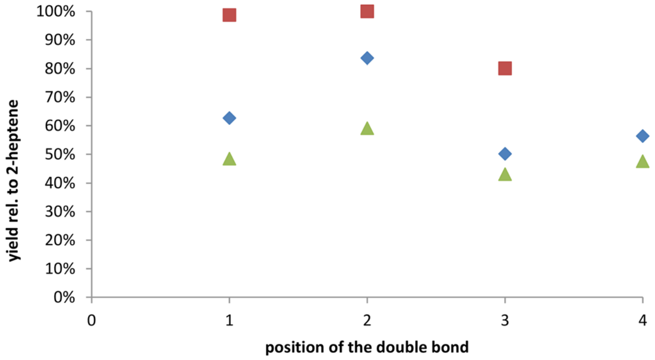


Figure 3. Structure–reactivity relationship in the oxidation of heptenes versus octenes versus nonenes with [Mn(nep)(OTf)$_2$]; ◆ = octene, ■ = heptene, ▲ = nonene.

Herein, we reported the synthesis of (NNNN)manganese(+II) complexes and some unexpected selectivity trends in the epoxidation of linear alkenes. All tested Mn complexes showed good to excellent epoxidation activity. Complex **7** possessing a naphthylmethylene substituent at the ethylenediamine backbone showed excellent performance. First indications for an odd–even-type selectivity trend were obtained. Although not exclusive, at the moment we think that this selectivity trend is interesting and might open the door toward more selective oxidation of isomeric, yet unfunctionalized, olefins.

Experimental Section

General procedure for catalytic epoxidation

The alkene (1 mmol, 1 equiv.) and HOAc (0.8 mL, 14 mmol) were dissolved in a mixture of 2,2,2-trifluoroethanol (1.8 mL) and ethyl acetate (0.2 mL). The catalyst (0.01 mmol, 1 mol%) and H_2O_2 (30% in water, 1.3 mmol, 1.3 equiv.) were diluted to 1 mL with 2,2,2-trifluoroethanol and simultaneously added at −20 °C over a period of 2 h by using a syringe pump. The mixture was then stirred for 1 h before dodecane (57 µL, 0.25 mmol) was added as an internal standard. After filtration over a short plug of silica gel (Et_2O), the crude product was analyzed by gas chromatography. For isolation of the product, the mixture was diluted with Et_2O (20 mL) and washed with a saturated aqueous solution of Na_2SO_3 (10 mL) and a saturated aqueous solution of Na_2CO_3 (10 mL). The solution was then dried with Na_2SO_4, and the solvent was removed under reduced pressure. The crude product was filtered over silica gel (Et_2O) and finally purified by flash column chromatography (silica gel).

Keywords: alkenes · diastereoselectivity · epoxidation · manganese · oxidation

[1] a) J. Mahatthananchai, A. M. Dumas, J. W. Bode, *Angew. Chem. Int. Ed.* **2012**, *51*, 10954–10990; *Angew. Chem.* **2012**, *124*, 11114–11152; b) J. Hu, Y. Wei, X. Tong, *Org. Lett.* **2011**, *13*, 3068–3071; c) T. Schabel, C. Belger, B. Plietker, *Org. Lett.* **2013**, *15*, 2858.

[2] a) W. P. Hems, M. Groarke, A. Zanotti-Gerosa, G. A. Grasa, *Acc. Chem. Res.* **2007**, *40*, 1340–1347; b) A. Pfenninger, *Synthesis* **1986**, 89–116; c) H. C. Kolb, M. S. VanNieuwenzhe, K. B. Sharpless, *Chem. Rev.* **1994**, *94*, 2483–2547; d) E. N. Jacobsen, *Acc. Chem. Res.* **2000**, *33*, 421–431; e) C. G. Frost, J. Howarth, J. M. J. Williams, *Tetrahedron: Asymmetry* **1992**, *3*, 1089–1122.

[3] a) D. H. Woodmansee, A. Pfaltz, *Chem. Commun.* **2011**, *47*, 7912–7916; b) M.-Z. Wang, M.-K. Wong, C.-M. Che, *Chem. Eur. J.* **2008**, *14*, 8353–8364; c) K.-P. Ho, W. L. Wong, L. Y. S. Lee, K.-M. Lam, T. H. Chan, K.-Y. Wong, *Chem. Asian J.* **2010**, *5*, 1970–1973.

[4] D. Weickmann, W. Frey, B. Plietker, *Chem. Eur. J.* **2013**, *19*, 2741–2748.

[5] a) M. Costas, A. K. Tipton, K. Chen, D.-H. Jo, L. Que, Jr., *J. Am. Chem. Soc.* **2001**, *123*, 6722–6723; b) S. R. Iyer, M. M. Javadi, Y. Feng, M. Y. Hyun, W. N. Oloo, C. Kim, L. Que, Jr., *Chem. Commun.* **2014**, *50*, 13777–13780.

[6] a) M. C. White, A. G. Doyle, E. N. Jacobsen, *J. Am. Chem. Soc.* **2001**, *123*, 7194–7195; b) M. S. Chen, M. C. White, *Science* **2007**, *318*, 783–787; c) M. S. Chen, M. C. White, *Science* **2010**, *327*, 566–571; d) P. E. Gormisky, M. C. White, *J. Am. Chem. Soc.* **2013**, *135*, 14052–14055.

[7] a) O. Cussó, I. Garcia-Bosch, D. Font, X. Ribas, J. Lloret-Fillol, M. Costas, *Org. Lett.* **2013**, *15*, 6158–6161; b) O. Cussó, I. Garcia-Bosch, X. Ribas, J. Lloret-Fillol, M. Costas, *J. Am. Chem. Soc.* **2013**, *135*, 14871–14878; c) O. Cussó, X. Rbas, J. Lloret-Fillol, M. Costas, *Angew. Chem. Int. Ed.* **2015**, *54*, 2729–2733; *Angew. Chem.* **2015**, *127*, 2767–2771; d) I. Garcia-Bosch, X. Ribas, M. Costas, *Adv. Synth. Catal.* **2009**, *351*, 348–352; e) I. Garcia-Bosch, L. Gómez, A. Polo, X. Ribas, M. Costas, *Adv. Synth. Catal.* **2012**, *354*, 65–70; f) I. Prat, L. Gómez, M. Canta, X. Ribas, M. Costas, *Chem. Eur. J.* **2013**, *19*, 1908–1913.

[8] a) B. Wang, C.-X. Miao, S.-F. Wang, F. E. Kühn, C.-G. Xia, W. Sun, *J. Organomet. Chem.* **2012**, *715*, 9–12; b) S. Yu, C.-X. Miao, D. Wang, S. Wang, C. Xia, W. Sun, *J. Mol. Catal. A* **2012**, *353–354*, 185–191; c) D. Shen, B. Qiu, D. Xu, C. Miao, C. Xia, W. Sun, *Org. Lett.* **2016**, *18*, 372–375; d) C. Miao, B. Wang, Y. Wang, C. Xia, Y.-M. Lee, W. Nam, W. Sun, *J. Am. Chem. Soc.* **2016**, *138*, 936–943; e) M. Wu, B. Wang, S. Wang, C. Xia, W. Sun, *Org. Lett.* **2009**, *11*, 3622–3625; f) B. Wang, S. Wang, C. Xia, W. Sun, *Chem. Eur. J.* **2012**, *18*, 7332–7335; g) D. Shen, C. Miao, S. Wang, C. Xia, W. Sun, *Org. Lett.* **2014**, *16*, 1108–1111.

[9] a) R. V. Ottenbacher, K. P. Bryliakov, E. P. Talsi, *Adv. Synth. Catal.* **2011**, *353*, 885–889; b) R. V. Ottenbacher, D. G. Samsonenko, E. P. Talsi, K. P. Bryliakov, *ACS Catal.* **2014**, *4*, 1599–1606; c) O. Y. Lyakin, R. V. Ottenbacher, K. P. Bryliakov, E. P. Talsi, *ACS Catal.* **2012**, *2*, 1196–1202; d) R. V. Ottenbacher, K. P. Bryliakov, E. P. Talsi, *Inorg. Chem.* **2010**, *49*, 8620–8628; e) R. V. Ottenbacher, D. G. Samsonenko, E. P. Talsi, K. P. Bryliakov, *ACS Catal.* **2016**, *6*, 979–988; f) R. V. Ottenbacher, D. G. Samsonenko, E. P. Talsi, K. P. Bryliakov, *Org. Lett.* **2012**, *14*, 4310–4313; g) R. V. Ottenbacher, E. P. Talsi, K. P. Bryliakov, *ACS Catal.* **2015**, *5*, 39–44.

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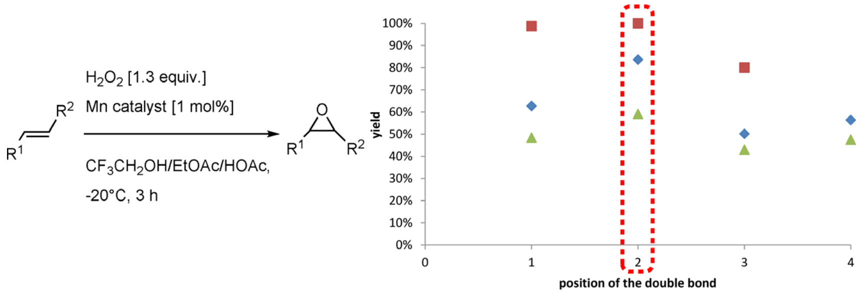

Evening out the odds: An unexpected odd–even-type selectivity trend in the diastereoselective epoxidation of unfunctionalized aliphatic alkenes by using a non-heme-type Mn catalyst in trifluoroethanol as the solvent is observed. (◆ = octene, ■ = heptene, ▲ = nonene)

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Selectivity Trends in Olefin Epoxidations Catalyzed by (NNNN)Manganese(+II) Complexes using Trifluoroethanol as the Solvent