Alkene Isomerization Catalyzed by a Mn(I) Bisphosphine Borohydride Complex

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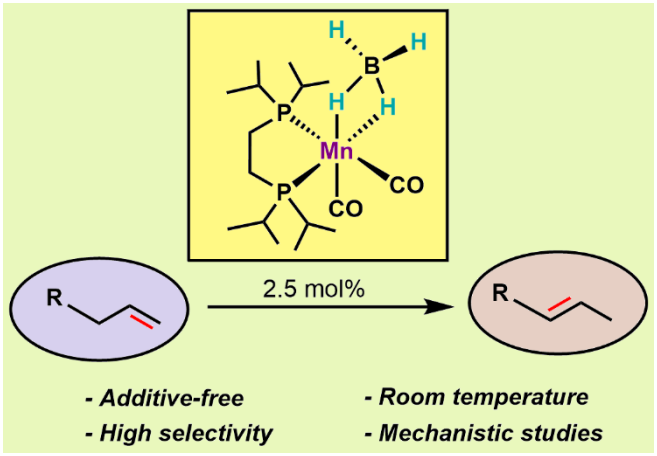
ABSTRACT: An additive-free manganese-catalyzed isomerization of terminal alkenes to internal alkenes is described. This reaction is atom economic, implementing an inexpensive, non-precious metal catalyst. The most efficient catalyst is the borohydride complex cis-[Mn(dippe)(CO)$_2$(κ^2-BH$_4$)]. This catalyst operates at room temperature with a catalyst loading of 2.5 mol %. A variety of terminal alkenes are effectively and selectively transformed to the respective internal E-alkenes. Preliminary results show chain walking isomerization at elevated temperature. Mechanistic studies were carried out including stochiometric reactions and in situ NMR analysis. These experiments are flanked by computational studies. Based on these, the catalytic process is initiated by liberation of "BH$_3$" as a hydroborated alkene. The catalytic process is initiated by double bond insertion into an M–H species leading to an alkyl metal intermediate, followed by β-hydride elimination at the opposite position to afford the isomerization product.



INTRODUCTION

Isomerization and translocation of double bonds inside a molecule are essential steps in a variety of catalytic processes. Monoisomerization and especially chain walking reactions enable the functionalization of a great variety of organic frameworks.[1] The compounds thus obtained are widely used as fragrances, agrochemicals and intermediates in the pharmaceutical industry.[2] The field of transpositional isomerization catalysis has long been dominated by complexes based on precious metals, such as rhodium[3], iridium[4], ruthenium[5] and palladium.[6] However, representatives of base metal catalysts in this field have been fathomed.[7] The early development of nickel-[8] and cobalt-based[9] isomerization catalysts as well as industrial application of the latter[10] represent some of the most established examples. Over the last years base metal catalysts based on nickel,[11] cobalt,[12] and iron,[13] have emerged in the field of alkene isomerization.[7,14] Selected base metal catalysts for the isomerization of alkenes are depicted in Figure 1.

As manganese is concerned, to the best of our knowledge, there is only one literature example described by Pidko and Filonenko.[15] The authors utilized a cationic Mn(I) CNP pincer carbonyl pre-catalyst which, in the presence of K[HBEt$_3$], was able to isomerize terminal carbon carbon double bonds at 60 °C.

We have recently demonstrated the broad application of manganese(I) complexes based on the *fac*-[Mn(dippe)(CO)$_2$(CH$_2$CH$_2$CH$_3$)] (dippe = 1,2-bis(di-*iso*-propylphosphino)ethane) for hydrogenation and hydrofunctionalization reactions.[16,17] Based on our recent findings, we describe here the activity of *fac*-[Mn(dippe)(CO)$_3$(CH$_2$CH$_2$CH$_3$)] (**Mn1**),[17a] *fac*-[Mn(dippe)(CO)$_3$(H)] (**Mn2**),[18] *cis*-[Mn(dippe)(CO)$_2$(κ^2-

HBpin)] (**Mn3**)[17c] and *cis*-[Mn(dippe)(CO)$_2$(κ^2-BH$_4$)] (**Mn4**) as pre-catalysts for the selective isomerization of terminal alkenes to internal alkenes. A plausible reaction mechanism based on detailed experimental and theoretical studies is presented.

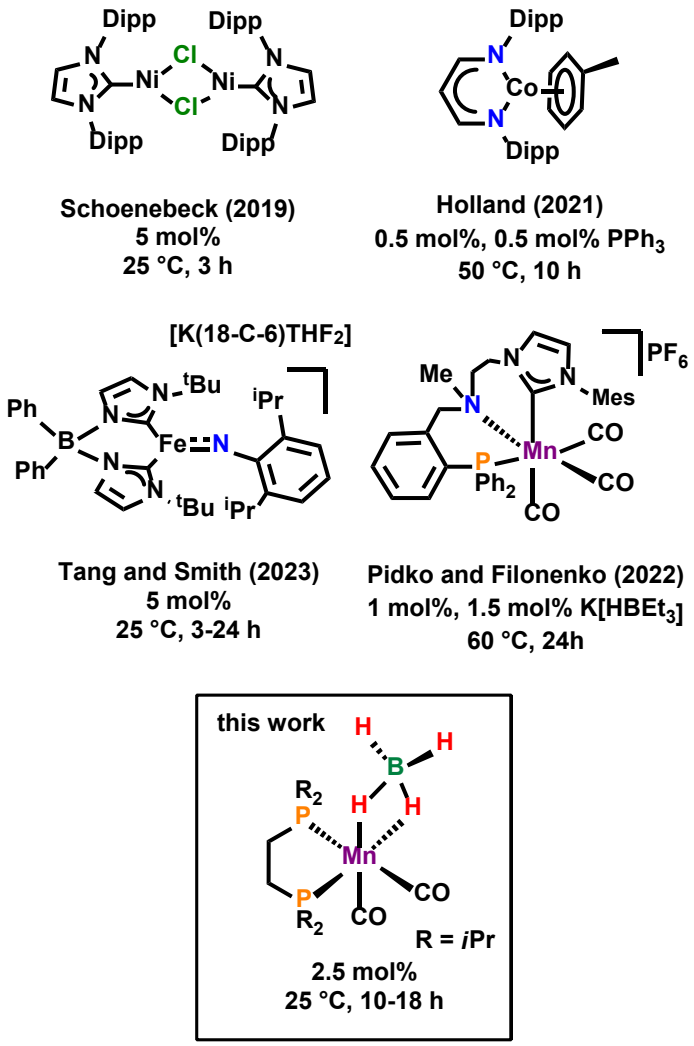


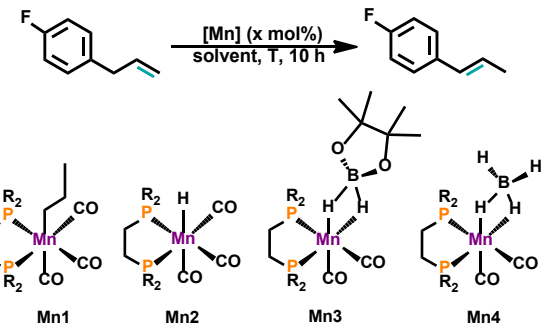
Figure 1. Selected Examples of Base Metal Olefin Isomerization Pre-Catalysts.

RESULTS AND DISCUSSION

The new Mn(I) borohydride complex **Mn4** was prepared in 79% yield by treatment of **Mn1** with NH_3BH_3 at 50 ºC for 3.5 h. It was fully characterized by ^{1}H, ^{13}C{^{1}H} and ^{31}P{^{1}H} NMR and IR spectroscopy, and high-resolution mass spectrometry. The catalytic performance of **Mn4** and the known Mn(I) complexes **Mn1**-**Mn3** were then investigated for the isomerization of 1-allyl-4-flurobenzene as model substrate in THF as solvent. Selected optimization experiments are depicted in Table 1. Although **Mn1** effectively catalyzes a variety of hydrofunctionalizations[16] it turned out to be catalytically inactive for isomerization purposes. Likewise, the hydride complex **Mn2** was found to be inactive for the desired transformation. With **Mn3** bearing the σ-B-H bound HBpin ligand full conversion to the internal alkene was achieved at 60 °C. However, lowering the temperature to 25 °C resulted in no catalytic activity. **Mn4** afforded high conversion and yield with very good selectivity towards the *E*-isomer even at room temperature within 10 h. Notably, no additives were required to activate either **Mn3** or **Mn4**. In other solvents such as CH_2Cl_2 and toluene **Mn4** was considerably less active and lower yields were achieved,

whereas in DMSO, acetone, and MeOH no reaction took place at all (Table 1, entries 8-12). Finally, in the absence of catalyst no reaction took place.

Table 1. Optimization Reactions for the Manganese-Catalyzed Transposition of 1-Allyl-4-fluorobenzene.[a]

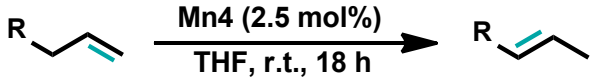


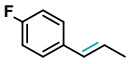
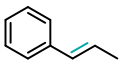
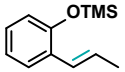
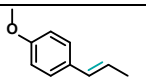
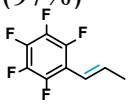
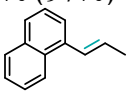
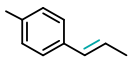
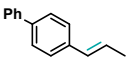
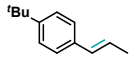
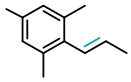
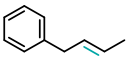
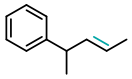
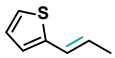
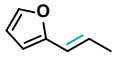
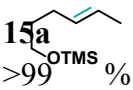
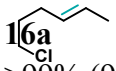
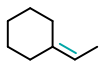
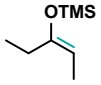
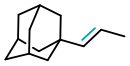
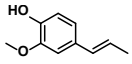
entry	**[Mn]** (mol%)	Solvent	Temp. (°C)	Conversion (%)	*E*/*Z* ratio
1	**Mn1** (3)	THF	60	-	-
2	**Mn2** (3)	THF	60	-	-
3	**Mn3** (3)	THF	60	> 99	94:6
4	**Mn4** (3)	THF	60	> 99	99:1
5	**Mn3** (3)	THF	25	-	-
6	**Mn4** (2.5)	THF	25	> 99	99:1
7	**Mn4** (1)	THF	25	8	91:9
8	**Mn4** (2.5)	CH_2Cl_2	25	60	91:9
9	**Mn4** (2.5)	toluene	25	42	95:5
10	**Mn4** (2.5)	DMSO	25	-	-
11	**Mn4** (2.5)	acetone	25	-	-
12	**Mn4** (2.5)	MeOH	25	-	-

[a]Reaction conditions: 1-Allyl-4-fluorobenzene (0.5 mmol), **[Mn]** and 1,4-dioxane as internal standard (0.13 mmol) in the respective solvent (0.5 mL) at 60 °C for 10 h. Conversion and *E*/*Z* ratio were determined by ^{1}H NMR spectroscopy.

Based on the optimized reaction conditions the substrate scope and limitations were investigated. In order to achieve sufficient conversion for a broad variety of substrates the reaction time was extended to 18 h. Starting with aromatic substrates the desired 1,2-isomerized compound were obtained in high yields. Allylbenzene derivatives featuring strong electron donating groups (e.g. -OTMS) to weak electron donating groups (e.g. alkyl moieties) or electron withdrawing groups (e.g. single or multiple fluorine atoms) were all converted successfully to the desired alkenes. A good performance on annulated systems is demonstrated by the isomerization of 1-allylnaphthalene (**6a**). Halides, ethers and trimethylsilylethers (Table 2, **1a**, **3a** and **4a**) were tolerated as well as the presence of a thiophene and furan moieties (Table 2, **13a** and **14a**). However, it should be noted that 40 °C were required for these heteroaromatic systems. Excellent *E*-selectivity could be observed for the above-mentioned substrates. No conversion could be observed for unprotected

Table 2. Catalytic 1,2-Transposition Reactions of Alkenes by Mn4.[a]



 **1a** >99 % (97%)	 **2a** >99 % (97%)	 **3a** >99 % (98%)	 **4a** >99 % (96 %)
 **5a** >99 % (94%)	 **6a** >99 % (96 %)	 **7a** >99 % (99 %)	 **8a** >99% (99 %)
 **9a** >99 % (99 %)	 **10a** >99 %	 **11a** 99 % (68 %)	 **12a** 96 % (95 %)
 **13a** 15 % 40 °C: 99 % (97 %)	 **14a** n.d. 40 °C: 87 %	 **15a** >99 % (72 %)	 **16a** >99% (98 %)
 **17a** 40 % 40 °C:	 **18a** 75 % (72 %)	 **19a** 93 % (92%)	 **20a** 81% (80 %)
	 **21a** n.d.	 **22a** n.d.	

[a]Reaction conditions: Alkene substrate (0.5 mmol), **Mn4** (2.5 mol%) and 1,4-dioxane as internal standard (0.13 mmol) in THF-d_8 (0.5 mL) at 25 °C for 18 h. Conversion, yield and *E*/*Z* ratio was determined by GC-MS and ^{1}H NMR spectroscopy. n.d. = not detected.

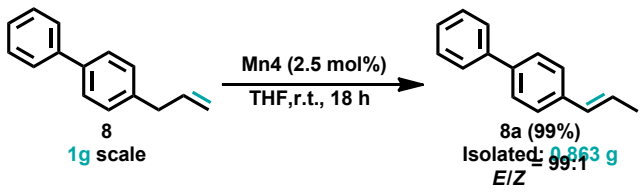
phenols such as eugenol (Table 2, **21a**). While high reactivity was achieved for aliphatic systems, a drop in selectivity was observed (Table 2, **15a** and **16a**). This effect increased to a mere 55:45 *E*/*Z* ratio for trimethyl(pent-1-en-3-yloxy)silane (Table 2, **18a**). Gratifyingly, more bulky olefins such as allyladamantane and allyltrimethylsilane underwent facile isomerization to yield **19a** and **20a** in high yields (Table 2). In comparison to the model substrate 1-allyl-4-fluorobenzene a slight decrease in catalytic performance was noted but high *E*/*Z* ratios were achieved.

A rather drastic decrease in selectivity was noted for the mesityl substrate **10a** (Table 2). Although excellent yield was upheld, a strong interference of the methyl groups can be presumed from the *E*/*Z* ratio

being lowered to about 3:2. The conversion of vinylcyclohexane to the trisubstituted olefin ethylidenecyclohexane (Table 2, **17a**) was explored. At room temperature a conversion of 40 % was not exceeded even with an extended reaction time of 36 h. However, heating to 40 °C for 18 h afforded **17a** in 99 % yield.

Taking into account the particularly mild reaction conditions and additive-free setup, **Mn4** could be a promising choice for transformations in pharmaceutical settings. Encouraged by these findings we envisioned the application of **Mn4** for the gram-scale synthesis of *E*-4-(prop-1-en-1-yl)-1,1'-biphenyl from 4-allyl-1,1'-biphenyl (Scheme 1, **8a**). With biphenyl scaffolds composing many biologically active molecules and pharmaceuticals,[19] this building block seemed a worthwhile target for this demonstration.

Scheme 1. Gram-scale Synthesis of 8a Catalyzed by Mn4.



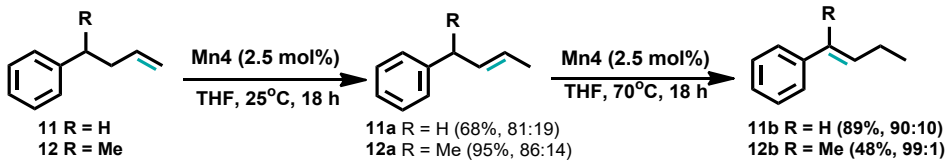
Preliminary studies on long distance isomerization (chain walking) were conducted by increasing the reaction temperature. At room temperature olefins **11** and **12** were converted into **11a** and **12b**, respectively in 68 and 95 % yields with E/Z ratios of 81:19 and 86:14 (Scheme 2). Upon addition of a new batch of catalyst, at 70 °C these olefins were further converted into the conjugated analogues **11b** and **12b** in 89 and 48 % yields, respectively, with E/Z ratios of 90:10 and 99:1. It should be noted that in the case of the non-branched terminal alkene **11** partial chain-walking occurred already at room temperature accounting for the lower yield of **11a**. For the sterically more demanding **12a**, the second transposition step is significantly more difficult even at a reaction temperature of 70 °C leading to a lower yield of **12b**. The formation of **11b** and **12b** from **11** and **12**, respectively, was also achieved in one step with similar yields and E/Z ratios upon performing the reaction at 70 ºC for 18 h. It has to be mentioned that in the case of the aliphatic substrates **15** and **16** no chain walking was observed.

Having established the scope of the isomerization procedure we turned our attention toward the investigation of the reaction mechanism. Over the last decades, different mechanisms for olefin isomerization by transition metals have been proposed.[7,13b,20] Among those, the alkyl and radical mechanism are the most prevalent. The alkyl mechanism involves the insertion of an olefin into a metal hydride followed by *β*-hydride elimination to furnish the product. Following a similar sequence, the radical mechanism is based on the transfer of hydrogen radicals. In contrast to the previously mentioned pathways, the π-allyl mechanism proceeds exclusively in an intramolecular fashion through a 1,3-hydrogen shift.

A well-established method to distinguish the possible pathways described above is the crossover labeling experiment.[15] We performed a crossover isomerization of allylbenzene-d_2 (**2-*d*$_2$**) and non-deuterated 4-allylanisole (**4**) (Scheme 3). An intramolecular hydrogen shift involved in the allyl mechanism would confine deuterium to the previously labeled substrate **2-*d*$_2$**. However, deuterium scrambling was found to extend to 4-allylanisole yielding partially deuterated (*E*)-anethole-*d* (**4a-*d***). Furthermore, a distribution of deuterium throughout the product propene chains was observed. Due to these findings, the involvement of an π-allyl mechanism in the isomerization catalyzed by **Mn4** was excluded.

To investigate the potential involvement of a radical mechanism we performed an experiment with TEMPO as a radical trap. The presence of TEMPO is presumed to inhibit an isomerization *via* radical pathway. However, the presence of the radical trap did not affect the isomerization of **1** (Table 3, entry 1). No products of a reaction between TEMPO and a substrate radical could be detected. Therefore, we deem the involvement of a radical mechanism unlikely. Further mechanistic investigations focused on the hydride functionality accompanied by an easily accessible coordination site. In order to test this assumption, pyridine and PMe_3 were used as additives.

Scheme 2. Preliminary Studies on Chain-walking Isomerization Catalyzed by Mn4.



Scheme 3. Deuterium Crossover Labeling Experiment with Mn4.

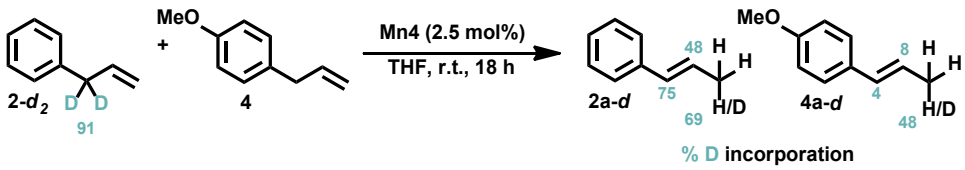
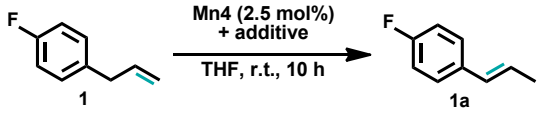


Table 3. Isomerization Experiments with Additives.[a]



entry	Additive (mol%)	Solvent	Yield (%)	*E*/*Z* ratio
1	TEMPO (12.5)	THF	97	99:1
2	Pyridine (12.5)	THF	77	96:4
3	PMe_3 (12.5)	THF	-	-

[a]Reaction conditions: 1-Allyl-4-fluorobenzene (0.5 mmol), **Mn4** (2.5 mol%), additive (12.5 mol%) and 1,4-dioxane as internal standard (0.13 mmol) in THF-d_8 (0.5 mL) at 25 °C for 10 h. Yield and *E*/*Z* ratio were determined by ^{19}F and ^{1}H NMR spectroscopy.

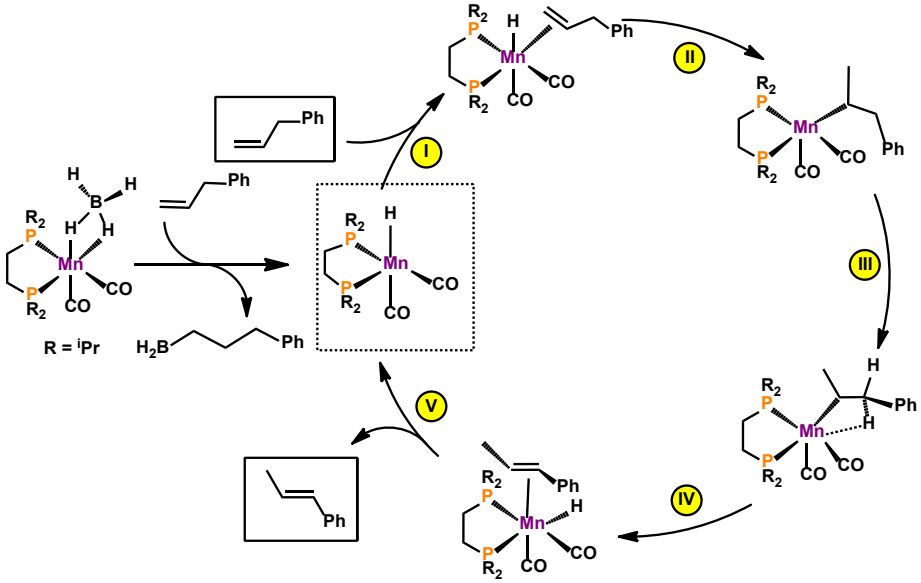
The addition of pyridine (Table 3, entry 2) resulted in a significant drop in reactivity of **Mn4**. The isomerization of allylbenzene resulted in a yield of 77 %, while in presence of PMe_3 no catalytic activity was observed (Table 3, entry 3). A deactivation by the strongly coordinating pyridine and PMe_3 ligands is in line with the presence of a vacant coordination site during catalysis. Monitoring of the experiments involving pyridine and PMe_3 by $^{31}P\{^{1}H\}$ NMR spectroscopy revealed the formation of new hydride species giving rise to signals at -4.52 (t, J_{HP} = 54.8 Hz) and -9.00 (q, J_{HP} = 49.3 Hz) ppm, respectively.

These species are assigned to complexes **Mn5** and **Mn6** as shown in Scheme 4. While **Mn5** could not be isolated in pure form, **Mn6** could be isolated in 87% yield. Both compounds were fully characterized by NMR spectroscopy and HR-MS (see Supporting Information).

Scheme 4. Syntheses of Hydride Complexes Mn5 and Mn6.

The above-mentioned findings strongly suggest an inner-sphere mechanism with a catalyst activation by loss of BH_3 as rate-determining step. Deuterium labeling and radical trap experiments are consistent with a hydride mechanism operating *via* olefin insertion and *β*-hydride elimination which is indeed supported by DFT calculations (*vide infra*).

Scheme 5. Simplified Catalytic Cycle for the Isomerization of Allylbenzene.



The reaction mechanism was explored in detail by means of DFT calculations,[21] with allylbenzene taken as model substrate and **Mn4** (**A** in the calculations as allylbenzene adduct) as pre-catalyst. The resulting free energy profiles are represented in Figures 2 - 4 while Scheme 5 depicts a summary of the catalytic cycle. The free energy profile for the initiation process, where the active catalyst is formed, is depicted in Figure 2. The first step is the addition of allylbenzene in **A** to a non-coordinated B-H bond of the BH_4 ligand thereby being hydroborated to form **B** containing a κ^2-*B,H*-coordinated borane (**B'** is a rotamer of **B**). This first step requires a high barrier of 30 kcal/mol and is slightly exergonic. This is in line with *in situ* NMR spectroscopy during catalysis. The dominant species throughout the reaction was found to be **Mn4** even upon full conversion. Dissociation of $H_2BCH_2CH_2CH_2Ph$ affords the catalytically active species **C** ([Mn(dippe)$(CO)_2$H]) in an endergonic step (ΔG = 15 kcal/mol) with a barrier of 17 kcal/mol (see also Scheme 5).

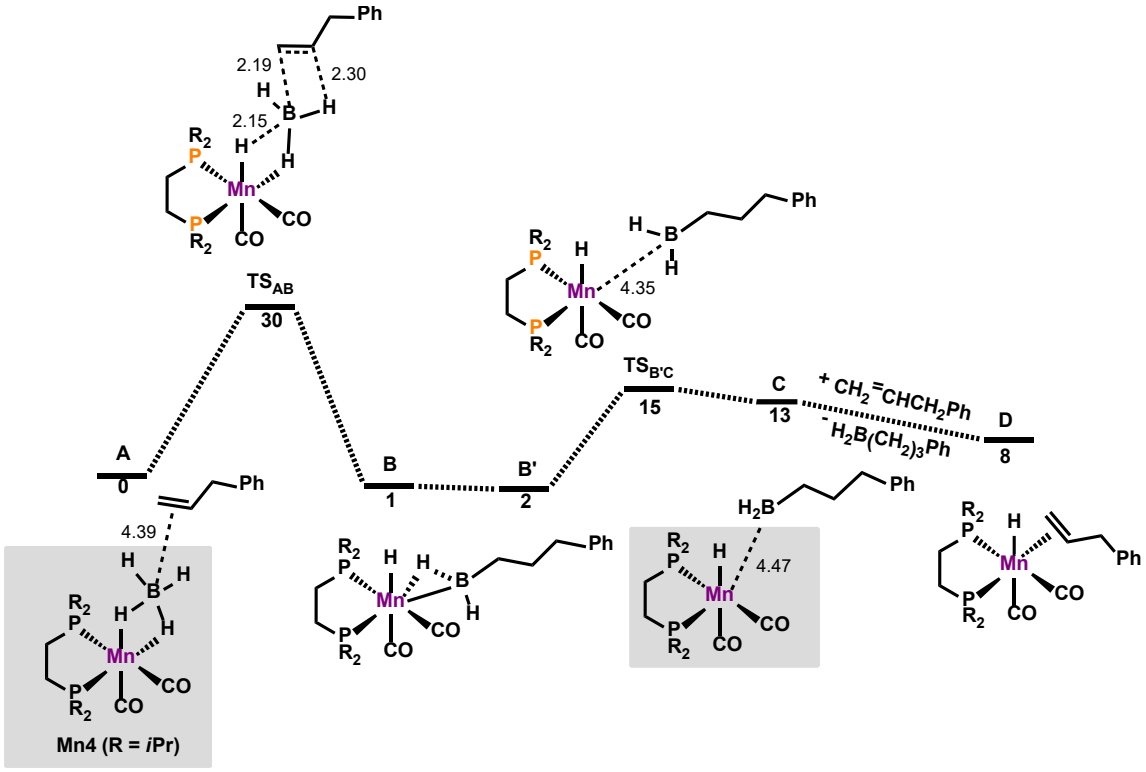


Figure 2. Free Energy Profile Calculated for the Activation of the Pre-catalyst by Hydroboration of Allylbenzene. Free Energies (kcal/mol) are Referred to *fac*-[Mn(dippe)(CO)$_2$(κ^2-BH$_4$)] (Mn4) (A in the calculation in the form of Mn4·CH$_2$=CHCH$_2$Ph).

Addition of another allylbenzene affords complex **D** bearing a η^2-bound CH$_2$=CHCH$_2$Ph ligand. In the next step of the reaction the hydride migrates to the terminal olefin C-atom resulting in an alkyl complex **E** stabilized by a C-H agostic interaction with the terminal C-H bond (Figure 3). This is a very facile step with a barrier of merely 5 kcal/mol and a free energy balance of ΔG = 1 kcal/mol. In the following steps, the agostic interaction is cleaved to yield **F** which is then further stabilized by forming an agostic interaction with the C-H bond adjacent to the phenyl substituent to give intermediate **G**. These processes are essentially thermoneutral and have a barrier of 11 kcal/mol.

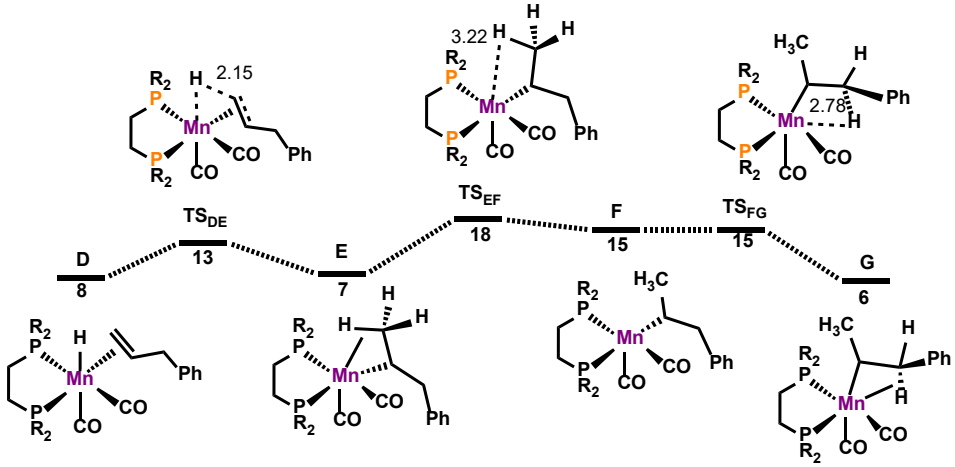


Figure 3. Free Energy Profile Calculated for the Isomerization of Allylbenzene. Free Energies (kcal/mol) are Referred to *fac*-[Mn(dippe)(CO)$_2$(κ^2-BH$_4$)] (Mn4) (A in the calculation in the form of Mn4·CH$_2$=CHCH$_2$Ph).

Complex **G** undergoes β-elimination to form complex **H** featuring the η^2-coordinated product olefin (Figure 4). The barrier is only 7 kcal/mol with a free energy balance of ΔG = 7 kcal/mol with respect to **G**. In the last step of the mechanism *E*-CH_3CH=CHPh (**2a**) is liberated from **H** to yield the coordinatively unsaturated hydride complex **J**. This complex undergoes facile isomerization to afford the catalytically active species **K** thereby closing the catalytic cycle (see Scheme 5). It has to be noted that this intermediate is essentially identical to **C** but without the loosely bound borane $H_2BCH_2CH_2CH_2Ph$ obtained in the initiating step (Figure 2). Closing the cycle, from **K** back to **D**, with addition of a fresh allylbenzene molecule has a free energy balance of ΔG = –5 kcal/mol. In summary, initiation is an endergonic (ΔG = 8 kcal/mol) process with a barrier of 30 kcal/mol, from **A** to $\mathbf{TS_{AB}}$, while the catalytic cycle has a barrier of $\Delta G^{\ddagger}$ = 11 kcal/mol, from **E** to $\mathbf{TS_{EF}}$.

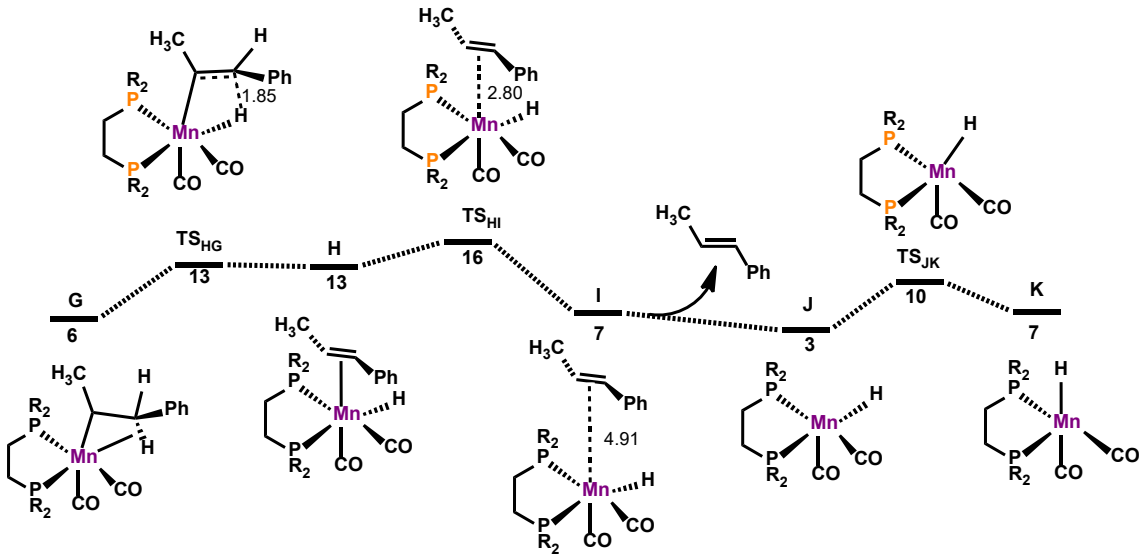


Figure 4. Free Energy Profile Calculated for the Isomerization of Allylbenzene to Form *E*-Prop-1-en-1-ylbenzene. Free Energies (kcal/mol) are Referred to *fac*-[Mn(dippe)(CO)$_2$(κ^2-BH$_4$)] (Mn4) (A in the calculation in the form of Mn4·CH$_2$=CHCH$_2$Ph).

Formation of the *Z*-isomer of the product was also addressed by the DFT mechanistic studies (see Supporting Information). The process involves a C-H agostic exchange in intermediate **G**, followed by β-elimination and loss of the corresponding product *Z*-CH_3CH=CHPh. The process has a barrier of 14 kcal/mol measured from **G** to the β-elimination transition state $\mathbf{TS_{LM}}$ being thus less favorable than formation of the *E* isomer. This is in good agreement with the experimental observations.

CONCLUSION

In sum, we have introduced an efficient protocol for the transposition of terminal alkenes catalyzed by the Mn(I) borohydride complex *fac*-[Mn(dippe)(CO)$_2$(κ^2-BH$_4$)]. The reported procedure operates at room temperature with a catalyst loading of 2.5 mol% and no additives. High reactivities and excellent *E*-selectivities were achieved for allylbenzene derivatives. While maintaining good reactivity, the selectivity was slightly diminished for aliphatic systems. Increasing the steric bulk in these substrates reestablished high *E*-selectivity. The protocol was also applied for gram-scale synthesis with 4-allyl-1,1'-biphenyl. Preliminary studies also showed a temperature-dependent chain walking process leading to a sequential migration of the double bond. Deuterium studies were carried out to gain insights in the reaction mechanism. The influence of additives such as pyridine and PMe_3 on the reactivity of *fac*-[Mn(dippe)(CO)$_2$(κ^2-BH$_4$)] was investigated ultimately leading to the detection of hydride species. Both

additives lead to deactivation by the strongly coordinating ligands being in line with the requirement of a vacant coordination site during catalysis. DFT calculations indeed disclosed a typical *inner sphere* mechanism with all reacting fragments coordinated to the metal. The reaction proceeds *via* a metal hydride mechanism involving hydride insertion of the terminal C=C bond of the olefin resulting in an alkyl complex. Consecutive β-elimination of internal C-H bond adjacent to the substituent yields the isomerization product. Notably, the formation of the *E*-isomer is favored both kinetically and thermodynamically.

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:
Synthetic procedures, ^{1}H, $^{13}C\{^{1}H\}$, and $^{31}P\{H\}$ NMR spectra of all compounds and complete computational details (PDF)
Cartesian coordinates for DFT-optimized structures (XYZ)

Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

Financial support by the Austrian Science Fund (FWF) is gratefully acknowledged (Project No. P 32570-N). Centro de Química Estrutural (CQE) and Institute of Molecular Sciences (IMS) acknowledge the financial support of Fundação para a Ciência e Tecnologia (Projects UIDB/00100/2020, UIDP/00100/2020, and LA/P/0056/2020).

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