

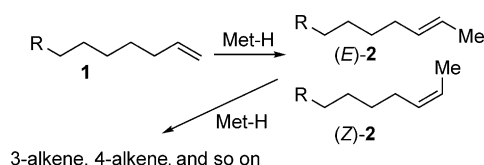
Synthetic Methods

An Alternative Mechanism for the Cobalt-Catalyzed Isomerization of Terminal Alkenes to (Z)-2-Alkenes**

Anastasia Schmidt, Alexander R. Nödling, and Gerhard Hilt*

Abstract: The cobalt-catalyzed selective isomerization of terminal alkenes to the thermodynamically less-stable (Z)-2-alkenes at ambient temperatures takes place by a new mechanism involving the transfer of a hydrogen atom from a Ph_2PH ligand to the starting material and the formation of a phosphonium complex, which recycles the Ph_2PH complex through a 1,2-H shift.

The isomerization of alkenes comprises two reaction modes. The first is the inversion of the double-bond configuration. This type of isomerization can be realized by various methods, such as by photochemical isomerization^[1] or by several chemical transformations.^[2] The second mode for the isomerization of an alkene is the translocation of the double bond along a carbon chain. When a terminal alkene, such as **1**, is subjected to the reaction, isomerization of the double bond to position 2 leads to an *E/Z* mixture of the 2-alkene (**2**). With transition-metal catalysts, the isomerization is often realized via a transition-metal hydride (Met-H) as the active catalyst species (Scheme 1).^[3] According to the general mechanism



Scheme 1. General mechanism for the isomerization of alkenes by metal hydride species.

for such isomerization reactions via metal hydride catalysts, the addition and β -hydride elimination by the Met-H result in isomerization by a formal 1,3-H shift.

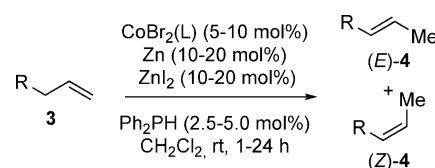
Of the several transition-metal-catalyzed isomerization reactions, Weix, Holland, and co-workers described a cobalt catalyst which exhibits a high preference for the formation of the (Z)-2-alkenes from 1-alkenes.^[4] Unfortunately, this particular cobalt catalyst also caused further isomerization of the double bond along the carbon chain so that higher isomers (3-alkenes and so on) were also detected. Furthermore, the primary (Z)-2-alkene product was isomerized to the thermodynamically more-stable (E)-2-alkene over time, and for

some alkenes, such as allylbenzene, the (E)-2-alkene was the primary product in the first place.

During the course of our continuing investigations of cobalt catalyst systems for the isomerization of 1,3-dienes,^[5] we found that the dpppBuEt ligand^[6] allowed the desired transformation of 1-hexadecene (**1**, $\text{R} = \text{C}_9\text{H}_{21}$; 95 % conversion, ambient temperature, 5 h) to *E/Z*-**2** with only minor amounts of the undesired higher homologues. Unfortunately, the results obtained with a catalyst mixture consisting of $[\text{CoBr}_2(\text{dpppBuEt})]$, zinc powder, and zinc iodide were difficult to reproduce and, therefore, we started a detailed investigation into the reason for the inconsistent results. Eventually, we realized that an impurity in the ligand, a remnant of the ligands synthesis (Ph_2PH), could be responsible for the formation of the active cobalt catalyst. Accordingly, when Ph_2PH was added in catalytic amounts to the precatalyst mixture, the reaction of 1-hexadecene proceeded within 1.5 h to 95 % conversion and an *E/Z* ratio of 15:85. From this point onward the cobalt-catalyzed isomerization was highly reproducible and could be performed under very convenient reaction conditions on a millimolar scale, often within 1–3 h. The transformations were conducted in anhydrous dichloromethane at ambient temperature (with few exceptions) under exclusion of oxygen and with commercially available starting materials, without the need for previous purification.

We were able to demonstrate in control experiments that all the components of the catalyst mixture must be present to obtain the desired transformation in a short reaction time at ambient temperatures. We also ascertained that the amount of Ph_2PH has an influence on the reaction rate as well as on the *E/Z* ratio. The reaction proceeds faster with a higher Ph_2PH content, but with a reduced excess of the *Z* isomer. The isomerization reaction of 1-alkenes using the cobalt precatalyst with dppp-type ligands (such as dppp, bdpp, or dpppBuEt)^[6] as well as Ph_2PH as an additive under the conditions exemplified in Scheme 2 could be applied to a variety of other terminal alkenes. The results of these transformations are summarized in Table 1.

The isomerization reactions with dppp are the fastest, but the *E/Z* ratios are inferior to those when other ligands are applied. The use of the bdpp ligand gave the best results for



Scheme 2. Cobalt-catalyzed isomerization of terminal alkenes.

[*] Dipl.-Chem. A. Schmidt, Dipl.-Chem. A. R. Nödling, Prof. Dr. G. Hilt
Fachbereich Chemie, Philipps-Universität Marburg
Hans-Meerwein-Strasse, 35043 Marburg (Germany)
E-mail: Hilt@chemie.uni-marburg.de

[**] The donation of dpppBuEt from BASF SE is gratefully acknowledged.

Supporting information for this article is available on the WWW under <http://dx.doi.org/10.1002/anie.201409902>.

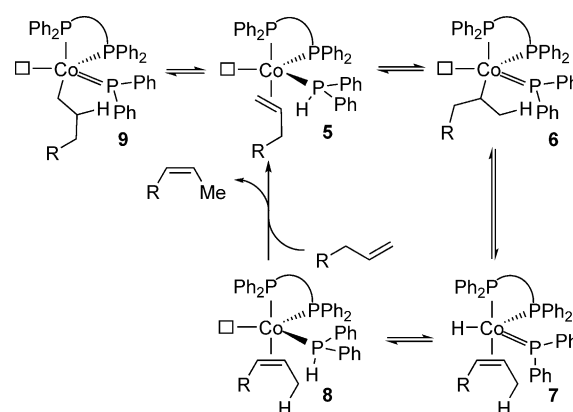
Table 1: Results of the cobalt-catalyzed isomerization of alkenes.^[a]

Entry	L	1-Alkene (3)	Main product (4)	Yield [%] (conversion [%])	E/Z ratio (sum of other isomers [%])
1	dpppBuEt			99 (95)	15:85 (3)
2	bdpp			92 (90)	14:86 (<1)
3	dppp			80 ^[b] (51)	55:45 (<1)
4	dppp			59 (100)	100:0 (<1)
5	bdpp			84 ^[c] (83)	8:92 (<1)
6	dpppBuEt			86 (89)	13:87 (<1)
7	bdpp			91 ^[d] (100)	19:81 (<1)
8	dpppBuEt			99 (92)	16:84 (<1)
9	dpppBuEt			95 (96)	14:86 (<1)
10	dpppBuEt			71 (93)	26:74 (<1)
11	bdpp			96 ^[e] (97)	4:96 (3)
12	bdpp			94 ^[d] (95)	14:86 (5)
13	bdpp			80 (95)	16:84 (<1)
14	dppp			84 ^[f] (93)	83:17 (9)
15	dpppBuEt			91 (88)	13:87 (<1)
16	dppp			99 (100)	100:0 (<1)
17	bdpp			84 ^[f] (84)	18:82 (<1)
18	bdpp			98 (100)	87:13 (<1)
19	dppp			72 (88)	22:78 (8)

[a] Conditions: CoBr₂(L) (5–10 mol%), Zn (10–20 mol%), ZnI₂ (10–20 mol%), Ph₂PH (2.5–5 mol%), and 1-alkene **3** (0.5 mmol, 1.0 equiv), CH₂Cl₂, 1–24 h, rt (unless otherwise noted). Unreacted starting material and other isomers were not separated and are included in the yield (unless otherwise noted). The conversion and E/Z ratio were determined by ¹H NMR spectroscopy, GC, or GC-MS analysis. The amount of other isomers was determined by GC or GC-MS analysis. [b] After 7 h, another 10 mol% CoBr₂(L), 20 mol% Zn, 20 mol% ZnI₂, and 5 mol% Ph₂PH were added. [c] 15 mol% CoBr₂(L), 30 mol% Zn, 30 mol% ZnI₂, and 7.5 mol% Ph₂PH were used. [d] The reaction proceeded at 3 °C. [e] The reaction proceeded at –3 °C. [f] The starting material was separated by flash chromatography. Bpin = (pinacolato)boron; TBS = *tert*-butyldimethylsilyl.

the branched and sterically more-demanding substrates, whereas the dpppBuEt ligand was the ligand of choice for the simple unbranched substrates. Simple alkenes without or with functional groups at least two carbon–carbon bonds away from the terminal alkene subunit, such as **3a**, **3b**, **3h–j**, and **3l**, react smoothly and give the desired (*Z*)-2-alkenes in high yields and good stereoselectivities. The amount of *E* isomer increased significantly when an aryl substituent was placed in the homoallylic position (**3c**), and the *E* isomer was obtained as a single isomer when allylbenzene **3d** or allyl ether **3p** were applied. Interestingly, additional methyl substituents in the homoallylic position (**3e**, **3f**, **3q**) were tolerated and, especially for **3e** (entry 5), significantly better results were obtained (compared to **3c**, entry 3), with the more complex starting material increasing the selectivity to *E/Z* = 8:92. Fortunately, the highest *Z* selectivity was observed for homoallylboronic pinacol ester **3k**. In this case, the cobalt catalyst led to the *Z*-configured allylboron building block **4k** in excellent yield and selectivity, with only minor amounts of other isomers. In some cases the reactivity was so high that lower reaction temperatures were necessary to obtain good results (**4g**, **4k**, **4l**). An interesting observation is that a carbonyl group in the vicinity of the alkene, such as in **3n**, leads to an inversion of the *E/Z* ratio (entries 14 and 15), which can be rationalized by additional coordination of the carbonyl moiety. Furthermore, a kinetic discrimination was observed for **3r**, where only the allylic ether double bond was isomerized predominantly to the *E* isomer. It is noteworthy that prolonged reaction times led to undesired isomerization of the (*Z*)-2-alkene to the (*E*)-2-alkene (see the Supporting Information). This process starts as soon as around 90 % of the starting material has been consumed. The most outstanding feature of the cobalt-catalyzed isomerization reaction is the fact that higher homologues are only found in trace amounts. Increased amounts are found only after prolonged reaction times (up to 9 % after 24 h reaction for 1-hexadecene (**3a**)). This finding led us to the conclusion that the isomerization does not follow the generally accepted mechanism of addition/elimination of a cobalt hydride species to the double bond.^[3] Instead, the role of the Ph₂PH additive in the reaction mechanism must be taken into consideration, which prompted us to the following mechanistic proposal (Scheme 3).

In the low-valent cobalt(I) complex **5**, generated by reduction of the cobalt(II) precatalyst, the terminal alkene, the dppp ligand, as well as the Ph₂PH additive are coordinated. This arrangement results in a vacant coordination site on the cobalt center.^[7] The outstanding activity of the cobalt complex can be explained by the transfer of the hydrogen atom from the P–H subunit to the terminal carbon atom of the double bond and the formation of an alkyl cobalt species (**6**). The vacant coordination site on the cobalt center allows β-hydride elimination from the allylic position, which leads to migration of the double bond. This results in an overall 1,3-hydrogen shift in the substrate and formation of a cobalt hydride species **7**. Accordingly, the Ph₂PH ligand in **5** is transformed into a phosphonium-type ligand in structures **6** and **7**.^[8] If intermediate **7** is short-lived and a 1,2-hydrogen shift from the cobalt to the phosphorus center (**7**→**8**) takes place, the lifetime of the cobalt-hydride intermediate **7** is reduced, which prohibits



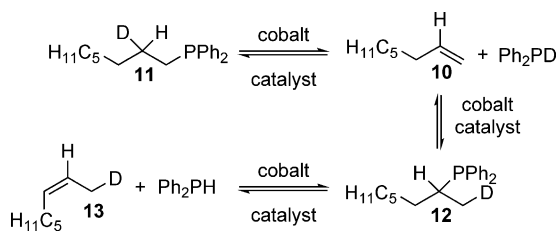
Scheme 3. Proposed mechanism of the cobalt-catalyzed isomerization of alkenes in the presence of a Ph₂PH additive.

the formation of higher homologues through re-addition of the cobalt hydride to the 2-alkene and so on. The steric bulk of the dppp ligand must be responsible for the kinetically controlled formation of the *Z* isomer. Furthermore, the lower binding affinity of the cobalt catalyst to the 2-alkene compared to terminal alkenes then causes the fast exchange of the product toward the starting material, and the active cobalt species **5** is formed to complete the catalytic cycle of the reaction.

The formation of the alkyl-cobalt species **9** through a nonproductive side reaction must also be taken into consideration. Although this process does not lead to the desired 2-alkene, the process is important to explain the incorporation of deuterium in the product when deuterium-labeled starting materials were used.

First, stoichiometric amounts of Ph₂PD (96 % D incorporation) were applied to verify that the deuterium atom is transferred to the terminal carbon atom (**5** to **6**) and to the carbon atom at position-2 via **5** to **9** of the 1-hexadecene in the first step. The deuterium content of the isolated (*E/Z*)-2-hexadecene in position-1 was found to be high (51 %) and a considerable amount of deuterium was detected at the olefinic carbon atom at position-2 (18 %, see the Supporting Information). As an alternative mechanistic proposal, we considered a reversible cobalt-catalyzed hydrophosphination,^[9] the *anti*-Markovnikov or Markovnikov addition of Ph₂PH to 1-octene (**10**, Scheme 4), for the formation of **11** and **12**. The 2-deuterated starting material can be generated from **11**, whereas the 1-deuterium-labeled starting material or the desired *Z*-configured product **13** would be accessible from **12**.

To verify that the alternative mechanism was relevant in the cobalt-catalyzed isomerization, the non-deuterated isomer of **11**, 1-octyldiphenylphosphine, was applied as the additive instead of Ph₂PH for the isomerization of 1-hexadecene (**3a**). The reaction proceeded very slowly (49 % conversion after 25 h), but (*Z*)-2-hexadecene (**4a**) was generated as with Ph₂PH as additive. 1-Octene or (*Z*)-2-octene should have been detected as side products if the alkyl phosphine was an intermediate in the reaction, which was not the case. Furthermore, no isomerization product (**4a**) was detected when the Markovnikov-type product of the hydrophosphination, 2-octyldiphenylphosphine (**12**), was used as the additive. Thus, the cobalt-catalyzed addition/elimination of Ph₂PH can be excluded as an alternative mechanism

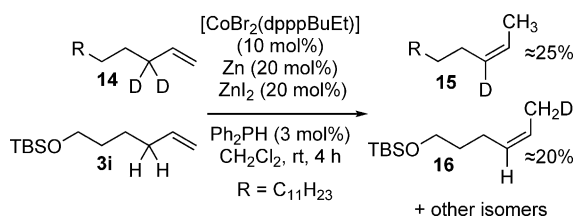


Scheme 4. Deuterium-labeling experiment to verify the addition/elimination by hydrophosphination.

because the 1- and 2-octyldiphenylphosphine were not found to be intermediates in the isomerization reaction.

We then treated 3,3-dideutero-1-hexadecene (**14**) with the catalyst mixture in the presence of non-deuterated alkene **3i** (Scheme 5) to prove that the isomerization does not proceed through an intramolecular 1,3-hydrogen shift reaction.

The 2-alkenes obtained from this scrambling experiment were separated and analyzed individually. The isomerization



Scheme 5. Deuterium-labeling experiment for the verification of intermolecular hydrogen transfer.

products derived from **14** (> 95 % D) exhibited a decreased deuterium incorporation, while the products derived from **3i** (natural abundance) showed an increased deuterium incorporation. The scrambling of the deuterium/hydrogen atoms among the starting materials was proven by the identification of about 25 % of product **15** in the mixture and about 20 % of **16** (see the Supporting Information). From these results we conclude that either the deuterium atom from **14** or the hydrogen atom from **3i** was transferred to the cobalt atom, an alkene exchange occurred, and that the isomerization is then catalyzed by the intermediate cobalt complexes **6**, **7**, and **8**.

In conclusion, we were able to show that a cobalt-catalyzed isomerization of terminal alkenes to (*Z*)-2-alkenes can be realized with Ph_2PH as the decisive additive to promote the isomerization. The desired *Z* isomers were generated predominantly, a number of functional groups were tolerated, and additional methyl groups in homoallylic positions were not only tolerated but led in one case to even better results. We are convinced that the new mechanism and the mild reaction conditions will be a boost for further developments in this field.

Experimental Section

Representative procedure: Anhydrous zinc iodide (10–20 mol%), zinc powder (10–20 mol%), and cobalt complex (5–10 mol%) were

suspended in anhydrous dichloromethane (0.5 mL) under argon. After stirring the mixture for 10 min, Ph_2PH (2.5–5 mol%; 0.125 M in CH_2Cl_2) was added and after additional stirring for 10 min, 1-alkene **3** (0.50 mmol; 1 equiv) was added. The reaction mixture was stirred at the required temperature and the progress of the reaction was monitored by GC or GC-MS analysis. The reaction mixture was filtered over a short pad of silica gel with pentane or pentane/diethyl ether as eluent. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel.

Received: October 9, 2014

Published online: November 27, 2014

Keywords: alkenes · cobalt · double-bond migration · isomerization · stereoselectivity

- [1] a) K. Singh, S. J. Straig, J. D. Weaver, *J. Am. Chem. Soc.* **2014**, *136*, 5275–5278; b) Y. Ito, Y. Uozu, T. Dote, M. Ueda, T. Matsuura, *J. Am. Chem. Soc.* **1988**, *110*, 189–198.
- [2] a) N. F. Jain, P. F. Cirillo, J. V. Schaus, J. S. Paneik, *Tetrahedron Lett.* **1995**, *36*, 8723–8726; b) J. Q. Yu, M. J. Gaunt, J. B. Spencer, *J. Org. Chem.* **2002**, *67*, 4627–4629; c) U. H. Andrews, J. E. Baldwin, M. W. Grayston, *J. Org. Chem.* **1982**, *47*, 287–292; d) M. T. Reetz, M. Plachky, *Synthesis* **1976**, 199–200.
- [3] a) R. H. Crabtree, *The Organometallic Chemistry of the Transition Metals*, 3rd ed., Wiley, New York, **2001**, pp. 226–228; b) G. W. Parshall, *Homogeneous Catalysis*, Wiley, New York, **1980**, pp. 31–35.
- [4] a) C. Chen, T. R. Dugan, W. W. Brennessel, D. J. Weix, P. L. Holland, *J. Am. Chem. Soc.* **2014**, *136*, 945–955; b) G. Hilt, *ChemCatChem* **2014**, *6*, 2484–2485; c) G. Erdogan, D. B. Grotjahn, *Org. Lett.* **2014**, *16*, 2818–2821; d) C. R. Larsen, G. Erdogan, D. B. Grotjahn, *J. Am. Chem. Soc.* **2014**, *136*, 1226–1229; e) S. M. M. Knapp, S. E. Shaner, D. Kim, D. Y. Shopov, J. A. Tendler, D. M. Pudalov, A. R. Chianese, *Organometallics* **2014**, *33*, 473–484; f) R. Jennerjahn, R. Jackstell, I. Piras, R. Franke, H. Jiao, M. Bauer, M. Beller, *ChemSusChem* **2012**, *5*, 734–739; g) L.-G. Zhuo, Z.-K. Yao, Z.-X. Yu, *Org. Lett.* **2013**, *15*, 4634–4637; h) M. Mayer, A. Welther, A. J. von Wangelin, *ChemCatChem* **2011**, *3*, 1567–1571; i) T. Kobayashi, H. Yorimitsu, K. Oshima, *Chem. Asian J.* **2009**, *4*, 1078–1083; j) H. J. Lim, C. R. Smith, T. V. RajanBabu, *J. Org. Chem.* **2009**, *74*, 4565–4572; k) D. B. Grotjahn, C. R. Larsen, J. L. Gustafson, R. Nair, A. Sharma, *J. Am. Chem. Soc.* **2007**, *129*, 9592–9593.
- [5] a) A. Schmidt, G. Hilt, *Chem. Asian J.* **2014**, *9*, 2407–2410; b) Y. N. Timsina, S. Biswas, T. V. RajanBabu, *J. Am. Chem. Soc.* **2014**, *136*, 6215–6218; c) F. Pünner, A. Schmidt, G. Hilt, *Angew. Chem. Int. Ed.* **2012**, *51*, 1270–1273; *Angew. Chem.* **2012**, *124*, 1296–1299; d) M. Sodeoka, H. Yamada, M. Shibasaki, *J. Am. Chem. Soc.* **1990**, *112*, 4906–4911; e) M. Sodeoka, S. Satoh, M. Shibasaki, *J. Am. Chem. Soc.* **1988**, *110*, 4823–4824.
- [6] dppp = 1,3-bis(diphenylphosphino)propane, bdpp = 2,4-bis(diphenylphosphino)pentane, dpppBuEt = 2-butyl-2-ethyl-1,3-bis(diphenylphosphino)propane.
- [7] L. Fiebig, J. Kuttner, G. Hilt, M. Schwarzer, G. Frenking, H.-G. Schmalz, M. Schäfer, *J. Org. Chem.* **2013**, *78*, 10485–10493.
- [8] Leading references: a) L. Rosenberg, *Coord. Chem. Rev.* **2012**, *256*, 606–626; b) J.-P. Bezombes, P. B. Hitchcock, M. F. Lappert, J. E. Nycz, *Dalton Trans.* **2004**, 499–501; c) W. Malisch, K. Grün, O. Fey, C. Abd El Baky, *J. Organomet. Chem.* **2000**, *595*, 285–291.
- [9] Leading reference: W. Malisch, B. Klüpfel, D. Schumacher, M. Nieger, *J. Organomet. Chem.* **2002**, *661*, 95–110.