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Asymmetric double-bond isomerization of cyclic allyl acetals by using diop and chiraphos modified nickel complexes

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Abstract

Diop or chiraphos modified dibromo- and dichloronickel complexes proved to be readily available catalyst precursors, which upon activation with lithium triethylborohydride (Super-Hydride®) gave enantioselectivities up to 92% ee for the asymmetric isomerization of 5-methylene-1,3-dioxanes **3** and up to 67% ee for the asymmetric isomerization of 4,7-dihydro-1,3-dioxepins **1**.

The excellent work of Otsuka, Tani and Noyori et al.[1–3] on the asymmetric isomerization of diethylgeranyl- or nerylamine with optically active $[Rh(binap)]^+$-complexes as catalysts has shown the asymmetric double-bond isomerization to be an important method in stereoselective organic synthesis.[4] However, high asymmetric induction could only be achieved with allylic amines as substrates probably via a nitrogen-triggered mechanism,[5,6] whereas use of other substrates leads to a significant drop in the enantioselectivity.[7,8]

Our previous work on this topic focused on cyclic allyl acetals such as 2-substituted 4,7-dihydro-1,3-dioxepins **1** and 5-methylene-1,3-dioxanes **3** as substrates and hydridic ruthenium complexes as catalysts modified by optically active ligands,[9] but with these substrates and catalysts the asymmetric induction obtained to date was also moderate (5–38% ee).[10,11]

More recently, the flash-isomerization of **1** with $NiCl_2$dppe activated with Grignard reagents in the presence of trimethylsilyl chloride was reported.[12] However, we found that the isomerization of **1** and **3** (R=*tert*-butyl) with $NiCl_2$dppe (dppe=diphenylphosphanoethane) and isopropylmagnesium bromide in the presence of trimethylsilyl chloride gave poor yields of **2** and **4** (Scheme 1), and 2,2,4-trimethyl-3-pentanol was formed as the major product (Table 1, entries 1, 2 and 12). This product probably arises either by cleavage of the substrates or the products to liberate pivalaldehyde, which can then react with the Grignard reagent.[13] The formation of 2,2,4-trimethyl-3-pentanol was suppressed by activation of the catalyst precursor ($NiCl_2$dppe) with lithium triethylborohydride (Super-Hydride®) (Table 1, entries 3 and 13).

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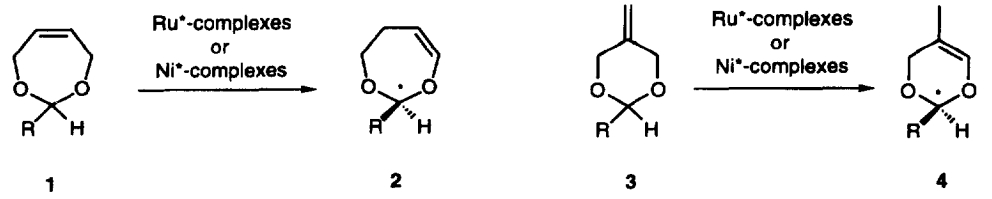

1 2 3 4

Scheme 1.

On the other hand, a surprisingly clean and fast reaction occurred, when $NiCl_2$diop was used as the catalyst precursor. The formation of 2,2,4-trimethyl-3-pentanol was not observed, even when the catalyst precursor was reacted with excess Grignard reagent (Table 1, entries 7 and 15).[14] Moreover, in comparison to ruthenium-catalyzed isomerizations significantly improved enantiomeric excesses of **2** and **4** (R=*tert*-butyl) were obtained especially when $NiCl_2$diop was activated with Super-Hydride® (Table 1, entries 9 and 17). However, with respect to the asymmetric induction the optimal chelate ring size of the nickel complex varies with the ring size of the substrate.[15] In the isomerization of 4,7-dihydro-1,3-dioxepins **1**, complex ligands forming a five-membered chelate ring gave better results than diop. Thus, the isomerization of **1** (R=*tert*-butyl) with $NiCl_2$chiraphos and lithium triethylborohydride at 60°C afforded **2** with 47% ee. The enantioselectivity could be increased by lowering the temperature. At room temperature, **2** was obtained with 67% ee (Table 1, entries 5 and 6).[16] As already observed in the reactions of **1** with $NiCl_2$dppe as precatalyst, activation of $NiCl_2$chiraphos with Grignard reagents predominantly caused ring cleavage of **1** or **2** and formation of 2,2,4-trimethyl-3-pentanol (Table 1, entry 4).

In contrast to the nickel-catalyzed isomerization of **1**, diop as the optically active ligand proved to be superior to chiraphos for the isomerization of 5-methylene-1,3-dioxanes **3** (Table 1, entries 14, 15 and 17). A further jump in the enantioselectivity could be achieved, when $NiBr_2$diop instead of $NiCl_2$diop was used as catalyst precursor (Table 1, entries 20–22). In this case, the isomerization reaction occurs with an acceptable rate even at lower temperatures, and **4** (R=*tert*-butyl) was obtained at −70°C in ether with 92% ee (Table 1, entry 26).

Preliminary investigations on the epoxidation of 5-methyl-4*H*-1,3-dioxins indicate, that **4** (R=*tert*-butyl) is an interesting precursor for the synthesis of carboxaldehyde **6**. Thus, the reaction of **4** with *m*-chloroperbenzoic acid in CH_2Cl_2 afforded *m*-chlorobenzoate **5** as an intermediate, which upon distillation immediately rearranged to give **6** in a high overall yield (Scheme 2).[17] Enantiomerically pure carboxaldehydes of type **6** have already found application as chiral building blocks in natural product syntheses, e.g. the synthesis of bicyclomycin[18] or vitamin E.[19]

In summary, a breakthrough was achieved in the asymmetric double-bond isomerization of cyclic allyl acetals by using diop- or chiraphos-modified nickel complexes as catalyst precursors and activation with Super-Hydride®. The catalysts are readily available, and the products are of potential interest in stereoselective organic synthesis. Further investigations in the improvement of the enantioselectivity of the isomerization process and use of the products **2** and **4** as chiral building blocks are in progress.

Acknowledgements

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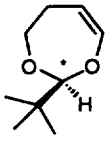
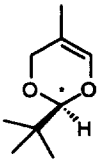
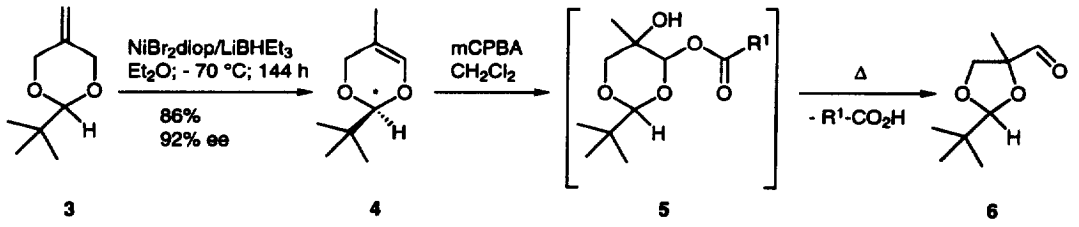
Table 1
Nickel-catalyzed isomerization of substrates **1** and **3** (R=*tert*-butyl)

Product [a]	Entry	Catalytic System [b]	Solv.	Temp. (°C)	Convers. (%) [c] / Time (h)	Yield [d] (%)	ee [e] (%)	$[\alpha]_D^{20}$ (neat)
 **2**	1	$NiCl_2$dppe/ RMgX	THF	0→20 [f]	100/0.75	13 [g]		
	2	$NiCl_2$dppe/ RMgX/TMSCl	THF	0→20 [f]	100/0.75	35 [h]		
	3	$NiCl_2$dppe/ $LiBHEt_3$	THF	60	100/72	62		
	4	$NiCl_2$[(-)-chiraphos]/RMgX	THF	0→20 [f]	100/72	21 [i]	22	
	5	$NiCl_2$[(-)-chiraphos]/ $LiBHEt_3$	THF	60	100/7.5	68	47	+ 15.9
	6		THF	20	100/48	72	67	+ 23.6
	7	$NiCl_2$[(-)-diop]/ RMgX	THF	0	100/0.5	86	22	+ 8.2
	8	$NiCl_2$[(-)-diop]/ $LiBHEt_3$	THF	66	100/1.5	82	32	+ 10.8
	9		THF	-57	100/16	79	45	+ 14.7
	10	$NiBr_2$[(-)-diop]/ $LiBHEt_3$	THF	66	100/2	75	20	+ 7.1
	11		THF	-55	100/24	83	39	+ 13.5
 **4**	12	$NiCl_2$dppe/ RMgX	THF	0→20 [f]	12/24	2 [j]		
	13	$NiCl_2$dppe/ $LiBHEt_3$	THF	66	23/18	23 [c]		
	14	$NiCl_2$[(-)-chiraphos]/ $LiBHEt_3$	THF	66	100/120	84	16	+ 15.9
	15	$NiCl_2$[(-)-diop]/ RMgX	THF	0	100/0.5	86	73	- 72.2
	16	$NiCl_2$[(-)-diop]/ $LiBHEt_3$	THF	66	100/2.5	82	38	- 38.5
	17		THF	0	83/24	83 [c]	63	
	18		THF	-54	0/24	0 [c]		
	19	$NiBr_2$[(-)-diop]/ RMgX	THF	0	100/0.5	86	72	- 70.8
	20	$NiBr_2$[(-)-diop]/ $LiBHEt_3$	THF	66	100/0.5	86	53	- 51.4
	21		THF	0	100/2	81	73	- 72.8
	22		THF	-57	100/24	86	89	- 89.3
	23	$NiBr_2$[(-)-diop]/ $LiBHEt_3$	Et_2O	34	100/0.5	82	56	- 54.3
	24		Et_2O	-56	100/24	83	89	- 87.8
	25		Et_2O	-63	100/48	85	91	- 90.3
	26		Et_2O	-70	100/144	86	92	- 91.1

[a] Absolute configuration unknown. [b] Substrate **1**: 0.04 molar equivalents of the nickel-catalyst precursor were used. Activation of the catalyst precursor was performed by using 4 molar equivalents of isopropylmagnesium bromide or 0.04 molar equivalents of Super-Hydride; Substrate **3**: 0.025 molar equivalents Ni-catalyst precursor and activation with 2.5 molar equivalents isopropylmagnesium bromide or 0.05 molar equivalents of the nickel-catalyst precursor and activation with 0.05 molar equivalents Super-Hydride®.[20] [c] Determined by GC.[21] [d] The results refer to isolated yields if not otherwise stated. [e] Determined by GC.[21] Reproducibility ± 0.5%. [f] After isopropylmagnesium bromide was added at 0 °C the mixture was allowed to warm up to 20 °C. [g] Major product 2,2,4-trimethyl-3-pentanol (45%)(GC). [h] Byproduct 2,2,4-trimethyl-3-pentanol (25%)(GC). [i] Major product 2,2,4-trimethyl-3-pentanol. [j] Major product 2,2,4-trimethyl-3-pentanol (7%)(GC).

References

1. Tani, K.; Yamagata, T.; Otsuka, S.; Akutagawa, S.; Kumobayashi, H.; Taketomi, T.; Takaya, H.; Miyashita, A.; Noyori, R. *J. Chem. Soc., Chem. Commun.* **1982**, 600.
2. Tani, K.; Yamagata, T.; Akutagawa, S.; Kumobayashi, H.; Taketomi, T.; Takaya, H.; Miyashita, A.; Noyori, R.; Otsuka, S. *J. Am. Chem. Soc.* **1984**, *106*, 5208.



Scheme 2.

3. Tani, K.; Yamagata, T.; Tatsumo, Y.; Yamagata, Y.; Tomita, K.; Akutagawa, S.; Kumobayashi, H.; Otsuka, S. *Angew. Chem.* **1985**, *97*, 232; *Int. Ed. Engl.* **1985**, *24*, 217.
4. *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press, Inc.: Orlando, FL, 1985; Vol. 5.
5. Inoue, S.; Takaya, H.; Tani, K.; Otsuka, S.; Sato, T.; Noyori, R. *J. Am. Chem. Soc.* **1990**, *112*, 4897.
6. For mechanistic aspects of the isomerization of allylic substrates, see also: (a) Davies, S. G. *Organo–Transition Metal Chemistry: Applications To Organic Synthesis*; Pergamon: Oxford, 1982. (b) Noyori, R. *Asymmetric Catalysis In Organic Synthesis*; Wiley: New York, 1994. (c) Cornils, B.; Herrmann, W. A. *Applied Homogeneous Catalysis with Organometallic Compounds*; Vol. 2; Verlag Chemie: Weinheim, 1996.
7. Tani, K. *Pure Appl. Chem.* **1985**, *57*, 1845.
8. Botteghi, C.; Giacomelli, G. *Gazz. Chim. Ital.* **1976**, *106*, 1131.
9. The hydridic ruthenium complexes were prepared in situ from $Ru_2Cl_4diop_3$ or the respective dichloro precursor by treatment with sodium borohydride or hydrogen.[10,11]
10. Frauenrath, H.; Philipps, T. *Angew. Chem.* **1986**, *98*, 261; *Int. Ed. Engl.* **1986**, *25*, 274.
11. Frauenrath, H.; Kaulard, M. *Synlett* **1994**, 517.
12. Malanga, C.; Urso, A.; Lardicci, L. *Tetrahedron Lett.* **1995**, *36*, 1133.
13. In another report Menicagli et al. also stated, that $NiCl_2$dppe causes ring cleavage to give quantitative yields of an alcohol via a formal alkylation at C_2 of **1** by reaction with a Grignard reagent: Menicagli, R.; Malanga, C.; Finato, B; Lardicci, L. *Gazz. Chim. Ital.* **1989**, *119*, 69.
14. It is noteworthy, that the same results were obtained, when the diop-modified nickel complex was activated by the Grignard reagent either in the presence or without addition of trimethylsilyl chloride.
15. We also found, that the catalytic activity of nickel complexes in the isomerization of acyclic allylic substrates strongly depends on the chelate ring size of the catalyst: Wille, A.; Tomm, S.; Frauenrath, H. *Synthesis* **1998**, 305; see also: Trost, B. M.; Murphy, D. J. *Organometallics* **1985**, *4*, 1143.
16. At lower temperatures $NiCl_2$chiraphos exhibited no catalytic isomerization activity.
17. Taken in part from the PhD thesis of Carsten Wattenbach: Wattenbach, C.; Maurer, M.; Frauenrath, H. to be published.
18. Tanner, D.; Somfai, P. *Tetrahedron* **1986**, *42*, 5985; and references cited therein.
19. Barner, R.; Schmid, M. *Helv. Chim. Acta* **1979**, *62*, 2384.
20. (−)-Diop was purchased from Merck and prepared by standard methods. The diop used for these investigations had an optical rotation of $[\alpha]_D^{20}$ −11.3 (c=2; benzene). (−)-Chiraphos was purchased from Aldrich; optical rotation $[\alpha]_D^{20}$ −191 (c=1.5; $CHCl_3$). Super-Hydride® was purchased from Aldrich.
21. GC analyses were performed by using an OV1-CB-0.5 column (25 m, 0.25 mm ID). The ee values were determined by GC on a FS-CYCLODEX beta-I/P column (50 m, 0.25 mm ID). Supplier: CS-Chromatographie Sercice GmbH, Am Parir 27, D-52379 Langerwehe. Separation of the enantiomers of **2** (R=*tert*-butyl): carrier H_2, 80 kPa, 100°C isothermal; retention times 13.89 and 14.33 min. Separation of the enantiomers of **4** (R=*tert*-butyl): carrier H_2, 70 kPa, temperature program (60°C isothermal for 1 min, 2.5°C/min to 130°C); retention times 23.61 and 24.22 min.