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Tetrahedron Letters 44 (2003) 4969–4971

TETRAHEDRON
LETTERS

Enantioselective hydrogenation of itaconate using rhodium bihelicenol phosphite complex. Matched/mismatched phenomena between helical and axial chirality

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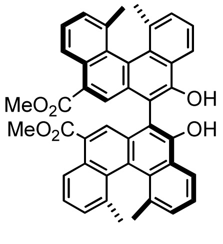
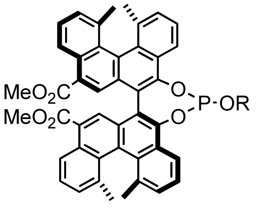
Received 14 April 2003; revised 8 May 2003; accepted 9 May 2003

Abstract—Phosphites prepared from bihelicenol, menthol (or 1-phenylethanol), and PCl_3 are effective ligands for the rhodium-catalyzed enantioselective hydrogenation of dimethyl itaconate. Stereochemistry of the helicene moiety plays an important role in the asymmetric induction, and matched/mismatched phenomena are observed between helical and axial chirality. © 2003 Elsevier Science Ltd. All rights reserved.

Helicenes are a group of aromatic compounds with helical structures. In spite of their unique chiral structure, they were rarely employed for ligands in asymmetric catalysis.[1] In view of successful achievement of 2,2′-binaphthol (binol) in asymmetric catalysis, we were interested in bihelicenols **1**, which are dimeric helicenols possessing helical and axial chirality. It was wondered whether **1** would be even a better ligand, because it should form a larger chiral pocket at the catalyst metal center. Also wondered was that **1** might exhibit different stereoselectivity between diastereomers. We previously reported the synthesis of all six isomers of bihelicenols (*M*,*M*,*S*)-**1**, (*M*,*M*,*R*)-**1**, (*P*,*P*,*S*)-**1**, (*P*,*P*,*R*)-**1**, (*P*,*M*,*S*)-**1**, and (*P*,*M*,*R*)-**1**.[2]



(*M,M,S*)-**1**



(*M,M,S*)-**2** (R = menthyl)
(*M,M,S*)-**3** (R = 1-phenylethyl)

Transition metal-catalyzed asymmetric hydrogenation is a highly efficient and practical way of producing optically pure organic compounds. Rhodium-catalyzed asymmetric hydrogenation of prochiral olefins has generally been conducted using bidentate phosphines. Monodentate phosphites,[3] however, have recently been shown to be excellent ligands by Pringle,[4] Reetz,[5] Feringa,[6] and Xiao.[7] They employed ligands derived from binol and an alcohol including chiral menthol or 1-phenylethanol, and showed that the enantiodiscrimination is controlled by the biaryl moiety and not the alcohol moiety.[5,7] Based on the studies, we started to investigate asymmetric hydrogenation of dimethyl itaconate **4** using phosphites **2** and **3** derived from **1**. A high selectivity was attained using (*M*,*M*,*S*,*l*)-**2** prepared from (*M*,*M*,*S*)-**1** and *l*-menthol, and matched/mismatched phenomena were observed between helical and axial chirality.

Phosphites **2** were conveniently synthesized from **1** and menthols (Table 1).[5,7,8] For example, the reaction of PCl_3 with 1 equiv. of *l*-(1*R*,2*S*,5*R*)-menthol in THF yielded *l*-menthyl phosphorodichloride, and the addition of the solution to (*M*,*M*,*S*)-**1** and triethylamine in THF at −78°C followed by warming to −20°C for 1 h afforded the phosphite (*M*,*M*,*S*,*l*)-**2** in 81% yield. 1-Phenylethanol derivatives **3** were also synthesized analogously.

The ligands thus obtained were used in the rhodium-catalyzed asymmetric hydrogenation of **4** (Table 2). The catalyst was formed in situ by treating $[Rh(cod)_2]BF_4$ (cod = 1,5-cyclooctadiene) (1 mol%) and (*M*,*M*,*S*,*l*)-**2** (3 mol%) in CH_2Cl_2, and **4** was hydrogenated with 90 atm

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0040-4039/03/$ - see front matter © 2003 Elsevier Science Ltd. All rights reserved.
doi:10.1016/S0040-4039(03)01183-3

Table 1. Synthesis of bihelicenol phosphites **2** and **3**

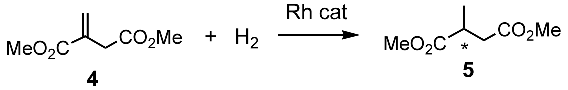
Phosphite	Yield (%)	$[\alpha]_D^{25}$ [a]	^{31}P NMR[b]
(*M*,*M*,*S*,*l*)-**2**	81	+603	139.6
(*M*,*M*,*S*,*d*)-**2**	82	+1014	153.4
(*M*,*M*,*R*,*l*)-**2**	82	+150	162.5
(*M*,*M*,*R*,*d*)-**2**	75	+160[c]	157.7
(*M*,*M*,*S*,*S*)-**3**	77	+1070	139.6
(*M*,*M*,*S*,*R*)-**3**	83	+958	141.2
(*M*,*M*,*R*,*S*)-**3**	78	+83	153.7
(*M*,*M*,*R*,*R*)-**3**	76	+95	150.9

[a] Optical rotation in $CHCl_3$ at the concentration of *c* 0.5.

[b] Chemical shift in $CDCl_3$ employing triphenylphosphate as external standard δ −18.0.

[c] At the concentration of *c* 0.25.

Table 2. Rh-catalyzed asymmetric hydrogenation of **4**[a]



Entry	Ligand	Temp. (°C)	Ee (%)[b]	Config.[c]
1	(*M*,*M*,*S*,*l*)-**2**	−78 to 20[d]	96	*S*
2		−78 to 20	90	*S*
3		20	77	*S*
4[e]		20	37	*S*
5	(*M*,*M*,*S*,*d*)-**2**	−78 to 20	85	*S*
6	(*M*,*M*,*R*,*l*)-**2**	−78 to 20	10	*R*
7	(*M*,*M*,*R*,*d*)-**2**	−78 to 20	1	*R*
8	(*M*,*M*,*S*,*S*)-**3**	20	77	*S*
9		−78 to 20	49	*S*
10[e]		20	53	*S*
11	(*M*,*M*,*S*,*R*)-**3**	20	73	*S*
12	(*M*,*M*,*R*,*S*)-**3**	20	37	*R*
13	(*M*,*M*,*R*,*R*)-**3**	20	54	*S*

[a] See Ref. 9 for experimental procedures. **5** was obtained in a quantitative yield.

[b] Ee was determined by GC using a chiraldex G-TA (30 m×0.25 mm) column.

[c] The absolute configuration was determined by the sign of optical rotation.

[d] Reacted at −78°C for 6 h, and then warmed to 20°C.

[e] Reacted with 40 atm of hydrogen.

hydrogen at −78°C for 6 h, which was followed by warming to 20°C for 18 h. Methylsuccinate (*S*)-**5** was obtained in a quantitative yield with 96% ee (entry 1). The selectivity compares favorably with those obtained with binol phosphites, and the same absolute configuration of **5** was obtained in regard to the axial chirality. The reaction was slower probably due to the narrower pocket of the rhodium complex with (*M*,*M*,*S*,*l*)-**2** than binol phosphite. When the mixture was immediately warmed from −78°C to 20°C, ee slightly lowered (entry 2). Enantioselectivity was reduced to 77% ee when reacted at 20°C (entry 3), and to 37% ee under 40 atm hydrogen (entry 4). Switching the ligand to (*M*,*M*,*S*,*d*)-**2** gave (*S*)-**5** in 85% ee (entry 5) indicating that (*M*,*M*,*S*)-bihelicenyl moiety is decisive for the stereoselectivity, and that the chirality of menthol is unimportant. In contrast, (*R*)-**5** was obtained in very low ee, when (*M*,*M*,*R*,*l*)-**2** or (*M*,*M*,*R*,*d*)-**2** was used (entries 6 and 7). The combination of (*M*)-helicene and (*S*)-axis of **2** represents the matched pair for this reaction.

Hydrogenation employing (*M*,*M*,*S*,*S*)-**3** under 90 atm hydrogen at 20°C gave (*S*)-**5** in 77% ee (entry 8). Enantioselectivity in this case lowered to 49% ee, when the reaction was conducted by warming from −78 to 20°C (entry 9). The higher pressure was again required for the higher ee (entry 10). Since use of (*M*,*M*,*S*,*R*)-**3** gave (*S*)-**5** in 73% ee (entry 11), the asymmetric induction is controlled by the (*M*,*M*,*S*)-bihelicenol moiety as was (*M*,*M*,*S*)-**2**. (*M*,*M*,*R*,*S*)-**3** and (*M*,*M*,*R*,*R*)-**3** gave **5** with lower ee (entries 12 and 13) exhibiting that (*M*)-helical and (*S*)-axial chirality of **3** are again the matched pair. It might be interesting to note that the diastereomers with larger $[\alpha]_D$ and higher field ^{31}P NMR chemical shifts exhibit higher selectivity for both **2** and **3** (Table 1). The mismatched case showed an interesting behavior: (*M*,*M*,*R*,*S*)-**3** and (*M*,*M*,*R*,*R*)-**3** gave enantiomeric **5**, in which the chirality of 1-phenylethanol moiety is important. Such phenomenon was not observed in the reactions using binol phosphites.

Catalytic hydrogenation of dimethyl itaconate **4** using $[Rh(cod)_2]BF_4$ and (*M*,*M*,*S*,*l*)-**2** results in full conversion and high ee. The stereochemistry at the helicene moiety plays an important role in the asymmetric induction, and (*M*)/(*S*) combination turned out to be the matched pair. It should be noted that the substitution of achiral naphthalene moiety of binol with the chiral helicene provides a method to fine-tune chiral environment of metal center for asymmetric catalysis.

Acknowledgements

This work was supported by grants from the Japan Society of Promotion of Science.

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9. Under an argon atmosphere, [Rh(cod)$_2$]BF$_4$ (4.0 mg, 0.01 mmol) and (*M*,*M*,*S*,*l*)-**2** (24 mg, 0.03 mmol) were added to degassed dichloromethane (5 mL), and the orange solution was stirred at room temperature for 5 min. In a stainless autoclave (50 mL) was added dimethyl itaconate **4** (158 mg, 1 mmol). An argon atmosphere was applied, and degassed dichloromethane (5 mL) was added. The rhodium complex solution was then added to the substrate solution in the autoclave, and the mixture was stirred for 1 min. Then, the solution was cooled to −78°C, and 90 atm of hydrogen was applied. The mixture was stirred for 6 h, and warmed to room temperature for 18 h. The gas was removed, and the solvents were evaporated under reduced pressure. After short silica gel column chromatography, bulb-to-bulb distillation gave (*S*)-**5** (158 mg, quant., 96% ee) as colorless oil.