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Transition Metal-catalyzed Asymmetric Vinylcyclopropane-Cyclopentene Rearrangements with Chiral Phosphine Ligands. Dramatic Solvent Effects on Asymmetric Induction

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A dramatic solvent effect was observed on the nickel-catalyzed asymmetric rearrangement of a cyclopropane system into an optically active cyclopentane derivative with chiral phosphine ligands. The stereochemistry of the product was readily controlled by selecting the catalyst, nickel or palladium, with extremely high enantioselectivity.

A transition metal-promoted carbon-carbon bond formation reaction$^{1)}$ is one of the useful tools for the stereoselective construction of complex organic structures and has recently received much attention in its stereoselectivity and stereospecificity.$^{2)}$

Thermal rearrangement of vinylcyclopropanes to cyclopentenes$^{3)}$ generally requires high reaction temperature, whereas transition metals such as nickel,$^{4)}$ palladium,$^{5)}$ rhodium,$^{6)}$ copper,$^{7)}$ molybdenum,$^{8)}$ chromium,$^{9)}$ and iron$^{10)}$ mediate the reactions to proceed under much milder reaction conditions. We wish to communicate herein a highly enantioselective asymmetric synthesis of a cyclopentane derivative by the nickel- or palladium-catalyzed asymmetric vinylcyclopropane-cyclopentene rearrangements with chiral phosphine ligands. We wish to report here also a dramatic solvent effect on the nickel-catalyzed asymmetric rearrangement and the enantioselection of the product controlled by the catalyst employed.

Upon treatment with a nickel catalyst, bis(cyclooctadiene)nickel [$Ni(COD)_2$], in the presence of a chiral phosphine ligand, a cyclopropane compound **1** resulted in facile conversion into an optically active cyclopentane derivative **2** in good yields with extremely high enantioselectivity, depending on solvents used. Effects of chiral ligands on the asymmetric induction were examined using (S)-(-)-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP), (4R,5R)-(-)-4,5-bis(diphenylphosphinomethyl)-2,2-dimethyl-1,3-dioxolane (DIOP), (4R,5R)-(+)-4,5-bis[bis(3,5-dimethylphenyl-4-methoxy)phosphinomethyl]-2,2-dimethyl-1,3-dioxolane (MOD-DIOP), and neomenthyldiphenyphosphine (NMDPP). The enantiomeric excess of **2** was calculated on the basis of the optical rotation ($[\alpha]_D$-158.4°(MeOH)) of optically pure (R)-(-)-**2,** which was determined by the NMR spectral analysis with a shift reagent, tris[3-(2,2,2-trifluoro-1-hydroxyethylidene)-*d*-camphorato]europium [$Eu(tfc)_3$]. Some of the results obtained are listed in Table 1. The chiral phosphines (+)-MOD-DIOP and (-)-BINAP served as extremely efficient ligands in the nickel-catalyzed reactions to give (R)-(-)-**2** in very high optical yields (84-90%), whereas the phosphine (-)-DIOP was less effective on the asymmetric induction, as shown in Table 1. Among the solvents examined, the nickel-catalyzed reaction was executed at room temperature successfully in dimethyl sulfoxide (DMSO), N,N-dimethylformamide (DMF), 1,2-dimethoxyethane (DME), and tetrahydrofuran (THF) except for benzene, however heating at 50 °C was required in acetonitrile. Dramatic solvent effects were

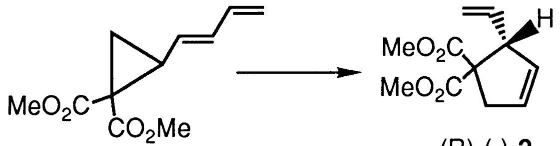
Table 1. The Nickel-catalyzed Asymmetric Rearrangements of **1** with Chiral Phosphine Ligands

Ligands	Solvent	Reaction conditions[a)]			Product **2**	
		Temp /°C	Time/h	Yields/%	$[\alpha]_D$/°(MeOH)	e.e./%[b)]
(-)-MOD-DIOP	DMSO	r.t.	4	77	-144.0	90
	CH_3CN	50	5	63	-108.0	68
	Benzene	r.t.	12	20	-5.0	3
	DMF	r.t.	12	66	-7.2	4
	DME	r.t.	12	71	-4.2	2
	THF	r.t.	12	56	-1.2	1
	THF-DMSO (10:1)	r.t.	12	67	-120.1	75
	THF-DMSO (100:1)	r.t.	12	57	-12.3	8
	THF-$DMSO_2$ (10:1)	r.t.	12	50	-1.4	1
(-)-DIOP	DMSO	r.t.	2	76	-2.6	2
(-)-BINAP	DMSO	r.t.	4	96	-133.9	84
	CH_3CN	50	4	50	-123.0	77

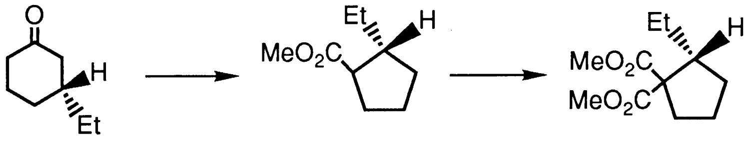
a) The compound **1** was treated with $Ni(COD)_2$ (0.15 equiv.) in the presence of the chiral ligands (0.2 equiv.).
b) The enantiomeric excess (e.e.) of **2** was determined on the basis of the optical rotation observed.

observed on the chemical yields and the enantioselectivity in this nickel-catalyzed reaction of **1**. The nickel-(+)-MOD-DIOP-catalyzed reactions in benzene, DMF, DME, and THF at room temperature provided (R)-(-)-**2** with exteremely low enantiomeric excess (1-4%). However, the highest optical yield (90%) of (R)-(-)-**2** was obtained in the nickel-(+)-MOD-DIOP-catalyzed reaction on the use of DMSO as a solvent. The optical yield decreased with the increasing dilution ratio of THF in DMSO. Use of dimethyl sulfone ($DMSO_2$) in THF (THF-$DMSO_2$ 10:1), instead of DMSO, was not effective on the asymmetric induction, leading to (R)-(-)-**2** in 50% yield with very low enantiomeric excess. The reaction in THF-dimethyl sulfide (100:1) at room temperature gave no rearranged product.

Stereochemical studies on the transition metal-catalyzed reactions of the cyclopropane system **1** were carried out employing various kinds of other transition metal catalysts such as tetrakis(triphenylphoshine)-palladium [$Pd(PPh_3)_4$], hexacarbonylmolybdenum [$Mo(CO)_6$], hexacarbonylchromium [$Cr(CO)_6$], hexacarbonyltungusten [$W(CO)_6$], and tetrakis(triphenylphosphine)platinum [$Pt(PPh_3)_4$]. Some of the results obtained are listed in Table 2. In contrast to the afore-mentioned nickel-catalyzed reactions, the palladium-catalyzed reactions of **1** in the presence of the chiral phosphines described above led to smooth formation of (S)-(+)-**2** in good yields with rather low enantiomeric excess. In the case of the platinum and molybdenum catalysts, heating at 50-110 °C in DMSO or acetonitrile was required to complete the rearrangement of **1** in the presence of (+)-MOD-DIOP and (-)-BINAP, producing (R)-(-)-**2** with rather low enantiomeric excess. Positive solvent



1 (R)-(-)-**2**



(R)-(+)-**3** (R)-(-)-**4** (R)-(-)-**5**

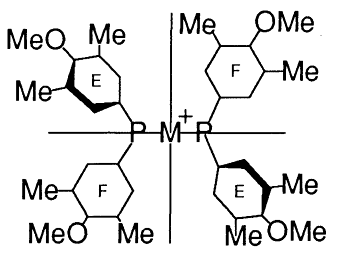
Table 2. The Transition Metal-catalyzed Asymmetric Rearrangements of **1** with Chiral Phosphine Ligands

Catalysts	Ligands	Solvent	Reaction conditions[a)] Temp /°C	Time/h	Yields/%	Product **2** [α]$_D$/°(MeOH)	e.e./%[b)]
Pd(PPh$_3$)$_4$	(+)-MOD-DIOP	DMSO	r.t.	2	100	+3.0	2
	(-)-DIOP	DMSO	r.t.	6	72	+32.5	21
		CH$_3$CN	50	5	68	+16.7	10
	(-)-BINAP	DMSO	r.t.	2	68	+64.4	40
		CH$_3$CN	r.t.	6	52	+20.5	13
	NMDPP	DMSO	r.t.	4	65	+50.0	31
		CH$_3$CN	50	4	50	+2.3	1
Pt(PPh$_3$)$_4$	(+)-MOD-DIOP	CH$_3$CN	80	12	87	-27.2	17
	(-)-BINAP	DMSO	110	12	69	-4.6	3
		CH$_3$CN	50	24	52	-4.2	3
Mo(CO)$_6$	(+)-MOD-DIOP	DMSO	110	12	37	-43.2	27
		CH$_3$CN	80	12	10	-9.2	6
	(-)-BINAP	DMSO	50	12	43	-47.0	30

a) The compound **1** was treated wih the catalysts (0.15 equiv.) in the presence of the chiral ligands (0.2 equiv.).
b) The enantiomeric excess (%) of **2** was determined on the basis of the optical rotation observed.

effects by DMSO on the asymmetric induction were observed also in the palladium- and molybdenum-catalyzed reactions. The chromium- or tungusten-catalyzed reactions of **1** in DMSO did not work well, eventhough under heating at 110 °C, resulting in a very poor yield (2-6%) of (R)-(-)-**2** with low enantiomeric excess. The cobalt-, rhodium-, and ruthenium-catalyzed reactions of **1** at 80-90 °C in DMSO or acetonitrile gave no rearranged product.

The absolute configuration of the product **2** was determined as follows. Oxidative ring contraction of (R)-(+)-3-ethylcyclohexanone (**3**) ([α]$_D$+4.2°(MeOH))[11)] with selene oxide-hydrogen peroxide in refluxing pyridine followed by esterification afforded (R)-**4** ([α]$_D$-21.1°(MeOH)).[12)] α-Methoxycarboxylation of the ester (R)-**4** thus obtained with methyl chloroformate was carried out in THF at -78 °C for 4 h in the presence of LDA, giving (R)-(-)-**5** ([α]$_D$-12.9°(MeOH), 59% e.e.). The Raney Ni-catalyzed hydrogenation of (R)-(-)-**2** ([α]$_D$ -105°(MeOH), 68% e.e.) obtained above gave (R)-(-)-**5** ([α]$_D$-14.4°(MeOH), 68% e.e.). Thus the absolute configuration of the product **2** obtained by the afore-mentioned nickel-catalyzed asymmetric synthesis was determined as (R)-(-)-**2**.



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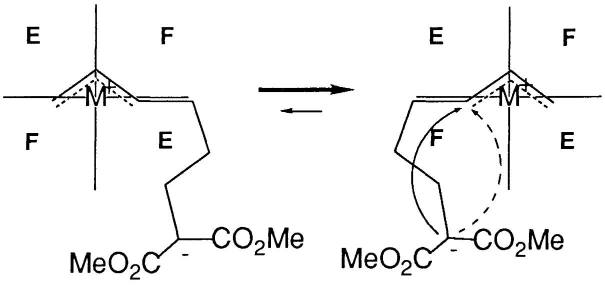

7a M=Ni, Pd, Pt, Cr, Mo, W **7b**

The mechanism for the asymmetric induction in the metal-(+)-MOD-DIOP-catalyzed reactions is rationalized as follows. The steric environment of the (+)-MOD-DIOP-metal complex is shown in **6** using the abbreviations, E (the edge of the phenyl ring) and F (the face of the phenyl ring). The cyclopropane ring in **1** would be dissected by the reaction with the transition metals, forming chiral π-allylmetallic complexes **7** in which the phospine groups in (+)-MOD-DIOP are chelated to the metals. The bulky ester part of the allylic substrate derived from **1** would be orientated in the most sterically preferred space (F) of the chiral pocket[13)] formed by the chelation of the chiral phosphine ligand (+)-MOD-DIOP to the transition metals, affording **7b,** not **7a** because of the rather severe steric hindrance between the ester part and the edge of the phenyl ring in **7a**. The carbanion in the intermediate **7b** would attack to the reaction site at the π-allylmetallic complex from the opposite direction to the metals in the case of the palladium, or from the same direction as the metal in the case of other transition metals (the nickel, platinum, molybdenum, chromium, and tungustem catalysts), presumably through the coordination of the carbanion to the transition metal catalyst, producing (S)-(+)-**2** or (R)-(-)-**2**, respectively. The sulfinyl function of DMSO would participate in these transition metal-catalyzed asymmetric reactions presumably by the direct coordination to the metal catalysts or the solvation.

In conclusion, as we have pointed out in this communication, it should be marked that the sulfinyl function played an important role for induction of new chirality with high efficiency in the nickel-catalyzed asymmetric rearrangements of a cyclopropane system **1** with chiral phosphine ligands (+)-MOD-DIOP and (-)-BINAP. Furthermore, it seems synthetically useful that the selection of the catalyst, $Ni(COD)_2$ or $Pd(PPh_3)_4$ could readily control the stereochemistry of the product, producing an optically active cyclopentane derivative **2** of (R)- or (S)-configuration, respectively. This method provides a facile entry to optically active cyclopentane derivatives which are expected to be synthetically useful chiral intermediates for attractive five-membered natural products.

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