(92%) of alcohol, pure by ^{1}HMR analysis with $[\alpha]^{25}_D$ −104° (c 4.4, $CHCl_3$).

(−)-*cis*-Bicyclo[3.3.0]octan-2-one (3). The alcohol obtained above was oxidized with Cr^{6+} by using the procedure of Ratcliffe.[6] From 41 mg of alcohol was obtained 36 mg (90%) of the ketone (−)-3, pure by spectral (^{1}HMR) and VPC (25% Carbowax on Chromasorb P, 150 °C) analyses: $[\alpha]^{25}_D$ −105° (c 3, $CHCl_3$); ORD α^{25} (λ, nm) −33.3° (450), −53.3° (400), −100° (350), −227° (318), 0° (291), +40° (280).

(6) Ratcliffe, R.; Rodehorst, R. *J. Org. Chem.* **1970**, *35*, 4000.

Acknowledgment. We are grateful to the National Institutes of Health (Grant No. CA 21852), the Robert A. Welch Foundation (Grant No. F-626), and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for financial support of the research.

Registry No. (±)-1, 85665-20-9; (+)-1, 85717-55-1; (−)-1, 85717-56-2; (−)-1·(−)-α-phenethylamine, 85760-67-4; (+)-3, 85717-57-3; (−)-3, 85717-59-5; (±)-4, 68317-62-4; (−)-4, 71048-52-7; (−)-4 (dihydro), 85717-58-4; (−)-5, 85665-21-0.

Chiral (β-Aminoalkyl)phosphines. Highly Efficient Phosphine Ligands for Catalytic Asymmetric Grignard Cross-Coupling[1]

Tamio Hayashi, Mitsuo Konishi, Motoo Fukushima, Koichi Kanehira, Takeshi Hioki, and Makoto Kumada*

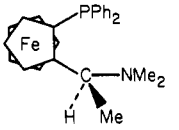
Department of Synthetic Chemistry, Faculty of Engineering, Kyoto University, Kyoto 606, Japan

Received October 27, 1982

New chiral (β-aminoalkyl)phosphines, $RCH(NMe_2)CH_2PPh_2$ [R = Me (Alaphos), *i*-Bu (Leuphos), $PhCH_2$ (Phephos), *i*-Pr (Valphos), *sec*-Bu (Ilephos), Ph (PhGlyphos), *c*-Hex (ChGlyphos), and *t*-Bu (*t*-Leuphos)], were prepared by starting with optically active amino acids. The phosphines were used as ligands for nickel-catalyzed asymmetric cross-coupling of 1-arylethyl Grignard reagents (ArMeCHMgCl) with vinyl bromide. Coupling products of over 70% enantiomeric excess (ee) were obtained in the reaction with the ligand Phephos, Valphos, Ilephos, PhGlyphos, ChGlyphos, or *t*-Leuphos. A mechanism involving complexation of the magnesium atom in the Grignard reagent with the amino group on the (β-aminoalkyl)phosphine ligand is proposed to account for the high stereoselectivity. The asymmetric cross-coupling was applied to the synthesis of optically active 2-arylpropionic acids.

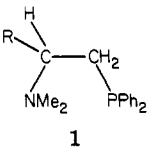
Asymmetric carbon–carbon bond-forming reactions are of great significance for the synthesis of optically active compounds, and the use of chiral transition-metal catalysts for such reactions has recently attracted considerable attention owing to a number of advantages of catalytic asymmetric synthesis.[2] Asymmetric cross-coupling of secondary alkyl Grignard reagents with alkenyl halides[3,4] has been effected by chiral phosphine–nickel or –palladium catalysts and is now recognized to provide an efficient route to the synthesis of optically active olefins, which could hardly be obtained by other methods.

Previously, we have shown[3a,b] that chiral [(aminoalkyl)ferrocenyl]phosphines, represented by (*S*)-*N*,*N*-dimethyl-1-[(*R*)-2-(diphenylphosphino)ferrocenyl]ethylamine [(*S*)-(*R*)-PPFA], are effective ligands for asymmetric



(*S*)-(*R*)-PPFA

cross-coupling. 3-Phenyl-1-butene (68% ee) was produced in the reaction of 1-phenylethylmagnesium chloride with vinyl bromide. Results obtained for the cross-coupling by using various kinds of modified ferrocenylphosphine ligands have proved that the amino group on the phosphine ligand is the first requisite for high stereoselectivity and that the surroundings around the nitrogen atom exert a strong effect on the stereoselectivity. On the basis of these data, we have devoted attention to the design and preparation of new phosphine ligands of higher ability for asymmetric cross-coupling. We have arrived at (β-aminoalkyl)phosphines (1) which seem to fulfull the nec-



1

essary conditions mentioned above and could be readily prepared from amino acids. Use of amino acids as optically active starting compounds is convenient because amino acids with various substitutents are readily available in an optically pure form. In this paper, we report the preparation of the (β-aminoalkyl)phosphines and their use for asymmetric Grignard cross-coupling. Application of the

(1) Part of this paper appeared previously: Hayashi, T.; Fukushima, M.; Konishi, M.; Kumada, M. *Tetrahedron Lett.* **1980**, *21*, 79.

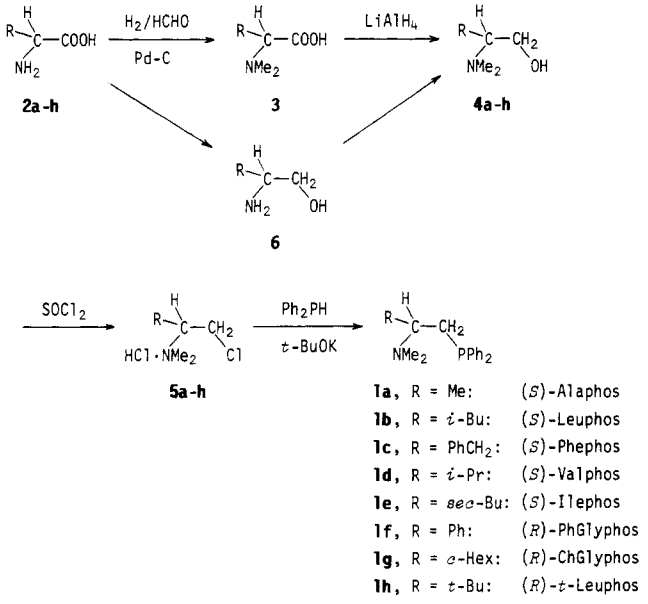
(2) For reviews: (a) Kagan, H. B.; Fiaud, J. C. *Top. Stereochem.* **1978**, *10*, 175. (b) Bosnich, B.; Fryzuk, M. D. *Ibid.* **1981**, *12*, 119.

(3) (a) Hayashi, T.; Konishi, M.; Fukushima, M.; Mise, T.; Kagotani, M.; Tajika, M.; Kumada, M. *J. Am. Chem. Soc.* **1982**, *104*, 180. (b) Hayashi, T.; Tajika, M.; Tamao, K.; Kumada, M. *Ibid.* **1976**, *98*, 3718. (c) Hayashi, T.; Konishi, M.; Hioki, T.; Kumada, M.; Ratajczak, A.; Niedbała, H. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 3615. (d) Hayashi, T.; Nagashima, N.; Kumada, M. *Tetrahedron Lett.* **1980**, *21*, 4623. (e) Tamao, K.; Hayashi, T.; Matsumoto, H.; Yamamoto, H.; Kumada, M. *Ibid.* **1979**, 2155. (f) Tamao, K.; Yamamoto, H.; Matsumoto, H.; Miyake, N.; Hayashi, T.; Kumada, M. *Ibid.* **1977**, 1389. (g) Brunner, H.; Pröbster, M. *J. Organomet. Chem.* **1981**, *209*, C1. (h) Consiglio, G.; Piccolo, O.; Morandini, F. *Ibid.* **1979**, *177*, C13. (i) Kiso, Y.; Tamao, K.; Miyake, N.; Yamamoto, K.; Kumada, M. *Tetrahedron Lett.* **1974**, 3. (j) Consiglio, G.; Botteghi, C. *Helv. Chim. Acta* **1979**, *56*, 460.

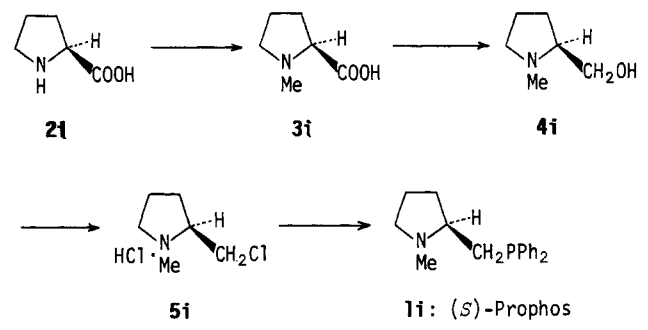
(4) For a review see: Hayashi, T. In "Asymmetric Reactions and Processes in Chemistry"; Eliel, E. L., Otsuka, S., Eds.; American Chemical Society: Washington, D.C., 1982; ACS Symp. Ser. No. 185, Chapter 12.

0022-3263/83/1948-2195$01.50/0

Scheme I



Scheme II

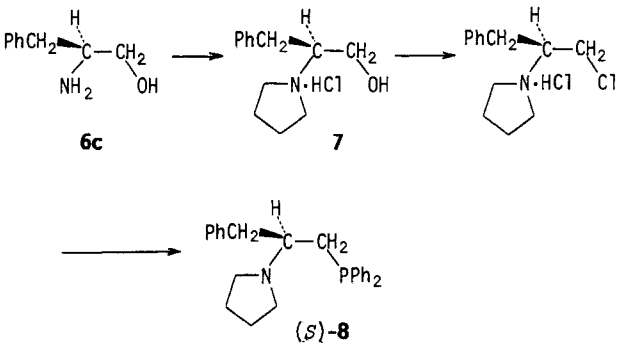


cross-coupling to the asymmetric synthesis of 2-arylpropionic acids is also described.

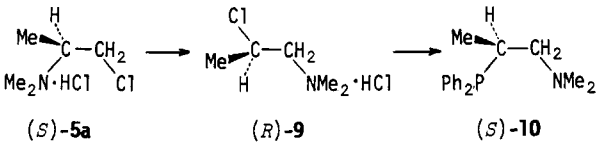
Results and Discussion

Synthesis of (β-Aminoalkyl)phosphines. The (β-aminoalkyl)phosphines (**1**) were prepared by a sequence of reactions (Schemes I and II) starting with amino acids **2**, viz., (*S*)-alanine (**2a**), (*S*)-leucine (**2b**), (*S*)-phenylalanine (**2c**), (*S*)-valine (**2d**), (*S*)-isoleucine (**2e**), (*R*)-phenylglycine (**2f**), (*R*)-cyclohexylglycine[5] (**2g**), (*R*)-*tert*-leucine[6] (**2h**), and (*S*)-proline (**2i**). N-Methylation of **2** by reductive condensation with formaldehyde and hydrogen in the presence of Pd/C[7] gave dimethylamino acids **3**, which were converted by reduction with lithium aluminum hydride in THF[8] to β-(dimethylamino)alkyl alcohols **4**. In cases in which amino acids have larger substituents (**2c,f,g**), the alcohols **4** were more conveniently obtained by reduction of amino acids **2** or their esters followed by N-methylation with formaldehyde and formic acid. The alcohols **4** were converted by treatment with hydrogen chloride and thionyl chloride in chloroform to β-(dimethylamino)alkyl chloride hydrochlorides **5**. According to the procedure reported by Whitesides,[9] **5** was treated with diphenylphosphine (1.0 equiv) and potassium *tert*-butoxide (2.0–2.5 equiv) in THF. [β-(Dimethylamino)alkyl]diphenylphosphines **1** were obtained in moderate to high yields except for the phosphines from **2f** and **2g**. In the reaction of **5f** (R = Ph), the elimination of hydrogen chloride, producing acetophenone after hydrolysis, was found to proceed as a side reaction, lowering the yield of the phosphine **1f**. The new phosphine ligands are named after the abbreviations of the starting amino acids. Thus, the phosphine **1a** prepared from (*S*)-alanine is named (*S*)-Alaphos. Likewise, **1b–h** are named Leuphos, Phephos, Valphos, Ilephos, PhGlyphos, ChGlyphos, and *t*-Leuphos, respectively. These phosphines are 100% optically pure except for the phosphine **1h** (R = *t*-Bu), which was prepared by starting with *tert*-leucine (**2h**) of 88% ee and considered to have the same optical purity though the attempts to check the optical purity of **1h** were unsuccessful.

Scheme III



Scheme IV



A similar sequence of reactions starting with (*S*)-proline (**2i**) gave the chiral phosphine with the pyrrolidine five-membered ring, (*S*)-Prophos[10] (**1i**), for which the preparation and application to asymmetric hydroformylation have been reported.[11]

(β-Aminoalkyl)phosphine **8** containing the pyrrolidino group instead of the dimethylamino group could be also prepared via the β-pyrrolidinoalkyl alcohol **7**, which was obtained by reaction of **6c** with 1,4-dibromobutane[12] (Scheme III).

All the (β-aminoalkyl)phosphines mentioned above have a chiral carbon center at the amino substituents. Preparation of the phosphine with a chiral carbon center at the diphenylphosphino group was achieved by thermal rearrangement of (*S*)-2-(dimethylamino)-1-chloropropane hydrochloride (**5a**) to (*R*)-2-chloro-1-(dimethylamino)propane hydrochloride (**9**) followed by phosphination with diphenylphosphine and potassium *tert*-butoxide (Scheme IV). The absolute configuration of the phosphine **10** is assigned to be *S* by considering that both steps proceed with inversion. The enantiomeric purity of (*S*)-**10** ($[\alpha]^{25}_D$ −18° (*c* 1.0, benzene)) obtained here was determined to be around 27% by the ^1H NMR spectra of its phosphine oxide

(5) Eisler, K.; Rudinger, J.; Sorm, F. *Collect. Czech. Chem. Commun.* **1966**, *31*, 4563.
(6) Hashimoto, S.; Yamada, S.; Koga, K. *J. Am. Chem. Soc.* **1976**, *98*, 7450 and references cited therein.
(7) Bowman, R. E.; Stroud, H. H. *J. Chem. Soc.* **1950**, 1342.
(8) Vogl, O.; Pöhm, M. *Monatsh. Chem.* **1952**, *83*, 541.
(9) (a) Wilson, M. E.; Nuzzo, R. G.; Whitesides, G. M. *J. Am. Chem. Soc.* **1978**, *100*, 2269. (b) Nuzzo, R. G.; Haynie, S. L.; Wilson, M. E.; Whitesides, G. M. *J. Org. Chem.* **1981**, *46*, 2861.
(10) Though "prophos" has been used as an abbreviation of 1,2-bis(diphenylphosphino)propane, we call the phosphine **1i** "Prophos" in this paper.
(11) Ogata, I.; Mizukami, F.; Ikeda, Y.; Tanaka, M. Japanese Koai 76 43754; *Chem. Abstr.* **1976**, *85*, 124144; Japanese Kokai 76 39662; *Chem. Abstr.* **1976**, *85*, 124143.
(12) Abbott, D. J.; Colonna, S.; Stirling, C. J. M. *J. Chem. Soc., Perkin Trans. 1* **1976**, 492.

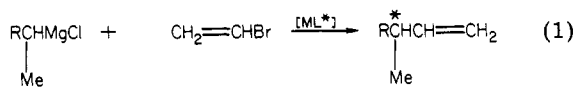
Table I. Asymmetric Cross-Coupling of Grignard Reagents 11 with Vinyl Bromide[a]

entry	Grignard reagent	chiral catalyst[b]	product (yield, %)[c]	$[\alpha]^{22}_D$ (neat), deg	% ee[d] (confign)
1	11a	$NiCl_2$/(S)-Alaphos (1a)	12a (>95)	+2.25	38 (S)
2	11a	$NiCl_2$/(S)-Leuphos (1b)	12a (>95)	+3.34	57 (S)
3	11a	$NiCl_2$/(S)-Phephos (1c)	12a (>95)	+4.19	71 (S)
4	11a	$NiCl_2$/(S)-Valphos (1d)	12a (>95)	+4.78	81 (S)
5	11a	$NiCl_2$/(S)-Valphos (1d)	12a (88)[e]	+4.30	72 (S)
6	11a	$NiCl_2$/(S)-Ilephos (1e)	12a (>95)	+4.78	81 (S)
7	11a	$NiCl_2$/(R)-PhGlyphos (1f)	12a (>95)	−4.11	70 (R)
8	11a	$NiCl_2$/(R)-ChGlyphos (1g)	12a (>95)	−4.55	77 (R)
9	11a	$NiCl_2$/(R)-t-Leuphos (1h)[f]	12a (>95)	−4.92	83 (R) (94)[g]
10	11a	$NiCl_2$/(S)-Prophos (1i)	12a (86)	−1.41	24 (R)
11	11a	$NiCl_2$/(S)-8	12a (70)	+2.96	50 (S)
12	11a	$NiCl_2$/(S)-10[h]	12a (>95)	−0.40	7 (R) (25)[g]
13	11a	$PdCl_2$[(S)-Alaphos(1a)]	12a (53)[i]	+0.30	5 (S)
14	11a	$PdCl_2$[(S)-Phephos(1c)]	12a (83)[i]	+3.28	55 (S)
15	11a	$PdCl_2$[(S)-Valphos(1d)]	12a (82)[i]	+2.00	34 (S)
16	11a	$NiCl_2$/(S)-Valphos (1d)	j (69)[k]	−30.5[l]	58 (S)
17	11b	$NiCl_2$/(S)-Valphos (1d)	12b (94)[k]	+6.78	83 (S)
18	11c	$NiCl_2$/(S)-Valphos (1d)	12c (88)[k]	+7.41[m]	72 (S)
19	11c	$NiCl_2$/(R)-ChGlyphos (1g)	12c (85)[k]	−7.83[m]	76[n] (R)
20	11d	$NiCl_2$/(S)-Valphos (1d)	12d (45)	−0.83[o]	6 (R)

[a] The reaction was carried out in ether at 0 °C for 2 days. RMeCHMgCl (11)/CH_2=CHBr/catalyst ratio of 2.0/1.0/5 × 10^{-3}. [b] Nickel catalysts were prepared in situ by mixing nickel chloride with 1 equiv of ligands. [c] Yields based on vinyl bromide used were determined by GLC. Isolated yields were usually over 70%. [d] Calculated on the basis of values for the optically pure compounds: (R)-12a, $[\alpha]^{22}_D$ −5.91° (neat);[3a] (R)-(E)-1,3-diphenyl-1-butene, $[\alpha]^{20}_D$ +52.9° (c 3, benzene);[3a] (R)-12b, $[\alpha]^{22}_D$ −8.15° (neat);[3e] (R)-12c (95% ee), $[\alpha]^{25}_D$ −9.83° (neat);[33] (S)-12d, $[\alpha]^{20}_D$ +14.6° (neat).[3a] [e] PhMeCHMgCl (11a)/CH_2=CHBr ratio of 1.0/2.0. The yield is based on 11a used. [f] Prepared from (R)-tert-leucine of 88% ee. [g] Optical yields corrected for the optical purity of the phosphine ligand used. [h] The phosphine 10 is 27% optically pure. [i] Styrene (>15%) was formed as a byproduct. [j] Reaction with (E)-β-bromostyrene at 0 °C for 24 h. [k] Isolated yields. [l] $[\alpha]^{20}_D$ (c 3, benzene). [m] $[\alpha]^{25}_D$ (neat). [n] This sample of 12c was converted into methyl 2-(2-naphthyl)propionate by oxidation ($NaIO_4$/$KMnO_4$) followed by treatment with diazomethane. ^{1}H NMR of the ester in the presence of Eu(dcm)$_3$ showed that the enantiomeric purity was 83%. [o] $[\alpha]^{20}_D$ (neat).

in the presence of Eu(dcm)$_3$.[13] These data are in good agreement with Kagan's recent report[14] that optically pure (R)-10 prepared from the (S)-lactamide has $[\alpha]_D$ +74.1° (c 1.34, benzene).

Asymmetric Grignard Cross-Coupling. The (β-aminoalkyl)phosphines were examined for their stereoselectivity as chiral ligands in the cross-coupling of 1-phenylethylmagnesium chloride (11a) with vinyl bromide producing 3-phenyl-1-butene (12a). Cross-coupling of 1-(p-tolyl)ethyl, 1-(2-naphthyl)ethyl, and 2-octyl Grignard reagents (11b,c,d) was also carried out by using some of the (β-aminoalkyl)phosphine ligands (eq 1). The reaction



(1)

11a, R = phenyl
b, R = p-tolyl
c, R = 2-naphthyl
d, R = n-hexyl

12a-d

conditions and results are summarized in Table I. The chiral catalyst used here (0.5 mol %) is the nickel complex prepared in situ by mixing nickel chloride and the ligand in a 1:1 ratio or the isolated palladium complex $PdCl_2L^*$ where both the phosphorus and nitrogen atoms in the aminophosphine L* are bonded to the palladium to form a chelate ring.[15]

Table I contains the following significant features. (1) The coupling product 12a of high optical purity was obtained when Phephos (1c), Valphos (1d), Ilephos (1e), PhGlyphos (1f), ChGlyphos (1g), or t-Leuphos (1h) was used as a ligand of the nickel catalyst (entries 3–9). The stereoselectivity of over 70% achieved here is among the highest for the asymmetric cross-coupling of the 1-phenylethyl Grignard reagent,[3,16] much higher than that reported with 1,2-bis(diphenylphosphino)propane[1] or 2,3-O-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane.[3i,j] In the reaction with t-Leuphos (1h), the selectivity corrected for the optical purity of the phosphine ligand was 94%. Optical purity of the coupling product was not largely affected by the ratio of 11a to vinyl bromide (entries 4 and 5), as has been previously reported in the reaciton with ferrocenylphosphine ligands.[3a] (2) The phosphines with the S configuration (1a–e) led to the product 12a with the S configuration while those with the R configuration (1f–h) led to the product with the R configuration (entries 1–9). The exception is (S)-Prophos (1i) which has a cyclic structure and hence different surroundings around the nitrogen atom from those of the others. (3) The phosphine ligand with the larger substituent at the chiral carbon atom induced the higher stereoselectivity; that is, the order of efficiency for asymmetric induction is 1h (R = t-Bu) > 1d (R = i-Pr) ≃ 1e (R = sec-Bu) ≃ 1g (R = c-Hex) > 1c (R = $PhCH_2$) ≃ 1f (R = Ph) > 1b (R = i-Bu) > 1a (R = Me) (entries 1–9). (4) Lower stereoselectivity was observed in the reaction with 10 than with 1a (entries 1 and 12). This indicates that the ligand with a chiral carbon center at the dimethylamino group is more effective than that with a chiral carbon center at the diphenylphosphino group. (5)

(13) McCreary, M. D.; Lewis, D. W.; Wernick, D. L.; Whitesides, G. M. *J. Am. Chem. Soc.* **1974**, *96*, 1038.
(14) Kagan, H. B.; Fiaud, J. C.; Hoornaert, C.; Meyer, D.; Poulin, J. C. *Bull. Soc. Chim. Belg.* **1979**, 923.
(15) The chelation is demonstrated by the NMR spectra which show the presence of inequivalent methyl groups on the nitrogen.
(16) Recently we have found that asymmetric cross-coupling of α-(trimethylsilyl)benzylmagnesium bromide gave optically active allylsilanes of up to 95% ee and that use of 1-phenylethylzinc reagents instead of the Grignard reagent for the cross-coupling by PPFA–palladium catalyst increased the stereoselectivity to 86%. See: Hayashi, T.; Konishi, M.; Ito, H.; Kumada, M. *J. Am. Chem. Soc.* **1982**, *104*, 4962. Hayashi, T.; Hagihara, T.; Katsuro, Y.; Kumada, M. *Bull. Chem. Soc. Jpn.*, in press.

Table II. Asymmetric Synthesis of 2-Arylpropionic Acids 16[a]

Grignard reagent	chiral ligand	ArMeCHCH=CH$_2$ (15) yield, %	ArMeCHCH=CH$_2$ (15) $[\alpha]^{20}_D$ (neat), deg	ArMeCHCOOH (16) yield, %	ArMeCHCOOH (16) $[\alpha]^{20}_D$[b] (95% EtOH), deg	ArMeCHCOOH (16) % ee[c] (confign)
14a	(S)-Valphos (1d)	81	+5.66	60	−34.0	80[d] (R)
14a	(R)-ChGlyphos (1g)	75	−5.74	62		79 (S)
14a	(R)-t-Leuphos (1h)	49	−5.84	62	+36.2	83 (S) (94)[e]
14b	(S)-Valphos (1d)			61[f]	−24.4	82[g] (R)
14b	(R)-ChGlyphos (1g)			64[f]	+17.4	82 (S)
14b	(R)-t-Leuphos (1h)			59[f]	+14.9	79 (S) (90)[e]

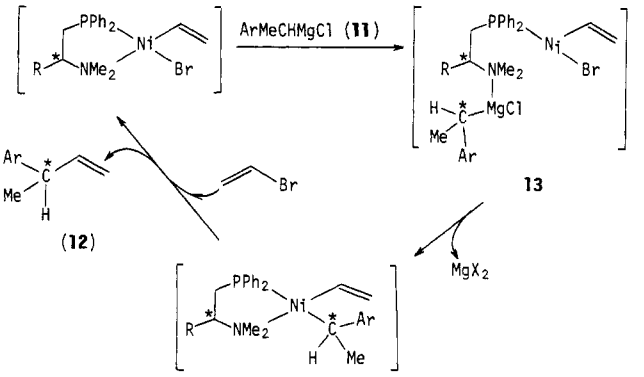
[a] Cross-coupling was carried out in ether at 0 °C for 2 days. ArMeCHMgCl (14)/CH$_2$=CHBr/ligand/NiCl$_2$ ratio of 2.0/1.0/0.01/0.01. [b] Optically pure (S)-16a has been reported to have $[\alpha]^{25}_D$ +60° (95% EtOH).[20] [c] Determined by ^{1}H NMR of methyl esters of 16 in the presence of Eu(dcm)$_3$. The signal of the methyl ester of the S isomers appeared at higher field than that of the R isomers. [d] Methyl 2-(4-isobutylphenyl)propionate has $[\alpha]^{20}_D$ −49.0° (c 1.82, benzene). [e] Corrected for the optical purity of t-Leuphos (88%). [f] Overall yields calculated on the basis of vinyl bromide. [g] Methyl 2-(4-biphenylyl)propionate has $[\alpha]^{20}_D$ −52.7° (c 2.06, benzene).

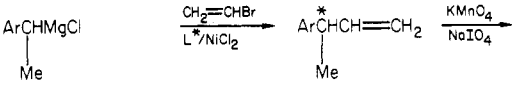
The ligand 8 which has the pyrrolidino group instead of the dimethylamino group showed a little lower selectivity than Phephos (1c) (entry 11). The effect of steric bulkiness of the dialkylamino groups on the stereoselectivity remains to be clarified. (6) Use of palladium catalysts lowered both the stereoselectivity and the yield of the coupling product 12a (entries 13–15). The low yield of 12a is ascribed to the side reaction forming styrene. The interrelation between a decrease in stereoselectivity and an increase in the formation of styrene has been rationalized by a mechanism involving racemization by β-hydride elimination on a diorganometal intermediate at the key step.[3a,17] (7) The (β-aminoalkyl)phosphines were also effective for the reaction of 11b and 11c (entries 17–19). The product 12b is a useful synthetic precursor of optically active α-curcumene.[3e] While the 1-arylethyl Grignard reagents (11a–c) gave the products of high optical purity, the (β-aminoalkyl)phosphines were not effective for 2-octylmagnesium chloride (11d) (entry 20).

The features described in 1–4 clearly demonstrate that the dimethylamino group in the phosphine ligands is playing an important role in the present asymmetric Grignard cross-coupling. The plausible mechanism is shown in Scheme V, which is analogous to that proposed for the asymmetric cross-coupling with chiral [(aminoalkyl)ferrocenyl]phosphines[3a] and appears consistent with all the results obtained above. The key intermediate is the diastereomeric one, 13, which involves coordination of the amino group on the ligand to the magnesium atom in the Grignard reagent. The coordination is considered to occur selectively with one of the enantiomers of the racemic Grignard reagent and allow it to readily undergo subsequent transmetalation. The stereoselectivity upon the coordination is affected by the steric bulkiness of the alkyl group substituted at the chiral carbon on the aminophosphine ligand.[18]

Ready availability of the present chiral (β-aminoalkyl)phosphine ligands from amino acids and high efficiency of the Grignard cross-coupling have made it possible to get optically active 3-aryl-1-butenes with a high percent enantiomeric excess, which could be readily converted by oxidation into optically active antiinflammatory agents, 2-arylpropionic acids.[19] Cross-coupling of 1-(4-isobutylphenyl)ethylmagnesium chloride (14a) and 1-(4-biphenylyl)ethylmagnesium chloride (14b) with vinyl bromide was carried out in a manner similar to that shown in eq 1 by using (S)-Valphos (1d), (R)-ChGlyphos (1g), and (R)-t-Leuphos (1h). Optically active olefins 15a,b formed were oxidized with potassium permanganate and sodium periodate to the 2-arylpropionic acids 16a,b (eq 2). The

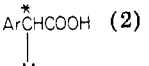
Scheme V





14a, Ar = p-(i-Bu)C$_6$H$_4$
b, Ar = p-PhC$_6$H$_4$

15a,b



(2)

16a,b

results obtained are summarized in Table II. Since the optical rotations of the acids 16 were strongly affected by small quantities of impurities, it was difficult to determine the optical purity of the acids by their specific rotations. The acids were converted into methyl esters, of which the enantiomeric purities were checked by ^{1}H NMR spectroscopy in the presence of a chiral shift reagent, Eu(dcm)$_3$.[13] It was found that 2-(4-isobutylphenyl)propionic acid (Ibuprofen,[20] 16a) and 2-(4-biphenylyl)propionic acid[21] (16b) were obtained in about 80% enantiomeric purity.

Experimental Section

Optical rotations were measured with a Perkin-Elmer 241 polarimeter. ^{1}H NMR spectra were measured with a JEOL

(17) It has been observed that palladium catalysts are more susceptible than nickel catalysts to β elimination in the cross-coupling of secondary alkyl Grignard reagents. For example, see: Hayashi, T.; Konishi, M.; Kumada, M. *Tetrahedron Lett.* **1979**, 1871.

(18) For a more detailed description concerning the mechanism of the asymmetric cross-coupling, see ref 3a.

(19) For reviews, see: (a) Shen, T. Y. *Angew Chem., Int. Ed. Engl.* **1972**, *11*, 460. (b) Flower, R. J. *Pharmacol. Rev.* **1974**, *26*, 33. (c) Kawabata, K.; Ogata, I. *Tokoshi Nyusu, Kagaku Kogyo Shiryo* **1978**, *13*, 85.

(20) Kaiser, D. G.; Vangiessen, G. J.; Reischer, R. J.; Wechter, W. J. *J. Pharm. Sci.* **1976**, *65*, 269.

(21) Shen, T. Y.; Dorn, C. P., Jr. *Chem. Abstr.* **1966**, *65*, 658.

MH-100 spectrometer. Gas chromatographic data were obtained with a Shimadzu GC-4B or GC-4C chromatograph (30% Silicone DC550 on Celite) by using an appropriate internal standard.

Amino acids **2** were commerically available except for cyclohexylglycine and *tert*-leucine.

(*R*)-Cyclohexylglycine (2g). (*R*)-Phenylglycine (2 g, 13.2 mmol) was hydrogenated (50 atm of H_2 for 10 days) in 10 mL of 2 N hydrochloric acid in the presence of rhodium black which was prepared by hydrogenation of $[RhCl(cyclooctadiene)]_2$ (30 mg) in water. The catalyst was removed by filtration, and addition of 6 mL of 28% ammonium hydroxide to the filtrate gave 2.45 g (79%) of (*R*)-**2g**, $[\alpha]^{25}_D$ −31.5° (*c* 0.52, 5 N HCl) (lit.[5] for (*S*)-**2g**, $[\alpha]^{25}_D$ +35.8° (*c* 0.47, 5 N HCl)).

(*R*)-*tert*-Leucine (2h) was prepared according to the reported procedure;[6] $[\alpha]^{20}_D$ +8.94° (*c* 5, H_2O) (lit.[22] for (*S*)-**2h**, $[\alpha]_D$ −10.15° (H_2O)).

Dimethylamino Acids (3). According to Bowman's procedure,[7] the amino acids **2a–e,h,i** were methylated by reductive condensation with formaldehyde and hydrogen in the presence of Pd/C in water. The dimethylamino acids **3a–e,h** and *N*-methylproline (**3i**) obtained by removing the catalyst, excess formaldehyde, and the solvent were subjected to the subsequent reduction without further purification by recrystallization.

β-(Dimethylamino)alkyl Alcohols (4). (*S*)-2-(Dimethylamino)-1-propanol (4a). The procedure reported[8] for the reduction of amino acids was modified as follows. To a suspension of 25 g (0.659 mol) of lithium aluminum hydride in 500 mL of dry THF was added 32 g (0.273 mol) of (*S*)-*N*,*N*-dimethylalanine in approximately 1-g portions over a period of 30 min. The mixture was refluxed for 4 h and was hydrolyzed at 0 °C by successive addition of 25 mL of water, 25 mL of 15% aqueous sodium hydroxide, and 75 mL of water. The white precipitates formed were removed by filtration and washed with THF. The combined filtrate was dried over anhydrous sodium sulfate and evaporated. The residue was distilled [44–47 °C (19 mm)] to give 12.7 g (45%) of (*S*)-**4a**: NMR ($CDCl_3$) δ 0.86 (d, *J* = 7 Hz, 3 H), 2.23 (s, 6 H), 2.06–2.47 (m, 1 H), 3.13 (br s, 1 H), 3.25–3.52 (m, 2 H); α^{25}_D +0.668° (0.1 dm, neat) (lit.[23] for (*R*)-**4a**, $[\alpha]^{23.5}_D$ −3.83° (*c* 2.9, ethanol)).

The alcohols, **4b,d,e,h,i**, were prepared in a similar manner.

(*S*)-2-(Dimethylamino)-4-methyl-1-pentanol (4b): 79% yield; bp 85–86 °C (17 mm); NMR ($CDCl_3$) δ 0.90 and 0.93 (2 d, *J* = 7 Hz, 6 H), 1.0–1.7 (m, 3 H), 2.26 (s, 6 H), 2.5–2.8 (m, 1 H), 3.30 (br s, 1 H), 3.37 (ABX, J_{A-B} = 10 Hz, J_{A-X} = 5 Hz, J_{B-X} = 10 Hz, Δν = 26 Hz, 2 H); α^{25}_D +1.249° (0.1 dm, neat).

(*S*)-2-(Dimethylamino)-3-methyl-1-butanol (4d): 57% yield; bp 82–84 °C (26 mm); NMR ($CDCl_3$) δ 0.84 and 1.01 (2 d, *J* = 7 Hz, 6 H), 1.82 (octet, 1 H), 2.16–2.40 (m, 1 H), 2.42 (s, 6 H), 3.28 (br s, 1 H), 3.39 (ABX, J_{A-B} = 10 Hz, J_{A-X} = 5 Hz, J_{B-X} = 10 Hz, Δν = 32 Hz, 2 H); α^{25}_D −0.368° (0.1 dm, neat).

(*S*)-2-(Dimethylamino)-3-methyl-1-pentanol (4e): 69% yield; bp 92–94 °C (22 mm); NMR ($CDCl_3$) δ 0.85 (d, *J* = 7 Hz, 3 H), 0.92 (t, *J* = 7 Hz, 3 H), 1.05–1.85 (m, 3 H), 2.41 (s, 6 H), 2.21–2.59 (m, 1 H)8 3.45 (ABX, J_{A-B} = 10 Hz, J_{A-X} = 5 Hz, J_{B-X} = 10 Hz, Δν = 18 Hz, 2 H); α^{25}_D +0.530° (0.1 dm, neat).

(*R*)-2-(Dimethylamino)-3,3-dimethyl-1-butanol (4h): 59% yield; bp 85–87 °C (17 mm); NMR ($CDCl_3$) δ 1.00 (s, 9 H), 2.35–2.50 (m, 1 H), 2.60 (s, 6 H), 2.87 (br s, 1 H), 3.45–3.66 (m, 2 H); α^{25}_D −0.066° (0.1 dm, neat).

(*S*)-1-Methyl-2-(hydroxymethyl)pyrrolidine (4i): 65% yield; bp 71–74 °C (21 mm); NMR ($CDCl_3$) δ 1.55–2.00 (m, 4 H), 2.12–2.35 (m, 2 H), 2.36 (s, 3 H), 2.97–3.17 (m, 1 H), 3.54 (ABX, J_{A-B} = 10 Hz, J_{A-X} = 4 Hz, J_{B-X} = 3 Hz, Δν = 13 Hz, 2 H), 3.79 (br s, 1 H); α^{25}_D −5.036° (0.1 dm, neat).

(*S*)-2-(Dimethylamino)-3-phenyl-1-propanol (4c). (a) (*S*)-**4c** was prepared in 90% yield by lithium aluminum hydride reduction of (*S*)-*N*,*N*-dimethylphenylalanine methyl ester in ether according to the reported procedure.[24] (b) A mixture of 4.9 g (33 mmol) of (*S*)-2-amino-3-phenyl-1-propanol[25] (**6c**), 10 mL (0.27 mol) of formic acid, and 9 mL (0.11 mol) of 37% aqueous formaldehyde was refluxed for 14 h. The solution was made alkaline with 10% aqueous sodium hydroxide and extracted with dichloromethane. The dichloromethane layer was dried over anhydrous sodium sulfate and evaporated. The residue was dissolved in ether and stirred with saturated ethanolic hydrogen chloride to give 2.9 g (41%) of the hydrochloride (*S*)-**4c**·HCl as white crystals: mp 132–133 °C; NMR ($CDCl_3$) δ 2.90 (s, 6 H), 2.25–4.03 (m, 5 H), 7.22 (s, 5 H); $[\alpha]^{22}_D$ +11.9° (*c* 4.0, H_2O) (lit.[26] for (*S*)-**4c**·HCl, mp 128–130 °C; $[\alpha]^{22}_D$ +12.1° (*c* 2.5, H_2O)).

(*R*)-2-(Dimethylamino)-2-phenylethanol (4f). The reported procedure[27] was modified as follows. (*R*)-2-Amino-2-phenylethanol[28] (**6f**; 3.66 g, 27 mmol) was converted to the hydrochloride by treating it with concentrated hydrochloric acid (4 mL) and removing the excess acid and water. To the hydrochloride were added 13 g (0.16 mol) of 37% aqueous formaldehyde and 7.5 mL (0.20 mol) of 98% formic acid. The mixture was refluxed for 24 h. The mixture was made alkaline with 10% aqueous sodium hydroxide and extracted with dichloromethane. The organic layer was washed with brine, dried over anhydrous sodium sulfate, and evaporated. To the residue was added saturated ethanolic hydrogen chloride, and the solvent was removed under reduced pressure to give hydrochloride of (*R*)-**4f**. Recrystallization from 2-propanol/ether afforded 3.61 g (67%) of pure sample: mp 104–105 °C; NMR ($CDCl_3$) δ 2.23 and 2.44 (2 d, *J* = 5 Hz, 6 H), 4.0–4.6 (m, 3 H), 7.48 (s, 5 H); $[\alpha]^{25}_D$ −30.8° (*c* 0.85, H_2O) (lit.[27] for (*R*)-**4f**·HCl, mp 105–106.5 °C; $[\alpha]^{25}_D$ −33.0° (*c* 0.82, H_2O)).

(*R*)-2-(Dimethylamino)-2-cyclohexylethanol (4g). To a suspension of 3.0 g (79 mmol) of lithium aluminum hydride in 50 mL of THF was added 3.8 g (24 mmol) of (*R*)-cyclohexylglycine (**2g**) in small portions. After refluxing for 5 h, the mixture was hydrolyzed by successive addition of 3 mL of water, 3 mL of 15% aqueous sodium hydroxide, and 9 mL of water. The white precipitates were removed by filtration. The filtrate was evaporated, and the residue was dissolved in chloroform and dried over anhydrous sodium sulfate. Evaporation of the solvent followed by recrystallization from ethanol/pentane gave 2.78 g (80%) of (*R*)-2-amino-2-cyclohexylethanol (**6g**): mp 73–73.5 °C; NMR ($CDCl_3$) δ 0.75–2.05 (m, 11 H), 2.40–2.70 (m, 1 H), 3.28 (t, *J* = 9 Hz, 1 H), 3.63 (dd, *J* = 4, 9 Hz, 1 H); $[\alpha]^{22}_D$ −11.7° (*c* 0.99, ethanol). Anal. Calcd for $C_8H_{17}NO$: C, 67.08; H, 11.97; N, 9.78. Found: C, 66.93; H, 11.91; N, 9.51.

(*R*)-**6g** (2.73 g, 19 mmol) was converted to its hydrochloride by treating it with concentrated hydrochloric acid (3 mL) and removing the excess acid and water. To the hydrochloride were added 9.3 g (0.11 mol) of 37% aqueous formaldehyde and 5.4 mL (0.11 mol) of formic acid. The mixture was refluxed for 39 h. The solution was made alkaline by adding 10% aqueous sodium hydroxide and was extracted with dichloromethane. The dichloromethane layer was washed with brine, dried over anhydrous sodium sulfate, and evaporated. The residue was distilled [99–100 °C (4 mm)] to give 2.78 g (85%) of (*R*)-**4g**: NMR ($CDCl_3$) δ 0.80–2.00 (m, 11 H), 2.44 (s, 6 H), 2.2–2.4 (m, 1 H), 3.5 (br s, 1 H), 3.22 (t, *J* = 10 Hz, 1 H), 3.55 (dd, *J* = 10, 5 Hz, 1 H); α^{25}_D +0.135° (0.1 dm, neat).

β-(Dimethylamino)alkyl Chloride Hydrochlorides 5. The procedures reported[29] for converting β-aminoalkyl alcohols to chlorides were modified. The following procedure for the preparation of (*S*)-2-(dimethylamino)propyl chloride hydrochloride (**5a**) is typical. (*S*)-2-(Dimethylamino)-1-propanol (**4a**; 11.4 g, 0.11 mol) was converted to the hydrochloride by treating it with an excess of concentrated hydrochloric acid (20 mL) in ethanol and removing the excess acid and solvent under reduced pressure. The hydrochloride of **4a** was dissolved in 40 mL of chloroform, and 20 mL (0.27 mol) of thionyl chloride was added dropwise at 0 °C over a period of 10 min. The mixture was refluxed for 2 h and concentrated to dryness under reduced pressure. The residue

(22) Abderhalden, E.; Faust, W.; Haase, E. *Hoppe-Seyler's Z. Physiol. Chem.* **1934**, *228*, 187.
(23) Beckett, A. H.; Harper, N. J.; Clitherow, J. W. *J. Pharm. Pharmacol.* **1963**, *15*, 349.
(24) Corey, E. J.; McCaully, R. J.; Sachdev, H. S. *J. Am. Chem. Soc.* **1970**, *92*, 2476.
(25) Seki, H.; Koga, K.; Matsuo, H.; Ohki, S.; Matsuo, I.; Yamada, S. *Chem. Pharm. Bull.* **1965**, *13*, 998.
(26) Ose, S.; Yoshimura, Y. *Yakugaku Zasshi* **1958**, *78*, 687.
(27) Nishimura, H. *Yakugaku Zasshi* **1964**, *84*, 824.
(28) Tseng, C. C.; Terashima, S.; Yamada, S. *Chem. Pharm. Bull.* **1977**, *25*, 166.
(29) (a) Minoura, Y.; Takebayashi, M.; Price, C. C. *J. Am. Chem. Soc.* **1959**, *81*, 4689. (b) Hall, L. A. R.; Stephens, V. C.; Burckhalter, J. H. "Organic Syntheses"; Wiley: New York, 1963; Collect. Vol. IV, p 333.

was dissolved in ethanol, followed by concentration again to dryness. The oily residue was then dissolved in 20 mL of dry ethanol, and ether was added slowly until white crystals were formed. After being cooled in a refrigerator, the cyrstals (10.5 g, 60%) were collected on a glass filter. Addition of ether to the filtrate followed by effective cooling gave an additional 6.3 g (36%) of the product. The hydrochlorides **5** are hygroscopic and must be dried at 50 °C over phosphorus pentoxide under reduced pressure before use.

(*S*)-5a: 96% yield; mp 113–114 °C; NMR ($CDCl_3$) δ 1.54 (d, J = 7 Hz, 3 H), 2.86 (d, J = 5 Hz, 6 H), 3.55–3.95 (m, 1 H), 3.96 (m, 2 H); $[\alpha]^{25}_D$ +17.8° (*c* 0.99, H_2O) (lit.[30] for *dl*-**5a**, mp 104 °C).

(*S*)-5b: 77% yield; mp 112–114 °C; NMR ($CDCl_3$) δ 1.86 and 1.90 (2 d, J = 7 Hz, 6 H), 2.27–2.93 (m, 3 H), 3.75 and 3.81 (2 d, J = 5 Hz, 6 H), 4.48 (m, 1 H), 4.94 (ABX, J_{A-B} = 13 Hz, J_{A-X} = 2 Hz, J_{B-X} = 4 Hx, $\Delta\nu$ = 32 Hz, 2 H); $[\alpha]^{25}_D$ +31.2° (*c* 0.94, H_2O). Anal. Calcd for $C_8H_{19}NCl_2$: C, 48.00; H, 9.57; N, 7.00. Found: C, 47.85; H, 9.77; N, 6.76.

(*S*)-5c: 96% yield; mp 160 °C; NMR ($CDCl_3$) δ 2.93 and 2.98 (2 d, J = 5 Hz, 6 H), 3.1–4.2 (m, 5 H), 7.25 (s, 5 H); $[\alpha]^{15}_D$ +30.0° (*c* 1.64, H_2O) (lit.[26] mp 163–164 °C; $[\alpha]^{15}_D$ +30.5° (*c* 2.0, H_2O)).

(*S*)-5d: 93% yield; mp 118–120 °C; NMR ($CDCl_3$) δ 1.16 and 1.27 (2 d, J = 7 Hz, 6 H), 2.45 (octet, J = 7 Hz, 1 H), 2.96 and 3.00 (2 d, J = 5 Hz, 6 H), 3.33 (m, 1 H), 3.98 (d, J = 4 Hz, 2 H); $[\alpha]^{25}_D$ +3.9° (*c* 1.02, H_2O). Anal. Calcd for $C_7H_{17}NCl_2$: C, 45.17; H, 9.21; N, 7.53. Found: C, 44.90; H, 9.45; N, 7.51.

(*S*)-5e. The hydrochloride was extremely hygroscopic and purification for analysis was not possible: 75% yield; NMR ($CDCl_3$) δ 1.03 (t, J = 7 Hz, 3 H), 1.13 (d, J = 7 Hz, 3 H), 1.36–1.78 (m, 2 H), 2.00–2.37 (m, 1 H), 3.03 (d, J = 5 Hz, 6 H), 3.30–3.56 (m, 1 H), 3.95 (d, J = 4 Hz, 2 H).

(*R*)-5f: 84% yield; mp 203–204 °C dec; NMR ($CDCl_3$) δ 2.63 and 2.97 (2 d, J = 5 Hz, 6 H), 4.25–4.50 (m, 1 H), 4.36 (ABX, J_{A-B} = 9 Hz, J_{A-X} = 3 Hz, J_{B-X} = 8 Hz, $\Delta\nu$ = 42 Hz, 2 h), 7.40–7.71 (m, 5 H). $[\alpha]^{25}_D$ +8.70° (*c* 1.79, H_2O) (lit.[27] for (*S*)-**5f**, mp 193–194 °C; $[\alpha]^{25}_D$ −6.7° (*c* 4.3, H_2O)).

(*R*)-5g: 61% yield; mp 120 °C; NMR ($CDCl_3$) δ 1.00–2.30 (br m, 11 H), 2.94 and 2.97 (2 d, J = 5 Hz, 6 H), 3.14–3.45 (m, 1 H), 3.96 (d, J = 4 Hz, 2 H); $[\alpha]^{25}_D$ −11.7° (*c* 1.03, ethanol). Anal. Calcd for $C_{10}H_{21}NCl_2$: C, 53.10; H, 9.36; N, 6.19. Found: C, 52.91; H, 9.58; N, 6.13.

(*R*)-5h: 81% yield; mp 140 °C; NMR ($CDCl_3$) δ 1.32 (s, 9 H), 3.10 and 3.17 (2 d, J = 5 Hz, 6 H), 3.20–3.22 (m, 1 H), 3.68–4.16 (m, 2 H). Anal. Calcd for $C_8H_{19}NCl$: C, 48.00; H, 9.57; N, 7.00. Found: C, 47.83; H, 9.70; N, 7.08.

(*S*)-5i: 82% yield; mp 151–153 °C; NMR ($CDCl_3$) δ 3.00 (d, J = 5 Hz, 3 H), 1.8–4.4 (m, 9 H); $[\alpha]^{25}_D$ −5.0° (*c* 1.05, H_2O). Anal. Calcd for $C_6H_{13}NCl_2$: C, 42.37; H, 7.70; N, 8.24. Found: C, 41.98; H, 7.93; N, 7.98.

[β-(Dimethylamino)alkyl]diphenylphosphines 1. The procedure reported[9] by Whitesides was modified. The procedure for the preparation of (*S*)-Alaphos (**1a**) is typical. In a 100-mL two-necked flask equipped with a reflux condenser and a septum rubber was placed 0.987 g (8.8 mmol) of potassium *tert*-butoxide. The flask was flushed with nitrogen and matintained under a slightly positive pressure of nitrogen thereafter. Dry THF (15 mL) and 0.62 mL (3.5 mmol) of diphenylphosphine were added successively via a syringe. The resulting red solution was stirred at ambient temperature for 20 min, and 0.555 g (3.5 mmol) of (*S*)-2-(dimethylamino)propyl chloride hydrochloride (**5a**) was added as crystals. The mixture was refluxed for 2 h. During that time the red color of the solution disappeared. The solvent was removed under reduced pressure, the residue was taken up in 10% aqueous hydrochloric acid, and the aqueous solution was washed with benzene. The aqueous solution was made alkaline with 10% aqueous sodium hydroxide and extracted with benzene. The benzene solution was washed with brine, dried over anhydrous sodium sulfate, and evaporated. The residue was passed through a short alumina column (ether) to remove a small amount of phosphine oxide, giving 0.756 g (80%) of (*S*)-Alaphos (**1a**) as a colorless syrup.

(*S*)-Alaphos (1a): 80% yield; NMR ($CDCl_3$) δ 1.08 (d, J = 7 Hz, 3 H), 2.18 (s, 6 H), 1.81–2.78 (m, 3 H), 7.24–7.56 (m, 10H); $[\alpha]^{25}_D$ −47.2: (*c* 1.16, benzene). Anal. Calcd for $C_{17}H_{22}NP$: C, 75.25; H, 8.17; N, 5.16. Found: C, 75.12; H, 8.28; N, 4.87.

(*S*)-Leuphos (1b): 68% yield; NMR ($CDCl_3$) δ 0.81 (d, J = 7 Hz, 6 H), 1.38 (deformed t, 2 H), 1.53–2.65 (m, 4 H), 2.15 (s, 6 H), 7.25–7.67 (m, 10 H); $[\alpha]^{25}_D$ −35.3° (*c* 1.09, chloroform). Anal. Calcd for $C_{20}H_{28}NP$: C, 76.65; H, 9.00; N, 4.47; P, 9.88. Found: C, 76.69; H, 8.85; N, 4.46; P. 10.11.

(*S*)-Phephos (1c): 47% yield; mp 45–46 °C; NMR ($CDCl_3$) δ 2.05–2.16 (m, 2 H), 2.20 (s, 6 H), 2.50–3.00 (m, 3 H), 6.91–7.38 (m, 15 H); $[\alpha]^{25}_D$ +32.9° (*c* 0.99, benzene). Anal. Calcd for $C_{23}H_{26}NP$: C, 79.51; H, 7.54; N, 4.03; P, 8.92. Found: C, 79.69; H, 7.62; N, 3.96; P, 8.75.

(*S*)-Valphos (1d): 91% yield; NMR ($CDCl_3$) δ 0.86 and 0.93 (2 d, J = 7 Hz, 6 H), 1.70–2.38 (m, 4 H), 2.17 (s, 6 H), 7.22–7.58 (m, 10 H). $[\alpha]^{25}_D$ +12.5° (*c* 1.00, benzene). Anal. Calcd for $C_{19}H_{26}NP$: C, 76.22; H, 8.75; N, 4.68. Found: C, 76.45; H, 8.87; N, 4.59.

(*S*)-Ilephos (1e): 70% yield; NMR ($CDCl_3$) δ 0.76 (t, J = 7 Hz, 3 H), 0.92 (d, J = 7 Hz, 3 H), 0.96–2.50 (m, 6 H), 2.17 (s, 6 H), 7.20–7.62 (m, 10 H). $[\alpha]^{25}_D$ +32.6° (*c* 0.84, chloroform). Anal. Calcd for $C_{20}H_{28}NP$: C, 76.65; H, 9.00; N, 4.47; P, 9.88. Found: C, 76.75; H, 8.89; N, 4.42; P, 9.98.

(*R*)-PhGlyphos (1f): 12% yield (this low yield is due to the β elimination as a side reaction, giving acetophenone after hhydrolysis); NMR ($CDCl_3$) δ 2.14 (s, 6 H), 2.63 (ABX J_{A-B} = 13 Hz, J_{A-X} = 7 Hz, J_{B-X} = 9 Hz, $\Delta\nu$ = 30 Hz, 2 H), 3.36 (m, 1 H), 7.09–7.58 (m, 15 H); $[\alpha]^{25}_D$ +40.1° (*c* 0.34, benzene). Anal. Calcd for $C_{22}H_{24}NP$: C, 79.25; H, 7.26; N, 4.20. Found: C, 79.17; H, 7.22; N, 4.11.

(*R*)-ChGlyphos (1g): 10% yield; NMR ($CDCl_3$) δ 0.78–1.90 (br m, 11 H); 2.04–2.39 (m, 3 H), 2.16 (s, 6 H), 7.24–7.45 (m, 10 H); $[\alpha]^{25}_D$ −5.8° (*c* 0.34, benzene). Anal. Calcd for $C_{22}H_{30}NP$: C, 77.84; H, 8.91; N, 4.13; P, 9.13. Found: C, 77.45; H, 9.05; N, 4.05; P, 8.85.

(*R*)-*t*-Leuphos (1h): 90% yield; NMR ($CDCl_3$) δ 0.88 (s, 9 H), 2.14–2.18 (m, 3 H), 2.46 (s, 6 H), 7.24–7.68 (m, 10 H); $[\alpha]^{25}_D$ −114.8° (*c* 1.53, benzene). Anal. Calcd for $C_{20}H_{28}NP$: C, 76.65; H, 9.00; N, 4.47. Found: C, 76.32; H, 8.95; N, 4.38.

(*S*)-Prophos (1i): 78% yield; NMR ($CDCl_3$) δ 1.4–2.3, 2.45–2.66, 2.91–3.17 (m, 9 H), 2.28 (s, 3 H), 7.20–7.60 (m, 10H); $[\alpha]^{25}_D$ −133° (*c* 0.81, chloroform) (lit.[11] $[\alpha]_D$ −131.5° (*c* 2.5, toluene)). Anal. Calcd for $C_{18}H_{24}NP$: C, 75.76; H, 8.48; N, 4.91; P, 10.85. Found: C, 75.77; H, 8.29; N, 4.77; P, 10.87.

[(*S*)-2-(1-Pyrrolidino)-3-phenylpropyl]diphenylphosphine (8). A solution of 3.15 g (21 mmol) of (*S*)-2-amino-3-phenyl-1-propanol (**6c**) and 5.06 g (23 mmol) of 1,4-dibromobutane in 40 mL of toluene was refluxed for 3 h. Sodium bicarbonate (3.9 g, 46 mmol) was added, and the mixture was refluxed for an additional 18 h. The mixture was made alkaline by adding 50% aqueous sodium hydroxide and extracted with ether. The ether layer was washed with brine, dried over anhydrous sodium sulfate, and evaporated. Saturated ethanolic hydrogen chloride was added and the solvent was removed under reduced pressure. The residue was recrystallized from 2-propanol/ether to give 4.24 g (84%) of (*S*)-2-(1-pyrrolidino)-3-phenyl-1-propanol hydrochloride (**7**): mp 97–99 °C; NMR (CD_3OD) δ 2.00–2.35 (m, 4 H), 3.02–4.12 (m, 9 H), 7.31 (s, 5 H); $[\alpha]^{25}_D$ +5.53° (*c* 1.01, H_2O).

To a solution of 3.26 g (13.5 mmol) of (*S*)-**7** in 45 mL of chloroform was added 5 mL (69 mmol) of thionyl chloride, and the mixture was refluxed for 2 h. The solvent was removed under reduced pressure, ethanol was added to decompose excess thionyl chloride, and ethanol was removed under reduced pressure. The residue was recrystallized from 2-propanol/hexane to give 2.03 g (58%) of (*S*)-2-(1-pyrrolidino)-3-phenylpropyl chloride hydrochloride: mp 108–109 °C; NMR ($CDCl_3$) δ 1.98–2.45 (m, 4 H), 3.00–3.48, 3.60–4.24 (m, 9 H), 7.31 (s, 5 H); $[\alpha]^{25}_D$ +19.0° (*c* 0.97, H_2O). The chloride (0.363 g, 1.4 mmol) was treated with diphenylphosphine (0.25 mL, 1.4 mmol) and potassium *tert*-butoxide (0.328, 2.9 mmol) in THF (15 mL) to give 0.280 g (54%) of (*S*)-**8** as a colorless syrup: NMR ($CDCl_3$) δ 1.53–1.75 (m, 4 H), 2.18–2.28 (m, 2 H), 2.50–2.68 (m, 4 H), 2.82–3.20 (m, 3 H), 7.05–7.50 (m, 15 H); $[\alpha]^{25}_D$ +29.9° (*c* 0.50, benzene). Anal. Calcd for $C_{25}H_{28}NP$: C, 80.40; H, 7.56; N, 3.75. Found: C, 80.40; H, 7.61; N, 3.68.

(*S*)-1-(Dimethylamino)-2-(diphenylphosphino)propane (10). According to the procedure reported[30] for the preparation of racemic 1-(dimethylamino)-2-chloropropane hydrochloride (**9**),

(30) Schultz, E. M.; Sprague, J. M. *J. Am. Chem. Soc.* **1948**, *70*, 48.

(S)-2-(dimethylamino)-1-chloropropane hydrochloride (**5a**; 1.10 g, 6.9 mmol) was sublimed at 150 °C and 2 mmHg. Recrystallization from 2-propanol gave 0.575 g (52%) of (R)-**9**: NMR ($CDCl_3$) δ 1.68 (d, J = 7 Hz, 3 H), 2.95 and 3.00 (2 d, J = 4 Hz, 6 H), 3.10–3.70 (m, 2 H), 4.45–4.80 (m, 1 H); $[\alpha]^{25}_D$ −15° (c 0.88, H_2O). Anal. Calcd for $C_5H_{13}NCl_2$: C, 37.99; H, 8.29; N, 8.86. Found: C, 37.84; H, 8.41; N, 8.87.

The chloride (R)-**9** (0.222 g, 1.4 mmol) obtained above was treated with diphenylphosphine (0.25 mL, 1.4 mmol) and potassium *tert*-butoxide (0.405 g, 3.6 mmol) in THF (10 mL) to give 0.326 g (86%) of (S)-**10**: NMR ($CDCl_3$) δ 1.08 (dd, J = 6.5, 14 Hz, 3 H), 2.19 (s, 6 H), 2.00–2.70 (m, 3 H), 7.10–7.60 (m, 10 H; $[\alpha]^{25}_D$ −18° (c 1.01, benzene) (lit.[14] for (R)-**10**, $[\alpha]_D$ +74° (c 1.34, benzene)). Anal. Calcd for $C_{17}H_{22}NP$: C, 75.25; H, 8.17; N, 5.16. Found: C, 75.19; H, 8.28; N, 4.91.

(S)-**10** was oxidized into 1-(dimethylamino)-2-(diphenylphosphinyl)propane (91% yield) by treating it with an excess of 30% hydrogen peroxide in acetone: NMR ($CDCl_3$) δ 1.08–1.38 (m, 3 H), 2.16 (s, 6 H), 2.30–2.69 (m, 3 H), 7.38–7.58, 7.65–7.96 (m, 10 H). The ^1H NMR of the phosphine oxide (0.15 M) in the presence of Eu(dcm)$_3$ (0.1 M) showed the presence of a pair of enantiomers in a ratio of 63.5:36.5, indicating that the enantiomeric purity is 27%.

PdCl$_2$[(S)-Valphos]. To a suspension of 83,5 mg (0.32 mmol) of dichlorobis(acetonitrile)palladium(II) in 3 mL of benzene was added with stirring a solution of 99.5 mg (0.33 mmol) of (S)-Valphos (**1d**) in 5 mL of benzene. After 12 h at room temperature, the yellow precipitate formed was collected by filtration, washed with benzene, and dried in vacuo. Recrystallization from dichloromethane/hexane gave 168 mg (91%) of the palladium complex as yellow-orange blocks: mp ~230 °C dec; NMR ($CDCl_3$) δ 0.94 and 1.04 (2 d, J = 7 Hz, 6 H), 2.10–2.70 (m, 4 H), 2.98 and 3.14 (2 s, 6 H), 7.22–8.25 (m, 10 H). Anal. Calcd for $C_{19}H_{26}NCl_2PPd$: C, 47.87; H, 5.50; N, 2.94. Found: C, 47.62; H, 5.55; N, 2.91.

Palladium complexes containing **1a** and **1c** were prepared in a similar manner in about 90% yield.

PdCl$_2$[(S)-Alaphos]: mp ~240 °C dec; NMR ($CDCl_3$) δ 1.25 (d, J = 7 Hz, 3 H), 2.4–2.9 (m, 3 H), 2.93 and 3.10 (2 s, 6 H), 7.2–8.3 (m, 10 H). Anal. Calcd for $C_{17}H_{22}NCl_2PPd$: C, 45.51; H, 4.94; N, 3.12. Found: C, 45.16; H, 4.90; N, 3.16.

PdCl$_2$[(S)-Phephos]: mp 235–240 °C dec; NMR ($CDCl_3$) δ 1.55–2.75 (m, 5 H), 3.08 and 3.23 (2 s, 6 H), 6.84–7.85 (m, 15 H). Anal. Calcd for $C_{23}H_{26}NCl_2PPd$: C, 52.65; H, 4.99; N, 2.67. Found: C, 50.52; H, 4.76; N, 2.54. The discrepancy in the analytical data is due to the presence of ~0.5 equiv of dichloromethane as a crystal solvent, which was shown by the NMR of the complex.

Asymmetric Grignard Cross-Coupling. The cross-coupling was carried out in essentially the same manner as that which we have previously reported.[3a] The reaction conditions and data obtained are listed in Table I. Densities of the products **12** are as follows: **12a**,[31] d^{22}_4 0.8809; **12b**, d^{22}_4 0.885; **12c**,[32] d^{25}_4 0.982; **12d**,[3a] d^{20}_4 0.7365.

Preparation of 2-Arylpropionic Acids 16. 1-(4-Isobutylphenyl)ethylmagnesium Chloride (14a). To a mixture of 150 mL of carbon disulfide and 132 g (0.99 mol) of anhydrous aluminum chloride was added dropwise below 0 °C a mixture of 130 g (0.95 mol) of isobutylbenzene and 81 g (1.0 mol) of acetyl chloride over a period of 2 h. The mixture was then kept stirring at room temperature for 7 h and poured upon 700 g of cracked ice to which 150 mL of concentrated hydrochloric acid was added. the mixture was extracted with ether, and the ether solution was dried over calcium chloride and evaporated. The residue was distilled [95 °C (3 mm)] to give 150 g (89%) of 4-isobutylacetophenone: NMR ($CDCl_3$) δ 0.91 (d, J = 7 Hz, 6 H), 1.95 (nonet, 1 H), 2.53 (br d, 2 H), 2.61 (s, 3 H), 7.15–7.94 (AA′BB′, 4 H) [lit.[33] bp 86–90 °C (0.5 mm)].

To a suspension of 13.4 g (0.35 mol) of lithium aluminum hydride in 300 mL of dry ether was added dropwise over a period of 30 min a solution of 88 g (0.50 mol) of 4-isobutylacetophenone in 150 mL of ether. The mixture was refluxed for 3 h and hydrolyzed at 0 °C by successive addition of 14 mL of water, 14 mL of 15% aqueous sodium hydroxide, and 42 mL of water. The white precipitates were removed by filtration. The filtrate was dried over anhydrous sodium sulfate, and the solvent was removed under reduced pressure to give 93 g of crude 1-(4-isobutylphenyl)ethanol, which was subjected to chlorination without further purification. In a separatory funnel are placed 100 mL of concentrated hydrochloric acid and the alcohol obtained above. After the flask was shaken vigorously, 100 mL of ether was added, and the mixture was shaken again. The ether layer was drawn off, shaken again with 100 mL of concentrated hydrochloric acid, dried over calcium chloride, and evaporated. The residue was distilled [103 °C (6 mm)] to give 90.2 g (92%) of 1-(4-isobutylphenyl)ethyl chloride: NMR (CCl_4) δ 0.90 (d, J = 7 Hz, 6 H), 1.84 (d, J = 7 Hz, 3 H), 1.86 (nonet, 1 H), 2.48 (d, J = 7 Hz, 2 H), 5.15 (q, 1 H), 7.10–7.44 (AA′BB′, 4 H). Anal. Calcd for $C_{12}H_{17}Cl$: C, 73.26; H, 8.71; Cl, 18.02. Found: C, 73.43; H, 8.99; Cl, 18.20. The Grignard reagent **14a** (0.5–1.0 M in ether) was prepared in ~70% yield by adding slowly a solution of the halide in ether to magnesium ribbons at 0 °C.

1-(4-Biphenylyl)ethylmagnesium Chloride (14b). To a solution of 75 mL (0.15 mol) of methylmagnesium bromide in ether (2.0 M) was added dropwise at 0 °C a solution of 25 g (0.137 mol) of 4-phenylbenzaldehyde in 140 mL of ether. The mixture was refluxed for 2 h and after cooling was added to 300 g of ice–water. Extraction with ether followed by evaporation of the solvent gave crude 1-(4-biphenylyl)ethanol. The crude alcohol was converted into 1-(4-biphenylyl)ethyl chloride by shaking with concentrated hydrochloric acid in ether in a similar manner to the preparation of 1-(4-isobutylphenyl)ethyl chloride. Recrystallization from hexane gave 19.6 g (71%) of the chloride: mp 52 °C (lit.[34] mp 52–52.5 °C); NMR ($CDCl_3$) δ 1.88 (d, J = 7 Hz, 3 H), 5.13 (q, 1 H), 7.20–7.70 (m, 9 H). The chloride was converted to the Grignard reagnet **14b** (~1.0 M in ether) in ~70% yield.

3-(4-Isobutylphenyl)-1-butene (15a). The following procedure for the reaction with the nickel–Valphos catalyst is typical. A 300-mL flask containing 26 mg (0.20 mmol) of anhydrous nickel chloride and 63 mg (0.21 mmol) of (S)-Valphos (**1d**) was filled with argon after evacuation. To it were added at −78 °C 2.8 mL (40 mmol) of vinyl bromide and 131 mL (80 mmol) of the Grignard reagent **14a** (0.61 M) in ether. The mixture was stirred at 0 °C for 2 days and hydrolyzed with 10% hydrochloric acid. The organic layer and ether extracts from the aqueous layer were combined, washed with saturated sodium bicarbonate solution, and dried over anhydrous sodium sulfate. After evaporation of solvent, distillation through a short Vigreux column [70–71 °C (2 mm)] gave 6.1 g (81%) of **15a**. An analytically pure sample was obtained by preparative GLC (silicone DC550): d^{20}_4 0.8645; NMR (CCl_4) δ 0.89 (d, J = 7 Hz, 6 H), 1.33 (d, J = 7 Hz, 3 H) 1.83 (nonet, 1 H), 2.40 (br d, J = 7 Hz, 2 H), 3.14–3.53 (m, 1 H), 4.83–5.10 (m, 2 H), 5.74–6.12 (m, 1 H), 6.86–7.10 (AA′BB′, 4 H). Anal. Calcd for $C_{14}H_{20}$: C, 89.29; H, 10.71. Found: C, 89.39; H, 10.79. Optical rotation data are listed in Table II.

2-(4-Isobutylphenyl)propionic Acid (16a). The reported procedure[35] for oxidation of 3-phenyl-1-butene was followed. To a solution of **15a** (0.576 g, 3.1 mmol; $[\alpha]^{20}_D$ +5.66° (neat)) in 80 mL of *tert*-butyl alcohol were added a solution of 1.24 g (9.0 mml) of potassium carbonate in 60 mL of water and a solution of 5.13 g (24 mmol) of sodium periodate and 0.63 g (4.0 mmol) of potassium permanganate in 60 mL of water. The solutin was adjusted to pH 8.5 with 2 N aqueous sodium hydroxide and was stirred overnight. After *tert*-butyl alcohol was removed under reduced pressure, the aqueous solution was acidified with concentrated hydrochloric acid to pH 2.5, and sodium bisulfite was added until the solution became off-white. The solution was extracted with ether, and the extracts were dried over sodium sulfate, concentrated, and distilled [120–140 °C (2 mm), Kugelrohr] to give 0.38 g (60%) of **16a**: NMR ($CDCl_3$) δ 0.91 (d, J = 7 H, 6 H), 1.50 (d, J = 8 Hz, 3 H), 1.84 (nonet, 1 H), 2.96 (br d, J = 7 Hz, 2 H), 3.72 (q, 1 H), 7.01–7.32 (AA′BB′, 4 H), 9.78 (br s, 1 H); $[\alpha]^{25}_D$ −34.0° (c 2, 95% ethanol) (lit.[20] for (S)-**16a**, $[\alpha]^{25}_D$ +60° (95% ethanol)).

(31) Cram, D. J. *J. Am. Chem. Soc.* **1952**, *74*, 2137.
(32) Menicagli, R.; Piccolo, O.; Lardicci, L.; Wis, M. L. *Tetrahedron* **1979**, *35*, 1301.
(33) Baddeley, G.; Wrench, E. *J. Chem. Soc.* **1956**, 4943.
(34) Tsuno, Y.; Kusuyama, Y.; Sawada, M.; Fujii, T.; Yukawa, Y. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 3337.
(35) Spencer, H. K.; Hill, R. K. *J. Org. Chem.* **1976**, *41*, 2485.

A solution of the acid **16a** obtained above (0.36 g, 1.8 mmol) and *p*-toluenesulfonic acid (40 mg) in 10 mL of methanol was refluxed for 3 h. The solvent was removed under reduced pressure, and the residue was taken up in ether. The solution was washed with 10% aqueous sodium hydroxide, dried over anhydrous sodium sulfate, and evaporated. The residue was distilled [110–130 °C (2 mm), Kugelrohr] to give 0.27 g (70%) of methyl 2-(4-isobutylphenyl)propionate: $[\alpha]^{20}_D$ −49.0° (*c* 1.82, benzene); NMR (CCl_4) δ 0.92 (d, *J* = 7 Hz, 6 H), 1.45 (d, *J* = 8 Hz, 3 H), 1.85 (nonet, 1 H), 2.44 (d, *J* = 7 Hz, 2 H), 3.44–3.71 (m, 1 H), 3.67 (s, 3 H), 6.92–7.21 (AA'BB', 4 H). NMR spectroscopy with the chiral shift reagent Eu(dcm)$_3$ indicated that the ester is 80% ee.

2-(4-Biphenylyl)propionic Acid (16b). The cross-coupling of **14b** was carried out in a similar manner to that of **14b**. After hydrolysis and the workup, short silica gel column (benzene) treatment gave a mixture of 3-(4-biphenylyl)-1-butene (**15b**) and 4-ethylbiphenyl in a ratio of 1:1. NMR ($CDCl_3$) of **15b**: δ 1.37 (d, *J* = 7 Hz, 3 H), 3.48 (q, 1 H), 4.92–5.23 (m, 2 H), 5.81–6.24 (m, 1 H), 7.15–7.75 (m, 9 H). The mixture was subjected, without further purification, to oxidation with sodium periodate and potassium permanganate in a manner similar to the preparation of **16a**. Extraction of organic products with 10% aqueous sodium hydroxide followed by acidification with concentrated hydrochloric acid and ether extraction gave a ca. 60% yield of the acid **16b**:[21] NMR ($CDCl_3$) δ 1.59 (d, *J* = 8 Hz, 3 H), 3.83 (q, 1 H), 7.25–7.90 (m, 9 H), 9.50 (br s, 1 H).

Esterification (TsOH/MeOH) of the acid **16b** ($[\alpha]^{20}_D$ −24.4° (95% ethanol)) gave methyl 2-(4-biphenylyl)propionate: $[\alpha]^{20}_D$ −52.7° (*c* 2.06, benzene); NMR ($CDCl_3$) δ 1.54 (d, *J* = 7 Hz, 3 H), 3.68 (s, 3 H), 3.68–3.85 (q, 1 H), 7.29–7.75 (m, 9 H). NMR spectroscopy with Eu(dcm)$_3$ indicated that the ester is 82% ee.

Acknowledgment. We thank the Ministry of Education, Japan, for Grants-in-Aid (No. 311709, 355370, 00547080) and Asahi Glass Foundation of the Contribution to Industrial Technology for financial support. We are grateful to Prof. K. Koga and Dr. K. Tomioka (The University of Tokyo) for helpful suggestions for the preparation of optically active *tert*-leucine.

Registry No. **1a**, 74492-06-1; **1b**, 82821-95-2; **1c**, 74492-07-2; **1d**, 74492-09-4; **1e**, 85711-05-3; **1f**, 74492-08-3; **1g**, 82821-97-4; **1h**, 74492-10-7; **1i**, 60365-87-9; **2a**, 56-41-7; **2b**, 61-90-5; **2c**, 63-91-2; **2d**, 72-18-4; **2e**, 73-32-5; **2f**, 875-74-1; **2g**, 14328-52-0; (*S*)-**2h**, 20859-02-3; (*R*)-**2h**, 26782-71-8; **2i**, 147-85-3; **3a**, 2812-31-9; **3b**, 2439-37-4; **3d**, 2812-32-0; **3e**, 2439-38-5; **3f**, 29810-09-1; **4a**, 40916-65-2; **4b**, 69150-45-4; **4c**, 27720-03-2; **4c**·HCl, 85711-08-6; **4d**, 64584-88-9; **4e**, 85711-06-4; **4f**, 2202-65-5; **4f**·HCl, 1128-33-2; **4g**, 85711-07-5; **4h**, 74492-02-7; **4i**, 34381-71-0; **5a**, 74524-03-1; **5b**, 85711-09-7; **5c**, 74492-03-8; **5d**, 74492-04-9; **5e**, 85711-10-0; **5f**, 2202-63-3; **5g**, 85711-11-1; **5h**, 74492-05-0; **5i**, 67824-38-8; **6c**, 3182-95-4; **6f**, 56613-80-0; **6f**·HCl, 85711-12-2; **6g**, 85711-13-3; **6g**·HCl, 85711-14-4; **7**, 85711-15-5; **8**, 85711-16-6; (*R*)-**9**, 57496-01-2; **10**, 79186-17-7; (*S*)-**12a**, 58717-85-4; (*R*)-**12a**, 36617-88-6; (*S*)-**12b**, 77693-46-0; (*R*)-**12b**, 72782-48-0; (*S*)-**12c**, 77693-47-1; (*R*)-**12c**, 73335-32-7; (*S*)-**12d**, 54541-45-6; (*R*)-**12d**, 54541-44-5; (+)-**15a**, 85711-17-7; (−)-**15a**, 85711-18-8; **15b**, 85711-21-3; (*R*)-**16a**, 51146-57-7; (*S*)-**16a**, 51146-56-6; (*R*)-**16b**, 10516-54-8; (*S*)-**16b**, 10532-14-6; $PdCl_2$[(*S*)-Valphos], 85719-55-7; $PdCl_2$[(*S*)-Alaphos], 85719-56-8; $PdCl_2$[(*S*)-Phephos], 85719-57-9; $NiCl_2$, 7718-54-9; (*S*)-1-(dimethylamino)-2-(diphenylphosphinyl)propane, 85711-20-2; (*R*)-1-(dimethylamino)-2-(diphenylphosphinyl)propane, 74098-44-5; dichlorobis(acetonitrile)palladium(II), 14592-56-4; (*S*)-*N*,*N*-dimethylphenylalanine methyl ester, 27720-05-4; diphenylphosphine, 829-85-6; 1,4-dibromobutane, 110-52-1; (*S*)-2-(1-pyrrolidino)-3-phenylpropyl chloride hydrochloride, 85711-19-9; (*R*)-methyl 2-(4-isobutylphenyl)propionate, 81576-57-0; (*R*)-methyl 2-(4-biphenylyl)propionate, 85711-22-4; (1-chloroethyl)benzene, 672-65-1; 1-(1-chloroethyl)-4-methylbenzene, 2362-36-9; 2-(1-chloroethyl)naphthalene, 58464-06-5; 2-chlorooctane, 628-61-5; 1-(1-chloroethyl)-4-(2-methylpropyl)benzene, 62049-65-4; 4-(1-chloroethyl)-1,1'-biphenyl, 58114-03-7.

Photochemistry of Phenyl-Substituted Benzobicyclo[3.1.0]hex-2-enes. A Reverse Di-π-methane Rearrangement

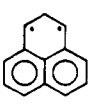
Joseph J. M. Lamberts and Wim H. Laarhoven*

Department of Organic Chemistry, University of Nijmegen, Toernooiveld, 6525 ED Nijmegen, The Netherlands

Received October 22, 1982

The photochemical rearrangements of phenyl-substituted benzobicyclo[3.1.0]hex-2-enes can generally be explained by assuming that homolytic fission of that cyclopropane bond which leads to the most stable diradical is the primary step. The final products are formed by 1,2 hydrogen shifts in the intermediate. An exception to this general pattern was observed with 5-phenylbenzobicyclo[3.1.0]hex-2-ene (**5**). The photoproducts of **5** could only be explained by assuming reverse di-π-methane rearrangements followed by 1,3 hydrogen shifts. It is argued that this reaction path is followed because of the high rate to the back-reaction of the homolytic bond fission of **5**.

Substituted cyclopropanes undergo two major photochemical reactions, viz., cis–trans isomerization and rearrangement to propenes. As a special class of cyclopropanes, bicyclo[3.1.0]hex-2-enes show epimerization at C(6) as their prominent photoreaction upon direct as well as sensitized irradiation[1,2] (Scheme I). Recently, a trimethylene diradical (**2**) has been shown to play a role in the photorearrangement of naphthobicyclo[3.1.0]hexane.[3] This study is aimed at the investigation of the influence of the position of the phenyl substitutent in the photorearrangement of



2

(1) (a) H. E. Zimmerman and G. A. Epling, *J. Am. Chem. Soc.*, **94**, 8749 (1972), and references cited therein; (b) J. S. Swenton, J. A. Hyatt, T. J. Walker, and A. L. Crumrine, *ibid.*, **93**, 4808 (1971).

(2) (a) S. S. Hixson and J. Borovsky, *J. Am. Chem. Soc.*, **97**, 2930 (1975); **98**, 2840 (1976); (b) D. L. Garin and D. J. Cooke, *J. Chem. Soc., Chem. Commun.*, 33 (1972).

(3) J. F. Muller, D. Muller, H. J. Dewey, and J. Michl, *J. Am. Chem. Soc.*, **100**, 1629 (1978).

0022-3263/83/1948-2202$01.50/0