1.6–2.5 (m, 4 H, H_2, H_3, OH). Anal. Calcd for $C_{11}H_{12}FeO_4$: C, 50.03; H, 4.58. Found: C, 49.70; H, 4.69.

Preparation of 3-Fp-5-hydroxy-2-pentanone (15b). The reaction of **8** (0.653 g, 2.04 mmol) with **9b** (0.316 g, 3.24 mmol) in the presence of $PhNMe_2$ (0.258 g, 2.13 mmol) gave no detectable **14b**. The product was directly reacted with 10 mL of 10% Na_2CO_3 with THF as a cosolvent. Chromatography on alumina (activity III, neutral) yielded **15b** upon elution with CH_3CN/CH_3OH (10/1); 0.200 g (34%). Recrystallization from CH_2Cl_2/hexane gave an analyticlaly pure solid, mp 93–94 °C. The crude material showed a mixture of diastereomers in the ^1H NMR spectrum (3:1). The reported NMR is for the major component: IR (film) 3500, 2010, 1970, 1630 cm^{-1}; ^1H NMR ($CDCl_3$) 4.77 (s, 5 H, Cp), 3.7 (m, 1 H, H_5), 2.80 (dd, 1 H, J = 2.0, 11.0 Hz, H_3), 2.22 (ddd, 1 H, J = 3.0, 11.0, 14.0 Hz, H_{4a}), 2.16 (s, 3 H, H_1), 1.49 (ddd, 1 H, J = 2.0, 8.0, 14.0 Hz, H_{4b}), 1.13 (d, 3 H, J = 6.0 Hz, H_6), the position of the OH signal was not determined. Anal. Calcd for $C_{13}H_{16}FeO_4$: C, 53.45; H, 5.52. Found: C, 53.44; H, 5.70.

Preparation of 2-Fp-4-hydroxy-4-methylpentanal (15c). Complex **11c** (0.118 g, 0.326 mmol) was reacted with Na_2CO_3 as with **15a** to yield **15c**: 0.097 g (100%), mp 94–95 °C dec; IR ($CDCl_3$) 2015, 1945, 1630 cm^{-1}; ^1H NMR (CD_3NO_2) δ 9.19 (d, 1 H, J = 3.2, H_1), 4.92 (s, 5 H, Cp), 2.72 (ddd, 1 H, J = 2.0, 3.2, 11.0 Hz, H_2), 2.30 (dd, 1 H, J = 11.0, 14.0 Hz, H_{3a}), 1.62 (dd, 1 H, J = 2.0, 14.0 Hz, H_{3b}), 1.09 (s, 6 H, CH_3's), 2.48 (s, 1 H, OH). Anal. Calcd. for $C_{13}H_{16}FeO_4$: C, 53.45, H, 5.52. Found: C, 53.42, 5.62. An NMR experiment in CO_3NO_2 showed that **15c** could be cleanly transformed back to **11c** by using trifluoroacetic acid.

Attempted Preparation of 11d. Compound **14d** (30 mg) was dissolved in CD_3NO_2 and filtered through Celite into an NMR tube. Upon addition of 10 μL of trifluoroacetic acid, new signals appeared as singlets at δ 5.37, 2.50, and 1.80. After 3 h at room temperature, the signals for **14d** and the new product had disappeared and were replaced by a singlet at δ 5.25. The rest of the spectrum was very broad.

Acknowledgment is made to the Research Corp., the donors of the Petroleum Research Fund, administerd by the American Chemical Society, and the Graduate Research Council of the University of Oklahoma, for support of this work. Appreciation is given to Barbara King and Keith Jones for preparing some of the starting materials.

Registry No. 7, 76983-90-9; 8, 46238-51-1; **9a**, 18913-31-0; **9b**, 40296-27-3; **9c**, 34761-53-0; **9d**, 2425-45-8; **11a**, 76983-93-2; **11b**, 79391-83-6; **11c**, 79391-85-8; **14c**, 79391-86-9; **14d**, 79391-87-0; **15a**, 79391-88-1; **15b**, 79391-89-2; **15c**, 79391-90-5; NaF_p, 12152-20-4; 4-chloro-2-butyn-1-ol, 13280-07-4.

Benzenesulfonylcarbonitrile Oxide. 3. Useful New Procedures for Generation

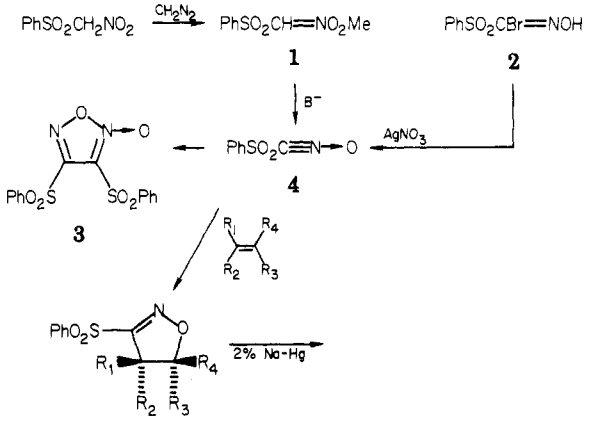
Peter A. Wade* and M. Krishna Pillay

Department of Chemistry, Drexel University, Philadelphia, Pennsylvania 19104

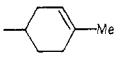
Received July 23, 1981

Chemoselective processes permitting the functionalization of isolated carbon–carbon double bonds are currently of major synthetic importance, and this importance continues to grow in concert with the development of improved methods for the preparation of alkenes. Nitrile oxides cycloadd to alkenes in one such process, many diverse functionalities being tolerated in the reacting partners. This, in conjunction with straightforward transformation procedures, has led to a number of useful new synthetic procedures.[1]

Scheme I

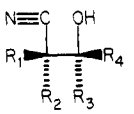


5a, $R_1 = R_2 = R_3 = H$; $R_4 = n$-Bu

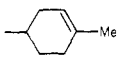
b, $R_1 = R_2 = H$; $R_3 = Me$; R_4 = 

c, $R_1 = H$; $R_2R_3 = -(CH_2)_4-$; $R_4 = Me$

d, $R_1 = R_2 = R_3 = R_4 = Me$



6a, $R_1 = R_2 = R_3 = H$; $R_4 = n$-Bu

b, $R_1 = R_2 = H$; $R_3 = Me$; R_4 = 

c, $R_2 = R_3 = H$; R_1R_4 = 

We have recently reported the use of benzenesulfonylcarbonitrile oxide (**4**) in the functionalization of alkenes.[2] For simple alkenes two limitations were encountered. Reaction with 2,3-dimethyl-2-butene gave only a 17% yield of cycloadduct, even with a large excess of the alkene. Also, the required precursor to nitrile oxide **4** involved a four-step preparation. Here we report two new procedures for generating this nitrile oxide each of which eliminates one of these problems.

The methyl nitronic ester **1** provides easy access to nitrile oxide **4**.[3] (Phenylsulfonyl)nitromethane is O-methylated with diazomethane and the derived crude **1** treated with aqueous sodium silicate or hydroxide in a two-phase system (Scheme I). In the absence of alkene, nitrile oxide dimer **3** is obtained in 44% yield, indicating some side reactions to the formation of the 1,3-dipole. However, when an excess of reagents is employed in the

(1) (a) Jager, V.; Buss, V. *Liebigs Ann. Chem.* **1980**, *101*. (b) Jager, V.; Buss, V.; Schwab, W. *Ibid.* **1980**, 122. (c) Confalone, P. N.; Lollar, E. D.; Pizzolato, G.; Uskovic, M. R. *J. Am. Chem. Soc.* **1978**, *100*, 6291. (d) Burri, K. F.; Cardone, R. A.; Chen, W. Y.; Rosen, P. *Ibid.* **1978**, *100*, 7069. (e) Huisgen, R.; Christl, M. *Chem. Ber.* **1973**, *106*, 3291. (f) Kalvoda, J.; Kaufmann, H. *J. Chem. Soc., Chem. Commun.* **1976**, 209. (g) Grund, H.; Jager, V. *Liebigs Ann. Chem.* **1980**, 80. (h) Jager, V.; Grund, H. *Angew. Chem., Int. Ed. Eng.* **1976**, *15*, 27. (i) Jager, V.; Grund, H.; Schwab, W. *Ibid.* **1979**, *18*, 78. (j) Kaufmann, H.; Kalvoda, J. *J. Chem. Soc., Chem. Commun*, **1976**, 210. (k) Kotera, K.; Takano, Y.; Matsuura, A.; Kitahonoki, K. *Tetrahedron* **1970**, *26*, 539.

(2) For the previous paper in this series, see: Wade, P. A.; Hinney, H. R. *J. Am. Chem. Soc.* **1979**, *101*, 1319.

(3) Nitronic anhydrides are common nitrile oxide precursors, but nitronic esters have rarely been employed. For one example, see: Young, A.; Levand, O.; Luke, W. K. H.; Larson, H. O. *J. Chem. Soc., Chem. Commun.* **1966**, 230.

0022-3263/81/1946-5425$01.25/0

presence of suitable alkenes, cycloadducts are readily obtained. For 1-hexene and *d*-limonene cycloadducts **5a** and **5b** were obtained in 72% and 46% yields, respectively, based on the alkene. It is interesting to note that for *d*-limonene only the disubstituted and not the trisubstituted double bond was attacked. This latter reaction can be performed in 65% yield with greater than 96% chemoselectivity for the disubstituted double bond by using base treatment of the α-bromo oxime **2**.

Besides allowing the convenient preparation of cycloadducts, the nitronic ester procedure can be combined with our previously reported[2] transformation of 3-(phenylsulfonyl)isoxazolines to β-cyanohydrins with 2% sodium amalgam. Without the isolation of cycloadducts, 1-hexene, *d*-limonene, and norbornylene were converted to the corresponding β-cyanohydrins **6a–c** in 69%, 44%, and 88% yield, respectively, based on the starting alkene. The dimer **3** formed along with the intermediate cycloadducts was conveniently destroyed in situ by 2% sodium amalgam.

The most versatile route for the preparation of a nitrile oxide involves portionwise base treatment of the corresponding α-halo oxime in the presence of substrate alkene.[4] This route is applicable to nitrile oxide **4** by using the α-bromo oxime **2**, obtained by sequential bromination, O-methylation, and mild thermolysis of the resulting nitronic ester. However, nitrile oxide **4** is sensitive to attack by basic reagents, especially amines. Thus, triethylamine is not generally suitable for preparing nitrile oxide **4** subsequent to cycloaddition. With difficult alkenes, our recommended two-phase aqueous sodium carbonate procedure also does not permit high yields of cycloadduct. An alternative procedure which is found to be more effective is to employ silver nitrate. Under these conditions, 1-hexene and 1-methylcyclohexene gave cycloadducts **5a** and **5c** in 81% and 72% yields, respectively. With aqueous sodium carbonate, yields of only 76% and 59%, respectively, were obtained. For 2,3-dimethyl-2-butene, only a 17% yield of cycloadduct **5d** could be obtained by using the base procedure. At 50 °C with silver nitrate, however, the yield of **5d** was increased to 44%. This result for 2,3-dimethyl-2-butene is particularly encouraging when compared to reports for other 1,3-dipoles.[5]

Other procedures for the generation of nitrile oxide **4** have also been investigated, including treatment of (phenylsulfonyl)nitromethane with phenyl isocyanate–triethyl amine and thermolysis of dimer **3**. These procedures were unsatisfactory, a complex mixture of products resulting in each case.

Experimental Section

General Methods. Diazomethane[6] and 2% Na–Hg[7] were prepared by standard procedures. *d*-Limonene was passed through a short column of alumina and distilled just prior to use; other alkenes were simply distilled unless otherwise noted. Reactions were routinely worked up by using anhydrous sodium sulfate as a drying agent and concentrating at reduced pressure. Column chromatography was carried out on Baker analyzed reagent silica gel (60–200 mesh) with methylene chloride as the eluting solvent unless otherwise noted. Other general details have recently been published.[8]

General Procedures for the Preparation of Nitrile Oxide Cycloadducts 5a–d. (A) Nitronic Ester Method. Nitrile oxide precursor **1** was prepared by adding three 5-mL portions of 0.4 M etheral diazomethane over 10 min to an ice-cold solution of (phenylsulfonyl)nitromethane[8,9] (1.0 g, 5.0 mmol) in 10 mL of methylene chloride. After the mixture was stirred for 10 min, solvent and excess diazomethane were removed at reduced pressure (0–5 °C), and methylene chloride (6 mL), alkene (1.20 mmol), and 1.0 M aqueous sodium metasilicate (6 mL) were added. The reaction mixture was stirred (300–600 rpm) at ambient temperature for 4 h and then methylene chloride and water were added. The organic layer was separated, washed with water, dried and concentrated. Column chromatography gave the pure product as listed below for the individual compounds.

(B) Silver Nitrate Method. To a mixture of alkene (5–15 mmol) and silver nitrate (170 mg, 1.0 mmol) under N_2 was added dropwise over 2 h (syringe pump) a solution containing bromo oxime **2**[2] (132 mg, 0.5 mmol), alkene (5–15 mmol), and THF (2 mL). The resulting mixture was stirred for 15 min and filtered, and the filtrate was concentrated to give the crude product. This was chromatographed as in procedure A. Reaction temperatures and total amounts of alkene used are listed individually below.

5-Butyl-4,5-dihydro-3-(phenylsulfonyl)isoxazole (5a) was prepared in 72% yield by procedure A and in 81% yield by procedure B (10 equiv of 1-hexene, 20–25 °C). The crude product was chromatographed with 80:20 hexane–ethyl acetate as the eluting solvent; dimer **3** eluted after compound **5a** under these conditions. Kugelrohr distillation gave the analytical sample: bp 140–150 °C (0.04 torr); IR (film) 1330, 1160 cm^{-1} (sulfone); NMR δ 7.3–8.0 (m, 5 H), 4.4–5.0 (m, 1 H), 3.27 (dd, 1 H, J_{AB} = 17 Hz, J_{AX} = 10 Hz), 2.87 (dd, 1 H, J_{AB} = 17 Hz, J_{BX} = 8 Hz), 0.7–1.9 (m, 9 H).

Anal. Calcd for $C_{13}H_{17}NO_3S$: C, 58.42; H, 6.41; N, 5.24. Found: C, 58.32; H, 6.58; N, 5.51.

4,5-Dihydro-5-(4-methyl-3-cyclohexenyl)-3-(phenylsulfonyl)isoxazole (5b). The cycloadduct was prepared in 46% yield by procedure A and in 65% yield from base treatment of bromo oxime **2**.[2] Distillation (Kugelrohr) gave the analytical sample: bp 150–160 °C (0.02 torr); IR (film) 1330, 1160 cm^{-1} (sulfone); NMR δ 7.5–8.15 (m, 5 H), 5.35 (br s, 1 H), 3.19 (d, 1 H of AB pattern, J = 17 Hz), 2.93 and 2.89 (2 d, 1 H of two AB patterns in equal intensity, J = 17 Hz), 1.2–2.2 (m, 13 H).

Anal. Calcd for $C_{17}H_{21}NO_3S$: C, 63.94; H, 6.63; N, 4.39. Found: C, 63.75; H, 6.37; N, 4.41.

3a,4,5,6,7,7a-Hexahydro-7a-methyl-3-(phenylsulfonyl)-1,2-benzisoxazole (5c). The cycloadduct was prepared in 72% yield by procedure B (60 equiv of 1-methylcyclohexene, 45–50 °C). It was necessary to free the alkene of isomeric methylenecyclohexane by spinning-band distillation; the alkene was passed through a short column of silica gel just prior to use. The analytical sample of cycloadduct **13** was Kugelrohr distilled: bp 150–160 °C (0.10 torr); IR (film) 1330, 1170 cm^{-1} (sulfone); NMR δ 7.5–8.2 (m, 5 H), 3.20 (m, 1 H), 1.2–2.2 (m) overlapping 1.27 (s, total of 11 H).

4,5-Dihydro-4,4,5,5-tetramethyl-3-(phenylsulfonyl)isoxazole (5d). Prepared in 44% yield by procedure B (60 equiv of 2,3-dimethyl-2-butene, 50–55 °C). It was necessary to free the alkene of all isomers by spinning-band distillation; the alkene was passed through a short column of silica gel just prior to use. The cycloadduct was obtained as an oil: IR (film) 1320, 1150 cm^{-1} (sulfone); NMR δ 7.5–8.1 (m, 5 H), 1.30 (s, 6 H), 1.23 (s, 6 H).

Anal. Calcd for $C_{13}H_{17}NO_3S$: C, 58.41; H, 5.24; N, 6.41. Found: C, 58.58; H, 5.43; N, 6.36.

Also isolated in 43% yield was dimer **3**.

Preparation of β-Cyanohydrins 6a–c. To an ice-cold solution of (phenylsulfonyl)nitromethane[8,9] (1.01 g, 5.0 mmol) in methylene chloride (10 mL) were added over 10 min three 5-mL portions of 0.4 M etheral diazomethane. The solution was stirred for 10 min and concentrated (0–5 °C) to a white pasty residue. Methylene chloride (6 mL) and the alkene (1.2 mmol) were added followed by 1 M aqueous sodium metasilicate (6 mL). The mixture

(4) For a review, see: Grundmann, C.; Grunanger, P. "The Nitrile Oxides"; Springer-Verlag: New York, 1971.

(5) (a) Grundmann, C.; Frommeld, H.-D.; Flory, K.; Datta, S. K. *J. Org. Chem.* **1968**, *33*, 1464. (b) Tartakovskii, V. A.; Chlenov, I. E.; Lagodzinskaya, G. V.; Novikov, S. S. *Dokl. Akad. Nauk. SSSR* **1965**, *161*, 136.

(6) Moore, J. A.; Reed, D. E. "Organic Syntheses"; Wiley: New York, 1973; Collect. Vol. 5, p 351.

(7) Fieser, L. F.; Fieser, M. "Reagents for Organic Synthesis"; Wiley: New York, 1967; Vol. 1, p 1030.

(8) Wade, P. A.; Hinney, H. R.; Amin, N. V.; Vail, P. D.; Morrow, S. D.; Hardinger, S. A.; Saft, M. S. *J. Org. Chem.* **1981**, *46*, 765.

(9) See also: Kelley, J. L.; McLean, E. W.; Williard, K. F. *J. Heterocycl. Chem.* **1977**, *14*, 1415.

was stirred (300–600 rpm) at ambient temperature for 4 h, and then water and methylene chloride were added. The organic layer was separated, washed with water, dried, and concentrated. Without purification, the crude product was dissolved in THF (15 mL). Water (0.50 mL) and 2% Na–Hg (6.5 g, 5.7 mmol of Na°) were added, and the mixture was stirred rapidly. After 1 h, more water (0.25 mL) and 2% Na–Hg (3.3 g, 2.9 mmol of Na°) were added, and stirring was continued for 1 h. Methylene chloride (15 mL) and anhydrous sodium sulfate were added, and after 10 min the mixture was filtered and concentrated. The crude product was purified by Kugelrohr distillation. In all cases the β-cyanohydrin was obtained in >90% purity (VPC), but traces of low-boiling impurities were present.

3-Hydroxyheptanenitrile (6a). The product (95% pure by VPC) was obtained in 69% yield as an oil, bp 65–75 °C (0.02 torr). The analytical sample was further purified by preparative VPC: IR (film) 3450 (OH), 2260 cm^{-1} (CN); NMR δ 3.6–4.1 (m, 1 H), 3.04 (br s, 1 H, exchanges with D_2O), 2.52 (d, 2 H, J = 5.5 Hz), 0.7–1.8 (m, 9 H).

3-Hydroxy-3-(4-methyl-3-cyclohexenyl)butanenitrile (6b). Prepared in 44% yield by the general procedure. The product (90% pure by VPC, several volatile constituents were present in low yield) was obtained as an oil, bp 80–95 °C (0.02 torr). The analytical sample was purified by preparative VPC (SE-30 column, 170 °C): IR (film) 3460 (OH), 2260 cm^{-1} (CN); NMR δ 5.35 (br s, 1 H), 2.72 (s, 1 H, exchanges with D_2O), 2.53 (s, 2 H; at 250 MNz[10] appears as two overlapping AB quartets), 1.1–2.1 (m, 13 H).

Anal. Calcd for $C_{11}H_{17}NO$: C, 73.70; H, 9.56. Found: C, 73.49; H, 9.61.

Starting with purified cycloadduct, an 87% yield of β-cyanohydrin **6b** was obtained.

***(exo,exo)*-3-Hydroxybicyclo[2.2.1]heptane-2-carbonitrile (6c).** The product was obtained in 88% yield as an oil (>95% pure by VPC) which refused to crystallize, bp 90–100 °C (0.025 torr) [lit.[1e] bp 110 °C (0.001 torr)]. The spectra were identical with those published.

Acknowledgment. This investigation was supported by PHS Grant No. CA 26943 awarded by the National Cancer Institute, DHHS.

Registry No. 1, 57359-33-8; 2, 70367-23-6; 3, 66074-00-8; 4, 70367-24-7; 5a, 70367-25-8; 5b, 79466-78-7; 5c, 79466-79-8; 5d, 70367-31-6; 6a, 70102-87-3; 6b, 79466-80-1; 6c, 79466-81-2; (phenylsulfonyl)nitromethane, 21272-85-5; 1-hexene, 592-41-6; *d*-limonene, 5989-27-5; 1-methylcyclohexene, 591-49-1; 2,3-dimethyl-2-butene, 563-79-1; norbornylene, 498-66-8.

(10) We thank Dr. George Furst (University of Pennsylvania, Department of Chemistry) for obtaining these spectra.

Use of Heterogeneous Asymmetric Hydrogenation for the Preparation of a Chiral Phosphinite and Its Application as a Ligand in Homogeneous Asymmetric Hydrogenation

József Bakos,* Imre Tóth, and László Markó

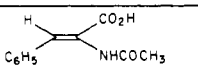
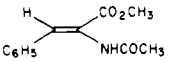
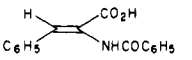
Department of Organic Chemistry, University of Chemical Engineering, H-8200 Veszprém, Hungary

Received January 26, 1981

The success of homogeneous asymmetric hydrogenation of prochiral olefins with rhodium complexes as catalysts depends mainly on the structure of the chiral ligand, a phosphine, or a phosphinite. Three different methods have been used up until now for the preparation of such compounds: resolvation of a racemic mixture,[1] use of a chiral natural product as the starting compound,[2] and asymmetric homogeneous hydrogenation.[3] We report now on a fourth procedure, the use of asymmetric heterogeneous hydrogenation.

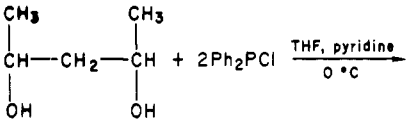
(1) W. S. Knowles and M. J. Sabacky, *Chem. Commun.*, 1445 (1968).

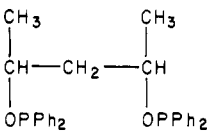
Table I. Hydrogenation of Prochiral Olefins with Rhodium Complex Catalysts Containing BDPOP[a]

olefin	Et_3N/Rh molar ratio	optical yield, % (*S,S*)-(+)-BDPOP[b]	optical yield, % (*R,R*)-(−)-BDPOP[d]
	0	53	63
	0.5	58	65
	1.0		54
	3.0		54
	3.0		48[c]
	8.0		10
	0	48	
	2.0		53
	0	78	

[a] Reaction conditions: substrate/[(nor-C_7H_8)RhCl]$_2$/BDPOP ratio of 100:1:2.2, solvent benzene/methanol (1/1), 1 bar of H_2, 25 °C. [b] The absolute configuration is *S* in all cases. [c] Catalyst [(nor-C_7H_8)Rh(BDPOP)]$^+$-ClO_4^-, substrate/Rh ratio of 100:1, solvent methanol. [d] The absolute configuration is *R* in all cases.

By use of the method of Izumi and co-workers[4] (−)-(2*R*,4*R*)- and (+)-(2*S*,4*S*)-2,4-pentanediol were prepared by hydrogenating acetylacetone in the presence of a Raney nickel catalyst modified with an aqueous solution of tartaric acid (the *R,R* or *S,S* enantiomer, respectively) and NaBr. The pentanediol enantiomers (optical purities above 97%) were transformed with Ph_2PCl to the two corresponding enantiomers of 2,4-bis[(diphenylphosphinyl)oxy]pentane (BDPOP).





BDPOP

Both chiral phosphinites were tested as ligands in the homogeneous catalytic hydrogenation of (acylamino)-cinnamic acid derivatives with (phosphine)rhodium complexes as catalysts. The results are compiled in Table I.

The optical yields achieved correlate well with that obtained with the only other diphosphinite containing an OC_3O bridge between the two phosphorous atoms.[5] Et_3N had no significant effect at low N/Rh ratios on the enantioselectivity, but large amounts of Et_3N were disadvantageous.

In addition the (*R,R*)-pentanediol was transformed in the usual way over the ditosylate into (−)-(2*S*,4*S*)-2,4-bis(diphenylphosphino)pentane.

This chiral ditertiary phosphine, however, proved to be an oily substance, and we could not obtain it in a sufficiently pure state necessary for complete characterization. With this oil as a ligand, 37–44% optical yields were

(2) T. P. Dang and H. B. Kagan, *Chem. Commun.*, 481 (1971).
(3) M. D. Fryzuk and B. Bosnich, *J. Am. Chem. Soc.*, 100, 5491 (1978).
(4) K. Ito, T. Harada, A. Tai, and Y. Izumi, *Chem. Lett.*, 1049 (1979).
(5) R. Jackson and D. J. Thompson, *J. Organomet. Chem.*, 159, C29 (1978).

0022-3263/81/1946-5427$01.25/0