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Poly(tertiary phosphines and arsines). 17. Poly(tertiary phosphines) Containing Terminal Neomenthyl Groups as Ligands in Asymmetric Homogeneous Hydrogenation Catalysts[1,2]

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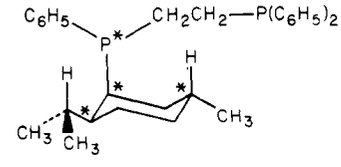
The addition of neomenthylphenylphosphine to $(C_6H_5)_2PCH{=}CH_2$ in boiling tetrahydrofuran catalyzed by potassium *tert*-butoxide gives the di(tertiary phosphine) $(Nmen)(C_6H_5)PCH_2CH_2P(C_6H_5)_2$ (I, Nmen = neomenthyl), which could be separated by fractional crystallization into pure diastereomers differing only in the configuration at the chiral phosphorus atom. Novel features in this new di(tertiary phosphine) are the chiral terminal neomenthyl group and the nonequivalent phosphorus atoms. Asymmetric homogeneous hydrogenations of the prochiral α-(acylamido)cinnamic acid derivatives $C_6H_5CH{=}C(NHCOR)(CO_2R')$ (R = CH_3, R′ = H and CH_3; R = C_6H_5, R′ = H and C_2H_5) result in significant differences in optical yield behavior when rhodium(I) complexes of each of the two diastereomers of $(Nmen)(C_6H_5)PCH_2CH_2P(C_6H_5)_2$ are used. In particular, the optical yield range for the above four prochiral α-(acylamido)cinnamic acid derivatives is 31–85% for one of the diastereomers of I but only 42–56% for the other diastereomer. The related polyphosphorus compounds $C_6H_5P[CH_2CH_2P(Nmen)(C_6H_5)]_2$ and $(Nmen)(C_6H_5)PCH_2CH_2P(S)(CH_3)_2$ have been obtained as mixtures of diastereomers from the additions of neomenthylphenylphosphine to $C_6H_5P(CH{=}CH_2)_2$ and $CH_2{=}CHP(S)(CH_3)_2$, respectively, in boiling tetrahydrofuran catalyzed by potassium *tert*-butoxide.

The original work with rhodium(I) complexes of chiral phosphines as asymmetric homogeneous hydrogenation catalysts used monodentate phosphines containing chirality either at the phosphorus or at one or more carbon atoms.[3-5] More recent work has shown that the use of asymmetric chelating di(tertiary phosphines) in such catalysts can result in systems which give much higher optical yields in the asymmetric hydrogenation of prochiral olefins. Examples of chiral di(tertiary phosphines) giving optical yields approaching 100% in the hydrogenation of prochiral olefins such as α-acetamidoacrylic acid are the ligand (−)-(*o*-$CH_3OC_6H_4$)(C_6H_5)$PCH_2CH_2P(C_6H_5)$-($C_6H_4OCH_3$-*o*) ("dipamp") of Knowles et al.[6] and the ligands (−)-(2*S*,3*S*)-$(C_6H_5)_2PCH(CH_3)CH(CH_3)P(C_6H_5)_2$ ("(*S*,*S*)-chiraphos")[7] and $(C_6H_5)_2PCH(CH_3)CH_2P(C_6H_5)_2$ ("*R*-prophos")[8] of Fryzuk and Bosnich. The high optical yields in asymmetric hydrogenations of prochiral olefins using catalysts containing these bidentate ligands may relate to the rigidity of the five-membered chelate rings in the catalytically active rhodium(I) species.

All of these reported chiral di(tertiary phosphines) have had the chirality in either the phosphorus atoms or the bridge between the two phosphorus atoms. This paper describes the preparation and properties of the new chiral di(tertiary phosphine) $(Nmen)(C_6H_5)PCH_2CH_2P(C_6H_5)_2$ (Nmen = neomenthyl) of structure I (chiral atoms are



I

starred in structures in this paper), as well as related polyphosphorus compounds containing terminal neo-

(1) Part 16: R. B. King and W. Z. M. Rhee, *Inorg. Chem.*, 17, 2961 (1978).
(2) Portions of this work were presented at the Joint Central-Great Lakes Regional Meeting of the American Chemical Society, Indianapolis, Ind., May, 1978; paper ORGN 58 in abstracts.
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(4) J. D. Morrison, W. F. Masler, and S. Hathaway in "Catalysis in Organic Syntheses, 1976", P. N. Rylander and H. Greenfield, Eds., Academic Press, New York, 1976.
(5) J. D. Morrison, W. F. Masler, and M. K. Neuberg, *Adv. Catal.*, **25**, 81 (1976).
(6) W. S. Knowles, M. J. Sabacky, B. D. Vineyard, and D. J. Weinkauff, *J. Am. Chem. Soc.*, **97**, 2567 (1975).
(7) M. D. Fryzuk and B. Bosnich, *J. Am. Chem. Soc.*, **99**, 6262 (1977).
(8) M. D. Fryzuk and B. Bosnich, *J. Am. Chem. Soc.*, **100**, 5491 (1978).

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menthyl groups. The new ligand I has the following novel features: (1) The terminal chiral neomenthyl group can be obtained from the inexpensive optically active natural product (−)-menthol. (2) This chiral neomenthyl group makes possible a pair of diastereomers, differing only in the configuration around the chiral phosphorus atom (starred in structure I). The two diastereomers of I can be separated by fractional crystallization thereby making I the first example of a self-resolving chiral di(tertiary phosphine) where the chirality in a terminal group can be used to resolve a chiral phosphorus atom. This paper examines both the separation of (Nmen)(C_6H_5)-$PCH_2CH_2P(C_6H_5)_2$ (I) derived from optically pure (−)-menthol into the pure diastereomers and the use of each pure diastereomer in a rhodium(I)-based homogeneous catalyst for the asymmetric hydrogenation of prochiral α-(acylamido)cinnamic acid derivatives. This represents the first time that it has been feasible to compare optical yields obtained from two diastereomeric chiral di(tertiary phosphines) used as ligands in an asymmetric homogeneous hydrogenation catalyst.

Experimental Section

Preparative Studies. Microanalyses were performed by Atlantic Microanalytical Laboratory and Schwarzkopf Microanalytical Laboratory. Proton NMR spectra were taken in $CDCl_3$ solutions and recorded at 60 MHz on a Varian T-60 spectrometer. The proton NMR spectra of the new neomenthylphosphines showed the correct ratios of the various types of protons but were too complex to analyze in detail. Phosphorus-31 and carbon-13 (Table I) NMR spectra were taken in dichloromethane solutions and recorded at 40.3 and 25.0336 MHz, respectively, on a Jeolco PFT-100 spectrometer operating in the pulsed Fourier transform mode with proton noise decoupling and a deuterium lock. Phosphorus-31 chemical shifts (δ) are reported in parts per million downfield from external 85% H_3PO_4 whereas carbon-13 chemical shifts (Table I) are reported in parts per million downfield from internal tetramethylsilane. Melting points were taken in capillaries and are uncorrected. Optical rotation measurements were done at ambient temperatures by using the sodium D line (589 nm) on a Perkin-Elmer Model 141 automatic polarimeter. Dichloromethane solutions prepared in a nitrogen-filled glovebox were used for the optical rotation measurements unless otherwise indicated.

All preparations of organophosphorus compounds were carried out in an efficient hood, using calcium hypochlorite traps to destroy any noxious effluent vapors before passing them into the hood exhaust. Air-sensitive organophosphorus and organometallic compounds were handled in a nitrogen atmosphere by using Schlenk tubes and associated equipment and a nitrogen-filled glovebox where necessary. Tetrahydrofuran was redistilled under nitrogen over sodium benzophenone ketyl.

Commercial (−)-menthol was converted into (−)-menthyl chloride[9] and (+)-neomenthyl chloride[10] by the cited published procedures. The organophosphorus compounds phenylphosphine,[11,12] diphenylvinylphosphine,[13,14] dimethylvinylphosphine sulfide,[15] and neomenthyldiphenylphosphine[16] were prepared by the cited published procedures. Phenyldivinylphosphine [bp 127–132 °C (36 mm) (lit.[17] bp 55 °C (0.5 mm)] was prepared in 41% yield by the reaction of phenyldichlorophosphine with vinylmagnesium bromide in tetrahydrofuran followed by

Table I. Carbon-13 NMR Spectra of Neomenthyl and Menthyl Groups[a] in Organophosphorus and Related Compounds

	carbon-13 NMR spectrum, δ[c]										
compd[b]	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	CH_2CH_2 bridge
MenOH[d]	32.2	45.9	71.2	50.7	23.8	35.3	22.6	26.1	16.3	21.3	
MenCl	34.3	47.8	63.7	51.5	25.3	35.4	22.9	28.0	16.1	21.9	
$MenPPh_2$[d]	34.0 (2.5)	37.9 (1.3)	38.2 (21.8)	45.7 (13.1)	25.9 (8.8)	35.3	22.6	28.5 (20.5)	15.5 (1.2)	21.7	
MenP(H)Ph[e]	35.0		39.5 (14.7)	46.7 (11.0)	26.3 (7.3)			29.6 (9.8)			
	34.3 (17.3)	41.7 (8.6)	37.7 (12.2)	48.1 (12.2)	25.9 (8.5)	36.1	23.6	29.5 (15.9)	16.1	22.6	
$NmenPPh_2$[d]	27.7 (5.8)	39.5 (2.5)	35.8 (19.9)	50.3 (15.8)	26.4 (9.8)	36.3	22.7	30.1 (9.6)	22.4 (1.2)	21.2 (0.9)	
NmenP(H)Ph[e]	28.4 (4.9)	40.2	36.5 (20.7)	50.8 (15.9)	27.0 (9.8)	37.0	23.4	30.8 (9.8)	23.1	21.9	
(Nmen)PhPCH$_2$CH$_2$PPh$_2$ (LS)	29.5 (6.1)	39.9	39.8 (18.3)	51.3 (14.7)	27.3 (11.0)	37.1	23.5	30.6 (8.6)	22.1	21.9	~25.1
(Nmen)PhPCH$_2$CH$_2$PPh$_2$ (MS)	28.4 (4.9)	40.4	40.0 (17.1)	50.5 (15.9)	27.0 (11.0)	37.0	23.3	31.3 (7.3)	22.9	22.1	~25.5
				51.2 (14.7)				31.3 (6.1)			
PhP[CH$_2$CH$_2$PPh(Nmen)]$_2$[e]	29.5 (4.9)	40.3	39.9	50.5 (14.6)	27.1 (11.0)	37.0	23.3	30.6 (8.5)	22.9	22.1	28.4, 25.4

[a] In addition to the resonances listed here, the compounds containing phenyl groups exhibited the expected complex phenyl carbon-13 pattern in the range δ 141–128. [b] Men = menthyl, Nmen = neomenthyl, Ph = phenyl, LS = less soluble isomer, MS = more soluble isomer. [c] The phosphorus–carbon coupling constants for the resonances observed as doublets (in hertz) are given in parentheses. [d] These data, listed for comparison, are taken from A. M. Aguiar, C. J. Morrow, J. D. Morrison, R. E. Burnett, W. F. Masler, and N. S. Bhacca, *J. Org. Chem.*, 41, 1545 (1976). [e] These compounds were mixtures of diastereomers.

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(10) L. Horner, H. Oedinger, and H. Hoffman, *Justus Liebigs Ann. Chem.*, **626**, 26 (1959).
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(15) R. B. King and J. C. Cloyd, Jr., *J. Am. Chem. Soc.*, **97**, 53 (1975).
(16) A. M. Aguiar, C. J. Morrow, J. D. Morrison, R. E. Burnett, W. F. Masler, and N. S. Bhacca, *J. Org. Chem.*, **41**, 1545 (1976).
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hydrolysis with aqueous tetrasodium ethylenediaminetetraacetate analogous to a recently reported[18] preparation of (diethylamino)divinylphosphine.

Preparation of Neomenthylphenylphosphine. A blue solution of 14.3 g (0.62 mol) of sodium metal in 1 L of liquid ammonia was treated dropwise with a solution of 68 g (0.62 mol) of phenylphosphine in 500 mL of tetrahydrofuran to give a red solution of sodium phenylphosphide. The liquid ammonia was then allowed to evaporate spontaneously by stirring the reaction mixture at room temperature for 10 h. A solution of 113.6 g (0.65 mol) of (−)-menthyl chloride ($[\alpha]^{8}_{D}$ −42.32° (neat)) was added in one portion. The reaction mixture was boiled under reflux for 22 h. The resulting light orange solution was treated with 125 mL of deoxygenated water. The organic layer was separated, washed with water, dried with sodium sulfate, and concentrated at ~25 mm. Distillation of the filtered solution after removal of the solvent gave 38.0 g of a forerun [bp 37–70 °C (0.15 mm)], followed by 71.6 g (46.5% yield) of neomenthylphenylphosphine: bp 120–123 °C (0.08 mm); $[\alpha]^{26}_{D}$ +93.5° (neat); IR ν(PH) 2295 cm^{-1}; ^{31}P NMR δ −55.5 and −66.0 of approximately equal relative intensities. Anal. Calcd for $C_{16}H_{25}P$: C, 77.4; H, 10.1; P, 12.5. Found: C, 77.2; H, 10.0; P, 12.1.

This product was very air sensitive, solidifying immediately upon exposure to air.

Preparation of 1-(Neomenthylphenylphosphino)-2-(diphenylphosphino)ethane (I). A mixture of 14.4 g (58 mmol) of neomenthylphenylphosphine, 12.3 g (58 mmol) of diphenylvinylphosphine, 3–4 spatula tips (~0.2 g, not weighed) of potassium *tert*-butoxide, and 150 mL of tetrahydrofuran was boiled under reflux for 42 h. Solvent was then removed at 30–40 °C (20 mm). The viscous oily residue was dissolved in 140 mL of degassed absolute ethanol. The solution was kept overnight at −15 °C to give 25.6 g (96% yield) of a diastereomeric mixture of (Nmen)(C_6H_5)$PCH_2CH_2P(C_6H_5)_2$ collected in several crops.

Anal. Calcd for $C_{30}H_{38}P_2$: C, 78.3; H, 8.3; P, 13.5. Found: C, 78.1; H, 8.3.

The two diastereomers were separated from this crude product by repeated fractional crystallization from ethanol. In this connection the diastereomeric mixture obtained from an experiment such as that described above was dissolved in 200 mL of boiling degassed absolute ethanol. Cooling the resulting solution to room temperature gave a white solid. Two more similar crystallizations of this white solid from 200-mL portions of degassed absolute ethanol and cooling to room temperature each time to isolate the product gave finally 3.6 g (13.5% yield) of the pure (by phosphorus-31 NMR) less soluble diastereomer: mp 92–94 °C; $[\alpha]^{18}_{D}$ −109.36° (*c* 4.26, CH_2Cl_2); ^{31}P NMR δ −12.6 (doublet) and −21.7 (doublet) ($|^3J$(P–P)|32 Hz). Anal. Found: C, 78.4; H, 8.3; P, 13.8.

The more soluble diastereomer was isolated from the filtrate from the first crystallization of the less soluble diastereomer. Cooling this filtrate overnight at −15 °C gave white crystals corresponding to about 10% of the original diastereomeric mixture and typically having an $[\alpha]^{20}_{D}$ value in the range +20–30°; this material was still a mixture of the two diastereomers (by phosphorus-31 NMR). After removal of this product, further cooling of the resulting filtrate to −20 °C gave 0.7 g (2.6% yield) of the pure (by phosphorus-31 NMR) more soluble diastereomer, which, because of its high solubility, was filtered with external cooling of the filter to −20 to −40 °C: mp 74–78 °C; $[\alpha]^{27}_{D}$ −24.45° (*c* 0.64, CH_2Cl_2); ^{31}P NMR δ −12.6 (doublet) and −17.4 (doublet) ($|^3J$(P–P)| 32 Hz). Anal. Found: C, 78.1; H, 8.5; P, 13.3.

During this separation of the two diastereomers of (Nmen)(C_6H_5)$PCH_2CH_2P(C_6H_5)_2$ by fractional crystallization as outlined above, most of the originally introduced material was recovered as mixtures of these two diastereomers as shown by the phosphorus-31 and/or carbon-13 NMR spectra and the widely varying optical rotations, which, however, were consistent with the amounts of each diastereomer indicated to be present from the NMR spectra.

Preparation of the Tri(tertiary Phosphine) Bis[2-(neomenthylphenylphosphino)ethyl]phenylphosphine. A mixture of 2.48 g (10 mmol) of neomenthylphenylphosphine, 0.81 g (5 mmol) of phenyldivinylphosphine, ~0.2 g of potassium *tert*-butoxide, and 70 mL of tetrahydrofuran was boiled under reflux for 42 h. Removal of solvent at 30 °C (30 mm) gave a yellow viscous oil. This oil was treated with 70 mL of deoxygenated ethanol. The resulting solution was kept overnight at −15 °C. The precipitated solid was filtered and dried at 30 °C (0.05 mm). Recrystallization from ethanol gave 1.6 g (48.6% yield) of a diastereomeric mixture of $C_6H_5P[CH_2CH_2P(C_6H_5)(Nmen)]_2$: mp 68–77 °C; $[\alpha]^{18}_{D}$ +61.51° (*c* 2.77, CH_2Cl_2); ^{31}P NMR spectrum δ −17.3 (complex multiplet), −22.1 (complex multiplet). Anal. Calcd for $C_{42}H_{61}P_3$: C, 76.6; H, 9.3; P, 14.1. Found: C, 76.4; H, 9.2; P, 13.8.

Addition of Neomenthylphenylphosphine to Dimethylvinylphosphine Sulfide. A mixture of 6.0 g (50 mmol) of dimethylvinylphosphine sulfide and 12.41 g (50 mmol) of neomenthylphenylphosphine in 150 mL of tetrahydrofuran was treated with sufficient (~0.2 g) potassium *tert*-butoxide for the reaction mixture to become brown-red. The resulting mixture was boiled under reflux for a total of 67 h. Solvent was then removed at 30–40 °C (18 mm). The brown solid residue was dissolved in 200 mL of ethanol. The ethanol solution was cooled to room temperature and then in a freezer. After 2 h the product was filtered and dried at 20 °C (0.1 mm) to give 12.9 g (70% yield) of a mixture of the diastereomers of (Nmen)(C_6H_5)-$PCH_2CH_2P(S)(CH_3)_2$: mp 102–103 °C; $[\alpha]^{20}_{D}$ 49.9° (*c* 3.04, tetrahydrofuran); ^{31}P NMR spectrum δ +38.1 and δ −21.5 ($|^3J$-(P–P)| 42 Hz) for the less soluble diastereomer and δ + 37.9 and δ −17.6 ($|^3J$(P–P)| 43 Hz) for the more soluble diastereomer. Anal. Calcd for $C_{20}H_{34}P_2S$: C, 65.2; H, 9.3; P, 16.8; S, 8.7. Found: C, 65.2; H, 9.1; P, 16.9; S, 8.9.

Fractional crystallization of this mixture of diastereomers from ethanol resulted in some changes in the ratios of the two diastereomers present in the separated crystals but did not allow the separation of either of the pure diastereomers. The observation of $[\alpha]^{20}_{D}$ values of +49.9° for material containing 60% of the less soluble isomer and of +44.3° for material containing 55% of the less soluble isomer allows an estimation of $[\alpha]^{20}_{D}$ values of +93° for the pure less soluble diastereomer and −15° for the pure more soluble diastereomer.

Preparation of Menthylphenylphosphine. A blue solution of 5.2 g (0.23 mol) of sodium metal in 500 mL of liquid ammonia was treated with 24.9 g (0.23 mol) of phenylphosphine in 250 mL of tetrahydrofuran to form a red solution of sodium phenylphosphide. The ammonia was allowed to evaporate. The resulting tetrahydrofuran solution was treated with a solution of 39.5 g (0.23 mol) of (+)-neomenthyl chloride ($[\alpha]^{26}_{D}$ +44.6° (neat)) dissolved in 200 mL of tetrahydrofuran over a period of 1 h. The reaction mixture was then treated with 100 mL of water. The organic layer was separated, washed with water, dried over anhydrous sodium sulfate, and distilled under vacuum. After removal of an extensive forerun (suggestive of major amounts of dehydrohalogenation of the (+)-neomenthyl chloride) 4.7 g (8.4% yield) of menthylphenylphosphine was collected: bp 125–133 °C (0.35 mm); $[\alpha]^{19}_{D}$ −119.18° (*c* 7.01, CH_2Cl_2); IR ν(P–H) 2273 cm^{-1}; ^{31}P NMR δ −32.2 and −43.9 of approximately equal relative intensities. Anal. Calcd for $C_{16}H_{25}P$: C, 77.4; H, 10.1; P, 12.5. Found: C, 77.1; H, 10.0; P, 12.1.

Attempted reactions of menthylphenylphosphine with diphenylvinylphosphine and dimethylvinylphosphine sulfide in boiling tetrahydrofuran in the presence of potassium *tert*-butoxide failed to give crystalline products under conditions similar to those described above for the preparations of (Nmen)(C_6H_5)-$PCH_2CH_2P(C_6H_5)_2$ and (Nmen)(C_6H_5)$PCH_2CH_2P(S)(CH_3)_2$, respectively.

Preparation of [(Nmen)(C_6H_5)$PCH_2CH_2P(C_6H_5)_2$Rh(nor-C_7H_8)][ClO_4]. A solution of 0.1145 g (0.25 mmol) of (Nmen)(C_6H_5)$PCH_2CH_2P(C_6H_5)_2$ (pure diastereomer with $[\alpha]_D$ +109°) and 0.0575 g (0.125 mmol) of $[(nor\text{-}C_7H_8)RhCl]_2$[19] in 40 mL of methanol was kept for 40 min under argon at room temperature and then treated slowly with a solution of 0.4 g (3.27 mmol) of sodium perchlorate in 40 mL of distilled water. The resulting yellow-orange precipitate was filtered, washed with water, and recrystallized from a mixture of methanol and water to give,

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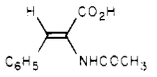
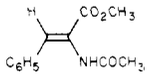
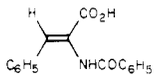
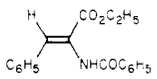
(19) E. W. Abel, M. A. Bennett, and G. Wilkinson, *J. Chem. Soc.*, 3178 (1959).

Table II. Optical Yields for the Asymmetric Hydrogenation of α-(Acylamido)cinnamic Acid Derivatives Using Rhodium(I) Complexes Containing (Nmen)(C_6H_5)$PCH_2CH_2P(C_6H_5)_2$ and (Nmen)(C_6H_5)$_2$P

prochiral olefin	hydrogenation optical yield,[a] %		
	(Nmen)(C_6H_5)$PCH_2CH_2P(C_6H_5)_2$		(Nmen)-(C_6H_5)$_2$P
	$[\alpha]_D$ +109°	$[\alpha]_D$ −24°	$[\alpha]_D$ +95.5°
	46 (62) [R]	60 [S]	0
	42 (66) [R]	58 [S]	2 [R]
	49 (44) [R]	85 [S]	13 [R]
	56 (58) [R]	31 [S]	12 [R]

[a] The optical yields in parentheses were obtained by using the preformed cationic complex [(Nmen)(C_6H_5)-$PCH_2CH_2P(C_6H_5)_2$Rh(nor-C_7H_8)][ClO_4] as the catalyst. The remaining optical yields were obtained by using catalysts prepared from [(nor-C_7H_8)RhCl]$_2$ and the phosphine in a phosphorus/rhodium molar ratio of 2.2/1 as described in the Experimental Section. The absolute configuration of the product (R or S) is given in the brackets.

after washing with water and diethyl ether and drying, 0.16 g (85% yield) of [(Nmen)(C_6H_5)$PCH_2CH_2P(C_6H_5)_2$Rh(nor-C_7H_8)][ClO_4].

Anal. Calcd for $C_{37}H_{46}ClO_4P_2Rh$: C, 58.9; H, 6.1; Cl, 4.7; P, 8.2; Rh, 13.6. Found: C, 58.7; H, 6.1; Cl, 4.8; P, 9.5; Rh, 13.2.

Catalytic Reactions (Table II). A 20 mL stainless steel autoclave was charged under argon with a weighed amount of the prochiral olefin followed by a catalyst solution prepared in a mixture of 4.5 mL of benzene and 4.5 mL of methanol from 5.75 mg of [(nor-C_7H_8)RhCl]$_2$ and sufficient pure (Nmen)(C_6H_5)-$PCH_2CH_2P(C_6H_5)_2$ diastereomer or (Nmen)(C_6H_5)$_2$P to give a phosphorus/rhodium molar ratio of 2.2/1. The quantity of prochiral olefin was calculated to give an olefin/catalyst molar ratio of 100/1. The loaded autoclave was flushed several times with prepurified hydrogen before hydrogenations at 70 bars of hydrogen pressure at room temperature for at least 1 day were carried out. After completion of the reaction, the solvent was removed at ~25 °C (35 mm). The product was separated from the catalyst by one of the following two methods. For esters, a methanol solution of the product was passed through a column of 200–400 mesh Dowex 50W-X2 ion-exchange resin in the H^+ form. For acids, the product was dissolved in 10% aqueous sodium hydroxide and filtered, and the filtrate was treated with 10% aqueous hydrochloric acid followed by extraction with diethyl ether. The resulting ether or methanol solutions of the products were concentrated under vacuum to give the product. The resulting products were either clear or only faintly yellow. The identities and chemical yields of these products were determined by proton NMR spectroscopy at 80 MHz, on a Tesla Model BS487C spectrometer. The optical rotations of the products were measured in methanol solutions on a Schmidt-Haensch LM visual polarimeter with approximately 0.01° precision. The optical yields were calculated by using reported[6,7] values for the optical rotations of the pure hydrogenation products. All optical yields listed in Table II were obtained from experiments where the chemical yields, as shown by proton NMR spectra, were greater than 95%.

A series of hydrogenations (Table II) was also carried out in methanol solution by using the preformed complex [(Nmen)-(C_6H_5)$PCH_2CH_2P(C_6H_5)_2$Rh(nor-C_7H_8)][ClO_4] and again a substrate/catalyst molar ratio of 100/1; otherwise the procedure was similar to that noted above.

Results and Discussion

Synthesis and Characterization of Ligands. The syntheses of neomenthyl poly(tertiary phosphines) described in this paper involve the construction of PCH_2CH_2P units by the base-catalyzed addition of phosphorus–hydrogen compounds to vinyl–phosphorus derivatives by the well-established scheme[15,18,20,21,22] of eq 1. A

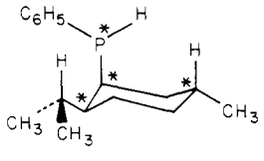
$$\text{PH} + \text{CH}_2{=}\text{CHP} \rightarrow \text{PCH}_2\text{CH}_2\text{P} \quad (1)$$

neomenthyl–phosphorus derivative containing either a phosphorus–hydrogen bond or a phosphorus–vinyl group is required in order to apply this synthetic principle to the preparation of chiral neomenthyl poly(tertiary phosphines). The neomenthylphosphorus derivative chosen for this work was neomenthylphenylphosphine, (Nmen)-(C_6H_5)PH (II), which can be prepared by the sequence of reactions in eq 2 and 3. The product is a distillable liquid

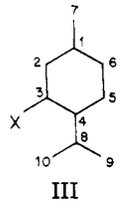
$$2C_6H_5PH_2 + 2Na \xrightarrow{NH_3} 2C_6H_5PHNa + H_2 \quad (2)$$

$$C_6H_5PHNa + MenCl \rightarrow (Nmen)(C_6H_5)PH + NaCl \quad (3)$$

which rapidly oxidizes in air to a solid. The carbon-13 NMR spectrum of this product (Table I) clearly indicates that the menthyl chloride has undergone inversion to give a neomenthyl group in its reaction with C_6H_5PHNa exactly analogous to the reported[16] reaction of menthyl chloride with (C_6H_5)$_2$PNa to give neomenthyldiphenylphosphine. The phosphorus-31 NMR spectrum of (Nmen)(C_6H_5)PH (II) exhibits two resonances of approximately equal relative



II



III

intensities indicating the presence of the expected two diastereomers. Because of the air sensitivity of (Nmen)(C_6H_5)PH, no attempt was made to separate the pure diastereomers. An attempt to prepare (Nmen)-(C_6H_5)PH by an alternative method involving the cleavage of one phenyl group in neomenthyldiphenylphosphine,[16] using sodium in liquid ammonia followed by addition of ammonium chloride, did not give a pure product, apparently owing to difficulties in separating (Nmen)-(C_6H_5)PH from unreacted (Nmen)(C_6H_5)$_2$P.

The base-catalyzed addition of (Nmen)(C_6H_5)PH (II) to diphenylvinylphosphine gives the crystalline chiral di(tertiary phosphine) (Nmen)(C_6H_5)$PCH_2CH_2P(C_6H_5)_2$ (I) according to reaction 4. The phosphorus-31 NMR

$$(Nmen)(C_6H_5)PH + (C_6H_5)_2PCH{=}CH_2 \rightarrow (Nmen)(C_6H_5)PCH_2CH_2P(C_6H_5)_2 \quad (4)$$

spectrum of this product exhibits a single doublet (C_6H_5)$_2$$PCH_2CH_2$ resonance at δ −12.6 but two doublet (C_6H_5)(Nmen)PCH_2CH_2 resonances at δ −17.4 and −21.7. This is again consistent with the presence of the expected two diastereomers with the latter resonance being much more sensitive to the configurational differences between the two diastereomers because of the closer proximity to the chiral atoms. The individual pure diastereomers can be separated by fractional crystallization from ethanol but this procedure is very wasteful since only the extreme fractions are diastereomerically pure. The carbon-13 NMR

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spectra of the neomenthyl groups in the individual diastereomers (Table I) also exhibit some differences, particularly in the chemical shifts of carbon atoms 1, 4, 8, and 9 (see structure III for the numbering of the neomenthyl carbon atoms).

Base-catalyzed additions of phosphorus–hydrogen compounds to vinylphosphine sulfides often give highly crystalline adducts,[15] which in the case of neomenthyl derivatives might be separable into pure diastereomers by fractional crystallization. The base-catalyzed addition of (Nmen)(C_6H_5)PH to dimethylvinylphosphine sulfide gives the expected crystalline 1:1 adduct (Nmen)(C_6H_5)-$PCH_2CH_2P(S)(CH_3)_2$ according to eq 5. Again the

$$(\text{Nmen})(C_6H_5)\text{PH} + CH_2{=}\text{CHP(S)}(CH_3)_2 \rightarrow (\text{Nmen})(C_6H_5)\text{PCH}_2\text{CH}_2\text{P(S)}(CH_3)_2 \quad (5)$$

phosphorus-31 NMR spectrum indicates this product to be the expected mixture of diastereomers. In this case both of the phosphorus atoms exhibit distinctly different chemical shifts in each diastereomer. However, attempts to separate pure diastereomers of (Nmen)(C_6H_5)-$PCH_2CH_2P(S)(CH_3)_2$ by fractional crystallization from ethanol were unsuccessful. The phosphorus-31 NMR spectra indicated some changes in the relative amounts of the individual diastereomers in different samples, but no fraction approaching 100% purity of either diastereomer was obtained.

A tri(tertiary phosphine) containing two neomenthyl groups was also obtained by using the base-catalyzed addition

$$2(\text{Nmen})(C_6H_5)\text{PH} + C_6H_5\text{P}(\text{CH}{=}\text{CH}_2)_2 \rightarrow C_6H_5\text{P}[\text{CH}_2\text{CH}_2\text{P}(C_6H_5)(\text{Nmen})]_2 \quad (6)$$

This tri(tertiary phosphine) appears to be the first example of a chiral tri(tertiary phosphine). The proton-decoupled phosphorus-31 NMR spectrum of this tri(tertiary phosphine) shows complex multiplets around δ −17 and −22. Comparison with the reported[21] phosphorus-31 NMR chemical shifts of $C_6H_5P[CH_2CH_2P(C_6H_5)_2]_2$ and those noted above for (Nmen)(C_6H_5)$PCH_2CH_2P(C_6H_5)_2$ suggests that in this phosphorus-31 NMR spectrum of C_6H_5P-$[CH_2CH_2P(C_6H_5)(Nmen)]_2$ the multiplet at δ −17 arises from the superimposed resonances of the center phosphorus atom and the outer phosphorus atoms in one of the two possible configurations whereas the resonance at δ −22 (an unsymmetrical "triplet" with ~24 Hz separations) arrises from the outer phosphorus atoms in the other possible configuration. In any case, this phosphorus-31 NMR spectrum is consistent with the tri(tertiary phosphine) $C_6H_5P[CH_2CH_2P(C_6H_5)(Nmen)]_2$ isolated from this preparation being a mixture of the expected three diastereomers. The obvious complexity of this system has precluded a more complete analysis or attempts to separate these diastereomers of the tri(tertiary phosphine).

Some attempts were also made to prepare poly(tertiary phosphines) containing menthyl rather than neomenthyl terminal groups by using analogous synthetic methods. The required secondary phosphine precursor, (Men)-(C_6H_5)PH, was obtained by the reaction of (+)-neomenthyl chloride with C_6H_5PHNa exactly analogous to the preparation of (Nmen)(C_6H_5)PH (II) although the yields appear to be considerably lower. However, the base-catalyzed additions of (Men)(C_6H_5)PH to diphenylvinylphosphine and dimethylvinylphosphine sulfide were found to give only viscous oils which could not be crystallized. Therefore, these systems were not investigated in detail.

Asymmetric Hydrogenation Studies (Table II). Rhodium(I) complexes of both diastereomers of (Nmen)(C_6H_5)$PCH_2CH_2P(C_6H_5)_2$ (I), prepared in situ from $[(\text{nor-}C_7H_8)\text{RhCl}]_2$ and the di(tertiary phosphine), were used as catalysts for the asymmetric homogeneous hydrogenation of the prochiral olefins $C_6H_5CH{=}C$-(NHCOR)(CO_2R') (R = CH_3, R′ = H and CH_3; R = C_6H_5, R′ = H and C_2H_5). The monophosphine (Nmen)(C_6H_5)$_2$P was also tested in order to evaluate the relative significance of the neomenthyl and phosphorus chiralities as well as the rigid five-membered chelate ring in influencing optical yields and absolute configurations of the products.

A characteristic of the two diastereomers of (Nmen)-(C_6H_5)$PCH_2CH_2P(C_6H_5)_2$ (I), which have opposite configurations around the chiral phosphorus atom but the same configuration in the neomenthyl group, is that they produce opposite enantiomers for each of the four prochiral α-(acylamido)cinnamic acid derivatives investigated. Furthermore, for a given diastereomer of I, the same absolute configuration of the chiral hydrogenation product is produced for each of the four prochiral α-(acylamido)cinnamic acid derivatives investigated. These observations suggest that the chirality of the phosphorus atom in I is more significant than that of the neomenthyl group in determining the optical yield and absolute configuration of the chiral hydrogenation product. In addition, another property of the $[\alpha]_D$ −24° stereoisomer of I (which unfortunately is the rarer and more difficultly separated isomer) is the high sensitivity of the product optical yield toward minor changes in the structure of the prochiral olefin. Most conspicuously (Table II), the relatively high optical yield (85%) in the asymmetric hydrogenation of the carboxylic acid $C_6H_5CH{=}C(NHCO$-$C_6H_5)(CO_2H)$ is lowered to 31% upon simple conversion of this carboxylic acid to its ethyl ester. That this is not some simple type of hydrogen bonding effect is indicated by the failure to observe a similar major decrease in optical yield in esterifying the other prochiral carboxylic acid used. A similar sensitivity of optical yield toward minor changes in the prochiral olefin structure is observed neither for the other diastereomer of I (that with $[\alpha]_D$ +109°) nor for any of the reported chelating di(tertiary phosphines) containing only achiral terminal groups and no potentially basic trivalent nitrogen functionalities.[23] This suggests that the chiral terminal group of I may increase the sensitivity of optical yield toward minor changes in the prochiral olefin structure in asymmetric hydrogenations by using its rhodium(I) complexes.

All of the optical yields for the asymmetric hydrogenation of the four prochiral α-(acylamido)cinnamic acid derivatives, using either diastereomer of (Nmen)(C_6H_5)-$PCH_2CH_2P(C_6H_5)_2$ (I), were found to be considerably higher than those found for the asymmetric hydrogenation of the same four prochiral olefins with the monophosphine (Nmen)(C_6H_5)$_2$P. This indicates that the chiral phosphorus atom and/or the rigid five-membered chelate ring in I are responsible for a major portion of the observed yields in asymmetric hydrogenations using I. Separation of the influence of the chiral phosphorus atom and the rigid five-membered chelate ring would require similar asymmetric hydrogenation studies using a pure diastereomer of a ligand such as (Nmen)(C_6H_5)(CH_3)P. Unfortunately, a recent attempt[24] to prepare this monophosphine resulted in a mixture of diastereomers which could not be separated.

Some asymmetric hydrogenation experiments were also performed on the four prochiral α-(acylamido)cinnamic acid derivatives by using the preformed [(diphos)Rh-(nor-C_7H_8)][ClO_4] catalyst derived from the [α] +109°

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(24) C. Fisher and H. S. Mosher, *Tetrahedron Lett.*, 2487 (1977).

diastereomer of (Nmen)(C_6H_5)$PCH_2CH_2P(C_6H_5)_2$ (I). Since the results were not substantially different from those obtained with the more convenient catalysts prepared in situ by reaction of $[(nor\text{-}C_7H_8)RhCl]_2$ with the phosphine (Table II), similar pure cationic salts of the other phosphines used in this work were not tested as catalysts.

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Registry No. I isomer 1, 70912-44-6; I isomer 2, 70912-45-7; II, 70912-46-8; (–)-menthol, 2216-51-5; (–)-menthyl chloride, 16052-42-9; (+)-neomenthyl chloride, 13371-12-5; phenylphosphine, 638-21-1; diphenylvinylphosphine, 2155-96-6; dimethylvinylphosphine sulfide, 42495-78-3; neomenthyldiphenylphosphine, 43077-29-8; phenyldichlorophosphine, 644-97-3; vinyl bromide, 593-60-2; sodium phenylphosphide, 51918-31-1; bis[2-(neomenthylphenylphosphino)ethyl]phenylphosphine, 70912-47-9; (Nmen)(C_6H_5)$PCH_2CH_2P(S)(CH_3)_2$ isomer 1, 70912-48-0; (Nmen)(C_6H_5)$PCH_2CH_2P(S)(CH_3)_2$ isomer 2, 70912-49-1; menthylphenylphosphine, 70912-50-4; [(Nmen)(C_6H_5)$PCH_2CH_2P(C_6H_5)_2Rh(nor\text{-}C_7H_8)$][$ClO_4$], 70940-72-6; $[(nor\text{-}C_7H_8)RhCl]_2$, 12257-42-0; menthyldiphenylphosphine, 43077-31-2; (*Z*)-2-(acetylamino)-3-phenylpropenoic acid, 55065-02-6; methyl (*Z*)-2-(acetylamino)-3-phenylpropenoate, 60676-51-9; (*Z*)-2-(benzoylamino)-3-phenylpropenoic acid, 26348-47-0; ethyl (*Z*)-2-(benzoylamino)-3-phenylpropenoate, 26348-46-9; *N*-acetyl-D-phenylalanine, 10172-89-1; *N*-acetyl-L-phenylalanine, 2018-61-3; methyl *N*-acetyl-D-phenylalaninate, 21156-62-7; methyl *N*-acetyl-L-phenylalaninate, 3618-96-0; *N*-benzoyl-D-phenylalanine, 37002-52-1; *N*-benzoyl-L-phenylalanine, 2566-22-5; ethyl *N*-benzoyl-D-phenylalaninate, 64896-35-1; ethyl *N*-benzoyl-L-phenylalaninate, 7200-18-2; phenyldivinylphosphine, 26681-88-9.

Convenient Preparation of 5′-Chloro-2′,5′-dideoxyadenosine

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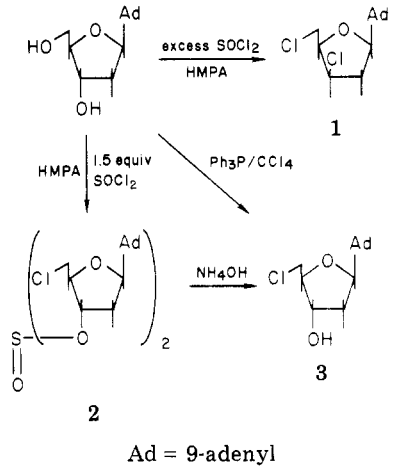
The title compound was prepared by treating 2′-deoxyadenosine with 1.5 equiv of $SOCl_2$ in hexamethylphosphoramide. An intermediate bis sulfite was isolated and characterized.

The chlorination procedure developed by Kikugawa and Inchino,[1] using hexamethylphosphoramide (HMPA) and $SOCl_2$, has been widely and successfully applied to the preparation of 5′-chloro derivatives of purine and pyrimidine ribonucleosides.[2-5] Attempts to employ this procedure in the preparation of the corresponding derivative (**3**) of 2′-deoxyadenosine, however, have in general given only the dichlorinated product, **1**.[2-4] In a single instance where selective chlorination at the 5′-position was reported,[5] **3** served as an intermediate and was not characterized.

The procedures which gave dichlorination used a considerable excess of $SOCl_2$. Our studies have revealed that reducing the amount of $SOCl_2$ to 1.5–1.8 equiv brought about a different reaction; the major product obtained, after removal of HMPA and adjustment of pH to neutrality, was the bis sulfite **2** (Scheme I), which was readily isolated and characterized by its elemental composition and NMR spectra. A similar product has been reported from the attempted chlorination of 1-(2,3-*O*-isopropylidene-β-D-ribofuranosyl)uracil, but in that case $SOCl_2$ was used in the absence of HMPA.[6]

The bis sulfite **2** was readily converted to the desired 5′-chloro derivative **3** upon standing overnight in a mixture of CH_3OH and concentrated NH_4OH. The reaction appears to proceed by sulfur–oxygen scission, since the product obtained was identical chromatographically and in its NMR spectrum with **3** prepared by chlorination of 2′-deoxyadenosine with triphenylphosphine and CCl_4.[7]

Scheme I



Ad = 9-adenyl

The latter method is unambiguous, but has the disadvantages of lower yield and higher cost, and is not well suited to larger scale preparations.

If **2** was dissolved in HMPA and treated with excess $SOCl_2$, conversion to the dichlorinated product (**1**) was rapid. This indicates that **2** may serve as an intermediate in the previously reported dichlorinations, although alternative mechanisms may be more important.

Experimental Section

Melting points were determined with a Thomas-Hoover capillary apparatus and are uncorrected. Elemental analyses were performed by Integral Microanalytical Laboratories, Inc., Raleigh, N.C. Thin-layer chromatograms (TLC) were run on Eastman silica gel plates with a UV indicator and developed with $CHCl_3$–CH_3OH (9:1). High-pressure liquid chromatograms (LC) were run on a Whatman ODS silica gel column using mixtures of CH_3OH and H_2O at a pressure of 1700 psi; compounds were

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