Organic and Biological Chemistry

Direct Configurational Correlation of Trialkyl- and Triarylphosphine Oxides[1]

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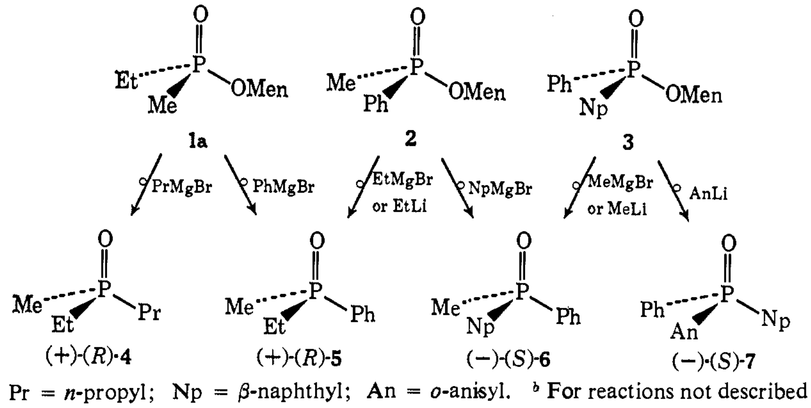
Abstract: The direct configurational correlation of a trialkyl- (ethylmethyl-*n*-propyl) and a triaryl- (*o*-anisyl-β-naphthylphenyl) phosphine oxide has been achieved by a sequence of nucleophilic displacements on phosphorus in appropriately substituted menthyl phosphinates, using Grignard or organolithium reagents (Chart I). The enhanced reactivity of organolithium reagents permits preparation of phosphine oxides from esters which fail to undergo the desired reaction with Grignard reagents, but the produced phosphine oxides are obtained in a significantly lower state of optical purity.

Optically active phosphine oxides are conveniently synthesized by reaction of organomagnesium halides with diastereomerically enriched (or pure) menthyl phosphinates.[3] The nucleophilic displacement at phosphorus is known to occur with inversion of configuration,[3] and the configurations of phosphine oxides prepared by this method are therefore correlated with those of their precursor esters. In a preliminary communication,[4] we noted that configurations of trialkyl- and triarylphosphine oxides could "in principle be correlated *via* the appropriately substituted phosphinates." However, the extreme sensitivity of the Grignard synthesis to variations in the groups on phosphorus and magnesium imposes a serious limitation on its scope and foiled previous attempts to accomplish the above-stated goal.[3] The present paper describes modifications in the method which have overcome these difficulties. The principal transformations are summarized in Chart I.[5]

Chart I[a,b]



[a] Men = (−)-menthyl; Pr = *n*-propyl; Np = β-naphthyl; An = *o*-anisyl. [b] For reactions not described in the text, see ref 3.

Trialkylphosphine Oxides. The route to these compounds by our method involves the nucleophilic displacement of alkoxide ion in a dialkylphosphinate by an alkyl group derived from an organometallic reagent. In previous work[3] it was shown that such esters are significantly less susceptible to nucleophilic attack than are similar alkylarylphosphinates; thus, whereas menthyl methylphenylphosphinate readily reacts with a variety of alkyl- and arylmagnesium halides to give the corresponding phosphine oxides, menthyl cyclohexylmethylphosphinate fails to undergo the desired nucleophilic displacement with phenylmagnesium bromide. In addition, steric effects are operative, since methyl (but not menthyl) cyclohexylmethylphosphinate reacts normally. Accordingly, two modifications were investigated: a structural modification of the phosphinate, to reduce the steric requirement at phosphorus, and modification of the organometallic reagent, to enhance its reactivity.

Reaction of *n*-propylmagnesium bromide with menthyl ethylmethylphosphinate (**1**) afforded ethylmethyl-*n*-propylphosphine oxide (**4**); the success of the displacement reaction is attributable to the lesser steric requirement of the ethyl, as compared to the cyclohexyl group. Partial separation of the diastereomers of **1** was achieved by fractional crystallization, and was monitored by the pmr signals (doublets) attributed to the PCH_3 group. Centered at τ 8.63 (for **1a**) and 8.60 (for **1b**), with $J = 14.5$ Hz, these signals permitted identification of the major diastereomer in the mixture of **1**

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[1] This work was supported by the Air Force Office of Scientific Research under Grant No. AF-AFOSR-1188-B.

[2] Public Health Service Predoctoral Fellow, 1966–1969.

[3] O. Korpiun, R. A. Lewis, J. Chickos, and K. Mislow, *J. Am. Chem. Soc.*, 90, 4842 (1968).

[4] O. Korpiun and K. Mislow, *ibid.*, **89**, 4784 (1967).

[5] Some of the transformations were carried out with the enantiomers of the compounds shown in Chart I.

but were too closely spaced to allow quantitative estimation of the composition of the mixture. Reaction of phenylmagnesium bromide with a mixture of diastereomers enriched in **1a** afforded (+)-(*R*)-ethylmethylphenylphosphine oxide[3] (**5**), $[\alpha]_{400}$ +40°,[6] 62% optically pure,[7] and reaction of phenylmagnesium bromide with a mixture of diastereomers enriched in **1b** afforded (*S*)-**5** with $[\alpha]_D$ −6.7°, 29% optically pure.[7] Since the Grignard reaction proceeds with inversion,[3] the chirality at phosphorus in **1a** is therefore $(R)_P$, and in **1b**, $(S)_P$. In like manner, reaction of *n*-propylmagnesium bromide with **1** enriched in $(S)_P$-**1b** as above afforded **4**, $[\alpha]_D$ −0.36°, $[\alpha]_{300}$ −1.9°, presumably *ca.* 30% optically pure. Given the inversion mechanism, the chirality of (−)-**4** is therefore *S*.

Because of their greater reactivity, organolithium reagents present an attractive alternative to the use of organomagnesium halides in the displacement reaction. These reagents have been employed with success in similar reactions when Grignard reagents have failed,[8] and they have been used in nucleophilic displacements at phosphorus to form phosphinamides (with inversion).[9] Our expectations were fulfilled. One of the diastereomers of menthyl cyclohexylmethylphosphinate,[3] mp 110–111°, which failed to yield phosphine oxide upon reaction with propylmagnesium bromide, reacted with *n*-propyllithium to give cyclohexylmethylpropylphosphine oxide (**8**), $[\alpha]_D$ +0.4°. Since catalytic hydrogenation[10] of (*S*)-methylphenylpropylphosphine oxide affords (+)-(*S*)-**8**, $[\alpha]_D$ +1.22°, and since reaction of alkyllithium reagents with phosphinates provide phosphine oxides of predominantly inverted configuration, as evidenced by formation of (+)-(*R*)-**5** in the reaction of ethyllithium with menthyl $(S)_P$-methylphenylphosphinate (**2**), it follows that the starting diastereomer (mp 110–111°) has the *R* configuration at phosphorus.[11]

Triarylphosphine Oxides. In previous work,[3] we recorded our observation that anisylmagnesium bromides fail to react with menthyl $(S)_P$-β-naphthylphenylphosphinate (**3**) to give the corresponding triarylphosphine oxides. The increased reactivity of organolithium reagents, exemplified above, proved once again to overcome the present difficulty; thus reaction of *o*- and *p*-anisyllithium with **3** at −70° afforded *o*-anisyl-β-naphthylphenylphosphine oxide (**7**), $[\alpha]_D$ −1.8°, and the *para* isomer (**9**), $[\alpha]_D$ −2.5°. Nucleophilic displacement on **3** occurs with inversion, as demonstrated by the observation that reaction of methyllithium with **3** affords (−)-methyl-β-naphthylphenylphosphine oxide (**6**), whose configuration is known[3] to be *S*. Consequently, (−)-**7** and (−)-**9** have the *S* and *R* configurations, respectively.

The sequences described in this and the preceding section, and summarized in Chart I,[5] complete the stated[4] goal of a direct configurational correlation between a trialkyl- and a triarylphosphine oxide.[12]

Optical Purities of the Products. In contrast to the reactions of **2** and **3** with organomagnesium halides, which proceed with nearly complete stereospecificity, it is evident (Table I) that reactions of organolithium reagents sometimes give products of significantly lower optical purity (the formation of **5** by the two types of displacements allows a direct comparison). In the examples cited in Table I, the starting esters were diastereomerically homogeneous by melting point and pmr,[3,13] and the optical purities of the products were, with one exception, estimated on the basis of the highest reported[3,10] rotations. The optical purity of (*S*)-**7**, $[\alpha]_D$ −1.81°, $[\alpha]_{400}$ −28.5°, was estimated as follows. Reduction with hexachlorodisilane[14] afforded (*S*)-*o*-anisyl-β-naphthylphenylphosphine (**10**), $[\alpha]_D$ −10.0°, $[\alpha]_{400}$ −43.8° (benzene), which upon reoxidation with hydrogen peroxide yielded (+)-(*R*)-**7** with $[\alpha]_{400}$ +9.0°. Reaction of a portion of the same sample of (−)-(*S*)-**10** with optically pure (+)-(*S*)-2-phenyl-2-methoxyethyl-1-d_2 bromide[15] (**11**) afforded the phosphonium salt; integration of the pmr singlets due to the diastereotopic anisyl O-methyl protons[15] gave a ratio of diastereomers of 82:62. The optical purity of the precursor, (−)-(*S*)-**10**, is therefore 14%, as is the optical purity of the derivative, (+)-(*R*)-**7**. It follows that the absolute rotation of **7** is $[\alpha]_{400} = 9.0/0.14 = 64°$, $[\alpha]_D = (1.81)\cdot(64)/28.5 = 4.1°$. The absolute rotation of **10** is $[\alpha]_{400} = 43.8/0.14 = 313°$, $[\alpha]_D = 10.0/0.14 = 71°$ (benzene). Finally, the optical purity of (−)-**7** obtained by the displacement reaction is 1.81/4.1 = 44%, revealing a marked loss of stereochemical integrity in the reaction of **3** with *o*-anisyllithium.

Table I. Optical Purity of Phosphine Oxides, $R_1R_2R_3PO$[a]

Compound no.	R_1	R_2	R_3	Chirality	$[\alpha]_D$,[b] deg	Optical purity, %
5	Me	Ph	Et	*R*	+15.5	70[c]
6	Ph	Np	Me	*S*	−11.5	95[d]
7	Ph	Np	An	*S*	−1.8	44[e]
8	Me	Chx	Pr	*S*	+0.4	35[f]

[a] See footnote *a*, Chart I; Chx = cyclohexyl. All phosphine oxides were prepared from $R_1R_2P(O)OMen$ and R_3Li. [b] Rotations refer to solvent methanol. [c] Based on the highest reported rotation (ref 3), $[\alpha]_D$ 23°. [d] Based on the highest reported rotation (ref 3), $[\alpha]_D$ 12°. [e] See text. [f] Based on highest reported rotation (ref 10), $[\alpha]_D$ 1.22°.

The loss of stereospecificity may be ascribed to one or a combination of factors which are operative at three stages of the reaction. The starting ester may be epimerized to a mixture of diastereomers (differing in configuration at phosphorus) at a rate comparable with that of the displacement reaction, perhaps through the intermediacy of a pentacoordinate phosphorus compound which, given a sufficiently long half-life, may suffer stereomutation through intramolecular exchange of lig-

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(6) All rotations reported in the text refer to solvent methanol, except as noted.

(7) Optically pure **5** (ref 3) has $[\alpha]_D$ 23° and $[\alpha]_{400}$ 65°.

(8) J. Jacobus and K. Mislow, *Chem. Commun.*, 253 (1968).

(9) A. Nudelman and D. J. Cram, *J. Am. Chem. Soc.*, 90, 3869 (1968).

(10) L. Horner, R. Luckenbach, and W. D. Balzer, *Tetrahedron Lett.*, 3157 (1968).

(11) By the same token, the other diastereomer of menthyl cyclohexylmethylphosphinate,[3] mp 80–81°, therefore has the $(S)_P$ configuration.

(12) As has been previously pointed out,[3] configurational correlations between phosphine oxides by this method are established even without information on the stereochemical course of the nucleophilic displacement (inversion *vs.* retention), provided only that the course remains the *same* in all the displacement reactions.

(13) R. A. Lewis, O. Korpiun, and K. Mislow, *J. Am. Chem. Soc.*, 90, 4847 (1968).

(14) K. Naumann, G. Zon, and K. Mislow, *ibid.*, **91**, 7012 (1969).

(15) J. P. Casey, R. A. Lewis, and K. Mislow, *ibid.*, **91**, 2789 (1969).

and positions (pseudorotation),[16] or the product phosphine oxide may suffer partial racemization under the conditions of the reaction. Mechanisms for these racemizations may involve exchange of groups bonded to phosphorus.[17] Reactions consequent upon α-lithiation,[18] similar to those discussed in the somewhat related methyl aryl sulfoxide systems,[19] may possibly play a role.[20]

Experimental Section[21]

Menthyl ethylmethylphosphinates 1a and **1b** were prepared as follows. A solution of ethyldichlorophosphine[22] (131 g, bp 107–111°) in ether (200 ml) was added dropwise to a vigorously stirred solution of triethylamine (222 g, distilled from barium oxide) and methanol (64 g) in ether (1 l.) at 0°, under nitrogen. The mixture was stirred for 1 hr, triethylamine hydrochloride was removed by filtration under nitrogen, the filtrate was distilled under aspirator vacuum, and material removed at 35–80° (210 mm) was redistilled to yield dimethyl ethylphosphonite, 48 g, bp 73–77° (210 mm) (lit.[23] bp 73–74.5° (225 mm)). This ester was added to methyl iodide (5 ml) contained in a three-necked flask, equipped with an addition funnel, nitrogen inlet, and reflux condenser, at a rate sufficient to maintain a rapid reflux. The resulting product phosphinate was distilled, bp 107–110° (47 mm), to yield 33.5 g of methyl ethylmethylphosphinate, 80% pure by glpc. A portion, redistilled, bp 40–44° (0.1 mm), was 93% pure by glpc; pmr CH_3O, d, τ 6.49, $J_{\mathrm{PCH}} = 11$ Hz; CH_3P, d, τ 8.56, $J_{\mathrm{PCH}} = 14$ Hz.

Phosphorus pentachloride (73 g) was added in small portions to a stirred solution of the once-distilled phosphinate (33.5 g) in carbon tetrachloride (200 ml). After the initial exothermic reaction had subsided, the solution was stirred 3 hr and filtered, and the filtrate was concentrated on a rotary evaporator. Distillation of the residual oil afforded ethylmethylphosphinyl chloride (25 g): bp 56–59° (0.5 mm) (lit.[24] bp 99–102° (15 mm)); pmr CH_3P, d, τ 8.00, $J_{\mathrm{PCH}} = 13$ Hz; CH_3CH_2, m, τ 8.70, $J_{\mathrm{PCCH}} = 22$ Hz. A solution of pyridine (10.4 g) in benzene (50 ml) was added dropwise, with stirring, to a solution of menthol (18.5 g) and the acid chloride (15 g) in benzene (100 ml), at 0°. The mixture was heated at reflux for 10 hr, cooled, washed with water (100 ml), three 50-ml portions of 1% hydrochloric acid, water (100 ml), and saturated sodium bicarbonate (100 ml), and dried over magnesium sulfate. Solvent was removed on a rotary evaporator, and menthol was removed at 65° (0.1 mm). The residual oil crystallized upon cooling. This material was recrystallized repeatedly from 2-methylbutane; eventually, a small amount of one pure diastereomer **1a** was obtained: mp 73–76°; pmr (10% in CCl_4, TMS reference) CH_3P, d, τ 8.63, $J_{\mathrm{PCH}} = 14.5$ Hz.

Anal. Calcd for $C_{13}H_{27}PO_2$: C, 63.88; H, 11.05; P, 12.99. Found: C, 63.25; H, 11.25; P, 12.83.

Although diastereomers **1a** and **1b** were very difficult to separate completely, several crops of crystals were obtained which were enriched in one or the other of the two diastereomers. The pmr spectra of these mixtures exhibited two CH_3P doublets, centered at τ 8.60 and 8.63, each with $J_{\mathrm{PCH}} = 14.5$ Hz. The separation of signals provided a measure of the ratio of diastereomers, but because of the small difference in chemical shift, quantitative estimates were not made. Three mixtures were used to prepare phosphine oxides: A, enriched in **1a**, and **B** and C, enriched in **1b**.

Optically Active Phosphine Oxides. A. The Grignard synthesis provided phosphine oxides from mixtures of **1a** and **1b** as described previously.[3] From mixture C and phenylmagnesium bromide was obtained (−)-(*S*)-ethylmethylphenylphosphine oxide, **5**, $[\alpha]_D$ −6.7°. Mixture A, treated with the same Grignard reagent, provided (+)-(*R*)-**5**, $[\alpha]_{400}$ +40°, $[\alpha]_{350}$ +60°; both samples of **5** were identical, except for rotation, with an authentic sample prepared from **2**.[3]

From mixture **B** (6 g) and *n*-propylmagnesium bromide was obtained **(−)-(*S*)-ethylmethyl-*n*-propylphosphine oxide** (0.5 g, 15%). The material was purified by chromatography on silica gel, eluting with benzene, chloroform, and 10% methanol–chloroform, and subsequently distilled (kugelrohr, bp 80° (0.05 mm)). The product thus obtained was homogeneous by glpc. Retention times were identical with those of the racemic material (see below) on Carbowax and silicon rubber columns, and pmr and ir spectra of active and racemic material were identical. That the small rotation ($[\alpha]_D$ −0.36°, $[\alpha]_{300}$ −1.9°) was not an artifact was further shown by reduction to the phosphine followed by oxidation to the inverted phosphine oxide, $[\alpha]_{300}$ +1.2°.[14]

B. Synthesis from Organolithium Reagents. (+)-(*S*)-Cyclohexylmethyl-*n*-propylphosphine Oxide (8).[10] A filtered solution of *n*-propyllithium, prepared from *n*-propyl bromide (15.35 g, 125 mmol) and lithium wire (2.2 g, 320 mg-atoms) in ether (50 ml), was added to diastereomerically pure menthyl cyclohexylmethylphosphinate[3] (1.5 g, 5 mmol), mp 109–111°, in benzene (10 ml). Most of the ether was removed by distillation and 25 ml of benzene was added. The mixture was heated to reflux for 12 hr, and worked up as described above. Purified by chromatography on silica gel (eluate, ethyl acetate) and subsequent distillation (kugelrohr, 100° (0.05 mm)), the material was homogeneous by tlc on silica gel, eluting with ethyl acetate, methanol, or benzene, and had $[\alpha]_D$ +0.42°, $[\alpha]_{300}$ +2.5°; pmr CH_3P, d, τ 8.66, $J_{\mathrm{PCH}} = 12$ Hz; mol wt: calcd for $C_{10}H_{21}PO$, M^+ m/e 188.13300 (found 188.13255). In like manner, (+)-(*R*)-**5** was prepared from **2** and ethyllithium. The product had $[\alpha]_D$ +15.5° and was identical except for rotation with **5** prepared above.

(−)-(*S*)-*o*-Anisyl-β-naphthylphenylphosphine Oxide (7). A solution of *o*-anisyllithium, prepared from *o*-anisyl bromide (0.91 g, 5.0 mmol) and *n*-butyllithium (5.0 mmol) in ether (10 ml), was added dropwise, with vigorous stirring, to a solution of **3** (2.2 g, 5.5 mmol) in ether (75 ml) at −70°, under nitrogen. After stirring 0.5 hr, water (5 ml) was added, and the mixture was warmed to room temperature. The organic layer was removed; the aqueous layer was acidified with 6 *N* hydrochloric acid and extracted with three 25-ml portions of chloroform. The combined organic layers were dried over magnesium sulfate and concentrated on the rotary evaporator. The residue, after purification by chromatography on silica gel (eluate, ethyl acetate) and subsequent distillation (kugelrohr, 220° (0.05 mm)), was a colorless glass, identical with racemic material by tlc, ir, and pmr, and had $[\alpha]_D$ −1.81°, $[\alpha]_{400}$ −28.5°.

(−)-(*R*)-*p*-Anisyl-β-naphthylphenylphosphine oxide (9) was prepared in like manner. Separation from two by-products observed by tlc was achieved by chromatography and distillation, as above. The colorless glass was identical with racemic material by tlc, ir, and pmr, and had $[\alpha]_D$ −2.5°, $[\alpha]_{400}$ −8.2°.

(−)-(*S*)-Methyl-β-naphthylphenylphosphine oxide (6), $[\alpha]_D$ −11.5°, prepared in like manner, was identical except for rotation with authentic material.[3]

Racemic Phosphine Oxides. These compounds were prepared from phosphinyl chlorides by the Grignard reaction, as illustrated for ***o*-anisyl-β-naphthylphenylphosphine oxide (7)**. A solution of β-naphthylphenylphosphinyl chloride[3] (4.1 g, 14 mmol) in ether (25 ml) was added to a solution of *o*-anisylmagnesium bromide (45 mmol) in ether (100 ml).

The mixture was stirred overnight and hydrolyzed with saturated ammonium chloride (10 ml), and the ether solution was removed. The aqueous layer was washed several times with chloroform, and the combined organic layers, dried over magnesium sulfate, were concentrated on the rotary evaporator. The residual oil was distilled (kugelrohr); the fraction removed at 210–220° (0.1 mm)

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[16] K. E. DeBruin, K. Naumann, G. Zon, and K. Mislow, *J. Am. Chem. Soc.*, **91**, 7031 (1969), and references cited therein.

[17] For example, D. Seyferth, D. E. Welch, and J. K. Heeren [*J. Am. Chem. Soc.*, **86**, 1100 (1964)] showed that triphenylphosphine reacts with alkyllithium reagents to give alkyldiphenylphosphine oxides as exchange products.

[18] Such mechanisms would be inapplicable to interconversions in aryl systems such as **3** → **7**, but must be considered in the other cases listed in Table I.

[19] J. Jacobus and K. Mislow, *J. Am. Chem. Soc.*, **89**, 5228 (1967).

[20] However, we have shown[3] that α-lithiation of cyclohexylmethylphenylphosphine oxide does not affect the optical purity of that compound.

[21] Elemental analyses were performed by Schwarzkopf Microanalytical Laboratories, Woodside, N. Y. Unless otherwise noted, pmr spectra were recorded on a Varian A-60A spectrometer, and refer to *ca.* 10% solutions in deuteriochloroform, with tetramethylsilane as internal standard. Optical rotatory dispersion spectra were taken on a Cary 60 recording spectropolarimeter; sodium D line rotations were also taken with a Schmidt and Haensch visual polarimeter. Rotations refer to solvent methanol, *c* 1.0–3.0, unless otherwise noted. Mass spectra were measured on an AEI MS-9 high-resolution mass spectrometer. We thank the National Science Foundation for providing the funds for the purchase of the mass spectrometer under Grant No. GP-5200.

[22] M. S. Kharasch, E. V. Jensen, and S. Weinhouse, *J. Org. Chem.*, **14**, 429 (1949).

[23] B. A. Arbusov and N. I. Rispoloshenskij, *Izv. Akad. Nauk SSSR*, 854 (1952); *Chem. Abstr.*, **47**, 9903 (1953).

[24] L. Maier, *Chem. Ber.*, **94**, 3056 (1961).

was crystallized from chloroform–hexane, and recrystallized from methylene chloride–hexane: mp 139–142°; pmr CH_3O, s, τ 6.54; naphthyl, d, τ 1.74, $J_{\mathrm{PCCH}} = 14$ Hz, 1 H. An analytical sample was sublimed at 160° (0.5 mm).

Anal. Calcd for $C_{23}H_{19}PO_2$: C, 77.08; H, 5.34; P, 8.64; mol wt, 358.11226. Found: C, 76.72; H, 5.45; P, 8.53; M^+ *m/e* 358.11874.

p-**Anisyl-β-naphthylphenylphosphine oxide (9)**, prepared in like manner, was obtained as a glass. Purified by chromatography on Florisil (eluate, ethyl acetate) and subsequent distillation (kugelrohr, bp 260° (0.50 mm)), the material was homogeneous by tlc on silica gel, eluting with ethyl acetate, methanol, or benzene: pmr CH_3O, s, τ 6.17; naphthyl, d, τ 1.72, $J_{\mathrm{PCCH}} = 14$ Hz, 1 H; mol wt: calcd for $C_{23}H_{19}PO_2$, M^+ *m/e* 358.11226 (found 358.11026).

Ethylmethyl-*n*-propylphosphine oxide (4), prepared from ethylmethylphosphinyl chloride and *n*-propylmagnesium bromide, was obtained as a colorless oil. Purified by distillation (kugelrohr, bp 90° (0.1 mm)), the material was homogeneous by glpc and transparent in the uv (ϵ_{210} 13, methanol); pmr CH_3P, d, τ 8.57, $J_{\mathrm{PCH}} = 14$ Hz.

Anal. Calcd for $C_6H_{15}PO$: C, 53.72; H, 11.27; mol wt, 134.08605. Found: C, 53.88; H, 11.20; M^+ *m/e* 134.08591.

Determination of Optical Purity by Pmr. (+)-(*S*)-2-Phenyl-2-methoxyethyl-1-d_2 Bromide (11). (+)-(*S*)-O-Methylmandelic acid (31 g, 187 mmol), mp 66.5–68°, $[\alpha]^{22}$D +162° (*c* 1.49, water) (lit.[25] $[\alpha]^{23}$D +162°), was esterified with diazomethane to yield (quantitatively) methyl (*S*)-O-methylmandelate (33.8 g, 187 mmol). After distillation (bp 59° (0.1 mm)), the ester had $[\alpha]^{25}$D +138° (*c* 1.0, methanol). A solution of 18 g (100 mmol) of this material in ether (50 ml) was added dropwise to a suspension of lithium aluminum deuteride (4.2 g, 100 mmol) in ether (150 ml), at a rate sufficient to maintain a rapid reflux. When addition was complete (*ca.* 45 min) the mixture was heated at reflux for an additional 15 min, cooled, and treated with ethyl acetate (10 ml) to consume excess lithium aluminum deuteride. The resulting mixture was hydrolyzed with water (4.2 ml), 15% sodium hydroxide solution (4.2 ml), and water (12.6 ml). The ether layer was dried over magnesium sulfate and concentrated on the rotary evaporator. The residue was distilled to yield **(+)-(*S*)-2-phenyl-2-methoxyethanol-1-d_2** (14.1 g, 91.5 mmol): bp 75° (1.0 mm); $[\alpha]^{22.7}$D +133° (neat); pmr CH_3O, s, τ 6.77; C_6H_5CH, s, τ 5.75; OH, s, τ 6.83; C_6H_5, s, τ 2.79. Methanesulfonyl chloride (9.6 g, 84 mmol) was added to a stirred solution of the alcohol (6.5 g, 42 mmol) in pyridine (100 ml). After 90 min, the mixture, which contained solid pyridine hydrochloride, was poured into an ice–water mixture (700 ml), and a precipitate formed. Removed by filtration, washed with water, and distilled (kugelrohr, 120° (0.025 mm)) the resulting **(+)-(*S*)-2-phenyl-2-methoxyethyl-1-d_2 methanesulfonate** (6.4 g, 28 mmol) had mp 46–49°; $[\alpha]^{24}$D +91.3°; pmr CH_3SO_2, s, τ 7.11; CH_3O, s, τ 6.78; C_6H_5CH, s, τ 5.58; C_6H_5, s, τ 2.78. A solution of the methanesulfonate (6.3 g, 27 mmol) in dimethyl sulfoxide (25 ml) was added to sodium bromide (8.2 g, 80 mmol) in dimethyl sulfoxide (100 ml) at 80°. After stirring for 12 hr, the mixture was cooled, poured over ice (500 g), and extracted with two 300-ml portions of ether. The ethereal solution was washed with two 300-ml portions of water, dried over magnesium sulfate, and concentrated on the rotary evaporator. The residue was purified by distillation, bp 74° (0.2 mm),[26] to yield **11** (4.25 g, 19.6 mmol): $[\alpha]^{24}$D +73°; $n^{22.5}$D 1.5399; pmr CH_3O, s, τ 6.79; C_6H_5CH, s, τ 6.03; C_6H_5, s, τ 2.80. The over-all yield from the starting acid was 42%.

o-**Anisyl-β-naphthylphenyl-((*S*)-2-phenyl-2-methoxyethyl-1-d_2)-phosphonium Bromide.** Reduction of (−)-(*S*)-**7** (294 mg, $[\alpha]^{27}_{400}$ −28.5° (*c* 1.016, methanol)) with hexachlorodisilane provided the phosphine **14** (244 mg, $[\alpha]^{27}_{400}$ −43.8° (*c* 2.387, benzene)).[14] A portion (95 mg, 0.26 mmol) of this material was combined with **11** (650 mg, 2.3 mmol) in benzene (4 ml) and heated at reflux for 12 hr. The phosphonium bromide which precipitated was washed several times with ether, dissolved in methylene chloride, filtered, precipitated with hexane, and dried (60°, 0.05 mm): pmr (benzonitrile, 100 MHz) $-C_6H_4OCH_3$, s, τ 6.26, 1.71 H, and τ 6.34, 1.29 H.

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[25] J. Jacobus, M. Raban, and K. Mislow, *J. Org. Chem.*, 33, 1142 (1968).

[26] W. M. Lauer and M. A. Spielman [*J. Am. Chem. Soc.*, **55**, 4923 (1933)] give bp 117–118° (15 mm) for the racemic unlabeled bromide.

The Use of Hexachlorodisilane as a Reducing Agent. Stereospecific Deoxygenation of Acyclic Phosphine Oxides[1]

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Abstract: Optically active acyclic phosphine oxides are reduced by hexachlorodisilane to phosphines with a high degree of stereospecificity and with inversion of configuration. Mechanisms for these deoxygenations are suggested which account for the observed stereochemistry. Factors are discussed which are responsible for the racemization of the produced phosphines under the conditions of the reduction. The ready availability of hexachlorodisilane, the simplicity and mildness of the reduction conditions, the high product yield, and the high stereospecificity of the reaction make this a most convenient method for the preparation of optically active phosphines from phosphine oxides. In an extension of this study, octachlorotrisilane was found to reduce acyclic phosphine oxides to phosphines with nearly complete inversion of configuration, and hexachlorodisilane was found to reduce amine oxides to amines and sulfoxides to sulfides. It is suggested that perchloropolysilanes may also be implicated in the reduction of optically active phosphine oxides with trichlorosilane in the presence of strongly basic tertiary amines.

Optically active phosphines constitute a class of compounds which has occupied a central position in the study of organophosphorus reaction mechanisms and stereochemistry.[2] Reported pathways leading to the synthesis of such compounds are cathodic reduc-

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[2] For comprehensive reviews giving citations to the original literature, see (a) L. Horner, *Pure Appl. Chem.*, 9, 225 (1964); (b) W. E. McEwen in "Topics in Phosphorus Chemistry," Vol. 2, M. Grayson and E. J. Griffith, Ed., Interscience Publishers, New York, N. Y., 1965, Chapter 1; (c) M. J. Gallagher and I. D. Jenkins in "Topics in Stereochemistry," Vol. 3, N. L. Allinger and E. L. Eliel, Ed., John Wiley & Sons, Inc., New York, N. Y., 1968, Chapter 1.