toluene. Such large fractions of disproportionation between radicals would be unusual, although not impossible.[12]

(12) P. J. Wagner and H. N. Schott, *J. Amer. Chem. Soc.*, 91, 5383 (1969).

(13) Alfred P. Sloan Fellow, 1968–1970; to whom correspondence should be addressed.

Peter J. Wagner,[13] Richard A. Leavitt

Department of Chemistry, Michigan State University
*East Lansing, Michigan 48823*
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Lithium Aluminum Hydride Induced Stereomutation of Secondary Phosphine Oxides[1]

Sir:

Recent reports[2,3] that the synthesis of optically active *secondary* phosphine oxides is accomplished by lithium aluminum hydride (LAH) reduction of diastereomerically enriched menthyl phosphinates appear to be at variance with our observation[4] that *tertiary* phosphine oxides undergo stereomutation in the presence of LAH *prior* to reduction. We now wish to report a resolution of this apparent discrepancy.

Diastereomers (**a** and **b**) of phenyl-α-phenylethylphosphine oxide (**1**)[5] were separated by a combination of column chromatography (silica gel, benzene–

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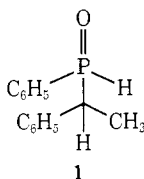
chloroform) and fractional crystallization (benzene–hexane). Diastereomeric compositions of **1** were measured by pmr spectroscopy.[7]

Upon treatment with LAH at room temperature in tetrahydrofuran or diethyl ether (0.35 mmol of LAH/mmol of **1**), followed by hydrolysis with aqueous ammonium chloride, each diastereomer of **1** was rapidly (<30 sec) transformed into an approximately equimolar

mixture of **1a** and **1b**. Although some decomposition occurred, recovery of **1** was at least 75–80%. Reaction of **1b** with an excess of LAH (2 mmol of LAH/mmol of **1**) also gave an approximately equimolar mixture of **1a** and **1b** in <30 sec, but recovery of epimerized **1** was only 40–50%.[8] Reaction of **1** with less than 0.35 mmol of LAH/mmol of **1** resulted in incomplete epimerization.[9,10]

The observation of stereomutation of **1** with LAH is readily accommodated by a mechanistic model similar to that which was invoked[4] for the tertiary phosphine oxides: addition–elimination of hydride reagent to the phosphine oxide.[11] In contrast to tertiary phosphine oxide systems, however, pseudorotation of the postulated trigonal-bipyramidal intermediate ($[R_1R_2HH'P(OAlL_3)]Li$) is not required to account for epimerization of secondary phosphine oxides. In the intermediate in which both hydrogens are apical, or in the three intermediates in which both hydrogen atoms occupy equatorial positions, addition of H followed by loss of H' leads directly to epimerization. For the other three isomers, such hydride exchange does not directly lead to epimerization.

The LAH-induced epimerization of **1** clearly reveals that LAH reduction of phosphinates is not a suitable method for the preparation of optically active secondary phosphine oxides. Repeated attempts in this laboratory to obtain optically active benzylphenylphosphine oxide (**2**), employing conditions identical with those previously described,[2] have provided only racemic **2**.[14] Furthermore, **1a** and **1b** do not undergo epimerization in methanolic solutions of dilute (0.05 *M*) hydrogen chloride or sodium methoxide during a 12-hr period.[15] The reported[2,3] racemization in such

(8) A sample of 1 recovered from a reaction mixture of 1b and LAH (2 mmol of LAH/mmol of 1) which had been quenched with D₂O showed no exchange of the benzylic hydrogen. It follows that epimerization at the chiral carbon center cannot be responsible for the stereomutation.

(9) For example, treatment of 1b with LAH (0.17 mmol of LAH/mmol of 1) gave a 40/60 mixture of 1a/1b.

(10) Some evolution of hydrogen was noted. While this observation suggests the possibility that stereomutation of 1 may in part occur by way of intermediate i, assuming that i is pyramidally unstable under

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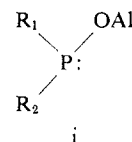
the conditions of the reaction, such a mechanism is rendered less likely by the finding that no detectable hydrogen evolution occurred during the stereomutation of 1 by lithium tri-*tert*-butoxyaluminum hydride.

(11) That stereomutation of 1 is not significantly due to a process involving reduction to a secondary phosphine[12] followed by adventitious oxidation during work-up was shown by LAH treatment (0.18 mmol of LAH/mmol of 1) of ¹⁸O-labeled 1 (3.11 ± 0.15 atom % ¹⁸O/mol).[13] The recovered phosphine oxide contained 2.79 ± 0.15 atom % ¹⁸O/mol.

(12) Secondary phosphines can be obtained by treatment of the corresponding phosphine oxide with excess LAH (L. Horner, H. Hoffmann, and P. Beck, *Chem. Ber.*, 91, 1583 (1958)).

(13) Prepared by treatment of 1 with an HCl-saturated solution of ¹⁸O-enriched water (3.25 atom % ¹⁸O/mol) and dioxane (D. B. Denney, A. K. Tsolis, and K. Mislow, *J. Amer. Chem. Soc.*, 86, 4486 (1964)).

(14) Treatment of (−)-menthyl benzylphenylphosphinate[2] with a twofold excess of LAH at 0° for 0.5 hr also gave racemic 2, even though the starting ester proved to be epimerically stable under these conditions.

(15) The diastereomeric compositions of two different mixtures of 1a and 1b remained invariant upon successive treatment with methanol-*d* and methanol. Thus, hydrogen–deuterium exchange in 1 occurs with *retention* of configuration.

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

(2) T. L. Emmick and R. L. Letsinger, *J. Amer. Chem. Soc.*, 90, 3459 (1968).

(3) O. Červinka, O. Bělovský, and M. Hepnerová, *Chem. Commun.*, 562 (1970).

(4) P. D. Henson, K. Naumann, and K. Mislow, *J. Amer. Chem. Soc.*, 91, 5645 (1969).

(5) Alkylation[6] of the sodium salt of *n*-butyl phenylphosphinate with α-phenylethyl bromide, followed by treatment with phosphorus pentachloride, afforded phenyl-α-phenylethylphosphinyl chloride, which yielded 1 upon reaction with lithium tri-*tert*-butoxyaluminum hydride.

(6) G. M. Kosolapoff, *J. Amer. Chem. Soc.*, 72, 4292 (1950).

(7) The pmr spectrum of the diastereomer (1a) eluted in the first fractions featured: CH_3, dd, τ 8.39, $^3J_{PH} = 17.5$ Hz, $^3J_{HH} = 7.2$ Hz; *PH*, dd, τ 2.73, $J_{PH} = 468$ Hz, $^3J_{HH} = 3.3$ Hz. The pmr spectrum of the other diastereomer (1b), mp 110–111°, featured: CH_3, dd, τ 8.41, $^3J_{PH} = 17.5$ Hz, $^3J_{HH} = 7.2$ Hz; *PH*, dd, τ 2.62, $J_{PH} = 468$ Hz, $^3J_{HH} = 1.3$ Hz. Diastereomeric compositions were determined by integration of the low-field half of the characteristic PH resonances. *Anal.* of 1: Calcd for $C_{14}H_{15}PO$: C, 73.03; H, 6.57; P, 13.45. Found: C, 72.77; H, 6.86; P, 13.50.

media cannot therefore be regarded as characteristic of secondary phosphine oxides.

(16) (a) Public Health Service Predoctoral Fellow, 1969–1970; (b) Public Health Service Predoctoral Fellow, 1966–1969; (c) Public Health Service Postdoctoral Fellow, 1969–1970, supported by the National Cancer Institute.
* Address correspondence to this author.

William B. Farnham,[16a] Robert A. Lewis[16b]
Roger K. Murray, Jr.,[16c] Kurt Mislow*
Department of Chemistry, Princeton University
Princeton, New Jersey 08540

Stereospecific Alkylation of Menthyl Phenylphosphinate[1]

Sir:

Diastereomerically enriched menthyl phosphinates are useful precursors in the synthesis of optically active tertiary phosphine oxides,[2] phosphinamides,[3] and phosphonothioates.[4] We now report a significant broadening of the scope of this method: diastereomerically enriched menthyl alkylarylphosphinates can be conveniently prepared by the stereospecific alkylation of diastereomerically enriched menthyl arylphosphinates, and *a single precursor thus suffices for the synthesis of a wide variety of mixed alkyldiaryl- and aryldialkylphosphine oxides of known absolute configuration.*[5]

Partial separation of the diastereomers (**a** and **b**) of menthyl phenylphosphinate (**1**)[6] was achieved by

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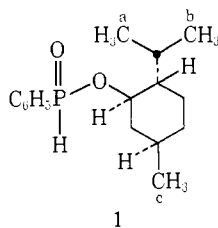
fractional crystallization.[7] The salient features of the pmr spectra of **1a** and **1b** are listed in Table I. Of particular interest are the isopropyl doublets, H_a and H_b. It has been established[8] in analogous menthyl alkylarylphosphinates (*e.g.*, menthyl methylphenylphosphinate (**2**)[2a]) that both isopropyl doublets of the S_P epimer are shifted upfield relative to the corresponding signals for the R_P epimer, and that the chem-
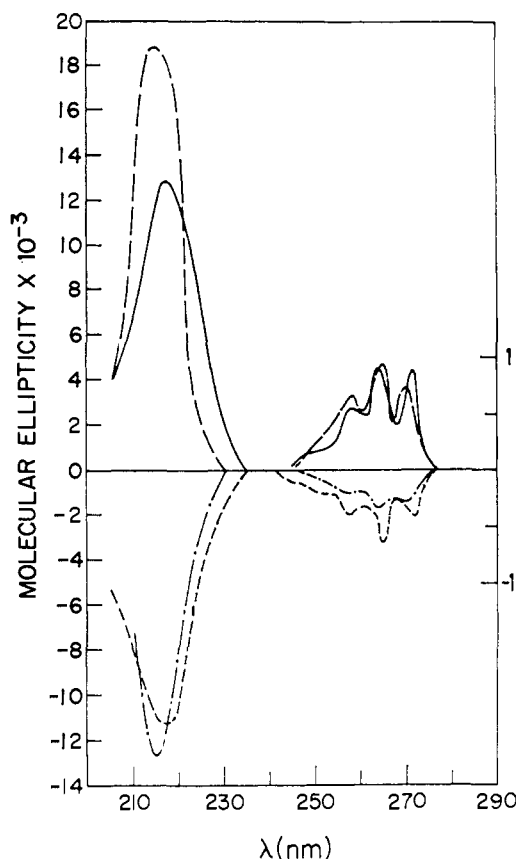
(1) This work was supported by the Air Force Office of Scientific Research under Grant No. AF-AFOSR-1188-B.

(2) (a) O. Korpiun, R. A. Lewis, J. Chickos, and K. Mislow, *J. Amer. Chem. Soc.*, **90**, 4842 (1968); (b) R. A. Lewis and K. Mislow, *ibid.*, **91**, 7009 (1969).

(3) A. Nudelman and D. J. Cram, *ibid.*, **90**, 3869 (1968).

(4) H. P. Benschop, D. H. J. M. Platenburg, F. H. Meppelder, and H. J. Boter, *Chem. Commun.*, 33 (1970).

(5) The extension of this reaction to alkylations of menthyl alkylphosphinates,[4] and thence to the synthesis of mixed aryldialkyl- and trialkylphosphine oxides of known absolute configuration, is readily envisaged.

(6) T. L. Emmick and R. L. Letsinger, *J. Amer. Chem. Soc.*, **90**, 3459 (1968).

(7) An initial crop of crystals of 1 precipitating from *n*-hexane at −78° consisted of a 95/5 mixture of 1a/1b, $[\alpha]^{22}D$ −21.0° (benzene). The mother liquors, after standing at −20°, deposited a 15/85 mixture of 1a/1b, $[\alpha]^{22}D$ −89.6° (benzene). Diastereomeric compositions were determined by integration of the low-field half of the characteristic P–H resonances in the pmr spectra (Table I).

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

Figure 1. CD spectra (isooctane solution) of menthyl phenylphosphinates: (—) for a 95/5 mixture of 1a/1b; (----) for a 15/85 mixture of 1a/1b; (— —) for 2a; and (-·-·) for 2b. The ordinate scale on the right refers to the long-wavelength transition, and the ordinate scale on the left to the short-wavelength transition.

ical-shift difference is greatest for the H_a (upfield) proton signal. Accordingly, the chirality at phosphorus in **1a** may be assigned as *R*, and that in **1b** as *S*. In support of this conclusion, mixtures diastereomerically enriched in **1a** and **1b** display CD curves which are enantiomeric in type and which correlate well with the corresponding CD curves of $(R)_P$-2 (**2a**) and $(S)_P$-2 (**2b**), respectively (Figure 1).[9]

Table I.[a,b] Pmr Chemical Shifts and Coupling Constants of Menthyl Phenylphosphinate (1) Diastereomers

	P–H	C–CH₃		
		H_a	H_b	H_c
1a	2.35 (553)	9.13 (7.0)	9.02 (7.0)	9.11 (4.5)
1b	2.34 (556)	9.30 (7.0)	9.11 (7.0)	9.03 (5.0)

[a] Chemical shifts are given in τ units, and coupling constants (in parentheses) are given in hertz. [b] Methyl doublets are assigned by comparison with corresponding signals of analogous menthyl alkylarylphosphinates.[8]

A 95/5 mixture of **1a/1b** (1.0 mmol) in dimethylformamide (DMF) was added to a mixture of sodium hydride (1.0 mmol) and methyl iodide (10.0 mmol) in DMF, and the resulting suspension was heated to 50° for 0.5 hr. Work-up of the reaction mixture afforded a 95/5 mixture (by pmr[8]) of **2a/2b** in 85% yield. Sim-

(9) We thank Drs. Franklin D. Saeva and Jeremiah P. Casey for measuring the CD spectra.