3-keto-9-methyl-$\Delta^{1,6}$-hexahydronaphthalene[12] (0.5 g) was reduced with lithium aluminum deuteride (0.12 g) in ether (40 ml) for 2 hr. Excess reagent was destroyed with a saturated solution of sodium sulfate and the ether-soluble material was heated with water (2.0 ml) and concentrated sulfuric acid (0.3 ml) at 97° for 2.5 hr. The mixture was cooled and the product was extracted into ether and vacuum distilled, yielding ***trans*-1-keto-9-methyl-$\Delta^{2,6}$-hexahydronaphthalene** (0.33 g), bp 65–70° (air-bath temperature) (1 mm), as a yellow oil. This product was dissolved in ethyl acetate (20 ml) and hydrogenated over 10% palladium–carbon catalyst at atmospheric pressure until gas absorption ceased (30 min, 42 cc). The catalyst was removed by filtration, the solvent was evaporated, and the residue was distilled (bath temperature 130–140°) at 18 mm to give ***trans*-9-methyl-1-decalone-3-d_1** (0.32 g). This decalone (0.06 g) in ethanol (0.6 ml) was treated with 15% aqueous sodium hydroxide solution (0.16 ml) and freshly distilled furfuraldehyde (0.04 ml) was added. After standing at room temperature in the dark for 18 hr, the mixture was filtered and the solid product recrystallized from methanol to afford ***trans*-2-furfurylidene-9-methyl-1-decalone-3-d_1 (IIIb)** as cream plates, mp 86–87° (λ_{max} 321 mμ (log ε 4.36, in ethanol)). The **benzylidene derivative (XIa)** was obtained as colorless plates, mp 92.5–93.5°, by using benzaldehyde (0.04 ml) instead of furfuraldehyde in the last step.

2-Furfurylidene-5,6-dimethyl-6-phenylcyclohexanone (XXII). A solution of 4,5-dimethyl-4-phenyl-Δ^2-cyclohexenone[5] (2.48 g) in methanol (20 ml) was treated with 30% hydrogen peroxide (5.15 ml). The mixture was cooled to 15° and 6 *N* caustic soda (1.48 ml) was added dropwise with stirring at 15–17° during 12 min. The mixture was kept at 15–20° for 3 hr, poured into water, and extracted with ether. The ethereal extract was washed and dried over anhydrous magnesium sulfate and the ether evaporated. **4,5-Dimethyl-4-phenylcyclohexanone 2,3-epoxide** was obtained as a colorless oil, ν_{CO} 1710 cm^{-1}. The crude epoxy ketone (2 g) was refluxed with 100% hydrazine hydrate (23 ml) containing hydrazine sulfate (7.4 g) for 20 min. The mixture was cooled, diluted with water, and extracted with ether. The ethereal extract was washed and dried over anhydrous magnesium sulfate, and the ether was removed, leaving a viscous brown gum. Distillation at 0.7 mm (bath temperature 150–170°) gave **5,6-dimethyl-6-phenyl-Δ^2-cyclohexenol** (0.6 g) as a pale yellow viscous oil, a portion of which was purified by glpc (10-ft 10% Apiezon L on 60–80 Chromosorb W, 180°).

Anal. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.79. Found: C, 83.0; H, 8.90.

Oxidation of the alcohol with excess 8 *N* Jones reagent[10] in acetone gave after ether extraction **5,6-dimethyl-6-phenyl-Δ^2-cyclohexenone** (0.4 g) as a yellow oil, ν_{CO} 1680 cm^{-1}.

Anal. Calcd for $C_{14}H_{16}O$: C, 83.96: H, 8.05. Found: C, 83.67; H, 8.33.

The cyclohexenone (0.32 g) in ethyl acetate (25 ml) was hydrogenated over 10% palladium–carbon catalyst (100 mg) at room temperature and pressure until hydrogen uptake ceased (47 ml). The catalyst was removed and the solvent evaporated, giving **5,6-dimethyl-6-phenylcyclohexanone** as a colorless oil, ν_{CO} 1725 cm^{-1}. A portion was purified for analysis by glpc (10-ft 10% Apiezon L on 60–80 Chromosorb W, 175°).

Anal. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.79. Found: C, 83.17; H, 9.06.

The cyclohexanone (0.25 g) was dissolved in methanol (5 ml) containing sodium methoxide (0.1 g), and redistilled furfuraldehyde (0.15 g) was added. The mixture was left at room temperature under nitrogen overnight and poured into water, and the product was isolated by ether extraction as usual. **2-Furfurylidene-5,6-dimethyl-6-phenylcyclohexanone (XXII)** (0.3 g) was obtained as a yellow viscous gum which did not crystallize and darkened rapidly on exposure to air. Purification was effected by glpc (5-ft 10% SE30 on 60–80 Chromosorb W, 250°).

Anal. Calcd for $C_{19}H_{20}O_2$: C, 81.40; H, 7.19. Found: C, 81.50: H, 7.26.

2-Furfurylidene-4,5,5-trimethylcyclopentanone (XXIV). 2,2,3-Trimethylcyclopentanone (0.126 g) and redistilled furfuraldehyde (0.096 g) were dissolved in methanol (2 ml), and sodium methoxide (0.050 g) was added. The mixture was left overnight under an atmosphere of nitrogen and poured into water, and the product was isolated by ether extraction and purified by glpc (5-ft SF96, 185°). The product was obtained as an unstable yellow oil which darkened immediately on exposure to air.

Anal. Calcd for $C_{13}H_{16}O_2$: mol wt, 204. Found: mol wt (mass spectroscopy), 204.

Similarly *cis*-8-methyl-d_3-hydrindanone (see above) was condensed with furfuraldehyde to give the **furfurylidene derivative (XIX)** as an unstable viscous yellow gum.

Anal. Calcd for $C_{13}H_{15}D_3O_2$: mol wt, 233. Found: mol wt (mass spectroscopy), 233.

Communications to the Editor

A New Route to the Preparation and Configurational Correlation of Optically Active Phosphine Oxides[1]

Sir:

Optically active phosphine oxides occupy a key position in the stereochemical investigations of phosphorus compounds.[2,3] Produced[3] from optically active quaternary phosphonium salts by reaction with sodium hydroxide, from optically active phosphoranes by the Wittig reaction, or from optically active phosphines by oxidation, phosphine oxides are themselves precursors to optically active phosphines by reduction with trichlorosilane.[4] Present synthetic routes to optically active phosphines ($R_1R_2R_3P$) and phosphine oxides ($R_1R_2R_3PO$) require resolution[2] of the individual phosphine oxides or, more commonly,[3] resolution of quaternary phosphonium salts ($R_1R_2R_3R_4P^+X^-$) with subsequent cleavage, either by cathodic reduction or by reaction with base, to effect the elimination of R_4. Consequently, whatever the method of preparation, the ultimate starting material has to be one in which the three groups, R_1, R_2, and R_3, are already present prior to optical resolution. This structural commitment severely restricts the scope of these methods and limits the pathways which are accessible for configurational intercorrelations, particularly so since, to achieve selective elimination, the ease of cleavage of R_4 must be substantially greater than that of the other three groups.

We have developed a synthetic scheme which overcomes these difficulties. Unsymmetrically substituted

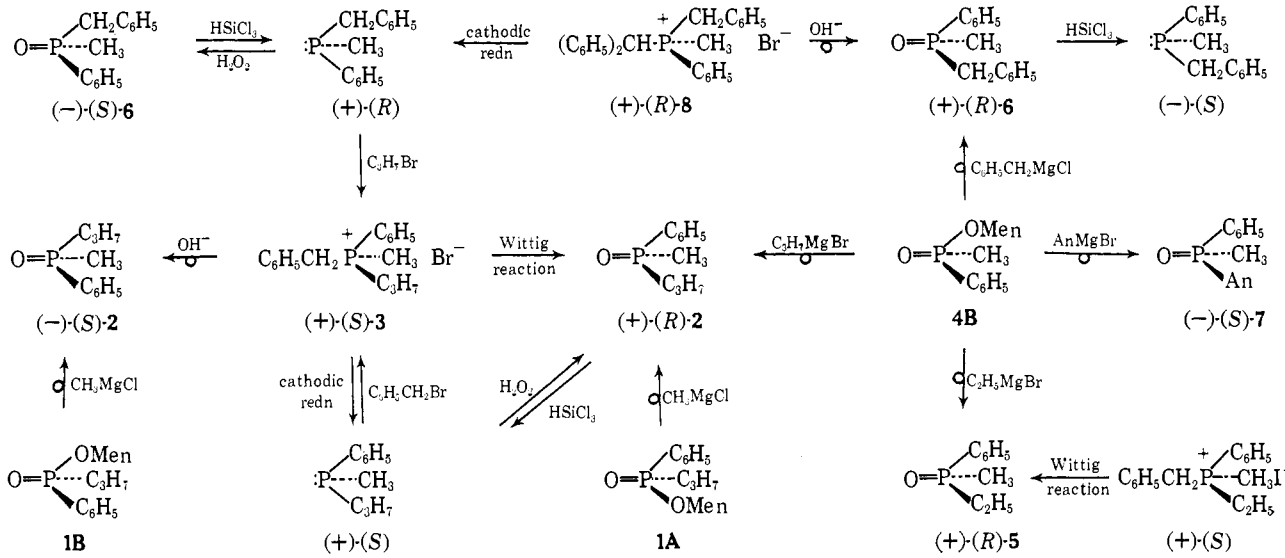
(1) This work was supported by the Air Force Office of Scientific Research under Grant No. AF-AFOSR-1188-67.

(2) Resolution of ethylmethylphenylphosphine oxide (5) provided the first example of an optically active phosphorus compound (J. Meisenheimer and L. Lichtenstadt, *Ber.*, 44, 356 (1911); J. Meisenheimer, J. Casper, M. Höring, W. Lauter, L. Lichtenstadt, and W. Samuel, *Ann.*, 449, 213 (1926)).

(3) For comprehensive reviews giving citations to the original literature, see R. F. Hudson and M. Green, *Angew. Chem. Intern. Ed. Engl.*, 2, 11 (1963); L. Horner, *Pure Appl. Chem.*, 9, 225 (1964); W. E. McEwen in "Topics in Phosphorus Chemistry," Vol. 2, M. Grayson and E. J. Griffith, Ed., Interscience Publishers, Inc., New York, N. Y., 1965, Chapter 1; G. Kamai and G. M. Usacheva, *Russ. Chem. Rev.*, 35, 601 (1966).

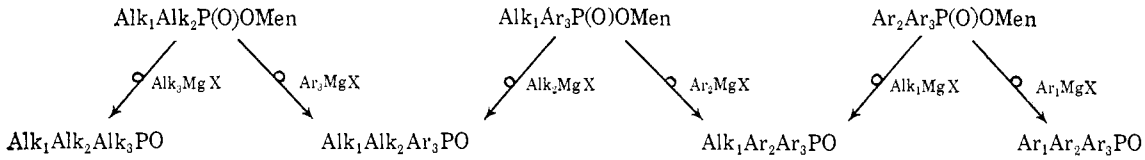
(4) L. Horner and W. D. Balzer, *Tetrahedron Letters*, 1157 (1965).

Chart I[a,b]



[a] Men = (−)-menthyl; An = *p*-anisyl; C_3H_7 = *n*-propyl. [b] Grignard reactions are described in the text; for other reactions, see ref 3 and 4.

Chart II[a]



[a] Alk = alkyl group; Ar = aryl group.

menthyl phosphinates ($R_1R_2P(O)OMen$) are readily separated into the diastereomeric forms. Reaction with alkyl or aryl Grignard reagents (R_3MgX) in benzene at 70° affords phosphine oxides[5] ($R_1R_2R_3PO$) with a high degree of stereospecificity. Thus, reaction of methylmagnesium chloride with diastereomerically pure[6] menthyl phenyl-*n*-propylphosphinate[7] (**1A**, mp 86°, $[\alpha]^{23}D$ −14° (benzene)) gives methylphenyl-*n*-propylphosphine oxide (**2**), $[\alpha]^{23}D$ +17.3° (methanol);[8] reaction with a mixture consisting of 87.4% of the epimer **1B** (mp 40°, $[\alpha]^{23}D$ −81.3° (benzene)) and 12.7% of **1A** gives **2** with $[\alpha]^{22}D$ −12.7° (methanol) (see Chart I). Since the chirality of the phosphorus atom in **1A** is *R*,[9] as determined by X-ray analysis,[10] and since the chirality of (+)-**2** is *R* by correlation[3,4] with (+)-(*S*)-benzylmethylphenyl-*n*-propylphosphonium bromide (**3**),[11] it follows that the Grignard reaction proceeds with inversion of configuration.[12] Similarly, reaction of *n*-propylmagnesium bromide with diastereomerically pure menthyl methylphenylphosphinate[6] (**4B**, mp 80°, $[\alpha]D$ −94° (benzene)) gives (+)-(*R*)-**2**, $[\alpha]^{23}D$ +17.1° (methanol);[8] since the reaction proceeds with inversion, the chirality of the phosphorus atom in **4B** is *S* and in **4A**[13] is *R*. Consequently, the configurations of all phosphine oxides prepared from **4** by the Grignard displacement reaction can be derived. For example, reaction of ethylmagnesium bromide, benzylmagnesium chloride, and *p*-anisylmagnesium bromide with **4B** gives, respectively, (+)-(*R*)-ethylmethylphenylphosphine oxide (**5**), $[\alpha]^{22}D$ +21.1° (water),[14] (+)-(*R*)-benzylmethylphenylphosphine oxide (**6**), $[\alpha]^{23}D$ +50.9° (methanol),[15] and (+)-(*S*)-anisylmethylphenylphosphine oxide[6] (**7**), $[\alpha]^{23}D$ −8.4° (methanol). In this manner, the configurations of **2** and **6** have been related by conversion from a *single* precursor (**4B**), whereas previous correlations[3,4] required the independent resolution of two phosphonium salts (**3** and **8**), coupled with a minimum of four reaction steps. The most important feature of the new method is indicated by Chart II, where it is shown that configurations of trialkyl-, dialkylaryl-,

(5) K. D. Berlin and R. U. Pagilagan, *J. Org. Chem.*, 32, 129 (1967), found that alkyldiphenylphosphine oxides can be obtained by reaction of alkyl diphenylphosphinates with alkyl Grignard reagents.

(6) R. A. Lewis, O. Korpiun, and K. Mislow, *J. Am. Chem. Soc.*, **89**, 4786 (1967).

(7) All new compounds gave elemental analyses (C, H, P) and nmr spectra consistent with their structures. Menthyl esters **1** and **4** were prepared by the conventional route: $C_6H_5PCl_2$ (+ROH) → $C_6H_5P(OR)_2$ (+RI) → $C_6H_5(R)P(O)OR$ (+PCl_5) → $(C_6H_5)(R)P(O)Cl$ (+(−)-menthol) → **1** (R = *n*-C_3H_7) and **4** (R = CH_3), and the epimers were separated by fractional crystallization.

(8) The highest reported rotation for **2** is $[\alpha]D$ +19.6° (methanol) (D. B. Denney and J. W. Hanifin, Jr., *Tetrahedron Letters*, 2177 (1963)).

(9) In the specification of chirality, contributions by d orbitals to bonds of quadriligand atoms are neglected (R. S. Cahn, C. Ingold, and V. Prelog, *Angew. Chem. Intern. Ed. Engl.*, 5, 385 (1966)).

(10) Unpublished work by E. B. Fleischer and R. Dewar. We thank Professor Fleischer for communicating these results to us prior to publication.

(11) A. F. Peerdeman, J. P. C. Holst, L. Horner, and H. Winkler, *Tetrahedron Letters*, 811 (1965).

(12) This result is analogous to the inversion accompanying transesterification of methyl ethylphenylphosphinate (M. Green and R. F. Hudson, *J. Chem. Soc.*, 540 (1963)), and to the inversion accompanying reaction of menthyl sulfinates with Grignard reagents (K. K. Andersen, *Tetrahedron Letters*, 93 (1962); P. Bickart, M. Axelrod, J. Jacobus, and K. Mislow, *J. Am. Chem. Soc.*, **89**, 697 (1967)).

(13) The epimer[6] of **4B** (*i.e.*, **4A**) has mp 89°, $[\alpha]D$ −16.3° (benzene).

(14) The highest reported rotation for **5** is $[\alpha]D$ +23.1° (water);[2] *cf.* also K. F. Kumli, W. E. McEwen, and C. A. VanderWerf, *J. Am. Chem. Soc.*, **81**, 3805 (1959).

(15) L. Horner and H. Winkler, *Tetrahedron Letters*, 3265 (1964), report $[\alpha]D$ +48.8° (methanol) for **6**.

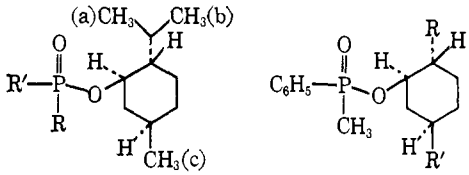
alkyldiaryl-, and triarylphosphine oxides may in principle be correlated *via* the appropriately substituted phosphinates; such correlations have not been possible by previously existing methods. We are currently exploring the scope and ramifications of this scheme.

Olaf Korpiun, Kurt Mislow
Department of Chemistry, Princeton University
Princeton, New Jersey 08540
Received June 27, 1967

Configurational Correlation of Phosphinates by Nuclear Magnetic Resonance and Optical Rotatory Dispersion[1]

Sir:

Menthyl phosphinates are useful precursors in the synthesis of optically active phosphorus compounds.[2] We now report that the nmr and ord spectra of these esters are characteristic of configuration and are thus important adjuncts to the assignment of chirality at phosphorus in this family of compounds.



1, R = *n*-C_3H_7; R′ = C_6H_5 **5**, R = *i*-C_3H_7; R′ = H
2, R = CH_3; R′ = C_6H_5 **6**, R = H; R′ = CH_3
3, R = CH_3; R′ = C_6H_{11}
4, R = R′ = C_6H_5

The absolute configuration of the menthyl esters **1** and **2** has been established.[2] As shown in Table I,

Table I.[a] Pmr Chemical Shifts and Coupling Constants of Phosphinate Esters

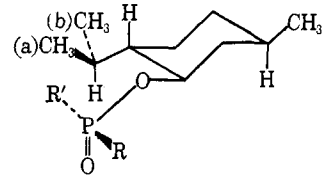
Compd	P-CH_3	C-CH_3 H_a	C-CH_3 H_b	C-CH_3 H_c
1A		9.11 (7.0)	9.05 (7.0)	9.25 (4.5)
1B		9.68 (7.0)	9.19 (7.0)	9.10 (5.0)
2A	8.38 (14.5)	9.11 (7.0)	9.05 (7.0)	9.24 (4.5)
2B	8.14 (14.5)	9.66 (7.0)	9.19 (7.0)	9.11 (5.0)
3A	8.64 (13.0)	9.19 (7.0)	9.08 (7.0)	9.10 (5.0)
3B	8.61 (13.0)	9.19 (7.0)	9.08 (7.0)	9.10 (5.0)
4		9.43 (7.0)	9.12 (7.0)	9.15 (5.0)
5A	8.38 (14.5)	9.10 (7.0)	9.05 (7.0)	
5B	8.32 (14.5)	9.59 (7.0)	9.20 (7.0)	
6A	8.42 (14.5)			*Ca.* 9.1 (5.0)
6B	8.42 (14.5)			*Ca.* 9.1 (5.0)

[a] Chemical shifts are given in τ units, and coupling constants (in parentheses) are given in Hz.

the epimers of **1** and **2** having the *S* configuration at phosphorus (**1B** and **2B**) exhibit a downfield shift of the H_c doublet and an upfield shift of the isopropyl doublets (H_a and H_b), relative to the corresponding signals for the epimers which have the *R* configuration at phosphorus (**1A** and **2A**). The large upfield shift of the H_a doublet (*ca.* 0.5 ppm) is particularly striking; its location in a region unencumbered by other signals provides an excellent measure of diastereomeric purity since contamination of **A** by **B** can be easily detected and estimated quantitatively.

The source of the shift experienced by H_a is traceable to the diamagnetic anisotropy of the phenyl ring rather than of the phosphoryl group, as shown by two observations. First, the C-CH_3 protons of the diastereomeric menthyl cyclohexylmethylphosphinates (**3**)[3,4] are indistinguishable at 60 MHz; second, the large upfield shift of H_a is also exhibited by menthyl diphenylphosphinate (**4**).[3] The C-CH_3 proton signals can be assigned by comparison (Table I) of the nmr spectra of esters containing portions of the menthyl group (**5** and **6**) with the spectra of **1–4**. First, both diastereomers of racemic *trans*-2-isopropyl-1-cyclohexyl methylphenylphosphinate (**5**)[3] feature two C-CH_3 doublets with J = 7.0 Hz; second, **5B** exhibits a 0.5-ppm upfield shift of one doublet relative to the corresponding signal in **5A**; third, both diastereomers of *cis*-3-methyl-1-cyclohexyl methylphenylphosphinate (**6**)[3] exhibit a C-CH_3 doublet with J = 5.0 Hz. Consequently, H_a must be located in the isopropyl portion of **1–5** and is diagnostic of configuration. For example, given the 1*R*,2*S*,5*R* configuration of menthol,[5] it can be deduced that **5A** is a mixture of enantiomers, one of which has the *R* configuration at phosphorus and the 1*R*,2*S* configuration in the cyclohexyl moiety, *i.e.*, $(R)_P$-$(1R,2S)_C$, while the other has the $(S)_P$-$(1S,2R)_C$ configuration; similarly **5B** is an equimolar mixture of $(S)_P$-$(1R,2S)_C$ and $(R)_P$-$(1S,2R)_C$ enantiomers.

The remaining question is to decide which of the two diastereotopic[6] methyl groups in the isopropyl portion of **1–5** is associated with the most highly shielded proton, H_a. If we assume minimal conformational strain in the menthol portion and an "up" conformation for the phosphinate ester grouping,[7] the most populated conformation of **1–4** (and, by extension, **5**) may be represented by stereoformula **7**. If this formulation is correct, it follows that when R′ = phenyl, as in **1B**, **2B**, **4**,



7

and $(S)_P$-$(1R,2S)_C$-**5**, the more highly shielded proton (H_a) is located on the methyl group which has the *pro-R* chirality[8,9] and the less highly shielded proton (H_b) on the methyl group which has the *pro-S* chirality.[8]

(1) This work was supported by the Air Force Office of Scientific Research under Grant No. AF-AFOSR-1188-67.
(2) O. Korpiun and K. Mislow, *J. Am. Chem. Soc.*, **89**, 4784 (1967).
(3) All new compounds gave elemental analyses (C, H, and P) and nmr spectra consistent with their structures.
(4) Prepared from $C_6H_{11}P(Cl)N(C_2H_5)_2$ (K. Issleib and W. Seidel, *Chem. Ber.*, **92**, 2681 (1959)) by the route (+CH_3OH) → $C_6H_{11}P(OCH_3)_2$ (+CH_3I) → $(C_6H_{11})(CH_3)P(O)OCH_3$ (+PCl_5) → $(C_6H_{11})(CH_3)P(O)Cl$ (L. Z. Soborovskij and J. M. Zinovjev, *Zh. Obshch. Khim.*, **24**, 516 (1954)), followed by reaction with (−)-menthol and separation of the epimers by fractional crystallization.
(5) V. Prelog, *Helv. Chim. Acta*, **36**, 308 (1953).
(6) K. Mislow and M. Raban in "Topics in Stereochemistry," Vol. I, N. L. Allinger and E. L. Eliel, Ed., John Wiley and Sons, Inc., New York, N. Y., 1967, Chapter 1.
(7) T. H. Siddall, III, and C. A. Prohaska, *J. Am. Chem. Soc.*, **84**, 3467 (1962); K. D. Berlin and R. U. Pagilagan, *Chem. Commun.*, 687 (1966); K. D. Berlin and R. U. Pagilagan, *J. Org. Chem.*, **32**, 129 (1967).
(8) K. R. Hanson, *J. Am. Chem. Soc.*, **88**, 2731 (1966).
(9) Similar arguments have been advanced by T. S. Sorensen, *Can. J. Chem.*, **45**, 1585 (1967), in a discussion of the nmr spectra of isopropylcyclopentenones.