of solid ammonium chloride, the ammonia was allowed to evaporate, and the crude product was worked up in the usual fashion to give 0.45 g (66%) of 1-anilino-1,2-diphenylethane (**32**), bp 168–170° (1 mm) [lit.[23] bp 168–170° (1 mm)]: hydrochloride, mp 198–199° (lit.[23] mp 192°); ir (neat) of **32**, 3115 (NH), 745, 728 and 689 cm^{-1} (ArH); nmr (CCl_4) of **32** δ 6.77 (m, 16, ArH, NCH), 4.08 (d, 2, $ArCH_2$), 3.67 (broad s, 1, NH).

B. *cis*-1-*p*-Chlorophenyl-2,3-diphenylaziridine (31).[24]—This reaction was effected essentially as described in part A by employing 0.92 g (0.04 g-atom) of sodium and 3.2 g (0.01 mol) of aziridine **31** to afford 2.2 g (73%) of 1-anilino-1,2-diphenylethane (**32**), bp 168–170°,[23] hydrochloride mp and mmp 198–199°. The ir and nmr of this product were identical with those in part A.

(23) M. Busch and A. Rinck, *Ber.*, **38**, 1761 (1905).
(24) Kindly provided by R. N. Loeppky and D. H. Smith.

C. 2,2-Diphenyl-3-methylaziridine (33).—This reaction was effected as described in part A by reducing 5.23 g (0.025 mol) of aziridine **33** by 1.15 g (0.05 g-atom) of sodium to give a reddish brown mixture which was, after 1 hr, poured into 200 ml of ammonia containing 15 g of ammonium chloride. The usual work-up gave 2.9 g (69%) of diphenylmethane, bp 84–85° (1 mm). The ir and nmr of this compound were identical with those of authentic samples.

Registry No.—Styrene oxide, 97-09-3; *trans*-stilbene oxide, 1439-07-2; **5**, 882-59-7; cyclohexene oxide, 286-20-4; **10**, 3146-39-2; 1,2-epoxybutane, 106-88-7; **12**, 6975-17-3; **18**, 4359-34-6; **19**, 6317-10-8; **21**, 2235-01-0; **22**, 26963-79-1; **24**, 14447-29-1; **25**, 26926-47-6; **26**, 26926-48-7.

A Stereochemical Reaction Cycle with Chiral Phosphorus[1]

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Cholesteryl and menthyl methylphenylphosphinates diastereomerically pure gave *N*-phenyl methylphenylphosphinic amide of the same rotation. The lithium salt of α-phenylethylamine with the same phosphinate esters gave the corresponding diastereomerically pure phosphinic amide of the same rotation. Treatment of these same esters with benzyl Grignard reagent gave benzylmethylphenylphosphine oxide of the same rotation. These results, coupled with reactions and configurational assignments of others, completed a three-reaction stereochemical cycle with three chiromers. The two reactions reported here proceed with inversion of configuration and high stereospecificity. Cholesteryl methylphenylphosphinate, absorbed on a solid support, failed to separate a series of racemates in a glc column.

From analogies drawn between the reactions of sulfinate[3,1b] and phosphinate esters, we anticipated the possibility that phosphinate esters might react with Grignard reagents and with substituted lithium amides to produce phosphine oxides and phosphinic amides, respectively. The stereochemical course of these reactions was of interest, particularly since they lead to compounds with phosphorus as the only chiral center. Indeed, since Horner and Winkler[4] had already demonstrated that benzylmethylphenylphosphine oxide was converted stereospecifically and with retention to *N*-phenyl methylphenylphosphinic amide, we envisioned closing a three-reaction stereochemical cycle by converting the same methylphenylphosphinate ester to these two substances. Finally, we planned to use these optically active compounds as liquid phases in attempts to resolve racemates by gas–liquid chromatography.

While our work was in progress, that of Korpium and Mislow[5a] appeared which established that in general, alkylarylphosphinate esters of menthol react with Grignard reagents to give phosphine oxides with high stereospecificity and inversion of configuration. In particular, they converted menthyl methylphenylphosphinate to benzylmethylphenylphosphine oxide. The absolute configuration of menthyl methylphenylphosphinate was known,[6] and that of the oxide was established.[5] Thus, by the time our work matured, the configurations of all three chiromers[7] II, III, and IV were in hand.

Initially, we failed to separate the diastereomers of menthyl methylphenylphosphinate, but successfully obtained pure one diastereomer of cholesteryl methylphenylphosphinate (I). Korpium and Mislow's[5a] recipe led us to the pure menthyl diastereomers (II). Treatment of either ester with benzylmagnesium Grignard reagent gave benzylmethylphenylphosphine oxide (IV) of essentially the same maximum rotation, a fact that establishes that both starting phosphinate esters possess the same configuration at phosphorus (*S*) (Scheme I). Both esters with lithium anilide gave *N*-phenyl methylphenylphosphinic amide (III) of the same sign and magnitude of rotation as that reported[4] by conversion of (+)-(*R*)-IV to (−)-(*S*)-III. These facts establish that the conversion of the phosphinic esters with lithium anilide proceeds with essentially complete inversion of configuration. The two, *three*-reaction stereochemical cycles are formulated. They are triligostatic (three ligands common to the three chiromers),[7] podal (number of chiromers equals the number of reactions),[7] contain no ligand metathesis,[7] and two of the reactions proceed with inversion and one with retention of configuration.

To determine the generality of the conclusion that lithium amides and phosphinate esters give phosphinic amides with high stereospecificity, (−)-(*S*)-I and (−)-(*S*)-II were treated with the lithium salt of optically

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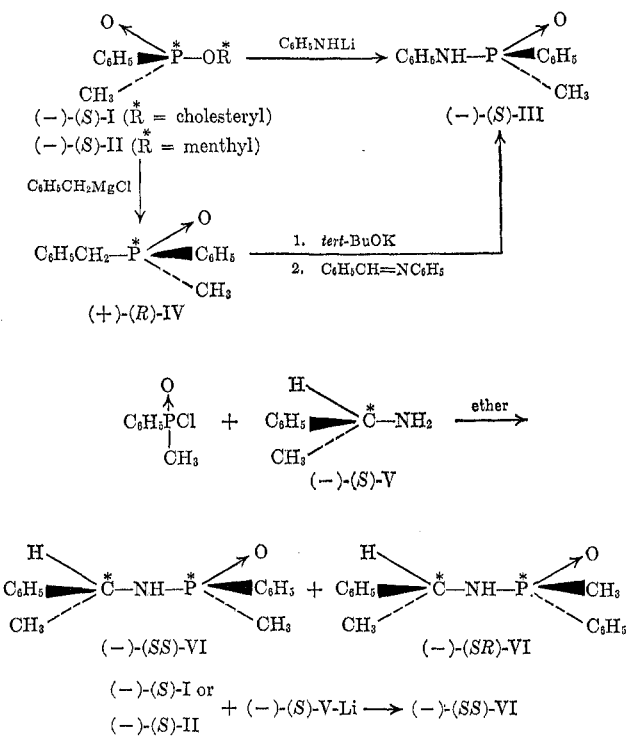
(2) This author thanks the Dow Chemical Co. and U. S. Rubber Co. for nonresident tuition grants.
(3) K. K. Andersen, *Tetrahedron Lett.*, 93 (1962).
(4) L. Horner and H. Winkler, *ibid.*, 3265 (1964).
(5) (a) O. Korpium and K. Mislow, *J. Amer. Chem. Soc.*, **89**, 4784 (1967); (b) O. Korpium, R. A. Lewis, J. Chickos, and K. Mislow, *ibid.*, **90**, 4842 (1968).
(6) E. B. Fleischer and R. Dewar, unpublished results, referred to in ref 5b, coupled with the results of ref 5b.
(7) D. C. Garwood and D. J. Cram, *J. Amer. Chem. Soc.*, **92**, 4575 (1970).

pure (−)-(*S*)-α-phenylethylamine[8] [(−)-(*S*)-V] and gave a single diastereomer of VI, very probably (−)-(*SS*)-VI. The same diastereomer [(−)-(*SS*)-VI] and its epimer at phosphorus [(−)-(*SR*)-VI] were obtained and separated by treating 2 mol of (−)-(*S*)-V with 1 mol of methylphenylphosphinic chloride in ether. The difference in nmr spectra of these diastereomers was used to demonstrate the absence of less than 5% diastereomeric impurity in each sample, and tlc experiments decreased the value to less than 2%.

SCHEME I



The feasibility of using phosphine oxides as the liquid phase in glc experiments was tested with racemic *o*-dodecyloxyphenylmethylphenylphosphine oxide, which was synthesized by conventional reactions. A column successfully separated a series of compounds of similar structure (see Experimental Section). However, a glc column with (−)-(*S*)-cholesteryl methylphenylphosphinate [(−)-(*S*)-I] as the stationary liquid phase failed to separate a number of racemates (see Experimental Section). These columns were vastly shorter than those used in Gil Av's successful experiments[9] with peptides as the liquid phase.

Experimental Section

Cholesteryl Methylphenylphosphinate [(−)-(*S*)-I].—Cholesterol (74 g, 0.192 mol) and pyridine (15.2 g, 0.19 mol) were dissolved in 350 ml of dichloromethane under dry conditions and under nitrogen. To this stirred solution was added dropwise 33.6 g (0.192 mol) of methylphenylphosphinic chloride[10] dissolved in 50 ml of dichloromethane. The mixture (heavy white precipitate) was stirred for 12 hr at 25° and shaken with ice-cold dilute sulfuric acid. The organic phase was washed with water, dried, and evaporated to a viscous oil, wt 94.5 g, which was chromatographed on 1200 g of silica gel. The unreacted cholesterol was eluted with 3:2 ether–pentane solution. The ester was eluted with 10% acetone–ether, and toward the end, 20% acetone–ether. Fractions (20) of about 500 ml were collected, and appearance of the desired ester was monitored by tlc (4:1 ether–pentane on silica gel plates). A total of 74.2 g (75%) of ester was distributed in the fractions, which were separated into the first ten rich in (−)-(*S*)-I, and the second ten rich in diastereomer (+)-(*R*)-I. The residues from evaporation of the first half of the fractions were crystallized and recrystallized twice from pentane and gave (−)-(*S*)-I: 11.9 g (12%); mp 134–135.5°; $[\alpha]^{25}D$ −81.4° (*c* 4.53, chloroform). Rotation and melting point did not change with further recrystallization. *Anal.* Calcd for $C_{34}H_{53}O_2P$: C, 77.82; H, 10.18. Found: C, 78.02; H, 10.38.

The second 10 fractions were evaporated and the residue repeatedly recrystallized from pentane (six times), but could not be brought to constant melting point or rotation, the maximum rotation being $[\alpha]^{25}D$ +6.13° (*c* 2.33, chloroform).

Menthyl Methylphenylphosphinates [(−)-(*S*)-II and (−)-(*R*)-II].—Menthol (31.2 g, 0.195 mol) and pyridine (15.4 g, 0.195 mol) were dissolved in 450 ml of anhydrous ether. To this dry solution stirred under nitrogen was added dropwise 34.1 g (0.195 mol) of methylphenylphosphinic chloride[10] in 50 ml of ether. The resulting mixture (heavy precipitate) was stirred for 8 hr and shaken with 10% hydrochloric acid. The organic phase was washed, dried, and evaporated to give 48.3 g of an oil which was chromatographed on 710 g of silica gel. The unreacted menthol eluted with 15% ether–pentane, and the desired ester with 25% ether–pentane. The ester was collected in twenty-five 400-ml fractions, evaporation of which gave 34.8 g (61%) of ester. The progress of the separation was followed by tlc on silica gel plates (ether as eluent, phosphomolybdic acid as developer). The first fraction [(−)-(*R*)-II, 1.2 g, 2%] gave mp 89° and $[\alpha]^{25}D$ −15.4° (*c* 4.8, benzene) [lit.[5] mp 89°, $[\alpha]^{25}D$ −16.3° (*c* 1.3, benzene)]. The next 16 fractions contained mixtures of diastereomers. The last 8 fractions contained (−)-(*S*)-II: 5.7 g or 10%; mp 80°, $[\alpha]^{25}D$ −93.8° (*c* 1.45, benzene) [lit.[5] mp 79–80°, $[\alpha]^{25}D$ −94° (*c* 1.3, benzene)]. *Anal.* Calcd for $C_{17}H_{27}O_2P$: C, 69.36; H, 9.25. Found for (−)-(*R*)-II: C, 69.49; H, 8.99. Found for (−)-(*S*)-II: C, 69.52; H, 9.31.

Benzylmethylphenylphosphine Oxide [(+)-(*R*)-IV].—A Grignard reaction between benzylmagnesium chloride (6.3 g of benzyl chloride and 1.2 g of magnesium) and 2.62 g of cholesteryl methylphenylphosphinate [(−)-(*S*)-I, see above] in benzene at reflux for 8 hr was carried out, and quenched with aqueous ammonium chloride. The organic phase was washed, dried, and evaporated to give 5.05 g of residue which was chromatographed on 50 g of silica gel. Impurities were eluted with 10% acetone–ether, the phosphine oxide with acetone to give 0.97 g (84%) of material, recrystallization of which from acetone–ether gave mp 135–135.2°, $[\alpha]^{25}D$ +49.94° (*c* 1.64, methanol) [lit.[5] mp 134–135°, $[\alpha]^{25}D$ +50.9° (*c* 1–3, methanol), lit.[11] mp 135°].

***N*-(α-Phenylethyl) Methylphenylphosphinic Amides [(−)-(*SS*)-VI and (−)-(*SR*)-VI].**—To a solution of 1.21 g (0.01 mol) of (−)-(*S*)-α-phenylethylamine, $[\alpha]^{25}D$ −40.1° (neat),[8] in 5 ml of anhydrous ether under dry nitrogen was added 6.25 ml of a 1.6 *M* solution of *n*-butyllithium (0.01 mol) in hexane. A solution of 1.74 g (0.01 mol) of methylphenylphosphinic chloride[10] in 10 ml of ether was added to the mixture. The resulting mixture was stirred for 5 hr and shaken with water, and the organic phase was washed with water. The solid that separated (2.36 g) was collected, dissolved in dichloromethane, and chromatographed on 50 g of silica gel. The separation of the diastereomeric amides was followed by tlc on silica gel with 9:1 acetone–methanol as eluent and iodine as developer. Ten fractions (75 ml) were collected of 4.5:1 acetone–ether eluent. Fraction 4 on evaporation gave crystalline material, $[\alpha]^{25}D$ −16.1° (*c* 1.58, chloroform), and fraction 5, $[\alpha]^{25}D$ −16.2° (*c* 1.58, chloroform), combined wt 0.23 g. After recrystallization of this material from ether–pentane, it gave mp 117–119° [(−)-(*SR*)-VI]. *Anal.* Calcd for $C_{15}H_{18}NOP$: C, 69.49; H, 7.00. Found: C, 69.68; H, 7.02.

Fractions 6–10 exhibited rotations that increased from an initial $[\alpha]^{25}D$ −62.6° to a maximum of $[\alpha]^{25}D$ −64.6° (*c* 1.96, chloroform),

(8) (a) A. Ault, *J. Chem. Educ.*, **42**, 269 (1965); (b) W. Leithe, *Chem. Ber.*, **64**, 2827 (1931).

(9) E. Gil Av and B. Feibush, *Tetrahedron Lett.*, 3345 (1967), and earlier references.

(10) C. S. Gibson and J. D. A. Johnson, *J. Chem. Soc.*, 92 (1928).

(11) J. Meisenheimer, J. Casper, M. Horning, W. Lauter, L. Lichtenstadt, and W. Samuel, *Justus Liebigs Ann. Chem.*, **449**, 213 (1926).

combined wt 0.6 g. After recrystallization, this material [(−)-(*SS*)-VI] from ether–pentane gave mp 133–134°. *Anal.* Found: C, 69.68; H, 6.93.

N-(α-**Phenylethyl**) **Methylphenylphosphinic Amide** [(−)-(*SS*)-VI] **from Menthyl or Cholesteryl Methylphenylphosphinates** [(−)-(*S*)-II **and** (−)-(*S*)-I].—The procedure is illustrated as applied to the cholesteryl ester (−)-(*S*)-I. To a solution (4.12 g or 34 mmol) of (−)-(*S*)-α-phenylethylamine, $[\alpha]^{25}D$ −40.1° (neat),[8] in 20 ml of dry benzene was added 21.3 ml of a 1.6 *M* solution of *n*-butyllithium (34 mmol) in hexane with stirring under dry nitrogen. The mixture was stirred at reflux for 1 hr. A solution of 0.92 g (1.7 mmol) of (−)-(*S*)-I, $[\alpha]^{25}D$ −81.4°, *c* 4.53, chloroform (or 1.7 mmol of (−)-(*S*)-II, $[\alpha]^{25}D$ −94°, *c* 1.45, benzene) in 20 ml of dry benzene was added with stirring, and the mixture was held at reflux for 5 hr. The reaction mixture was shaken with 10% hydrochloric acid and dichloromethane. The organic layer was washed, dried, and evaporated to give 0.97 g of residue which was chromatographed on 25 g of silica gel. The first 4 fractions (75 ml each) were eluted with 1:1 ether–acetone, fractions 5–8 with pure acetone. The yellow oil from 5 and 6 was crystallized (nonfractionally) from ether–pentane to give 0.11 g (25%) of (−)-(*SS*)-VI, $[\alpha]^{25}D$ −63° (*c* 1.55, chloroform), mp 132–133.5°. An identical yield, melting point, and rotation were obtained from (−)-(*S*)-II. Examination of the crude amides from both preparations of (−)-(*SS*)-VI with tlc on silica gel plate, acetone–methanol, 9:1, showed the absence of other diastereomers. Control experiments with both diastereomers demonstrated that as little as 1–2% could have been detected.

N-**Phenyl Methylphenylphosphinic Amide** [(−)-(*S*)-III].—Application of the above procedure to lithium anilide (10 mol excess) and either cholesteryl or menthyl methylphenylphosphinate [(−)-(*S*)-I or (−)-(*S*)-II] gave (−)-(*S*)-III. The yield after chromatography and nonfractional crystallization of (−)-(*S*)-III (acetone–pentane) from (−)-(*S*)-I was 35%, mp 161–163°, $[\alpha]^{25}D$ −26.2° (*c* 1.33, methanol). The yield after chromatography and nonfractional crystallization (acetone–pentane) from (−)-(*S*)-II was 38%, mp 161–163°, $[\alpha]^{25}D$ −26.1° (*c* 0.83, methanol). The literature[4] reported mp 164°, $[\alpha]^{25}D$ −25.8° (c 0.76, methanol).

o-**Dodecyloxybromobenzene**.—A mixture of *o*-bromophenol (82.5 g), 250 ml of 95% ethanol, and 21 g of sodium hydroxide pellets was heated into solution, and 113.2 g of dodecyl bromide was added. After 24 hr at reflux, the product was isolated by extraction and distillation, wt 142 g (92%), bp 153° (0.14 mm). *Anal.* Calcd for $C_{18}H_{29}BrO$: C, 63.34; H, 8.56. Found: C, 63.47; H, 8.54.

o-**Dodecyloxyphenylmethylphenylphosphine Oxide** (VII).—The Grignard reagent of *o*-dodecyloxybromobenzene was prepared by the "entrainment method"[12] from 34.1 g of bromide and 2.6 g of magnesium in 500 ml of dry ether. To this stirred mixture under nitrogen was added dropwise 17.4 g of methylphenylphosphinic chloride[10] in 200 ml of dry ether. The resulting viscous mixture was shaken with dilute hydrochloric acid, and the organic phase was washed with water, dried, evaporated, and distilled to give 19.6 g (49%) of VII as a viscous and slowly crystallizing oil, bp 188° (0.14 mm). *Anal.* Calcd for $C_{25}H_{37}O_2P$: C, 74.97; H, 9.31. Found: C, 75.01; H, 9.29.

Attempted Resolution by Glc.—A 0.25 in. (i.d.) × 10 ft column was packed with a 10% mixture by weight of diastereomerically pure cholesteryl methylphenylphosphinate [(−)-(*S*)-I] on Chromosorb W (80–100 mesh). About 15 g of mixture filled the column, which was cured in an oven at 170° for 90 min and at 155° for 3 hr. A small sample of pure (−)-(*S*)-I was found not to change its rotation when held at 165° for 12 hr. The chromatographic experiments were carried out on a Perkin-Elmer vapor fractometer, Model 154, at a column temperature of 144° with helium as a carrier. On this column, the following racemates had the indicated retention times, and the peaks were sharp: 2-octanol, 14 min; 2-phenylpropionitrile, 32 min; 3-methoxy-3-phenyl-2-butanone, 34 min; 2-methyl-1-phenyl-1-propanol, 28 min; 3-methoxy-2-methyl-3-phenyl-2-butanol, 44 min. In experiments that involved *o*-dodecyloxyphenylmethylphenylphosphine oxide (VII), 5% by weight of VII on Chromosorb W was employed in the same type of column and in the same machine and carrier gas. At 85°, 1-butanol, 2-butanol, and *tert*-butyl alcohol gave 6.3, 2.9, and 1.3 min retention times, respectively. At 105°, 1-octanol and 2-octanol gave 14.7 and 4.7 min retention time, respectively. At 87°, 1-butanol, 2-butanol, and 2-pentanol gave 2.7, 1.5, and 2.4 min retention times, respectively.

Registry No.—(−)-(*S*)-I, 20752-41-4; (−)-(*S*)-II, 16934-93-3; (−)-(*R*)-II, 26963-82-6; (−)-(*SR*)-VI, 20752-44-7; (−)-(*SS*)-VI, 20752-43-6; VII, 26910-10-1; *o*-dodecyloxybromobenzene, 26910-11-2.

(12) D. E. Pearson, D. Cowan, and J. D. Beckler, *J. Org. Chem.*, **24**, 504 (1959).

Carbon-14 Tracer Study of the Dehydrocyclization of *n*-Heptane

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The ^{14}C distribution in toluene from the dehydrocyclization of *n*-heptane-1-^{14}C and -4-^{14}C, both over the same chromia on "nonacidic" alumina preparation, is consistent with 80% or more of the aromatic being formed by direct six-carbon ring formation. Thus, chromia on "nonacidic" alumina can give results similar to other chromia and chromia–alumina. In general, a dehydrocyclization mechanism involving various size intermediates is not necessary even for the "nonacidic" catalyst.

The mechanism for the heterogeneous catalytic conversion of paraffins to aromatics, dehydrocyclization, has been widely studied.[1] Early workers, guided by aromatic product distributions and kinetics, supported a dehydrocyclization mechanism involving direct six-carbon ring formation. An early ^{14}C tracer study[2] also supported this mechanism.

Results of more recent ^{14}C tracer studies[3,4] were incompatible with this mechanism. To explain their ^{14}C distributions, Pines and Chen[4] proposed that cyclization to both six- and seven-membered-ring intermediates participate in the mechanism. The contribution of these intermediates varied with time on stream and catalyst. Such competition between various size ring intermediates would not allow the dehydrocyclization mechanism to have predictive value. On the other hand, Feighan and Davis[5] found that *n*-heptane-4-^{14}C

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(1) For a review of the literature, see (a) A. H. Steiner in "Catalysis," Vol. 4, P. H. Emmett, Ed., Reinhold, New York, N. Y., 1957, p 529; (b) H. Hansch, *Chem. Rev.*, **52**, 353 (1953); (c) H. Pines and C. T. Goetschel, *J. Org. Chem.*, **30**, 3530 (1965).

(2) R. W. Wheatcroft, Dissertation, University of California, 1949.

(3) J. J. Mitchell, *J. Amer. Chem. Soc.*, **80**, 5848 (1958).

(4) H. Pines and C. T. Chen, *J. Org. Chem.*, **26**, 1057 (1961).

(5) J. A. Feighan and B. H. Davis, *J. Catal.*, **4**, 594 (1965).