The apparatus for base-cleavage and separation of diacetylene from xylene and acetone consists principally of a decomposition flask (A), an acetone–xylene condensation receiver (B), a graduated diacetylene trap (C), and a reactor flask (D).

Flask A is a 500-ml., 29/42 standard taper, three-necked flask equipped with a thermometer well or joint. One neck is equipped with a gas inlet tube for introduction of nitrogen while the furthest neck is equipped with a 10-in. Vigreux column (29/42 joints, 1-in. o.d.). The middle neck is equipped with a Tru-bore stirrer and mineral oil seal to minimize possible loss of diacetylene. The top of the Vigreux column is equipped with a standard distillation head, which condenses acetone (water cooling below 25°) yet allows the major part of the evolved diacetylene to be swept (nitrogen) into C or D. The condensed acetone can be allowed to reflux or led directly to B.

Collection flask B is a 250-ml., three-necked flask equipped with a 0.5-in. (o.d.) delivery tube leading from the distillation head of A into receiver B. A stopcock (0.25-in. bore) located 2 in. above the neck of B serves to isolate B from A and collect acetone. The furthest neck of B is fitted with a 10-in. packed (stainless steel 0.25-in. Podbielniak) column, the top of which is equipped with a total return condenser for acetone, but allows diacetylene gas to be collected in C or D. The receiver is kept at a temperature 55–60° to minimize diacetylene solubility in acetone.

Diacetylene–nitrogen sweep gas lines (0.25-in. i.d., Pyrex) leading from distillation head (A) and total return condenser (B) meet at a T-connection prior to leading into the diacetylene trap (C). Trap C (1-in. i.d.) is graduated to 0.20-ml. accuracy and has a capacity of about 50 ml. It is equipped with an entrance tube ending approximately at the 20-ml. mark, and an exit tube used to vaporize the diacetylene slowly under a slow nitrogen current into the cooled reactor (D) containing an appropriate solvent. Trap C is cooled to approximately −50 to −70° by the use of Dry Ice and alcohol, and by immersing the trap up to the 20-ml. mark. However, care must be exercised to avoid freezing (−36°) the diacetylene in the entrance line and causing a plug. The bath is lowered somewhat if crystallization is noted, otherwise a bath temperature of −30 to −35° can be used safely for several hours if the diacetylene is to be used in a reaction.

The generation of diacetylene is started by first adding to flask A, 100 ml. of xylene, 0.10 mole (16.6 g.) of 2,7-dimethylocta-3,5-diyne-2,7-diol, and 0.10 g. of powdered 90–98% potassium or sodium hydroxide (latter preferred). The reaction system previously well purged with nitrogen is now purged again with nitrogen for 10 min. using a moderate flow through a mineral oil bubble counter. The reaction slurry is stirred at a speed sufficient to maintain good mixing, but to prevent splashing, as the reaction slurry is heated.

As the reaction temperature approaches 90° some gradual volatilization of possibly acetone and diacetylene is noted. With the use of constant heat input, the reaction temperature rises to 92–94° and then falls to 87–88° whereupon active distillation of both acetone and diacetylene is observed. When approximately 50% (by volume) of the expected amounts of products have been collected in B and C, the rate of distillation decreases as the reaction temperature increases. By the time the boiling point of xylene (139°) is reached, distillation of acetone and condensation of diacetylene have essentially ceased. Slowing the rate of heating after distillation starts has been observed to be detrimental to the conversion to diacetylene. The acetone collection chamber is kept at 60° to minimize solubility of diacetylene in acetone. Both flasks A and B are swept with slow currents of nitrogen during the cleavage and for 15 min. after heating was halted. The nitrogen sweep for both A and B can be operated independently of each other. The conversion to diacetylene is measured directly by noting the volume of liquefied gas (d^0_4 0.7364) or by weighing the cold tared trap. If stored overnight, it should be cooled to −70 to −80° under a nitrogen atmosphere. Exposure to air and alkali must be avoided at all times, and a safety face shield should be worn when handling this material. A well-ventilated hood with a sliding glass or Plexiglas window should be used. It is preferable to lead the diacetylene directly into reaction vessel (D) or shortly after (within several hours) it is collected in C to vaporize it slowly into D using a current of nitrogen and a water bath at 5–10°. Recommended solvents for dissolving diacetylene and for carrying out the reactions are methylal, dioxane, liquid ammonia, N-methylpyrolidone, and dimethyl sulfoxide. The diacetylene collected on redistillation leaves no residue and boils at 9–10°.

The physical constants are diacetylene,[12] b.p. 10.3° (760 mm.); m.p. −36 to −35°; d^0_4 0.7364; vapor pressure 1.6 mm. (−78°), 93.5 (−35.5°), 519 (0°).

(12) F. Straus and L. Kollek, *Ber.*, **59B**, 1664 (1926).

α-Methyldopa. Resolution and Configuration

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The hypotensive activity of 3-(3,4-dihydroxyphenyl)-2-methylalanine (α-methyldopa) resides in the optical isomer with a negative rotation,[1] $[\alpha]^{25}D$ −4° (*c* 2, 0.1 *N* hydrochloric acid).

The same isomer inhibits the decarboxylation of L-3,4-dihydroxyphenylalanine (L-dopa) by mammalian decarboxylase while the other isomer is totally inactive.[2] This suggests that the biologically active isomer has the L configuration. The rotatory dispersion curve for (−)-α-methyldopa (Fig. 1) supports this sug-

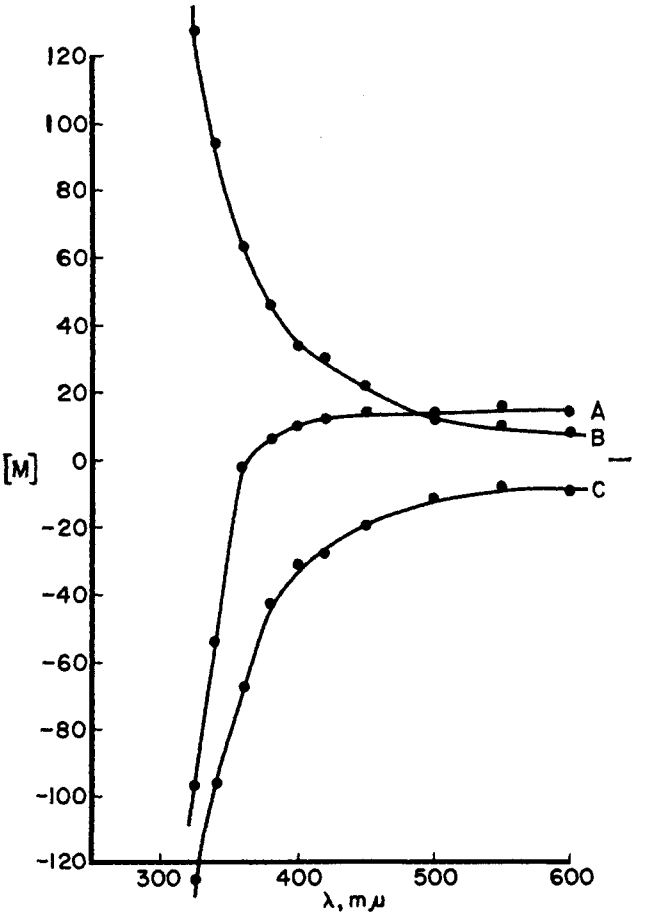


Fig. 1.—Rotatory dispersion curves: A, D-dopa; B, L-α-methyldopa; C, D-α-methyldopa. Measurements were made at 25° on 1% solutions of the amino acids in 6 *N* hydrochloric acid.

(1) A. Sjoerdsma and S. Udenfriend, *Biochem. Pharmacol.*, **8**, 164 (1961).

(2) S. M. Hess, R. H. Connamacher, M. Ozaki, and S. Udenfriend, *J. Pharmacol. Exptl. Therap.*, **134**, 129 (1961); C. C. Porter, J. A. Totaro, and C. M. Leiby, *ibid.*, **134**, 139 (1961).

gestion; the curve is similar to the curves for L-phenylalanine and L-tyrosine reported by Schellman.[3] The rotations for all three amino acids become strongly positive in the 300-mμ region. The dispersion curve of (+)-α-methyldopa is similar to the D-dopa[4] curve.

The assignment of the L-configuration to the active isomer is supported by three other rotational criteria. First, the Lutz–Jirgensons rule,[5] that L-amino acids show a positive shift in rotation upon going from neutral to acidic solution, is obeyed by (−)-α-methyldopa; $[\alpha]^{25}D$ −13.5° (*c* 2, phosphate buffer, pH 6.5), $[\alpha]^{25}D$ +4° (*c* 2, 6 *N* hydrochloric acid). The molecular rotation difference, [M]HCl − [M]pH 6.5, +40.5°, is larger than that of most amino acids but close to that of L-phenylalanine,[6] [M]HCl − [M]H_2O, +49.6°; D-dopa[4] shows a negative shift of the same magnitude [M]6 *N* HCl − [M]pH 6.5, −45°. It is of interest that (−)-α-methyldopa follows the rule at all the wave lengths employed (see Table I).[7] Second, L-amino acids give hydantoin derivatives with large negative rotations.[8] The hydantoin of (−)-α-methyldopa was prepared in these laboratories[9] and has a negative rotation, $[\alpha]^{25}D$ −52.1° (*c* 1, water).

TABLE I

DEPENDENCY OF OPTICAL ROTATION ON ACID CONCENTRATION

Wave length, mμ	$[\alpha]^{25}$ (*c* 2) 6 *N* HCl	1 *N* HCl	0.1 *N* HCl	pH 6.5, phosphate
	A. L-α-Methyldopa			
578	+4	−0.1	−4	−14
546	+5	−0.1	−4.5	−16
436	+11.5	+1	−5.5	−25
405	+15	+3	−5	−29
	B. D-α-Methyldopa			
578	−4	+1.5	+5.5	+13
546	−4	+1.5	+6	+14
436	−10	−0.5	+8	+25
405	−15	−3	+7	+29
	C. D-Dopa[a,b]			
578	+7.5	+9.5	+13	+31.5
546	+8	+10	+14	+35.5
436	+8	+13	+19.5	+61
405	+6	+12.5	+20.5	+72.5

[a] 0.1 *N* hydrochloric acid, *c* 1.0. [b] pH 6.5, phosphate, *c* 0.5.

Finally, the rotatory dispersion curve for the copper salt of (−)-α-methyldopa (Fig. 2) is similar to that of L-tyrosine copper salt measured under the same conditions. Upon going from 400 mμ to longer wave lengths a positive shift in rotation occurs until, at about 600 mμ, a positive extremum is reached. The copper salt of D-dopa undergoes the opposite shift, becoming more negative as the wave length is increased from 400 mμ. Measurements of copper salt rotations have been used as evidence of configuration.[10,11] In this previous work the isolated copper salts were dissolved in water or

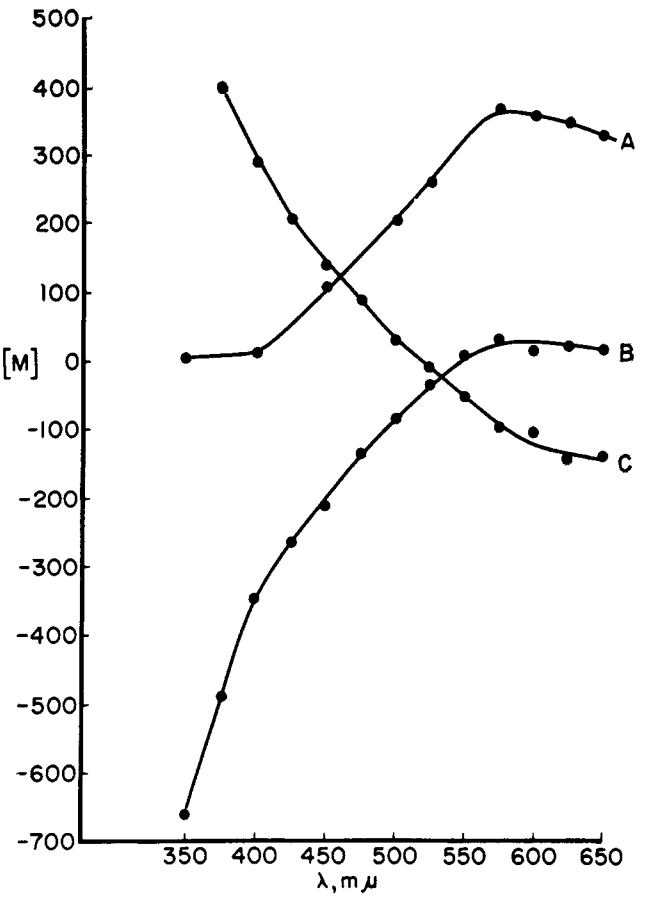


Fig. 2.—Rotatory dispersion curves of copper salts: A, L-α-methyldopa; B, L-tyrosine; C, D-dopa. Measurements were made at 25° on 0.5% solutions of the amino acids in 0.25 *M* cupric sulfate buffered at pH 3.4.

1 equiv. of cupric acetate was added to aqueous solutions of the amino acids. However solutions of the copper salt of α-methyldopa prepared in the same way were too unstable to air oxidation to be useful for rotation studies. A relatively stable solution of the copper salt can be prepared in acidic solution. Rotatory dispersion measurements were made on (−)-α-methyldopa, D-dopa, and L-tyrosine in the presence of excess cupric sulfate buffered at pH 3.4.[12] The high positive rotation of (−)-α-methyldopa at 589 mμ ($[\alpha]^{25}D$ 170–175°, for optically pure isomer) in the buffered cupric sulfate solution provides a useful assay for optical purity.

Inherent in all the rotational evidence is the assumption that the substitution of methyl for the α-hydrogen of an optically active amino acid does not alter greatly the rotatory characteristics. This assumption appears valid for amino acids in which the other alkyl substituent on the α-carbon is large compared with methyl.[13]

(3) J. A. Schellman and C. S. Schellman, *Arch. Biochem. Biophys.*, **65**, 58 (1956).

(4) Purchased from California Corporation for Biochemical Research, Los Angeles, Calif.

(5) O. Lutz and B. Jirgensons, *Ber.*, **63**, 448 (1930).

(6) J. P. Greenstein, L. M. Birnbaum, and M. C. Otey, *J. Biol. Chem.*, **204**, 307 (1953).

(7) The shift of rotation with pH has the effect of giving (−)-α-methyldopa an anomalous dispersion curve in 0.1 *N* hydrochloric acid (negative rotation in the visible region of the spectrum and a positive rotation in the ultraviolet) and a plain positive dispersion curve in 6 *N* hydrochloric acid.

(8) G. W. Clough, *J. Chem. Soc.*, **113**, 526 (1918).

(9) R. A. Vitali and T. Jacob, in press.

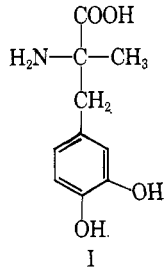
(10) P. Pfeiffer and W. Christeleit, *Z. Physiol. Chem.*, **245**, 197 (1937).

(11) N. Izumiya, M. Winitz, S. M. Birnbaum, and J. P. Greenstein, *J. Am. Chem. Soc.*, **78**, 1602 (1956).

(12) The rotations obtained for L-tyrosine differ considerably from the published values.[10] In the 400–500-mμ range rotations were negative rather than positive and the positive extremum at 525 mμ, observed by Pfeiffer and Christeleit,[10] was shifted to 575 mμ. The differences, attributable to the acidity or the excess cupric sulfate content of our solutions, emphasize the necessity of making configurational comparisons under identical conditions.

(13) M. Winitz, S. M. Birnbaum, and J. P. Greenstein [*J. Am. Chem. Soc.*, **77**, 716 (1955)], after observing the rotational shifts with change of pH for (+)-isovaline, generalized that the Lutz–Jirgensons rule applies only to α-amino acids which contain an α-hydrogen atom. However, in isovaline the two groups on the α-carbon, methyl and ethyl, are comparable in size, while for α-methylphenylalanines, methyl is small compared with benzyl.

Based on the above evidence (−)-α-methyldopa is assigned the L- or *S*-configuration (I).



I

The resolution of α-methyldopa[14] was achieved using 3-(3,4-dimethoxyphenyl)-2-methylalanine,[15] which was converted to the N-acetyl derivative. Upon treatment with (−)-1-phenylethylamine,[16] $[\alpha]^{25}D$ −36.5° (neat), a diastereoisomeric salt was obtained, $[\alpha]^{25}D$ +69° (*c* 1, methanol). From the salt was isolated (−)-*N*-acetyl-3-(3,4-dimethoxyphenyl)-2-methylalanine, $[\alpha]^{25}D$ −56° (*c* 1, methanol), which upon acid hydrolysis gave (−)-α-methyldopa, $[\alpha]^{25}D$ −4° (*c* 2, 0.1 *N* hydrochloric acid). Exactly the same operations using dextrorotatory 1-phenylethylamine gave (+)-α-methyldopa, $[\alpha]^{25}D$ +4° (*c* 2, 0.1 *N* hydrochloric acid).

In a second resolution, α-methyldopa[15] was the starting material. Acetylation gave N-acetyl-3-(3,4-diacetoxyphenyl)-2-methylalanine which upon treatment with quinine gave a 1:1 salt. The quinine salt of the desired enantiomer was crystalline and insoluble in acetone, $[\alpha]^{25}D$ −72.5° (*c* 1, 96% ethanol), while the undesired enantiomer formed an acetone-soluble glass. The acetylated acid, $[\alpha]^{25}D$ −74.5° (*c* 1, 96% ethanol), was liberated from crystalline quinine salt with hydrochloric acid. Acid hydrolysis of the acetyl groups gave (−)-α-methyldopa, $[\alpha]^{25}D$ −3° (*c* 2, 0.1 *N* hydrochloric acid).

Experimental

Rotatory Measurements.—Two instruments were used to measure the optical rotatory dispersion. Measurements in the range 600 to 325 mμ were made with an instrument constructed in this laboratory on the Keston[17] principle. This instrument contains ultraviolet transmitting polarizing and analyzing prisms and it was calibrated against reagent grade sucrose. The values thereby determined were checked at 405, 436, 546 and 578 mμ with a Zeiss precision photoelectric polarimeter. The pH dependency of the rotations was investigated with the Zeiss instrument.

The optical rotatory dispersions of D-α-methyldopa, L-α-methyldopa and D-dopa are plotted in Fig. 1. The rotations of these compounds at selected acid concentrations and wave lengths are summarized in Table I.

The optical rotatory dispersions of the copper salts of L-α-methyldopa, L-tyrosine, and D-dopa are plotted in Fig. 2. The copper salts were prepared at 0.5% (w./v.) concentration by dissolving the amino acid in an aqueous solution containing per liter 20 g. of anhydrous sodium acetate, 50 ml. of glacial acetic acid, and 62.5 g. of $CuSO_4 \cdot 5H_2O$. The pH of the reagent is 3.4.

DL-N-Acetyl-3-(3,4-dimethoxyphenyl)-2-methylalanine.—A mixture of 69.0 g. (0.288 mole) of DL-3-(3,4-dimethoxyphenyl)-2-methylalanine in 207 ml. (2.56 moles) of pyridine and 276 ml. (2.92 moles) of acetic anhydride was heated at 90° with stirring for 3 hr. The solution was concentrated under vacuum to a thick sirup. The residue was poured into 300 ml. of ice–water and stirred for 10 min. The product crystallized on addition of 250 ml. of 2.5 *N* hydrochloric acid.[18] The mixture was aged at 5° for 1 hr. and filtered. After washing successively with cold water and 100 ml. of ethanol, and drying over phosphorus pentoxide, the N-acetyl derivative weighed 70.0 g. (86.% yield) and melted at 213–215°; λ_{max}^{Nujol} 3.1, 3.8, 5.87, 6.1, 6.16, and 6.6 μ.

Anal. Calcd. for $C_{14}H_{19}NO_5$: C, 59.78; H, 6.81. Found: C, 60.05; H, 6.60.

L-N-Acetyl-3-(3,4-dimethoxyphenyl)-2-methylalanine (−)-1-Phenylethylamine Salt.—To a slurry of 77 g. (0.274 mole) of DL-N-acetyl-3-(3,4-dimethoxyphenyl-2-methylalanine) in 200 ml. of methanol slowly was added a solution of 33.2 g. (0.274 mole) of (−)-1-phenylethylamine in 50 ml. of methanol. The methanol was distilled under vacuum until copious crystallization occurred. The precipitate was dissolved in 1 l. of water at 90°. The hot solution was filtered, cooled slowly to 25°, and aged at 8° for 40 hr. The collected salt was dried under vacuum at 55°. The yield was 54.5 g. (99%); $[\alpha]^{25}D$ +55° (*c* 1, methanol). Recrystallization from water gave 42.5 g. (77%), m.p. 212–215°, $[\alpha]^{25}D$ +69° (*c* 1, methanol). Titration with base gave an equivalent weight of 396 (theory, 402.5).

Anal. Calcd. for $C_{22}H_{30}N_2O_5$: C, 65.65; H, 7.51. Found: C, 65.55; H, 7.43.

L-N-Acetyl-3-(3,4-dimethoxyphenyl)-2-methylalanine.—The L-N-acetyl-3-(3,4-dimethoxyphenyl)-2-methylalanine (−)-1-phenylethylamine salt (25 g., 0.062 mole) was dissolved in 100 ml. of water and 27.5 ml. of 2.5 *N* sodium hydroxide. The solution was extracted with two 50-ml. and two 25-ml. portions of chloroform. The solution was heated to 70° and 30 ml. of 2.5 *N* hydrochloric acid was added. The N-acetyl acid, which crystallized immediately, was cooled to 10°, filtered, washed with cold water, and dried under vacuum at 60°. The product weighed 16.8 g. (96%); m.p. 192–194°; $[\alpha]^{25}D$ −55° (*c* 1, methanol); $\lambda_{max}^{CH_3OH}$ 230 mμ (ε 8950), 279 (2950).

Anal. Calcd. for $C_{14}H_{19}NO_5$: C, 59.78; H, 6.81. Found: C, 59.74: H, 6.77.

L-(−)-3-(3,4-Dihydroxyphenyl)-2-methylalanine.—A solution of L-N-acetyl-3-(3,4-dimethoxyphenyl)-2-methylalanine (10.0 g., 0.0356 mole) in 100 ml. of 48% hydrobromic acid was heated at reflux under a nitrogen atmosphere for 12 hr. The solution was concentrated to dryness and flushed successively with 50-ml. portions of water, *t*-butyl alcohol, and water. The partly crystalline residue was dissolved in 80 ml. of water by warming. The pH was adjusted to 6.4 with 6 *N* ammonium hydroxide under a nitrogen atmosphere. The hot solution was treated with 1.2 g. of decolorizing carbon and filtered. The amber-colored filtrate was concentrated under vacuum to a volume of 30 ml. The mixture was aged in an ice bath for 1 hr., filtered, and washed with a minimum amount of cold water. After drying under vacuum at 100°, the product weighed 5.38 g. (72%); m.p. 306–308°; $[\alpha]^{25}D$ −4° (*c* 2, 0.1 *N* hydrochloric acid); λ_{max}^{Nujol} 2.79, 3.08, 4.2, 5.3, 6.17, 6.33, and 6.58 μ.

Anal. Calcd. for $C_{10}H_{13}NO_4$: C, 56.87; H, 6.20. Found: C, 57.06; H, 6.37.

DL-N-Acetyl-3-(3,4-diacetoxyphenyl)-2-methylalanine.—A slurry of 50 g. (0.237 mole) of α-methyldopa in 50 ml. (0.62 mole) of pyridine and 125 ml. (1.32 moles) of acetic anhydride was heated on the steam bath with stirring. The solid dissolved and the temperature rose to 118°. After 3 hr. on the steam bath (96°), the reddish solution was concentrated under vacuum. The residual oil was dissolved in 50 ml. of acetone and was diluted with 200 ml. of water and 50 ml. of 2.5 *N* hydrochloric acid.[18] After holding at 0–5° for 2 hr., the precipitated product was filtered, washed with water, and dried under vacuum at 50°. The product weighed 74 g. (92.6% yield); m.p. 197–199°; λ_{max}^{Nujol} 3.1, 3.8, 5.68, 5.86, 6.08, 6.4, and 6.61 μ; $\lambda_{max}^{CH_3OH}$ 265 mμ (ε 540), 271 (506).

Anal. Calcd. for $C_{16}H_{19}NO_7$: C, 56.97; H, 5.68. Found: C, 56.93; H, 6.00.

L-(−)-N-Acetyl-3-(3,4-diacetoxyphenyl)-2-methylalanine Quinine Salt.—Quinine (96.4 g., 0.297 mole) and 100 g. (0.297 mole) of D,L-N-acetyl-3-(3,4-diacetoxyphenyl)-2-methylalanine were placed in a 2-l. flask and 960 ml. of acetone was added. The solids dissolved upon stirring and product started to precipitate within 15 min. After stirring at 0–5° for 4 hr., the product was filtered, washed with acetone, and dried under vacuum at

(14) Merck & Co., Inc., South African Patent 61/950 (1962).

(15) G. A. Stein, H. A. Bronner, and K. Pfister, III, *J. Am. Chem. Soc.*, **77**, 700 (1955).

(16) A. W. Ingersol, "Organic Syntheses," Coll. Vol. II, A. H. Blatt, Ed., John Wiley and Sons, Inc., New York, N. Y., 1943, p. 506.

(17) *Cf.* Carl Djerassi, "Optical Rotatory Dispersion," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, p. 32.

(18) The acid is added to speed hydrolysis of the azlactone.

40°. The yield was 91 g. (93%); m.p. 164–166°; $[\alpha]^{25}D$ −72.7° (*c* 1, 96% ethanol). The quinine salt titrated with base gave an equivalent weight of 665 (theory, 661.8).

L-(−)-N-Acetyl-3-(3,4-diacetoxyphenyl)-2-methylalanine.—The quinine salt of L-(−)-N-acetyl-3-(3,4-diacetoxyphenyl)-2-methylalanine (17.7 g., 0.0268 mole) was dissolved at 0–5° in 11.0 ml. of 2.5 *N* hydrochloric acid and 60 ml. of water. To the clear solution was added 10.6 ml. of 2.5 *N* hydrochloric acid which caused product to precipitate. After holding overnight at 0–5°, the product was filtered, washed with cold water, and dried under vacuum at 40°. The yield was 7.49 g. (83%); m.p. 181–183°; $[\alpha]^{25}D$ −74.5° (*c* 1, 96% ethanol). Base titration showed an equivalent weight of 336 (theory, 337.3).

L-(−)-3-(3,4-Dihydroxyphenyl)-2-methylalanine.—A solution of L-(−)-N-acetyl-3-(3,4-diacetoxyphenyl)-2-methylalanine (25.0 g., 0.074 mole) in 200 ml. of 6 *N* hydrochloric acid was refluxed for 2 hr. The solution was concentrated to dryness under vacuum and the residual yellow oil was concentrated to dryness three times with 50-ml. portions of *t*-butyl alcohol to remove hydrochloric acid. The gummy residue was dissolved in 45 ml. of water and the solution was filtered to remove a trace amount of insoluble material. The filtrate was adjusted to pH 7.0 with concentrated ammonia. After adding 1.0 g. of sulfur dioxide, the mixture was held at 0–5° overnight. The crystals were filtered, washed with cold water, and dried under vacuum at 50°. The product weighed 14.9 g., but contained 11.3% water by Karl Fischer titration (84.5% yield calculated for $C_{10}H_{13}NO_4 \cdot 1.5\ H_2O$).[19]

The L-(−)-α-methyldopa, m.p. 295° dec., $[\alpha]^{25}D$ −3° (*c* 2, 0.1 *N* hydrochloric acid) had an equivalent weight by base titration of 239 (theory, 238) and had an absorption maximum at 281 mμ (ε 2780). The dried product gave an infrared spectrum identical with material resolved through the 1-phenylethylamine salt.

(19) X-Ray analysis reveals that L-(−)-α-methyldopa exists in three crystalline forms. Normally, when isolated from aqueous solutions, a sesquihydrate is obtained. Vigorous drying of the sesquihydrate (100°, under vacuum) gives an anhydrous form which, when exposed to air, absorbs water and is transformed back to the hydrate. A second, nonhygroscopic, anhydrous form has been isolated from isopropyl alcohol solutions.

Condensation of Catechol with Phenylphosphonous Dichloride. A Novel Ring-Cleavage Reaction[1]

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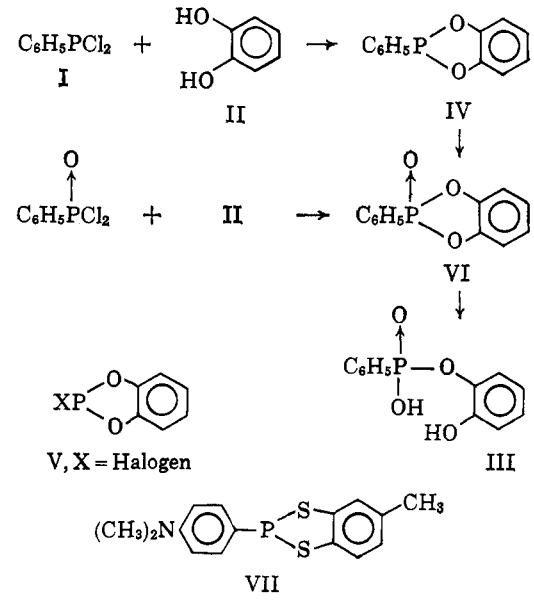
Received November 1, 1963

The chemistry of cyclic compounds derived from trivalent and pentavalent phosphorus has been investigated in some detail and an excellent review[3] has appeared recently which included data on the reaction of phosphorus trichloride with catechol (II). No detailed investigation on the synthesis of 2-aryl-substituted 1,3,2-benzodioxaphospholes has been described.

The reaction between catechol (II) and phenylphosphonous dichloride (I) is more complicated than might be anticipated. When the condensation was performed with equimolar quantities of I and II in the presence of pyridine or triethylamine in various solvents, the only isolable product was 2-phenyl-1,3,2-benzodioxaphosphole 2-oxide (VI) (Scheme I). In addition the phosphonate VI is exceedingly unstable since,

SCHEME I



upon standing for a short time (even in desiccator), it is converted quantitatively to a strong acid, *o*-hydroxyphenylhydrogen phenylphosphonate (III).[4] Reaction of I and II in bromobenzene at reflux led to the cyclic derivative IV.[5] From the cool solution, relatively pure 2-phenyl-1,3,2-benzodioxaphosphole (IV) was obtained in excellent yield. The structure of the product was tentatively established by the infrared spectral data. However, the spectrum changed rapidly when the impure ester IV was subjected to purification by recrystallization or upon storage in a desiccator. Structural confirmation of III was provided *via* hydrolysis with hydrochloric acid to yield phenylphosphonic acid and catechol. The P–O bond in III is readily cleaved by treatment with mineral acid as well as alkali. Thus, it appears that 2-phenyl-1,3,2-benzodioxaphosphole (IV) is formed initially but undergoes rapid oxidation followed by hydrolysis to III. The extreme sensitivity to oxidation of the heterocyclic ring in IV is somewhat surprising in view of the isolation of corresponding 2-halogen analogs (V),[3] although they are reported to be inherently sensitive to cleavage because of ring strain.[6] Although a related, stable sulfur compound (VII) was recorded recently, attempts to prepare other members in the series failed.[7]

Phenylphosphonic dichloride reacted with II in bromobenzene to give VI[8] (infrared analysis confirmed

(1) We gratefully acknowledge support of the National Institutes of Health, GM-10367-01. Partial support by the Research Foundation of the Oklahoma State University is also acknowledged.

(2) Postdoctorate Fellow, 1963–1964.

(3) R. S. Edmundson, *Chem. Ind.* (London), 1770 (1962).

(4) This compound may have been obtained (no analytical data) from the reaction of phenylphosphonic dichloride and II, but it now seems the previous material (m.p. 115–118°) may not have been sufficiently pure [W. W. Coover, Jr., R. L. McConnell, and M. A. McCall, *Ind. Eng. Chem.*, **52**, 409 (1960)].

(5) The procedure is similar to that used for the preparation of dihydro-1,3,2-benzodiazaphosphole 2-oxides: see R. L. Dannley and D. Zazaris, Abstracts, 142nd National Meeting of the American Chemical Society, Atlantic City, N. J., Sept., 1962, p. 62-Q.

(6) The corresponding 2-alkoxy derivatives of this system were reported to be extremely sensitive at low temperature: see W. S. Reich, *Nature*, **157**, 133 (1946).

(7) I. G. M. Campbell and J. K. Way, *J. Chem. Soc.*, 5034 (1960).

(8) Actually, VI was claimed to have been prepared from phenylphosphonic dichloride and II, but the melting point was 124–125°, identical with the melting point found for III in our work [L. Anschütz and H. Walbrecht, *J. prakt. Chem.*, **133**, 65 (1932)].