at 140° and a flow rate of 55 cc. helium/min. The estimated per cents of apocamphane and 1-bromoapocamphane were 22% and 78%, respectively. The per cents were estimated by comparison with standard chromatograms.

Reduction of *cis*-α-Bromostilbene with Triphenyltin Hydride. Reduction No. 10.—A mixture of 5.18 g. (0.02 mole) of *cis*-α-bromostilbene[24] and 7.02 g. (0.02 mole) of triphenyltin hydride was stirred at *ca.* 26°. During 10 min. the reaction temperature rose to 42°, remained at this temperature for 5 min., and then gradually decreased to *ca.* 26°. After 1 hr. the reaction mixture had completely solidified. The mixture was allowed to remain at *ca.* 26° overnight before processing. It was then slurried with 25 ml. of petroleum ether (b.p. 30–60°) and poured onto 100 g. of Woelm neutral alumina (activity I–II). The column was eluted with petroleum ether until 700 ml. of eluate was obtained. Distillation of the petroleum ether *in vacuo* left 6.2 g. of solid material which was recrystallized from 95% ethanol to give 3.18 g. of *trans*-stilbene, m.p. 120–122°, no depression on admixture with a known sample of *trans*-stilbene, infrared and ultraviolet spectra superimposable on that of a known sample of *trans*-stilbene.

The mother liquor was evaporated to dryness, slurried with 25 ml. of petroleum ether and poured onto 70 g. of Woelm neutral alumina (activity I–II). The column was eluted with petroleum ether until 500 ml. of eluate was obtained. Evaporation of the petroleum ether followed by recrystallization of the solid residue from 95% ethanol gave 350 mg. of *trans*-stilbene, m.p. 120–122°, total yield of *trans*-stilbene 3.53 g. (98.0%).

The first column (100 g. of alumina) was eluted with methylene chloride–methanol (9:1) until 700 ml. of eluate was obtained, and the second column was eluted with methylene chloride–methanol (9:1) until 500 ml. of eluate was obtained. The two fractions were combined, and the solvent was distilled *in vacuo*. There remained 6.6 g. of solid material, m.p. 95–98°, which upon recrystallization from *n*-propyl alcohol gave 6.35 g. (73.8%) of triphenyltin bromide, m.p. 116–118°.

In another run using 2.59 g. (0.01 mole) of *cis*-α-bromostilbene and 3.51 g. (0.01 mole) of triphenyltin hydride there was obtained, using essentially the same isolation procedure as above, *trans*-stilbene (88.8%) and triphenyltin bromide (72.1%).

In another run using 5.18 g. (0.02 mole) of *cis*-α-bromostilbene and 7.02 g. (0.02 mole) of triphenyltin hydride and carried out at *ca.* 26 to 29°, there was obtained *trans*-stilbene (61.1 %), *cis*-stilbene (30.5%), and triphenyltin bromide (72.0%).

Reduction of *trans*-α-Bromostilbene with Triphenyltin Hydride. Reduction No. 11.—A mixture of 7.0 g. (0.027 mole) of *trans*-α-bromostilbene[24] and 9.47 g. (0.027 mole) of triphenyltin hydride was stirred at *ca.* 26°. During the course of 10 min. the temperature rose to 30°, remained at that temperature for 15 min., and then returned to *ca.* 26°. After 24 hr. the reaction mixture had become a thick paste. The mixture was slurried with 25 ml. of petroleum ether and poured onto 70 g. of Woelm neutral alumina (activity I–II, column I). The column was eluted with petroleum ether. The first 250-ml. portion of eluate yielded no residue. The next two 500-ml. portions of eluate were combined and yielded, after removal of the solvent, 7.4 g. of a semisolid, which was slurried with 20 ml. of *n*-hexane and cooled overnight in a refrigerator. The crystals which were present were collected on a filter (1.65 g.), m.p. 112–114°. Recrystallization from 95% ethanol gave 1.60 g. of *trans*-stilbene, m.p. 120–122°, no depression on admixture with an authentic sample of *trans*-stilbene.

The hexane was removed from the first mother liquor *in vacuo*, and the residue was distilled to give 1.87 g. (38.6%) of *cis*-stilbene, b.p. 93–97° (2 mm.); authentic *cis*-stilbene had b.p. 93–96° (2 mm.). The infrared and ultraviolet spectra were superimposable upon that of an authentic sample of *cis*-stilbene.

The residue from the distillation was slurried with 25 ml. of petroleum ether and poured onto 70 g. of Woelm neutral alumina (activity I–II, column II). The column was eluted with petroleum ether until 250 ml. of eluate was obtained. Removal of the petroleum ether *in vacuo* gave 1.5 g. of a semisolid which yielded after two recrystallizations from 95% ethanol 1.03 g. of *trans*-stilbene, m.p. 120–122°. The total yield of *trans*-stilbene was 2.63 g. (54.1%).

Column I was further eluted with methylene chloride–methanol (98:2) until 1 l. of eluate was obtained. Column II was eluted with methylene chloride–methanol (98:2) until 250 ml. of eluate was obtained. The two eluates were combined, and the solvent was removed *in vacuo* leaving 8.65 g. of solid material which afforded after recrystallization from *n*-propyl alcohol 8.32 g. (71.7 %) of triphenyltin bromide, m.p. 116–118°.

Separation of a Known Mixture of *trans*-Stilbene, *cis*-Stilbene, and Triphenyltin Bromide.—A known mixture consisting of 1.62 g. of *trans*-stilbene, 0.180 g. of *cis*-stilbene, and 4.30 g. of triphenyltin bromide was slurried with 25 ml. of petroleum ether and poured onto 70 g. of Woelm neutral alumina (activity I–II). The column was eluted with petroleum ether until 500 ml. of eluate was obtained. Removal of the solvent *in vacuo* left 1.85 g. of a semisolid which gave after recrystallization from 95% ethanol 1.55 g. of *trans*-stilbene, m.p. 120–122°.

The mother liquor was evaporated to dryness, and the residue was dissolved in 5 ml. of hexane and allowed to stand at −5° overnight. The crystals were collected on a filter giving 50 mg. of *trans*-stilbene, m.p. 120–122°. The total yield of *trans*-stilbene was 1.60 g. (98.7%).

Removal of the hexane from the filtrate followed by distillation of the residue gave 0.180 g. (100%) of *cis*-stilbene, b.p. 93–96° (2 mm.).

The column was further eluted with methylene chloride–methanol (9:1) until 500 ml. of eluate was obtained. Removal of the solvent *in vacuo* left 3.4 g. of solid material which afforded after recrystallization from *n*-propyl alcohol 3.4 g. (79.0%) of triphenyltin bromide, m.p. 116–118°.

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[24] J. Wislicenus, *Ber. Verhandl. sachs. Akad. Wiss. Leipzig Math. phys. Kl.*, **52**, 117 (1900).

The Absolute Configuration of Citrinin[1]

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One of the first compounds with antibiotic activity isolated in Raistrick's classic investigations on fungal metabolites was the substance citrinin, obtained in 1931 from *Penicillium citrinum*.[2] Though it proved too toxic for medical use, the discovery of its activity intensified the search which subsequently led to practical antibiotics.

The structure of citrinin (I) was established in 1949, primarily by the investigations of Robertson and his co-workers,[3] and several syntheses have been recorded.[4] An ingenious suggestion of Cram[5] led to the assignment of relative stereochemistry. Hydrolysis of citrinin gives the levorotatory phenol (II) which is partially or wholly racemized by acid. Cram pointed out that if the methyl groups on the asymmetric carbons of citrinin were *trans*, participation of the aromatic ring in the formation of a carbonium ion from II would afford a symmetrical intermediate and consequently lead to racemization; his subsequent studies with model compounds confirmed this proposal.[6]

Further degradation of citrinin has now made it possible to complete the stereochemical assignment by showing the absolute configuration. The dimethyl

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[1] This investigation was supported by a research grant (GM 06568-04) from the Public Health Service, to whom the authors express their appreciation.

[2] A. C. Hetherington and H. Raistrick, *Phil. Trans. Roy. Soc. London*, **220B**, 269 (1931).

[3] (a) J. P. Brown, N. J. Cartwright, A. Robertson, and W. B. Whalley, *J. Chem. Soc.*, 859 (1949); (b) J. P. Brown, A. Robertson, W. B. Whalley, and N. J. Cartwright, *ibid.*, p. 867.

[4] (a) N. J. Cartwright, A. Robertson, and W. B. Whalley, *ibid.*, 1563 (1949); (b) H. H. Warren, G. Dougherty, and E. S. Wallis, *J. Am. Chem. Soc.*, **71**, 3422 (1949); (c) T. S. Gore, R. V. Talavdekar, and K. Venkataraman, *Current Sci.* (India), **19**, 20 (1950); *Chem. Abstr.*, **44**, 7313 (1950).

[5] D. J. Cram, *J. Am. Chem. Soc.*, **70**, 4244 (1948).

[6] D. J. Cram, *ibid.*, **71**, 3863 (1949); **72**, 1001 (1950).

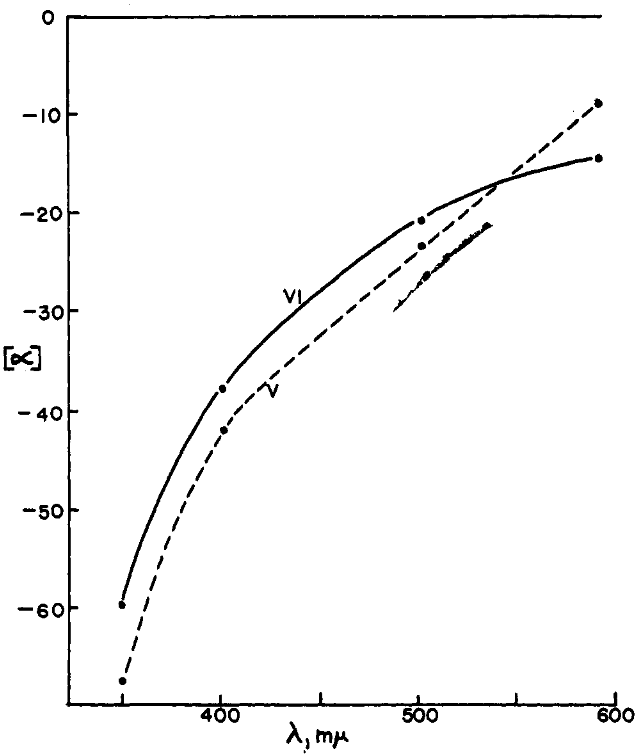
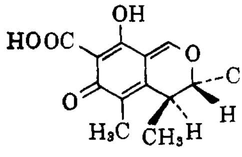
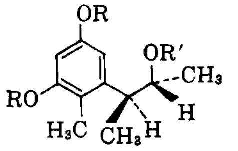


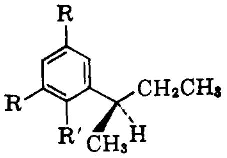
Fig. 1.—O.R.D. curves (chloroform) of 2-(2-methyl-3,5-dimethoxyphenyl)butane (V) and 2-phenylbutane (VI).



I



II, R = R' = H
III, R = CH_3; R' = H
IV, R = CH_3; R' = $SO_2C_7H_7$



V, R = OCH_3; R' = CH_3
VI, R = R' = H

ether (III) of the phenol II was converted to its *p*-toluenesulfonate (IV). Lithium aluminum hydride reduction of the tosylate gave the levorotatory ether (V), with only one asymmetric carbon. Though there is no guarantee of the optical purity of V, since partial racemization could occur during reduction[7] *via* the same symmetrical phenonium ion which participates in the acid hydrolysis of citrinin, its optical rotation is sufficient to establish its configuration by optical rotatory dispersion measurements. Comparison of the O.R.D. curves of (−)-V and (−)-2-phenylbutane (VI), shown in Fig. 1, clearly proves their configurational identity.[8] Since the configuration of (−)-2-phenylbutane has been proven to be that shown in VI,[7a] this result establishes the configuration shown in formula I as the correct expression of absolute stereochemistry of citrinin.[9]

Experimental

(−)-2-(3,5-Dimethoxy-2-methylphenyl)butane (V).—To a solution of 13.3 g. of 3-(3,5-dimethoxy-2-methylphenyl)butan-2-ol (III, "phenol A dimethyl ether")[3a] in 150 ml. of pyridine, cooled to 0°, 15.25 g. of *p*-toluenesulfonyl chloride was added slowly with stirring, and the mixture was kept in the refrigerator for 48 hr. The reaction mixture was poured onto 500 g. of ice and water and was extracted with ether; the ether extracts were washed with cold 1:1 hydrochloric acid, then with water, dried, and concentrated at reduced pressure. The residual oily tosylate was not purified further but showed characteristic sulfonate bands in the infrared at 7.4 and 8.5 μ along with the complete lack of hydroxyl absorption.

A solution of the tosylate in 175 ml. of anhydrous ether was added dropwise to a stirred suspension of 2.75 g. of lithium aluminum hydride in 100 ml. of ether, and the reaction mixture refluxed for 12 hr. The excess hydride was decomposed with dilute sodium hydroxide, and the mixture was filtered. The ether layer, after washing with dilute base and water, was dried and distilled, affording 10.9 g. (80%) of V, b.p. 91.5–93° (0.5 mm.), $[\alpha]^{17}\mathrm{D}$ −8.70° (*c* 10, chloroform).

Anal. Calcd. for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 75.19; H, 9.46.

The infrared spectrum, in chloroform, was identical with that of authentic racemic material.[3a]

(−)-2-Phenylbutane (VI).—An authentic sample of the hydrocarbon was obtained by hydrogenation of (−)-3-phenyl-1-butene,[10] $[\alpha]^{20}\mathrm{D}$ −7.36° (chloroform), over palladium–charcoal in methanol. The product had $[\alpha]^{19}\mathrm{D}$ −14.2° (*c* 10, chloroform).

Acknowledgment.—The authors wish to thank Dr. Erwin Schwenk for a generous gift of citrinin.

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[7] (a) D. J. Cram, *J. Am. Chem. Soc.*, **74**, 2149 (1952); (b) **74**, 2152 (1952).

[8] For evidence that simple aryl substituents do not change the general shape of the O.R.D. curves of aromatic compounds, see (a) J. H. Brewster and S. F. Osman, *ibid.*, **82**, 5754 (1960); (b) F. Nerdel and H. Härter, *Ann.*, **621**, 22 (1959); (c) F. Nerdel and H. Würgau, *ibid.*, **621**, 34 (1959); (d) F. Nerdel and H. Liebig, *ibid.*, **621**, 42 (1959).

[9] Recently the same conclusion has been independently reached by P. P. Mehta and W. B. Whalley, *J. Chem. Soc.*, 3777 (1963).

[10] D. J. Cram, *J. Am. Chem. Soc.*, **74**, 2137 (1952). The authors wish to thank Dr. M. Rabinovitz for supplying this material.

Elimination Reactions. IV. Phenylspiropentane by γ-Elimination

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Treatment of a number of 3-phenylpropylamine derivatives with sodium amide in liquid ammonia has been found to produce phenylcyclopropanes *via* γ-elimination.[1] To extend the scope of this reaction we synthesized methiodide I where the β-carbon atom is incorporated into a three-membered ring. Structure I also provided an additional opportunity to study the behavior of carbanions generated adjacent to a small ring.[2]

Reaction of quaternary salt I with sodium amide in liquid ammonia led exclusively to the γ-elimination product phenylspiropentane (II) which was isolated in about 50% yield. Assignment of structure II follows from analysis of the n.m.r. spectrum. Signals are observed at 7.1 (5 protons), 2.2 (1 proton, a quartet), 1.4 (1 proton, a quartet), and 0.9 p.p.m. (5 protons,

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[1] C. L. Bumgardner, *J. Am. Chem. Soc.*, **83**, 4420 (1961); **83**, 4423 (1961).

[2] C. L. Bumgardner, *ibid.*, **85**, 73 (1963).