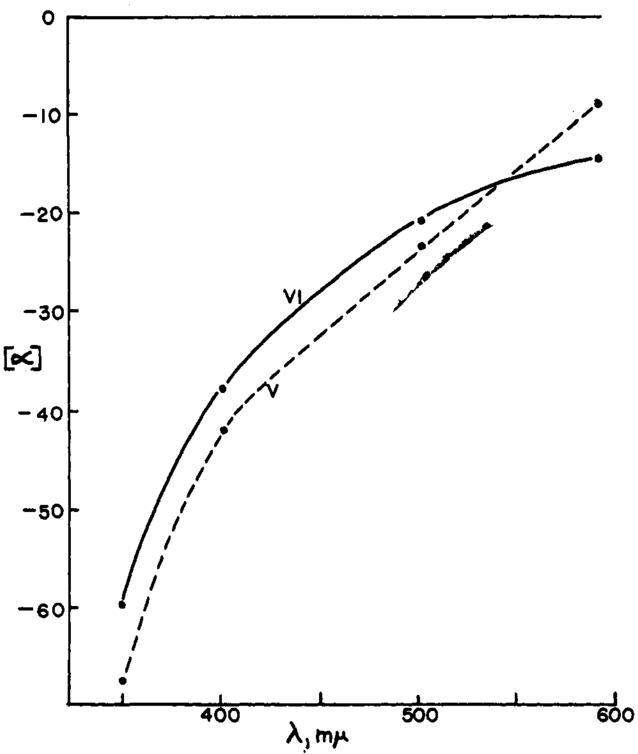
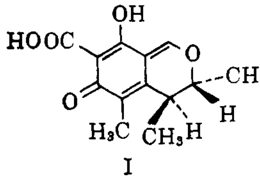
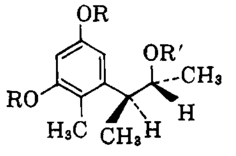
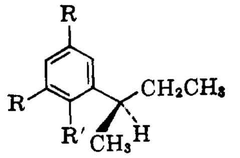


Fig. 1.—O.R.D. curves (chloroform) of 2-(2-methyl-3,5-dimethoxyphenyl)butane (V) and 2-phenylbutane (VI).


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.), $[\alpha]^{17}D$ −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] $[\alpha]^{20}D$ −7.36° (chloroform), over palladium–charcoal in methanol. The product had $[\alpha]^{19}D$ −14.2° (*c* 10, chloroform).

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

---

[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

Carl L. Bumgardner

Gorgas Laboratory, Rohm and Haas Company,
Redstone Arsenal Research Division, Huntsville, Alabama

Received September 23, 1963

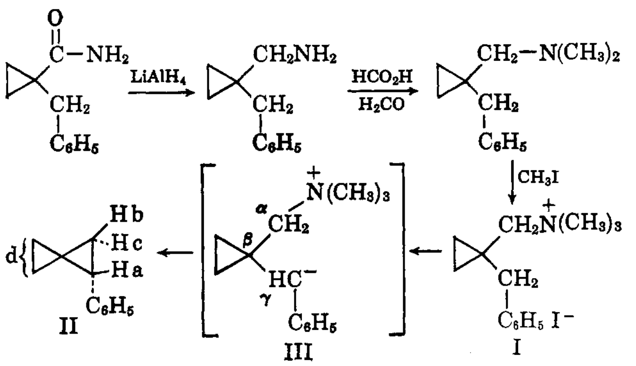
Treatment of a number of 3-phenylpropylamine derivatives with sodium amide in liquid ammonia has been found to produce phenylcyclopropanes *via* γ-elimination.[1] To extend the scope of this reaction we synthesized methiodide I where the β-carbon atom is incorporated into a three-membered ring. Structure 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,

---

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

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



a multiplet underneath another peak). The low-field signal may be attributed to the aromatic protons, the 2.2-p.p.m. quartet to the proton adjacent to the phenyl ring (proton a in structure II), the 1.4-p.p.m. quartet to proton b, and the high-field multiplet to proton c, which is more highly shielded than proton b due to the *cis*-phenyl ring.[3] Analysis of the splitting leads to the following values: $J_{ab} = 8.1$, $J_{ac} = 4.5$, $J_{bc} = -4.1$ c.p.s. Protons d account for the remainder of the 0.9-p.p.m. signal. The spectrum resembles that described for chlorospiropentane.[4] Bands in the infrared spectrum at 3100 (cyclopropyl hydrogen), 1010 (cyclopropyl ring), and 700 and 760 cm.$^{-1}$ (monosubstituted benzene) also indicate structure II as does the ultraviolet spectrum which is similar to that of phenylcyclopropane.[1]

Interestingly, no evidence for isomerization or rearrangement of zwitterion III, probably an intermediate in the reaction, was obtained. Since methiodide I can be obtained readily by the steps shown above, γ-elimination constitutes a practical synthetic route to spiropentane II, previously unknown. Furthermore, structure II, which carries an aromatic handle, may serve as a starting point for other transformations in the spiropentane series.

Experimental[5]

(1-Benzylcyclopropyl)carbinyltrimethylammonium Iodide (I).—Reduction of 8.09 g. of 1-benzylcyclopropanecarboxamide[6] with 6.6 g. of lithium aluminum hydride in anhydrous ether gave (1-benzylcyclopropyl)carbinylamine, b.p. 62° (0.3 mm.), ν_{N-H} 3330 cm.$^{-1}$, ν_{Δ} 1020 cm.$^{-1}$, in 42% yield. The n.m.r. spectrum showed signals at 7.1 (phenyl), 2.5 (methylene), 2.25 (methylene), 0.95 (N-H), and 0.1 p.p.m. (cyclopropyl) in the proper ratios for (1-benzylcyclopropyl)carbinylamine. The primary amine (3.1 g.) was converted (45% yield) into (1-benzylcyclopropyl) carbinyldimethylamine, b.p. 64° (0.3 mm.), ν_{Δ} 1035 cm.$^{-1}$, by the Eschweiler-Clarke procedure[7] using 17 ml. of 90% formic acid and 17 ml. of 37% formaldehyde. Treatment of 1.64 g. of the tertiary amine with 7.4 g. of methyl iodide in ether yielded after recrystallization from absolute ethanol 1.8 g. (63%) of (1-benzylcyclopropyl)carbinyltrimethylammonium iodide (I), m.p. 146-147°.

Anal. Calcd. for $C_{14}H_{22}NI$: C, 50.76; H, 6.70. Found: C, 50.63; H, 6.67.

Phenylspiropentane.—To 100 ml. of a liquid ammonia solution containing sodium amide made from 0.08 g. of sodium was added 0.85 g. of methiodide I over a period of 10 min. After the mixture was stirred for 3 hr., 0.2 g. of ammonium chloride was added followed by 50 ml. of ether. The ammonia was allowed to evaporate overnight, and then 50 ml. of water and 25 ml. of ether were introduced. The ether layer was separated and washed successively with 30 ml. of 10% hydrochloric acid solution, 30 ml. of water, 30 ml. of 5% sodium bicarbonate solution, and 30 ml. of water. Distillation of the dried ether solution yielded 0.17 g. (46%) of phenylspiropentane; $n^{20}\text{D}$ 1.5435; λ_{max} 223, 260, 268, 272 mμ (*c* 95% ethanol).

Anal. Calcd. for $C_{11}H_{12}$: C, 91.61; H, 8.39. Found: C, 91.56; H, 8.72.

Acknowledgment.—This work was carried under Army Ordnance Contract DA-01-021 ORD-11878. The author wishes to thank Mr. Kirt Keller for technical assistance and Dr. F. A. Johnson for a discussion of the n.m.r. spectra.

---

(3) D. Y. Curtin, H. Gruen, Y. G. Hendrickson, and H. E. Knipmeyer, *J. Am. Chem. Soc.*, **83**, 4838 (1961).

(4) D. E. Applequist, G. F. Fanta, and B. W. Henrikson, *ibid.*, **82**, 2368 (1960).

(5) Melting points and boiling points are uncorrected. Infrared spectra were determined with a Perkin-Elmer Infracord spectrophotometer with a sodium chloride prism. N.m.r. spectra were obtained with either a Varian Associates, Model V-3000-B, high resolution spectrometer using a 40-Mc. probe or a Varian Associates A-60 spectrometer. A-60 spectra (deuteriochloroform solutions, probe temperature 38°) were measured using tetramethylsilane as internal standard. Spectra (40-Mc.) (pure liquids, probe temperature 30°) were measured from external tetramethylsilane. Ultraviolet spectra were determined with a Beckman recording spectrophotometer, Model DK-1.

(6) F. J. Piehl and W. G. Brown, *J. Am. Chem. Soc.*, **75**, 5023 (1953).

(7) R. N. Icke, B. B. Wisegarver, and G. A. Allis, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 723.