products to be mixtures consisting of about 80% furanosides and 20% pyranosides.

Crude 3,5-di-O-benzoyl-2-deoxy-D-ribose, (I). The sirupy product described above (8.4 g.) was dissolved in 200 ml. of acetone, and 60 ml. of water followed by 45 ml. of 6*N* hydrochloric acid was added. After 2 days at room temperature, when the mutarotation had become essentially constant, the solution was deionized over Duolite A-4 (wet with 75% acetone) and concentrated at reduced pressure to a sirup. This was dissolved in chloroform, dried over sodium sulfate, and again concentrated to a sirup (7.2 g.). The methoxyl content of the sirupy product was about 1.8%, presumably due to unhydrolyzed methyl pyranosides.

5-O-Benzoyl-D-glycero-4,5-dihydroxy-2-pentenal benzylphenylhydrazone (II). The crude 3,5-di-*O*-benzoyl-2-deoxy-D-ribose (7.2 g.) was diluted with a small volume of ethanol and 4.7 g. of 1-benzyl-1-phenylhydrazine was mixed in to give a homogeneous solution. After 1 day, the mixture was extracted by trituration with petroleum ether (b.p. 33–58°) and the residue was diluted with ethanol followed by water to give 3.4 g. of crystals in two crops. After recrystallization from benzene-ether, the 5-*O*-benzoyl-D-*glycero*-4,5-dihydroxy-2-pentenal benzylphenylhydrazone melted at 138–139°, $[\alpha]_D^{26}$ −14° in benzene, *c* 2.

Anal. Calcd. for $C_{25}H_{24}O_3N_2$: C, 75.0; H, 6.04; N, 7.00. Found: C, 74.7; H, 5.80; N, 6.97.

The same unsaturated benzylphenylhydrazone was formed, but somewhat more slowly, when an equivalent amount of acetic acid was added with the 1-benzyl-1-phenylhydrazine in the above reaction.

5-O-Benzoyl-D-glycero-4,5-dihydroxypentanal benzylphenylhydrazone, (III). The unsaturated benzylphenylhydrazone (3.4 g.) was hydrogenated at room temperature and atmospheric pressure in ethyl acetate solution in the presence of 0.5 g. of 10% palladium-on-carbon catalyst. The hydrogenation was complete in 2 hr. with the absorption of approximately one molecular equivalent of hydrogen. Filtration and evaporation gave a crystalline residue. Recrystallization from ether yielded 2.66 g. of 5-*O*-benzoyl-D-*glycero*-4,5-dihydroxypentanal benzylphenylhydrazone, m.p. 98–99°, $[\alpha]_D^{25}$ +3.7° in benzene, *c* 3.6.

Anal. Calcd. for $C_{25}H_{26}O_3N_2$: C, 74.6; H, 6.51; N, 6.96. Found: C, 74.6; H, 6.43; N, 7.15.

D-*Glycero-4,5-dihydroxypentanal benzylphenylhydrazone*, (IV). A solution of 1.5 g. of III in 300 ml. of methanol containing 0.3 g. of sodium was refluxed for 5 hr. The solution was then cooled, deionized, and concentrated, finally with water to remove methyl benzoate. The resulting crystals (1.05 g.) were recrystallized from ethanol-ether–petroleum ether (b.p. 32–37°) to give pure IV, m.p. 77–78°, $[\alpha]_D^{25}$ −14° in absolute ethanol, *c* 3.4.

Anal. Calcd. for $C_{18}H_{22}O_2N_2$: C, 72.5; H, 7.43; N, 9.39. Found: C, 72.5; H, 7.49; N, 9.31.

Degradation of IV *to succinic acid.* An amount of 570 mg. of III was shaken for 1 day with 1 ml. of benzaldehyde, 0.3 g. of benzoic acid, and 15 ml. of water. The mixture was then extracted three times with ether and the remaining aqueous phase was further treated with 5.3 ml. of 0.4*M* sodium metaperiodate solution for 7 hr. at room temperature. A few drops of ethylene glycol then were added, the solution was deionized, and the effluent and washings were treated with 1 g. of potassium permanganate. After 6 hr., excess permanganate was destroyed with acetaldehyde, manganese dioxide was removed by filtration and potassium ion by ion exchange, and the solution was concentrated to a semicrystalline residue. This was dissolved in dilute sodium hydroxide, extracted thoroughly with ethyl acetate, decolorized with carbon, again freed of sodium ion by ion exchange, and concentrated. The resulting crude succinic acid (m.p. 178–180°) was converted to the *p*-bromobenzyl pseudothiuronium salt,[3] m.p. 167°; yield, 100 mg.

The melting point of this product was undepressed by admixture with the *p*-bromobenzyl pseudothiuronium salt (m.p. 167°) prepared from authentic succinic acid, and the x-ray diffraction patterns given by the two preparations were identical.

1-O-Acetyl-3,5-di-O-benzoyl-2-deoxy-D-ribose. Thoroughly dried, crude 3,5-di-*O*-benzoyl-2-deoxy-D-ribose (840 mg.) was acetylated at 0° with acetic anhydride and pyridine in the usual manner. Addition of the reaction mixture to ice-water yielded a semicrystalline precipitate. This was separated by decantation, triturated with fresh ice-water, and recrystallized from ethanol to yield 205 mg. of crystalline product. Further recrystallization from ether–petroleum ether (b.p. 63–69°) yielded pure 1-*O*-acetyl-3,5-di-*O*-benzoyl-2-deoxy-D-ribose, m.p. 88–89°, $[\alpha]_D^{27}$ −23.7°, constant in USP chloroform, *c* 2.

Anal. Calcd. for $C_{21}H_{20}O_7$: C, 65.6; H, 5.25. Found: C, 65.7; H, 5.42.

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(3) B. T. Dewey and H. G. Shasky, *J. Am. Chem. Soc.*, **63**, 3526 (1941).

The Structure and Synthesis of Rhetsinine (Hydroxyevodiamine)

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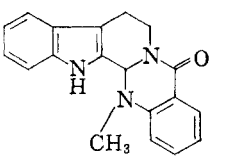
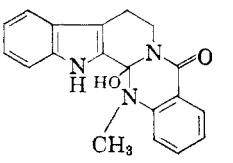
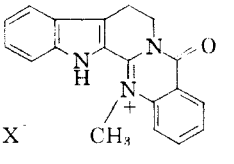
The chemistry of the alkaloid evodiamine (I), derived from the Chinese drug plant *Evodia rutecarpa* Benth. and Hook., was studied many years ago by Asahina and his co-workers. During the course of their investigations, a yellow base, $C_{19}H_{17}N_3O_2$, was derived upon potassium permanganate oxidation of the alkaloid.[1] The product was named hydroxyevodiamine and was assigned structure II. Later Ohta[2] observed that hydroxyevodiamine may react with acids with loss of water and suggested formula III for the salts. Upon addition



I



II



III

(1) Y. Asahina and T. Ohta, *J. Pharm. Soc. Japan*, **530**, 293 (1926); *Chem. Abstr.* **21**, 2134 (1927).

(2) T. Ohta, *J. Pharm. Soc. Japan* **65B**, 89 (1945).

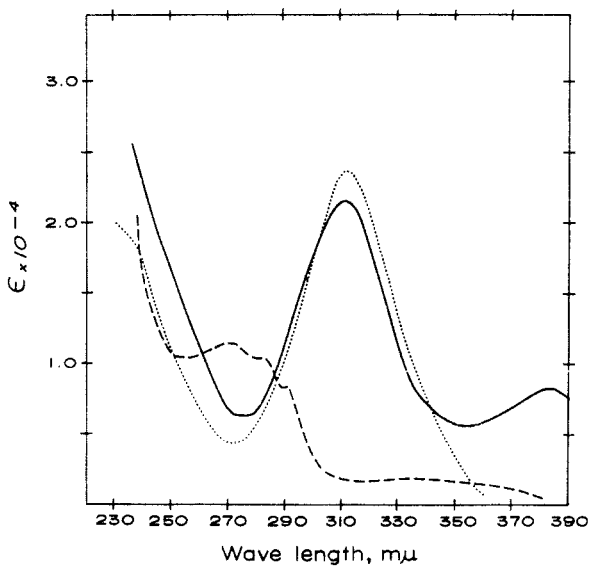
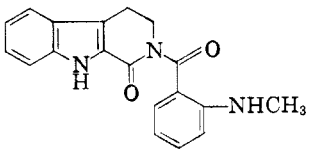


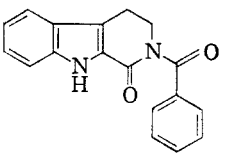
Fig. 1. Rhetsinine (hydroxyevodiamine), ————; evodiamine, - -; 2-benzoyl-1-oxo-1,2,3,4-tetrahydropyrid-[3,4-b]indole, ... Spectra in absolute acetonitrile

of base to III, he suggested, the quaternary base (III. X = OH) first arises and then forms II. Very recently Chatterjee and co-workers[3] proposed formula I for the alkaloid rhetsine and formula II for the alkaloid rhetsinine derived from *Xanthoxylum rhetsa* D.C.

It seemed probable to us, on the basis of some previous work in these laboratories, that the evodiamine oxidation product should be formulated as the dicarbonyl compound IV. A sample of the yellow substance was prepared from evodiamine[4] and was spectrally related, *in non-hydroxylic media*, to 2-benzoyl-1-oxo-1,2,3,4-tetrahydropyrid[3,4-b]indole (V) rather than to evodiamine (Fig. 1).



IV

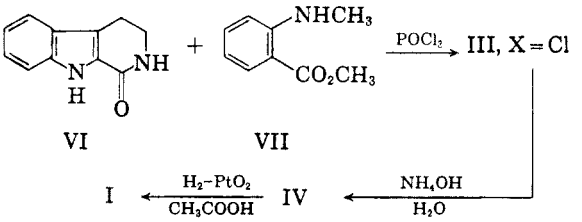


V

Its infrared spectrum in mineral oil mull, showing carbonyl bands at 5.97 and 6.05 μ and NH bands at 2.97 and 3.10 μ, also eliminates the quaternary base structure (III. X = OH) as a possible one for the *crystalline* alkaloid, since the quaternary chloride (III. X = Cl) shows only a single carbonyl band at 5.87 μ. Hydroxyevodiamine thus should be formulated as IV.

A sample of rhetsinine, isolated from *Xanthoxylum rhetsa* D.C. and kindly sent to us by Professor S. M. Kupchan of the University of Wisconsin, had infrared and ultraviolet spectra identical with those of hydroxyevodiamine and gave no depression of melting point upon admixture. Rhetsinine is a more suitable name for the compound than hydroxyevodiamine.

Rhetsinine was also synthesized through reaction of 1-oxo-1,2,3,4-tetrahydropyrid[3,4-b]indole (VI), methyl *N*-methylanthranilate (VII), and phosphorus oxychloride followed by addition of base. The hydrolysis to IV may be reversed by dilute hydrochloric acid, which immediately reconverts IV to III (X = Cl). Catalytic reduction of rhetsinine in acetic acid yielded *dl*-evodiamine (rhetsine).



EXPERIMENTAL

2-Benzoyl-1-oxo-1,2,3,4-tetrahydropyrid[3,4-b]indole. A mixture of 10 ml. of benzoyl chloride, 1 g. of 1-oxo-1,2,3,4-tetrahydropyrid[3,4-b]indole and 1 ml. of pyridine was heated under reflux for 1 hr. Excess benzoyl chloride was removed *in vacuo* and the residue was thoroughly triturated with 5% aqueous sodium carbonate. The solid was collected and recrystallized twice from chloroform–ethyl acetate to give 0.9 g. of product, m.p. 266.5–267.5°

Anal. Calcd. for $C_{18}H_{14}N_2O_2$: C, 74.47; H, 4.86. Found: C, 74.07; H, 4.95.

Synthesis of rhetsinine (hydroxyevodiamine). To 5.0 g. of 1-oxo-1,2,3,4-tetrahydropyrid[3,4-b]indole dissolved in 120 ml. of hot, dry toluene was added 3 ml. of freshly distilled phosphorus oxychloride. The reaction mixture was heated under reflux for 15 min. during which time a small second phase separated. A 7.5-g. portion of methyl *N*-methylanthranilate was then added. The reaction mixture was stirred vigorously under reflux for 2.5 hr. The toluene was then removed by distillation. The residue was cooled and treated with aqueous ammonia and chloroform. The chloroform layer was separated, concentrated, filtered, diluted with benzene, and treated with hydrogen chloride. A solid yellow hydrochloride separated and was recrystallized first from 300 ml. of water and then from 95% ethanol containing a little 5% hydrochloric acid to give 6.2 g. (68% yield) of *anhydrohetsinine hydrochloride* (III. X = Cl), m.p. 238° dec.

Anal. Calcd. for $C_{19}H_{16}N_3OCl$: C, 67.55; H, 4.77; N, 12.44. Found: C, 67.30; H, 4.84; N, 12.52.

A sample of the hydrochloride was shaken with aqueous ammonia and chloroform. The red chloroform solution was concentrated, diluted with 80% ethanol, and allowed to stand. The color faded to pale orange and yellow crystals of rhetsinine, m.p. 196° dec. after turning red at *ca.* 175°, separated from solution.

Anal. Calcd. for $C_{19}H_{17}N_3O_2$: C, 71.45; H, 5.37; N, 13.16. Found: C, 71.35; H, 5.25; N, 13.26.

dl-Evodiamine. To a solution of 2.3 g. of rhetsinine in 100 ml. of glacial acetic acid was added 65 mg. of platinum oxide catalyst. The mixture was shaken under 45 p.s.i. of hydrogen for 45 min. The product crystallized from solution during the reduction. The mixture was diluted with water and the product collected, dried, and recrystallized from a 1:1 mix-

(3) A. Chatterjee, S. Bose and C. Ghosh, *Tetrahedron* **7**, 257 (1959).

(4) We are indebted to Professor T. Ohta of the Tokyo College of Pharmacy, Tokyo, Japan, for providing an authentic sample of evodiamine.

ture of ethanol and ethyl acetate to give 1.9 g. of prisms which soften at 269° and melt at 275–277° when heated at a rate of 5° per min. The compound was compared with a specimen of natural evodiamine from Professor T. Ohta[4] and had the same ultraviolet and infrared spectral properties.

Anal. Calcd. for $C_{19}H_{17}N_3O$: C, 75.22; H, 5.65. Found: C, 75.32, 75.25; H, 5.77, 5.85.

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Chlorination of Polyfluoroalkyl Borates[1a]

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In connection with recent studies on fluoro heterocycles an interest developed in the synthesis of perfluorinated *n*-alkyl borates. Orthoboric acid esters are generally prepared by reaction of the respective alcohol with either a boron halide, boron trioxide, or orthoboric acid. Perfluorinated alcohols were desired in this work, but primary perfluorinated alcohols are not isolable. However, work was started with alcohols of the type R_FCH_2OH which are commercially available. The orthoborates expected from these alcohols require final fluorination either by direct exchange of hydrogen for fluorine by silver difluoride or similar agents, or by halogenation with bromine or chlorine followed by replacement of bromine or chlorine by fluorine by means of an inorganic fluorinating agent such as silver fluoride.

Preliminary experiments showed that boron trifluoride etherate did not react with trifluoroethanol, pentafluoropropanol, and heptafluorobutanol even under reflux, whereas boron trichloride in petroleum ether solution reacted instantaneously at −20° to give the desired borates. Thus tris(trifluoroethyl)borate (I), tris(pentafluoropropyl)borate (II), and tris(heptafluorobutyl)borate (III) were obtained in a 60–70% yield.

While bromination was unsuccessful, compound I was chlorinated rapidly when exposed to ultraviolet light. Surprisingly, the absorption of chlorine never stopped and the volume of the reaction mixture started to decrease after a certain interval of time. The reaction mixture thus obtained was distilled under vacuum to give two compounds, bis(trifluoromonochloroethyl) chloroboronate (VII) and the higher boiling tris(trifluoromonochloroethyl)borate (IV).

This result proved that the chlorination first proceeds as desired with the substitution of three of the six available hydrogen atoms by chlorine. The resulting compound IV then chlorinates further, not by exchange of residual hydrogen for chlorine, but by splitting off an alkoxy group with the formation of VII.

$$(R_FCH_2O)_3B \xrightarrow{Cl_2,\ h\nu} (R_FCHClO)_3B \xrightarrow{Cl_2,\ h\nu} (R_FCHClO)_2BCl$$

I, II, III — IV, V, VI — VII, VIII, IX

I, IV, VII. $R_F = CF_3$
II, V, VIII. $R_F = C_2F_5$
III, VI, IX. $R_F = C_3F_7$

We assume that compound VII is also not stable to chlorine and is probably converted into trifluoromonochloroethyldichloroboronite (X) which in turn undergoes further reaction with chlorine to form boron trichloride.

Chlorination of II and III led to the corresponding compounds V, VI, VIII, and IX. Bis(heptafluoromonochlorobutyl)chloroboronate (IX) was obtained contaminated with heptafluoromonochlorobutyldichloroboronite (XI).

For proof of structure, IX was also prepared from VI and boron trichloride as another method of preparation of dialkyl chloroboronates.[2] When

$$2\ (CF_3CF_2CF_2CHClO)_3B + BCl_3 \longrightarrow 3\ (CF_3CF_2CF_2CHClO)_2BC$$

VI — IX

the preparation of XI, the monoalkoxy derivative, was attempted by using an excess of boron trichloride, surprisingly only the dialkoxy derivative, IX, was obtained.

Since bromination and chlorination had failed to produce a perhalogenated orthoborate, an attempt was made to prepare the desired perfluoroalkyl orthoborates by direct fluorination of the hydrogen atoms attached to the α-carbon atoms of the alkyl groups by means of silver difluoride. The only product obtained from III was a boron-free material, probably di-1,1-dihydroheptafluorobutyl ether.

EXPERIMENTAL[3]

Tris(heptafluorobutyl) borate (III). The solution of 23 g. of boron trichloride in 200 ml. of petroleum ether (b.p. 30–38°) was added dropwise to a stirred mixture of 100 g. of 1,1-dihydroheptafluorobutanol and 100 ml. of petroleum ether with ice-salt cooling during 40 min. To ensure complete reaction, the mixture was then kept for 20 min. at 20°. The separated solid, boric acid, was filtered off and the petroleum ether evaporated. Distillation of the residual product gave a forerun of heptafluorobutanol and then 66.5 g. of III (66%); b.p. 137° (200 mm.); n_D^{23} 1.2596. The use of pyridine as hydrogen chloride scavenger decreased the yield.

(1)(a) This article is based on work performed under Project 116-B of The Ohio State University Research Foundation sponsored by The Olin Mathieson Chemical Corporation, New York, N. Y. (1)(b) Present address: Olin Mathieson Chemical Corporation, New Haven, Conn.

(2) W. Gerrard and M. F. Lappert, *J. Chem. Soc.*, 501 (1957).

(3) Analyses are by Galbraith Microanalytical Laboratories, Knoxville, Tenn. Despite the fact that considerable care was taken in the purification of the reaction products, some variance was observed between the analyses and the calculated values which is typical of compounds containing high percentages of fluorine.