1-(β-Dimethylaminoethyl)-2-phenylindoline Hydrochloride.—The procedure described above was employed, using an equivalent amount of β-dimethylaminoethyl chloride hydrochloride. From 12.9 g. (0.66 mole) of 2-phenylindoline there was obtained 12.6 g. (71.5%) of the free base. The free base is a colorless liquid boiling at 183–184° at 3.8 mm. The hydrochloride, prepared as described above, after four recrystallizations from absolute ethanol consisted of fine colorless needles melting at 210.5–212.5°.

Anal. Calcd. for $C_{18}H_{22}N_2 \cdot HCl$: C, 71.38; H, 7.65; N, 9.25. Found: C, 71.38; H, 7.50; N, 9.00.

9-[β-(1-Pyrrolidyl)-ethyl]-carbazole.—Sodamide[6] was prepared from 3.8 g. (0.17 mole) of sodium. A mixture of sodamide, 150 cc. of dry xylene and 25.1 g. (0.15 mole) of carbazole was stirred and heated in an oil-bath at 130° for three hours. To the mixture was added 20.0 g. (0.15 mole) of β-(1-pyrrolidyl)-ethyl chloride and the mixture stirred and heated under reflux for eight hours. The mixture was filtered and the precipitate washed with about 200 cc. of xylene. The xylene filtrate was extracted with dilute hydrochloric acid, the acid extracts made basic by the addition of a cold solution of sodium hydroxide, whereupon a light brown precipitate formed. This was filtered and dried in air. The weight of crude product was 38.4 g. (96%); m. p. 80–81°. Two recrystallizations from petroleum ether (Skelly B) after treatment with charcoal gave light yellow needles melting at 80.5–81.0°.

Anal. Calcd. for $C_{18}H_{20}N_2$: C, 81.77; H, 7.63; N, 10.60. Found: C, 81.80; H, 7.47; N, 10.51.

9-[β-(1-Pyrrolidyl)-ethyl]-1,2,3,4-tetrahydrocarbazole Hydrochloride.—The procedure given above for 9-[β-(1-pyrrolidyl)-ethyl]-carbazole was followed using 25.6 g. (0.15 mole) of 1,2,3,4-tetrahydrocarbazole.[12] The product, which separated as an oil, was taken up in ether and the ethereal solution dried over anhydrous magnesium sulfate. The drying agent was filtered off and the hydrochloride precipitated by bubbling dry hydrogen chloride through the solution. The yield of crude product, melting at 211–220°, was 38.1 g. (83%). Three recrystallizations from an ethyl acetate–absolute ethanol mixture (3:1) using decolorizing carbon gave light yellow needles melting at 232.5–233.0°.

Anal. Calcd. for $C_{18}H_{24}N_2 \cdot HCl$: C, 70.91; H, 8.27; N, 9.19. Found: C, 70.74; H, 8.01; N, 9.42.

9-[β-(1-Pyrrolidyl)-ethyl]-1,2,3,4,10,11-hexahydrocarbazole Hydrochloride.—The procedure given above for 1-[β-(1-pyrrolidyl)-ethyl]-2-phenylindoline was followed using the appropriate quantity of 1,2,3,4,10,11-hexahydrocarbazole.[13] The free base was obtained as a light yellow, slightly fluorescent liquid boiling at 147–149° (0.5 mm.); yield 62%.

The hydrochloride was prepared as described in the same procedure. The crude product, upon five recrystallizations from ethyl acetate, in the presence of decolorizing charcoal, gave light yellow needles melting at 135–137.5°. The hydrochloride darkens upon standing.

Anal. Calcd. for $C_{18}H_{26}N_2 \cdot HCl$: C, 70.45; H, 8.87; N, 9.13; Cl, 11.55. Found: C, 70.40; H, 8.67; N, 9.07; Cl, 11.55.

Summary

1. Four new 1-[β-(1-pyrrolidyl-ethyl]-indole derivatives, three new 9-[β-(1-pyrrolidyl)-ethyl]-carbazole derivatives, and 1-β-(dimethylaminoethyl)-2-phenylindoline hydrochloride have been prepared.

2. The results of preliminary pharmacological tests on these compounds for antihistaminic activity is reported.

(12) Rogers and Corson, THIS JOURNAL, **69**, 2910 (1947).

(13) Borsche, Witte and Bothe, *Ann.*, **359**, 70 (1908).

KALAMAZOO, MICHIGAN RECEIVED SEPTEMBER 20, 1948

[CONTRIBUTION FROM THE LABORATORIES OF GORDON A. ALLES, PH.D.]

Characterization of Certain Alkaloids from *Fagara coco*

BY C. ERNST REDEMANN, BURNETT B. WISEGARVER AND GORDON A. ALLES

Stuckert[1] and co-workers in 1925 began the isolation and separation of the alkaloids of *Fagara coco* (Gill.) Engl. Six alkaloids were listed, only four of which, α-, β-, γ-, and δ-fagarine, were sufficiently well characterized to be considered discrete compounds. Merck and Company of Darmstadt subsequently carried out the isolation of the fagara alkaloids on a large scale and reported only two alkaloids, designated fagarine I, m.p. 163°, and fagarine II, m.p. 202°. Fagarine I is to be identified with α-fagarine, but fagarine II appears to be a new alkaloid. Later Deulofeu[2] and co-workers isolated α-, β-, and γ-fagarine from a sample of *Fagara coco* supplied by Stuckert. β-Fagarine has been identified[2] as skimmianine[3,4] and γ-fagarine as 8-methoxydictamnine.[5]

The structure of α-fagarine has been of interest since the report of Stuckert and Sartori[6] that it exerts a depressant action upon cardiac function, and the subsequent finding of Moisset de Espanés[7] that it raises the threshold for both auricular and ventricular fibrillation arising from faradic stimulation. It has more recently been reported as a superior substitute[8] for quinidine for controlling cardiac arrythmias. Stuckert[1] arrived at the empirical formula $C_{19}H_{22}NO_4$ for α-fagarine, while Merck[1] gave $C_{19}H_{23}NO_5$. Deulofeu[2,8,9] and co-workers concluded that the empirical formula is $C_{19}H_{23}NO_4$ and suggest a provisional structure.

Dried ground leaves and twigs of *Fagara coco* were extracted by the method of Deulofeu.[2]

(1) "Investigaciones del Laboratorio de Química Biológica, Cordoba, Argentina," Vol. I 1933, and Vol. II, 1938.

(2) Deulofeu, Labriola and de Langhe, THIS JOURNAL, **64**, 2326 (1942).

(3) Honda, *Arch. exp. Path. Pharmakol.*, **52**, 83 (1904).

(4) Asahina and Inubuse, *Ber.*, **63**, 2052 (1930).

(5) Berinzaghi, Muruzabal, Labriola and Deulofeu, *J. Org. Chem.*, **10**, 181 (1945).

(6) Stuckert and Sartori, *Rev., Univ. Nac. Cordoba, Argent.*, **19**, 12 (1932).

(7) Moisset de Espanés and Navarro, *Rev. Soc. Arg. Biol.*, **12**, 137 (1936); **13**, 112 (1937); **13**, 259 (1937).

(8) Deulofeu, Labriola, Orias, Moisset de Espanés and Taquini, *Science*, **102**, 69 (1945).

(9) Deulofeu, Labriola and Berinzaghi, *J. Org. Chem.*, **12**, 217 (1947).

The α-fagarine thus obtained melted at 159–160° instead of either 163° or 169–170°, both values having been reported by Deulofeu. Analyses and molecular weight determination of our α-fagarine[10] indicated an empirical formula $C_{21}H_{23}NO_5$. The failure of Deulofeu and co-workers to determine neutral equivalent weights of the base and halogen analyses of the halogen acid salts of α-fagarine is probably responsible for the erroneous empirical formula they reported, for had they determined these quantities it would have been apparent that some of their analytical values were in error. Treatment of α-fagarine with phosphorus oxychloride gave an anhydromethochloride which is impossible with a compound having the provisional structure given by Deulofeu. In addition a careful repetition of Deulofeu's oxidative degradation in acid medium confirmed the presence of methanal, but failed to show any *m*-methoxybenzaldehyde. The identity of our α-fagarine with that described by Deulofeu is based upon the fact that five derivatives of our α-fagarine had melting points in agreement with the corresponding derivatives reported by Deulofeu.

α-Fagarine and α-allocryptopine[11] were found to be identical. Schmidt and co-workers[12] have shown that allocryptopine exists in two isomeric modifications, the α-melting at 160°, and the β-melting at 169–170°, which they were able to interconvert,[13] thus suggesting that these two modifications may arise from dimorphism. The melting points of α-allocryptopine and the α-fagarine we isolated are the same, while the higher melting point of β-allocryptopine is the same as that recently reported by Deulofeu[9] and co-workers for their α-fagarine. Deulofeu in an earlier paper[2] reported the m.p. of α-fagarine as 163°, which he subsequently attributed to a solvate. Jowett and Pyman[14] have isolated β-allocryptopine (γ-homochelidonine) from a closely related species of Fagara, *Xanthoxylum brachyacanthum*, F. Muell., more recently classified as *Fagara brachyacanthum* (F. Muell.) Engl.

α-Fagarine hydrochloride melted at 190–192° dec. which is in agreement with the dec. temperature of 190° reported by Haworth and Perkin[15] for α-allocryptopine hydrochloride. α-Fagarine aurichloride melted at 187° dec. in agreement with that given by Schmidt and Wintgen[12b] for α-allocryptopine aurichloride. When treated with phosphorus oxychloride α-fagarine gave an anhydromethochloride, m.p. 205°, which is close to the m.p. 200–201° reported by Gadamer[16] for the anhydromethochloride produced from α-allocryptopine by similar treatment.

An authentic sample of α-allocryptopine isolated from another plant source was kindly supplied by Dr. R. H. F. Manske. After recrystallizing both his α-allocryptopine sample and our α-fagarine from the same solvent a determination of the mixed melting point showed no depression. A comparison of crystal forms showed the two substances to be identical in crystal habit. The ultraviolet absorption spectra of α-fagarine and α-allocryptopine (Fig. 1) are identical, the two curves falling upon each other so exactly as to be indistinguishable. Our α-fagarine was shown to be identical with the α-fagarine commercially available in Argentina by direct comparison with an authentic sample purchased from the Laboratories Apotarg, Cordoba, Argentina. Both samples melted at 159–160° and in admixture showed no depression in m.p.

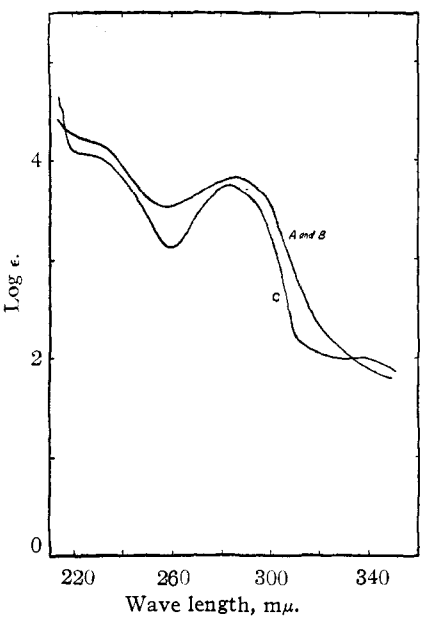

Fig. 1.—A, α-Allocryptopine; B, α-fagarine; C, α-fagarine hydrochloride.

It was found that a small quantity of hydrochlorides crystallized upon cooling a hot aqueous solution of the crude fagarine in dilute hydrochloric acid. The bases obtained from the crystalline hydrochlorides were separated into two fractions, one melting at 181–183° and the other at 198–199°. The base melting at 198–199° is to be identified with Merck fagarine II, while that melting at 181–183° appears to be new and will be referred to as fagarine III in this paper.

(10) Much difficulty was experienced in obtaining correct analyses of α-fagarine. Analyses were run by three commercial microanalytical laboratories and in our own laboratory before it was possible to get consistent analytical values.

(11) Stuckert annotated on p. 199 of his later report[1] that Merck suggested that α-fagarine was similar to α-allocryptopine, but this suggestion does not seem to have been followed. α-Allocryptopine is also called β-homochelidonine.

(12) (a) Schmidt and Fischer, *Arch. Pharm.*, **239**, 409 (1901); (b) Schmidt and Wintgen, *ibid.*, **239**, 438 (1901).

(13) We attempted the interconversion following their directions, but all attempts were unsuccessful, probably because we had no seed crystals of the β-allocryptopine. The same difficulty is encountered with many polymorphic organic compounds.

(14) Jowett and Pyman, *J. Chem. Soc.*, **103**, 290 (1913).

(15) Haworth and Perkin, *ibid.*, 445 (1926).

(16) Gadamer, *Arch. Pharm.*, **258**, 148 (1919).

Analyses of fagarine II, its hydrochloride, hydrobromide, aurichloride and methiodide indicate an empirical formula of $C_{21}H_{23}NO_5$ for the base, with a methylimide, a methylenedioxy and two methoxy groups present. The lack of optical activity would indicate either the absence of an asymmetric carbon atom, or easy isomerization. Treatment with phosphorus oxychloride gave an anhydromethochloride. The ultraviolet absorption spectra of fagarine II and its hydrochloride (Fig. 2) are very similar to those of α-fagarine. The two molecules probably differ only in the positions occupied by the methylenedioxy and methoxy groups.

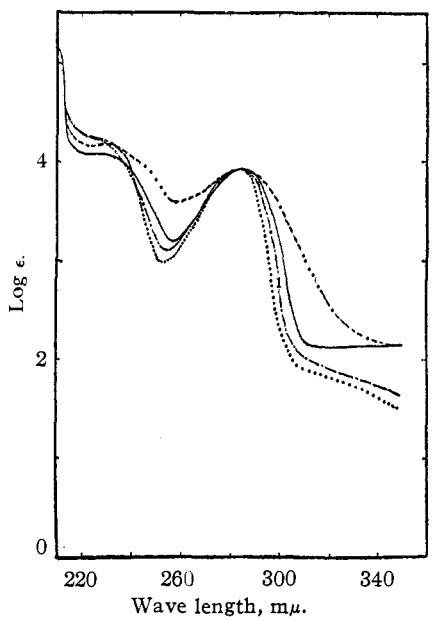

Fig. 2.— - - - -, Fagarine II; ——, fagarine II hydrochloride; — — — —, fagarine III; . . . . . , fagarine III hydrochloride.

The amount of fagarine III obtained has been too small for an extensive study of its properties and derivatives. This alkaloid gives no color with concentrated sulfuric acid, a negative Labat test for a methylenedioxy group, and is strongly levo-rotatory. Its ultraviolet absorption spectrum (Fig. 2) is similar to that of α-fagarine and fagarine II.

Experimental[17,18]

Purification of Crude α-Fagarine.—Crude α-fagarine, extracted from ground *Fagara coco* by the method of Deulofeu,[2] was reprecipitated from its hydrochloride solution and then crystallized from ethanol giving pure α-fagarine, m. p. 159–160°. Samples of purified α-fagarine were crystallized from ethyl acetate, acetone, benzene and chloroform–petroleum ether, with no change in m. p. A sample of α-fagarine crystallized from ethyl acetate and dried at 100° *in vacuo* over phosphorus pentoxide at 2 mm. for nine hours was analyzed.

(17) All melting points are uncorrected.

(18) The methoxy and methylimide determinations were made by the Elek Micro Analytical Laboratories, Los Angeles.

Anal. Calcd. for $C_{21}H_{23}NO_5$: C, 68.27, H, 6.27; N, 3.79; CH_3O, 16.80; mol. wt., 369.4; neut. eq., 369.4. Found: C, 68.47, 68.37; H, 6.18, 6.20; N, 3.37, 3.71; CH_3O, 16.93, 16.96; mol. wt., 362, 368, 370 (ebullioscopic in benzene); neut. eq., 368.5, 368.5, 369.5.

α-Fagarine Hydrochloride.—The hydrochloride was obtained from absolute ethanol solution in nearly the theoretical yield as a crystalline powder, m. p. 190–192° dec.; Deulofeu[9] gave the m. p. 192–193°. A sample of this hydrochloride was dried at 100° over phosphorus pentoxide at 2 mm. for six hours before analysis.

Anal. Calcd. for $C_{21}H_{23}NO_5 \cdot C_2H_5OH \cdot HCl$: C, 61.1; H, 6.64; Cl, 7.87, CH_3O, 20.33. Found: C, 60.76, 60.78; H, 6.56, 6.60; Cl, 7.85, 7.89; CH_3O, 18.96, 19.17. (The ethyl alcohol of crystallization would be estimated as a methoxyl group, thus giving the equivalent of three methoxyl groups.)

The presence of ethanol in the analytical sample of α-fagarine hydrochloride was shown by distilling 5 g. with 20 ml. of 2 *N* hydrochloric acid and then redistilling the first 5 ml. of distillate. The first 0.5 ml. from the second distillation (b. p. 78°) was treated with 3 ml. of pyridine and 0.5 g. of 3,5-dinitrobenzoyl chloride, giving a 3,5-dinitrobenzoate, m. p. 92.5°, which is the melting point of ethyl 3,5-dinitrobenzoate. Concentration of the aqueous boiler residue from the first distillation gave a white crystalline product which turned slightly yellow when dried at 130° over phosphorus pentoxide at 2 mm. for two hours.

Anal. Calcd. for $C_{21}H_{23}NO_5 \cdot HCl \cdot 0.5H_2O$: Cl, 8.54. Found: Cl, 8.54, 8.56.

The ionization constant of α-fagarine was estimated from the hydrolysis of its hydrochloride in aqueous solution. A 0.022 *M* solution of the hydrochloride in doubly distilled water had a *p*H of 5.38 at 25° from which the basic ionization constant, K_b, was calculated to be 1.3×10^{-5}.

α-Fagarine Hydrobromide.—This was prepared in ethanol by the procedure of Deulofeu.[9] The crystals were collected and dried at 100° over phosphorus pentoxide at 2 mm. for two hours; m. p. 185–188° dec.; Deulofeu gave 186–188° dec.

Anal. Calcd. for $C_{21}H_{23}NO_5 \cdot HBr \cdot 0.5C_2H_5OH$: C, 55.7; H, 5.75; Br, 17.05. Found: C, 55.55; H, 5.77, Br, 16.95.

α-Fagarine Hydroiodide.—A solution of 300 mg. of α-fagarine in 5 ml. of ethanol and 0.5 ml. of freshly distilled hydroiodic acid (d. 1.57) was prepared by warming. Two crystal forms were observed after standing overnight. These were thought to be different solvates, since after drying they showed identical melting points, m. p. 192–194° dec. Deulofeu[9] gave 190–192° dec.

Anal. (A) Sample dried at 50° in air. Calcd. for $C_{21}H_{23}NO_5 \cdot HI \cdot C_2H_5OH$: I, 23.4. Found: I, 23.4. (B) Sample dried at 100° *in vacuo* over phosphorus pentoxide for three hours. Calcd. for $C_{21}H_{23}NO_5 \cdot HI$: C, 50.7; H, 5.52; I, 25.5. Found: C, 50.6; H, 5.52; I, 24.84, 24.95.

α-Fagarine Methiodide.—This was obtained by a slight variation of Deulofeu's procedure as a fine crystalline powder, m. p. 205–206°. Deulofeu gave 205°.

Anal. Calcd. for $C_{21}H_{23}NO_5 \cdot CH_3I$: C, 51.6; H, 5.08; I, 24.84. Found: C, 51.77; H, 5.27; I, 24.82.

α-Fagarine Picrate.—This was prepared by the procedure of Deulofeu[9]; observed m. p. 207–208°; Deulofeu gave 208–209°.

Anal. Calcd. for $C_{21}H_{23}NO_5 \cdot C_6H_3N_3O_7$: C, 54.1; H, 4.34. Found: C, 53.9; H, 4.45.

α-Fagarine Aurichloride.—A solution of 74 mg. of α-fagarine, 80 mg. of gold chloride, a few drops of diluted hydrochloric acid and 3 ml. of ethanol was prepared by warming slightly. Water was added to the warm solution, a few drops at a time, until just turbid. Garnet-red, warty, crystal masses gradually formed; m. p. 187° dec.

Anal. (A) Sample dried at 50° in air. Calcd. for $C_{21}H_{23}NO_5 \cdot HAuCl_4 \cdot H_2O$: Au, 27.0. Found: Au, 27.0.

(B) Sample dried at 100° over phosphorus pentoxide *in vacuo* for three hours. Calcd. for $C_{21}H_{23}NO_5 \cdot HAuCl_4$: Au, 27.80. Found: Au, 27.82.

Oxidation of α-Fagarine with Acid Permanganate.—One gram of α-fagarine was oxidized by the procedure of Deulofeu.[9] An excess of a solution of 2,4-dinitrophenylhydrazine in 6 *N* hydrochloric acid was added to the steam distillate and the solution allowed to stand until precipitation was complete, in place of the ether extraction used by Deulofeu. The precipitate was collected and recrystallized from ethanol, giving yellow crystals, m.p. 165°, whose m.p. was not lowered in admixture with an authentic sample of formaldehyde 2,4-dinitrophenylhydrazone. The alcoholic mother liquor was evaporated to dryness leaving 30 mg. of a dinitrophenylhydrazone, m.p. 160–164°, whose m.p. was not depressed in admixture with formaldehyde 2,4-dinitrophenylhydrazone. In addition, Deulofeu[9] reported isolating *m*-methoxybenzaldehyde 2,4-dinitrophenylhydrazone, m.p. 220°, but we were not able to find any trace of such a substance.

The adequacy of our isolation procedure was demonstrated by a model experiment with 20 mg. of *m*-methoxybenzaldehyde which gave a copious yield of its 2,4-dinitrophenylhydrazone, m.p. 220°.

Treatment of α-Fagarine with Phosphorus Oxychloride.—A mixture of 2 g. of α-fagarine and 2 ml. of phosphorus oxychloride was allowed to stand without external heating for ten minutes, after which the mixture was heated in an 110° oil-bath for forty-five minutes. The excess phosphorus oxychloride was removed *in vacuo* and the residue was dissolved in hot water from which it crystallized upon cooling as very small needle crystals. Recrystallization from 2% hydrochloric acid gave crystals, m.p. 205° with previous browning and dec. A sample dried *in vacuo* at 130° decomposed.

Anal. (A) Dried at 50° in the air. Calcd. for $C_{21}H_{22}NO_4 \cdot HCl \cdot 3H_2O$: Cl, 8.01. Found: Cl, 8.04. (B) Dried at 65° for eight hours *in vacuo* over phosphorus pentoxide. Calcd. for $C_{21}H_{22}NO_4 \cdot HCl \cdot H_2O$: Cl, 8.71. Found: Cl, 8.63.

Mixed Melting Point of α-Allocryptopine and α-Fagarine.—A sample of authentic α-allocryptopine was kindly furnished by Dr. Manske. Both his sample and our α-fagarine were recrystallized from ethyl acetate. Each sample melted at 159–160° and no depression was shown in the melting point of their mixture.

Isolation of Fagarines II and III.—While working up a composite lot of 200 g. of crude α-fagarine from the first precipitation at *p*H 12–13, the dark-brown granular mass was dissolved in 2 l. of hot 1 *N* hydrochloric acid and the filtered solution was allowed to stand overnight at room temperature. The 43 g. of sparingly soluble hydrochloride which separated was dissolved in 2 l. of boiling water and the base liberated with sodium hydroxide. The crude base (26.5 g.) which separated was crystallized from "Cellosolve" and then from ethanol, giving 13.8 g. of fine white needles, m.p. 198–199°, of crude fagarine II. From the mother liquors 1.6 g. of another base, fagarine III, was obtained by taking advantage of its much smaller rate of crystallization. Fagarine III separated as large, pale yellow octahedral prisms, m.p. 181–183°.

Fagarine II.—Pure fagarine II was obtained by repeated crystallization of the crude fagarine II from "Cellosolve," ethanol, ethyl acetate and benzene. The melting point of the long fine white needles remained constant at 198–199°. This base showed no optical activity in chloroform solution, had a bitter taste and gave a red-violet color with concd. sulfuric acid which slowly changed to a purple color. The Labat test[19] for the methylenedioxy group was strongly positive.

Anal. Calcd. for $C_{21}H_{23}NO_5$: C, 68.27: H, 6.27; N, 3.79; 2 CH_3O, 16.80; mol. wt., 369.4; neut. eq., 869.4: 1 CH_3N, 7.8. Found: C, 68.4, 68.2; H, 6.31, 6.38; N, 3.61, 3.71; CH_3O, 15.29; mol. wt., 374 (ebullioscopic in benzene); neut. eq., 373, 374; CH_3N, 5.6.

(19) Labat, *Bull. soc. chim.*, [4] 5, 745 (1909).

Fagarine II Aurichloride.—A solution of 160 mg. of fagarine II, 160 mg. of gold chloride trihydrate, 5 ml. of water and a few drops of hydrochloric acid was prepared by heating moderately. The aurichloride separated as a granular orange-colored solid, m.p. 218–219°. After boiling with ethanol and drying *in vacuo* at 130° this solid was analyzed.

Anal. Calcd. for $C_{21}H_{23}NO_5 \cdot HAuCl_4$: Au, 27.80. Found: Au, 27.97, 27.49, 27.80.

Fagarine II Methiodide.—A suspension of 1.0 g. of fagarine II in 10 ml. of absolute ethyl acetate and 2 ml. of methyl iodide was heated in a sealed tube at 80° for four hours. The fine crystalline powder was collected and dried at 60°; weight 1.37 g. (99% yield); m.p. 234° dec.; sparingly soluble in hot water and hot ethanol.

Anal. Calcd. for $C_{21}H_{23}NO_5 \cdot CH_3I$: C, 51.66; H, 5.13; I, 24.82. Found: C, 51.5; H, 5.18; I, 24.91, 24.78.

Fagarine II Anhydromethochloride.—A mixture of 1.0 g. of fagarine II and 2 ml. of phosphorus oxychloride was allowed to stand for ten minutes at room temp. During this time the solid dissolved with slight evolution of heat. After heating in an oil-bath at 110° for forty-five minutes the excess phosphorus oxychloride was distilled under reduced pressure and the residue was dissolved in 60 ml. of boiling water. The crystals which separated were recrystallized from 200 ml. of boiling 2% hydrochloric acid, giving pale yellow scales which turned red upon exposure to light. These crystals were dried in the dark at 50° and then in a brown glass vial at 65° for four hours *in vacuo* over phosphous pentoxide, weight 0.8 g.; m.p. 210–215° with previous sintering and browning.

Anal. Calcd. for $C_{21}H_{22}ClNO_4$: C, 65.01; H, 5.72; Cl, 9.14. Found: C, 64.5, 64.5; H, 6.05, 6.08; Cl, 8.57.

There may have been a slight contamination of unreacted fagarine II hydrochloride present in this material since the hydrochloride is much less soluble than the anhydromethochloride.

Fagarine II Hydrochloride.—A solution of 2.3 g. of fagarine II dissolved in a slight excess of hot dilute hydrochloric acid was evaporated to dryness. The residue was crystallized from ethanol–ether, giving 1.9 g. of microscopic needle crystals, m.p. 200–202° dec., but on rapid heating a m.p. as high as 215° dec. was observed. The sample for analysis was dried for four hours at 100° *in vacuo* over phosphorus pentoxide.

Anal. Calcd. for $C_{21}H_{23}NO_5 \cdot HCl \cdot 0.5H_2O$: C, 60.79; H, 6.07; Cl, 8.54. Found: C, 60.5, 60.8; H, 6.29, 6.33; Cl, 8.47, 8.52.

Fagarine II Hydrobromide.—A suspension of 1.0 g. of fagarine II in 15 ml. of warm ethanol was treated dropwise with 48% aqueous hydrobromic acid until the solid dissolved and the solution was acidic. Ether was added to incipient turbidity and after standing for some time the crystalline hydrobromide was collected and dried four hours at 130° *in vacuo* over phosphorus pentoxide; weight 0.8 g.; m.p. 208–210° dec.

Anal. Calcd. for $C_{21}H_{23}NO_5 \cdot HBr \cdot 0.5H_2O$: C, 54.91; H, 5.49; Br, 17.40. Found: C, 54.55, 54.30; H, 5.66, 5.73; Br, 17.60, 17.67.

Fagarine II Picrate.—A solution of 37 mg. of fagarine II in 25 ml. of hot ethanol was treated with 25 mg. of picric acid in 10 ml. of ethanol. Upon cooling, the bright yellow picrate crystallized as microscopic needles, m.p. 214°.

Anal. Calcd. for $C_{21}H_{23}NO_5 \cdot C_6H_3N_3O_7$: C, 54.2; H, 4.38. Found: C, 54.4; H, 4.65.

Fagarine III.—After recrystallizing from ethanol, pure fagarine III was obtained as almost colorless large octahedral prisms, m.p. 181–183°. This melting range could not be reduced by repeated crystallization from ethanol. $[\alpha]^{27}D$ −300° (112.4 mg. made up to 10.00 ml. with chloroform, $[\alpha]^{27}D$ −3.37°, *l*, 1 dm.). Fagarine III is tasteless, gives a colorless solution with concd. sulfuric acid, even when heated, and a negative Labat test[18] for a methylenedioxy group.

Anal. Calcd. for $C_{22}H_{26}NO_4$: C, 71.7; H, 7.07; N, 3.80. Found: C, 71.5, 71.6; H, 7.11, 7.17; N, 2.98, 3.03.

Fagarine III Hydrochloride.—Upon dissolving 1.6 g. of fagarine III in 200 ml. of dilute hydrochloric acid and cooling, very fine needle crystals of the hydrochloride separated. These were collected and dried at 130° *in vacuo* over phosphorus pentoxide; m.p. 232–234° dec.

Anal. Calcd. for $C_{22}H_{26}NO_4 \cdot HCl$: C, 65.2; H, 6.68; Cl, 8.77. Found: C, 64.4, 64.6; H, 6.87, 6.93; Cl, 9.15.

Ultraviolet Absorption Spectra.—The ultraviolet absorption spectra were determined using a Beckman model DU quartz spectrophotometer. The solvent was 99% ethanol for the bases, and 0.1 *N* aqueous hydrochloric acid for the hydrochlorides. Minimum slit widths were used with a 1.00 cm. quartz cell. All measurements were made against a blank of an identical sample of the pure solvent to eliminate its absorption.

Acknowledgment.—The authors wish to express their gratitude to Dr. R. H. F. Manske for supplying us with an authentic sample of α-allocryptopine.

Summary

1. A re-investigation of α-fagarine and its derivatives has shown it to be identical with α-allocryptopine.

2. A second alkaloid, fagarine II, has been isolated and several derivatives have been prepared and analyzed. These data would suggest that fagarine II is isomeric with α-fagarine, differing only in the positions of the substituents.

3. Fagarine III has been isolated in very small amount. The ultraviolet absorption spectra of this alkaloid and its hydrochloride would suggest that it, also, belongs to the cryptopine group of alkaloids.

PASADENA 2, CALIFORNIA RECEIVED SEPTEMBER 7, 1948

[CONTRIBUTION FROM THE BUREAU OF ENTOMOLOGY AND PLANT QUARANTINE, AGRICULTURAL RESEARCH ADMINISTRATION, U. S. DEPARTMENT OF AGRICULTURE]

The Action of Ultraviolet Light on DDT

BY ELMER E. FLECK

The prolonged residual action of DDT (I) is due to its low vapor pressure[1] and to its stability toward oxidation.[2] Recently evidence has been accumulating to show that DDT is not so stable when exposed to direct sunlight in solution as when it is exposed in the solid state.[3]

Attempts have been made to explain this phenomenon by isolating the decomposition products of DDT produced by ultraviolet light. The isolation of 4,4′-dichlorobenzophenone (IV) was accomplished during 1945 in this laboratory by irradiating DDT dissolved in γ-valerolactone in an open Petri dish with ultraviolet light from a 100-watt mercury-vapor lamp. Since that time Wichmann, *et al.*,[4] have confirmed the formation of this compound by isolating the 2,4-dinitrophenylhydrazone of 4,4′-dichlorobenzophenone from the products obtained by irradiation of a benzene solution of DDT in an open Petri dish with ultraviolet light.

The formation of 4,4′-dichlorobenzophenone from DDT has been assumed to proceed first by elimination of hydrogen chloride from the trichloroethane group and then by oxidation of the resulting double bond. This mechanism of reaction was tested by irradiation of solutions of DDT in completely filled quartz cells. A wide variety of solvents were tried, and in every case hydrogen chloride was evolved but dehydrochlorinated DDT could not be isolated.

When a solution of DDT in ethyl alcohol was irradiated with a 360-watt mercury-vapor lamp for sixteen hours, about 1 mole of hydrogen chloride was evolved. A strong odor of acetaldehyde was present, and cooling the solution yielded about 10% of a crystalline compound which melted at 230–231°. This was shown to be 2,3-dichloro-1,1,4,4-tetrakis-(*p*-chlorophenyl)-2-butene (II) by analysis and by mixed melting point determinations with authentic material made by the method of Brand and Bausch.[5] These authors prepared II by hydrogenation of DDT in the presence of Pd–$CaCO_3$ catalyst. The identity of the two compounds was further substantiated by conversion of the irradiation product into 1,1,4,4-tetrakis-(*p*-chlorophenyl)-1,-2,3-butatriene (III) by refluxing with alcoholic sodium hydroxide. This procedure eliminated 2 moles of hydrogen chloride from II and resulted in a yellow crystalline product which melted with decomposition at 286°. Brand and Bausch give 288° with decomposition for this same compound. Mixed melting points of the two preparations showed no depression.

The butatriene (III), obtained by irradiation and reaction with alkali, was oxidized with chromic anhydride to form IV. This is in accordance with the oxidation of III prepared by the method of Brand and Bausch.[5]

In order to eliminate the possibility of an unknown impurity being present in the *p,p′*-DDT, the irradiation was repeated with a second preparation of *p,p′*-DDT made from DDT produced by a different manufacturer. The same yield of II was obtained.

(1) E. E. Fleck, *J. Econ. Entomol.*, **37**, 353 (1944).
(2) O. Zeidler, *Ber.*, **7**, 1181 (1874).
(3) E. E. Fleck, *Ind. Eng. Chem.*, **40**, 707 (1948).
(4) H. J. Wichmann, W. I. Patterson, P. A. Clifford, A. K. Klein and H. V. Claborn, *J. Assoc. Offic. Agr. Chem.*, **29**, 222 (1946).
(5) K. Brand and W. Bausch, *J. prakt. Chem.*, **127**, 219 (1930).