805. *The Constituents of* Casimiroa edulis *Llave* et *Lex. Part II.* The Bark.*

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Investigation of the trunk and root bark of the Mexican tree *Casimiroa edulis* Llave *et* Lex. has yielded twelve substances. Of these, three (edulein, edulitine, and edulinine) appear to be new. The remainder are shown to be coumarins (bergapten, *iso*pimpinellin, and scopoletin), furanoquinoline alkaloids (dictamnine, γ-fagarine, and skimmianine), a flavonoid (5 : 6-dimethoxyflavone), and two substances (zapotin and casimiroin) previously isolated from the seed.

IN Part I,* the isolation of thirteen substances from the seed of the tree *Casimiroa edulis* Llave *et* Lex. was described. We here report a similar investigation of the bark. Besides casimiroin and zapotin, already obtained from the seed, the trunk bark yielded eight substances (see Table), of which three (edulein, edulitine, and edulinine) appear to be new. It is of interest that casimiroedin, the major constituent of the seed, was absent from the bark.

Compounds obtained from trunk and root bark of Casimiroa edulis.

Compound	Extraction solvent	Yield (%) from trunk bark	root bark
Zapotin	" Acid " benzene	0·122	0·425
Bergapten	,,	—	0·0035
*iso*Pimpinellin	,,	—	0·0122
5 : 6-Dimethoxyflavone	,, benzene and methylene chloride	0·0122	0·645
Casimiroin	,, ,, ,,	0·0052	0·225
Edulein	,, methylene chloride	0·0021	0·0430
Edulitine	,, ,, ,,	0·0006	—
Scopoletin	,,	0·0015	—
Dictamnine	" Alkaline " benzene	0·0008	0·0038
γ-Fagarine	,, ,,	0·0024	0·0106
Skimmianine	,, ,,	0·0020	—
Edulinine	,, methylene chloride	0·0030	0·0026

The extraction procedure was that used previously. The " acid " benzene extract of the trunk bark on chromatography on alumina yielded zapotin and casimiroin, and a compound, $C_{15}H_8O_2(OMe)_2$, shown to be 5 : 6-dimethoxyflavone by successive demethylation and acetylation to 5 : 6-diacetoxyflavone. This flavone has not previously been observed in Nature, but has been obtained by a synthesis [1] which was carried out since it was erroneously believed that the naturally occurring primetin possessed the 5 : 6-dihydroxyflavone structure.

The " acid " methylene chloride extract furnished successively edulein, edulitine, and the known coumarin scopoletin. Edulein, $C_{17}H_{15}O_2N$, contained one methoxyl and one *N*-methyl group, but no active hydrogen; its neutral character pointed to the presence of an amide group and the infrared spectrum was compatible with this.

Edulitine (m. p. 235—236°), $C_{11}H_{11}O_3N$, contained two methoxyl but no *N*-methyl groups, and the presence of a hydroxyl group was shown by the active-hydrogen determination and formation of a monoacetate. It therefore appears to be a hydroxydimethoxyquinoline or -*iso*quinoline. It was suspected that it might be 4-hydroxy-6 : 7-dimethoxyquinoline [2] (m. p. 236—237°), but was found to differ from this. Nevertheless, the general resemblance of the infrared and ultraviolet spectra confirms the quinoline structure. Further work on edulein and edulitine is in progress.

Scopoletin (7-hydroxy-6-methoxycoumarin) was identified by the close agreement

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* Part I, preceding paper.

[1] Baker, *J.*, 1939, 956.

[2] Riegel, Lappin, Adelson, Jackson, Albisetti, Dodson, and Baker, *J. Amer. Chem. Soc.*, 1946, **68**, 1264.

between its physical properties as well as those of the 7-acetate and 7-methyl ether with those reported.[3, 4, 5, 6]

The " alkaline " benzene extract on chromatography gave dictamnine,[7] γ-fagarine,[8] and skimmianine,[9] identified by comparison with authentic samples.

The " alkaline " methylene chloride extract furnished an apparently new alkaloid, edulinine, $C_{16}H_{21}O_4N$, containing one methoxyl but no *N*-methyl group.

The root bark was found similarly to contain all these substances (mostly in larger amounts; cf. Table), except edulitine, scopoletin, and skimmianine. In addition, the two furanocoumarins bergapten [10] and *iso*pimpinellin [11] were isolated. Bergapten was identified by conversion into bergaptenquinone, identical with that described in Part I. The structure of *iso*pimpinellin was confirmed by direct comparison.

EXPERIMENTAL

For general experimental details see Part I.

Extraction Procedure.—(a) *Trunk bark*. The bark was collected in the Federal District of Mexico during the month of April. The sun-dried and ground material (50 kg.) was extracted by the procedure outlined for the fruit, the " acid " hexane extraction being omitted.

(b) *Root bark*. The root bark, obtained from the same source, was dried in the sun and ground and 16·5 kg. were processed in the same way as the trunk bark.

5 : 6-*Dimethoxyflavone*.—This (from both trunk and root bark) was isolated from the " acid " benzene and methylene chloride extracts and was eluted from the column with benzene–ether (9 : 1). It formed plates (from acetone–methanol), m. p. 198—199°, $\lambda_{max.}$ 270, 300, and 325—327 mμ (log ε 4·45, 4·14, and 3·83, respectively), $\lambda_{max.}$ (mull) 6·03, 6·18, and 6·29 μ (Found : C, 72·5; H, 5·1; OMe, 22·1%; *M*, 262. Calc. for $C_{17}H_{14}O_4$: C, 72·35; H, 5·0; 2OMe, 22·0%; *M*, 282) (lit.,[1] m. p. 196°).

With refluxing hydrobromic acid in acetic acid it gave 5 : 6-dihydroxyflavone, m. p. 185—187°, $\lambda_{max.}$ 282 and 362 mμ (log ε 4·44 and 3·42, respectively) (Found : C, 70·6; H, 4·1. Calc. for $C_{15}H_{10}O_4$: C, 70·85; H, 3·95%) (lit.,[1] m. p. 189—190°), converted by acetic anhydride and pyridine into 5 : 6-diacetoxyflavone, needles (from methanol), m. p. 161—162° (Found : C, 67·45; H, 4·3. Calc. for $C_{19}H_{14}O_6$: C, 67·45; H, 4·15%). The m. p. was undepressed on admixture with an authentic sample (m. p. 162—163°) and the infrared spectra were identical.

Edulein.—This *substance* (both trunk and root bark) was obtained from the " acid " methylene chloride extract and was eluted from the column with benzene–ether (4 : 1). It formed needles (from ethyl acetate–methanol), m. p. 200—201°, $\lambda_{max.}$ 250 and 316 mμ (log ε 4·59 and 4·19, respectively), $\lambda_{max.}$ (in $CHCl_3$) 6·09, 6·15, 6·20, 6·26, and 6·35 μ (Found : C, 76·95; H, 5·7; N, 5·3; OMe, 11·6; *N*-Me, 5·5%; *M*, 255. $C_{17}H_{15}O_2N$ requires C, 76·95; H, 5·7; N, 5·3; 1OMe, 11·65; 1*N*-Me, 5·65%; *M*, 265). Edulein gave a yellow colour with tetranitromethane and an orange colour with alcoholic ferric chloride. *Edulein picrate* formed yellow needles (from methanol), m. p. 191—192° (Found : C, 55·6; H, 3·6. $C_{17}H_{15}O_2N,C_6H_3O_7N_3$ requires C, 55·85; H, 3·65%).

Edulitine.—Edulitine (from the trunk bark only) was eluted from the column, directly after edulein, by ether. Crystallization from ethyl acetate gave needles, m. p. 235—236°, $\lambda_{max.}$ 222, 248, 280, and 320 mμ (log ε 4·43, 4·52, 3·88, and 3·57, respectively), $\lambda_{max.}$ (mull) 6·08, 6·16, and 6·28 μ (Found : C, 64·25; H, 5·45; N, 6·85; OMe, 29·7; active H, 0·49%; *M*, 201. $C_{11}H_{11}O_3N$ requires C, 64·4; H, 5·4; N, 6·85; 2OMe, 30·25; active H, 0·49%; *M*, 205). A m. p. depression was observed on admixture with 4-hydroxy-6 : 7-dimethoxyquinoline,[2] m. p. 232—234°, $\lambda_{max.}$ 224, 246, 318, and 330 mμ (log ε 4·25, 4·47, 3·99, and 4·01, respectively), $\lambda_{max.}$ (mull) 6·08, 6·19, and 6·43 μ. Edulitine gave a yellow colour with 20% aqueous potassium hydroxide and a magenta colour with alcoholic ferric chloride. The *picrate* formed small yellow needles (from methanol), m. p. 189—191° (Found : C, 47·05; H, 3·05. $C_{11}H_{11}O_3N,C_6H_3O_7N_3$ requires C,

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[3] *Inter al.*, Schmidt, *Arch. Pharm.*, 1898, **236**, 324.

[4] Power and Rogerson, *J.*, 1912, **101**, 5.

[5] Sera and Shibuye, *J. Agric. Chem. Soc. Japan*, 1930, **6**, 600.

[6] Araki and Miyashita, *J. Pharm. Soc. Japan*, 1929, **49**, 736.

[7] *Inter al.*, Asahina, Ohta, and Inubuse, *Ber.*, 1930, **63**, 2045.

[8] *Inter al.*, Deulofeu, Labriola, and de Langhe, *J. Amer. Chem. Soc.*, 1942, **64**, 2326.

[9] *Inter al.*, Asahina and Inubuse, *Ber.*, 1930, **63**, 2052.

[10] *Inter al.*, Thomas and Baetcke, *Ber.*, 1912, **45**, 3705; Howell and Robertson, *J.*, 1937, 293.

[11] *Inter al.*, Wessely and Kallab, *Monatsh.*, 1932, **59**, 161.

47·0; H, 3·25%). The *monoacetate* had m. p. 200—201°, $\lambda_{max.}$ 238, 314, and 326 mμ (log ε 4·36, 3·87, and 3·89, respectively) (Found: C, 62·95; H, 5·3. $C_{13}H_{13}O_4N$ requires C, 63·15; H, 5·3%).

Scopoletin.—The chromatogram (from the trunk bark only) after removal of edulein and edulitine was washed with ethyl acetate–methanol (1 : 1); the resulting yellow solid which did not melt below 330° was dissolved in water. Amberlite ion-exchange resin IR-120 (3 parts) was added, the supernatant liquid decanted, and the resin washed with methanol. The combined solutions were evaporated and the residue was crystallized from methanol–ether. This procedure yielded scopoletin as needles, m. p. 203—204°, $\lambda_{max.}$ 228, 297, and 347 mμ (log ε 4·12, 3·67, and 4·07, respectively), $\lambda_{max.}$ (in $CHCl_3$) 5·80, 6·16 (w), and 6·30 μ (Found: C, 62·75; H, 4·25; OMe, 16·2%; *M*, 202. Calc. for $C_{10}H_8O_4$: C, 62·5; H, 4·2; 1OMe, 16·15%; *M*, 192) (lit.,[4] m. p. 203—204°). Scopoletin acetate formed plates (from acetone), m. p. 177°, $\lambda_{max.}$ 224, 277, and 335 mμ (log ε 4·44, 4·07, and 3·95, respectively) (Found: C, 61·7; H, 4·35. Calc. for $C_{12}H_{10}O_5$: C, 61·55; H, 4·3%) (lit.,[4] m. p. 177°). Scopoletin methyl ether, made by means of diazomethane, separated as needles (from methanol), m. p. 144—145° (Found: C, 64·35; H, 4·95; O, 31·05. Calc. for $C_{11}H_{10}O_4$: C, 64·05; H, 4·9; O, 31·05%) (lit., m. p. 145° [5]; 147—148° [6]).

Dictamnine.—This furanoquinoline (from both trunk and root bark) was isolated from the " alkaline " benzene extract and was eluted with benzene–ether (9 : 1). It formed needles (from acetone–hexane), m. p. 132—133°, $\lambda_{max.}$ 236, 309, and 328 mμ (log ε 4·78, 3·96, and 3·88, respectively), $\lambda_{max.}$ (mull) 6·10, 6·27, and 6·41 μ (w) (Found: C, 72·7; H, 4·4; N, 7·05; OMe, 15·5%; equiv., 196; *M*, 194. Calc. for $C_{12}H_9O_2N$: C, 72·35; H, 4·55; N, 7·05; 1OMe, 15·6%; equiv. ≡ *M*, 199). Identity with a sample (m. p. 131—132°) was established through mixed m. p. and infrared comparison. Dictamnine picrate separated from methanol as light yellow prisms, m. p. 165—166° (Found: C, 50·55; H, 2·9; N, 13·3. Calc. for $C_{12}H_9O_2N,C_6H_3O_7N_3$: C, 50·45; H, 2·85; N, 13·1%) (lit.,[7] m. p. 163°).

γ-Fagarine.—This substance (from trunk and root bark) was eluted after dictamnine with benzene–ether (7 : 3). Crystallization from acetone–ether gave rhombs, m. p. 141—142°, $\lambda_{max.}$ 244, 310, and 336 mμ (log ε 4·79, 3·86, and 3·78, respectively), $\lambda_{max.}$ (mull) 6·10, 6·27, and 6·41 μ (w) (Found: C, 68·1; H, 4·85; N, 6·3; OMe, 27·05%; equiv., 215; *M*, 201. Calc. for $C_{13}H_{11}O_3N$: C, 68·1; H, 4·85; N, 6·1; 2OMe, 27·05%; equiv. ≡ *M*, 229). An authentic sample, m. p. 141—142°, was identical (mixed m. p.; infrared). The picrate, yellow plates from methanol, had m. p. 175—176° (Found: C, 49·95; H, 3·0; N, 12·4. Calc. for $C_{13}H_{11}O_3N,C_6H_3O_7N_3$: C, 49·8; H, 3·1; N, 12·2%) (lit.,[8] m. p. 177°).

Skimmianine.—Skimmianine (from trunk bark only) was eluted with benzene–ether (1 : 1) directly after γ-fagarine. It separated from methanol as wedges, m. p. 178°, $\lambda_{max.}$ 248, 320, and 331 mμ (log ε 4·88, 3·91, and 3·91, respectively), $\lambda_{max.}$ (mull) 6·10, 6·25, and 6·40 μ (w) (Found: C, 64·7; H, 4·9; N, 5·65; OMe, 32·45; equiv., 223; *M*, 236. Calc. for $C_{14}H_{13}O_4N$: C, 64·85; H, 5·05; N, 5·4; 3OMe, 35·9%; equiv. ≡ *M*, 259). Identity with an authentic specimen, m. p. 178—179°, was established in the usual way. The picrate formed yellow needles (from methanol), m. p. 195—196° (Found: C, 49·2; H, 3·55; N, 11·6. Calc. for $C_{14}H_{13}O_4N,C_6H_3O_7N_3$: C, 49·2; H, 3·3; N, 11·5%) (lit.,[9] m. p. 195—197°).

Edulinine.—This *alkaloid* (from both trunk and root bark) was obtained by chromatography of the " alkaline " methylene chloride extract on silica. The fractions eluted with ethyl acetate separated from this solvent as plates, m. p. 140—142°, $\lambda_{max.}$ 228, 274, 282, and 324 mμ (log ε 4·61, 3·93, 3·90, and 3·91, respectively), $\lambda_{max.}$ (mull) 6·10 and 6·25 μ (Found: C, 65·85; H, 7·2; N, 4·8; OMe, 10·8; *M*, 262. $C_{16}H_{21}O_4N$ requires C, 65·95; H, 7·25; N, 4·8; 1OMe, 10·65%; *M*, 291). The methylenedioxy-group was absent, as indicated by the gallic acid colour test. Likewise the vanillin test for indoles was negative. Edulinine gave an intense yellow colour with tetranitromethane.

Bergapten.—This substance (from root bark only) was isolated from the " acid " benzene extract by repeated chromatography on alumina. The first fractions eluted with benzene–ether (9 : 1) on crystallization from methanol gave bergapten as needles, m. p. 187—188°, $\lambda_{max.}$ 250, 260, 268, and 310 mμ (log ε 4·24, 4·21, 4·24, and 4·16, respectively), $\lambda_{max.}$ (mull) 5·78, 6·13, 6·21, and 6·30 μ (Found: C, 66·7; H, 4·0; O, 29·3; OMe, 14·7%; *M*, 212. Calc. for $C_{12}H_8O_4$: C, 66·65; H, 3·75; O, 29·6; 1OMe, 14·35%; *M*, 216) (lit.,[10] m. p. 188—189°).

Successive nitration, reduction, and oxidation of bergapten, carried out as described previously,[10] yielded bergaptenquinone, m. p. and mixed m. p. 250—253°.

iso*Pimpinellin.*—This compound (from root bark only) was eluted with benzene–ether (9 : 1) after bergapten. It formed pale yellow needles (from methanol), m. p. 149—150° (Found: C, 63·6; H, 4·25. Calc. for $C_{13}H_{10}O_5$: C, 63·4; H, 4·1%). The m. p. was undepressed on admixture with the sample (m. p. 150—151°) described in the previous paper and the infrared and ultraviolet spectra were identical.

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