[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF WAYNE UNIVERSITY]

TERPENOIDS. II.[1] EXPERIMENTS IN THE CAFESTOL SERIES

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One of the important constituents of the non-saponifiable fraction of coffee oil is a substance $C_{20}H_{28}O_3$ named cafestol (formerly "cafesterol") which is invariably accompanied by a closely related substance referred to as kahweol. Initial isolation experiments by Bengis and Anderson (1) and by Slotta and Neisser (2) were soon followed by extensive structure investigations by Slotta (3) and Hauptmann (4, 5) in Brazil; by Wettstein and collaborators (6–11) in Switzerland; and by Chakravorty, Levin, and co-workers (12–14) in this country. These studies were prompted by the erroneous report (2) of the estrogenic activity of cafestol, subsequently corrected (6, 13, 15) and by the original impression that the substance possessed a steroid skeleton.

The extensive degradation experiments of the Swiss workers (6–11), though not leading to a definite structure proposal, resulted in the conclusion that cafestol is diterpenoid in nature. In addition to the earlier elucidated (3, 4) presence of two of the oxygen atoms in a glycol grouping —C(OH)—CH_2OH, the Swiss investigators (9) concluded that the third oxygen atom, previously assumed to be an inert hydroxyl (3), carbonyl (4), or cyclic enol ether (14) function, formed part of a furan ring. Kahweol, though never isolated in a pure state because of its lability, is believed to be a tetradehydrocafestol on the basis of reduction and peracid titration experiments (11).

Recently, two alternate suggestions concerning the nature of the third oxygen atom of cafestol have been advanced: (a) Fieser and Fieser (16) suggested that the third oxygen atom was actually present as a lactonic carbonyl joined to the tertiary hydroxyl group and they interpreted the ultraviolet absorption maximum at 226 mμ (14) as indicating an α,β-unsaturated lactone grouping.

(b) Ferrari (17) repeated the isolation of cafestol and on the basis of the infrared spectrum of cafestol *acetate* concluded that *cafestol* possessed a carbonyl group (*sic*), which would automatically eliminate a furan ring from consideration. Subsequently (18), Ferrari claimed the conversion of cafestol to androstane, thus reintroducing the earlier discarded (7, 9, 13) postulate of a steroid skeleton, and he indicated also a general similarity—structurally as well as therapeutically (19) — between cafestol and cortisone.

In view of these conflicting reports and the fact that the structure of this intriguing substance is still unknown, we have undertaken an investigation of this problem in this laboratory. The first experiments were concerned with establishing the identity of the third oxygen atom and to determine whether cafestol is diterpenoid or steroidal in nature. Our initial conclusions, based to a consid-

[1] Paper I, Djerassi, Geller, and Lemin, *J. Am. Chem. Soc.*, **75**, 2254 (1953).

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erable extent upon an examination of the infrared and ultraviolet spectra of certain key derivatives of cafestol are reported in the present paper and are in substantial agreement with the partial structures proposed by Wettstein, *et al.* (10).

The extraction of cafestol from the oil of green Santos Bourbon coffee was carried out essentially according to published procedures (2, 5b) and yielded approximately 10% of crude cafestol. In a representative experiment described in the experimental section, the first crop (*ca.* 5%) exhibited m.p. 152–155°, $[\alpha]_D^{24}$ −148°, $\lambda_{max.}^{EtOH}$ 223, 290 mμ, log ε 3.75, 3.28 while the second crop (*ca.* 5%) possessed m.p. 150–153°, $[\alpha]_D^{24}$ −177°, $\lambda_{max.}^{EtOH}$ 223, 290 mμ, log ε 3.66, 3.63. These data are in good agreement with those observed by other workers (5, 6, 8, 11) and indicate (11) the presence of approximately 15–20% of kahweol. As demonstrated clearly by Wettstein, *et al.*, (11) the accompanying kahweol (as the acetate) should possess strong levorotation ($[\alpha]_D$ *ca.* −350°) and a pronounced ultraviolet absorption maximum at 290 mμ (log ε *ca.* 4.1); it is thus possible to estimate the kahweol content of crude cafestol preparations simply on the basis of these two physical constants. It is noteworthy that our crude preparations were practically colorless and proved to be stable to exposure to air and light. The infrared spectrum of such a crude sample of cafestol is shown in Fig. 3 and demonstrates unequivocally the complete absence of carbonyl absorption. This automatically excludes from consideration the presence of a lactone ring (16) in either cafestol or kahweol and similarly eliminates the claim of Ferrari (17, 18) that cafestol contains an inert keto group, a conclusion based upon the infrared spectrum of cafestol *acetate* and the presence of an ultraviolet absorption maximum at 288 mμ, log ε 2.18, presumably typical of an isolated carbonyl group (*vide infra*). We were fortunate in obtaining[4] a sample of Ferrari's cafestol and its infrared and ultraviolet spectra proved to be identical in all respects with our material. Acetylation of our crude cafestol produced a monoacetate with constants in good agreement with those reported in the literature (6) (ultraviolet absorption spectrum in Fig. 1). Its infrared spectrum exhibited a pronounced hydroxyl band at 2.82 μ, due to the tertiary hydroxyl group, and the expected ester carbonyl band at 5.80 μ.

Attempts in our hands to remove the acid-labile kahweol impurity from crude cafestol by chromatography on Florex or silica gel (8) did not result in any appreciable reduction of the negative rotation or the ultraviolet absorption at 290 mμ. However, purification was readily accomplished by sodium-ethanol reduction[5] (11) and one such treatment yielded cafestol with $[\alpha]_D^{24}$ − 97°, $\lambda_{max.}^{EtOH}$ 224, 290 mμ, log ε 3.77, 1.43. The infrared spectrum of this purified material is shown in Fig. 4, while that of the corresponding acetate is reproduced in Fig. 5. The latter was identical with that of "isocafesterol acetate" (14),[6] thus confirming

[4] We are indebted to Simes, S.P.A., Milano, Italy for this specimen.

[5] Ferrari (17) used this same purification scheme and it is not clear how a carbonyl group, even if it had been present originally, could have survived such treatment since even 11-keto steroids are reduced readily under such conditions (*inter al.*, Herzog, Oliveto, Jevnik, and Hershberg, *J. Am. Chem. Soc.*, **74**, 4470 (1952)).

[6] We are indebted to Dr. R. H. Levin of the Upjohn Company, Kalamazoo, Michigan for sending us a sample of "isocafesterol acetate".

Wettstein's suggestion (11) that "isocafesterol" is essentially purified cafestol and does not involve a rearrangement of the double bond system. It is interesting to note that no appreciable differences were noted in the infrared spectra of

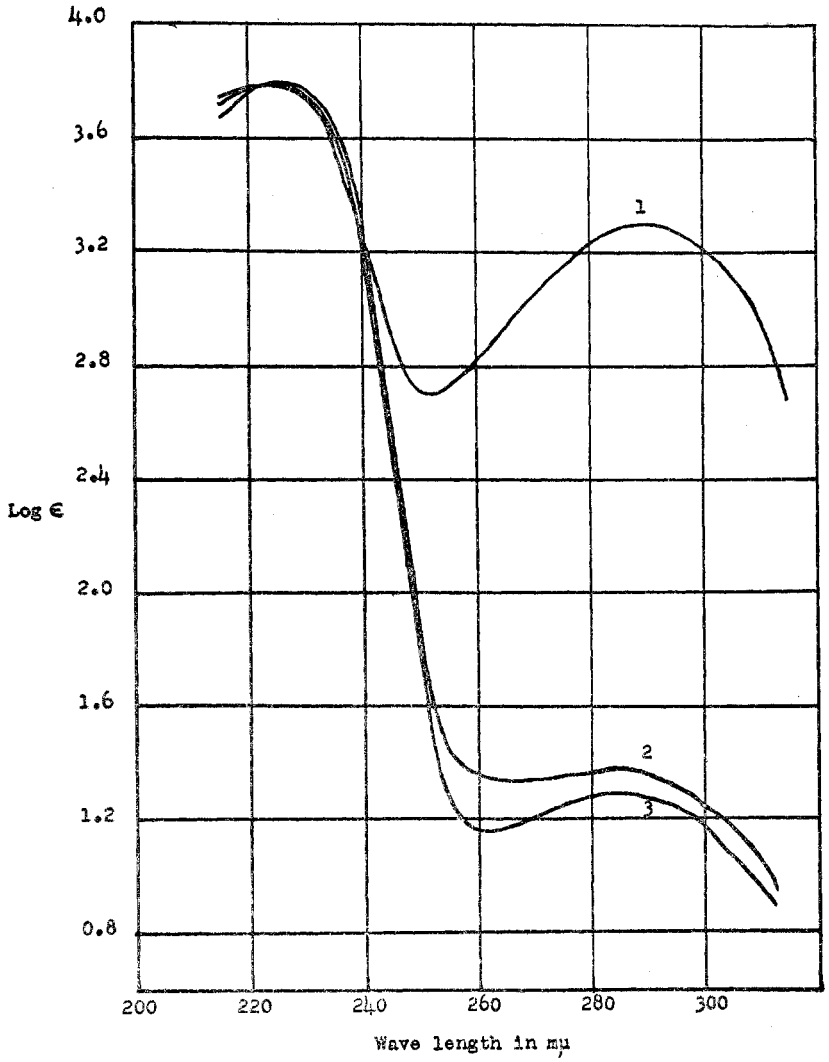


FIG. 1. ULTRAVIOLET ABSORPTION SPECTRA OF: 1. Acetate of crude cafestol. 2. Cafestol acetate regenerated from maleic anhydride adduct of acetate of purified cafestol. 3. Acetate of purified cafestol.

crude and purified cafestol samples. As demonstrated by the absence of a carbonyl band in the infrared absorption spectrum (Fig. 4) of purified cafestol, the low extinction (log ϵ 1.43) at 288 mμ cannot be due to an isolated carbonyl group as suggested by Ferrari (17, 18) but rather is due to traces of kahweol which was not reduced during the sodium-ethanol treatment.

Having disposed of the presence of a ketonic or lactonic carbonyl group in cafestol, we now turn to a consideration of the chromophoric systems found in cafestol and cafestol-kahweol mixtures. Wettstein, *et al.*, (6) recorded the smooth

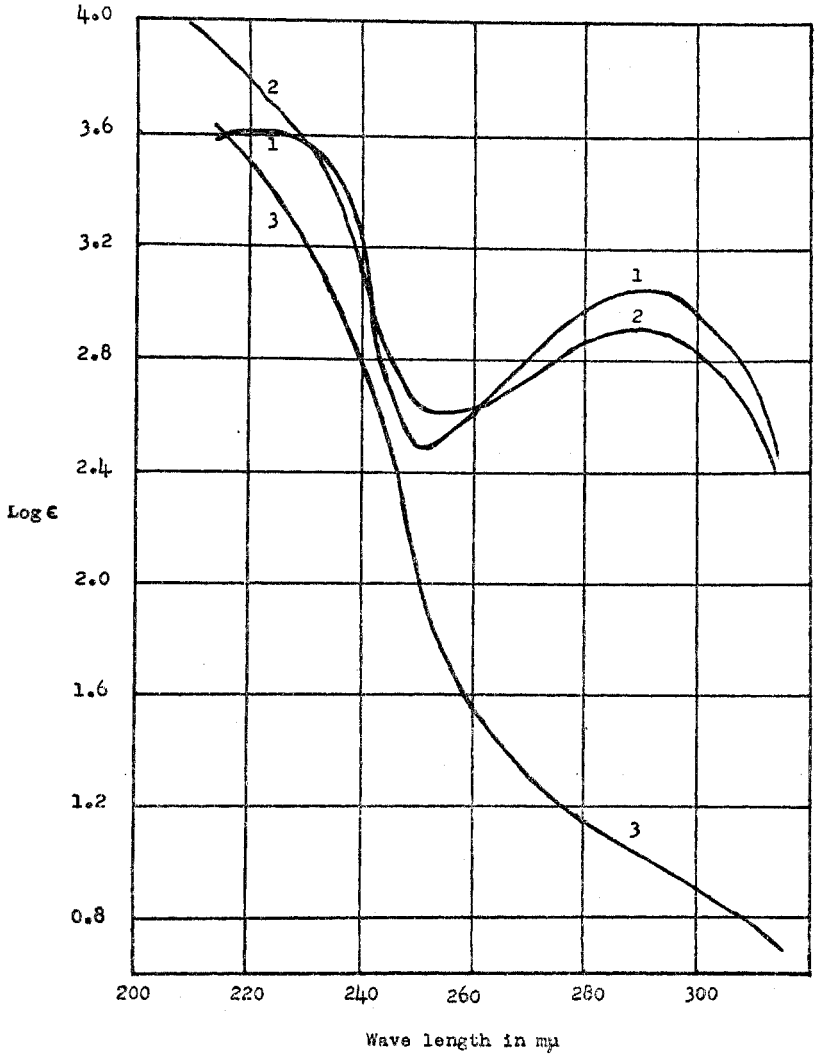
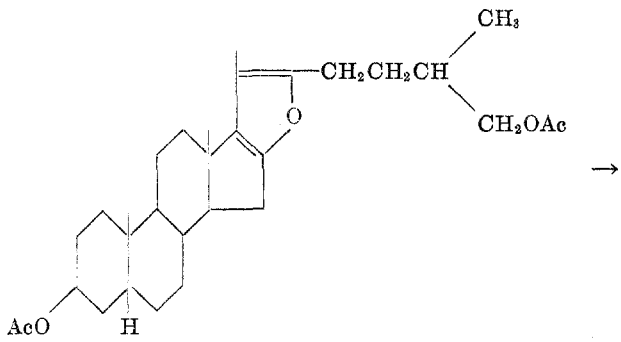


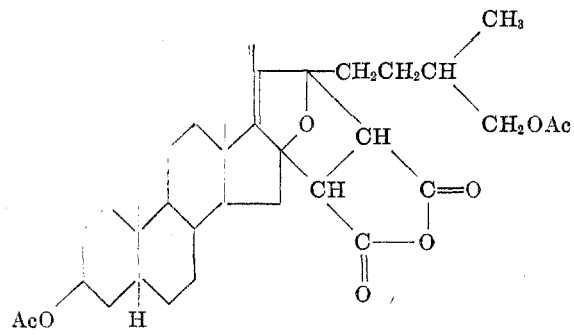
FIG. 2. ULTRAVIOLET ABSORPTION SPECTRA OF: 1. Acetate of crude cafestol. 2. Maleic anhydride adduct of acetate of crude cafestol (1). 3. Maleic anhydride adduct of acetate of purified cafestol.

formation of a maleic anhydride adduct of cafestol with disappearance of the maximum at 290 mμ. Whether the chromophore responsible for the 224 mμ maximum in cafestol is involved in maleic anhydride formation cannot be deduced from Wettstein's spectroscopic data (6), since measurements were only started from *ca.* 230 mμ onwards and the maleic anhydride adduct itself shows high end

absorption (*cf.* Fig. 2). In fact, Wettstein's results have been interpreted (16) as possibly involving only reaction of maleic anhydride with the kahweol impurity but this appears unjustified because of the high yield of adduct obtained. This point has now been settled unambiguously. When *crude* cafestol acetate containing *ca.* 10% of kahweol (*cf.* Fig. 2) was treated with maleic anhydride, there was obtained very readily an adduct, the ultraviolet absorption spectrum (Fig. 2) of which shows *practically the same extinction at 290 mμ as the starting material*, but which does not exhibit anymore the band at 224 mμ. Instead, there is observed continuous increased absorption down to 200 mμ[7] and precisely the same observation was made with the steroidal furan derivative I (20) ($\lambda_{max.}^{EtOH}$ 226 mμ), the maleic anhydride adduct (II) of which exhibits only terminal absorption.[8] It is clear, therefore, that adduct formation involves only *a furan ring in cafestol* and the present spectroscopic (*cf.* analogy to I) and earlier chemical data (9) coupled with the characteristic color reactions (9) are completely compatible with such a view.



I



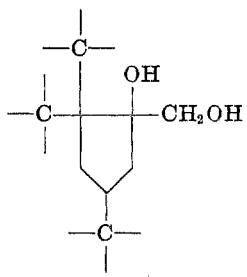
II

[7] Kindly measured by Mr. A. Bowers, University of Manchester, England, with a Unicam SP 500 spectrophotometer.

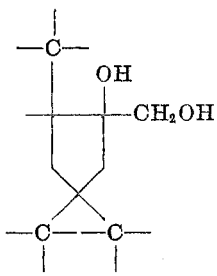
[8] The extinction values down to 200 mμ in each case are typical of tetrasubstituted double bounds (*Cf.* Halsall, *Chemistry & Industry*, 867 (1951); Bladon, Henbest, and Wood, *J. Chem. Soc.*, 2737 (1952)) but this may be fortuitous and is hardly interpretable in view of the presence of the anhydride grouping. A tetrasubstituted olefinic linkage in the cafestol derivative would require fusion of the furan ring to the rest of the molecule at the 3,4-positions which appears excluded on the basis of the hydrogenation experiments (ref. 7).

The ultraviolet absorption spectrum of the maleic anhydride adduct of *pure* cafestol acetate (Fig. 2) is the same as that of the adduct of the crude material except for the fact that the 290 mμ maximum is now missing. Regeneration of cafestol acetate from this pure adduct again shows (Fig. 1) the pronounced furan maximum at 224 mμ and only very slight absorption at 290 mμ. It can safely be concluded, therefore, that the 290 mμ maximum in crude cafestol is due to the kahweol impurity (*cf.* ref. 11) and that *the chromophore in kahweol responsible for this maximum is a homoannular diene system, unreactive towards maleic anhydride (under the conditions used), and not in conjugation with the furan ring.* The hypothetical diunsaturated lactone formulation (16) has already been eliminated by the infrared absorption spectrum. It may be pertinent to mention at this point that Ferrari (18) in his recent formulation of cafestol as a keto steroid implies that a diene system is responsible for the 224 mμ absorption maximum. It should be noted that it is patently impossible to place a heteroannular diene system (the only type that would absorb at such a low wave length), which reacts readily with maleic anhydride, into an intact C_{19} steroid nucleus. It is obvious, therefore, that Ferrari's steroid formulation for cafestol is untenable.

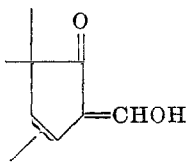
There are two other structural aspects of the cafestol problem which can be solved unambiguously by a spectroscopic investigation, namely the size of the rings connected to the furan ring and the glycol grouping respectively. Wettstein and co-workers (6) were able to show that the glycol grouping of cafestol is attached to a ring since lead tetra-acetate oxidation furnished a C_{19} cyclic ketone, epoxynorcafestadienone. The corresponding tetrahydro ketone upon ring opening with sodium hypoiodite led to a C_{19} dibasic acid which furnished an anhydride. On the basis of Blanc's rule, this would indicate that the original ring was five-membered but it was found that one of the carboxyl groups in the dibasic acid was extremely hindered, and hence probably attached to a quaternary carbon atom, and that the ketone did not condense (8) with aromatic aldehydes, in contrast to 17-keto steroids. This led to the partial formulation IIIa or IIIb, a type of structure in which Blanc's rule for the corresponding six-membered ketone has been known to fail several times (21).



IIIa



IIIb



IV

We have repeated the preparation of epoxynorcafestadienone by lead tetra-acetate oxidation of both crude and purified cafestol. In each instance, there was obtained a ketone which showed only a single, sharp infrared band in chloroform solution at 5.76 μ (Fig. 6). Infrared examination in carbon disulfide solution in

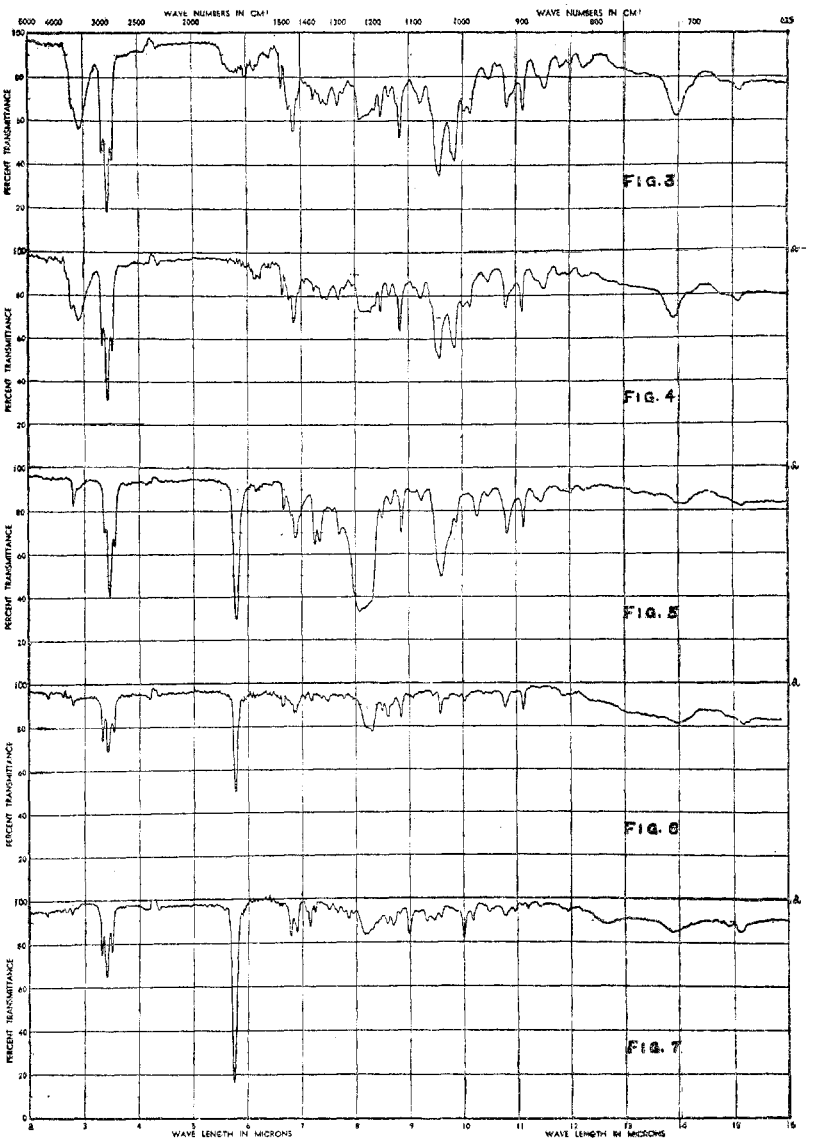


FIG. 3. INFRARED ABSORPTION SPECTRUM OF CRUDE CAFESTOL
FIG. 4. INFRARED ABSORPTION SPECTRUM OF PURIFIED CAFESTOL (sodium-ethanol reduction)
FIG. 5. INFRARED ABSORPTION SPECTRUM OF THE MONOACETATE OF PURIFIED CAFESTOL
FIG. 6. INFRARED ABSORPTION SPECTRUM OF EPOXYNORCAFESTADIENONE
FIG. 7. INFRARED ABSORPTION SPECTRUM OF DIKETONE X

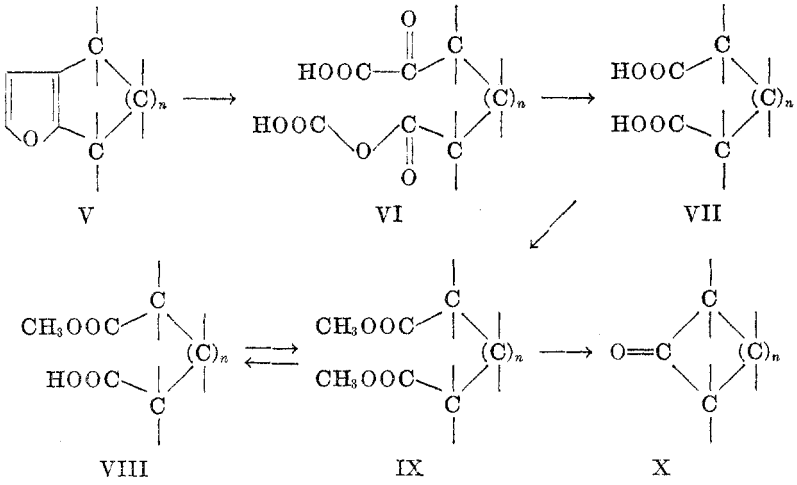
an instrument of high resolution[9] (± 1 cm.$^{-1}$) gave a value of 1742 cm.$^{-1}$ in excellent agreement with the recorded value for five-membered ketones in 17-

[9] We are grateful to Dr. R. Norman Jones of the National Research Council, Ottawa, for this information.

keto steroids (22) and even in cases where this five-membered ring is fused to two adjacent rings (23). The assumption of *a five-membered ring bearing the glycol grouping in cafestol* is thus justified and furthermore, it can be stated that the homoannular diene system of kahweol is not present adjacent to the glycol grouping since no evidence (infrared or ultraviolet) of α,β-unsaturated ketone formation could be detected in the lead tetra-acetate oxidation product of kahweol-containing cafestol.

While the Swiss workers (8) were unable to effect condensation of epoxynorcafestadienone with aromatic aldehydes and therefore were led to the assumption of the presence of one or two substituents (*cf.* IIIa and IIIb) adjacent to the methylene group, we found that epoxynorcafestadienone condensed readily with ethyl formate to yield the corresponding α-hydroxymethylene ketone (IV). We conclude from this observation that the presence of a substituent adjacent to the methylene group of the ketone is not necessarily justified since the adjoining ring juncture might possibly have an effect on the reactivity of this methylene group and, hence, prevent ready condensation with aromatic aldehydes.

The attachment of the furan ring to the rest of the molecule was indicated chiefly through oxidation experiments, notably the course of the ozonization (10), and the latter was formulated as follows:



The dibasic acid VII, obtained from the ozonization of epoxynorcafestadienone (V), could not be crystallized, but upon methylation afforded a crystalline dimethyl ester (IX). Saponification of the latter yielded a crystalline monomethyl ester (VIII) which could be reconverted to IX thus demonstrating the tertiary or quaternary nature of the carbon atom to which one of the carboxyl groups of the ozonization product VII was attached. Dieckmann condensation of the dimethyl ester IX or pyrolysis of the original dibasic acid VII led to a diketone X, in which one of the keto groups is known to be part of a five-membered ring (*vide supra*). The above reaction sequence does not differentiate between a five-

(X, n = 2) or six-membered ring ketone (X, n = 3) for the second carbonyl group in the diketone X, and this in turn leaves open the question whether the ring adjacent to the furan ring is six or seven-membered.

We have repeated the above described conversion of epoxynorcafestadienone (V) to the diketone X since the latter appeared to us an eminently suitable intermediate for further degradation experiments now under way in this laboratory. In our hands, the pyrolysis of VII (via the previously undescribed anhydride) was superior to the sequence proceeding through the dimethyl ester IX and we were able to confirm and extend the observations recorded by the Swiss workers (10). The infrared spectrum of the diketone X, shown in Fig. 7, exhibits a single carbonyl band at 5.76 μ, of considerably greater intensity than that found in the starting material, epoxynorcafestadienone (Fig. 6) thus proving the presence of *two* five-membered ring ketones, and this was confirmed by infrared examination of the diketone in an instrument of very high resolution.[9] *The presence in cafestol of a six-membered ring fused to a furan nucleus is thus established.* It is hoped that the connection between this moiety and the terminal five-membered ring bearing the glycol grouping will be established by degradation experiments of the diketone X. It should be noted that unless one assumed the presence of a masked and hitherto undetected double bond, cafestol must possess five rings. The formation of such a double bond, unreactive towards perbenzoic acid (*cf.* 24) and catalytic hydrogenation, is by no means excluded since it could have been produced in the sodium-alcohol reduction by 1,4-addition to the homoannular diene system of kahweol.

EXPERIMENTAL[10]

Isolation of cafestol. The isolation procedure is patterned after that of Slotta (2) and Hauptmann and Franca (5b).

In initial experiments, ground, green Santos Bourbon coffee beans were extracted with peroxide-free ether in a Soxhlet extractor continuously for 26 hours in an atmosphere of nitrogen and the ether was evaporated to dryness yielding about 10% of coffee oil. For our subsequent work, aliquots were taken of one homogenous 10 kg. batch of coffee oil, which was generously supplied by General Foods, Inc., Hoboken, N. J., and which had been obtained by trichloroethylene extraction of green Santos Bourbon beans.

A mixture of 125 g. of coffee oil (General Foods, Inc.) and 300 cc. of petroleum ether (b.p. 30–60°) was cooled overnight and the insoluble material, predominantly containing caffeine, was centrifuged and discarded. The solvent was removed under reduced pressure and the oil was stirred under at atmosphere of nitrogen overnight at 23° with 175 cc. of 10% aqueous sodium hydroxide solution. At the end of this period, 350 cc. of water and 235 cc. of 95% ethanol were added, stirring was continued for five hours, and the solution was then extracted continuously in an atmosphere of nitrogen with ether for 42 hours. The ether extract was washed several times with water, the washings were passed once through ether, and the combined organic solutions were dried over sodium sulfate, concentrated to a small volume, and diluted with 600 cc. of petroleum ether (this addition was not always necessary). After cooling overnight, the light tan-colored crystals were collected and dried *in*

[10] Melting points are uncorrected. Rotations were measured in chloroform and ultraviolet absorption spectra in 95% ethanol solution. The infrared spectra were obtained with a Baird Associates recording double beam spectrophotometer using a cell thickness of 0.1 mm. (chloroform solution).

vacuo; yield, 5.97 g., m.p. 152–155°, $[\alpha]_D^{24}$ −148°, $\lambda_{max.}^{EtOH}$ 223, 290 mμ, log ε 3.75, 3.28, infrared spectrum in Fig. 3. Concentration of the filtrate and chilling yielded a second crop (6.07 g.) with m.p. 150–153°, $[\alpha]_D^{24}$ −177°, $\lambda_{max.}^{EtOH}$ 223, 290 mμ, log ε 3.66, 3.63.

Acetylation of a sample of the first crop of crude cafestol with acetic anhydride and pyridine at room temperature overnight afforded in 93% yield the crude acetate with m.p. 159–162°. One recrystallization from methanol gave colorless crystals with m.p. 163–166°, $[\alpha]_D^{24}$ −123°, $\lambda_{max.}^{EtOH}$ 223, 290 mμ, log ε 3.79, 3.29 (Fig. 1), which corresponds (11) to cafestol acetate containing *ca.* 15% of kahweol acetate.

Purification of cafestol. Attempts to purify the above described cafestol or cafestol acetate by chromatography on Florex (Floridin Co., 60–100 mesh) or silica gel (Fisher Scientific Co., 28–200 mesh) resulted in 86–98% recovery of material with essentially the same physical constants as the starting material.

Satisfactory purification was accomplished by following the directions of Wettstein, *et al.*, (11). In one representative experiment, 12.5 g. of crude cafestol ($\lambda_{max.}^{EtOH}$ 224, 289 mμ, log ε 3.74, 3.39) upon reduction with 108 g. of sodium in 1 l. of abs. ethanol yielded 64% of material, m.p. 154–157° ($\lambda_{max.}^{EtOH}$ 288 mμ, log ε 2.15) and 18% of a second crop with $\lambda_{max.}^{EtOH}$ 288 mμ,g ε 2.34. Repeated reduction of the first crop followed by recrystallization from ether afforded 74% of cafestol with m.p. 156–158°, $[\alpha]_D^{24}$ −97°, $\lambda_{max.}^{EtOH}$ 224, 290 mμ, log ε 3.77, 1.43; infrared absorption spectum in Fig. 4.

Acetylation of this material in the usual manner and recrystallization from methanol yielded an analytical sample of cafestol acetate with m.p. 164–166° (corr.), $[\alpha]_D^{24}$ −90°, $\lambda_{max.}^{EtOH}$ 224, 288 mμ, log ε 3.80, 1.30 (Fig. 1), infrared absorption spectrum, Fig. 5.

Anal. Calc'd for $C_{22}H_{30}O_4$: C, 73.74; H, 8.35.

Found: C, 73.98; H, 8.44.

Maleic anhydride adduct of cafestol acetate. Crude cafestol acetate (m.p. 151–157°, $\lambda_{max.}^{EtOH}$ 224, 288 mμ, log ε 3.74, 3.07) was treated with maleic anhydride in benzene solution at room temperature for 4 days exactly as described by Wettstein, *et al.*, (6) and the crude adduct which precipitated from the benzene solution was dried; yield, 83%, m.p. 182–184°, $\lambda_{max.}^{EtOH}$ 289 mμ, log ε 2.95. The ultraviolet absorption spectrum of the starting material and adduct are reproduced in Fig. 2.

Anal. Calc'd for $C_{26}H_{32}O_7$: C, 68.42; H, 7.02.

Found: C, 68.89; H, 7.24.

A similar reaction with cafestol acetate, purified by sodium-ethanol reduction, yielded 85% of adduct with m.p. 188–190° (after recrystallization from acetone), no selective absorption in the ultraviolet (*cf.* Fig. 2).

Anal. Calc'd for $C_{26}H_{32}O_7$: C, 68.42; H, 7.02.

Found: C, 68.49; H, 6.90.

A small sample (49 mg.) of this adduct was sublimed for 1.6 hours at 165° and 0.01 mm., yielding a sublimate of cafestol acetate with m.p. 162–164°, $[\alpha]_D^{24}$ −89.5° $\lambda_{max.}^{EtOH}$ 224, 288 mμ, log ε 3.80, 1.35 (Fig. 1).

Epoxynorcafestadienone. The small scale lead tetra-acetate oxidation reported by Wettstein, *et al.*, (6) was found to be applicable to larger amounts without change. Thus, oxidation of 4.0 g. of the above described purified cafestol with 6.5 g. of lead tetra-acetate yielded 71% of the ketone with m.p. 173–174°. Two additional recrystallizations furnished the analytical sample with m.p. 176–178°, $[\alpha]_D^{24}$ − 102°, $\lambda_{max.}^{EtOH}$ 224, 289 mμ, log ε 3.82, 1.71. The infrared spectrum (Fig. 6) shows a carbonyl band in chloroform solution at 5.76 μ ($\nu_{max.}^{CS_2}$ 1742 ± 1 cm.$^{-1}$ in an instrument of high resolution),[9] typical (22, 23) of five-membered ring ketones. Reported (6), m.p. 176–178°, $[\alpha]_D$ − 99°.

Anal. Calc'd for $C_{19}H_{24}O_2$: C, 80.24; H, 8.51.

Found: C, 80.22; H, 8.38.

Lead tetra-acetate cleavage of a kahweol-containing sample of cafestol ($\lambda_{max.}^{EtOH}$ 290 mμ, log ε 3.42) furnished in essentially the same yield a pale yellow crude ketone with m.p. 155–169°, $\lambda_{max.}^{EtOH}$ 224, 290 mμ, log ε 3.76, 3.29, $\lambda_{max.}^{CHCl_3}$ 5.76 μ, thus demonstrating that the kahweol chromophore was not in conjugation with the keto group.

A small sample of epoxynorcafestadienone (79 mg.) was converted into its maleic anhydride adduct in the above-mentioned manner and recrystallized from acetone-ether; yield, 78 mg., m.p. 192° (dec.), no selective absorption in the ultraviolet but progressively high log ϵ values down to 200 mμ.[7]

Sodium borohydride reduction of epoxynorcafestadienone resulted in smooth reduction of the keto group (no carbonyl absorption in the infrared) but the alcohol could not be crystallized, possibly due to the formation of two epimers. The ultraviolet absorption was identical with that of the starting ketone.

α-Hydroxymethylene-epoxynorcafestadienone (IV). A solution of 454 mg. of epoxynorcafestadienone was added with swirling to a cooled mixture of 240 mg. of ethyl formate, 170 mg. of commercial sodium methoxide, and 2 cc. of dry benzene. After standing overnight in an atmosphere of nitrogen, ether and water were added, and the organic layer was separated and extracted several times with dilute sodium hydroxide solution. The combined alkaline extracts were acidified and the colorless hydroxymethylene derivative was collected (417 mg., m.p. 195–196° (dec.)) and recrystallized from benzene-ethanol; m.p. 209–210° (dec.), $[\alpha]_D^{24}$ −218°, $\lambda_{max.}^{CHCl_3}$ 5.95 μ, purple color with alcoholic ferric chloride. From the original ether solution, there was recovered 64 mg. of starting material.

Anal. Calc'd for $C_{20}H_{24}O_3$: C, 76.89; H, 7.74.
Found: C, 76.60; H, 7.99.

Ozonization of epoxynorcafestadienone. The following modification has proved quite reproducible and superior to that recorded earlier (10); furthermore, it does not involve standardization of the ozone generator.

Oxygen containing *ca.* 2% of ozone was bubbled slowly through a solution of 3.0 g. of epoxynorcafestadienone in 150 cc. of C.P. ethyl acetate cooled in a Dry Ice-acetone bath until a blue color first appeared (85 minutes) and then continued for an additional 42 minutes. The resulting solution did not give any color with tetranitromethane (in contrast to the strong yellow color produced initially). The solvent was removed *in vacuo* and the residual, colorless, gummy ozonide was decomposed by heating on the steam-bath with 150 cc. of water containing 50 cc. of 6% hydrogen peroxide and the solution was extracted thoroughly with ether and with chloroform. After washing several times with 5% sodium hydroxide solution, the organic layer was washed with water until neutral, dried, and evaporated leaving 140 mg. of neutral material (m.p. 150–205°). The infrared spectrum of this neutral fraction indicated the presence of a five-membered ring ketone as well as a five-membered lactone but a study of its structure has been deferred until larger amounts become available. The alkaline extracts were acidified, extracted with chloroform, washed with water, dried, and evaporated yielding 2.39 g. (73%) of the crude oily dibasic acid VII, ($\lambda_{max.}^{CHCl_3}$ 5.76 and 5.84 μ) which resisted all attempts at crystallization; a similar observation was made by Wettstein and co-workers (10).

The above diacid (500 mg.) was refluxed for four hours with 7.2 cc. of acetic anhydride, the solvent was removed *in vacuo*, and the residue on recrystallization from chloroform-ether yielded 220 mg. (47%) of crystalline, light tan *anhydride* with m.p. 197–199°, $[\alpha]_D^{24}$ −137°, $\lambda_{max.}^{CHCl_3}$ 5.53 and 5.73 μ. Further recrystallization raised the m.p. to 201–202°.

Anal. Calc'd for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64.
Found: C, 69.78; H, 7.99.

The crystalline anhydride was heated at 190–200° and 15 mm. for four hours, the temperature was lowered to 140° and the product was sublimed overnight at that temperature and 0.01 mm. The colorless sublimate (50%) exhibited m.p. 192–195° and showed only a single infrared absorption band at 5.76 μ. Recrystallization from ether and repeated sublimation furnished the analytical sample of the *diketone* X with m.p. 196–198°, $[\alpha]_D^{24}$ −156°, $\lambda_{max.}^{CHCl_3}$ 5.76 μ (Fig. 7); in a high precision instrument,[9] $\nu_{max.}^{CS_2}$ 1744 cm.$^{-1}$ and $\nu_{max.}^{CHCl_3}$ 1737 cm.$^{-1}$ was observed.

Anal. Calc'd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00.
Found: C, 77.93; H, 8.89.

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SUMMARY

Infrared and ultraviolet spectroscopic data are presented for cafestol and a number of transformation products which support the presence in cafestol of a glycol grouping attached to a five-membered ring as well as that of a furan nucleus connected to a six-membered ring.

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