production of glutathione in the TPN system is inhibited by the addition of DPN. Thus, it would appear that TPN is preferentially reduced by the photochemical reducing system produced in bacterial photosynthesis. However, this could be due to the use of spinach pyridine nucleotide reductase, which is specific for TPN with chloroplasts.[3]

TABLE I

PHOTOREDUCTION OF TPN BY *Rhodospirillum rubrum* CHROMATOPHORES AS DEMONSTRATED BY COUPLED ENZYMIC REDUCTION OF OXIDIZED GLUTATHIONE

The reaction mixture consisted of 20 μmoles phosphate buffer *p*H 7.4, 1.2 μmoles TPN, 40 μmoles oxidized glutathione neutralized to *p*H 7.0, 5.4 mg. of a glutathione reductase preparation prepared according to reference 4, 1.8 mg. of a pyridine nucleotide reductase preparation prepared according to directions furnished by A. San Pietro, and *R. rubrum* chromatophores equal to 0.20 mg. bacterial chlorophyll in a final volume of 3.2 ml. The reaction mixture was placed in a Thunberg tube, made anaerobic by evacuations with four alternate flushings with nitrogen gas, following which half the mixture was placed in the side arm and covered with aluminum foil. The Thunberg tube (thus containing an internal dark control of identical composition) was immersed in a water-bath at 30° and illuminated for two hours at approximately 2000 foot candles. Following illumination the glutathione content of the illuminated and non-illuminated portions was determined according to the method of Grunert and Phillips.[6]

Conditions	μmoles GSH present Light	Dark	Light − dark
Complete system	1.81	0.85	0.96
Minus TPN	0.30	.33	− .03
Minus oxidized glutathione	.13	.20	− .07
Boiled GSH reductase	.48	.53	− .05
Boiled pyridine nucleotide reductase	.68	.72	− .04
Boiled chromatophores	.46	.32	.14

(6) R. R. Grunert and P. H. Phillips, *Arch. Biochem.*, **30**, 217 (1951).

DEPARTMENT OF CHEMISTRY
BRIGHAM YOUNG UNIVERSITY
PROVO, UTAH LEO P. VERNON

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TERPENOIDS. XXXIII.[1] THE STRUCTURE AND PROBABLE ABSOLUTE CONFIGURATION OF CAFESTOL

Sir:

Recently[2] we proposed structure I—without the stereochemical implications—for the coffee constituent cafestol and rigorous evidence for the furanoperhydrophenanthrene skeleton was adduced by dehydrogenation[3] and synthesis.[2] The nature of the substituted cyclopentane ring follows from a series of reactions[2,3,4] but its point of attachment is so far based only on the virtual identity of the rotatory dispersion curves[5] of certain 17-nor-16-ketones (II) in the cafestol and phyllocladene series where this structural point has been established[6] by dehydrogenation to retene. The angular methyl group of cafestol (I) was placed[2] at C-10 by analogy to phyllocladene,[6] which in turn is based on analogy to other diterpenes. Quite recently, Haworth and Johnstone[7]—on the basis of certain dehydrogenations—have suggested that the angular methyl group in cafestol (and by inference[8] also in the other members of the phyllocladene group of diterpenes) should be placed at C-5, which would be of considerable biogenetic significance. We wish now to place on the record certain relevant experiments which show that our original[2] structure I with the angular methyl group at C-10 is correct and that Haworth's dehydrogenation results[7] are probably best interpreted as involving rearrangements or reduction of a carboxyl group to methyl.

Hydrogenolytic opening of the furan ring of epoxynorcafestadiene (III)[3] with platinum oxide in acetic acid led to several products including the 3-hydroxy-4-ethyl derivative (m.p. 130–132°, $[\alpha]_D$ −64° (all rotations in $CHCl_3$), found for $C_{19}H_{32}O$: C, 82.58; H, 11.81; O, 6.07) which upon chromium trioxide oxidation and passage over *alkaline* alumina yielded the ketone V (m.p. 86–88°, $\lambda_{max.}^{CHCl_3}$ 5.84 μ, found for $C_{19}H_{30}O$: C, 83.42; H, 11.02; O, 5.99), while a similar reaction sequence on cafestadiene (IV) (m.p. 69–70, $[\alpha]_D$ −156°, found for $C_{20}H_{28}O$: C, 84.05; H, 9.86) provided the ketone VI (m.p. 81–83°, found for $C_{20}H_{32}O$: C, 83.32; H, 11.19). *Both ketones exhibited a negative single Cotton effect curve* (*cf.* ref. 5) *in contrast to the positive one* of 4α-ethyl-cholestan-3-one (m.p. 120–122°, $[\alpha]_D$ +38°, $\lambda_{max.}^{CHCl_3}$ 5.83 μ, found for $C_{29}H_{50}O$: C, 83.69; H, 11.92) prepared by lithium–ammonia reduction of 4-ethyl-Δ^4-cholesten-3-one[9] (m.p. 87–89°, $\lambda_{max.}^{EtOH}$ 251 mμ, log ε 4.07, found for $C_{29}H_{48}O$: C, 84.20; H, 12.04; O, 4.19).

It has been demonstrated[10] with the triterpene ketone friedelin, where the same A/B stereochemistry obtains, that an angular methyl group at C-5 favors the production of an axial alcohol in the lithium aluminum hydride reduction while the equatorial epimer is formed with lithium–ammonia. On the other hand, if the angular methyl group is located at C-10, both methods of reduction should provide the equatorial alcohol as shown by the formation of 4α-ethylcholestan-3β-ol (m.p. 141–143°, $[\alpha]_D$ +24°, found for $C_{29}H_{52}O$: C, 83.62; H, 12.23) from the model 4α-ethylcholestan-3-one. When the ketone V, derived from cafestol, was subjected to *either* reduction procedure, the principal product in each case was the *same* alcohol VII (m.p. 151–153°, $[\alpha]_D$ −73°, found for $C_{19}H_{32}O$: C, 82.69; H, 11.38; O, 5.98) with an equatorial hydroxyl group.[11]

(1) Paper XXXII, C. Djerassi and J. S. Mills, THIS JOURNAL, **80**, Feb. (1958).

(2) H. Bendas and C. Djerassi, *Chemistry and Industry*, 1481 (1955).

(3) C. Djerassi, H. Bendas and P. Sengupta, *J. Org. Chem.*, **20**, 1046 (1955).

(4) See A. Wettstein, F. Hunziker and K. Miescher, *Helv. Chim. Acta*, **26**, 1197 (1943), and earlier references cited therein.

(5) C. Djerassi, R. Riniker and B. Riniker, THIS JOURNAL, **78**, 6362 (1956).

(6) C. W. Brandt, *New Zealand J. Sci. Technol.*, **34B**, 46 (1952).

(7) R. D. Haworth and R. A. W. Johnstone, *J. Chem. Soc.*, 1492 (1957).

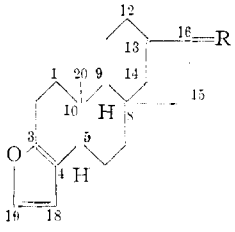
(8) See *Ann. Repts. Chem. Soc.*, **53**, 209 (1957).

(9) Synthesized from Δ^4-cholesten-3-one by the same procedure used recently for the corresponding 4-methyl analog (G. D. Meakins and O. Rodig, *J. Chem. Soc.*, 4679 (1956); F. Sondheimer and Y. Mazur, THIS JOURNAL, **79**, 2906 (1957)).

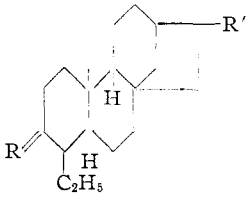
(10) *Cf.* G. Brownlie, F. S. Spring, R. Stevenson and W. S. Strachan, *J. Chem. Soc.*, 2419 (1956).

(11) The orientation of the hydroxyl group in this and several other alcohols derived from cafestol was confirmed by infrared data (alcohol and acetate) and by the elegant quantitative micro-oxidation procedure of J. Schreiber and A. Eschenmoser (*Helv. Chim. Acta*, **38**, 1529 (1955); *cf. ibid.*, **40**, 1391 (1957)).

Further evidence for the location of the angular methyl group at C-10[2] rather than C-5[7] could be provided by bromination experiments. If the angular methyl group were located at C-5, the monobromo derivative of the ketone V should be the axial isomer[12] as demonstrated in the case of friedelin[13] and 19-nor-androstan-17β-ol-3-one acetate (present authors). On the other hand, if the angular methyl group is situated at C-10, an equatorial bromo derivative would be predicted[12] as was indeed found to be the case in the monobromination of the model 4α-ethyl-cholestan-3-one (m.p. 112–114°, $[\alpha]D$ +33°, no u.v. shift but $\lambda_{max.}^{CHCl_3}$ 5.75 μ, found for $C_{29}H_{49}BrO$: C, 70.56; H, 9.73; Br, 16.49) and of the ketone V (m.p. 127–127.5°, $\lambda_{max.}^{CHCl_3}$ 5.73 μ, equatorial type bromo-ketone R.D. curve,[14] found for $C_{19}H_{29}BrO$: C, 64.84; H, 8.21; O, 4.71).



I, R = OH, $-CH_2OH$
II, R = O
III, R = H_2
IV, R = H, $-CH_3$



V, R = O; R′ = H
VI, R = O; R′ = CH_3
VII, R = H, ...OH; R′ = H

The negative Cotton effect of the rotatory dispersion curves of V, VI and the corresponding mono-bromo derivative requires *that the A/B ring juncture is antipodal to that of the other polyterpenes and steroids* and this apparently also applies[5] to the other members of the phyllocladene group including the *Garrya* alkaloids. That diterpenes with the "wrong" absolute configuration are more common than has hitherto been assumed was demonstrated recently with eperuic acid,[15] which possesses an unrearranged diterpene skeleton. The possible biogenetic significance of this unexpected stereochemical feature and additional evidence in favor of stereoformula I for cafestol will be discussed in a detailed paper.

DEPARTMENT OF CHEMISTRY
WAYNE STATE UNIVERSITY
DETROIT, MICHIGAN

CARL DJERASSI
M. CAIS[16a]
L. A. MITSCHER[16b]

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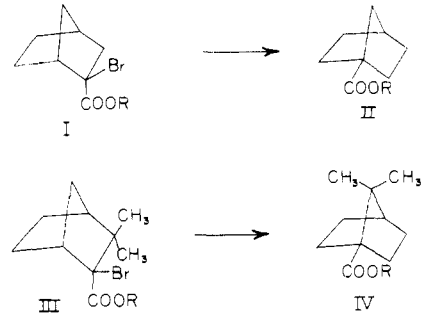
(12) E. J. Corey, THIS JOURNAL, **76**, 175 (1954).
(13) E. J. Corey and J. J. Ursprung, *ibid.*, **78**, 5041 (1956).
(14) *Cf.* C. Djerassi, J. Osiecki, R. Riniker and B. Riniker, *ibid.*, **80**, Feb. (1958).
(15) F. E. King and G. Jones, *J. Chem. Soc.*, 658 (1955); J. D. Cocker and T. G. Halsall, *ibid.*, 4262 (1956); C. Djerassi and D. Marshall, *Tetrahedron*, **1**, 238 (1957).
(16) (a) General Foods Corporation postdoctorate research fellow (1956-1957); (b) U. S. Public Health Service predoctorate research fellow (1956-1957).

THE OBSERVATION OF REARRANGEMENT DURING HYDROGENOLYSIS; A NEW METHOD OF PREPARING BRIDGEHEAD CARBOXYLIC ACIDS

Sir:

Previous studies on the mechanism of hydrogenolysis by means of metals have stressed the occurrence of retained configuration.[1-6] For these cases ionic reaction mechanisms have been suggested. In contrast, the occurrence of almost complete racemization as a result of the hydrogenolysis of carbon–sulfur bonds has been attributed to the intermediacy of free radicals.[7,8] We wish to report the incidence of rearrangement accompanying the hydrogenolysis of carbon–halogen bonds in certain bicyclo[2,2,1]heptane compounds. Well characterized cases of rearrangement during hydrogenolysis have not been discussed previously, to the best of our knowledge.

This observation also affords a novel and a comparatively simple route to the synthesis of bridgehead compounds of bicyclo[2,2,1]heptane, and very possibly other bicyclic skeletons. These substances heretofore have been available only through rather lengthy sequences of reaction.[9,10] Good yields of product were obtained in each of the cases examined. Thus, the bromoacid I (R = H),[11]



when shaken under 40 lb. hydrogen pressure with 10% palladium–charcoal in dilute methanolic potassium hydroxide[12] and the product worked up in the customary manner, gave II (R = H), m.p. 112–113° after one recrystallization from pentane. An elemental analysis, mixed melting point and comparison of infrared spectrum with that of an authentic sample[13] established the identity of the product. The bromoester I (R = CH_3), when treated with powdered zinc in glacial acetic acid

(1) W. A. Bonner, J. A. Zderic and G. S. Casaletto, THIS JOURNAL, **74**, 5086 (1952).
(2) W. A. Bonner, *ibid.*, **76**, 6350 (1954).
(3) W. A. Bonner and J. A. Zderic, *ibid.*, **78**, 3218, 4369 (1956).
(4) E. J. Corey and R. A. Sneen, *ibid.*, **78**, 6269 (1956).
(5) E. J. Corey, M. G. Howell, A. Boston, R. L. Young and R. A. Sneen, *ibid.*, **78**, 5036 (1956).
(6) E. Ott and K. Kramer, *Ber.*, **68**, 1655 (1935).
(7) H. Hauptmann and B. Wladislaw, THIS JOURNAL, **72**, 710 (1950).
(8) W. A. Bonner, *ibid.*, **74**, 1033, 1034, 5089 (1952).
(9) W. von E. Doering, M. Levitz, A. Sayigh, M. Sprecher and W. P. Whelan, Jr., *ibid.*, **75**, 1009 (1953), and private communication with Dr. Doering.
(10) P. D. Bartlett and L. H. Knox, *ibid.*, **61**, 3189 (1939).
(11) The structures of the compounds I and II have been established and will be discussed in a forthcoming publication, from this laboratory.
(12) According to the directions of reference 6 and L. F. Fieser and Wei-Tuan Huang, THIS JOURNAL, **75**, 4837 (1953).
(13) We are indebted to Dr. W. von E. Doering for supplying this reference compound.