

the pellet of CmF_4 . The solution was then centrifuged, the supernatant liquid was transferred to a quartz absorption cell and an aliquot taken for radiochemical assay. Care was taken to maintain the solution at $\leq 10^\circ$ during these manipulations. The cell, containers, etc., all were prechilled in a refrigerator prior to use.

The spectrum was recorded immediately on a Model 14 Cary Spectrophotometer with sample and reference compartments held at 10.5° . Cesium fluoride ($15 M$) was used as the reference solution.

Aqueous $\text{Cm}^{244}(\text{IV})$ is not stable with time but disappears within *ca.* one hour as expected. The diminution of the two principal peaks was followed as a function of time with eleven different readings being obtained for each maximum. A zero-order rate constant of $-1.3 \pm 0.2\%$ /minute was obtained at 10.5° which is consistent with the predicted alpha-induced reduction and curium half-life as described above. The reduction of $\text{Cm}(\text{IV})$ is hastened by some other reaction at 25° as complete disappearance of the oxidized state was noted within 20 minutes at that temperature.

By extrapolation to the time of assay, estimates of the molar extinction coefficients for the two principal maxima were obtained. The location of the observable maxima ($\pm 10 \text{ \AA.}$) in solution and the previously determined maxima for solid CmF_4 ¹² are compared in Table I.

TABLE I

Maxima of aqueous $\text{Cm}(\text{IV})$ in $15 M$ CsF at 10.5°	Maxima of anhydrous CmF_4
3310 \AA.	
3380	
3506	
3565	
3830	3865 \AA.
	4010 } $\text{CmF}_3?$
	4118 }
4514 $\epsilon \cong 160$	4504
4620	4607
6650	6730
6960	6960
7820	7650
8000	7915
8640 $\epsilon = 130$	8560
9100	9100
	10975
	16120

Note that the molar extinction coefficients of $\text{Cm}(\text{IV})$ are considerably greater than those of either aqueous $\text{Cm}(\text{III})$ or $\text{Am}(\text{IV})$. In fact, the positions and magnitudes of the two principal peaks of $\text{Cm}(\text{IV})$ are strongly reminiscent of aqueous $\text{Am}(\text{III})$ with which it is isoelectronic.

After the $\text{Cm}(\text{IV})$ maxima had disappeared (within one hour), diminished $\text{Cm}(\text{III})$ maxima were apparent at *ca.* 4000 \AA. However, most of the $\text{Cm}(\text{III})$ formed from the self-reduction is in the insoluble CmF_3 state and floats on the surface of the sirupy solution.

In addition to the $\text{Cm}(\text{III})$, we noted a small amount of $\text{Am}(\text{III})$ ($\epsilon = 400$) at 5000 \AA. present only after the $\text{Cm}(\text{IV})$ had disappeared. The curium stock was known to contain some americium

impurity; therefore, the americium must have been present as $\text{Am}(\text{IV})$ in solution (with $\epsilon = 30$ for $\text{Am}(\text{IV})$ at 4559 \AA. , such a small concentration could not be detected spectrophotometrically) until after the $\text{Cm}(\text{IV})$ had reduced.

Attempts were made to dissolve CmF_4 in saturated potassium or rubidium fluoride solution but rapid reduction of the curium was observed. Further work is in progress to examine thoroughly the behavior of $\text{Cm}(\text{IV})$ in fluoride media and to obtain a crystalline alkali $\text{Cm}(\text{IV})$ fluoride for X-ray studies.

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OPTICAL ROTATORY DISPERSION STUDIES. LVIII.¹
THE COMPLETE ABSOLUTE CONFIGURATIONS OF
STEVIOI, KAURENE AND THE DITERPENE
ALKALOIDS OF THE GARRYFOLINE AND ATISINE
GROUPS²

Sir:

The recently announced³ interconversion of steviol (I)⁴ and the diterpene alkaloid garryfoline (II)⁵ through $(-)\text{-}\beta\text{-dihydrokaurene}$ ⁶ (dihydro derivative of III)—coupled with various rotatory dispersion measurements^{4,5a,7,8} on ketonic degradation products of these diterpenoids—has resulted in mutually consistent, absolute configurational assignments at all asymmetric centers with the exception of C-9. Earlier summarized, circumstantial arguments^{3,5a,9} led us to favor a 9,10-*anti* backbone in garryfoline (II); if this is correct, then our experimental interconversion⁸ requires a similar stereochemical feature in steviol (I) and $(-)\text{-kaurene}$ (III).^{6,8b} We should now like to report rotatory dispersion measurements on some new steviol and kaurene derivatives, which settle this remaining stereochemical question for this entire group of naturally occurring diterpenoids. Incidental to these studies, it was observed that $(+)\text{-mirene}$ ⁶ is actually a difficultly separable mixture of $(+)\text{-kaurene}$ (antipode of III) and phyllocladene; its stereochemistry,^{8b} therefore, is of no further concern.

Ozonolysis of steviol (I) methyl ester yields⁴ the norketol V, whose positive Cotton effect (Fig. 1) is very similar to that¹⁰ of ketonorepiallogibberic acid

(1) Paper LVII, C. Djerassi, E. J. Warawa, J. M. Berdahl and E. J. Eisenbraun, *J. Am. Chem. Soc.*, **83**, 3334 (1961).

(2) The work at Stanford University was supported by grant No. CRTY-5061 from the National Cancer Institute of the National Institutes of Health, U. S. Public Health Service.

(3) E. Mosettig, P. Quitt, U. Beglinger, J. A. Waters, H. Vorbrueggen and C. Djerassi, *J. Am. Chem. Soc.*, **83**, 3163 (1961).

(4) F. Dolder, H. Lichti, E. Mosettig and P. Quitt, *ibid.*, **82**, 246 (1960).

(5) (a) H. Vorbrueggen and C. Djerassi, *Tetrahedron Letters*, 119 (1961); (b) C. Djerassi, C. R. Smith, A. E. Lippman, S. K. Figdor and J. Herran, *J. Am. Chem. Soc.*, **77**, 4801, 6533 (1955).

(6) L. H. Briggs, B. F. Cain, B. R. Davis and J. K. Wilmshurst, *Tetrahedron Letters*, No. 8, 8 (1959).

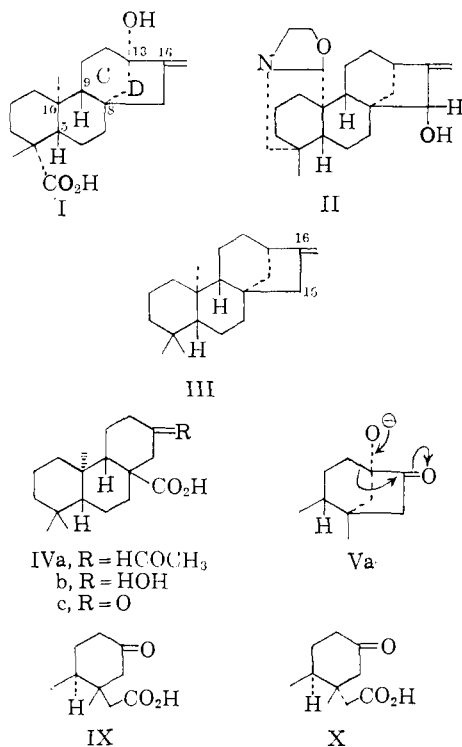
(7) C. Djerassi, R. Riniker and B. Riniker, *J. Am. Chem. Soc.*, **78**, 6362 (1956).

(8) (a) L. H. Briggs, B. F. Cain, B. R. Davis and J. K. Wilmshurst, *Tetrahedron Letters*, No. 8, 13 (1959); (b) L. H. Briggs, B. F. Cain, R. C. Cambie and B. R. Davis, *ibid.*, no. 24, 18 (1960).

(9) A. J. Solo and S. W. Pelletier, *Chem. & Ind.*, 1108 (1960).

(10) See J. F. Grove and T. P. C. Mulholland, *J. Chem. Soc.*, 3007 (1960); J. F. Grove, J. MacMillan, T. P. C. Mulholland and W. B. Turner, *ibid.*, 3049 (1960).

and which possesses the identical C/D absolute configuration. Treatment of the norketol V with potassium *t*-butoxide (4 hr. reflux in *t*-butanol-tetrahydrofuran) or preferably with butyllithium (3 hr. refluxing in ether-tetrahydrofuran) furnished in over 50% yield the *isonorketol* VII (m.p. 197–199°, $[\alpha]_D -62.5^\circ$ (all rotations in chloroform); *Anal.* found for $C_{20}H_{30}O_4$: C, 71.76; H, 9.42), the change resembling mechanistically (Va) the usual steroid D-homo rearrangement. The *isonorketol* VII exhibited a strong negative Cotton effect (Fig. 1), as was the case with *isosteviol* (VII, hydroxyl group replaced by methyl) or *gibberic acid*.¹⁰ Periodate cleavage of the norketol V provided the corresponding *seco*-acid VI (m.p. 178–181°, $[\alpha]_D -69.5^\circ$; *Anal.* found for $C_{20}H_{30}O_5$: C, 68.34; H, 8.85), whose weak positive rotatory dispersion curve (Fig. 1) was essentially the mirror image of that of a 5β -3-keto steroid.¹¹ Similar oxidation of the *isonorketol* VII led to the *iso-seco* acid VIII (double m.p. 141° and 198–200°, $[\alpha]_D -46.4^\circ$; *Anal.* found for $C_{20}H_{30}O_5$: C, 68.60; H, 8.73), which exhibited a negative Cotton effect (Fig. 1)—qualitatively the mirror image of the R.D. curve of a 5α -3-keto steroid.¹¹



The base-catalyzed conversion (Va) of the norketol (V) to the *isonorketol* (VII) involves only carbon atoms 8 and 13, while the configuration at C-9 must have remained unchanged. Consequently, if *steviol* possesses a 9,10-*anti* backbone, the derived *seco* acids must be represented by the pair VI and VIII, while a 9,10-*syn* stereochemistry in *steviol* would lead to the C-8 isomeric *seco* acids IX and X. As has already been noted earlier,¹²

(11) C. Djerassi, "Optical Rotatory Dispersion," McGraw-Hill Book Co., New York, N. Y., 1960.

(12) C. Djerassi, M. Cais and L. A. Mitscher, *J. Am. Chem. Soc.*, **81**, 2386 (1959).

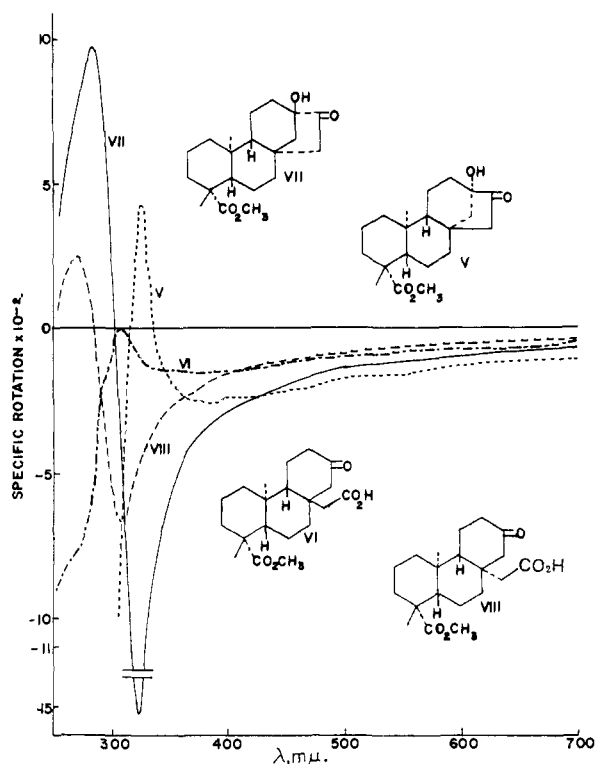


Fig. 1.—Optical rotatory dispersion studies (methanol solution) of *steviol* degradation products V-VIII.

the octant rule^{11,13} predicts a weak positive Cotton effect for VI and a negative one for VIII in agreement with the experimental results (Fig. 1). Turning to the C-9 isomeric pair, IX would be expected to have a much stronger positive Cotton effect than VI, but most importantly, X would exhibit a positive Cotton effect in contrast to the observed negative one, which according to the tenets of the octant rule¹³ is only consistent¹² with VIII.

(-)-*Isokaurene*⁶ (15–16 double bond isomer of III) upon permanganate oxidation provided the methyl ketone IVa (m.p. 140°; *Anal.* Found for $C_{20}H_{32}O_3$: C, 74.44; H, 10.08; neut. equiv., 322), which was subjected¹⁴ to Bayer–Villiger oxidation followed by saponification. The resulting hydroxy acid IVb (m.p. 254–256°; *Anal.* Found for $C_{18}H_{30}O_3$: C, 73.27; H, 10.40) was oxidized to the keto acid IVc (m.p. 169–170°; *Anal.* Found for $C_{18}H_{28}O_3$: C, 73.92; H, 9.77), whose positive rotatory dispersion curve (peak at $[\alpha]_{305}^{MeOH} +150^\circ$) was similar to that (Fig. 1) of the *steviol seco*-acid VI and antipodal to that¹¹ of a 5β -3-keto steroid.

These rotatory dispersion studies¹⁵ remove the last doubt concerning the absolute configuration of this group of diterpenoids. The above conclusions from the *steviol* (I) and (-)-*kaurene* (III) series are directly applicable to *garryfoline* (II), because of their mutual experimental interconversion.³

(13) W. Moffitt, R. B. Woodward, A. Moscovitz, W. Klyne and C. Djerassi, *ibid.*, **83**, October (1961).

(14) For analogous reaction sequence in the phyllocladene series, see P. K. Grant and R. Hodges, *Tetrahedron*, **8**, 261 (1960).

(15) We are indebted to Mrs. T. Nakano and Mrs. Ruth Record for the O.R.D. measurements.

Furthermore, garryfoline (II) has been related^{5b} to the other *Garrya* alkaloids¹⁶ as well as to members of the atisine class,¹⁷ so that the complete absolute stereochemistry of these alkaloids is now known.

(16) K. Wiesner and Z. Valenta in L. Zechmeister's "Progress in the Chemistry of Organic Natural Products," Springer, Vienna, 1958, Vol. XVI, pp. 26-89.

(17) S. W. Pelletier, *J. Am. Chem. Soc.*, **82**, 2398 (1960).

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NON-CHAIR CONFORMATIONS.
EQUILIBRATION OF *CIS*- AND *TRANS*-
2,5-DI-*t*-BUTYL-1,4-CYCLOHEXANEDIONE

Sir:

Equilibrations of *cis*- and *trans*-1,3-di-*t*-butyl-cyclohexane¹ and of *cis*- and *trans*-2,4-di-*t*-butyl-cyclohexanone² demonstrate that in these molecules, the *t*-butyl groups prefer the equatorial orientation in chair conformations. This communication describes the equilibration of *cis*- and *trans*-2,5-di-*t*-butyl-1,4-cyclohexanedione (*cis*-I and *trans*-I). Although *trans*-I can exist in a chair conformation with both *t*-butyl groups equatorial (1), the equilibrium favors *cis*-I. We conclude that *cis*-I prefers a *nonchair* conformation such as 7.

The diones, *cis*-I and *trans*-I, were prepared stereospecifically in good yield by the Jones oxidation³ of two isomeric 2,5-di-*t*-butyl-1,4-cyclohexanediols, diol A (*t*-butyl groups *cis*) and diol B (*t*-butyl groups presumed *trans*). Oxidation of diol A,⁴ m.p. 157.5-158.5°, yielded *cis*-I, m.p. 140-140.5°. Rapid reaction of 3 moles of hydrogen with 2,5-di-*t*-butylhydroquinone in acetic acid solution (containing one drop of concentrated hydrochloric acid) with platinum oxide catalyst at 75-80° under 2-4 atm. pressure gave a product mixture from which a 2,5-di-*t*-butyl-1,4-cyclohexanediol, diol B, m.p. 220-221°, was isolated by fractional recrystallization in *ca.* 5% yield.⁵ Oxidation³ of diol B yielded *trans*-I, m.p. 151.5-152°.⁶

Acid catalyzed equilibrations at 25-100° of the diones, *cis*-I and *trans*-I, 0.1-0.2 *M* solutions in acetic acid-water, 0.1-1 *N* in hydrogen chloride, and in carbon tetrachloride, 0.1 *N* in hydrogen chloride, gave mixtures containing 20 ± 10% *trans*-I and 80 ± 10% *cis*-I at equilibrium. The results of equilibrations in an acetic acid-water

(1) N. I. Allinger and L. A. Freiberg, *J. Am. Chem. Soc.*, **82**, 2393 (1960).

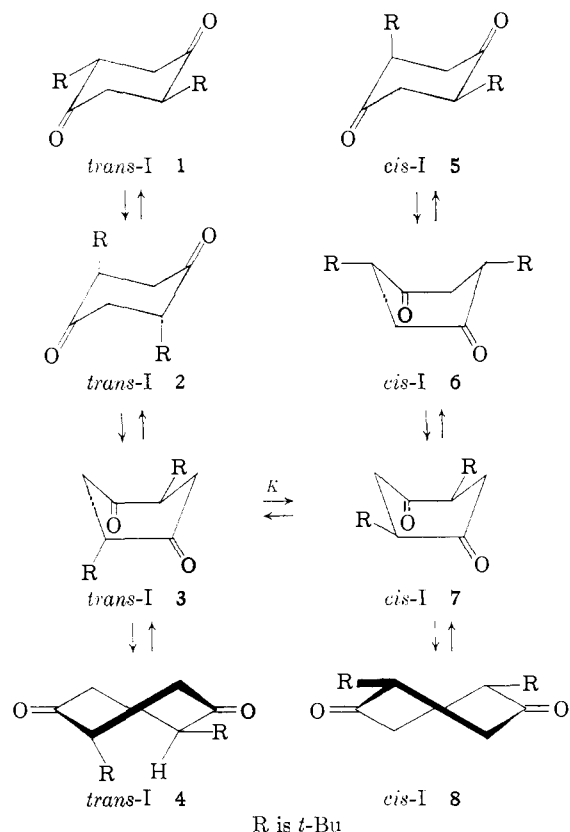
(2) N. I. Allinger and H. M. Blatter, *ibid.*, **83**, 994 (1961).

(3) R. G. Curtis, I. Heilbron, E. R. H. Jones and G. F. Woods, *J. Chem. Soc.*, 457 (1953).

(4) R. D. Stolow, *J. Am. Chem. Soc.*, **83**, 2592 (1961). Assignment of the *cis* configuration to the *t*-butyl groups in diol A is considered to be unequivocal, and is based upon the observation that diol A exhibits intramolecular hydrogen bonding.

(5) Diol B does not exhibit intramolecular hydrogen bonding.

(6) The diones, *cis*-I and *trans*-I, gave acceptable carbon and hydrogen analyses and have been characterized further by their infrared, ultraviolet and nuclear magnetic resonance spectra, as well as by gas chromatography.



solution 0.58 *N* in hydrogen chloride (prepared from 5.00 ml. of concentrated hydrochloric acid plus sufficient glacial acetic acid to bring the total volume to 100.0 ml.) are given in Table I.

TABLE I
EQUILIBRATION: *trans*-I ⇌ *cis*-I

<i>T</i> , °C.	Time, hr.	% <i>cis</i> ^a	<i>K</i> ^b	Δ <i>F</i>
44.9	37	81.5 ± 0.4	4.41 ± 0.2	-0.94 ± 0.04
85.0	3.0	79.1 ± 0.2	3.78 ± 0.1	-0.95 ± 0.02

^a Analyses by gas chromatography were carried out in duplicate at 180° with a 10 ft. 0.25 in. copper column packed with 20% silicone gum rubber on 60-80 mesh firebrick. The analyses were calibrated against known mixtures, one containing 79.1% *cis*-I. ^b From a graph of ln *K* as a function of 1/*T*, the approximate values of the enthalpy and entropy of equilibration were determined: Δ*H*, -0.87 ± 0.3 kcal./mole; Δ*S*, 0.2 ± 0.7 e.u.

For *cis*-I and *trans*-I, the three different possible chair conformations (1, 2 and 5) and three of the nine different possible boat conformations (3, 6 and 7) are illustrated. The other possible boat conformations are predicted to have higher energies than 3, 6 and 7 because of stronger repulsions between non-bonded groups. In addition, other conformations, such as twist⁷ conformations 4 and 8, require consideration.

A simple argument can be given in support of the conclusion that *cis*-I prefers a *non-chair* conformation. If a *t*-butyl group preferred an equatorial orientation when 1,4-cyclohexanedione was in the chair conformation, then 1 (the diequatorial chair conformation of *trans*-I) would be more stable than 5.

(7) W. S. Johnson, V. J. Bauer, J. L. Margrave, M. A. Frisch, L. H. Dreger and W. N. Hubbard, *J. Am. Chem. Soc.*, **83**, 606 (1961).