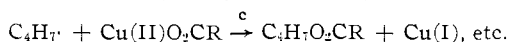
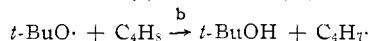
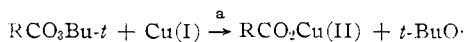
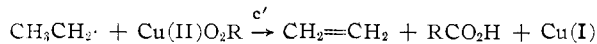
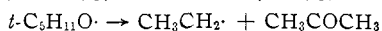


The isomer ratios of the butenyl esters are also insensitive to solvent composition, which ranged from benzene, acetonitrile, methanol, *tert*-butyl alcohol, 20% aqueous *tert*-butyl alcohol to acetic acid. In the last solvent *tert*-butyl perbenzoate and butene-2 yielded the same mixture of butenyl acetates<sup>7</sup> as was derived from *tert*-butyl peracetate in benzene. In the other protic solvents (alcohol and water) there were formed besides the butenyl esters, products (butenyl ethers and alcohols arising from the solvent). The distributions between the 3-but-1-enyl and crotyl derivatives in these latter products were the same as those of the corresponding esters.

These experiments indicate that the butenyl intermediate leading to products is *free* to undergo isomerization. We prefer to postulate the reaction occurring via the steps



Ethyl radicals derived in 70–80% yield from the cuprous-catalyzed decomposition of *tert*-amyl perbenzoate in benzene, methanol or cumene yielded ethylene (90–98%) and ethane (7–1%).



The catalysis by cuprous ion (step a) and the oxidation-reduction reactions<sup>8</sup> (steps c and c') will be commented on later.

Similar results have been reported to us by D. B. Denney, who currently is investigating the allylbenzene-propenylbenzene system.

(7) The butenyl benzoates did not interchange with solvent to form butenyl acetates under these conditions.

(8) H. E. De La Mare, J. Kochi and F. F. Rust, *J. Am. Chem. Soc.*, **83**, 2013 (1961).

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#### A DIRECT CORRELATION OF THE DITERPENE ALKALOIDS AND HYDROCARBONS OF THE PHYLLACLADENE GROUP. INTERCONVERSION OF GARRYFOLINE AND STEVIOL<sup>1</sup>

Sir:

Recently,<sup>2</sup> we reported on the transformation of the alkaloid garryfoline (I)<sup>3</sup> into the hydrocarbon II, which was not identical with either of the two C-16 isomeric hydrogenation products<sup>4</sup> of phyllocladene (VII), a diterpene of known relative and absolute stereochemistry.<sup>5</sup> We have now found that our hydrocarbon II is identical (mixture melting point, gas-phase chromatographic mobility)

(1) Paper XXXI in the series (by C. Djerassi) "Alkaloid Studies." For preceding article see C. Djerassi, A. A. P. G. Archer, T. George, B. Gilbert and L. D. Antonaccio, *Tetrahedron*, in press.

(2) H. Vorbrueggen and C. Djerassi, *Tetrahedron Letters*, 119 (1961).

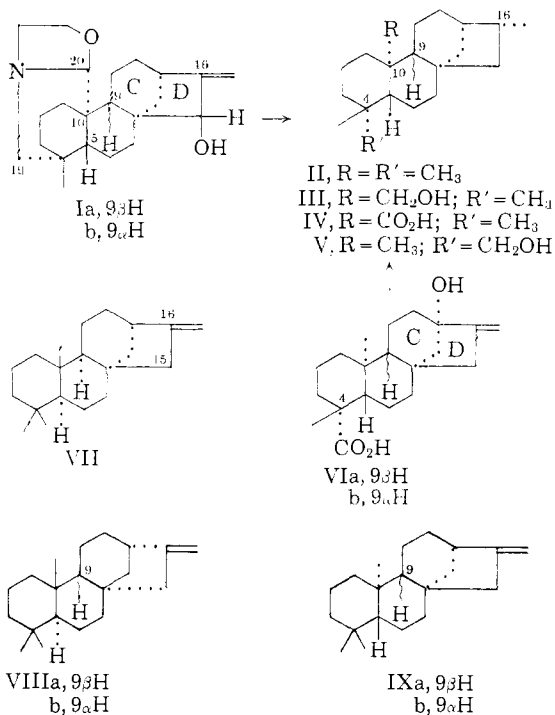
(3) C. Djerassi, C. R. Smith, A. E. Lippmann, S. K. Figdor and J. Herran, *J. Am. Chem. Soc.*, **77**, 4801, 6633 (1955).

(4) C. W. Brandt, *New Zealand J. Sci. Techn.*, **20**, 8B (1938).

(5) L. H. Briggs, B. F. Cain and R. C. Cambie, *Tetrahedron Letters*, No. 8, 17 (1959); P. K. Grant and R. Hodges, *Tetrahedron*, **8**, 261 (1960).

with a newly synthesized<sup>6</sup> specimen of "Stevane-B" (m.p. 54–55°,  $[\alpha]_D -56^\circ$ ) derived from steviol.<sup>7</sup> The precursor alcohol III<sup>2</sup> from garryfoline (I) proved to be completely different from the corresponding isomeric alcohol (m.p. 142–144°,  $[\alpha]_D -62^\circ$ ), which now has been prepared from steviol (VI) and related to "Stevane-B" (II). It follows, therefore, that the alcohol from steviol must be V and that the carboxyl group in steviol (VI) must be located at C-4, thus settling the remaining structural question of this interesting diterpene acid. Further confirmation of this conclusion could be provided by  $pK^*_{MCS}$  measurements<sup>8</sup> (kindly performed by Dr. V. P. Arya) on five different steviol and isosteviol derivatives, which ranged between 8.52–8.68, in contrast to  $pK^*_{MCS}$  9.49 reported earlier<sup>2</sup> for the isomer IV with the carboxylic acid at C-10. The apparent dissociation constants of steviol (VI) and its derivatives are in excellent agreement with that<sup>8</sup> of deoxypodocarpic acid<sup>9</sup> ( $pK^*_{MCS}$  8.45), which also possesses an axial carboxyl group at C-4 and an A/B *trans* ring juncture.

"Stevane-A,"<sup>6</sup> the C-16 epimer of "Stevane-B" (II), has been shown<sup>6</sup> to be identical with (–)- $\alpha$ -dihydrokaurene, the principal hydrogenation product of (–)-kaurene.<sup>10,11</sup> "Stevane-B" (II), there-



fore, is (–)- $\beta$ -dihydrokaurene (m.p. 51–52°)<sup>10</sup> and the interconversions shown thus represent the

(6) The degradation procedure was essentially identical with that published earlier by F. Dolder, H. Lichti, E. Mosettig and P. Quitt, *J. Am. Chem. Soc.*, **82**, 246 (1960).

(7) E. Mosettig and W. R. Nes, *J. Org. Chem.*, **20**, 884 (1955).

(8) P. F. Sommer, V. P. Arya and W. Simon, *Tetrahedron Letters*, No. 20, 18 (1960).

(9) E. Wenkert and B. G. Jackson, *J. Am. Chem. Soc.*, **80**, 217 (1958).

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

(11) L. H. Briggs, B. F. Cain, R. C. Cambie and B. R. Davis, *ibid.*, No. 24, 18 (1960).

first direct chemical connection between a diterpene of the phyllocladene class and the diterpenoid alkaloids.<sup>12</sup> In view of the rigorous structure proof of the *Garrya* alkaloids,<sup>12</sup> this interconversion also represents a confirmation of Briggs' structure proposal<sup>10</sup> for kaurene (IX).

The absolute configuration of garryfoline (I) and the other diterpenoid alkaloids already has been settled<sup>2</sup> in terms of stereoformula I. The earlier rotatory dispersion arguments<sup>6</sup> in the steviol series applied only to the absolute stereochemistry of positions 8 and 13, but the present interconversion with garryfoline *via* II allows expansion to the absolute configurational representation VI. The only point still open for discussion is the absolute configuration at C-9. Several circumstantial arguments have been raised in favor of an *anti*-backbone, *i.e.*, Ia (and hence VIa) with a 9 $\beta$ -hydrogen atom, among them the very great steric hindrance of C-20 substituted derivatives<sup>2</sup> of garryfoline (I)<sup>13</sup> which is also reflected in the preference<sup>14</sup> of various methine double bonds toward termination at C-20 (establishment of trigonal center) rather than C-19, as well as certain rotational shifts<sup>15</sup> in the related alkaloid ajaconine. If these arguments are accepted, then (-)-kaurene must have absolute configuration IXa rather than IXb.<sup>11</sup> This, in turn, requires that (+)-mirene be represented by VIIIa, since the earlier suggested<sup>11</sup> absolute configuration VIIIb would then imply that kaurene and mirene are antipodes, which is not the case.<sup>11</sup>

Except for this possible uncertainty relating to the stereochemistry of C-9, all structural features as well as the relative and absolute configuration of steviol, mirene, kaurene and the diterpene alkaloids (of the *Garrya* and atisine groups) are now settled.

(12) Garryfoline (I) already has been related (ref. 3) to garryine and veatchine (see 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) as well as to the atisine group (S. W. Pelletier, *J. Am. Chem. Soc.*, **82**, 2398 (1960)).

(13) Stereochemistry Ib requires that ring B be a boat and this presumably reduces steric hindrance to an appreciable extent.

(14) See K. Wiesner and J. A. Edwards, *Experientia*, **11**, 255 (1955); D. Dvornik and O. E. Edwards, *Can. J. Chem.*, **35**, 840 (1957).

(15) D. Dvornik and O. E. Edwards, *Proc. Chem. Soc.*, 305 (1958); A. J. Solo and S. W. Pelletier, *Chem. & Ind.*, 1108 (1960).

(16) The postdoctorate research fellowship of H. V. at Stanford University was supported by grant No. 2G-682 from the National Heart Institute of the National Institutes of Health, U. S. Public Health Service.

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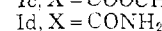
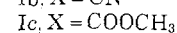
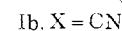
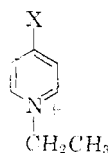
RECEIVED JUNE 16, 1961

#### FORMATION OF STABLE FREE RADICALS ON ELECTROREDUCTION OF N-ALKYLPYRIDINIUM SALTS

Sir:

The intensely colored free radical species formed by the one electron reduction of 1,1'-dialkyl-4,4'-dipyridinium salts were characterized by Weitz

and co-workers.<sup>1</sup> Recently Wallenfels and Gellrich<sup>2</sup> reported that colored radicals are formed by chemical reduction of N-dichlorobenzylpyridinium salts in which thiazole or thiazolium substituents are in the 4-position of the ring. In addition, it was reported that free radicals are obtained by chemical reduction of the N-dichlorobenzyl analog of Id. We have investigated the electrochemical reduction of the N-ethylpyridinium salts Ib, Ic, and Id, where the substituents are electron withdrawing, and have detected the presence of stable free radical species. The reduction of Ia was used as a "standard" of behavior for the simple pyridinium salts. The reductions of 10<sup>-3</sup> and 10<sup>-4</sup> M solutions of the various pyridinium salts were carried out in both aqueous and acetonitrile solutions.



#### Buffered Aqueous Potassium Chloride Solution.

—Polarographically, Ia gave two waves: a reversible one electron reduction at -0.71 v. and an irreversible two electron reduction at -1.09 v.<sup>3</sup> In general, the results are comparable to those obtained for similar 4,4'-dipyridinium salts.<sup>4</sup> A controlled potential coulometric reduction of Ia at -0.85 v. yielded the expected blue dipyridinium ion radical with nearly a 100% current efficiency.

In basic solution, Ib also gave two polarographic waves: a reversible one electron reduction at -0.87 v., and a pH dependent second wave at -1.16 v. (pH 8.5). In neutral or acidic solution the second wave is shifted to less negative potentials, obscuring the first wave. In solutions more basic than pH 8.5, the rate of the base catalyzed hydrolysis of the cyano group is increased markedly.<sup>5</sup>

Macroscopic constant potential coulometric reductions of Ib were carried out in buffered solution (pH 8.5) at a potential of -0.93 v., corresponding to the diffusion current region of the first wave. After a short induction period the solutions gradually turned deep blue. Spectroscopic and polarographic measurements showed that the main reduction product was the same radical which was formed from Ia.<sup>6</sup> Apparently the initially formed Ib radical slowly dimerizes with the elimination of two cyanides to produce Ia. Since Ia is more easily reducible than Ib, however, it immediately adds another electron to produce Ia radical. Current efficiencies based on an over-all 1.5 electron reduction of Ib were high, indicating some side reactions were taking place.

(1) See E. Weitz, *Angew. Chem.*, **66**, 658 (1959), and references therein.

(2) K. Wallenfels and M. Gellrich, *Ann.*, **621**, 198 (1959).

(3) All potentials are referred to the aqueous saturated calomel electrode.

(4) R. Eloffson and R. Edsberg, *Can. J. Chem.*, **35**, 646 (1957).

(5) J. W. Patton, Ph.D. Thesis, University of Wisconsin, 1961.

(6) Reduction of Ib with sodium dithionite in buffered aqueous solution led to the same radical: J. L. Cotter and E. M. Kosower, unpublished results.