face-to-face. In V the *trans* relation of the aromatic rings allows overlap of rings only at the 2-positions.

The electronic spectra of 1:1 methanol–water solutions of all these compounds were anomalous—the absorption intensities were greater than the sums of the intensities of the separate chromophores (approximated by *p*-toluidine and *p*-nitrotoluene). Absorption in the visible region resulted in definite coloration. The maxima in the anomalous absorption of these compounds are summarized in Table I.

TABLE I

ANOMALOUS ABSORPTION[a] OF 4-$NO_2C_6H_4$–$(CH_2)_x$–C_6H_4-NH_2-4′

Cpd.	x	λ'_{max}	ϵ'_{max}	$kf\epsilon'd\nu$[b]
I	1	324	1620	115
II	2	313	1330	114
III	3	310	1480	100
IV	2 (*cis*)	312	2420	155
V	2 (*trans*)	308	2470	168

[a] $\epsilon' = \epsilon$(compound) $- [\epsilon(4\text{-}NO_2C_6H_4CH_3) + \epsilon(4\text{-}NH_2C_6H_4CH_3)]$. [b] Relative integrated intensity from 280 to 650 mμ.

Despite the great differences in the orientations of the donor and acceptor rings in these molecules, all showed the spectral characteristics of molecular complexes–increased absorption intensity over that expected and an absorption shift toward the visible.[2,3] Therefore, the geometrical orientation of the donor and acceptor in a molecular complex is not critical in determining whether charge-transfer interaction will occur.[4]

If the maximum in the anomalous absorption corresponds to the charge-transfer band, then the prediction of Orgel and Mulliken[1] regarding the intensities (variable) and the wave lengths (relatively invariant) of this band for complexes with different orientations of donor and acceptor is firmly supported by this work.

(2) L. J. Andrews, *Chem. Revs.*, **54**, 713 (1954).

(3) Studies at different concentrations gave the same results indicating the anomalies must be attributed to intramolecular rather than intermolecular interactions.

(4) Direct charge-transfer interaction of nitro and amino groups, sometimes suggested for nitroaromatic-amine complexes, is very improbable here. The rings must interact.

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MECHANISM OF FORMATION OF ISOPENTENYL PYROPHOSPHATE

Sir:

During the enzymatic synthesis of squalene the carboxyl groups of six mevalonic acid (MVA) molecules are eliminated.[1] When this reaction is allowed to take place in D_2O, approximately 4 atoms of D, or less than 1 atom per molecule of MVA, are incorporated into the hydrocarbon.[2] We have interpreted this result as showing that decarboxylation occurs without protonation of the carbon chain, that it is concerted with the elimination of OH (or OR) from C-3 of MVA and that the reaction product is a derivative of Δ^3-isopentenol, (3-methyl-3-butenol-1).[2] With the identification of isopentenylpyrophosphate[3,4] as the condensing unit in squalene synthesis, these conclusions have been greatly strengthened. We now wish to present more direct evidence for the concerted nature of the decarboxylation process. A yeast enzyme, approximately 100-fold purified,[5] catalyzes the irreversible transformation: MVA-5-pyrophosphate[3] + ATP → isopentenylpyrophosphate + CO_2 + ADP + P_i. All four products are formed in stoichiometric amounts (Table I). Furthermore, kinetic experiments show that CO_2 evolution and ADP formation occur at identical rates and without a lag period. When T_2O is present during this reaction the isopentenyl moiety of the isolated isopentenylpyrophosphate is essentially free of T (T:C^{14} ratios in two experiments 0.010 and 0.040) demonstrating that the above reaction occurs without protonation of the carbon chain.[6] It is established by this finding and by the synchronous appearance of the products that the reaction of the substrate with ATP, the removal of the OH function and the decarboxylation of the MVA ester cannot be separate, consecutive events. Since ADP and P_i are formed from ATP in stoichiometric amounts and since the elements of ATP are not found in the reaction product,[5] the substrate must be phosphorylated and the same phosphate residue again eliminated in the course of the reaction.

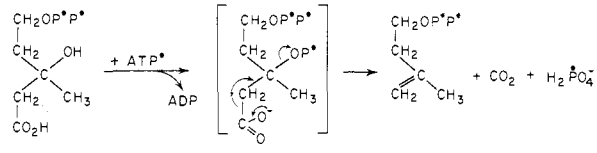
TABLE I

STOICHIOMETRY OF PRODUCTS FORMED IN THE ENZYMATIC DECARBOXYLATION OF MVA-PYROPHOSPHATE TO ISOPENTENYLPYROPHOSPHATE

The enzyme was obtained from yeast autolysate[3] by steps including precipitation with $(NH_4)_2SO_4$ (45–68% saturation), and with ethanol (13–35%), and chromatography on diethylaminoethyl cellulose column.[5] The incubation system contained $MnSO_4$ 0.004 *M*, phosphate buffer, *p*H 7, 0.04 *M*, ATP^{32} 0.0002 *M* and 1.5 mg. of enzyme in a total volume of 2.5 ml. The reaction products were separated by chromatography on Dowex-1 formate.

	μ moles
C^{14}-MVA-pyrophosphate added	0.41
Isopentenylpyrophosphate formed	.40
$C^{14}O_2$[a]	.39
ADP formed	.44
Inorganic P	.44

[a] The substrate in this flask was 1-C^{14} MVA pyrophosphate incubated under the same conditions as above in stoppered Warburg flasks. $C^{14}O_2$ was absorbed in KOH and precipitated as $BaCO_3$.



(1) P. A. Tavormina and M. H. Gibbs, THIS JOURNAL, **78**, 6210 (1956).

(2) H. Rilling, T. T. Tchen and K. Bloch, *Proc. Nat. Acad. Sci. (U. S.)*, **44**, 167 (1958).

(3) S. Chaykin, J. Law, A. H. Phillips, T. T. Tchen and K. Bloch, *ibid.*, **44**, 998 (1958).

(4) F. Lynen, H. Eggerer, U. Henning and I. Kessler, *Angew. Chem.*, **70**, 738 (1958).

(5) K. Bloch, S. Chaykin, A. H. Phillips and A. de Waard, manuscript in preparation.

(6) These values are sufficiently small to exclude any possible masking of protonation by an isotope effect.

Therefore the indications are that the transitory phosphorylation product is either unstable or remains enzyme-bound. The results presented support the concerted mechanism shown below.

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(8) Holder of a Postdoctoral Fellowship from the United States Public Health Service.

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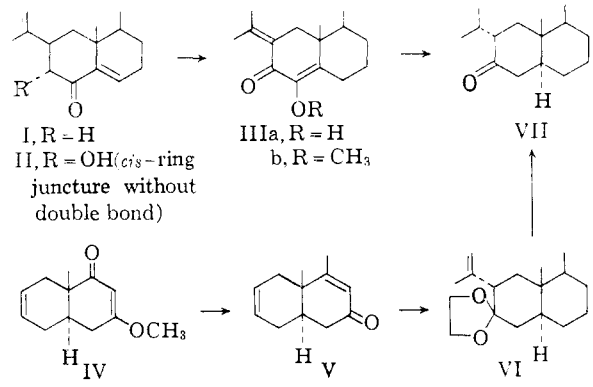
TERPENOIDS. XL.[1] ABSOLUTE CONFIGURATION OF EREMOPHILONE[2]

Sir:

The *relative* configuration of eremophilone (I)[3] has been established recently[4] by relating it, as well as naturally occurring[3] hydroxyeremophilone (IIIa), to hydroxydihydroeremophilone (II),[3] which already has been submitted to X-ray analysis.[5] In order to gain insight into the biogenetic precursor of these three sesquiterpenes (I,II,IIIa) which do not follow the isoprene rule, it was necessary to determine their absolute configuration and this now has been accomplished.

The (+)-antipode of IV of known absolute configuration[6] upon treatment with methyl lithium and acid cleavage afforded (+)-*trans*-2-keto-4,10-dimethyl-$\Delta^{3,6}$-hexahydronaphthalene (V) (m.p. 42–44°, λ_{max}^{MeOH} 236 mμ, log ϵ 4.02, rotatory dispersion curve very similar to that[7] of analog lacking C-4 methyl group; *anal.* found for $C_{12}H_{16}O$: C, 81.68; H, 9.18). Palladium-catalyzed hydrogenation of V in the presence of alkali provided (+)-*trans*-4,10-dimethyl-Δ^{6}-octalone-2[8] (b.p. 110–111° (1.5 mm.), negative R.D. Cotton effect; *anal.* found for $C_{12}H_{18}O$: C, 81.16; H, 10.18). Wolff-Kishner reduction led to (+)-*trans*-1,9-dimethyl-Δ^{6}-octalin,[9] which was transformed with perbenzoic acid to the 6α,7α-epoxide,[9] reduced with lithium aluminum hydride to the alcohol[9] and oxidized to (+)-*trans*-5,10-dimethyldecalone-2 (m.p. 29–30°, positive R.D. Cotton effect (amplitude reduced 68% upon addition of HCl—see ref. 8); *anal.* found for $C_{12}H_{20}O$: C, 79.72; H, 10.95). Condensation with ethyl oxalate and sodium hydride gave the glyoxalate,[9] which was decarbonylated thermally in the presence of powdered glass to (+)-*trans*-3-ethoxycarbonyl-5,10-dimethyldecalone-2 (b.p. 65° (0.01 mm.)), purple ferric chloride test; *anal.* found for $C_{15}H_{24}O_3$: C, 70.89; H, 9.14). Conversion to the cycloethylene ketal,[9] treatment with methylmagnesium iodide and dehydration of the crystalline (m.p. 55–60°) carbinol with phosphorus oxychloride in pyridine yielded (+)-*trans*-2-ethylenedioxy-3-isopropenyl-5,10-dimethyldecalin (VI) (b.p. 90–105° (0.1 mm.), $\lambda_{max}^{CHCl_3}$ 6.08, 11.15 μ; *anal.* found for $C_{17}H_{28}O_2$: C, 76.94; H, 10.89). Hydrogenation of VI provided (+)-*trans*-2-ethylenedioxy-3-isopropyl-5,10-dimethyldecalin,[9] which was cleaved with hydrochloric acid–methanol to *trans*-3-isopropyl-5,10-dimethyldecalone-2 (VII) (b.p. 75–85° (0.04 mm.), infrared spectrum unchanged after equilibration with alkali, *positive* R.D. Cotton effect with peak at $[\alpha]_{312\ m\mu}^{MeOH}$ +530° (*c*, 0.21); *anal.* found for $C_{15}H_{26}O$: C, 80.79; H, 11.69; yellow 2,4-dinitrophenylhydrazone, m.p. 169–172°).

In order to provide an experimental connection with VII, hydroxyeremophilone (IIIa)—which has already been related[3,4] to eremophilone (I)—in the form of its methyl ether IIIb[3] was hydrogenated with palladium-charcoal in ethanol solution to its tetrahydro derivative.[9] Equilibration of the latter with alkali followed by demethoxylation with calcium in liquid ammonia led to *trans*-3-isopropyl-5,10-dimethyldecalone-2 (VII), identical in all respects (including rotatory dispersion curve with *positive* Cotton effect) with the above-described synthetic specimen.



These interconversions demonstrate that eremophilone and its relatives possess the absolute configurations[10] implicit in stereoformulas I, II and IIIa and that the eudalenoid biogenetic precursor[11] has the same absolute configuration as eudesmol.[12]

We are deeply indebted to Dr. Maurice D. Sutherland of the University of Queensland for a generous gift of hydroxyeremophilone and to Monsanto

(1) Paper XXXIX, C. Djerassi and S. Burstein, *Tetrahedron*, in press.

(2) Supported by the Division of Research grants (No. RG-3863) of the National Institutes of Health, U. S. Public Health Service.

(3) J. Simonsen and D. H. R. Barton, "The Terpenes," Cambridge University Press, New York, N. Y., 1952, Vol. III, pp. 212–224.

(4) C. Djerassi, R. Mauli and L. H. Zalkow, THIS JOURNAL, **81**, July (1959).

(5) D. F. Grant and D. Rogers, *Chemistry and Industry*, 278 (1956); D. F. Grant, *Acta Crystal.*, **10**, 498 (1957).

(6) A. J. Speziale, J. A. Stephens and Q. E. Thompson, THIS JOURNAL, **76**, 5011 (1954).

(7) C. Djerassi, R. Riniker and B. Riniker, *ibid.*, **78**, 6377 (1956).

(8) The equatorial orientation of the C-4 methyl group was demonstrated by the ease of hemiketal formation using rotatory dispersion (C. Djerassi, L. A. Mitscher and B. J. Mitscher, *ibid.*, **81**, 947 (1959)).

(9) All compounds were characterized by analysis, infrared spectrum and rotatory dispersion.

(10) The earlier (opposite) assignment of absolute configuration involving rotatory dispersion comparisons (C. Djerassi, R. Riniker and B. Riniker, THIS JOURNAL, **78**, 6362 (1956)) was predicated on an α-oriented isopropenyl substituent in I. See also footnote 8 in ref. 4.

(11) R. Robinson, "The Structural Relations of Natural Products," Oxford University Press, New York, N. Y., 1955, p. 12.

(12) B. Riniker, J. Kalvoda, D. Arigoni, A. Fürst, O. Jeger, A. M. Gold and R. B. Woodward, THIS JOURNAL, **76**, 312 (1954).