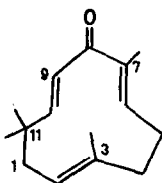


PHOTOCHEMISTRY OF ZERUMBONE

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PHOTOIRRADIATION of zerumbone (I), a medium-ring all-trans dienone¹, appeared of considerable interest because of the variety of pathways available to such a substrate. We now report on such an investigation.



I

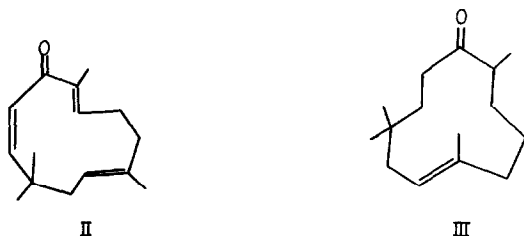
trans-6-cis-9-Zerumbone and μ -photozerumbone

Irradiation (N_2) of 1% heptane solution of zerumbone (3 g), without cooling (consequently heptane got heated to reflux), with a 100-Watt high-pressure mercury vapour lamp (reflector type)², furnished at the photostationary state (6 hr), a product which consisted of at least eight constituents (GLC), besides some unchanged zerumbone (9%). Of these, two components, with relative (to zerumbone) retention times of 0.2 and 0.84, constituted 23% and 35% respectively of the product; the remaining six products were formed in essentially equal quantities. The two major constituents could be separated by fractionation and finally purified by column chromatography.

trans-6-cis-9-Zerumbone. The compound with $RRT_{\text{zerumbone}} = 0.84$ was obtained as a colorless solid, m.p. 64-64.5° and is shown to be the cis- Δ^9 -isomer (II) of zerumbone.

The compound, $C_{15}H_{22}O$, is clearly an $\alpha\beta$ -unsaturated ketone:
 $\lambda_{\text{max}}^{\text{EtOH}}$ 238 $m\mu$ (ϵ 8,230), 318 $m\mu$ (ϵ 43); IR (Nujol): C=O 1662 cm^{-1} .

Its PMR spectrum³ shows signals for two quaternary methyls (6H singlet at 57 c/s), two vinylic methyls (3H doublet at 93 c/s with $J = 1$ c/s and a 3H singlet at 103 c/s) and four vinyl protons, which clearly fall in three groups: a 1H triplet centred at 312 c/s ($J = 8.5$ c/s), a 1H broad singlet at 390 c/s ($W_H = 13$ c/s) and, a 2H AB-quartet centred at 342 c/s ($J = 13$ c/s). It is clear from these data that the compound has the same functionality as zerumbone (I) and is monocyclic, and hence, in all probability



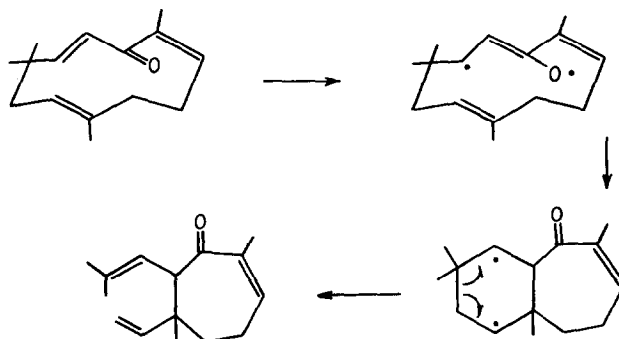
is a geometrical isomer of I. This was proved by its partial hydrogenation ($\text{Pd-CaCO}_3/\text{H}_2$) to a tetrahydroderivative, identified (GLC, IR) as tetrahydrozerumbone (III)^{1a}. Since in the IR spectrum of this isomer, the trans-CH=CH- out-of-plane deformation, which occurs in zerumbone at 970 cm^{-1} is absent, this bond must now have the cis-configuration. Thus, this product could be either trans-6-cis-9-zerumbone (II) or cis-6-cis-9-zerumbone*. Of these, structure II is assigned to this compound, in view of the thermal behaviour of another cis-isomer described later.

✧ -Photozerumbone. The second major component also analyses for $\text{C}_{15}\text{H}_{22}\text{O}$, and was obtained as a liquid: b.p. $84-86^\circ/0.7\text{ mm}$
 n_D^{30} 1.5048, $\lambda_{\text{max}}^{\text{EtOH}}$ $235\text{m}\mu$ ($\epsilon 6,250$), $315\text{ m}\mu$ ($\epsilon 100$); IR: C=O 1685 cm^{-1} , C=C 1650 cm^{-1} . Its PMR spectrum displays signals assignable to one quaternary methyl (3H singlet at 57 c/s), three vinylic methyls (3H doublet at 92 c/s, $J = 1.5$ c/s; 6H singlet

* In all the isomers of zerumbone, described in this communication, the non-conjugated $\Delta^{2,3}$ must remain trans-configured as in zerumbone.

at 106 c/s) and five olefinic protons in which three types are easily discernible: $C-\overset{|}{\underset{|}{C}}-CH=CH_2$ (a 12-line ABC type spectrum located between 283 and 363 c/s) $-CH_2-CH=C-\overset{Me}{|}$ (a 1H broadened triplet at 383 c/s; possibly conjugated with the C=O) and $-CH-CH=C-\overset{Me}{|}$ (a 1H pair of quintets centred at 317 c/s, $J = 10$ c/s); besides, a 1H doublet ($J = 10$ c/s) centred at 212 c/s and assignable to $-\overset{R}{\underset{|}{C}}-CH-CH-$ is, in all likelihood, spin-coupled with the olefinic proton centred at 317 c/s (same J value). The presence of a terminal vinyl group is supported by the deformation bands at 920 and 1010 cm^{-1} in the IR spectrum.

The structural features, described above, point to a skeletal rearrangement of the zerumbone frame-work during the formation of this product. The mechanistic sequence*, shown below,



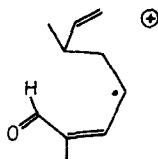
IV

*The net change is a Cope rearrangement⁴, the photochemical equivalent of which has been recently reported⁵. A concerted mechanism, involving a 6-membered transition-state is contra-indicated on orbital symmetry considerations⁶. However, it must be pointed out that this product may be of thermal origin (irradiation being carried out in refluxing heptane). This appears to be supported by the isolation of cis-6-trans-9-zerumbone (VI), which at $160 \pm 10^\circ$ smoothly passes into IV (vide infra) but, since this thermal reaction does not occur in refluxing heptane, no clear-cut conclusion is possible. In view of its doubtful photo-origin, the ketone has been termed \neq -photozerumbone.

leads to the structure (IV)[†] which meets all the spectral data requirements. This formulation is supported by its quantitative hydrogenation (Pt/AcOH) to a saturated hexahydroketone ($\nu^{C=O}$ 1700 cm^{-1}) and Na-EtOH reduction to a stereoisomeric mixture of dihydroalcohols. The latter, as required, gives acetone and formaldehyde on ozonolysis and is oxidised by pyridine-CrO₃ to a dihydroketone ($\nu^{C=O}$ 1695 cm^{-1} ; n_D^{30} 1.4900) having all the required PMR spectral characteristics.

The mass spectrum (molecular ion at m/e 218, relative abundance 19%, Σ_{28} 1.6%) shows the base peak (Σ_{28} 8.2%) corresponding to C₁₀H₁₄O (m/e 150), readily rationalised in terms of ion V. A full discussion of the spectrum is reserved for the detailed communication.

Passage of a hexane solution through an Al₂O₃/I column gave a mixture of epimers (AgNO₃-SiO₂ gel TLC; GLC) in which the



V

original ketone and the new epimer were present in the ratio 35:65 respectively.

Since, ψ -photozerumbone is a cycloheptenone the ring-olefinic bond must be cis and consequently, in its genesis, a cis-6-zerumbone must be involved.

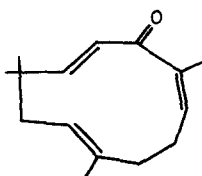
cis-6-trans-9-Zerumbone and cis-6-cis-9-zerumbone

When the irradiation was carried out with cooling (effective temp. $\sim 30^\circ$; immersion-type lamp²), keeping other variables essentially the same, photostationary state was reached after

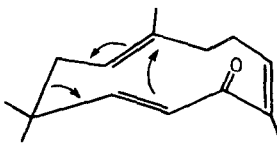
[†]This was presented at the Symposium on 'Recent Advances in the Chemistry of Terpenoids' held at the National Chemical Laboratory, Poona, during June 7-10, 1965.

50 hr and the product contained, besides zerumbone (8%) and trans-6-cis-9-zerumbone (30%), two new components (18% and 27% with $RRT_{\text{zerumbone}}$ of 0.58 and 0.39 respectively) and practically none (TLC) of ψ -photozerumbone. When the total product was refluxed in heptane, no change occurred but, after heating at $160 \pm 10^\circ$ for 3 hr the resulting product was practically devoid (GLC) of the two new components, mentioned above and, instead, considerable amount (TLC, GLC) of ψ -photozerumbone had been formed. The separation of these new components from the initial photoirradiation product proved exceedingly difficult and ultimately success could be attained by reducing the total reaction product with $LiAlH_4$ and separating the alcohol by inverted-column-chromatography⁷ over $AgNO_3$ - SiO_2 gel and, oxidising (pyridine- CrO_3) the pure alcohol back to the parent ketone.

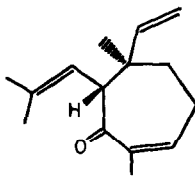
cis-6-trans-9-Zerumbone. The compound with $RRT_{\text{zerumbone}}$ 0.58, from its spectral characteristics ($\nu^{C=O}$ 1660 cm^{-1} ; λ_{max} $225\text{ m}\mu$ ϵ $9,280$. PMR: two quaternary methyls, 6H signal at 70 c/s; two



VI



VII



VIII

vinyllic methyls, 3H signals at 101 and 112 c/s; and, four olefinic protons signals in the region 300-380 c/s, containing an AB-quartet centred at 359 c/s with $J = 17\text{ c/s}$) is clearly a geometrical isomer of zerumbone and since, it still displays a strong

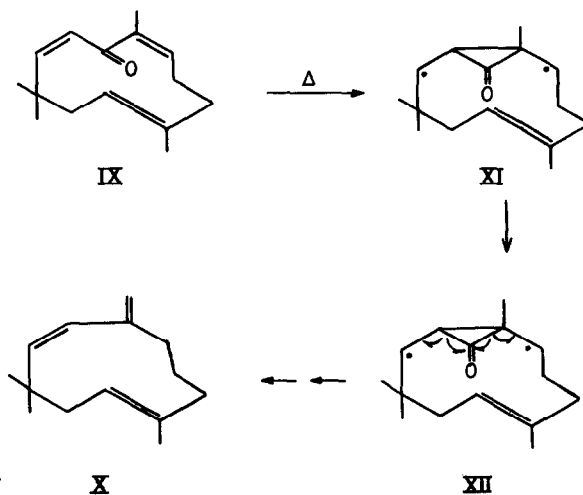
band at 978 cm^{-1} in its IR spectrum, must have the $\Delta^{9,10}$ -olefinic linkage trans and consequently, $\Delta^{6,7}$ -bond must be cis (VI).

This ketone, on being heated to $160 \pm 10^\circ$, smoothly passed into a new product, identified (GLC) as the ψ -photozerumbone (IV). The $\Delta^{9,10}$ and $\Delta^{2,3}$ bonds in VII, which have a 1,5-relationship can be readily accommodated in a quasi-chair conformation (VII), the preferred geometry for the Cope rearrangement⁸ and this will lead to the stereochemistry shown in VIII for the product.

Cis-6-cis-9-Zerumbone. The product with RRT_{zerumbone} 0.39 has the following characteristics: $\nu^{C=O}$ 1662 cm^{-1} ; λ_{max} $240\text{ m}\mu$; two quaternary methyls (6H singlet at 68.5 c/s), two vinylic methyls (3H signals at 88 and 112 c/s) and four ethylenic protons (1H broad triplet centred at 301 c/s, $J = 7.5\text{ c/s}$; an AB-quartet centred at 339 c/s, $J = 13\text{ c/s}$; 1H broad multiplet centred at 347 c/s). These data require the compound to be stereoisomeric with zerumbone, a conclusion confirmed by its catalytic reduction to tetrahydrozerumbone (III)^{1a}. Since the compound does not display a strong band at $\sim 970\text{ cm}^{-1}$ in its IR spectrum, $\Delta^{9,10}$ must be cis-configured.

When the compound was heated at $\sim 160^\circ$ for 3 hr the major product (60%) obtained proved to be a nor-hydrocarbon: $C_{14}H_{22}$, highest m/e at 190 (Σ_{28} 11.8%)*. In view of its spectral characteristics (λ_{max} $231\text{ m}\mu$, ϵ 12,500; IR: 1615, 888, 823 cm^{-1} . PMR: 2 quaternary methyls, 6H signal at 62 c/s; one vinylic methyl 3H signal at 108 c/s; $-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-$, 2H AB quartet centred at 342 c/s with $J = 10\text{ c/s}$; $>\text{C}=\text{CH}_2$, a2H quartet centred at 291 c/s with $J = 1.5\text{ c/s}$; $-\text{C}=\text{CH}-$, 1H broad signal centred at 348 c/s) the hydrocarbon has been assigned the structure X, the ready formation of which from a cis-cis-zerumbone (IX) is readily

* The base peak occurs at m/e 175 (Σ_{28} 16.8%). A fuller discussion of the fragmentation will be reported later.



understood (XI \rightarrow XII). In view of this, this zerumbone isomer has been assigned the cis-cis-structure (IX).

REFERENCES

- 1 (a) Sukh Dev, Tetrahedron **8**, 171 (1960).
(b) N.P. Damodaran and Sukh Dev, Tetrahedron Letters 1977 (1965).
- 2 Supplied by Engelhard Industries, Newark (USA).
- 3 All PMR spectra were taken on 10-20% solutions in CCl_4 on a Varian A-60 spectrometer; the signals are recorded in c/s from tetramethylsilane as zero.
- 4 S.J. Rhoads in Molecular Rearrangements (Edited by P.de Mayo), part 1, pp. 684-696, Interscience, New York (1963).
- 5 R.C. Cookson, V.N. Gogte, J.Hudec and N.A. Mirza, Tetrahedron Letters 3955 (1965).
- 6 R.B. Woodward and R. Hoffmann, J. Amer. Chem. Soc. **87**, 2511 (1965).
- 7 V.K. Bhalla, U.R. Nayak and Sukh Dev, J. Chromatog. (in press)
- 8 W. von E. Doering and W. Roth, Tetrahedron **18**, 67 (1962).