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A CONTRIBUTION TO THE STRUCTURE OF VALERANONE

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IN a previous communication,[1] we proposed two alternative formulae I and II for valeranone. Shortly afterwards, structure III was ascribed to valeranone by Govindachari *et al.*;[2,3] the authors used, incorrectly in our opinion,[4] the term jatamansone instead of the name valeranone. The configuration of methyl group on $C_{(10)}$ was studied by Djerassi and co-workers[5] who suggested

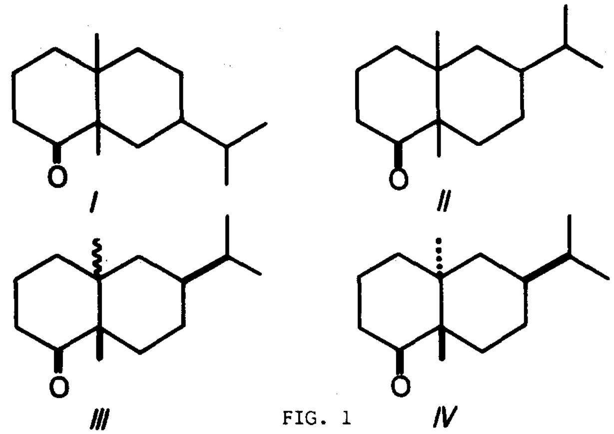
I II III IV

FIG. 1

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[1] J. Křepinský, M. Romaňuk, V. Herout and F. Šorm, Tetrahedron Letters No. 7, 9 (1960).

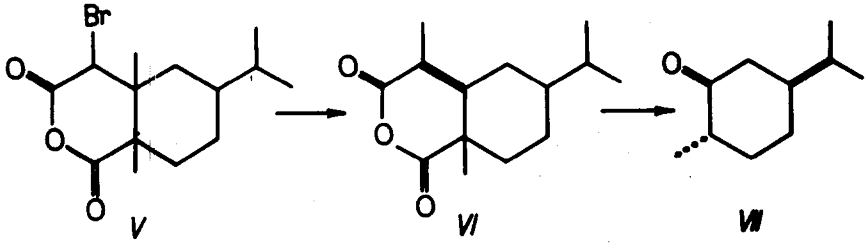
[2] T.R. Govindachari, B.R. Pai, K.K. Purushothaman and S. Rajadurai, Chem. & Ind. 1059 (1960).

[3] T.R. Govindachari, B.R. Pai, K.K. Purushothaman and S. Rajadurai, Tetrahedron 12, 105 (1961).

[4] J. Křepinský, V. Herout and F. Šorm, Tetrahedron Letters No. 3, 9 (1960).

[5] C. Djerassi, T.R. Govindachari, B.R. Pai and K.K. Purushothaman, Tetrahedron Letters No. 6, 226 (1961).

structure IV for valeranone on the basis of rotatory dispersion arguments which assumed that II represented the correct skeletal structure. The main sequence of reactions which led Govindachari et al. to structure III is outlined in Scheme 1 (V-VII); on treatment with dimethyl aniline the substance V was dehydrobrominated to α,β-unsaturated anhydride VI and this on Lemieux and Rudloff oxidation[6] afforded, according to the work of Govindachari et al.[3], 1-trans-carvomentone. In our preliminary note[1] we reported already that on treatment of substance V with collidine or dimethyl aniline, no product of normal dehydrobromination could be obtained. As the absorption bands of the dehydrobromination product obtained both by the Indian authors[3] (1786, 1672, 1695 cm^{-1}) and in this Laboratory as well (1782, 1682, 1496, 1598, 3062 cm^{-1}) had been at variance with the formula VI, we re-investigated the reaction in a greater detail. We ascertained that besides trimethyl phenylammonium bromide VIII, a substance of molecular formula $C_{21}H_{29}O_3N$ (IX) was formed, m.p. 144° (diisopropyl ether), $[\alpha]_D^{20}$ + 200°. The absorption bands of IX in the infra-red region showed the presence of an aromatic system (1496, 1598, 3062 cm^{-1}), a lactone (1782 cm^{-1}) and an amide group (1682 cm^{-1}). We have explained the unexpected formation of IX by a rearrangement,* the course of which may be seen in Scheme 2.



Scheme 1

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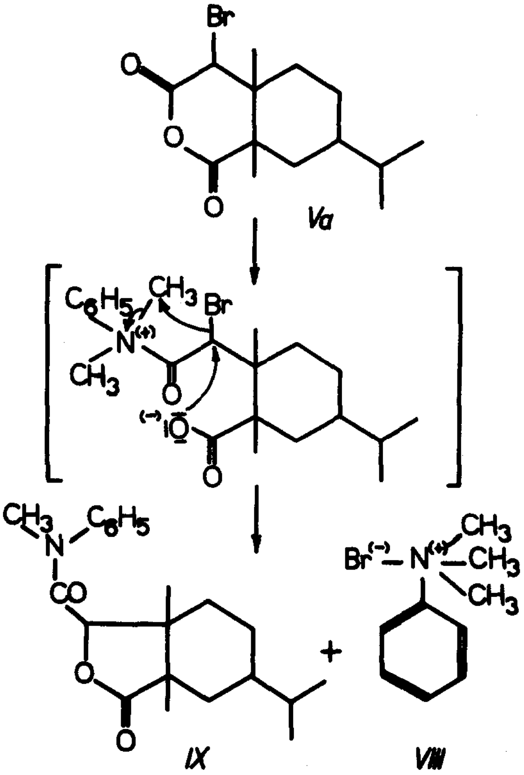
* The rearrangement is studied in detail at present.

[6] R.V. Lemieux and E. v. Rudloff, Canad. J. Chem. 33, 1701, 1710 (1955).



Scheme 2

As the physical data of both the compounds VI and IX strikingly resembled, we anticipated the possibility that both compounds in question might be identical; this proved to be true when an authentic sample of VI[*] melted undepressed on admixture of IX. The infra-red spectra of both VI and IX were identical in all respects as well; in addition, the sample prepared by the Indian authors contained 3.81% nitrogen (for IX calculated 4.08% N). Nevertheless, we attempted to carry out the oxidation of IX by

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[*] Our thanks are due to Professor T.R. Govindachari, Presidency College, Madras, India, who kindly sent us a sample for comparison.

means of Lemieux and Rudloff method[6] which, according to the Indian authors, should result in formation of 1-trans-carvomentone; in our hands, however, only starting material could be recovered. In the light of the results discussed above we cannot consider well-founded structure III for valeranone, while the arguments adduced for absolute configuration IV are now not applicable, since they were based on skeleton II rather than I.

In order to decide between both structures I and II suggested by us for valeranone, we used following sequence of reactions (cf. Scheme 3): on treatment with perbenzoic acid, valeranone afforded ε-lactone X, m.p. 61-62° (pentane), which on alkaline hydrolysis and subsequent treatment with diazomethane yielded methyl ester of hydroxy-acid XI. On dehydration and ozonization, the compound XI afforded desmethyl keto methyl ester XII; the latter on bromination with N-bromo-succinimide and subsequent dehydrobromination with collidine yielded α,β-unsaturated keto methyl ester XIII, $C_{15}H_{24}O_3$, λ_{max} 234 mμ (log ε = 4.131); (By comparison with values for the monocyclic compounds, 3-methyl-6-isopropylcyclohex-2-enone (235 mμ) and 4-isopropylcyclohex-2-enone (226 mμ) we found that our value (234 mμ) was in good agreement with structure XIII[7]) infra-red bands at 1744, 1429 cm^{-1} (methyl ester) and at 1672, 1634 cm^{-1} (carbonyl group). This conclusion is in good agreement with NMR spectrum of compound XIII: the band at $\tau = 4.2$ corresponds to the hydrogen of an -C=CH group and its intensity shows that there is only one such hydrogen atom in the molecule. The corresponding structure derived from II contains two ethylenic hydrogen atoms and we feel sure that these would have given separate peaks in the 4 to 5 region. The other main features in the spectrum are also more consistent with structure XIII.* On ozonization, the α,β-unsaturated keto ester XIII

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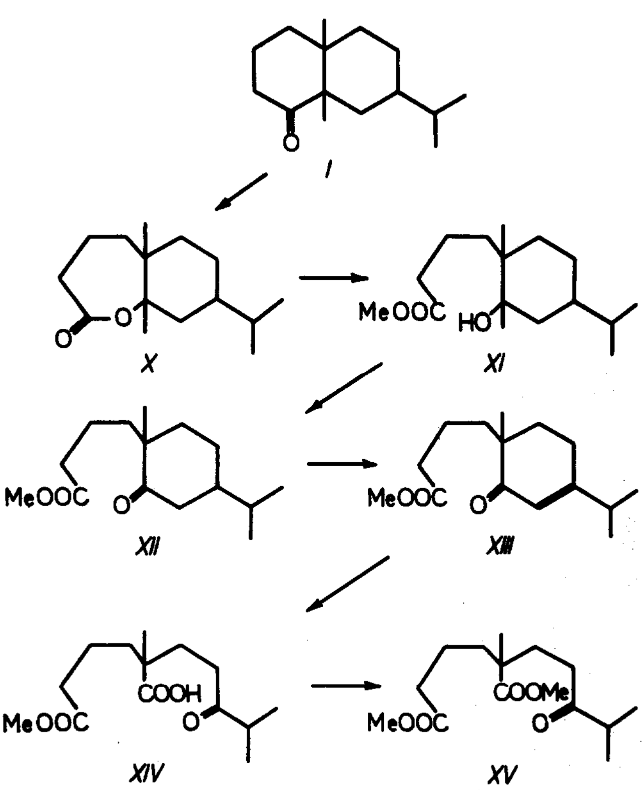
* Our thanks are due to Dr. N. Sheppard, University Chemical Laboratory, Cambridge, for the measurement of the NMR spectrum and valuable discussion.

[7] R.B. Woodward, J. Amer. Chem. Soc. 63, 1123 (1941).



Scheme 3

afforded an ester of keto dicarboxylic acid XIV, which on subsequent treatment with diazomethane yielded keto dimethyl ester XV (infra-red bands 1748 cm^{-1} - methyl ester, and at 1725 cm^{-1} - keto group on an aliphatic chain; the ultra-violet spectrum showed absorption band at 280 mμ log ϵ = 1.540; the sample contained 22.40% - OCH_3, calculated for XC 21.66% - OCH_3. For tricarboxylic ester assumed from the alternative structure II was calculated 29.43% - OCH_3).

Professor Govindachari has informed us that he has re-investigated the compound called dehydronorjatamansic anhydride and its oxidation with periodate, after perusing this paper sent to him in advance of publication. He has concluded that the view expressed by him about the nature of this compound was incorrect and that the claim made in his paper to have oxidized this compound to 1-*trans*-carvomenthone was erroneous.