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THE CONSTITUTION OF TWO NEW SESQUITERPENIC KETONES

FUROPELARGONES A AND B[1]

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Abstract—Furopelargones A and B are shown to have structures III and IV, respectively. Ozonolysis of furopelargone A led to the optical antipode VIIa of *trans-cis*-nepetonic acid, the structure and stereochemistry of which was ascertained by degradation to (−)-*trans-cis*-nepetic acid (XIIa) and to (+)-3-methylcyclopentanone (XVIIIc). Only four structures (XIX to XXII) were then possible for furopelargone A. Hydrogenation of the natural product afforded a ketol, the mass spectrum of which was found to be compatible only with XXIII, arising from XIX. Furopelargone B was shown to be an epimer of furopelargone A in the position α to the carbonyl group.

THE essential oil of *Geranium bourbon* is obtained not from Geranium species but from different types of Pelargonium, in particular *Pelargonium roseum*.[3] It is produced in various countries, chiefly in the Reunion Island (formerly Bourbon Island). The main constituents of this essential oil are geraniol, citronellol and their esters (75–80%). Several investigations have led to the identification of various minor constituents, monoterpenoids and smaller molecules. Fractional distillation nevertheless permits the isolation of 5–10% substances of higher molecular weight, which have not been studied to any great extent. Pfau and Plattner[4] have identified S-guaiazulene in the essential oil, but also mostly among its dehydrogenation products, which is an indication of the presence of sesquiterpenoids. Sfiras[5] has studied more closely the carbonyl compounds contained in this essential oil; in addition to isomenthone and other noncharacterized ketones he isolated a ketone $C_{15}H_{22}O_2$ (semicarbazone: m.p. 153–154°) and another ketone, somewhat higher boiling (2,4-DNP: m.p. 88–89°).

We have undertaken the study of the carbonyl compounds, probably sesquiterpenoids, which can be found in the residue from fractional distillation under vacuum. In this way the more volatile components (90%) are eliminated and there remains a residue (10%) which distils in major part between 70° and 110° (0·1 mm).

Using Girard Reagent T, it was possible to isolate a mixture of carbonyl compounds (2% of the distillation residue). Vapour phase chromatography showed that this mixture contained two major components, which were named, following the order of elution, furopelargones A and B.[1] Column chromatography led first to a mixture of

[1] A preliminary report of this work has been published, *C.R. Acad. Sci. Paris.* **257**, 1784 (1963). We have adopted there the name pelargone as suggested by Herout *et al.* (Ref. 6.). We have since noticed that pelargone is the name occasionally given to di-n-octylketone. We wish therefore to avoid further confusion and propose the names given above.

[2] To whom all inquiries concerning this paper should be addressed.

[3] E. Guenther, *The Essential Oils* Vol. IV; p. 67. Van Nostrand, New York (1952)

[4] A. St. Pfau and Pl. Plattner, *Helv. Chim. Acta* **19**, 858 (1936).

[5] J. Sfiras, *Ind. Parfum.* **1**, 154 (1946); *Chem. Abstr.* **42**, 5170f (1948).

these substances in a ratio 55:45. The pure compounds could be obtained by more elaborate chromatography. On this occasion it was noticed that they are rather unstable to air at room temperature and had to be kept in a sealed tube in the cold; they are also unstable under acidic conditions. It will be shown in the present paper that furopelargones A and B have structures III and IV, respectively.

Furopelargone A, b.p.$_{0.05}$: 60–62°; $[\alpha]_D^{26}$, −105°, λ_{max} 219 mμ, (ε 7400), possesses formula $C_{15}H_{22}O_2$. It gives a 2,4-DNP $C_{21}H_{26}O_5N_4$ (m.p. 98°) and a semicarbazone $C_{16}H_{25}O_2N_3$ (m.p. 150–153°). It seems likely that furopelargone A is identical to the ketone $C_{15}H_{22}O_2$, isolated by Sfiras.[5] Furopelargone A is also identical to a ketone named pelargone, studied by Herout *et al.*[6] The communications of the Czech and Swiss authors and our own investigations[1] led to different conclusions.

Furopelargone B, b.p.$_{0.1}$: 81–83°; $[\alpha]_D^{24}$, +49°, λ_{max} 219 mμ (ε 8500), also has formula $C_{15}H_{22}O_2$; its semicarbazone has a m.p. 160–164°.

As can be seen, the UV spectra of both substances are practically identical; moreover, it was noticed that their IR and NMR spectra differed only very slightly and that their mass spectra were identical, which led us to expect very closely related structures. The optical rotatory dispersion curves of the two ketones[7] showed a strong Cotton effect, negative for furopelargone A, positive for furopelargone B, and were practically mirror images of one another. This led us to believe that the compounds might be epimers in a position α to the carbonyl function. Indeed, treatment by base of a 55:45 mixture of the ketones led to an approximately 85:15 mixture of the same substances. The following discussion of the various spectra of furopelargone A is equally applicable to the epimer B.

We first examined the nature and environment of the carbonyl group. The IR spectrum shows a strong band at 1715 cm^{-1}. The absence of absorption between 2650 and 2880 cm^{-1} and the lack of a peak above 500 c/s in the NMR spectrum showed that an aldehydic function was not present. The absence of carbonyl absorption in the IR spectrum of the 2,4-DNP indicated a monoketone. Further, the NMR spectrum shows a singlet (3 protons) at 119 c/s, which could originate either from the methyl group of a methyl ketone, or from a vinylic methyl group. The reduction of furopelargone A (III) by sodium borohydride led to an alcohol $C_{15}H_{24}O_2$ (V), whose NMR spectrum no longer bore a peak in this region, indicating a methyl ketone grouping in III. It should be mentioned here that this methyl ketone grouping did not react in the iodoform test; however, similar cases have already been described.[8] Since IV could be transformed into III by epimerization in the position α to the carbonyl group, the system CH_3—CO—$CH(R_1R_2)$, R_1 and $R_2 \neq H$, was certainly present. This was confirmed by deuterium exchange of the hydrogen atoms α to the carbonyl group. In the mass spectrum of III the molecular peak appeared at m/e 234; in the mass spectrum of the deuterated III it was found at m/e 238, showing the presence of four α hydrogens. Further, the presence of a peak at m/e 237 (d_3), twice

[6] M. Romanuk, V. Herout, F. Sorm, Y. R. Naves and P. Tullen, XIX*th Congress of Pure and Applied Chemistry* Abstract A9/9, London (1963). We thank Professor V. Herout, Prague, for the kind supply of a sample of the semi-carbazone of his pelargone; it was found identical to our sample by mixed m.p. Professor Herout also informed us (July 1963) that he considered the structure we demonstrate here as a possibility.

[7] We wish to thank here Professor G. Ourisson, Strasbourg, in whose laboratory these curves, as well as our first NMR spectra were measured.

[8] G. Büchi, M. Schach v. Wittenau and D. M. White, *J. Amer. Chem. Soc.* **81**, 1968 (1959).

the intensity of m/e 238, agrees well with three exchangeable hydrogen atoms on a methyl group and one in a tertiary position. Furthermore, the mass spectrum of III showed an intense peak at m/e 191 (M-43), which can arise from the loss of $CH_3CO\cdot$. In the spectrum of the deuterated product there appeared a new peak at m/e 194 (M-46), corresponding to loss of $CD_3CO\cdot$.

We have seen earlier that the equilibrium between III and IV is around 85:15, which renders very probable the attachment of the methyl ketone group to a ring. Should it be linked to an aliphatic chain, an equilibrium near 50:50 would be expected. In the present case, the *cis*- or *trans*-position of the methyl ketone group with respect to another ring substituent would account for the difference in stability of the two epimeric compounds.

We next turned our attention to the second oxygen atom in the molecule. As the IR spectrum showed no absorption band around 3500 cm^{-1}, a hydroxyl function appeared unlikely. In addition, an intense band was found at 1528 cm^{-1}, which could originate from an enolized β-diketone system,[9] impossible here, or from an aromatic system, either carbocyclic or furanic. Since the presence of the second oxygen atom in an ether function was probable, and since the compounds were rather unstable in air and under acidic conditions, it seemed likely that a furan ring was present. The IR spectrum cannot give conclusive proof of the presence of a furan ring; nevertheless, bands were found at 700, 733, 891, 1014, 1528 cm^{-1} (all intense) and at 1560 cm^{-1} (weak), which, according to Kubota,[10] Nakanichi[11] and Fetizon[12] should be consistent with the presence of a furan ring. Furthermore, the NMR spectrum of III bore two doublets (1 proton each) centered at 370 and 431 c/s. These positions are indicative of α and β protons of furans.[13] The coupling constants measured for these two doublets were both equal to 2 c/s. According to Abraham and Bernstein[14] as well as Reddy and Goldstein[15] the coupling constant of an α-proton with a β-proton on a furan ring is about 2 c/s while that of an α-proton with a β'-proton is less than 1 c/s. This would indicate that the furan ring in III is probably substituted in an α and the vicinal β position.

The UV absorption of III (λ_{max}, 219 mμ; ε 7400) must be due to the furan ring alone, i.e. not conjugated to the carbonyl function.[12,16]

In addition to the furan ring, the NMR spectrum indicated two further elements of the structure: a doublet (3 protons) centred at 42 c/s (J = 8 c/s) showed the presence of a secondary methyl group; another doublet (6 protons) centred at 69·5 c/s (J = 9 c/s) would be consistent with an isopropyl group attached (because of the slight deshielding) to the furan ring.

[9] R. Norman Jones and C. Sandorfy, *Chemical Applications of Spectroscopy*, in *Techniques of Organic Chemistry* (Edited by A. Weissberger) Vol. IX; pp. 494 and 569 Interscience, New York (1957).
[10] T. Kubota, *Tetrahedron* **4**, 68 (1958).
[11] K. Nakanichi, *Infrared Absorption Spectroscopy* p. 62. Holden Day Publ. (1962).
[12] M. Fetizon and P. Baranger, *Bull. Soc. Chim. Fr.* 1311 (1957); *C.R. Acad. Sci. Paris.* **247**, 1182 (1958).
[13] L. M. Jackman, *Applications of NMR Spectroscopy in Organic Chemistry*, p. 64. Pergamon Press (1959).
[14] R. J. Abraham and H. J. Bernstein, *Canad. J. Chem.* **39**, 905 (1961).
[15] G. S. Reddy and J. H. Goldstein, *J. Phys. Chem.* **65**, 1539 (1961).
[16] Y. R. Naves, *Helv. Chim. Acta* **43**, 466 (1960); H. Stetter and R. Lautenbach, *Chem. Ber.* **93**, 603 (1960); C. Djerassi, E. Wilfred, L. Visco and A. J. Lemin, *J. Org. Chem.* **18**, 1449 (1953).

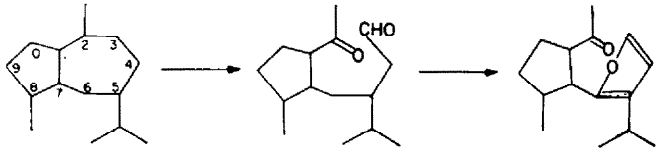
If we admit the presence of a carbonyl group and a furan ring in furopelargone A ($C_{15}H_{22}O_2$), this molecule must then contain another double bond or another ring. The latter possibility is more likely because the CH_3CO-grouping is probably attached to a ring, which is not the furan, and because no other vinylic protons appear in the NMR spectrum in addition to the furanic ones.

We then tried to construct a sesquiterpenic molecule which could be derived from farnesol according to the biogenetic mechanisms accepted for other sesquiterpenes,[17] and at the same time satisfy the following structural requirements:

$CH_3—CO—CH<$}ring,
α,β-disubstituted furan (or α,β'-)
one secondary methyl group,
one isopropyl group (or two tertiary methyl groups).

This was found impossible, unless extensive rearrangements, unlikely to happen during the biogenesis of a monocarbocyclic sesquiterpene, were involved. Then, during stimulating discussions, Büchi[18] considered the possibility that furopelargone A could rise from a bicarbocyclic sesquiterpene through opening of a ring.

If a sesquiterpene having the carbon skeleton (I) of S-guaiazulene with appropriate functions and double bond were cleaved by oxidation at the C-2, C-3 bond, one could easily derive by further oxidation structure (II) for furopelargone A, as follows:



I II

This structure is in agreement with all the structural features which have been derived above. The degradation of III, which will now be discussed, proved the correctness of this assumption.

Ozonolysis of III affords, in addition to a mixture of neutral materials,[19] an acidic compound. This was esterified to a keto ester VIIb, $C_{10}H_{16}O_3$, $[\alpha]_D^{20}$, $-30°$ (semicarbazone: m.p. 159–161°). The IR spectrum of this compound shows two carbonyl bands, at 1719 and 1740 cm^{-1}. Its NMR spectrum involves a singlet (3 protons) at 215 c/s (methyl group of the methyl ester) and a singlet (3 protons) at 125 c/s which should correspond to the methyl ketone group, already present in III. A doublet (3 protons) centred at 53 c/s ($J = 7$ c/s) represents the secondary methyl group, found previously. The absence of any other methyl absorption in this spectrum

[17] L. Ruzicka, *Proc. Chem. Soc.* 341 (1959).

[18] We wish to express here our thanks to Professor George Büchi, M.I.T., Cambridge, Mass., U.S.A., who suggested to us this possibility (August, 1962) and derived structure (II) as a consequence of this argument.

[19] The neutral fraction is a mixture of at least three compounds (by v.p.c.). It has been shown by B. P. Jibben and J. P. Wibaut, *Rec. Trav. Chim.* 79, 342 (1960) that ozonolysis of furans can lead to α-dicarbonyl compounds. Our neutral fraction, which was not further studied, could contain the triketone (VI) and/or its cyclization products.

further confirms the presence in III of an isopropyl group attached to the furan ring. It can thus be concluded that ester VIIb is monocyclic (ring not larger than C_5). If the structure hypothesis is correct, the keto acid VIIa must be one of the eight possible stereoisomeric nepetonic acids, three of which are known as degradation products of nepetalactone and isonepetalactone.[20] Our keto ester (VIIb) is neither methyl *trans-trans*-nepetonate (VIIIb) nor its optical antipode. Acid VIIa affords a 2,4-DNP (m.p. 170–172°), which depresses the melting point when mixed with an authentic sample of the 2,4-DNP of VIIIa (m.p. 174–175°).[21] Furthermore, the semicarbazone of VIIb melts at 159–161°, while that of VIIIb melts at 180–181°.[22]

Our keto acid (VIIa) is neither *cis-trans*-nepetonic acid (IXa) nor its antipode because IXa epimerizes so easily to VIIIa that it is difficult to isolate.[20] The unknown *cis-cis*-nepetonic acid (Xa) or its antipode would be expected to epimerize even more easily than IXa. Keto acid VIIa could then be *trans-cis*-nepetonic acid (XIa) or its antipode; indeed, the 2,4-DNP of our keto acid (VIIa) melts at 170–172° while the same derivative of *trans-cis*-nepetonic acid melts at 170–171°.[20] Due to lack of comparison samples or IR spectra, we then had to degrade further the keto acid VIIa.

Degradation of VIIa by sodium hypobromite afforded a crystalline diacid (XIIa), $C_8H_{12}O_4$, m.p. 106–110°, $[\alpha]_D^{25}$, −76°, which might then be *trans-cis*-nepetic acid (XIIIa). The three nepetic acids corresponding to the three nepetonic acids (VIIIa, IXa and XIa) are known,[20] and the synthesis of the four racemates of the stereoisomeric nepetic acids has been described.[23] (±)-*trans-cis*-Nepetic acid (XIIIa) has m.p. 114° and $[\alpha]_D$ +85°. Our diacid furthermore afforded a liquid dimethyl ester (XIIb) whose IR spectrum is identical in all respects with that of synthetic dimethyl (±)-*trans-cis*-nepetate.[23] Our diacid is therefore (−)-*trans-cis*-nepetic acid.[24] This result establishes the relative and absolute configurations in III.

Nevertheless, structure VIIa for the keto acid still had to be ascertained because XIVa would also lead to the diacid (XIIa) by hypobromite oxidation. We therefore submitted our keto ester (VIIb) to a Baeyer–Villiger oxidation, which afforded the acetoxy ester (XVb). Saponification followed by esterification led to the hydroxy ester (XVIb) which was oxidized to the keto ester (XVIIb). This was then saponified and decarboxylated to (+)-3-methylcyclopentanone, of absolute configuration XVIIIc. Comparison with an authentic sample was done by IR spectra and optical rotation; in addition, the dibenzylidene derivative of our ketone did not depress the melting point of an authentic sample (XVIIId) and had the same rotation. This result confirms the absolute configuration of furopelargones A and B as well as structure

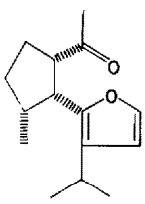
[20] R. B. Bates, E. J. Eisenbraun and S. M. McElvain, *J. Amer. Chem. Soc.* **80**, 3420 (1958). It should be noted here that the correct stereochemistry in the nepetalactone series has been elucidated by these authors in a later communication (Ref. 23).

[21] We wish to thank Professor E. J. Eisenbraun, Oklahoma State University, Stillwater, Okla., U.S.A., for having kindly provided this and other samples.

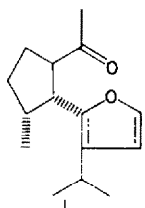
[22] S. M. McElvain, R. D. Bright and P. R. Johnson, *J. Amer. Chem. Soc.* **63**, 1558 (1941).

[23] R. B. Bates, E. J. Eisenbraun and S. M. McElvain, *J. Amer. Chem. Soc.* **80**, 3413 (1958).

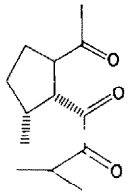
[24] The slight difference in the m.p. and in the absolute value of the rotation, as well as the difficulties we met in efforts to purify our compound, further indicate that our diacid might contain a small amount of a steroisomer. *Added in proof:* Professor E. J. Eisenbraun has recently found our diacid to be identical with (—) *trans-cis* nepetic acid synthesized in his laboratory (mixed m.p.). We wish to thank him for running this comparison.



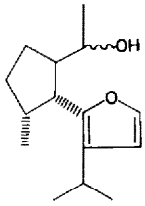
IV



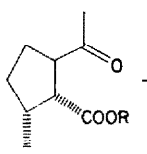
III



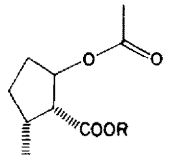
VI



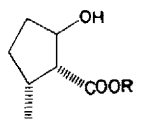
V



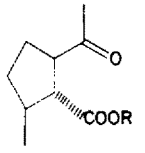
VII



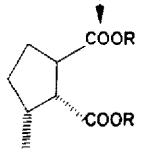
XV



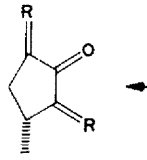
XVI



VIII

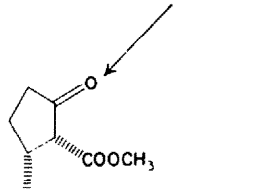


XII

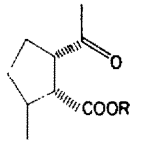


XVIII

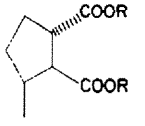
(c) R = H_2
(d) R = C_6H_5CH-



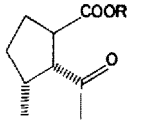
XVII



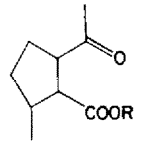
IX



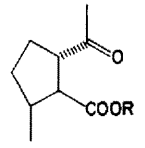
XIII



XIV



X



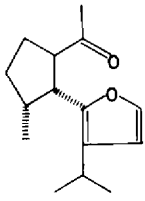
XI

(a) R = –H
(b) R = $-CH_3$

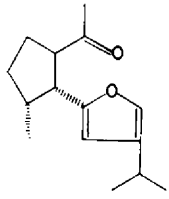
VIIa for the keto acid obtained by ozonization. Had this acid been XIVa, 2-methylcyclopentanone should have been obtained.

The distribution of the two substituents (isopropyl group and substituted cyclopentane ring) on the furan ring had still to be determined. Four structures can be written, with the furan ring bearing one α and one β or β' substituent (XIX to XXII).

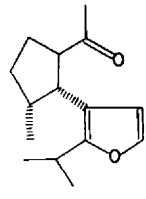
On catalytic hydrogenation, III consumed three moles of hydrogen and afforded a compound $C_{15}H_{28}O_2$. Its IR spectrum showed a carbonyl band at 1700 cm^{-1} and a hydroxyl band at 3740 cm^{-1}. The NMR spectrum indicated the absence of an aldehyde group. The absence of a methyl peak around 120 c/s showed that the ketone function of III must have been reduced, apparently to an alcohol, whereas the new ketonic function had to arise from a hydrogenolytic cleavage of the furan ring. Such a cleavage is by no means unusual under our working conditions,[25] to give a ketone group at the more substituted α position of the former furan ring.[26] It is then possible to write structures XXIII to XXVI for this ketol. In order to assign one of these four structures to our ketol, and accordingly, one of the four structures (XIX to XXII) to furopelargone A, the ketol was deuterated in positions α to the carbonyl group, and a detailed and comparative study of the mass spectra of undeuterated and deuterated compounds was undertaken. It will be shown that the ketol can be represented only by XXIII, and consequently furopelargone A by XIX $\equiv$ III.[27] Furopelargone B is then represented by IV.



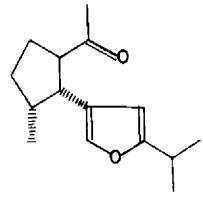
XIX



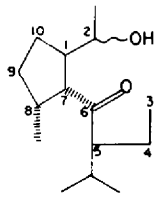
XX



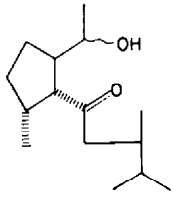
XXI



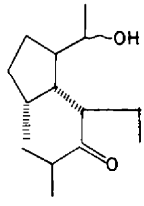
XXII



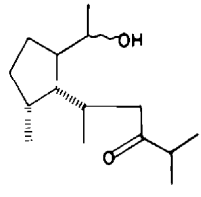
XXIII



XXIV



XXV



XXVI

The mass spectrum (Fig. 1) of the unlabelled ketol exhibits the expected molecular peak at m/e 240,which shifts cleanly to m/e 242 in the case of the deuterated compound. Thus, the incorporation of two atoms of deuterium is consistent with structures

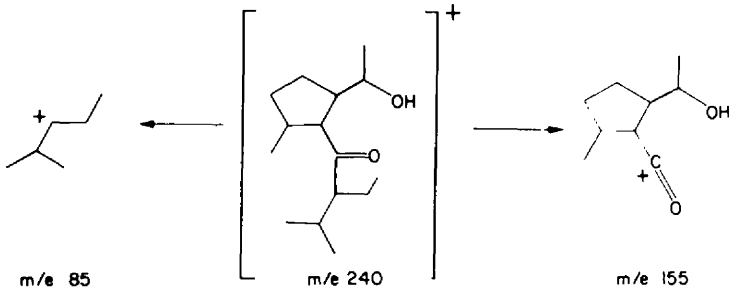
[25] Hydrogenation in ethanol with Pt or Pd—C catalysts yielded only starting material.

[26] H. A. Smith and J. F. Fuzek, *J. Amer. Chem. Soc.* **71**, 415 (1949). In the case of simple, unhindered furans, these authors observed a further reduction to an alcohol. This is prevented in our case, due to considerable steric hindrance.

[27] *Added in proof:* We have been informed by Professor G. Büchi and Mr. H. Wüest that they have completed a synthesis of furopelargone A, and found that the synthetic and natural products had identical IR and NMR spectra as well as v.p.c. retention time.

XXIII and XXV, but not with XXIV and XXVI, since the latter would contain three exchangeable hydrogens each. The possibility of selective exchange of only two hydrogens out of the three in XXIV and XXVI is excluded, since it will be later shown that the two exchanged hydrogens are not attached to the same carbon atom.

The assignment of structure XXIII is indicated by cleavage of the C-5, C-6 bond, yielding m/e 155 and 85.



Charge retention is well stabilized on either the carbonyl group (m/e 155), a common process in the mass spectra of aliphatic ketones,[28] or the secondary carbon atom of the hydrocarbon fragment (m/e 85).[29] Fragments expected from structures XXIV to XXVI do not correspond to both the observed m/e values and the necessary charge stabilization on both halves. Further evidence for the above structural assignment of m/e 155 and 85 to XXIII is their complete shift to m/e 156 and 86, respectively, in the spectrum of the deuterated compound. In addition, the shift of only one mass unit each indicates a virtual certainty that there are not two deuterium atoms attached to one carbon atom, which further excludes XXIV and XXVI, as mentioned previously.

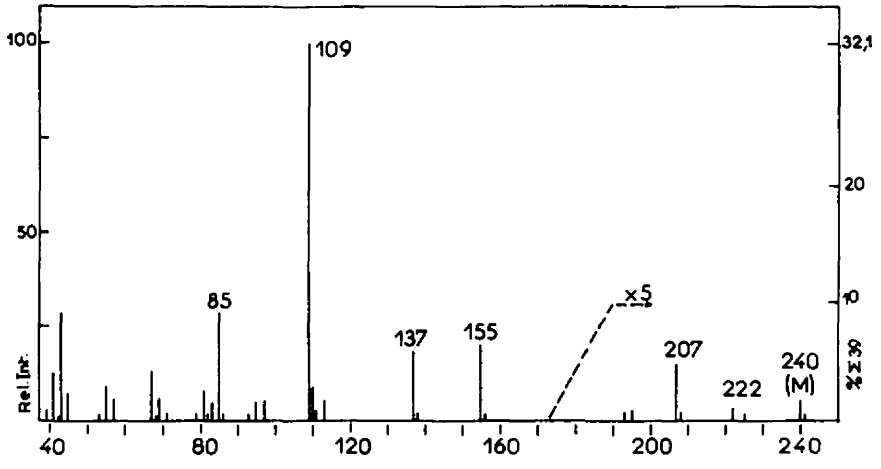


FIG. 1. Mass spectrum of hexahydrofuropelargone A.

[28] A. G. Sharkey, G. L. Schultz and R. A. Friedel, *Analyt. Chem.* **28**, 934 (1956).

[29] For interpretation of mass spectra, see K. Biemann, *Mass Spectrometry*, McGraw-Hill, New York (1962).

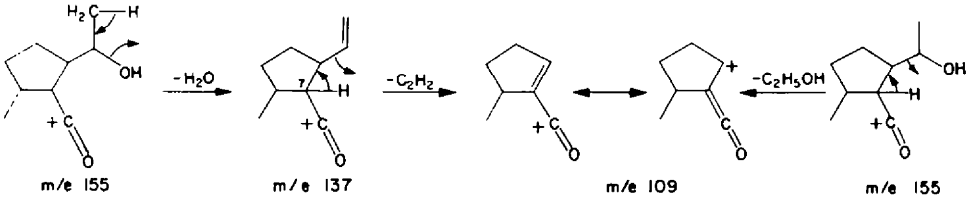
Formation of the most intense peak in the spectrum, m/e 109, occurs through several different paths, as indicated by (i) metastable peaks shown in Table 1, (ii) the splitting of m/e 109 into approximately 40% m/e 109 — 60% m/e 110 in the spectrum of the deuterated compound.

TABLE 1. METASTABLE PEAKS FROM THE MASS SPECTRUM OF HEXAHYDROFUROPELARGONE A (FIG. 1)

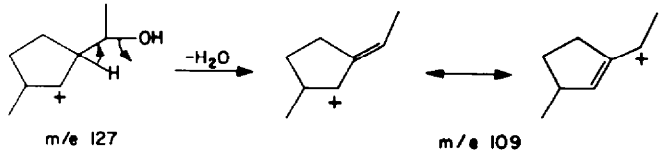
m* calc	m* obs	Transition indicated
121·1	121·2	$155^+ \rightarrow 137^+$
86·7	86·9	$137^+ \rightarrow 109^+$
76·7	77·2	$155^+ \rightarrow 109^+$
93·5	93·8	$127^+ \rightarrow 109^+$

Loss of water from m/e 155 to yield m/e 137 can occur by a 1,2-elimination, forming a vinyl group. Further elimination of ethylene, involving the hydrogen atom on C-7 yields the well stabilized ion at m/e 109 (also m/e 109 in the spectrum of the deuterated compound). Elimination of ethanol in the same manner directly from m/e 155 yields an ion of the same formal structure.

A clue to the formation of the m/e 109 ion which contains the hydrogen on C-7 (hence appearing at m/e 110 in the spectrum of the labelled compound) is provided by a weak metastable peak at m/e 93·8, which indicates the transition $127^+ \rightarrow 109^+$ (Table 1). Formation of m/e 127[30] may occur by rupture of the C-6, C-7 bond, with



charge retention on the secondary carbon atom of the ring.[31] Rapid decomposition (hence low intensity) of the m/e 127 ion by loss of water yields m/e 109. A 1,2-elimination would be especially attractive since the resulting olefin would provide allylic stabilization of the positive charge:



Another possibility for the formation of the m/e 109 ion shown above is from m/e 222 (M-18), in which case the double bond resulting from 1,2-elimination of water would provide allylic activation of the bond to be broken (C-6, C-7). This

[30] Relative intensity 0·9%, too low for representation in Fig. 1.

[31] Charge retention on the carbonyl group would yield m/e 113, a peak of low intensity in Fig. 1.

however, does not seem to be the case, since there is no metastable peak observed corresponding to $222^+ \rightarrow 109^+$, and since initial loss of water is not a 1,2 process as shown by the shift of m/e 222 to 223 (M-HDO) in the spectrum of the deuterated compound.

EXPERIMENTAL

IR spectra were recorded either on a Perkin-Elmer Infracord 137-B (I) or on a Unicam S.P. 100 (U) spectrophotometer. UV spectra were recorded on a Perkin-Elmer Spectracord 202 spectrophotometer, using ethanol as solvent. NMR spectra were recorded on a Varian A-60 spectrometer using tetramethylsilane as internal standard. Mass spectra were determined with an Atlas-Werke CH4 mass spectrometer; ionizing energy 70 eV; ionizing current 40 μA; inlet temp. 140°. Rotations were measured either on a Hilger Standard Polarimeter (H), or on a Roussel-Jouan electronic Quick-Polarimeter (R). Solutions were made in $CHCl_3$ unless otherwise stated. Optical rotatory dispersion curves were measured with a Rudolph photoelectric spectropolarimeter using dioxan as solvent. Aerograph A-90-P vapor-phase chromatograph was used, with a 20% D.C. silicone grease on Celite column. Thin layer chromatoplates made of Kieselgel-G Merck, were eluted with hexane—ethyl acetate (85:15), sprayed with 50% H_2SO_4 and heated under an IR lamp. Microanalyses were performed by the microanalytical department of Messrs. Firmenich and Cie, Geneva, and by the microanalytical department of the Centre National de la Recherche Scientifique.

Isolation of furopelargones A *and* B[32]

Fractional distillation of the oil of *Geranium bourbon* yields 90% material boiling under 70° (0·1 mm). The remaining residue was used as starting material. To 500 g of this residue dissolved in 500 ml absolute ethanol, were added 30 g Girard Reagent T and 5 g Amberlite IRC-50 in its dry, acidic, commercial form.[33] The mixture was heated to boiling for 2 hr under N_2. Most of the ethanol was then removed *in vacuo*. After cooling and dilution with 850 ml ether, the resin was filtered off. Extraction of the ethereal solution successively with 850 ml and then 250 ml water gave an aqueous solution of the hydrazones T. These were hydrolyzed by acidification with HCl aq to pH 2, and after 1 hr at room temp, the carbonyl compounds were extracted with ether. The ethereal solution was washed with water to neutrality and dried (Na_2SO_4). After evaporation of the solvent a dark brown oil (18 g) was obtained, which, after a crude distillation under high vacuum furnished a light yellow oil (9 g). According to v.p.c., this oil contains 2 major components, named in the order of elution furopelargones A and B, in a proportion 55:45 as calculated from the ratio of peak areas. Both compounds appear as pink spots on chromatoplates under the conditions described previously (R_f about 0·7 and 0·5, respectively). Furopelargones A (2·3 g) and B (1·7 g) could be obtained pure after 2 successive chromatographies on silicic acid (elution with hexane–ether 19:1). Both substances are unstable to air and acidic conditions; they were kept in sealed tubes at 0°.

Furopelargone A, b.p.$_{0\cdot05}$: 60–62°; $[\alpha]_D^{25}$, −105° (*c*, 0·6) (H); optical rotatory dispersion: $[\alpha]_D$ −88°;[34] $[\alpha]_{305\ m\mu}$ −1547°: $[\alpha]_{290\ m\mu}$ −500°. UV spectrum: λ_{max} 219 mμ (ε 7400). IR spectrum (U) (10% solution in CCl_4 and CS_2): 2950, 2870, 1715, 1528, 1472, 1388, 1369, 1270, 1260, 1232, 1174, 1150, 1070, 1014, 891, 841, 759, 733 and 700 cm^{-1}. NMR spectrum (CCl_4): 38 and 46 c/s (doublet, 3H) 63 and 74 c/s (doublet, 6H). 119 c/s (singlet, 3H), 369 and 371 c/s (doublet, 1H), 429 and 431 c/s (doublet, 1H). (Found: C, 77·09; H, 9·50. $C_{15}H_{22}O_2$ requires: C, 76·88; H, 9·46%). Mol. wt: 234 (by mass spectrometry).

Semicarbazone: m.p. 152–153° (CH_3OH). (Found: C, 65·40; H, 8·90; N, 13·93. $C_{16}H_{27}O_2N_3$ requires: C, 65·49; H, 9·28, N, 14·32%).

2,4-Dinitrophenylhydrazone: m.p. 98° (CH_3OH). (Found: C, 60·75; H, 6·79. $C_{21}H_{26}O_5N_4$ requires: C, 60·85; H, 6·32; N, 13·52%). IR spectrum: no band in the carbonyl region.

Furopelargone B, b.p.$_{0\cdot1}$: 81–83°; $[\alpha]_D^{26}$, +49° (*c*, 1·5) (H); Optical rotatory dispersion: $[\alpha]_D$ +59°[34]; $[a]_{305\ m\mu}$ +1266°; $[\alpha]_{290\ m\mu}$ +189°. U.V. spectrum: λ_{max} 219 mμ (ε 8500). IR spectrum (U) (10% solutions in CCl_4 and CS_2): 2960, 2880, 1721, 1525, 1475, 1390, 1365, 1295, 1190, 1160, 1135, 1080, 1020, 898, 848, 752, 718 cm^{-1}. NMR spectrum (CCl_4): 40 and 47 c/s (doublet, 3H) 66 and 73 c/s

[32] We wish to thank here Dr. F. Bruderlein who carried out the first isolation of these two ketones.
[33] C. L. Teitelbaum, *J. Org. Chem.* **23**, 646 (1958).
[34] The discrepancy between the two $[\alpha]_D$ given here is due to the lower accuracy of the spectropolarimeter in this wavelength range.

(doublet, 6H), 106 c/s (singlet, 3H), 371 and 373 c/s (doublet, 1H) 433 and 435 c/s (doublet, 1H). (Found: C, 76·85; H, 9·46. $C_{15}H_{22}O_2$ requires: C, 76·88; H, 9·46%). Mol. wt: 234 (by mass spectrometry); the mass spectra of furopelargones A and B are identical. Semicarbazone: m.p. 160–164°.

Epimerization of IV *to* III. To 5·2 g of a mixture (ratio 55:45) of the two ketones dissolved in 30 ml methanol were added 10 ml 2N Na_2CO_3 and 15 ml water. After boiling under N_2 for 2 hr and cooling, 50 ml water was added and the reaction product extracted with ether. The ethereal solution was washed with water to neutrality and dried over Na_2SO_4. After evaporation of the ether 5 g oil was obtained. According to v.p.c. this was a 88:12 mixture of furopelargones A and B, which gave easily the semicarbazone of III in good yield.

For degradation studies of III, the distilled carbonyl fraction from the Girard reaction was treated by base, as indicated above, and the reaction product further purified by column chromatography on silicic acid.

Reduction of furopelargone A *by sodium borohydride.* Furopelargone A (556 mg, 2·4 mmoles) and $NaBH_4$ (70 mg, 1·85 mmoles) were dissolved in 25 ml absolute methanol and kept at room temp for 24 hr. After addition of a few drops glacial acetic acid and water, the reaction product was extracted with ether. The ethereal solution was washed with sat. NaCl aq to neutrality, then dried (Na_2SO_4). Evaporation of the solvent left 425 mg colorless oil, $b.p._{0·06}$: 95°; $[\alpha]_D^{28}$ −18° (*c*, 0·9) (H). IR spectrum (liquid film): 3500, 2950, 1520, 1465, 1340, 1150, 1100, 1060, 1000, 950, 890, 855, 840, 760, 720, 700 cm^{-1}. NMR spectrum (CCl_4): 36 and 43 c/s (doublet, 3H), 60, 66 and 73 c/s; 82 c/s; 205, 212, 218, 225, 231 c/s (multiplet, 1H), 378 and 380 c/s (doublet, 1H), 434 and 436 c/s (doublet, 1H). (Found: C. 76·33; H, 10·31. $C_{15}H_{24}O_2$ requires: C, 76·22; H, 10·24%). Mol. wt: 236 (by mass spectrometry).

Deuteration of furopelargone A. To a solution of 96 mg III in 5 ml anhydrous, peroxide-free dioxan were added 2 ml D_2O (99·75%) and 45 mg anhydrous Na_2CO_3. After boiling 30 min under dry N_2, most of the solvent was removed *in vacuo*. The residue was extracted with anhydrous ether. The ethereal solution was washed once with 2 ml D_2O and dried over Na_2SO_4. After removal of the solvent, 71 mg colorless oil was obtained, $b.p._{·1}$: 90° (bath temp). Its IR spectrum is identical with that of III.

Ozonization of III. *Methyl* trans-cis-*nepetonate* (VIIb). A stream of oxygen + ozone was bubbled through a solution of 6·6 g furopelargone A in 150 ml dry ethyl acetate at −70° for 4 hr. The reaction mixture became green-blue and did not react further with tetranitromethane. The solvent was then evaporated *in vacuo* at room temp. Water (150 ml) and 6% H_2O_2 (50 ml) were added and the mixture was heated in a water bath for 1 hr with intermittent shaking. Organic material was extracted from the cooled mixture with ether. The ethereal phase was washed twice with 1N NaOH, then with a sat. NaCl aq to neutrality. After evaporation of the solvent from the dried solution 1·4 g neutral material was obtained. This yellow oil was a mixture (v.p.c.) and was not studied further. The basic extracts were then acidified with HCl aq and extracted with ether. The ethereal solution was washed with a sat. NaCl aq and dried as usual. Evaporation of the solvent afforded 3·8 g acidic material. It was treated with excess diazomethane in ether. After evaporation of the ether, distillation yielded, in addition to some nondistillable, tarry material, 2·4 g of an oil, $b.p._{·03}$: 54–60°, which was further purified by chromatography on silicic acid. The pure compound (by v.p.c. and t.l.c.) was eluted with hexane–ether (9:1).

$B.p._{·03}$: 54–57; $[\alpha]_D^{20}$ −30°(R) (*c*, 1). IR spectrum (U) (10% solutions in CCl_4 and CS_2): 2950, 2870, 1740, 1719, 1465, 1441, 1386, 1360, 1237, 1203, 1170, 1035, 1000, 963, 924, 760 cm^{-1}. NMR spectrum (CCl_4): 48 and 55 c/s (doublet, 3H), 125 c/s (singlet, 3H), 215 c/s (singlet, 3H). Mol. wt: 184 (by mass spectrometry). (Found: C, 65·07; H, 8·77. $C_{10}H_{16}O_3$ requires: C, 65·19; H, 8·75%). Semicarbazone: m.p. 159–161° ($CH_3OH—H_2O$). (Found: C, 54·88, H, 8·14; N, 17·80. $C_{11}H_{19}O_3N_3$ requires: C, 54·75; H, 7·94; N, 17·42%).

Saponification of keto ester (VIIb) *to keto acid* (VIIa). A mixture of 530 mg keto ester (VIIb) and 50 ml 2·5 N NaOH aq was heated with stirring at 90° for 45 min. After cooling, the homogeneous solution was washed once with ether, then acidified and extracted with ether. The ethereal solution was washed and dried as usual. After evaporation of the solvent, 430 mg acidic material was obtained. As this keto acid seemed to distil with partial decomposition, it was used without purification for further reactions.

2,4-Dinitrophenylhydrazone: m.p. 171–173°, soluble in NaOH aq with a deep brown-violet color. (Found: C, 51·48, H, 5·56; N, 15·61. $C_{15}H_{18}O_6N_4$ requires: C, 51·42; H, 5·18; N, 15·99%). A mixture of this compound with authentic 2,4-dinitrophenylhydrazone of *trans-trans*-nepetonic acid

(m.p. 170–172°) had a lower m.p. (151–159°). The two compounds could not be distinguished by thin layer chromatography.

(−)-trans-cis-*Nepetic acid* (XIIa) *and its ester* (XIIb). To a solution of 117 mg (0·65 mmole) keto acid in 5 ml 2·5N NaOH aq was added NaOBr aq (625 mg Br_2 in 5·5 ml 2·5N NaOH); these proportions correspond to a tenfold excess of hydroxide and a twofold excess of Br_2.[35] The mixture was stirred for 30 min at room temp during which period crystalline CBr_4 separated. It was filtered off and 1 g Na_2SO_3 was added to the filtrate. The solution was then acidified with H_2SO_4 aq. Continuous extraction with ether during 6 hr, drying the ethereal solution over Na_2SO_4 and evaporation of the solvent afforded 110 mg crude diacid (XIIa). Chromatography on silicic acid (elution with benzene–ether 9:1) gave colorless crystals, which after 2 recrystallizations from chloroform–hexane melted at 106–110°. This m.p. did not change after further recrystallizations. $[\alpha]_D^{19}$, −76° (*c*, 1) (R). (Found: C, 55·60; H, 6·80. $C_8H_{12}O_4$ requires: C, 55·80; H, 7·03%).

This diacid was then esterified by ethereal diazomethane. The IR spectrum of XIIb is identical to the spectrum of (±)-*trans-cis*-nepetic acid methyl ester[23] and different from the spectra published of the other stereoisomers. IR (I) (liquid film): 2950, 1720, 1455(sh), 1430, 1375, 1350, 1325, several shoulders between 1300 and 1230, 1200, 1175, 1140(sh), 1115(sh), 1050(sh), 1030, 1005, 920, 875, 815(sh), 780, 760, 720 cm^{-1}.

Baeyer-Villiger oxidiation of the keto ester (VIIb) *to acetoxy ester* (XVb). An ice-cold, homogeneous solution of trifluoroacetic anhydride (2·5 ml) and 0·5 ml 85% H_2O_2 in 20 ml methylene chloride was added in 5 min to a stirred mixture of the keto ester (1·7 g) and anhydrous Na_2HPO_4 (6 g) in 20 ml methylene chloride at 0°. The mixture was stirred at 0° for 8 hr, then allowed to stand at room temp for 2 days. After filtration of the insoluble salts the solution was washed successively with $NaHSO_3$ aq, water, $NaHCO_3$ aq, water and a sat. NaCl aq. After drying over Na_2SO_4 and removal of the solvent, a colorless oil (1·9 g) was obtained. Chromatography over silicic acid afforded a pure product (1·3 g), eluted with hexane–ether (9:1), $b.p._{0·1}$: 150° (bath temp); $[\alpha]_D^{25}$, −26° (*c*, 2,) (R). IR spectrum (U) (liquid film): 2950, 1740, 1460, 1435, 1375, 1365, 1290, 1235, 1200, 1150, 1110, 1030, 1000, 980, 920, 765 cm^{-1}. NMR spectrum (CCl_4): 52 and 59 c/s (doublet, 3H), 118 c/s (singlet, 3H), 221 c/s (singlet, 3H). (Found: C, 60·43; H, 7·99. $C_{10}H_{16}O_4$ requires: C, 59·98; H, 8·05%).

Hydrolysis of XVb. *Hydroxy ester* (XVIb). The acetoxy ester (XVb; 1·15 g) was heated and stirred on the steam bath with a Na_2CO_3 aq (1·3 g in 50 ml water) for 1 hr. The cooled homogeneous solution was washed once with ether to remove any unreacted material, and it was then acidified with dil. HCl. Solid NaCl was then added until saturation. Continuous extraction of the solution with ether provided a viscous colorless oil (550 mg). It was esterified with diazomethane and the hydroxy ester (XVIb) was used for the next step without further purification.

Jones oxidation of the hydroxy ester (XVIb) *to the keto ester* (XVIIb). A standard solution[36] of CrO_3 in dil. H_2SO_4 aq was added dropwise to a solution of the crude hydroxy ester (520 mg) in acetone (40 ml, freshly distilled from $KMnO_4$ until the orange color persisted. The mixture was allowed to stand 10 min, then it was decolorized with a few frops of methanol, filtered and evaporated. The residue was dissolved in ether and the solution was washed several times with sat. NaCl aq. Evaporation of the solvent from the dried solution left a colorless oil (420 mg). Chromatography over silicic acid afforded the pure keto ester (XVIIb), $[\alpha]_D^{25}$, +78° (*c*, 2) (R); IR spectrum (liquid film) (I): 2950, 1770, 1740, 1460, 1430, 1410, 1370, 1340, 1300, 1260, 1230, 1210, 1180, 1160, 1130, 1100, 1080, 1050, 1025, 1010, 960, 930, 915, 850, 780 cm^{-1}.

Hydrolysis and decarboxylation of the keto ester (XVIIb) *to* (+)-3-*methylcyclopentanone* (XVIIIc). A mixture of XVIIb (195 mg), *p*-toluenesulfonic acid monohydrate (65 mg), ethylene glycol (0·5 ml) and water (1·5 ml) was heated to boiling for 3 hr in a 120° oil bath and then allowed to stand at room temp overnight. It was diluted with water and extracted several times with ether. The combined ethereal extracts were washed successively with $NaHCO_3$ aq and a sat. NaCl aq then dried over Na_2SO_4. Careful evaporation of the solvent through a short Vigreux column left a liquid residue. Distillation from a bubble tube under atm. press. yielded (+)-3-methylcyclopentanone (32 mg) as a colorless, volatile liquid, possibly contaminated with a small amount of solvent, $[\alpha]_D^{25}$, +101° (*c*, 2 in ethanol) (R); an authentic sample[37] had $[\alpha]_D^{25}$, +124°. The ethanolic solution of the ketone (XVIIIc) was mixed with freshly distilled benzaldehyde (85 mg) and was diluted with ethanol to 3 ml. To this vigorously stirred colorless solution, sodium hydroxide (300 mg) in water (3 ml) was

[35] K. J. Morgan, J. Bardwell and C. F. Cullis, *J. Amer. Chem. Soc.* **72**, 3190 (1950).

[36] C. Djerassi, R. R. Engle and A. Bowers, *J. Org. Chem.* **21**, 1547 (1956).

added in one portion. A light yellow precipitate was formed after 2 min. This crystalline product was collected after 30 min, washed thoroughly with water to remove all alkalinity and dried in a desiccator. Recrystallization from ethanol afforded the (−)-2,5-dibenzylidene-3-methylcyclopentanone (XVIIId), m.p. 150–151°, $[\alpha]_D^{25}$, −54° (*c*, 1). (Found: C, 87·34; H, 6·47. $C_{20}H_{18}O$ requires: C, 87·56; H, 6·61%). It did not depress the m.p. of an authentic sample prepared the same way from authentic XVIIIc.[37] (m.p. 150–152°), $[\alpha]_D^{25}$ −52°(H) (*c*, 1).

Hydrogenation of III *and acetylation of the crude hexahydrofuropelargone* A. A solution of III (580 mg) in 20 ml acetic acid was hydrogenated at atm. press., using Pt catalyst prepared from 180 mg PtO_2. The solution consumed 194 ml H_2 (theory: 180 ml for 3 moles of H_2 per mole of III, corrected for temp) and the uptake stopped after 2 hr. The filtered solution was diluted with ether and the acetic acid was removed by washing the ethereal phase successively with NaCl aq, NaOH aq and again NaCl aq to neutrality. Evaporation of the solvent from the dried solution yielded 570 mg hydrogenated material. Thin layer chromatography indicated two hardly separated major components in addition to other minor impurities. The crude product was therefore acetylated with 1·5 ml acetic anhydride in 5 ml dry pyridine overnight at room temp followed by 1 hr at 110°. The cooled reaction mixture was taken up in ether. After washing successively with 2N HCl (twice), then sat. NaCl aq to neutrality, the solvent was evaporated from the dried solution to yield 550 mg crude product. Chromatography over silicic acid (elution with pet. ether–ether 19:1) gave the pure keto acetate (300 mg, one spot by t.l.c.), $b.p._{\cdot 0\cdot 1}$: 95° (bath temp), $[\alpha]_D^{20}$, −4·5° (*c*, 1·67) (R); IR spectrum (I) (liquid film): 2950, 1735, 1700, 1460, 1370, 1245, 1175, 1145, 1125, 1095, 1060, 1040, 955, 940, 850, 800, 790 cm^{-1}. Mol. wt: 282 (by mass spectrometry). (Found: C. 72·38; H, 10·55. $C_{17}H_{30}O_3$ requires: C, 72·30; H, 10·71%).

Hexahydrofuropelargone A (XXIII). A 155 mg portion of the purified keto acetate was saponified by heating for 2 hr with 10 ml methanol and 5 ml NaOH aq. After addition of 50 ml water to the cooled solution and extraction with ether, the organic layer was washed to neutrality. Evaporation of the solvent from the dried solution left a colorless oil (127 mg). Thin layer chromatography of this material showed two slightly separated spots of comparable intensity. By careful chromatography, some material corresponding to one spot could be obtained. It had a mass spectrum identical to that of the material before chromatography. Accordingly, the two substances are most likely the epimers arising from hydrogenation of the ketone group of III. The following data correspond to the mixture of these epimers: $b.p._{\cdot 0\cdot 1}$: 100° (bath temp); $[\alpha]_D^{24}$ −3° (*c*, 2·5) (R); IR spectrum (U) (10% solutions in CCl_4 and CS_2): 3630, 3470, 2960, 2870, 1700, 1467, 1390, 1309, 1276, 1238, 1183, 1105, 1065, 963, 916, 808, 766, 680 cm^{-1}. Mol. wt: 240 (by mass spectrometry).

Deuteration of XXIII. Experiments showed that exchange did not occur under the conditions previously used for the deuteration of III. The following conditions were necessary: in a 25 ml flask fitted with a reflux condenser and $CaCl_2$ drying tube, and containing 2 ml D_2O (99·75%), freshly cut metallic Li (about 50 mg) was added. It reacted vigorously but without burning. To this solution of LiOD in D_2O was added 56 mg XXIII dissolved in 3 ml anhydrous dioxan. After 60 hr at room temp the mixture was heated for 2 hr. Anhydrous ether (15 ml) and anhydrous Na_2SO_4 were added to the cooled solution. After 2 hr, the ethereal solution was decanted, the residue washed with anhydrous ether and the combined solvents evaporated to leave 51 mg deuterated product (neutral to indicator paper) $b.p._{\cdot 0\cdot 05}$: 70° (bath temp). It had an IR spectrum identical to that of XXIII. The mass spectrum (discussed in the theoretical part) showed a mol. wt of 242.

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Note added in proof (14 *May* 1964): The structure of pelargone has recently been reported by Romanuk *et al. Coll. Czech. Chem. Comm.* **29**, 1048 (1964) and is identical with that of furopelargone A reported above.[6]

[37] We wish to thank here Dr. J. Jacques, Collège de France, Paris for the generous supply of this compound.