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THE FORMATION AND X-RAY CRYSTAL STRUCTURE OF A NOVEL BRIDGED DILACTONE DERIVED FROM CHRYSANTHEMIC ACID BY DIMERIZATION OF LAVANDULYLIC ACIDS

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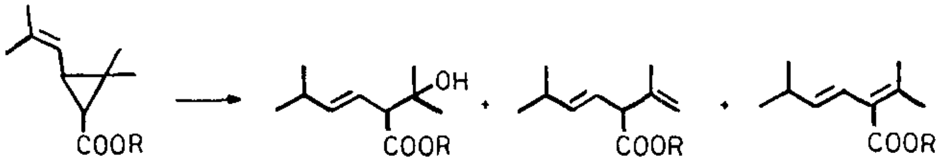
Abstract - Thermal acid catalysed rearrangement of chrysanthemic acid or its ethyl ester afforded 5,8-[1-(2-methylpropyl)]-ethano-3,3,8-trimethyl-5-(2-methylethyl)-3,4,4a,5,8,8a-hexahydro-1H,6H-pyrano[3,4-c]-pyran-1,6-dione, the structure of which was confirmed by X-ray analysis.

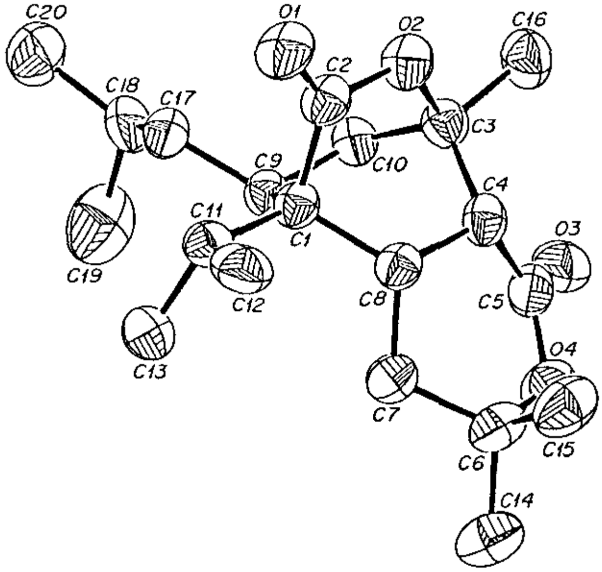
It has been reported that chrysanthemic acid and its esters (1) undergo acid catalysed rearrangements to give mainly lavandulylic acid ester derivatives (2), (3) and (4),[1-3] which at high temperatures (>130°C) cyclize to lactones.[1-2]
As part of our investigations of the two-phased acid catalysed rearrangements of chrysanthemic acid esters we have isolated the novel ethano-bridged δ,δ-dilactone (5), a formal dimer of two isomeric lavandulylic acids (3) and (4).
Thus, after refluxing cis/trans chrysanthemic acid or its ethyl ester (1) in a mixture of 65% aqueous sulphuric acid and heptane for 24 h, a colourless crystalline compound, mp 202-203°C, insoluble in pentane, was isolated in low yield. The ir spectrum indicated the presence of two lactone functional groups, which absorbed at ν_{max} 1720 and 1740 cm^{-1}.
The mass spectrum and elemental analysis ($[M]^+$, m/z 336, $C_{20}H_{32}O_4$) as well as the ^{13}C and ^{1}H nmr spectra (two isopropyl and three methyl groups) suggested the structure of a lavandulylic acid dimer in which one of the original methyl groups has entered into the reaction.[4]



(1) (2) (3) (4)

R = H, Me, Et

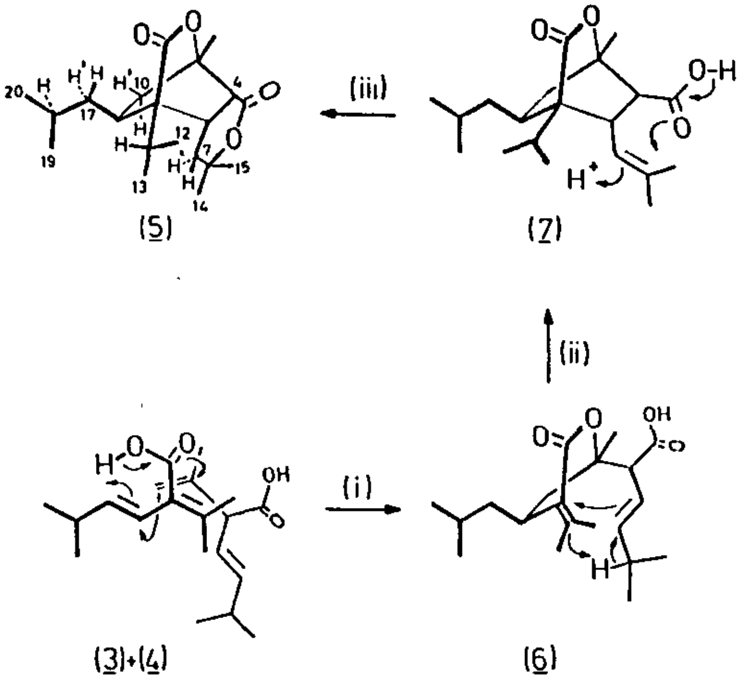
Slow crystallization of (5) from ethyl acetate-pentane afforded crystals suitable for X-ray analysis.[5] The molecular structure of (5) reveals the formation of a novel bridged dilactone in which three sigma bonds (C1-C8, C9-C10 and C3-O2) were formed between two lavandulylic acid fragments. An additional lactonisation within one acid moiety occurred forming the C6-O4 sigma bond.



X-Ray crystal structure of (5)

Careful analysis of the chemical shifts and proton-proton coupling constants in $CDCl_3$ allows a full assignment of the protons,[4] and reveals that the principal conformation of (5) in solution is essentially the same as in the crystalline form. We note in particular the large W coupling constant [J 2.3 Hz] between protons 4 and 10', and the coupling between the protons in the staggered least crowded conformation of the isobutyl side chain. Also notable is the strong deshielded H(11) [δ2.53 ppm] which lies in the plane of the carbonyl C(2)-O(1), and conversely the shielding effect of the same carbonyl on H'(17) [δ0.96 ppm] which lies above the carbonyl plane.[4]

A reasonable mechanism for the formation of (5) involves a three step dimerization of the two isomeric lavandulylic acids (3) and (4) [R=H].



The initial step (i) is an acid catalysed addition of (4) across the terminal double bond of (3) to form the monocyclic lactone (6). This is followed by an unusual intramolecular ene reaction (ii)[6] to form the bicyclic lactone (7). This step is unlikely to be acid catalysed since protonation at the β-position of the unsaturated lactone (6) will result in the formation of an unfavourable carbonium ion adjacent to a carbonyl group. On the other hand, the ene reaction is stereochemically favoured as shown in the scheme, and is likely to proceed concertedly.[6] Finally, the bicyclic lactone (7) being a γ,δ-unsaturated acid, lactonises readily under acid conditions (iii) to the bridged dilactone product (5).

It is interesting to note that the base catalysed reaction of the related chrysanthemyl nitrile in NaH-DMF gave a methano-bridged bicyclic system derived from the reaction of formaldehyde with two molecules of the open chain isomeric artemisic nitrile.[7]

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4. ^{1}H NMR ($CDCl_3$, 300 MHz): δ0.89, 0.90 (Me-19,Me-20), 0.92(H'-17), 0.96 (Me-13), 1.10(Me-12), 1.26(H-17), 1.31(H'-10), 1.40, 1.49(Me-14, Me-15), 1.59(H-18), 1.72(Me-16), 1.73(H'-7), 1.91(H-7), 2.19(H-9), 2.35(H-10), 2.53(H-11), 2.81(H-8), 2.81(H-8), 2.83(H-4), $J_{4,8}{}^{12.1}$, $J_{4,10'}{}^{2.3}$, $J_{7,7'}{}^{13.8}$, $J_{7,8}{}^{6.1}$, $J_{7',8}{}^{12.1}$, $J_{9,10}{}^{9.9}$, $J_{9,10'}{}^{5.2}$, $J_{9,17}{}^{2.5}$, $J_{9,17'}{}^{12.0}$, $J_{10,10'}{}^{14.3}$, $J_{11,12}{}^{6.8}$, $J_{11,13}{}^{7.4}$, $J_{14,15}{}^{0.3}$, $J_{17,17'}{}^{12.8}$, $J_{17,18}{}^{10.8}$, $J_{17',18}{}^{2.9}$, $J_{18,19} = J_{18,20}{}^{6.5}$ Hz.
5. Crystal data: $C_{20}H_{32}O_4$, M=336.5, monoclinic, space group $P2_1/c$, a=8.926(1), b=11.586(1), c=18.750(1) Å, β=91.00(1)°, U=1938.8(5) Å^3; Z=4, D_c=1.153 g cm^{-3}, F(000)=744, μ(Mo-K_α)=0.45 cm^{-1}, λ=0.71069 Å. Crystal size ca 0.5x0.5x0.33 mm. Data were collected on an Enraf-Nonius CAD-4 automated diffractometer with graphite monochromated Mo-K_α radiation using ω-2θ scans (θ_{max} of 25°C), and were corrected for absorption. The structure was solved by direct methods and refined anisotropically using absorption corrected data to R=0.045,R_w=0.082. The unit cell dimensions were obtained by a least-squares fit of 24 centred reflections in the range of 10<θ<15°. Intensities were corrected for Lorentz and polarization effects. All non-hydrogen atoms were found by using the results of the multan direct method analysis.[8]

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