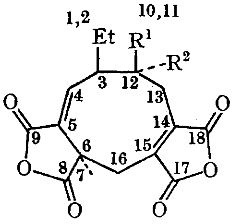
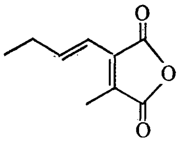
A Novel Synthesis of a Nine-membered Ring

By R. K. HUFF, C. E. MOPPETT, and J. K. SUTHERLAND*
(*Chemistry Department, Imperial College, London S.W.7*)

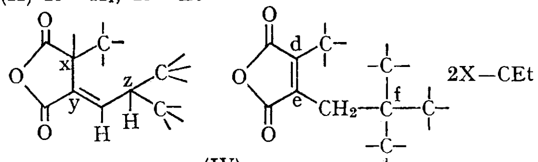
WE have previously shown[1] that glaucanic acid (I) arises biosynthetically by dimerisation of the anhydride (III). In an attempt to realise this reaction chemically (III) was treated with sodium hydride in dimethylformamide and from the reaction a crystalline solid (II), $C_{18}H_{20}O_6$, was obtained in 2% yield (improved to 4% by using triethylamine as base). The spectral data for (I) and (II) summarised in the Table establish the part-structures (IV) for the synthetic product (II) and show that it is mono-carbocyclic and that there are seven chain-terminating groups (methyl or oxidized equivalent) present. This also implies that there are seven branches from the single carbocyclic ring present. However in the part structures (IV) there are eight branches indicated, so that one, or more, of these must be common to both units. By examining the possible identity of any pair of the atoms d, e, f, x, y, and z in (IV) it becomes obvious that only x and f can be common to both part structures; this allows extension of the structure to (V), a major portion of which was confirmed by ozonolysis of (II) to yield the crystalline propane-1,2,2-tricarboxylic acid.[2] The other fragment from the ozonolysis was a liquid glutaric acid, $C_9H_{16}O_4$ (anhydride, ν_{max} 1810 and 1760 cm.$^{-1}$), the properties of which were distinct from those of the two 2,4-diethylglutaric acids but identical (i.r., mass spec., n.m.r., g.l.c., t.l.c.) with those of *threo*-2,3-diethylglutaric acid.† By



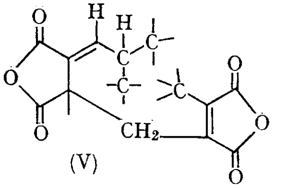
(I) R^1=Et, R^2=H
(II) R^1=H, R^2=Et



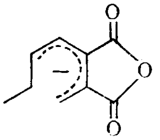
(III)



(IV)



(V)



(VI)

Spectral properties

		Isoglaucanic acid (II)	Glaucanic acid (I)
λ_{max} (cyclohexane)		220 nm. (ϵ 10700), infl. 250 nm.	220 nm. (ϵ 10700), infl. 250 nm.
ν_{max} (Nujol)		1850, 1830, 1765, 1670, 1655	1850, 1830, 1765, 1670, 1655
Mass spectrum	Parent ion	332	332
	Base peak	166	166

N.m.r. spectrum ($CDCl_3$, 100 MHz) (position in τ J in c./sec)

H on:		
C-1, C-10	9·22 (t, J 6), 8·83 (t, J 5)	9·21 (t, J 6), 8·92 (t, J ?)
C-4	3·13 (d, J 11)	3·08 (d, J 12)
C-7	8·51 (s)	8·53 (s)
C-10	7·48, 6·82 (AB, J 13)	7·37, 6.80 (AB, J 13)

---

† Synthesis by the method described in ref. 2 but from (±)-diethylsuccinic acid.

the same criteria the dimethyl and di-*p*-phenylphenacyl esters were identical. However this series showed only minor differences from the *erythro*-2,3-diethylglutaric[2] one but the argument in favour of the *threo*-arrangement of ethyl groups can be strengthened by considering the stereochemistry of (II). Only if the C-3 ethyl and C-7 methyl in (I) and (II) are *trans* can the hydrogens at C-3 and C-4 approach the antiperiplanar stereochemistry‡ required to account for the magnitude of the coupling constant; thus (I) and (II) can only differ in stereochemistry at C-12. The foregoing evidence puts the constitution of (II) beyond doubt and it is virtually certain that the synthetic product is isomeric with the natural at C-12.

We have pointed out[1] that this may be an electrocyclic [6 + 4] addition and the stereo- and position specificity of the reaction tends to support this; no other bisanhydrides of this type are formed in the reaction. The difference between the chemical and biochemical reaction is most readily explained by postulation, in the former case, of isomerisation of the initially formed anion of (II) to the anion (VI) which then adds to (II).

(*Received, July 23rd,* 1968; *Com.* 995.)

---

‡ The n.m.r. argument is supported by the antiperiplanar arrangement found for these hydrogens in the conformation of the related glauconic acid *m*-iodobenzoate as determined by *X*-ray crystallography (G. Ferguson, G. A. Sim, and J. M. Robertson, *Proc. Chem. Soc.*, 1962, 385).

[1] C. E. Moppett and J. K. Sutherland, *Chem. Comm.*, 1966, 772.
[2] D. H. R. Barton, L. D. S. Godinho, and J. K. Sutherland, *J. Chem. Soc.*, 1965, 1779.