The 2,2′-, 3,3′- and 4,4′-Thiodi-(γ-valerolactones)

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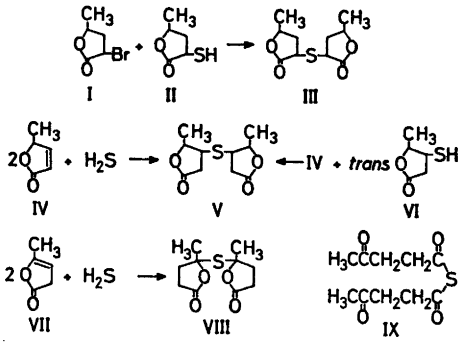
In previous publications,[1,2] the addition of thioacetic acid to α- and β-angelica lactones (VII and IV), respectively, was investigated. During those studies, 2,2′-thiodi-(γ-valerolactone) (III) was obtained as a by-product.[1] The preparation of III from 2-mercapto-γ-valerolactone (II) and 2-bromo-γ-valerolactone (I) is now described. It was shown, by mixed melting point and IR, to be identical with that obtained previously.

III can exist in three diastereomeric forms, *cis,cis-*, *cis,trans-*, and *trans,trans-*, owing to the fact that both I and II exist in *cis-* and *trans*-forms, the latter predominating.[1] III is probably the most stable *trans,trans*-isomer.

3,3′-Thiodi-(γ-valerolactone) (V) is a new compound. This compound was prepared by two independent paths: A. By a base catalysed Michael addition of hydrogen sulphide to IV. B. By the addition of *trans*-3-mercapto-(γ-valerolactone)[2] (VI) to IV.



The first step in A is the formation of VI and the second step is the consecutive addition of VI to IV. VI could also be formed as a by-product. The theoretically possible diastereomers of V are *cis,cis-*, *cis,trans-*, and *trans,trans-*. The stereochemistry of the addition of thioacetic acid to IV was studied by GLC and NMR.[2] It was established that the *S*-acetyl group was predominantly *trans-* to the γ-methyl group in the lactone. The position of the 3-CH was of importance in the determination of the isomeric relationship since this proton was shielded by a neighbouring methyl group in the *trans*-isomer. The 3-CH in V gives a multiplet at $\delta = 3.26$ ppm. The corresponding proton in the *trans*-3-(acetylthio)-γ-valerolactone and in the *trans*-VI showed multiplets at $\delta = 3.81$ and 3.12 ppm, respectively.[2] The corresponding δ values for the *cis*-isomers of the two last compounds were 4.28 and 3.82 ppm, respectively. These considerations indicated that V has the *trans,trans*-configuration. The formation of this stereoisomer might be favored by the steric hindrance exerted by the γ-methyl group and the bulky lactone ring.

B. The addition of the *trans*-VI to IV was also a base catalysed reaction. The addition product from this reaction was shown to be identical with the sample described in A (above). Possible stereoisomers of V in this case were the *cis,trans-* and the *trans,trans*-V. The *trans,trans*-isomer predominates even in this case. This follows from the fact that two samples of V, prepared as described in A and B, were shown to be identical by m.p., IR, and NMR.

Iwakura *et al.*[3] have examined the reaction between VII and hydrogen sulphide in the presence of *p*-toluenesulphonic acid. The possible isomeric products in this reaction are: the 4,4′-thiodi-(γ-valerolactone) (VIII) (ψ-thioanhydride), the n-thioanhydride (IX), *cis-* and *trans*-3,4′-thiodi-(γ-valerolactone) and V (three stereoisomers). Iwakura suggested structures VIII and IX, but did not use spectra as structural proof. No translation was available, but a report of their work mentioned only IX as the product of this reaction. Pryor[4] stated that "in acidic media thiols and hydrogen sulphide add to olefins to give the products which would be predicted from Markownikov's rule." This statement explains the formation of the cyclic isomer (VIII). The fact that the addition product between VII and hydrogen sulphide prepared in the present work gave no semicarbazone, supported also the presence of VIII. The 3,4′-thiodi-(γ-valerolactones) structure and structure V were excluded since the NMR spectrum of the addition product did not show methyl

splitting. The methyl group gave a singlet at $\delta = 2.02$ ppm, indicating the cyclic structure VIII. Similarly, the cyclic levulinylchloride [5] and the cyclic 4-(acetylthio)-γ-valerolactone [2] gave singlets for the γ-methyl group at $\delta = 2.03$ and 1.82 ppm, respectively. The corresponding protons in levulinic acid [6] and n-methyl levulinate [5] gave singlets at $\delta = 2.12$ and 2.13 ppm, respectively. This is good evidence for the structure VIII.

A study of the remaining 2,3′-, 2,4′- and 3,4′-thiodi-(γ-valerolactones) will be published at a later date.

Experimental. α-Angelicalactone (VII) was prepared according to Helberger *et al.*,[7] b.p. 48–50°/9 mm, $n_D^{25} = 1.4460$.

β-Angelicalactone (IV) was prepared from VII according to Thiele *et al.*,[8] b.p. 81–83°/9 mm, $n_D^{25} = 1.4552$.

2-Bromo-γ-valerolactone (I),[1] *2-mercapto-γ-valerolactone (II)* [1] and the trans-*3-mercapto-γ-valerolactone (VI)* [2] were authentic samples from the previous work.[1,2]

2,2′-Thiodi-(γ-valerolactone) (III) 9.0 g I, 6.6 g II and 30 ml benzene were mixed. A solution of 7.0 ml triethylamine in 20 ml benzene was added dropwise to this solution over 30 min with stirring and cooling. The cooling bath was removed and the mixture was allowed to stand at room temperature for 24 h. The reaction mixture was extracted with 50 ml water. The benzene solution was dried and the benzene removed under reduced pressure on a rotary evaporator to yield 10.9 g of an oil. Scratching with a glassrod induced crystallisation. After several days the crystals were filtered at the pump and recrystallised twice from benzene-petroleum ether. 1.0 g crystals, m.p. 93–94°C, were collected. (Ref. 1: 90–92°C). The identity was established with IR and NMR. The NMR spectrum ($CHCl_3$ solution) showed the following signals at δ pm: 1.43 doublet, 1.92 multiplet, 2.78 multiplet, 4.52 multiplet.

3,3′-Thiodi-(γ-valerolactone) (V). (A) In a simple laboratory apparatus described by Olsson,[9] hydrogen sulphide was passed over IV (19.6 g) and triethylamine (three drops) for 1 h with vigorous stirring. The reaction was exothermic and cooling with cold water was necessary. The reaction mixture was heated on a water bath for 1 h. The oil crystallized on cooling and scratching. After several days the crystals were filtered at the pump. Recrystallisation first from benzene-ethanol yielded 4.2 g. Repeated recrystallisation from ethanol gave white crystals (3.3 g), m.p. 92–93°C. (Found: C 52.18; H 6.06; S 13.88; Calc. for $C_{10}H_{14}O_4S$ (230.2): C 52.13; H 6.13; S 13.92). The IR-spectrum (KBr disc): 2980 m, 2938 w, 1790 s, 1450 w, 1420 m, 1390 s, 1340 w, 1297 w, 1277 m, 1239 m, 1210 s, 1175 m, 1090 m, 1068 s, 1044 m, 939 s, 906 w, 830 m, 789 m, 660 m, 593 w, 532 m, 450 cm^{-1} w. NMR ($CHCl_3$ solution) showed the following signals at δ ppm: 1.49 doublet (3 H), 2.77 multiplet (2 H), 3.26 multiplet (1 H), 4.36 multiplet (1 H).

(B) 4.9 g IV, 6.6 g VI, and two drops of triethylamine were mixed. A slightly exothermic reaction occurred. The reaction was completed by heating on a water bath for 30 min. The reaction mixture crystallised on standing and the crystals were filtered at the pump and recrystallised twice from benzene-petroleum ether (Yield 2.7 g, m.p. 90–91°C). The IR and NMR-spectra were identical for samples of V prepared by methods A and B.

4,4′-Thiodi-(γ-valerolactone) (VIII) was prepared according to Iwakura *et al.*,[3] m.p. 130–135°C (Ref. 3: 134–134.5°C). The IR-spectrum (KBr disc): 3012 w, 2998 w, 2961 w, 2945 w, 2932 w, 1770 s, 1460 m, 1420 s, 1382 s, 1318 w, 1280 m, 1250 s, 1196 s, 1136 s, 1100 m, 1074 s, 1002 m, 935 s, 895 s, 835 m, 799 m, 668 m, 644 m, 566 m, 530 w, 513 cm^{-1} m. NMR-spectrum ($CHCl_3$ solution) δ ppm: 2.02 singlet (3 H), 2.48 multiplet (4 H).

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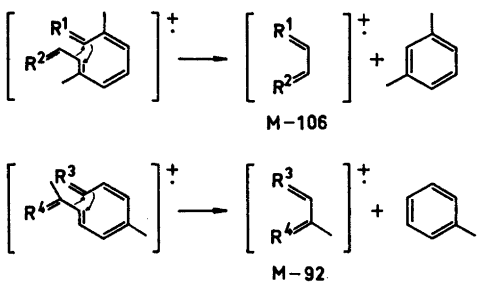

Mass Spectrometric Studies of Carotenoids

I. Occurrence and Intensity Ratios of M − 92 and M − 106 Peaks

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This communication discusses some preliminary findings of an investigation of the scope and limitations of mass spectrometry in the structural elucidation of carotenoids.

A previous study by Schwieter *et al.*,[1] has shown that various carotenes give rise to abundant M − 92 and M − 106 ions on electron impact. The formation of these was ascribed to the elimination of part of the central acyclic chain of the carotenoid skeleton, and the mechanism below was invoked to account for these losses. M − 92 and M − 106 ions have also been encountered in a later study of the mass spectra of carotenoid epoxides and furanoid oxides [2] and it has been claimed that these ions are a typical feature of the mass spectra of carotenoids.[3,4]

Examination of a wide variety of carotenoids, mainly of natural occurrence, shows that all those with C_{40}-skeletons and an acyclic chain of at least 9 conjugated double bonds give rise to significant M − 92 and M − 106 ions. These ions may thus now be regarded as characteristic of carotenoids. Since in many cases they are more abundant than the molecular ion, they can be useful indicators of the

Table 1. Intensity ratios of the (M−92)/(M−106) peaks (R) in the mass spectra of carotenoids with a varying number of conjugated carbon-carbon double bounds in the acyclic polyene chain (DB).

	Polyene	*R*	*DB*
Bicyclic	Zeaxanthin	10.0	9
	Echinenone	4.46	9
	3-Hydroxy-3′-keto-α-carotene	3.19	9
	3-Hydroxy-3′-methoxy-α-carotene	2.73	9
	Canthaxanthin	2.56	9
	Iso-zeaxanthin	2.17	9
	Lutein diacetate	1.73	9
	Lutein	1.59	9
Monocyclic	Chlorobactene	1.00	10
	Rubixanthin	0.70	10
	Rhodoxanthin*	0.55	10
	Rubixanthin acetate	0.44	10
Acyclic	Lycophyll	0.36	11
	Lycopen-16-al	0.34	11
	Lycopene	0.34	11
	Lycoxanthin	0.34	11
	1,2,1′,2′-Tetrahydro-1,1′-dihydroxy-lycopene	0.34	11
	Rhodopin	0.27	11
	3,4,3′,4′-Tetrahydro-spirilloxanthin	0.26	11
	Anhydro-rhodovibrin	0.068	12
	Rhodovibrin	0.057	12
	OH-Spirilloxanthin	0.029	13
	Spirilloxanthin	0.018	13

* Rhodoxanthin is a bicyclic retro-compound, whereas the other compounds having 10 double bonds are monocyclic.