*Monascoflavin**

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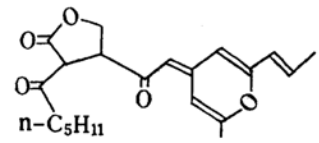
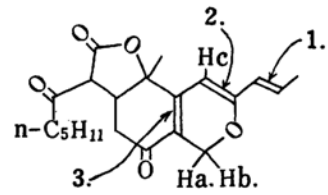
Structure Ia[1] was forwarded as a working hypothesis for monascoflavin[2-4], $C_{21}H_{26}O_5$, $[\alpha]_{700}^{16}+418$ (c: 0.0062 in ethanol), plain positive RD curve, one active hydrogen, three C–CH_3, no OH and OCH_3. However, the NMR spectra[5], especially the AB type quartet around 140 cps (vs. chloroform, at 56.4 Mc) arising from two protons in monascoflavin and dihydromonascoflavin could not be satisfactorily accounted for by the structure. Further studies on new derivatives, corrections of the molecular formula of hydrogenated products, a re-interpretation of the NMR spectra, and considerations of the biogenetic relations with monascorubrin[6] have led to structure I (or Ib). The mentioned quartet is now comfortably assigned to the methylene protons Ha and Hb. Some pertinent compounds are listed in Table I. The dihydro (II), tetrahydro (III) and hexahydro (IV) derivatives are those in which the double bonds (1), (2) and (3) in I have successively been hydrogenated. The 116 cps peak in I and



Ia



I

II is absent in III and IV, and the peak can be assigned to Hc. Presence of the n-$C_5H_{11}CO$ side-chain was shown by the production of capronic acid upon ozonolysis, oxidation with potassium permanganate, or fusion with potassium hydroxide, and production of amylamine upon Beckmann rearrangement of the oxime and hydrolysis. The lactone ring is cleaved and amides are formed, though sluggishly, when monascoflavin and hydrogenated products are treated with various amines, i. e., tetrahydromonascoflavin hexyl amide (V, R=C_6H_{13}). The amides, unlike the starting materials, no more showed the appearance or intensification of a ca. 288 mμ peak upon addition of base, and thus an enolizable β-keto-γ-lactone moiety is present in monascoflavin. Compound V (R=H) did not consume lead tetraacetate and this suggested it was not

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1) Presented at the 3rd Symposium on the Organic Chemistry of Natural Products, Tokyo, 1959.

2) A. Nishikawa, *J. Arg. Chim. Soc. Japan* (*Nippon Nogeikagaku Kaishi*), 5, 1007 (1932).

3) H. Salomon and P. Karrer, *Helv. Chim. Acta*, 15, 18 (1931); P. Karrer and A. Geiger, ibid., 25, 289 (1941).

4) A. D. G. Powell, A. Robertson and W. B. Whalley, *Chem. Soc. Spec. Publ.* No. 5, 27 (1956).

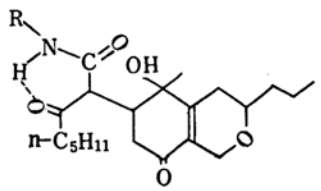
5) M. Ohashi, A. Terahara, K. Nakanishi, I. Yamaguchi and N. Hayakawa, This Bulletin, 33, 1312 (1960).

6) K. Nakanishi, M. Ohashi, S. Kumasaki and S. Yamamura, *J. Am. Chem. Soc.*, 81, 6339 (1959).

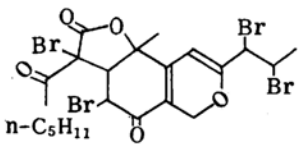
TABLE I. IR AND UV ABSORPTIONS

Compound	M.p., °C	Solvent	IR -COO-	IR -CO-	IR $\Delta^{\alpha\beta}$CO	UV λ_{max}^{MeOH} mμ(log ε)
Mf1.[a] (I) $C_{21}H_{26}O_5$	143~145	$CHCl_3$	1786	1720	1673	225(4.21), 288(3.41), 385(4.21)
2H-Mf1. (II) $C_{21}H_{28}O_5$	122	〃	1791	1723	1672	220(3.77), 237(3.61), 364(3.91)
4H-Mf1. (III)[b] $C_{21}H_{30}O_5$	136~137	〃	1790	1725	1703	244(4.03)[c]
6H-Mf1. (IV)[b] $C_{21}H_{32}O_5$	211~212	〃	1778	1742[d] 1723		
4H-Mf1.-C_6-amide[e] (V) $C_{27}H_{41}O_5N$	177~178	〃		1702	1665	241[c]
nor-4H-Mf1. (VI) $C_{20}H_{30}O_3$	41~ 44	CCl_4		1712	1668	242[c]
4Br-Mf1. (VII) $C_{21}H_{24}O_5Br_4$	162~164	$CHCl_3$	1786	1711	1690	225(3.93), 365(3.95)

a) Abbreviation for monascoflavin.
b) Tetra- and hexahydromonascoflavin were formulated as the hexa- and octahydro derivatives, respectively, in reference 5.
c) The difference with the calculated λ_{max} of 249 mμ is presumably caused by a transannular effect of the oxygenic *p* electrons on the $\alpha\beta$-unsaturated system. A similar effect has been reported for nitrogen: A. Marchant and A. R. Pinder, *J. Chem. Soc.*, **1956**, 327.
d) This unusually high $\nu_{C=O}$ value for a six-membered ring ketone is due to ring strain imposed by the γ-lactone. A similar effect is observed when the 1703 cm^{-1} band in III is compared with the 1668 cm^{-1} band in VI.
e) Amide I and II bands at 1665 and 1520 cm^{-1}, respectively.

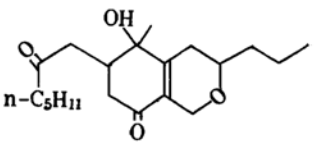


V

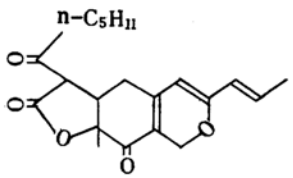


VII

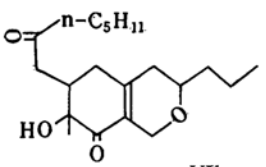
an α-ketol. Ozonolysis of I and II gave acetaldehyde and butyric acid, respectively, while base hydrolysis of I and II gave crotonic acid and butyric acid, respectively. These results show that a propenyl side-chain is attached to the α-position of the pyran ring and that it should be conjugated with the α, β-unsaturated carbonyl group (to permit the occurrence of a vinylogous β-diketone cleavage). The conspicuous methyl peak at 330 cps in I remains constant and uncoupled in II–IV[5], and the position is lower than ordinary methyl peaks by ca. 30 cps. This, coupled with the production of methylglyoxal from the ozonolysis of I places a methyl group on a tertiary carbon atom bearing a oxygenic function (the lactone ring). Tetrabromomonascoflavin (VII) has no active hydrogen. Furthermore, the +17 cm^{-1} shift of the 1673 cm^{-1} band of I suggests that the α-position of the α, β-unsaturated carbonyl group must be substituted by an equatorial bromine. Boiling III in 20% alkali under nitrogen yielded VI. The facts mentioned are best explained by structure I.



VI



Ib



VIb

The alternative structure Ib is also conceivable

but it is difficult to account for the 1690 cm^{-1} band in tetrabromo-monascoflavin and the non-consumption of lead tetraacetate by V(R=H). However, Ib is the conclusion reached by English chemists[7] who base their conclusion on analogies with other azaphilones, e. g., monascorubrin[8], the structure of which also differs from that of the present authors[6,9], and the fact that nortetrahydromonascoflavin (VIb instead of VI) consumed periodic acid with the production of a methyl ketone. These inconsistencies will be settled in the near future.

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7) The authors are most grateful to Dr. W. B. Whalley, University of Liverpool, for informing us of their results prior to publication and for discussion at the IUPAC Symposium.

8) B. C. Fielding, F. J. Haws, J. S. E. Holker, A. D. G. Powell, A. Robertson, D. N. Stanway and W. B. Whalley, *Tetrahedron Letters*, No. 5, 24 (1960).

9) M. Ohashi, A. Terahara and K. Nakanishi, This Bulletin, 33, 1311 (1960).