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THE STRUCTURE OF POLYGONAQUINONE

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Abstract—Polygonaquinone, obtained from the roots of *Polygonatum* species, is shown to have structure D.

THE roots of *Polygonatum falcatum* A. Gray (Japanese name: Narukoyuri) have been widely used as a drug in eastern Asia. From the ether extracts of the root, an orange pigment named *polygonaquinone* has been isolated. Although its physiological action is not yet entirely clear, the authors initiated the structural elucidation of this pigment in view of its interesting chemical properties.

Polygonaquinone (I), m.p. 133–134°, has a molecular formula $C_{28}H_{48}O_4$, and gives a deep reddish-violet solution in dilute alkali. The IR spectrum of I has no carbonyl band around 1700 cm^{-1} but a strong absorption at 1615 cm^{-1}. The formation of a dimethyl ether, $C_{30}H_{52}O_4$ (II), m.p. 79–80°, on treatment with an ethereal solution of diazomethane shows the presence of two acidic hydroxyl groups. The positive ferric chloride test and a large bathochromic shift of the UV spectrum in alkaline solution suggest that these hydroxyl groups are either enolic or phenolic. With acetic anhydride and pyridine I gives a diacetate, $C_{32}H_{52}O_6$ (III), m.p. 92–93°, the acetate band being only at 1780 cm^{-1}. The appearance of an α,β-unsaturated carbonyl absorption in II (1655 and 1610 cm^{-1}) and III (1672 and 1635 cm^{-1}) indicates that the intense band of I at 1615 cm^{-1} is attributable to the strongly hydrogen-bonded carbonyl group. Reductive acetylation of I with acetic anhydride and zinc dust yields a colorless tetraacetate, $C_{36}H_{58}O_8$ (IV), m.p. 120–121°. The UV spectrum of IV, $\lambda_{max}^{CHCl_3}$ 263 mμ (log ε 2·58), is similar to that of 2,3,5,6-tetraacetoxytoluene.[1] These properties, particularly the UV spectrum of I, indicate the chromophore of I as a dihydroxy-*p*-benzoquinone. Some pertinent data is shown in Table 1.

The dimethyl ether (II) exhibits only five signals in the NMR spectrum and none are in the vinyl hydrogen region. A sharp singlet (3 H) at 1·90 ppm, assigned to a methyl group on an olefinic carbon, should be on the quinone nucleus since I and its derivatives have the carbon-carbon double bond only in the quinone ring.[4] Two methoxyl groups appear at 4·00 ppm as a singlet (6 H), and the other three signals—a broad triplet at 0·88 ppm (3 H), a singlet at 1·25 ppm (38 H), and a broad triplet at 2·40 ppm (2 H)—probably originated from an alkyl side chain, $C_{21}H_{43}$. The diacetate (III) shows a similar NMR spectrum—a singlet at 1·93 ppm (3 H) (methyl on the quinone ring), a broad triplet at 0·87 ppm (3 H) (terminal methyl), a singlet at 1·22 ppm (38 H) (methylenes), and a singlet at 2·32 ppm (8 H) (benzylic methylene and

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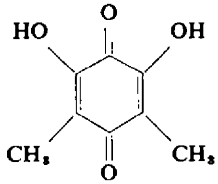
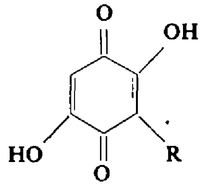
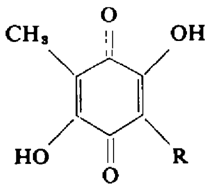
[1] J. C. Sheehan, W. B. Lawson and R. J. Gaul, *J. Amer. Chem. Soc.* **80**, 5536 (1958).

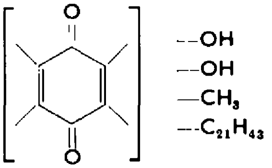
[2] B. W. Bycroft and J. C. Roberts, *J. Org. Chem.* **28**, 1429 (1963).

[3] S. Natori and E. Nishikawa, VII*th Symposium on the Chemistry of Natural Products*, Abstracts of Papers, p. 149. Fukuoka (October 1963).

TABLE 1. THE UV SPECTRA OF DIHYDROXY-*p*-BENZOQUINONES

Compound		λ_{max}^{EtOH} mμ(log ε)	Ref.
		297 (4·26), 426 (2·26)	2
	R: $C_{11}H_{23}$ R: $C_{13}H_{27}$	291 (4·25), 427 (2·45) 291 (4·26), 425 (2·46)	3 3
	R: $CH(CH_3)_2$ R: C_8H_{15} R: $C_{19}H_{39}$	293 (4·31), 435 (2·36) 297 (4·15), 430 (2·47) 292 (4·37)	2 3 3
Polygonaquinone (I)		295 (4·28)	

two acetyl groups). Hence, it appears that I is a dihydroxy-*p*-benzoquinone with one methyl group and a long alkyl side chain, as in formula A, which has been confirmed by oxidation.



A

Mild oxidation of I with alkaline hydrogen peroxide or with potassium permanganate in pyridine yields an acid, $C_{22}H_{44}O_2$ (V), m.p. 76–77°, the molecular formula of which was determined by mass spectrum of its methyl ester. The IR spectrum of V exhibits a group of bands between 1200 and 1300 cm^{-1}, characteristic of the long paraffin chain, which is in accordance with a simple NMR spectrum. The mass spectrum of the methyl ester is typical of the C_{22} straight chain fatty acid, behenic acid. This was proved by the identity of the IR spectrum and the mixed melting point determination with authentic behenic acid. These results are supported by three possible structures for I.

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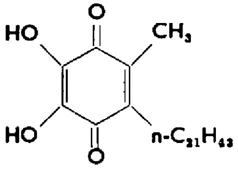
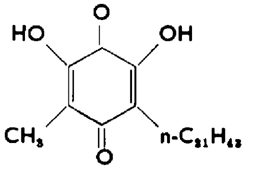
[4] The corresponding methyl signal of maesaquinone[5] and of helicobasidin[3] appeared at 1·95 and 1·93 ppm, respectively.

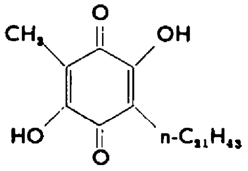
[5] H. Ogawa, Y. Shigehisa, S. Natori and K. Kawaguchi, XIX*th Meeting of the Pharmaceutical Society of Japan*, Abstracts of Papers, p. 127. Tokyo (April 1964).



B

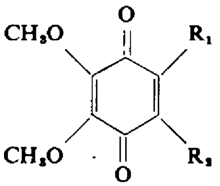
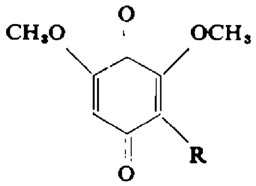
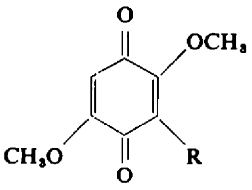


C



D

TABLE 2. THE UV SPECTRA OF DIMETHOXY-*p*-BENZOQUINONES

Compound	Solvent	λ_{max} mμ (log ε)	Ref.
			
R_1: R_2:			
H H	$CHCl_3$	254 (4·17), 398 (3·17)	6
CH_3 H	EtOH	265 (4·15)	7
CH_3 CH_3	EtOH	275 (4·19)	7
CH_3 $C_{50}H_{81}$	Cyclohexane	272 (4·14), 407 (2·39)	8
CH_3 $C_{50}H_{81}$	EtOH	275 (4·14), 407 (2·56)	8
			
R: H	$CHCl_3$	287 (4·28), 377 (2·78)	6
CH_3	Cyclohexane	~280	8
			
R: H	$CHCl_3$	284 (4·38), 377 (2·78)	6
CH_3	Cyclohexane	~280	8
Polygonaquinone dimethyl ether (II)	EtOH	287 (4·06)	
	$CHCl_3$	288 (4·12), 398 (2·60)	

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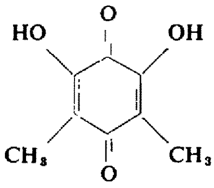
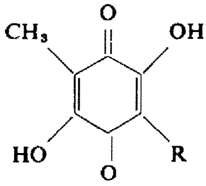
[6] W. Flaig, J. C. Salfeld and E. Baume, *Liebigs Ann.* **618**, 117 (1958).

[7] E. B. Vischer, *J. Chem. Soc.* 815 (1953).

[8] R. A. Morton, U. Gloor, O. Schindler, G. M. Wilson, L. H. Chopard-dit-Jean, F. W. Hemming, O. Isler, W. M. F. Leat, J. F. Pennock, R. Rüegg, U. Schwieter and O. Wiss, *Helv. Chim. Acta* **41**, 2343 (1958).

Re-examination of the UV spectrum excludes structure B. As is shown in Table 2, there is a marked difference between the spectrum of the dimethyl ether (II) and that of 2,3-dimethoxy-*p*-benzoquinone derivatives. If the structure of I is of this type, an absorption maximum at a shorter wave-length could be expected. The structures C and D may be distinguished on the basis of IR spectra. Compounds of the type C would show two carbonyl bands since one of the carbonyl groups would not have a strong intramolecular hydrogen bond in the solid state (Table 3). Polygonaquinone (I) has only one carbonyl band at a very low frequency and this fact establishes its structure as D. Polygonaquinone (I) is thus closely related to other natural products such as maesaquinone[5,9–11] and helicobasidin.[3]

TABLE 3. THE IR SPECTRA OF DIHYDROXY-*p*-BENZOQUINONES

Compound	$\nu_{C=O}$ (cm^{-1})		Ref.
	KBr	$CHCl_3$	
	1660, 1641	1653, 1645	2
			
R:			
C_8H_{15}	1609	1638	3
$CH(CH_3)_2$	1616	1640	2
$C(CH_3){=}CHCH_3$	1617	1642	2
Polygonaquinone (I)	1615	1635	

EXPERIMENTAL

M. ps were determined on a micro hot stage and are uncorrected. The UV spectra have been measured with a Beckman DK-2 spectrophotometer and the IR spectra on a Koken IR-S spectrometer. Unless otherwise stated, the NMR spectra were run on a Nihon-denshi model JNM-3 instrument (60 Mc) in $CDCl_3$ solution using tetramethylsilane as internal standard, and recorded in ppm. The mass spectrum was kindly measured by Naka Division of Hitachi Co. Ltd.

Extraction of polygonaquinone (I). About 10 kg of commercially available dried roots of *Polygonatum* species were cut into small pieces and extracted with ether at room temp for 2 days. After removal of ether from the extracts, the residue was recrystallized from ethanol several times to give pure I as orange prisms, m.p. 133–134° (Found: C, 75·26; H, 11·00. $C_{28}H_{48}O_4$ requires: C, 74·95; H, 10·78%). Mol. Wt. (Rast): 440, 450; Calcd. 448·66. λ_{max}^{EtOH} 295 mμ (log ε 4·28), $\lambda_{max}^{CHCl_3}$ 295 mμ

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[9] M. Hiramoto, *Proc. imp. Acad. Japan* **15**, 220 (1939).

[10] M. Hiramoto, *J. Pharm. Soc. Japan* **62**, 460 (1942).

[11] M. Hiramoto, *J. Pharm. Soc. Japan* **62**, 464 (1942).

(4·32), 417 mμ (2·33). $\nu_{C=O}^{KBr}$ 1615 cm^{-1}, $\nu_{C=O}^{CHCl_3}$ 1635 cm^{-1}. NMR spectrum in pyridine: 0·87 (broad triplet, 3 H), 1·27 (singlet, 38 H), 2·10 (singlet, 3 H), and 2·68 (broad triplet, 2 H).

Dimethyl ether (II). An ethereal solution of diazomethane was added in slight excess with stirring to a solution of 100 mg I in 200 ml ether and the mixture set aside overnight. The solvent was removed and the residual oil triturated with methanol. Recrystallization from ethanol gave 63 mg II as yellow needles, m.p. 79–80° (Found: C, 75·65; H, 11·01. $C_{30}H_{52}O_4$ requires: C, 75·58; H, 11·00%). λ_{max}^{EtOH} 287 mμ (log ε 4·06), $\lambda_{max}^{CHCl_3}$ 288 mμ (4·12), 398 mμ (2·60). $\nu_{C=O}^{KBr}$ 1655 cm^{-1}, $\nu_{max}^{CHCl_3}$ 1651 cm^{-1}. NMR spectrum: 0·88 (broad triplet, 3 H), 1·25 (singlet, 38 H), 1·90 (singlet, 3 H), 2·40 (broad triplet, 2 H), and 4·00 (singlet, 6 H).

Diacetate (III). Polygonaquinone (I) (200 mg) was dissolved in a mixture of 6 ml acetic anhydride and 6 ml pyridine. After 12 hr water was added and the product extracted with ether. The ether extracts were washed with water and then evaporated under red. press. Recrystallization from ethanol gave 145 mg III as yellow needles, m.p. 92–93° (Found: C, 72·03; H, 9·68. $C_{32}H_{52}O_6$ requires: C, 72·14; H, 9·84%). λ_{max}^{EtOH} 269 mμ (log ε 4·02), $\lambda_{max}^{CHCl_3}$ 269 mμ (4·20), 343 mμ (2·61). $\nu_{C=O}^{KBr}$ 1780, 1672 cm^{-1}, $\nu_{C=O}^{CHCl_3}$ 1775, 1672 cm^{-1}. NMR spectrum: 0·87 (broad triplet, 3 H), 1·22 (singlet, 38 H), 1·93 (singlet, 3 H) and 2·32 (singlet, 8 H).

Tetraacetate (IV). A mixture of 150 mg I and 500 mg Zn dust in 15 ml acetic anhydride was refluxed for 3 hr at 150–160° and the cooled mixture was poured into ice-water to give white solid. Recrystallization from ethanol afforded 165 mg IV as colorless plates, m.p. 120–121° (Found: C, 69·93; H, 9·45. $C_{36}H_{58}O_8$ requires: C, 69·87; H, 9·45%). λ_{max}^{EtOH} 263 mμ (log ε 2·58). $\nu_{C=O}^{KBr}$ 1760 cm^{-1}, $\nu_{C=O}^{CHCl_3}$ 1779 cm^{-1}.

$KMnO_4$ *oxidation of* I. Pulverized $KMnO_4$ (1·5 g) was added in small portions to a stirred solution of 800 mg I in a mixture of 30 ml pyridine and 1 ml water. The excess $KMnO_4$ was destroyed by addition of $NaHSO_3$ and the mixture diluted with water. The colorless solid was collected and its $CHCl_3$ solution was chromatographed on a silica-gel column (20 g). Most of the material was eluted in one fraction with $CHCl_3$. The product was recrystallized from pet. ether to give 380 mg V as colorless plates, m.p. 76–77° (Found: C, 77·74; H, 12·90. $C_{22}H_{44}O_2$ requires: C, 77·58; H, 13·02%). $\nu_{C=O}^{KBr}$ 1705 cm^{-1}. NMR spectrum: 0·89 (broad triplet, 3 H), 1·22 (singlet, 38 H), and 2·33 (broad triplet, 2 H). This substance (V) was identified as behenic acid, n-$C_{21}H_{43}$—COOH, by comparison of its IR spectrum and mixed m.p. with authentic behenic acid. The m.p. was depressed on admixture with the lower homologue, arachidic acid, n-$C_{19}H_{39}$—COOH. Mass spectrum of methyl ester (m.p. 54–55°) of V in m/e (relative intensity): 354 (95), 325 (6), 323 (11), 311 (27), 297 (14), 255 (13), 199 (12), 143 (30), 129 (12), 101 (10), 87 (67), 74 (100). The pattern is very much similar to that of methyl stearate.[12]

Alkaline H_2O_2 *oxidation of* I. H_2O_2 (30% aq) (50 ml) was added to a solution of 700 mg I in 250 ml 1/10 N KOH aq. The mixture was allowed to stand overnight and the precipitated solid collected. Recrystallization from pet. ether gave 175 mg of V as colorless plates, m.p. 76–77°.

Acknowledgement—This work was supported in part by a grant from the Parke, Davis and Co., Ann Arbor, Michigan, U.S.A.

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[12] R. Ryhage and E. Stenhagen, *J. Lipid Research* **1**, 361 (1960).