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Hydroxybenzoquinones from Myrsinaceae Plants. III.[1] The Structures of 2-Hydroxy-5-methoxy-3-pentadecenylbenzoquinone and Ardisiaquinones A, B and C from *Ardisia* spp.[2]

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From the rhizomes of *Ardisia japonica* 2–hydroxy–5–methoxy–3–pentadecenylbenzoquinone contaminated with 3–tridecenyl and 3–tridecyl compounds (Ia) was obtained. Novel type bisbenzoquinonyl–olefin derivatives, designated ardisiaquinones A, B and C, were isolated from the root bark of *Ardisia sieboldii* and the structures (V—VII) have been elucidated.

Examinations on the distribution of benzoquinone derivatives among Myrsinaceae plants growing in Japan[1] revealed the presence of several hitherto unknown compounds. This paper describes the details of the isolation and the structural elucidation of the new compounds.[2]

From the benzene extract of the rhizomes and the fruits of *Ardisia japonica* (THUNB.) BLUME. (Japanese name: Yabukoji), collected at Sayama, a benzoquinone mixture (Ia), yellow plates of mp 66.5—67°, was obtained in an yield of 0.01%,[5] besides embelin (IIa) contaminated with rapanone (IIb)[6] and an unknown deep red compound of mp 161—164°. Although Ia has been proved to be contaminated with two homologs as revealed by the gas chromatography of the oxidation product (*vide infra*) and by the mass spectrum of Ia, further work has been carried out using the mixture of the homologs, since the separation is practically impossible and the yield is rather poor.

Ia dissolves in sodium carbonate to show violet color, which is decolorized by the addition of sodium dithionite. Infrared (IR) spectrum (Table I) shows the presence of conjugated carbonyl groups, an aromatic ether and a hydroxyl group. Ultraviolet (UV) spectrum (Table I) is similar to that of 3–alkyl–2,5–dihydroxybenzoquinone such as embelin (IIa) and rapanone (IIb). Elemental analyses and a mass spectrum showed the molecular formula, $C_{22}H_{34}O_4$ (M^+ m/e 362), though it is contaminated with the compounds, $C_{20}H_{30}O_4$ (M^+ m/e 334) and $C_{20}H_{32}O_4$ (M^+ m/e 336).

Ia formed the following derivatives: Catalytic hydrogenation followed by aerial oxidation afforded the dihydro derivative (M^+ m/e 364, 336) (Ib), yellow plates of mp 90—91°. Demethylation of Ib afforded a dihydroxy compound (IIc), orange red plates of mp 138°, while methylation of Ib gave dimethoxy compound (IIIa), pale yellow plates of mp 64°. Nuclear

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1) Part II: H. Ogawa and S. Natori, *Phytochemistry*, **7**, 773 (1968).
2) The preliminary communication of a part of this work has been published.[4]
3) Location: *Kamiyoga–1–chome, Setagaya–ku, Tokyo.*
4) H. Ogawa, S. Sakaki, K. Yoshihira, and S. Natori, *Tetrahedron Letters*, **1968**, 1387.
5) From the fruits of *Ardisia crenata* SIM. (Japanese name: Manryo) and *A. quinquegona* BLUME (Japanese name: Shishiakuchi) and the rhizomes of *A. japonica* var. *angusta* (NAKAI) MAMINO et NEMOTO (Japanese name: Hosobayabukoji) and *A. montana* SIEB. (Japanese name: Otsurukoji) a fraction showing nearly identical mp, UV and IR spectra and TLC with Ia was obtained. Due to the scarcity of the sample, further characterization has not been carried out.[1]
6) As reported in the previous paper IIa and IIb generally exist in nature as a mixture.[1] The presence of IIb in the plant had been recorded.[7]
7) M. Hiramoto, *Yakugaku Zasshi*, **59**, 665 (1939).

Table I. UV and IR Spectra of the Benzoquinone Derivatives

	UV λ_{max}^{EtOH} mμ (log ε)		IR (KBr) cm^{-1}			
			ν_{O-H}	$\nu_{C=O}$ (acetyl)	$\nu_{C=O}$ (C=C)	ν_{C-O-C}
Rapanone (IIb)	292.5(4.24)	425(2.43)	3305	—	1605(s)	—
Rapanone 5-methyl ether (Ic)	289.5(4.24)	420(2.63)	3315	—	1655(sh) 1630(m) 1595(s)	1200
Rapanone dimethyl ether (IIIb)	286(4.23)	390(2.65)	—	—	1600(s) 1655(s)	1208
2-O-Acetylrapanone 5-methyl ether (IV)	274(4.17)	370(2.83)	—	1763—1770 (br)	1660—1635 (br) 1604(s)	1240
Maesaquinone (XVIII)	294—296(4.36)	440(2.58)	3320	—	1605(s)	—
Acetylmaesaquinone	275(4.18)	415(2.85)	3315	1782	1655(s) 1639(sh) 1615(m)	—
Di-O-acetylmaesaquinone	266(4.14)	340—345(3.00)	—	1765	1665(s) 1632(br)	—
2-Hydroxy-5-methoxy-3-pentadecenylbenzoquinone (Ia)	289(4.21)	420(2.65)	3318	—	1655(sh) 1632(m) 1595(s)	1202
2-Hydroxy-5-methoxy-3-pentadecylbenzoquinone (Ib)	289(4.22)	420(2.64)	3320	—	1655(sh) 1630(m) 1595(s)	1200
2,5-Dihydroxy-3-pentadecylbenzoquinone (IIc)	292(4.27)	425(2.47)	3305	—	1637(sh) 1605(s)	—
2,5-Dimethoxy-3-pentadecylbenzoquinone (IIIa)	286(4.23)	392(2.36)	—	—	1655(s) 1603(s)	1210
Ardisiaquinone A (V)	289(4.60)	415—425(2.83)	3315	—	1655(sh) 1633(m) 1598(s)	1203
Dihydroardisiaquinone A (VIII)	289(4.59)	410—420(2.86)	3315	—	1655(sh) 1633(m) 1598(s)	1203
Demethylardisiaquinone A (X)	293—294(4.40)	418—425(2.68)	3300	—	1605(s)	—
Di-O-acetylardisiaquinone A (XII)	……	……	—	1765	1660—1640 (br) 1610(s)	1238
Di-O-acetyldihydroardisiaquinone A (VIV)	274(4.48)	370(3.06)	—	1765	1660—1640 (br) 1610(s)	1238
Ardisiaquinone B (VI)	291(4.56)	420—428(2.82)	3300	—	1605(s)	1203
Dihydroardisiaquinone B (IX)	291(4.58)	420—430(2.89)	3300	—	1605(s)	1203
Demethylardisaquinone B (XI)	294(4.44)	420—430(2.77)	3300	—	1605(s)	—
Tri-O-acetylardisiaquinone B (XIII)	……	……	—	1775	1665(s) 1610(s)	1235
Tri-O-acetyldihydroardisiaquinone B (XV)	271(4.66)	360(3.04)	—	1775	1665(s) 1610(s)	1238
Ardisiaquinone C (VII)	281(4.41)	420(2.87)	3328	1774	1657(sh) 1635(m) 1603(s)	1203

Table II. NMR Spectra of the Benzoquinone Derivatives (τ Values)

Compound	Solvent	–OH	$\rangle$=–H	–CH=CH–	–OCH$_3$	–C$\underline{H}_2$–CH=	–OCOCH$_3$	$\rangle$=–CH$_2$–	$\rangle$=–CH$_3$	–CH$_2$–	–CH$_2$–C$\underline{H}_3$
Rapanone (IIb)	CDCl$_3$	2.37 (2H, br.)	4.03 (1H, s)	—	—	—	—	7.4—7.8 (2H)	—	8.5—8.9 (centered at 8.74)	9.11[a]
Rapanone 5–methyl ether (Ic)	CCl$_4$	2.84 (1H, br.)	4.25 (1H, s)	—	6.14 (3H, s)	—	—	7.4—7.9 (2H)	—	8.5—8.8 (8.72)	9.12[a]
Rapanone dimethyl ether (IIIb)	CCl$_4$	—	4.41 (1H, s)	—	5.97, 6.23 (3H, s)(3H, s)	—	—	7.8—7.9 (2H)	—	8.5—8.9 (8.72)	9.14[a]
2–O–Acetylrapanone 5–methyl ether (IV)	CCl$_4$	—	4.23 (1H, s)	—	6.21 (3H, s)	—	7.72 (3H, s)	7.5—7.9 (2H)	—	8.3—8.9 (8.72)	9.11[a]
Di–O–acetylrapanone	CCl$_4$	—	3.58 (1H, s)	—	—	—	7.71 (6H, s)	7.5—7.9 (2H)	—	8.4—8.9 (8.73)	9.11[a]
Maesaquinone (XVIII)	CDCl$_3$	2.37 (2H, br.)	—	4.68 (2H, t, J=5 cps)	—	7.8—8.2 (4H)	—	7.4—7.8 (2H)	8.05 (3H, s)	8.3—8.9 (8.71)	9.10[a]
Acetylmaesaquinone[10]	CCl$_4$	3.01 (1H, br.)	—	4.68 (2H, t, J=5 cps)	—	7.8—8.2 (4H)	7.69 (3H, s)	7.4—7.8 (2H)	8.09 (3H, s)	8.3—9.0 (8.74)	9.16[a]
2–Hydroxy–5–methoxy–3–pentadecenylbenzoquinone(Ia)	CCl$_4$	2.83 (1H, br.)	4.27 (1H, s)	4.70 (2H, m)	6.17 (3H, s)	7.9—8.3 (4H)	—	7.3—7.8 (2H)	—	8.5—8.9 (8.72)	9.10[a]
2–Hydroxy–5–methoxy–3–pentadecylbenzoquinone (Ib)	CCl$_4$	2.85 (1H, br.)	4.22 (1H, s)	—	6.12 (3H, s)	—	—	7.4—7.8 (2H)	—	8.5—8.9 (8.70)	9.10[a]
Ardisiaquinone A (V)	CDCl$_3$	2.7	4.16 (2H, s)	4.67 (2H, t, J=6 cps)	6.13 (6H, s)	7.9—8.1 (4H)	—	7.4—7.8 (4H)	—	8.4—8.8 (8.70)	—
Dihydroardisiaquinone A (VIII)	CDCl$_3$	2.7	4.16 (2H, s)	—	6.14 (6H, s)	—	—	7.4—7.8 (4H)	—	8.4—8.8 (8.76)	—
Di–O–acetylardisiaquinone A (XII)	CCl$_4$	—	4.23 (2H, s)	4.73 (2H, t, J=5 cps)	6.21 (6H, s)	7.9—8.0 (4H)	7.73 (6H, s)	7.5—7.8 (4H)	—	8.4—8.9 (8.72)	—
Ardisiaquinone B (VI)	CDCl$_3$	2.42 (3H, br.)	4.14 (1H, s)	4.67 (2H, br. t, J=6 cps)	6.13 (3H, s)	7.8—8.2 (4H)	—	7.5—7.8 (4H)	8.07 (3H, s)	8.5—8.8 (8.70)	—
Dihydroardisiaquinone B (IX)	CDCl$_3$ +d$_6$DMSO	2.37 (3H, br.)	4.22 (1H, s)	—	6.19 (3H, s)	—	—	7.5—7.8 (4H)	8.16 (3H, s)	8.2—8.9 (8.72)	—
Tri–O–acetylardisiaquinone B (XIII)	CDCl$_3$	—	4.25 (1H, s)	4.72 (2H, br. t, J=*ca.* 5 cps)	6.23 (3H, s)	7.8—8.2 (4H)	7.73 (9H, s)	7.5—7.9 (4H)	8.08 (3H, s)	8.2—8.9 (8.72)	—
Ardisiaquinone C (VII)	CDCl$_3$	2.79 (2H, br.)	4.26 (1H, s)	4.72 (2H, br. t, J=5 cps)	6.24 (3H, s)	7.8—8.2 (4H)	7.71 (3H, s)	7.5—7.8 (4H)	8.06 (3H, s)	8.3—8.9 (8.71)	—

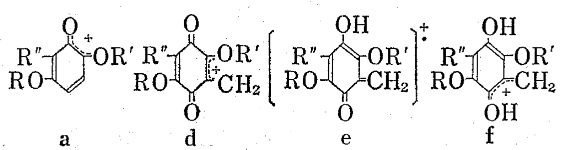
[a] 3H, t, J=5—7 cps

Table III. Characteristic Peaks of Mass Spectra of the Benzoquinone Derivatives

	m/e (relative intensity in %)									
	a	b	c	d	e	f[a]	g	M^+-28	M^+	M^++2[a]
Embelin (IIa)	125 (10)		142 (22)	153 (26)	154 (100)	155 (38)			294 (30)	
Rapanone (IIb)	125 (11)		142 (23)	153 (28)	154 (100)	155 (40)			322 (31)	
Rapanone 5-methyl ether (Ic)	139 (18)	153 (15)	156 (16)	167 (27)	168 (100)	169 (44)			336 (50)	
Rapanone dimethyl ether (IIIb)	153 (38)	154 (22)	167 (38) 169 (34)	181 (13)	182 (34)	183 (31)			350 (100)	352 (20)
Maesaquinone (XVIII)	139 (11)			167 (25)	168 (52)	169 (51)			418 (100)	420 (6)
2-Hydroxy-5-methoxy-3-pentadecenyl(tridecyl, tridecenyl)benzoquinone (Ia)	139 (14)	153 (16)	156 (11)	167 (18)	168 (100)	169 (64)			334 (12) 336 (13) 362 (50)	364 (13)
2-Hydroxy-5-methoxy 3-pentadecyl(tridecyl)benzoquinone (Ib)	139 (13)	153 (12)	156 (16)	167 (30)	168 (100)	169 (46)			336 (43) 364 (29)	
Ardisiaquinone A (V)	139 (50)	153 (31)		167 (31)	168 (80)	169 (100)	193[b] (19)	500 (9)	528 (50)	530 (31)
Dihydroardisiaquinone A (VIII)	139 (87)	153 (55)		167 (56)	168 (82)	169 (100)	193 (18)	502 (84)	530 (66)	532 (35)
Ardisiaquinone B (VI)	139 (39)	153 (26)		167 (24)	168 (82)	169 (100)	193[b] (16)	500 (7)	528 (97)	530 (48)
Dihydroardisiaquinone B (IX)	139 (59)	153 (26)		167 (32)	168 (53)	169 (100)	193 (9)	502 (41)	530 (38)	532 (38)
Demethylardisiaquinone B (XI)	125 (10) 139 (27)			153 (27) 167 (30)	154 (36) 168 (70)	155 (49) 169 (80)	193 (12)	488 (9)	514 (100)	516 (10)
Ardisiaquinone C (VII)	139 (23)	153 (21)		167 (23)	168 (80)	169 (100)	193 (14)	528 (60) 530 (60)	570 (7)	572 (10)

[a] Formation of $(M+2)^+$ ions and the fragments thereof, *i.e.* fragment f, in the ionization chamber has reported.[25–27]

[b] Slight peaks m/e 264. 264.5, 265, 265.5, corresponding to M^{2+}, $(M+1)^{2+}$, $(M+2)^{2+}$ and $(M+3)^{2+}$ were observed.



a d e f

magnetic resonance (NMR) spectra of Ia and Ib (Table II) are quite informative and the presence of one each of hydroxyl, methoxyl and alkyl side chain with one double bond, and ring proton in Ia was confirmed.

The alkenyl side chain was characterized by hydrogen peroxide oxidation of Ia, Ib and IIc and the examination of the fatty acids thus formed with the gas chromatography of their methyl esters. The methyl ester mixture formed from Ib and IIc showed a main peak identical with that of methyl palmitate accompanied by a peak identical with that of methyl myristate, while that of Ia showed three peaks, the main peak being assigned as that of hexadecenoic acid and the minor two, myristic and tetradecenoic acids (Table IV). These results showed a good accord with the M^+ peaks in the mass spectra and the side chain of the mixture is characterized as pentadecenyl as the major and tridecyl and tridecenyl as the minor. Due to the scarcity of the sample and difficulty in the separation of the mixture, the position of the double bond has not been examined.

The disposition of one each of the alkenyl, hydroxyl and methoxyl groups on benzoquinone nucleus was examined by spectroscopic methods. Three isomers of alkyldihydroxybenzoquinones are distinguishable by IR and UV spectra.[8–12] UV maximum of IIIa (286 mμ) excludes 2,3-dihydroxy type compound;[12] while UV maximum (292 mμ) and IR absorption band (1605 cm^{-1}) of IIc clearly demonstrate 2,5-dihydroxy type compound.[8–11] The relative position of the hydroxyl group and the methoxyl group has been established by a comparison with a model compound, 2-hydroxy-5-methoxy-3-tridecylbenzoquinone (rapanone 5-methyl ether) (Ic), prepared by the methylation of rapanone (IIb) under a controled condition.

Ic afforded monoacetate (IV) and the relative position of the methoxyl group and the hydroxyl group in Ic has been established by the examination of NMR spectra of Ic and IV. Shielding values of substituents on benzene nucleus have been reported by many workers[13] and the effects of the substituents at 2-position to the proton at 3-position in naphthoquinones are reported in the case of many compounds.[14] Although the effects of substituents at

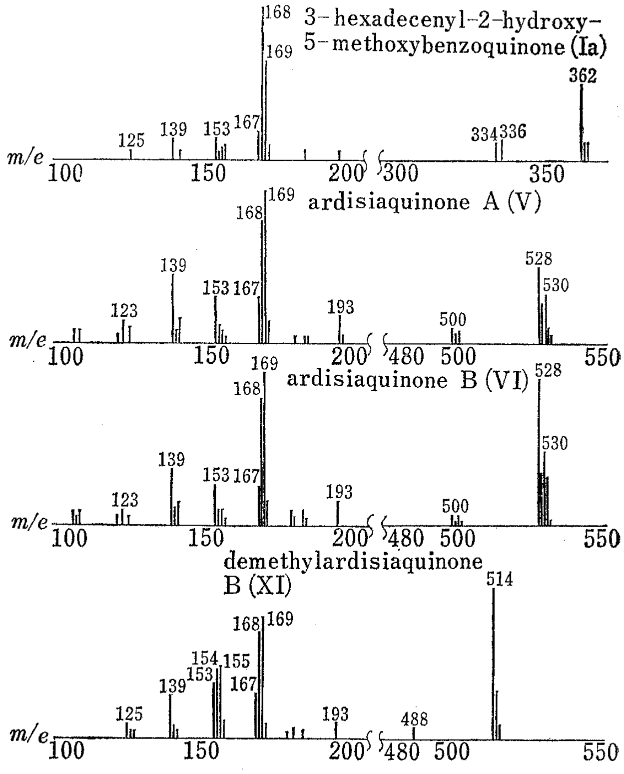


Fig. 1. Mass Spectra of 3-Hexadecenyl-2-hydroxy-5-methoxybenzoquinone, Ardisiaquinones A and B and Demethylardisiaquinone B

Ions having an abundance greater than 5% of that of the base peak are recorded.

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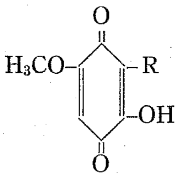
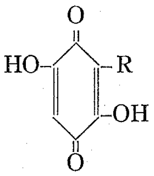
8) B.W. Bycraft and J.C. Roberts, *J. Org. Chem.*, **28**, 1429 (1963).
9) S. Natori, H. Ogawa, and H. Nishikawa, *Chem. Pharm. Bull.* (Tokyo), **12**, 236 (1964).
10) H. Ogawa and S. Natori, *Chem. Pharm. Bull.* (Tokyo), **13**, 511 (1965).
11) H. Nakata, K. Sasaki, I. Morimoto, and Y. Hirata, *Tetrahedron*, **20**, 2319 (1964); K. Yoshihira and S. Natori, *Chem. Pharm. Bull.* (Tokyo), **14**, 1052 (1966).
12) G. Pettersson, *Acta Chem. Scand.*, **18**, 2303 (1964).
13) J.A. Ballantine and C.T. Pillinger, *Tetrahedron*, **23**, 1961 (1967); and the references cited therein.
14) R.E. Moore and P.J. Scheuer, *J. Org. Chem.*, **31**, 3272 (1966).

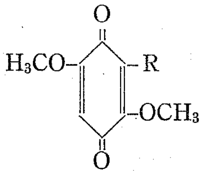
1,3– and 1,4–positions are not negligible, it should be concluded from the examinations on the chemical shifts of the ring protons on benzoquinone nucleus so far reported that the proton adjacent to acetoxyl or alkyl group appearring in lower field (3.4—3.7 τ) will be differentiated from that adjacent to hydroxyl or methoxyl group in higher field (4.0—4.4 τ). As an example 5–alkyl–2–hydroxybenzoquinone shows two ring protons at 4.01 τ (s, 3–position) and 3.49 τ (t, 6–position), in which the former shifts to a lower field (3.59 τ) by acetylation while the latter remains at nearly the same field (3.51 τ). Thus the comparison of the ring proton of IIb, Ic and IV (Table II) clearly demonstrated that the methoxyl group should be at 5–position adjacent to the ring proton. Since all the spectral data of Ia and Ib except the NMR signals due to the olefinic double bond in the side chain of Ia are almost superimposable with those of Ic, Ia is assumed to have the same substitution pattern.



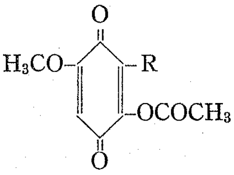
Ia : R=$C_{15}H_{29}(C_{13}H_{27}$, $C_{13}H_{27})$
Ib : R=$C_{15}H_{31}(C_{13}H_{26})$
Ic : R=$C_{13}H_{27}$



IIa : R=$C_{11}H_{23}$
IIb : R=$C_{13}H_{27}$
IIc : R=$C_{15}H_{31}(C_{13}H_{27})$



IIIa : R=$C_{15}H_{31}(C_{13}H_{27})$
IIIb : R=$C_{13}H_{27}$



IV : R=$C_{13}H_{27}$

Thus the mixture (Ia) has been characterized as 2–hydroxyl–5–methoxy–3–pentadecenyl–benzoquinone contaminated with 3–tridecyl and 3–tridecenyl compounds.

The benzene extract of the root bark of *Ardisia sieboldii* Miquel. (Japanese name: Mokutachibana), collected at Tanegashima, after removing a triterpene 'ilexol',[15] was introduced onto a column of acid–treated silica gel and was successively eluted with the solvent system of increasing polarity to give i) an oily fraction containing a mixture of triterpenoids, mp 218°, ii) a mixture of embelin (IIa) and rapanone (IIb), mp 144°,[20] iii) an orange red compound of mp 119° (ardisiaquinone B) (VI), iv) yellow crystalline powder of mp 69—70° (ardisiaquinone C) (VII), and v) yellow crystalline powder of mp 154° (ardisiaquinone A) (V). The yields of the new quinones were 0.02, 0.0005 and 0.02% respectively.

V, VI and VII show quite similar properties; they dissolve in sodium carbonate in violet color, which is decolorized with sodium dithionite. UV absorptions (Table I) suggested hydroxybenzoquinone chromophores in these compounds.[8–12] The molecular formulae of the

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15) Ilexol was first isolated from *Ilex* spp.[16] and then from *Ardisia japonica* BLUME[17] and *A. colorata* ROXB.[18] Although a structure has been proposed for the compound,[16] it has also been suggested that it might be a mixture of bauerenol and the corresponding 7,9(11)–diene.[19]

16) K. Yagishita, *Bull. Agric. Chem. Soc. Japan*, **21**, 160 (1957); K. Yagishita and S. Iseda, *ibid.*, **21**, 274 (1957); K. Yagishita, *ibid.*, **22**, 123, 131 (1958); **23**, 217 (1959).

17) M. Aritomi, *Yakugaku Zasshi*, **83**, 659 (1963).

18) P. Kanchanapee, H. Ogawa, and S. Natori, *Shoyakugaku Zasshi*, **21**, 68 (1967).

19) F.N. Lahey and M.V. Leeding, *Proc. Chem. Soc.*, **1958**, 342.

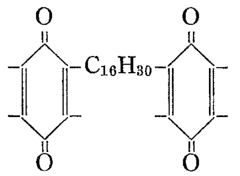
20) The presence of rapanone in the bark of the plant had been reported.[21]

21) J. Kawamura, *Repts. Japan Sci. Assoc.*, **12**, 377 (1937).

quinones are established as $C_{30}H_{40}O_8$ for A and B and $C_{32}H_{42}O_9$ for C from elemental analyses, molecular ions in mass spectra and molecular weights determined by osmometry.

Catalytic hydrogenation of V and VI, followed by aerial oxidation, gave the respective dihydro compounds, $C_{30}H_{42}O_8$ (by elemental analyses and mass spectra) (VIII and IX), showing nearly the same UV and IR spectra as V and VI. Treatment of V and VI with alkaline[22] afforded the respective demethyl compounds (X and XI). The same treatment of VII gave the demethyldeacetyl compound, which was identified with the demethyl compound from VI (XI). Acetylation of V and VIII gave the respective diacetates (XII and XIV), while VI and IX gave the triacetates (XIII and XV), the number of the phenolic acetyl groups being proved by IR and NMR spectra (Table I and II). Catalytic hydrogenation followed by acetylation of VII gave the same acetate (XV) from IX; thus ardisiaquinone C (VII) has been proved to be the monoacetate of ardisiaquinone B (VI).

Formation of these derivatives and the spectral data, especially IR (Table I) and NMR spectra (Table II) revealed the presence of the following functional groups in ardisiaquinones: V, two each of identically situated methoxyl groups, hydroxyl groups and ring protons and an aliphatic chain with one double bond ($C_{16}H_{30}$); VI, one methoxyl group, three hydroxyl groups, one olefinic methyl, one ring proton and the aliphatic chain ($C_{16}H_{30}$); and VII, the same as VI except one phenolic acetoxyl group instead of one of the three hydroxyl groups. The most characteristic feature of the NMR spectra in these compounds is the absence of aliphatic methyl group, indicating the both ends of the chain are attached probably to the benzoquinone nuclei. The molecular formulae, the proton numbers in NMR spectra and the molecular extinction values in UV spectra, which are about two times of 3-alkyl-2,5-dihydroxybenzoquinone derivatives (Table I), suggested that in the molecules of ardisiaquinones two benzoquinone nuclei are linked by the olefinic chain and the partial formula (A) is suggested.



A

V	VI	VII
$-OCH_3$	$-OCH_3$	$-OCH_3$
$-OCH_3$	$-OH$	$-OCOCH_3$
$-OH$	$-OH$	$-OH$
$-OH$	$-OH$	$-OH$
$-H$	$-CH_3$	$-CH_3$
$-H$	$-H$	$-H$

The mass spectra of benzoquinone derivatives especially ubiquinones and the related compounds have been reported[23–28] and the formation of the corresponding hydroquinones by dismutation reactions in an ionization chamber with water and the fragments thereof has been noticed.[25,27,28] As shown in Table III alkyl-dihydroxy(methoxy)benzoquinones show prominent peaks corresponding to benzylium ion (d), d+1 (e), d+2 (f), which are informative guide for learning the substituents on the quinone rings. In the mass spectra of ardisiaquinones and the dihydro derivatives (V, VI, VIII, and IX) (Fig. 1 and Table III) the base peak at *m/e* 169 and the fairly strong peaks at *m/e* 167 and 168 were observed, while in the demethylated compound from the quinone B (XI) at 153, 154, 155, 167, 168 and 169 *m/e*. These fragmentations indicate the presence of one each of hydroxyl and methoxyl group in both of the two quinone nuclei of V and in one of them of VI and the presence of two hydroxyl and one C-methyl groups in the other ring in VI.

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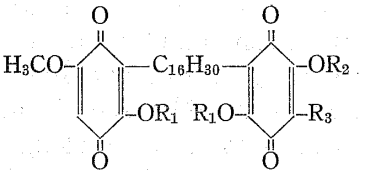
As has been discussed in this paper, the UV absorptions especially those of V, VI, X and XI (289, 291, 293, and 294 mμ respectively) exclude the presence of 2,3–dihydroxy (or hydroxy–methoxy) substitution pattern which should show the absorption in lower wave length.[9,12] The carbonyl streching vibration is diagnostic for the distinction between 2,5–dihydroxy and 2,6–dihydroxy compounds[8–11] and the similarity of the absorption of V and VIII with Ia, Ib, and Ic and of X and XI (1605 cm^{-1}, unsplitted) with IIb, IIc and XVIII (Table I) prove the presence of the former substitution pattern. UV absorptions of V and VI agree with the summation of the absorption of two moles of Ic for V and of one mole each of Ic and XVIII for VI. Such similarity was also observed in all the spectral data of the derivatives.

The relative positions of the methoxyl and the hydroxyl groups was learned from the comparison of the chemical shifts of the ring protons in V and VI with those of XII and XIII (Table II). Since the acetylation of V and VI does not affect the shielding of the ring proton(s), it should be concluded that the adjacent position(s) to the ring proton(s) in V and VI have been occupied by the methoxyl group (s).

Thus the substitution pattern in V, VI and VII except the position of the acetoxyl group in VII has been established as B.



B

V : $R_1=H$, $R_2=CH_3$, $R_3=H$
VI : $R_1=H$, $R_2=H$, $R_3=CH_3$
VII : monoacetate of VI

Finally the olefinic chain linking the two quinone rings was confirmed by the oxidation by alkaline hydrogen peroxide. From the dihydro derivatives (VIII and IX) the same dicarboxylic acid, mp 118—120°, was obtained and identified by a mixed fusion and IR spectra with octadecane–1,18–dioic acid. A mixed fusion, IR spectra and gas chromatography of the methyl ester also approve the identity. The same oxidation of V and VI afforded acidic products, the main fractions of which were proved to be identical both from V and VI by gas chromatography of the methyl ester prepared thereof. The acidic fractions were then directly ozonized and oxidized with silver oxide to give a same product, mp 97°, which was identified with azelaic acid by a mixed fusion, IR spectra and gas chromatography of the methyl ester. Thus the chain linking the two quinone rings must be 8–hexadecene. Due to the scarcity of the oxidation products from V and VI and of the authentic sample of *cis*–9–octadecene–1,18–dioic acid,[29–31] prepared from octadec-9-yne-1,18-dioic acid,[30] and to the difficulty encountered in the course of purification, we could not obtain the specimens showing sharp mp. However they showed entirely the same IR absorption and were clearly different from the spectrum of the *trans* isomer.[31] The identity was also confirmed by the IR comparison of S–benzylisothiouronium salts prepared from the oxidation product of V and from the authentic *cis* acid.

Thus the double bond has been determined as *cis* and the structures of ardisiaquinones A, B and C have been proved to be expressed by the formulae V, VI and VII.

The substitution pattern and the chain length has been confirmed by the unequivocal synthesis of 1,16–bis (2,5–dimethylamino–3–benzoquinonyl)hexadecane (XVI) and its identity with the compound prepared from dihydroardisiaquinone A (VIII); the results will be published in a forthcoming paper.[32]

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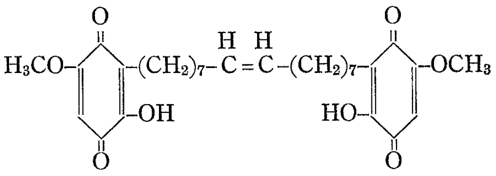
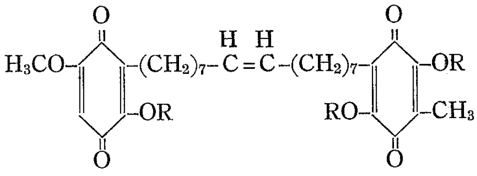
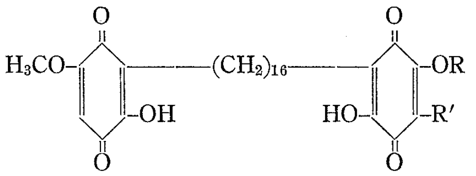


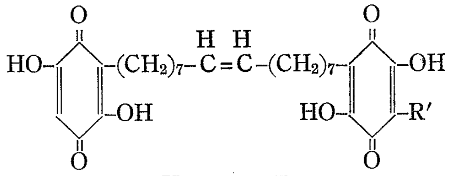
V



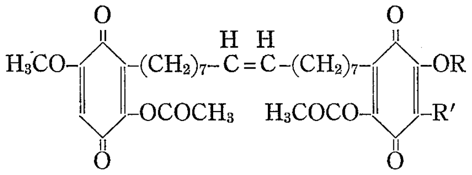
VI : $R=H$, H and H
VII : $R=H$, H and CH_3CO



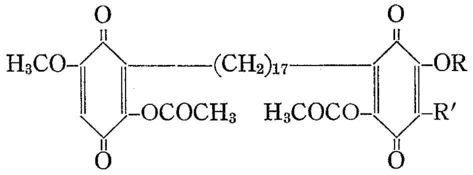
VIII : $R=CH_3$, $R'=H$
IX : $R=H$, $R'=CH_3$



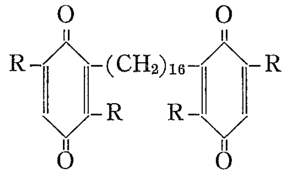
X : $R'=H$
XI : $R'=CH_3$



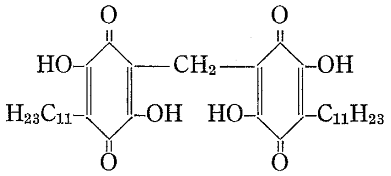
XII : $R=CH_3$, $R'=H$
XIII : $R=CH_3CO$, $R'=CH_3$



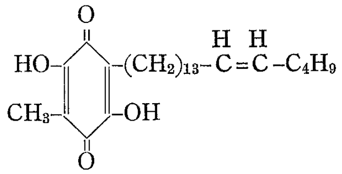
XIV : $R=CH_3$, $R'=H$
XV : $R=CH_3CO$, $R'=CH_3$



XVI : $R=CH_3NH-$



XVII



XVIII

The structures of these compounds are assumed to be unique from biogenetical feature. The quinones are obviously derived from acetate–malonate units as other 3–alkyl–2,5–dihydroxybenzoquinone derivatives, though there exists no experimental proof. Although there have been many polyketides assumed to be formed by the oxidative coupling of two units or by the linking of the two units with C_1–unit such as in the case of vilangin[33] (XVII), the compound having two aromatic rings linked by more than two carbon atoms has, as far as the authors are aware, never been reported in polyketides. The biogenesis of ardisiaquinones are assumed to be initiated from *cis*–9–octadecene–1,18–dioic acid, which is assumed to be the precursor of civetone[29] and phloionic acid,[34] and the two rings have been formed by the simultaneous malonate condensation at the both ends of the dicarboxylic acid.

Experimental[35]

Isolation of 2-Hyrdoxy-5-methoxy-3-pentadecenyl(tridecenyl, tridecyl)benzoquinone (Ia) from *Ardisia japonica*——Dried and cutted rhizomes of *Ardisia japonica* (THUNB.) BLUME. (4.3 kg), collected at Sayama,

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33) Ch.B. Rao and V. Venkateswarlu, *J. Org. Chem.*, **26**, 4529 (1961).
34) A. Chicoisne, G. Dupont, and R. Dulou, *Bull. Soc. Chim. France*, **1957**, 1237.
35) Melting points were determined in a Yanagimoto Melting Point Apparatus and are incorrected; the UV spectra were taken on a Hitachi EPU–2A Spectrophotometer; the IR spectra were measured on a Nihon Bunko DS–301 Spectrophotometer in KBr discs; the NMR spectra were run on a Varian Associates A–60 (60 Mc) and recorded in τ values with the internal standard (TMS); the mass spectra were determined on a Hitachi RMU–6D Mass Spectrometer with direct inlet system operating at the ionization potential (70 eV) and the ionization temperature (*ca.* 200°); and gas chromatography was carried out on a Shimadzu GC–1B Gas Chromatograph.

Saitama Prefecture, in January 1965, were extracted with boiling benzene (10 liter × 25) and the extract, after the evaporation of benzene, was dissolved in 5% NaOH under ice cooling. The alkaline solution was washed with ether, acidified and then extracted with ether (500 ml × 9). After the evaporation of ether, the residue (20 g) showing four spots positive for alkaline reagents was dissolved in hexane and divided into hexane–soluble portion and insoluble portion. The former fraction was chromatographed on a column of $CaHPO_4$ (6 × 40 cm × 5). The elution with hexane afforded colorless oil (5 g). The elution with hexane–benzene (1:1) afforded embelin (IIa) contaminated with a small amount of rapanone (IIb) (20 mg), orange plates of mp 138—140° (from benzene and then from EtOH) which was identified with an authentic sample.[36] Further elution with benzene gave a fraction containing the objective compound (Ia), which was repeatedly chromatographed through the same column till it showed a single spot on thin–layer chromatography. Recrystallization from 80% EtOH afforded yellow plates (400 mg) of mp 62—66° and further recrystallization from the same solvent raised the mp 66.5—67°. The hexane–insoluble part was washed with benzene–hexane (1:2) and the residue was recrystallized from EtOH and then from benzene to give further amount of IIa (30 mg). The benzene–hexane washings afforded red plates of mp 161—164° (from MeOH), which has not been characterized yet.

2-Hydroxy-5-methoxy-3-pentadecenyl(tridecenyl, tridecyl)benzoquinone (Ia)——Yellow platelets of mp 66.5—67° from 80% MeOH. The contamination of tridecenyl (*ca.* 13%) and tridecyl (*ca.* 13%) compounds was revealed by the mass spectrum and gas chromatography of the oxidation product (*vide infra*). *Anal.* Calcd. for $C_{22}H_{34}O_4$: C, 72.89; H, 9.45. Calcd. for $C_{20}H_{30}O_4$: C, 71.82; H, 9.04. Calcd. for $C_{20}H_{32}O_4$: C, 71.39; H, 9.59. Found: C, 72.46; H, 9.20.

2-Hydroxy-5-methoxy-3-pentadecyl(tridecyl)benzoquinone (Ib)——Ia (100 mg) in EtOH was catallytically hydrogenated in the presence of PtO_2 (10 mg). After removing the catalyst, the solution was added with a few drop of ferric chloride solution, acidified and refluxed for 3 hr. The solvent was evaporated and the ethereal solution of the residue was washed with water, dried and evaporated. Recrystallization of the residue from 80% MeOH afforded yellow needles of mp 90—91° (70 mg). The mass spectrum and gas chromatography of the oxidation product showed the contamination of tridecyl compound (*ca.* 30%).

2,5-Dihydroxy-3-pentadecyl(tridecyl)benzoquinone (IIc)——Ib (34 mg) in benzene (4 ml) was refluxed for 1 hr with $AlCl_3$ (400 mg). The solvent was evaporated, water was added and the reaction product was extracted with ether. The ethereal layer was washed with 5% $NaHCO_3$ and then evaporated. The residue

TABLE Ⅳ. Gas Chromatography of Fatty Acid Methyl Esters Formed by Oxidation of Benzoquinones (by Hitachi–Perkin Elmer F6–D)

Column	Column temp. (°C)	Sample	t_R (min)			
SE 52 (1.5%) on gaschrom P (1.5 m)	200	methyl ester from Ia	8.05	8.30	16.70[a]	—
		methyl ester from Ia (hexane eluate of the column chromatography[b])	—	8.25	—	—
		methyl ester from Ia (hexane–ether eluate of the chromatography)	8.05	—	16.70	—
		methyl ester from Ib	—	8.25	—	17.00
		methyl ester from Ⅱc	—	8.25	—	17.00
		methyl myristate	—	8.20	—	—
		methyl palmitate	—	—	—	17.00
SE 52 (5%) on diasolid H (2.0 m)	250	methyl ester from Ⅴ	9.40			
		methyl ester from Ⅵ	9.35			
		methyl ester from Ⅷ		10.1		
		methyl ester from Ⅸ		10.15		
		methyl *cis*–9–octadecene–1,18–dioate	9.35			
		methyl octadecane–1,18–dioate		10.07		
SE 52 (5%) on diasoild H (2.0 m)	175—178	methyl ester from the ozonization product from Ⅴ		4.70		
		methyl ester from the ozonization product from Ⅵ		4.72		
		methyl azelate		4.75		

[b] main peak
[a] by the method of B. de Vries (*J. Am. Oil Chem. Soc.*, 40, 186 (1963)).

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[36] For the identification of embelin and rapanone, see ref. 1).

in hexane–benzene (1:1) was passed through a column of $CaHPO_4$ and the fraction eluted with benzene–acetone (5:1) was recrystallized from benzene to orange–red plates (20 mg) of mp 136—138°.

2,5-Dimethoxy-3-pentadecyl(tridecyl)benzoquinone (IIIa)——Methylation of Ib (70 mg) with dimethyl sulfate–K_2CO_3–acetone afforded IIIa, pale yellow plates (23 mg) of mp 64° from MeOH.

Alkaline Hydrogen Peroxide Oxidation of Ia, Ib and IIc and the Identification of the Oxidation Products by Gas-Liquid Chromatography——To the solution of the quinone (2—3 mg) in 1 N KOH (1 ml), hydrogen peroxide (30%, 2—3 drops) was added and warmed on a water bath for 30 min. The acidified reaction mixture was extracted with ether and treated directly with ethereal diazomethane and evaporated. The methyl esters thus obtained were applied for gas chromatography and the results are shown in Table IV.

Rapanone 5-Methyl Ether (Ic)[37]——Rapanone (2.0 g) was refluxed with dimethyl sulfate (1 g, 2/3 mole), K_2CO_3 (0.5 g) and acetone (70 ml) for 2 hr. The reaction mixture was filtered while hot, acidified and evaporated. The residue was added with water and extracted with ether. The ethereal extract was evaporated and the residue was dissolved in hexane and chromatographed on a column of silica-gel (Mallinckrodt) treated beforehand with 2% HOAc (6×40 cm). The fraction eluted by benzene was evaporated and recrystallized from EtOH to yellow plates of mp 90—91° (0.63 g). *Anal.* Calcd. for $C_{20}H_{32}O_4$: C, 71.39; H, 9.59. Found: C, 71.46; H, 9.58.

2-O-Acetylrapanone 5-Methyl Ether (IV)——Ic (50 mg) was acetylated with Ac_2O and H_2SO_4. After working up usual, the acetate was recrystallized from 90% EtOH to pale yellow plates (*ca.* 20 mg) of mp 76—77°. *Anal.* Calcd. for $C_{22}H_{34}O_5$: C, 69.81; H, 9.05. Found: C, 69.70; H, 9.05.

Isolation of Ardisiaquinone A, B, and C(V—VII) from *Ardisia sieboldii* Miquel——Dried root bark of *Ardisia sieboldii* Miqul (8.37 kg), collected at Tanegashima, Kagoshima Prefecture, in November 1966, was extracted with benzene (8 liter×4). The extract (104 g) was dissolved in acetone and acetone–insoluble substance (23 g) was removed by filtration. The insoluble substance was recrystallized from acetone to colorless needles of mp 222—225°. It forms the acetate, mp 280—288°, and the benzoate, mp 247—250°, and was identified with the sample of 'ilexol' from *Ilex* sp.[16] The acetone solution was evaporated, leaving the residue (*ca.* 80 g). The residue in benzene was chromatographed on a column of silica–gel (Mallinckrodt) treated with 2% HOAc (8×40 cm×16) and eluted successively with benzene, benzene–AcOEt (100: 2.5), and benzene–EtOAc (100:5). From the benzene fraction pale yellow oily substance (36 g)[38] and then rapanone (IIa) contaminated with embelin (IIa) (35 g),[36] mp 144°, and 'ilexol' (5 g) were obtained. From the benzene–AcOEt (100:2.5) layer red crystalline powder of mp 108—112° (ardisiaquinone B) (1.8 g) and then yellow crystalline powder of mp 64—70° (ardisiaquinone C) (0.06 g) were obtained. The benzene–EtOAc (100:5) fraction afforded ardisiaquinone A, yellow crystalline powder of mp 147—152° (1.4 g).

Ardisiaquinone A (V)——The crude sample was recrystallized from benzene–hexane (3:7) to yellow crystalline powder of mp 154°. *Anal.* Calcd. for $C_{30}H_{40}O_8$: C, 68.16; H, 7.63; mol. wt. 528. Found: C, 67.74; H, 7.28; mol. wt. 528 (M^+ by mass spectrum), 538 (osmometry).

Ardisiaquinone B (VI)——The crude sample was recrystallized from benzene–hexane (1:9) to red crystalls of mp 119°. *Anal.* Calcd. for $C_{30}H_{40}O_8$: C, 68.16; H, 7.63; mol. wt. 528. Found: C, 68.06; H, 7.38; mol. wt., 528 (M^+ of mass spectrum), 525 (osmometry).

Ardisiaquinone C (VII)——Recrystallized from hexane, yellow crystalline powder of mp 69—70°. *Anal.* Calcd. for $C_{32}H_{42}O_9$: C, 67.35; H, 7.42; mol. wt., 570. Found: C, 67.13; H, 7.42; mol. wt., 570 (M^+ of mass spectrum).

Dihydroardisiaquinone A (VIII)——V (100 mg) in EtOH was catalytically hydrogenated in the presence of PtO_2 (10 mg). In the course of the hydrogenation the color of the solution changed from yellow to violet-red, violet and finally to colorless. After removing the catalyst the filtrate was evaporated. The color of the solution returned to yellow and the residue was recrystallized from benzene–hexane (3:7) to yellow crystals of mp 174—176° (70 mg). *Anal.* Calcd. for $C_{30}H_{42}O_8$: C, 67.90; H, 7.98; mol. wt., 530. Found: C, 67.61; H, 7.90; mol. wt., 530 (M^+ of the mass spectrum).

Dihydroardisiaquinone B (IX)——VI (100 mg) was hydrogenated as before and IX, orange powder thus obtained, showed mp 145—148° (from benzene–hexane (1:9)). *Anal.* Calcd. for $C_{30}H_{42}O_8$: C, 67.90; H, 7.98; mol. wt., 530. Found: C, 68.45; H, 7.82; mol. wt., 530 (M^+ of mass spectrum).

Demethylardisiaquinone A (X)——V (50 mg) was dissolved in 2 N NaOH (5 ml) and warmed on a water bath for 5 min. The solution was acidified and extracted with ether. The residue was recrystallized from benzene–hexane (1:1) to orange–red crystalline powder (12 mg) of mp 174.5—175°. *Anal.* Calcd. for $C_{28}H_{36}O_8$: C, 67.18; H, 7.25. Found: C, 67.19; H, 7.41.

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37) H. Ogura and K. Furuhata, the 86th Annual Meeting of the Pharmaceutical Society of Japan, Abstracts of Papers p. 141 (1966).

38) From this fraction a mixture of triterpenoids, mp 218°, was obtained. From the IR spectrum and the hydrolysis the mixture is assumed to be triterpene acetate, though it has been proved to be a mixture of three compounds by gas–liquid chromatography.

Demethylardisiaquinone B (XI)——i) VI (50 mg) was treated as in the case of X from V. Orange red needles (15 mg) of mp 165—167° from benzene-hexane (1:1). *Anal.* Calcd. for $C_{29}H_{38}O_8$: C, 67.68; H, 7.44. Found: C, 67.49; H, 7.38.

ii) Ardisiaquinone C (VII) (10 mg) was treated with 2N NaOH at room temperature. After working up usual orange-red product was recrystallized from bezene-hexane (1:1), mp 162—165° (7 mg). The identity with XI from VI was confirmed by a mixed fusion and IR spectra.

Ardisiaquinone A Diacetate (XII), Ardisiaquinone B Triacetate (XIII), Dihydroardisiaquinone A Diacetate (XIV) and Dihydroardisiaquinone B Triacetate (Dihydroardisiaquinone C Diacetate) (XV)——i) V, VI, VIII or IX (20—50 mg) was acetylated by Ac_2O and a drop of H_2SO_4. V gave diacetate (XII) of yellow oil, while VI gave triacetate (XIII) of yellow oil (*cf.* Table I and II). VIII gave diacetate (XIV), yellow crystals of mp 84° from hexane, while IX gave triacetate (XV) of yellow wax (*cf.* Table I).

ii) Ardisiaquinone C (VII) (30 mg) was hydrogenated as before and the product, yellow crystals of mp 81° from hexane was acetylated to afford yellow wax, wihch was identified with XV by IR and thin-layer chromatography.

The Oxidation of VIII and IX. Formation of Octadecane-1,18-dioic Acid——VIII or IX (100 mg) was dissolved in 1 N KOH (20 ml) and, after the addition of 30% H_2O_2 (1 ml), warmed on a water bath for 30 min. After standing at room temperature for 3 hr, the reaction mixture was acidified and the precipitate was collected by centrifugation. The precipitate was washed with water, dissolved in ether, dried and evaporated. The residue was extracted with hexane-benzene (8:2) and the deposited crystals from the extract was recrystallized from hexane-benzene (8:2). The same acid, mp 118—120°, was obtained from VIII and IX. The acid derived from the both afforded the same methyl ester, mp 43—50°, by methylaton with diazomethane. The identity with octadecane-1,18-dioic acid was established by mixed fusions and IR spectra comparison of the free acid and the methyl ester and also by the gas-liquid chromatography retention times (Table IV) of the methyl ester with the authentic samples.

The Oxidation of V and VI. Formation of *cis*-9-Octadecene-1,18-dioic Acid——V or VI (100 mg) was oxidized as before and, after the decolorization of the reaction mixture, it was warmed on a water bath for 5 min and acidified. The reaction mixture was extracted with a mixture of benzene-hexane (8:2) and the extract was washed, dried and evaporated under N_2-stream. The acidic products thus obtained from V (mp 59—71°) and VI (mp 65—72°) were proved to be identical by the comparison of the peaks of gas-liquid chromatography carried out by their methyl esters. Although it was impossible to obtain the samples showing a sharp mp,[39] the comparison of the IR spectra with those[31] of *cis*- and *trans*-9-octadecene-1,18-dioic acids clearly demonstrated the identity with the *cis* acid. The *cis*-acid prepared from 9-octadecyne-1,18-dioic acid[30] also did not show a sharp mp, but again proved the identity with the oxidation product by IR spectra. S-Benzylisothiouronium salt prepared from the oxidation product of V, mp 162°, also showed the identical IR spectrum with that from the prepared sample. Comparison by the methyl esters by gas-liquid chromatography was also carried out (Table IV).

The acid from V or from VI (2—3 mg) was dissolved in $CHCl_3$ (2 ml) and ozonized for 30 min. The solvent was removed, silver oxide (prepared from 0.15 g of $AgNO_3$) and water (5 ml) were added. After standing at room temperature for overnight, the reaction mixture was filtered and evaporated. The residue was recrystallized from acetone to colorless crystals of mp 95—96° from V and mp 91—97° from VI and they were identified with azelaic acid by the comparison of the IR spectra and the gas chromatography of the methyl ester prepared by diazomethane (Table IV).

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[39] *cis*-Acid, mp 69—70°,[30] 70—71.5°,[29] and 74°;[31] *trans*-acid, mp 98.5—99.5°,[29] and 99°.[31]