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Synthetic Study of Siccanin, an Antifungal Antibiotic. II.[1] An Attempt to Synthesis of Siccanin Skeleton

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A synthesis of a perhydrobenzo[*a*]xanthene related to the skeleton of siccanin (3), an antifungal antibiotic, was described. A series of reactions starting from $\Delta^{1(9)}$-octal-2-one (**5**) gave 1-(2-hydroxy-6-methoxy-4-methylbenzyl)-2-methylene-9-vinyl-*cis*-decalin (**19**), whose acid-catalysed cyclization reaction yielded a perhydrobenzo[*a*]xanthene (**20a**) with *cis*/*anti*/*cis* ring junctures. The structure of the latter compound was determined by three dimensional X-ray analysis of its brosyl derivative (**20c**).

In the previous paper[1] of this series, it was reported that acid-catalyzed cyclization of an orcinol derivative (**1a**) bearing an hydroxy function at the γ-position of the side chain easily provided a hexahydroxanthene compound (**2a**) which involves the B, C, and D rings of siccanin[3] (**3**), an antifungal antibiotic. In addition, it was found that, no matter which *cis* or *trans* alcohol was cyclized, the resulting hexahydroxanthene (**2a**) was the same and the ring juncture of **2a** was postulated as being *trans* refering to the foregoing analogous study of Mechoulam, *et al.*[4] Accordingly, some difficulties in preparing a hexahydroxanthene with a *cis* ring juncture, which corresponds to that of the B and C rings of siccanin (**3**), might be anticipated through this type cyclization reaction. However, it was assumed that a benzo[*a*]perhydroxanthene compound (**2b**) with a *cis*/*anti*/*trans* structure to be obtained by an analogous cyclization of a *cis*-decalin analog of **1a** (**1b**) would be converted into a *cis*/*syn*/*cis* derivative with the siccanin skeleton by the successive introduction of a carbonyl function at the benzylic position (C-12, see Chart 1) and an epimerization of the 12a-hydrogen adjacent to this carbonyl group by base. This is based on an observation of Hirai, *et al.*,[5] that a ketone derivative (**4**) derived from siccanin resisted ring epimerization on treatment with various bases and the *cis*/*syn*/*cis* structure of **4** is thermodynamically stable. Some investigation of this synthetic scheme directed towards siccanin forms the subject of this paper.

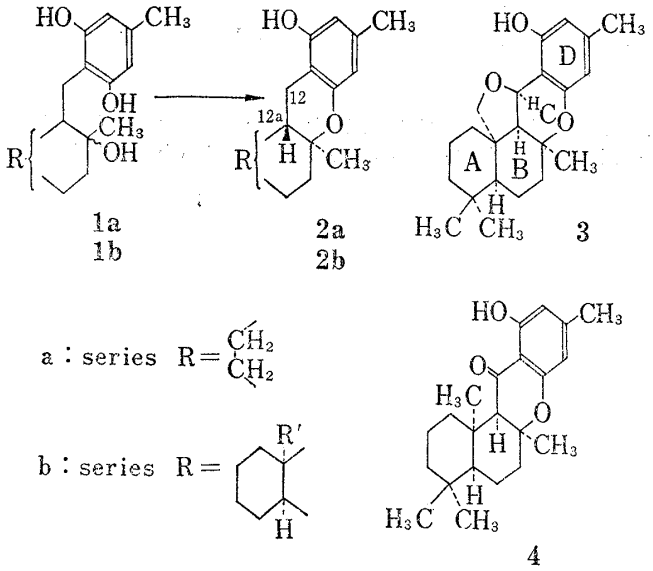

Chart 1

1) Part I: S. Oida, Y. Ohashi, A. Yoshida, and E. Ohki, *Chem. Pharm. Bull.* (Tokyo), **20**, 2634 (1972).
2) Location: *Hiromachi, Shinagawa-ku, Tokyo.*
3) K. Ishibashi, K. Hirai, M. Arai, S. Sugawara, A. Endo A. Yasumura, H. Masuda, and T. Muramatsu, *Ann. Sankyo Res. Lab.*, **22**, 1 (1970) and references cited therein.
4) R. Mechoulam and B. Yagen, *Tetrahedron Letters*, **1969**, 5349.
5) Private communication. Also see ref. 3.

As for access to a *cis*-fused decalin system, there are a number of methods developed which are available at present. In addition to the Diels-Alder reaction between substituted dienes and quinones,[6] hydrogenation of $\Delta^{1(9)}$-octal-2-ones,[7] or hydroboration reaction of $\Delta^{1(9)}$-octalins,[8] the cuprous ion-catalyzed conjugate 1,4-addition of organometallic reagents to $\Delta^{1(9)}$-octal-2-ones furnishes a versatile and useful process for the introduction of an alkyl angular substituent to afford a *cis*-fused decalin system.[9] Thus, it was assumed that an application of a vinylmetallic reagent[10] to the 1,4-addition reaction would provide a *cis*-fused decalin with an angular vinyl group amenable to forming a hydroxymethyl group which involves the angular substituent on the A and B rings of siccanin. Following the procedure of House, *et al.*,[11] treatment of $\Delta^{1(9)}$-octal-2-one (**5**) with vinylmagnesium chloride[12] was carried out in the presence of tetrakis[iodo(tri-*n*-butylphosphine)copper(I)][13] in tetrahydrofuran and 9-vinyl-*cis*-decalone (**6**) was obtained in 72% yield.[14] Characterization of **6** was conducted by formation of a crystalline 2,4-dinitrophenylhydrazone, mp 87.5—89°.

Having obtained the decalone (**6**), it was now necessary to attempt the introduction of an orcinol moiety at the C-1 position of **6**. First, a condensation of **6** with 2,6-dimethoxy-4-methylbenzaldehyde[17] (**7**) was attempted in the presence of potassium *t*-butoxide, but this resulted in exclusive formation of a C-3 substituted decalone (**8**). The structure of **8** was secured by a characteristic doublet of doublets absorption at 2.38 and 2.62 ppm, J_{ab}=17.5 Hz, due to the C-1 methylene protons in its nuclear magnetic resonance (NMR) spectrum. Next, we attempted a reaction of the octalone (**5**) with the Grignard reagent followed by trapping of the intermediate enolate anion (**9**) with the aldehyde (**7**); however, this resulted in a formation of a complex mixture, from which a possible C-1 substituted product could not be isolated except for a 25% yield of the C-3 substituted product (**8**) and a small amount of the unsubstituted product (**6**). Accordingly, we turned to blocking the C-3 position prior to the introductrion of the orcinol moiety as follows. Following the procedure of Ireland, *et al.*,[18] treatment of **6** with ethylformate in the presence of sodium methoxide and successive treatment of the resulting hydroxymethylene ketone with *n*-butylmercaptan afforded a C-3 blocked ketone (**10**) in 74% yield. Successively, a base-catalyzed condensation between **10** and the aldehyde (**7**) was carried out under various conditions; however, no reaction was observed, suggesting that the C-1 position is too hindered to allow close approach of the bulky aldehyde

6) L.S. Butz and A.W. Rytina, *Org. Reactions*, **5**, 136 (1949).
7) T.E. McMurry, *J. Am. Chem. Soc.*, **90**, 6821 (1968) and its related references.
8) J.A. Marshall, M.T. Pike, and R.D. Carroll, *J. Org. Chem.*, **31**, 2933 (1966).
9) A.I. Birch and R. Robinson, *J. Chem. Soc.*, **1943**, 501; J.A. Marshall and R. Roebke, *J. Org. Chem.*, 33, 840 (1968); E. Piers and R.J. Keziere, *Can. J. Chem.*, **47**, 137 (1969); E. Piers, W. de Waal, and R.W. Britton, *J. Am. Chem. Soc.*, **93**, 5113 (1971).
10) Vinyl group transfer to the β-carbon atom of an alicyclic conjugated enones using divinylcopperlithium-tributylphosphine has been already reported. See J. Hooz and R.B. Layton, *Can. J. Chem.*, **48**, 1626 (1970); An application of this method with divinylcopperlithium to $\Delta^{1(8)}$-inden-2-one was carried out and announced during this study. See E.J. Corey and R.L. Carney, *J. Am. Chem. Soc.*, **93**, 7318 (1971).
11) H.O. House, W.L. Respess, and G.M. Whitesides, *J. Org. Chem.*, **31**, 3128 (1966).
12) S.D. Rosenberg, *J. Org. Chem.*, **22**, 1201 (1957).
13) Inorganic Synthese VII, McGraw-Hill Book Co., Inc., New York, 1963, p. 10.
14) In this reaction, divinylcopperlithium-tributylphosphine prepared by the method of Whitesides, *et al*,[15] was used, but the result was almost the same as above. Moreover, prior to this study, we attempted an addition reaction of methoxymethylmagnesium chloride[16] to **5** in the presence of cuprous ion, but this mainly resulted in formation of a 1,2-addition product. A further study on this reaction under different conditions was not carried out owing to some difficulties associated with a preparation of the Grignard reagent.
15) G.M. Whitesides, W.F. Fisher, Jr., J.S. Filippo, R.W. Bashe, and H.O. House, *J. Am. Chem. Soc.*, **91**. 4871 (1969).
16) E. Taeger, Ch. Fiedler, A. Chiari, and H.P. Berndt, *J. Prakt. Chem.*, **28**, 1 (1965).
17) R. Adams and R.B. Carlin, *J. Am. Chem. Soc.*, **65**, 360 (1943).
18) R.E. Ireland and J.A. Marshall, *J. Org. Chem.*, **27**, 1615, 1620 (1962).

(**7**) necessary to effect reaction. Accordingly, a stepwise introduction of the substituent at the C-1 position was carried out in the following way. An enolate anion prepared from **10** by means of sodium methylsulfinylmethide yielded a methylene compound[19] (**11**) as a syrup on treatment with paraformaldehyde, which was found to be unstable. Without purification, the 1-methylene-2-one (**11**) thus obtained was submitted to a treatment with the lithium salt of orcinol dimethylether, giving an isomeric mixture of ketones (**13**). The yield of **13** from **10** was about 62%. The components of **13** were distinguishable on a thin-layer chromatogram and separated by a column of silica gel, one as a syrup and the other as crystals, mp 82—84°. Moreover, acid-catalyzed condensation between the 1-methylene-2-one (**11**) and orcinol was attempted and this resulted in a formation of a tetracyclic compound (**14**) in a low yield.

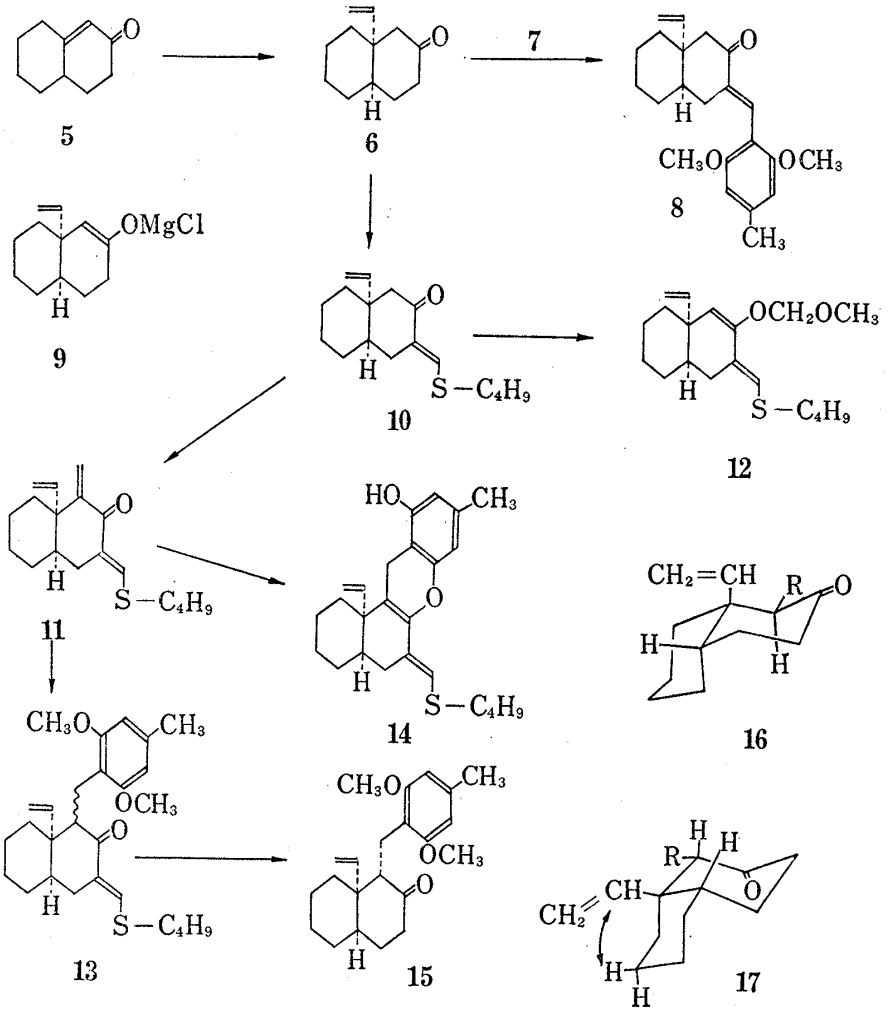

Chart 2

Removal of the C-3 blocking group from each epimeric ketone (**13**) or their mixture gave a crystalline ketone (**15**), mp 143—144°, in a good yield, along with a small amount of an isomeric ketone, mp 79—80°. The stereochemistry of **15** thus obtained required brief comment. Obviously, the C-1 substituent adjacent to the carbonyl in **15** is epimerizable. The predominant formation of one epimer in **15** shows that one of the two possible epimers (**16** and **17**) is considerably more stable than the other. This can be seen on the basis of con-

19) Moreover, treatment of the enolate anion prepared from **10** with methoxymethylchloride afforded a methoxymethyl enolether (**12**) as a syrup, whose structure was suggested by ultraviolet (λ_{max} 279.5 mμ), infrared (no carbonyl absorption), and NMR (4.67 ppm as singlet due to the C-1 proton) spectrometries.

formational analysis where the favored chair-chair conformation of **16** is indeed appreciably more stable than the other (**17**). This is mainly due to the presence of a surplus 1,3-diaxial interaction between the C-7 proton and the angular vinyl substituent in **17** as compared to similar interactions present in **16**. Thus, the ketone (**15**) would be designated as a *cis*-fused decalone with a bulky side chain oriented *cis* with respect to the angular vinyl group.

Next, the synthesis of the tetracyclic compound (**2b**) from **15** was attempted. As described in the preceding paper,[1] either epimeric alcohol (**1a**) or the C-2 methylene compound gave the same hydroxanthene compound (**2a**); therefore, synthesis of **2b** from **15** was carried out *via* the corresponding methylene compound easily accessable as follows. Treatment of **15** with methylenetriphenylphosphorane generated in dimethyl sulfoxide in tetrahydrofuran gave a C-2 methylene derivative (**18**), mp 113—114.5°, in 87% yield. Demethylation of **18** was conducted by the method of Feutrill, *et al.*:[20] Refluxing **18** in dimethylformamide in the presence of thioethoxide gave a phenol (**19**), mp 75.5—76.5°, in 93% yield. Treatment of **19** with *p*-toluenesulfonic acid in benzene gave a cyclic compound (**20a**) as a syrup in 89% yield, which formed a crystalline phenolic compound (**20c**), mp 138.5—140.5°, on further treatment with thioethoxide. As for the structure of this final product (**20b**), its NMR spectra from various solvents unfortunately did not furnish any reliable data for assigning its stereochemistry. Consequently, a crystalline brosylate (**20c**) derived from **20b** was submitted

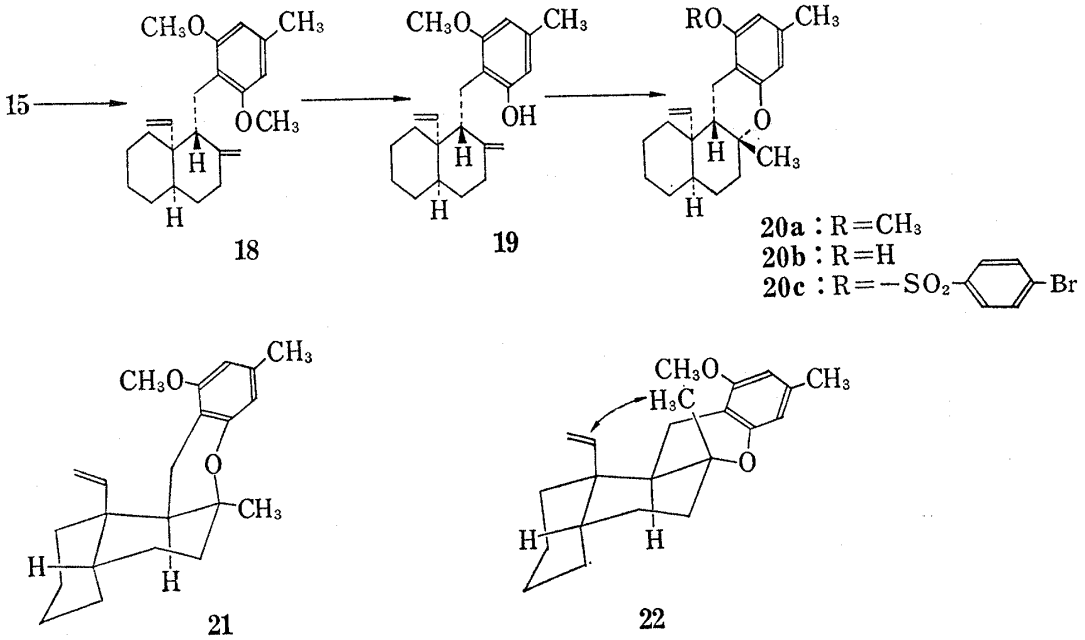

Chart 3

to a three-dimensional X-ray diffraction analysis. Thus, the result of the X-ray analysis, as will be described in the following section, revealed that the juncture of the B and C rings in **20c** was *cis* as shown in a steric formula (**21**), contrary to our initial scheme for the synthesis of a *trans* juncture. The formation of the B-C *cis* fusion would be interpreted also in terms of conformational analysis. The acid-catalyzed cyclization reaction into a hydroxanthene skeleton proceeds through a carbonium ion and is strongly influenced by the sterochemical environment of the C-3 reactive center. In a possible *cis/anti/trans* isomer (**22**), the newly-built angular methyl group would fall into a 1,3-diaxial interaction with the angular vinyl substituent and subsequently, the *cis/anti/cis* isomer (**21**) less subject to these steric effects is preferentially formed. Some other synthetic programs directed towards siccanin are still in progress and will be the subject of the forthcoming papers.

20) G.I. Feutrill and R.N. Mirrington, *Tetrahedron Letters*, **1970**, 1327.

TABLE I. Final Atomic Co-ordiantes and Isotropic Temperature Factors for Light Atoms, Anisotropic for Br and S

Atom	x/a	y/b	z/c	B
Br	−0.084	0.799	0.549	a)
S	0.280	0.615	0.594	a)
C 1	0.482	0.427	0.844	3.42
C 2	0.602	0.419	0.881	3.63
C 3	0.631	0.352	0.905	4.87
C 4	0.555	0.316	0.746	4.56
C 5	0.434	0.326	0.713	3.43
C 6	0.359	0.290	0.551	3.56
C 7	0.365	0.314	0.396	3.43
C 8	0.338	0.378	0.368	3.24
C 9	0.402	0.416	0.518	2.72
C 10	0.399	0.393	0.685	2.90
C 11	0.363	0.481	0.481	3.17
C 12	0.243	0.485	0.384	2.84
C 13	0.179	0.436	0.313	3.30
C 14	0.065	0.440	0.227	3.02
C 15	0.012	0.495	0.215	3.97
C 16	0.076	0.545	0.270	3.46
C 17	0.188	0.539	0.357	2.93
C 18	−0.109	0.498	0.122	3.86
C 19	0.290	0.403	0.698	3.61
C 20	0.233	0.366	0.739	4.52
C 21	0.352	0.400	0.205	3.39
C 22	0.019	0.744	0.552	3.49
C 23	0.107	0.763	0.528	3.82
C 24	0.192	0.723	0.546	3.76
C 25	0.175	0.664	0.576	3.33
C 26	0.087	0.644	0.596	3.71
C 27	0.006	0.685	0.578	3.76
O 28	0.222	0.382	0.328	3.18
O 29	0.249	0.590	0.411	2.68
O 30	0.274	0.567	0.695	4.39
O 31	0.376	0.646	0.632	4.66

a) The anisotropic temperature factors for Br and S are in the form
$T_i = \exp(-\beta_{11}h^2 - \beta_{22}k^2 - \beta_{33}l^2 - 2*(\beta_{12}hk + \beta_{13}hl + \beta_{23}kl))$

	β_{11}	β_{12}	β_{33}	β_{12}	β_{13}	β_{23}
Br	0.00619	0.00174	0.02947	0.00094	0.00603	0.00027
S	0.00519	0.00192	0.01604	0.00038	0.00284	−0.00013

TABLE II. Deviations (Å) of Atoms from Various Planes

a) plane through C(1), C(2), C(4), C(5);
b) plane through C(5), C(7), C(8), C(10);
c) plane through C(8), C(11), C(12), O(28);
d) plane through C(9), C(11), C(13), O(28).

Plane	Atom	Deviation	Plane	Atom	Deviation
a)	C(3)	−0.70	c)	C(9)	−0.60
	C(10)	0.70		C(13)	0.10
b)	C(6)	0.70	d)	C(8)	0.65
	C(9)	−0.61		C(12)	−0.07
	C(1)	−0.77		C(10)	−1.53
	C(19)	1.43		C(14)	−0.22
	C(21)	−0.78			

Crystal Data and Structural Determination of 20c

The sample of **20c** for the X-ray analysis were grown from MeOH as colorless needles, approximately 0.2 mm in diameter and 0.4 mm long. The *a*-axis of the crystal was the normal direction to the X-ray beam. The crystal data for $C_{27}H_{31}O_4SBr$, mol. wt.=531.52, showed for the monoclinic and the space group $P2_1/c$: a=13.40 Å, b=22.52 Å, c=8.67 Å, β=114.8°, Z=4.

Intensities of 2017 independent reflections were collected with the Rigaku four-circle diffractometer with Mo-Kα radiation, 2θ up to 60°. The structure was solved by location

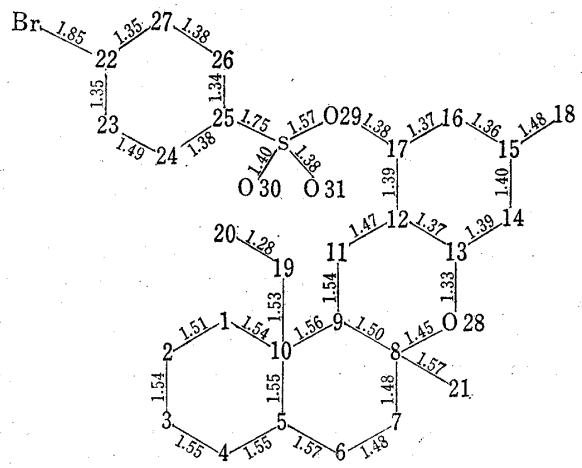

Fig. 1

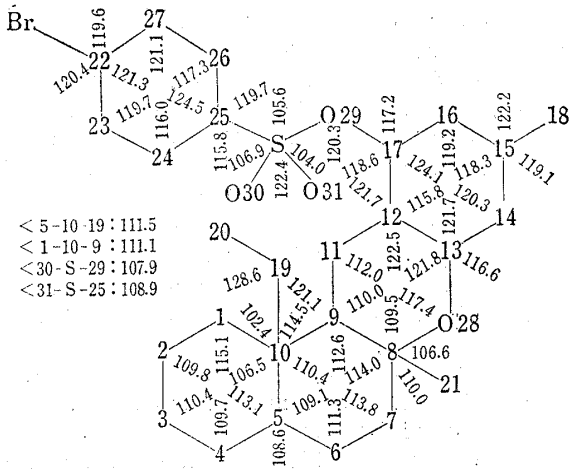

Fig. 2

of the bromine atom from a three-dimensional Patterson function and by a series of least squares refinements to reduce the R-value to 0.12. The final positional parameters are shown in Table I, the bond lengths in Fig. 1, the bond angles in Fig. 2, the molecular skeletal form projected along the *b*-axis in Fig. 3, and deviations of atoms from each least squares plane in Table II respectively.[21] Considering the data presented in discussion thus far the following points are evident: (a) The A and B rings have essentially chair conformations. (b) In the C ring, the best least squares plane is through four atoms of C(9), C(11), C(13), and O(28), which has an envelop-like form. (c) The junctures of these rings are thereafter a *cis*/*anti*/*cis*.

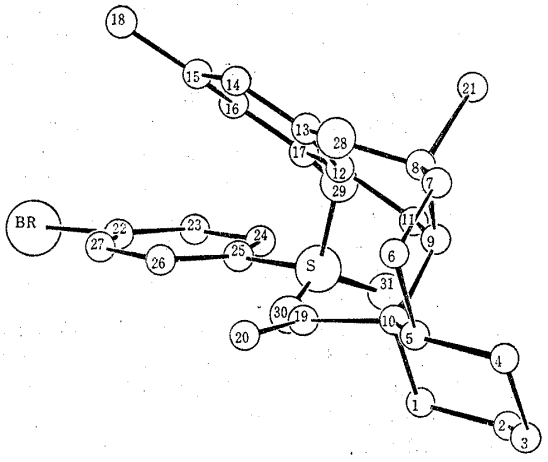

Fig. 3

Experimental

Melting points are uncorrected. Infrared (IR) spectra were determined on a Perkin-Elmer Model 221 or Perkin-Elmer Infracord, ultraviolet (UV) spectra on a Beckman Model DK-2, and NMR spectra on a Varian A-60 spectrometer. Removal of solvent *in vacuo* was accomplished with a rotating flash evaporator at 20—30 mmHg and usually at 35—50°. Thin-layer chromatography (TLC) was performed on TLC-plates Silica Gel F_{254} pre-coated (E. Merck AG) and visualization of spots was effected by spraying iodine or a solution of NH_4VO_3 in 50% H_2SO_4, followed by heating. Columns for ordinary chromatography

21) Numbering of atoms is arbitrary and inconsistent with that of the formal formulation.

were prepared with Wako Gel Q-22 or Alumina II-III (E. Merck AG). The abbreviations used are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br., broad; sh., shoulder.

9-Vinyl-*cis*-decal-2-one (6)——To 640 ml of an ice-cold and stirred solution of 2.5M vinylmagnesium chloride in tetrahydrofuran, which was prepared from Mg and vinylchloride by the Rosenberg's procedure,[12] was added dropwise a solution of 174.2 g (1.16 mole) of $\Delta^{1(9)}$-octal-2-one (**5**) and 12.5 g of tetrakis[iodo(tri-*n*-butylphosphine)copper(I)][13] in 350 ml of tetrahydrofuran over a period of 2.5 hr and the resulting dark violet mixture was further stirred for 30 min at room temperature. The mixture was poured into ice-cold aqueous HCl and extracted with dichloromethane several times. The combined extracts were washed with H_2O, dried and evaporated, leaving a colored syrup which was distilled to give 146.1 g (71.6%) of **6**, $bp_{2.5-3.5}$ 98—104°, as a colorless syrup. IR $\nu_{max}^{liq.}$ cm^{-1}: 1716, 1642, 998, 918. NMR ($CDCl_3$) δ ppm: 2.23 (1H, d, J=14.5 Hz), 2.58 (1H, d, J=14.5 Hz), 4.8—5.2 (2H, m), 5.4—6.0 (1H, m).

The syrup of **6** thus obtained formed 2,4-dinitrophenylhydrazone which was recrystallized from AcOEt–MeOH to colored needles of mp 87.5—89°. IR ν_{max}^{Nujol} cm^{-1}: 3300, 3160, 1625, 1589, 1340, 997, 923. NMR ($CDCl_3$) δ ppm: 4.8—5.4 (2H, m), 5.6—6.2 (1H, m), 8.10 (1H, d, J=10.5 Hz), 8.30 (1H, dd, J=10.5, 4 Hz), 9.11 (1H, d, J=4 Hz), 11.27 (1H, br. s). *Anal.* Calcd. for $C_{18}H_{22}O_4N_4$: C, 60.32; H, 6.19; N, 15.63. Found: C, 60.44; H, 6.06; N, 15.77.

3-(2,6-Dimethoxy-4-methylbenzylidene)-9-vinyl-*cis*-decal-2-one (8)——To a solution prepared by dissolving 10 mg of potassium in 10 ml of *t*-BuOH was added a solution of 53 mg of **6** in 1 ml of *t*-BuOH and successively a solution of 51 mg of **7** in 1 ml of *t*-BuOH at room temperature. After stirring at room temperature for 3 hr, the mixture was diluted with H_2O and extracted twice with dichloromethane. The extract was dried and evaporated to give 112 mg of syrup which was chromatographed over 3 g of silica gel. Elution with hexane–dichloromethane (2:1.5, v/v) and removal of the solvent gave 80 mg of **8** as a syrup. IR $\nu_{max}^{liq.}$ cm^{-1}: 1687, 1615, 1579, 1129, 968, 910. NMR ($CDCl_3$) δ ppm: 2.35 (1H, d, J=17.5 Hz), 2.38 (3H, s), 2.62 (1H, d, J=17.5 Hz), 3.75 (6H, s), 4.8—5.2 (2H, m), 5.5—6.1 (1H, m), 6.36 (2H, s), 7.2—7.3 (1H, m). Elementary analysis of **8** did not furnish a satisfactory data. *Anal.* Calcd. for $C_{22}H_{28}O_3$: C, 77.61; H, 9.15. Found: C, 77.11; H, 8.33.

3-*n*-Butylthiomethylene-9-vinyl-*cis*-decal-2-one (10)——To an ice-cold and stirred suspension of NaH in 400 ml of benzene, which was prepared from 2.9 g of 50% NaH dispersion by washing with hexane, was added dropwise 0.5 ml of MeOH and, successively, 7.1 g of **6** and 12.4 g of ethyl formate under N_2 atmosphere and the mixture was stood overnight at room temperature. The mixture containing some precipitate was carefully poured into ice water and the benzene layer was collected and washed with 2% aqueous KOH. The combined aqueous layer and washings was further washed with benzene, then acidified with dil. HCl and extracted twice with dichloromethane. The extract was washed with aqueous NaCl, dried and evaporated, giving 7.25 g of an α-hydroxymethylene ketone as a faint yellow syrup whose TLC chromatogram revealed a single spot.

A solutjion of 7.25 g of the hydroxymethylene ketone thus obtained, 3.92 g of *n*-BuSH and 14 mg of TsOH in 50 ml of benzene was refluxed for 6 hr under N_2 atmosphere. The reaction mixture was cooled and washed with 5% aqueous $NaHCO_3$ and dried. Evaporation of the solvent left 10.3 g of a syrup which was distilled to give 7.3 g (74%) of **10**, bp_3 186—190°. IR $\nu_{max}^{liq.}$ cm^{-1}: 1668, 1545, 1226, 995, 912. NMR ($CDCl_3$) δ ppm: 2.30 (1H, d, J=18 Hz), 2.72 (1H, d, J=18 Hz), 4.75—5.15 (2H, m), 5.6—6.1 (1H, m), 7.55 (1H, q, J=1.5, 2.5 Hz). UV λ_{max}^{EtOH} 312.5 mμ (ε 16900). *Anal.* Calcd. for $C_{17}H_{26}OS$: C, 73.32; H, 9.41. Found: C, 73.03; H, 9.65.

3-*n*-Butylthiomethylene-1-methylene-9-vinyl-*cis*-decal-2-one (11)——After washing with hexane, 132 mg of 50% NaH dispersion was dissolved in 1.5 ml of dimethylsulfoxide. The mixture was warmed for 1 hr at 70° and diluted with 1 ml of tetrahydrofuran. To the ice-cold solutuon thus obtained was added dropwise a solution of 690 mg of **10** in 1.5 ml of tetrahydrofuran with stirring and the mixture was further stirred for 10 min. Then, 110 mg of paraformaldehyde was added in one portion and the mixture was stirred for 10 min with cooling. The mixture was poured into ice water and extracted with benzene. The extract was washed with H_2O, dried and evaporated, giving 540 mg of **11** as a syrup whose TLC chromatogram revealed a single spot. The sample did not give a satisfactory data of elementary analysis and, on standing in air, was converted into a colored gum. IR $\nu_{max}^{liq.}$ cm^{-1}: 1561, 1634, 1597, 1545, 992, 917. NMR ($CDCl_3$) δ ppm: 4.80 (1H, dd, J=17, 2 Hz), 4.99 (1H, dd, J=11, 2 Hz), 5.49 (1H, d, J=1.5 Hz), 5.85 (1H, dd, J=17, 11 Hz), 6.75 (1H, d, J=1.5 Hz), 7.73 (1H, q, J=1.5, 2.5 Hz). UV λ_{max}^{EtOH} mμ (ε): 264, 340 (8400, 28900.)

3-*n*-Butylthiomethylene-1-(2,6-dimethoxy-4-methylbenzyl-9-vinyl-*cis*-deca-2-one (13)——To a solution of 611 mg of orcinol dimethylether in 13 ml of tetrahydrofuran was added 2.7 ml of 1.5M *n*-BuLi solution in hexane with stirring and the mixture was stood for 5 min at room temperature. To the resulting mixture containing a suspension of precipitates was added dropwise a solutuion of 736 mg of **11** in 4 ml of tetrahydrofuran at −45——50° with stirring and thus, the precipitates dissolved gradually into the solution. The resulting red-colored mixture was further stirred with cooling for 30 min and poured into ice water and then extracted with $CHCl_3$. The extract was dried and evaporated, leaving 1.468 g of a syrup which was dissolved in 20 ml of $CHCl_3$. After addition of 500 mg of silica gel, the mixture was refluxed for 1 hr, filtered and evaporated. The residue (1.501 g) thus obtained was chromatographed over 25 g of silica gel. Fractions eluted with hexane–$CHCl_3$ (4:1, v/v) recovered 290 mg of the unchanged orcinol dimethylether.

Further elution with hexane–$CHCl_3$ (1:1, v/v) and evaporation of the solvent gave 923 mg (83%) of an isomeric mixture of **13** whose TLC chromatogram exhibited the presence of two isomeric components. Without purification, this crude product was transfered to the next reaction.

In another run, the crude product (1.56 g) was chromatographed over 20 g of silica gel and eluted with hexane containing a gradient amount of $CHCl_3$. After removal of the solvent from fractions, the fast running fractions afforded 268 mg of one isomer as syrup. IR $\nu_{max}^{liq.}$ cm^{-1}: 1672, 1610, 1586, 1552, 1119, 967, 908. NMR ($CDCl_3$) δ ppm: 2.30 (3H, s), 3.78 (6H, s), 4.98 (1H, dd, J=16.5, 2 Hz), 5.10 (1H, dd, J=11.5, 2 Hz), 5.72 (1H, dd, J=16.5, 11.5 Hz), 6.32 (2H, s), 7.28 (1H, t, J=2 Hz).

After collecting 188 mg of the isomeric mixture of **13** from the successive fractions, the fractions gave 226 mg of a crystalline isomer which was recrystallized from hexane to give prisms of mp 82—84°. IR ν_{max}^{Nujol} cm^{-1}: 1662, 1604, 1591, 1120, 975, 920. NMR ($CDCl_3$) δ ppm: 2.27 (3H, s), 3.68 (6H, s), 5.09 (1H, dd, J=18, 2 Hz), 5.25 (1H, dd, J=11, 2 Hz), 5.86 (1H, dd, J=18, 11 Hz), 6.27 (2H, s), 7.33 (1H, t, J=2 Hz). *Anal.* Calcd. for $C_{27}H_{38}O_3S$: C, 73.27; H, 8.65. Found: C, 73.43; H, 8.88.

6-*n*-Butylthiomethylene-9-methyl-12-bα-vinyl-12b,1,2,3,4,4aα,5,6-octahydro-12*H*-benzo[*a*]xanthen-11-one(14)——A mixture of 110 mg of **11**, 70 mg of orcinol, 10 mg of TsOH, and 1.5 ml of dichloromethane was allowed to stand overnight at room temperature with stirring. Then, the mixture was poured into dil. $NaHCO_3$ and the organic layer collected was dried and evaporated, leaving 145 mg of a syrup which was chromatographed over 6 g of silica gel. Elution with hexane-benzene (1:9, v/v) and evaporation of the solvent gave 80 mg of **14** as a thick syrup. IR $\nu_{max}^{liq.}$ cm^{-1}: 3380, 1652, 1624, 1598. UV λ_{max}^{EtOH} 284 mμ. NMR ($CDCl_3$) δ ppm: 0.93 (3H, m), 2.13 (3H, s), 3.06 (2H, s), 4.7—5.2 (2H, m), 5.12 (1H, br., OH), 5.67 (1H, m), 6.38 (2H, s), 6.58 (1H, br. s). *Anal.* Calcd. for $C_{25}H_{32}O_2S$: C, 75.71; H, 8.13. Found: C, 75.28; H, 8.02.

1-(2,6-Dimethoxy-4-methylbenzyl)-9-vinyl-*cis*-decal-2-one (15)——A mixture of 5.33 g of the epimeric mixture of **13**, 12 ml of 25% aqueous KOH, and 21 ml of diethyleneglycol was refluxed at 150—160° (bath temp.) for 30 hr under N_2 atmosphere. The cooled mixture was diluted with benzene and washed with H_2O. After drying, the organic layer was evaporated to leave 3.63 g of a crystalline mass which was recrystallized from hexane, giving 2.37 g of **15** as prisms of mp 143—144°. IR ν_{max}^{Nujol} cm^{-1}: 1711, 1611, 1589, 1245, 1122, 967, 902, 809. NMR ($CDCl_3$) δ ppm: 2.29 (3H, s), 3.74 (6H, s), 5.10 (1H, dd, J=17.5, 2 Hz), 5.25 (1H, dd, J=11, 2 Hz), 5.86 (1H, dd, J=17.5, 11 Hz), 6.31 (2H, s). *Anal.* Calcd. for $C_{22}H_{30}O_3$: C, 77.15; H, 8.83. Found: C, 77.02; H, 8.83.

The mother liquor left by recrystallization of **15** was collected and evaporated. A part of the residue (630 mg) was chromatographed over 18 g of alumina. Fractions eluted with hexane–$CHCl_3$ (2:1, v/v) were evaporated to give 322 mg of crystals which was recrystallized from hexane, giving 32 mg of a second crop of **15**. The recrystallization mother liquor was evaporated and chromatographed again over 18 g of alumina. Elution with hexane–$CHCl_3$ (1:1, v/v), evaporation of the solvent and recrystallization of the residue (82 mg) afforded 17 mg of an isomeric compound as mp 79—80°, as prisms. IR ν_{max}^{Nujol} cm^{-1}: 1719, 1607, 1589, 1193, 1124, 968, 801. NMR ($CDCl_3$) δ ppm: 2.28 (3H, s), 3.77 (6H, s), 5.03 (1H, dd, J=17, 2 Hz) 5.17 (1H, dd, J=11, 2 Hz), 5.77 (1H, dd, J=17, 11 Hz), 6.30 (2H, s). *Anal.* Calcd. for $C_{22}H_{30}O_3$: C, 77.15; H, 8.83. Found: C, 76.89; H, 8.86.

1-(2,6-Dimethoxy-4-methylbenzyl)-2-methylene-9-vinyl-*cis*-decalin (18)——To a cooled and stirred NaH solution prepared by dissolving 115 mg (2.4 mmole) of 50% NaH mineral oil suspension (after washing twice with hexane) in 1.4 ml of dimethyl sulfoxide was added dropwise a solutuion of 821 mg (2.3 mmole) of triphenylmethylphosphonium bromide in 2.2 ml of dimethyl sulfoxide over a period of 5 min under N_2 atmosphere and the mixture was further stirred for 15 min at room temperature. To the resulting solution was added a solution of 383 mg (1.12 mmole) of **15** in 2.5 ml of tetrahydrofuran during 10 min and the mixture was stirred for 1 hr at room temperature. Then the mixture was poured into ice-water and extracted twice with hexane. The extract was washed with H_2O and dried and evaporated. The residue was recrystallized from EtOH, affording 305 mg of **18** as prisms, mp 114—115.5°. The mother liquor was collected and evaporated and the residue was chromatographed over 5 g of silica gel. Elutuion with benzene–hexane (9:1, v/v) evaporation of the solvent and recrystallization of the residue afforded 26 mg of the second crop of **18**, mp 113—114.5°. The yield of **18** was 331 mg (87%). IR ν_{max}^{Nujol} cm^{-1}: 1647, 1606, 1588, 915, 885. NMR ($CDCl_3$) δ ppm: 2.28 (3H, s), 2.7—3.0 (2H, m), 3.70 (6H, s), 4.10 (1H, d, J=3 Hz), 4.44 (1H, dd, J=3, 1.5 Hz), 4.9—5.45 (2H, m), 5.88 (1H, dd, J=17.5, 11.5 Hz), 6.28 (2H, s). *Anal.* Calcd. for $C_{23}H_{32}O_2$: C, 81.13; H, 9.47. Found: C, 80.97; H, 9.38.

1-(2-Hydroxy-6-methoxy-4-methylbenzyl)-2-methylene-9-vinyl-*cis*-decalin (19)——A solution of 207 mg of **18** and 0.5 g of EtSNa in 5 ml of dimethylformamide was refluxed for 1 hr under N_2 atmosphere. The cooled mixture was diluted with H_2O and extracted with benzene. The extract was washed with H_2O, dried and evaporated, leaving 261 mg of a syrup which was chromatographed over 6 g of silica gel. Fractions eluted with benzene–hexane (1:1, v/v) were evaporated to give 7 mg of unchanged **18** containing some byproducts. Fractions eluted with benzene–hexane (7:3, v/v) gave 186 mg (93%) of **19** which crystallized on standing. Recrystallization from petroleum ether gave prisms, mp 75.5—76.5°. IR ν_{max}^{Nujol} cm^{-1}: 3520, 1648, 1623, 1593, 902. NMR ($CDCl_3$) δ ppm: 2.22 (3H, s), 3.68 (3H, s), 4.22 (1H, m), 4.54 (1H, t, J=2 Hz), 4.67 (1H, s, OH), 4.9—5.5 (2H, m), 6.01 (1H, dd, J=17.5, 11.5 Hz), 6.22 (2H, s). *Anal.* Calcd. for $C_{22}H_{30}O_2C$, 80.93; H, 9.26. Found: C, 80.90; H, 9.23.

6aβ,9-Dimethyl-11-methoxy-12bα-vinyl-1,2,3,4,4aα,5,6,6a,12b,12aβ-decahydro-12*H*-benzo[*a*]xanthene (20a)——A mixture of 132 mg of **19**, 3 ml of benzene, and 3 mg of TsOH was refluxed for 1 hr and the cooled mixture was washed with aqueous $NaHCO_3$. The collected benzene layer was dried and evaporated, giving 115 mg of a pale yellow syrup which was chromatographed over 6 g of silica gel. Fractions eluted with benzene–hexane (1:1, v/v) were evaporated to give 118 mg (89%) of **20a** as a colorless syrup. The product was found to be contaminated with a small amount of by products which was shown by TLC chromatography. IR $\nu_{max}^{liq.}$ cm^{-1}: 1623, 1590, 1110, 999, 905, 810. NMR ($CDCl_3$) δ ppm: 1.20 (3H, s), 2.26 (3H, s), 3.77 (3H, s), 4.4—5.0 (2H, m), 6.13 (1H, dd, J=17.5, 11.5 Hz), 6.23 (2H, br. s). *Anal.* Calcd. for $C_{22}H_{30}O_2$: C, 80.93; H, 9.26. Found: C, 81.32; H, 9.50.

The NMR spectrum of **20a** exhibited some singlet absorptions at 1.17 and 3.80 probably due to the contamination of a *trans* isomer (**21**) with 1/5 intensity in absorption area as compared to that of **20a**.

6aβ,9-Dimethyl-12bα-vinyl-1,2,3,4,4aα,5,6,6a,12aβ,12b-decahydro-12*H*-benzo[a]xanthen-11-ol (20b)——A solution of 1.031 g of **20a** and 2.0 g of NaSEt in 10 ml of dimethylformamide was refluxed for 1 hr under N_2 atmosphere and the cooled mixture was diluted with H_2O and extracted with benzene. The extract was washed with H_2O, dried and evaporated, leaving 1.055 g of a syrup which was chromatographed over 16 g of silica gel. Elution with benzene–hexane (1:1, v/v) and evaporation of the solvent afforded 930 mg of a syrup which crystallized on standing. Recrystallization from hexane gave 462 mg of **20b** as needles, mp 138.5—140.5°. IR ν_{max}^{Nujol} cm^{-1}: 3370, 1625, 1586, 1050, 992, 908, 819. NMR ($CDCl_3$) δ ppm: 1.23 (3H, s), 2.20 (3H, s), 4.58 (1H, dd, J=2, 11 Hz), 4.75 (disappeared with addition of D_2O), 4.80 (1H, dd, J=17.5, 2 Hz), 6.13 (1H, s), 6.18 (1H, dd, J=17.5, 11 Hz), 6.22 (1H, s). *Anal.* Calcd. for $C_{21}H_{28}O_2$: C, 80.73; H, 9.03. Found: C, 80.69; H, 8.89.

By treatment in the usual manner, **20b** formed a brosylate (**20c**) which was recrystallized from MeOH as needles, mp 140.5—141°. IR ν_{max}^{Nujol} cm^{-1}: 1633, 1575, 1391, 1190, 972, 900, 793. NMR ($CDCl_3$) δ ppm: 1.08 (3H, s), 2.19 (3H, s), 4.48 (1H, dd, J=2, 11 Hz), 4.72 (1H, dd, J=2, 17.5 Hz), 5.95 (1H, dd, J=17.5, 11 Hz), 6.37 (1H, br. s), 650 (1H, br. s), 7.73 (4H, s). *Anal.* Calcd. for $C_{27}H_{31}O_4SBr$: C, 60.67; H, 5.84; S, 6.00. Found: C, 60.51; H, 5.97; S, 6.18.