Tetrahedron. Vol. 27, pp. 6063 to 6071. Pergamon Press 1971. Printed in Great Britain

THE ISOLATION AND STRUCTURE OF SICCANOCHROMENES

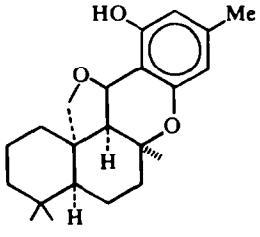
S. NOZOE and K. T. SUZUKI

Institute of Applied Microbiology, University of Tokyo, Bunkyo-ku, Tokyo, Japan

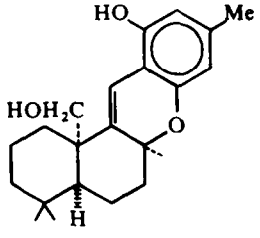
(*Received in Japan* 22 *July* 1971; *Received in the UK for publication* 18 *August* 1971)

Abstract—A number of chromene derivatives have been isolated from the cultured broth of *Helminthosporium siccans* Drechsler, some of which were considered to be the possible intermediates of the biosynthesis of an antibiotic, siccanin. The structures of these compounds were elucidated from their chemical and spectral properties.

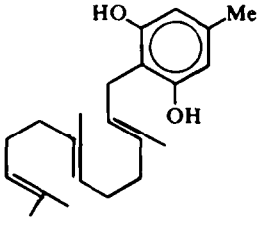
IN THE PRECEDING PAPER[1] we reported the structure and the chemistry of a new antibiotic, siccanin (I) and its congener, siccanochromene-E (II), both isolated from the cultured broth of the plant pathogenic fungus, *Helminthosporium siccans* Drechsler. Inspection of structures I and II suggests that these compounds might be derived biogenetically by the combination of sesquiterpene and orsellinate entities and can be classified as "prenyl phenols", similar to grifolin (III)[2] and tauranin (IV).[3] The sesquiterpene portion of siccanin (I) contains a drimane type carbon skeleton; however, the junction of the rings A, B, and C possesses an unusual *cis*-syn-*cis* type.



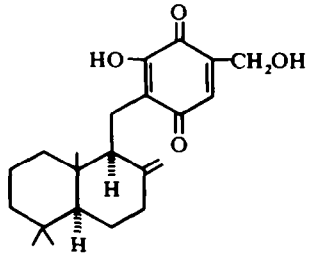
I



II



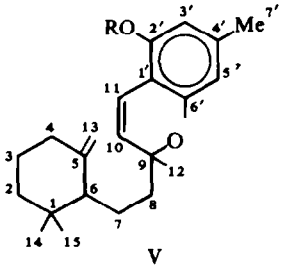
III



IV

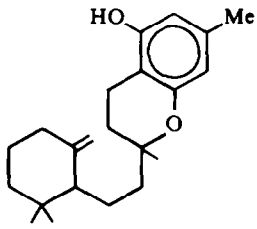
We are interested in the mechanism of cyclization of the acyclic precursors into this compound. It was found that the fermentation broth and mycelia of the above fungus contain many chromene derivatives as minor metabolites. Eight chromenes were isolated and purified: These substances were designated siccanochromene-A. -H. -B ~ -G in the order of their polarities on silica gel plates. Siccanochromene-A and -B are assumed to be possible intermediates in the biosynthesis of siccanin. Herein is described the structural elucidations and the spectral properties of these compounds.

Siccanochromene-A (Va).[4] $C_{22}H_{30}O_2$. $[\alpha]_D = +68{\cdot}8°$ (EtOH). showed a characteristic UV absorption maxima at 229·5. 278·5 and 286·5 nm (ε. 25.700. 9.320. 8.900). and IR bands at 1.630 and 1.580 cm^{-1} due to chromene chromophore. The NMR spectrum of siccanochromene-A (Va) indicated the presence of a geminal dimethyl group (0·82. 0·92). a Me group on α etheral carbon (1·26). an aromatic Me group (2·17). an exocyclic methylene group (4·71. 4·48. 2H. d. $J = 2$ Hz). protons on a disubstituted double bond conjugated with aromatic ring (6·55. 5·31. 2H. $J = 11$ Hz. AB pattern) and two aromatic protons (6·10. 5·96). The details of the NMR spectra of Va and its

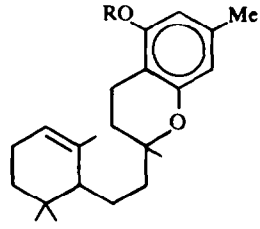


V

a: R = H
b: R = COMe

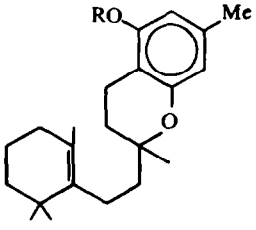


VI



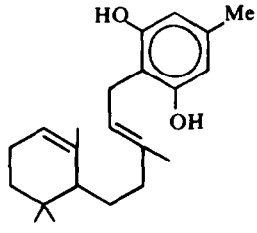
VII

a: R = H
b: R = COMe



VIII

a: R = H
b: R = COMe



IX

derivatives were summarized in Table 1. The significant diamagnetic shift (35 Hz) of the proton on the disubstituted double bond upon acetylation of the phenolic OH group of Va indicates the substitution pattern of the aromatic ring[5] as shown in V. The mass spectrum of siccanochromene-A exhibited main peaks at *m/e* 326 (M^+). 311 (M-15). 247 (M-79) and 175 (base peak). From the spectral properties mentioned above.

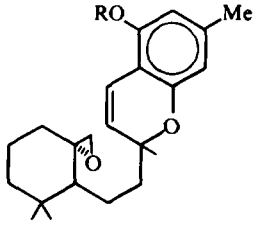
TABLE 1. NMR SPECTRA OF SICCANOCHROMENE-A AND ITS DERIVATIVES

Compounds	C_{14}-Me C_{15}-Me	C_{12}-Me	$C_{7'}$-Me	C_{13}-H	C_{10}-H	C_{11}-H	$C_{3'}$-H $C_{5'}$-H	OAc
Va	0·92 0·82 (6H. s)	1·26 (3H. s)	2·17 (3H. s)	4·48 4·71 (2H. J = 2)	5·31 (2H. AB. J = 11	6·55	5·96 6·10 (2H. s)	
Vb	0·85 0·77 (6H. s)	1·27 (3H. s)	2·16 (3H. s)	4·43 4·65 (2H. J = 2)	5·31 (2H, AB, J = 11)	6·20	6·27 6·36 (2H. s)	2·20 (3H. s)
VI	0·84 0·86 (6H. s)	1·21 (3H. s)	2·15 (3H. s)	4·77 4·46 (2H. J = 2)		2·50 (2H. t. J = 7)	5·98 6·10 (2H. s)	
VIIa	0·84 0·90 (6H. s)	1·20 (3H. s)	2·13 (3H. s)	1·62 (3H. s)		2·50 (2H. t. J = 7)	6·12 5·95 (2H. s)	
VIIIa	0·94 0·99 (6H. s)	1·25 (3H. s)	2·13 (3H. s)	1·52 (3H. s)		2·52 (2H. t. J = 7)	6·12 5·95 (2H. s)	

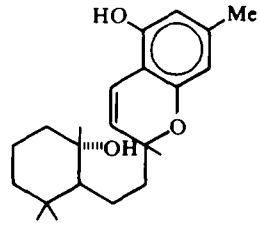
it was possible to postulate structure Va for siccanochromene-A. The structure was confirmed by chemical interrelation with a synthetically derived compound as follows. Hydrogenation of siccanochromene-A with Pd/C in EtOH afforded a dihydro derivative VI. $C_{22}H_{32}O_2$ (M^+. 328). λ_{max}: 274. 281 nm (ε. 800. 780). NMR : 2·50 (2H. t. J = 7 Hz).

Treatment of VI with $SnCl_4$ in benzene yielded the isomerized chromane derivatives VIIa and VIIIa in a ratio of 1:9. which were separated as their acetate by column chromatography over $AgNO_3$ impregnated silica gel. On the other hand. compound VIIIa was synthesized from dihydro-α-ionone *via* compound IX.[6] The identity of the naturally derived compound and the synthetic one was confirmed by a comparison of TLC. VPC as well as spectral data.

Siccanochromene-B (Xa).[4] $C_{22}H_{30}O_3$. $[\alpha]_D$ +121° (EtOH). showed the same UV spectrum as that of siccanochromene-A. The NMR spectrum of Xa exhibits signals at 2·36 and 2·53 (2H. AB q. J = 5 Hz) due to the methylene protons of the oxirane ring instead of the exocyclic methylene proton signals in Va. The remainder of the spectrum was similar to that of Va and the details are listed in Table II. The mass spectrum of Xa showed peaks at *m/e* 342 (M^+). 327 (M-15). 324 (M-18). 309 (M-33) and 175 (base peak). These spectral data suggested structure Xa for siccanochromene-B. Reduction of siccanochromene-B with LAH in THF led quantitatively to a tertiary alcohol XI. $C_{22}H_{32}O_3$. $[\alpha]_D$ +115° (EtOH). The NMR spectrum of XI showed a new signal at 1·32 (3H. s) instead of the signals due to oxirane protons. Treatment of the carbinol XI with $SOCl_2$ in pyridine gave siccanochromene-A in 80% yield. The direction of dehydration mentioned above indicated the stereochemistry of oxirane in which the C—O bond occupies an equatorial position. The synthetic episiccanochromene-B which possesses an axial OH group afforded mainly the Δ^5-isomer by the same treatment.[6]



X
a: R = H
b: R = COMe

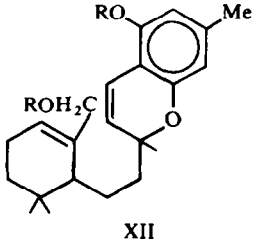


XI

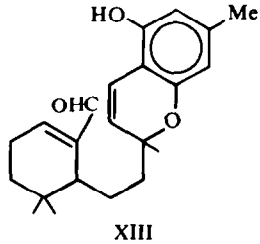
TABLE II. NMR SPECTRA OF SICCANOCHROMENE-B AND ITS DERIVATIVES

compounds	C_{14}-Me C_{15}-Me	C_{12}-Me	$C_{7'}$-Me	C_{13}-H	C_{10}-H	C_{11}-H	$C_{3'}$-H $C_{5'}$-H	-OAc
Xa	0·82 1·04 (6H. s)	1·28 (3H. s)	2·16 (3H. s)	2·36 2·53 (2H. AB. J = 5)	5·33	6·55 (2H. AB. J = 11)	5·97 6·08 (2H. s)	
Xb	0·77 0·99 (6H. s)	1·31 (3H. s)	2·21 (3H. s)	2·30 2·48 (2H. AB. J = 11)	5·41	6·34 (2H. AB. J = 11)	6·31 6·41 (2H. s)	2·26 (3H. s)
XI	0·93 0·80 (6H. s)	1·24 (3H. s)	2·14 (3H. s)	1·32 (3H. s)	5·50	6·57 (2H. AB. J = 11)	6·09 5·91 (2H. s)	

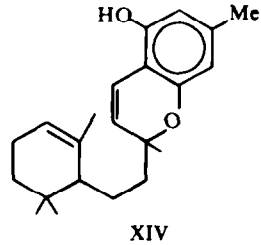
Siccanochromene-C (XIIa). $C_{22}H_{30}O_3$ (M^+. 342). showed similar UV and IR absorption spectra as those of aforementioned chromenes. The NMR spectrum of XIIa indicated the presence of an unsaturated primary alcohol (3·95. 2H. s. which changed to AB type quartet at 4·29 and 4·43. J = 12 Hz. upon acetylation) and an olefinic proton (5·54. 1H. multiplet). The details of the NMR spectra of XIIa and its derivatives are listed in Table III. The oxidation of siccanochromene-C with Jones' reagent yielded the α.β-unsaturated aldehyde XIII. $C_{22}H_{28}O_3$. which showed UV absorption maxima at 230·5. 237. 281 and 289 nm (ε. 31.100. 25.400. 8.350 and 7.930.



XII
a: R = H
b: R = COMe
c: R = Ms



XIII



XIV

respectively). IR bands at 1684 1.634 and 1.580 cm^{-1}. and NMR peaks at 9·35 (aldehydic proton) and 6·56 (an olefinic proton. 1H. t. $J = 4$ Hz). Treatment of siccanochromene-C with $MeSO_2Cl$ in pyridine afforded a dimesylate XIIc. LAH reduction XIIc in THF yielded compound XIV. This compound was identical with a sample synthesized from α-ionone.[6]

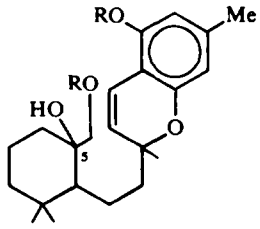
TABLE III. NMR SPECTRA OF SICCANOCHROMENE-C AND ITS DERIVATIVES

Compounds	C_{14}-Me C_{15}-Me	C_{12}-Me	$C_{7'}$-H	C_{13}-H	C_{10}-H	C_{11}-H	$C_{3'}$-H $C_{5'}$-H	C_4-H	-OAc	Ms
XIIa	0·82 0·91 (6H. s)	1·27 (3H. s)	2·09 (3H. s)	3·92 (2H. s)	5·28 (2H. AB. $J = 11$)	6·54	5·97 6·06 (2H. s)	5·54 (1H. m)		
XIIb	0·84 0·92 (6H. s)	1·31 (3H. s)	2·19 (3H. s)	4·29 4·43 (2H. AB. $J = 12$)	5·43 (2H. AB. $J = 11$)	6·26	6·31 6·41 (2H. s)	5·57 (1H. t. $J = 4$)	2·24 1·94 (6H, s)	
XIIc	0·89 0·95 (6H. s)	1·35 (3H. s)	2·26 (3H. s)	3·85 4·00 (2H. AB. $J = 12$)	5·51 (2H. AB. $J = 11$)	6·56	6·48 6·55 (2H. s)	6·55 (1H. t. $J = 4$)		2·75 3·00 (6H. s)
XIII	0·79 1·01	1·25 (3H. s)	2·13 (3H. s)	9·35 (1H. s)	5·27 (2H. AB. $J = 11$)	6·50	5·97 6·05 (2H. s)	6·56 (1H. t. $J = 4$)		
XIV	0·83 0·89	1·29 (3H. s)	2·13 (3H. s)	1·61 (3H. s)	5·23 (2H. AB. $J = 11$)	6·52	5·93 6·10 (2H. s)	5·20 (1H. t. $J = 4$)		

Siccanochromene-F (XVa). $C_{22}H_{32}O_4$. gave a diacetate which was shown to be an epimeric mixture at C-5. The IR spectrum of the diacetate still showed the absorption due to a OH group at 3.600 cm^{-1}. The spectral properties resemble those of other chromenes. One of the epimers separated in pure form XVb-A showed NMR peaks at 4·00 and 4·25 (2H. AB q. $J = 11$ Hz) due to methylene protons of the primary alcohol. The mass spectrum exhibited peaks at *m/e* 444 (M^+). 429. 426. 371 (M-73). 353 (M-91) and 217 (base peak). The NMR spectra of the free alcohol and its derivatives are listed in Table IV.

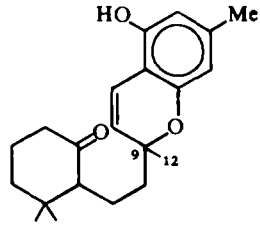
Both epimers (XVa-A and -B) of siccanochromene-F yielded the same norketone XVI. $C_{21}H_{28}O_3$ (M^+. 328). IR band at 1710 cm^{-1}. upon treatment with HIO_4 in THF. The norketone XVI was proved to be identical in all respects with a specimen synthesized from mesityl oxide and diethyl malonate.[6]

Three other chromenes. siccanochromene-D (XVIIa). $C_{22}H_{32}O_3$ (M^+. 344). siccanochromene-G (XVIIIa). $C_{22}H_{30}O_4$ (M^+. 358). and siccanochromene-H (XIXa). $C_{22}H_{30}O_3$ (M^+. 342) were isolated. and found to occur as epimeric mixtures at C-5. The NMR spectra are listed in Table V. Siccanochromene-G. -D and -H are chemically interrelated by oxidation and reduction. The saturated aldehyde function in siccanochromene-H (XIXa) might be formed by isomerization of the oxirane ring in siccanochromene-B (Xa) during isolation and purification. Compounds XVIIa and XVIIIa are also considered to be artifacts. generated by a Canizzaro type reaction of XIXa.



XV

a: R = H
b: R = COMe



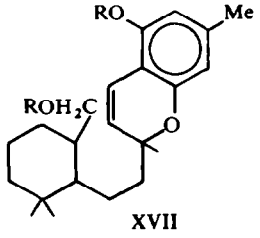
XVI

TABLE IV. NMR SPECTRA OF SICCANOCHROMENE-F AND ITS DERIVATIVES

Compounds	C_{14}-Me C_{15}-Me	C_{12}-Me	$C_{7'}$-Me	C_{13}-H	C_{10}-H	C_{11}-H	$C_{3'}$-H $C_{5'}$-H	OAc
XVa-A*	0·75 0·97 (6H. s)	1·34 (3H. s)	2·17 (3H. s)	3·56 (2H. s)	5·47 (2H. ABq. J = 11)	6·64	6·13 6·23 (2H. s)	
XVb-A	0·81 0·99 (6H. s)	1·34 (3H. s)	2·25 or 2·28 (3H. s)	4·00 4·25 (2H. ABq. J = 11)	5·55 (2H. ABq. J = 11)	6·33	6·42 6·52 (2H. s)	2·07 2·25 or 2·28 (6H. s)
XVa-B*	0·88 0·97 (6H. s)	1·34 (3H. s)	2·15 (3H. s)	3·22 3·47 (2H. ABq. J = 11)	5·43 (2H. ABq. J = 11)	6·61	6·11 6·22 (2H. s)	
XVb-B	0·88 0·95 (6H. s)	1·37 (3H. s)	2·24 or 2·27 (3H. s)	3·76 3·89 (2H. ABq. J = 11)	5·53 (2H. ABq. J = 11)	6·34	6·39 6·52 (2H. s)	2·04 2·24 or 2·27 (6H. s)
XVI	0·75 1·00 (6H. s)	1·27 (3H. s)	2·16 (3H. s)		5·45 (2H. ABq. J = 11)	6·64	6·03 6·08 (2H. s)	

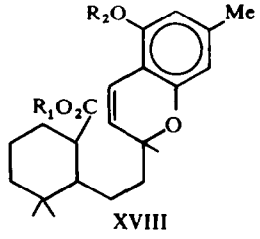
* measured in $CDCl_3$ solution

Some of the chromenes reported herein exhibit anti-bacterial activity against *Staphyllococcus aureus.*



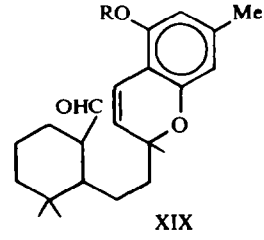
XVII

a: R = H
b: R = COMe



XVIII

a: R_1 = H, R_2 = H
b: R_1 = Me, R_2 = H
c: R_1 = Me, R_2 = COMe



XIX

a: R = H
b: R = COMe

TABLE V. NMR SPECTRA OF SICCANOCHROMENE-D. -G. -H AND THEIR DERIVATIVES

Compounds	C_{14}-Me C_{15}-Me	C_{12}-Me	$C_{7'}$-Me	C_{10}-H	C_{11}-H	C_{13}-H or OMe	$C_{3'}$-H $C_{5'}$-H	-OCOCH$_3$
XVIIa	0·75. 0·87 (0·84. 0·91)* (6H. s)	1·27 (3H. s)	2·10 (3H. s)	5·25 (2H. ABq. J = 11)	6·49	3·20 ~ 3·65 (2H. m)	5·92 6·03 (2H. s)	
XVIIb	0·78. 0·91 (0·88. 0·96)* (6H. s)	1·34 (3H. s)	2·20 (3H. s)	5·40 (2H. ABq. J = 11)	6·22	3·70. 4·06 (2H. AB of ABX) (3·60. 4·10. 2H. m)*	6·26 6·23 (2H. s)	1·92(1·82)* 2·20 or 2·24 (6H. s)
XVIIIb	0·77. 0·94 (0·91. 0·99)* (6H. s)	1·26 (3H. s)	2·28 (3H, 2)	5·26 (5·29. 6·58)* (2H. ABq. J = 11)	6·58	3·53 (3·51)* (3H. s)	6·02 6·08 (2H. s)	
XVIIIc	0·78. 0·94 (0·90. 0·98)* (6H. s)	1·30 (3H. s)	2·20 or 2·25 (3H. s)	5·35 (5·40. 6·23)* (2H. ABq. J = 11)	6·23	3·46 (3·40)* (3H. s)	6·31. 6·41 (2H. s)	2·20 or 2·25 (3H. s)
XIXa	0·78. 0·94 (0·86. 0·97)* (6H. s)	1·27 (1·30)* (3H. s)	2·14 (3H. s)	5·21 (5·26. 6·46)* (2H. ABq. J = 11)	6·46	9·50 (1H, d, J = 4) (9·78, 1H, s)*	5·94 6·02 (2H. s)	

* δ values in parentheses are for the epimer.

EXPERIMENTAL

All m.ps are uncorrected. UV spectra were determined on a Shimadzu SV-50 recording spectrometer in EtOH. All chromenes mentioned in text showed absorption maxima at 229–231. 279–282. and 287–291 nm (ε. 26.000. 9.300. 8.900). IR spectra were determined on a JASCO IR-S or DS-301 Infrared spectrometer in $CHCl_3$. NMR spectra were determined in CCl_4 unless otherwise mentioned on a Jeol 100 M spectrometer. The signals are reported in δ values from TMS as internal standard. To some solutions. D_2O was added to check on exchangeable hydrogens. Silica gel plates (Kieselgel G nach Stahl. Merck) were developed with 0 ~ 50% acetone in C_6H_6 or 0 ~ 10% MeOH in $CHCl_3$ plus 1 ~ 2% AcOH. depending on the polarity of compounds. All compounds were visualized with a diazotized benzidine salt solution in spray and with a conc H_2SO_4 in spray plus heating. Typical R_f values are shown as follows: system A (C_6H_6 100%). siccanochromene-A (0·46). siccanin (0·80). siccanochromene-H (0·10). system B (C_6H_6: acetone = 10:1). siccanochromene-H (0·81). siccanin (0·80). siccanochromene-B (0·75). siccanochromene-G methyl ester (0·75). siccanochromene-G (0·37). −D (0·37). −E (0·29). and −F (0·09). Silica gel (Wakogel C-200 for Column Chromatography. Wako) and Florisil (100–200 mesh. Wako) were used in ratio of 10–50:1 of applied material. and columns were packed by the most nonpolar solvents used on elution and developed. Gas chromatographic analyses were determined on a Shimadzu 4APTF using 1·5% OV-17 and 1·0% XE-60 on chromosorb W 100/200. 150 cm × 4 mm. Mass spectra were determined on a Hitachi Mass Spectrometer RMU-6D at 70 eV.

Fermentation of H.siccans. *H. siccans* was inoculated in 500 ml Sakaguchi flask containing 100 ml culture (consisted of 3% polypeptone. 4% glucose. 0·5% $KHSO_4$ and 0·25% $MgSO_4$) and fermented for 5 days at 26–27°. 120 rpm. *H. siccans* needed about 60 hr for lag time and reached a stationary state in about 120 hrs after inoculation. Siccanochromene-A. -B. siccanin. presiccanochromenic acid[7] and siccanochromenic acid[7] were found at the end of the lag phase in the broth and mycelia. Ergosterol was also found in the mycelia at that time. At the end of the log phase siccanochromene-C appeared. Siccanochromene-E and -F existed as trace metabolites. Hydroxylated derivatives of siccanin were found after prolonged fermentation.

Extraction of mycelia and broth. The mycelia were separated from the fermented broth by filtration and extracted with hot acetone two or three times and then most of the acetone was evaporated *in vacuo* and combined with the filtrated broth. The combined filtrates were extracted with ether or EtOAc two or three times. dryed (Na_2SO_4) and evaporated to dryness.

Fractionation of crude metabolites. The crude metabolites were directly or after hydrolysis (in 5% KOH–EtOH at room temp overnight in usual manner) fractionated on silica gel columns and/or florisil columns repeatedly. Changing eluting solvents from 0–100% ether in C_6H_6 on silica gel columns, siccanochromene-A. -H. siccanin. siccanochromene-B. -C. -D. -E. -F and -G were eluted out successively and each fraction was further purified by changing solvent systems (to 0–100% MeOH in $CHCl_3$ and/or packing material to florisil) until no impurity was detected by TLC. GC. NMR and/or MS. The purity was also confirmed on acetylation.

Acetylation and deacetylation. All compounds were acetylated by dissolving in Ac_2O pyridine and standing overnight at room temp. Usual work-up afforded a quantitative yield of acetates. Deacetylation was carried out by saponification in 5% KOH–EtOH.

Hydrogenation of siccanochromene-A (Va). Siccanochromene-A (15 mg) and 5% Pd/C (15 mg) were dissolved in abs EtOH (2 ml) and shaken under normal pressure until one equivalent mole of hydrogen was taken up. The catalyst was filtered off and the solvent evaporated under red. press. to afford gas-chromatographically pure chromane VI.

Isomerization of chromane VI. One drop of anhyd $SnCl_4$ was added to the dry C_6H_6 solution (1·5 ml) of VI (50 mg) and stirred for 20 min at room temp. Then the solution was washed with water three times, dried (Na_2SO_4), and evaporated to dryness under red. press. The same treatment of IX afforded an essentially identical mixture of VIIa and VIIIa in a ratio of 1 : 9.

Transformation of siccanochromene-5 (Xa) *to siccanochromene-A* (Va). To the dry solution THF (1 ml) of Xa (22 mg). LAH (2 mg) was added and refluxed until no more Xa was detected on TLC. The mixture was worked up in the usual manner to give pure XI (19 mg). XI (15 mg) was dehydrated by $SOCl_2$ (one drop) in dry pyridine (0·3 ml) at 0° with stirring. Excess $SOCl_2$ was destroyed by adding ice and the products extracted with ether. The organic layer was washed with water and dried (Na_2SO_4). Removal of solvent under red. press. yielded an oil. On silica gel column chromatography with n-hexane-C_6H_6 siccanochromene-A was obtained as pure oil (12 mg).

Oxidation of siccanochromene-C (XIIa). XIIa (20 mg) was dissolved in acetone (1 ml) and one drop of 8 N Jones' reagent added with stirring at room temp. The mixture was extracted with ether after addition of ice. The extracted oil was pure on TLC but easily decomposed on silica gel column and also decomposed on acetylation.

Transformation of siccanochromene-C (XIIa) to XIV. To the pyridine solution (1 ml) of XIIa (120 mg) $MeSO_2Cl$ (one drop) was added and allowed to stand for 4 hr at 0°. After adding ice to the mixture the products were extracted with ether. washed with water. dried (Na_2SO_4). and evaporated to dryness. The products (90 mg) consisted of a mixture of dimesylate XIIc (*m/e*. 498 (M^+). 483 (M-15). 402 (M-96). and 253 (base peak)) and monochloro-monomesylate (*m/e*. 437 and 439 (M^+). 424 and 422 (M-15). 402 (M-35). and 253 (base peak)). The mixture was reduced without separation by LAH in THF. Crude product (40 mg) was obtained by usual work-up. Purification on silical gel afforded pure XIV (22 mg) and its identity with the synthesized one was confirmed in all respects except optical activity.

Ketone XVI. Each epimer of siccanochromene-F (XVa) (10 mg) was dissolved in THF (1 ml) and equimolecular amount of HIO_4 (6·5 mg) was added with stirring. Usual work-up and purification on silica gel column (n-hexane-benzene) afforded pure XVI (6 mg). The identities of each ketone and with a independently synthesized one were confirmed on TLC. IR. NMR and MS.

Acknowledgement—The authors are grateful to Professor Emeritus K. Tsuda and Professor S. Okuda University of Tokyo, for their encouragements and interests in this work. Thanks are also due to Sankyo Co., Ltd. for giving us the strain of *H. siccans* and the fermented materials.

REFERENCES

[1] K. Hirai. K. T. Suzuki and S. Nozoe. *Tetrahedron* **27**, 6057 (1971)
[2] T. Goto. H. Kakisawa and Y. Hirata. *Ibid.* **19**. 2079 (1963)
[3] K. Kakisawa. K. Nakanishi and H. Nishikawa. *Chem. Pharm. Bull. Tokyo* **12**, 796 (1964)
[4] S. Nozoe. K. T. Suzuki and S. Okuda. *Tetrahedron Letters* 3643 (1968)

[5] A. Arnone, G. Cardillo, L. Merlini and R. Mondelli, *Ibid.* 4021 (1967)
[6] S. Nozoe and K. Hirai, *Ibid.* 3017 (1969)
[7] S. Nozoe and K. T. Suzuki, *Ibid.* 2457 (1969)