Tetrahedron. Vol. 27, pp. 6073 to 6081. Pergamon Press 1971. Printed in Great Britain

THE SYNTHESES OF SICCANOCHROMENE-A AND THE RELATED TRIPRENYL-PHENOLS[1]

S. NOZOE and K. HIRAI*

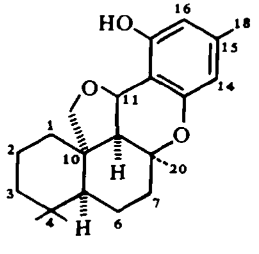
Institute of Applied Microbiology, University of Tokyo, Bunkyo-ku, Tokyo, Japan

(*Received in Japan* 17 *August* 1971; *Received in the UK* 25 *August* 1971)

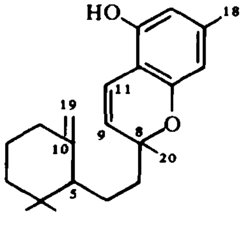
Abstract—Siccanochromene-A (II), episiccanochromene-B (XI) were synthesized from orcinol and a corresponding α,β-unsaturated aldehyde. Dihydro-γ-ionone which was used for the synthesis of presiccanochromene-A (XVII) was prepared photochemically from dihydro-α-ionone.

SICCANOCHROMENE-A (II) and siccanochromene-B (III)[2] isolated from a plant pathogenic fungus. *Helminthosporium siccans* Drechsler as minor metabolites were shown to be possible intermediates in the biosynthesis of an antibiotic. siccanin (I). The present paper describes the syntheses of the siccanochromene derivatives.

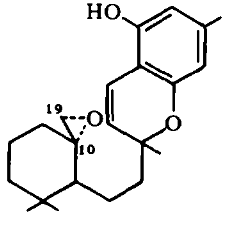
The keto-ester IV. prepared from mesityl oxide and diethyl malonate by a known method[3] was converted into the ethylene ketal V. which was then treated with methylsulfinyl carbanion[4] in DMSO to afford β-ketosulfoxide VI. The ketosulfoxide VI. ν_{max} 1.710 cm^{-1}. NMR δ 2·56 (CO–C$\underline{H}$—S—) was successively treated with aluminium amalgam in aqueous THF to give the methyl ketone VII in 80% yield from the ketal



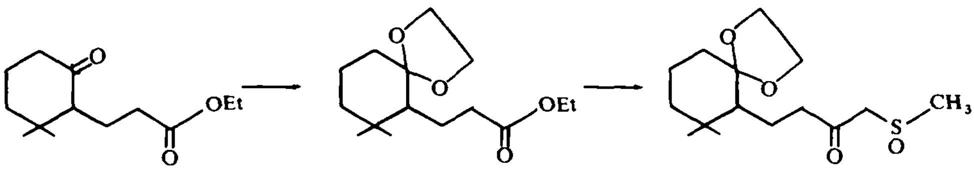
siccanin I



siccanochromene-A II



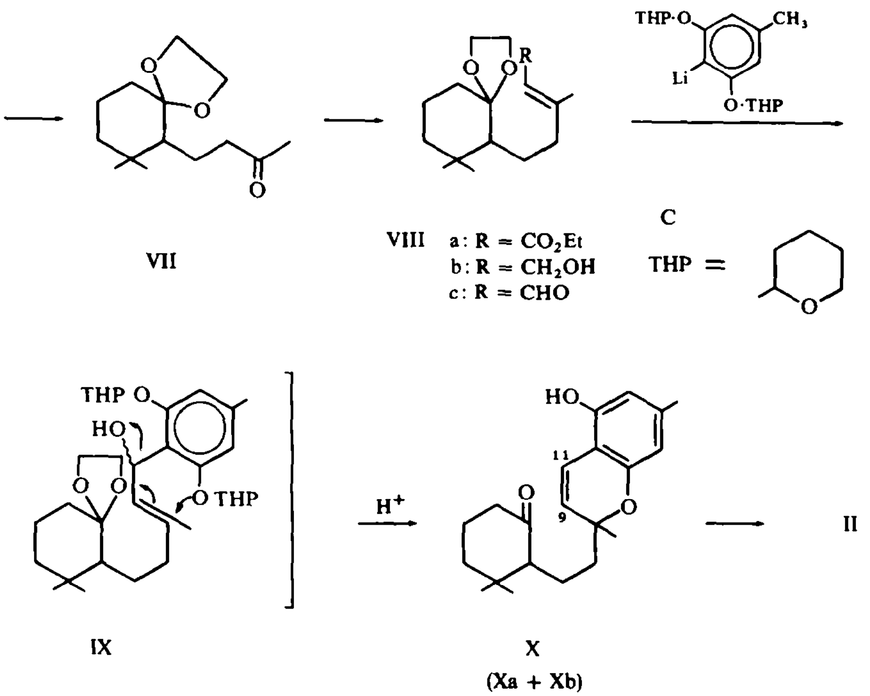
siccanochromene-B III



IV V VI

---

* Present address: Central Research Laboratories, Sankyo Co., Ltd., Hiromachi, Shinagawa-ku, Tokyo. Japan.



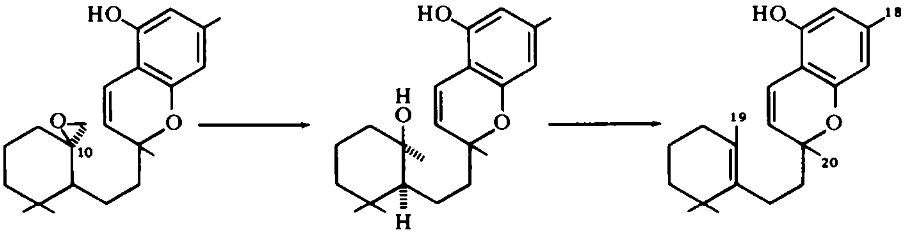
V. The resulting keto-ester was condensed with ethyl diethylphosphonoacetate in the presence of NaH in DMSO[5] to afford the α.β-unsaturated ester VIIIa as a mixture of *cis*- and *trans*- geometrical isomers in a ratio *ca.* 1 :3.

The mixture was separated into the *cis*- and *trans*-isomers by means of silica gel column chromatography. The *cis*-isomer shows the β-Me signal at δ 1·84 and the *trans*-isomer at δ 2·10. The unsaturated ester VIIIa was converted into the corresponding aldehyde VIIIc by LAH reduction followed by oxidation with active MnO_2. The aldehyde VIIIc showed a UV absorption maximum at 238 nm. IR bands at 2,730, 1,680 and 1,630 cm^{-1} and NMR signals at δ 0·87, 0·94 (6H, gem-dimethyls), 2·15 (3H, s, olefinic Me), 3·86 (4H, oxymethylene), 5·77 and 10·0 (each 1H, d, $J = 7$ Hz; α,β-unsaturated aldehyde). The olefinic Me and aldehydic proton signals of the *cis*-isomer appear at δ 1·94 and 9·90 respectively.

Orcinol bis-tetrahydropyranyl ether obtained from orcinol and dihydropyran was converted to its 2-lithio compound by treatment with n-BuLi in ether.[6] The lithio compound was condensed with the aldehyde VIIIc at room temp. The resulting benzyl alcohol derivative IX was immediately hydrolyzed with oxalic acid in aqueous THF. to give the expected keto-chromene (X) as 1:1 diastereomeric mixture. The keto-chromene (X). $C_{21}H_{28}O_3$ (M^+. 328) exhibits UV absorption maxima at 220. 278. and 284·5 nm (ε. 22.000. 8.100 and shoulder) and IR bands at 1.710. 1.630 and 1.580 cm^{-1}. Repeated chromatographic separations of the diastereomeric mixture of X was carried out on silica gel columns to yield isomers Xa and Xb in pure form. both of which showed an almost identical IR spectrum. Compound Xa showed the olefinic proton signals at 5·45 and 6·64 and Xb at 5·30 and 6·57 as an AB type quartet (J = 11

Hz). The synthetic ketone Xa was shown to be identical with the compound derived from naturally occurring siccanochromene-F[7] by oxidation with periodate. The methylenation ofXa with methylenetriphenylphosphorane afforded siccanochromene-A (II),* proved to be identical with natural compound in all respects VPC, TLC, NMR, IR. MS and analysis. The same treatment of Xb yielded the diastereoisomer of II, which exhibits the same NMR spectrum except for the olefinic proton signals at 5·35 and 6·55 (2H, AB pattern, $J = 11$ Hz), instead of the corresponding signals at 5·31 and 6·55 in the natural compound.

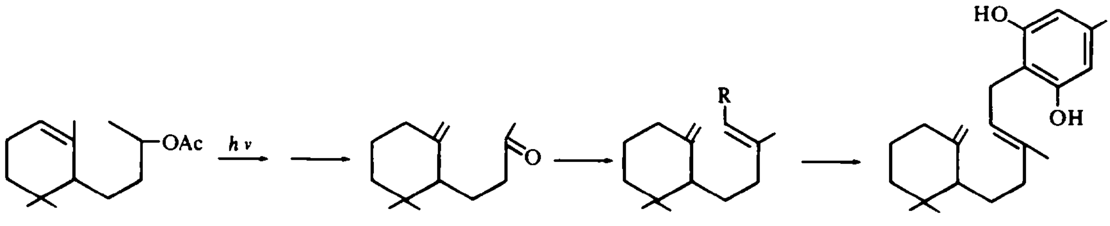
Reaction of the acetate of the keto-chromene Xa with excess dimethylsulfonium methylide[8] gave an oxirane derivative XI, $C_{22}H_{30}O_3$, (M^+, 342), λ_{max}231 and 281 nm (ε, 25.500, 6.700); ν_{max}1.628, 1.580, 3.620 and 3.400 cm^{-1}. NMR δ 2·42 and 2·52 (2H, AB quartet, $J = 5·0$ Hz; oxirane ring methylene protons). The synthetic compound XI was found to be epimeric at C-10 with the natural siccanochromene-B. The tertiary alcohol XII derived from XI by LAH reduction was dehydrated to afford compound



XI XII XIII

XIII as major product by treatment with $SOCl_2$ in pyridine; while, as previously reported, the tertiary alcohol derived from the natural siccanochromene-B gave siccanochromene-A as major product by the same treatment.[2]

Presiccanochromene-A (XVII), which has been isolated from culture filtrates as a minor constituent, was synthesized from dihydro-α-ionyl acetate by the following reaction sequence.



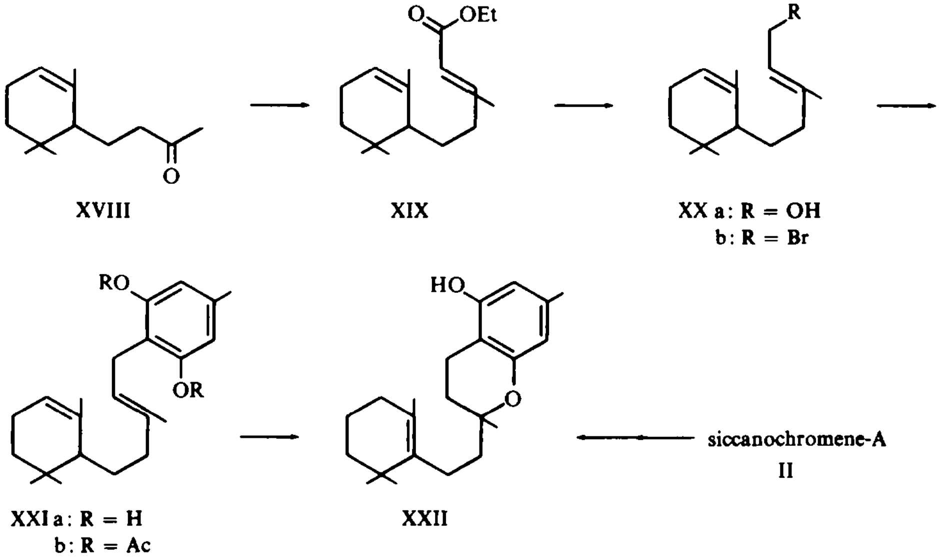
XIV XV XVI a: R = CO_2Et
b: R = CH_2OH
c: R = CH_2Br
XVII

Irradiation of a solution of dihydro-α-ionyl acetate (XIV) in isopropyl alcohol by a 450-W high pressure mercury vapour lamp in the presence of xylene as a photosensitizer[9] induced double bond isomerization to give dihydro-γ-ionyl acetate, which

---

* The absolute and relative stereochemistry at C_5 and C_8 have not been decided.

was then hydrolyzed and oxidized with CrO_3 in pyridine. The allyl alcohol XVIb. prepared as the same procedure described for compound VIIIb was converted into the bromide XVIc with PBr_3 in petroleum ether containing pyridine. Condensation of XVIc with the lithium salt of orcinol bis-tetrahydropyranyl ether in hexane followed by mild hydrolysis with oxalic acid gave the phenolic compound XVII. which was found to be identical in all respects with the natural presiccanochromene-A.[10] The prenyl phenol derivative XXIa prepared from dihydro-α-ionone (XVIII)



XVIII XIX XX a: R = OH
b: R = Br

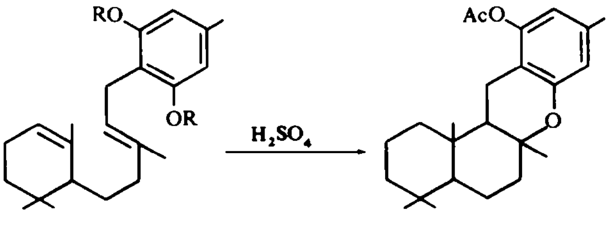
XXI a: R = H
b: R = Ac

XXII

siccanochromene-A
II

as described above was treated with acid to give the chromane derivative XXII. which was identical with the compund derived from siccanochromene-A (II) by hydrogenation followed by acid treatment.

Treatment of the di-acetate XXIb with H_2SO_4 in nitropropane[11] at −70° gave a complex mixture of the products. from which a crystalline compound. XXII. m.p. 131°. $C_{24}H_{34}O_3$ (M^+. 370). ν_{max} 1.760 cm^{-1}. λ_{max} 275 nm (shoulder). 283 nm (3.300). was isolated. The NMR spectrum of XXII shows four new tertiary Me signals at 0·92. 1·19. and 1·22 (3H. 3H. and 6H). The olefinic proton signals at δ 1·63 and 1·68 in XXIb disappeared. From these data the structure XXII was tentatively assigned for this product.



XXIb XXII

EXPERIMENTAL

All m.ps are uncorrected. UV spectra were measured on a Shimadzu SV-50 spectrometer. IR spectra were taken on a Jasco DC-301 spectrometer. NMR spectra were determined in CCl_4 on a Jeol 100 Mz spectrometer. The signals are reported in δ values from TMS as internal standard. VPC's were performed on Shimadzu model 14-APTF instrument equipped with H_2-flame detector. Mass spectra were determined on a Hitachi Mass spectrometer RMU-6D at 70 eV. Merck "Kieselgel G" was used for TLC on 0·25 mm layers. Spots were detected by charring with H_2SO_4 or diazotized benzidine salt solution.

Keto-ester (IV). This compound was prepared from mesityl oxide and diethyl-malonate by the reported procedure.[3] b.p. 112°–117°/0·1 mm. $\nu_{\max}^{\text{film}}$ 1.730. 1.709 cm^{-1}. VPC: 2·6 min. (140°) 3% OV-17. 75 cm × 4 mm. N_2: 1 Kg/cm^2. NMR: 0·77. 1·09 (6H. gem-dimethyls). 1·23 (3H. triplet. $J = 7$ Hz). 4·01 (2H. quart. $J = 7$ Hz).

Ethylene ketal ester (V). A mixture containing 4·5 g of *keto-ester* (IV). 8 ml ethylene glycol and 3·0 mg of *p*-TsOH in 120 ml C_6H_6 was refluxed for 7 hr. with continuous azeotropic removal of water and ethylene glycol by means of a Dean–Stark trap. The cooled mixture was washed with water and 5% aq. $NaHCO_3$. saturated brine and dried (Na_2SO_4). The solvent was distilled under red. press. yielding 5·5 g of crude *ethylene ketal ester* (V). b.p. 87°/0·05 mm. $\nu_{\max}^{\text{film}}$ 1.730 cm^{-1}. NMR: 0·85. 0·95 (6H. gem-dimethyls). 1·23 (3H, t., $J = 7$ Hz), 4·02 (2H, quart., $J = 7$ Hz), 2·30 (2H. m), 3·85 (4H, m). VPC: 4·5 min. (140°) 3% OV-17, 75 cm × 4 mm. N_2: 1 Kg/cm^2. (Calc. for $C_{15}H_{26}O_4$: C. 66·66; H. 9·80. Found: C. 66·63; H. 9·69%).

β-Keto sulfoxide (VI). Methyl sulfinyl carbanion was prepared from 55% NaH (360 mg) and DMSO (5 ml) by the method of Corey and Chaykovsky.[4] To this was added THF (5 ml) and then THF (4 ml) solution of V (1 g). The mixture was stirred for 1·5 hr and poured into 5 × volume of water and extracted with $CHCl_3$ eight times. The combined extracts were washed with water and dried (Na_2SO_4). Removal of solvent gave crude VI (900 mg). $\nu_{\max}^{CHCl_3}$ 1,710 cm^{-1}. NMR: 0·88. 0·97 (6H. gem-dimethyls). 1·25 (2H. t., $J = 7$ Hz). 2·58 (—SO—Me). 3·85 (6H. complex). 2·65 (2H).

Methyl ketone (VII). The above obtained VI (900 mg) was dissolved in 10% aq. THF (60 ml). To this solution was added aluminium–amalgam (1 g) prepared by the reported procedure.[4] The whole was heated at 55° for 1 hr. The mixture was filtered and the filtrate concentrated to remove most of the solvent. Ether was added and the ethereal phase separated from the water. dried (Na_2SO_4) and evaporated to leave crude VII (700 mg). b.p. 64°/0·045 mm. $\nu_{\max}^{\text{film}}$ 1,717 cm^{-1}. NMR: 0·86. 0·94 (6H. gem-dimethyls). 2·00 (MeCO). 2·42 (2H, m), 3·82 (4H, m). VPC: 3 min. (140°) 3% OV-17, 75 cm × 4 mm. N_2: 0·95 Kg/cm_2. (Calc. for: $C_{14}H_{24}O_3$: C. 69·64; H. 10·07. Found: C. 69·15; H. 10·04%).

Ketal ester (VIIIa). To the methylsulfinyl carbanion-DMSO solution which was prepared from 480 mg NaH (55% dispersed in mineral oil) and dry DMSO (8 ml) by Corey's method.[4] was added 2·24 g ethyl diethylphosphonoacetate for ten min. After stirring for twenty min at room temp. the methyl ketone VII (1·6 g) was added dropwise through a syringe to the above solution and the mixture stirred at 30° for 20 hr. Petroleum ether was added and the organic layer washed with 5% aq. HCl and water and dried (Na_2SO_4). Removal of solvent afforded 1·65 g of *cis*- and *trans*-isomer mixture. b.p. 98–105°/0·03 mm. $\lambda_{\max}^{EtOH} = 220$ nm. VPC: 5·2 min. (*cis*-) and 6·8 min. (*trans*-) (160°) 3% OV-17 on Shimalite W (80/100 mesh). N_2: 1·05 Kg/cm^2. (Calc. for $C_{18}H_{30}O_4$: C. 69·64; H. 9·74; O. 20·62. Found: C. 69·85; H. 9·78; O. 20·48%).

The mixture was chromatographed on silica gel (20 times). Elution with n-hexane: $C_6H_6 = 10:1$ afforded *cis*-ester. (25%) $\lambda_{\max}^{EtOH} = 220$ nm. $\nu_{\max}^{\text{film}}$ 1,718. 1,648 cm^{-1}. NMR: 0·84. 0·99 (6H. gem-dimethyls). 1·23 (3H. t., $J = 7$ Hz). 4·02 (2H. quart., $J = 7$ Hz). 1·84 (Me). 2·60 (br. triplet). 3·85 (4H. m). 5·50 (br. singlet). M^+ at *m/e* 310 ($C_{18}H_{30}O_4$). Elution with n-hexane: $C_6H_6 = 8:2$ gave *trans*-ester. (75%). $\lambda_{\max}^{EtOH} = 220$ nm. $\nu_{\max}^{\text{film}} = 1.718$. 1.648 cm^{-1}. NMR: 0·86. 0·925 (6H, gemdimethyls). 1·24 (3H. t., $J = 7$ Hz). 4·025 (2H quart., $J = 7$ Hz). 2·10 (Me). 3·85 (4H. m) 5·55 (br. singlet). M^+ at *m/e* 310 ($C_{18}H_{30}O_4$).

Allylic alcohol (VIIIb). 1 g of the *ketal ester* mixture (VIIIa) was dissolved in 25 ml dry ether and 250 mg of LAH was added at 0° over twenty min. Stirring was continued for fifty min and then moist ether added slowly. The product was isolated with ether. The ethereal extract was washed with water and dried (Na_2SO_4). Removal of solvent gave 850 mg of the *allylic alcohol* VIIIb. TLC: $R_f = 0·28$ (C_6H_6 acetone = 9:1). $\nu_{\max}^{\text{film}} = 3.400$ cm^{-1}. NMR: 0·86. 0·93 (6H. gem-dimethyls). 1·63 (Me). 3·85 (6H). 5·32 (1H. t., $J = 7$ Hz). VPC: 4 min. (*cis*-) and 4·7 min. (*trans*-) (154°) 3% OV-17 on Shimalite W. 75 cm × 4 mm. N_2: 1·1 Kg/cm^2. M^+ at *m/e* 268 ($C_{16}H_{28}O_3$).

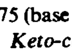
α.β-*Unsaturated aldehyde mixture* (VIIIc). (a) *Method by active manganese dioxide*: *Allylic alcohol* mixture (VIIIb) (180 mg) was dissolved in 10 ml dry petroleum ether (b.p. 50–63°) and to this was added active MnO_2 (500 mg) with stirring. Stirring was continued at 18° for 22 hr. Filtration and removal of solvent afforded 120 mg of VIIIc. TLC: $R_f = 0·53$ (C_6H_6: acetone = 9:1).

(b) *Method by* CrO_3-Py. *complex*: *Allylic alcohol* mixture (VIIIb) (2·0 g) was dissolved in 7 ml pyridine and CrO_3-Py. complex (CrO_3 (1 g)–Py. 10 ml) was added to the solution. The mixture was allowed to stand at 18° for 16 hr. Water was added and the product isolated with ether. The ethereal layer was washed in the usual manner and removal of solvent afforded 1·9 g of crude *α,β-unsat. aldehyde* (VIIIc). Rapid chromatography on silica gel (10 times. C_6H_6) gave 1·1 g of VIIIc. TLC: R_f = 0·53 (C_6H_6 : acetone = 9 ; 1). λ_{max}^{EtOH} 238 nm. ν_{max}^{film} 2730. 1680 and 1630 cm^{-1}. NMR: 0·87. 0·94 (6H. gem-dimethyls). 1·94 (Me. *cis*-). 2·15 (Me. *trans*-). 3·86 (4H). 5·77 (1H. *J* = 7 Hz). 9·90 (1H. d.. *J* = 7 Hz. *cis*-) 10·0 (1H. d. *J* = 7 Hz. *trans*-). VPC: 4·8 min. (*cis*-). 5·6 min. (*trans*-) (154°) 3% OV-17 on Shimalite W. 75 cm × 4 mm. N_2 : 1·1 Kg/cm^2.

Keto-chromene (X). To a solution of 1·22 g of orcinol bis-tetrahydropyranylether in 8 ml dry n-hexane was added 2·8 ml of n-BuLi/n-hexane solution (15·23%) through a syringe. Being stirred for 1 hr at room temp. this solution was allowed to stand overnight for complete conversion of the pyranylether into its lithio derivative. To the above solution was added dropwise the α,β-unsaturated *aldehyde* VIIIc (1·1 g) in 5 ml n-hexane through a syringe and stirring was continued for 60 min. The mixture was poured into ice-water and the product taken up with ether. The ethereal extract was washed with water and dried (Na_2SO_4). Removal of solvent afforded 2·1 g of product which immediately chromatographed on 21 g of silica gel and the early fraction eluted with C_6H_6 gave almost pure 1·6 g of the *carbinol* (IX). The above obtained *carbinol* was dissolved in 23 ml THF and 8 ml 5% aq. oxalic acid and the whole heated at 60° for 2·5 hr with stirring. After cooling the mixture was extracted with ether and the ethereal extract washed with 5% aq. $NaHCO_3$. water. dried (Na_2SO_4) and evaporated under vacuum to give product (1 g). The residual oil was chromatographed on silica gel (10 g) and elution with n-hexane: C_6H_6 = 1 :2 and C_6H_6 afforded 400 mg of the desired *keto-chromene* (X). (44% yield). TLC: R_f = 0·5 (C_6H_6: acetone = 10:1). VPC: 12·2 min. (196°) 1·5% OV-17 on chromosorb P (80/100 mesh). 1·5 m = 4 mm. N_2: 0·75 Kg/cm^2. λ_{max}^{EtOE} 229 (ε. 22.000). 278 (8.100) and 284·5 nm (sh.). M^+ at *m/e* 328 ($C_{21}H_{28}O_3$). NMR shows the *keto-chromene* (X) is a 1 : 1 mixture of the two diastereomers (Xa and Xb). The *keto-chromene* (X) (150 mg) was chromatographed on 4·5 g silica gel with a gradient system (V_6H_6 :n-hexane) to separate into the diastereomer Xa (40 mg) and Xb (27 mg).

Keto-chromene (Xa). $\nu_{max}^{CHCl_3}$ 3.620. 3.380. 1.710. 1.630 and 1.580 cm^{-1}. NMR : 0·75. 1·00 (6H. gem-dimethyls). 1·27 (Me). 2·16 (C_{17}–Me). 6·03. 6·08 (2H. aromatic protons). 5·45 (1H. d.. *J* = 11 Hz). 6·64 (1H. d.. *J* = 11 Hz). (Calc. for $C_{21}H_{28}O_3$: C. 76·79; H. 8·59; O. 14·61. Found: C. 76·58; H. 8·63; O. 14·78%).

Keto-chromene (Xb). $\nu_{max}^{CHCl_3}$ 3.620. 3.380. 1.710. 1.630 and 1.580 cm^{-1}. NMR : 0·80. 1·02 (6H. gem-dimethyls). 1·32 (Me). 2·17 (C_{18}–Me). 6·06 (2H, aromatic protons). 5·35 (1H. d.. *J* = 11 Hz). 6·58 (1H. d.. *J* = 11 Hz).

Siccanochromene-A (II). Methyl sulfinyl carbanion was prepared from 55% NaH (100 mg) and 4 ml DMSO by the method of Corey and Chaykofsky.[4] 1·6 ml of the above solution was injected into 286 mg triphenyl methylphosphonium bromide through a syringe. After stirring for 15 min. *keto-chromene* (Xa) (27 mg) in DMSO (1 ml) was injected into this solution through a syringe and the whole heated with stirring at 55° for one hr. The mixture was poured into ice-water and extracted with ether. The ethereal extract was washed with water and dried (Na_2SO_4). Solvent was distilled and the product chromatographed on silica gel (10 times). Elution with n-hexane: C_6H_6 = 10:1 gave *siccanochromene*-A (II) (20 mg). TLC: R_f = 0·57 (C_6H_6: acetone = 14 : 1). λ_{max}^{EtOH} 229·5 (ε. 25.700). 278·5 (9.320). and 286·5 nm (8.900). $\nu_{max}^{CHCl_3}$ 3.640. 3.370. 3.060. 1.630. 1.580. 9.80. 892. and 817 cm^{-1}. NMR: 0·82. 0·92 (6H. gem-dimethyls). 1·26 (C_{20}–Me). 2·17 (C_{18}–Me), 4·48 and 4·71 ( $=\!<^{H}_{H}$). 5·31 (1H, d., *J* = 11 Hz). 6·55 (1H, d., *J* = 11 Hz). 5·96 and 6·10 (2H, aromatic). VPC: 8 min. (196°) 1% XE-60 on chromosorb W. 1·5 m × 4 mm (100/120 mesh). N_2 : 1·4 Kg/cm^2. 6·1 min (229°) 1·5% OV-17 on chromosorb W (100/120 mesh). 1·5 m × 4 mm. N_2 flow rate 73 ml/min. M^+ at *m/e* 326 ($C_{22}H_{30}O_2$). 175 (base peak).

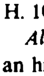
Episiccanochromene-B (XI). *Keto-chromene* (Xa) was acetylated by the usual method (Ac_2O/Py). The acetate (M^+ : 370. δ2·23 and 2·27 (acetyl and aromatic Me) (25 mg) was dissolved in 0·4 ml dry THF and this solution was added through a syringe to the dimethylsulfonium methylide. prepared from 2M-methylsulfinyl carbanion (0·135 ml) and the same volume of THF and trimethyl sulfonium iodide (55·2 mg) in 0·4 ml DMSO by the method of Corey *et al.*[8] The mixture was stirred at 24° for 30 min and poured into ice-water and extracted with ether. The ethereal extract was washed with water and dried (Na_2SO_4). After removal of solvent. the crude product was chromatographed on silica gel (PLC). The part of R_f = 0·5 (C_6H_6: acetone = 10 : 1) was gather and extracted with $CHCl_3$. VPC: 15·7 min (210°) 1·5% OV-17 on Shimalite W. 1·5 m × 4 mm. N_2 : 1·3 Kg/cm^2 (*cf.* siccanochromene-B is at 14·9 min. under the same conditions). λ_{max}^{EtOH} 231 (ε. 25.500). 281 mn (6.700). $\nu_{max}^{CHCl_3}$ 3.620. 3.400. 1.628 and 1.580 cm^{-1}. NMR : 0·92. 0·98 (6H. gem-dimethyls). 1·27 (C_{20}-Me). 2·14 (C_{18}-Me) 2·42 and 2·52 (2H.  . *J* = 5 Hz). 5·34 (1H.

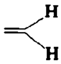
d. J = 11 Hz). 6·58 (1H. d. J τ 11 Hz). 6·01 and 6·09 (2H. aromatic protons). M^+ at m/e 342 ($C_{22}H_{30}O_3$).

Carbinol (XII). To a THF (1·5 ml) solution of 20 mg of the above obtained *episiccanochromene*-B (XI) was added 50 mg of LAH and refluxed for one hr. Work up as usual and silica gel PLC (R_f = 0·5; C_6H_6 : acetone = 10:1) afforded *carbinol* XII. VPC: 14·0 min. (210°). 1·5% OV–17 on Shimalite W (80/100mesh). 1·5 m × 4 mm. N_2: 1·33 Kg/cm^2. (*cf. carbinol* derived from the natural one appeared at 14·2 min. under same conditions.) NMR: 0·86. 0·93 (6H. gem-dimethyls). 1·10 and 1·31 (two Me's). 2·14 (C_{18}–Me). 5·36 (1H d. J = 11 Hz). 6·57 (1H. d. J = 11 Hz). 5·98 and 6·12 (2H. aromatic protons). M^+ at m/e 344 ($C_{22}H_{32}O_3$).

Dehydration of the carbinol (XII). The above obtained *carbinol* XII (6 mg) was dissolved in 0·15 ml pyridine and then two drops of $SOCl_2$ were added by micropipet at 0° and stirring continued for 2 min. The mixture was poured into ice-water and extracted with ether. The gas chromatogram showed a peak at 8·45 min. (XIII). 87·5% pf the isolated product. TLC: 0·57 (C_6H_6: acetone = 14:1). λ_{max}^{EtOH} 231 (ε. 25.600). 281 nm (7.200). $\nu_{max}^{CHCl_3}$ 3.610. 3.390 (br.). 1.610 and 1.580 cm^{-1}. NMR: 0·93. 0·97 (6H. gem-dimethyls). 1·32 and 1·52 (two Me's). 2·11 (C_{18}–Me). 5·36 (1H. d. J = 11 Hz). 6·58 (1H. d. J = 11 Hz). 5·95 and 6·11 (2H. aromatic protons). VPC: 8·45 min. (210°) 1·5% OV-17 on Shimalite W (80/100 mesh). 1·5 m × 4 mm. N_2: 1·3 Kg/cm^2. M^+ at m/e 326 ($C_{22}H_{30}O_2$).

Dihydro γ-ionone (XV). *Dihydro α-ionyl acetate* (XIV) (1·5 g) was dissolved in iso-PrOH (150 ml) and to this was added 1·5 ml of xylene as sensitizer in a water jacketed Vycor immersion well. The solution was irradiated with 450-W high pressure mercury lamp under bubbling argon gas with ice-cooling for 7 hr. The solvent was distilled under red. press. and distillation of the product afforded 1·3 g of crude dihydro γ-ionyl acetate (b.p. 130°/7 mm). The crude *dihydro γ-ionyl* acetate (1 g) was hydrolysed by the usual method and oxidized by CrO_3 (600 mg) in Py. (7 ml) at room temp. Ethereal extract gave 700 mg crude dihydro γ-ionone. forming semicarbazone by the usual method; m.p. 189° (lit. 190°). 5% aq. Phthalic acid hydrolysis of the semicarbazone gave pure *dihydro γ-ionone*. b.p. 111–112°/8 mm. ν_{max}^{film} 1.712. 890 cm^{-1}. NMR: 0·86. 0·90 (6H. gemd-methyls). 1·98 (COMe). 2·20 (2H. m.). 4·43 (1H. d.. J = 2·5 Hz). 4·67 (1H. br. singlet).

Unsaturated ester (XVIa). Ethyl diethylphosphonoacetate (2 g) was added with stirring to a methylsulfinyl carbanion solution prepared from NaH (0·39 g) in DMSO (6 ml). To the above solution *dihydro γ-ionone* (1·15 g) was added at room temp and the mixture heated at 30° for 20 hr. After extraction with petroleum ether and removal of solvent. 1·4 g crude XVIa was isolated. NMR spectrum showed the product consisted of a *trans*:*cis* = 3:1 mixture. Elution with n-hexane on silica gel column chromatograph gave first the *cis*-isomer then the *trans*- (XVIa): λ_{max}^{EtOH} 220 nm, $\nu_{max}^{CHCl_3}$ 3,080, 1,716, 1,645, 906 cm^{-1}. NMR: 0·86, 0·93 (6H), gem-dimethyls). 1·25 (Me. t.. J = 7 Hz). 4·03 (CH_2. quartet. J = 7 Hz). 2·10 (Me). 4·51 and 4·72 (2H. ). 5·53 (1H. s.) M^+ at m/e 264 ($C_{17}H_{28}O_2$). (Calc. for $C_{17}H_{28}O_2$: C. 77·22; H. 10·67. Found: C. 77·10: H. 10·71%).

Allyl alcohol (XVIb). XVIa (210 mg) was reduced with 80 mg of LAH in 8 ml of ether at 0°. After stirring an hr at 0°. work up as usual gave *allyl alcohol* (XVIb). ν_{max}^{film} 3.640. 3.480. 3.060. 1.670. 892 cm^{-1}. NMR: 0·84. 0·90 (6H. gem-dimethyls). 1·60 (Me). 3·97 (2H. d.. J = 7 Hz). 5·25 (1H. t.. J = 7 Hz). 4·48. 4·69. (2H. ).

Allyl bromide (XVIc). *Allyl alcohol* (1 g) was dissolved in 2 ml of petroleum ether and 0·11 g of pyridine at −7°. A solution of 0·53 g of PBr_3 in 1·5 ml of petroleum ether was added and the stirring continued for an hr at this temp. Ice-water was added and the product extracted with petroleum ether three times. The petroleum extract was washed with 5% aq. $NaHCO_3$. water and dried (Na_2SO_4). Petroleum ether was distilled under red. press. at room temp to afford 1·2 g of *allyl bromide* (XVIc). IR: no OH absorption. NMR: 3·90 (2H. d.. J = 8 Hz). 5·52 (1H. t.. J = Hz). Beilstein test: (+).

Pre-siccanochromene-A (XVII). To a solution of orcinol bis-tetrahydro pyranyl ether Li salt which was prepared from 520 mg orcinol bis-tetrapyranyl ether and n-BuLi was added to the above *allyl bromide* (XVIc) (520 mg) in 3·5 ml of abs. xylene and the mixture refluxed for two hr (white precipitate appeared). After cooling. the mixture was extracted with ether and the extract washed with 5% aq. NaOH. 2% aq. $NaHCO_3$ and water. dried (Na_2SO_4) and evaporated. The residual oil (10·6 g) was dissolved in MeOH (60 ml) and 5% aq. oxalic acid and the whole heated with stirring at 55° for two hr. After removal of MeOH. the mixture was extracted with ether and the extract washed with water and dried (Na_2SO_4). Evaporation under red. press. gave 680 mg of crude XVII. chromatographed on silica gel (10 g). Elution with C_6H_6 afforded pure XVII (240 mg). TLC: R_f = 0·5 (C_6H_6: acetone = 10:1). λ_{max}^{EtOH} 274 (ε. 1.080). 283 nm (1.015). $\lambda_{max}^{CHCl_3}$ 3.630. 3.480. 1.635. 1.592. 895 cm^{-1}. NMR: 0·83. 0·91 (6H. gemdimethyls). 3·29 (2H. d.. J = 7·5 Hz). 5·22 (1H. t..

J = 7·5 Hz). 4·47 and 4·69 (2H. $=\!\!<^{\mathrm{H}}_{\mathrm{H}}$). 5·07 (—O$\underline{\mathrm{H}}$. disappear with D_2O). 6·10 (2H. aromatic protons). VPC: 11·0 min. (220°) 1·5% OV-17 on Shimalite W (80/100 mesh), 1 m × 4 mm. H_2: 0·7 Kg/cm^2. M$^+$ at m/e 328 ($C_{22}H_{32}O_2$). All these data are in good agreement with naturally occurring pre-siccanochromene-A.

α.β-*Unsaturated ester* (XIX). XIX was obtained from α-ionone (XVIII) by the same procedure as that of XVIa. *cis-*: *trans-* = 1:3.

cis-isomer; λ_{max}^{EtOH} 220 nm, $\nu_{max}^{CHCl_3}$1·722, 1·650 cm^{-1}. NMR; 0·87, 0·98 (6H, gem-dimethyls) 1·23 (Me, t., J = 7 Hz). 4·07 (Me. quart.. J = 7 Hz). 1·70 (Me), 1·85 (Me), 2·55 (2H), 5·26 (1H, m.), 5·57 (1H). VPC: 9·65 min. (135°) 2% OV-17 on Gas Chrom-P (60/80 mesh), 1 m × 3 mm N_2: 1 Kg/cm^2. (Calc. for $C_{17}H_{28}O_2$: C. 77·22; H. 10·67; O. 12·10. Found: C. 77·15; H. 10·68; O. 11·86%).

trans-isomer (XIX); λ_{max}^{EtOH} 220 nm, $\nu_{max}^{CHCl_3}$1,722, 1650 cm^{-1}. NMR: 93 (6H, gem-dimethyls), 1·25 (Me, t.. J = 7 Hz). 4·07 (CH_2. quart.. J = 7 Hz), 1·65 (Me), 2·13 (Me), 5·26 (1H, m.), 5·60 (1H). VPC: 13·73 min. (the same conditions as *cis*-isomer). Calc. for $C_{17}H_{28}O_2$: C. 77·22; H. 10·67; O. 12·10. Found: C. 77·16; H. 10·67. O. 12·09%). *Allyl alcohol* (XXa). XXa was obtained by the same procedure as that of XVIb. b.p. 116°/3mm. TLC: R_f = 0·57 (C_6H_6:acetone = 4:1), ν_{max}^{film} 3,350, 1,660, 1,020 cm^{-1}. NMR: 0·87, 0·92 (6H, gem-dimethyls), 1·65 (two Me's), 4·07 (2H, d., J = 7 Hz), 5·35 (1H. t., J = 7 Hz), 5·25 (1H. m.). VPC: 6·8 min. (135°), 2% OV-17 on Gas Chrom-P (60/80 mesh), 1 m × 3 mm, N_2: 1 Kg/cm^2.

Allyl bromide (XXb). XXb was obtained by the same procedure as that of XVIc. NMR: 0·88, 0·94 (6H. gem-dimethyls), 1·65 (Me) 1·72 (Me), 3·88 (2H, d., J = 8 Hz), 5·50 (1H, t., J = 8 Hz), 5j25 (1H, m.).

Triprenyl phenol (XXIa). XXIa was obtained by the same procedure as that of XVII in 40% yield. TLC: R_f = 0·5 (C_6H_6 : acetone = 10:1), λ_{max}^{EtOH} 273·5 (ε, 1.250), 282·5 nm (sh.). $\nu_{max}^{CHCl_3}$ 3.630. 3.480. 1.638. 1.592 cm^{-1}. NMR ($CDCl_3$): 0·85. 0·90 (6H. gem-dimethyls). 1·63 (Me), 1·78 (Me). 2·12 (C_{18}–Me). 5·22 (1H). 5·15 (1H. t.. J = 7 Hz). 3·27 (2H. d.. J = 7 Hz). 6·06 (2H. aromatic protons). M$^+$ at m/e 328 ($C_{22}H_{32}O_2$). (Calc. for $C_{22}H_{32}O_2$: C. 80·44; H. 9·83; O. 9·74. Found: C. 80·06; H. 9·82; O. 9·42%).

Diacetate (XXIb). Triprenyl phenol (XXIa) (40 mg) was acetylated with Ac_2O (0·3 ml) and pyridine (0·7 ml) at room temp overnight. TLC: R_f = 0·36 (C_6H_6) λ_{max}^{EtOH} 255 nm), $\nu_{max}^{CHCl_3}$1,760, 1,632, 1,580 cm^{-1}. NMR: 0·84. 0·89 (6H. gem-dimethyls). 1·63. 1·68 (two Me's). 2·22 (two acetyls). 2·28 (C_{18}–Me). 3·10 (2H. d.. J = 7 Hz). 4·98 (1H. t.. J = 7 Hz). 5·24 (1H, m.) 6·74 (2H. aromatic protons). M$^+$ at m/e 412 ($C_{26}H_{36}O_4$). VPC: 11·4 min. (225°) 1·5% OV-17 on Shimalite W (80/100 mesh), 1·5 m × 4 mm, N_2: 47·5 ml/min.

Chromane (XXII). A solution of 50 mg of triprenyl phenol (XXIa) in 1·5 ml of abs C_6H_6 at 25° was treated with $SnCl_4$ (0·1 ml) with stirring for 20 min. The mixture was poured onto ice–water and ether added. The ethereal solution was washed with 5% aq. $NaHCO_3$. H_2O and dried (Na_2SO_4). The ether was removed to give the chromane (XXII) (40 mg). TLC: R_f = 0·33 (C_6H_6), λ_{max}^{EtOH} 260 (sh.), 274 (sh.), 284 nm (sh). $\nu_{max}^{CHCl_3}$ 3.640. 3.400. 1.637. 1593 cm^{-1}. NMR: 0·94, 0·99 (6H. gem-dimethyls). 1·25 (Me). 1·52 (Me). 2·13 (C_{18}–Me). 2·52 (2H. t.. J = 7 Hz). 6·12 and 5·95 (2H. aromatic protons). VPC: 6·3 min. (225°) 3% OV-17 on Shimalite W. 1 m × 3 mm. N_2: 1·05 Kg/cm^2. All these data were identical with that of chromane derived from naturally occurring siccanochromene-A.[2]

Acid treatment of XXIb. A cooled solution of 100% H_2SO_4 (0·3 ml) in nitro-propane (1·5 ml) was added at −70° to a well stirred solution of 250 mg of XXIb in nitro-propane (5 ml). The resulting yellow solution was kept at −70° for 20 min and poured into a mixture of ether and ice-cooled water. The aqueous layer was extracted with ether and the extract washed with 5% aq. $NaHCO_3$. water and dried (Na_2SO_4). After removal of solvent. the product was chromatographed on silica gel (6 g). The early 5% C_6H_6-n-hexane fraction afforded 25 mg of XXIII and then afforded 64 mg of *product*-A and 76 mg of *product*-B successively. XXIII: m.p. 131° (recry. from n-hexane). TLC: R_f = 0·7 (C_6H_6:acetone = 20:1). λ_{max}^{EtOH} 283 (ε, 2,300), 275 nm (sh.). $\nu_{max}^{CHCl_3}$ 1.760. 1.630. 1.580 cm^{-1}. VPC: 12·75 min. (225°) 1·5% OV-17 on Shimalite W (80/100 mesh), 1·5 m × 4 mm. N_2: 1·2 Kg/cm^2. M$^+$ at m/e 370 ($C_{24}H_{34}O_3$). NMR: 0·92, 1·19 (gem-dimethyls). 1·22 (two Me's). 2·25 and 2·31 (acetyl and C_{18}–Me). 6·44 and 6·52 (2H. aromatic protons).

Product-A: m.p. 117–119° (prism, recry. from MeOH). λ_{max}^{EtOH} 267 (ε, 500), 274 nm (sh.). $\nu_{max}^{CHCl_3}$ 1,761, 1,628, 1.370 cm—^{1}. VPC: 9·7 min. (under same conditions as XXIII). M$^+$ at m/e 412.

Product-B: m.p. 114–115° (recry. from n-hexane). λ_{max}^{EtOH} 267 (ε. 500), 274 nm (sh.). $\nu_{max}^{CHCl_3}$ 1.763. 1.627· 1.370 cm^{-1}. VPC: 10·8 min. (under the same condition.). M$^+$ at m/e 412.

Acknowledgement—The authors are grateful to Professor Emeritus K. Tsuda and Professor S. Okuda. University of Tokyo, for their encouragements and interest in this work. We also thank the Takasago

Perfumery Co., Ltd., for providing us with α- and β-ionones and Dr. G. Sunagawa of Sankyo Co., Ltd., for his generous support of this work.

REFERENCES

[1] [a] Presented at the 12th Symposium on the Chemistry of Natural Products. Sendai. October (1969); [b] S. Nozoe and K. Hirai. *Tetrahedron Letters* 3017 (1969)
[2] S. Nozoe. T. Suzuki and S. Okuda. *Ibid.* 3643 (1968)
[3] D. Stauffacher and H. Schninz. *Helv. Chim. Acta* **37**, 1223 (1965)
[4] E. J. Corey and M. Chaykovsky. *J. Am. Chem. Soc.* **87**. 1345 (1965)
[5] W. S. Wadsworth. Jr., and W. D. Emmons. *Ibid.* **83**, 1733 (1961)
[6] M. Isobe and T. Goto. *Tetrahedron* **24**, 945 (1968)
[7] S. Nozoe and K. T. Suzuki. *Ibid.* (preceding paper)
[8] E. J. Corey and M. Chaykovsky. *J. Am. Chem. Soc.* **87**. 1353 (1965)
[9] P. K. Kropp. *Ibid.* **88**, 4092 (1966)
[10] S. Nozoe and K. T. Suzuki. *Tetrahedron Letters* 2457 (1969)
[11] I. G. Mursakulov. A. K. Semenovsky. W. A. Smit and V. F. Kucherov. *Tetrahedron* **23**. 1621 (1967)