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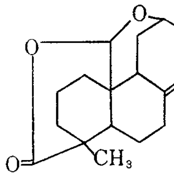
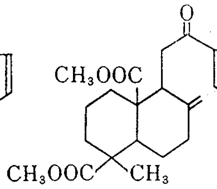
Relative Configuration of Sciadin, Dimethylsciadinonate, and Sciadinone, and Substitution of Oxygen in the Lactone Ring of Sciadin with Nitrogen

Three furanoid diterpenes, sciadin,[1a)] dimethylsciadinonate, and sciadinone[1b)] obtained from the leaves of *Sciadopitys verticillata* Sieb. et Zucc. have been proved to have the structures (I, II, and III), respectively. Since the latter two compounds were correlated[1b)] with sciadin, it was concluded that they have the same carbon skeleton, including its relative configuration in common, represented as IV (To economize space, we shall develop our argument by reference to the three dimensional structures, established in the sequel for the compounds in this series, rather than employ the two dimensional formulae which have already been elucidated[1a),1b)]). Presence of a lactone bridge between C-17 and C-19 of sciadin and sciadinone requires that the carbonyl carbon (C-19) and C-17 be in a 1,3-*cis*-diaxial relation to each other in ring A. Considering the presence of an ether bridge between C-12 and C-17 of sciadin, only two structures, *cis*-octahydro-3*H*-2-benzopyran system with A/B-*trans*-fusion (V), and *trans*-octahydro-3*H*-2-benzopyran system with A/B-*cis*-fusion (VI) satisfy the above requirements.



I



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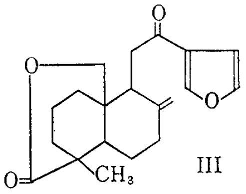
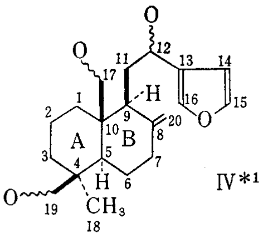
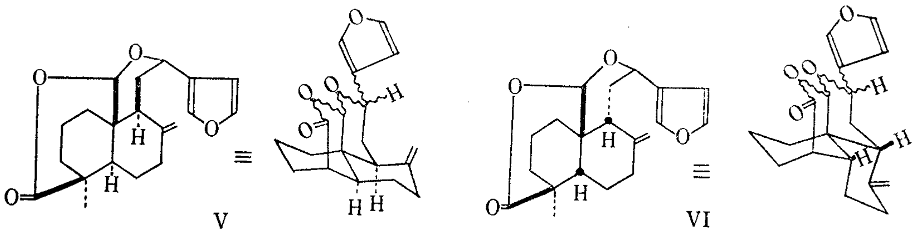


III



IV[*1,2)]



Possible Configuration for Sciadin

[*1] Three-dimensional formula used in this paper. This does not indicate absolute configuration.

1) *a*) M. Sumimoto, Y. Ito, H. Yokoi : Abstract of papers, Symposium on Organic Chemistry of Natural Products, Sapporo, Japan (1962). After this work had been completed, Sumimoto's original paper concerning the structure of sciadin appeared in Tetrahedron, **19**, 643 (1963); *b*) C. Kaneko, T. Tsuchiya, M. Ishikawa : This Bulletin, **11**, 271 (1963).

2) For the numbering system, cf. J. Cocker, T. Halsall : J. Chem. Soc., **1956**, 4262.

The fact that the ketone (VII) ($C_{15}H_{20}O_5 \cdot \frac{1}{4}H_2O$, m.p. 198~201°. *Anal.* Calcd. : C, 63.25; H, 7.25. Found : C, 63.13; H, 6.93., methyl ester, m.p. 194~196°. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1} : 1721 (two carbonyl), 1749 (one carbonyl). *Anal.* Calcd. for $C_{16}H_{22}O_5$: C, 65.60; H, 7.64. Found: C, 65.29; H, 7.53) obtained from sciadinone on ozonolysis was recovered unchanged after boiling with potassium hydroxide-ethanol solution, showed the equatorial orientation of the side chain at C-9, and this fact is consistent with the two structures shown above. Differentiation between V and VI became possible on the basis of the following novel reaction.[*2] Treatment of dimethylsciadinonate with BF_3-etherate in methanol afforded two oily products, (A) ($C_{21}H_{26}O_6$. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1} : 1775, 1730, 1686. *Anal.* Calcd. : C, 67.36; H, 7.00; Found : C, 66.60; H, 7.33. G.P.C.,[*3] R.R.T. to that of dimethylsciadinonate as standard, 1.34.) and (B) (IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1730 (two carbonyl), 1692 (one carbonyl). G.P.C. R.R.T. to that of dimethyl sciadinonate as standard, 0.98.) in 80% and 10% yield after separation by chromatography over silica gel. Purity of each compound was assured by a single sharp peak in their gas chromatogram. The nuclear magnetic resonance spectra of both compounds are shown in Table I. From the nuclear magnetic resonance and other spectral data, together with its elemental analysis, it is established that the former should be represented as VIII. Although insufficient amount of the latter compound (B) prevented to its through examination, spectral data agree well with the structure (IX) for this compound. The structure of compound (A) was further assured through its hydrolysis with a base to a crystalline acid (X) ($C_{21}H_{28}O_7$, m.p. 216~217°. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: broad absorption around 3300, 1737, 1700, 1668. *Anal.* Calcd. : C, 64.27; H, 7.19. Found: C, 64.65; H, 7.59).

TABLE I. N.M.R. Data for VIII and IX[a)]

VIII			IX		
Peak (τ)	Area	Assignment	Peak (τ)	Area	Assignment
1.89	1	$C(16)\underline{H}$	1.90	1	$C(16)\underline{H}$
2.56	1	$C(15)\underline{H}$	2.55	1	$C(15)\underline{H}$
3.23	I	$C(14)\underline{H}$	3.22	1	$C(14)\underline{H}$
6.38	3	$C(19)OOC\underline{H}_3$	6.38	5	$COOC\underline{H}_3+C(11)\underline{H}_2$
7.18	2	$C(11)\underline{H}_2$	6.42	3	$COOC\underline{H}_3$
8.78	3	$C\underline{H}_3$(tert.)	8.47	3	$\rangle$-$C\underline{H}_3$
8.82	3	$C\underline{H}_3$(tert.)	8.78	3	$C\underline{H}_3$(tert.)

a) Samples were dissolved in deuterochloroform at room temperature using tetramethylsilane as an internal reference and adopting the τ scale. The spectra were obtained on a JNM-3H-60 spectrometer operated at 60 Mc.

Newly formed lactone bridge between C-8 and C-17 in VIII requires that the lactone-oxygen (not its carbonyl side) and C-17 be in a 1,3-*cis*-diaxial relation to each other in ring B. Since, only the *trans*-A/B-system (V) satisfies this requirement, the alternate *cis*-A/B-system, such as VI, is abondoned. For these reasons, it is clear that sciadin, dimethylsciadinonate, and sciadinone can have only *cis*-octahydro-3*H*-2-benzopyran

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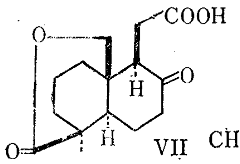
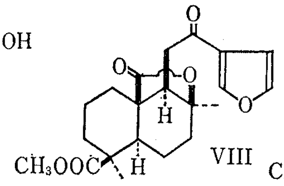
[*2] The detail study on this experiment, along with the application of this reaction to other diterpenes in this series will be published at a later date.

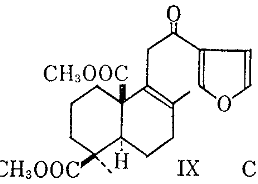
[*3] Gas chromatography was conducted on the following conditions: Apparatus, Shimadzu GC-1B, HFD-1; column, 6×150 mm.; 1% SE-30 on chromosorb-w; column temp., 230°; flash heater temp., 280°; N_2 pressure, 2 kg., 30 ml./min.; H_2 pressure, 0.8 kg., 35 ml./min. The following abbreviations are used throughout this paper; G.P.C. for gas-phase chromatography and R.R.T. for relative retention time.

with *trans*-A/B-system like IV, as their common carbon skeleton, or its mirror image, and thus, must be represented as XI, XII, and XIII, respectively. Only the configuration of two hydrogens at C-12 and C-17 in sciadin remains uncertain.

The configuration of sciadin, thus obtained is exactly same as that proposed recently by Sumimoto,[1α)] though the ways to the conclusion are different from ours.


VII


VIII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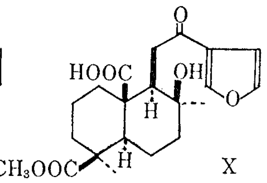
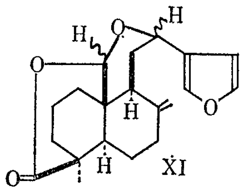
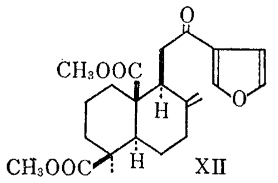
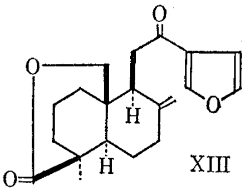
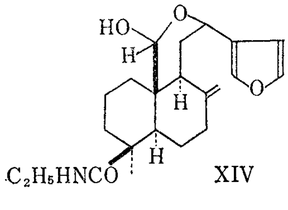

X

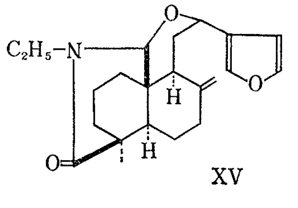

XI


XII


XIII

Stereochemistry of these diterpenes so far elucidated is exactly same as that of the atisine-type diterpene alkaloids.[3)] Of significance relative to the problem of converting these diterpenes to the above-mentioned alkaloids of established absolute configuration is to find a method for introducing the nitrogen atom. Such introduction of the nitrogen atom into sciadin has been achieved by the following method. Treatment of sciadin with ethylamine at 100° gave rise to a hydroxyamide (XIV) (m.p. 147~148°, IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 3400 (broad), 1615, 1063, 1028, 898, 876. *Anal.* Calcd. for $C_{22}H_{31}O_4N \cdot \frac{1}{2}H_2O$: C, 69.08; H, 8.43; N, 3.66. Found: C, 68.67; H, 8.11; N, 3.47. G.P.C.: R.R.T. 0.82 (sciadin as a standard)). Dissolution of this amide in acetic acid at room temperature afforded a δ-lactam (XV) (m.p. 112~114°, IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 1635, 1070~1080, 895, 875. *Anal.* Calcd. for $C_{22}H_{29}O_3N$: C, 74.33; H, 8.22; N, 3.94. Found: C, 74.35; H, 8.13; N, 3.96. G.P.C.: R.R.T. 0.82 (sciadin as a standard)). The same retention time of XIV and XV in the gas chromatography suggests that the former is dehydrated as soon as it was injected, owing to the high temperature of the injection tube. Yield of the lactam from sciadin is almost quantitative.[*4] Such a ready lactamization can only be explained if the carbon bearing the "alkyl"-oxygen of the δ-lactone group in sciadin is also "acetalic" in character and thus has ethereal oxygen attached to it.[4)] Not only this reaction gave the additional evidence for the correctness of the structure in the lactone moiety


XIV


XV

[*4] The lactamization has been effected by using ammonia, methylamine and ethanolamine. Detail of this study will be published soon.

3) S.W. Pelletier: Tetrahedron, **14**, 76 (1961) and papers quoted therein.

4) D.R. Barton, H.J. Cheung, A.D. Cross, L.M. Jackman, M. Martin-Smith: J. Chem. Soc. **1961**, 5061.

of sciadin, but also afforded the key step to convert sciadin to the above-mentioned atisine-type diterpene alkaloids (or their mirror images). The work along this line is now in progress.

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Syntheses of (+)-Isosophoramine and (−)-13-Alkylsubstituted Sophoramine from (+)-Matrine

Recently Sadykov showed that (+)-isosophoramine, isolated from *Sophora pachycarpa*, is (+)-11,13-didehydroallomatrine (I).[1] We previously reported the syntheses of (−)-sophocarpine (V) and (−)-sophoramine (VI) from (+)-matrine (II) as shown below.[2]

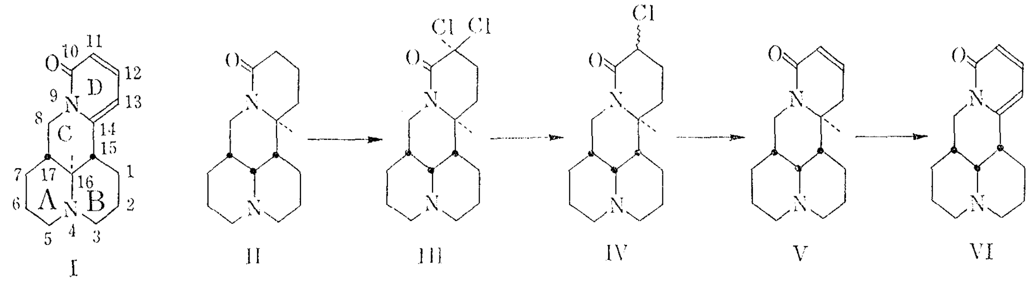

Chart 1.

This paper deals with the syntheses of (+)-isosophoramine (I) directly from dichloromatrine (III) or *via* (−)-sophoramine (VI) and also of (−)-13-alkylsubstituted sophoramines (Xa and Xb) from (−)-sophocarpine (V).

When III was heated in pyridine at 250° overnight, an aromatic base was obtained in 58% yield: its analytical data (Calcd. for $C_{15}H_{20}ON_2$: C, 73.73; H, 8.25; N, 11.47. Found.: C, 73.50; H, 8.22; N, 11.14) and physical constants—m.p. 149° (ether-petroleum ether), $[\alpha]_D^{18}$ +53.3° (c=1.005, EtOH), UV λ_{max}^{EtOH} mμ (log ε): 309 (3.88), 233.5 (3.78), IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2830, 2770 (*trans*-quinolizidine), 1655, 1575, 1550 (α-pyridone)—are in quite good agreement with those of (+)-isosophoramine (I).[1] Furthermore the catalytic hydrogenation of this base offered (+)-allomatrine (VII) in a quantitative yield. Consequently, I was synthesized from III in one step, involving aromatization of ring D and inversion at the C_{16}-position.[*1] Although the isomerization from VI to I did not occur by heating

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[*1] When the reaction temperature was ca. 200°, the mixture of I and VI was obtained.

[1] A. S. Sadykov, Yu. K. Kushmuradov, Kh. A. Aslanov: Dokl. Akad. Nauk S. S. S. R., **145**, 829 (1962); C. A., **57**, 15170 (1962).

[2] S. Okuda, H. Kamata, K. Tsuda, I. Murakoshi: Chem. & Ind. (London), **1962**, 1326.