Fra le sostanze naturali, la più attiva è la furocumarina fondamentale, psoralene, seguita da due suoi metossiderivati, xantotoxina e bergaptene. Anche alcuni metilpsoraleni di sintesi sono molto attivi.

Gli autori hanno anche stabilito, esaminando una cinquantina di alimenti di origine vegetale, che le furocumarine fotosensibilizzatrici possono entrare nella nostra dieta, ponendo il problema di una loro possibile funzione biologica a livello cutaneo.

Inoltre, per affrontare lo studio del meccanismo di azione di queste furocumarine, essi le hanno confrontate con altre note sostanze fotodinamiche, rispetto a quattro test scelti fra i più significativi: fotoossidazione dell'α-terpinene ad ascaridolo; emolisi dei globuli rossi; fotoossidazione delle proteine del siero di sangue; effetto ottenuto per applicazione epicutanea od iniezione intradermica nella cavia e successiva irradiazione.

Le furocumarine fotosensibilizzatrici hanno dimostrato di possedere proprietà particolari, diverse da quelle delle altre sostanze fotodinamiche, cioè il loro meccanismo d'azione, a differenza di queste ultime, non può essere riportato ad una fotoossidazione di substrati proteici.

Nonostante queste e successive ricerche degli autori e di altri ricercatori, il meccanismo d'azione delle furocumarine è rimasto oscuro.

Solo in questi ultimi tempi gli autori sono riusciti a mettere in evidenza alcuni fatti che possono servire a chiarire la complessa questione. Essi hanno trovato che il flavin-mononucleotide (FMN) e le furocumarine fotosensibilizzatrici per irradiazione ultravioletta danno luogo alla formazione di nuove sostanze, talune delle quali sono derivati flavinici complessi ed altre sono composti cumarinici derivanti da trasformazioni che intervengono nella parte furanica delle furocumarine.

Ci sono indicazioni per ritenere che questa fotoreazione possa servire per interpretare l'attività sulla cute. Solo le furocumarine attive infatti fotoreagiscono con l'FMN, quelle inattive non danno alcuna reazione; inoltre con l'FMN si può ottenere una protezione nelle cavie trattate con furocumarine e poi irradiate.

# Brèves communications – Kurze Mitteilungen – Brevi comunicazioni – Brief Reports

Les auteurs sont seuls responsables des opinions exprimées dans ces communications. – Für die kurzen Mitteilungen ist ausschliesslich der Autor verantwortlich. – Per le brevi comunicazioni è responsabile solo l'autore. – The editors do not hold themselves responsible for the opinions expressed by their correspondents.

## Oxygen Heterocycles[1]. Maackiain, a New Naturally Occurring Chromanocoumaran[2]

Previous papers[1,3] have been concerned with the isolation and elucidation of the structure of sophorol, a new isoflavanone from *Maackia amurensis* Rupr. et Maxim. var. Buergeri (Maxim.) C. K. Schneid. In a continued investigation of the heartwood constituents of the same plant material, the present author has isolated a further new oxygen heterocyclic compound, named maackiain, the presence of which has been forecast from biogenetical considerations[1].

Maackiain, $[\alpha]_D^{20} -251.7°$ ($CHCl_3$), $R$ D[4] in methanol (C, 0.074), 26°; $[\alpha]_{700} -175.8°$, $[\alpha]_{589} -227.0°$, $[\alpha]_{400} -559.0°$, $[\alpha]_{360} -684.0°$, formed colourless leaflets (m.p. 178.5° ~ 179.0°) containing a half equivalent molecule of water from aqueous methanol. Analytical data of the crystals are in excellent agreement with the formula $C_{16}H_{12}O_5$ $^1/_2H_2O$. (Found: C, 65.68; H, 4.69; $H_2O$, 3.7, 3.6%. $C_{16}H_{12}O_5$ $^1/_2H_2O$ requires: C, 65.53; H, 4.46; $^1/_2H_2O$, 3.6%. Found: (In a sample, m.p. 180.0° ~ 181.0°, dried at 100° ~ 110° *in vacuo*) C, 67.67, 67.33; H, 4.41, 4.58. $C_{16}H_{12}O_5$ requires C, 67.60; H, 4.26).

Maackiain has a phenolic hydroxyl group (IR OH 3472 $cm^{-1}$ in Nujol) and gave a mono-O-methyl ether, m.p. 168 ~ 169°. (Found: C, 67.92; H, 4.74; $OCH_3$, 10.35%. $C_{17}H_{14}O_5$ requires C, 68.45; H, 4.37; $OCH_3$, 10.40%.) The remaining four oxygen atoms were indifferent to reagents under standard conditions. The IR-spectrum of maackiain showed characteristic absorption bands[5] at 1035 $cm^{-1}$ and 929 $cm^{-1}$, assigned to a methylenedioxy group. The methylenedioxy protons were confirmed by the 56.4 mc/sec N.M.R. spectrum[6] of O-methylmaackiain, which shows sharp singlet lines of the type Ar–O–$CH_2$–O–Ar and $OCH_3$ at higher fields of 77 cps and 196 cps each from the signal of solvent chloroform. Pterocarpin[7] as a reference compound showed the corresponding singlet peaks at 76 and 196 cps respectively.

On the basis of the above evidence, the formulation of maackiain can be expanded into the formula $C_{15}H_9$, –O–$CH_2$–O–, –O–, –O–, –OH.

Biogenetic considerations and the above results suggested the chromanocoumaran skeleton, having a 2,4-di-

[1] Paper IV. Paper III in this series see H. Suginome, Tetrahedron Letters No. 19, 16 (1960).

[2] Read before the 14th Annual Meeting of the Chemical Society of Japan, Tokyo (April 1961).

[3] H. Suginome, J. org. Chem. *24*, 1655 (1959).

[4] The R.D.-curve was kindly determined by Dr. M. Maruyama through the courtesy of Professor S. Fujise of Tohoku University.

[5] L. H. Briggs, L. D. Colebrook, H. M. Fales, and W. C. Wildman, Anal. Chem. *29*, 904 (1957).

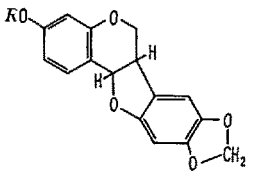
[6] Spectra were determined in chloroform solution. The band positions were read by the side-band method.

[7] A. McGookin, A. Robertson, and W. B. Whalley, J. chem. Soc. *1940*, 787; *1954*, 2794. – F. E. King, C. B. Cotterill, D. H. Godson, L. Jurd, and T. J. King, J. chem. Soc. *1953*, 3693. – A. Akisanya, C. W. L. Bevan, and J. Hirst, J. chem. Soc. *1959*, 2679.

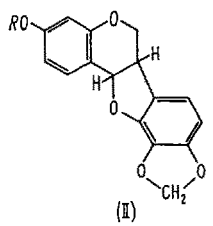
oxygenated alkyl phenyl and 5-oxygenated 6-alkyl-1,3-benzodioxole nuclei in the molecule.

The ultraviolet absorption spectrum of maackiain ($\lambda_{max}$ 280 ($\varepsilon$; 4420), 286 ($\varepsilon$; 5120), and 310 m$\mu$ ($\varepsilon$; 8500)). compared with those of model compounds is compatible with the presence of the above two groupings. However, the alternative possibility that maackiain has a 4-oxygenated-5-alkyl substitution pattern in the 1,3-benzodioxole ring as in pterocarpin (II; $R = CH_3$) is not excluded since ultraviolet absorption spectra of maackiain and pterocarpin are also superimposable (Figure).

On the basis of this spectral evidence, the possible structure of maackiain is restricted to formula (I; $R$=H) or (II; $R$ = H).



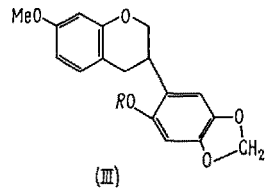
(I)



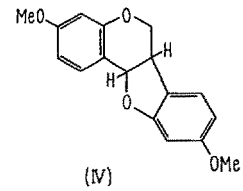
(II)

The following evidence proved unequivocally formula I for the structure of maackiain. Catalytic reduction of O-methylmaackiain gave rise to a new phenolic substance, dihydro-O-methylmaackiain, $C_{17}H_{14}O_5$, melting at 146° to 148° which gave an optically active mono-O-methyl ether ($[\alpha]_D^{18}$° $-21.0$°, chloroform, m.p. 116° ~ 117°). The same dihydro compound was also produced almost quantitatively by BIRCH reduction[8] with the sodium-liquid ammonia-toluene system.

On the basis of formula (I; $R$=H) for maackiain, the structure of this phenolic compound is reasonably explained by the isoflavan formula (III; $R$ = H), formed by hydrogenolysis of a benzilic ether type linkage.



(III)



(IV)

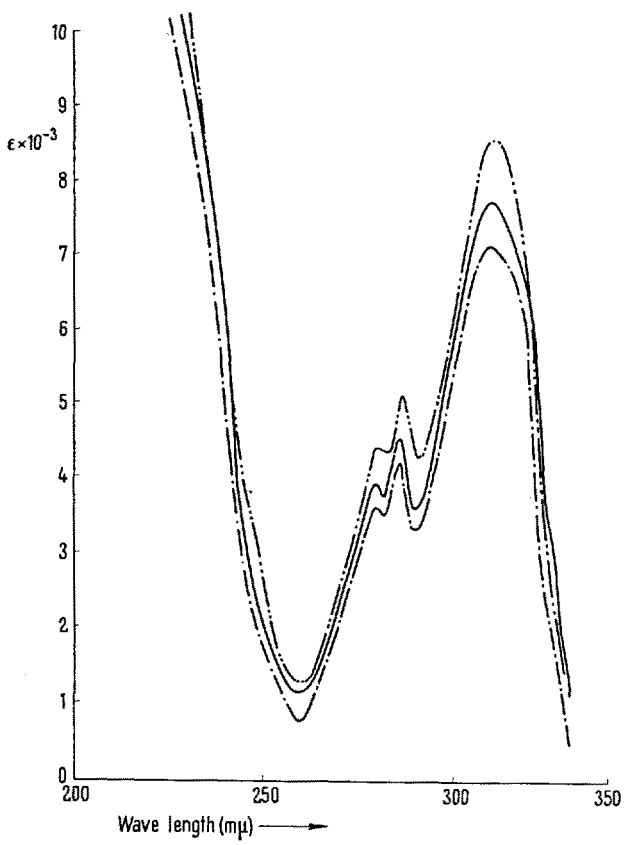
The structure of the O-methyl ether of dihydro-O-methylmaackiain has been confirmed by a synthesis of racemic 2′,7-dimethoxy-4′,5′-methylenedioxy isoflavan (III; $R = CH_3$). Catalytic reduction of 2′-7-dimethoxy-4′,5′-methylenedioxy-isoflavone gave an oily mixture of the corresponding isoflavan-4-ol and isoflavanone, Clemmensen reduction of which gave racemic 2′,7-dimethoxy-4′,5′-methylenedioxyisoflavan (m.p. 111° ~ 113°) (III; $R = CH_3$); the latter and O-methyldihydro-O-methylmaackiain gave identical infrared spectra in chloroform solution, thus establishing structure (I; $R$=H) for maackiain[9].

Although no direct evidence has so far been presented, examination of the models of the feasible structures[10] of maackiain shows that maackiain almost certainly has a *cis* configuration.

Maackiain is the third chromanocoumaran[11] so far discovered in Nature, pterocarpin and homopterocarpin (IV)[7,12] being the first examples.

The absolute stereochemistry of maackiain (I; $R$=H) pterocarpin (II; $R = CH_3$) and homopterocarpin (IV) is very probably the same.

Studies concerning the absolute stereochemistry of maackiain and related isoflavans are now in progress[13,14].




UV-spectra
—·— maackiain, —— O-methyl-maackiain, —·—·— pterocarpin

[8] A. J. BIRCH, Quart. Rev. *4*, 69 (1950). – A. J. BIRCH, J. W. CLARK-LEWIS, and A. V. ROBERTSON, J. chem. Soc. *1957*, 3586. – See also for 1,3-benzodioxole system: A. J. BIRCH, J. chem. Soc. *1947*, 102. – D. B. CLAYSON, J. chem. Soc. *1949*, 2016.

[9] After the correction to the formula of pterocarpin (J. B-SON BREDENBERG and J. N. SHOOLERY, Tetrahedron Letters Nr. 9, 285 (1961)) which showed the heterocycle to have structure (I; $R$ = H), comparison of IR-spectra in chloroform solution confirmed this conclusion.

[10] E. M. PHILBIN and T. S. WHEELER, Proc. chem. Soc. *1958*, 167. – H. HART and C. R. WAGNER, Proc. chem. Soc. *1958*, 284.

[11] S. WAWZONECK in R. C. ELDERFIELD, *Heterocyclic Compounds* (J. Whiley and Sons, Inc., 1951), vol. 2, p. 391. – W. KARRER, *Konstitution und Vorkommen der organischen Pflanzenstoffe* (Birkhäuser Verlag, Basel 1958), p. 691.

[12] E. SPÄTH and J. SCHLÄGER, Ber. dtsch. chem. Ges. *73*, 1 (1940).

[13] *Acknowledgements.* The author is grateful to Professors T. IRIE, T. MATSUMOTO, and T. MASAMUNE for their encouragement.
The author also wishes to express his sincere thanks to Drs. F. E. KING and J. W. W. MORGAN for a generous gift of a specimen of pterocarpin, and to Drs. I. YAMAGUCHI and N. HAYAKAWA of the Radiation Application Division, Japan Atomic Energy Research Institute for determination of N.M.R. spectra.
Grateful thanks are also due to Mr. T. IWADARE and Mr. Y. KIO for help in experiments.

[14] *Note added in proof.* Subsequent to the completion of this work COCKER et al.[15] have published the structure of an oxygen heterocycle inermin isolated from *Andira inermis* H.B.K. Inermin and maackiain are identical. Furthermore, both are the same as the aglycone of trifolirhizin, isolated from *Trifolium pratense*, and shown to have structure (I; $R$ = H) by BREDENBERG and HIETALA[16].

[15] W. COCKER, T. DAHL, C. DEMPSEY, and T. B. H. MCMURRY, Chem. and Ind. *1962*, 216.

[16] J. B-SON BREDENBERG and P. K. HIETALA, Acta chem. Scand. *15*, 936 (1961).

*Zusammenfassung.* Aus *Maackia amurensis* Rupr. et Maxim. var. *Buergeri* (Maxim.) C. K. Schneid wurde ausser dem bekannten Sophorol ein Phenol $C_{16}H_{12}O_5$ isoliert. Auf Grund spektroskopischer Untersuchungen und dem Vergleich mit einem synthetisch hergestellten Derivat (III; $R=CH_3$) wird dem Maackiain die Struktur (I; $R=H$) eines Chromanocumarans zugeschrieben.

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*Department of Chemistry, Faculty of Science, Hokkaido University, Sapporo (Japan), November 30, 1961.*

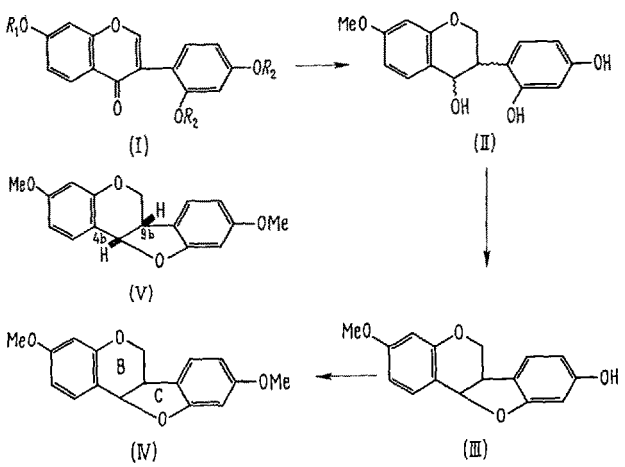
[17] Present address: University Chemical Laboratory, Cambridge (England).

## Sauerstoff-Heteroringe[1]. Die Konfiguration und Synthese des *d,l*-Homopterocarpins

Homopterocarpin, ein farbloser Inhaltsstoff des roten Sandelholzes sowie anderer Pterocarpus-Spezies[2], wurde bereits im Jahre 1874 von CAZENEUVE[3] isoliert. Im Jahre 1940 ist die Struktur dieser Verbindung von ROBERTSON et al.[4] sowie von SPÄTH und SCHLÄGER[5] im Sinne der Formel IV aufgeklärt worden.

An dieser Stelle soll über den Konstitutionsbeweis dieses Naturstoffes durch die Synthese berichtet werden. Wir synthetisierten *d,l*-Homopterocarpin auf dem von uns früher[6] mitgeteilten Wege.

Die Entalkylierung des 2',4',7-Trimethoxyisoflavons (I) $R_1 = R_2 = Me$[4,5,7] mit Aluminiumchlorid in Benzol[8] unter Rückfluss ergab das entsprechende Trihydroxyisoflavon (I) $R_1 = R_2 = H$ vom Smp. 272° (Zers.) (Acetylderivat Smp. 148–150°) in guter Ausbeute.




Bei der selektiven Methylierung des letzteren mit Methyljodid in Aceton in Gegenwart von Kaliumcarbonat bei Zimmertemperatur entstand 2',4'-Dihydroxy-7-methoxyisoflavon (I) $R_1 = CH_3$, $R_2 = H$ (Smp. 207–208°) in 73%iger Ausbeute.

Dieses partiell methylierte Isoflavon gab bei der Reduktion mit $NaBH_4$[6,9] in Dioxan nur in schlechter Ausbeute das Stereoisomerengemisch der entsprechenden Isoflavan-4-ole II.

Das rohe Stereoisomerengemisch liess sich durch 1stündiges Kochen in Essigsäure leicht in ein Gemisch von tetracyclischer Verbindung III und entsprechendem Isoflav-3-en überführen. Letzteres konnten wir nur durch ein UV-Maximum bei 327 mμ charakterisieren. Die Verbindung III wurde ohne weitere Reinigung durch Methylierung mit Methyljodid in Aceton in *d,l*-Homopterocarpin (IV) übergeführt.

Das so erhaltene *d,l*-Homopterocarpin (IV) schmolz bei 123–125°, während das natürliche, optisch aktive Homopterocarpin den Schmelzpunkt 87°[4,10] aufweist. Die synthetische Verbindung ergab jedoch völlig gleiche IR- (Chloroform) und UV-Spektren ($\lambda_{max}$ 285 mμ, ε; 9250) wie der Naturstoff.

Modellbetrachtungen[11] zeigen, dass die *trans*-Verknüpfung der beiden Ringe B und C des Homopterocarpins (IV), im Gegensatz zur *cis*-Verknüpfung, zu einer spannungsreichen Struktur führt.

Der glatte Ringschluss der Substanz II mit Säure scheint *cis*-Verknüpfung wahrscheinlich zu machen. Im 56,4 Mhz NMR-Spektrum[12] von IV[13] werden die Resonanzen des Protons an $C_{4b}$ als Dublett mit Zentrum bei 99,3 C/S und die Methoxylgruppen bei 196,0 C/S bei höherer Feldstärke als das Signal des Chloroforms beobachtet. Am Modell des Homopterocarpins (IV) mit *cis*-verbundenen B-C-Ringen ergeben sich für die Winkel zwischen den durch die Atome $H–C_{4b}–C_{9b}$ und $C_{4b}–C_{9b}–H$ bestimmten Ebenen Werte von ungefähr 0–10°, die nach CONROY[14] J = 7,7–8 C/S ergeben würden. Die Kupplungskonstante des Protons an $C_{4b}$, J = 5,9, weist auf *cis*-Stellung[15] der Ringe B-C des Homopterocarpins (IV) hin. Alle oben erwähnten Resultate lassen sich am besten durch die Formel V interpretieren.

[1] V. Mitteilung. IV. Mitteilung siehe H. SUGINOME, Exper. *18*, 161 (1962).

[2] P. L. SAWHNEY und T. R. SESHADRI, J. sci. industr. Res. *13B*, 5 (1954), und darin angeführte Literaturreferenzen. – F. E. KING, C. B. COTTERILL, D. H. GODSON, L. JURD und T. J. KING, J. chem. Soc. *1953*, 3693. – A. AKISANYA, C. W. L. BEVAN und J. HIRST, J. chem. Soc. *1959*, 2679.

[3] P. CAZENEUVE, Ber. dtsch. chem. Ges. *7*, 1798 (1874).

[4] A. MCGOOKIN, A. ROBERTSON und W. B. WHALLEY, J. chem. Soc. *1940*, 787.

[5] E. SPÄTH und J. SCHLÄGER, Ber. dtsch. chem. Ges. *73*, 1 (1940).

[6] H. SUGINOME und T. IWADARE, Bull. chem. Soc. Japan *33*, 567 (1960).

[7] H. SUGINOME, J. org. Chem. *24*, 1655 (1959).

[8] W. B. WHALLEY, J. chem. Soc. *1953*, 3366.

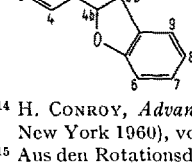
[9] M. MIYANO und M. MATSUI, Chem. Ber. *91*, 2044 (1958).

[10] Literatur [5] gibt als Schmelzpunkt 87–88° an.

[11] Es wurden Dreiding-Modelle verwendet.

[12] J. A. POPLE, W. G. SCHNEIDER und H. J. BERNSTEIN, *High-resolution Nuclear Magnetic Resonance* (McGraw Hill, New York 1959). – J. D. ROBERTS, *Nuclear Magnetic Resonance, Application to Organic Chemistry* (McGraw Hill, New York 1959). – L. M. JACKMAN, *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry* (Pergamon Press, London 1957). Die Spektren wurden mit einem Variant-Spektrometer in Chloroform als Lösungsmittel durchgeführt.

Den Herren Drs. I. YAMAGUCHI und N. HAYAKAWA, die diese Messungen im japanischen Atomenergie-Forschungsinstitut durchführten, sei an dieser Stelle bestens gedankt.

[13] 

Wir möchten vorschlagen, das Chromanocumaranringsystem[6], das heisst 4bH,9bH,10H-(1)-Benzopyrano-(4,3-b)-(1)-benzofuran, wie (A) zu numerieren und Substanzen, welche dasselbe Skelett haben, als «Pterocarpinoide» zu bezeichnen.

[14] H. CONROY, *Advances in Organic Chemistry* (Interscience Publ., New York 1960), vol. 2, p. 310.

[15] Aus den Rotationsdispersionskurven von Homopterocarpin, Pterocarpin[4] und Maackiain[1] ergibt sich, dass diese Naturstoffe dieselbe Konfiguration haben. H. SUGINOME, unveröffentlichte Beobachtung.