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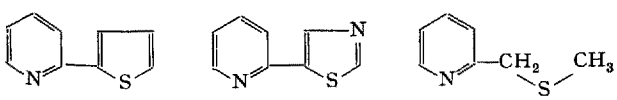
Schwefel als Ligandatom in Chelatkomplexen

Die Mitteilung von KOMSER und SEN[1] über Chelatkomplexe mit β-Furfuraldoxim, von denen vermutet wird, dass in ihnen das Furan-O-Atom sich als eine der basischen Haftstellen betätigt, veranlasst uns, über eigene Versuche zu berichten, die wir unternommen haben, um das Komplexbildungsvermögen des Schwefels in einem aromatischen Bindungssystem zu untersuchen.

Wir haben zu diesem Zweck die folgenden drei noch unbekannten Verbindungen synthetisiert: 2-(2'-Thienyl)-pyridin (I), 5-(2'-Pyridyl)-thiazol (II) und als Vergleichsverbindung[2] Methyl-α-picolyl-sulfid (III).



I II III

I wurde ausgehend von 2-Bromthiophen über dessen Grignardverbindung durch Erhitzen mit Pyridin im Autoklaven gewonnen, liess sich durch Sublimation im Vakuum oder Kristallisation aus Petroläther reinigen und zeigt den Smp. 90–91°. Das Thiazolderivat II konnte aus dem Oxim des 2-Acetylpyridins hergestellt werden, dessen Tosylat zum ω-Aminoacetylpyridin umgelagert wurde. Sodann wurde die Aminogruppe thioformyliert und das erhaltene Derivat mit konz. H_2SO_4 cyclisiert. Die farblose Reinsubstanz schmilzt bei 63–64°. Die Vergleichsverbindung III erhält man aus dem Hydrochlorid des 2-Chlormethylpyridins und dem Natriumsalz von Methylmercaptan. Die wasserhelle Flüssigkeit vom Sdp. 100–105°/17 Torr bildet ein Pikrat vom Smp. 98–99°.

Von diesen Verbindungen gibt das Thiazolderivat II mit Fe^{2+}-Ionen sofort eine sehr deutliche rotviolette Färbung, die wir einem Chelatkomplex zuordnen[3]. Spektrophotometrische Messungen ergaben bei pH 2,5 ein Maximum bei ca. 530 mμ. Der Ligand allein absorbiert in diesem Bereich praktisch nicht, sein Absorptionsmaximum liegt im UV-Gebiet. Über experimentelle Einzelheiten werden wir an anderer Stelle berichten.

Summary. The hitherto unknown compounds 5-(2'-pyridyl)thiazole, 2-(2'-thienyl)pyridine and methyl-α-picolyl sulphide have been synthesized. The structure of all three substances allows the formation of a chelate ring with N and S as ligand atoms. 5-(2'-Pyridyl)thiazole yields with Fe^{2+} at a pH of 2.5 a significant change in absorption, which is attributed to chelate formation.

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und H. ERLENMEYER

Institut für Anorganische Chemie der Universität Basel (Schweiz), 13. März 1964.

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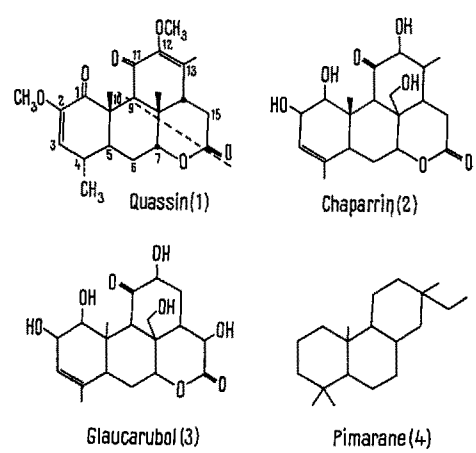
[3] Fe^{3+} gibt keine sichtbare Reaktion.

A Biogenetic Proposal for the Simaroubaceous Bitter Principles[1]

In recent years chemical studies on C-20 bitter principles from the plant family Simaroubaceae have resulted in structural proposals for quassin[2,3] (1), chaparrin[4,5] (2), and glaucarubol[4–6] (3). The known chemistry of other bitter principles of yet unassigned structure from the Simaroubaceae indicates a close relationship to the quassin structure[7–11].

VALENTA et al.[2] have advanced two different biogenetic hypotheses to account for the formation of quassin (1): (a) oxidative coupling of two identical C-10 units as in (1); and (b) rearrangement of a diterpenoid pimarane skeleton (4) through a series of 1, 2 shifts.

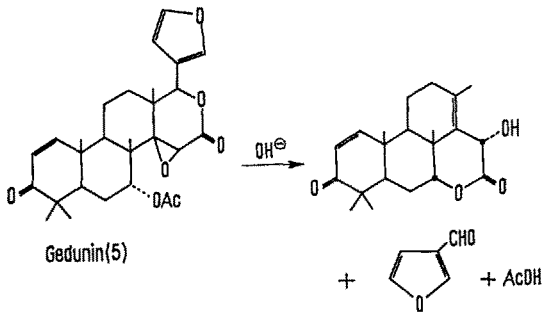
On the basis of arguments to follow, a third pathway is now proposed: That C-26 terpenoids are the precursors of the C-20 bitter principles by loss of a C-5 fragment in a limonol to merolimonol type conversion followed by loss of a methyl group from C_4. The Simaroubaceae, Meliaceae, and the Rutaceae are closely related plant families belonging to the suborder Geraniinese (order Geraniales)[12]. A series of C-26 terpenoids, the limonoids[13], occurs in the families Meliaceae and Rutaceae.



Quassin(1) Chaparrin(2)

Glaucarubol(3) Pimarane(4)

Some of the more important limonoids of these families are cedrelone[14], anthothecol[15], khivorin[16], gedunin[17,18] (5), obacunone[19], limonin[20,21], evodol[22], and nimbin[23]. These C-26 bitter principles form a consistent biogenetic pattern of increasing oxidation level arising from a butyrospermol type tetracyclic triterpene intermediate, as first suggested by ARIGONI et al.[21]. One of the more novel reactions of limonin compounds is the base catalyzed limonol to merolimonol conversion[20], as illustrated in the case of gedunin (5).

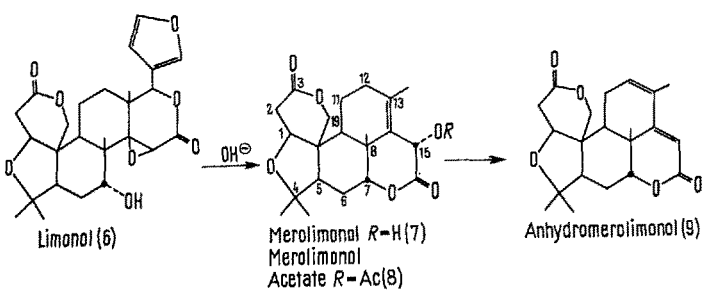


Gedunin(5)

This reaction, which depends upon the presence of an α-hydroxy group at C_7[24], has been used as a diagnostic test for assigning natural products to the limonoid group. The close botanical relationship of these plant families and close structural resemblance of the merolimonol compounds to the C-20 bitter principles suggests that a similar biogenetic pathway with loss of a C-5 fragment occurs in the Simaroubaceae.

Further, the stereochemistry of merolimonol compounds coincides with that advanced for quassin[25] (1) at the asymmetric centers C_5, C_8, C_9, C_{10}, and in particular at C_7. The asymmetric center at C_7 is not uniquely defined by either of the previous biogenetic hypotheses. Since all the known limonoid compounds with a 7-hydroxy group undergo the merolimonol conversion, they must all have the α-configuration at C_7.

Inspection of the NMR spectra of merolimonol (7) and several of its derivatives (Table) show that the H_7 proton is a triplet at ca. δ 4.5 with a small coupling constant of <3 cps. A coupling constant of this magnitude is consistent with an equatorial proton at H_7 which approximately bisects the angle formed by the hydrogens of the adjacent methylene group[26] at C_6.



Limonol(6) Merolimonol R=H(7) Merolimonol Acetate R=Ac(8) Anhydromerolimonol(9)

The coupling pattern of merolimonol (7) is in complete agreement with the values reported for quassin and its derivatives[2] and with arguments advanced for the stereochemistry of quassin[25] at C_7.

Further, GEISSMAN and ELLESTAD[4] have reported that the H_7 proton in chaparrin (2) is a symmetrical triplet occurring at about δ 4.5, thus defining the stereochemistry at C_7. The proton at this position must be equatorial to the B-ring, analogous to merolimonol and quassin.

Merolimonol shows quite different physical properties from limonin derivatives and remarkably similar properties to quassin. Merolimonol and quassin both exhibit high solubility in polar solvents and both are intensely bitter. The absolute configuration of quassin is apparently not known.

Removal of the axial methyl from the gem dimethyl group at C_4 of the merolimonol intermediate to give the C-20 bitter principles occurs presumably through an oxidative decarboxylation process. Nimbin, which on the basis of the available chemical data[23] and biogenetic considerations is best represented by (10), appears to be such an intermediate. One of the C_4 methyls has been

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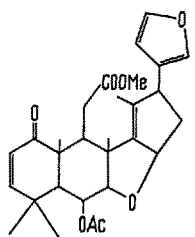
NMR spectra of merolimonol derivatives and quassin[a]

	H_{15}	H_7	H_{19}	H_1	C_{13}	C-methyls at C_8	C_4	Other assignments
Merolimonol (7)	5.09	4.43[e] (<3)	4.29 4.44 (12)	3.98 (3)	1.72 (2)	1.27	1.13 1.05	
Merolimonol acetate (8)	6.09	4.56[d] (<3)	4.32 4.45 (14)	4.01 (3)	1.82	1.27	1.13 1.05	Acetate 2.22
Anhydromerolimonol (9)		4.39[d] (<3)	4.45 4.58 (13)	3.96 (3)	1.87 (1)	1.28	1.18 1.10	H_{12}, H_{14}, 5.57[b] H_{15}, H.., 5.51[c]
Quassin (1)		4.37[d] (<3)				1.22	1.13 (6)	H_3 5.38 (2) H_9, 3.00

[a] The NMR spectra were recorded at 60 mc on a Varian A-60, in deuterochloroform relative to TMS. Coupling constants given in parenthesis c/s. [b] Sharp singlet. [c] Broad, unresolved band. [d] Unsymmetrical; X part of an ABX pattern. [e] Partly obscured by H_{19} resonance.

oxidized to a carboxylic acid group. Decarboxylation can now easily lead to a quassin type A-ring.



Nimbin (10)

This overall biogenetic process would impose certain obvious structural and stereochemical restrictions consistent with structural variations to be found in the limonoids on those simaroubaceous bitter principles of unassigned structure. One could predict that in addition to having the same general stereochemistry as quassin, the C_{15} hydroxy group in glaucarubol (3) should be in the α-configuration[27].

Zusammenfassung. Ein biogenetischer Vorschlag für Simaruba-Bitterstoffe, welcher ihre chemische Struktur, Stereochemie und ihre Entstehung in der Pflanze erklärt, wird vorgelegt.

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[27] *Note added in proof:* J. B-SON BREDENBERG (Chem. and Ind. *1964*, 73) has proposed an identical biogenetic pathway for the simaroubaceous bitter principles. C. R. NARAYANAN et al. (Chem. and Ind. *1964*, 322) has proposed a complete structure for Nimbin[10].

In vitro and *in vivo* Effects of X-Rays and of Iodoacetic Acid on P^{32} Incorporation into Phosphoethanolamine of Rat Thymus Cells

Orthophosphate labelled with P^{32} has been very largely employed in the study of the effects of ionizing radiation on nucleic acid synthesis and on turnover of nucleotides related to that synthesis, in many living systems[1,2]. Only a few authors so far have studied, with the same precursor, the radiation effects on the turnover of phosphorylated non-nucleotide intermediates in nature[3].

The incorporation of P^{32}-orthophosphate into these intermediates has been examined in previous experiments carried out in this laboratory *in vitro* with isolated rat thymus cells[4]. These experiments, dealing with the study of the mechanism of radiosensitizing effect of iodoacetic acid (IAA), showed that both X-rays and IAA induced an inhibition of P^{32}-incorporation only on a single component, which was identified as phosphoethanolamine (PEA).

In the present paper the results of a more detailed study of the effects of X-rays and of IAA on the incorporation of P^{32}-orthophosphate in rat thymocytes *in vivo* and *in vitro* are reported.

Carrier free P^{32}-orthophosphate, from Radiochemical Centre, Amersham, was diluted with inert KH_2PO_4-

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