[1] Tumor Inhibitors. 99. For previous paper in the series, see S. M. KUPCHAN, Recent Adv. Phytochem., in press.
[2] For a recent review see M. N. GALBRAITH, D. H. S. HORN, S. ITÔ, M. KODAMA and J. M. SASSE, Agric. Biol. Chem. *36*, 2393 (1972).
[3] Tumor-inhibitory activity and cytotoxicity were assayed under the auspices of the National Cancer Institute, by the procedures described by R. I. GERAN, N. H. GREENBERG, M. M. MCDONALD, A. M. SCHUMACHER and B. J. ABBOTT (Cancer Chemother. Rep. part 3, *3*, 1 (1972)). Podolide showed significant activity in vivo against P-388 leukemia in mice and cytotoxicity in vitro towards cells derived from both human carcinoma of the nasopharynx (KB) and P-388 murine leukemia.
[4] Podolide was accompanied by trace amounts of its 2,3-dihydro derivative which could be removed by fractional crystallization from methanol.
[5] S. ITÔ, M. KODAMA, M. SUNAGAWA, T. TAKAHASHI, H. IMAMURA and O. HONDA, Tetrahedron Lett. *1968*, 2065.
[6] The diol (**2**) was characterized as its diacetate (**3**), $C_{23}H_{30}O_7$, mp 144–145°.
[7] G. GERMAIN, P. MAIN and M. M. WOOLFSON, Acta cryst. A *27*, 368 (1971).
[8] R. BUCOURT and D. HAINAUT, Bull. Soc. Chim. Fr. *1966*, 501.
[9] S. ITÔ, M. KODAMA, M. SUNAGAWA, M. KOREEDA and K. NAKANISHI, Chem. Commun. *1971*, 855.
[10] S. M. KUPCHAN and R. M. SCHUBERT, Science *185*, 791 (1974).
[11] We thank Dr. R. E. PERDUE, JR., U.S.D.A., for supplying the plant material (collected in Ethiopia in November, 1964). The work was supported by grants from the National Cancer Institute (CA-11718 and CA-11760) and the American Cancer Society (CI-102J), and a contract with the Division of Cancer Treatment, National Cancer Institute (NO1-CM-12099).

A stereoscopic representation of the molecular structure of (**1**) is shown in the Figure. The double bond in ring *A* is identified as C (2)–C (3). The lactone ring is a C (5) envelope, the cyclohexene and cyclohexane rings have slightly distorted 1,2-diplanar (*sofa*) conformations, while the pyran ring has a slightly distorted 1,3-diplanar conformation[8].

The absolute configuration of podolide (**1**) was assigned on the basis of the observation of a negative Cotton effect in the CD spectrum, $[\Phi]_{262}^{MeOH} - 15{,}090$[5,9]. Studies are in progress to determine the relative importance of the α,β-unsaturated δ-lactone, epoxide[10], and other functions with respect to the tumor-inhibitory activity of podolide[11].

Zusammenfassung. Nachweis, dass Podolid, ein neues antileukämisches norditerpinisches Dilacton aus *Podocarpus gracilior* Pilg. die Struktur (**1**) besitzt.

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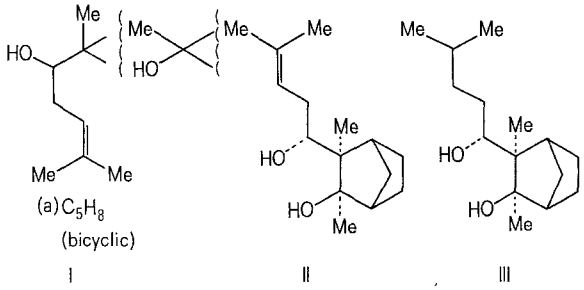
The Structure of Clausantalene, a New Sesquiterpene from *Clausena indica* Oliv.[1]

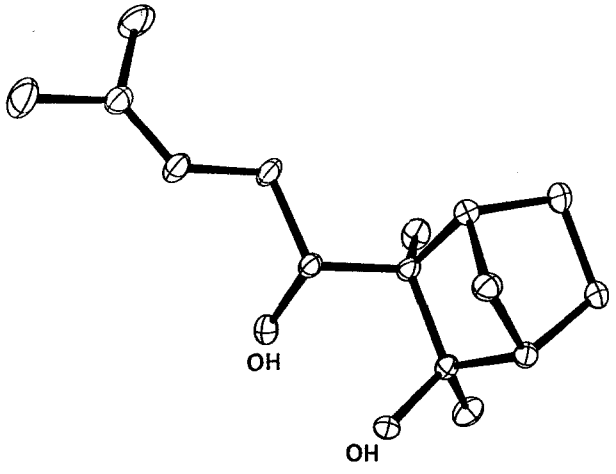
From the roots of *Clausena indica* Oliv. (Rutaceae) some known coumarins[2], a new cyclopropyl coumarin[3] and two new carbazole alkaloids[4,5] have been isolated. In this communication we report isolation of a new sesquiterpene designated clausantalene and its structure determination based on spectral and X-ray crystallographic data. Hexane extract of the roots, on careful chromatographic separation on silica gel and preparative TLC, gave about 0.01% yield of colourless crystals of clausantalene $C_{15}H_{26}O_2$, m.p. 114°, $[\alpha]_D + 27.7°$ (C 1.9, $CHCl_3$) (Rf 0.55, $CHCl_3 - 2\%$ MeOH; TLC Si gel). It has no UV-absorption and its IR-spectrum indicated the presence of hydroxyl groups (3380 cm^{-1}). Its mass spectrum showed a negligible molecular ion peak at *m/e* 238 and a base peak at *m/e* 220 ($M^+ - H_2O$). The other major fragment ions at *m/e* 177 ($220 - C_3H_7$), 151 ($220 - C_5H_9$) suggested the presence of an isopentenyl chain. This was confirmed by its NMR spectrum (100 MHz, $CDCl_3$) which showed gem-dimethyls at δ 1.65 and 1.72 (3H each, J = 1 Hz), and a slightly split triplet at δ 5.25 (1H, J = 7 Hz) assigned to an olefinic proton adjacent to an unsubstituted methylene group appearing at δ 2.1 (confirmed by decoupling). Irradiation at δ 1.72 sharpened the triplet at δ 5.25. A one-proton triplet at 3.88 (J = 7 Hz), also coupled to the methylene protons at δ 2.1 as shown by double resonance experiments, indicated that the proton should be placed on a methylene carbon having an oxygen function. 2 broad signals (1H each) at δ 2.7 and 3.3 vanished on deuteration, indicating the presence of 2 hydroxyl groups. 2 tertiary methyls appeared at δ 0.9 and 1.2, of which the latter should be due to a methyl on a carbon bearing a hydroxyl group. Hydrogenation over Pd-C or PtO_2 afforded dihydroclausantalene $C_{15}H_{28}O_2$, m.p. 102° $[\alpha]_D + 16.6°$ (C 2, $CHCl_3$) by reduction of the isopentenyl double bond. Since the dihydroderivative does not contain any unsaturation (NMR; no tetranitromethane colour), clausantalene should be a bicyclic sesquiterpene containing the 5-carbon chain (a). A partial structure (I) could be written on the evidence cited above and clausantalene should therefore belong to the sesquicarane, bergamotane or β-santalane types[6].



I II III

[1] Contribution No. 377 from Ciba-Geigy Research Centre.
[2] B. S. JOSHI, V. N. KAMAT and D. H. GAWAD, Phytochemistry *10*, 480 (1971).
[3] B. S. JOSHI, V. N. KAMAT and D. H. GAWAD, Experientia *30*, 223 (1974).
[4] B. S. JOSHI and D. H. GAWAD, Indian J. Chem. *10*, 1123 (1972).
[5] B. S. JOSHI and D. H. GAWAD, Indian J. Chem. *12*, 437 (1974).
[6] T. K. DEVON and A. I. SCOTT, *Handbook of Naturally Occurring Compounds* (Academic Press, New York 1972), Vol. 2, p. 55.

Clausantalene and dihydroclausantalene failed to give an acetyl derivative under mild acetylation conditions. As attempts to correlate the carbocyclic ring system with one of the already known sesquiterpene skeleta failed, and a variety of reactions yielded unsaturated products or intractable mixtures, an X-ray study was undertaken.



Clausantalene ($C_{15}H_{26}O_2$) crystallizes as clear regular rectangular blocks; they are *ortho*rhombic, space group $P2_12_12_1$, a = 8.205, b = 8.488, c = 20.616 Å, Z = 4 mols/cell. Intensities of 1594 reflections were measured on a Siemens diffractometer with Cu-K_α radiation (to $\Theta = 70°$), and of these 45 were reckoned unobserved. The structure was solved by direct methods and is currently refined to R = 0.11. The molecular arrangement is given by II, and, by implication, that of dihydroclausantalene by III. The Figure shows a perspective view of the molecule (or its enantiomorph). The hydroxy groups are linked by both intra-(2.68 Å), and inter-(2.82 Å) molecular hydrogen bonds to form continuous chains running parallel to a.

An attempt will be made to determine the absolute configuration by allowing for anomalous scattering by oxygen, but this cannot be done until the structure is fully refined and may not prove possible in view of the small amount of oxygen in the molecule.

The occurrence of a santalane type sesquiterpene from the Rutacea family may be of some taxonomic interest[7].

Zusammenfassung. Es wurde ein neues Sesquiterpen $C_{15}H_{26}O_2$ (Clausantalene) aus den Wurzeln von *Clausena indica* Oliv. (Rutacene) isoliert. Spektralanalytische und röntgenkristallographische Daten ermittelten ein β-Santalan-Derivat.

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The Structure of Quimbeline, a New Bisindole Alkaloid from *Voacanga chalotiana*

The root bark of *Voacanga chalotiana* has been found to contain, beside a number of known indole alkaloids and three new bases[1], considerable quantities of vobtusine (II) and minor amounts of a closely related compound, which we have named quimbeline, $C_{43}H_{48}N_4O_6$, m.p. 270°, $[\alpha]_D$ — 195° (c1, $CHCl_3$). The gross structure of vobtusine has been determined mainly on the basis of spectroscopic considerations[2], while the location of the hydroxyl function at C-2′ and the configuration of the C-7 spiral centre were established by X-ray investigation[3]. The complete structural proposal I for quimbeline is based almost entirely on a mass spectrometric and ^{13}C-NMR investigation in comparison with vobtusine, the information to be gained from ^{1}H-NMR-spectrum being minimal owing to the complexity of the molecule.

The close relationship between the 2 alkaloids is apparent from the similarity of their IR- and UV-spectra. Quimbeline shows UV-absorption maxima (MeOH) at 221, 263, 301, 327 nm (lg ε 4.54, 4.05, 4.15, 4.21 respectively) and IR stretching bands ($CDCl_3$) at 3390 (NH), 1675 and 1610 (–N–C=C–CO_2Me) cm^{-1}, which agree for the presence of the N-alkyl-methoxy-indoline and β-anilino-acrylic ester groupings[2]. The ^{1}H-NMR-spectrum of quimbeline ($CDCl_3$, 100 MHz) shows a broad singlet at δ 8.95 (NH), an aromatic pattern superimposable to that of vobtusine, 2 singlets at δ 3.80 and 3.74 (CO_2*Me* and ArO*Me*) and 1 proton at δ 4.95 as a doublet (J = 14 Hz). The latter signal is due to one of the C-8 protons, which demonstrates the deshielding effect of the lone pair of the indoline N_a nitrogen atom, and is diagnostic for the configuration at C-7. In vobtusine this signal falls at δ 5.14, whereas the ^{1}H-NMR-spectrum of amataine[4], an alkaloid possessing the vobtusine skeleton with an opposite configuration at C-7, lacks of such signal.

Quimbeline contains 2 less hydrogens than vobtusine. Owing to the lack of further sp^2 carbon atoms in the ^{13}C-NMR-spectrum and to the presence of only 1 active hydrogen (NH), the additional unsaturation is due to the formation of an ethereal linkage involving the hydroxyl function of vobtusine and 1 of the neighbouring carbon

[1] B. Gabetta, E. M. Martinelli and G. Mustich, Fitoterapia *45*, 32 (1974).
[2] J. Poisson, M. Plat, H. Budzikiewicz, L. J. Durham and C. Djerassi, Tetrahedron *22*, 1075 (1966).
[3] J. Naranjo, M. Hesse and H. Schmid, Helv. chim. Acta *55*, 1849 (1972), footnote.
[4] N. Kunesch, B. C. Das and J. Poisson, Bull. Soc. Chim. fr., *1970*, 4370. – V. Agwada, M. B. Patel, M. Hesse and H. Schmid, Helv. chim. Acta *53*, 1567 (1970).