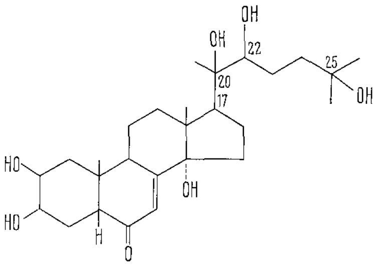
Isolation of Commisterone, a New Phytoecdysone from *Cyanotis vaga*[1]

A report[2] on the supposed effective control of cancer of the breast through the external application of a poultice prepared from the herb *Cyanotis vaga* (Lour.) Schultes[3] (Commelinaceae; Chinese name 'que che hong', tongue of a rooster) has induced us to undertake the present chemical study. It is further reported that a decoction of this plant relieves high fever and causes a feeling of well-being or elation.

Very little work has been done on the Commelinaceae. The flowers of *C. communis* are reported[4] to contain commelinin, a crystalline blue metalloanthocyanin believed to consist of 4 molecules of awokinin (delphinidine-3, 5-diglucoside plus coumaric acid held together with one atom of magnesium and weakly linked to a yellowish substance of unknown structure).

In the present study, the comminuted leaves of *Cyanotis vaga* were extracted in a soxhlet first with n-hexane and afterwards with benzene. Chromatography of the vacuum distillation residue of benzene on silica gel (70–325 mesh, E. Merck) and elution with ethylacetate yielded, in the middle fractions, colorless prisms melting at 146–151 °C in about 0.7% yield. The crystals were slightly soluble in benzene and chloroform, and moderately soluble in acetone, methanol and ethanol. They were chromatographically uniform: Silica gel G: Rf 0.37 (acetone), 0.55 (ethylacetate), 0.7 (ethanol).

The spectrometric properties of this substance, for which we propose the name commisterone, suggest strongly that it is either the insect-moulting hormone 20-hydroxy-ecdysone[5] (variously named 'crustecdysone', 'ecdysterone', 'polypodine A'), or a stereoisomer.



I. Crustecdysone

The IR-spectrum is characterized by an intense absorption centered at 3400 cm^{-1} (νOH) and a carbonyl absorption at 1660 cm^{-1} (β,β-disubstituted enone). This enone grouping is confirmed by the UV-absorption at 244 nm ($\varepsilon = 10{,}500$, MeOH). The mass spectrum[6] shows a weak molecular ion M^+ at *m/e* 480 and a series of peaks at *m/e* 462 (M-H_2O), 444 (M-2H_2O), 426 (M-3H_2O) and 408 (M-4H_2O), which have been reported to be characteristic of crustecdysone (I)[5,7,8] and its isomers 22-isocrustecdysone[9] and pterosterone (2, 3, 14, 20, 22, 24-Hexahydroxy-coprost-7-en-6-on)[10]. High resolution mass measurement of peak *m/e* 462 (M-H_2O) shows that commisterone itself has the molecular formula $C_{27}H_{44}O_7$. We also find peaks at *m/e* 99 (parent peak) and at *m/e* 81 (35% relative intensity), corresponding to side chain cleavage at C_{20}/C_{22} (Figure), as well as the nuclear fragment at

Table I. Mass spectral[6] data of commisterone, isolated from *Cyanotis vaga*

m/e	Exact mass		Composition	Origin	Metastable ion, m*	
	Found	Calculated			Found	Calculated
462	462.2980	462.2981	$C_{27}H_{42}O_6$	M-H_2O		
444			$C_{27}H_{40}O_5$	M-2H_2O		
426	426.2772	426.2770	$C_{27}H_{38}O_4$	444-H_2O	408.8	408.73
408			$C_{27}H_{36}O_3$	426-H_2O	390.7	390.76
363	363.2172	363.2171	$C_{21}H_{31}O_5$			
345			$C_{21}H_{29}O_4$	363-H_2O	328.0	327.89
327			$C_{21}H_{27}O_3$	345-H_2O	310.2	309.94
309			$C_{21}H_{25}O_2$	327-H_2O (?)	292.5	291.99
300	300.1730	300.1725	$C_{19}H_{24}O_3$			
285	285.1849 (73%)	285.1854	$C_{19}H_{25}O_2$			
	285.1488 (27%)	285.1491	$C_{18}H_{21}O_3$			
269	269.1544	269.1541	$C_{18}H_{21}O_2$			
250	250.1565	250.1569	$C_{15}H_{22}O_3$			
99	99.0810 (86%)	99.0810	$C_6H_{11}O$			
	99.0446 (14%)	99.0446	$C_5H_7O_2$			
143			$C_8H_{14}O_2$			
125			$C_8H_{12}O$	143-H_2O	109.3	109.27
81			C_6H_9	99-H_2O	66.25	66.27

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[1] Dedicated to Prof. Dr. R. Tschesche, Organisch-Chemisches Institut, Universität Bonn (Germany) on the occasion of his 65th birthday, for the invaluable help and inspiration he has given us.

[2] Reported by Forester Marcelino Punzalan of Canaman, Camarines Sur (Philippines) who provided us with a generous supply of plant material, for which we express our gratitude.

[3] We thank Prof. C. G. G. J. van Steenis and Dr. R. C. Bakhuizen van den Brink jr., Leiden (Netherlands) and Mr. Hermes Gutierrez, Chief Botanist, National Museum of the Philippines, for the identification of the specimen.

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[6] The mass- and NMR-spectra were made through the kindness of Prof. R. Tschesche and Dr. H.-W. Fehlhaber of the Organisch-Chemisches Institut, Universität Bonn (Germany), to whom we express our gratitude. Mass spectrometer: MS 9 (Associated Electrical Industries, London); direct inlet system, ion source temperature = 200 °C; ionization energy = 70 eV, with an ionizing current of 100 μa; resolution = 14,000. NMR: Varian A-60.

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m/e 363 ($C_{21}H_{31}O_5$) produced by this cleavage. In addition, we also find fragments at *m/e* 345 ($C_{21}H_{29}O_4$, 363-H_2O, m* 328.0), 327 ($C_{21}H_{27}O_3$, 345-H_2O, m* 310.2), 300 ($C_{19}H_{24}O_3$), all of which constitute characteristic fragments obtained with crustecdysone[5,11]. These and other significant peaks are reproduced in Table I.

On the basis of the spectroscopic data and melting points, commisterone (mp 146–151°) is not identical with any of the related compounds with molecular formula of $C_{27}H_{44}O_7$, with insect-moulting properties so far reported: crustecdysone (I), mp 235–236°[7], 22-isocrustecdysone, mp 259–260°[9], pterosterone, mp 229–230°[10], inokosterone, mp 255 (decomp.)[12], and ponasterone C, mp 270–272°[13]. Pterosterone[10] and ponasterone C[13] would be excluded since they give doublets at 9.00 (J = 6, pyridine), while commisterone as also crustecdysone[14] give singlets at 8.91[15] and 8.87[16] respectively.

Comparison of the IR-spectrum of commisterone with that of crustecdysone[5] in KBr shows essential identity in the region 400–1500 cm^{-1} but great dissimilarity in the fingerprint region. Similarly, comparison of the NMR-spectra of the 2 compounds shows close resemblance but not identity of the resonance signals of principal groups (Table II).

Table II. Proton chemical shifts of commisterone and crustecdysone in τ values, relative to TMS

Compound	C-18, C-19	O-H	H-7	C-26,
Crustecdysone[14,16]	9.18 (3 H) 9.10 (3 H)	5.43 (1 H) 5.66 (2 H) 5.79 (1 H) 5.91 (1 H) 6.50 (1 H)	4.35	8.87 (9 H)
Commisterone[15]	9.21 (3 H) 9.15 (3 H)	5.29 (1 H) 5.56 (1 H) 5.64 (2 H) 5.85 (1 H) 6.41 (1 H)	4.32	8.91 (9 H)

From the foregoing information, we infer that commisterone has the same skeletal and side chain structure as crustecdysone and must be stereoisomeric with it. Work is now in progress on the stereochemistry of commisterone[17].

Zusammenfassung. Aus den zerkleinerten Blättern von *Cyanotis vaga* (Commelinaceae) wurde durch Benzolextraktion und Chromatographie mit Silikagel eine neue Substanz isoliert: $C_{27}H_{44}O_7$ (Sp. 146–151°), die nach den spektrometrischen Daten (IR, NMR, UV, MS) mit dem Insektenhormon Ecdysteron stereoisomer ist.

A. C. Santos[18], M. T. Chua[19],
N. Eufemio[18] and C. Abela[18]

National Research Council of the Philippines
Diliman, Q. C. (Philippines), 6 April 1970.

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[16] In hexadeuterodimethylsulfoxide containing deuterochloroform, using hexamethyldisiloxane (HMDS) as internal standard. Value given has been corrected to give chemical shift relative to tetramethylsilane.

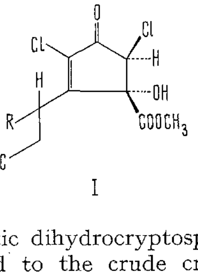
[17] We wish to express our gratitude to the National Research Council of the Philippines for supporting this work.

[18] Chemistry Department, Araneta University Foundation.

[19] Department of Chemistry, Ateneo de Manila University.

The Total Synthesis of Racemic Cryptosporiopsin, a Fungitoxic Antibiotic

Synthesis of a racemic dihydro derivative (I, R=H) of the fungitoxic metabolite cryptosporiopsin II[1,2], by a four-step sequence involving skeletal rearrangement of *meta-n*-propyl phenol through the agency of alkaline hypochlorite, has recently been reported[3]. Conversion of synthetic dihydrocryptosporiopsin to racemic cryptosporiopsin has now been realized, constituting a total synthesis of the antibiotic.



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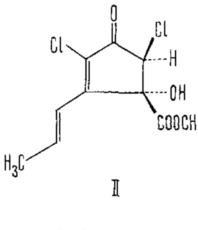

II

Synthetic dihydrocryptosporiopsin[3] was converted in 98% yield to the crude crystalline allylic bromide I (R=Br) by the Wohl-Ziegler reaction[4]. A sample, recrystallized from cyclohexane, had mp 116–121°; it displayed a molecular ion at *m/e* 344 (with appropriate isotope peaks[5]) in the mass spectrum, and UV λ_{max} (EtOH) at 252 nm (ε 7500).

Reaction with dimethylformamide[6] proved to be the most effective method for converting I (R=Br) to racemic cryptosporiopsin. Attempts to effect the required dehydrobromination under a variety of other conditions were attended by extensive decomposition. Thus, a solution of I (R=Br) (1.03 m*M*) in dry dimethylformamide (5 ml) was heated at 135–140 °C for 20 min in a nitrogen atmosphere. Preparative layer chromatography of the

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