

Table IX. 7-Acetoxy-3,5,8-trimethoxyflavones 5, 5,7-Diacetoxy-3,8-dimethoxyflavones 6, and 3,7-Diacetoxy-5,8-dimethoxyflavones 7

compd	mp (°C)	recrystn solvent	formula	found		calcd	
				C	H	C	H
5a	174-175	MeOH	C ₂₁ H ₂₀ O ₈	62.95	4.99	62.99	5.04
5b	166-167	MeOH	C ₂₂ H ₂₂ O ₉	61.04	5.01	61.39	5.15
5c	169-170	MeOH	C ₂₃ H ₂₄ O ₁₀	60.02	5.18	60.00	5.25
5d	156-157	MeOH	C ₂₃ H ₂₂ O ₁₀	60.36	4.92	60.26	4.84
5e	168-169	MeOH	C ₂₄ H ₂₂ O ₁₁	59.19	4.43	59.26	4.56
(lit. ² 172-173)							
6a	165-166	MeOH	C ₂₂ H ₂₀ O ₉	61.63	4.68	61.68	4.71
(lit. ¹⁰ 166.5-167.5)							
6b	144-145	MeOH	C ₂₃ H ₂₂ O ₁₀	60.35	4.83	60.26	4.84
6c	136-137	MeOH	C ₂₄ H ₂₄ O ₁₁	58.89	4.88	59.01	4.95
(lit. ¹⁴ 165-167)							
(lit. ¹⁵ 152)							
6d	138-139	MeOH	C ₂₄ H ₂₂ O ₁₁	59.26	4.65	59.26	4.56
(lit. ¹¹ 140-141 and 147-148.5)							
6e	156-157	MeOH	C ₂₅ H ₂₂ O ₁₂	58.10	4.25	58.37	4.31
(lit. ² 158-160)							
(lit. ¹² 157-158)							
7a	148-150	aqueous MeOH	C ₂₂ H ₂₀ O ₉	61.58	4.91	61.68	4.71
(lit. ¹³ 154)							
7b	170-171	MeOH	C ₂₃ H ₂₂ O ₁₀	60.24	4.62	60.26	4.84
7c	146-147	MeOH	C ₂₄ H ₂₄ O ₁₁	58.93	4.78	59.01	4.95
7d	157-158	aqueous MeOH	C ₂₄ H ₂₂ O ₁₁	59.00	4.58	59.26	4.56
7e	99-101	MeOH	C ₂₅ H ₂₂ O ₁₂	58.08	4.56	58.37	4.31

with chloroform-ethyl acetate (10:1). The 5- and 3-hydroxyflavones were obtained from the first and second eluates, respectively. The demethylated products from 1d and 1e were separated by preparative HPLC using methanol as eluent. 5-Hydroxy-3,4',7,8-tetramethoxyflavone (9):¹⁰ yellow needles from methanol, mp 167-168 °C. 3-Hydroxy-4',5,7,8-tetramethoxyflavone (10):¹ yellow prisms from methanol, mp 198-200 °C.

5-Hydroxy-3,4',7-trimethoxyflavone (12): yellow prisms from ethyl acetate-hexane, mp 145-146.5 °C (lit.²³ mp 152-153 °C). 3-Hydroxy-4',5,7-trimethoxyflavone (13): yellow needles from chloroform-ethyl acetate, mp 147.5-148.5 °C (lit.²³ mp 149-150 °C). 5-Hydroxy-3,4',6,7-tetramethoxyflavone (15):¹⁰ pale yellow prisms from chloroform-ethyl acetate, mp 168-169 °C. The other flavones 2 and 3 as yellow needles or prisms are shown in Table VIII.

Acetylation of the Hydroxyflavones. All of the hydroxyflavones were easily acetylated by the hot acetic anhydride-pyridine method to give the corresponding acetates as colorless needles. The results are shown in Table IX.

Registry No. 1a, 85734-53-8; 1b, 33554-63-1; 1c, 110193-72-1; 1d, 22109-96-2; 1e, 7678-88-8; 2a, 1570-09-8; 2b, 42923-42-2; 2c, 62953-00-8; 2d, 14965-08-3; 2e, 4988-22-1; 3a, 95125-09-0; 3b, 110193-74-3; 3c, 110193-75-4; 3d, 33554-57-3; 3e, 110193-76-5; 4a, 110193-77-6; 4b, 110193-78-7; 5a, 110193-79-8; 5b, 110193-80-1; 5c, 110193-81-2; 5d, 23344-33-4; 5e, 20972-77-4; 6a, 5128-43-8; 6b, 110193-82-3; 6c, 62953-04-2; 6d, 15085-75-3; 6e, 4853-12-7; 7a, 95626-26-9; 7b, 110193-83-4; 7c, 110193-84-5; 7d, 110193-85-6; 7e, 110193-86-7; 8, 24027-55-2; 9, 15486-34-7; 10, 24027-55-2; 11, 16692-52-7; 12, 15486-34-7; 13, 5631-70-9; 14, 4472-73-5; 15, 14787-34-9; 2,4-dihydroxy-3,6, ω -trimethoxyacetophenone, 42923-40-0; 4'-(benzyloxy)-7-hydroxy-3,3',5,8-tetramethoxyflavone, 110205-36-2; 3',4'-bis(benzyloxy)-7-hydroxy-3,5,8-trimethoxyflavone, 110193-73-2; 4-methoxybenzoic anhydride, 794-94-5; 3,4-dimethoxybenzoic anhydride, 24824-54-2; 3,4,5-trimethoxybenzoic anhydride, 1719-88-6; 4-(benzyloxy)-3-methoxybenzoic anhydride, 1592-47-8; 3,4-bis(benzyloxy)benzoic anhydride, 1592-48-9; potassium 4-methoxybenzoate, 52509-81-6; potassium 3,4-dimethoxybenzoate, 25635-53-4; potassium 3,4,5-trimethoxybenzoate, 29970-25-0; potassium 4-(benzyloxy)-3-methoxybenzoate, 110193-70-9; potassium 3,4-bis(benzyloxy)benzoate, 110193-71-0.

(23) Guider, J. M.; Simpson, T. H.; Thomas, D. B. *J. Chem. Soc.* 1955, 170-173.

Marine Alkaloids. 12.¹ Chartellines, Halogenated β -Lactam Alkaloids from the Marine Bryozoan *Chartella papyracea*

Uffe Anthoni, Lionel Chevotot,² Charles Larsen, Per H. Nielsen, and Carsten Christophersen*

Marine Chemistry Section, Department of General and Organic Chemistry, The H. C. Ørsted Institute, University of Copenhagen, DK-2100 Copenhagen, Denmark

Received December 4, 1986

The isolation and structure elucidation of three new β -lactam indole alkaloids, chartellines B and C and methoxydechlorochartelline A, from the marine bryozoan *Chartella papyracea* are described. The chartellines only differ in the number and position of the bromo substituents. Dechloro-3-methoxychartelline A is an artifact formed during the isolation procedure and is synthesized from chartelline A. All four alkaloids have the S configuration.

Bryozoans have lately emerged as a source of biologically active compounds. The prospect of identifying new interesting compounds from this large invertebrate phylum is thus quite encouraging. The limited number of studies reported so far³ is at least in part due to difficulties in

securing enough material for serious investigations to be performed. Many bryozoan species are adapted to an

(3) (a) Christophersen, C. *Acta Chem. Scand., Ser. B* 1985, B39, 517 and references cited therein (review). (b) Blackman, J.; Matthews, D. J. *Heterocycles* 1985, 23, 2829. (c) Laycock, M. V.; Wright, J. L. C.; Findlay, J. A.; Patil, A. D. *Can. J. Chem.* 1986, 64, 1312. (d) Keil, P.; Nielsen, E. G.; Anthoni, U.; Christophersen, C. *Acta Chem. Scand., Ser. B* 1986, B40, 555. (e) Pettit, G. R.; Kamano, Y.; Aoyagi, R.; Herald, C. L.; Doubek, D. L.; Schmidt, J. M.; Rudloe, J. J. *Tetrahedron* 1985, 41, 985. (f) Pettit, G. R.; Kamano, Y.; Herald, C. L. *J. Nat. Prod.* 1986, 49, 661.

(1) Part 11: Reference 4.

(2) Present address: UA CNRS 322, Université de Bretagne Occidentale, 29287 Brest, France.

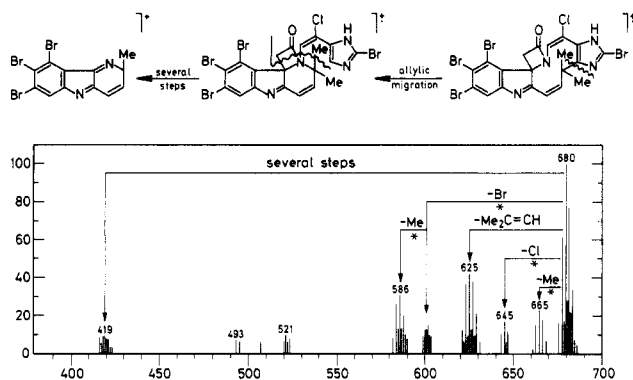
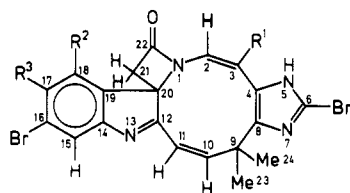


Figure 1. Mass spectrum of chartelline A (3). Fragmentation routes marked with an asterisk are supported by metastable ions. Only the main peaks of the isotopic clusters are given.

epiphytic way of life, making the collection of sufficient amounts an extremely tedious task. Furthermore, the taxonomy is complicated and requires the intervention of a trained taxonomist in order to identify and sort a collection. On the other hand, some marine bryozoans are free growing and can be collected in large quantities when their habitats are known. Among the latter is *Flustra foliacea* L., the source of a series of bromo-substituted indole alkaloids.^{3a,c,d} Recently another member of the same family (Flustridae) namely *Chartella papyracea* (Ellis and Solander) has yielded a new type of indole alkaloid named chartelline A.⁴ Owing to the extraordinary structural



1. $R^2 = R^3 = H$, $R^1 = Cl$, Chartelline C
2. $R^3 = H$, $R^1 = Cl$, $R^2 = Br$, Chartelline B
3. $R^1 = Cl$, $R^2 = R^3 = Br$, Chartelline A
4. $R^1 = OMe$, $R^2 = R^3 = Br$, Methoxy-dechlorochartelline A

features of chartelline A, i.e., a β -lactam ring condensed with a 10-membered ring, the remaining alkaloids of *C. papyracea* were further studied. We now report the isolation and structure elucidation of three novel alkaloids secured from this bryozoan, together with assignments of the spectral data of chartelline A.

Results and Discussion

Isolation. The alkaloids were isolated from the ethyl acetate extract of lyophilized bryozoans defatted with petroleum ether. Cellulose chromatography followed by recrystallization from ethyl acetate afforded a crude alkaloid mixture that yielded to HPLC separation. Chartelline A was the main alkaloid (ca. 75%), while about 10% of the mixture consisted of methoxydechlorochartelline A, chartellines B and C, and at least 10 minor alkaloids. The mother liquor from the recrystallization contained about 15% of two β -lactam alkaloids with a new skeleton. The structures of these compounds will be published elsewhere.

Structure Elucidation. The spectral data indicated that the three components of the most polar fraction of

Table I. 1H NMR Assignments of Selected Isomers of 1-4^a

	1 ^b	2 ^b	3 ^b	4 ^b
H2	7.09 (s)	7.07 (s)	7.06 (s)	6.29 (s)
H5	9.02 (s)	9.01 (s)	9.10 ^c (s)	9.28 (s)
H10	6.07 (d)*	6.05 (d)*	6.02 (d)*	5.98 (d)*
H11	6.10 (d)*	6.10 (d)*	6.08 (d)*	6.09 (d)*
H15	7.61 (d)	7.56 (d)*	7.71 (s)	7.72 (s)
H17	7.42 (dd)	7.52 (d)*		
H18	7.17 (d)			
	3.18 (d)	3.22 (d)	3.21 (d)	3.13 (d)
2 H21	3.33 (d)	3.42 (d)	3.43 (d)	3.41 (d)
3 H23	1.51 (s)*	1.49 (s)*	1.49 (s)*	1.46 (s)*
3 H24	1.54 (s)*	1.55 (s)*	1.55 (s)*	1.54 (s)*
CH ₃ O				3.62 (s)

^a Assignments of chemical shifts (ppm, in CDCl₃) for closely spaced peaks are marked with an asterisk and may be reversed.
^b Coupling constants (hertz) for 1-4 are essentially the same: $J_{10,11} = 12$; $J_{15,17} = 1$; $J_{17,18} = 8$; $J_{21,21'} = 15-16$.
^c This value may vary.

C. papyracea possessed identical skeletons, differing in the number of bromine substituents in the benzene ring. Since one of the components was identical with chartelline A (3) for which a complete X-ray structure has been reported,⁴ it served as a convenient starting point for the structure determination of the two other components, chartelline B (2) and chartelline C (1).

The EI mass spectrum of chartelline A displayed an intense molecular ion peak (m/z 680) with the isotopic pattern characteristic for Br₄Cl (see Figure 1). The most abundant fragment ion at m/z 625 indicated an initial allylic fission with subsequent loss of Me₂C=CH from the isoprene unit linking the indolenine and imidazole rings. Less intense fragment peaks at m/z 665 and 645 represent loss of methyl and chlorine radicals from the molecular ion, respectively. The latter fragmentations are supported by metastable ions. A pronounced fragmentation pathway, m/z 680 \rightarrow 601 \rightarrow 586 (also supported by metastable ions), corresponds to loss of a bromine radical from the molecular ion followed by loss of a methyl radical from m/z 601. The main peak of the M⁺ - Br cluster is actually m/z 602, presumably signifying a small impurity of chartelline B. Analogously, m/z 521 may contain a minor impurity of chartelline C (m/z 522). Otherwise this cluster ion may originate from M⁺ by successive loss of a methyl radical and the dihydrobromoimidazole fragment. Another important fragmentation route, involving loss of ketene from the β -lactam ring, was indicated by the prominent metastable near m/z 599, though the corresponding fragment ion at m/z 638 is not very abundant. In support, an isotopic cluster centered at m/z 419 may represent the pyridoindole cation arising from allylic migration followed by loss of the N-substituents. Since the mass spectra of the two other chartellines displayed virtually identical fragmentation patterns (see the Experimental Section) they are assigned a similar skeleton structure. The characteristic isotopic patterns of the molecular ions established the elemental compositions C₂₀H₁₅Br₂ClN₄O for chartelline C and C₂₀H₁₄Br₃ClN₄O for chartelline B.

The possibility remained that the peaks assigned to molecular ions for 1 and 2 were in fact fragment ions. However, the 1H NMR spectra of 1-3 (Table I) showed conclusively that the bromine substitution increased stepwise from chartelline C to chartelline A. It should be noted that the chartellines in solution occur as a mixture of two tautomers arising from the N5-N7 shift of hydrogen in the imidazole ring. The spectral data given in Table I correspond to the major isomer (also shown in Scheme I), which contains the N5-H group (9-9.3 ppm in CDCl₃).

At high field, chartelline A (3) showed two singlets from the methyl groups (1.49 and 1.55 ppm) followed by the AB

(4) Chevolut, L.; Chevolut, A.-M.; Gajhede, M.; Larsen, C.; Anthoni, U.; Christophersen, C. *J. Am. Chem. Soc.* 1985, 107, 4542.

Table II. ^{13}C NMR Assignments of Selected Isomers of 3 and 4^a

carbon	2	3 ^b	4
2	148.7	148.7	102.8
3	113.6*	113.9*	148.7*
4	132.6*	131.8	143.4*
6	121.2*	119.3*	132.0*
8	126.3*	127.6*	130.2*
9	37.5	37.6	37.5
10	122.2*	122.2*	123.8*
11	122.8*	123.9*	127.3*
12	177.9	178.9	179.3
14	152.2	153.9	154.1
15	115.6	115.8	116.1*
16	125.0*	126.4*	125.9*
17	133.8*	120.9*	120.9*
18	124.5*	118.3*	118.4*
19	137.5*	137.5	137.8*
20	71.9	72.8	72.9
21	44.8	44.9	43.7
22	161.9	162.0	163.4
23	26.9*	26.7*	26.2*
24	29.1*	29.0*	29.3*
OCH ₃			56.2

^a Assignments of chemical shifts (ppm, in CDCl₃) for closely spaced peaks are marked with an asterisk and may be reversed. ^b Quaternary carbon, CH, CH₂, and CH₃ were identified by DEPT sequence.

pattern of the lactam CH₂ group [3.21 and 3.43 ppm (J_{gem} = 16 Hz)]. At low field the *cis*-ethylenic protons were found [6.02 and 6.08 ppm (J = 12 Hz)], while a further low-field shift of the remaining ethylenic proton (7.06 ppm) was caused by the deshielding effect of the nitrogen function at C2. The close correspondence of the data obtained for 1 and 2 established the common structure of this part of the molecule. On the other hand, the signals arising from the aromatic protons reflected the difference in Br substitution. Thus, in 3 the peak at 7.71 ppm could unambiguously be assigned the C15-H. In 1, a corresponding signal at 7.61 ppm showed a meta coupling to C17-H (7.42 ppm), the latter coupling ortho to C18-H (7.17 ppm). This supports the formulation of chartelline C as the C16-Br isomer (1). In 2, the two signals at 7.52 and 7.56 ppm with a coupling constant of 1 Hz corresponded to the presence of C15-H and C17-H, and chartelline B is therefore assigned the structure of the C16-Br, C18-Br isomer 2. These data do not unambiguously exclude the C17-Br substitution pattern for 1 and the C16-Br, C17-Br substitution pattern for 2. However, support for the proposed structures was obtained from solvent dependence studies of the ¹H NMR signals of 2 and 3.⁵

The mass spectrum of methoxydechlorochartelline A (4) displayed an abundant molecular ion at m/z 676 identified by the isotopic cluster as C₂₁H₁₆Br₄N₄O₂ corresponding to chartelline A, in which Cl has been substituted with OCH₃ or CH₂OH. Fragment ions at m/z 661 (-Me) and 621 (-Me₂C=CH) indicated that the isoprene unit of the chartellines was retained. Abundant peaks at m/z 645 and 31 (base peak) corresponding to loss of CH₃O indicated the presence of CH₃O in 4. The IR spectra of methoxydechlorochartelline A and chartelline A were superimposable in large regions, even in the fingerprint range, pointing to a close relationship. New bands at 1059 and 1260 cm⁻¹ in 4 provided supporting evidence for the presence of CH₃O.

The ¹³C NMR spectrum of 4 (Table II) established the presence of 20 carbon atoms consistent in chemical shift

and intensity with those of chartelline A. The extra signal at 56.1 ppm was compatible with the presence of CH₃O in 4. Also, the ¹H NMR spectrum of 4 (Table I) was remarkably similar to that of 3, apart from the additional signals from CH₃O in 4 (3 H, 3.62 ppm).

Methoxydechlorochartelline A (4) was prepared from chartelline A (3), in 80% yield, by addition of methoxide in methanol. Transformation of 3 to 4 in boiling methanol was observed. The latter reaction is slow and is of little synthetic utility, since the prolonged reaction time favors formation of a considerable amount of decomposition products. In light of these observations there remains little doubt that methoxydechlorochartelline A (4) is an artifact formed during the isolation procedure. This conclusion was borne out by investigations of new material under rigorous exclusion of methanol where even traces of 4 could not be detected.

Reaction between chartelline A (3) and aqueous sodium hydroxide gave rise to a complicated product mixture, which was not investigated further.

Chartelline A (3) has the *S* absolute configuration.⁴ Chartellines A (3), B (2), and C (1) all have qualitatively identical CD curves with a positive maximum between 217 and 225 nm followed by two negative maxima at 253–257 and 308–324 nm. On the basis of these findings we conclude that 2 and 3 also have the *S* configuration. In the case of 4, the CD curve has nearly identical positive and negative maxima as observed for 3. Apparently a positive inflection at 230 nm is developed into a positive maximum at 236 nm in 4, and two new negative maxima at 273 and 308 nm appear. We ascribe the appearance of the new maxima to a lowered symmetry caused by the introduction of the methoxyl group in 4 in place of the chlorine substituent of 1, 2, or 3. Accordingly, 4 is assigned the *S* configuration.

Although the complexity of the CD curves precludes the assignment of the chromophore responsible for the dichroic absorption, it is noteworthy that a negative maximum is present in the region between 240 and 290 nm where the indolenine chromophore appears.⁶ ORD studies of indolenine alkaloids indicate that a negative Cotton effect is associated with the β configuration at C3 of the indolenine ring.^{7–10} If the macrocyclic ring of the chartellines is identified, stereochemically, with the condensed ring system of the indolenine alkaloids, the rule predicts correctly the *S* absolute configuration of the chartellines.

Preliminary investigations of *Flustra papyracea* (syn. *C. papyracea*)¹¹ collected also in North Brittany waters around Roscoff gave two wide-spectrum *in vitro* antibacterial alkaloids. One of these, named papyraceabromine A, was unstable and assigned the composition C₂₂H₁₇Br₄N₃O₅. Minor alkaloids of a structurally different type, named papyraceabromine B and C, are structurally similar except that papyraceabromine C has a hydrogen atom substituted with bromine as compared with papyraceabromine B. Clearly, the elemental composition of papyraceabromine A is not compatible with the findings for

(6) Legrand, M.; Rougier, M. J. In *Stereochemistry, Fundamentals and Methods*; Kagan, H. B., Ed.; Georg Thieme: Stuttgart, 1977; Vol. 2, p 101.

(7) Strandtmann, M. v.; Eilertsen, R.; Shavel, J., Jr. *J. Org. Chem.* 1966, 31, 4202.

(8) Finch, N.; Gemenden, C. W.; Hsu, I. H.-C.; Kerr, A.; Sim, G. A.; Taylor, W. I. *J. Am. Chem. Soc.* 1965, 87, 2229.

(9) Klyne, W.; Swan, R. J.; Bycroft, B. W.; Schuman, D.; Schmid, H. *Helv. Chim. Acta* 1965, 48, 443.

(10) Savaakan, S.; Kompiš, I.; Hesse, M.; Schmid, H. *Helv. Chim. Acta* 1972, 55, 2861.

(11) Guella, G.; Guerriero, A.; Mancini, I.; Pietra, F., unpublished results mentioned in: Pietra, F. *Gazz. Chim. Ital.* 1985, 115, 443.

(5) Nielsen, P. H.; Anthoni, U.; Larsen, C.; Christophersen, C., in preparation.

chartelline A or any other at present known alkaloids from *C. papyracea*. Moreover, chartelline A as well as the crude mixture of alkaloids is devoid of any significant antimicrobial activity against a representative series of microorganisms, including gram-negative and gram-positive bacteria as well as molds.¹² Chartelline A was found inactive in NCI's leukemia screen (3PS31) at a dose level of 5.60 mg/kg and exhibited ED₅₀ of 29 and 31 mcg/mL in the in vitro KB and PS tests, respectively.¹³

The conflicting results regarding the chemistry as well as the biological activity are deplorable, since the organisms were collected in the same area, namely Morlaix Bay. We collected samples of *C. papyracea* on the location "Chateau du Taureau" around Roscoff in 1979, 1981, and several times during 1985. Although the total alkaloid content varies in different collections, the ratio between the alkaloids is roughly constant. The collection of Pietra¹¹ originated from the location "Les Pierres Noires". In view of the current suspicion concerning the role of microorganisms in the secondary metabolite patterns of many marine organisms,¹⁴ the above-mentioned discrepancy is currently investigated.

Experimental Section

Instrumental details have been reported previously.^{3d} NMR (500-MHz) data were obtained from a Bruker instrument.

All solvents were twice distilled, and all extractions were carried out at room temperature.

Isolation of Chartellines A, B and C and Methoxydechlorochartelline A. *C. papyracea* collected from Roscoff Marine Biological Station, Sept 1985, yielded 800 g of lyophilized material. Extraction with petroleum ether (4×) gave after evaporation 0.6% lipid material. Ethyl acetate extraction (3×) left after evaporation 0.7% (5.7 g) material. Cellulose chromatography (Avicel) with hexane as eluent gave 21% material with low nitrogen content (0.27%). Successive elution with methylene chloride gave 72% (4.1 g) alkaloid-containing mixture (C, 41.16; H, 3.35; N, 6.95). The methylene chloride fraction was recrystallized from ethyl acetate to give 1.36 g of crude alkaloid mixture containing chartellines A, B and C and methoxydechlorochartelline A. The crude material gave 1, 2, and 4 by HPLC separation.⁴ Chartelline B (2) and chartelline C (1) were present in amounts approximately 7% and 4% of that of chartelline A (3), while the amount of 4 varied considerably in different preparations. The mother liquor from the recrystallization contains two alkaloids with a new skeleton. The latter compounds will appear in a future publication. The crude alkaloid mixture contains at least 10 alkaloids, which could be separated by repeated HPLC on reversed phase (RP-18) with acetonitrile-water (60:40) or methanol-water (80:20) as eluent.

Chartelline C (1): 270-MHz ¹H NMR, see Table I; IR (KBr) 3420, 3240, 3080, 2970, 2925, 2850, 1777 (vs), 1760 (vs), 1665, 1605, 1550, 1475, 1455, 1368, 1340, 1250, 1052, 987, 973, 922, 885, 850, 757 cm⁻¹; MS, *m/z* 522 (M⁺, ClBr₂ pattern), 487 (M⁺ - Cl), 467

(M⁺ - Me₂C=CH), 443 (M⁺ - Br), 261 (C₁₂H₈N₂⁸¹Br); UV (EtOH) λ_{max}, nm (log ε) 227 (4.41), 234 (4.41); CD (c 0.023, EtOH) λ_{max}, nm (Δε) 308 (-13.6), 253 (-29.5), 225 (44.5); [α]²⁰ (c 0.023, EtOH) (λ, nm) -217.4° (589), -234.8° (578), -286.9° (546), -678.3° (436), -652.2° (365).

Chartelline B (2): 500-MHz ¹H NMR, see Table I; IR (KBr) 3240, 3080, 2970, 2925, 2850, 1780 (vs), 1765 (vs), 1665, 1600, 1568, 1554, 1475, 1439, 1387, 1367, 1338, 1255, 1234, 1080, 939, 926, 870, 850, 765, 735 cm⁻¹; MS, *m/z* 602 (M⁺, ClBr₃ pattern), 587 (M⁺ - Me), 567 (M⁺ - Cl), 547 (M⁺ - Me₂C=CH), 521 (M⁺ - Br, ClBr₂ pattern), 339 (C₁₂H₇N₂Br₂), 259 (C₁₂H₈N₂⁸¹Br); UV (EtOH) λ_{max}, nm (log ε) 225 (4.44), 235 (4.43); CD (c 0.023, EtOH) λ_{max}, nm (Δε) 315 (-17.3), 254 (-36.1), 221 (46.0); [α]²⁰ (c 0.023, EtOH) (λ, nm) -339.1° (589), -343.5° (578), -413.0° (546), -973.9° (436), -743.5° (365).

Chartelline A (3): mp, UV, HRMS, and [α]²⁰, see ref 4; 500-MHz ¹H NMR, see Table I; ¹³C NMR, see Table II; IR (KBr) 3200, 3080, 2965, 2920, 2850, 1780 (vs), 1765 (vs), 1665, 1594, 1555, 1475, 1430, 1368, 1337 (s), 1248, 1127, 972, 926, 870, 846, 799, 765 cm⁻¹; for MS, see Scheme I; UV (EtOH) λ_{max}, nm (log ε) 230 (4.59), 243 (4.57); CD (c 0.038, EtOH) λ_{max}, nm (Δε) 324 (-21.5), 257 (-41.2), 230 (44.7, inflection), 217 (71.6).

Methoxydechlorochartelline A (4): 500-MHz ¹H NMR, see Table I; ¹³C NMR, see Table II; IR (KBr) 3185 (s), 3080, 2965, 2930, 1770 (vs), 1750 (vs), 1690, 1675, 1594, 1555, 1489, 1460, 1452, 1435, 1415, 1400, 1340 (vs), 1260, 1230, 1210, 1170, 1145, 1128, 1059, 1019, 976, 940, 909, 890, 870, 759, 750 cm⁻¹; MS, *m/z* 676 (M⁺, Br₄ pattern), 661 (M⁺ - Me), 645 (M⁺ - CH₃O), 621 (M⁺ - Me₂C=CH); UV (EtOH) λ_{max}, nm (log ε) 230 (4.50), 245 (4.41); CD (c 0.055, EtOH) λ_{max}, nm (Δε) 323 (-10.9), 308 (-7.9), 273 (-10.4), 255 (-12.7), 236 (14.9), 217 (37.2); [α]²⁰ (c 0.055, EtOH) (λ, nm) -196.3° (589), -201.8° (578), -245.9° (546), -620.2° (436), -297.2° (365).

Preparation of Methoxydechlorochartelline A. To chartelline A (80 mg, 0.12 mmol) dissolved in dry methanol (5 mL) was added sodium methoxide (0.13 mmol) in dry methanol (200 μL) at room temperature. The reaction mixture, which turned yellow instantly, was left 24 h at room temperature. After addition of acetic acid (one drop) and evaporation, the product mixture was purified by HPLC on RP-18 with methanol-water (80:20) as eluent: yield 66 mg, 83% material; all spectral data identical with those described for methoxydechlorochartelline (4) above.

Refluxing of a methanol solution of 3 (more than 98% pure) resulted in a slow formation of 4 as determined by HPLC [RP-18, acetonitrile-water (60:40) with UV detection at 265 nm and automatic integration of the peaks of the chromatogram]. The amount of 4 formed after 8, 16, and 36 h of reflux was 2, 6, and 10%, respectively. In this experiment, the remaining 3 was only 92, 88, and 49%, respectively, indicating the increasing amount of decomposition products formed. Continued reflux resulted in increasing decomposition.

Chartelline A, dissolved in aqueous sodium hydroxide, developed a yellow coloration immediately. After neutralization with acetic acid followed by lyophilization, HPLC analyses showed complete absence of starting material and a complex mixture of products.

Acknowledgment. We are indebted to the Thomas B. Thrige Foundation, The Carlsberg Foundation, The NOVO Foundation, and to the Danish Natural Science Research Council for financial support. We are grateful to Station Marine de Roscoff and especially to Yvon Craignou for the collection of material and to Lise Penzien for skilfull technical assistance.

(12) The antimicrobial tests were carried out by Leo Pharmaceutical Co.

(13) These data are the result of screening performed under the auspices of the Developmental Therapeutics Program, Division of Cancer Treatment, National Cancer Institute, Bethesda, MD.

(14) Tischler, M.; Ayer, S. W.; Andersen, R. J. *Comp. Biochem. Physiol.*, B: *Comp. Biochem.* 1986, 84B, 43.