Communications to the Editor

## Chartelline A: A Pentahalogenated Alkaloid from the Marine Bryozoan *Chartella papyracea* [1a]

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Received January 21, 1985

Only six species of an estimated 4000 extant bryozoans have so far been investigated in any detail. Biologically active compounds have been identified from *Alcyonidium gelatinosum* (L.),[2a,b] *Bugula neritina* (L.),[2c,d] *Flustra foliacea* (L.),[2e,f] *Phidolopora pacifica*,[2g] *Sessibugula translucens* Osburn 1950,[2h] and *Zoobotryon verticillatum* (Delle Chiaja, 1828).[2i] Secondary metabolites from marine bryozoans have recently been reviewed[3a] as have indole derivatives[3b] and alkaloids[3c] from these organisms. This report deals with the isolation and structure elucidation of Chartelline A, an unusual pentahalogenated alkaloid from the
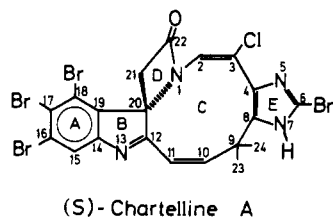
(S)- Chartelline A

marine bryozoan *Chartella papyracea* (Ellis and Solander) belonging to the same family (Flustridea) as *F. foliacea.*

The bryozoans were collected from Roscoff Marine Biological Station by diving during the autumn of 1981. After lyophilization and defatting with cyclohexane the alkaloids were secured by extraction with methylene chloride giving a yield of crude extract, 1.6% of dry weight. Further purification was effected by silica gel chromatography using cyclohexane/ethyl acetate (3:1) and cyclohexane/ethyl acetate (1:1) successively as eluents. The most polar eluent gave material which after LH 20 chromatography or preparative thin-layer chromatography (silica gel, ethyl acetate/methanol 19:1) could be induced to crystallize by addition
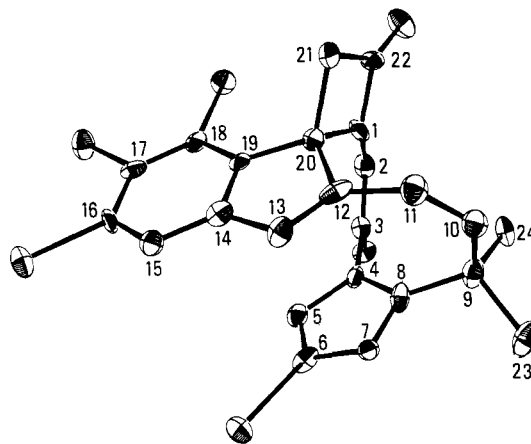

Figure 1. ORTEP drawing[4] of chartelline A.

of ethyl acetate. Homogeneity was confirmed by HPLC analysis (RP-8 Merck 25 cm × 4 mm, 7 μm, methanol/acetonitrile/water, 32.5:32.5:35). The total yield of chartelline A was around 0.07% of dry weight.

The elemental composition $C_{20}H_{13}Br_4ClN_4O$ was determined from HRMS (calcd for $C_{20}H_{13}{}^{79}Br_2{}^{81}Br_2{}^{35}ClN_4O$, 679.747 and for $C_{20}H_{13}{}^{79}Br_3{}^{81}Br^{37}ClN_4O$, 679.746; found 679.745 ± 0.005). Chartelline A, mp 214–216 °C dec (EtOAc), exhibited IR absorption bands (KBr disk) at 3195 (m, br), 1780 (s), 1765 (s), and 1338 (s) cm^{-1}, UV absorption (EtOH) λ_{max} 230 nm (br, log ε 4.59), and $[\alpha]^{20}{}_D$ −421° (c 0.038, EtOH).

^{1}H NMR spectroscopy (270 MHz, CDCl$_3$) revealed the presence of 13 hydrogen atoms. Two methyl groups appear at δ 1.50 (s, 3 H) and 1.56 (s, 3 H). An AB system at δ 3.21 (d, 1 H, J = 15.4 Hz) and 3.43 (d, 1 H, J = 15.4 Hz) was assigned to the hydrogen atoms of an isolated methylene group and another AB system at δ 6.01 (d, 1 H, J = 11.9 Hz) and 6.10 (d, 1 H, J = 11.9 Hz) to the hydrogen atoms of a cis-substituted double bond. The remaining three hydrogen atoms appear at δ 7.07 (s, 1 H), 7.71 (s, 1 H), and 9.45 (br s, N H). ^{13}C noise-decoupled and off-resonance-decoupled NMR spectroscopy accordingly exhibit methyl group signals at δ 26.7 and 29.0, a methylene group at δ 44.8, and quaternary carbon atoms at δ 38.0 and 72.7. The remaining carbon atoms are sp^2 hybridized and appear between δ 115.3 and 179.0. These data did not allow an unambiguous structure determination to be carried out. Consequently a single-crystal X-ray structure determination was undertaken.

Chartelline A was induced to crystallize from a chromatographic fraction by addition of ethyl acetate. The resulting crystals contain one molecule of ethyl acetate for each chartelline. Figure 1 shows an ORTEP drawing of the molecule after final refinement (R = 4.9%, R_w = 6.1%). The absolute configuration around C(20) was determined to be S at a better than 99.5% significance level according to Hamilton's R-factor test.[5] Apart from the pentahalogeno substitution pattern the structure is unique in formally being derived from five condensed ring systems. The central aza-2,4,7-cyclodecatriene system adopts a boatlike conformation forming a groove lined with the four nitrogen atoms. The dihedral angle between the least-square planes of the ring system derived from indolenine and the imidazole ring is 11 (1)°, close to coplanar with a distance between C(6) and the least-square plane of the indolenine system of 3.07 (3) Å. Chartelline A is colorless in the crystalline state. Accordingly the crystal structure determination indicate that apart from the imidazole ring and the phenyl ring

(1) (a) Contribution 10 of the series "Marine Alkaloids". For part 9, see: Grøn, C.; Christhopersen, C. *Acta Chem. Scand., Sect. B* **1984**, *B38*, 709. (b) Laboratorie d'Océanographie Chimique, Université de Bretagne Occidentale, Brest 29283, France. (c) Centre National pour l'Exploitation des Océans, Centre Océanologique de Bretagne, 29N-Plouzané, 29273 Brest, France. (d) Department of Physical Chemistry, The H. C. Ørsted Institute, University of Cophenhagen, Universitetsparken 5, DK-2100 Copenhagen, Denmark. (e) Marine Chemistry Section, Department of General and Organic Chemistry, The H.C. Ørsted Institute, University of Cophenhagen, Universitetsparken 5, DK-2100 Copenhagen, Denmark.

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very little conjugation is present in the remaining ring systems. The C(10)–C(11) and the C(2)–C(3) double bonds are virtually isolated double bonds (1.31 (2) and 1.34 (1) Å, respectively) as is the C(12)–N(13) double bond (1.27 (1) Å).[6] Furthermore conjugation is insignificant between the C(2)–C(3) double bond and the β-lactam ring system (C(2)–N(1) 1.40 (1) Å). The β-lactam ring is close to perpendicular to the plane of the indolenine system, the dihedral angle C(14)–C(19)–C(20)–C(21) is 120 (1)°. The distance between the imidazole N(7) and the carbonyl O in the ethyl acetate is 2.82 (2) Å indicating a strong hydrogen bond.

Biogenetically, chartelline A seems to be composed of modified tryptamine and histamine residues linked via an isoprene unit. The biosynthesis of this new class of alkaloids is at present totally unexplored as is the question whether chartelline A is a true bryozoan metabolite or originates with some symbiotic or associated organism. The chemical and biological properties of chartelline A and related natural products from bryozoans are at present being investigated.

Registry No. (*S*)-Chartelline A, 96845-55-5.

Supplementary Material Available: Tables of structure factors, atomic coordinates, thermal parameters, bond angles, and bond lengths (4 pages). Ordering information is given on any current masthead page.

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(6) The dihedral angle C(10)–C(11)–C(12)–N(13) is 104 (1)° and the torsion angle C(2)–C(3)–C(4)–N(5) is 113 (1)°.

Cyclization and Disproportionation Kinetics of Triplet Generated, Medium Chain Length, Localized Biradicals Measured by Time-Resolved CIDNP[1]

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Received January 8, 1985

With the advent of more reliable MO calculations and very fast experimental techniques the chemistry of biradicals has moved to the forefront of physical organic chemistry.[2] Ideally one would like to know static and dynamic properties associated with biradicals represented by a simple polymethylene chain, $\dot{C}H_2$-$(CH_2)_n\dot{C}H_2$. Presumably because of experimental difficulties, no direct kinetic measurements have been reported for any of its members. In this paper we wish to report kinetics obtained for a series of compounds similar to polymethylenes except that one of the terminal methylenes is replaced by a carbonyl group. At present this series comes closest to the ideal mentioned above.

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(1) Supported by NSF Grant CHE 8218164.
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Scheme I
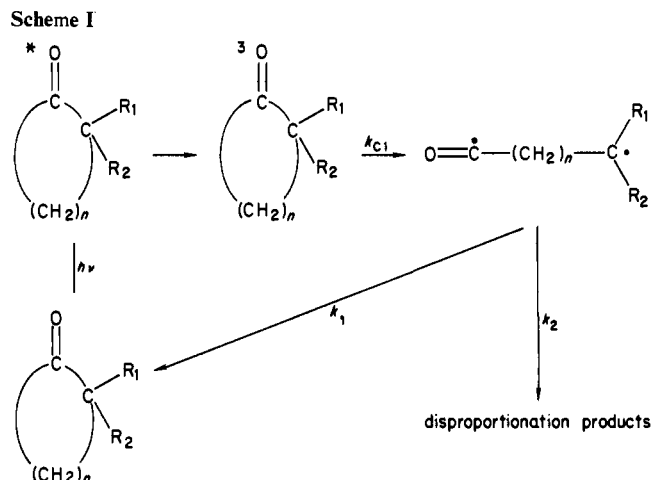
Table I

biradical	length	τ, ns[a]	disprop/ cycliz	EF[b]	(EF/ EF$_{max}$)10²
$\dot{C}H_2(CH_2)_6\dot{C}O$ (1)	1,8	100	0.48	202	0.62
$(CH_3)_2\dot{C}(CH_2)_6\dot{C}O$ (2)	1,8	83	2.4	392	2.28
$\dot{C}H_2(CH_2)_7\dot{C}O$ (3)	1,7	100 (150)[c]	0.51	305	0.94
$CH_3\dot{C}H(CH_2)_5\dot{C}O$ (4)	1.7	100	0.61	334	1.47
$(CH_3)_2\dot{C}(CH_2)_5\dot{C}O$ (5)	1,7	130	2.0	639	3.72
$\cdot\boxed{}-(CH_2)_2\dot{C}O$	1,6	77	7.0	335	1.25

[a] The errors are estimated to be ±20%. [b] EF, the enhancement factor is defined as the ratio of the CIDNP signal intensity, *I*, and the corresponding Boltzmann equilibrated signal, I^0, at equal concentrations: $I/(I^0 \times$ conversion). Conversion is the fraction of the reactant converted to product per laser pulse. [c] From a biexponential fit it cannot be stated which exponent belongs to which reaction step. Both exponents are listed here.

The biradicals are generated by photolysis of cyclic ketones and the chemistry is represented by Scheme[3] I. It is well established that intersystem crossing in ketones is very fast and that the cleavage occurs from a triplet state.[4] In our work we measure the formation kinetics of the cyclic ketone and disproportionation products. In cases where cleavage (k_{cl}) is fast relative to the sum of the biradical decay rates, this yields directly the lifetime τ of the biradical ($1/\tau = k_1 + k_2$).

The experimental technique used is based on NMR detected laser flash photolysis recently developed in this laboratory.[5] The method, an extension of CIDNP spectroscopy, samples the nuclear magnetization of the products formed after a time interval τ' between the laser pulse initiating the chemistry and the rf probing pulse. Only the magnetization of the diamagnetic products formed during τ' contributes to the spectrum. With our present equipment, operating at 60 MHz with a flip angle of 7° we are able to measure lifetimes as short as 25 ns.[6] The advantage over faster optically detected flash photolysis lies in more positive product identification and the independence of the presence of a strong chromophore in the biradical.

The lifetime τ of the biradicals **1**, **2**, and **4–6** were obtained by fitting the formation rates of the products with a single ex-

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(6) Deconvolution for the finite rf pulse width was accomplished by fitting the signal intensities to $I(\tau') = \int_0^\infty dc(t) \int_t^\infty F(t,\tau') \, dt \, dt$ where τ' is the delay between the laser pulse and the center of the rf pulse, $c(t)$ is the product concentration and $F(t,\tau')$ is the shape function of the rf pulse envelop.