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Brianthein Z, A New Polyfunctional Diterpene From the Gorgonian *Briareum polyanthes*[1]

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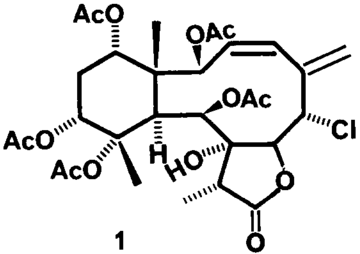
Summary: A novel diterpene and possible chemotaxonomic marker has been isolated from the gorgonian *Briareum polyanthes*. The gross structure has been determined and relative configuration is proposed.

Representatives of the order Gorgonaceae are now well known sources of diterpenes.[2] *Briareum asbestinum*, a species common throughout the Caribbean, produces a series of novel, highly oxidized diterpenes headed by briarein A, **1**,[3] and the asbestinins.[4] Although no species of *Briareum* had been reported previously from Bermudian waters, we found, in 1979, a moderately large community of a new species, *B. polyanthes*,[5] at the eastern end of the archipelago. Our study of this organism has resulted in the isolation and identification of a new metabolite possessing the briarein carbon skeleton; the identification of this highly oxidized compound and its potential chemotaxonomic significance comprise this report.



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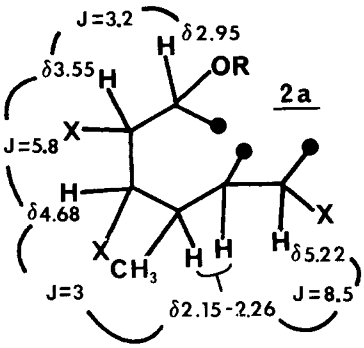
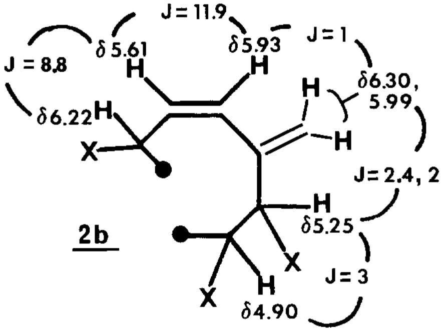
The dichloromethane soluble extracts (24.52 g) were partitioned using a scheme popularized by Kupchan.[6] The chloroform soluble fraction was separated by step-gradient gel permeation chromatography on Sephadex LH-20.[7] A large fraction, eluted with hexane-dichloromethane (1:4) appeared to be rich in terpenoid materials. Additional gel permeation of this material through Sephadex LH-60 (CH_2Cl_2-CH_3CN, 3:1), followed by HPLC (Ultrasphere-Cyano column, hexane/i-PrOH, 2:1) gave 30 mg of a crystalline solid assigned the trivial name brianthein Z.[8]

An intense absorption at 1739 cm^{-1} in the IR and three singlets (each 3H) in the ^{1}H-NMR at δ 2.15, 2.06 and 2.04 indicated the presence of three acetate groups; however, four ester type carbonyls were disclosed by ^{13}C-NMR analysis (δ 174.27, 170.07, 169.98 and 169.75). Inclusion of a γ-lactone in brianthein Z accounted for the fourth carbonyl and an IR absorption at 1790 cm^{-1}. A hydroxyl group was also required by the IR absorption at 3540 cm^{-1}. Brianthein Z gave a positive Beilstein test and isotopic abundances in mass spectral fragments indicated a single chlorine atom was present. The molecular formula could be deduced by counting carbons (in the ^{13}C-NMR) and hydrogens (^{1}H and ^{13}C NMR data) and comparing those totals with the molecular weight determined by mass spectrometry--540. Nine oxygens were mandated by the acetate, lactone and hydroxyl functionalities; addition of one more oxygen gave the formula $C_{26}H_{33}ClO_{10}$.

^{1}H-NMR decoupling experiments at 250 MHz revealed three isolated systems, **2a–c**. Left to be assigned were a methyl singlet (δ 1.09) and a 1H singlet at δ 3.2 (OH). The 1,3 disubstituted butadiene of **2b** was formulated after consideration of the chemical shifts and coupling constants of the associated hydrogens and the four sp_2 carbon resonances between δ 118 and 137. The chemical shifts of the two allylic methines in **2b** suggested that they both resided on carbons bearing heteroatoms; this substructure's striking resemblance to its counterpart in briarein A led to assemblage of these known pieces to give **2d**. The chemical shifts of the heteroatom bearing methines in the "A" ring seemed to require placement of the third acetate at C-11.[9] Since one oxygen and one site of unsaturation remained untendered, an epoxide linkage was assigned to connect C-9 and C-10,[9] yielding structure **2** for brianthein Z. In support of this proposal, SFORD experiments revealed that the proposed epoxide proton at δ2.95 resided on a carbon resonating at δ61.85, while its companion at δ3.55 was borne by the carbon resonating at δ52.70.

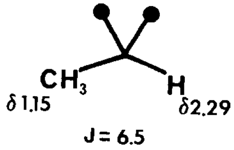


2a

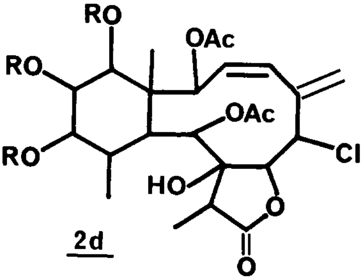


2b

2c



$X = Cl$ or OR

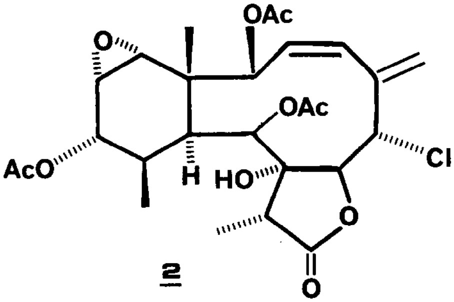


2d

The relative configuration of the substituents decorating the cyclohexane ring in **2** was deduced by comparison with briarein A, whose structure and absolute configuration were determined by x-ray diffraction studies.[3] The striking feature of the conformation of briarein A is the axial disposition of the two methyl groups and the C-11[9] acetate on the cyclohexane ring. The ^{1}H-NMR coupling constants for the cyclohexane ring protons in **2** fit nicely for that same conformation and relative configuration at C-8, C-11, C-12, and C-13[9] in brianthein Z. Extension of the coupling constant arguments required that the epoxide bonds be α. The coupling constant between the C-2 and C-3 methines required the chlorine to be axial (α) as well. Steric considerations and the coupling constant of the proton on C-7 indicated a pseudoequatorial disposition (β) of the acetoxyl group on C-7. Examination of Dreiding models strongly suggested that the C-1 hydroxyl and C-17 methyl groups should be axial (α). Thus, the relative configuration of **2** can be completely assigned, except for the acetate on C-14, which, by analogy to **1**, should be axial (β).

The chemotaxonomic significance of this discovery lies in the confusion surrounding the identity of the producing organism. It has been variously described as *Ammothea polyanthes*

Duchassaing & Michelotti (1860), *Erythropodium polyanthes* Deichmann (1936) and synonymous with *Briareum asbestinium* Bayer (1961). The absence, in our extracts, of briarein A, **1**, and the presence of **2**, bearing the same carbon skeleton, but with an unprecedented array of functionalities, lends considerable support to its current identification as a distinct species of *Briareum*.[5,10]



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1. Contribution #909 from the Bermuda Biological Station. Part of this work was presented at the 23rd Annual Meeting of the American Society of Pharmacognosy, Pittsburgh, PA, August 1982.
2. a) W. Fenical in "Marine Natural Products. Chemical and Biological Perspectives," P. J. Scheuer, ed., Academic Press Inc., New York, Vol. II, 1978, 173-245; b) B. Tursch, J. C. Braekman, D. Daloze and M. Kaisin, *ibid.*, 247-96.
3. J. E. Burks, D. van der Helm, C. Y. Chang and L. S. Ciereszko, *Acta Crystallogr.*, *Sect. B*, **33**, 704 (1977).
4. a) D. B. Stierle, B. Carte, D. J. Faulkner, B. Tagle, and J. Clardy, *J. Am. Chem. Soc.*, **102**, 5088 (1980); b) S. J. Selover, P. Crews, B. Tagle and J. Clardy, *J. Org. Chem.*, **46**, 964 (1981).
5. The specimens have been identified by Dr. Frederick Bayer of the Smithsonian Institution; we are grateful for his interest and assistance.
6. S. M. Kupchan, R. W. Britton, M. F. Ziegler and C. W. Sigel, *J. Org. Chem.*, **38**, 178 (1973).
7. J. H. Cardellina II, *J. Nat. Prod.*, in press.
8. $\nu_{max}^{CHCl_3}$ 3540, 2930, 1790, 1739, 1365 cm^{-1}; ^{13}C-NMR ($CDCl_3$): δ174.27(s), 170.07(s), 169.98(s), 169.75(s), 136.80(s), 131.07(d), 127.92(d), 118.94(t), 84.64(s), 77.10(d), 75.66(d), 69.45(d), 69.18(d), 62.42(d), 61.85(d), 52.70(d), 44.78(d), 40.81(s), 36.78(d), 32.86(d), 21.78(q), 20.76(q), 20.29(q), 15.81(q), 12.41(q), 6.04(q); MS: m/z 540/542 (M^+), 504, 498/500, 480/482.
9. Numbering system used in ref. 3.
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