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PTILOSARCONE, THE TOXIN FROM THE SEA PEN PTILOSARCUS GURNEYI

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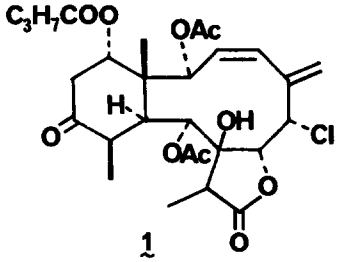
The north Pacific sea pen Ptilosarcus gurneyi Gray was shown to contain a mild toxin which was soluble in organic solvents[1]. The LD_{50} of purified toxin in mouse (i.p.) was determined to be 7.4 mg/Kg. In methanol solution, the toxin decomposed to give a non-toxic product. Both the toxin and its decomposition product inhibited acetylcholinesterase and serum cholinesterase. We wish to suggest structures for the toxin, ptilosarcone (1), and its decomposition product, ptilosarcenone (2), that are very similar to that of briarein A (3), a metabolite of the gorgonian Briareum asbestinum, whose structure was determined by X-ray analysis.

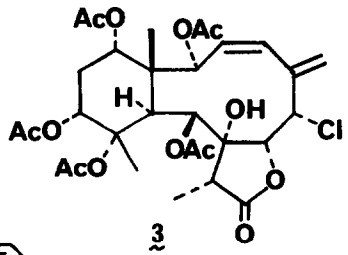
Ptilosarcone (1), obtained in low yield as a glass, had the molecular formula $C_{28}H_{37}O_{10}Cl$[1]. On decomposition, it lost the elements of butyric acid to give ptilosarcenone (2), $C_{24}H_{29}O_8Cl$, which showed a uv absorption at λ 220 nm (ε 9,000) and a new band in the infrared spectrum at 1682 cm^{-1}, both typical of an α,β-unsaturated ketone. The infrared spectra of both compounds showed bands at 3560 (-OH), 1783 (γ-lactone) and 1732 cm^{-1} (acetate). The infrared spectrum of 3 showed similar bands at 3560, 1785 and 1730 cm^{-1}, the latter band being more intense.

Many signals in the richly detailed 220 MHz pmr spectra of ptilosarcone (1) and ptilosarcenone (2) were strikingly similar to those of briarein A (3). Whereas briarein A (3) contained five acetate groups with signals at δ 1.97 (3H), 1.99 (9H) and 2.24 (3H), ptilosarcenone (2) contained two acetate groups at δ 2.16 and 2.21, while ptilosarcone (1) contained two acetate groups at δ 1.98 and 2.20 and a group of signals due to a butyrate ester at δ 2.25 (t, 2H), 1.60 (m, 2H) and 0.95 (t, 3H).

Spin decoupling experiments have allowed us to assign every signal in the pmr spectrum of briarein A (3) to the structure obtained by X-ray analysis[2]. Spin decoupling studies on ptilosarcone (1) and ptilosarcenone (2) allowed the assignment of the pmr signals as shown in the table. Comparison of the pmr spectra suggested that the substitution pattern about the 10-membered ring was the same for all three compounds, with the exception of the stereochemistry at C-9. The substitution pattern about the 6-membered ring in 1 and the stereochemical arrangement of the substituents could be assigned on the basis of pmr coupling constants. The protons at C-13 appeared as an AB quartet δ 2.35 (eq) and 2.91 (ax) , further split by coupling to a single equatorial proton (δ 5.22) at C-14. The facile decomposition therefore involved a trans-diaxial elimination of the butyrate group at C-14. The pmr spectrum of 2 contained the expected pair of doublets at δ 5.90 and 6.61 assigned to the protons at C-13 and C-14. In the pmr spectrum of 1, the proton at C-11 appeared as a complex multiplet at δ 2.78 which was coupled to the methyl doublet at 1.38 (J = 7 Hz), the equatorial proton at 2.35 (J = 1 Hz), and the bridgehead proton at 3.10 ppm (J = 6 Hz). The magnitudes of the coupling constants and the existence of W-coupling provide evidence for an axial methyl group and an equatorial proton at C-11. The bridgehead proton is also coupled to an α-acetoxy proton at δ 5.50 ppm (J = 5.5 Hz). Since the coupling constant between these protons in briarein A is very small (<0.5 Hz), we have assumed that the 5.5 Hz coupling constant indicates the alternative stereochemistry at C-9. The remaining signals in the pmr spectra of 1 and 2 all have counterparts having identical coupling constants in the pmr spectrum of 3. We believe that the similarities between the pmr spectra provide compelling evidence for the gross structures of ptilosarcone (1) and



1



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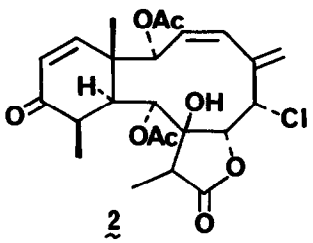

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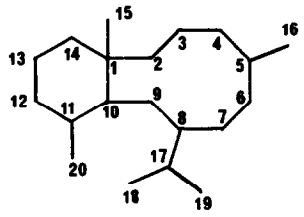

Table. Chemical Shifts (ppm from TMS), Coupling Constants (Hz) in Parentheses

H at C-#	Ptilosarcone (1)	Ptilosarcenone (2)	Briarein A (3)
2	6.26 (9)	5.72 (9)	6.12 (10)
3	5.70 (12, 9)	5.63 (12, 9)	5.84 (12, 10)
4	5.96 (12)	5.99 (12)	6.00 (12)
6	5.22 (3.7, 2, 1)	5.26 (3.7, 2, 1)	5.12 (3.7, 1, 1)
7	4.94 (3.7)	5.01 (3.7)	4.87 (3.7)
9	5.50 (5.5)	5.49 (7.3)	5.58 (s)
10	3.10 (6.2, 5.5)	2.82 (m)	3.10 (s)
11	2.78 (6.2, 7, 7, 7, 1)	2.82 (m)	---
12	---	---	5.71* (3.4, 2.8)
13 ax	2.91 (15, 2.5)	5.90 (11)	2.35 (17, 2.8, 2.5)
13 eq	2.35 (15, 4.2, 1)		1.99 (17, 3.4, 3)
14	5.22 (4.2, 2.5)	6.61 (11)	4.87* (3, 2.5)
15	1.23 (s)	1.18 (s)	1.40 (s)
16	5.93 (2, 1)	5.96 (2, 1)	5.48 (1, 1)
16	6.13 (1, 1)	6.12 (1, 1)	5.60 (1, 1)
17	2.58 (7, 7, 7)	2.41 (7, 7, 7)	3.14 (7, 7, 7)
18	1.22 (7)	1.21 (7)	1.34 (7)
20	1.38 (7)	1.30 (7)	1.54 (s)

*Assignment could be reversed.

ptilosarcenone (2), but we recognize that the stereochemistry at C-8 and C-17 cannot be determined by this method.

Acknowledgements

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References and Notes

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2. J. E. Burks, D. van der Helm, C. Y. Chang and L. S. Ciereszko, Acta Cryst., in press.