Pergamon

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Tetrahedron Letters 44 (2003) 2637–2640

TETRAHEDRON LETTERS

Aldingenin A, new brominated sesquiterpene from red algae *Laurencia aldingensis*

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Received 31 January 2003; accepted 7 February 2003

Abstract—A new brominated bisabolene derivative, aldingenin A, was isolated from red alga *Laurencia aldingensis* Saito et Womersley (Ceramiales, Rodophyta). Its structure was determined by analysis of spectroscopic data (^{1}H and ^{13}C NMR, IR, MS), including bidimensional NMR (^{1}H–^{1}H COSY, HMQC, HMBC and NOESY) and biogenetic considerations.

Our chemical studies on the constituents of the red alga *Laurencia aldingensis* Saito et Womersly[1] (Rhodomelaceae, Ceramiales), found for the first time in Brazil and in the Atlantic ocean resulted in the isolation of a new bisabolene-type sesquiterpene named aldigenin A. This compound has been fully characterized by spectroscopic methods, including two-dimensional NMR analysis. Considering that sesquiterpenes have important taxonomic significance[2–4] allied to first occurrence of *L. aldingensis* in Brazil, this work contributes to the taxonomic investigation of Brazilian species of *Laurencia*.

Column chromatography over silica gel and Sephadex LH-20 of the CH_2Cl_2 extract of *L. aldingensis* resulted in the isolation of aldigenin A.[5] Its LREIMS showed peaks at m/z 332/330 $[M]^+$, with relative intensities suggestive of one bromine atom that correspond to the empirical formula $C_{15}H_{23}O_3Br$ (m/z 330.0799 in the HREIMS). The ^{13}C NMR spectra displayed fifteen signals (Table 1) and their multiplicity was determined from DEPT 135° and 90° spectra: four methyl, three methylene, five methine (four of these bearing heteroatoms) and three nonprotonated carbons (all of these bearing heteroatoms). Since the IR spectrum revealed the absence of absorption for hydroxyl and carbonyl groups the oxygen atoms are involved in ether linkages. The ^{1}H NMR spectrum in deuterated-benzene[6] displayed signals corresponding to hydrogen atoms, which are linkage at heterosubstituted carbons, at δ 4.31 (1H, dt, J=13.2, 4.1 Hz), 4.26 (1H, dd, J=12.9, 4.2 Hz), 3.88 (1H, m) and 2.77 (1H, t, J=3.0 Hz). Signals corresponding to four tertiary methyls groups appeared at δ 1.93 (3H, s), 1.28 (3H, s), 1.25 (3H, s) and 0.80 (3H, s). All the hydrogen bearing carbon signals were assigned by HMQC NMR spectrum (Table 1).

The ^{1}H–^{1}H COSY spectrum established two proton sequences. The coupling between the proton at δ 4.31 and the methylene protons at δ 1.84 and δ 2.13 as well as these signals and the proton at δ 2.77 established the connectivity of the H-10/H-9/H-8 in the moiety **a**. This spectrum showed also the correlation of the signal at δ 3.88 and δ 1.74, δ 2.10 and δ 1.59, indicating the connectivity of the H-5/H-4a, H-5/H-4b and H-5/H-6. The cross-peaks between the hydrogen atoms at δ 2.21 and 4.26; δ 2.05 and 4.26; δ 1.59 and 2.05, were due to the couplings of H-2/H-1b, H-2/H-1a and H-6/H-1a in the moiety **b**.

The occurrence of three cyclic ether groups would allow the existence of ten planar structures. The chemical shifts of carbinol carbons were not compatible to the presence of 1,2-epoxide system and, considering the sterical hindrance and the coupling constants between H-9/H-10 (J=13.2 Hz), the planar structure, as depicted in Figure 1, was suggested.

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0040-4039/03/$ - see front matter
doi:10.1016/S0040-4039(03)00379-4

Table 1. ^{13}C, ^{1}H, ^{1}H–^{1}H COSY, HMBC and NOESY NMR data of aldingenin A (500 MHz, δ ppm (J) Hz, benzene-d_6)

Position	δ_C*	δ_H	^{1}H–^{1}H COSY	HMBC (H→C)	NOESY
1	33.4 (CH_2)	a_{endo}: 2.05 dddd (12.9, 4.2, 2.6, 1.5)	H-2, H-6	C-3, C-5	H-2, H-8
		b_{exo}: 2.21 q (12.9)	H-1a, H-2, H-6	C-6, C-5, C-3, C-2	H-6, H-2, H-14
2	64.0 (CH)	4.26 dd (12.9, 4.2)	H-1a, H-1b	C-3, C-1, C-15	H-6, H-4a, H-1a, H-1b
3	72.2 (C)	–	–	–	–
4	51.5 (CH_2)	a_{exo}: 1.74 dd (14.5, 2.7)	H-4b, H-5, H-15	C-3, C-15	H-5, H-2
		b_{endo}: 2.10 dd (14.5, 3.1)	H-4a, H-5, H-6	C-6, C-5, C-3, C-2, C-15	H-5, H-15
5	67.1 (CH)	3.88 m	H-4a, H-4b, H-6	C-3, C-1	H-6, H-4a, H-4b, H-14
6	49.9 (CH)	1.59 dt (12.9, 2.7)	H-1a, H-1b, H-5	C-1, C-7, C-14	H-5, H-2, H-14
7	77.3 (C)	–	–	–	–
8	72.7 (CH)	2.77 t (3.0)	H-9a, H-9b	C-10	H-1a, H-9a, H-9b, H-14
9	37.3 (CH_2)	a_{eq}: 1.84 dt (14.1, 3.0)	H-9b, H-8, H-10	C-10, C-8, C-7, C-11	H-10, H-8
		b_{ax}: 2.13 ddd (14.1, 13.2, 3.0)	H-8, H-9a, H-10	C-10	H-13, H-14
10	52.9 (CH)	4.31 dd (13.2, 4.1)	H-9a, H-9b	C-9, C-8, C-11, C-12, C-13	H-9a, H-12
11	75.0 (C)	–	–	–	–
12_{eq}	31.4 (CH_3)	1.28 s	–	C-10, C-11, C-13	H-10
13_{ax}	24.2 (CH_3)	1.25 s	–	C-10, C-11, C-12	H-9b, H-14
14	23.3 (CH_3)	0.80 s	–	C-6, C-7, C-8	H-8, H-9b, H-13
15	28.6 (CH_3)	1.93 s	–	C-2, C-3, C-4	H-4b

* Multiplicity obtained from DEPT 135° and 90° spectra.

HMBC data were used to confirm the moieties **a** and **b** and established the connectivity between the protons and carbon atoms. The correlation of signals at δ 1.84 (H-9a)/4.31 (H-10)/0.80 (H-14) with 72.7 (C-8) as well as the correlated signals at δ 1.28 (H-12)/1.25 (H-13)/2.77 (H-8)/1.84 (H-9a)/2.13 (H-9b) with 52.9 (C-10) confirmed the positioning of the *gem*-dimethyl groups at carbon C-11 which is vicinal to bromine atom, located at C-10. The NMR data to C-10 of aldingenin A and the related sesquiterpene laucapyranoid B[7] are similar, suggesting the same configuration to bromine atom. The structure of the moiety **b** of the molecule was again determined by the HMBC correlations between the signal at δ 72.2 (C-3) and δ 4.26 (H-2)/3.88 (H-5)/2.05 (H-1a)/2.21 (H-1b)/1.74 (H-4a)/2.10 (H-4b)/1.93 (H-15) and between the signals at δ 49.9 (C-6) and δ 2.21 (H-1b)/2.10 (H-4a). The connectivity between the **a** and **b** moieties was determined by long-range correlation between the signals at δ 1.59 (H-6) with 77.3 (C-7) and 23.3 (C-14) (Table 1).

The relative stereochemistry was assigned on the basis of a study of the coupling constants and NOESY experiments (Fig. 2). The small value to coupling constant observed to H-8 indicated equatorial position. This information, associated to a minute analysis of the coupling constants and the strong NOE observed between H-8 and H-1a, indicated a norbornene type conformation to C-1/C-6 system, which was confirmed by the cross-peaks between H-6/H-2, H-5, H-14 as well as H-4b/H-5, H-15. The coupling constant for the H-10 is typical of an axial proton, confirming the bromine atom in the equatorial configuration. In the NOESY spectrum, a strong correlation between H-10 and H-12 was observed, positioning the C-12 methyl group at the equatorial position. On the other hand, a strong NOE between H-9b/H-13/H-14 was in agreement with these methyl groups being in the axial position.

A biogenetic route was proposed for aldingenin A, involving an α-bisabolene precursor (Fig. 3). Similar to the biogenetic pathway described previously to *L. pannosa*[8] and *L. obtusa*,[9] the oxidation of the positions

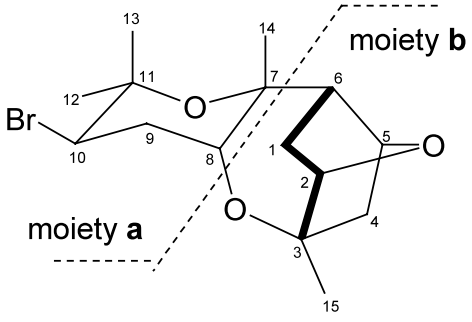

Figure 1.

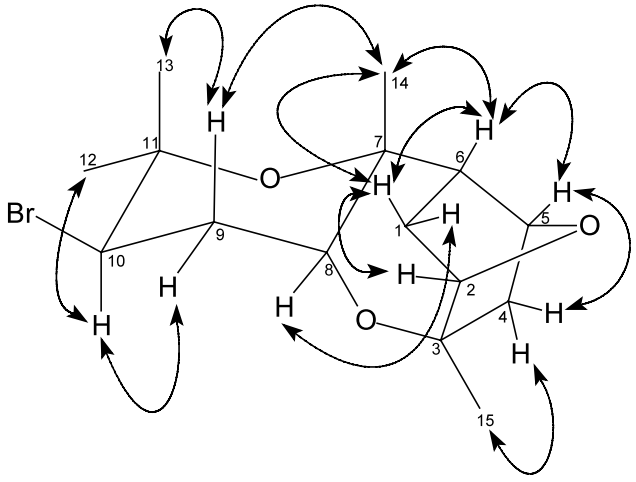

Figure 2. Important NOE correlation observed in the NOESY spectrum of aldigenin A.

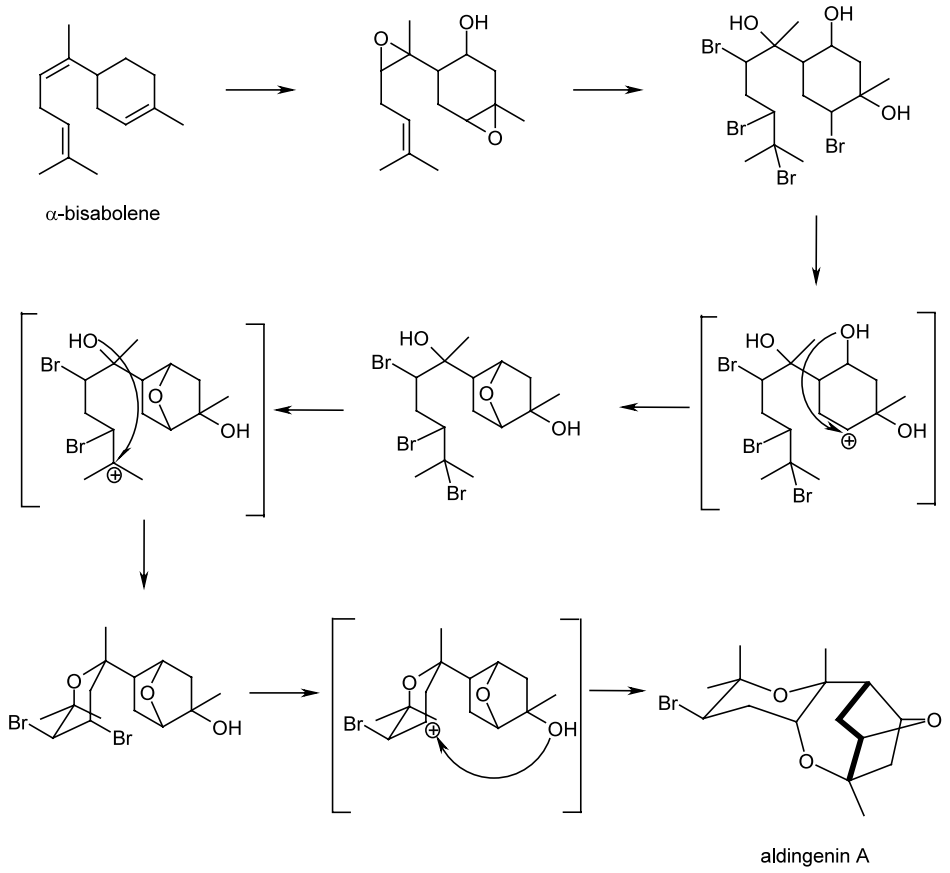

Figure 3. Biogenetic mechanism for formation of aldigenin A from α-bisabolene.

C-8/C-7 and C-10/C-11 followed by nucleophilic attack by bromide at C-10, C-8, C-3 and C-2, yields a halidrine derivative. The hydroxylation at C-5 position was previously observed in chamigrene derivatives isolated from *L. obtusa*.[9] Bromide elimination followed by successive ether ring formation, would give aldingenin A. The conversion of γ-bisabolene yielding chamigrane derivatives, has been previously described in several *Laurencia* species,[8–11] thus accordingly the α-bisabolene should be the precursor of the sesquiterpene aldigenin A.

Acknowledgements

This work was supported by CNPq and FAPESP.

References

1. Saito, Y.; Womersly, H. B. S. *Aust. J. Bot.* **1974**, *22*, 815–874.
2. Howard, B. M.; Nonomura, A. M.; Fenical, W. *Biochem. Syst. Ecol.* **1980**, *8*, 329–336.
3. Masuda, M.; Abe, T.; Sato, S.; Suzuki, T.; Suzuki, M. *J. Phycol.* **1997**, *33*, 194–206.
4. Faulkner, D. J. *Nat. Prod. Rep.* **2001**, *18*, 1–49 and previous reports in this series.
5. *General procedure for isolation and purification of aldigenin A*: The air dried algae (wet wt. 24 g) was ground in a Wiley mill and extracted at room temperature four times with CH_2Cl_2 (1.6 L) for 2 days each time. Combined extracts were concentrated under reduced pressure and the resulting oily residue (2.75 g) was chromatographed on a silica gel column using increasing amounts of EtOAc in n-C_6H_{14}. The fractions eluted with n-C_6H_{14}:EtOAc (85:15; v/v) yielded a dark green fraction (192 mg), which was chromatographed on a Sephadex LH-20 column with n-C_6H_{14}:CH_2Cl_2 (1:4; v/v), to give 56 mg of a white powder. This powder was further re-chromatographed on a silica gel column using n-C_6H_{14}:EtOAc (3:1 v/v) to afford aldigenin A **1** (36 mg); $[\alpha]_D^{25} = -10$ (c 0.05, $CHCl_3$); mp (MeOH) 169–171°C; IR (film) ν_{max} cm^{-1}: 2984, 2927, 2855, 1459, 1380, 1287, 1256, 1225, 1115, 1089, 1063, 1037, 982, 824, 755, 644, 547, 442; LREIMS: m/z 332 (2), 330 (2), 317 (4), 316 (5), 251 (9), 233 (9), 199 (10), 165 (10), 163 (16), 123 (15), 119 (36), 109 (28), 107 (11), 105 (10), 95 (32), 93 (28), 92 (12), 91 (32), 83 (12), 82 (10), 81 (18), 79 (17), 77 (17), 71 (21), 69 (30), 67 (16), 55 (22), 53 (15), 43 (100), 41 (47); HREIMS: m/z 330.0799; calcd for $C_{15}H_{23}O_3{}^{79}Br$: 330.0831. For ^1H and ^{13}C NMR data, see Table 1.
6. Since the ^1H NMR signals for H-1, H-4 and H-9 in $CDCl_3$ overlapped, the experiments were carried out in benzene-d_6. However, for comparison, the NMR data in $CDCl_3$ are listed as follows: ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.1 (q, C-14), 24.2 (q, C-13), 28.1 (q, C-15), 30.8 (q, C-12), 32.1 (t, C-1), 36.0 (t, C-9), 50.0 (t, C-4), 50.3 (d,

C-6), 52.3 (d, C-10), 64.1 (d, C-2), 67.8 (d, C-5), 71.8 (s, C-3), 72.4 (d, C-8), 76.1 (s, C-11), 78.1 (s, C-7); ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.51 (m, H-5), 4.37 (dd, $J=12.9$, 4.3 Hz, H-2), 4.34 (dd, $J=13.2$, 4.1 Hz, H-10), 3.66 (t, $J=3.0$ Hz, H-8), 2.60–2.51 (m, H-1a, H-9b), 2.37–2.19 (m, H-1b, H-4a, H-4b, H-9a), 1.95 (ddd, $J=12.9$, 3.2, 2.6 Hz, H-6), 1.91 (s, H-15), 1.42 (s, H-12), 1.37 (s, H-13), 1.29 (s, H-14).

7. Chang, M.; Vazquez, J. T.; Nakanishi, K.; Cataldo, F.; Estrada, D. M.; Fernandez, J.; Gallardo, A.; Martin, J. D.; Norte, M.; Perez, R.; Rodriguez, M. L. *Phytochemistry* **1989**, *28*, 1417–1424.
8. Suzuki, M.; Daioh, M.; Vairappan, C. S.; Abe, T.; Masuda, M. *J. Nat. Prod.* **2001**, *64*, 597–602.
9. Brito, I.; Cueto, M.; Díaz-Marrero, A. R.; Darias, J.; Martin, A. S. *J. Nat. Prod.* **2002**, *65*, 946–948.
10. Francisco, M. E. Y.; Erickson, K. L. *J. Nat. Prod.* **2001**, *64*, 790–791.
11. Suzuki, M.; Nakano, S.; Takahashi, Y.; Abe, T.; Masuda, M.; Takahashi, H.; Kobayashi, K. *J. Nat. Prod.* **2002**, *65*, 801–804.