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New bromotriterpene polyethers from the Indian alga *Chondria armata*

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Abstract—Six new bromotriterpene polyethers, armatol A–F (**1**–**6**), with a rearranged carbon skeleton, were isolated from the Indian Ocean red alga *Chondria armata*. The structures were characterized by spectroscopic techniques, in particular 1D- and 2D-NMR. © 2001 Elsevier Science Ltd. All rights reserved.

Red algae represent a rich source of halogenated metabolites[2] that include mono-, sesqui- and di-terpenes as well as C_{15} and C_{30} ether lipids. Genus *Laurencia*, the most investigated, has provided interesting bioactive metabolites among those mentioned above. In particular, thyrsiferol[3] and venustatriol[4] are the first examples of squalene-derived polyethers found in this genus. From then on, a series of bromotriterpene polyethers have been found in specimens of *Laurencia*[5] collected all around the world. More recently, a new bromotriterpene, aurilol,[6] characterized by the presence of an oxepane ring in the molecule, was isolated from the gland of the sea hare *Dolabella auricularia* thus suggesting a dietary origin. In fact, a similar compound, enshuol,[7] was found in the red alga *Laurencia omaezakiana*. An overview of marine polyether triterpenes has just appeared in the literature:[8] the authors give a complete summary of the chemical structures, biogenetic considerations and biological activity of molecules coming from red algae, sponges or molluscs.

In our ongoing search for bioactive compounds from the Indian Ocean we have investigated *Chondria armata*, an alga of the same family of *Laurencia* (Rhodomelaceae, Ceramiales), that contained six new brominated polyether squalene derivatives, armatols A–F (**1**–**6**).

Preliminary screening of the chloroformic extract of the alga showed antiviral, antibacterial and antifungal activities[9] thus suggesting that the active agent(s) could be unusual lipophilic metabolite(s).

1. Results and discussion

Chondria armata was exhaustively treated with ethanol and the chloroform soluble fraction from this extract was submitted to chromatography (see Experimental) affording six new polyether bromotriterpenes.

Armatol A (**1**) had the molecular formula $C_{30}H_{51}BrO_6$ deduced by EIMS fragment and by ^{13}C NMR. The presence of one bromine atom was suggested by the characteristic pattern 1:1 of the molecular ion at *m/z* 588/586 and by the signal at δ 59.2 in the carbon spectrum. The ^{13}C NMR accounted for thirty carbons: eight methyls, nine methylenes, five methine groups, six quaternary carbons α to oxygens and, in the lowfield region, two disubstituted olefinic carbons. Analysis of the ^1H NMR spectrum exhibited the presence in the lowfield region of five methine signals at δ 3.89, 3.28, 3.25, 3.38 and 3.72 and two olefinic protons at δ 5.42 and 5.35 that were linked to nine methylenes. In fact in the COSY spectrum the signal resonating at δ 3.89 (H-3) correlated with the methylene at δ 2.33–2.00 (H_2-4) which in turn was linked to another methylene at δ 1.74–1.49 (H_2-5); the signal at δ 3.28 (H-7) correlated with the methylene at δ 1.65–1.43 (H_2-8) which in turn correlated with another methylene at δ 1.50–1.33 (H_2-9); the methine at δ 3.25 (H-11) correlated with the methylene at δ 1.64 (H_2-12) which in turn correlated with the methylene at δ 1.66 (H_2-13) which were linked to the other methine signal at δ 3.38 (H-14); this latter sequence was also confirmed by a TOCSY experiment; the methine signal at δ 3.72 (H-18) was linked to the methylene at δ 1.85–1.65 (H_2-17) which in turn correlated with the other methylene at δ 1.74 (H_2-16); and finally the signal at δ 5.35 (H-22) correlated with the other olefinic proton at δ 5.42 (H-21) which in turn correlated with the allylic methylene at δ 2.48–2.11

Keywords: polyethers; *Chondria armata*; bromotriterpenes.
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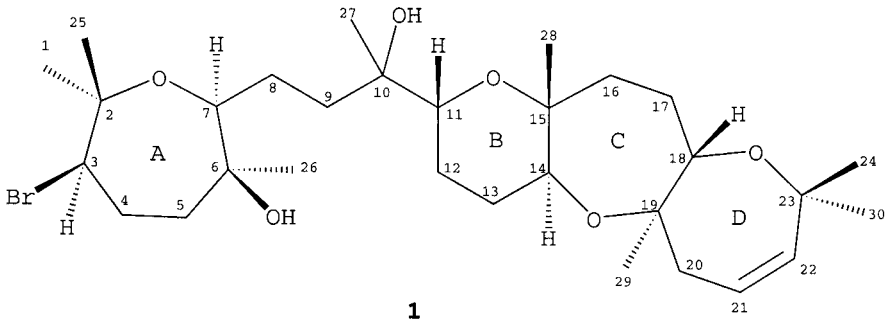
Table 1. ^{1}H NMR data (Bruker AMX 500 MHz, $CDCl_3$; δ values are referred to $CHCl_3$ (δ 7.26); assignments determined by ^{1}H–^{1}H COSY, HMQC experiments) for armatol A–F (**1**–**6**)

Position	δ 1H m Hz **1**	δ 1H m Hz **2**	δ 1H m Hz **3**	δ 1H m Hz **4**	δ 1H m Hz **5**	δ 1H m Hz **6**
1	1.36 s	1.36 s	1.35 s	1.36 s	1.36 s	1.36 s
2						
3	3.89 d 11.0	3.90 d 11.0	3.99 d 10.4	3.89 d 11.0	4.01 d 10.4	3.89 d 11.4
4	2.33ax–2.00eq	2.35ax–2.04eq m	2.33ax–2.05eq m	2.33ax–2.01eq m	2.30ax–2.00eq m	2.35ax–2.05eq m
5	1.74eq–1.49ax	1.77eq–1.48ax m	1.83eq–1.44ax m	1.75eq–1.48ax m	1.85eq–1.54ax m	1.75eq–1.49ax m
6						
7	3.28 dd 10.4, 3.0	3.31 dd 10.3, 2.9	3.28 dd 9.2, 2.4	3.30 dd 9.9, 2.6	3.28 dd 9.8, 3.0	3.31 dd 10.2, 3.0
8	1.65–1.43 m	1.63–1.48 m	1.65–1.44 m	1.63–1.47 m	1.62–1.43 m	1.64 m
9	1.50–1.33 m	1.52–1.35 m	1.52–1.34 m	1.50–1.35 m	1.53–1.33 m	1.54–1.34 m
10						
11	3.25 dd 10.8, 3.1	3.27 dd 12.4, 2.6	3.25 dd 10.1, 1.8	3.27 dd 11.7, 1.8	3.25 dd 11.8, 2.4	3.44 dd 5.0, 2.4
12	1.64 m	1.65 m	1.65 m	1.64 m	1.65 m	1.73–1.58 m
13	1.66 m	1.63 m	1.63 m	1.66 m	1.63 m	1.72 m
14	3.38 dd 11.3, 4.3	3.50 dd 11.0, 4.0	3.48 dd 10.7, 3.0	3.44 dd 10.6, 4.8	3.45 dd 10.4, 3.9	3.74 dd 11.0, 4.2
15						
16	1.74 m	1.88–1.73 m	1.87–1.70 m	1.77 m	1.88–1.72 m	2.02–1.58 m
17	1.85–1.65 m	2.05–1.45 m	2.00–1.48 m	1.90–1.50 m	2.00–1.56 m	2.28ax–1.88eq m
18	3.72 dd 11.2, 3.9	3.14 dd 11.4, 2.6	3.13 dd 10.9, 2.4	3.72 dd 11.4, 3.3	3.73 dd 10.9, 3.1	3.34 dd 7.4, 1.7
19						
20	2.48–2.11 m	1.75eq–1.52ax m	1.77eq–1.54ax m	2.13eq–1.64ax m	2.10eq–1.67ax m	2.12–1.18 m
21	5.42 m	2.21ax–2.05eq m	2.22ax–2.04eq m	2.04 m	2.06 m	2.43–2.09 m
22	5.35 d 12.1	4.10 d 10.6	4.10 d 10.9	4.31 dd 7.4, 2.6	4.33 dd 7.3, 2.5	4.22 bt 3.7
23						
24	1.19 s	1.32 s	1.32 s	1.27 s	1.27 s	1.31 s
25	1.40 s	1.41 s	1.41 s	1.42 s	1.40 s	1.42 s
26	1.11 s	1.12 s	1.18 s	1.11 s	1.19 s	1.12 s
27	1.08 s	1.09 s	1.09 s	1.09 s	1.10 s	1.10 s
28	1.19 s	1.19 s	1.18 s	1.22 s	1.22 s	1.22 s
29	1.26 s	1.22 s	1.23 s	1.24 s	1.24 s	1.32 s
30	1.24 s	1.31 s	1.33 s	1.40 s	1.34 s	1.40 s

Table 2. ^{13}C NMR data (Bruker AMX 500 MHz, $CDCl_3$; δ values are reported referred to $CDCl_3$ (δ 77.0); assignments aided by DEPT sequence, HMQC and HMBC) for armatol A–F (**1**–**6**)

Position	δ 13C m **1**	δ 13C m **2**	δ 13C m **3**	δ 13C m **4**	δ 13C m **5**	δ 13C m **6**
1	25.3 q	25.3 q	25.5 q	25.8 q	25.8 q	25.3 q
2	77.7 s	78.1 s	78.1 s	78.3 s	78.2 s	79.1 s
3	59.1 d	59.2 d	60.1 d	59.7 d	60.4 d	59.2 d
4	30.4 t	30.4 t	31.4 t	30.9 t	30.2 t	30.4 t
5	44.3 t	44.3 t	44.3 t	44.9 t	45.5 t	44.3 t
6	72.3 s	72.3 s	72.4 s	72.8 s	72.8 s	72.2 s
7	76.4 d	76.5 d	76.5 d	76.9 d	78.8 d	79.5 d
8	23.4 t	23.4 t	23.3 t	23.9 t	23.5 t	25.1 t
9	33.4 t	33.5 t	33.4 t	34.0 t	33.7 t	33.1 t
10	73.1 s	73.2 s	73.4 s	73.7 s	73.7 s	72.9 s
11	74.9 d	75.4 d	75.5 d	75.7 d	75.3 d	76.6 d
12	26.9 t	25.2 t	25.3 t	25.7 t	25.7 t	24.5 t
13	27.3 t	27.1 t	27.3 t	27.8 t	27.5 t	23.3 t
14	73.5 d	70.5 d	70.5 d	71.9 d	71.4 d	74.5 d
15	77.2 s	77.2 s	77.3 s	77.7 s	77.6 s	73.2 s
16	38.4 t	40.3 t	40.2 t	40.2 t	40.3 t	35.6 t
17	27.3 t	28.7 t	28.6 t	28.9 t	28.8 t	21.7 t
18	76.4 d	77.4 d	77.5 d	76.7 d	76.2 d	76.6 d
19	80.1 s	78.1 s	78.8 s	79.4 s	79.3 s	79.5 s
20	41.8 t	44.7 t	44.7 t	40.8 t	39.6 t	27.0 t
21	121.9 d	31.4 t	31.4 t	29.2 t	31.4 t	26.2 t
22	136.4 d	59.7 d	59.5 d	65.6 d	65.1 d	59.7 d
23	77.8 s	77.8 s	77.8 s	77.4 s	77.6 d	73.2 s
24	25.9 q	25.6 q	25.3 q	30.9 q	30.9 q	32.6 q
25	25.7 q	25.7 q	25.7 q	26.6 q	26.6 q	27.8 q
26	25.9 q	25.0 q	21.3 q	24.0 q	21.3 q	24.9 q
27	23.4 q	23.5 q	23.5 q	25.5 q	23.5 q	23.4 q
28	25.9 q	19.7 q	19.8 q	19.6 q	19.1 q	14.9 q
29	18.0 q	16.6 q	16.8 q	17.9 q	17.4 q	24.5 q
30	29.3 q	24.3 q	24.3 q	26.3 q	26.8 q	27.8 q



1

(H_2-20). Furthermore in the ^{1}H NMR spectrum two D_2O exchangeable resonances (3.01 and 2.35 ppm) were assigned to two OH groups, further confirmed by the band at 3450 cm^{-1} in the ir spectrum. 2D-NMR studies allowed all resonances to be assigned (Tables 1 and 2). In particular, HMBC and NOESY experiments helped us to link together these subunits and to give structure **1**.

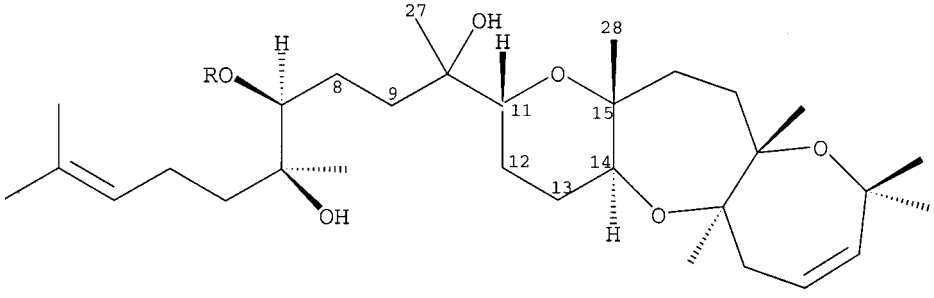
In fact, a long range correlation between C-2 (δ 78.1) and H-7 (δ 3.28) confirmed the presence of the ether ring A whereas the long range correlation between C-15 (δ 77.2) and H-18 (δ 3.72) and between C-19 (δ 78.1) and H-14 (δ 3.38) confirmed the presence of the ether ring C. On the other hand, NOESY cross-peaks between H-11 (δ 3.25) and H_3-28 (δ 1.19) and between H-18 (δ 3.72) and H_3-24 (δ 1.19) suggested the presence of the other two ether rings B and D, respectively. Furthermore C-6, CH_3-26 and C-7 had long-range correlations with the signal at δ 3.01 whereas C-10, CH_3-27 and C-11 had correlation with the signal at δ 2.35, locating the first OH group at C-6 and the second at C-10.

The relative stereochemistry of armatol A (**1**) was inferred by NOESY and NOE difference experiments as follows: H-3 had cross-peaks with H-5ax, H-7, H_3-1, whereas H-7 had correlations with H_3-1, H-3, H-5ax and H_3-26, thus establishing the axial orientation of the OH group at C-6. Proton H-11 had strong NOE effects with H_3-27 and H_3-28 thus suggesting that ring B assumed an ordinary chair conformation and H-11 was β oriented, whereas H-14 had a NOE with H_3-29 and H-17ax; H-18 exhibited cross-peaks with H-20ax and H_3-30 establishing the all-*trans* junction for the rings B–D. Finally a monodimensional experiment confirmed the *cis* configuration of the double bond. All these data were confirmed by carrying out 1D- and 2D-experiments in C_6D_6 and are reported in the Experimental. Lacking a secondary alcohol function, it was impossible to perform any chemical method to establish the absolute stereochemistry on the unmodified molecule; however, as reported in the literature, treatment with Zn and acetic acid[6] yielded compound **7** suitable for application of the modified Mosher method to the secondary alcohol obtained from the opening of ring A. The chemical shift analysis of the (*S*)-MTPA and (*R*)-MTPA esters (Table 3) was consistent with the absolute configuration *S* at C-7; according to the relative stereochemistry of the ring A, the absolute stereochemistries at C-3 and C-6 should be *R* and *S*, respectively.

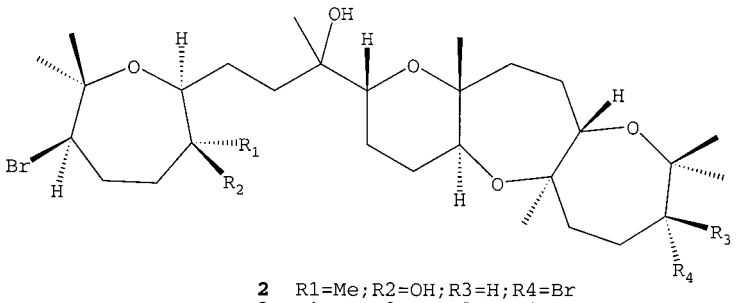
Table 3. Selected ^{1}H NMR chemical shifts (Bruker AMX 500 MHz, $CDCl_3$; δ values are referred to C_6H_6 (δ 7.15); $\Delta\delta$ ($\Delta\delta$ ($\delta_{(S)\text{-ester}}-\delta_{(R)\text{-ester}}$) values are given in ppm) for the MTPA esters of **7**)

H	7a	7b	$\Delta\delta$
H-7	5.27	5.33	−0.06
H-11	3.09	3.16	−0.07
H_3-27	0.98	1.07	−0.09
H-3	5.10	5.09	+0.01
H_3-1	1.58	1.57	+0.01
H_3-26	1.07	1.03	+0.04
H_2-4	2.10	2.08	+0.02

Armatol B (**2**) had the molecular formula $C_{30}H_{52}Br_2O_6$ deduced by the FAB mass fragment (MH^+, 667) and by the ^{13}C NMR spectrum. The presence of two bromine atoms was suggested by the characteristic 1:2:1 pattern of the molecular ion in the FAB mass spectrum and by two resonances at δ 59.2 and δ 59.7 in the carbon spectrum. The ^{1}H NMR data of **2** revealed the presence of eight methyl singlets, ten methylenes, five downfield methines and two D_2O exchangeable resonances (3.01 and 2.35 ppm) confirmed by the band at 3450 cm^{-1} in the ir spectrum attributable to two OH groups. The ^{13}C NMR spectrum of



7 R= H
7a, **7b** {MTPA



2 R1=Me;R2=OH;R3=H;R4=Br
3 R1=OH;R2=Me;R3=H;R4=Br
4 R1=Me;R2=OH;R3=Br;R4=H
5 R1=OH;R2=Me;R3=Br;R4=H

2 accounted for thirty carbons: 8 methyls, 6 oxygenated quaternary carbons, 4 oxygenated tertiary carbons, 2 brominated tertiary carbons and 10 methylenes.

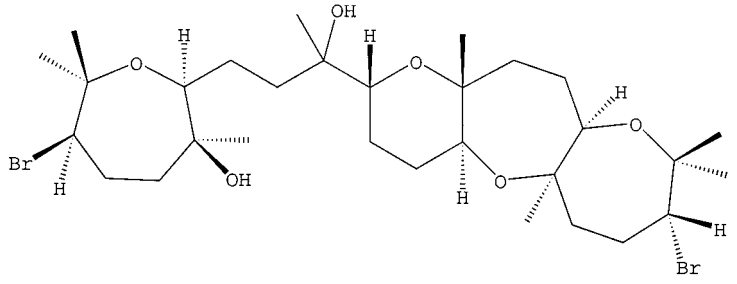
Analysis of the COSY spectrum revealed the presence of the following partial structures, confirmed also by TOCSY: H3–H5, H7–H9, H11–H14, H16–H18, H20–H22. The most remarkable difference between **2** and **1** was the presence of the methine signal at δ 4.10 (H-22) which correlated with the methylene at δ 2.21–2.05 (H_2-21) in turn linked to the methylene at δ 1.75–1.52 (H_2-20). In fact, this methine correlated, in the HMQC experiment, with the carbon resonance at δ 59.7, allowing us to locate the second bromine atom at C-22 (Tables 1 and 2). Furthermore, a strong crosspeak between H-22 and H-18, in the NOESY experiment, suggested the equatorial position of the bromine group. The relative stereochemistry of the rings A and B–D was inferred by 1D and 2D-NOE experiments and was very similar to that of **1** with the exception due to the presence of the second bromine group on the ring D.

Armatol C (**3**) presented the same fragment in FAB mass (MH^+, 667) and the 1:2:1 pattern suggested the presence of two bromine atoms. It differred from **2** only for a few resonances in the ^{1}H- and ^{13}C NMR spectra: 1) the protonic resonance of H-3 was shifted from δ 3.89 to δ 4.00 most likely due to the inverse stereochemistry at C-6; in fact, in Armatol B (**2**) a crosspeak between H-7 and H_3-26 located the OH group in axial orientation while in this case the absence of this effect located the OH group in equatorial position, which in turn had a steric influence on H-3 that therefore resonated at slightly lower field; 2) the ^{13}C NMR shift of C-26 (δ 21.5) further supports its axial orientation as it resonates at δ 25.0 in the equatorial orientation. All data are reported in Tables 1 and 2 and in the Experimental.

Armatol D (**4**) showed the same FAB mass fragment as **2** and **3**, characterized by the presence of two bromine atoms. The majority of the protonic signals appeared similar to armatol B (**2**), only a double doublet in the lowfield region (δ 4.33) which resonated at δ 65.4 in the HMQC experiment, suggested a different stereochemistry for C-22. This proved that the bromine on this carbon was axially oriented, which further explained the downfield shift of H-18 (δ 3.72), and was further confirmed by the absence of a NOE crosspeak in the NOESY experiments between H-22 and H-18 as occurred in armatol B (**2**). COSY, TOCSY, NOESY and HMBC were very similar to Armatol B with the exception of the differences caused by the inverse stereochemistry at C-22.

Armatol E (**5**), with the same FAB mass fragment as the above compounds, was spectroscopically very close to **4** and showed the same signals in the proton spectrum with the exception of the stereochemistry at C-6, as occurred in Armatol C (**3**). In fact, the value of H-3 was slightly shifted at δ 4.00 probably due to the steric effect of the OH group at C-6. Furthermore, an axial orientation for C-26 was also suggested by the ^{13}C NMR value, that confirmed the inversion of the stereochemistry at C-6.

Finally Armatol F (**6**) had the molecular formula $C_{30}H_{52}Br_2O_6$ deduced by FAB mass fragment and by ^{13}C NMR spectrum. The presence of two bromine atoms was suggested by the characteristic 1:2:1 pattern of the molecular ion in the FAB mass spectrum and by two resonances at δ 59.2 and δ 59.7 in the carbon spectrum. The ^{1}H NMR spectrum presented, in the lowfield region, six methine resonances δ 3.31, 3.34, 3.44, 3.74, 3.89 and finally a broad triplet at δ 4.22 (H-22) assigned to one of the two brominated carbon atoms: this signal correlated (in the COSY and TOCSY spectra) with the methylenes at δ 2.43–2.09



(H_2-21) and δ 2.12–1.18 (H_2-20); the proton at δ 3.34 (H-18) correlated with the methylene at δ 2.28–1.88 (H_2-17) which in turn correlated with another methylene at δ 2.02–1.58 (H_2-16); the proton at δ 3.74 (H-14) correlated with the methylene at δ 1.72 (H_2-13) that correlated with the methylene at δ 1.73–1.58 (H_2-12), which in turn had correlation with the proton at δ 3.44 (H-11). The proton at δ 3.31 (H-7) correlated with the methylene at δ 1.64 (H_2-8), which in turn correlated with the methylene at δ 1.54–1.34 (H_2-9). Finally, the proton at δ 3.89 (H-3) correlated with the methylene at δ 2.35–2.05 (H_2-4), which in turn correlated with the methylene at δ 1.75–1.49 (H_2-5) (see Table 1).

Careful analysis of the ^{13}C NMR spectrum showed some differences with respect to the other compounds: in fact, the resonance of the methyl group at C-19 was downfield shifted with respect to the same methyl group in Armatol D (**4**) (δ 24.5 vs δ 17.9): this was due to the different type of junction between rings C and D that appeared to be *cis*; furthermore C-17 and C-20 appeared highfield with respect to the compounds with all *trans*-junctions (δ 21.7 vs 28.9, C-17; 27.05 vs δ 40.8, C-20). NOESY experiments and monodimensional NOE difference spectroscopy showed that the relative configuration of ring A remained unvaried, as ring B; since H-18 had a NOE with a signal at δ 1.31 attributable both to H_3-30 and H_3-29 this problem was solved by assigning the molecule in a different NMR solvent (C_6D_6, see Experimental). Starting from the signal at δ 3.53 attributable to one of the brominated proton (δ 59.5), the COSY spectrum showed correlation with the methylene at δ 2.18–1.86 (H_2-4), which in turn was linked to the methylene at δ 1.50–0.96 (H_2-5). The signal at δ 2.81 (H-7) showed a cross peak with the methylene at δ 1.78–1.70 (H_2-8), which in turn correlated with the methylene at δ 1.55–1.45 (H_2-9). The proton at δ 3.42 (H-11) correlated with the methylene at δ 1.78–1.48 (H_2-12), which in turn was linked to the methylene at δ 1.75–1.48 (H_2-13), which in turn correlated with the proton at δ 3.81 (H-14): this sequence was also confirmed in a TOCSY experiment. The proton at δ 3.31 (H-18) correlated with the methylene at δ 2.32–1.86 (H_2-17), which in turn had cross peaks with the methylene at δ 2.15–1.66 (H_2-16). Finally, the other brominated proton at δ 3.70 (H-22) had a correlation with the methylene at δ 1.88–1.70 (H_2-21), which in turn was linked to the methylene at δ 1.98–0.79 (H_2-20). HMBC helped us to link these five subunits, the eight methyls and the oxygenated quaternary carbons to give structure **6**. Only NOESY and NOE difference experiments were diagnostic to establish the relative stereochemistry of the molecule. In fact, H-3 (δ 3.53) had a strong effect with H-7 (δ 2.81), with H_3-1 (δ 1.28), H-5ax (δ 0.96), whereas H-7 (δ 2.81) had a cross-peak with H_3-1, H-3, H-5ax and with H_3-26 (δ 1.01) that suggested the axial orientation of the exchangeable hydroxyl group located at C-6. Proton H-11 (δ 3.42) had correlation with H_3-27 (δ 1.16) and H_3-28 (δ 1.23), whereas H-14 (δ 3.81) had strong NOE with H-17ax (δ 2.32) and H_3-29 (δ 1.20). Proton H-18 (δ 3.31) had cross-peaks with H_3-24 (δ 1.31), H-20ax (δ 0.79) and H_3-29 (δ 1.20): this latter signal was diagnostic for suggesting the *cis* junction for the rings C–D. Finally, H-22 (δ 3.70) had NOESY correlations with both H_3-24 (δ 1.31) and H_3-30 (δ 1.04), suggesting its equatorial position, and with H-20ax (δ 0.79).

2. Conclusion

Armatols A–F represent the first example of a new class of bromotriterpenes found in the red alga *Chondria armata*. The triterpenoids isolated from *Laurencia* including the armatols could arise from (6*S*,7*S*,10*R*,11*R*,14*R*,15*R*,18*S*,19*S*)-squalene tetraepoxide, a common precursor. However, from a biogenetic point of view, the discovery of several molecules with different stereocenters suggest the hypothesis that the biosynthesis of these molecules may occur in a not concerted way.

Interestingly, Fernandez[8] et al. reported the strong cytotoxic properties of these squalene-derived compounds, suggesting that further biological assay should be directed to an evaluation of this activity.

3.1. Experimental

3.1.1. General experimental procedures. Precoated TLC plates Merck Si gel 60 F254 were used for analytical TLC. Sephadex LH-20 Pharmacia and Merck Kieselgel 60 powder were used for preparative column chromatography (150×4 cm). Analytical Novapak C-18 column Waters was used on a Waters HPLC with refractometer index detector. The mass spectra were obtained from AEI MS-30 (EIMS) and ZAB VG (FABMS) instruments. IR spectra were recorded in a liquid film on a BIORAD FTS 155 FTIR. Optical rotations were measured on a Jasco DIP 370 polarimeter. ^1H- and ^{13}C NMR spectra were recorded on a Bruker AMX 500 (500 MHz) spectrometer.

3.2. Biological material

The alga was collected along the Indian coasts of Goa (off Anjuna). A sample has been deposited at NIO Repository and Taxonomy Centre no. 1316 (Goa, India). The alga was identified by Geeta Deshmukh of the National Institute of Oceanography.

3.3. Extraction and isolation

The alga (60 g dry weight) was extracted exhaustively with ethanol. Further fractionation of the crude extract into petroleum ether, chloroform, *n*-butanol and water soluble fraction and testing of the fractions led to the location of the antiviral activity in chloroform soluble fraction. The chloroform extract (ca 1 g) was submitted to a LH-20 sephadex column in $CHCl_3/CH_3OH$ 1:1 to yield several fractions. Further purification of these fractions were carried out on silica gel column using petroleum ether and increasing amounts of diethyl ether. Finally some fractions from the silica column were submitted to further purification on HPLC RP-18 analytical column using as eluent CH_3CN/H_2O 9:1 and CH_3CN/H_2O 8:2.

3.3.1. Armatol A (1). (White oil, 20 mg, 0.034 mmol); $[\alpha]_D$= +43.4 (*c* 2.0, $CHCl_3$), IR (liquid film) ν_{max}: 3452, 2988, 2942, 2872, 1722, 1444, 1377, 1084, 757 cm^{-1}; HREIMS *m/z*: [586.2876 calculated for $C_{30}H_{51}{}^{79}BrO_6$ 586.2870]; EIMS 588, 586 $(M)^+$, 570, 568 $(M-H_2O)^+$, 506 $(M-HBr)^+$. ^1H- and ^{13}C NMR data in $CDCl_3$ are reported in Tables 1 and 2. ^1H NMR data in C_6D_6 (ppm, *J*

Hz): 1.24 (H_3-1, s), 3.53 (H-3, d 11.2), 2.18–1.86 (H_2-4, m), 1.50–0.97 (H_2-5, m), 2.80 (H-7, dd 9.9, 3.0), 1.75–1.65 (H_2-8, m), 1.60–1.43 (H_2-9, m), 3.22 (H-11, 10.8, 3.1), 1.52 (H_2-12, m), 1.75 (H_2-13, m), 3.45 (H-14, 11.3, 4.3) 1.73 (H_2-16, m), 1.97–1.78 (H_2-17, m), 3.84 (H-18, 11.2, 3.9), 2.56–2.23 (H_2-20, ddd 15.2, 5.6, 1.8), 5.42 (H-21, m), 5.20 (H-22, d 12.1), 1.09 (H_3-24, s), 1.33 (H_3-25, s), 1.00 (H_3-26, s), 1.14 (H_3-27, s), 1.20 (H_3-28, s), 1.28 (H_3-29, s), 1.24 (H_3-30, s); ^{13}C NMR data in C_6D_6 (ppm): 25.3 (C-1), 77.6 (C-2), 59.3 (C-3), 30.6 (C-4), 44.3 (C-5), 71.9 (C-6), 76.6 (C-7), 23.7 (C-8), 34.1 (C-9), 73.0 (C-10), 75.7 (C-11), 25.6 (C-12), 27.3 (C-13), 74.1 (C-14), 77.4 (C-15), 38.7 (C-16), 27.5 (C-17), 76.5 (C-18), 80.3 (C-19), 42.3 (C-20), 122.3 (C-21), 136.7 (C-22), 77.9 (C-23), 26.1 (C-24), 25.7 (C-25), 25.2 (C-26), 23.5 (C-27), 17.5 (C-28), 18.1 (C-29), 29.5 (C-30).

3.3.2. Armatol B (2). (White oil, 12 mg, 0.018 mmol): $[\alpha]_D$=+25.4 (*c* 0.4, $CHCl_3$); IR (liquid film) ν_{max}: 3475, 2988, 2942, 2880, 1467, 1382, 1142, 1088, 764 cm^{-1}; HR-FABMS *m/z*: [667.2143 calculated for $C_{30}H_{52}{}^{79}Br_2O_6$ 666.2131 [MH]; FABMS 667, 669, 671 (M+H, 1:2:1), 649, 651, 653 (M+H−H_2O), 591, 589 (M+H−HBr), 511 (M+H−2HBr); ^{1}H and ^{13}C NMR data are reported in Tables 1 and 2.

3.3.3. Armatol C (3). (White oil, 1.5 mg, 0.002 mmol): $[\alpha]_D$=+20.4 (*c* 0.15, $CHCl_3$); IR (liquid film) ν_{max}: 3475, 2988, 2942, 2880, 1467, 1382, 1142, 1088, 764 cm^{-1}; HR-FABMS *m/z*: [667.2150 calculated for $C_{30}H_{52}{}^{79}Br_2O_6$ 666.2131 [MH]; FABMS 667, 669, 671 (M+H, 1:2:1), 649, 651, 653 (M+H−H_2O), 591, 589 (M+H−HBr), 511 (M+H−2HBr); ^{1}H and ^{13}C NMR data are reported in Tables 1 and 2.

3.3.4. Armatol D (4). (White oil, 21 mg, 0.031 mmol): $[\alpha]_D$=+25.1 (*c* 2.0, $CHCl_3$); IR (liquid film) ν_{max}: 3475, 2988, 2934, 2880, 1459, 1374, 1135, 1073, 764 cm^{-1}; HR-FABMS *m/z*: [667.2148 calculated for $C_{30}H_{52}{}^{79}Br_2O_6$ 666.2131 [MH]; FABMS 667, 669, 671 (M+H, 1:2:1), 649, 651, 653 (M+H−H_2O), 591, 589 (M+H−HBr), 511 (M+H−2HBr); ^{1}H and ^{13}C NMR data are reported in Tables 1 and 2.

3.3.5. Armatol E (5). (White oil, 1.8 mg, 0.003 mmol): $[\alpha]_D$=+13.6 (*c* 0.18, $CHCl_3$); IR (liquid film) ν_{max}: 3475, 2988, 2934, 2880, 1459, 1374, 1135, 1073, 764 cm^{-1}; HR-FABMS *m/z*: [667.2140 calculated for $C_{30}H_{52}{}^{79}Br_2O_6$ 666.2131 [MH]; FABMS 667, 669, 671 (M+H, 1:2:1), 649, 651, 653 (M+H−H_2O), 591, 589 (M+H−HBr), 511 (M+H−2HBr); ^{1}H and ^{13}C NMR data are reported in Tables 1 and 2.

3.3.6. Armatol F (6). (White oil, 15 mg, 0.022 mmol): $[\alpha]_D$=+17.9 (*c* 1.5, $CHCl_3$), IR (liquid film) ν_{max}: 3459, 2988, 2942, 2872, 1449, 1374, 1142, 1073, 757 cm^{-1}; HR-FABMS *m/z*: [667.2146 calculated for $C_{30}H_{52}{}^{79}Br_2O_6$ 666.2131 [MH]; FABMS 667, 669, 671 (M+H, 1:2:1), 649, 651, 653 (M+H−H_2O), 591, 589 (M+H−HBr), 511 (M+H−2HBr); ^{1}H and ^{13}C NMR data in $CDCl_3$ are reported in Tables 1 and 2; ^{1}H NMR data in C_6D_6 (ppm, *J* Hz): 1.28 (H_3-1, s), 3.53 (H-3, d 11.0), 2.18–1.86 (H_2-4, m), 1.50–0.96 (H_2-5, m), 2.81 (H-7, dd 9.4, 2.7), 1.78–1.70 (H_2-8, m), 1.55–1.45 (H_2-9, m), 3.42 (H-11, dd 9.0, 5.1), 1.78–1.48 (H_2-12, m), 1.75–1.48 (H_2-13, m), 3.81 (H-14, dd 10.5, 4.7), 2.15–1.66 (H_2-16 m,), 2.32–1.86 (H_2-17, m), 3.31 (H-18, dd 6.9, 3.1), 1.98–0.79 (H_2-20, m), 1.88–1.70 (H_2-21 m), 3.70 (H-22, t 3.2), 1.31 (H_3-24, s), 1.35 (H_3-25, s), 1.01 (H_3-26, s), 1.16 (H_3-27, s), 1.23 (H_3-28, s), 1.20 (H_3-29, s), 1.04 (H_3-30, s); ^{13}C NMR data in C_6D_6 (ppm): 25.5 (C-1), 77.6 (C-2), 59.5 (C-3), 30.6 (C-4), 44.3 (C-5), 72.0 (C-6), 76.6 (C-7), 23.7 (C-8), 33.8 (C-9), 73.2 (C-10), 75.9 (C-11), 25.2 (C-12), 25.6 (C-13), 74.6 (C-14), 73.3 (C-15), 36.2 (C-16), 21.7 (C-17), 79.2 (C-18), 78.9 (C-19), 27.6 (C-20), 26.3 (C-21), 59.8 (C-22), 73.4 (C-23), 32.5 (C-24), 25.7 8C-25), 25.3 (C-26), 23.5 (C-27), 15.6 (C-28), 24.4 (C-29), 27.7 (C-30).

3.4. Reductive dehalogenation

Armatol A (**1**) (5 mg, 0.008 mmol) was refluxed in EtOH (0.30 mL) with zinc powder (11 mg) and NH_4Cl (10 mg) for 40 min. and then filtered through a pad of Celite. The residue was washed with EtOAc (5 mL) to afford compound **7**. ^{1}H- and ^{13}C NMR (C_6D_6): 5.44, 5.20, 3.84, 3.45, 3.40, 3.17, 2.58–2.20, 2.19, 1.33–1.45 1.67, 1.59, 1.27, 1.24, 1.20, 1.14, 1.09; 137.1, 125.8, 122.9, 78.0, 76.8, 75.8, 74.6, 42.6, 39.8, 39.0, 35.9, This compound was submitted to the modified Mosher's method to give the two (*R*)- and (*S*)- esters **7b** and **7a**, respectively.

3.5. Biological assays

Antiviral, antibacterial and antifungal tests were performed on the crude extract, as described in Ref. 9a and b.

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