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NEW POLYACETYLENES FROM THE SPONGE SIPHONOCHALINA SP.

M. Rotem and Y. Kashman*

Department of Chemistry, Tel-Aviv University, Tel Aviv, Israel

Abstract

Six new compounds, characterized by a long unsaturated alkyl chain (nC_{22}), were isolated from a marine sponge. All compounds except for one, possess an enyne terminus on one side of the molecule and either a terminal acetylene (in four) or a propargyl alcohol on the other end. Four of the compounds were unequivocally identified mainly by spectroscopic methods.

Acetylenic compounds are well-known constituents of plants: only few, however, are known from marine organisms and to our knowledge only one group of compounds contains more than a single triple bond. Among the acetylene containing marine natural products are: A group of halogenated ethers, characterized by a straight-chain C-15 carbon skeleton and a terminal enyne function which has been isolated from algae[1] and a sea hare[2], carotenoids[3], two steroids[4], a sesquiterpene[5] and polyketids[6,7].

A diacetylene was found in a group of several n C-22 straight-chain compounds isolated from a marine sponge[8]. One of the compounds found in the latter sponge contains, again, the enyne terminus - an end group which turns out to be quite abundant in the above and the herewith discussed compounds.

In our continuing search for bioactive compounds from marine organisms we have isolated from the sponge Siphonochalina sp.[9] collected at several places in the southern part of the Gulf of Eilat (the Red Sea) six n C-22 straight-chain acetylenic compounds.

Extraction of the freeze-dryed sponge (petrol ether, 4% dry weight) and subsequent repeated chromatographies (LH-20 and Silica gel)[10,11] gave six closely related new compounds, named in order of polarity, Δ^{15}-docos-1-yne (1; $Rf^{12a}=0.65$; 0.2% based on the dry weight of the animal), octahydrosiphonochalyne (2; $Rf^{12a}=0.55$; 0.4%), dihydrosiphonochalyne (4; $Rf^{12a}=0.44$; 0.1%) siphonochalyne (3; $Rf^{12b}=0.34$; 0.2%), dehydrosiphonochalynol (6; $Rf^{12b}=0.55$; 0.1%) and siphonochalynol (5; $Rf^{12b}=0.43$; 0.3%).

Δ^{15}-docos-1-yne (1), $C_{22}H_{40}$; m/e 304(12%), 278(6%) and 275(4%) followed by a series of peaks with 14 m.u. intervals[13]. The IR, UV and NMR spectra of 1 suggested the presence of a terminal acetylene and an additional unconjugated double bond: λ_{max}^{hexane} end absorption; $\nu_{max}^{CHCl_3}$ 3300 and 2120 (terminal-C≡CH group); 2920, 2850, 1460, 1380, 930, 630 cm^{-1}; $\delta(CCl_4$, 60 MHz) 0.90t($J=5Hz, CH_2-C\underline{H}_3$) 1.35 brs($28H, -(CH_2)_n-$), 1.80t($J=2.2Hz, -CH_2C{\equiv}C\underline{H}$)[14], 2.05m(6H) and 5.35t($J=6Hz$, $-C\underline{H}=C\underline{H}-$). Hydrogenation of 1 over Pd-C gave n-docosane[15]. The above data suggested the following general formula: $CH_3-(CH_2)_m-CH=CH-(CH_2)_n-C{\equiv}CH$ The size of m and n was established by the mass spectrum of the hydroxy dimethylamino derivative of 1[16] obtained by mono peroxidation of the double bond, using m-chloroperbenzoic acid (3 hrs at 50° in CH_2Cl_2)[17], followed by 8 hr heating of the epoxide solution in Me_2NH in a mini pressure reactor at 120°. The two main significant fragments obtained in the mass spectrum, the ammonium ions $Me_2\overset{+}{N}=CH(CH)_2)_{12}-C{\equiv}CH$ (m/e 250, 44%) and $CH_3(CH_2)_5$ -

$-CH{=}\overset{+}{N}Me_2$ (m/e 142, 50%), determined unequivocally the size of m and n as 12 and 5 respectively. Assignment of a cis configuration of the isolated double bond was based on the absence of IR absorption at 970 cm^{-1} [8,18].

Siphonochalyne - (3), $C_{22}H_{24}$. All five siphonochalynes (2-6) have in common, apart from the linear C-22 alkyl chain (which was confirmed by hydrogenation, accompanied by hydrogenolysis in case of alcohols 5 and 6) a cis -CH=CH-C≡CH terminus. This end group was confirmed by IR, UV, ^1H and ^{13}C-NMR spectra: λ_{max}^{hexane} 225 nm; ν_{max} 3300 and 2100 cm^{-1}; δ($CDCl_3$, 270 MHz) 2.90d (J=1.7Hz,≡CH)[14],5.44dd(J=10 and 1.7Hz,=CH-C≡) and 6.0dt(J=10 and 7.5Hz, CH_2-CH=); δ($CDCl_3$,22.63 MHz) 82.0, 80.6, 108.7 and 146.0 (C-22, 21, 20 and 19 respectively).

The spectral data of 3 suggested the presence of two additional unsaturated sites, that is, a terminal acetylene and a $(C{\equiv}C)_3$ unit: λ_{max}^{hexane} 310, 284, 268, 253 nm[19]; $\nu_{max}^{CCl_4}$ 3300 (C≡CH), 3020 (=CH), 2930, 2830, 2220s[20], 2120, 2100 (C≡CH), 1540, 1460, 1430, 1350, 1020, 825, 720 cm^{-1}; δ($CDCl_3$,90MHz) 1.53m(12H), 2.00t(J=2.4Hz ≡CH), 2.28m(8H), 3.08d(J=2.1Hz, =CH-C≡CH), 5.46dd(1H) and 6.00dt(1H). The highly characteristic UV spectra with the very sharp vibrational fine structure[19] confirms unequivocally the triyne unit; the exact location of which had next to be established. Epoxidation of 3 with m-chloroperbenzoic acid (6 hrs, 50° in CH_2Cl_2)[21] gave the mono epoxide on which an LIS experiment was performed in order to determine the triyne location in the molecule ($CDCl_3$, 270 MHz):

a. 1.53-1.66m (12H), 1.95t (1H) 2.35-2.40m (8H), 3.04m (2H), 3.44dd (1H)
b. 1.53brs(4H), 1.95t (1H), 2.31-2.61(16H), 3.94-4.42m (3H)

a. Pure 3 b. After adding 0.5eq. of $Eu(fod)_3$-d_{27}.

The paramagnetic shift of eight protons from the 1.53-1.66 region, leaving behind four unaffected ones, indicated that a six methylene chain (the allyl, propargyl and the four shifted CH_2 groups) connects the enyne (the complexation site) to the triyne (see formula 3).

Octahydrosiphonochalyne-(2), $C_{22}H_{32}$; λ_{max}^{neat} 3300, 2920, 2850, 2200, 2120, 2100, 1610, 1460, 1430, 690 cm^{-1}; δ($CDCl_3$, 90MHz) 1.32m(20H), 1.93t(J=2.6Hz, -C≡CH), 2.3m(8H), 3.07d(J=2.1Hz, =CH-C≡CH), 5.3dd(1H) and 5.85dt(1H); no molecular ion could be observed in the mass spectrum, the highest peak appeared at m/e 205(10%), (the parent peak being m/e 91 (100%)). The existence of a third acetylenic bond, apart from the two in the termini (-HC=CH-C≡CH and C≡CH) was clear from the IR (three C≡C bonds) and from the existence of eight allylic and propargylic protons in the δ2.3 region (two CH_2 groups next to the end groups + two groups from both sides of the additional C≡C group). The exact location of the central triple bond could not yet be determined. a similar approach to the one described for compound 3 failed to provide unequivocal results. Furthermore, a microzonolysis experiment[22] gave too many fragments avoiding unambiguous conclusions.

Dihydrosiphonochalyne - (4), $C_{22}H_{26}$; the IR, UV and NMR spectra indicated the presence of the enyne and yne termini as in 2 and 3 and the existence of an additional $-(C{\equiv}C)_2CH{=}CH$ group: λ_{max}^{hexane} 284, 263 and 252 nm[19]; ν_{max}^{neat} 3300, 3020, 2920, 2850, 2200, 2100, 2080, 1450, 1430 and 730 cm^{-1}; δ($CDCl_3$,270MHz)1.30m(14H), 1.96s(≡CH), 2.31m(6H), 3.00d(J=2Hz,=CH-C≡CH), 5.45dd(2H) and 5.95dt(2H), no molecular ion could be obtained in the mass spectrum even at 15 eV or by the use of chemical ionization.

According to the above data two general formulas 4a and 4b can be suggested for this compound, differentiation between the two needs, however, more material and further work (the microozonolysis results were as unambiguous as with 3).

<u>Siphonochalynol</u> - (<u>5</u>), $C_{22}H_{24}O$; m/e (CI), 305 $(M+I)^+$ accompanied by m/e 287 $(M+1-H_2O)^+$; $\nu_{max}^{CCl_4}$ 3600-3100, 3300, 2920, 2860, 2210s, 2090, 1425, 1300, 1215, 1130, 1100, 900, 630 cm^{-1}; λ_{max}^{MeOH} 308, 283, 267 and 252 nm[19]; δ($CDCl_3$, 270MHz) 1.50m(10H), 2.30m(8H), 3.09d(J=2.3Hz, $=CH-C\equiv C\underline{H}$), 4.25t(J=2.2Hz, $-CH_2-C\equiv C-C\underline{H}_2OH$), 5.47dd(J=10.9 and 2.3Hz, 1H) and 5.96dt(J=10.9 and 6.7, 1H). The above data suggested the structure of the two ends of the molecule that is, the enyne function on one end and the propargyl alcohol on the other. The latter group was also confirmed by MnO_2 oxidation to the corresponding aldehyde.

The location of the triyne was unequivocally confirmed by an LIS experiment (270 MHz):

						8	7	6	5	4	3	2	1	
	$HC\equiv C-CH=CH-$	CH_2-	$(CH_2)_2-$	CH_2-	$(C\equiv C)_3-$	CH_2-	CH_2-	CH_2-	CH_2-	CH_2-	C	$\equiv C-$	CH_2OH	<u>5</u>
a.		2.3	1.5	2.3		2.3	1.5	1.5	1.5	2.3			4.25	
b.		2.3dt	1.5m	2.3m		2.5t	1.9	2.1	2.2	3.0t			6.50	
								quintets, (J=7.5Hz)						

a. Pure compound <u>5</u> b. Compound <u>5</u> with 0.4eq. of $Eu(fod)_3-d_{27}$.

<u>Dehydrosiphonochalynol</u> - (<u>6</u>), $C_{22}H_{22}O$; m/e (CI), 303 $(M+1)^+$ the IR and UV are practically identical with those of compound <u>5</u>[23]; δ($CDCl_3$, 90MHz)1.55m(6H), 2.3m(9H), 3.08d(J=2Hz, $=CH-C\equiv C\underline{H}$), 4.43d (J=2Hz, $C\underline{H}_2OH$), 5.52m(2H) and 5.90m(2H). The above data suggested for <u>6</u> one enyne terminus, a triyne function and a $-CH=CH-C\equiv C-CH_2OH$ end (the $C\underline{H}_2OH$ gives rise to a slightly paramagnetic shifted doublet, in the NMR spectrum, (rather than a triplet) as compared to compound <u>5</u>). The location of the triyne, as shown below in formula <u>6</u>, was established, as with compound <u>5</u>, by an LIS experiment (270MHz):

	$HC\equiv C-CH=CH$ —	CH_2 —	$(CH_2)_2$ —	CH_2 —	$(C\equiv C)_3-$	CH_2 —	CH_2 —	CH_2 —	$CH =$	CH —	$C\equiv C-CH_2OH$	
a.		2.3	1.55	2.3		2.3	1.55	2.3	5.9	5.52	4.45d	
b.		2.3m	1.55quin	2.3m		2.63t	2.0quin	3.05dt		6.24m(2H)	8.83	<u>6</u>
							(J=7Hz)	(J=7Hz)				

a. Pure compound <u>6</u>. b, Compound <u>6</u> with 0.7eq of $Eu(fod)_3-d_{27}$.

<u>1</u>. $CH_3-(CH_2)_5-\overset{16}{CH}=\overset{15}{CH}-(CH_2)_{12}-\overset{2}{C}\equiv\overset{1}{CH}$

<u>2</u>. $HC\equiv\overset{21}{C}-CH=\overset{19}{CH}-(CH_2)_m-C\equiv C-(CH_2)_n-\overset{2}{C}\equiv\overset{1}{CH}$ (m+n=14) (m,n>1)

<u>3</u>. $HC\equiv C-CH=CH-(CH_2)_6-\overset{7}{(C\equiv C)}_3-(CH_2)_4-\overset{2}{C}\equiv\overset{1}{CH}$

<u>4</u>.a. $HC\equiv C-CH=CH-(CH_2)_m-CH=CH-(C\equiv C)_2-(CH_2)_n-C\equiv CH$ (m+n=10) (m or n=1)

b. $HC\equiv C-CH=CH-(CH_2)_m-(C\equiv C)_2-(CH=CH)-(CH_2)_n-C\equiv CH$

<u>5</u>. $HC\equiv C-CH=CH-(CH_2)_4-(C\equiv C)_3-(CH_2)_5-\overset{3}{C}\equiv\overset{2}{C}-\overset{1}{CH_2}OH$

<u>6</u>. $HC\equiv C-CH=\overset{19}{CH}-(CH_2)_4-\overset{9}{(C\equiv C)}_3-(CH_2)_3-\overset{5}{CH}=\overset{4}{CH}-\overset{3}{C}\equiv\overset{2}{C}-\overset{1}{CH_2}OH$

Interesting is the finding of the same chain length (nC-22) in the described compounds as in the *Reniera fulva* sponge acetylenes[8]. Accordingly, a nC-23 fatty acid precursor could also be suggested for the above compounds however, the fact that compounds 5 and 6 bearing the propargyl terminus (first stage in a possible oxidative degradation) are C-22 and not C-23 casts doubt on such a biogenesis in our case.

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References and Notes

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9. This sponge appears in the form of soft brown tubes, part of which open up into horn forms
10. Separation between 1-4 and 5-6 was achieved on a LH-20 column (chloroform petrol-ether 2:1). On the same column the separation of 5 from 6 was also performed. Compound 6, the minor alcoholic isomer, was purified on a Porasil-A column by HPLC (ethyl acetate benzene 2:98). Compounds 1-4 were separated by the aid of pre-packed silica gel 60 lobar column (petrol-ether ether 95:5).
11. The purity of the individual compounds was established by UV spectra, TLC (see ref. 12) and HPLC using a porasil-A column with RI and UV detectors. Minor quantities of other isomers may exist in the crude extract.
12. TLC was performed on silica gel with: a) petrol-ether ether 9:1 or b) ethyl acetate toluene 1:9 systems. The spots were developed by vanillin-sulfuric acid spray upon which each compound gave its specific colourification (brown-yellow through bordo to purple).
13. The two most abundant peaks in the spectra are 219(40%) $[C_{16}H_{27}]^+$ and 96(100%) $[C_7H_{12}]^+$ resulting both from fragmentations in the double bond neighborhood.
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15. The n-alkane was identified by VPC and a characteristic mass spectrum.
16. H. Budzikiewicz, C. Djerassi and D.H. Williams, "Structure Elucidation of Natural Products by Mass Spectrometry" Vol. 2, Holden-Day 1964.
17. $\delta(CDCl_3, 90MHz)$ 0.88t(J=4.5Hz,3H), 1.29 brs(28H), 1.92t(J=2Hz,1H), 2.2m(6H) and 2.9m(2H).
18. Worth mentioning is the location of the double bond in 1 which is as in palmitoleic acid.
19. F. Bohlmann, T. Burkhardt, C. Zdero, "Naturally Occurring Acetylenes", Academic Press, N.Y. 1973. All measured UV ε-values, and vibrational band intensity ratios, were found to be in the correct order of magnitude although the ε-values were in some cases higher than expected.
20. The intensity of the $(C{\equiv}C)_n$ absorption at 2220 cm^{-1} is proportional to n[19].
21. $\delta(CDCl_3, 90MHz)$ 1.6m(10H), 1.95t(J=2.6Hz,1H), 2.36m(8H), 3.04m(2H) and 3.44dd(J=3.8 and 2Hz,1H).
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23. Compound 5 exhibits a higher ε-value at 225nm.

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