Synthesis and a study of the ^{13}C NMR spectroscopic properties of positional isomers of some C_{18} acetylenic thia fatty esters†

Marcel S.F. Lie Ken Jie,* Oladapo Bakare, and Maureen M.L. Lau

Department of Chemistry, The University of Hong Kong
Pokfulam Road, Hong Kong (Special Administrative Region), China
E-mail: hrsclkj@hkucc.hku.hk

This paper is dedicated to Dr. Douglas Lloyd on his 80th birthday

Abstract

The carbon magnetic resonance spectra of four positional acetylenic thia fatty acid methyl ester isomers have been recorded to investigate the effect of the sulfur atom on the chemical shifts of the carbon nuclei adjacent to it.

Keywords: Acetylenic thia fatty acid, chemical shifts, carbon-13 NMR

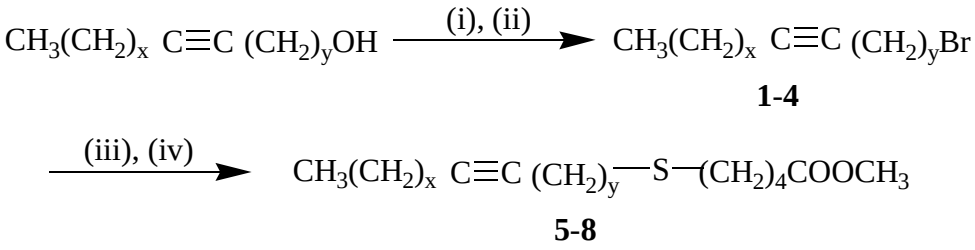
Introduction

Unsaturated thia fatty acids, such as 13-thia-9*Z*,11*E*-octadecadienoic acid and 13-thia-9*E*,11*E*-octadecadienoic acid are found to be reversible competitive inhibitors of lipoxygenase.[1-5] Corey *et al*.[6,7] reported that the 7-thia-, 10-thia- and 13-thia-arachidonic acids are potent inhibitors in leukotriene (lipoxin) biosynthesis. This implies a possible means of controlling inflammatory diseases caused by an overproduction of the leukotrienes in the human body. Buist's group have demonstrated the enzymatic biomethylenation of 6-thia-oleic acid by the microorganism, *Lactobacillus plantarum*.[8] Skrede *et al.* have reviewed the metabolism of thia fatty acids.[9]

Our group have synthesized and studied spectroscopic and mass spectrometric properties of the positional isomers of the methyl thialaurate,[10-13] ten methyl dithiastearate isomers[14] and the corresponding sulfinyl and sulfonyl derivatives of methyl thialaurate.[15] In this paper, we describe the synthesis of a set of positional isomers of C_{18} acetylenic thia fatty esters (**5-8**, Scheme 1) in an effort to study the effect of the sulfur atom on the chemical shifts of the carbon nuclei in the alkynyl chain of these thia fatty ester isomers by nuclear magnetic resonance spectroscopy.

Results and Discussion

The acetylenic thia fatty esters (**5-8**) were synthesized by the reaction of the 5-mercapto-pentanoic acid and the corresponding 1-bromo-5-decyne, 1-bromo-4-decyne, 1-bromo-3-decyne and 1-bromo-2-decyne, respectively, in ethanolic KOH under a nitrogen atmosphere. The key 1-bromo-decyne intermediates (**1**-**4**) were prepared by bromination of the corresponding 1-hydroxy-decyne, which in turn were prepared by conventional chain extension of acetylenic intermediates (Scheme 1).



Compound	x	y
5	5	4
6	6	3
7	7	2
8	8	1

(i) $MeSO_2Cl$, Et_3N, CH_2Cl_2; (ii)LiBr, acetone; (iii) $HS(CH_2)_4COOH$, KOH, EtOH, N_2; (iv) BF_3, MeOH.

Scheme 1. Synthesis of isomeric acetylenic thia fatty esters (**5-8**).

The ^{13}C NMR chemical shifts of carbon nuclei are very susceptible to changes in the positions of the functional groups on the alkyl chains of fatty acids, making this analytical technique a much more informative one than ^{1}H NMR, especially in the confirmation of the structure of closely related fatty ester isomers. Bus *et al.*[16] have determined the shift parameters due to the acetylenic, *cis*-olefinic and *trans*-olefinic system on the carbon shifts of the adjacent methylene carbon atoms (Table 1).

Table 1. Chemical shift parameters of the carbomethoxy, methylenic and acetylenic functional groups on the shift of adjacent methylene carbon atoms

α β γ δ ε ζ
X-$CH_2CH_2CH_2CH_2CH_2CH_2$-

-X	α	β	γ	δ	ε	ζ
—$COOCH_3$	+4.40	-4.75	-0.50	-0.45	-0.20	-0.10
—CH_3	-7.00	+2.15	-0.35	-0.10	-	-
—C≡C—	-11.00	-0.65	-0.80	-0.45	-0.10	-

To establish the shift effects due to a sulfur atom on the neighbouring methylene carbon nuclei, di-*n*-decyl sulfide was used as a model compound for this purpose. We have used the same base values employed for an unperturbed carbon nucleus of a methylene group as reported by Bus *et al.*[16] and also the shift for a methyl and the carbonyl atom of the methyl ester group as 29.75, 14.10 and 174.35 ppm, respectively. The shift parameters due to a sulfur atom on the adjacent methylene carbons can therefore be established from the result of the ^{13}C NMR spectroscopic analysis of the di-*n*-decyl sulfide (Table 2). In the Table-2 we show the carbon shift values of the unperturbed methylene groups, but have included the shift values reported by Bus *et al.* for the methylene adjacent to the methyl group (namely the methylenes at the ω-1, ω-2, ω-3 and ω-4 position).

Table 2. Shift parameters due to the effect of the sulfur atom on the ^{13}C NMR shift values of the methylene carbon atoms of di-*n*-decyl sulfide

	C-1 (α)	C-2 (β)	C-3 (γ)	C-4 (δ)	C-5 (ε)	C-6 (ω-4)	C-7 (ω-3)	C-8 (ω-2)	C-9 (ω-1)	C-10 (ω)
Observed	32.31	29.85	29.04	29.36	29.63	29.63	29.36	31.99	22.76	14.11
Reported[16]	29.75	29.75	29.75	29.75	29.75	29.65	29.40	31.90	22.75	14.10
δobs - δrep.	+2.56	+0.10	-0.71	-0.39	-0.12	-0.02	-0.04	+0.09	+0.01	+0.01

The shift effect for a sulfur atom on the adjacent methylene carbon shifts was derived from the difference in values between the observed and the reported values of the shifts of the corresponding methylene carbon. From these results, it appeared that the sulphur atom exercised

a deshielding effect on the α– and β–methylene groups while the sulphur atom showed a slight shielding effect on the γ, δ and ε–methylene shifts. It was possible by application of the 'the additivity rule' to estimate the carbon shifts of the various methylene carbon nuclei, including those of the acetylenic carbons, of the acetylenic thia isomers (**5**-**8**). The observed and estimated shift values are shown in Table 3. The detail calculation of the shift values of the carbon nuclei of the methyl 6-thia-10-octadecynoate (**6**) is given below as an example:

C (2) 29.75 + (-0.39) [δ (S)] + 4.4 [α (COOMe)] = 33.76 (33.64)*
C (3) 29.75 + (-0.71) [γ (S)] + (-4.75) [β (COOMe)] = 24.29 (24.16)
C (4) 29.75 + 0.10 [β (S)] + (-0.50) [γ (COOMe)] = 29.35 (29.15)
C (5) 29.75 + 2.56 [α (S)] + (-0.10) [ε (C=C)]
+ (-0.45) [δ (COOMe)] = 31.76 (31.72)
C (7) 29.75 + 2.56 [α (S)] + (-0.80) [γ (C=C)]
+ (-0.10) [ζ (COOMe)] = 31.41 (31.10)
C (8) 29.75 + 0.10 [β (S)] + (-0.65) [β (C=C)] = 29.20 (29.15)
C (9) 29.75 + (-0.71) [γ (S)] + (-11.00) [α (C=C)] = 18.04 (17. 99)
C (10) 80.20 + (-0.39) [δ (S)] + (-0.05) [C-10 (COOMe)] = 79.76 (78.98)
C (11) 80.20 + (-0.12) [ε (S)] + 0.05 [C-11 (COOMe)] = 80.13 (81.07)
C (12) 29.75 + (-11.00) [α (C=C)] = 18.75 (18.77)
C (13) 29.75 + (-0.65) [β (C=C)] = 29.10 (29.15)
C (14) 29.75 + (-0.80) [γ (C=C)] + (-0.10) [δ (Me)] = 28.85 (28.87)
C (15) 29.75 + (-0.45) [δ (C=C)] + (-0.35) [γ (Me)] = 28.95 (28.87)
C (16) 29.75 + (-0.10) [ε (C=C)] + 2.15 [β (Me)] = 31.80 (31.80)
C (17) 29.75 + (-7.00) [α (Me)] = 22.75 (22.64)
*Observed values in brackets.

Bus *et al.*[17] have reported the basic shift value of an unperturbed acetylenic carbon atom in a long chain fatty acid ester as 80.20 ppm. In the spectrum of compound **5**, the effect of the sulfur atom allowed the acetylenic carbon nuclei to be characterized. The more downfield acetylenic signal was attributed to the shift of C-12. The effect of the sulfur atom increases when the acetylene is interrupted by two methylene groups from the sulfur atom as seen for the carbon shifts of compound **6**. The shifts of C-9 (17.99), C-10 (78.98), C-10 (81.07) and C-12 (18.77) are very close to the calculated shifts of these carbon nuclei.

ARKIVOC 2002 (iii) 188-197

Table 3. ^{13}C NMR chemical shift values of positional isomers of methyl 6-thia-octadecynoate (**5-8**)

Isomer	x	y		C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11	C-12	C-13	C-14	C-15	C-16	C-17	C-18	COOMe
6-thia-11-yne (**5**)	5	4	Obs.	173.73	33.64	24.19	29.15	31.69	S	31.69	29.15	28.22	18.41	79.53	80.72	18.77	28.71	28.58	31.42	22.59	14.03	51.44
			Calc.	-	33.76	24.29	29.35	31.86		31.76	29.05	28.39	18.36	80.03	80.18	18.75	29.00	28.60	31.45	22.65	-	-
			δobs - δcalc	-	-0.12	-0.10	-0.20	-0.17		-0.07	0.10	-0.17	0.05	-0.5	0.54	0.02	-0.29	-0.02	-0.03	-0.06	-	-
6-thia-10-yne (**6**)	6	3	Obs.	173.71	33.64	24.16	29.15	31.72	S	31.10	29.15	17.99	78.98	81.07	18.77	29.15	28.87	28.87	31.80	22.64	14.09	51.44
			Calc.	-	33.76	24.29	29.35	31.76		31.41	29.20	18.04	79.76	80.13	18.75	29.10	28.85	28.95	31.80	22.75	-	-
			δobs - δcalc	-	-0.12	-0.13	-0.20	-0.04		-0.31	-0.05	-0.05	-0.78	0.94	0.02	0.05	0.02	-0.08	0.00	-0.11	-	-
6-thia-9-yne (**7**)	7	2	Obs.	173.65	33.59	24.13	29.15	31.69	S	31.80	20.45	78.33	81.50	18.77	29.10	28.90	29.15	29.25	31.88	22.67	14.09	51.44
			Calc.	-	33.76	24.29	29.25	31.41		31.56	18.65	79.39	79.96	18.63	29.10	28.95	29.20	29.30	31.90	22.75	-	-
			δobs - δcalc	-	-0.17	-0.16	-0.10	0.28		0.24	1.80	-1.06	1.54	0.14	0.00	-0.05	-0.05	-0.05	-0.02	-0.08	-	-
6-thia-8-yne (**8**)	8	1	Obs.	173.68	33.61	24.13	28.50	31.01	S	19.80	83.51	75.68	18.85	28.93	28.93	29.20	29.55	29.33	31.90	22.70	14.11	51.44
			Calc.	-	33.76	24.19	28.90	31.06		21.21	80.1	79.74	18.36	28.98	28.95	29.30	29.55	29.40	31.90	22.75	-	-
			δobs - δcalc	-	-0.15	-0.16	-0.40	-0.05		-1.41	3.41	-4.06	0.49	-0.05	-0.02	-0.10	0.00	-0.07	0.00	-0.05	-	-

ISSN 1424-6376

Bus *et al.*[16] have reported 80.20 ppm as the basic value for an unperturbed acetylenic carbon atom in a long chain fatty acid ester. They have also reported the shift effect of the methoxycarbonyl group on the acetylenic carbon atoms at different positions (C2/C3 to C11/C12) from the methoxycarbonyl group, while the terminal methyl group was reported not to have any effect on the acetylenic carbon atoms beyond the ω-3 position. From their report, the shift effects of the methoxycarbonyl group on the chemical shift of the acetylenic center located between positions 8 and 12 from the methoxycarbonyl group in a long chain fatty ester are as follows:

Position	Shift effect of COOMe
C8/C9	-0.20/+0.25
C9/C10	-0.10/+0.15
C10/C11	-0.05/+0.05
C11/C12	-0.05/0.00

Assuming that the additivity rule employed for the calculation of the shift of the methylene carbon atoms is valid for the acetylenic group, the shift effect of a sulphur atom on an acetylene carbon atom can be deduced by subtracting the basic value (80.20 ppm) and the combined shift effects due to the methoxycarbonyl group and terminal methyl, from the observed chemical shift value for such acetylenic carbon. The results of this calculation are presented in Table 4 for the positional isomers of methyl 6-thia-octadecynoate (**5-8**).

These results show that the sulphur atom consistently exerts a shielding effect on the acetylenic carbon atom proximal to it and a deshielding effect on the carbon remote from it.

Table 4. Chemical shift effects due to a sulphur atom on the acetylenic carbon atoms in positional isomers of methyl 6-thia-octadecynoate (**5-8**)

Compound	y	Observed values		Shift parameter due to COOMe		Shift parameter due to sulphur	
		Ca	Cb	Ca	Cb	Ca	Cb
5	4	79.53	80.72	-0.05	-	-0.62	+0.52
6	3	78.98	81.07	-0.05	+0.05	-1.17	+0.82
7	2	78.33	81.50	-0.10	+0.15	-1.77	+1.15
8	1	75.68	83.51	-0.20	+0.25	-4.32	+3.06

Experimental Section

General Procedures. Thin layer chromatographic (TLC) analyses were performed on microscopic glass plates coated with normal silica gel type 60 (about 0.1 mm layers, E. Merck no. 7730). Preparative TLC separations were carried out on glass plates (20 x 20 cm) coated with silica gel GF254 type 60 (0.7 mm layers, E. Merck no. 7730). Column chromatography was performed by gradient elution on silica gel 60 (E. Merck no. 7734) using mixtures of *n*-hexane:diethyl ether as eluent. Infrared spectra were recorded on a Nicolet 20SXC-FTIR spectrophotometer or a Shimadzu model 470 infrared spectrometer and were calibrated against polystyrene absorption peak at 1601 cm^{-1}. Samples were run as neat films. ^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectra were obtained on a JEOL FX 90Q (90 MHz) with proton observation at 90 MHz and carbon observation at 22.5 MHz. Samples were dissolved in $CDCl_3$ and chemical shifts obtained relative to tetramethylsilane as an internal standard. Gas-liquid chromatographic (GLC) analyses were carried out on a Hewlett Packard HP5890 gas chromatograph fitted with a 30 m capillary column (0.25 mm internal diameter, 0.25 μm film thickness, SPB-1 or 0.53 mm internal diameter, 0.20 μm film thickness, SP-2380). Helium (2 ml/min) was used as the carrier gas under isothermal conditions (240ºC or 180 ºC on SPB-1 and 120 ºC, 160 ºC or 190 ºC on SP-2380) with a flame ionization detector. Gas chromatography-mass spectrometric (GC-MS) analyses were carried out on a Hewlettt Packard HP5890 gas chromatograph fitted with a capillary glass column (12 m x 0.2 mm i.d.), coated with crosslinked methyl silicone gum (HP.1, 0.33 μm film thickness). The compounds were submitted to on column injection at 140 ºC for 3 min, then temperature programmed at 5 ºC min^{-1} to 250 ºC using helium as the carrier gas. The column outlet was connected to a Hewlett Packard HP5970 series mass selective detector, operating at an ionization energy of 70eV. Microanalysis was performed on Perkin Elmer PE 2400 series II CHNS/O analyzer. All chemicals and reagents were of analytical reagent grade.

General method for the preparation of 1-bromododecyne 1-4 as exemplified by the synthesis of 1-bromo-2-dodecyne (4)

A mixture of methane sulphonyl chloride (5.03 g, 43.97 mmol), triethylamine (4.5 cm^3), 2-dodecyn-1-ol (4.0 g, 21.98 mmol) and CH_2Cl_2 (40 cm^3) was stirred at 0ºC for 1 h. The reaction mixture was filtered and the residue washed with CH_2Cl_2 (40 cm^3). The combined CH_2Cl_2 layer was washed with dil. HCl (2 mol dm^{-3}, 30 cm^3), water (2 x 25 cm^3), dried (Na_2SO_4) and the solvent removed under reduced pressure. The solution of the residue (5.68 g) in dry acetone (10 cm^3) was added to a solution of LiBr (2.54 g, 29.3 mmol) in dry acetone (15 cm^3) and the mixture refluxed for 1 h. Ice cold water (60 cm^3) was added and the oil that separated out removed. The aqueous layer was extracted with *n*-hexane (2 x 25 cm^3). The *n*-hexane extract was combined with the oily liquid, washed with water (20 cm^3) and dried over anhydrous sodium sulphate. Evaporation of the solvent, followed by column chromatography of the residue

on silica gel, using *n*-hexane-diethyl ether (95:5) as eluent, gave 1-bromo-2-dodecyne **4** (4.43 g, 82.3%).

1-Bromo-5-dodecyne (1). ^{1}H-NMR δ 3.43 (2H, t, *J* = 6.6, 1-H), 1.9-2.3 (6H, m, CH_2), 1.2-1.8 (10H, m, CH_2), 0.88 (3H, t, Me); ^{13}C-NMR δ 81.07, 79.09, 33.18 (1-C), 31.85, 31.42, 29.12, 28.58, 27.57, 22.62, 18.77, 17.99, 14.06 (Me); IR ν 2231, 1453, 1432, 1251, 759, 647 cm^{-1}.

1-Bromo-4-dodecyne (2). ^{1}H-NMR δ 3.52 (2H, t, *J* = 6.5, 1-H), 1.8-2.45 (6H, m, 2-H, 3-H and 6-H), 1.2-1.6 (10H, m, CH_2), 0.88 (3H, t, Me); ^{13}C-NMR δ 81.58, 77.90, 32.45 (1-C), 32.10, 31.83, 29.12, 28.87, 22.67, 18.77, 17.61, 14.09 (Me); IR ν 2230, 1457, 1430, 1247, 734, 645 cm^{-1}.

1-Bromo-3-dodecyne (3). ^{1}H-NMR δ 3.41 (2H, t, *J* = 7.0, 1-H), 2.5-2.8 (2H, m, 2-H), 2.0-2.2 (2H, m, 5-H), 1.2-1.6 (12H, m, CH_2), 0.88 (3H, t, Me); ^{13}C-NMR δ 82.72, 76.90, 31.88, 30.26 (1-C), 29.23, 29.15, 29.01, 28.87, 23.46 (2-C), 22.70, 18.74 (5-C), 14.09 (Me); IR ν 2230, 1459, 1436, 1267, 1207, 720, 639 cm^{-1}.

1-Bromo-2-dodecyne (4). ^{1}H-NMR δ 3.92 (2H, t, *J* = 2.4, 1-H), 2.15-2.26 (2H, m, 4-H), 1.2-1.6 (14H, m, CH_2), 0.88 (3H, t, Me); ^{13}C-NMR δ 88.33, 75.36, 31.94, 29.50, 29.31, 29.15, 28.87, 28.44, 22.73, 19.01 (4-C), 15.63 (1-C), 14.11 (Me); IR ν 2230, 1458, 1426, 1206, 719, 607 cm^{-1}.

General method for the preparation of positional isomers of methyl 6-thia-octadecynoate 5-8 as exemplified by the synthesis of methyl 6-thia-10-octadecynoate (6)

A mixture of 5-mercaptopentanoic acid (821 mg, 6.118 mmol), 1-bromo-4-dodecyne (1.5 g, 6.117 mmol), KOH (700 mg, 12.475 mmol) and ethanol (60 cm^3) was refluxed for 5 h. under nitrogen. Water (80 cm^3) was added to the cooled reaction mixture, which was then extracted with hexane (2 x 30 cm^3). The aqueous layer was acidified with conc. HCl and extracted again with diethyl ether (2 x 40 cm^3). The ethereal extract was washed with water (30 cm^3) and saturated NaCl solution (25 cm^3), then dried over anhydrous Na_2SO_4. Evaporation of solvent gave 6-thia-10-octadecynoic acid (1.762 g, 96.5%). The latter was refluxed with methanol (25 cm^3) and BF_3-MeOH (15%, w/w. 5 cm^3) under N_2 for 20 min. Water (40 cm^3) was added to the cooled reaction mixture and extracted with hexane (2 x 30 cm^3). The extract was washed, dried and evaporated to dryness. Preparative TLC separation (0.7 mm thick layer of silica, using a mixture of *n*-hexane-diethyl ether, 85:15, v/v as developer) gave pure methyl 6-thia-10-octadecynoate **6** (1.503 g, 78.6%).

Methyl 6-thia-11-octadecynoate (5). Yield: 81.4%; Rf 0.4 (PE10); ^{1}H-NMR δ 3.66 (3H, s, OMe), 2.52 (4H, t, *J* = 6.8, 5-H and 7-H), 2.34 (2H, t, *J* = 7.0, 2-H), 2.0-2.2 (4H, m, 10-H and 13-H), 1.6-1.9 (6H, m, CH_2), 1.2-1.5 (10H, m, CH_2), 0.88 (3H, t, Me); ^{13}C-NMR δ 173.73 (1-C), 80.72 (12-C), 79.53 (11-C), 51.44 (OMe), 33.64 (2-C), 31.69(5-C and 7-C), 31.42 (16-C), 29.15, 28.71, 28.58, 28.22, 24.19 (3-C), 22.59 (17-C), 18.77 (13-C), 18.41 (10-C), 14.03 (Me); IR ν 2928, 2856, 1740, 1456, 1436, 1258, 1204, 1172, 757 cm^{-1}; GLC (ECL): 20.0 (SPB-1), 25.9 (SP-2380); GCMS m/z (%): 312 (M^+, 1). 281 (7), 198 (13), 197 (50), 127 (53), 115 (39),

114 (29), 101 (100); microanalysis: calculated for $C_{18}H_{32}O_2S$ (%): C, 69.18; H, 10.32; S, 10.26; found (%): C, 69.05; H, 10.66; S, 10.48.

Methyl 6-thia-10-octadecynoate (6). Rf 0.4 (PE10); ^{1}H-NMR δ 3.66 (3H, s, OMe), 2.61 (2H, t, *J* = 6.8, 7-H), 2.52 (2H, t, *J* = 6.8, 5-H), 2.34 (2H, t, *J* = 7.0, 2-H), 2.0-2.2 (4H, m, 9-H and 12-H), 1.6-1.9 (6H, m, CH_2), 1.2-1.5 (10H, m, CH_2), 0.88 (3H, t, Me); ^{13}C-NMR δ 173.71 (1-C), 81.07 (11-C), 78.98 (10-C), 51.44 (OMe), 33.64 (2-C), 31.80 (16-C), 31.72 (5-C), 31.10 (7-C), 29.15, 28.87, 24.16 (3-C), 22.64, 18.77 (12-C), 17.99 (9-C), 14.09 (Me); IR ν 2950, 2930, 2856, 1740, 1456, 1435, 1257, 1205, 1173, 757 cm^{-1}; GLC (ECL): 19.9 (SPB-1), 25.6 (SP-2380); GCMS m/z (%): 313 (1), 312 (M^+, 1), 281 (18), 198 (14), 197 (90), 115 (32), 114 (25), 113 (57), 87 (100); microanalysis: calculated for $C_{18}H_{32}O_2S$ (%): C, 69.18; H, 10.32; S, 10.26; found (%): C, 69.15; H, 10.47; S, 10.56.

Methyl 6-thia-9-octadecynoate (7). Yield: 79.7%; Rf 0.4 (PE10); ^{1}H-NMR δ 3.66 (3H, s, OMe), 2.64 (2H, t, *J* = 6.8, 7-H), 2.57 (2H, t, *J* = 6.8, 5-H), 2.34 (4H, t, *J* = 7.0, 2-H and 8-H), 2.0-2.2 (2H, m, 11-H), 1.6-1.9 (4H, m, CH_2), 1.2-1.5 (12H, m, CH_2), 0.88 (3H, t, Me); ^{13}C-NMR δ 173.65 (1-C), 81.50 (10-C), 78.33 (9-C), 51.44 (OMe), 33.59 (2-C), 31.88 (16-C), 31.80 (7-C), 31.69 (5-C), 29.25, 29.15, 29.10, 28.90, 24.13 (3-C), 22.67 (17-C), 20.45 (8-C), 18.77 (11-C), 14.09 (Me); IR ν 2950, 2929, 2856, 1741, 1457, 1435, 1203, 1172, 733 cm^{-1}; GLC (ECL): 20.0 (SPB-1), 25.6 (SP-2380); GCMS m/z (%): 312 (M^+, 1). 281 (12), 198 (14), 197 (100), 115 (54), 100 (29); microanalysis: calculated for $C_{18}H_{32}O_2S$ (%): C, 69.18; H, 10.32; S, 10.26; found (%): C, 69.17; H, 10.32; S, 10.38.

Methyl 6-thia-8-octadecynoate (8). Yield: 77%; Rf 0.4 (PE10); ^{1}H-NMR δ 3.66 (3H, s, OMe), 3.24 (2H, t, *J* = 2.3, 7-H), 2.67 (2H, t, *J* = 7.0, 5-H), 2.1-2.45 (4H, m, 2-H and 10-H), 1.6-1.9 (4H, m, CH_2), 1.2-1.5 (14H, m, CH_2), 0.88 (3H, t, Me); ^{13}C-NMR δ 173.68 (1-C), 83.51 (9-C), 75.68 (8-C), 51.44 (OMe), 33.61 (2-C), 31.90 (16-C), 31.01 (5-C), 29.55, 29.33, 29.20, 28.93, 28.50, 24.13 (3-C), 22.70 (17-C), 19.80 (7-C), 18.85 (10-C), 14.11 (Me); IR ν 2951, 2926, 2854, 1740, 1457, 1436, 1257, 1205, 1173, 733 cm^{-1}; GLC (ECL): 20.0 (SPB-1), 25.4 (SP-2380); GCMS m/z (%): 281 (M-31, 8), 200 (28), 197 (13), 117 (20), 116 (59), 115 (63), 87 (49), 85 (100), 55 (51); microanalysis: calculated for $C_{18}H_{32}O_2S$ (%): C, 69.18; H, 10.32; S, 10.26; found (%): C, 69.12; H, 10.55; S, 10.61.

Acknowledgements

This project was supported by the CRCG of the University of Hong Kong and by the Lipid Research Fund and a Commonwealth Scholarship (O.B.).

References

† One of the authors (MSFLKJ) was a Ph.D. student under F.D. Gunstone of the Department of Chemistry, The University of St. Andrews, at which time Dr. Lloyd was also a staff member of the Department. MSFLKJ also wishes to express his appreciation to Dr. Lloyd for introducing him to the art of enjoying fine French Bordeaux wines.

1. Larsen, L.N.; Hørvik, K.; Sørensen, H.I.N.; Bremer, J. *Biochim. Biophys. Acta* **1997**, *1348*, 346.
2. Pitt, M.J.; Easton, C.J.; Ferrante, A.; Poulos, A.; Rathjen, D.A. *Chem. Phy. Lipids.* **1998**, *92*, 63.
3. Robinson, B.S.; Huang, Z.H.; Parashakis, G.; Hii, C.S.T.; Ferrante, J.V.; Poulos, A.; Rathjen, D.A.; Pitt, M.J.; Easton, C.J.; Ferrante, A. *Lipids* **1999**, *34*, S341.
4. Easton, C.J.; Robertson, T.A.; Pitt, M.J.; Rathjen, D.A.; Ferrante, A; Poulos, A. *Bioorg. Med. Chem.*, **2001**, *9*, 317.
5. Funk, Jr., M.O.; Alteneder, A.W. *Biochim. Biophys. Res. Commun.* **1983**, *114*, 937.
6. Corey, E.J.; Cashman, J.R.; Eckrich, T.M.; Corey, D.R. *J. Am. Chem. Soc.* **1985**, *107, 713.*
7. Corey, E.J.; d'Alarcao, M.; Kyler, K.S. *Tetrahedron Lett.* **1985**, *27*, 3585.
8. Buist, P.H.; Dimnik, G.P. *Tetrahedron Lett.* **1986**, *27*, 1457.
9. Skrede, S.; Sørensen, H.N.; Larsen, L.N.; Steineger, H.H.; Høvik, K.; Spydevold, O.S.; Horn, R.; Bremer, J. *Biochim. Biophys. Acta* **1997**, *1344*, 115.
10. Lie Ken Jie, M.S.F.; Bakare, O.; Davies, J.E.D. *Chem. Phys. Lipids* **1990**, *56*, 223
11. Lie Ken Jie, M.S.F.; Bakare, O. *J. Chem. Soc., Perkin 1* **1989**, 2121.
12. Christie, W.W.; Brechany, E.Y.; Lie Ken Jie, M.S.F.; Bakare, O. *Biol. Mass Spectrom* **1991**, *20*, 629.
13. Lie Ken Jie, M.S.F.; Bakare, O.; Davies, J.E.D. *Chem. Phys. Lipids* **1997**, *85*, 175.
14. Lie Ken Jie, M.S.F.; Bakare, O. *Chem. Phys. Lipids* **1990**, *53*, 203.
15. Lie Ken Jie, M.S.F.; Bakare, O. *Chem. Phys. Lipids* **1992**, *61*, 139.
16. Bus, J.; Sies, I.; Lie Ken Jie, M.S.F. *Chem. Phys. Lipids* **1976**, *17*, 501.
17. Bus, J.; Sies, I.; Lie Ken Jie, M.S.F. *Chem. Phy. Lipids* **1977**, *18*, 130.
18. Gunstone, F.D.; Pollard, M.R.; Scrimgeour, C.M. *Chem. Phy. Lipids* **1976**, *17*, 1.