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Synthesis and physical properties of some unsaturated and hydroxy alkylseleno fatty acid derivatives

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Abstract

Three unsaturated 12-alkylseleno (alkyl = Me, Et, Pr) C18 derivatives were prepared by reaction of sodium alkylselenide with the tosyloxy derivative of methyl ricinoleate. Reaction of sodium alkylselenide (alkyl = Me, Et, Pr, hexyl) or phenylselenide with methyl 10,11-epoxyundecanoate gave the corresponding ethyl 10-hydroxy-11-alkyl-(phenyl)seleno-undecanoates. The ^{1}H-NMR spectroscopic analysis revealed strong hydrogen-bonding between the selenium atom and the hydroxy function. Acid-catalyzed dehydration of methyl 10-hydroxy-11-methylseleno-undecanoate gave methyl 10-undecenoate as the major product, due to neighboring participation reaction of the selenium atom in the alkyl chain. To demonstrate the stability of unsaturated selenium-containing fatty acid analogues, the total synthesis of methyl 11-methyl-seleno-9-*cis*-undecenoate was elaborated.

Keywords: Synthesis; Alkylseleno; Phenylseleno; 1,3-Hydroxy-selena; Unsaturated selena fatty esters; Physical properties

1. Introduction

We have reported the synthesis and NMR studies on the positional isomers of methyl selenalaurate and telluralaurate [1]. The synthesis of several selena C16–C20 long-chain fatty acid homologues, containing radioactive ^{75}Se in the alkyl chain, have been reported by Sadek et al. [2] in order to study their potential as myocardial imaging agents. An earlier investigation by us into the antimicrobial action of some selena fatty acids against *Streptococcus pyogenes* has shown that the activity is more effective in the selena C14 acid than the corresponding C15 or C16 homologues. Also, the position of the selenium atom in the alkyl chain in these fatty acids appears to be more effective when positioned furthest from the carboxyl group [3]. Schwarz and Fredga have also studied the biological potency of selena fatty acids and noted the relationship between the structure of aliphatic selena fatty acids in preventing dietary liver necrosis in rats [4]. The nutritional importance of selenium has been extensively researched and many organic compounds containing selenium have been found to be potential chemotherapeutic agents [5].

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We report in this paper (a), the substitution of the hydroxy function in methyl ricinoleate (12-hydroxy-9-*cis*-octadecenoate) by various alkyl (phenyl)seleno groups; (b), the preparation of 1,3-hydroxy-selena fatty acid derivatives via the ring-opening reaction of an epoxy fatty ester and (c), the total synthesis of an unsaturated selena fatty ester analogue.

2. Materials and methods

Methyl ricinoleate was obtained from castor oil [6]. Selenium powder, propargyl alcohol, 8-bromooctanoic acid, 10-undecenoic acid and carbontetrabromide were purchased from Aldrich Chemical Co. (Milwaukee, WI). Methyl 10,11-epoxyundecanoate was prepared by the method described elsewhere [7].

Thin-layer chromatographic analysis was performed on microscope glass plates coated with silica (~0.1 mm thick) and a mixture of petroleum ether/diethyl ether (4:1 v/v), used as the developing solvent. Infrared spectra were obtained on a Nicolet 20SX-FTIR spectrophotometer and spectra were recorded as neat samples on NaCl cells. NMR spectra were obtained for solutions in $CDCl_3$ (0.2 mM) on a JEOL FX9OQ (90 MHz) Fourier-transformed NMR spectrometer. Chemical shifts are given in δ-values in ppm downfield from internal tetramethylsilane (TMS).

3. Experimental

3.1. Substitution of the hydroxy function in methyl ricinoleate by alkylseleno groups

3.1.1. Methyl 12-tosyloxy-9-cis-octadecenoate

A mixture of methyl ricinoleate (5g, 16 mmol), *p*-toluenesulfonylchloride (4.0g, 20.8 mmol) and anhydrous pyridine (30 ml) was stirred at room temperature for 24 h. The reaction mixture was poured into cold dilute HCl (2M, 100 ml) and the mixture was extracted with dichloromethane (2 × 100 ml). The organic extract was successively washed with aqueous sodium carbonate (5%, 50 ml), water (50 ml) and dried over anhydrous sodium sulfate. The solvent was evaporated under reduced pressure to give crude methyl 12-tosyloxy-9-*cis*-octadecenoate (5.0 g, 65%) as an oil. IR (NaCl) 1740 (s, C=O str.), 1600 (m, C=C arom. str.), 1370 (s, S=O asymm. str.), 1180 (s, S=O symm. str.) and 910 (m) cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ): 0.83 (t, 3H, CH_3), 1.1–1.8 (m, 22H, CH_2), 2.40 (s, 3H, $PhCH_3$), 2.28 (t, J = 7.3 Hz, 2H, 2–*H*), 2.42 (m, 2H, 11–*H*), 3.66 (s, 3H, $COOCH_3$), 4.45 (m, 1H, 12–*H*), 5.3–5.5 (m, 2H, 9–*H*, 10–*H*), 7.23 (d, J = 7.3 Hz, 2H, arom.) and 7.71 (d, J = 7.3 Hz, 2H, arom.).

3.2. General method for the preparation of ethyl 12-alkylseleno-9-cis-octadecenoates (**1a–1c**) *as exemplified by the synthesis of ethyl 12-methylseleno-9-cis-octadecenoate* (**1a**)

Absolute ethanol (30 ml) was added to a mixture of selenium powder (2.9 g, 3.4 mmol) and sodium borohydride (0.09 g, 2.3 mmol) under nitrogen. The reaction mixture was stirred for 15 min and refluxed for an additional 1 h. Methyl iodide (0.3 g, 2.3 mmol) was added and the reaction mixture was refluxed for 6 h. A solution of sodium borohydride (0.09 g, 0.23 mmol) in absolute ethanol (10 ml) was added and the reaction mixture refluxed for 4 h. The reaction mixture was cooled and methyl 12-tosyloxy-9-*cis*-octadecenoate (1.0 g, 2.1 mmol) in ethanol (10 ml) was added. The mixture was stirred for a further 12 h at room temperature. The reaction mixture was poured into dilute HCl (2M, 100 ml) and the mixture was extracted with diethyl ether (3 × 100 ml). The organic extract was washed with aqueous NaCl solution (10%, 2 × 30 ml) and dried over anhydrous sodium sulfate. Silica-gel (30 g) column chromatographic separation, using a mixture of petroleum ether:diethyl ether (4:1 v/v) as the eluent, gave ethyl 12-methylseleno-9-*cis*-octadecenoate (**1a**, 0.55 g, 67%) as a viscous oil.

3.3. General method for the preparation of ethyl 10-hydroxy-11-alkyl(phenyl)seleno-undecanoates (**2a–2e**) *as exemplified by the synthesis of ethyl 10-hydroxy-11-methylseleno-undecanoate* (**2a**)

A mixture of selenium powder (0.6 g, 7.6 mmol), sodium borohydride (0.19 g, 5.1 mmol) and absolute ethanol (30 ml) was refluxed for 1 h under nitrogen. Methyl iodide (0.7 g, 5.1 mmol) in ethanol (5 ml) was added and the reaction mixture refluxed

for 6 h. Sodium borohydride (0.19 g, 5.1 mmol) in ethanol (10 ml) was added and the reaction mixture was refluxed for 4 h. Methyl 10,11-epoxy-undecanoate (1.0 g, 4.7 mmol) in ethanol (10 ml) was then added and the total mixture refluxed for an additional 12 h. The cooled reaction mixture was poured into dilute HCl (2M, 100 ml) and the aqueous solution was extracted with diethyl ether (3 × 80 ml). The organic extract was washed with aqueous NaCl solution (10%, 2 × 30 ml) and dried over anhydrous sodium sulfate. Silica-gel (30 g) column chromatographic separation using a mixture of petroleum ether/diethyl ether (4:1 v/v) as the eluent, furnished ethyl 10-hydroxy-11-methylseleno-undecanoate (**2a**, 1.26 g, 83%) as an oil.

3.4. Preparation of ethyl 10-acetoxy-11-methylseleno-undecanoate (3)

A mixture of ethyl 10-hydroxy-11-methylseleno-undecanoate (0.5 g, 1.5 mmol), acetic anhydride (5 ml) and pyridine (1.5 ml) was stirred at ambient temperature for 18 h. The excess reagent was removed under reduced pressure. The residue was dissolved in a mixture of petroleum ether/diethyl ether (9:1 v/v, 200 ml). The ethereal solution was percolated through a silica-gel (10 g) chromatographic column. Evaporation of the solvent gave ethyl 10-acetoxy-11-methylseleno-undecanoate (**3**, 0.47 g, 91%) as an oil. $R_f = 0.6$ (petroleum ether/diethyl ether, 4:1 v/v); IR (NaCl) 1736 (C=O, str.) cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ) 1.25 (t, $J = 7.3$ Hz, 3H, $COOCH_2CH_3$), 1.2–1.8 (m, 14H, CH_2), 2.03 (s, 3H, $OCOCH_3$), 2.06 (s, 3H, $SeCH_3$), 2.29 (t, $J = 7.4$ Hz, 2H, 2–*H*), 4.12 (q, $J = 7.3$ Hz, 2H, $COOCH_2CH_3$) and 4.98 (m, 1H, $>CHOCOCH_3$, 10–*H*); ^{13}C-NMR ($CDCl_3$, ppm) 4.93 ($SeCH_3$), 14.27 ($COOCH_2CH_3$), 21.13 ($OCOCH_3$), 24.95 (C3), 25.33 (C8), 29.06, 29.12, 29.23, 33.75 (C9), 34.32 (C2), 60.05 ($COOCH_2CH_3$), 73.38 (C10), 179.48 ($OCOCH_3$) and 173.65 (C1).

3.5. Preparation of methyl 11-methylseleno-9-cis-undecenoate (5)

3.5.1. Methyl 11-hydroxy-9-cis-undecenoate (4)

Propargyl alcohol (3.0 g, 54 mmol) in anhydrous tetrahydrofuran (THF, 10 ml) was added to a suspension of lithium amide, prepared from lithium (1.1 g), liquid ammonia (1500 ml) and Fe(III) nitrate (0.5 g), and the reaction mixture stirred for 2 h. Then, 8-Bromo-octanoic acid (10 g, 44.8 mmol) in THF (50 ml) was added and the reaction mixture stirred for an additional 6 h. Ammonia was allowed to evaporate. Dilute HCl (2M, 200 ml) was added and the reaction mixture was extracted with diethyl ether (3 × 70 ml). The organic extract was washed with water (2 × 30 ml) and dried over anhydrous sodium sulfate. The solvent was evaporated and the residue was recrystallized from petroleum ether (100 ml) to give 11-hydroxy-9-undecynoic acid (7.4 g, 83%) as a white crystalline solid (m.p. 57.0–58.0°C, lit. 56.5–57.0°C [8]).

A mixture of 11-hydroxy-9-undecynoic acid (7.0 g), borontrifluoride/methanol complex (15%, 5 ml) and absolute methanol (30 ml) was refluxed for 10 min. Water (50 ml) was added and the reaction mixture was extracted with diethyl ether (3 × 60 ml). The organic extract was washed with water (20 ml) and dried over anhydrous sodium sulfate. Evaporation of the solvent gave methyl 11-hydroxy-9-undecynoate (5.1 g, 83%).

A mixture of methyl 11-hydroxy-9-undecynoate (5.0 g, 23.6 mmol), ethyl acetate (100 ml), Lindlar's catalyst (0.1 g) and quinoline (0.5 g) was shaken in an atmosphere of hydrogen at 780 mmHg pressure for 6 h. The reaction mixture was filtered and the organic solution was successively washed with dilute HCl (2M, 10 ml), water (30 ml) and dried over anhydrous sodium sulfate. Evaporation of the solvent under reduced pressure furnished methyl 11-hydroxy-9-*cis*-undecenoate (**4**, 3.7 g, 73%) as an oil. IR (NaCl) 3400 (br., O—H str.), 1741 (C=O, str.), 1460, 1210 cm^{-1}.

3.5.2. Methyl 11-bromo-9-cis-undecenoate

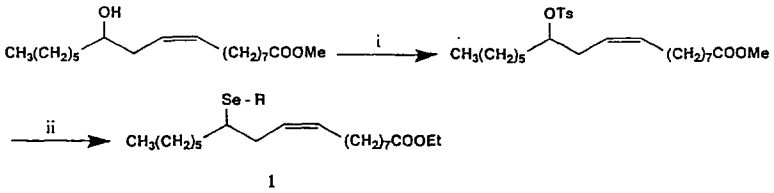
A mixture of methyl 11-hydroxy-9-*cis*-undecenoate (2.0 g, 9.3 mmol), carbontetrabromide (3.0 g, 4.7 mmol), triphenylphosphine (5.8 g, 7.6 mmol) and methylene dichloride (50 ml) was stirred for 8 h at room temperature. The solvent was evaporated under reduced pressure. Petroleum ether (30 ml) was added to the residue and the resulting mixture was filtered. The filtrate was evaporated and silica-gel (20 g) column chromatographic separation, using a mixture of petroleum ether/diethyl

ether (4:1 v/v) as the eluent, gave methyl 11-bromo-9-*cis*-undecenoate (1.8 g, 86%) as an oil. IR (NaCl) 1738 (C=O, str.), 1460 (m), 1200 (m), 720 (m) cm^{-1}.

3.5.3. *Methyl 11-methylseleno-9-cis-undecenoate* (5)

Methyl 11-bromo-9-*cis*-undecenoate (1.0 g, 3.6 mmol) in ethanol (10 ml) was added to a solution

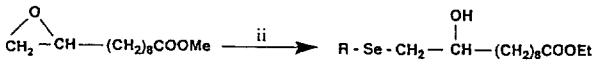
(a) Ethyl 12-alkylseleno-9-*cis*-octadecenoates (**1a-1c**)



1

R = CH_3 (1a), CH_3CH_2 (1b) or $CH_3CH_2CH_2$ (1c)

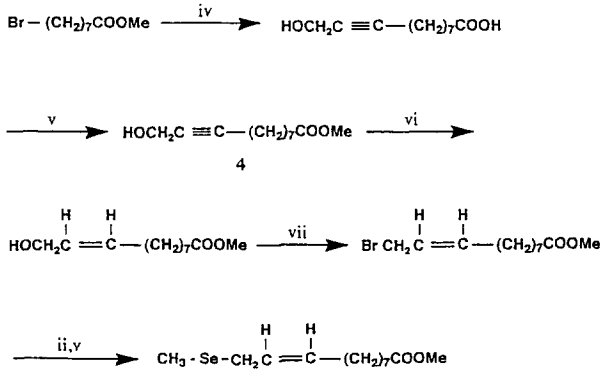
(b) Ethyl 10-hydroxy-11-alkyl(aryl)selenoundecanoates (**2a-2e**)



2a-2e

R = CH_3 (2a), CH_3CH_2 (2b), $CH_3(CH_2)_2$ (2c), $CH_3(CH_2)_5$ (2d), or C_6H_5 (2e)

(c) Methyl 11-methylseleno-9-*cis*-undecenoate (5)



4

5

(i) tosyl chloride, pyridine (ii) NaSeR, EtOH (iii) acetic anhydride, pyridine (iv) LiC ≡ CCH_2OH, liq. NH_3 (v) BF_3-MeOH (vi) H_2, Lindlar catalyst (vii) CBr_4, PPh_3, CH_2Cl_2

Scheme 1.

of sodium methylselenide, prepared from selenium (0.47 g, 6.0 mmol), sodium borohydride (0.18 g, 4.8 mmol), methyl iodide (1.2 g, 3.9 mmol) and ethanol (50 ml), and stirred at room temperature for 12 h. The reaction mixture was poured into dilute HCl (2M, 50 ml) and the mixture was extracted with diethyl ether (3 × 50 ml). The ethereal extract was washed with aqueous NaCl solution (10%, 2 × 20 ml) and dried over anhydrous sodium sulfate. The filtrate was evaporated and the residue was refluxed with borontrifluoride/methanol complex (10%, 15 ml) for 30 min. Water (50 ml) was added and the reaction mixture was extracted with diethyl ether (2 × 50 ml). The ethereal extract was washed with water (30 ml) and dried over anhydrous sulfate. The filtrate was evaporated and silica-gel column chromatographic separation of the residue furnished methyl 11-methylseleno-9-*cis*-undecenoate (**5**, 0.65 g, 72%) as an oil. $R_f = 0.7$ (petroleum ether:diethyl ether, 4:1 v/v); IR (NaCl) 1740, 1480 (m), 1230 (m) cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ) 1.1–1.9 (m, 12H, CH_2), 1.90 (s, 3H, $SeCH_3$), 2.31 (t, $J = 7.5$ Hz, 2H, 2–*H*), 3.10 (d, $J = 6.1$ Hz, 2H, CH_2SeCH_3, 11–*H*), 3.67 (s, 3H, $COOCH_3$) and 5.46 (m, 2H, *CH*=*CH*).

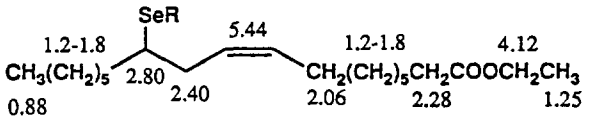
3.6. Reaction of ethyl 10-hydroxy-11-methylseleno-undecanoate (2a) with p-toluenesulfonic acid

A mixture of methyl 10-hydroxy-11-methylseleno-undecanoate (**2a**, 1.0 g, 3.1 mmol), benzene (50 ml) and *p*-toluenesulfonic acid (0.2 g) was refluxed for 6 h. Aqueous sodium bicarbonate (10%, 20 ml) was added and the benzene layer isolated. The organic extract was washed with water (10 ml) and dried over anhydrous sodium sulfate. The filtrate was evaporated under reduced pressure and silica-gel column chromatographic separation of the residue yielded methyl 10-undecenoate (0.6 g, 90%) as an oil. R_f = 0.7 (petroleum ether:diethyl ether, 4:1 v/v); IR (NaCl) 3100 (w, —CH=CH_2), 1736 (s, C=O str.), 1620 (m, C=C str.) cm^{-1}; ^{13}C-NMR ($CDCl_3$, ppm) 14.27 ($COOCH_2CH_3$), 25.03 (C3), 28.96, 29.09, 29.17, 29.23, 29.31, 33.80 (C9), 34.4 (C2), 60.11 ($COOCH_2CH_3$), 114.14 (C11), 139.12 (C10) and 173.79 (C1).

4. Results and discussion

For the preparation of 12-alkylseleno unsaturated C_{18} fatty acid derivatives (**1a–1c**) (Scheme 1a), methyl ricinoleate was used as the substrate. The hydroxy group of methyl ricinoleate was converted to the tosyloxy function to provide a better leaving group. Sodium alkylselenide was generated in situ from dialkyldiselenide by sodium borohydride reduction [9]. Hydrazine was not used as the reducing agent, as any excess of this reagent would reduce the unsaturated center of the substrate [10]. Treatment of methyl 12-tosyloxy-9-*cis*-octadecenoate with sodium alkylselenide yielded the corresponding alkylseleno derivatives (**1a–1c**) with an average yield of 65%. Inter-esterification

Table 1
Results of the proton chemical shifts (δ) of unsaturated alkylseleno fatty acid derivatives (**1a–1c**)



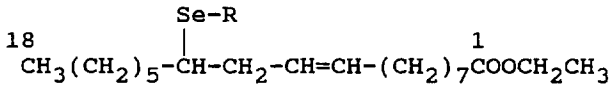
1.94
(**1a**) R = CH_3
2.58 1.39
(**1b**) R = CH_2 CH_3
2.54 0.99
(**1c**) R = CH_2 CH_2CH_3
1.25

of the methyl ester group to the ethyl ester function occurred during the reaction, due to the presence of ethanol in the ethanolic sodium borohydride solution [11].

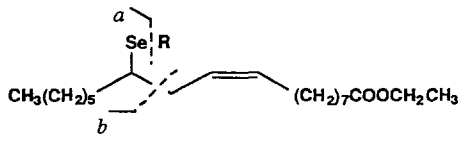
The alkylseleno derivatives (**1a–1c**) were stable and could be readily purified by silica column chromatography. The ^{1}H-NMR spectra of these derivatives displayed a multiplet at δ 5.44, which confirmed the presence of the *cis*-ethylenic bond. The deshielding effect of the selenium atom caused the methine proton (12–*H*) to appear at ca. δ 2.80 (m). Compounds **1a–1c** can be distinguished from each other by signals arising from the chemical shifts of the protons associated with the alkylseleno function (Table 1).

In the ^{13}C-NMR analysis of compounds **1a–1c**, the alkylseleno groups at C12 produced interesting effects on the shifts of the neighbouring carbon nuclei (Table 2). The presence of the ethylenic system in these derivatives was apparent from the signals at about 127 and 131 ppm for the shift of C9 and C10 carbon nuclei, respectively. The shift of the methine carbon atom (C12) appeared at ca. 41 ppm, which was confirmed by the application of the APT test (Attached Proton Technique). Compound **1a** was readily characterized by the shift of the methyl carbon nucleus of the methylseleno group, which appeared at 2.30 ppm. The shift of the methylene and methyl carbon nuclei of the ethylseleno group in compound **1b** ap-

Table 2
^{13}C-NMR chemical shift values (ppm) of ethyl 12-alkylseleno-9-*cis*-octadecenoate (**1a–1c**)



Carbon nucleus	Compound		
	1a (R = CH_3)	**1b** (R = CH_3CH_2)	**1c** (R = $CH_3CH_2CH_2$)
C1	173.71	173.71	173.82
C2	34.37	34.37	34.40
C3	25.00	24.97	25.00
C4	29.17	29.15	29.20
C5	29.17	29.15	29.20
C6	29.17	29.15	29.20
C7	29.58	29.55	29.61
C8	27.52	27.52	27.57
C9	127.31	127.33	127.42
C10	131.53	131.51	131.53
C11	33.15	33.64	33.75
C12	41.93	40.98	41.31
C13	34.97	35.40	35.51
C14	27.82	27.74	27.79
C15	29.17	29.15	29.20
C16	31.80	31.80	31.83
C17	22.64	22.62	22.67
C18	14.06	14.06	14.08
Se-*R*	2.30	15.90	14.74
		16.28	24.13
			25.24
$COOCH_2CH_3$	14.27	14.25	14.27
$COOCH_2CH_3$	60.08	60.08	60.13



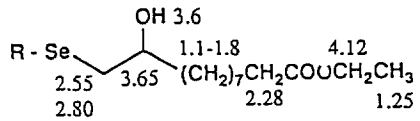
R =	Molecular ion (M^+)	a	b
(1a) Me	404 (12)	389 (100)	193 (92)
(1b) Et	418 (3)	389 (100)	207 (44)
(1c) Pr	432 (4)	389 (100)	221 (72)

Fig. 1. Results of the mass spectral analysis of unsaturated alkylseleno fatty acid derivatives.

peared at 16.28 and 15.90 ppm, respectively. In compound **1c**, the shift of the carbon atoms of the propylseleno moiety appeared at 25.24 and 24.13 ppm for the α- and β-methylene carbon atoms from the selenium atom, and the shift of the methyl carbon nucleus was found at 14.74 ppm.

The mass spectra of compounds **1a–1c** were simple and characteristic (Fig. 1). The intensity of the molecular ion (M^+) was low (3–12%). Cleavage of the Se—C bond at the alkylseleno moiety resulted in a base peak *a* (*m/z* = 389, 100%) in each case. Cleavage of the C—C bond at

Table 3
Results of the proton chemical shifts (δ) of 10-hydroxy-11-alkyl(phenyl)seleno-undecanoate (**2a–2d**)

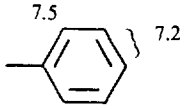


(2a) R = CH_3 (2.0)

(2b) R = CH_2—CH_3 (2.59, 1.40)

(2c) R = CH_2—CH_2—CH_3 (2.6, 1.7, 0.99)

(2d) R = CH_2—$(CH_2)_5$—CH_3 (2.55, 1.2–1.8, 0.89)

(2e) R =  (7.5, 7.2)

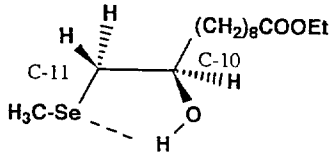
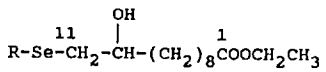


Fig. 2. Intramolecular hydrogen-bonding between selenium and hydroxy function in compound **2a**.

C11/C12 resulted in an intense peak (*b*) which revealed the structure of the alkylseleno moiety.

In the preparation of 1,3-hydroxy-selena fatty acid derivatives (Scheme 1b), reaction of sodium alkylselenide or phenylselenide with methyl-10,11-epoxyundecanoate gave exclusively the corresponding 10-hydroxy-11-alkylseleno-undecanoate derivatives (**2a–2d**) or 10-hydroxy-11-phenylseleno-undecanoate (**2e**) in high yield (average 80%). As sodium borohydride was used in the preparation of sodium alkylselenide and phenylselenide in ethanol, inter-esterification occurred during the ring-opening reaction. The IR spectra of compounds **2a–2d** showed characteristic absorption bands at 3450 (br, O—H str.), 1735 (s, C=O str.) cm^{-1}. Compound **2e** showed additional and characteristic absorption bands at 1600, 1550 and 1455 cm^{-1} for the aromatic system. The results of the ^{1}H-NMR spectral analysis of compound **2a–2e** are presented in Table 3. Of special interest was the shift of the 11-*H* protons. These protons displayed two sets of double doublets at δ 2.80 (dd, J = 12.7, 3.4 Hz, 1H) and 2.55 (dd, J = 12.7, 8.6 Hz, 1H). The chemical non-equivalence of these methylene protons was due to the restricted rota-

Table 4
^{13}C-NMR chemical shift values (ppm) of ethyl 10-hydroxy-11-alkyl(phenyl)seleno-undecanoate (**2a–2d**)



Carbon nucleus	Compound 12 **2a** (R = CH_3)	12 13 **2b** (R = CH_2CH_3)	12 - 14 **2c** (R = $(CH_2)_2CH_3$)	12 - 17 **2d** (R = $(CH_2)_5CH_3$)	**2e** (R = C_6H_5)
C1	173.79	173.76	173.84	173.84	173.68
C2	34.37	34.35	34.40	34.40	34.29
C3	24.97	24.95	24.97	24.97	24.89
C4	29.09	29.09	29.12	29.12	29.04
C5	29.17	29.15	29.17	29.20	29.12
C6	29.33	29.33	29.36	29.36	29.28
C7	29.55	29.52	29.55	29.55	29.44
C8	25.84	25.84	25.87	25.87	25.65
C9	26.68	36.76	36.76	36.76	36.62
C10	69.64	69.96	69.91	69.88	70.07
C11	34.75	32.80	33.32	33.37	36.81
Se	—	—	—	—	—
C12	4.52	17.82	26.82	24.68	—
C13	—	15.87	23.97	29.20	—
C14	—	—	14.46	29.55	—
C15	—	—	—	31.34	—
C16	—	—	—	22.54	—
C17	—	—	—	14.00	—
C_6H_5	—	—	—	—	129.93
				—	132.75 (*o*)
60.13 14.25				—	129.04 (*m*)
COO—CH_2—CH_3				—	126.96 (*p*)

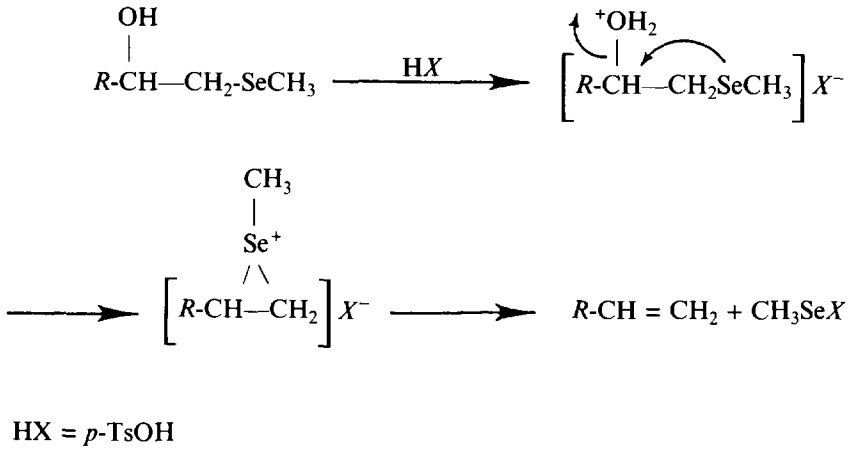
tion between C10 and C11 resulting from the intramolecular hydrogen-bonding between the hydroxy group and the selenium atom (Fig. 2). Reich et al. reported a similar situation in the ^{1}H-NMR analysis of [1-(trimethylsilyl)-2-(phenylseleno)-3-phenyl-1-propanol] [12]. The silyl and phenylseleno groups are in an anti-periplanar position with the selenium atom hydrogen-bonded to the hydroxy group.

The results of the ^{13}C-NMR spectral analysis of compounds **2a-2e** are presented in Table 4. From the carbon chemical shifts of the C9, C10 and C11 carbon nuclei, it could be confirmed that the selenium atom was attached to the C11 carbon atom of the fatty ester derivatives. The results demonstrate that the attack of the alkylselenide or phenylselenide anion preferred the less hindered carbon atom of the epoxy system of methyl 10,11-epoxyundecanoate.

In order to support the presence of hydrogen-bonding between the hydroxy group and the selenium atom in compounds **2a–2e**, the hydroxy function in compound **2a** was acetylated. Examination of the ^{1}H-NMR spectrum of the acetoxy derivative (**3**) showed only a doublet at δ 2.68 (d, J = 3.3 Hz, 2H) for the 11–*H* protons. This result indicates that in the absence of a hydroxy group, the protons of the methylene (C11) adjacent to the selenium atom are chemically equivalent.

Efforts were made to induce an acid-catalyzed elimination of the hydroxy function in compound **2a** with the hope of obtaining the corresponding unsaturated selena fatty acid derivative. However, when compound **2a** was treated with *p*-toluenesulfonic acid in benzene, the reaction gave methyl undecenoate instead as the major product. This product was readily identified by a combination of chromatographic and spectroscopic methods. It appeared, therefore, that elimination of the hydroxy function was followed by the cleavage of the Se—C bond. In order to ascertain that *p*-toluenesulfonic acid was not the cause of the Se—C bond cleavage, methyl 11-selenalaurate was refluxed with *p*-toluenesulfonic acid for 8 h in benzene and found to be unchanged. It could also be inferred that the reaction of compound **2a** with *p*-toluenesulfonic acid induced neighboring group participation of the selenium atom. A plausible mechanism for this reaction is proposed as illustrated below.

Despite numerous attempts to vary the experimental conditions, the reaction of compound **2a** with *p*-toluenesulfonic acid did not result in the production of any unsaturated selena fatty acid derivatives. It could also be argued that the anticipated unsaturated selena fatty acid derivative might itself be unstable. In order to show the stability of unsaturated selena fatty esters, the



synthesis of a methylene-interrupted unsaturated selena fatty ester (**5**) was elaborated (Scheme 1c).

In the synthesis of compound **5** (methyl 11-methylseleno-9-*cis*-undecenoate), the key intermediate **4** (11-hydroxy-9-undecynoic acid) was obtained from propargyl alcohol. Partial hydrogenation of the methyl ester of compound **4** gave methyl 11-hydroxy-9-*cis*-undecenoate. Bromination of the latter, followed by reaction with sodium methylselenide, furnished the requisite product (**5**). Compound **5** was stable and could be readily purified by silica-gel chromatography. The presence of the *cis*-ethylenic bond was confirmed by the signal at δ 5.46 (m) for the olefinic protons in the ^{1}H-NMR spectrum, and by signals at 126.47 (C9) and 133.10 (C10) ppm for the ethylenic carbon nuclei in the ^{13}C-NMR spectrum.

This study of selena fatty acid derivatives shows that the incorporation of a selenium atom into fatty acids can be readily achieved. However, the presence of a selenium atom may induce neighboring group participation reactions during further chemical transformations.

5. Acknowledgements

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6. References

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