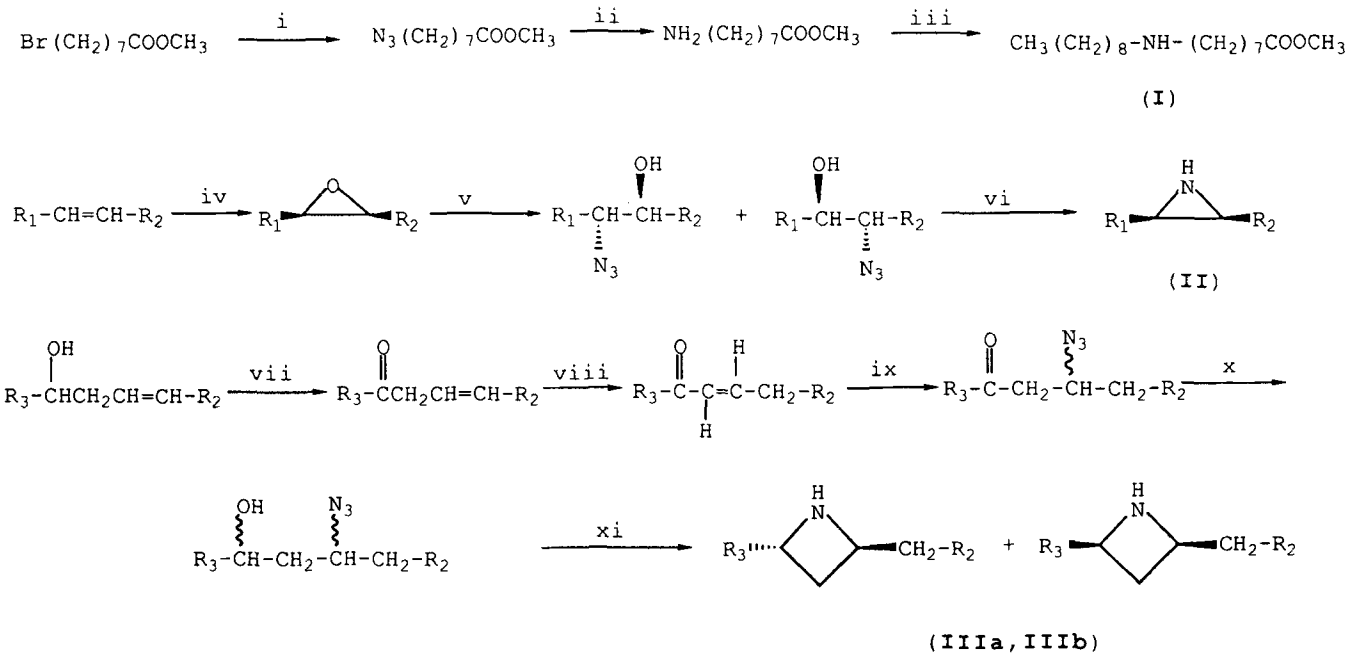
Synthesis and Spectroscopic Properties of Long-Chain Aza, Aziridine and Azetidine Fatty Esters

Marcel S.F. Lie Ken Jie* and **M.S.K. Syed-Rahmatullah**
Department of Chemistry, University of Hong Kong, Hong Kong

Reaction of 1-mesyloxynonane with methyl 8-aminooctanoate gives methyl 9-azastearate (I, 20%); treatment of methyl 9(10),10(9)-azidohydroxyoctadecanoate and methyl 10-azido-12-hydroxyoctadecanoate with triphenylphosphine furnishes the corresponding aziridine derivative (II, 75%) and two geometric azetidine isomers (IIIa and IIIb, 37%), respectively. The aza function in compound I, the aziridine nucleus in compound II and the azetidine system in compounds IIIa, IIIb were characterized by ^1H nuclear magnetic resonance (NMR) and ^{13}C NMR spectral analysis. The infrared spectral analyses of compounds (I), (II) and (IIIa,IIIb) showed characteristic absorption bands at 3200–3300 cm^{-1} for the N-H stretching vibration.

KEY WORDS: Aza, azetidine, aziridine, fatty esters, ^1H NMR, ^{13}C NMR, spectroscopy, synthesis.

Recently, there has been an upsurge in interest in the biological properties of long-chain fatty acids containing nitrogen atoms. A number of synthetic aza prostenoids have been prepared to study the anti-inflammatory properties and the effect of such analogues on the activity of prostaglandin synthetase (1-3). Zamboni and Rokach (4) have synthesized the aza analogue of Leukotriene A_4 (LTA_4) to study the inhibitory effects on enzymes leading to the formation of Leukotrienes B_4 and C_4. Aziridine derivatives of long-chain fatty acids exhibit antimicrobial properties towards Gram(+) bacteria (5). We have synthesized a large number of long-chain fatty acids containing an amino, amido, azido, pyrrolinyl or pyrrolidinyl group (6-9), and currently we are investigating their biological behavior with emphasis on their antimicrobial properties. In our continuing effort to prepare novel nitrogen-containing fatty acid derivatives for biological applications, we report in this paper a novel approach to the synthesis of long-chain aza, aziridine and azetidine fatty ester derivatives involving azido fatty ester intermediates (Scheme 1).



SCHEME 1

*To whom correspondence should be addressed at Dept. of Chemistry, University of Hong Kong, Pokfulam Rd., Hong Kong.

MATERIALS AND METHODS

Instruments. Gas chromatographic analysis was conducted on a Hewlett Packard HP5970 gas chromatograph (Palo Alto, CA) fitted with a 10-m microbore glass column (0.53 mm diam., 2.65 μm film thickness SE-30 stationary phase and a flame ionization detector. Nitrogen (20 mL/min) was used as the carrier gas at an isothermal column temperature of 190°C. External standards of methyl myristate, palmitate and stearate were used as reference compounds, and the equivalent chainlength (ECL) value was calculated accordingly for each component (10). Thin-layer chromatography (TLC) analysis was performed on microscope glass plates coated with silica gel (*ca.* 0.1 mm thickness) and a mixture of petroleum ether (b.p. 40–60°C)/diethyl ether was used as the developer [PE30 denotes a mixture of petroleum ether/diethyl ether (70:30, v/v) where the numeral stands for the percentage of ether in the developer]. Preparative TLC separation was carried out on alumina-coated glass plates (20 × 20 cm, 0.7 mm thickness) (Alumina 60, GF_{254}, type E, Merck, Darmstadt, Germany). Column chromatographic purifications were carried out on silica gel, and mixtures of petroleum ether and ether were used as eluant unless otherwise stated. Infrared (IR) spectra were obtained on a Perkin-Elmer model 577 spectrophotometer (Norwalk, CT), and nuclear magnetic resonance (NMR) spectra were derived from either a JEOL FX-90Q (90 MHz) or JEOL GSX-270 (270 MHz) instrument (Jeol, Ltd., Japan).

Reagents. The following compounds were obtained and used without further purification—methyl oleate, sodium azide, triphenylphosphine, BF_3-etherate, methanesulfonyl chloride and 8-bromooctanoic acid (Aldrich Chemical Co., Milwaukee, WI). Ricinoleic acid (12-hydroxy-9-*cis*-octadecenoic acid) was isolated from castor oil by the procedure described by Gunstone (11) and was converted to the methyl ester by refluxing with BF_3-methanol complex (12). All solvents were dried and distilled before use. Methyl 8-bromooctanoate was prepared by refluxing 8-bromooctanoic acid with BF_3-methanol complex, and methyl 12-oxo-9-*cis*-octadecenoate was prepared by the method described previously (13).

Preparation of methyl 8-azidooctanoate. A mixture of methyl 8-bromooctanoate (2.0 g, 8.4 mmol), sodium azide (1.0 g, 15.4 mmol) and dimethylformamide (25 mL) was stirred at 70°C for 4 hr. Water (50 mL) was added, and the reaction mixture was extracted with diethyl ether (2 × 40 mL). The ethereal extract was washed with water (2 × 30 mL) and dried (Na_2SO_4). Silica column separation gave methyl 8-azidooctanoate (1.6 g, 95%) as an oil. R_F 0.6 (PE20). ^1H NMR ($CDCl_3$, δ): 3.25 (t, *J* 6.6 Hz, 2H, $-C\underline{H}_2$-Br) and the normal fatty ester signals. ^{13}C NMR ($CDCl_3$, ppm): 24.9 (t, C-3), 26.6 (t, C-7), 28.9–29.9 (t, 3xCH_2), 34.1 (t, C-2), 51.4 (q, $COO\underline{C}H_3$), 51.5 (t, C-8), 174.1 (s, C-1). IR (NaCl, cm^{-1}): 2100 ($-CH_2-\underline{N}_3$) and 1740 ($\underline{CO}OCH_3$).

Preparation of methyl 8-aminooctanoate. A mixture of methyl 8-azidooctanoate (1.4 g, 7 mmol), Lindlar's catalyst (0.1 g) (14,15) and methanol (25 mL) was shaken in an atmosphere of hydrogen at 780 mm Hg pressure for 12 hr. The reaction mixture was filtered, and the solvent was distilled under reduced pressure. Silica column chromatographic separation gave methyl 8-aminooctanoate (1.13 g, 93%) as an oil; R_F 0.1 ($CHCl_3$/MeOH, 1:1, v/v). ^1H NMR ($CDCl_3$, δ): 1.85 (s, 2H, $-CH_2-N\underline{H}_2$), 2.65 (t, *J* 6.3 Hz, 2H, $-C\underline{H}_2HN_2$) and the normal fatty ester signals. ^{13}C NMR ($CDCl_3$, ppm): 24.9 (t, C-3), 26.7 (t, C-6), 29.1 (t, C-4 and C-5), 33.7 (t, C-7), 34.1 (t, C-2), 42.1 (t, C-8), 51.4 (q, $COO\underline{C}H_3$) and 174.2 (s, C-1); IR (NaCl, cm^{-1}): 3100–3400 (br, $-\underline{C}H_2\underline{N}H_2$ str.) 1740 ($-\underline{CO}CH_3$) and 1580 ($-CH_2\underline{N}H_2$ bend).

Preparation of 1-mesyloxynonane. To a cooled mixture of 1-nonanol (3.0 g, 2.3 mmol), triethylamine (14 mL) and dry dichloromethane (40 mL) at 0°C, methanesulphonyl chloride (4 mL) was added dropwise over a period of 5 min. The reaction mixture was stirred for 20 min, and water (30 mL) was added. The organic layer was isolated, and the aqueous solution was extracted with dichloromethane (20 mL). The combined organic extract was successively washed with ice water (30 mL) and dried (Na_2SO_4), and the solvent was distilled under reduced pressure to give 1-mesyloxynonane (4.9 g, 96%) as an oil. IR (NaCl, cm^{-1}): 2960, 2860, 1480, 1370 (SO_2 asymm. str), 1200 (SO_2 symm. str), 980, 860 and 780 cm^{-1}.

Preparation of methyl 9-azastearate (I). A mixture of methyl 8-aminooctanoate (0.3 g, 1.73 mmol), 1-mesyloxynonane (0.3 g, 1.35 mmol), triethylamine (1 mL) and dichloromethane (15 mL) was refluxed under nitrogen for 48 hr. Water (20 mL) was added to the cooled reaction mixture followed by dil. NaOH (5%, 2 mL). The reaction mixture was extracted with diethyl ether (2 × 25 mL), washed with water (20 mL) and dried (Na_2SO_4). Silica column chromatographic separation with a mixture of petroleum ether/diethyl ether/methanol (2:2:1, v/v/v) as eluant afforded methyl 9-azastearate (I, 0.1 g, 20%) as an oil. Elemental analysis $C_{18}H_{37}O_2N$ calc.: C, 72.19, H, 12.45, N, 4.68%; found: C, 72.3, H, 12.3, N, 4.5%. R_F 0.2 ($CHCl_3$/MeOH, 1:1, v/v), ECL 18.4 (SE30). ^1H NMR ($CDCl_3$, δ): 0.88 (t, 3H, $-C\underline{H}_3$), 1.2–1.8 (m, 26H, $-C\underline{H}_2$-), 1.7 (s, $-CH_2-N\underline{H}-CH_2$-), 2,3 (t, 2H, $-C\underline{H}_2COOCH_3$), 2.6 (t, 4H, $-C\underline{H}_2-NH-C\underline{H}_2$), 3.6 (s, 3H, $-COOC\underline{H}_3$). ^{13}C NMR ($CDCl_3$, ppm): 14.12 (q, C-18), 22.68 (t, C-17), 24.89 (t, C-3), 27.20 (t, C-6), 27.42 (t, C-12), 29.08 (t), 29.18 (t), 29.29 (t), 29.59 (t), 29.97 (t), 30.00 (t, C-7), 30.05 (t, C-11), 31.90 (t, C-16), 34.08 (t, C-2), 50.03 (t, C-8), 50.09 (t, C-10), 51.46 (q, $COO\underline{C}H_3$) and 174.31 (s, C-1). IR (NaCl, cm^{-1}): 3200–3400 (br, $-CH_2-N\underline{H}-CH_2$-), 1740 ($-\underline{CO}OCH_3$) and 1650 ($-CH_2-\underline{NH}-CH_2$-bend).

Preparation of methyl 9(10)-azido-10(9)-hydroxyoctadecanoate. A mixture of methyl *cis*-9,10-epoxyoctadecanoate [1.0 g, 3.2 mmol, prepared by epoxidation of methyl oleate (16)], sodium azide (0.8 g, 12 mmol), ammonium chloride (0.65 g, 12 mmol), water (5 mL) and ethanol (50 mL) was refluxed for 24 hr. Water (50 mL) was added, and the reaction mixture was extracted with diethyl ether (2 × 50 mL). The ethereal extract was washed with water (20 mL) and dried (Na_2SO_4). Silica column chromatographic separation of the isolated product gave a mixture of methyl 9-azido-10-hydroxyoctadecanoate and methyl 10-azido-9-hydroxyoctadecanoate (1.0 g, 87%) as an oil. R_F 0.4 (PE30). ^1H NMR ($CDCl_3$, δ): 2.4 (s, 1H, >CH-O-H, D_2O exchangeable), 3.2 (m, 1H, >C$\underline{H}$-N_3), 3.5 (m, 1H, >C$\underline{H}$-OH) and the normal fatty ester signals. ^{13}C NMR ($CDCl_3$, ppm): 14.1 (q, C-18), 22.7 (t, C-17), 24.9 (t, C-3), 25.7 (t, C-7 or C-14), 26.3 (t, C-12 or C-7), 29.0 (t), 29.2 (t), 29.5 (t), 29.5 (t), 30.8 (t, $-C\underline{H}_2-CHN_3-CHOH-$, 34.0 (t, C-2), 34.3 (t, $-C\underline{H}_2-CHOH-CHN_3-$), 51.3 (q, $-COOC\underline{H}_3$), 67.2 (d, $-C\underline{H}N_3-CHOH-$), 73.6 (d, $-CHN_3-C\underline{H}OH-$). IR (NaCl, cm^{-1}): 3460 (br, >CH-O$\underline{H}$), 2100 (>C$\underline{H}$-$\underline{N}_3$) and 1740 ($-\underline{CO}OCH_3$).

Preparation of methyl 8-(cis-3-octyl-2-aziridinyl)octanoate (II). A mixture of the methyl 9(10)-azido-10(9)-hydroxyoctadecanoate (0.5 g, 1.4 mmol), triphenylphospine (0.4 g, 1.5 mmol) and anhydrous tetrahydrofuran (20 mL) was stirred at 70°C for 3 hr. The solvent was removed under reduced pressure. The residue was chromatographed on silica gel (30 g), eluting with PE20 (50 mL) followed by a mixture of petroleum ether/diethyl ether/methanol (150 mL, 2:2:1, v/v/v), to give methyl 8-(*cis*-3-octyl-2-aziridinyl)octanoate (II, 0.34 g, 75%) as an amorphous solid (m.p. 51°C). R_F 0.45 (petroleum ether/diethyl ether/methanol, 2:2:1, v/v/v). ^1H NMR ($CDCl_3$, δ): 0.88 (t, 3H, -C$\underline{H}_3$), 1.2–1.8 (m, 26H, -C$\underline{H}_2$-), 1.9 (s, 1 H, >N$\underline{H}$), 1.92 (m, 2H, 2 × C$\underline{H}$ of aziridine ring), 2.3 (t, 2H, -C$\underline{H}_2$COOCH$_3$), 3.6 (s, 3H, -COOC$\underline{H}_3$). ^{13}C NMR ($CDCl_3$, ppm): 14.1 (q, C-18), 22.7 (t, C-17), 25.0 (t, C-3), 28.0 and 28.1 (t, C-7 and C-12), 28.9 (t, C-8 and C-11), 29.1 (t), 29.3 (t), 29.4 (t), 29.6 (t), 31.9 (t, C-16), 34.1 (t, C-12), 35.0 (d, -C$\underline{H}$- of aziridine ring), 51.4 (q, -COOC$\underline{H}_3$) and 174.2 (s, C-1). IR (NaCl, cm^{-1}): 3150 (br, >N$\underline{H}$), 1740 (-$\underline{CO}$OCH$_3$) and 880 (s, ring C$\underline{H}$).

Preparation of methyl 12-oxo-10-trans-octadecenoate. A mixture of methyl 12-oxo-9-*cis*-octadecenoate (1.0 g, 3.2 mmol), BF_3-etherate (1 mL, 7.0 mmol) and dichloromethane (50 mL) was heated at 60°C for 2 hr. Water (50 mL) was added to the reaction mixture, and the organic layer was isolated. The aqueous layer was extracted with dichloromethane (30 mL). The combined organic extract was washed with water (20 mL) and dried (Na_2SO_4). The solvent was distilled under reduced pressure, and silica column chromatographic separation gave methyl 12-oxo-10-*trans*-octadecenoate (0.7 g, 70%) as an oil. R_F 0.5 (PE10). ^1H NMR ($CDCl_3$, δ): 2.1 (m, 2H, -CO-CH=CH-C$\underline{H}_2$-), 2.5 (t, 2H, *J* 7.5 Hz, -C$\underline{H}_2$-CO-CH=CH-), 6.04 (d, 1H, *J* 17 Hz, -CO-C$\underline{H}$=CH-), 6.8 (m, 1H, *J* 17 Hz, -CO-C$\underline{H}$=CH-) and the normal fatty ester signals. ^{13}C NMR ($CDCl_3$, ppm): 14.1 (q, C-18), 22.6 (t, C-17), 25.0 (t, C-3), 28.3 (t, C-8), 29.2 (t), 31.8 (t, C-16), 32.5 (t, C-9), 34.2 (t, C-2), 40.3 (t, C-13), 51.4 (q, -COOC$\underline{H}_3$), 130.5 (d, C-11), 147.2 (d, C-10), 174.3 (s, C-1) and 200.9 (s, C-12). IR (NaCl, cm^{-1}): 1740 (-$\underline{CO}$OCH$_3$), 1680 (-$\underline{CO}$-CH=CH-), 1620 (CH=CH, conj. str) and 950 (-$\underline{CH}$=$\underline{CH}$, *trans*).

Preparation of methyl 10-azido-12-oxo-octadecanoate. A mixture of methyl-12-oxo-10-*trans*-octadecenoate (3.0 g, 9.7 mmol), sodium azide (1.25 g, 19.2 mmol) and glacial acetic acid (40 mL) was stirred at room temperature for 12 hr. Brine (50 mL) was added, and the reaction mixture was extracted with diethyl ether (2 × 60 mL). The ethereal extract was washed with saturated $NaHCO_3$ solution (2 × 20 mL), water (20 mL) and dried (Na_2SO_4). The solvent was distilled and silica column chromatographic separation gave methyl-10-azido-12-oxo-octadecanoate (2.8 g, 82%) as an oil. R_F 0.5 (PE20). ^1H NMR ($CDCl_3$, δ); 2.43 (t, 2H, *J* 7.5 Hz, 13-H), 2.56 (dd, *J* 2.5 Hz, 4 Hz, 2H, 11-H), 3.8 (m, 2H, -C$\underline{H}$-N_3) and the normal fatty ester signals. ^{13}C NMR ($CDCl_3$, ppm): 14.0 (q, C-18), 22.5 (t, C-17), 23.6 (t, C-14), 25.0 (t, C-3), 26.0 (t, C-8), 28.9 (t, C-15), 29.1 (t), 29.2 (t), 29.4 (t), 31.6 (t, C-16), 34.1 (t, C-2), 34.6 (t, C-9), 43.6 (t, C-13), 47.1 (t, C-11), 51.3 (s, -COOC$\underline{H}_3$), 58.3 (t, C-10, -C$\underline{H}$-N_3), 174.1 (s, C-1) and 208.1 (s, C-12). IR (NaCl, cm^{-1}): 2100 (> CH-$\underline{N}_3$), 1740 (-$\underline{CO}$OCH$_3$), and 1710 (-$\underline{CO}$-CH$_2$-CHN$_3$-).

Preparation of methyl 10-azido-12-hydroxyoctadecanoate. A solution of $NaBH_4$ (0.2 g, 5.2 mmol) in methanol (5 mL) was added to a cooled solution of methyl 10-azido-12-oxooctadecanoate (1.0 g, 2.8 mmol) in MeOH (20 mL) at 0°C. The reaction mixture was stirred for 30 min at 0°C. The solvent was evaporated under reduced pressure, and water (25 mL) was added to the residue. The aqueous mixture was extracted with diethyl ether (2 × 30 mL). The ethereal extract was washed with water (30 mL) and dried (Na_2SO_4). Silica column chromatography gave a mixture of stereoisomers of methyl 10-azido-12-hydroxyoctadecanoate (0.72 g, 71%) as an oil. R_F 0.5 (PE20). ^1H NMR ($CDCl_3$, δ): 3.45 (m, 1H, > C$\underline{H}$-N_3), 3.60 (s, 4H, -COOC$\underline{H}_3$, -CHO$\underline{H}$ D_2O exchangeable), 3.65 (m, 1H, > C$\underline{H}$-OH) and the normal fatty ester signals. ^{13}C NMR ($CDCl_3$, ppm): 14.1 (q, C-18), 22.6 (t, C-17), 25.0 (t, C-3), 25.4, 25.6 (t, -C$\underline{H}_2$-CH$_2$-CHN$_3$), 25.8, 26.1 (t, -C$\underline{H}_2$-CH$_2$-CHOH-), 29.1 (t), 29.3 (t), 29.5 (t), 31.8 (t, C-16), 34.1 (t, C-2), 34.4, 35.0 (t, C-9), 37.7, 38.2 (t, C-13), 41.5, 41.9 (t, C-11), 51.4 (q, -COOC$\underline{H}_3$), 59.9, 61.1 (d, C-10), 68.6, 70.1 (d, C-12), 174.3 (s, C-1), IR (NaCl, cm^{-1}): 3200–3400 (br, -CH-O$\underline{H}$), 2100 (-CH-$\underline{N}_3$) and 1740 (-$\underline{CO}$CH$_3$).

Preparation of methyl 9-(4-hexyl-2-acetidinyl)nonanoate (IIIa,IIIb). A mixture of methyl 10-azido-12-hydroxyoctadecanoate (0.64 g, 1.8 mmol), triphenylphosphine (0.47 g, 1.8 mmol) and dry acetonitrile (10 mL) was heated at 100°C for 20 hr. The solvent was distilled off under reduced pressure. Cold petroleum ether (15 mL) was added to the residue. The filtrate was evaporated under reduced pressure, and preparative TLC separation on alumina with PE30 as the developing solvent gave methyl 9-(4-hexyl-2-azetidinyl)nonanoate (IIIa, IIIb, 0.21 g, 37%) as an oil. R_F 0.55 (petroleum ether/diethyl ether/MeOH, 2:2:1, v/v/v). ^1H NMR ($CDCl_3$, δ): 0.88 (t, 3H, -C$\underline{H}_3$), 1.2–1.8 (m, 24H, -C$\underline{H}_2$-), 2.0 (t, 2H, *J* 6.6 Hz, -C$\underline{H}_2$ of azetidine ring, 11-H), 2.3 (t, 2H, -C$\underline{H}_2$-COOCH$_3$), 2.48 (s, 1H, >N-$\underline{H}$), 3.54 (m, 2H, -CH- of acetidine ring, 10-H and 12-H), 3.66 (s, 3H, -COOC$\underline{H}_3$). ^{13}C NMR ($CDCl_3$, ppm): 14.1 (q, C-18), 22.6 (t, C-17), 25.0 (t, C-3), 25.5 (t, C-14), 25.7 (t, C-8), 29.1 (t), 29.5 (t), 31.9 (t, C-16), 32.6 (t, C-11, azetidine ring methylene), 34.1 (t, C-2), 38.1 (t, C-9 and C-13, *trans*-isomer), 39.0 (t, C-9 and C-13 *cis*-isomer), 51.3 (q, -COOC$\underline{H}_3$), 54.8 (d, 2C, ring -C$\underline{H}$- of *cis*-isomer), 55.6 (d, 2C, ring-C$\underline{H}$- of *trans*-isomer). IR (NaCl, cm^{-1}): 3300 (br, > N$\underline{H}$), 1740 (-$\underline{CO}$CH$_3$), 790, 770 and 740 (azetidine ring breathing, -C-N-C-).

RESULTS AND DISCUSSION

Difficulties were encountered when attempts to prepare long-chain aza fatty esters by reacting n-alkylamines with methyl ω-bromoalkanoates (17) resulted in the formation of intractable polar material. The reaction of aminoalkanoates with mesyloxyalkanes was considered for two reasons: i) A mesyloxy group is a better leaving group than a bromide ion in nucleophilic substitution reactions (18); and ii) possible amide formation is prevented when alkylamines react with the methyl ester function. Methyl 8-aminooctanoate was readily prepared from methyl 8-bromooctanoate by reaction with sodium azide followed by hydrogenation of the intermediate, methyl 8-azidooctanoate, over Lindlar catalyst. Treatment of 1-mesyloxynonane with methyl 8-aminooctanoate in the presence of triethylamine afforded methyl 9-azastearate (I) in low yield (20%). The N-H group in compound (I) was char-

acterized by the singlet at δ 1.7 (1H) and by the triplet at 2.6 (4H) for the chemical shift of the protons of the adjacent methylene protons to the aza function in the alkyl chain. In the ^{13}C NMR spectral analysis of compound (I) the α-methylene carbon atoms adjacent to the -NH function appeared at 50.03 and 50.09 ppm downfield from TMS.

The ring-opening reaction involving methyl *cis*-9,10-epoxyoctadecanoate (obtained from epoxidation of methyl oleate) and sodium azide gave a mixture of methyl *threo*-9,10- and 10,9-azidohydroxyoctadecanoate isomers. Heating the latter mixture in anhydrous tetrahydrofuran with triphenylphosphine furnished the desired methyl 8-(*cis*-3-octyl-2-aziridinyl)-octanoate (II) in good yield (75%). Foglia *et al.* (19) have prepared the same aziridine derivative from methyl oleate by the addition of *N,N*-dichlorourethane in 50–60% yield. The aziridine ring was characterized by the signals at δ 1.90 (s) for the shift of the proton of the N-H group and by the signal at 1.92 (m) for the shifts of the methine protons of the aziridine ring. In the ^{13}C NMR spectral analysis of compound II, the shift of the methine carbons atoms of the aziridine nucleus appeared at 35.0 (d) ppm and was confirmed by the Attached Proton Test (APT) technique. This synthesis method constitutes a novel approach to the preparation of aziridine fatty esters.

Treatment of methyl 12-oxo-*cis*-9-octadecenoate with BF_3-etherate furnished the corresponding conjugated keto-ene, which gave methyl 10-azido-12-oxooctadecanoate when reacted with sodium azide. Reduction of methyl 10-azido-12-oxooctadecanoate with sodium borohydride furnished methyl 10-azido-12-hydroxyoctadecanoate as the key intermediate for cyclization involving triphenylphosphine to the azetidine derivative in 37% yield. The reaction was non-stereospecific and gave a mixture of *cis*- and *trans*-isomers (IIIa, IIIb), which could not be separated by silica or alumina column chromatography, due to the extreme polar nature of the azetidine nucleus. However, the presence of both geometric isomers in the product was readily established by ^{13}C NMR spectral analysis. The methine carbon atoms of the *cis*- and *trans*-azetidine nucleus gave characteristic signals at 54.8 (d) and 55.6 (d) ppm for the chemical shifts of these carbon nuclei, respectively (20,21). The shift of the methylene carbon atom in the azetidine ring appeared at 32.6 ppm from TMS. In the ^1H NMR analysis of the mixture of compounds (IIIa, IIIb), the shifts of the methylene and methine protons of the azetidine ring appeared as a triplet at δ 2.0 (J 6.6 Hz) and as a multiplet at δ 3.54, respectively (22). The IR spectral analysis of compounds I, II, and IIIa, IIIb gave (in each case) the characteristic absorption band at 3200–3300 cm^{-1} for the N-H stretching vibration of medium intensity, and bands at 740, 770 and 790 cm^{-1} were due to the C-H bending vibrations of the *cis*- and *trans*-azetidine ring systems.

The physical properties recorded in this study show the ease of characterization of aza, aziridine and azetidine derivatives of long-chain fatty esters.

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