*Fatty Acids: Part 27. Olefin Inversion Involving Unsaturated Fatty Esters

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ABSTRACT

Unsaturated long chain fatty esters gave the corresponding bromochloro ester derivatives when treated with N-bromosuccinimide and hydrogen chloride. Treatment of the intermediate halo esters with sodium iodide furnished the same positional unsaturated fatty ester isomers, but of opposite geometric configuration. This olefin isomerization method was found to be high yielding, stereospecific and to cause no double bond migration.

INTRODUCTION

Sommerfeld recently has reviewed the occurrence of *trans* fatty acids in natural products and processed foods (2). *Trans* fatty acids are produced readily during catalytic hydrogenation of vegetable oils in the manufacture of margarine and during deodorization processes involving high temperatures, where *cis* unsaturated fatty acids are liable to *trans*-isomerization (3).

Isomerization of *cis* unsaturated fatty acids to the more stable *trans* isomer has been studied widely (4-7), but no proper investigation has yet been carried out to examine the conversion of *trans* fatty acids to the corresponding *cis* isomers. Sonnet (8) has reviewed olefin inversion including oxidative additions to alkenes followed by reductive elimination. In this publication we report the interconversion of Z and E isomers of C_{18} monenoic and dienoic fatty esters.

EXPERIMENTAL PROCEDURES

Thin layer chromatography (TLC) plates were coated with silica gel G impregnated with 20% silver nitrate (by weight) and developed with a mixture of light petroleum-diethyl ether (4:1, v/v). The spots were visualized by spraying with a 10% ethanolic solution of phosphomolybdic acid (followed by heating at 150 C for 10 min) or a 0.1% ethanolic solution of 2′, 7′ - dichloro-(R)-fluorescein and viewed under an ultraviolet source.

Gas liquid chromatographic (GLC) analyses were conducted using a Varian model 2400 Chromatograph equipped with a flame ionization detector. Stainless steel chromatographic columns of 0.3 cm diameter by 2 m length containing 10% Silar 10C on Chromosorb W, at 190 C and 40 ml N_2 flow, were used.

Infrared (IR) spectra were obtained with a Perkin-Elmer 577 spectrophotometer. Nuclear magnetic resonance (NMR) was recorded on a JEOL FX-90Q spectrophotometer (90 MHz). Chemical shifts are given in (δ) ppm from TMS. The samples were run as 10% solution in $CDCl_3$.

Dichloromethane and dimethyl formamide were distilled over calcium hydride. N-Bromosuccinimide was recrystallized from water (10 ml/g) and dried (m.p. 171-2 C). Hydrogen chloride gas was dried by bubbling through conc. H_2SO_4. Sodium iodide crystal (anhydrous) was obtained from Merck, and all solvents used were purified by standard procedures.

Methyl oleate and linoleate (99% purity) were obtained from the University of St. Andrews, Scotland, and methyl elaidate (98% pure) from Merck. Methyl *cis,cis*-8,12-; *cis,cis*-5,10- and *trans,trans*-5,9-octadecadienoate were prepared by total synthesis (9).

General Procedures for Olefin Inversion

Formation of Vicinal Bromochloro Ester. The unsaturated C_{18} fatty ester (0.5 g) was stirred in CH_2Cl_2 (25 ml) and cooled to -70 C with solid carbon dioxide. Dry HCl gas was passed slowly (60 ml/min) through this solution for 40 min. A solution of N-bromosuccinimide (1.05 mole/double bond equivalent) in CH_2Cl_2 (20 ml) was added in one portion to the reaction mixture while HCl gas continued to be passed for a further 30 min. The reaction mixture was allowed to reach 20 C and then poured into a saturated aqueous solution of sodium bisulfite (100 ml). The organic layer was isolated, washed successively with water (50 ml), saturated sodium bicarbonate (50 ml), water (50 ml) and dried over anhydrous sodium sulphate. The bromochloro-ester derivative was purified by SiO_2 column chromatography using a mixture of light petroleum/diethyl ether (9:1, v/v) as eluate. The yield of the purified halo esters varied from 64-79%.

Sodium Iodide Reduction of Vicinal Bromochloro Ester. A mixture of halo esters (0.4 g), dimethylformamide (30 ml) and sodium iodide (4 g) was heated at 80 C for 24 hr. The reaction mixture was poured into water (250 ml), and sodium thiosulfate (0.5 g) was added. The mixture was extracted with light petroleum in a continuous liquid-liquid extractor for 24 hr. The organic extract was washed with water and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure. The yield of the unsaturated fatty ester varied from 64-86%.

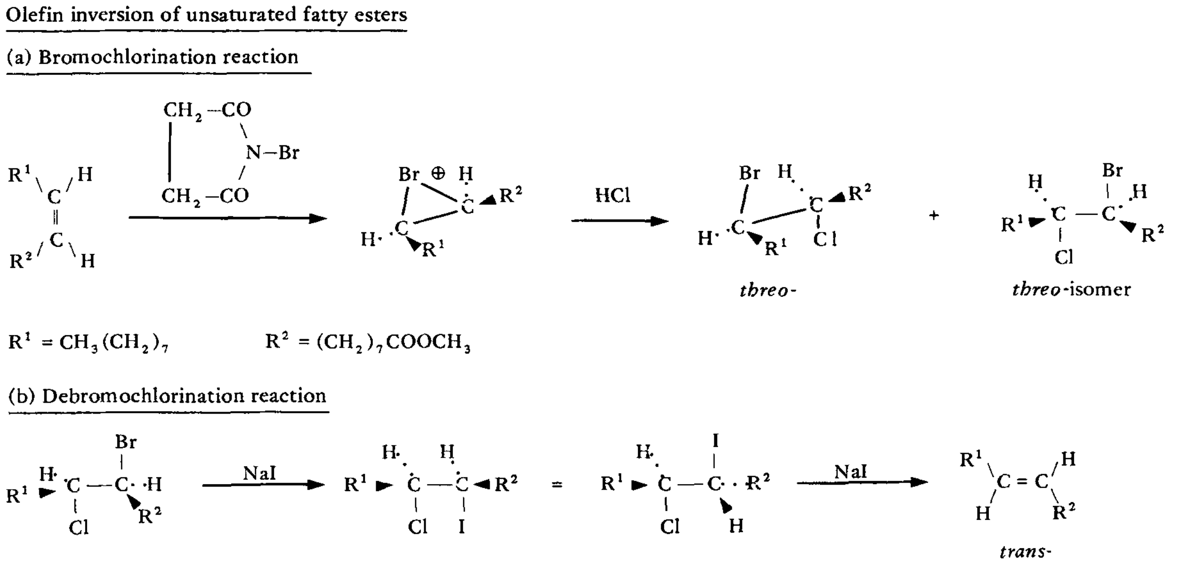
RESULTS AND DISCUSSION

Results of the bromochlorination reaction of the unsaturated fatty esters and subsequent NaI reduction of the halo esters are given in Table I.

Reaction of the ethylenic system of the unsaturated fatty ester with N-bromosuccinimide (NBS) followed by HCl resulted in the *trans*-addition of Br-Cl across the double bond giving a mixture of two positional isomers via a bromonium intermediate (10). Methyl oleate, for instance, would therefore yield two *threo*-bromochloro esters (Scheme 1), while methyl elaidate furnished the corresponding *erythro*-bromochloro esters.

On treatment of the bromo-chloro esters with sodium iodide, one iodide ion would displace the bromide via a bimolecular substitution reaction mechanism. The newly formed chloroiodo ester would be free to rotate to place the chloro and iodo substituents in a more favored *trans* orientation. Subsequent elimination reaction of the chloroiodo ester with another iodide ion gave the inverted unsaturated fatty acid (11) (Scheme 1). The reaction products were analyzed by a combination of IR (showing C-H out-of-plane deformation of *trans*-olefin bond at 965 cm^{-1}), $AgNO_3$-TLC (where the *trans*-isomers have relatively higher R_f values than their corresponding *cis*-isomers), and by GC separation on Silar 10C stationary phase. The results indicated that this chemical inversion of olefin was stereospecific and no geometric isomeric mixtures were obtained. In cases where two ethylenic bonds were present in the fatty ester, olefin inversion was complete for both ethylenic bonds. Each product was subjected to von Rudlof's oxidation to determine the position of the double bonds, and in no instance was there any migration of the double bond's position along the chain.

In order to eliminate any possible allylic bromination via free-radical mechanism when N-bromosuccinimide was used as the brominating agent, light and other free radical initia-



SCHEME 1

TABLE I

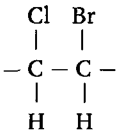
Olefin Inversion of Unsaturated Fatty Esters

Bromo-chlorination of unsaturated fatty esters					NaI reduction reactions			
			Bromochloro ester				Product	
Methyl ester isomer	Mole $(\times 10^{-3})$	Mole $(\times 10^{-3})$ NBS[a]	Mole $(\times 10^{-3})$	Percentage yield (%)	Mole $(\times 10^{-3})$ NaI	Reaction time (h)	Mole $(\times 10^{-3})$	Percentage yield (%)
18:1(9c)	2.19	2.24	1.61	73	13.2	24	18:1(9t) 1.38	86
18:1(9t)	1.68	1.68	1.29	76	13.2	24	18:1(9c) 0.91	70
18:2(9c,12c)	3.40	6.25	2.17	64	33.1	96	18:2(9t,12t) 1.53	71
18:2(9t,12t)	3.33	6.82	2.40	72	33.1	48	18:2(9c,12c) 1.63	68
18:2(5c,10c)	2.38	5.11	1.81	76	26.5	40	18:2(5t,10t) 1.15	64
18:2(8c,12c)	0.78	1.65	0.53	68	6.6	40	18:2(8t,12t) 0.37	70
18:2(5t,9t)	0.98	2.04	0.78	79	13.2	48	18:2(5c,9c) 0.54	69

[a]NBS = N-bromosuccinimide.

tors were carefully excluded (purifying the N-bromosuccinimide and solvents before use) (12). Low temperature condition for this reaction was recommended (10).

Slightly different chemical shifts were observed between the *erythro* and *threo* protons of the ethylenic protons after bromochlorination and appeared as multiplets. The *erythro* isomers exhibited shifts between 3.91-4.15 (δ), while the *threo* isomers gave 3.96-4.09 (δ) shifts for



$-\underset{\mathrm{H}}{\overset{\mathrm{Cl}}{\mathrm{C}}}-\underset{\mathrm{H}}{\overset{\mathrm{Br}}{\mathrm{C}}}-$ in the case of methyl elaidate and oleate respectively. For the methylene interrupted dibromo-dichloro esters (derived from methyl linelaidate and linoleate) the *erythro*, *erythro*- and *threo*, *threo*-protons at $C_{9,10,12,13}$ appeared between 3.90-4.60 and 3.85-4.50 (δ) respectively. In the dimethylene interrupted dibromo-dichloro derivatives the same type of protons appeared at 3.95-4.25 and 3.85-4.30 (δ) for the *erythro*, *erythro* and *threo*, *threo*-isomers.

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