SYNTHESIS OF 20-IODOEICOSANOIC AND 20-[^{125}I]-IODOEICOSANOIC ACIDS

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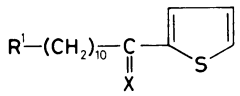
20-Iodoeicosanoic acid (*X*) was prepared in 9 steps, its carbon chain being constructed from thiophene and ethyl ester chlorides of dodecanedioic and butanedioic acids. Isotope exchange afforded 20-[^{125}I]-iodoeicosanoic acid required for scintigraphic studies of the myocardium. Desulfuration of the thiophene precursor *VIII* was accompanied by formation of side products *XI*—*XIX* arising by cleavage of the thiophene C–C bonds. Desulfuration of the model compounds *XX* and *XXI* has shown that the formation of these products is general.

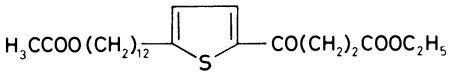
Saturated fatty acids, containing ω-placed radioactive iodine or a substituent with this isotope, are studied and used as myocardial imaging agents for diagnosis of heart deseases[1,2]. Recent investigations have studied the optimal length of the carbon chain, the label-carrying substituents and the β-fragmentation blockade in the myocardium by substitution in the chain[3–6]. Our present communication concerns the synthesis of 20-iodoeicosanoic acid (*X*) as well as this acid labelled with ^{125}I. The acid *X* has already been prepared from the corresponding hydroxy acid *IX* (ref.[7]) isolated from natural material or by reduction of the corresponding oxo compounds[8].

Our synthesis makes use of thiophene as the chain-lengthening building block[9]. Its reaction with ethyl ester chloride of dodecanedioic acid, catalyzed by tin tetrachloride, afforded ethyl 11-thenoylundecanoate (*I*) which without isolation was hydrolyzed to give the keto acid *II*. The acid *II* was reduced according to Huang–Minlon and the obtained acid *III* on reduction with lithium aluminium hydride in ether was converted into the corresponding alcohol *IV*. The hydroxy group in *IV* was protected by acetylation and the resulting acetate *V* was further acylated in position 5 of the thiophene nucleus with ethyl ester chloride of butanedioic acid, again with tin tetrachloride as catalyst. The obtained diester *VI* was hydrolyzed with ethanolic potassium hydroxide to give the corresponding acid *VII*. Its reduction according to Huang–Minlon led to the hydroxy acid *VIII* which was desulfurized

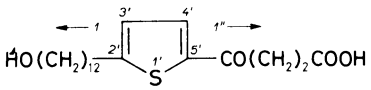
with Raney nickel in ethanol in the usual manner. Besides the desired 20-hydroxyeicosanoic acid (*IX*), obtained in 65% yield, column chromatography furnished a fraction (27%) consisting of 9 compounds as shown by the GC-MS method. The first four components were homologous primary alcohols 1-tridecanol (*XI*), 1-tetradecanol (*XII*), 1-pentadecanol (*XIII*) and 1-hexadecanol (*XIV*) which had arisen by cleavage of the thiophene C—C bonds or the bond linking the thiophene ring with the butanoic acid moiety. Their structure has been proven by mass spectra which fully agreed with those published for the authentic compounds[10].



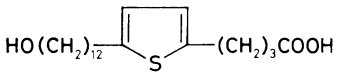
I, X = O ; $R^1 = COOC_2H_5$
II, X = O ; $R^1 = COOH$
III, $X = H_2$; $R^1 = COOH$
IV, $X = H_2$; $R^1 = CH_2OH$
V, $X = H_2$; $R^1 = CH_2OCOCH_3$



VI



VII

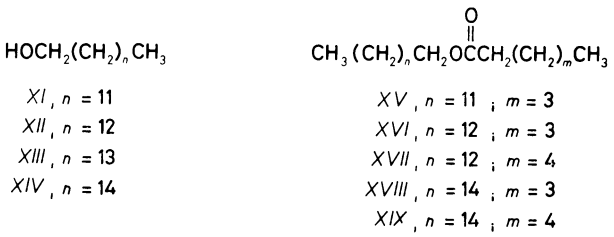


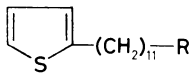
VIII

$R—CH_2(CH_2)_{18}COOH$

IX, R = OH
X, R = I

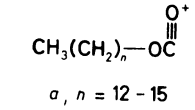
Further five compounds were esters of the mentioned alcohols with the formed short carboxyl-bearing fragments: tridecyl hexanoate (*XV*), tetradecyl hexanoate (*XVI*), tetradecyl heptanoate (*XVII*), hexadecyl hexanoate (*XVIII*) and hexadecyl heptanoate (*XIX*). The structure of these esters has been elucidated again using mass



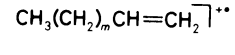


XX, R = CH_2OH
XXI, R = COOH

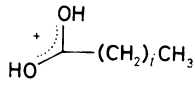
spectrometry. Their mass spectra are very characteristic. Esters of hexanoic and heptanoic acid lose the radical C_5H_{11} and C_6H_{13}, respectively, under formation of ion *a*. Further important ions *b* arise by McLafferty rearrangement in the chain of the original alcohol, combined with charge transfer. The most abundant ions in the spectra are unusual ions of the type *c*, *m/z* 117 for hexanoates and *m/z* 131 for heptanoates. Ions of the type *d* are less abundant. Reports on fission of the thiophene C—C bonds in the Raney nickel desulfuration are very rare[11]. In order to study the scope of this reaction we performed an analogous desulfuration of two model thiophene derivatives *XX* and *XXI*. In both cases the reaction mixture contained derivatives formed by cleavage of C—C bonds in the thiophene ring. Thus, the formation of those side products can be considered as general. The formation



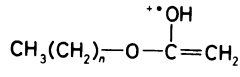
a, *n* = 12 - 15



b, *m* = 10 - 13



c, *m/z* 117 (*i* = 4)
m/z 131 (*i* = 5)



d, *n* = 12 - 15

of esters *XV*–*XIX* under the desulfuration conditions is very surprising, both from the viewpoint of formation and mechanism and it will be (as well as the cleavage of the thiophene ring) the topic of another study.

Reaction of 20-hydroxyeicosanoic acid (*IX*) with trimethyliodosilane in dichloromethane afforded 20-iodoeicosanoic acid (*X*) which on treatment with $Na^{125}I$ in 2-butanone gave 20-[^{125}I]-iodoeicosanoic acid in radiochemical yield of 37%.

EXPERIMENTAL

Melting points were determined on a Boetius block (G.D.R.) and are uncorrected. ^{1}H and ^{13}C-NMR spectra were measured on a Varian XL-200 instrument (^{1}H at 200·057 Hz, ^{13}C at 50·309 MHz) in deuteriochloroform. Tetramethylsilane was used as internal standard for the ^{1}H NMR spectra; the ^{13}C NMR spectra are referenced to the $CDCl_3$ signal, using the conversion relationship δ ($CDCl_3$) = 77·0. All chemical shifts are given in ppm (δ-scale). Coupling constants (*J*) were obtained by first-order analysis and are given in Hz. The numbering of carbon atoms for the purpose of the NMR spectra is given in formula *VII*. Mass spectra were obtained with a Finnigan MAT 90 (F.R.G.) spectrometer, electron energy 70 eV, ion source temperature 250°C, ion current 1 mA, direct inlet temperature 25–150°C; the GC-MS measurements were performed on an Incos 50 (Finnigan) instrument. Infrared spectra were recorded in chloroform solutions on a Perkin–Elmer 1760 FT-IR instrument, wavenumbers are given in cm^{-1}. Thin-layer chromatography was carried out on Silufol sheets (Kavalier, Votice, Czechoslovakia); detection by spraying with 5% phosphomolybdic acid and subsequent heating, or with a UV-lamp. Column chromatography was carried out on silica gel Silpearl (Kavalier, Votice). Analytical samples were dried in vacuo over phosphorus pentoxide for 24 h.

Ethyl ester chloride of dodecanedioic acid was obtained according to Jones[12] by treatment of monoethyl dodecanedioate with thionyl chloride. The product had b.p. 188–192°C/0·8 kPa (reported[12] b.p. 147–150°C/0·4 kPa). Ethyl ester chloride of succinic acid was obtained in an analogous manner, b.p. 90°C/2·65 kPa (reported[14] b.p. 92°C/2·67 kPa).

11-Thenoylundecanoic Acid (*II*)

Freshly distilled tin tetrachloride (62 g, 0·24 mol) was added at 0°C to a stirred mixture of ethyl ester chloride of dodecanedioic acid (50 g, 0·18 mol), thiophene (15·8 ml, 0·2 mol) and benzene (180 ml). The reaction mixture was stirred for 20 min at 0°C, for 1 h at 20°C and then decomposed with a mixture of dilute hydrochloric acid (1 : 1, 70 ml) and crushed ice (100 g). The benzene layer was separated and the aqueous one extracted with chloroform (50 ml). The combined organic portions were washed with water, dried over anhydrous magnesium sulfate and concentrated. The residue was mixed with ethanol (100 ml) and the solvent was evaporated. The dry residue was dissolved in 10% ethanolic potassium hydroxide (150 ml) and refluxed for 3 h. The mixture was diluted with water (200 ml), concentrated to a half, washed with ether and acidified with dilute (1 : 1) hydrochloric acid. The separated product was extracted with chloroform, the chloroform solution was dried and the solvent evaporated. Crystallization from benzene–light petroleum, and then from methanol–toluene afforded 37 g (69%) of the acid *II*, m.p. 68–69°C. IR spectrum: 1 709 (COOH); 1 660 (CO). ^{1}H NMR spectrum: 1·29 s, 12 H (2 × H-4 – H-9); 1·63 p, 2 H (2 × H-3; $J = J' = 8$); 1·74 p, 2 H (2 × H-10; $J = J' = 7·3$); 2·34 t, 2 H (2 × H-2; $J = 8·4$); 2·89 t, 2 H (2 × H-11; $J = 8·8$); 7·11 dd, 1 H (H-4′; $J = 3·8$; $J' = 5·1$); 7·61 dd, 1 H (H-5′; $J = 5·1$; $J' = 1·5$); 7·70 dd, 1 H (H-3′; $J = 3·8$; $J' = 1·5$); 10·61 bs, 1 H (COOH): ^{13}C NMR spectrum: 24·6, 24·8, 29·0, 29·1, 29·3 t (C-3 – C-10); 34·0 t (C-11); 39·4 t (C-2);

128·0, 131·7, 133·3 d (C-3′, C-4′, C-5′); 144·4 s (C-2′); 180·0 s (C-12); 193·6 s (C-1). Mass spectrum, *m/z* (%): 296 M^+ (5), 139 (15), 126 (100), 111 (68), 97 (5), 83 (5), 69 (5), 60 (3). For $C_{16}H_{24}O_3S$ (296·4) calculated: 64·83% C, 8·16% H, 10·82% S; found: 64·80% C, 8·05% H, 10·90% S.

12-Thienyldodecanoic Acid (*III*)

A mixture of acid *II* (29·6 g, 0·1 mol), diethylene glycol (150 ml) and 80% hydrazine hydrate (25 ml) was heated to 120°C for 30 min. A solution of potassium hydroxide (40 g) in diethylene glycol (100 ml) was added and the mixture was refluxed for 30 min. The excess hydrazine and water were distilled off and the mixture was kept at 200–220°C for 3 h (until the nitrogen evolution ceased). After cooling, water (400 ml) was added and the obtained solution was washed with ether (2 × 200 ml). The aqueous phase was acidified with dilute (1 : 1) hydrochloric acid and extracted with ether (4 × 200 ml). The extract was washed with water (2 × 350 ml), dried over anhydrous magnesium sulfate, the solvent was evaporated and the residue (27·6 g) crystallized from ether–light petroleum, affording 23·8 g (84%) of acid *III*, m.p. 38–40°C (reported[13] m.p. 41–42·5°C). IR spectrum: 1 708 (COOH). ^{1}H NMR spectrum: 1·27 s, 14 H (2 × H-4 – H-10); 1·63 p, 2 H (2 × H-3; $J = J' = 7·9$); 1·66 p, 2 H (2 × H-11, $J = J' = 7·5$); 2·34 t, 2 H (2 × × H-2, $J = 7·3$); 2·81 t, 2 H (2 × H-12, $J = 6·9$); 6·76 dd, 1 H (H-3′, $J = 3·2$; $J' = 1·2$); 6·89 dd, 1 H (H-4′, $J = 3·2$; $J' = 5·1$); 7·08 dd, 1 H (H-5′, $J = 1·2$; $J' = 5·1$); 11·5 bs, 1 H (COOH). ^{13}C NMR spectrum: 24·6, 29·0, 29·1, 29·2, 29·3, 29·4, 29·5 (2 C); 29·9 t (C-2 – C-10); 31·8 t (C-1); 34·1 t (C-11); 122·7, 123·8, 126·6 d (C-3′, C-4′, C-5′); 145·8 s (C-2′); 180·4 s (C-12). Mass spectrum, *m/z* (%): 282 M^+ (30), 167 (5), 153 (5), 139 (8), 111 (38), 97 (100), 85 (3), 69 (5), 60 (6). For $C_{16}H_{26}O_2S$ (282·4) calculated: 68·04% C, 9·28% H, 11·35% S; found: 68·17H C, 9·25% H, 11·41% S.

12-Thienyldodecan-1-ol (*IV*)

A solution of acid *III* (9·8 g, 35 mmol) in ether (130 ml) was added dropwise during 15 min to a solution of 0·5M lithium hydride (150 ml) in ether. In the course of the addition, the mixture spontaneously warmed to reflux temperature and was then stirred and refluxed for 1 h. After cooling, the excess hydride was decomposed with water and 10% sulfuric acid (100 ml) was added. The ethereal layer was separated and the aqueous one was extracted with ether (2 × 100 ml). The combined ethereal phases were washed with 2% solution of potassium hydroxide (80 ml) and water (2 × 150 ml), dried over anhydrous magnesium sulfate and the ether was evaporated. Crystallization of the residue (9·5 g) from light petroleum afforded 8·5 g (91%) of alcohol *IV*, m.p. 27–29°C. IR spectrum: 3 623, 3 436 (OH). ^{1}H NMR spectrum: 1·27 s, 14 H (2 × J-3 – H-9); 1·45–1·70 m, 7 H (2 × H-2, H-10, H-11, OH); 2·81 t, 2 H (2 × H-1, $J = 8·2$); 3·62 t, 2 H (2 × H-12, $J = 6·4$); 6·76 dd, 1 H (H-3′, $J = 3·3$; $J' = 1$); 6·90 dd, 1 H (H-4′, $J = 3·3$; $J' = 5·1$); 7·08 dd, 1 H (H-5′, $J = 1$; $J' = 5·1$). ^{13}C NMR spectrum: 25·7, 29·1, 29·3 (2 C); 29·4 (2 C); 29·6 (2 C); 29·9 t, (C-2 – C-10); 31·7 t (C-1); 32·8 t (C-11); 63·0 t (C-12); 122·6, 123·8, 126·6 d, (C-3′, C-4′, C-5′); 145·8 s (C-2′). Mass spectrum, *m/z* (%): 268 M^+ (20), 240 (4), 167 (5), 153 (5), 139 (7), 123 (10), 111 (27), 100 (21), 97 (100), 95 (5), 83 (9), 69 (11). For $C_{16}H_{28}OS$ (268·5) calculated: 71·58% C, 10·51% H, 11·94% S; found: 71·51% C, 10·40% H, 11·74% S.

1-Acetoxy-12-thienyldodecane (*V*)

A mixture of alcohol *IV* (9·5 g, 35 mmol), acetic anhydride (15 ml) and anhydrous pyridine (30 ml) was allowed to stand at room temperature for 24 h. Water (150 ml) was added and the product was extracted with chloroform (2 × 80 ml). The chloroform extract was washed

with dilute hydrochloric acid (1 : 10, 2 × 100 ml) and water (3 × 100 ml) and dried over anhydrous magnesium sulfate. The solvent was evaporated and the residue chromatographed on a column of silica gel. Elution with benzene gave 9·9 g (90%) of the oily acetate *V*. IR spectrum: 1 728 ($OOCCH_3$). ^{1}H NMR spectrum: 1·26 bs, 16 H (2 × H-3 — H-10); 1·63 m, 4 H (2 × H-2, H-11); 2·04 s, 3 H (CH_3CO); 2·81 t, 2 H (2 × H-1, *J*-7); 4·05 t, 2 H (2 × H-12, $J = 6·2$); 6·77 dd, 1 H (H-3′, $J = 1·1$; $J' = 3·5$); 6·90 dd, 1 H (H-4′, $J = 3·5$; $J' = 5·2$); 7·09 dd, 1 H (H-5′, $J = 1·1$; $J' = 5·2$). Mass spectrum, *m/z* (%): 310 M^+ (39), 267 (8), 250 (5), 168 (3), 153 (5), 139 (11), 123 (38), 111 (40), 110 (42), 97 (100), 85 (5), 67 (5), 55 (10), 43 (28). For $C_{18}H_{30}O_2S$ (310·5) calculated: 69·63% C, 9·74% H, 10·33% S; found: 69·72% C, 9·62% H, 10·12% S.

2-(1,4-Dioxo-4-ethoxybutyl)-5-(12-acetoxydodecyl)thiophene (*VI*)

A solution of freshly distilled tin tetrachloride (10·88 g, 41 mmol) was added in the course of 15 min at 0°C to a stirred solution of acetate *V* (11·4 g, 36 mmol) and ethyl ester chloride of succinic acid (5·92 g, 36 mmol) in benzene (60 ml). The mixture was stirred at 0°C for 30 min and then at room temperature for 1·5 h. After decomposition of the reaction mixture with dilute (1 : 1) hydrochloric acid and crushed ice (100 g), the benzene layer was separated and the aqueous one extracted with chloroform (2 × 30 ml). The organic phases were combined, dried over anhydrous sodium sulfate and the solvent was evaporated. The obtained crude product (13 g) was crystallized from benzene–ethanol and then from methanol; yield 7 g (55%) of derivative *VI*, m.p. 49°C. IR spectrum: 1 659 (CO); 1 729 (COOR and $OOCCH_3$). ^{1}H NMR spectrum:-1·25 t, 3 H ($COOCH_2\mathbf{CH_3}$, $J = 7·4$); 1·26 s, 16 H (2 × H-3 — H-10); 1·57—1·71 m, 4 H (2 × H-2, H-11); 2·04 s, 3 H (CH_3); 2·72 t, 2 H (2 × H-3″, $J = 6·6$); 2·82 t, 2 H (2 × H-1, $J = 7·3$); 3·19 t, 2 H (2 × H-2″, $J = 6·6$); 4·04 t, 2 H (2 × H-12, $J = 6·9$); 4·14 q, 2 H ($COO\mathbf{CH_2}$–CH_3, $J = 7·4$); 6·80 d, 1 H (H-4′, $J = 3·9$); 7·59 d, 1 H (H-4′, $J = 3·9$). ^{13}C NMR spectrum: 14·1 q ($\mathbf{CH_3}$–CH_2OOC); 21·0 q ($\mathbf{CH_3}$–CO); 25·9, 28·3, 28·5, 28·9, 29·2, 29·3, 29·4 (2 C); 29·46, 29·5, 30·6, 31·3, 33·4, t (C-1 — C-11, C-2″, C-3″); 60·6 t ($\mathbf{CH_2}$–CH_3); 64·6 t (C-12); 125·5 d (C-3′); 132·3 d (C-4′); 141·0 s (C-5′); 155·8 s (C-2′); 171·1 s (C-4″); 172·7 s (CO–CH_3); 190·6 s (C-1″). Mass spectrum, *m/z* (%): 438 M^+ (58), 393 (65), 392 (85), 350 (15), 332 (19), 295 (20), 277 (18), 225 (17), 193 (100), 180 (28), 151 (18), 141 (50), 129 (76), 97 (46), 69 (18), 55 (39), 43 (70). For $C_{24}H_{38}O_5S$ (438·6) calculated: 65·73% C, 8·73% H, 7·29% S; found: 65·76% C, 8·61% H, 7·54% S.

2-(1-Oxo-3-carboxypropyl)-5-(12-hydroxydodecyl)thiophene (*VII*)

Diester *VI* (7 g, 15 mmol) was refluxed with 10% ethanolic potassium hydroxide (50 ml) for 6 h. The mixture was cooled, concentrated in vacuo, diluted with water (150 ml) and the obtained solution was acidified with dilute hydrochloric acid (1 : 1) to pH 4. The separated compound was collected, washed with water and dried. Crystallization from ethanol afforded 5·6 g (95%) of the title acid *VII*, m.p. 116—117°C. IR spectrum: 3 623, 3 436 (OH); 1 723 (COOH); 1 659 (CO). ^{1}H NMR spectrum: 1·23 s, 16 H (8 × CH_2); 1·38 p, 2 H (CH_2, $J = J' = 6·5$); 1·61 p, 2 H (CH_2, $J = J' = 6·6$); 2·53 t, 2 H (2 × H-3″, $J = 6·7$); 2·81 t, 2 H (2 × H-1, $J = 7·8$); 3·12 t, 2 H (2 × H-2″, $J = 7·5$); 3·35 t, 2 H (2 × H-12, $J = 6·6$); 4·30 bs, 1 H (OH); 6·96 d, 1 H (H-3′, $J = 4·2$); 7·78 d, 1 H (H-4′, $J = 4·2$). ^{13}C NMR spectrum: 25·7, 28·6, 28·9, 29·15 (2 C); 29·2 (2 C); 29·3, 29·9, 31·1, 32·7, 33·1 t (C-1 — C-11, C-2″, C-3″); 60·9 t (C-12); 126·5 d (C-3′); 133·6 d (C-4′); 141·0 s (C-5′); 154·9 s (C-2′); 173·8 s (C-4″); 191·2 s (C-1″). Mass spectrum, *m/z* (%): 368 M^+ (70), 350 (63), 338 (17), 295 (20), 249 (10), 211 (17), 197 (38), 183 (82), 167 (42), 141 (100), 137 (45), 111 (30), 97 (75). For $C_{20}H_{32}O_4S$ (368·5) calculated: 65·18% C, 8·75% H, 8·77 % S found: 65·02% C, 8·83% H, 8·60% S.

2-(3-Carboxypropyl)-5-(12-hydroxydodecyl)thiophene (*VIII*)

A mixture of acid *VII* (11·9 g, 32 mmol), diethylene glycol (50 ml) and 100% hydrazine hydrate (20 ml) was heated to 120°C for 30 min. A solution of potassium hydroxide (13 g) in diethylene glycol (50 ml) was then added and the mixture was refluxed for 30 min. Water and the excess hydrazine hydrate were distilled off and the temperature was kept at 220–230°C for 4 h (until the nitrogen evolution ceased). After cooling, water (200 ml) was added and the mixture was acidified with hydrochloric acid to pH 4. The separated compound was collected on filter, washed with water and dried over phosphorus pentoxide. Chromatography on a column of silica gel (elution with benzene–ether) gave 7·6 g (66%) of hydroxy acid *VIII*, m.p. 71–72°C (ethanol–ether). IR spectrum: 3 623, 3 418 (OH); 1 711 (COOH). ^{1}H NMR spectrum: 1·26 bs, 16 H (2 × H-3 – H-10); 1·59 m, 4 H (2 × H-2, H-11); 1·97 q, 2 H (2 × H-2″, J = 7·4); 2·40 t, 2 H (2 × H-3″, J = 7·7); 2·73 t, 2 H (2 × H-1″, J = 7·8); 2·81 t, 2 H (2 × H-1, J = 7·8); 3·64 t, 2 H (2 × H-12, J = 7); 5·72 bs, 2 H (OH, COOH); 6·55 and 6·57 AB system (H-3′, H-4′, J(AB) = 3·6). ^{13}C NMR spectrum: 25·7 t (CH_2); 26·5, 29·0, 29·26, 29·29, 29·4, 29·5, 29·53 (3 C); 30·1, 31·6, 32·7, 33·0 t (CH_2); 63·1 t (C-12); 123·4 and 124·0 d (C-3′, 4′); 142·2 and 143·9 s (C-2′, C-5′); 178·6 s (C-4″). Mass spectrum, *m/z* (%): 354 (M^+ (56), 336 (20), 308 (8), 294 (20), 281 (51), 267 (9), 183 (100), 165 (7), 151 (6), 137 (19), 123 (100), 11 (24), 97 (18). For $C_{20}H_{34}O_3S$ (354·6) calculated: 67·75% C, 9·67% H, 9·04% S; found: 67·71% C, 9·52% H, 9·17% S.

Reduction of Hydroxy Acid *VIII* with Raney Nickel

Raney nickel W-2 (prepared from 100 g of the alloy) was added in portions during 2·5 h to a stirred boiling solution of hydroxy acid *VIII* (7·6 g, 21 mmol) in ethanol (100 ml). After the addition the mixture was stirred and boiled for additional 2 h, the nickel was filtered off and extracted successively with boiling ethanol (3 × 100 ml) and ethanol–acetic acid (20 : 1, 100 ml). The combined organic portions were concentrated in vacuo, and the residue was chromatographed on a column of silica gel in benzene–ether (9 : 1). Fractions 7–9 weighed 1·9 g (27%); R_F 0·65 and 0·70 in benzene–ether (1 : 1), m.p. 24–25°C; IR spectrum 3 628, 3 442 (OH); 1 714 (CO); GC-MS analysis showed that this side product fraction consisted of the following 9 compounds.

1-Tridecanol (XI, 3·5%). MS, *m/z* (%): 199 (M-1, 0·2), 182 (18), 154 (19), 139 (8), 125 (22), 111 (42), 97 (75), 83 (100), 69 (92), 55 (96), 43 (80).

1-Tetradecanol (XII, 6%). MS, *m/z* (%): 196 (M-18, 18). 168 (17), 139 (10), 125 (22), 111 (42), 97 (78), 83 (100), 69 (87), 55 (90), 43 (74).

1-Pentadecanol (XIII, 2·8%). MS, *m/z* (%): 227 (M-1, 0·2), 210 (12), 182 (10), 154 (6), 139 (9), 125 (20), 111 (40), 97 (74), 83 (100), 69 (85), 55 (89), 43 (84).

1-Hexadecanol (XIV, 12·6%). MS, *m/z* (%): 224 (M-18, 16), 196 (11), 168 (4), 154 (6), 139 (10), 125 (22), 111 (43), 97 (85), 83 (100), 69 (84), 55 (88), 43 (75).

Tridecyl hexanoate (XV, 0·5%). MS, *m/z* (%): 298 (M, 2), 242 (*d*, 1), 227 (*a*, 10), 182 (*b*, 25), 154 (10), 125 (11), 117 (*c*, 100), 111 (18), 99 (31), 97 (35), 83 (36), 69 (34), 55 (38), 43 (59).

Tetradecyl hexanoate (XVI, 0·6%). MS, *m/z* (%): 312 (M, 2), 256 (*d*, 1), 241 (*a*, 8), 196 (*b*, 20), 182 (14), 168 (9), 125 (12), 117 (*c*, 100), 111 (23), 97 (38), 83 (45), 69 (40), 57 (56), 43 (77).

Tetradecyl heptanoate (XVII, 0·4%). MS, *m/z* (%): 326 (M, 5), 256 (*d*, 1), 241 (*a*, 5), 196 (*b*, 25), 131 (*c*, 100), 125 (15), 113 (25), 97 (34), 83 (38), 69 (35), 57 (41), 55 (41), 43 (70).

Hexadecyl hexanoate (XVIII, 0·25%). MS, *m/z* (%): 340 (M, 2), 269 (*a*, 3), 224 (*b*, 12), 196 (3), 125 (8), 117 (*c*, 100), 111 (20), 97 (31), 83 (31), 69 (32), 57 (35), 55 (35), 43 (58).

Hexadecyl heptanoate (XIX, 0·1%). MS, *m/z* (%): 354 (M, 2), 269 (*a*, 3), 224 (*b*, 13), 196 (3), 139 (5), 131 (*c*, 100), 113 (21), 97 (32), 83 (35), 69 (22), 57 (45), 43 (64).

Fractions 11—14 afforded 4·6 g (65%) of acid *IX*.

20-Hydroxyeicosanoic acid (IX), m.p. 96—97°C (reported[8] m.p. 97·4—97·8°C). IR spectrum: 3 630, 3 441 (OH); 1 718 (COOH). ^{1}H NMR spectrum: 1·25 bs, 30 H (2 × H-4 — H-18); 1·59 m, 4 H (2 × H-3, H-19); 2·35 t, 2 H (2 × H-2, J = 7·4); 3·65 t, 2 H (2 × H-20, J = 6·7). ^{13}C NMR spectrum: 23·9, 24·9, 28·1, 28·2, 28·4, 28·5 (11 C); 31·9, 33·2 t (18 × CH_2); 61·0 t (C-20); 174·6 s (C-1). Mass spectrum, *m/z* (%): 310 (M-18, 10), 298 (4), 129 (10), 112 (21), 98 (65), 84 (38), 83 (45), 69 (65), 55 (100), 43 (57), 41 (76). For $C_{20}H_{40}O_3$ (328·5) calculated: 73·12% C, 12·27% H; found: 73·31% C, 12·14% H.

20-Iodoeicosanoic Acid (*X*)

A mixture of acid *IX* (4·5 g, 10 mmol), trimethyliodosilane (5 g, 25 mmol) and dichloromethane (30 ml) was stirred under argon at room temperature for 24 h. A solution of sodium metabisulfite (5%, 50 ml) was added and the mixture was extracted with dichloromethane (5 × 50 ml). The organic phases were combined, washed with 5% solution of sodium metabisulfite and water and dried over anhydrous sodium sulfate. The solvent was evaporated and the residue chromatographed on a column of silica gel in benzene–ether (5 : 1). Fractions 24—25 furnished 2·41 g (40%) of acid *X*, m.p. 72—74°C (benzene–light petroleum). IR spectrum: 1 709 (COOH). ^{1}H NMR spectrum: 1·25 bs, 30 H (2 × 4-H — 18-H); 1·63 p, 2 H (2 × H-3, $J = J'$ = 7·3); 1·82 p, 2 H (2 × H-19, $J = J'$ = 7·1); 2·34 t, 2 H (2 × H-2, J = 7·3); 3·18 t, 2 H (2 × H-20, J = 7·1). ^{13}C NMR spectrum: 7·3 t (C-20); 24·7, 28·5, 29·1, 29·2, 29·4 (2 C); 29·5 (2 C); 29·7 (7 C); 30·5, 33·6, 34·1 t (18 × CH_2); 180·1 s (C-1). Mass spectrum, *m/z* (%): 439 $M^+ + 1$ (5), 438 M^+ (3), 421 (8), 401 (3), 311 (31), 393 (36), 275 (8), 139 (12), 125 (18), 111 (21), 97 (38), 85 (40), 83 (46), 69 (64), 55 (100), 43 (92), 41 (97). For $C_{20}H_{39}IO_2$ (438·4) calculated: 54·79% C, 8·97% H, 28·94% I; found: 54·60% C, 8·73% H, 28·10% I.

20-[^{125}I]-Iodoeicosanoic Acid

A mixture of acid *X* (2 mg), sodium iodide [^{125}I] (0·55 MBq, without carrier; Amersham) and 2-butanone (5 ml) was refluxed for 5 h, cooled and poured into water (20 ml), containing 1M-hydrochloric acid (0·5 ml). The product was taken up in ether (3 × 5 ml), the combined ethereal extracts were washed with 5% sodium thiosulfate solution and dried over anhydrous sodium sulfate. The solvent was evaporated in a stream of nitrogen and the residue was purified by preparative thin-layer chromatography in chloroform–methanol (8 : 2). The activity of the obtained labelled acid *X* was 0·21 MBq (radiochemical yield 37%).

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