# Synthesis and Evaluation of Radioiodinated Terminal-Substituted 5-Iodo-(2-thienyl) Fatty Acids as New Myocardial Imaging Agents



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In order to evaluate the stability of radioiodide attached to the 5 position of thiophenes substituted at the 2-position with tissue-specific groups as new radiopharmaceuticals, two [$^{125}$I]iodothienyl-substituted long-chain fatty acids have been prepared and evaluated in rats. Radioiodide was introduced into the 5 position of 17-(2-thienyl)heptadecanoic acid and 13-(2-thienyl)tridecanoic acid by K-$^{125}$I treatment of their corresponding 5-[*bis*-(trifluoroacetoxy)]thallium derivatives. Tissue distribution studies in rats with 17-[5-[$^{125}$I]iodo(2-thienyl)]heptadecanoic acid shows significant heart uptake and prolonged retention accompanied by *in vivo* deiodination and moderate blood levels. A comparison of the heart uptake of the 17 carbon fatty acid with a 13 carbon analogue, 13-[5-[$^{135}$I]iodo(2-thienyl)]tridecanoic acid, demonstrated a significantly greater myocardial uptake for the 17 carbon fatty acid than the 13 carbon analogue. These results suggest that the 5-iodothienyl moiety substituted at the terminal position of long chain fatty acids does not interfere with myocardial uptake and that such compounds may be of value as a new class of myocardial imaging agents.

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## Introduction.

External nuclear medicine imaging of the heart, using long chain fatty acid analogues bearing gamma-emitting radionuclides, has valuable potential applications for the clinical detection of coronary artery disease. Long chain free fatty acids are the major physiological substrates for the heart. Iodine-123 labeled agents such as 17-[$^{123}$I]iodoheptadecanoic acid are the most extensively evaluated radiolabeled fatty acids [2,3]. The results of studies with the radioiodinated fatty acid have demonstrated that significant levels of radioactivity are initially localized in the heart after intravenous administration [2,3]. However, terminal radioiodinated fatty acids such as 17-[$^{123}$I]iodoheptadecanoic acid undergo *in vivo* deiodination which results in a rapid loss of radioiodide from the heart with a concomitant increase of radioactivity in the blood pool. Significant levels of radioiodide in the blood pool interfere with clear images of the heart. The rapid loss of radioiodide may in part result from the direct cleavage of the carbon-iodine bond of the fatty acid. Several strategies have been investigated to chemically stabilize radioiodide on fatty acids in order to overcome facile *in vivo* iodine bond cleavage. One approach is the attachment of radioiodide to the phenyl ring of a terminal substituted fatty acid [4-8]. Studies with a model agent, 15-[$^{123}$I](*p*-iodophenyl)pentadecanoic acid [9-11], have shown that this agent exhibits pronounced heart uptake and *in vivo* stability to deiodination.

Terminal 5-iodothienyl-2-substituted long chain fatty acids are also prime candidates as new myocardial imaging agents. Since the terminal phenyl ring does not appear to interfere with myocardial uptake of long chain fatty acids, a terminal thiophene ring is also an attractive moiety for introduction of radioiodine. The thiophene ring system is of interest because it can be more readily iodinated in comparison to the phenyl ring. Iodination of 2-alkylsubstituted thiophene with thallium(III)trifluoroacetate regiospecifically introduces the *bis*-(trifluoroacetoxy)thallium group into the 5-position. The substituted thallium group can be rapidly (< 15 minutes) displaced with iodine. Such a rapid, high yield, specific method is ideally suited for radiolabeling with the 13 hour half-life iodine-123 radioisotope. The goals of the present investigation were to develop a general synthesis of the preparation of radioiodinated 5-iodothienyl-substituted long chain fatty acids and to evaluate the biological distribution properties of model agents in rats.

## Results and Discussion.

### Chemistry.

Our synthetic approach began with a Friedel-Crafts condensation of a terminal halogenated acid chloride. We selected 16-iodohexadecanoic acid (**1a**) and 12-bromododecanoic acid (**1b**) as the starting materials since they are commercially available and have the appropriate chain lengths. The terminal halide provides a convenient functional group that can subsequently be fabricated into a carboxylic acid by homologation *via* a nitrile. In this manner 17-(2-thienyl)heptadecanoic acid was prepared as the key parent fatty acid by the 4-step sequence shown in Scheme 1. The quantitative conversion of 16-hydroxyhexadecanoic acid (juniperic acid) to 16-iodohexadecanoic acid (**1a**) by treatment with iodotrimethylsilane has recently been described by us [12]. The iodinated acid **1a** was treated with dimethylformamidium chloride with 10%, of an equivalent of dimethylformamide. The acid chloride **2a** was not isolated but subjected to Friedel-Crafts acylation utilizing anhydrous tin tetrachloride and methylene chlor-

Table 1

Distribution of Radioactivity in Tissues of Fischer 344 Female Rats Following i.v. Adminstration of 17-[5-[$^{125}$I]iodo-(2-thienyl)]heptadecanoic Acid (**7a**; R = $(CH_2)_{15}$) [a]

| Time after injection | Mean Percent injected dose/gram (range) Tissue | | | | | Heart: Blood |
|---|---|---|---|---|---|---|
| | Heart | Blood | Liver | Lungs | Thyroid | |
| 5 minutes | 3.97 (2.73-4.72) | 1.25 (1.10-1.33) | 9.06 (5.77-12.6) | 1.24 (0.89-1.03) | 12.6 (11.5-13.9) | 3.2:1 |
| 30 minutes | 3.99 (3.12-4.60) | 1.30 (1.17-1.44) | 6.10 (5.68-6.54) | 1.11 (1.08-1.17) | 36.4 (26.8-47.4) | 3.3:1 |
| 60 minutes | 4.18 (2.80-6.42) | 0.95 (0.79-1.09) | 3.78 (3.67-4.48) | 1.04 (0.84-1.25) | 49.2 (39.3-55.4) | 4.4:1 |
| 2 hours | 2.49 (2.10-3.04) | 0.71 (0.58-0.85) | 2.26 (1.98-2.47) | 1.03 (0.95-1.13) | 131 (129-137) | 3.6:1 |
| 4 hours | 1.26 (1.21-1.41) | 0.50 (0.46-0.55) | 1.62 (1.43-1.75) | 0.86 (0.78-0.93) | 239 (179-339) | 2.5:1 |
| 1 day | 0.26 (0.21-0.29) | 0.08 (0.06-0.09) | 0.31 (0.28-0.34) | 0.42 (0.33-0.48) | 484 (402-536) | 3.1:1 |

[a] Four rats were used for each time period. [$^{125}$I] **7a** (sp act 400 mCi/mmole, dose 22 $\mu$Ci/animal) was administered by injection in a lateral tail vein in 6% bovine serum albumin solution.

ide to afford 16-iodo-1-(2-thienyl)hexadecan-1-one (**4a**) in 66% yield based upon compound **1a**. The nmr spectrum of compound **4b** exhibited two multiplets centered at $\delta$ 7.13 for the 4-thienyl proton and at $\delta$ 7.70 for the 3- and 5-thienyl protons. The iodoketone **4b** was converted to the nitrile **5b** by treatment with sodium cyanide in dimethyl sulfoxide. The keto function of compound **5a** was reduced by the Wolff-Kishner (Huang-Minlon) method which concomitantly hydrolyzed the nitrile function to give 17-(2-thienyl)heptadecanoic acid (**6a**). The nmr spectrum of compound **6a** exhibited triplets at $\delta$ 2.37 and $\delta$ 2.85 corresponding to the C-2 and C-17 methylene protons, respectively, and a broad multiplet from $\delta$ 6.85-7.25 for the thienyl protons.

The treatment of iodine with magnesium (MgO) or mercuric oxide (HgO) are classic procedures [13-15] for the introduction of iodide into the 5-position of 2-substituted thiophenes. This method is not applicable to preparation of radioiodinated thiophenes in high yields since a minimum iodide:thiophene ratio of 2:1 is required which indicates that only a 50% incorporation of radioiodide would be expected. McKillop and Taylor [16] have reported the preparation of 5-iodo-2-substituted thiophenes in quantitative yield by aromatic thallation followed by treatment with aqueous iodide. Recently, we have successfully employed this method for the preparation of a model methyl-branched fatty acid, 15-([$^{125}$I]*p*-iodophenyl)-3-*(R,S)*-methylpentadecanoic acid [17]. Using this approach, aromatic thallation of compound **6b** with thallium(III)trifluoroacetate in acetonitrile gave the corresponding 5-[*bis*-(trifluoroacetoxy)]thallium derivative. Following removal of acetonitrile, the thallium product was treated with aqueous potassium iodide to give 17-[5-iodo-(2-thienyl)]heptadecanoic acid (**7a**) in 62% yield after purification by silica gel column chromatography. The nmr spectrum displayed the characteristic AB pattern of a 2,5-disubstituted thiophene centered at $\delta$ 6.77 (J = 4 Hz). The signals for the protons at ring positions 3 and 4 appeared as doublets corresponding at $\delta$ 6.50 and $\delta$ 7.07, respectively.

In order to investigate the effects of chain length of the thienyl fatty acids on myocardial uptake, a 13 carbon analogue, 13-[5-iodo-(2-thienyl)]tridecanoic acid (**7b**) was prepared in the same manner. The radioiodinated thienyl fatty acids, 17-[5-[$^{125}$I]iodo-(2-thienyl)]heptadecanoic acid and 13-[5-[$^{125}$I]iodo-(2-thienyl)]tridecanoic acid were prepared by K-$^{125}$I treatment of the 5-[*bis*-(trifluoroacetoxy)]thallium derivatives of the corresponding free acids as described for the synthesis of the unlabeled compounds.

Biological Studies.

The distribution of radioactivity in tissues of female Fischer rats at 5, 30 and 60 minutes and 2, 4, and 24 hours after intravenous administration of 17-[5-[$^{125}$I]iodo-(2-thienyl)]heptadecanoic acid (**7a**) is shown in Table 1. The level of accumulation of radioactivity in the heart is significantly higher with [$^{125}$I] **7a** (4.18% dose/gram, 60 minutes) than observed under the same conditions with 15-([$^{125}$I]*p*-iodophenyl)pentadecanoic acid (2.34% dose/gram) [17]. The high heart uptake reached a maximum at 5 minutes (3.97% dose/gram) and remained constant at 60 minutes (4.18% dose/gram). The heart:blood ratio was 3.2:1 at 5 minutes and reached a maximum of 4.4:1 at 60 minutes. The accumulation of activity in the thyroid was low; 12.6% dose/gram at 5 minutes and exhibited a significant increase to 49% dose/gram at 60 minutes and 484% dose/gram at 24 hours. This observation was not anticipated in

Table 2

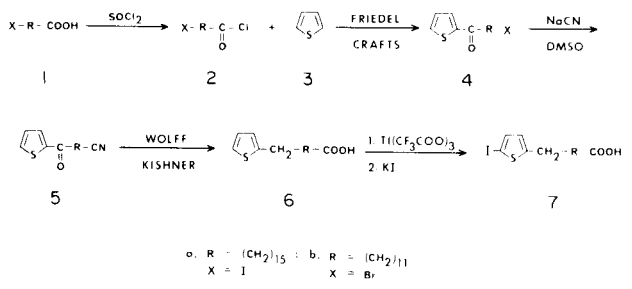
Distribution of Radioactivity in Tissues of Fischer 344 Female Rats Following i.v. Adminstration of 13-[5-[$^{125}$I]iodo-(2-thienyl)]tridecanoic Acid (**7b**; R = $(CH_2)_{11}$) [a]

| Time after injection | Mean Percent injected dose/gram (range) Tissue | | | | | Heart: |
|---|---|---|---|---|---|---|
| | Heart | Blood | Liver | Lungs | Thyroid | Blood |
| 5 minutes | 0.73 (0.64-0.75) | 0.51 (0.31-0.65) | 10.3 (7.66-11.9) | 0.84 (0.81-0.89) | 8.60 (7.22-9.98) | 1.4:1 |
| 30 minutes | 0.95 (0.78-1.09) | 0.94 (0.72-1.16) | 6.96 (6.03-8.05) | 0.87 (0.81-0.91) | 17.5 (14.5-22.4) | 1.0:1 |
| 2 hours | 0.54 (0.46-0.66) | 0.52 (0.50-0.55) | 3.54 (2.98-3.52) | 0.83 (0.74-0.96) | 69.7 (65.4-77.0) | 1.0:1 |
| 1 day | 0.07 (0.06-0.09) | 0.06 (0.05-0.06) | 0.13 (0.11-0.14) | 0.16 (0.11-0.22) | 478 (392-587) | 1.2:1 |
| 3 days | 0.03 (0.02-0.03) | 0.02 (0.02-0.02) | 0.04 (0.03-0.05) | 0.07 (0.04-0.15) | 321 (191-418) | 1.5:1 |

[a] Four rats were used for each time period. [$^{125}$I] **7b** (sp act 400 mCi/mmole, dose 12.2 $\mu$Ci/animal) was administered by injection in a lateral tail vein in 6% bovine serum albumin solution.

light of the expected stability of the iodothienyl bond. The high accumulation of free iodide by the thyroid may result from oxidation of the sulfur atom in a metabolically active organ such as the liver which results in the formation of a reactive non aromatic sulfone **8** or maleic acid derivative **9** which then may readily deiodinate.

Scheme 1

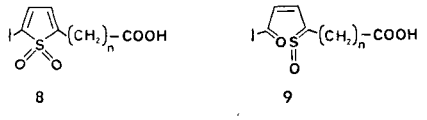



Tissue distribution studies in rats of the 13 carbon analogue, 13-[5-[$^{125}$I]iodo(2-thienyl)]tridecanoic acid (**7b**), are shown in Table 2. The heart uptake of radioiodinated **7b** is not as high as observed with 17-[5-[$^{125}$I])iodo(2-thienyl)]-heptadecanoic acid. The heart for 13-[5-[$^{125}$I]iodo(2-thienyl)]tridecanoic acid reaches a maximum of only 0.95% dose/gram at 30 minutes with heart:blood ratio of 1:1. These results demonstrate that heart specificity of iodothienyl-substituted fatty acids is dependent upon chain length. The uptake in liver and thyroid of [$^{125}$I] **7b** was very similar to the uptake observed with [$^{125}$I] **7a**.

Conclusion.

A synthesis has been developed for radioiodinated 5-thienyl fatty acids. A model agent, 17-[5-[$^{125}$I]iodo(2-thienyl)]-heptadecanoic acid, shows significant myocardial uptake and retention. As expected, the shorter $C_{13}$ chain analogue shows much lower heart uptake. Although both agents show moderate deiodination over a 2 hour period, the high myocardial uptake of the $C_{17}$ chain analogue make it an attractive alternative to iodophenyl fatty acids for diagnostic imaging. Studies are now in progress to chemically stabilize radioiodide at the 3 or 4 position of the thiophene ring to circumvent *in vivo* deiodination.

Scheme 2




## EXPERIMENTAL

The melting points were determined in capillary tubes using a Buchi SP apparatus and are uncorrected. The thin-layer chromatographic analysis were performed using 250-um thick layers of silica gel G PF-254 coated on glass plates (Analtech, Inc.). The low-resolution mass spectra (ms) were recorded using a Kratos MS25/DS55 system low-resolution instrument under the following conditions: ionizing energy, 70 eV; accelerating potential, 2000 eV; trap current 100 $\mu$A; and probe temperature, 180°. The proton nuclear magnetic resonance spectra (nmr) were obtained at 60 MHz with a Varian 360-L instrument or at 190 MHz with a Nicolet high resolution instrument. Samples (30-40 mg) were dissolved in deuteriochloroform and the resonances are reported downfield ($\delta$) from the internal tetramethylsilane standard.

Materials.

The petroleum ether had a 30-60° boiling range. The sodium [$^{125}$I]iodine was purchased from New England Nuclear, Inc. (North Billerica, MA). The specific activity of the radioiodide was adjusted to ~250 mCi/mmole by the addition of sodium iodide. All chemicals and solvents were analytical grade and were used without further purification.

Animal Tissue Distribution Experiments.

The distribution of radioactivity was determined in tissues of 10-12 week old female Fischer 344 rats (170-200 g) after intravenous administration of the labeled fatty acid. The animals were allowed food and

water *ad libitum* prior to and during the course of the experiment. The radioiodinated fatty acid was dissolved in 0.5 ml of absolute ethanol and added dropwise to a stirred solution of 6% bovine serum albumin at 40°. The final ethanol concentration was 10%. The solution was filtered through a 0.22 μm Millipore filter and injected *via* a lateral tail vein into the ether-anesthetized animals. The animals were anesthetized with ether, killed by cervical fracture, and the organs excised, rinsed, and blotted to remove adhering blood. Blood samples were obtained by cardiac puncture. The organs were then placed in tared vials. The vials were weighed, the radioactive contents were determined in a multi-channel Ge(Li) analyzer, and the percent injected dose/gram of tissue values were then calculated.

16-Iodo-1-(2-thienyl)hexadecan-1-one (**4a**).

A solution of 1.5 g (3.9 mmoles) of 16-iodohexadecanoic acid (**1a**), 36 mg (0.5 mmole) of dimethylformamide (DMF), and 595 mg (5 mmoles) of thionyl chloride was stirred at 80° for one hour. The resulting amber-coloured solution of 16-iodohexadecanoyl chloride (**2a**) was cooled to room temperature and added to a solution of 420 mg (5 mmoles) of thiophene (**3**) in 40 ml of methylene chloride. To the stirred mixture at 0° was added dropwise 1.52 g (6 mmoles) of anhydrous tin tetrachloride. The resulting purple-coloured mixture was then stirred at 0° for 30 minutes, room temperature for two hours, and treated with 6*N* aqueous hydrochloric acid until a yellow-coloured solution was obtained. The methylene chloride layer was separated, washed with 1*N* aqueous hydrochloric acid (2 × 50 ml), with aqueous sodium hydroxide (2 × 50 ml), with water (2 × 50 ml) and dried over anhydrous sodium sulfate. After removal of the methylene chloride the residue was dissolved in 1 ml of petroleum ether and applied to a silica gel column (30 g) slurried in petroleum ether. Fractions 1-10 (10 ml each) were eluted with petroleum ether followed by fractions 11-40 (10 ml each) with benzene. Fractions 28-32 were combined to give a solid which was crystallized from petroleum ether giving 1.19 g (66%) of **4a** as yellow crystals, mp 44-46°; nmr (deuteriochloroform): δ 1.27 (s, 26, $CH_2$), 2.9 (t, 2, $CH_2$-C=O), 3.15 (t, 2, I-$CH_2$) and 7.07-7.83 (m, 3, thienyl); ms: m/z 488 ($M^+$).

*Anal.* Calcd. for $C_{19}H_{33}IOS$: C, 53.57; H, 7.37. Found: C, 53.80; H, 7.66.

12-Bromo-1-(2-thienyl)dodecan-1-one (**4b**).

A mixture of 5.58 g (20 mmoles) of 12-bromododecanoic acid, 180 mg (2.5 mmoles) of dimethylformamide, and 2.89 g (22 mmoles) of thionyl chloride was stirred at 80° for 1 hour. The resulting 12-bromododecanoyl chloride was added to 60 ml of methylene chloride containing 1.82 g (22 mmoles) of thiophene. The mixture was cooled to 0° and reacted with 6.08 g (24 mmoles) of anhydrous tin tetrachloride as described for **4a**. Fractions 27-34 (10 ml in volume) were combined and concentrated *in vacuo* to afford 5.85 g (83%) of colorless oil; nmr (deuteriochloroform): δ 1.27 (s, 20, $CH_2$), 2.9 (t, 2, $CH_2$-C=O), 3.4 (t, 2, Br-$CH_2$) and 7.05-7.84 (m, 3, thienyl); ms: m/z 346 ($M^+$).

16-Cyano-1-(2-thienyl)hexadecan-1-one (**5a**).

A mixture of 896 mg (2 mmoles) of the iodoketone **4a** and 150 mg (3 mmoles) of sodium cyanide was stirred at 60° for 3 hours in 10 ml dimethyl sulfoxide. The resulting mixture was cooled to room temperature, added to 100 ml of water and extracted with ethyl ether (2 × 30 ml). The combined ether fractions were washed with water (4 × 50 ml), a saturated sodium chloride solution (2 × 50 ml), and dried over anhydrous sodium sulfate. The ethyl ether was removed *in vacuo* and the resulting residue was recrystallized from petroleum ether yielding 510 mg (76%) of a yellow-white solid mp 60-62°; nmr (deuteriochloroform): δ 1.23 (s, 26, $CH_2$), 2.31 (t, 2, $CH_2CN$), 2.89 (t, 2, $CH_2C$=O), 7.05-7.80 (m, 3, thienyl); ms: m/z 448 ($M^+$).

*Anal.* Calcd. for $C_{20}H_{33}NO$: C, 72.62; H, 9.51; N, 4.03. Found: C, 72.76; H, 9.78; N, 3.97.

12-Cyano-1-(2-thienyl)dodecan-1-one (**5b**).

The bromoketone **4b** 5.0 g (14.4 mmoles) and 1.5 g (30 mmoles) of sodium cyanide in 40 ml of dimethyl sulfoxide were stirred and heated at 80° for 12 hours. The crude product was isolated as described for **5a**. Recrystallization of the amber solid from petroleum ether gave 2.85 g (74%) of light yellow crystals mp 45-47°; nmr (deuteriochloroform): δ 1.27 (s, 18, $CH_2$), 2.33 (t, 2, $CH_2CN$), 2.9 (t, 2, $CH_2$), and 7.05-7.75 (m, 3, thienyl); ms: m/z 291 ($M^+$).

*Anal.* Calcd. for $C_{17}H_{25}NO$: C, 70.10; H, 8.59; N, 4.81. Found: C, 70.58; H, 9.16; N, 4.94.

17-(2-Thienyl)heptadecanoic Acid (**6a**).

To a stirred mixture of 168 mg (3 mmoles) of potassium hydroxide and 500 mg (1.67 mmoles) of 85% hydrazine hydrate in 20 ml of diethylene glycol was added 347 mg (1 mmole) of 16-cyano-1-(2-thienyl)hexadecan-1-one (**5a**). The mixture was refluxed for 1 hour, distilled until the solution reached a temperature of 210°, and then heated under reflux for 3 hours. After cooling to room temperature, the yellow colored solution was added to 100 ml of water acidified to *p*H 2 with 6*N* aqueous hydrochloric acid and extracted with (2 × 50 ml) of ethyl ether. The ethyl ether layers were combined, washed with water (4 × 50 ml), dried over anhydrous sodium sulfate and the ethyl ether removed to afford a yellow solid. Recrystallization of the solid from petroleum ether gave 189 mg (60%) of yellow crystals mp 66-67°; nmr (deuteriochloroform): δ 1.27 (s, 28, $CH_2$), 2.33 (t, 2, $CH_2C$=O), 2.73 (t, 2, $CH_2$-thienyl) and 6.85-7.3 (m, 3, thienyl); ms: m/z 352 ($M^+$).

*Anal.* Calcd. for $C_{21}H_{36}O_2S$: C, 71.59; H, 10.23. Found: C, 71.64; H, 10.48.

13-(2-Thienyl)tridecanoic Acid (**6b**).

The nitrile **5b** (2.6 g, 8.9 mmoles) was added to 20 ml of diethylene glycol containing 1.5 g (26.7 mmoles) of potassium hydroxide and 1 g (30 mmoles) of 85% hydrazine hydrate. The resulting mixture was reacted as described for **6a**. Recrystallization of the yellow solid from methanol-water afforded 1.86 g (72%) of yellow crystals, mp 58-59°; nmr (deuteriochloroform): δ 1.27 (s, 20H, $CH_2$), 2.33 (t, 2, $CH_2C$=O), 2.85 (t, 2, $CH_2$-thienyl) and 6.8-7.17 (m, 3, thienyl); ms: m/z 296 ($M^+$).

*Anal.* Calcd. for $C_{21}H_{35}O_2S$: C, 68.92; H, 9.46. Found: C, 69.06; H, 9.61.

17-[5-Iodo-(2-thienyl)]heptadecanoic Acid (**7a**).

A mixture of 125 mg (0.36 mmole) of 17-(2-thienyl)heptadecanoic acid (**6a**) and 272 mg (0.5 mmole) of thallium(III)trifluoroacetate in 100 ml of acetonitrile was stirred at 50° under red lights for 15 minutes. The resulting homogeneous solution was then stirred at room temperature and protected from light for 3 days. A solution of 266 mg (2 mmoles) of potassium iodide in 10 ml of water was added and the resulting mixture was stirred for 15 minutes. Sodiumthiosulfite (500 mg) was then added and the mixture stirred an additional 15 minutes, poured into 100 ml of water and extracted with ether (2 × 50 ml). The combined ether extracts were washed with water (3 × 50 ml) dried over anhydrous sodium sulfate and the ether removed *in vacuo*. The resulting solid was recrystallized from methanol-water giving 107 mg (62%) of **7a** as yellow rosettes mp 87-88°; nmr (deuteriochloroform): δ 1.27 (s, 28, $CH_2$), 2.35 (t, 2, $CH_2COOH$), 2.83 (t, 2, -$CH_2$-thienyl) and 6.77 (AB, 2, thienyl); ms: m/z 478 ($M^+$).

*Anal.* Calcd. for $C_{21}H_{35}ISO_2 \cdot H_2O$: C, 50.81; H, 7.46. Found: C, 50.83; H, 7.37.

13-[5-Iodo-(2-thienyl)]tridecanoic Acid (**7b**).

The acid **6b** (150 mg, 0.51 mmole) was added to 10 ml of acetonitrile containing 407 mg (0.75 mmole) of thallium(III)trifluoroacetate. The resulting mixture was reacted as described for **7a**. Recrystallization of the yellow residue from methanol-water gave 117 mg (55%) of light yellow platelets, mp 76-77°; nmr (deuteriochloroform): δ 1.27 (s, 20, $CH_2$), 2.36 (t, 2, -$CH_2COOH$), 2.83 (t, 2, -$CH_2$-thienyl), 6.77 (AB, 2, thienyl); ms: m/z 422 ($M^+$).

*Anal.* Calcd. for $C_{17}H_{27}IO_2S$: C, 48.34; H, 6.40; I, 30.09. Found: C, 48.45; H, 6.62 I, 30.16.

Radioiodinated ω-(2-Thienyl) Fatty Acids (**7a** and **7b**).

The acid (0.1 mmole) and 54 mg (0.1 mmole) of thallium(III)trifluoroacetate in 3 ml of acetonitrile were stirred at room temperature under

red lights for 48 hours. Sodium [$^{125}$I]iodide (no carrier added) in 1 ml of water was added and the resulting solution stirred 5 minutes. One ml of water containing 17 mg (0.1 mmole) of potassium iodide was then added and the mixture stirred 5 minutes. A second addition of 83 mg (0.5 mmole) of potassium iodide in 1 ml of water was added and the resulting mixture stirred 20 minutes. Sodium bisulfite (1 g) was added and the solution stirred 5 minutes, poured into 50 ml of water and extracted with ether (3 × 25 ml). The combined ether extracts were washed with 10% aqueous sodium bisulfite (3 × 25 ml), water (3 × 25 ml), dried over anhydrous sodium sulfate and the ether evaporated under a stream of argon. The crude radioiodinated acid was dissolved in 1 ml of chloroform and applied to a silicic acid column (30 g, acid form) slurried in chloroform. The column was eluted with chloroform and fractions 7-13 (20 ml in volume) were combined and the chloroform removed by a stream of argon to afford the radioiodinated ω-thienyl fatty acid [$^{125}$I-labeled (**7b**) 25.3 mCi, 62%)]. The radiochemical and chemical purity were confirmed by tlc ($SiO_2GF$) in methanol-chloroform 4:96, $R_f$ (0.40).

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