16, 86238-98-4; 17, 86238-99-5; 3-fluoro-4-methylbenzoic acid, 350-28-7; ethyl 3-fluoro-4-methylbenzoate, 86239-00-1; ethyl 4-(dibromomethyl)benzoate, 26496-95-7; ethyl 4-(bromomethyl)-3-fluorobenzoate, 86239-01-2; methyl 3-methoxy-4-methylbenzoate, 3556-83-0; 3-hydroxy-4-methylbenzoic acid, 586-30-1; ethyl 4-(bromomethyl)-3-methoxybenzoate, 86239-02-3; ethyl 3-methoxy-4-methylbenzoate, 86239-03-4; β-ionyltriphenylphosphonium bromide, 66556-69-2; diethyl pyridine-2,5-dicarboxylate, 5552-44-3; 2-formyl-5-(hydroxymethyl)pyridine, 40749-33-5; 2-carbethoxy-5-(hydroxymethyl)pyridine, 50501-35-4; 4-carbethoxybenzyl fluoride, 86239-04-5; acetone, 67-64-1; 2,5-pyridinedicarboxylic acid, 100-26-5; β-ionone, 29-77-6.

New Myocardial Imaging Agents: Stabilization of Radioiodine as a Terminal Vinyl Iodide Moiety on Tellurium Fatty Acids

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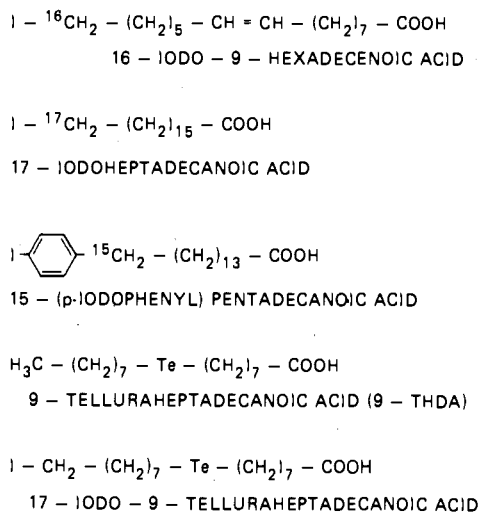
To determine the myocardial uptake and retention properties of radioiodinated tellurium fatty acids, we prepared two new tellurium fatty acids in which iodine-125 has been chemically stabilized by attachment as a *trans*-vinyl iodide (I–CH=CH–R–Te–R′–COOH) and evaluated them in rats. Fabrication of 18-iodo-13-tellura-17-octadecenoic acid was accomplished by coupling 1,5-diiodo-1-pentene with sodium 12-(methoxycarbonyl)-*n*-dodecan-1-yl telluride. The [5-^{125}I]-1,5-diiodo-1-pentene was prepared by an organoborane technique involving $^{125}I^+$ treatment of 5-iodo-1-penten-1-ylboronic acid [$I(CH_2)_3CH{=}CHB(OH)_2$]. The absolute heart uptake of this agent was moderate (1.47–2.52% dose/g after 60 min), but the heart/blood ratios were low (~2.6:1). Only marginal in vivo deiodination occurred, since the thyroid uptake was low (15–18% dose/g after 60 min). The effect of tellurium in position 13 was unexpected. To determine if the low heart specificity and low heart/blood ratios were dependent upon the position of the tellurium, we prepared an analogue with the same chain length, 18-[^{125}I]iodo-7-tellura-17-octadecenoic acid, in the same manner by reaction of [11-^{125}I]-1,11-diiodo-1-undecene with sodium 6-(methoxycarbonyl)-*n*-hexan-1-yl telluride. This agent showed pronounced heart uptake (2.47–3.94% dose/g after 60 min) and prolonged retention (1.76–3.14% dose/g after 4 h) in rats. Furthermore, the heart/blood ratios remained high for several hours (13:1 after 60 min; 9:1 after 4 h). Iodine-123 labeled 18-iodo-7-tellura-17-octadecenoic acid is an attractive new compound for evaluation as a myocardial imaging agent.

Radioiodinated long-chain fatty acids are important agents for the clinical evaluation of regional myocardial perfusion and fatty acid metabolism.[1] 17-[^{123}I]Iodoheptadecanoic acid[2-5] and 16-[^{123}I]iodo-9-hexadecenoic acid[6,7] have been widely used as myocardial imaging agents (Chart I). Clinical studies with 16-[^{123}I]iodohexadecanoic acid have also been reported.[8,9] The problem of deiodination of these agents results in relatively rapid loss of radioactivity from the myocardium with accumulation of radioiodide in the thyroid and blood. Radioactivity in the blood pool interferes with the measurement of myocardial fatty acid uptake, so a correction method is required to account for blood levels of free radioiodide.[3-5] In order to overcome the problem of radioiodide loss, iodine has been chemically stabilized by attachment to the para position of the phenyl ring of 15-phenylpentadecanoic acid.[10-12] Tissue distribution studies in mice with 15-(*p*-[^{123}I]iodophenyl)pentadecanoic acid have shown that this agent is relatively stable to facile in vivo deiodination and shows moderate myocardial washout.[12,13] This agent has also been used in humans.[14]

A different strategy that has been studied involves the introduction of the tellurium heteroatom in the fatty acid to inhibit β-oxidation and "trap" the fatty acid in the myocardium.[15] Tellurium-123m labeled 9-telluraheptadecanoic acid (9-THDA) shows rapid and pronounced myocardial uptake in rats[15-17] and dogs.[18,19] The unique properties of 9-THDA and similar tellurium fatty acids are the prolonged myocardial retention and high heart/blood ratios. In order to take advantage of the more attractive radionuclidic properties of the iodine-123 radioisotope (13.3 h half-life) in comparison to tellurium-123m (119 days half-life), we have explored the development of radioiodinated fatty acids containing stable tellurium.[1,16] Evaluation in rats indicated that the myocardial uptake

Chart I. Structures of the Iodinated Long-Chain Fatty Acids



† Oak Ridge National Laboratory.
‡ University of Tennessee.

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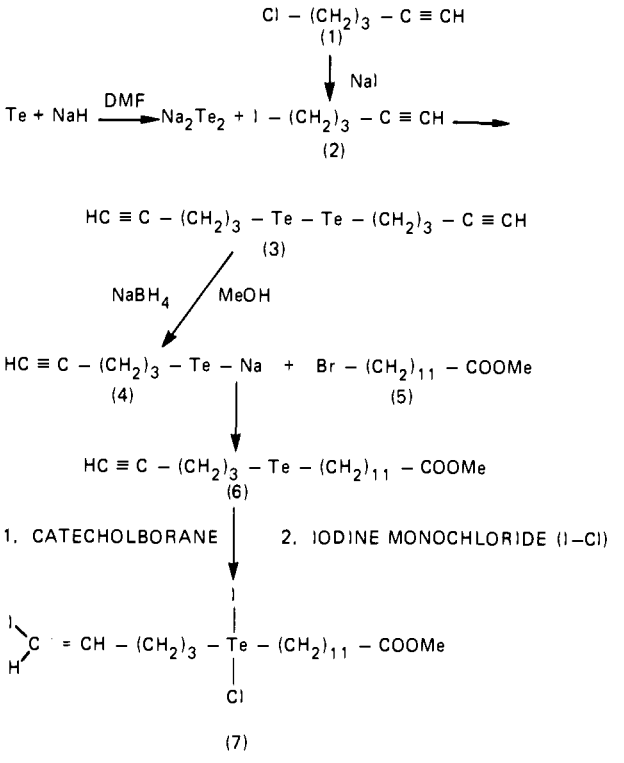
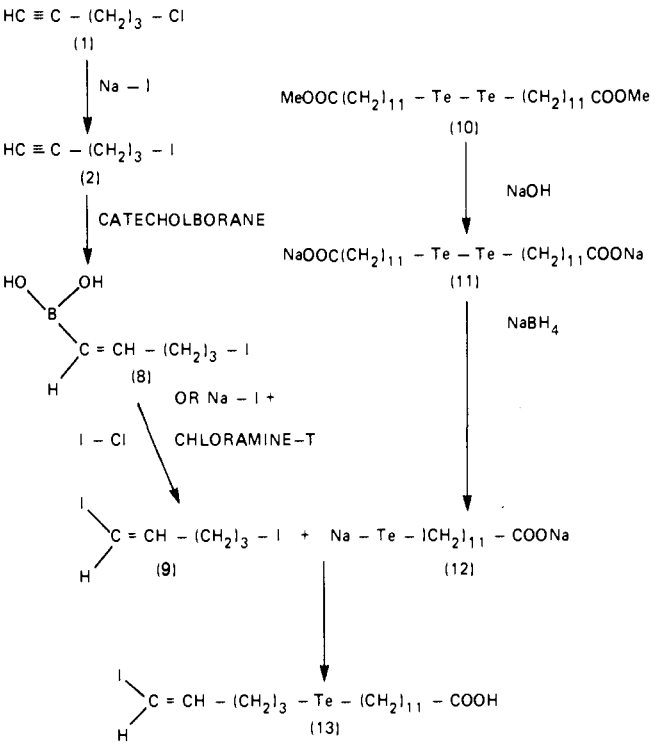
Scheme I



of 17-[^{131}I]iodo-9-telluraheptadecanoic acid (17-[^{131}I]iodo-9-THDA) is accompanied by significant in vivo deiodination.[20] A comparison of the heart uptake and deiodination of 17-[^{131}I]iodo-9-THDA and 16-[^{131}I]iodopalmitic acid has

Scheme II



demonstrated a close similarity in blood levels of radioactivity and thyroid uptake of radioiodide after administration of these agents to rats.

In order to overcome the problem of facile deiodination of the radioiodinated tellurium fatty acids, methods have now been evaluated to chemically stabilize the iodide on model compounds. The conversion of terminal *trans*-vinylboronic acids to the corresponding vinyl iodides with I_2 has been known for some time.[21,22] More recently, formation of vinyl iodides from vinylboronic acids with iodine monochloride[23,24] or via the in situ oxidation of I^- with chloramine-T[25] has been reported. Vinyl iodides can also be prepared by electrophilic iodination of vinylstannanes, and the synthesis of (*E*)-17α-[^{125}I]iodovinylestradiol from (*E*)-17α-[(tributylstannyl)vinyl]estradiol has been recently reported.[26] The goals of the present investigation were to develop a synthesis of vinyl iodide substituted tellurium fatty acids and to evaluate the biodistribution properties of the iodine-125 labeled agents in rats.

Results and Discussion

The initial synthetic approach involved fabrication of the intact acetylenic tellurium fatty acid substrate, methyl 13-tellura-17-octadecynoate (**6**; Scheme I). Commercially available 5-chloro-1-pentyne (**1**) was converted to 5-iodo-1-pentyne (**2**) by treatment with NaI in refluxing 2-butanone. The 6,7-ditelluradodeca-1,11-diyne (**3**) was prepared by treatment of **2** with sodium ditelluride (Na_2Te_2) gen-

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Table I. Distribution of Radioactivity in Tissues of Fischer 344 Rats Following Intravenous Administration of 18-[^{125}I]Iodo-13-tellura-17-octadecenoic Acid ([^{125}I]**13**)[a]

tissue	mean % injected dose/g (range) at the following times after injection					
	5 min	30 min	60 min	2 h	4 h	3 days
heart	1.46 (1.28–1.58)	1.52 (1.23–1.65)	1.81 (1.47–2.52)	1.03 (0.89–1.17)	0.76 (0.71–0.80)	0.09 (0.06–0.12)
blood	0.15 (0.14–0.16)	0.61 (0.58–0.68)	0.69 (0.61–0.74)	0.68 (0.62–0.80)	0.65 (0.56–0.68)	0.03 (0.03–0.04)
lungs	0.92 (0.77–1.03)	0.89 (0.79–0.96)	1.02 (0.90–1.17)	0.81 (0.25–0.91)	0.71 (0.65–0.76)	0.10 (0.07–0.08)
kidneys	1.01 (0.89–1.22)	1.04 (0.95–1.15)	1.15 (1.06–1.29)	0.96 (0.87–1.13)	0.93 (0.85–0.98)	0.08 (0.07–0.10)
liver	8.78 (7.90–10.14)	5.32 (5.02–5.59)	4.39 (3.77–5.57)	2.45 (1.89–2.71)	1.95 (1.84–2.09)	0.09 (0.07–0.13)
thyroid	1.62 (1.44–1.92)	5.64 (5.07–5.97)	13.41 (10.5–15.9)			

[a] Four rats were used for each time period. Each rat received ~8.6 μCi of the ^{125}I-labeled fatty acid (sp act. ~20 mCi/mmol) administered by injection in a lateral tail vein in 6% bovine serum albumin solution (0.5 mL).

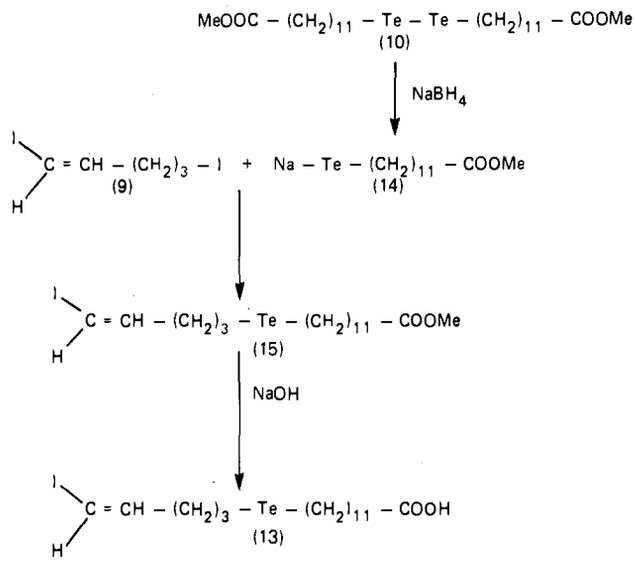
erated by NaH reduction of tellurium metal in DMF. In situ $NaBH_4$ reduction of the orange-colored ditelluride gave a colorless solution of the telluride **4**, which readily reacted with methyl 12-bromododecanoate (**5**) to give methyl 13-tellura-17-octadecynoate (**6**) in 35% yield after purification by silicic acid column chromatography. Reaction of **6** with catecholborane, followed by treatment with ICl gave an intractable product which appeared to contain a major component in which the ICl had added to the tellurium[27] to form a telluronium product (**7**). Although the halogens could probably be subsequently removed with a mild reducing agent [Te(IV) → Te(II)], a more convenient route was pursued in which the iodovinyl moiety was introduced prior to fabrication of the tellurium fatty acid chain.

In the second approach (Scheme II), the 5-iodo-1-pentyne (**2**) was treated with catecholborane, and the vinylboronic acid **8** was obtained as a white crystalline solid after hydrolysis. Treatment with ICl smoothly converted the boronic acid **8** to 1,5-diiodo-1-pentene (**9**). The overall yield of **9** from 5-iodo-1-pentyne (**2**) was about 30%. While the primary iodide of **9** was susceptible to nucleophilic displacement, the vinyl iodide moiety was stable under these reaction conditions. Our first successful synthesis of 18-iodo-13-tellura-17-octadecenoic acid (**13**) involved coupling of excess **9** with the sodium salt **12**, generated by the in situ $NaBH_4$ reduction of the disodium salt of 13,14-ditellurahexacosane-1,26-dioate (**11**). The disodium salt **11** was prepared by NaOH hydrolysis of the dimethyl ester **10**. The crude reaction product was crystallized from petroleum ether to give **13** in 62% yield. While this route worked well on a large scale (2–5 mmol), an alternate method was required for the microscale synthesis of the radiolabeled fatty acids.

In this route (Scheme III), methyl 18-iodo-13-tellura-17-octadecenoate (**15**) was prepared first and purified by column chromatography prior to basic hydrolysis to the free acid **13**. The 1,5-diiodo-1-pentene (**9**) was coupled with the sodium salt **14**, generated by $NaBH_4$ reduction of dimethyl 13,14-ditellurahexacosane-1,26-dioate (**10**), to give methyl 18-iodo-13-tellura-17-octadecenoate (**15**). Subsequent basic hydrolysis then gave 18-iodo-13-tellura-17-octadecenoic acid (**13**). The trans stereochemistry of the vinyl iodide moiety in these compounds was readily established by proton nuclear magnetic resonance spectrometry (NMR). The chemical shift values and coupling constants (J) for the olefinic protons exhibited the expected characteristic trans ABX_2 coupling pattern.

Iodine-125 labeled **13** with a specific activity of about 20 mCi/mmol was prepared in the same manner by using $^{125}I^+$ for substitution of the boronic acid. Tissue distribution studies in female Fischer rats demonstrated modest

Scheme III



myocardial uptake (Table I), but the heart/blood ratios were low. The low blood levels and marginal thyroid uptake, however, demonstrated that this agent is stable to in vivo deiodination. Introduction of the vinyl iodide moiety is, thus, an effective method of stabilizing the radioiodide in the tellurium fatty acid. The decreased heart uptake and low heart/blood ratios in comparison to 9-telluraheptadecanoic acid were unexpected. To determine the fate of the tellurium in comparison to the radioiodide, we also synthesized tellurium-123m labeled 18-iodo-13-tellura-17-octadecanoic acid. Evaluation of [^{123m}Te]**13** in rats gave similar results to the ^{125}I-labeled analogue (Table II).

The moderate myocardial uptake and low heart/blood ratios were unexpected, since 18-iodo-13-tellura-17-octadecenoic acid (**13**) has a total chain length (C_{18}) that is optimal for efficient extraction by the myocardium. These results could indicate that tellurium in position 13 exhibits some special effect that decreases the myocardial specificity of **13**. Earlier studies, however, have demonstrated that heart uptake in rats was similar with telluraheptadecanoic acid analogues with the tellurium heteroatom in the 6-, 9-, and 11-positions. A second explanation for the low heart uptake observed with **13** could be the perturbation on heart uptake resulting from the introduction of the terminal trans-vinyl iodide moiety. Both these possibilities were studied by the synthesis and evaluation of an analogue of **13** having the same chain length with tellurium in a different position of the chain.

The 7-tellura isomer of 18-iodo-17-octadecenoic acid (**24**) was prepared as illustrated in Scheme IV by the same method described earlier for the synthesis of **13**. The 11-iodo-1-undecyne (**17**) was prepared from commercially

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Table II. Distribution of Radioactivity in Tissues of Fischer 344 Rats Following Intravenous Administration of 18-Iodo-13-[^{123m}Te]tellura-17-octadecenoic Acid ([^{123m}Te]13)[a]

tissue	mean % injected dose/g (range) at the following times after injection		
	5 min	30 min	60 min
heart	2.09 (1.93–2.37)	1.98 (1.79–2.17)	1.92 (1.85–2.00)
blood	0.32 (0.29–0.34)	0.84 (0.79–0.90)	0.95 (0.83–1.03)
lungs	0.91 (6.67–1.13)	1.03 (0.96–1.10)	1.00 (0.94–1.04)
kidneys	1.46 (1.42–1.56)	1.73 (1.61–1.84)	1.85 (1.71–2.03)
liver	7.78 (7.18–8.03)	5.53 (5.33–5.74)	4.49 (4.03–4.84)

[a] Four rats were used for each time period. Each rat received ~8.4 μCi of the ^{123m}Te-labeled fatty acid (sp act. ~20 mCi/mmol) administered by injection in a lateral tail vein in 6% bovine serum albumin solution (0.5 mL). Other tissues analyzed included the brain, intestines, pancreas and spleen.

Table III. Distribution of Radioactivity in Tissues of Fischer 344 Rats Following Intravenous Administration of 18-[^{125}I]Iodo-7-tellura-17-octadecenoic Acid ([^{125}I]24)[a]

tissue	mean % injected dose/g (range) at the following times after injection					
	5 min	30 min	60 min	2 h	4 h	24 h
heart	3.47 (2.82–4.15)	2.78 (1.47–3.45)	2.96 (2.47–3.94)	2.86 (2.71–2.96)	2.37 (1.76–3.14)	1.18 (0.65–1.58)
blood	0.26 (0.24–0.30)	0.22 (0.15–0.27)	0.22 (0.18–0.26)	0.23 (0.20–0.26)	0.27 (0.24–0.31)	0.22 (0.20–0.24)
lungs	1.29 (1.19–1.36)	0.96 (0.71–1.10)	1.00 (0.86–1.17)	1.00 (0.91–1.04)	0.84 (0.69–1.06)	0.53 (0.51–0.58)
kidneys	1.05 (0.91–1.17)	0.89 (0.60–1.10)	0.95 (0.77–1.10)	0.88 (0.74–0.94)	0.77 (0.61–0.87)	0.47 (0.41–0.58)
liver	6.18 (3.77–7.40)	5.63 (2.90–7.58)	5.33 (4.17–6.66)	4.78 (4.37–5.04)	4.40 (3.06–5.63)	2.75 (2.49–3.03)
thyroid	8.54 (7.34–9.79)	13.5 (7.89–14.51)	22.2 (16.2–25.7)	43.8 (34.4–51.8)	69.8 (45.5–114.0)	173.0 (155–184)

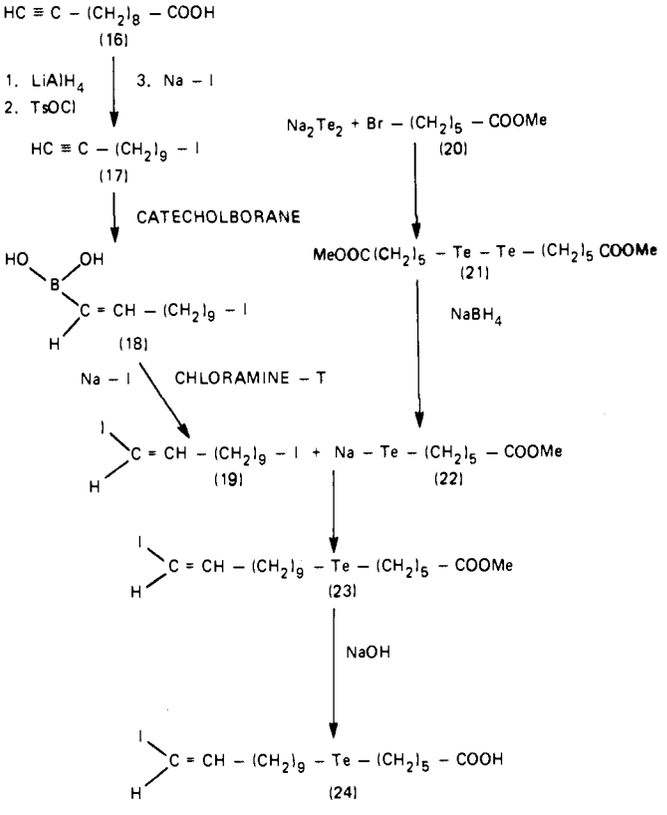
[a] Four rats were used for each time period. Each rat received ~4.1 μCi of the ^{125}I-labeled fatty acid (sp act. ~20 mCi/mmol) administered by injection in a lateral tail vein in 6% bovine serum albumin solution (0.5 mL).

available 10-undecynoic acid (**16**). Reduction of **16** with $LiAlH_4$ gave 1-undecyn-11-ol, which was converted to the *p*-toluenesulfonyl (tosyl) ester by reaction with tosyl chloride. Sodium iodide treatment of the tosyl ester then gave **17**. The boronic acid **18** was prepared by catecholborane addition across the acetylenic bond of **17**, followed by hydrolysis. Treatment of **18** with NaI in the presence of chloramine-T gave 1,11-diiodo-1-undecene (**19**) in 29% overall yield after purification. Coupling of **19** with the telluride **22**, generated by in situ $NaBH_4$ reduction of dimethyl 7,8-ditelluratetradecane-1,14-dioate (**21**), then gave **23**, which was purified by silicic acid column chromatography. Basic hydrolysis and crystallization from petroleum ether gave 18-iodo-7-tellura-17-octadecenoic acid (**24**).

The 18-[^{125}I]iodo-7-tellura-17-octadecenoic acid was prepared by the same method with Na^{125}I to radiolabel the 1,11-diiodo-1-undecene intermediate. Iodine-125 labeled **24** was evaluated in female Fischer rats and showed pronounced heart uptake (Table III). This agent also showed the anticipated prolonged myocardial retention. After 30 min, the heart uptake (1.47–3.45% dose/g) appeared to decrease only slightly (~20%), 20% from the peak levels detected 5 min after injection (2.82–4.15% dose/g). After 4 h, the heart uptake remained high (1.76–3.14% dose/g) and decreased to only 1.18% dose/g after 24 h. More importantly, the low blood levels resulted in high heart/blood ratios for all the time periods studied: 5 min, 13:1; 30 min, 13:1; 60 min, 13:1; 4 h, 12:1; 24 h, 5:1. The optimal properties of rapid and pronounced heart uptake, low in vivo deiodination, and high heart/blood ratios exhibited by 18-iodo-7-tellura-17-octadecenoic acid suggest this agent should be further evaluated as a new myocardial agent.

These results also demonstrate that tellurium in position 13 must have some special effect in decreasing heart uptake, since both **13** and **24** have the same chain length. Earlier studies had suggested that the position of the tellurium heteroatom in a series of telluraheptadecanoic acid analogues did not effect heart uptake, since the 6-, 9-, and 11-telluraheptadecanoic acid analogues all showed high heart uptake in rats.[16] To determine further the effect of tellurium position on the myocardial specificity of this

Scheme IV



type of compound, we prepared 13-[^{123m}Te]telluraheptadecanoic acid (13-THDA) and evaluated it in rats. To our surprise, this analogue shows markedly decreased heart uptake and much lower heart/blood ratios than 9-THDA (Table IV).

The inhibitory effect of tellurium in position 13 was unexpected, since studies described earlier had indicated that the position of the Te heteroatom did not appear to affect heart uptake of these agents in rats and dogs.[16] In addition, the reduced myocardial uptake in rats with the shorter-chain 6- and 9-telluratridecanoic acid analogues

Table IV. Distribution of Radioactivity in Tissues of Fischer 344 Rats Following Intravenous Administration of 13-[^{123m}Te]Telluraheptadecanoic Acid (13-[^{123m}Te]THDA)[a]

tissue	mean % injected dose/g (range) at the following times after injection		
	5 min	30 min	60 min
heart	1.06 (0.89–1.23)	0.98 (0.93–1.05)	0.83 (0.73–0.97)
blood	0.25 (0.21–0.30)	0.89 (0.78–1.05)	1.12 (0.97–1.26)
lungs	1.27 (0.98–1.44)	1.40 (1.20–1.56)	1.49 (1.27–1.87)
kidneys	1.54 (1.41–1.66)	1.62 (1.48–1.93)	1.59 (1.49–1.75)
liver	8.26 (8.10–8.58)	5.71 (4.66–6.25)	6.01 (5.43–6.43)

[a] Four rats were used for each time period. Each rat received ~6.8 μCi of the ^{123m}Te-labeled fatty acid (sp act. ~20 mCi/mmol) administered by injection in a lateral tail vein in 6% bovine serum albumin solution (0.5 mL). Other tissues analyzed included the brain, intestines, pancreas, and spleen.

further suggested that the total chain length was the critical structural feature that dictated myocardial specificity.[16] More recently we have also observed that Te in position 13 has the same effect on the heart uptake of terminal phenyl tellurium fatty acids. While 15-phenyl-6-[^{123m}Te]pentadecanoic acid shows pronounced myocardial specificity and high heart/blood ratios,[28] the 15-phenyl-13-[^{123m}Te]tellurapentadecanoic acid analogue shows reduced heart uptake and markedly increased blood levels, resulting in low heart/blood ratios. These results are similar to the data reported here for 13-[^{123m}Te]telluraheptadecanoic acid and 18-[^{125}I]iodo-13-tellura-17-octadecenoic acid.

Thus, the present studies have demonstrated that the terminal vinyl iodide moiety of selected tellurium long-chain fatty acids is an effective method of stabilizing radioiodide to overcome facile in vivo deiodination. The presence of the vinyl iodide moiety is compatible with the pronounced myocardial uptake that has been reported previously with alkyl-substituted tellurium fatty acids.[15-19] We have also stabilized radioiodide to in vivo deiodination by attachment to the para position of a phenyl ring,[29] and radioiodinated 15-(*p*-iodophenyl)-6-tellurapentadecanoic acid shows pronounced heart uptake in rats with little deiodination.[30] Radioiodinated 18-iodo-7-tellura-17-octadecenoic acid is presently being evaluated in a canine model to determine the myocardial uptake (extraction) under conditions of normal and reduced (ischemia) blood flow (myocardial perfusion). In addition, the distribution of this agent in relation to regional myocardial fatty acid metabolism is being evaluated.

Because of the attractive radionuclidic properties of the iodine-123 isotope (13.2 h half-life) for nuclear medicine imaging procedures, the iodine-123 labeled vinyl iodide substituted tellurium fatty acid is an attractive agent for evaluation. The most desirable route for introducing the radioiodide would be at a final stage of the synthesis. Attempts to prepare **24** by iodination of the intact tellurium fatty acid boronic acid "kit" are now being pursued. We have found that oxidative decomposition of tellurium fatty acids can be avoided if these agents are handled correctly and if prolonged exposure to light and the atmosphere are avoided. In fact, 18-[^{125}I]iodo-7-tellura-17-octadecenoic acid (**24**) has been stored under argon at 0–4 °C for up to 8–10 weeks with only minimal decomposition. The rapid formation of the iodine-123 labeled fatty acid in the clinic should be feasible for potential clinical evaluation of this new agent.

Experimental Section

All solvents and chemicals were analytical grade and were used without further purification. The ^{123m}Te metal was produced by neutron bombardment of enriched ^{122}Te in the Oak Ridge high flux isotope reactor (HFIR), and the Na^{125}I, Na^{131}I, and [^{125}I]iodine monochloride (ICl) were obtained from New England Nuclear Corp. (North Billerica, MD). The silicic acid (acidic grade, 60–200 mesh) used for column chromatography was obtained from Sigma Chemical Co. (St. Louis, MO). The thin-layer chromatography analyses (TLC) were performed with 250-μm thick layers of silica gel G PF-254 coated on glass plates (Analtech, Inc.) with the solvent systems indicated. The melting points were determined in capillary tubes with a Buchi SP apparatus and are uncorrected. The infrared spectra (IR) were recorded on a Beckman 18-A spectrophotometer with NaCl plates or KBr pellets. The low-resolution mass spectra (MS) were recorded with a Kratos MS-25 low-resolution instrument under the following conditions: ionizing energy, 70 eV; accelerating potential, 8000 V; trap current, 100 μA; probe temperature, 200–300 °C. The proton nuclear magnetic resonance spectra (NMR) were obtained at 60 MHz with a Varian 360-L instrument or at 200 MHz with a Nicolet high-resolution instrument. Samples (30–40 mg) were dissolved in deuteriochloroform, and the resonances are reported in parts per million (ppm) downfield (δ) from the internal tetramethylsilane standard. The yields indicated for the radioactive compound are radiolabeling yields.

Animal Tissue Distribution Experiments. The tissue distribution studies were performed with 10–12 week old female Fischer 344 rats (170–200 g). 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 °C. The final ethanol concentration was 10%. The solution was filtered through a 22-μm Millipore filter and injected via a lateral tail vein into ether-anethestized animals. After the times indicated in Tables I–IV, the animals were killed by cervical fracture, and blood samples were obtained by cardiac puncture. The organs were then removed, rinsed with saline solution, and blotted dry to remove residual blood. The organs were weighed and counted in a NaI autogamma counter (Packard Instruments). Samples of the injected radioactive solutions were also assayed as a standard to calculate the percent injected dose per gram of tissue values. The thyroid glands were not weighed directly. The weight of the thyroid glands was calculated in the usual manner by multiplying the animal weight by (7.5 mg/100 g).[31]

Syntheses. General Comments. All reactions with the tellurium compounds were performed in an argon atmosphere under red lights in dry, three-necked flasks. The reaction vessel was fitted with a rubber septum and an argon-purged addition funnel for the introduction of reactants and was equipped with a magnetic stirrer. Condensers were protected with a $CaCl_2$ drying tube, and a slight positive argon atmosphere was maintained by an oil pressure-release valve.

Ditelluride Intermediates 10 and 21. The dimethyl 13,14-ditellurahexacosane-1,26-dioate (**10**) was prepared (Scheme II) as described earlier[20] and exhibited the expected physical prop-

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erties. The dimethyl 7,8-ditelluratetradecane-1,14-dioate (21) was prepared in the same manner (Scheme IV) by methyl 6-bromohexanoate (20) alkylation of Na_2Te_2 generated in DMF by reduction of metallic Te with NaH under an inert atmosphere.

5-Iodo-1-pentyne (2). Commercial (K&K Laboratories, Inc.) 5-chloro-1-pentyne (1; 10.25 g, 100 mmol) was refluxed on a steam bath in 2-butanone (600 mL) with NaI (45 g, 300 mmol). The majority (~550 mL) of the solvent was distilled, and the mixture was cooled and diluted with pentane (100 mL). After filtration, H_2O (250 mL) was added, and the mixture was extracted with Et_2O (250 mL). The organic layer was washed with H_2O and dried over anhydrous $MgSO_4$. The solvent was removed in vacuo to give 17 g (87%) of 5-iodo-1-pentyne: low-resolution MS, m/z 194 (M^+, 100%) 67 (M^+ - I, 88%); NMR ($CDCl_3$) δ ~2.0 (m, 3 H, $CH_2C{\equiv}CH$) ~2.2 (m, 2 H, $CH_2CH_2C{\equiv}CH$), 3.30 (t, $J \simeq 6$ Hz, 2 H, CH_2I). Anal. (C_5H_7I) C, H.

(*E*)-1,5-Diiodo-1-pentene (9). The 5-iodo-1-pentyne (2; 14.6 g, 75 mmol) was treated under nitrogen with catecholborane (10.9 mL, 100 mmol) at 0 °C. The mixture was heated at 60 °C for 6 h, cooled, and diluted with 500 mL of H_2O. After the mixture was stirred overnight at room temperature, the flocculent white boronic acid (8) precipitate was filtered, and the residue was washed thoroughly with H_2O and then with C_6H_6 (50 mL) to remove any catechol. After the residue was dried in vacuo, 13.5 g (75%) of 5-iodo-1-penten-1-ylboronic acid (8) was obtained as a tan solid: mp 100–102 °C; low-resolution MS, m/z 240 (M^+, 39%), 113 (M^+ - I, 12%) and 69 (100%); NMR (acetone-d_6) δ 2.05 (m, 4 H, $CH_2CH_2CH{=}C$), 3.10 (t, 2 H, CH_2 I), 4.4 [s, $(OH)_2$ and H_2O], 5.30 [d, J = 16 Hz, 1 H, $=CHB(OH)_2$], ~6.3 [doublet of triplets, 1 H, $CH_2CH{=}CHB(OH)_2$]. The boronic acid 8 was sensitive to both light and heat but could be stored indefinitely in the freezer with minimal decomposition. Anal. ($C_5H_{10}O_2IB$) C, H, I.

The boronic acid 8 (2.4 g, 10 mmol) was dissolved in 10 mL of dry THF under a nitrogen atmosphere. The solution was cooled to −78 °C; after the addition of 20 mL of a 1 M solution of NaOAc (20 mmol) in MeOH, 10 mL of a freshly prepared 1 M methanol solution of ICl (10 mmol) was added, and the solution was stirred 5 min at −78 °C. After the solution was warmed to ~−10 °C, a saturated solution of $Na_2S_2O_3$ was added to destroy the excess ICl. The mixture was diluted with H_2O and extracted with pentane. The organic layer was washed thoroughly with H_2O and dried over anhydrous $MgSO_4$, and the solvent was removed in vacuo. The crude product was purified by chromatography on SiO_2 by elution with pentane to give 1.28 g of (*E*)-1,5-diiodo-1-pentene (40%) as a clear oil: TLC R_f 0.36 (petroleum ether); IR (NaCl) 660 (m), 685 (s), 945 (vs), 1170 (s), 1200 (vs), 1230 (vs), 1435 (m), 1615 (m), 2840 (w), 2930 (vs), 3050 (w) cm^{-1}; low-resolution MS, m/z 322 (M^+, 40%); NMR ($CDCl_3$) δ 2.10 (m, 4 H, $CH_2CH_2CH{=}CHI$), 3.10 (d, $J \simeq 6$ Hz, 2 H, CH_2I). The spectrum exhibited the expected ABX_2 two proton vinyl iodide coupling pattern at δ ~5.8–6.8 (2 H, $ICH{=}CHCH_2$). The terminal vinyl proton H_A is located as a doublet (J = 14.42 Hz) at 1210 Hz, with the components broadened by four J_{HH}. The olefinic H_B proton is located as a doublet of triplets centered at 1802 Hz, with $J_{doublet}$ = 14.4 Hz and $J_{triplet}$ = 7.2 Hz. The expected 1:2:2:2:1 intensity pattern is observed for this multiplet. Anal. (C_5H_8I) C, H, I.

Methyl 18-Iodo-13-tellura-17-octadecenoate (15). Dimethyl 13,14-ditellurahexacosane-1,26-dioate (10; 343 mg, 0.5 mmol) was reduced under argon (Scheme III) in 20 mL of MeOH at room temperature by the addition of excess $NaBH_4$. After the addition of 1,5-diiodo-1-pentene (9; 354 mg, 1.1 mmol), the colorless mixture was stirred under argon for 30 min. Following dilution with H_2O, the product was extracted twice with Et_2O, the combined extracts were washed twice with H_2O, dried over anhydrous Na_2SO_4, and evaporated under argon to give a yellow-colored gum. Analysis by TLC (C_6H_6) indicated the presence of three products: R_f 0.74, excess 1,5-diodo-1-pentene (9); R_f 0.45, methyl 18-iodo-13-tellura-17-octadecenoate (15); and R_f 0.15, the ditelluride 10. The crude product was dissolved in ~2 mL of C_6H_6 and applied to a silicic acid column (1 × 20 cm) slurried in petroleum ether. Fractions (20 mL in volume) were collected as follows: 1–10, petroleum ether; 11–30, C_6H_6. Aliquots of each fraction were analyzed by TLC (SiO_2-G, C_6H_6). Fractions 16–19 (R_f 0.45) were combined to give 130 mg (22%) of 15 as a light yellow oil: IR (neat, NaCl) 945 (w), 1170 (m), 1200 (m), 1440 (m), 1745 (s), 2850 (s), 2930 (s) cm^{-1}; low-resolution MS, M^+ at m/z 538 absent, 410 (M^+[^{130}Te], M^+ - HI, 63); NMR ($CDCl_3$) δ 2.34 (t, $J \simeq 6$ Hz, 2 H, CH_2COOCH_3), 2.64 (t, $J \simeq 6$ Hz, 4 H, CH_2TeCH_2), 3.67 (s, 3 H, $COOCH_3$), ~5.85–6.85 (complex m, 2 H, ABX_2, $ICH{=}CHCH_2$).

18-Iodo-13-tellura-17-octadecenoic Acid (13). Method A. From Direct Synthesis of the Free Acid (Scheme II). Dimethyl 13,14-ditellurahexacosane-1,26-dioate (10; 340 mg, 0.5 mmol) was refluxed under argon in 15 mL of EtOH containing 3 mL of 1 N NaOH for 1 h. After this solution was cooled to room temperature, a solution of 1,5-diiodo-1-pentene (9; 366 mg, 1.1 mmol) in 15 mL of THF was added to the orange-colored solution of the ditelluride (11). An aqueous solution of $NaBH_4$ was added dropwise to the reaction mixture until a colorless solution was obtained. The mixture was stirred for 2 h under argon at room temperature, diluted with H_2O, and washed three times with petroleum ether to remove the excess diiodopentene. After careful acidification of the aqueous layer to pH 2–3 with 10% H_2SO_4 at 0 °C, the cloudy mixture was extracted three times with Et_2O. The combined organic extracts were washed thoroughly with H_2O and dried over anhydrous Na_2SO_4, and the solvent was removed under argon. The resulting light yellow-colored solid was boiled in petroleum ether. The solution was decanted from a small amount of insoluble material. Crystallization of 0 °C gave 300 mg (62%) of 13, mp 57–59 °C. The product was homogeneous (R_f 0.26) upon TLC analysis ($CHCl_3$–MeOH, 4:9) and exhibited the following properties: IR (KBr) 660 (w), 680 (w), 710 (m), 730 (m), 940 (s), 1150 (s), 1200 (s), 1230 (s), 1280 (s), 1415 (s), 1445 (s), 1470 (s), 1700 (w), 2805 (vs), 2920 (vs) cm^{-1}; low-resolution MS, M^+ at m/z 524 not observed, 396 (M^+[^{130}Te] - HI, 29); high-resolution MS calcd for $C_{17}H_{31}O_2TeI$, 397.1397; found, 397.1403; NMR ($CDCl_3$, 200 MHz) δ 2.16 (m, 4 H, $CH_2CH_2TeCH_2CH_2$), 2.36 (t, $J \simeq 6$ Hz, 2 H, $-CH_2COOH$), 2.62 (m, 4 H, CH_2TeCH_2), ~6.02–6.54 (2 H, ABX_2, $ICH{=}CHCH_2$). Anal. ($C_{17}H_{31}O_2TeI$) C, H, I.

Method B. From Basic Hydrolysis of Compound 15 (Scheme III). The ester 15 was refluxed for 30 min under argon in 20 mL of EtOH containing 1 mL of 1 N NaOH. After cooling, the reaction mixture was poured into H_2O and then acidified to pH 2–3 with 1 N HCl, and the cloudy mixture extracted twice with Et_2O. The combined extracts were washed thoroughly with H_2O, dried over anhydrous Na_2SO_4, and evaporated under argon to give a light-yellow solid. Crystallization from petroleum ether gave 62 mg of 13: mp 55–59 °C; IR, NMR, and TLC identical with properties of 13 prepared as described in method A above.

(*E*)-1,11-Diiodo-1-undecene (19) (Scheme IV). Commercial 10-undecyn-1-oic acid (16; 18.2 g, 100 mmol) was dissolved in Et_2O (100 mL) and reduced to 10-undecyn-1-ol with $LiAlH_4$ (3.8 g, 100 mmol) by stirring at 0 °C for 4 h (Scheme IV). After the cautious addition of H_2O (3.8 mL), 15% NaOH (3.8 mL) was added followed by H_2O (7.6 mL), and the solution was filtered through Celite. The organic layer was washed with H_2O, and the solvent evaporated to give crude 1-undecyn-11-ol. The product was purified by distillation to give 10.5 g (63%) of 1-undecyn-11-ol: NMR ($CDCl_3$) δ ~1.3 (br s, 14 H, alkane), 1.93 (t, J = 2.5 Hz, 1 H, HC≡C), 2.13 (m, 2 H, $HC{\equiv}CCH_2$), 2.50 (s, 1 H, OH), 3.56 (t, 2 H, CH_2O).

The 1-undecyn-11-ol (8.4 g, 50 mmol) was dissolved in pyridine (50 mL), and the solution cooled to 0 °C and added slowly (30 min) to a pyridine solution (200 mL) containing tosyl chloride (19 g, 100 mmol). The solution was left to stand at 10 °C for 24 h, diluted with H_2O (200 mL), and extracted with Et_2O (200 mL). The organic layer was washed with 10% HCl and then H_2O and dried over anhydrous K_2CO_3–Na_2SO_4, and the solvent removed in vacuo to give the crude 1-(tosyloxy)-10-undecyne: NMR ($CDCl_3$) δ ~1.3 (br s, 14 H, alkane), 1.90 (t, J = 2.5 H_2, 1 H, CH≡C), 2.13 (m, 2 H, $HC{\equiv}CCH_2$), 2.43 (s, 3 H, CH_3), 3.93 (t, 2 H, CH_2O), 7.46 (A_2X_2, 4 H, aromatic).

The tosylate (3.22 g, 10 mmol) was refluxed in 100 mL of 2-butanone with NaI (7.5 g, 50 mmol) for 12 h. The 2-butanone was distilled off, and the mixture was cooled and diluted with pentane. The product was then filtered, and the filtrate was washed with H_2O. Evaporation of the solvent gave the product, which was chromatographed on silicic acid (petroleum ether) to give 2.1 g (75%) of 11-iodo-1-undecyne (17): NMR ($CDCl_3$) δ 1.3 (br s, 14 H, alkane), 1.90 (t, $J \simeq 2.5$ Hz, 1 H, HC≡C), 2.13 (m, 2 H, $HC{\equiv}CH_2$), 3.30 (t, 2 H, CH_2I). Anal. ($C_{11}H_{19}I$), C, H.

The 11-iodo-1-undecyne (2.78 g, 10 mmol) was treated with catecholborane (1.64 mL, 15 mmol) at 0 °C and then heated at 60 °C for 6 h under nitrogen. After the addition of H_2O (100 mL), the mixture was stirred for 18 h, the solid boronic acid **18** was filtered, and the residue was washed thoroughly with cold H_2O to give the product (2.61 g, 80%): NMR (acetone-d_6) δ 1.3 (br s, 14 H, alkane), 2.03 (m, 2 H, HC=CHCH_2), 3.23 (t, 2 H, CH_2I), 5.33 (d, J = 18 Hz, 1 H, HC=C*H*B), 6.5 (m, 1 H, *H*C=CHB), ~6.5 [s, 2 H, $(OH)_2$]. The boronic acid **18** (0.65 g, 2 mmol) was dissolved in THF–H_2O (8 mL, 1:1), cooled to 0 °C, and treated with 2 mL of a 1 M NaI solution (2 mmol) and chloramine-T (0.91 g, 4 mmol) in 8 mL of the THF–H_2O mixture. After 15 min, the mixture was extracted with petroleum ether, the organic extract was washed with H_2O and dried over anhydrous $MgSO_4$, and the solvent was evaporated in vacuo. The product was chromatographed on SiO_2 by elution with petroleum ether to give 1,11-diiodo-1-undecene (**19**; 620 mg, 76%): NMR ($CDCl_3$) δ 1.26 (br s, 14 H, CH_2's), 2.00 (m, 2 H, HC=CHCH_2), 3.16 (t, 2 H, CH_2I), 5.93 (d, J = 15 Hz, 1 H, CH=C*H*I), 6.40 (m, 1 H, C*H*=CHI). Anal. ($C_{11}H_{20}I_2$) C, H.

Methyl 18-Iodo-7-tellura-17-octadecenoate (23). This fatty acid methyl ester was prepared (Scheme IV) in the same manner as that described in detail for methyl 18-iodo-13-tellura-17-octadecenoate (**13**). An ethanolic solution (10 mL) of dimethyl 7,8-ditelluratetradecane-1,14-dioate (**21**; 150 mg, 0.3 mmol) was reduced under argon at room temperature with excess $NaBH_4$ to a colorless solution of the sodium tellurol (**22**). Following the addition of 1,11-diiodo-1-undecene (**19**; 100 mg, 0.25 mmol), the mixture was stirred at room temperature for 1 h, and the product was obtained in the usual manner. Purification by SiO_2 column chromatography gave methyl-18-iodo-7-tellura-17-octadecenoate (**23**; 130 mg, 98%): TLC R_f 0.50 (C_6H_6); IR (neat, NaCl) 950 (w), 1170 (m), 1200 (m), 1430 (m), 1745 (s), 2850 (s), 2925 (s) cm^{-1}; low-resolution MS, m/z 528 ([M^+[^{130}Te], ~10), 507 (M^+[^{130}Te] – MeO, 15), 490 (M^+[^{130}Te] – 48, 18), 411 (M^+[^{130}Te] – I, 30); high-resolution MS calcd for $C_{18}H_{33}O_2Te$ (M^+ – I), 411.1547; found, 441.1541; NMR ($CDCl_3$) δ 2.33 (t, $J \simeq$ 6 Hz, CH_2COOCH_3), 2.64 (t, $J \simeq$ 6 Hz, 4 H, CH_2TeCH_2), 2.68 (s, 3 H, $COOCH_3$), ~5.85–6.80 (complex pattern, 2 H, ABX_2, IC*H*=C*H*CH_2).

18-Iodo-7-tellura-17-octadecenoic Acid (24). The methyl ester (**23**; 75 mg, 0.14 mmol) was hydrolyzed in ethanolic KOH as described for **15**, and the product was crystallized from petroleum ether to give 18-iodo-7-tellura-17-octadecenoic acid (**24**) as white microcrystals (50 mg, 68%): mp 49–50 °C; TLC R_f 0.27 (4% MeOH–$CHCl_3$); IR (KBr) essentially identical with that described above for **13**; low-resolution MS, m/z 524 (M^+[^{130}Te], 12), 397 (M^+[^{130}Te] – I, 38); high-resolution MS calcd for $C_{17}H_{31}O_2Te$ (M^+ – I), 397.1391; found, 397.1387; NMR ($CDCl_3$, 60 MHz) δ 2.22 (t, $J \simeq$ 6 Hz, 2 H, CH_2COOH), 2.60 (t, $J \simeq$ 6 Hz, 4 H, CH_2TeCH_2), ~5.84–6.75 (complex multiplet, 2 H, ABX_2, IC*H*=C*H*CH_2). Anal. ($C_{17}H_{31}O_2TeI$) C, H, I.

18-Iodo-13-[^{123m}Te]tellura-17-octadecenoic Acid ([^{123m}Te]13). Tellurium-123m (4.5 mCi; 64 mg, 0.5 mmol) was stirred in 3 mL of H_2O at 80 °C under argon. An argon-purged aqueous solution of $NaBH_4$ was added until a clear, colorless solution was obtained. After this solution was cooled to room temperature, a solution of 1,5-diiodo-1-pentene (**9**; 177 mg, 0.6 mmol) and methyl 12-iodododecanoate (162 mg, 0.4 mmol) in THF (35 mL) was added, and the mixture was stirred at room temperature for 60 min. After dilution with H_2O, the mixture was extracted with Et_2O, and the organic layer was washed well with water, dried over anhydrous Na_2SO_4, and evaporated to dryness under argon. The crude product was chromatographed on a silicic acid column by elution with petroleum ether (fractions 1–10) and C_6H_6 (fractions 11–30). Aliquots of each fraction were analyzed by TLC (SiO_2-G, C_6H_6) and for radioactive content. Fractions 13–17 contained 423 μCi (9%) of methyl 18-iodo-13-[^{123m}Te]-tellura-17-octadecenoic acid. The product showed a major radioactive component that cochromatographed with authenic **6** on TLC analysis (R_f 0.50; SiO_2-G, C_6H_6). The product was refluxed for 60 min under argon in EtOH (20 mL) containing 2 mL of 1 N NaOH. The hydrolysis product was obtained as described for **6** to yield 245 μCi of 18-iodo-13-[^{123m}Te]tellura-17-octadecenoic acid ([^{123m}Te]**13**) (5.4% overall yield from ^{123m}Te).

[5-^{125}I]-1,5-Diiodo-1-pentene ([^{125}I]9). Method A. The boronic acid **8** was dissolved in dry THF (10 mL) under argon, and the solution was cooled to –78 °C. After the addition of 2 mL of a 1 M methanolic solution of NaOAc (2 mmol), 0.8 mmol of ^{125}ICl (20 mCi) in CCl_4 (2 mL) was added dropwise, and the solution was stirred for 10 min at –78 °C. After the solution was warmed to –30 °C, an aqueous solution of $Na_2S_2O_3$ was added to decolorize the iodine monochloride. The reaction mixture was diluted with H_2O and extracted with pentane. The organic layer was washed four times with H_2O and dried over Na_2SO_4, and the solvent was removed under argon. Analysis of the crude product by TLC (SiO_2-G; 5% EtOAc–petroleum ether) demonstrated the presence of a major radioactive product cochromatographing with 1,5-diiodo-1-pentene (R_f 0.78) and two additional products, R_f 0.65 and 0.60. The crude product was chromatographed on silicic acid by elution (20-mL fractions) with petroleum ether (fractions 1–20) and 5% Et_2O–petroleum ether (fractions 21–40). The homogeneous [5-^{125}I]-1,5-diiodo-1-pentene ([^{125}I]**9**; 2.5 mCi) was eluted in fractions 8–13. Fractions 25–35 contained significant amounts (10.1 mCi) of an unknown component. The 5-[^{123}I]**9** showed a single radioactive component (98%) on thin-layer radiochromatographic analysis (SiO_2-G, petroleum ether) that cochromatographed with a 1,5-diiodo-1-pentene standard (R_f 0.57).

Method B. A THF–H_2O mixture (1:1, 2 mL) of the 5-iodo-1-penten-1-ylboronic acid (**8**; 23.9 mg, 0.1 mmol) was cooled to 0 °C. After the addition of 15 mg of NaI, Na^{125}I (2.5 mCi) was added. Chloramine-T (45 mg, 0.2 mmol) was added in 1 mL of the THF–H_2O mixture, and the solution was stirred for 15 min. After dilution with Et_2O, the reaction mixture was washed with dilute $NaHSO_3$ (25 mL) and then H_2O (3 times). After the mixture was dried over anhydrous Na_2SO_4, the organic layer was evaporated under argon to give an oil, which was chromatographed on SiO_2. Elution with petroleum ether (25-mL fractions) gave the [^{125}I]**9** in fractions 8–13, which were combined to give 925 μCi (37%).

18-[^{125}I]Iodo-13-tellura-17-octadecenoic Acid ([^{125}I]13). Method A (Scheme II). The ditelluride (**11**; 67.3 mg, 0.1 mmol) was dissolved in EtOH (5 mL) and refluxed under argon with 1 N NaOH (1 mL) for 1 h. The mixture was cooled and reduced with $NaBH_4$ to a colorless solution of the sodium tellurol. The [^{125}I]**9** (2.5 mCi, 0.1 mmol) was combined with 41 mg of carrier 1,5-diodo-1-pentene (0.23 mmol total) in 5 mL of dry THF and added dropwise to the above tellurol solution. After stirring for 1 h at room temperature, the solution was poured into H_2O and washed with petroleum ether. The aqueous layer was acidified with 10% H_2SO_4, and the product was obtained as described for **13** to give 18-[^{125}I]iodo-13-tellura-17-octadecenoic acid.

Method B (Scheme III). The ditelluride **10** (68 mg, 0.1 mmol) was dissolved in 10 mL of EtOH and reduced under argon with $NaBH_4$ with warming in a H_2O bath. The colorless solution was cooled to room temperature and [5-^{125}I]-1,5-diiodo-1-pentene (**9**; 3.32 mCi; prepared as described under method B, above) added in EtOH. The mixture was stirred at room temperature for 1 h, diluted with H_2O, and extracted with Et_2O (2 times). The combined organic extracts were washed with H_2O (3 times) and dried over anhydrous Na_2SO_4, and the solvent was evaporated under argon. The oily product was dissolved in C_6H_6 and applied to an SiO_2-B column. Fractions 25 mL in volume were eluted with C_6H_6. Fractions 3–6 were combined to give 1.5 mCi (55%) of methyl 18-[^{125}I]iodo-13-tellura-17-octadecenoate ([^{125}I]**15**): TLC (C_6H_6) one radioactive spot (R_f 0.50) cochromographing with authentic **11**. Ethanolic basic hydrolysis in the usual manner gave 18-[^{125}I]iodo-13-tellura-17-octadecenoic acid ([^{125}I]**13**).

[11-^{125}I]-1,11-Diiodo-1-undecene ([^{125}I]19). This ^{125}I-labeled diiodoalkene was prepared as described in detail (method B) for the synthesis of [5-^{125}I]-1,5-diiodo-1-pentene ([^{125}I]**9**). 11-Iodo-1-undecen-1-ylboronic acid (**18**, 324 mg, 0.1 mmol) was dissolved in a mixture of THF–H_2O (1:1, 3 mL) and cooled to 0 °C. After the addition of Na^{125}I (10 mCi) in H_2O (15 mL) containing carrier NaI (15 mg), chloramine-T (45 mg, 0.2 mmol) in 2 mL of the THF–H_2O mixture was added to the solution, which was stirred at 0 °C for 15 min. The product was obtained as usual and purified by chromatography with petroleum ether on SiO_2 to give 2.69 mCi (27%) of [^{125}I]**9**.

18-[^{125}I]Iodo-7-tellura-17-octadecenoic Acid ([^{125}I]24). Methyl 18-[^{125}I]iodo-7-tellura-17-octadecenoate ([^{125}I]**23**) was prepared as described for methyl 18-[^{125}I]iodo-13-tellura-17-octadecenoate ([^{125}I]**15**; method B, Scheme III). After $NaBH_4$

reduction of ditelluride **21** (75 mg, 0.3 mmol) to a colorless solution of the tellurol **18** at room temperature, the [11-^{125}I]-1,11-diiodo-1-undecene ([^{125}I]**19**; 2.69 mCi) was added in EtOH, and the mixture was stirred for 1 h. The product was worked up in the usual manner as for [^{125}I]**15** and chromatographed on SiO_2 to give 547 μCi of [^{125}I]**23**, homogeneous upon thin-layer radiochromatographic analysis, R_f 0.50 (C_6H_6). Basic hydrolysis in the usual manner gave 532 μCi (97%) of 18-[^{125}I]iodo-7-tellura-17-octadecenoic acid ([^{125}I]**24**) showing a single radioactive component on TLC, R_f 0.27 (4% MeOH–$CHCl_3$). The product was stored under argon in sealed amber break-seal tubes at 0 °C until further use.

13-[^{123m}Te]Telluraheptadecanoic Acid (13-[^{123m}Te]THDA). The ^{123m}Te-labeled fatty acid was prepared by basic hydrolysis of the purified fatty acid methyl ester obtained by simultaneous butyl bromide and methyl 12-bromododecanoate alkylation of $Na_2{}^{123m}Te$ generated by $NaBH_4$ reduction of ^{123m}Te. The details of the chemical synthesis and properties of this tellurium fatty acid will be reported elsewhere.

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A Polymeric Drug for Treatment of Inflammatory Bowel Disease[1]

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Sulfasalazine (SASP) consists of salicylic acid azo linked at the 5-position to a pyridine-containing sulfonamide. This drug, currently used in inflammatory bowel disease treatment, is reductively cleaved by anaerobic bacteria in the lower bowel to 5-aminosalicylic acid (5-ASA) and sulfapyridine (SP). Recent reports indicate that 5-ASA is the active therapeutic moiety and that SP is responsible for a variety of adverse clinical side effects. Water-soluble polymer **7**, which contains salicylate residues azo linked at the 5-position to an inert polymer backbone, has been synthesized for the site-specific reductive release of 5-ASA in the lower bowel. Preparations of **7** deliver (chemical reduction) >1.96 mmol of 5-ASA/g of polymer. In vitro studies with the polymer in anaerobic rat cecal bacteria demonstrated a reduction rate of approximately 1 μequiv of azo bond h^{-1} (mL of cecal content)$^{-1}$. A pharmacokinetic comparison of polymer and SASP showed similar deliveries of 5-ASA and metabolites to the lower bowel, blood, and urine of orally dosed rats. Polymer **7** proved more active than SASP or 5-ASA in the guinea pig ulcerative colitis model. Potential therapeutic advantages of **7** include nonabsorption/nonmetabolism in the small intestine, direct 5-ASA release at the disease site, and nonabsorption/nonmetabolism of the reduction-released carrier polymer.

Sulfasalazine (salicylazosulfapyridine, Azulfidine, SASP)[3] is the most effective of various sulfonamides for the treatment of ulcerative colitis and has been used clinically for over 30 years.[4] Results of recent studies suggest that SASP may also be effective for treatment of Crohn's disease of the colon.[5] SASP (**1**) consists of salicylic acid linked to a pyridine-containing sulfonamide by an azo bond at the 5-position. The disposition and metabolism (Scheme I) of the drug in man have been well studied.[6-8] When administered orally, about 30% of the intact drug is absorbed from the small intestine. The absorbed portion undergoes enterohepatic circulation with 2–10% excreted intact in the urine, and the remainder returned to the gut via the bile. SASP in the gut travels to the lower bowel where anaerobic bacteria reductively cleave the azo bond, producing sulfapyridine (SP, **2**) and 5-aminosalicylic acid (5-ASA, **3**).[7] Approximately one-third of the 5-ASA is absorbed and excreted in urine as *N*-acetyl derivative **6**, with the remainder being excreted unchanged in the feces. SP is absorbed and undergoes N-acetylation (to **4**) and 5′-hydroxylation (to **5**). These two compounds are further metabolized and excreted in the urine as glucuronide conjugates.[9,10]

Limitations to the use of SASP are the development of adverse gastrointestinal, hematological, and generalized side effects, or more serious reactions, including agranulocytosis, toxic epidermal necrolysis, paresthesia, hepatotoxicity, pancreatitis, pulmonary disease, and male infer-

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