

$J \approx 13$  Hz,  $2\alpha_{\text{eq}}\text{-H}$ ), 4.45 (d, m, 1 H,  $J \approx 12$  Hz,  $8\alpha_{\text{ax}}\text{-H}$ ); MS (70 eV),  $m/e$  317 ( $M^+$ ).

**(4 $\alpha$ ,5 $\alpha$ ,8 $\alpha$ )-1-(Ethoxycarbonyl)-5-(hydroxymethyl)-decahydroquinoline (36).** To a solution of 31 (190 mg, 0.71 mmol) in toluene (10 mL) was added 1 mL of DIBAL (25% solution in toluene) at  $-60^\circ\text{C}$ . After 0.5 h, the mixture was decomposed with excess saturated ammonium chloride solution and poured into ice- $\text{H}_2\text{O}$ . The  $\text{H}_2\text{O}$  layer was extracted with  $\text{Et}_2\text{O}$  and the  $\text{Et}_2\text{O}$  layer was washed with  $\text{H}_2\text{O}$  and dried ( $\text{Na}_2\text{SO}_4$ ). Removal of the solvent under reduced pressure afforded 145 mg (85%) of a colorless oil (36) which was not further purified but used as such in subsequent reactions: IR (neat) 3400, 1660  $\text{cm}^{-1}$ ; NMR ( $\text{CDCl}_3$ )  $\delta$  1.23 (t, 3 H,  $J \approx 7$  Hz,  $\text{CH}_2\text{CH}_3$ ), 1.2-2.0 (m, 12 H), 2.4 (s, 1 H, OH), 2.80 (t, m, 1 H,  $J \approx 11$  Hz,  $2\beta\text{-H}$ ), 3.65 (d, 2 H,  $J \approx 7$  Hz,  $\text{CH}_2\text{O}$ ), 3.9 (d, 1 H,  $2\alpha\text{-H}$ ), 4.17 (q, 2 H,  $J \approx 7$  Hz,  $\text{CH}_2\text{CH}_3$ );  $8\alpha\text{-H}$  is hidden under the  $\text{CH}_2\text{CH}_3$  resonance signals.

**(4 $\alpha$ ,5 $\alpha$ ,8 $\alpha$ )-1-(Ethoxycarbonyl)decahydroquinoline-5-carboxaldehyde (37).** A mixture of 36 (140 mg, 0.58 mmol) and pyridinium chlorochromate<sup>16</sup> (150 mg, 0.70 mmol) in  $\text{CH}_2\text{Cl}_2$  (10 mL) was stirred at room temperature for 1 h and excess  $\text{Et}_2\text{O}$  was added. The solvent was removed from the precipitate by decanting.  $\text{Et}_2\text{O}$  was added several times to the residue. Following decantation, the combined solutions were concentrated under reduced pressure and the residual oil was chromatographed on silica gel using  $\text{EtOAc}$ -benzene (1:10) as the eluent. After solvent removal, 37 (105 mg, 76%) was obtained as a colorless oil, which was used without further purification in the next reaction: IR (neat) 1725, 1690  $\text{cm}^{-1}$ ; NMR ( $\text{CDCl}_3$ )  $\delta$  1.23 (t, 3 H,  $J \approx 7$  Hz,  $\text{CH}_2\text{CH}_3$ ), 1.3-2.0 (m, 11 H), 2.26 (s, 1 H, half-height width  $\approx 6$  Hz,  $5\beta\text{-H}$ ), 2.78 (t, m, 1 H,  $J \approx 11$  Hz,  $2\beta\text{-H}$ ), 3.9 (d, 1 H,  $2\alpha\text{-H}$ ),

4.05 (q, 2 H,  $J \approx 7$  Hz,  $\text{CH}_2\text{CH}_3$ ), 8.95 (s, 1 H, CHO);  $8\alpha\text{-H}$  is hidden under the  $\text{CH}_2\text{CH}_3$  signals. Upon standing at room temperature, the aldehyde 37 [MS (70 eV),  $m/e$  239 ( $M^+$ )] air oxidizes to carboxylic acid 34 [ $m/e$  225 ( $M^+$ )].

**(4 $\alpha$ ,8 $\alpha$ )-1-(Ethoxycarbonyl)decahydroquinoline (38).** A solution of 37 (38 mg, 0.16 mmol) and tris(triphenylphosphine)rhodium(I) chloride<sup>26</sup> (190 mg) in benzonitrile (10 mL) was heated at  $170^\circ\text{C}$  for 40 min. The reaction mixture was chromatographed over silica gel using  $\text{EtOAc}$ -benzene (1:10) as eluent. Following removal of the solvent under reduced pressure, 38 (18 mg, 54%) was obtained as a colorless oil [oil bath temperature  $130^\circ\text{C}$  (1.0 mm)]. This compound was identical in all respects with 38 prepared as follows: to a solution of *cis*-decahydroquinoline (39) (from 68 mg of *cis*-decahydroquinoline HCl salt<sup>30</sup>) in acetone (10 mL) was added  $\text{K}_2\text{CO}_3$  (0.2 g) and ethyl chloroformate (0.1 g) at room temperature. The mixture was stirred for 3 h, poured into ice- $\text{H}_2\text{O}$ , and extracted with  $\text{Et}_2\text{O}$ . The  $\text{Et}_2\text{O}$  extract was washed with dilute HCl, aqueous  $\text{Na}_2\text{CO}_3$ , and  $\text{H}_2\text{O}$  and dried ( $\text{Na}_2\text{SO}_4$ ). Removal of the solvent under reduced pressure afforded 60 mg (73%) of 38 as a colorless oil [oil bath temperature  $130^\circ\text{C}$  (1.0 mm)]: IR (neat) 1690  $\text{cm}^{-1}$ ; NMR ( $\text{CDCl}_3$ )  $\delta$  1.16 (t, 3 H,  $J \approx 7$  Hz,  $\text{CH}_2\text{CH}_3$ ), 1.1-2.2 (m, 13 H), 2.77 (t, m, 1 H,  $J \approx 12$  Hz,  $2\beta\text{-H}$ ), 3.9 (d, m, 1 H,  $J \approx 12$  Hz,  $2\alpha\text{-H}$ ), 4.07 (q, 2 H,  $J \approx 7$  Hz,  $\text{CH}_2\text{CH}_3$ );  $8\alpha\text{-H}$  is hidden under the  $\text{CH}_2\text{CH}_3$  signals; MS (70 eV),  $m/e$  211 ( $M^+$ ). Anal. ( $\text{C}_{12}\text{H}_{21}\text{NO}_2$ ) C, H, N.

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## Potential Pancreatic Imaging Agents. Tellurium-123m Labeled DL- $\alpha$ -Amino- $\gamma$ -(phenyltelluro)butyric Acid

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This report describes the first successful preparation of a  $^{123\text{m}}\text{Te}$ -labeled  $\alpha$ -amino acid as a potential pancreatic imaging agent. Tellurium-123m labeled DL- $\alpha$ -amino- $\gamma$ -(phenyltelluro)butyric acid was prepared by basic hydrolysis of the radiolabeled 5- $[\beta$ -(phenyltelluro)ethyl]hydantoin. The hydantoin was prepared by the reaction of  $^{123\text{m}}\text{Te}$ -labeled phenyltelluro, generated by sodium borohydride reduction of diphenyl ditelluride, with 5-( $\beta$ -bromoethyl)hydantoin. Tissue distribution studies in rats with the  $^{123\text{m}}\text{Te}$ -labeled amino acid for periods varying from 30 min to 24 h demonstrated only marginal pancreatic accumulation of radioactivity. The significant result of these studies is that a general synthetic method has been developed for the preparation of  $^{123\text{m}}\text{Te}$ -labeled amino acids.

The 159-keV  $\gamma$  photon (84% abundance) emitted from  $^{123\text{m}}\text{Te}$  is within the optimal energy range for detection with the sodium iodide detectors presently used clinically for nuclear medicine imaging procedures. The potential use of tissue-specific  $^{123\text{m}}\text{Te}$ -labeled radiopharmaceuticals has been recognized for several years,<sup>1</sup> and we have recently described the pronounced adrenal uptake of two  $^{123\text{m}}\text{Te}$ -labeled steroids in several animal species.<sup>2-4</sup> Prior to these studies, however, there were no reported attempts to chemically incorporate  $^{123\text{m}}\text{Te}$  into tissue-specific imaging agents. Tellurium succeeds selenium in group 4A of the periodic table and in some respects these two elements exhibit similar properties, although their specific chemical

properties quite often differ dramatically.<sup>5</sup> Despite several major disadvantages,  $^{75}\text{Se}$ -labeled selenomethionine<sup>6,7</sup> is still used for the clinical detection and diagnosis of pancreatic disease.<sup>8</sup> The more efficient collimation and detection of the single 159-keV  $\gamma$  photon from  $^{123\text{m}}\text{Te}$  suggested that  $^{123\text{m}}\text{Te}$ -labeled telluromethionine would be an attractive alternative to  $^{75}\text{Se}$ -labeled selenomethionine for pancreatic imaging.<sup>1</sup> Although selenomethionine has been prepared by a variety of microbiological and chemical methods,<sup>9,10</sup> attempts to prepare telluromethionine by microbiological methods have been unsuccessful.<sup>11</sup> The

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attractive imaging properties of  $^{123m}\text{Te}$  have prompted us to investigate the chemical synthesis of telluro amino acids.

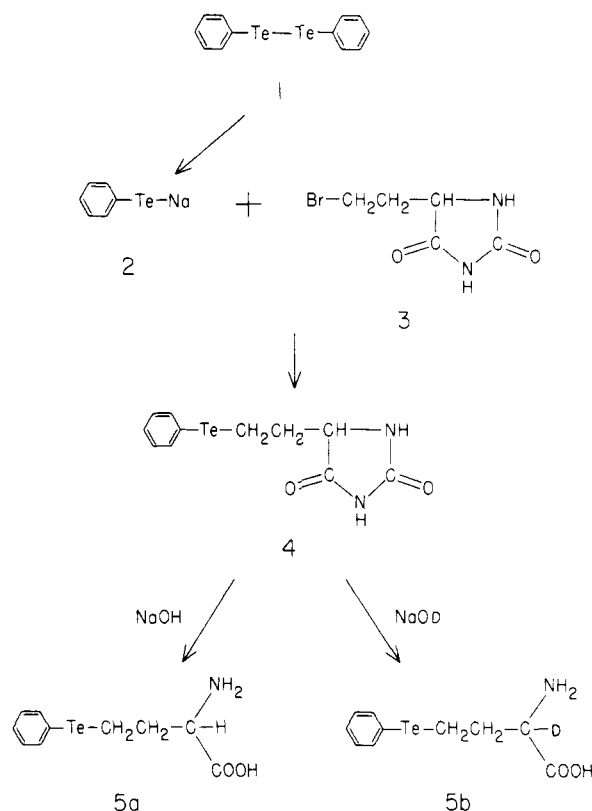
The unpredictable chemical properties and instability of many organotellurium compounds are well documented.<sup>5</sup> Nonetheless, attempts to prepare novel tellurium compounds generally follow methods that have been used successfully to prepare the analogous selenium compounds. In our earlier studies, we attempted to prepare telluromethionine by various methods that had been reported for the synthesis of selenomethionine. Most of the routes involved as the initial step the attempted introduction of the benzyltelluro moiety into suitable substrates. These strategies included the attempted addition of benzyltellurol across the olefinic bond of acrolein with the subsequent reaction of the product under Strecker conditions<sup>12</sup> and displacement of the *p*-toluenesulfonyl moiety,<sup>13</sup> halogen, or other suitable leaving group of a  $\gamma$ -substituted derivative of homoserine with an alkali metal salt of benzyltellurol. In both instances, it was envisioned that the resulting products could be methylated with methyl iodide after reduction in sodium-liquid ammonia (du Vigneaud conditions) and the protecting groups removed to give telluromethionine. Dibenzyl ditelluride has been prepared by a variety of methods,<sup>14,15</sup> but it is unstable in solution under many reaction conditions. Although the crucial benzyltellurol intermediate can be generated by in situ reductive cleavage of the ditelluride, benzyltellurol rapidly decomposes with deposition of tellurium metal, even under conditions where reaction mixtures have been carefully protected from the presence of oxidizing species. These disadvantages indicated that benzyltellurol was a particularly unsatisfactory reagent for the microscale synthesis of telluro amino acids. The benzyltellurol route was therefore abandoned and telluromethionine was successfully prepared<sup>16</sup> by the direct introduction of the methyltelluro moiety by nucleophilic displacement of bromide from 5-( $\beta$ -bromoethyl)hydantoin with sodium methyltellurol. Although telluromethionine was isolated and characterized, it rapidly decomposed upon standing in solution.<sup>16</sup> The instability of telluromethionine precluded the preparation and testing of the  $^{123m}\text{Te}$ -labeled amino acid.

Since phenyltelluro-substituted compounds are often considerably more stable than the alkyltelluro-substituted counterparts,<sup>5</sup> our attention has now focused on the preparation of an  $\alpha$ -amino acid substituted with the phenyltelluro moiety. The goals of the present investigation were to develop a synthesis of DL- $\alpha$ -amino- $\gamma$ -(phenyltelluro)butyric acid and to determine the tissue distribution of the  $^{123m}\text{Te}$ -labeled amino acid in rats.

### Synthesis and Biological Studies

Our approach for the synthesis of DL- $\alpha$ -amino- $\gamma$ -(phenyltelluro)butyric acid (**5a**) is similar to the method used earlier to prepare telluromethionine.<sup>16</sup> In the present studies, phenyltellurol (**2**) was coupled with 5-( $\beta$ -bromoethyl)hydantoin (**3**) and the resulting 5-[( $\beta$ -(phenyltelluro)ethyl]hydantoin (**4**) was cleaved by basic hydrolysis to **5a** (Scheme I). The 5-( $\beta$ -bromoethyl)hydantoin in-

Scheme I



intermediate (**3**) was prepared by the method of Livak and co-workers<sup>17</sup> and exhibited the expected physical properties. Coupling of **3** with phenyltellurol proceeded smoothly in refluxing methanol and 5-[( $\beta$ -phenyltelluro)ethyl]hydantoin (**4**) was isolated in 58% yield as a white crystalline solid and exhibited TLC, UV, and IR properties that were consistent with the proposed structure. The expected molecular ion was observed at  $m/z$  334 in the 70-eV low-resolution mass spectrum of 5-[( $\beta$ -phenyltelluro)ethyl]hydantoin, and the fragmentation pattern was consistent with the proposed structure (**4**). The composition of the fragmentation ions was confirmed by high-resolution mass spectral measurements. The 100-MHz NMR spectrum further substantiated the identity of **4** and integrated correctly for the expected proton population.

The DL- $\alpha$ -amino- $\gamma$ -(phenyltelluro)butyric acid (**5a**) was obtained in 49% yield by high-temperature basic hydrolysis of the hydantoin (**4**). The identity of **5a** was also confirmed by TLC, UV, and IR measurements (vide infra). A molecular ion was detected at  $m/z$  309 in the 70-eV mass spectrum of **5a** and fragmentation ions were observed which were consistent with the expected electron-induced decomposition of DL- $\alpha$ -amino- $\gamma$ -(phenyltelluro)butyric acid. The 100-MHz nuclear magnetic resonance data of **5a** were also clearly consistent with the proposed structure. Further confirmation of the identity of **5a** was obtained by NaOD hydrolysis of the hydantoin **4** to give DL- $\alpha$ -amino- $\gamma$ -(phenyltelluro)butyric acid (**5b**) deuterated at position 2. The expected exchange of the C-2 hydrogen was substantiated by an analysis of the 70-eV mass spectrum of **5b** in which the molecular ion was observed at  $m/z$  310. In addition, examination of the 100-MHz nuclear magnetic resonance spectrum of **5b** revealed the absence of the C-2 methine proton which is present at approximately 3 ppm in the spectrum of **5a**. Other features of the

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**Table I.** Distribution of Radioactivity in Female Rat Tissues at Various Time Intervals Following Intravenous Administration of  $^{123}\text{mTe}$  Labeled-DL- $\alpha$ -Amino- $\gamma$ -(phenyltelluro)butyric Acid

tissue	mean % dose/g of tissue for 3 rats $\pm$ SD			
	30 min	60 min	4 h	24 h
blood	0.208 $\pm$ 0.004	0.497 $\pm$ 0.048	0.451 $\pm$ 0.054	0.485 $\pm$ 0.057
liver	0.320 $\pm$ 0.007	0.534 $\pm$ 0.047	1.046 $\pm$ 0.363	2.139 $\pm$ 0.109
spleen	0.129 $\pm$ 0.004	0.238 $\pm$ 0.015	0.234 $\pm$ 0.037	0.280 $\pm$ 0.040
pancreas	0.206 $\pm$ 0.018	0.654 $\pm$ 0.072	0.434 $\pm$ 0.036	0.334 $\pm$ 0.059
kidneys	1.019 $\pm$ 0.070	2.628 $\pm$ 0.535	2.169 $\pm$ 0.198	1.489 $\pm$ 0.061

spectrum of **5b** were very similar to those exhibited by **5a**, with the exception of the altered  $\beta$ -methylene two-proton multiplet which was less complex in the spectrum of **5b** due to the absence of coupling between the  $\beta$ -methylene and methine protons.

Tellurium-123m labeled DL- $\alpha$ -amino- $\gamma$ -(phenyltelluro)-butyric acid was prepared by the same sequence of reactions described for the preparation of unlabeled **5a**. For this synthesis,  $^{123}\text{mTe}$ -labeled diphenyl ditelluride was generated from reactor-produced  $^{123}\text{mTe}$ . Tellurium-123m labeled products **4** and **5a** both exhibited single radioactive components upon thin-layer radiochromatographic analyses that cochromatographed with the unlabeled standards. The results of tissue distribution studies with racemic  $^{123}\text{mTe}$ -labeled **5a** in white female rats did not indicate pancreatic uptake of this agent (Table I).

## Conclusions

The attractive imaging properties of  $^{123}\text{mTe}$  prompted us to investigate the chemical synthesis and biological studies of  $^{123}\text{mTe}$ -labeled amino acids as a potential new class of pancreatic imaging agents. Telluromethionine was found to be unstable in earlier studies,<sup>16</sup> which indicated that the preparation and testing of the  $^{123}\text{mTe}$ -labeled amino acid would not be feasible. Since phenyltelluro-substituted compounds are often relatively stable, the present studies were initiated to prepare DL- $\alpha$ -amino- $\gamma$ -(phenyltelluro)butyric acid (**5a**) and to determine if the  $^{123}\text{mTe}$ -labeled amino acid showed pancreatic uptake in rats. Although radiolabeled **5a** did not show pancreatic uptake in rats, the most important feature of our studies is the demonstration that  $^{123}\text{mTe}$ -labeled amino acids can be prepared. The preparation and testing of such compounds could be important as a result of interest in the potential use of  $^{123}\text{mTe}$ -labeled amino acids for pancreatic imaging.

## Experimental Section

The melting points were determined in capillary tubes using a Büchi SP apparatus and are uncorrected. The thin-layer chromatographic analyses (TLC) were performed using 250- $\mu\text{m}$  thick layers of silica gel G PF-254 coated on glass plates obtained from Analtech, Inc. The following solvent systems were used: S-1, EtOAc- $\text{CHCl}_3$  (2:1); S-2, MeOH- $\text{CHCl}_3$  (4:96); S-3, BuOH-HOAc- $\text{H}_2\text{O}$  (4:1:1). Ultraviolet spectra (UV) were determined in either absolute ethanol or water using a Beckman DB double-beam instrument. The infrared spectra (IR) were recorded on KBr pellets with a Beckman 18-A spectrophotometer. The low-resolution mass spectra (MS) were recorded using the Oak Ridge National Laboratory low-resolution instrument under the following conditions: ionizing energy, 70 eV; accelerating potential, 8000 V; trap current, 100  $\mu\text{A}$ ; probe temperature, 200–300  $^\circ\text{C}$ . Fragmentation data are tabulated for ions detected in the low-resolution spectra of compounds **3**, **4**, **5a** and **5b** (mass, percent relative abundance). The high-resolution mass spectral measurements were determined with an AEI MS-50 instrument equipped with a DS-50 data system under the following conditions: ionizing energy, 70 eV; accelerating potential, 8000 V; trap current, 500  $\mu\text{A}$ ; probe temperature, 200–400  $^\circ\text{C}$ ; resolution,  $10^4$ ; scan rate, 10/s/decade. The nuclear magnetic resonance spectra (NMR) were obtained at 100 MHz with a Varian XL-100 instrument.

Samples were dissolved in the appropriate deuterated solvent (as indicated). The resonances are reported downfield ( $\delta$ ) from the internal tetramethylsilane standard.

**Materials.** Tellurium metal was purchased from Alfa Inorganics and was ground to a fine 45- $\mu\text{m}$  powder before use. The phenylmagnesium chloride solution was also obtained from this supplier and DL-homoserine was purchased from Sigma Chemical Co, Inc. All other chemicals and solvents were analytical grade and were used without further purification. The  $^{123}\text{mTe}$  was prepared by neutron irradiation of isotopically enriched  $^{122}\text{Te}$  (97.6%) by the  $^{122}\text{Te}(\eta, \gamma)^{123}\text{mTe}$  nuclear reaction as previously described<sup>4</sup> and had a specific activity of 1.2 mCi/mg. Diphenyl ditelluride (**1**) was prepared by the reaction of phenylmagnesium chloride with metallic tellurium as described by Irgolic and co-workers.<sup>18</sup> The yields varied from 20 to 40% when the reaction was conducted on the 10–100 mmol scale and the product (**1**) exhibited the expected UV, MS, and NMR properties. Preparation of  $^{123}\text{mTe}$ -labeled **1** was conducted on the microscale (1–2 mmol) and necessitated alterations of the reaction conditions (vide infra).

**Animal Tissue Distribution Experiments.** The distribution of radioactivity was determined in tissues of 10–12 week old female Fischer 344 rats (180–210 g) after intravenous administration of the labeled amino acid. The animals were allowed food and water ad libitum prior to and during the course of the experiment. The basic solution of  $^{123}\text{mTe}$ -labeled **5** was neutralized to pH  $\sim$ 8 with 1 N HCl, filtered through a 0.22- $\mu\text{m}$  Millipore filter, and injected via a lateral tail vein to the ether-anesthetized animals. The animals were sacrificed by decapitation, and the organs were removed, rinsed with saline solution, and placed in tared vials. The vials were then weighed, the radioactive contents were determined in a multichannel Ge(Li) analyzer, and the percent dose per gram of tissue values were then calculated.

**5-( $\beta$ -Bromoethyl)hydantoin (**3**).** The DL-homoserine (36 g, 0.30 mol) was dissolved in  $\text{H}_2\text{O}$  (100 mL) and the solution was heated to 60  $^\circ\text{C}$  in an oil bath. A mixture of KCNO (26 g, 0.32 mol) in  $\text{H}_2\text{O}$  (10 mL) was added dropwise to the amino acid solution over a 5-min period and the resulting mixture was stirred for 3 h at 60–65  $^\circ\text{C}$ . The temperature was elevated to 90  $^\circ\text{C}$  after the cautious dropwise addition of a 48% HBr solution (100 mL). The temperature was maintained at 90–95  $^\circ\text{C}$ , and the solution was then cooled to room temperature and allowed to stand overnight. After evaporation in vacuo and addition of 300 mL of acetone, the solution was vigorously stirred and the resulting white precipitate was removed by filtration. The filter cake was washed thoroughly with acetone, and the combined acetone filtrates were evaporated in vacuo to yield a red gum, which was dissolved in 48% HBr (50 mL) and heated at 90–95  $^\circ\text{C}$  for 3 h. Following evaporation of the liquid in vacuo, the gummy product was dissolved in  $\text{H}_2\text{O}$  (100 mL) and placed in the refrigerator to give a tan-colored precipitate, which was recovered by filtration and dissolved in acetone. Hexane was added to the rapidly stirred acetone solution, resulting in the deposition of a fine white solid. Filtration and drying gave 9.42 g (15%) of **3**: mp 140–140.5  $^\circ\text{C}$  (lit. 141.5–142  $^\circ\text{C}$ );<sup>17</sup> IR (KBr) 1775 (C=O), 1740 (C=O), 1425, 745 and 635 (CBr)  $\text{cm}^{-1}$ ; NMR ( $\text{Me}_2\text{SO}-d_6$ )  $\delta$  2.23 (m, 2 H,  $\alpha$ - $\text{CH}_2$ ), 2.66 (s, 1 H), 3.55 (d of d,  $J$  = 6 Hz, 2 H,  $\beta$ - $\text{CH}_2$ ), 4.11 (m, 1 H, ring CH), 6.65 (s, 1 H); MS,  $m/z$  208 ( $\text{M}^+$ ,  $^{81}\text{Br}$ , 7), 137 ( $^{81}\text{Br}$ , 3), 126 (8), 133 (42), 100 (100), 95 ( $^{81}\text{Br}$ , 7), 80 ( $^{81}\text{Br}$ , 6), 70 (7), 57 (40), 44 (30); high-resolution MS calcd for  $\text{C}_5\text{H}_7\text{O}_2\text{N}_2\text{Br}$ , 207.9696; found, 207.9683.

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**5-[ $\beta$ -(Phenyltelluro)ethyl]hydantoin (4).** In a typical preparation, diphenyl ditelluride (1; 1.0 g, 2.4 mmol) was dissolved in MeOH (25 mL) under an argon atmosphere and the orange-colored solution reduced by the addition of sodium borohydride to a colorless solution of phenyltellurol (2). The 5-( $\beta$ -bromoethyl)hydantoin (3; 932 mg, 4 mmol) was dissolved in a small volume of MeOH and added to the solution of 2. After the solution refluxed for 5 min, TLC analysis (S-1) indicated the absence of 3 ( $R_f$  0.26) and the presence of a UV-absorbing, less polar material ( $R_f$  0.34). The mixture was poured into water and washed thoroughly with C<sub>6</sub>H<sub>6</sub>. The aqueous solution was then acidified to pH 1–2 with 1 N HCl and extracted several times with Et<sub>2</sub>O. The combined Et<sub>2</sub>O extracts were washed with water and taken to dryness in vacuo to give a light yellow solid. Crystallization from Me<sub>2</sub>CO–H<sub>2</sub>O (2 times) and Me<sub>2</sub>CO–hexane (3 times) gave a fine white solid (770 mg, 58%) of 4: mp 140–140.5 °C; UV  $\lambda_{\max}$  225 nm (log  $\epsilon$  4.55) and 324 (0.27); IR (KBr) 1775 (C=O), 1730 (C=O), 1420, 1195, 930, 730, 690 (phenyl) cm<sup>-1</sup>; NMR (Me<sub>2</sub>SO-*d*<sub>6</sub>) 2.15 (m, 2 H,  $\alpha$ -CH<sub>2</sub>), 2.71 (s, 1 H), 2.92 (d of d,  $J$  = 7 Hz, 2 H,  $\beta$ -CH<sub>2</sub>), 4.03 (t,  $J$  = 7 Hz, 1 H, ring CH), 7.20 (m, 2 H, ortho and para aromatic H's), 7.41 (s, 1 H), 7.64 (m, 2 H, meta aromatic H's). The ortho, meta, and para hydrogens experience different shielding effects when the Te heteroatom is attached directly to the aromatic ring.<sup>5</sup> MS 334 (M<sup>+</sup>, <sup>130</sup>Te, 19), 284 (Te<sub>2</sub> (C<sub>6</sub>H<sub>5</sub>)<sub>2</sub>, dec ion), 256 (M<sup>+</sup>, <sup>130</sup>Te – C<sub>6</sub>H<sub>5</sub>, 4), 235 (M<sup>+</sup>, <sup>130</sup>Te – hydantoin ring, 5), 207 ([C<sub>6</sub>H<sub>5</sub>Te]<sup>+</sup>, 45), 154 ([C<sub>6</sub>H<sub>5</sub>]<sub>2</sub><sup>+</sup>, 29), 127 (M<sup>+</sup> – [C<sub>6</sub>H<sub>5</sub>Te], 82), 99 (hydantoin ring – H, 27), 77 ([C<sub>6</sub>H<sub>5</sub>]<sup>+</sup>, 100), 56 (19), 51 (50); high-resolution MS calcd for C<sub>11</sub>H<sub>12</sub>O<sub>2</sub>N<sub>2</sub>Te, 333.9976; found, 333.9938.

**DL- $\alpha$ -Amino- $\gamma$ -(Phenyltelluro)butyric Acid (5a).** The hydantoin 4 (334 mg, 1 mmol) was dissolved in 1 N NaOH (3 mL) in a small Pyrex vial which was placed in a stainless-steel bomb. The bomb was heated at 165 °C for 1 h and, after cooling, the solution was acidified to pH 4–5 with 1 N HCl. The precipitate was collected by centrifugation and crystallized from MeOH–H<sub>2</sub>O to give 5a: 120 mg (49%); mp 223–224 °C dec; UV  $\lambda_{\max}$  223 nm (log  $\epsilon$  4.10), 262 (1.42), 312 (0.22); IR (KBr) 3000 (–OH), 1585 (C=O), 1500, 1410, 720, 685 cm<sup>-1</sup> (phenyl); NMR (0.1 N NaOD)  $\delta$  1.86 (m, 2 H,  $\beta$ -CH<sub>2</sub>), 2.69 (m, 2 H,  $\gamma$ -CH<sub>2</sub>), 3.12 (1 H, m,  $\alpha$ -CH), 7.20 (m, 3 H, ortho and para, aromatic H's) and 7.64 (m, 2 meta H, aromatic H's); MS,  $m/z$  309 (M<sup>+</sup>, <sup>130</sup>Te, 11), 284 ([C<sub>6</sub>H<sub>5</sub>]<sub>2</sub>Te, dec ion, 4), 235 (M<sup>+</sup> <sup>130</sup>Te – hydantoin ring, 8), 207 ([C<sub>6</sub>H<sub>5</sub><sup>130</sup>Te]<sup>+</sup>, 21), 130 ([<sup>130</sup>Te]<sup>+</sup>, 14), 102 (44), 91 ([C<sub>7</sub>H<sub>7</sub>]<sup>+</sup>, 18), 77 ([C<sub>6</sub>H<sub>5</sub>]<sup>+</sup>, 100), 61 ([HO<sub>2</sub>C – NH<sub>2</sub>]<sup>+</sup>, 74), 56 (76), 51 (61), 44 (66); high resolution MS calcd for C<sub>10</sub>H<sub>13</sub>O<sub>2</sub>N<sub>2</sub>Te, 309.0013; found, 308.9969. Only one ninhydrin-positive component ( $R_f$  0.65) was detected upon TLC analysis (S-3). In addition, the  $R_f$  0.65 species was the only UV-absorbing component detected on the chromatogram. The results of ion-exchange chromatographic analysis using a Beckman amino acid auto-analyzer indicated the presence of a single ninhydrin-positive component. In a parallel experiment, the hydantoin 4 (67 mg, 0.20 mmol) was hydrolyzed at 165 °C for 1 h in 1 N NaOD (2 mL). The amino acid product 5b was obtained in the usual manner, mp 219–220 °C, and exhibited TLC and UV

properties similar to those reported for 5a: NMR (1 N NaOD),  $\delta$  2.08 (m, 2 H,  $\beta$ -CH<sub>2</sub>), 2.90 (m, 2 H,  $\gamma$ -CH<sub>2</sub>), 7.18 (m, 3 H, ortho and para, aromatic H's), and 7.64 (m, 2 H, meta aromatic H's); MS,  $m/z$  310 (M<sup>+</sup> <sup>130</sup>Te).

**<sup>123m</sup>Te-Labeled DL- $\alpha$ -Amino- $\gamma$ -(phenyltelluro)butyric Acid.** Reactor-produced <sup>123m</sup>Te (65.5 mg, 26.3 mCi) was combined with 188.5 mg of carrier tellurium powder. This material (2 mmol) was stirred in tetrahydrofuran (5 mL) to which was added phenylmagnesium chloride (4 mmol) in the same solvent (2 mL). The mixture was rapidly stirred under reflux, but the reaction did not commence until after the addition of a small crystal of benzoyl peroxide. The orange-colored solution was refluxed for 1 min, and the reaction flask was flushed with oxygen and then cooled in an ice bath. After warming to room temperature, the solution was stirred for 30 min and filtered, the orange-colored filtrate was diluted with benzene to a final volume of 25 mL, and aliquots of this solution were counted. The <sup>123m</sup>Te-labeled diphenyl ditelluride contained 9.22 mCi of radioactivity. The benzene solution was diluted to 50 mL with MeOH and the <sup>123m</sup>Te-labeled diphenyl ditelluride was reduced with sodium borohydride in the usual manner and refluxed for 1 h after the addition of the hydantoin 4 (208 mg, 1 mmol). Analysis by TLC (S-1) demonstrated the absence of the substrate (4) and the presence of a strongly UV-absorbing polar product ( $R_f$  0.30). The mixture was poured into water and extracted with benzene to remove diphenyl ditelluride and other nonpolar material. The aqueous layer was acidified to pH 1–2 and 6 N HCl and extracted thoroughly with ether. The combined organic extracts were washed well with water and dried over anhydrous sodium sulfate, and the solvent was removed in vacuo to give 2.2 mCi of <sup>123m</sup>Te-labeled 4. Only one major radioactive component ( $R_f$  0.30) was detected upon thin-layer radiochromatographic analysis (S-1) which cochromatographed with 4. In a typical hydrolysis, the <sup>123m</sup>Te-labeled hydantoin (370  $\mu$ Ci) was dissolved in 1 N NaOH (2 mL) and hydrolyzed at 165 °C in the usual manner. The bomb was cooled, the tan-colored solution was extracted with benzene, and then 1 N HCl was added to pH 7–8. Analysis by thin-layer radiochromatographic analysis (S-3) indicated the presence of only one major radioactive component which cochromatographed ( $R_f$  0.61) with authentic 5. In addition, the UV spectrum for this product was identical with that described earlier for DL- $\alpha$ -amino- $\gamma$ -(phenyltelluro)butyric acid (5).

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