Synthesis of 5-Alkyl- and 5-Aryl-L-Tryptophan Analogues via Palladium-Catalyzed Cross-Coupling of an Iodinated Cyclic Tryptophan Tautomer†

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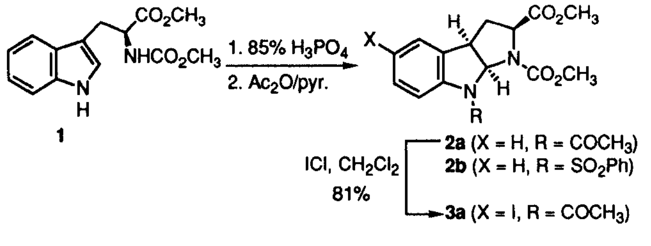
Received 2 May 1994; revised 8 July 1994

Cyclic tryptophan tautomers have been shown to be useful intermediates in the preparation of optically pure tryptophans substituted in the benzenoid ring. We have utilized cyclic tautomer **2a** for the preparation of L-tryptophan derivatives bearing 5-alkyl and 5-aryl functionalities. Treatment of **2a** with 4 equivalents of iodine monochloride provided the 5-iodo species **3a** in 81 % yield. Cross-coupling of **3a** with arylboronic acids or *B*-alkyl-9-borabicyclo[3.3.1]nonane derivatives, catalyzed by 3 mol% [bis(1,1'-diphenylphosphino)ferrocene]palladium(II) chloride, afforded the 5-aryl and 5-alkyl cyclic tryptophan tautomers **3b–g** in 59–79 % yields. The cyclic tautomers were easily decyclized and deprotected to give the corresponding 5-aryl- and 5-alkyl-L-tryptophans.

L-Tryptophan is an essential amino acid which provides the biosynthetic precursor for many naturally occurring indole alkaloids.[1] The ability to synthesize enantiomerically pure tryptophan analogues substituted in the benzenoid ring constitutes a useful approach toward the total synthesis of chiral indole alkaloids of natural and non-natural origin, and provides a general entry into non-natural amino acid derivatives of potential pharmacologic value. As part of our research utilizing substituted tryptophan analogues as probes for elucidating the biochemistry of carcinoid tumors,[2] we have developed a general, efficient method for the preparation of enantiomerically pure analogues of L-tryptophan substituted specifically in the 5-position.

Previous work by Hino[3] demonstrated the powerful utility of cyclic tryptophan tautomers as intermediates for direct functionalization of chiral tryptophans. Formation of cyclic tautomers allowed standard electrophilic substitution chemistry upon the 5-position of the benzenoid ring, due to deactivation of the reactive C-2 and C-3 positions. Thus, analogue **2a** (Scheme 1) was used for the preparation of 5-nitro-[4], 5-bromo-[4], 5-chloro-[4] and 5-hydroxytryptophan[5] analogues. In addition to functionalization of the benzenoid ring, cyclic tryptophan tautomers allowed stereospecific alkylations at the α- and β-carbons. Analogue **2b**, now commercially available, was a key intermediate in the syntheses of stereochemically pure α-[2,6] and β-substituted[7] tryptophans.

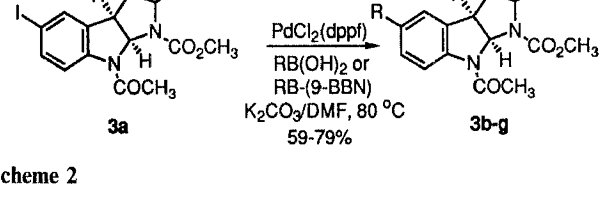


Scheme 1

Palladium-catalyzed cross-coupling is a mild, efficient method for the formation of carbon–carbon bonds. This methodology has enjoyed considerable attention in the past decade due to the versatility and mild conditions of the reaction, and has been particularly important in the functionalization of heterocyclic compounds.[8] One reaction of particular note is the efficient cross-coupling of aryl halides with aryl- and alkylboron derivatives. This method is extremely versatile because arylboronic acids containing many varieties of substituents are easily synthesized, and appropriate boron-containing alkyl moieties are readily prepared by simple hydroboration of alkenes and alkynes with either catecholborane or 9-borabicyclo[3.3.1]nonane (9-BBN). We have pursued palladium-catalyzed cross-coupling using aryl- and alkylboron compounds as a general method for the synthesis of optically pure 5-substituted tryptophans. There have been previous reports concerning palladium-catalyzed cross-coupling as a route to substituted indoles[9] and tryptamines,[10] but to our knowledge, there has been no study devoted to the derivatization of tryptophans using this methodology.

Although preparation of the 5-chloro and 5-bromo analogues of cyclic tryptophan tautomer **2a** had been previously reported,[4] we desired the 5-iodinated analogue **3a** because of the enhanced reactivity of aryl iodides over aryl bromides and chlorides in the cross-coupling reaction.[11] We first prepared **3a** via reaction of **2a** with 1.2 equivalents of thallium(III) trifluoroacetate[12] and 1 equivalent of molecular iodine in refluxing CCl_4. Workup followed by filtration through silica gel ($CHCl_3$) and recrystallization from EtOAc/hexane provided **3a**, but only in 35–40 % yield. A more desirable iodination method was developed using iodine monochloride (ICl). Treatment of a dichloromethane solution of **2a** with 4 equivalents of ICl provided greater than 95 % conversion of **2a** to **3a** in less than 5 minutes, determined by HPLC. Use of less than 4 equivalents of ICl resulted in decreased conversions, while greater amounts of ICl did not significantly improve the yield. Aqueous workup followed by recrystallization from EtOAc/hexane afforded **3a** in 81 % yield. Attempts to iodinate the N_a-phenylsulfonyl-protected analogue **2b** under the same conditions resulted in a noncrystallizable oil, and thus were not pursued further.

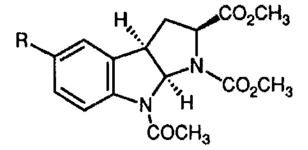
Cross-coupling of **3a** with arylboronic acids and *B*-alkyl-9-BBN derivatives, using conditions described by Miyaura and co-workers,[11] was investigated next (Scheme 2). The cross-coupling reaction was best catalyzed by [bis(1,1'-diphenylphosphino)ferrocene]palladium(II) chloride [$PdCl_2$(dppf)], a commercially available, air-stable reagent.[13] Arylboronic acids were purchased (Aldrich), and the *B*-alkyl-9-BBN derivatives were prepared by reacting 1.1 equivalents of the corresponding alkene with 1.1 equivalents of 9-BBN in THF for 6 hours at room temperature. Cross-coupling was conducted by stirring 1.0 equivalent of **3a** with 1.1 equivalents of boron derivative in the presence of 2.0 equivalents of K_2CO_3 and 3 mol% $[PdCl_2(dppf)]$ at 80 °C. The reaction progress was monitored by reverse-phase HPLC, which indicated that complete conversion was achieved within 16 hours. Following aqueous workup and purification by column chromatography, the 5-aryl and 5-alkyl cyclic tryptophan analogues **3b–g** were obtained in good yield (Table 1). The reaction proceeded equally well for arylboronic acids (entries 1 and 2) and *B*-alkyl-9-BBN analogues derived from styrenes (entries 3 and 4) or simple alkenes (entries 5 and 6). Of particular note was the efficient coupling with the 9-BBN adduct of 4-chlorostyrene (entry 4) which further emphasizes the enhanced reactivity of aryl iodides over aryl chlorides in the cross-coupling reaction. The reaction was also catalyzed with tetrakis(triphenylphosphine)palladium(0), but the reaction rate was slower, requiring greater than 24 hours for completion. Alternatively, cross-coupling was performed with the acyclic 5-iodotryptophan analogue **4a**, but product yields were lower and TLC analysis of the crude product indicated several byproducts.

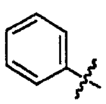
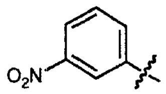
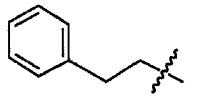
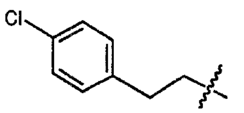
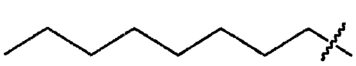
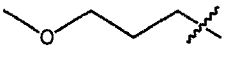


Scheme 2

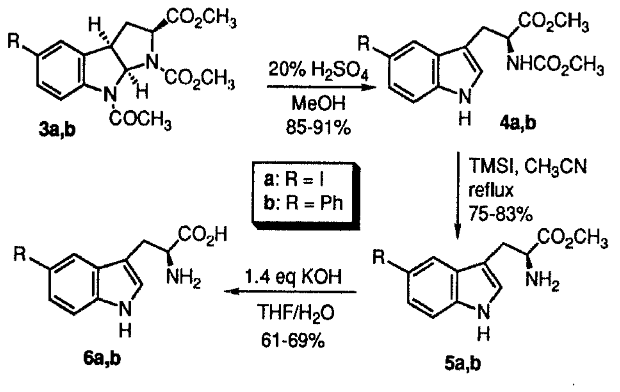
To serve as examples, the cyclic tautomers **3a** and **3b** were readily decyclized/deprotected to provide the corresponding 5-substituted L-tryptophans (Scheme 3). Treatment of **3a** and **3b** with 20% H_2SO_4 in methanol resulted in decyclization and removal of the N_a-acetyl group to provide **4a** and **4b** in 85 and 91 % yields, respectively. The decyclization/deprotection step was also performed using crude **3b**, which provided a greater overall yield for the two-step conversion of **3a** to **4b**. Thus, treatment of crude **3b** (no chromatography) with 20% H_2SO_4/MeOH followed by chromatographic purification afforded **4b** in 70% yield from **3a**, as opposed to the 58% yield obtained when **3b** was purified. Reaction of **4a** and **4b** with 1.5 equivalents of trimethylsilyl iodide (TMSI) in refluxing acetonitrile gave **5a** and **5b** in 75 and 83 % yields, respectively. In the preparation of **5a**, the corresponding hydroiodide salt was isolated directly by quenching the reaction of **4a** with TMSI. The hydroiodide salt was more conveniently isolated because of its highly crystalline character; the free base was a viscous oil. However, analogue **5b** was crystalline as the free base, and thus the hydroiodide salt was not isolated. Saponification (KOH, THF/H_2O) of **5a** and **5b** afforded the completely deprotected amino acids **6a** and **6b**. The use of the TMSI/saponification pathway in the deprotection of chiral N_b-methoxycarbonyltryptophan derivatives was previously reported to proceed without racemization.[14]

Table 1. Cyclic Tryptophan Analogues **3** Prepared



Compound	R	% Yield
3b[a]		64
3c[a]		64
3d[b]		79
3e[b]		74
3f[b]		59
3g[b,c]		59

[a] Prepared by cross-coupling with the corresponding arylboronic acid. [b] Prepared by cross-coupling with the 9-BBN adduct of the corresponding primary olefin. [c] 3-Methoxy-1-propene was prepared as described: Brown, H.C.; Lynch, G.J. *J. Org. Chem.* **1981**, *46*, 531-38.



Scheme 3

Our method provides a convenient, versatile route to enantiomerically pure 5-aryl- and 5-alkyl-substituted tryptophans via an easily accessible chiral building block (**3a**). Formation of cyclic tautomer **2a** allowed iodination specifically at the 5-position due to deactivation of the reactive C-2 and C-3 indole positions, affording **3a** in 81 % yield. Decyclization and deprotection of **3a** provided a simple synthesis of enantiomerically pure 5-iodo-L-tryptophan (**6a**), which had previously been prepared only as a racemate.[15] Palladium-catalyzed cross-coupling of **3a** with aryl- and alkylboron derivatives allowed carbon functionalization at the 5-position under mild conditions, while maintaining the stereochemical integrity of the α-carbon. Although this study was restricted to cross-coupling with aryl- and alkylboron analogues, derivatization of **3a** should be just as readily accomplished using other transition metal catalyzed techniques involving aryl iodides. Our general method should be useful in the construction of chiral indole alkaloids of natural and non-natural origin, as well as providing access to potentially useful tryptophan-like amino acid derivatives for biochemical and pharmacological research.

Melting points were determined with a Mel-Temp melting point apparatus and are uncorrected. ^1H NMR spectra were recorded on a Bruker AMX 500 spectrometer (500 MHz); chemical shifts are reported on the δ scale downfield from tetramethylsilane, in ppm. High resolution mass spectra were obtained using a Finnegan MAT 900 or Finnegan MAT 95Q mass spectrometer. Elemental analyses were obtained from Atlantic Microlab (Norcross, Georgia). Optical rotations were recorded with a Jasco DIP-370 digital polarimeter at ambient temperature using a path length of 50 mm. Column chromatography was performed with Merck Kieselgel 60 silica gel (70–230 mesh) with the eluents indicated. Dry tetrahydrofuran was obtained by refluxing over sodium/benzophenone and distilled immediately prior to use. Acetonitrile and DMF were passed through activated alumina and stored over 3Å molecular sieves. $PdCl_2$(dppf) was purchased from Aldrich Chemical Company. Compounds **3–5a, b** and **6b** all gave satisfactory C, H and N analyses (± 0.35) except **3b** (H −0.42), **4b** (H −0.44), and **6b** (H −0.40).

Dimethyl (2*S*,3a*R*,8a*S*)-8-Acetyl-5-iodo-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole-1,2-dicarboxylate (3a):
To a solution of **2a**[16] (2.30 g, 7.23 mmol) in CH_2Cl_2 (25 mL) was added iodine monochloride (1 M in CH_2Cl_2, 28.9 mL, 28.9 mmol), and the resulting deep red solution was stirred at r.t. for 15 min. The solution was then poured into a mixture of 10% $Na_2S_2O_5$ and 10% $NaHCO_3$ (1:1, 100 mL), and the solution carefully agitated until the red color was dispelled. The organic phase was collected and the aqueous phase extracted once with $CHCl_3$. The combined organic layers were washed sequentially with 10% $NaHCO_3$ and sat. brine, dried (Na_2SO_4) and evaporated to provide a colorless oil which, upon addition of EtOAc/hexane (1:1), formed colorless plates. The crystals were collected and recrystallized from EtOAc/hexane to afford the pure product; yield 2.59 g (81%); mp 161 °C; $[\alpha]_D = +148.7°$ (c = 1.18, $CHCl_3$).

^1H NMR ($CDCl_3$): δ = 2.52–2.66 (m, 2 H), 2.66 (s, 3 H), 3.24 (s, 3 H), 3.71 (br s, 3 H), 4.04 (t, 1 H, J = 6.5 Hz), 4.60 (br s, 1 H), 6.20 (br s, 1 H), 7.44 (br s, 1 H), 7.54 (dd, 1 H, J = 8.6, 1.0 Hz), 7.76 (br s, 1 H).

EIMS: m/z = 444.0172 (M^+, requires 444.0180), 402, 319, 277.

Cross-Coupling of 3a with Aryl- and Alkylboron Derivatives; General Procedure:
Into an oven-dried flask were placed **3a** (1.0 mmol), the arylboronic acid or *B*-alkyl-9-BBN derivative (1.1 mmol), K_2CO_3 (2.0 mmol), and $PdCl_2$(dppf) (0.03 mmol), and the flask flushed with N_2. The contents were dissolved in DMF (5 mL) and the mixture stirred at 80 °C under N_2 for 16 h. The reaction mixture was cooled and then poured into EtOAc/water.[17] The organic layer was extracted sequentially with 2 N HCl, 5% $NaHCO_3$, and sat. brine. Drying (Na_2SO_4) and evaporation gave the crude product as a brown oil. Purification via silica gel chromatography (EtOAc/hexane, 4:1) provided the desired 5-substituted analogues **3b–g**.

Dimethyl (2S,3aR,8aS)-8-Acetyl-5-phenyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole-1,2-dicarboxylate (**3b**):
White foam; $[\alpha]_D$ + 149.4° (c = 1.26, $CHCl_3$).

^1H NMR ($CDCl_3$): δ = 2.60–2.73 (m, 4 H), 2.81 (d, 1 H, J = 12.6 Hz), 3.09 (s, 3 H), 3.72 (br s, 3 H), 4.12 (br s, 1 H), 4.62 (br s, 1 H), 6.27 (br s, 1 H), 7.33 (t, 1 H, J = 7.5 Hz), 7.34 (s, 1 H), 7.42 (t, 2 H, J = 7.5 Hz), 7.47 (d, 1 H, J = 7.5 Hz), 7.52 (m, 2 H), 8.08 (br s, 1 H).

CIMS: m/z 395.1597 (MH^+, requires 395.1606), 319, 277, 257, 177, 149.

Dimethyl (2S,3aR,8aS)-8-Acetyl-5-(2-nitrophenyl)-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole-1,2-dicarboxylate (**3c**):
Light-yellow foam; $[\alpha]_D$ = + 154.3° (c = 1.09, $CHCl_3$).

^1H NMR ($CDCl_3$): δ = 2.63 (m, 4 H), 2.83 (d, 1 H, J = 13.1 Hz), 3.13 (s, 3 H), 3.74 (br s, 3 H), 4.15 (br s, 1 H), 4.66 (br s, 1 H), 6.32 (br s, 1 H), 7.40 (s, 1 H), 7.52 (d, 1 H, J = 8.0 Hz), 7.60 (t, 1 H, J = 8.0 Hz), 7.85 (d, 1 H, J = 7.6 Hz), 8.11 (br s, 1 H), 8.18 (dd, 1 H, J = 8.0, 1.8 Hz), 8.37 (t, 1 H, J = 1.8 Hz).

CIMS: m/z = 440.1415 (MH^+, requires 440.1457), 410, 395, 353.

Dimethyl (2S,3aR,8aS)-8-Acetyl-5-(2-phenylethyl)-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole-1,2-dicarboxylate (**3d**):
White semi-solid; $[\alpha]_D$ = + 76.1° (c = 2.80, $CHCl_3$).

^1H NMR ($CDCl_3$): δ = 2.35–2.69 (m, 4 H), 2.71 (d, 1 H, J = 12.8 Hz), 2.86 (s, 4 H), 3.07 (s, 3 H), 3.71 (br s, 3 H), 4.02 (br s, 1 H), 4.59 (br s, 1 H), 6.23 (br s, 1 H), 6.95 (s, 1 H), 7.07 (dd, 1 H, J = 8.0, 1.3 Hz), 7.20 (m, 3 H), 7.28 (m, 3 H), 7.88 (br s, 1 H).

CIMS: m/z = 423.1909 (MH^+, requires 423.1919), 353, 319, 311, 277.

Dimethyl (2S,3aR,8aS)-8-Acetyl-5-[2-(4-chlorophenyl)ethyl]-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole-1,2-dicarboxylate (**3e**):
Light-yellow semi-solid; $[\alpha]_D$ = + 75.3° (c = 1.45, $CHCl_3$).

^1H NMR ($CDCl_3$): δ = 2.51–2.65 (m, 4 H), 2.69 (d, 1 H, J = 13.0 Hz), 2.82 (s, 4 H), 3.10 (s, 3 H), 3.72 (br s, 3 H), 4.02 (br s, 1 H), 4.60 (br s, 1 H), 6.24 (br s, 1 H), 6.91 (s, 1 H), 7.04 (dd, 1 H, J = 8.0, 1.5 Hz), 7.09 (d, 2 H, J = 8.4 Hz), 7.24 (d, 2 H, J = 8.4 Hz), 7.86 (br s, 1 H).

CIMS: m/z = 457.1517 (MH^+, requires 457.1530), 353, 319, 311, 277.

Dimethyl (2S,3aR,8aS)-8-Acetyl-5-octyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole-1,2-dicarboxylate (**3f**):
White foam; $[\alpha]_D$ = + 75.0° (c = 1.04, $CHCl_3$).

^1H NMR ($CDCl_3$): δ = 0.88 (t, 3 H, J = 6.9 Hz), 1.27 (m, 10 H), 1.54 (m, 2 H), 2.52 (br s, 2 H), 2.54 (t, 2 H, J = 7.5 Hz), 2.66 (br s, 2 H), 2.72 (d, 1 H, J = 13.1 Hz), 3.11 (s, 3 H), 3.71 (br s, 3 H), 4.03 (br s, 1 H), 4.58 (br s, 1 H), 6.22 (br s, 1 H), 6.94 (s, 1 H), 7.04 (d, 1 H, J = 8.0 Hz), 7.87 (br s, 1 H).

CIMS: m/z = 431.2554 (MH^+, requires 431.2545), 410, 391, 279.

Dimethyl (2S,3aR,8aS)-8-Acetyl-5-(3-methoxypropyl)-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole-1,2-dicarboxylate (**3g**):
Colorless oil; $[\alpha]_D$ = + 82.0° (c = 1.33, $CHCl_3$).

^1H NMR ($CDCl_3$): δ = 1.83 (m, 2 H), 2.35–2.72 (m, 6 H), 3.11 (s, 3 H), 3.71 (br s, 3 H), 4.03 (br s, 1 H), 4.58 (br s, 1 H), 6.22 (br s, 1 H), 6.96 (s, 1 H), 7.06 (d, 1 H, J = 7.4 Hz), 7.87 (br s, 1 H).

CIMS: m/z = 391.1868 (MH^+, requires 391.1869), 349, 319, 277.

5-Iodo-N_b-methoxycarbonyl-L-tryptophan Methyl Ester (4a):
A solution of **3a** (1.16 g, 2.61 mmol) in 20% H_2SO_4/MeOH (25 mL) was stirred at r.t. for 3 h. The solution was poured into water (100 mL) and extracted with EtOAc. The organic extract was washed with 5% $NaHCO_3$ and sat. brine, dried (Na_2SO_4) and evaporated to afford the product as a light-yellow oil in quantitative yield. The oil was chromatographed through silica gel (EtOAc/hexane, 1:1) to provide the purified product as a colorless oil which, upon standing, formed a white solid. Trituration with boiling CCl_4 afforded a white powder; yield 896 mg (85%); mp 110 °C; $[\alpha]_D$ = + 58.0° (c = 1.12, $CHCl_3$).

^1H NMR ($CDCl_3$): δ = 3.26 (d, 2 H, J = 5.2 Hz), 3.70 (s, 3 H), 3.72 (s, 3 H), 4.76 (dt, 1 H, J = 8.0, 5.2 Hz), 5.29 (d, 1 H, J = 8.0 Hz), 6.94 (d, 1 H, J = 1.9 Hz), 7.11 (d, 1 H, J = 8.6 Hz), 7.41 (dd, 1 H, J = 8.6, 1.5 Hz), 7.83 (d, 1 H, J = 1.5 Hz), 8.36 (br s, 1 H).

EIMS: m/z = 402.0075 (M^+, requires 402.0075), 306, 256, 130.

N_b-Methoxycarbonyl-5-phenyl-L-tryptophan Methyl Ester (4b):
Prepared in 91% yield (faint-yellow foam) from **3b** as described above for the preparation of **4a** from **3a**; $[\alpha]_D = +29.9°$ ($c = 1.16$, $CHCl_3$).

^{1}H NMR ($CDCl_3$): $\delta = 3.35$ (t, 2H, $J = 6.0$ Hz), 3.65 (s, 3H), 3.67 (s, 3H), 4.74 (dt, 1H, $J = 7.9$, 6.0 Hz), 5.27 (d, 1H), 7.04 (d, 1H, $J = 2.2$ Hz), 7.31 (tt, 1H, $J = 7.4$, 1.2 Hz), 7.40–7.47 (m, 4H), 7.65 (dd, 1H, $J = 7.4$, 1.3 Hz), 7.74 (d, 1H, $J = 1.3$ Hz), 8.10 (br s, 1H).

CIMS: $m/z = 352.1411$ (M^+, requires 352.1423), 256, 206, 130.

5-Iodo-L-tryptophan Methyl Ester (5a):
To a solution of **4a** (700 mg, 1.74 mmol) in acetonitrile (7 mL) was added TMSI (525 mg, 2.61 mmol) and the solution stirred at reflux for 1 h. The solution was cooled to r.t., quenched with MeOH (1 mL), and the solvent evaporated to produce an off-white solid. Recrystallization from isopropanol afforded the hydroiodide salt of **5a** as a white crystalline solid in near-quantitative yield; mp 205–206 °C (dec); $[\alpha]_D = +31.4°$ ($c = 1.14$, MeOH).

^{1}H NMR (DMSO-d_6): $\delta = 3.20$ (m, 2H), 3.70 (s, 3H), 4.29 (t, 1H, $J = 6.2$ Hz), 7.21 (d, 1H, $J = 2.0$ Hz), 7.24 (d, 1H, $J = 8.4$ Hz), 7.35 (d, 1H, $J = 8.4$ Hz), 7.86 (br s, 1H), 8.29 (br, 2H), 11.23 (s, 1H).

CIMS: $m/z = 345.0022$ (MH^+, requires 345.0100), 328, 256, 202.

The free base was obtained by partitioning the hydroiodide salt between EtOAc and 5% $NaHCO_3$, drying the organic phase (Na_2SO_4) and evaporating. Column chromatography (silica gel, EtOAc/MeOH, 4:1) provided the free base as a colorless oil; yield: 450 mg (75%).

5-Phenyl-L-tryptophan Methyl Ester (5b):
Prepared in 83% yield from **4b** as described above for the preparation of **5a** from **4a**, except the hydroiodide salt was not isolated; mp 154 °C (*i*-PrOH); $[\alpha]_D = +42.4°$ ($c = 1.24$, MeOH).

^{1}H NMR ($CDCl_3$): $\delta = 3.10$ (dd, 1H, $J = 14.4$, 7.7 Hz), 3.33 (dd, 1H, $J = 14.4$, 4.8 Hz), 3.71 (s, 3H), 3.87 (dd, 1H, $J = 7.7$, 4.8 Hz), 7.12 (d, 1H, $J = 2.3$ Hz), 7.32 (t, 1H, $J = 7.5$ Hz), 7.45 (m, 4H), 7.66 (d, 2H, $J = 7.5$ Hz), 7.82 (br s, 1H), 8.09 (br s, 1H).

CIMS: $m/z = 294.1350$ (M^+, requires 294.1368), 278, 206

5-Iodo-L-tryptophan (6a):
To a solution of **5a** (580 mg, 1.67 mmol) in a mixture of THF (5 mL) and H_2O (10 mL) was added 1 N NaOH (2.3 mL, 1.4 equiv). The mixture was stirred for 16 h at r.t., and then neutralized with 1 N HCl (2.3 mL, 1.4 equiv). The solution was evaporated under reduced pressure to approximately 10 mL, at which time the desired product precipitated. The precipitate was collected and recrystallized from 70% EtOH to provide **6a** as an off-white crystalline solid; yield: 385 mg (69%); mp 165–166 °C (Lit.[15] mp 164 °C, racemate); $[\alpha]_D = -12.3°$ ($c = 1.08$, CF_3CO_2H).

^{1}H NMR (DMSO-d_6): $\delta = 2.96$ (dd, 1H, $J = 15$, 8.3 Hz), 3.22 (dd, 1H, $J = 15$, 4.2 Hz), 3.39 (dd, 1H, $J = 8.3$, 4.2 Hz), 7.20 (s, 1H), 7.21 (d, 1H, $J = 8.4$ Hz), 7.31 (dd, 1H, $J = 8.4$, 1.6 Hz), 7.92 (d, 1H, $J = 1.6$ Hz), 11.16 (s, 1H).

CIMS: $m/z = 330.9921$ (MH^+, requires 330.9942), 307, 137.

5-Phenyl-L-tryptophan (6b):
Prepared in 61% yield from **5b** as described above for the preparation of **6a** from **5a**; $[\alpha]_D = -19.5°$ ($c = 1.68$, CF_3CO_2H).

^{1}H NMR (D_2O/DCl): $\delta = 2.34$ (m, 2H), 3.27 (t, 1H, $J = 6.5$ Hz), 6.21 (s, 1H), 6.22 (t, 1H, $J = 8.2$ Hz), 6.34 (m, 3H), 6.41 (d, 1H, $J = 8.5$ Hz), 6.55 (d, 2H, $J = 8.2$ Hz), 6.70 (s, 1H).

CIMS: $m/z = 281.1283$ (MH^+, requires 281.1290), 205, 188.

We wish to thank the National Cancer Institute for a Postdoctoral Training Grant Fellowship (CA09441) to D.E.Z. Additional financial support was provided by R01 grant CA58450 (NIH).

† This work was presented at the 207th National Meeting of the American Chemical Society, San Diego, California, March 1994; Division Organic Chemistry Abstract #68.

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(17) In the preparation of analogues **3d–g**, 30% hydrogen peroxide (1 mL) was added to the cooled reaction mixture to destroy any excess of 9-BBN. After 5 min stirring, the workup proceeded as described.