# Enantioselective Synthesis of Marine Indole Alkaloid Hamacanthin B

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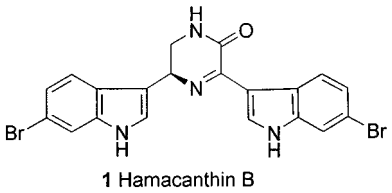
*Received August 9, 2001*

**Abstract:** An enantioselective total synthesis of hamacanthin B (**1**) is described. This synthesis is based on the asymmetric synthesis of (*S*)-2-azido-(indol-3-yl)ethylamine **7**, which is coupled with the 3-indolyl-α-oxoacetyl chloride **8** and subsequently used in a successful intramolecular Staudinger−aza Wittig cyclization to form the central dihydropyrazinone ring. The stereochemistry of naturally isolated hamacanthin **B** is revealed as the (*S*)-configuration.

Over the past few years, much attention has been paid to the search for certain bisindole secondary metabolites, containing either an imidazole- or piperazine-derived spacer unit, due to their novel structural features and broad spectrum of powerful biological activities.[1,2] Hamacanthin B (**1**), one member of the family of naturally occurring bis(indol-3-yl)dihydropyrazinones, was isolated from a deep-water marine sponge *Hamacantha* sp. and has been reported to show significant antimicrobial activity against *Candida albicans* and *Cryptococcus neoformans*. On the basis of NMR spectroscopy, its structure was elucidated to be 3,5-bis(6-bromoindol-3-yl)-5,6-dihydro-2(1*H*)-pyrazinone, but its absolute configuration was not assigned.[3] In this Note, we describe the first enantioselective synthesis of hamacanthin B (**1**, Figure 1) and demonstrate that the stereochemistry of natural hamacanthin B is (*S*).

Recently, we developed methodology for the preparation of an antipode of hamacanthin A, which has the bisindolyl group linking the 5,6-postion of dihydropyrazinone. It is revealed that natural hamacanthin A has the (*S*)-configuration. The (*R*)-chiral center in the antipode of hamacanthin A was created by using (*S*)-1-(indol-3-yl)-1,2-ethanediol as starting material, which was generated by the osmium tetraoxide-catalyzed asymmetric dihydroxylation (Sharpless AD reaction) of vinyl indole **2** using AD-mix-α.[4]




**1** Hamacanthin B

**Figure 1.**

With the above results in mind, we envisioned that hamacanthin B had the same (*S*)-configuration as hamacanthin A. Thus, vinyl indole **2** was subjected to AD-mix-$\beta$ to give (*R*)-1-(indol-3-yl)-1,2-ethanediol **3** in 89% yield and 98% ee. Selective tosylation of the primary hydroxyl group in vicinal diol **3** was accomplished in 75% yield using dibutyltin oxide and tosyl chloride in dichloromethane.[5] Displacement of tosylate **4** with $NaN_3$ in DMF gave the azide **5** in 80% yield. Although many useful methods have been reported for reduction of an azido to amino group,[6] most of them were with limited success. For example, $LiAlH_4$ could not only reduce the azido group but could also induce partial debromination of the 6-bromo substituent in the indole ring. Triphenylphosphine did not produce the desired product at all. However, we found that the reduction procedure using tin(II) chloride dihydrate as reductant worked well for our desired transformation.[7] Treatment of azide **7** with an excess of tin(II) chloride dihydrate in methanol at 30 °C for 20 h and subsequent protection of the resulting amino group with $(Boc)_2O$ provided **6** in 74% yield in two steps. Mitsunobu's procedure[8] was employed to convert the secondary hydroxyl in compound **6** to an azido group to give **7** in 83% yield (Scheme 1).

With (*S*)-2-azido-(indol-3-yl)ethylamine **7** in hand, the central pyrazinone ring was constructed by coupling amine with 6-bromo-3-indolyl-α-oxoacetyl chloride **8**,[9] followed by an intramolecular Staudinger−aza-Wittig cyclization[10] which we have successfully employed for the synthesis of the antipode of hamacantin A.[4] As shown in Scheme 2, key intermediate **7** underwent $CF_3COOH$-mediated cleavage of the Boc group followed by coupling with 6-bromo-3-indolylacetyl chloride **8** to readily afford compound **9** in 93% yield for two steps. Subsequent formation of the central pyrazinone ring was achieved by reaction of azide **9** and tributylphosphine in toluene at ambient temperature for 2 h and then refluxing for 12 h to provide the expected cyclized product **10** in 82% yield. The tosyl group used in indole protection can be removed with $LiAlH_4$, alkaline hydrolysis,[11] or a milder and chemoselective method involving the use of an excess

(1) Faulkner, D. J. *Nat. Prod. Rep.* **2001**, *18*, 1 and references therein.

(2) For related bisindole natural alkaloids, see: (a) Tsujii, S.; Rinehart, K. L.; Gunasekera, S. P.; Kashman, Y.; Cross, S. S.; Lui, M. S.; Pomponi, S. A.; Diaz, M. C. *J. Org. Chem.* **1988**, *53*, 5446. (b) Kohmoto, S.; Kashman, Y.; McConnell, O. J.; Rinehart, K. L.; Wright, A.; Koehn, F. *J. Org. Chem.* **1988**, *53*, 3116. (c) Wright, A. E.; Pomponi, S. A.; Cross, S. S.; McCarthy, P. *J. Org. Chem.* **1992**, *57*, 4772. (d) Capon, R. J.; Rooney, F.; Murray, L. M.; Collins, E.; Sim, A. T. R.; Rostas, J. A. P.; Butler, M. S.; Carrol, A. R. *J. Nat. Prod.* **1998**, *61*, 660. (e) Cutignano, A.; Bifulco, G.; Bruno, I.; Casapullo, A.; Gomez-Paloma, L.; Riccio, R. *Tetrahedron* **2000**, *56*, 3743. (f) Casapullo, A.; Bifulco, G.; Bruno, I.; Riccio, R. *J. Nat. Prod.* **2000**, *63*, 447.

(3) Gunasekera, S. P.; McCarthy, P. J.; Kelly-Borges, M. *J. Nat. Prod.* **1994**, *57*, 1437.

(4) Jiang, B. Yang, C.-G.; Wang, J. *J. Org. Chem.* **2001**, *66*, 4865.

(5) David, S.; Hanessian, S. *Tetrahedron* **1985**, *41*, 643.

(6) For a review, see: Scriven, E. F. V.; Turnbull, K. *Chem. Rev.* **1988**, *88*, 297.

(7) Boger, D. L.; Patane, M. A.; Zhou, J. *J. Am. Chem. Soc.* **1994**, *116*, 8544.

(8) Mitsunobu, O. *Synthesis* **1981**, 1.

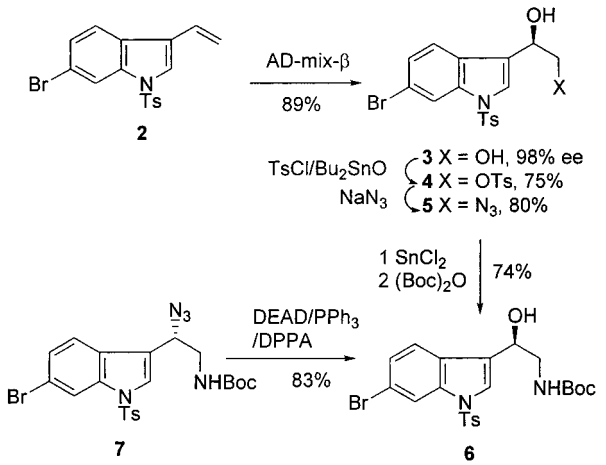
(9) Da Settimo, A.; Saettone, M. F.; Nannipieri, E.; Barili, P. *Gazz. Chim. Ital.* **1967**, *97*, 1304.

(10) (a) For an excellent review, see: Molina, P.; Vilaplana, M. J. *Synthesis* **1994**, 1197. (b) For recent examples of intramolecular aza-Wittig reaction in organic synthesis, see: (i) Sugimori, T.; Okawa, T.; Eguchi, S.; Yashima, E.; Okamoto, Y. *Chem. Lett.* **1997**, 869. (ii) Fresneda, P. M.; Molina, P.; Sanz, M. A. *Synlett* **2000**, 1190. (iii) Kamal, A.; Laxman, E.; Reddy, P. S. M. M. *Tetrahedron Lett.* **2000**, *41*, 8631.

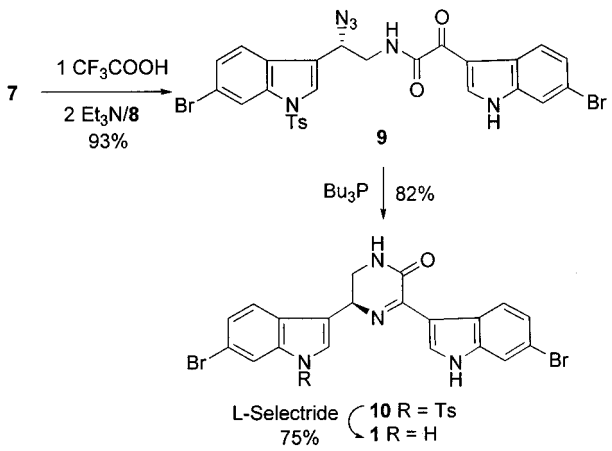
(11) Bowman, R. E.; Evans, D. D.; Islip, P. J. *Chem. Ind.* **1971**, 33.

10.1021/jo0108109 CCC: $22.00 
Published on Web 01/24/2002

**Scheme 1**




**Scheme 2**




Mg in methanol;[12] however, we found that all the known procedures proved less successful for the removal of the tosyl group in compound **10**. Finally, treatment of **10** with L-Selectride in refluxing THF for 3 h gave **1** in 75% yield. The specific rotation of **1** was +183 (*c* 0.1, $CH_3OH$). Comparison with naturally isolated hamacanthin B, which has a positive specific rotation of +176 (*c* 0.1, $CH_3OH$), revealed that natural hamacanthin B has the (*S*)-configuration. The $^1H$ and $^{13}C$ NMR chemical shifts and coupling constants of synthetic hamacanthin B corresponded to those reported for hamacanthin B isolated from Nature.

## Experimental Section

**General.** Anhydrous reactions were performed in oven-dried glassware under a positive pressure of nitrogen. Melting points were determined in an apparatus and uncorrected. Optical rotations were recorded at the Na-D line in a 1 dm cell at 20 °C. Infrared (IR) spectra were determined on thin film. $^1H$ NMR spectra were recorded at 300 or 600 MHz and were referenced to tetramethylsilane (TMS) at 0.00 ppm. $^{13}C$ NMR spectra were recorded at 75 or 100 MHz. Flash chromatography was performed using silica gel H (10−40 $\mu$m).

**(*R*)-1-(*N*-Tosyl-6-bromoindol-3-yl)-1,2-ethanediol (3).** Vinyl indole **2**[4] (3.0 g, 8.0 mmol) was subjected to AD-mix-$\beta$ (12 g) in *tert*-butyl alcohol/water (100 mL, 1:1) to give (*R*)-1-(indol-3-yl)-1,2-ethanediol **3** in 89% yield and 98% ee.[4] The enantiomeric excess was determined by HPLC using a Chiral OD column with an eluent of 2-propanol/hexane (2/8). $[\alpha]^{20}_D = -44.7$ (*c* 0.945, $CHCl_3$); IR (KBr) 3352 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz) $\delta$ 8.15 (d, $J$ = 1.6 Hz, 1H), 7.76 (d, $J$ = 8.4 Hz, 2H), 7.55 (s, 1H), 7.46 (d, $J$ = 8.4 Hz, 1H), 7.33 (dd, $J$ = 8.5 and 1.7 Hz, 1H), 7.25 (d, $J$ = 8.4 Hz, 2H), 5.02 (m, 1H), 3.84 (m, 2H), 2.72 (d, $J$ = 3.9 Hz, 1H), 2.36 (s, 3H), 2.18 (t, $J$ = 5.8 Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 75 MHz) $\delta$ 145.4, 135.8, 134.6, 130.0, 127.6, 127.8, 126.8, 126.6, 123.8, 121.8, 121.2, 118.6, 116.6, 68.3, 66.4, 21.5; EIMS *m/e* (relative intensity) 411/409 (8/8), 155 (62). Anal. Calcd for $C_{17}H_{16}BrNO_4S$: C, 49.76; H, 3.90; N, 3.41. Found: C, 49.38; H, 4.20; N, 3.28.

**(*R*)-1-(*N*-Tosyl-6-bromoindol-3-yl)-2-[(tosyl)oxy]-1-ethanol (4).** A mixture of diol **3** (1.36 g, 3.3 mmol) and $Bu_2SnO$ (0.91 g, 3.65 mmol) in benzene (30 mL) was refluxed for 2 h to remove water. After cooling to room temperature, the solvent was removed, and $CH_2Cl_2$ (30 mL) and tosyl chloride (0.69 g, 3.65 mmol) were added. Refluxing was continued for 6 h, after which the mixture was diluted with 30 mL of $CH_2Cl_2$ and washed with saturated $NaHCO_3$ and brine successively. The organic phase was dried over $Na_2SO_4$ overnight, filtered, and concentrated to give a syrupy residue which was purified by flash chromatography (silica, Hex/AcOEt 2:1) to give **4** (1.4 g, 75%) as a white solid. Mp 154 °C; $[\alpha]^{20}_D = -17$ (*c* 0.525, acetone); IR (KBr) 3518, 1598 $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$, 300 MHz) $\delta$ 7.99 (d, $J$ = 1.3 Hz, 1H), 7.90 (d, $J$ = 8.4 Hz, 2H), 7.68 (s, 1H), 7.42 (m, 5H), 7.32 (dd, $J$ = 8.5 and 1.5 Hz, 1H), 7.16 (d, $J$ = 8.1 Hz, 2H), 5.92 (d, $J$ = 4.95 Hz, 1H), 5.01 (m, 1H), 4.16 (d, $J$ = 4.95 Hz, 2H), 2.35 (s, 3H), 2.33 (s, 3H); $^{13}C$ NMR (DMSO-$d_6$, 100 MHz) $\delta$ 145.9, 144.7, 135.0, 134.0, 131.6, 130.4, 129.6, 127.4, 127.2, 126.7, 126.1, 124.7, 122.3, 121.9, 121.8, 117.4, 115.5, 72.4, 63.9, 21.1, 21.0; ESIMS *m/e* 563.6. Anal. Calcd for $C_{24}H_{22}BrNO_6S_2$: C, 51.06; H, 3.90; N, 2.48. Found: C, 51.13; H, 3.90; N, 2.54.

**(*R*)-1-(*N*-Tosyl-6-bromoindol-3-yl)-2-azido-1-ethanol (5).** To a solution of compound **4** (1.2 g, 2.13 mmol) in anhydrous DMF (20 mL) was added $NaN_3$ (0.52 g, 8 mmol). The mixture was stirred for 12 h at 80 °C and then allowed to cool to room temperature. Then water (50 mL) was added to quench the reaction. The aqueous layer was extracted with ethyl acetate (3 × 50 mL). The combined organic layers were washed with water and brine successively, dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was purified by flash chromatography (silica, Hex/AcOEt 3:1) to give **5** (0.74 g, 80%) as a white solid. Mp 164 °C; $[\alpha]^{20}_D = -65$ (*c* 0.580, acetone); IR (KBr) 3360, 2113 $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$, 300 MHz) $\delta$ 8.05 (d, $J$ = 1.3 Hz, 1H), 7.89 (d, $J$ = 8.4 Hz, 2H), 7.77 (s, 1H), 7.72 (d, $J$ = 8.5 Hz, 1H), 7.46−7.41 (m, 3H), 5.95 (br d, $J$ = 4.3 Hz, 1H), 5.03 (m, 1H), 3.59−3.46 (m, 2H), 2.33 (s, 3H); $^{13}C$ NMR (DMSO-$d_6$, 100 MHz) $\delta$ 145.8, 135.2, 133.9, 130.4, 127.8, 126.7, 126.3, 124.3, 123.8, 122.8, 117.5, 115.6, 65.6, 55.5, 21.0; EIMS *m/e* (relative intensity) 436/434 (1). Anal. Calcd for $C_{17}H_{15}BrN_4O_3S$: C, 46.89; H, 3.45; N, 12.87. Found: C, 46.61; H, 3.48; N, 12.80.

**(*R*)-2-*N*-(*tert*-Butyloxycarbonyl)-1-(*N*-tosyl-6-bromoindol-3-yl)-1-ethanol (6).** To a suspension of compound **5** (690 mg, 1.58 mmol) in MeOH (30 mL) under argon was added tin(II) chloride dihydrate (1.08 g, 4.8 mmol). The reaction mixture was stirred for 20 h at 30 °C and diluted with water (10 mL) and 6 N NaOH (10 mL). The resulting mixture was stirred for 30 min and then extracted with ethyl acetate (3 × 50 mL). The combined organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated to give the amine as a foam, which was used in the next step without purification. To a mixture of the crude amine and $Et_3N$ (0.5 mL, 3 mmol) in dichloromethane (20 mL) was added di-*tert*-butyl dicarbonate (415 mg, 1.9 mmol) in an ice-cooled bath. The reaction was stirred at room temperature for 3 h and diluted with dichloromethane (10 mL), then washed with water and brine, dried ($Na_2SO_4$), and concentrated in vacuo. The crude product was purified by flash chromatography (silica, Hex/AcOEt 2:1) to provide compound **6** (600 mg, 74% yield in two steps) as a white solid. $[\alpha]^{20}_D = -43$ (*c* 0.475, $CHCl_3$); IR (KBr) 3421, 1691 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz) $\delta$ 8.16 (d, $J$ = 1.7 Hz, 1H), 7.76 (d, $J$ = 8.4 Hz, 2H), 7.53 (d, $J$ = 1.0 Hz, 1H), 7.48 (d, $J$ = 8.5 Hz, 1H), 7.34 (dd, $J$ = 8.5 and 1.7 Hz, 1H), 7.25 (d, $J$ = 8.4 Hz, 2H), 5.03 (m, 1H), 4.94 (br, 1H), 3.6 (m, 1H), 3.33 (m, 2H), 2.36 (s, 3H), 1.45 (s, 9H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 157.1, 145.4, 136.0, 134.9, 130.1, 127.5, 126.8, 126.6, 123.6, 123.2, 121.4, 118.6, 116.7, 80.2, 68.0, 47.0, 28.3, 21.6;

(12) Muratake, H.; Natsume, M. *Heterocycles* **1989**, *29*, 783.

ESIMS *m/e* 533.2 (M + Na). Anal. Calcd for $C_{22}H_{25}BrN_2O_5S$: C, 51.87; H, 4.91; N, 5.50. Found: C, 51.75; H, 5.11; N, 5.28.

**(*S*)-*N*-(*tert*-Butyloxycarbonyl)-2-(*N*-tosyl-6-bromoindol-3-yl)-1-azidoethylamine (7).** To a solution of compound **6** (0.54 g, 1.06 mmol) in anhydrous THF (20 mL) were added triphenylphosphine (1.05 g, 4 mmol), diethyl azodicarboxylate (40% in toluene, 1.84 mL, 4 mmol), and diphenylphosphoryl azide (0.86 mL, 4 mmol) at −20 °C. The mixture was stirred for 6 h at this temperature and then allowed to warm to room temperature and stirred overnight. The solvent was evaporated under reduced pressure, and the residue was directly subjected to flash chromatography (silica, Hex/AcOEt 4:1) to give intermediate **7** (0.47 g, 83%) as a syrup. $[\alpha]^{20}_D = +68$ (*c* 0.415, $CHCl_3$); IR (KBr) 3423, 2106, 1709 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz) $\delta$ 8.17 (d, *J* = 1.6 Hz, 1H), 7.77 (dd, *J* = 6.7 and 1.7 Hz, 2H), 7.56 (d, *J* = 0.8 Hz, 1H), 7.52 (d, *J* = 8.4 Hz, 1H), 7.38 (dd, *J* = 8.5 and 1.6 Hz, 1H), 7.27 (d, *J* = 8.4 Hz, 2H), 4.89 (br, 2H), 3.58 (m, 1H), 3.32 (m, 1H), 2.37 (s, 3H), 1.45 (s, 9H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 155.8, 145.6, 136.0, 134.6, 130.2, 127.3, 126.9, 124.5, 121.3, 119.1, 118.5, 116.9, 80.1, 58.5, 44.8, 28.3, 28.3, 21.6; ESIMS *m/z*: 556.2 (M + Na). Anal. Calcd for $C_{22}H_{24}BrN_5O_4S$: C, 49.44; H, 4.49; N, 13.11. Found: C, 49.68; H, 4.66; N, 12.96.

**(*S*)-*N*-[2-Azido-2-(*N*-tosyl-6-bromo-indol-3-yl)ethyl]-2-(6-bromo-1*H*-indol-3-yl)-2-oxoacetamide (9).** To a stirred solution of compound **7** (440 mg, 0.82 mmol) in $CH_2Cl_2$ (20 mL) was added trifluoroacetic acid (3.1 mL, 40 mmol) in an ice−water bath under argon. The reaction solution was stirred at room temperature overnight and quenched by the addition of water (20 mL). The water phase was neutralized with aqueous 1 N NaOH and extracted with $CH_2Cl_2$ (2 × 20 mL). The combined organic layer was washed with saturated $NaHCO_3$ and brine successively, then dried over $Na_2SO_4$, and concentrated in vacuo to give the crude amine as a yellow oil. To a solution of the yellow oil and triethylamine (0.42 mL, 3 mmol) in dry DMF (15 mL) cooled in an ice bath was added dropwise a solution of 6-bromo-3-indolyl-α-oxoacetyl chloride **8**[4] (432 mg, 1.5 mmol) in dry DMF (5 mL). After 4 h, water (30 mL) was added and the resulting mixture was extracted with ethyl acetate (3 × 20 mL). The organic phase was washed with water and brine successively, dried ($Na_2SO_4$), and then concentrated in vacuo. Flash chromatography (silica, Hex/AcOEt 3:1) gave compound **9** (490 mg, 93%) as a light yellow solid. Mp 160 °C; $[\alpha]^{20}_D = +37$ (*c* 0.48, $CHCl_3$); IR (KBr) 3377, 2105, 1636 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz) $\delta$ 8.98 (d, *J* = 3.2 Hz, 1H), 8.78 (br s, 1H), 8.28 (d, *J* = 8.5 Hz, 1H), 8.17 (d, *J* = 1.7 Hz, 1H), 7.75 (d, *J* = 8.4 Hz, 2H), 7.64 (s, 1H), 7.61 (d, *J* = 1.7 Hz, 1H), 7.54 (d, *J* = 8.5 Hz, 1H), 7.46 (dd, *J* = 8.5 and 1.6 Hz, 1H), 7.39 (dd, *J* = 8.5 and 1.6 Hz, 1H), 4.96 (dd, *J* = 8.1 and 5.0 Hz, 1H), 3.88 (m, 1H), 3.63 (m, 1H), 2.32 (s, 3H); $^{13}C$ NMR (DMSO-$d_6$, 100 MHz) $\delta$ 181.5, 163.4, 145.8, 139.4, 137.2, 135.1, 133.6, 130.3, 127.8, 126.7, 125.9, 125.5, 125.2, 122.9, 122.1, 118.2, 118.1, 116.0, 115.8, 115.4, 112.0, 56.1, 41.7, 20.9; EIMS *m/e* 640 (M − $N_3$). Anal. Calcd for $C_{27}H_{20}Br_2N_6O_4S$: C, 47.37; H, 2.92; N, 12.28. Found: C, 47.34; H, 3.20; N, 11.91.

**(*S*)-3-(6-Bromoindol-3-yl)-5-(*N*-tosyl-6-bromoindol-3-yl)-5,6-dihydro-2(1*H*)-pyrazinone (10).** To a solution of compound **9** (330 mg, 0.48 mmol) in dry toluene (25 mL) was added tributylphosphine (202 μL, 0.80 mmol). The mixture was stirred at room temperature for 2 h and then warmed to reflux for 20 h under an argon atmosphere. After the removal of toluene, the residue was subjected to flash chromatography (silica, Hex/AcOEt 1:1 and 1:2) to give compound **10** (270 mg, 82%) as a yellow solid. Mp 166 °C; $[\alpha]^{20}_D = +116$ (*c* 0.20, $CH_3OH$); IR (KBr) 3397, 1682 $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$, 300 MHz) $\delta$ 11.69 (br s, 1H), 8.61 (br s, 1H), 8.43 (s, 1H), 8.19 (d, *J* = 8.5 Hz, 1H), 8.08 (d, *J* = 1.6 Hz, 1H), 7.89 (d, *J* = 8.4 Hz, 2H), 7.79 (d, *J* = 8.5 Hz, 1H), 7.75 (d, *J* = 0.8 Hz, 1H), 7.65 (d, *J* = 1.7 Hz, 1H), 7.47 (dd, *J* = 10.2 and 1.7 Hz, 1H), 7.43 (d, *J* = 8.2 Hz, 2H), 7.19 (dd, *J* = 10.2 and 1.8 Hz, 1H), 5.26 (dd, *J* = 10.0 and 4.9 Hz, 1H), 3.63 (dd, *J* = 12.9 and 5.0 Hz, 1H), 3.52 (dd, *J* = 12.9 and 10.2 Hz, 1H), 2.34 (s, 3H); $^{13}C$ NMR (DMSO-$d_6$, 100 MHz) $\delta$ 157.6, 157.2, 145.8, 137.2, 135.4, 133.8, 133.3, 130.4, 128.5, 126.7, 126.4, 124.9, 124.3, 123.8, 123.5, 122.8, 117.8, 115.8, 114.9, 114.5, 110.9, 53.2, 42.4, 21.0. Anal. Calcd for $C_{27}H_{20}Br_2N_4O_3S$: C, 50.63; H, 3.13; N, 8.75. Found: C, 50.89; H, 3.31; N, 8.55.

**Hamacanthin B (1).** To a solution of compound **10** (32 mg, 0.05 mmol) in 4 mL of THF was added L-Selectride (1M in THF, 0.5 mL, 0.5 mmol) under an argon atmosphere. After the resulting solution was refluxed for 4 h, the reaction was quenched with methanol (2 drops) and diluted by the addition of water (5 mL). The mixture was extracted with ethyl acetate (3 × 10 mL). The organic layer was washed with water and brine successively, dried ($Na_2SO_4$), and concentrated in vacuo. Purification by flash chromatography (silica, $CH_2Cl_2$/MeOH 50:1) gave hamacanthin B (**1**) (18 mg, 75%) as a yellow solid. $[\alpha]^{20}_D = +183$ (*c* 0.10, $CH_3OH$) {lit.[3] $[\alpha]^{20}_D = +176$ (*c* 0.10, $CH_3OH$)}; IR (KBr) 1674 $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$, 600 MHz) $\delta$ 11.62 (br, 1H), 11.13 (s, 1H), 8.48 (br, 1H), 8.41 (s, 1H), 8.30 (d, *J* = 9 Hz, 1H), 7.66 (d, *J* = 9 Hz, 1H), 7.63 (d, *J* = 1.7 Hz, 1H), 7.59 (d, *J* = 1.7 Hz, 1H), 7.28 (d, *J* = 1.8 Hz, 1H), 7.18 (dd, *J* = 8.4 and 1.6 Hz, 1H), 7.14 (dd, *J* = 8.4 and 1.6 Hz, 1H), 3.62 (dd, *J* = 12.8 and 5.0 Hz, 1H), 3.46 (dd, *J* = 12.8 and 9.0 Hz, 1H); $^1H$ NMR ($CDCl_3$/15% $CD_3OD$, 600 MHz) $\delta$ 8.52 (br, 1H), 8.29 (d, *J* = 8.4 Hz, 1H), 7.60 (m, 3H), 7.29 (d, *J* = 8.4 Hz, 1H), 7.27 (s, 1H), 7.22 (dd, *J* = 8.4 and 1.8 Hz, 1H), 5.43 (dd, *J* = 9.0 and 5.4 Hz, 1H), 3.84 (dd, *J* = 13.2 and 4.8 Hz, 1H), 3.70 (dd, *J* = 13.2 and 9.0 Hz, 1H); $^{13}C$ NMR (DMSO-$d_6$, 100 MHz) $\delta$ 157.3, 157.1, 137.4, 137.1, 132.9, 125.1, 124.1, 123.8, 123.4, 121.4, 120.9, 114.9, 114.8, 114.3, 114.2, 114.0, 111.1, 53.7, 43.3; EIMS *m/e* (relative intensity) 486/482 (32/32); HREIMS calcd for $C_{20}H_{14}{}^{79}Br_2N_4O$: 483.9545; found 483.9544. Anal. Calcd for $C_{20}H_{14}Br_2N_4O$: C, 49.41; H, 2.90; N, 11.52; Found: C, 49.44; H, 2.98; N, 11.50.

**Acknowledgment.** We are grateful for financiall support from Shanghai Municipal Committee of Science and Technology.

**Supporting Information Available:** $^1H$ and $^{13}C$ NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0108109