Pergamon

Tetrahedron: *Asymmetry* 13 (2002) 2261–2266

TETRAHEDRON: *ASYMMETRY*

Asymmetric synthesis of amathamides A and B: novel alkaloids isolated from *Amathia wilsoni*

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Received 29 August 2002; accepted 17 September 2002

Abstract—Syntheses of the amathamides A and B ((2*S*)-*N*-[(*E* and *Z*)-2(2,4-dibromo-5-methoxyphenylethenyl]-1-methyl-2-pyrrolinecarboxamides), new alkaloids isolated from the Tasmanian marine bryozoan *Amathia wilsoni*, were accomplished by a sequence of reactions starting from 3-hydroxybenzaldehyde.

1. Introduction

The enamides form a small but important group of naturally occurring compounds which have been isolated from a number of different sources, including terrestrial plants,[1–3] microorganisms,[4–6] and marine organisms.[7–11] In general, compounds belonging to this class of enamides show an array of biological effects, including antibiotic,[4] protein kinase inhibition,[5] and antitumor activity.[12] In addition to these acyclic enamides, several cyclopeptide alkaloids having the enamide (styrylamide) unit have also been isolated from terrestrial plants. Some of these cyclic enamide peptides have pharmacological activity.[13]

Marine invertebrates are currently the focus of an intense worldwide search for new pharmacologically active cytotoxic and antineoplastic agents. The marine invertebrate *Amathia wilsoni* Kirkpatrick,[14] a bryozoan endemic to the Australian subcontinent, has yielded five novel enamide alkaloids **1**–**5** (Fig. 1). It has been suggested that these alkaloids are biosynthetically-derived from phenylalanine,[14] which is enzymatically brominated followed by acylation with proline and further transformation to give the corresponding alkaloids **1**–**5**. It was originally suggested that the amathamides were metabolites from *A. wilsoni*,[14] but new evidence suggests that they may be derived from a symbiotic bacterium living in the bryozoan.[15] Additionally, the recently isolated brominated spiran compounds, amathaspiramides A–F,[16] are believed to be biosynthetically-derived from amathamides.

Our previous studies relating to the synthesis of *N*-formyl enamides, for example tuberine (isolated from *Streptomyces amakusaensis*)[17] and *N*-benzoyl cinnamoyl and nicotinoyl amides[18] (obtained from several species of the Rutaceae family), prompted us to investigate the synthesis of amathamides using the same general synthetic route.

2. Results and discussion

Bromination of 3-hydroxybenzaldehyde (**6**, Scheme 1),[19] gave either **7a** (2 equiv. Br_2 in $CHCl_3$, rt, 92%) or **7b** (4 equiv. in H_2O, rt, 90%) in excellent yields. Aldehydes **7a** and **7b** were then treated with methyl iodide in DMF in the presence of K_2CO_3 to give methyl ethers **8a** and **8b**, respectively, and subsequently condensed with nitromethane in the presence of ammonium acetate to give the nitroolefins **9a** and **9b** in 50–44% yields. Michael addition of thiophenol with a catalytic amount of *N*-isopropylcyclohexylamine to each nitroolefin gave the adducts **10a** and **10b** in 92–95% yields. Reduction of the dibromo compound **10a** with lithium aluminum hydride at −15°C gave the desired amine **11a** in 95% purity along with some mono-bromo reduction product. However, on reaction of the tribromo compound **10b** with lithium aluminum hydride at a variety of temperatures, displacement of the C-2 bromine atom by hydride occurred to give the unwanted product **11a**. Having explored a number of methods for the nitro reduction, we found that using samarium diiodide[20] as

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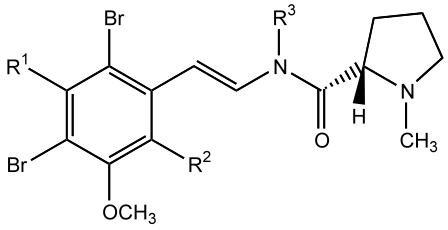
0957-4166/02/$ - see front matter
PII: S0957-4166(02)00586-4

	R^1	R^2	R^3	
1	H	H	H	Amathamide A
2	Br	H	CH_3	Amathamide C
3	Br	H	H	Amathamide E



	R^1	R^2	R^3	
4	H	H	H	Amathamide B
5	Br	H	H	Amathamide F

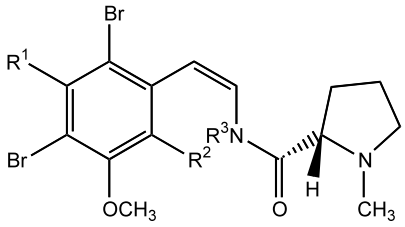


Figure 1. Structures of Amathamides **A**, **B**, **C**, **E** and **F**.

the reducing agent (rt, THF), gave the desired amine **11b** cleanly, with no substitution of bromine (Scheme 1).

Acylation of **11a** and **11b** with L-(*S*)-*N*-methylproline in the presence of DCC gave the thioacylated products **12a** and **12b** in 33–30% yields. Oxidation of **12a** and **12b** with sodium periodate and subsequent elimination of thiophenol led to the desired amathamides A **1** and B **4** in 23 and 1.1% yields, respectively. ^{1}H NMR indicated the amathamide was formed as a mixture of *trans* and *cis* isomers (95:5), which were then separated by chromatography on a Chromatotron to afford the *trans* amathamide **A 1** and *cis* **B 4**. Amathamide **A** gave a rotation of $[\alpha]_D^{25} = -46$ (*c* 0.005) in dichloromethane (no specific rotation value has previously been reported for the natural product Amathamide **A 1**). Using circular dichroism, Blackman and coworkers predicted the natural product amathamide **A** to be derived from (*S*)-proline, which is in agreement with our synthetic material. Using the same route we also synthesized the tribromoamathamide **13**, an isomer of amathamide **E** isolated from *A. wilsoni*. Further comparison of the ^{1}H NMR spectrum of the synthetic material **13** with the natural product amathamide **E**, established that the isolated natural material has the bromine atoms adjacent to each other as proposed by the authors (δ 7.05 for aromatic ring proton (amathamide **E**) and δ 7.78 for aromatic ring proton of isomer **13**).

One of the attractive features of our synthetic route is its flexibility, since a variety of non-natural analogues could be made available for biological testing by simply altering the acyl group or the aryl group.

3. Experimental

3.1. 2,4-Dibromo-5-hydroxybenzaldehyde, 7a

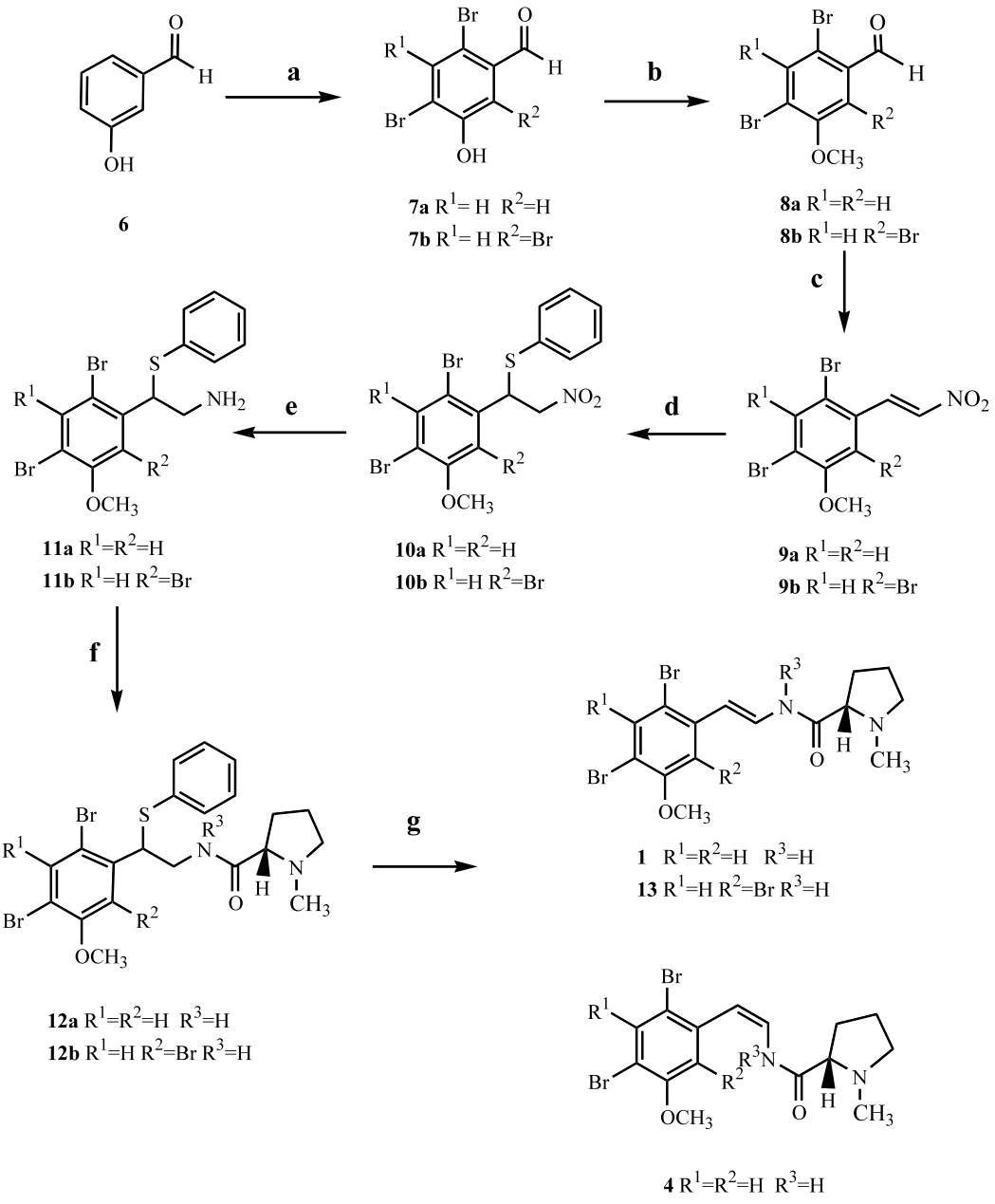
To a solution of 3-hydroxybenzaldehyde (40.9 mmol, 5.00 g) in $CHCl_3$ (100 mL) was added bromine (81.7 mmol, 4.2 mL). The resulting solution was stirred at rt for 3 days. The excess bromine was removed with a saturated solution of sodium thiosulfate (20 mL), the organic phase was washed with water and dried over anhydrous Na_2SO_4. Removal of solvent gave a solid which was recrystallized from acetic acid to give **7a** (10.5 g, 92%); mp 134–5°C, lit.[19] 134°C; IR (KBr) 3440, 3076, 2877, 1675, 1553, 1085 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.23 (s, 1H), 7.80 (s, 1H), 7.54 (s, 1H), 6.33 (s, 1H) ppm; MS (EI) *m*/*z* (%) 278 (M,$^+$ 15), 63 (100).

3.2. 2,4,6-Tribromo-5-hydroxybenzaldehyde, 7b

To a solution of 3-hydroxybenzaldehyde (24.6 mmol, 3.00 g) in water (200 mL) was slowly added bromine (94.9 mmol, 4.8 mL). The resulting solution was stirred at rt for 1 day, the excess bromine was removed with a saturated solution of sodium thiosulfate (20 mL) and the residue extracted into diethyl ether. The organic layer was separated, dried over anhydrous sodium sulfate and the solvent removed to give a yellow solid. The crude product was recrystallized from acetic acid to give **7b** as a pale yellow solid (8.79 g, 90%); mp 115–16°C, lit.[19] 119°C; IR (KBr) 3356, 1687, 1002 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 10.17 (s, 1H), 7.84 (s, 1H), 6.35 (bs, 1H) ppm; MS (EI) *m*/*z* (%) 358 (M,$^{+2}$ 100), 356 (M,$^+$ 35).

3.3. 2,4-Dibromo-5-methoxybenzaldehyde, 8a

To a solution of **7a** (5.6 mmol, 1.56 g) and K_2CO_3 (1.50 g) in dry DMF (50 mL) was added methyl iodide (6.13 mmol, 0.38 mL) and the mixture was stirred for 4 h at rt. The reaction mixture was quenched with water (50 mL) and the organic phase extracted into diethyl ether, dried over anhydrous sodium sulfate and the solvent removed to give a white solid (1.60 g, 98%); mp 110–11°C, lit.[19] 110°C; IR (KBr) 3010, 2993, 1679, 1575 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.25 (s, 1H), 7.85 (s, 1H), 7.40 (s, 1H), 3.95 (s, 3H) ppm; MS (EI) *m*/*z* (%) 294 (M,$^{+2}$ 100), 292 (M,$^+$ 55).



Scheme 1. *Reagents and conditions*: (a) i. $CHCl_3$, Br_2, **7a** 92%; ii. H_2O, Br_2, **7b** 90%; (b) CH_3I, DMF, K_2CO_3, **8a** 98%, **8b** 81%; (c) CH_3NO_2, AcOH, $AcONH_4$, **9a** 50%, **9b** 44%; (d) PhSH, Base, CH_2Cl_2, **10a** 95%, **10b** 92%; (e) SmI_2, THF, **11a** 65%, **11b** 60%; (f) DCC, DMAP, HOBT, (*S*)-*N*-methyl-L-Proline, **11a** 33%, **11b** 30%; (g) i. $NaIO_4$, MeOH; ii. Toluene, K_2CO_3, reflux, **1** 23%, **13** 20%, **4** 1.15%

3.3.1. 2,4,6-Tribromo-3-methoxybenzaldehyde, 8b. Using **7b** (14.0 mmol, 5.00 g), compound **8b** was obtained as a white solid using the procedure described above for **8a** (4.20 g, 81%); mp 97–98°C; IR (KBr) 3020, 1693, 1527, 1018 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 10.15 (s, 1H), 7.89 (s, 1H), 3.91 (s, 3H) ppm; MS (EI) m/z (%) 372 ($M,^{+2}$ 100), 370 ($M,^{+}$ 37).

3.4. (*E*)-2,4-Dibromo-5-methoxy-β-nitrostyrene, 9a

To a solution of **8a** (35.2 mmol, 10.3 g) in glacial AcOH (30 mL) was added ammonium acetate (35.5 mmol, 2.71 g) and nitromethane (242 mmol, 13.1 mL). The solution was heated under reflux with magnetic stirring for 1 h. The mixture was cooled to rt, the green yellowish precipitate was collected by filtration and it was washed with water. The solid was then dissolved in dichloromethane (100 mL), filtered through a plug of silica gel and then the organic phase was dried over anhydrous sodium sulfate and concentrated under reduced pressure to give a yellowish green solid (5.92 g, 50%); mp 167–168°C; IR (KBr) 3122, 2856, 1626, 1517 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 8.29 (d, 1H, $J=13.6$ Hz), 7.86 (s, 1H), 7.55 (d, 1H, $J=13.6$ Hz), 6.98 (s, 1H), 3.94 (s, 3H) ppm; MS (EI) m/z (%) 335 ($M,^{+}$ 30). Anal. calcd for $C_9H_7Br_2NO_3$: C, 32.05; H, 2.08. Found: C, 32.09; H, 2.11%.

3.4.1. (*E*)-2-4-6-Tribromo-5-methoxy-β-nitrostyrene, 9b. Compound **9b** was synthesized from **8b** (13.4 mmol, 5.00 g), using the same procedure described above for **9a**. A brownish yellow solid was obtained (2.46 g, 44%); mp 93°C; IR (KBr) 3127, 2848, 1644, 1527 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.98 (d, 1H, $J=13.8$ Hz), 7.89 (s, 1H), 7.56 (d, 1H, $J=14.0$ Hz), 3.91 (s, 3H) ppm; MS (EI) m/z (%) 417 ($M,^{+4}$ 100), 413 ($M,^{+}$ 34). Anal. calcd for $C_9H_6Br_3NO_3$: C, 25.96; H, 1.44. Found: C, 26.01; H, 1.49%.

3.5. 2-(2,4-Dibromo-5-methoxyphenyl)-2-(thiophenyl)-1-nitroethane, 10a

Compound **9a** (1.4 mmol, 0.47 g) was dissolved in methylene chloride (20 mL) and to the solution was added thiophenol (1.9 mmol, 0.20 mL) and 4 drops of *N*-isopropylcyclohexylamine. The resulting solution was stirred for 1 h at rt. The solution was concentrated and the crude reaction mixture was poured on silica gel, agitated to remove solvent and then was subjected to flash chromatography on silica gel using methylene chloride: hexane (20:80) as eluting solvent. Removal of the solvent gave a dark yellow oil (0.60 g, 95%); IR (CH_2Cl_2) 3070, 2847, 2937, 1554 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.26–7.36 (m, 5H), 6.60 (s, 1H), 5.27–5.35 (m, 1H), 4.70–4.91 (m, 2H), 3.76 (s, 3H) ppm; MS (EI) m/z (%) 443 ($M,^{+}$ 4), 292 (100). Anal. calcd for $C_{15}H_{13}Br_2NO_3S$: C, 40.27; H, 2.90. Found: C, 40.31; H, 2.93%.

3.6. 2-(2,4,6-Tribromo-3-methoxyphenyl)-2-(thiophenyl)-1-nitroethane, 10b

Compound **10b** was synthesized from **9b** (1.00 g, 2.4 mmol), using the procedure for **10a**. Light yellow liquid (1.19 g, 92%); IR (KBr) 3070, 2935, 1554 cm^{-1}; The ^1H NMR showed a mixture 1:1 of atropoisomers. ^1H NMR (400 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.78 (s, 1H), 7.52–7.32 (m, 10H) for two isomers, 5.86 (t, 1H, $J=7.4$ Hz), 5.72 (t, 1H, $J=7.2$ Hz), 5.36–5.26 (m, 2H), 5.12–5.02 (m, 2H), 3.89 (s, 3H), 3.82 (s, 3H) ppm; MS (EI) m/z (%) 523 ($M,^{+}$ 10), 370 (100). Anal. calcd for $C_{15}H_{12}Br_3NO_3S$: C, 34.22; H, 2.28. Found: C, 34.24; H, 2.29%.

3.7. Reduction of 2-(2,4-dibromo-5-methoxyphenyl)-2-(thiophenyl)-1-nitroethane, 10a, with samarium diiodide to give 11a

To a solution of samarium diiodide (0.1N, 45.0 mL, 4.5 mmol) under argon at rt, was added **10a** (0.44 mmol, 0.19 g) in dry methanol (0.25 mL). The solution was stirred for 30 h and the reaction was quenched by adding saturated sodium thiosulfate solution (3 mL) and the mixture was concentrated in vacuo. The residue was extracted into methylene chloride (50 mL), the organic phase dried over anhydrous sodium sulfate and the solvent was removed under reduced pressure to give amine **11a** as pale brown oil (0.12 g, 65%). The amine **11a** was then used in the next step without further purification. IR (CH_2Cl_2) 3361, 3175, 3004, 1581, 1469 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.25 (m, 5H), 6.85 (s, 1H), 5.15 (t, 1H, $J=7.2$ Hz), 3.80 (s, 3H), 3.30 (dd, 2H, $J=7.2$ and 3.2 Hz).

3.8. 2-(2,4,6-Tribromo-3-methoxyphenyl)-2-(thiophenyl)-1-aminoethane, 11b

Compound **11b** was synthesized from **10b** (0.95 mmol, 0.500 g), using the same procedure described for amine **11a**. Compound **11b** was obtained as atropoisomers: Yellow liquid (0.284 g, 71%); IR (CH_2Cl_2) 3448, 3363, 2935, 1581 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) 7.79 (s, 1H), 7.75 (s, 1H), 7.50 (m, 5H), 7.30 (m, 5H), 5.43 (t, 1H, $J=7.9$ Hz), 5.43 (t, 1H, $J=7.9$ Hz), 3.89 (s, 3H), 3.81 (s, 3H).

3.9. 2(*S*)-*N*-[2(2,4-Dibromo-5-methoxyphenyl)-2-(thiophenyl)ethane]-1-methyl-2-pyrrolinecarboxamide, 12a

To a stirred solution of (*S*)-*N*-methylproline (0.28 mmol, 0.036 g) in dry tetrahydrofuran (20 mL) was added dicyclohexylcarbodiimide (0.28 mmol, 0.057 g), 1-hydroxybenzotriazole (0.28 mmol 0.0378 g) and 4-*N*,*N*-dimethylaminopyridine in catalytic amounts. A solution of amine **11a** (0.28 mmol, 0.12 g) in dry THF (10 mL) was added to the suspension. The suspension was stirred for 18 h, filtered and the solvent removed in vacuo. The residue was purified by circular chromatography using methylene chloride as eluting solvent. Removal of the solvent gave a yellow oil (0.078 g, 33%); IR (CH_2Cl_2) 3327, 3058, 2937, 1668, 1580 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.68 (s, 1H), 7.51 (bs, 2H), 7.36–7.32 (m, 4H), 7.28–7.24 (m, 6H), 6.87 (s, 1H), 6.85 (s, 1H), 4.84–4.78 (m, 2H), 3.92–3.82 (m, 2H), 3.80 (s, 3H), 3.79 (s, 3H), 3.68–3.60 (m, 2H), 3.06–2.98 (m, 2H), 2.86–2.76 (m, 2H), 2.32–2.24 (m, 2H), 2.26 (s, 3H), 2.16 (s, 3H), 2.20–2.02 (m, 4H), 1.84–1.4 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.64, 138.82, 136.33, 136.29, 133.27, 132.89, 132.85, 129.22, 128.15, 115.37, 115.30, 112.37, 112.33, 111.63, 111.60, 68.98, 56.84, 56.77, 56.66, 51.25, 51.16, 42.49, 42.43, 41.89, 41.69, 31.11, 31.06, 24.50, 24.43 ppm; MS (EI) m/z (%) 526 ($M,^{+}$ 23), 84 (100). Anal. calcd for $C_{21}H_{24}Br_2N_2O_2S$: C, 47.72; H, 4.55. Found: C, 47.76; H, 4.59%.

3.10. (*S*)-*N*-[2(2,4,6-Tribromo-5-methoxyphenyl)-2-(thiophenyl)ethane]-1-methyl-2-pyrrolinecarboxamide, 12b

Compound **12b** was synthesized from **11b** (0.38 mmol, 0.200 g), using the same procedure described for amide **12a**. Compound **12b** was obtained as a yellow liquid (0.069 g, 30% yield); IR (CH_2Cl_2) 3348, 2938, 2847, 2789, 1673, 1508, 1452 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.80 (s, 1H), 7.74 (s, 1H), 7.6–7.2 (m, 10H) for both isomers, 5.47–5.18 (m, 2H) for both isomers, 4.3–4.1 (m, 2H), 4.05–3.88 (m, 2H), 3.90 (s, 3H), 3.80 (s, 3H), 3.04–2.9 (m, 2H), 2.85–2.77 (m, 2H), 2.40–2.00 (m, 2H), 2.22 (s, 3H), 2.18 (s, 3H), 1.8–1.4 (m, 8H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 155.07, 153.99, 139.74, 139.58, 137.65, 136.27, 135.99, 135.83, 132.24, 132.19, 132.12, 132.09, 129.27, 127.75, 127.71, 125.89, 124.06, 121.61, 121.29, 118.81, 117.43, 117.35, 77.48, 77.22,

76.97, 68.92, 60.90, 60.54, 56.92, 56.85, 55.54, 55.32, 54.91, 54.68, 42.00, 41.85, 41.66, 31.10, 24.57, 24.51. Anal. calcd for $C_{21}H_{23}Br_3N_2O_2S$: C, 41.52; H, 3.79. Found: C, 41.57; H, 3.83%.

3.11. (*E*)- and (*Z*)-2(*S*)-*N*-[-2(2,4-Dibromo-5-methoxyphenyl)ethanyl]-1-methyl-2-pyrroline carboxamide, 1 and 4

To a solution of **12a** (0.36 mmol, 0.190 g) in methanol was added a solution of sodium periodate (0.43 mmol, 0.093 g) in water (2 mL) and the resulting mixture heated under reflux for 2 h. The methanol was removed in vacuo and the aqueous residue was extracted into methylene chloride, dried over anhydrous sodium sulfate and the solvent removed to give sulfoxide as an oil. The crude product was then used in the next step without further purification. The sulfoxide was dissolved in toluene (25 mL), sodium carbonate was added (0.030 g) and the mixture heated under reflux for 4 h. The solvent was removed in vacuo and the residue extracted into methylene chloride (30 mL), dried over anhydrous sodium sulfate and the solvent removed to give an oil. The crude mixture was separated on preparative thin layer chromatography using methylene chloride–methanol (95:5) as the eluting solvent into the isomers (*E*)-1 and (*Z*)-4.

3.11.1. (2*S*)-*N*-[(*E*)-2(2,4-Dibromo-5-methoxyphenyl)-ethanyl]-1-methyl-2-pyrrolinecarboxamide, 1. White solid (0.034 g, 23% yield); mp 188–191°C, lit.[15] 189–190°C; $[\alpha]_D^{25} = -46$ (*c* 0.002, CH_2Cl_2); IR (CH_2Cl_2) 3259, 1676, 1643 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.32 (d, 1H, $J = 11.55$ Hz), 7.67 (s, 1H), 7.47 (dd, 1H, $J = 14.55$ and 11.55 Hz), 7.00 (s, 1H), 6.43 (d, 1H, $J = 14.57$ Hz), 3.91 (s, 3H), 3.19 (m, 1H), 3.03 (dd, 1H, $J = 10.37$ and 4.96 Hz), 2.44 (s, 3H), 2.44 (m, 1H), 2.29 (m, 1H), 1.92 (m, 1H), 1.86 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.2, 155.8, 136.7, 136.7, 125.1, 114.2, 111.9, 110.8, 108.6, 69.2, 57.2, 57.0, 42.5, 31.6, 25.1; MS (EI) *m*/*z* (%) 416 ($M,^+$ 40), 84(100). Anal. calcd for $C_{15}H_{18}Br_2N_2O_2$: C, 43.06; H, 4.31. Found: C, 43.11; H, 4.36%.

3.11.2. (2*S*)-*N*-[(*Z*)-2(2,4-Dibromo-5-methoxyphenyl)-ethanyl]-1-methyl-2-pyrrolinecarboxamide, 4. Yellow liquid (0.002 g, 1.1% yield); IR (CH_2Cl_2) 3310, 1689, 1647 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 9.44 (d, 1H, $J = 12.10$ Hz), 7.78 (s, 1H), 7.00 (dd, 1H, $J = 12.10$ and 9.70 Hz), 6.90 (s, 1H), 5.75 (d, 1H, $J = 9.73$ Hz), 3.88 (s, 3H), 3.03 (m, 2H), 2.35 (s, 3H), 2.33 (m, 2H), 1.80 (m, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 172.38, 155.46, 136.89, 135.80, 123.00, 114.61, 112.00, 108.76, 68.97, 56.74, 56.35, 42.15, 31.00, 24.47; MS (EI) *m*/*z* (%) 416 ($M,^+$ 40); HRMS (FAB) calcd for $C_{15}H_{19}Br_2N_2O_2$ $(M+H)^+$ 416.9813. Found: 416.9816.

3.11.3. 2(*S*)-*N*-[(*E*)-2(2,4,6-Tribromo-5-methoxyphenyl)-ethenyl]-1-methyl-2-pyrrolinecarboxamide, 13. Compound **13** was obtained from **12b** (0.24 mmol, 0.145 g) using the same procedure described above for compound **1**. Yellow liquid (0.023 g, 20% yield); $[\alpha]_D^{25} = -9.8$ (*c* 0.01, CH_2Cl_2); IR (CH_2Cl_2) 3288, 3069, 2935, 1693, 1650, 1488 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 9.21 (dd, 1H, $J = 11.20$ Hz), 7.78 (s, 1H), 7.4 (dd, 1H, $J = 15.00$ and 11.20 Hz), 6.04(d, 1H, $J = 15.00$ Hz), 3.86 (s, 3H), 3.2 (m, 1H), 3.0 (dd, 1H, $J = 10{,}37$ and 4.96 Hz), 2.44 (s, 3H), 2.2–2.4 (m, 3H), 1.8 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 172.78, 154.29, 137.66, 135.87, 129.84, 120.96, 118.85, 116.03, 110.61, 69.04, 60.68, 56.97, 42.28, 31.26, 24.72. Anal. calcd for $C_{15}H_{17}Br_3N_2O_2$: C, 36.22; H, 3.42. Found: C, 36.27; H, 3.46%.

Acknowledgements

We gratefully acknowledge support for this project by CONACYT.

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