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Total synthesis of alboatrin, a phytotoxic metabolite from *Verticillium alboatrum*

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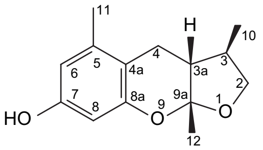
Abstract

A synthesis of the phytotoxic metabolite alboatrin **1** is described. An intramolecular ketene–olefin cycloaddition followed by an oxidative ring enlargement was employed to generate the tricyclic ring system.

Keywords: Alboatrin; Total synthesis; Intramolecular ketene–olefin cycloaddition

1. Introduction

Alboatrin is a phytotoxic metabolite isolated from the culture filtrate of *Verticillium alboatrum* by Ichihara et al.[1] The originally assigned structure was later modified to **1** involving inversion of the configuration of the secondary methyl group at C-3.[2] It inhibits the root growth of the host plant (Maris Kabul) and causes vascular-wilt disease in alfalfa. Alboatrin incorporates a linearly fused tetrahydrofurano benzopyran ring system rarely encountered in natural products and has three contiguous stereogenic centres. The recently isolated xyloketals are another group of marine metabolites, which possess this ring structure.[3] The unusual structural feature of **1** and the associated biological activity have prompted its synthesis.[1,2,4] In connection with our previous efforts on the synthesis of the aplysia group of marine sesquiterpenes, we had employed an intramolecular ketene–alkene cycloaddition followed by a ring expansion to generate the cyclopentanobenzofuran network of the natural products.[5] It occurred to us that a similar intramolecular ketene–alkene cycloaddition followed by an oxidative ring enlargement can provide a convenient access to the central tricyclic core of alboatrin. We describe here the successful application of this strategy to realize the synthesis of this metabolite.



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2. Results and discussion

The synthesis was started with orcinol monomethyl ether **2**.[6] This was alkylated with allyl bromide in acetone at reflux in the presence of potassium carbonate to furnish the allyl ether **3** in 96% yield. Thermal Claisen rearrangement of this allyl ether afforded a mixture of the rearranged phenols **4a** and **4b** in 86% yield in 2:1 proportion. An efficient separation was achieved through column chromatography. To enable the assignment of correct structures to these isomers, samples of both were converted to the dimethyl ethers **5a** and **5b**. The ^{13}C NMR spectra enabled the ready identification of both isomers with **5b** showing the expected nine signals due to its symmetrical nature (Scheme 1). Continuing with the synthesis, the phenol **4a** was alkylated with α-bromopropionic acid in

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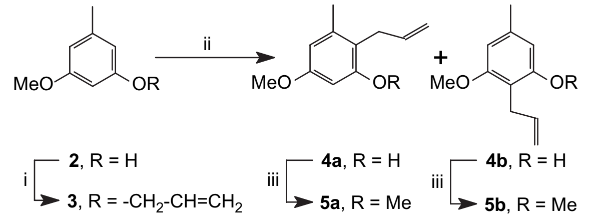
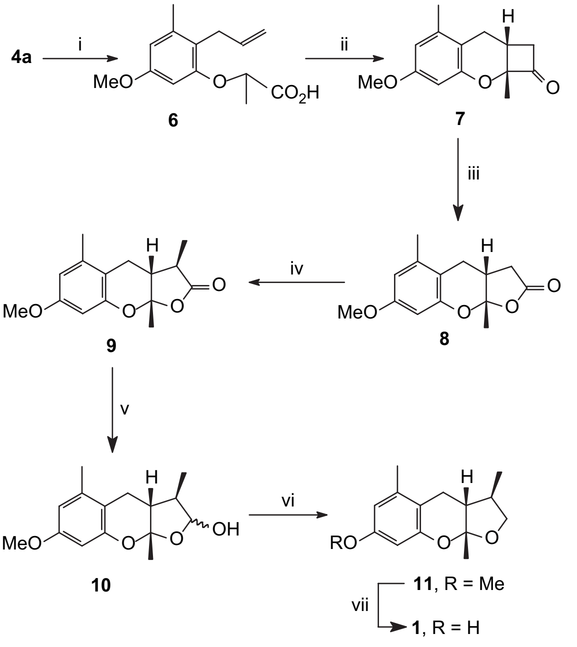
THF employing sodium hydride as the base, and furnished the alkylated carboxylic acid **6** in 83% yield as a colourless solid, mp 101–102 °C. The acid **6** on heating with toluene-*p*-sulfonyl chloride and triethylamine in benzene at reflux, underwent an intramolecular ketene–alkene cycloaddition[7,8] reaction and delivered the tricyclic cyclobutanone **7** as a colourless solid in 50% yield, mp 75–76 °C. The lower yield in the formation of bicyclic(4.2.0) ring systems from such cycloadditions was in conformity with the experience of others.[7,8] The structure of cyclobutanone **7** was adequately supported by analytical and spectral data. The assignment of the cis ring junction to this cyclobutanone was based on analogy with previous reports of such cycloadditions.[7,8]



Scheme 1. Reagents and conditions: (i) K_2CO_3, $CH_2{=}CHCH_2Br$, acetone, reflux, 5 h, 96%; (ii) 200 °C, 1 h, 86%; (iii) K_2CO_3, MeI, acetone, reflux, 8 h, 93%.

For carrying out the next step of oxidative ring enlargement, cyclobutanone **7** was treated with *m*-chloroperbenzoic acid in methylene chloride with added sodium bicarbonate and furnished the γ-lactone **8** as a colourless solid in 80% yield, mp 63–64 °C. The synthesis of lactone **8** thus generated the key tricyclic core of alboatrin **1**. The next step involved the stereocontrolled introduction of a secondary methyl group adjacent to the lactone carbonyl group. It was anticipated that during methylation of the lactone **8**, the methyl group will preferentially approach from the more accessible *exo* face of the molecule leading to the desired β-configuration of the secondary methyl group. In the event, when the lactone **8** was subjected to a methylation with iodomethane in the presence of LDA, it afforded the methylated lactone **9** as a colourless solid in 94% yield as a single isomer. The ^{1}H NMR spectrum showing a doublet at δ 1.25 confirmed the introduction of the methyl group and was assigned the β-configuration based on the arguments stated above. A final confirmation of this assignment however, hinged on its conversion to alboatrin **1** itself. For the reductive removal of the carbonyl oxygen it was reduced first with DIBAL-H to furnish lactol **10** as a mixture of isomers in 95% yield. No effort was made to separate the mixture since the next step involved a reductive removal of the hydroxy group. Treatment of the lactols **10** with triethylsilane in dichloromethane in the presence of trifluoroacetic acid[9] followed by chromatographic purification of the product afforded *O*-methylalboatrin **11** in 38% yield as a colourless low melting solid, mp 53–54 °C. Finally demethylation of **11** with boron tribromide in dichloromethane at −78 °C yielded the desired (±)-alboatrin **1** as colourless crystals, mp 146–147 °C (Scheme 2), which displayed spectral data [^{1}H and ^{13}C NMR] fully matching with reported values.[1,4] The synthesis thus additionally confirmed the assignment of the β-configuration to the C-3 methyl group.



Scheme 2. Reagents and conditions: (i) NaH, $CH_3CH(Br)CO_2H$, THF, reflux, 10 h, 83%; (ii) *p*-TsCl, Et_3N, benzene, reflux, 12 h, 50%; (iii) *m*-CPBA, $NaHCO_3$, CH_2Cl_2, rt, 6 h, 80%; (iv) LDA, HMPA, MeI, THF, −78 °C to rt, 10 h, 94%; (v) DIBAL-H, Et_2O, −78 °C, 2 h, 95%; (vi) CF_3CO_2H, Et_3SiH, CH_2Cl_2, −40 °C to rt, 15 min, 38%; (vii) BBr_3, CH_2Cl_2, −78 °C, 5 h, 80%.

In summary, we have described a synthesis of the phytotoxic metabolite alboatrin, employing an intramolecular ketene–olefin cycloaddition followed by an oxidative ring enlargement to generate the tricyclic structure of the compound.

3. Experimental

3.1. General

All non aqueous reactions were carried out under an inert atmosphere (nitrogen). Melting points were taken in open capillary tubes in a sulfuric acid bath and are uncorrected. Dry solvents and reagents were prepared from reagent grade materials by conventional methods. Petroleum ether refers to the fraction of bp 60–80 °C. The purity of the products was routinely monitored by TLC. Drying of organic layers was done with sodium sulfate. ^{1}H NMR spectra were recorded at 300 MHz in $CDCl_3$ solutions. ^{13}C NMR spectra were recorded in $CDCl_3$ solution at 75 MHz. Peak positions are indicated in parts per million downfield from an internal TMS standard. IR spectra of liquid products were recorded as thin films or in $CHCl_3$ solution. IR spectra of solids were recorded as KBr pellets.

3.1.1. 1-Allyloxy-3-methoxy-5-methylbenzene (**3**)

A mixture of monomethyl orcinol **2** (1.30 g, 9.40 mmol), anhydrous potassium carbonate (1.60 g, 11.6 mmol) and allyl bromide (1.40 g, 11.6 mmol) in acetone (30 mL) was heated at reflux for 5 h. The reaction mixture was then cooled and most of the acetone was distilled off. The residue was poured into water and extracted with ether (3×20 mL). The organic extract was washed with water, brine and dried. The residue after removal of solvent was subjected to column chromatography over silica gel. Elution with ethyl acetate–petroleum ether (1:24) furnished the allyl ether **3** (1.61 g, 96%) as a colourless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.30 (s, 3H), 3.77 (s, 3H), 4.50 (d, J=4.6 Hz, 2H), 5.26–5.30 (m, 1H), 5.37–5.44 (m, 1H), 6.00–6.10 (m, 1H), 6.31 (br s, 1H), 6.34 (br s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.2, 55.6, 69.2, 98.7, 107.7, 108.3, 117.9, 133.7, 140.6, 160.1, 161.0. Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.09; H, 7.93.

*3.1.2. 2-Allyl-5-methoxy-3-methylphenol (**4a**) and 2-allyl-3-methoxy-5-methylphenol (**4b**)*

The allyl ether **3** (200 mg, 1.12 mmol) was quickly heated to 220 °C and kept at that temperature for 1 h. Then it was allowed to cool to room temperature and the dark-brown rearranged product was subjected to column chromatography over silica gel. Elution with ethyl acetate–petroleum ether (1:24) furnished the rearranged phenol **4b** (57 mg, 28%) as a viscous oil. IR (neat) 3444 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.26 (s, 3H), 3.38 (d, J=6.9 Hz, 2H), 3.77 (s, 3H), 5.02–5.16 (m, 2H), 5.89–6.02 (m, 1H), 6.29 (s, 1H), 6.31 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.6, 27.2, 55.8, 104.4, 109.5, 110.7, 115.1, 136.6, 137.7, 154.9, 158.0. Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.14; H, 7.89.

Continued elution afforded the phenol **4a** (115 mg, 58%) as a colourless oil. IR (neat) 3440 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.16 (s, 3H), 3.26 (d, J=5.7 Hz, 2H), 3.64 (s, 3H), 4.87–4.97 (m, 2H), 5.80–5.89 (m, 1H), 6.18 (d, J=2.4 Hz, 1H), 6.27 (d, J=2.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.3, 30.5, 55.6, 99.9, 108.8, 115.5, 116.7, 136.5, 139.3, 155.3, 158.9. Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.11; H, 7.90.

*3.1.3. 2-Allyl-1,5-dimethoxy-3-methylbenzene (**5a**)*

A mixture of the phenol **4a** (50 mg, 0.28 mmol), anhydrous potassium carbonate (50 mg, 0.29 mmol) and iodomethane (45 mg, 0.32 mmol) in acetone (5 mL) was heated at reflux for 6 h. The reaction mixture was cooled and most of the acetone was distilled off. The residue was poured into water and extracted with ether (2×20 mL). The organic extract was washed with water and dried. The residue after removal of the solvent was subjected to column chromatography over silica gel. Elution with ethyl acetate–petroleum ether (1:19) furnished the dimethyl ether (**5a**) (50 mg, 93%) as a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.17 (s, 3H), 3.26 (d, J=6.0 Hz, 2H), 3.69 (s, 6H), 4.78–4.86 (m, 2H), 5.74–5.87 (m, 1H), 6.25 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.2, 30.2, 55.6, 56.0, 96.6, 107.0, 114.3, 119.3, 137.1, 138.9, 158.8, 158.9. Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 75.01; H, 8.35.

*3.1.4. 2-Allyl-1,3-dimethoxy-5-methylbenzene (**5b**)*

Similarly the phenol **4b** was converted to the dimethyl ether **5b**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.25 (s, 3H), 3.28 (d, J=6.0 Hz, 2H), 3.70 (s, 6H), 4.79–4.90 (m, 2H), 5.79–5.92 (m, 1H), 6.29 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.4, 27.4, 56.2, 105.2, 113.9, 114.2, 137.5, 137.6, 158.5. Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 75.92; H, 8.41.

*3.1.5. 2-(2-Allyl-5-methoxy-3-methylphenoxy)-propionic acid (**6**)*

To a magnetically stirred solution of 2-allyl-5-methoxy-3-methylphenol **4a** (300 mg, 1.68 mmol) and α-bromopropionic acid (257 mg, 1.68 mmol) in freshly distilled THF (10 mL) at −10 °C was added sodium hydride (150 mg, 60% dispersion in mineral oil, 3.74 mmol) portionwise during 45 min. Stirring was continued at −10 °C for 20 min and at room temperature for 30 min. The reaction mixture was then heated at reflux with vigorous stirring for 10 h. Upon cooling the reaction mixture was diluted with water, acidified with dilute HCl (6 M), and extracted with ether. The ether extract was washed with water, dried and concentrated. The residue was chromatographed through silica gel eluting with ethyl acetate–petroleum ether (1:4) to afford the acid **6** (350 mg, 83%) as a colourless solid, crystallized from ether–petroleum ether, mp 101–102 °C; IR (KBr) 1708 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.67 (d, J=6.9 Hz, 3H), 2.30 (s, 3H), 3.34–3.51 (m, 2H), 3.78 (s, 3H), 4.78 (q, J=6.9 Hz, 1H), 4.92–4.99 (m, 2H), 5.88–5.99 (m, 1H), 6.26 (s, 1H), 6.41 (s, 1H), 10.44 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.8, 20.2, 30.5, 55.6, 72.7, 97.9, 108.4, 114.6, 120.0, 136.9, 139.5, 156.2, 158.7, 178.1. Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25. Found: C, 67.19; H, 7.32.

*3.1.6. 5-Methoxy-2a,7-dimethyl-8,8a-dihydro-1H,2aH-3-oxacyclobuta[b]naphthalen-2-one (**7**)*

To a magnetically stirred solution of triethylamine (600 mg, 5.94 mmol) and toluene-*p*-sulfonyl chloride (460 mg, 2.4 mmol) in dry benzene (50 mL) at reflux was added dropwise a solution of the acid **6** (300 mg, 1.20 mmol) in dry benzene (50 ml) over 6 h. After addition was complete, reflux was continued for another 6 h. The reaction mixture was then cooled and washed with water (3×50 mL) and concentrated to one-third of the volume. This concentrated solution was stirred with 3% aqueous sodium hydroxide solution (100 mL) for 10 h. The benzene layer was washed with water, dried and concentrated. The residue was purified by column chromatography over silica gel. Elution with ethyl acetate–petroleum ether furnished the cycloaddition product cyclobutanone **7** (140 mg, 50%) as a colourless solid, crystallized from ether–petroleum ether; mp 75–76 °C; IR (KBr) 1786 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.55 (s, 3H), 2.22 (s, 3H), 2.35 (dd, J=18.3,5.7 Hz, 1H), 2.79–2.81 (m, 2H), 2.86–2.92 (m, 1H), 3.12 (dd, J=18.3, 9.5 Hz, 1H), 3.72 (s, 3H), 6.38 (d, J=2.4 Hz, 1H), 6.41 (d, J=2.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.8, 20.3, 24.7, 35.0, 48.1, 55.6, 92.9, 101.4, 111.3, 114.4, 138.2, 156.2, 159.1, 210.8. Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.43; H, 6.92.

*3.1.7. 7-Methoxy-5,9a-dimethyl-3a,9a-dihydro-3H,4H-1,9-dioxacyclopenta[b]naphthalene-2-one (**8**)*

A mixture of sodium bicarbonate (150 mg, 1.79 mmol) and *m*-chloroperbenzoic acid (220 mg, 50% pure; 0.64 mmol) was added portionwise to a vigorously stirred solution of the ketone **7** (130 mg, 0.56 mmol) in dry methylene chloride (10 mL) at 0 °C during 5 min. The reaction mixture was then stirred at ambient temperature for 3 h, diluted with methylene chloride (30 mL) and quenched with 10% aqueous sodium carbonate solution. The organic layer was washed with 10% aqueous sodium carbonate solution, brine and dried. The residue after evaporation of the solvent was chromatographed over silica gel. Elution with ethyl acetate–petroleum ether (1:9) furnished the γ-lactone **8** (111 mg, 80%) as a colourless solid, crystallized from ether–petroleum ether, mp 63–64 °C; IR (KBr) 1791 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.76 (s, 3H), 2.20 (s, 3H), 2.31 (dd, $J=17.7$, 10.0 Hz, 1H), 2.61 (dd, $J=17.7$, 8.9 Hz, 1H), 2.74–2.75 (m, 2H), 2.94–2.99 (m, 1H), 3.73 (s, 3H), 6.35 (d, $J=2.5$ Hz, 1H), 6.44 (d, $J=2.5$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.5, 22.9, 25.2, 33.7, 39.2, 55.7, 101.0, 108.3, 111.2, 111.3, 138.3, 153.5, 159.5, 174.9. Anal. Calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.78; H, 6.70.

*3.1.8. 7-Methoxy-3,5,9a-trimethyl-3a,9a-dihydro-3H,4H-1,9-dioxacyclopenta[b]naphthalene-2-one (**9**)*

To a well-stirred solution of LDA [prepared from *n*-butyllithium (0.26 mL of 1.6 M solution in hexane, 0.42 mmol) and diisopropylamine (45 mg, 0.44 mmol)] in THF (1 mL) at −78 °C, a solution of the γ-lactone **8** (100 mg, 0.40 mmol) in THF (1 mL) was added dropwise under argon and the resulting solution was stirred for 30 min. Then the reaction mixture was allowed to warm to −30 °C and kept at that temperature for another 30 min. Again the reaction mixture was cooled to −78 °C and HMPA (0.1 mL) followed by freshly distilled methyl iodide (170 mg, 1.20 mmol) was added dropwise. After 2 h the reaction mixture was allowed to attain room temperature and stirred for 10 h. The reaction mixture was then quenched with saturated aqueous ammonium chloride solution and extracted with ether (3×15 mL). The combined ethereal extracts were washed with water, dried, and the solvent removed. The residue was subjected to column chromatography over silica gel. Elution with ethyl acetate–petroleum ether (2:23) afforded the methylated lactone **9** (98 mg, 94%) as a colourless solid, crystallized from methylene chloride–petroleum ether, mp 68–70 °C; IR (KBr) 1790 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25 (d, $J=6.7$ Hz, 3H), 1.72 (s, 3H), 2.22 (s, 3H), 2.42–2.45 (m, 2H), 2.70–2.80 (m, 2H), 3.74 (s, 3H), 6.31 (d, $J=2.4$ Hz, 1H), 6.43 (d, $J=2.4$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.4, 19.3, 21.2, 23.9, 37.8, 46.0, 55.2, 99.9, 105.1, 109.2, 110.6, 138.1, 153.2, 159.1, 177.5. Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. Found: C, 68.74; H, 6.89.

*3.1.9. 7-Methoxy-3,5,9a-trimethyl-2,3,3a,9a-tetrahydro-4H-1,9-dioxa-cyclopentan[b]naphthalene-2-ol (**10**)*

To a well-stirred solution of the lactone **9** (50 mg, 0.19 mmol) at −78 °C in dry diethyl ether (3 mL), diisobutylaluminum hydride solution (0.20 mL of 1.0 M solution in hexane, 0.20 mmol) was added dropwise. After stirring at that temperature for 2 h, the reaction was quenched with aqueous saturated ammonium chloride solution. The organic layer was separated and the aqueous part thoroughly extracted with ether (3×15 mL). The combined ethereal extract was washed with water and dried. The residue after evaporation of the solvent was chromatographed over silica gel. Elution with ethyl acetate–petroleum ether (1:4) furnished the lactol(s) **10** (48 mg, 95%) as a colourless solid, crystallized from methylene chloride–petroleum ether, mp 118–119 °C; IR (neat) 3436 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.95, 1.09 (2d, $J=6.6$ Hz, 3H), 1.39, 1.60 (2s, 3H), 1.76–1.98 (m, 1H), 2.11, 2.13 (s, 3H), 2.22–2.29 (m, 1H), 2.55–2.67 (m, 2H), 3.64, 3.64 (2s, 3H), 4.99, 5.31 (2d, $J=5.1$ Hz, 1H), 6.12, 6.17 (2d, $J=2.6$ Hz, 1H), 6.22, 6.23 (2d, $J=2.6$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) 11.4, 14.8, 19.4, 19.5, 20.9, 21.7, 22.7, 25.5, 39.5, 44.2, 45.2, 48.0, 54.8, 54.8, 98.8, 99.7, 99.9, 105.3, 105.5, 107.3, 108.5, 109.6, 109.8, 110.7, 136.9, 137.5, 153.2, 153.7, 158.7, 158.9. Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.15; H, 7.65.

*3.1.10. O-Methylalboatrin (**11**)*

To a cooled and stirred solution of lactol **10** (30 mg, 0.114 mmol) in dichloromethane (2 mL), trifluoroacetic acid (0.02 mL, 0.228 mmol) and triethylsilane (0.018 mL, 0.114 mmol) were added dropwise at −40 °C, and stirred for 5 min and left to warm to room temperature. After stirring for 15 min at room temperature the reaction mixture was quenched with water. The organic layer was separated and the aqueous layer was extracted with methylene chloride (3×10 mL). The combined organic extracts were washed with sodium bicarbonate and brine, dried and concentrated. The residue was subjected to column chromatography over silica gel. Elution with ethyl acetate–petroleum ether (2%) furnished *O*-methylalboatrin **11** (11 mg, 38%) as a colourless solid, mp 53–54 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.06 (d, $J=6.5$ Hz, 3H), 1.51 (s, 3H), 1.93 (ddd, $J=10.9$, 5.3, 2.5 Hz, 1H), 2.10–2.16 (m, 1H), 2.21 (s, 3H), 2.69–2.71 (m, 2H), 3.51 (t, $J=8.5$ Hz, 1H), 3.73 (s, 3H), 4.18 (t, $J=8.5$ Hz, 1H), 6.27 (d, $J=2.1$ Hz, 1H), 6.36 (d, $J=2.1$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) 16.4, 19.9, 21.9, 23.2, 35.8, 48.6, 55.5, 74.4, 100.0, 107.4, 109.6, 109.8, 138.3, 154.2, 159.2; HRMS (ES +ve) calcd for $C_{15}H_{21}O_3$ $[M+H]^+$ 249.1492, found 249.1476.

*3.1.11. Alboatrin (**1**)*

To a stirred mixture of *O*-methylalboatrin **11** (40 mg, 0.028 mmol) in dry methylene chloride (3 mL) at −78 °C, boron tribromide (0.01 mL, 0.034 mmol) was added dropwise. The reaction mixture was stirred to −60 °C and this temperature was maintained for 2 h. Then the reaction mixture was quenched with ice cold water, and the organic layer was separated and the aqueous layer was further extracted with methylene chloride. The organic layers were combined and dried and then subjected to column chromatography with silica gel. Purification with petroleum ether–ethyl acetate (25:3) finally produced alboatrin **1** (32 mg, 80%) as a colourless solid. The compound was further crystallized from ether–petroleum ether, mp 146–147 °C (lit.[1,2,4] mp 146–148 °C).

^{1}H NMR (300 MHz, $CDCl_3$) δ 0.84 (d, J=6.0 Hz, 3H), 1.54 (s, 3H), 1.92–1.98 (m, 1H), 2.10–2.14 (m,1H), 2.18 (s, 3H), 2.68 (d, J=2.7 Hz, 2H), 3.51 (t, J=8.5 Hz, 1H), 4.17 (t, J=8.5 Hz, 1H), 6.31 (br s,1H), 6.33 (s, 1H), 6.37 (s 1H); ^{13}C NMR (75 MHz $CDCl_3$) 16.0, 19.4, 21.6, 23.2, 35.5, 48.4, 74.0, 101.9, 107.5, 109.5, 110.1, 138.2, 153.7, 155.3. HRMS (ES +ve) calcd for $C_{14}H_{17}O_3Na$ $[M+Na]^+$ 257.1153, found 257.1154.

The spectral data of **1** were identical with the reported values.[1,4]

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