Synthesis and antibacterial activity of amoenylin, a metabolite of *Dendrobium amoenum*¹

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Amenylin 6, a dihydrostilbene from *Dendrobium amoenum*, has been synthesised from syringaldehyde 1, in three steps with an overall yield of 40%. The spectral data of synthetic 6 are in good agreement with those of natural product. Amenylin 6 shows weak antibacterial activity.

Amenylin 6, a dihydrostilbene was isolated recently, from the orchid *Dendrobium amoenum.*¹ Dihydrostilbenes like batatasin III, have been reported as endogenous growth regulators.² As a part of our synthetic studies on stilbenes we have synthesised amenylin for the first time and the results are reported in this note.

4-Methoxybenzytriphenyolphosphonium bromide 4 was prepared from 4-methoxybenzyl alcohol 3 by treatment with phosphorous tribromide followed by triphenyl phosphate in 89% yield. Wittig condensation of 4 with 4-O-benzisyringaldehyde 2 in presence of n-butyl lithium gave stilbene derivative 5 (Z and E isomers, 77%), which was then hydrogenated over Pd-C to give amenylin 6 in 74% yield (Scheme I). The spectral data of synthetic 6 agree well with those of reported for natural 6. Thus, 6 was obtained starting from syringaldehyde in three steps with an overall yield of 40%.

Amenylin 6 showed weak antibacterial activity against Gram +ve (*Bacillus subtilis*) and Gram -ve (*Pseudomonas aeruginosa* and *Escherichia coli*) bacteria at a concentration of 500 µg/mL.

**Experimental Section**

Melting points were recorded on a V Scientific melting point apparatus, in open capillaries and are uncorrected. UV spectra was recorded on a Shimadzu UV-190 Spectrophotometer, IR spectra on a Perkin-Elmer BX1 FTIR Spectrophotometer, ¹H NMR (400 MHz) spectra on a Varian Gemini 400 MHz NMR spectrometer and Mass spectra on VG micromass 70-70H mass spectrometer. Acme silica gel G and silica gel (100-200 mesh) were used for analytical TLC and column chromatography, respectively.

4-O-Benzisyringaldehyde 2. A mixture of syringaldehyde (0.5 g, 2.75 mmole), benzyl bromide (0.4 mL, 3.37 mmole), potassium carbonate (0.6 g, 4.35 mmole) and acetone (15 mL) was heated under reflux for 2 hr. After completion of the reaction, the solid was filtered off and the solvent evaporated. The residue obtained was chromatographed over silica gel column using mixtures of pet. ether and ethyl acetate (90:10) as eluent to give 2 (0.58 g, 78%), m.p. 61-63°C; IR(neat) : 1692, 1587, 1497, 1327, 1230, 1217, 980, 836, 739 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): 6 3.90 (6H, s, Ar-2×OCH₃), 5.13 (2H, s, O-CH₃-Ph), 7.11 (2H, s, Ar-H), 7.29-7.48 (5H, m, Ar-H), 9.86 (1H, s, -CHO).

4-Methoxybenzytriphenyolphosphonium bromide 4. 4-Methoxybenzyl alcohol (3, 1.5 g, 10.86 mmole) in dry tetrahydrofuran (5 mL) and dry benzene (15 mL) was treated with stirring at 0°C, by dropwise addition of phosphorus tribromide (1.6 mL, 16.3 mmole) in dry THF (1 mL) and dry benzene (5 mL). After the reaction mixture had been stirred for 2 hr at rt, it was poured into ice cold water and the product extracted with ether. The ether extract was washed with brine, dried over Na₂SO₄ and the solvent was evaporated. The crude product obtained was dissolved in dry benzene (20 mL) and treated with triphenyl phosphate (4.26 g, 16.3 mmole). The reaction mixture was then heated under reflux for 3 hr, and then cooled and filtered to give 4 (4.1 g, 89%), m.p. 218-220°C; IR(KBr) : 1604, 1504, 1244, 1109, 844, 744, 717, 686 cm⁻¹.

5-[(4-Methoxyphenyl)ethenyl]-1,3-dimethoxy-2(phenylmethoxy)benzene 5. To a solution of 4-methoxybenzytriphenyolphosphonium bromide (1.23 g, 2.65 mmole) in THF (5 mL) was added n-butyl lithium (1.9 mL, 1.6 M in hexane) at 0°C and stirred for 90 min. A solution of 2 (0.6 g, 2.21 mmole) in THF (5 mL) was then added to the reaction mixture and was allowed to warm to rt and stirred for 16 hr.

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After usual workup, the residue was chromatographed over silica gel column using mixtures of pet. ether and ethyl acetate (95:5) as eluent to give 5 (Z-isomer, 190 mg, 23%) as an oil; UV (MeOH): 213 (4.58), 290 nm (4.14); IR(neat): 1605, 1578, 1507, 1247, 1127, 1032, 734 (Z-isomer) cm\(^{-1}\); \(^1\)H NMR (400 MHz,CDCl\(_3\)): \(\delta\) 3.65 (6H, s, 3"-,5"-OCH\(_3\)), 3.79 (3H, s, 4'-OCH\(_3\)), 5.01 (2H, s, -OCH\(_2\)), 6.41-7.48 (13 H, m, Ar-H). Further elution of the column with pet.ether and EtOAc (95:5) as eluent gave 5 (E-isomer, 450 mg, 54%), m.p. 82-84°C; UV (MeOH): 212 (4.62), 323 nm (4.30); IR(neat): 1604, 1579, 1510, 1247, 1126, 1032, 968 (E-isomer), 830 cm\(^{-1}\); \(^1\)H NMR (400 MHz,CDCl\(_3\)): \(\delta\) 3.83 (3H, s, 4'-OCH\(_3\)), 3.87 (6H, s, 3"-,5"-OCH\(_3\)), 5.02 (2H, s, -OCH\(_2\)), 6.71-7.51 (13 H, m, Ar-H).

2,6-Dimethoxy-4-[2-(4-methoxyphenyl)ethyl]phenol 6. To a solution of 5 (E-isomer, 300 mg) in ethyl acetate (10 mL) was added palladium – charcoal (10%, 50 mg) and the reaction mixture was stirred under hydrogen atmosphere for 2 hr. The catalyst was removed by filtration and the solvent evaporated. The residue obtained was chromatographed over silica gel column using pet.ether : ethyl acetate (90:10) as eluent when 6 (170 mg, 74%) was obtained as white solid, crystallised from chloroform-hexane, m.p. 78-80°C (Lit.\(^1\) semi-solid); UV (MeOH): 209 (4.64), 274 nm (3.46); IR(neat): 3507, 1611, 1512, 1459, 1241, 1214, 1114, 1033, 827 cm\(^{-1}\); \(^1\)H NMR (400 MHz,CDCl\(_3\)): \(\delta\) 2.71-2.78 (4H, br s, 1,2-H), 3.72 (3H, s, Ar-OCH\(_3\)), 3.77 (6H, s, Ar-OCH\(_3\)), 5.30 (1H, s, Ar-OH), 6.28 (2H, s, 1',4'-H), 6.75 (2H, d, J=8.6 Hz, 3',5'-H), 7.00 (2H, d, J=8.6 Hz, 2',6'-H); \(^{13}\)C NMR (100 MHz,CDCl\(_3\)): \(\delta\) 57.9 (C-4'), 146.9 (C-3''",5''), 133.9 (C-1"'), 132.9 (C-1',4'''), 129.4 (C-2',6'), 113.7 (C-3',5'), 105.2 (C-2''",6''), 56.2 (OCH\(_3\)), 55.2 (OCH\(_3\)), 38.3 (C-1), 37.2 (C-2); EIMS : m/z (\%) 289 (M+1, 18), 288 (M\(^+\), 67), 168 (18), 167 (100), 123 (6), 122 (16), 121 (83), 91 (2), 77 (3). Hydrogenation of 5 (Z-isomer)
under the above reaction conditions also gave 6 in 74% yield.

**Antibacterial activity**

Antibacterial activity of 6 was determined by the agar cup-plate diffusion method\(^4\). The zone of inhibition (diameter in mm) at a concentration of 500 \(\mu\)g/mL against *Pseudomonas aeruginosa* (Gram-ve), *Escherichia coli* (Gram-ve) and *Bacillus subtilis* (Gram+ve) were 8.5, 8.5 and 9.0 mm respectively. Compound 6 did not show any appreciable antifungal activity against *Aspergillus wentii* or *Aspergillus niger* even at 500 \(\mu\)g/mL concentration.

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**References**