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NOTE

Synthesis and Antimicrobial Activity of Lysichitalexin†

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Lysichitalexin [2-(4-methoxyphenyl)-1-nitroethane] **1**, a stress induced metabolite from *Lysichitum americanum*, has been synthesized starting from 4-methoxybenzaldehyde in two steps with an overall yield of 64%. The intermediate product, 2-(4-methoxyphenyl)-1-nitroethene 3 showed excellent antimicrobial activity.

Key words: Synthesis, Antimicrobial activity, Lysichitalexin

Lysichitalexin **1** was isolated as a cupric chloride induced stress metabolite from the leaves of *Lysichitum americanum*[1]. It exhibited antifungal activity against *Fusarium oxysporum* and *Cladosporium herbarum*[1]. In a continuing study on synthesis of simple bioactive molecules[2–6], we have synthesised **1** starting from commercially available 4-methoxybenzaldehyde **2** in two steps with an over all yield of 64% and the results are reported in this note.

Melting points were determined on a Mel Temp apparatus and are uncorrected. UV spectra were recorded on a Shimadzu 190 spectrometer, IR spectra on a Perkin Elmer BX FTIR spectrometer, ^{1}H NMR spectra on a amx 400 MHz NMR spectrometer and mass spectra on a VG micromass spectrometer. TLC was carried out on silica gel (ACME) thin layers. Petroleum ether is the fraction of bp 60–80°C.

2-(4-Methoxyphenyl)-1-nitroethene 3: A mixture of 4-methoxybenzaldehyde (**2**, 3.32 g, 0.02 mmoles), nitromethane (1.34 g, 0.02 mmoles), ammonium acetate (0.78 g, 0.01 mmoles) and glacial acetic acid (5 mL) was refluxed on a water bath (80–90°C) for 1 h. After the completion of reaction, the reaction mixture was poured into the cold water (50 mL) and the precipitated solid was filtered and recrystalized from a mixture of acetone and methanol to give **3** (4.3 g, 89%), mp 86–88°C; UV (MeOH): 353, 244 nm; IR ($CHCl_3$); 2359, 1624, 1605, 1424, 1343, 1258, 1177, 972 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (1H, d, J = 13.7 Hz, H-1), 7.53 (1H, d, J = 13.7 Hz, H-2), 7.51 (2H, d, J = 8.7 Hz, H-2′ and H-6′), 6.96 (2H, d, J = 8.7 Hz, H-3′ and H-5′), 3.87 (3H, s, OMe); EIMS: 179 [M$^+$](65), 132 (100), 121 (22), 89 (50), 77 (53), 64 (42).

2-(4-Methoxyphenyl)-1-nitroethane 1: To a solution of nitro-ethene (3, 0.5 g, 0.02 mmoles) in ethanol (5 mL) at 0°C was added $NaBH_4$ (100 mg;

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0.02 mmoles) over a period of 20 minutes in portions. After continuing the reaction for 2 h at 0°C, the alcohol was removed and 2N HCl (5 mL) was added carefully under cooling and the product was extracted into dichloromethane, washed with brine and the organic layer was dried over anhydrous sodium sulphate to give 1 (320 mg, 72%); semisolid, UV (MeOH); 274 nm; IR ($CHCl_3$) : 2935, 2838, 1612, 1557, 1441, 1377, 1180 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$): δ 7.13 (2H, d, J = 8.7 Hz, H-2′ and H-6′), 6.86 (2H, d, J = 8.7 Hz H-3′ and H-5′), 4.57 (2H, t, J = 7.4 Hz H-1), 3.79 (3H, s, OMe), 3.26 (2H, t, J = 7.4 Hz H-2); EIMS: 182 [M^+H] (24), 135 (90), 134 (98), 121 (100).

Condensation of **2** with nitromethane in presence of ammonium acetate gave 2-(4-methoxyphenyl)-1-nitroethene **3** in 89% yield. Reduction of **3** with $NaBH_4$ in ethanol[7] at 0°C gave **1** in 72% yield. The spectral data of the synthetic **1** corroborated well with those of natural **1**.

Compound **3** showed excellent antibacterial and antifungal activities against the test organisms and the results are noted in Table 1.

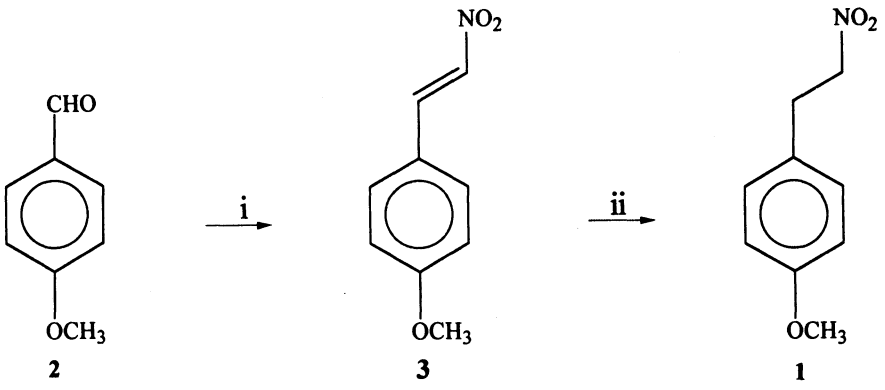
TABLE-1
ANTIMICROBIAL ACTIVITY OF 3 AND 1

Compound	Concentration (μg/mL)	Antibacterial activity*				Antifungal activity*
		a	b	c	d	e
3	50	20.5	14.0	16.0	15.0	22.0
	10	17.0	12.0	12.5	12.0	19.0
	5	12.0	10.0	10.0	11.0	11.0
	1	10.0	9.5	9.5	10.0	9.5
	0.1	10.0	9.0	9.5	10.0	—
1	500	10.5	10.0	9.5	11.0	16.0
	200	10.0	9.5	9.0	10.0	14.0
	100	10.0	9.0	9.0	9.0	11.0
	50	9.0	9.0	9.0	9.0	10.5
	5	—	—	—	—	9.0
	1	—	—	—	—	9.0
Nistatin	1	—	—	—	—	17.0
Ampicillin	1	17.0	19.0	17.0	16.0	—

*Zone of inhibition in mm
a: *E. coli*, b: *P. aeroginosa*, c: *S. epidermis*, d: *S. aureus*, e: *A. niger*
Cup dia: 8 mm; 0.05 mL.

The antibacterial activity was determined by Agar cup-plate method[8] against *Escherichia coli*, *Pseudomonas aeroginosa*, *Staphylococcus epidermis*, and *Staphylococcus aureus*. The compounds were tested at different concentrations (Table-1). The antifungal activity was also determined by a similar procedure[8] against *Aspergillus niger* using Nistatin as standard. **3** exhibited significant

antibacterial and antifungal activity where as compound **1** is found to posses moderate antibacterial and antifungal activity.



Scheme 1
(i) Nitromethane, ammonium acetate, glacial acetic acid, reflux, 1 h, 89%;
(ii) $NaBH_4$, ethanol, 0.5 h, 72%.

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