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A BRIEF SYNTHESIS OF NATURAL ANTIFEEDANT, 1-(2,4,6-TRIMETHOXYPHENYL) BUT-2(E)-EN-1-ONE

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ABSTRACT

1-(2,4,6-Trimethoxyphenyl) but-2(E)en-1-one, an antifeedant isolated from *Arachniodes standischii* has been synthesized in two steps from 2,4,6-trimethoxyacetophenone in good yield.

INTRODUCTION

The practical usefulness of antifeedants[1] in integrated pest management programme is gaining momentum in recent years. Several of the natural feeding deterrents having diverse structures have been isolated and characterised. Recently Tanaka *et al*[2] during their phytochemical studies of the fronds of *Arachniodes standichii* (Moore) Ohwi, isolated an active constituent having antifeedant activity for the larvae of the yellow butterfly and identified as 1-(2,4,6-trimethoxyphenyl) but-2(E)-en-1-one (1). Numata *et al* reported[3] the antifeedant activity of 1 and synthesised it via the Friedel-crafts alkylation in 16% yield from 1,3,5-trimethoxybenzene and crotonyl chloride. This low yield prompted us to report herein, a short and efficient synthesis of 1, (**Scheme 1**) from commercially available starting material 2,4,6-trimethoxyacetophenone (2).

EXPERIMENTAL

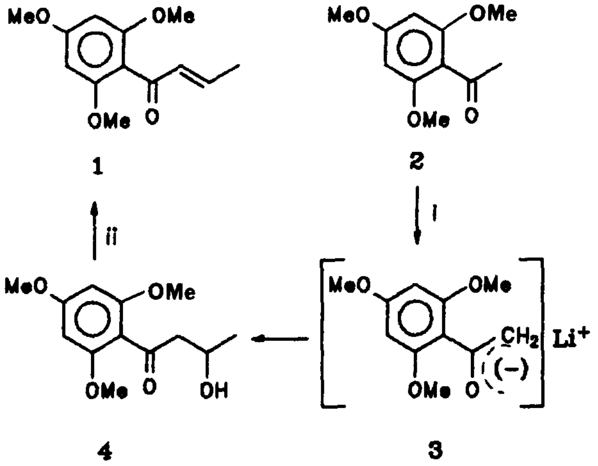
2,4,6-Trimethoxycetophenone was procured from Bioorganics (Madras, India) and was used as such ^{1}PMR spectra were obtained on a Varian (A 60) 60 MHz spectrometer in $CDCl_3$ using $SiMe_4$ as internal standard. IR spectra were recorded on a Perkin Elmer 783 spectrophotometer and UV spectra on Shimadzu UV-240 spectrophotometer. Mass spectra were recorded on a VG micromass 7070F instrument.

1-(2,4,6-Trimethoxyphenyl)-1-oxo-butan-3-ol (**4**): To a solution of lithium diisopropylamide (LDA) prepared from n-butyl lithium (20 mmol, 12.6 ml of 1.6 mol solution in hexane) and diisopropylamine (20 mmol, 2,8 ml) in dry THF (50 ml) at -10°C was added the ketone (2) (4.2 g, 20 mmol) in dry THF (25 ml) at -25°C to 30°C. The reaction mixture was stirred at this temperature for 1 h. The temperature was then lowered to -40°C and freshly distilled acetaldehyde (30 mmol, 1.3 g) was injected dropwise. After stirring for 2 h., the mixture was acidified with 2N HCl and extracted with ether. The organic layer was washed with brine and dried (Na_2SO_4). The residue obtained after removal of solvent was recrystallised from hexane resulting in colourless shining crystals of **4** (3.8 g, 75%), m.p. 97°C; (Found: C, 61.20; H, 6.9; $C_{13}H_{18}O_5$ requires C, 61.42; H, 7.1%); IR: vmax/cm^{-1} (KBr) 3500, 2995, 1720, 1620, 1425, 1230, 1140, 1020 and 825; PMR (δ) 1.25 (3H, d, J 6 H_z), 2.85 (2H, m), 3.80 (6H, s), 3.90 (3H, s), 4.3 (1H, m) and 6.1 (2H, s).

1-(2,4,6-Trimethoxyphenyl)-but-2(E)-en-1-one (1): To a solution of **4** (2.54 g, 10 mmol) in dry benzene, catalytic amount of para-tolouenesulfonic acid was added and mixture was refluxed for 2 h. After completion of the raction (monitored by TLC, SiO_2, benzene-ethyl acetate, 9:1) the cooled reaction mixture was washed with water, brine and dried (Na_2SO_4). Removal of the solvent under reduced pressure gave an oily residue, which solidified at room temperature. This was crystallised from hexane-acetone followed by sublimation at 160°C/0.5 mm to give pure colourless crystals of 1 (1.53 g, 65%); m.p. 87-88°C (lit.[3] m.p. 91-92°C); (Found C, 65.95; H, 6.60%. $C_{13}H_{16}O_4$ requires C, 66.10; H, 6.78%); IR; vmax/cm^{-1} (Nujol) 2950, 1650, 1605, 1280, 1250, 1160, 980 and 815; UV λ max/nm (MeoH) 222 (log ε 4.25), 302 (log ε 3.49); PMR: (δ) 1.85 (3H, d, J 6Hz), 3.75 (6H, s, Ar-OCH_3), 3.85 (3H, s, Ar-OCH_3), 6.10 (2H, s, ArH), 6.30-6.70 (2H, m, olefinic H); M.S.: 236 (M^+), 221, 208, 195 .

RESULTS AND DISCUSSION

The antifeedant 1 has been synthesized in two steps from commercially available 2,4,6-trimethoxyacetophenone (2) in good yield. The key steps in our synthesis are electrophilic reaction on lithium enolate and dehydration of hydroxy function of β-hydroxy carbonyl. The reaction of acetaldehyde with lithium enolate of 2 generated *in situ* from LDA[4,5] gave the desired β-hydroxyketone (4) in 75% yield. The IR bands at 3500, 1720 and 1620 cm^{-1} confirm the functional group as hydroxy, carbonyl and aromatic. The ^{1}PMR spectrum revealed the presence of three proton doublet at δ 1.25 and a two proton multiplet at 2.85. The compound 4 on refluxing with catalytic amount of *p*-toluenesulfonic acid (PTS)[6] in benzene afforded the antifeedant (1) in 65% yield. The compound 1 showed the characteristic IR band for conjugated α,β unsaturated carbonyl at 1650 cm^{-1} and E-double bond at 970 cm^{-1}. The structure of 1 is further confirmed from ^{1}PMR spectrum which displayed a doublet at 1.85 for methyl protons and a multiplet between 6.30-6.60 due to olefinic and aromatic protons integrated for 4 hydrogens. The physical (mp) and spectroscopic (IR, UV and MS) and elemental analysis were in good agreement with those reported[2,3] for structure 1.



Scheme 1 Reagents: i) LDA, -25°C, CH$_3$CHO; ii) PTS/C$_6$H$_6$/Δ.

The compound 1 was screened for antifeedant activity[3] against the larvae of polyphagas tobacco caterpillar (*Spodoptera litura*) and was found to possess moderate activity. With the substrate concentration of 0.1% of the diet, the insect feeding ratio was found to be 50.5%.

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