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Synthesis of (*E)* Stilbenes from 2, 4, 5-Trimethoxybenzyltriphenyl phosphonium Ylide and their Fungicidal Activity

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ABSTRACT

Plants use multiple defense mechanisms in order to prevent entering of phytopathogenic microorganisms. In many plant species one of the most efficient responses to combat attacking microbes is the rapid synthesis of antimicrobial low molecular weight phytoalexins, for example, stilbenes produced by several plants may be a useful lead structure for the chemical synthesis of antimicrobials. In this study, a series of novel 2, 4, 5-trimethoxy stilbene derivatives have been synthesized *via* the Wittig reaction. The starting material 2, 4, 5- trimethoxy benzaldehyde (asaronaldehyde) was obtained from β-asarone of sweet flag oil. The key intermediate 2, 4, 5-trimethoxybenzyltriphenyl phosphonium chloride was prepared for the first time from the corresponding benzyl chloride. All the *trans*-stilbenes were characterized by HRMS, ^{1}H and ^{13}C NMR spectral analysis and tested *in vitro* for their fungicidal activity against two plant pathogenic fungi viz., *Phytophthora capsici* and *Sclerotium rolfsii*.

Keywords: Sweet flag oil, 2, 4, 5-Trimethoxybenzyltriphenyl phosphonium chloride, Stilbenes, Wittig reaction, Antifungal

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INTRODUCTION

Acorus calamus Linn., commonly known as Sweet Flag belongs to the family Araceae (Adoraceae), also called as *Acorus odoratus.* This perennial herb is commonly grown wild in the hilly areas and cultivated as a commercial crop. The sweet flag oil present in the rhizomes of this plant is a unique source of compounds with structural diversity[1] and known for their medicinal[2] insecticidal[3-6] fungicidal[7] and bactericidal[8] properties. β- Asarone [*(Z)* - 1-propenyl-2, 4, 5-trimethoxybenzene] (Fig. 1) is one of the main constituent present in the sweet flag oil[9] was shown to possess *in vivo* carcinogenic effects[10] and *in vitro* mutagenic activities[11].

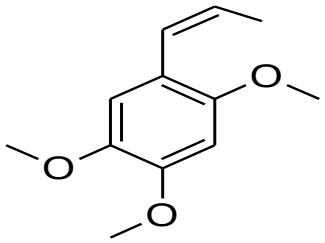


Figure 1: Structure of β- Asarone

It was reported by Saxena *et al.*[12], that the toxicity of asarone is mainly due to the propenyl side chain but not due to the presence of three methoxy groups on phenyl ring of the nucleus. Besides its toxicity, β- asarone showed some beneficial effects in cognititive impairment associated disorder such as, Alzheimer disease[13]. In many cases, natural stilbenes more specifically polyhydroxy stilbenes that exist in *trans*- geometry have been shown to protect plants against attack by fungal pathogens[7, 14-17]. In view of this anti phytopathogenic effect of asarone and stilbenes, we decided to synthesize new stilbene compounds with *E*- geometry by keeping 2, 4, 5-trimethoxy phenyl ring as a common moiety and studied their antifungal effect against selected plant pathogens.

MATERIALS AND METHOD

Experimental:

All chemicals were purchased of Laboratory Reagent (LR) grade; solvents used were of the commercial grade. Melting points were determined on Acro melting point apparatus (using a calibrated thermometer). Thin-layer chromatography (TLC) was run on silica gel pre-coated on aluminium sheet (silica gel 60 F_{254}.Merck). Analytical HPLC was recorded with Shimadzu (CLASS-VP) equipped with LC-10AT VP high-pressure pumps, a SPD-M10A VP photodiode array detector, a CTO-10AS VP oven and a SCL-10A VP controller (RP column: Atlantis-T3, 5.0µm, 4.6x150mm; Mobile phase: 50:50 acetonitrile: water- isocratic elution; UV detector:

290nm). Chromatographic separation of mixtures was performed in open glass columns packed with silica gel (Merck Grade 7734, 70-230 mesh) and eluted with ethyl acetate/hexane solvent mixture. The Mass spectra were recorded on GCMS-QP2010S (direct probe) instrument and High-resolution mass spectral (HRMS) data were obtained on the Micromass Q-Tof micro instrument using electro spray ionization (ESI). ^{1}H (400MHz) and ^{13}C NMR (100MHz) spectra were recorded on a Bruker spectrometer using $CDCl_3$ as a solvent and TMS as an internal reference. The chemical shifts were recorded in δ (ppm) units.

Synthesis of 2, 4, 5- trimethoxybenzyl alcohol (**2**)

To compound **1** (12 g, 61 mmol) in methanol (50 mL) at room temperature was added sodium borohydride (1 g, 26 mmol) portion wise for about 40 min. and stirred at same temperature for another 3-4 h. TLC was checked, methanol was evaporated under vacuum. A thick mass thus obtained was taken in water (150 mL), acidified to pH = 4-5 using glacial AcOH and extracted with dichloromethane. The organic layer was washed with water, dried over anhydrous sodium sulfate and evaporated under vacuum to give compound **2** as white to off-white solid. This was purified by column chromatography over silica gel using Hexane/EtOAc (9:1) to get pure white solid (11.4 g, 93%), mp 68-70 °C (lit. 70 °C) (Anthony *et al*., 1975). ^{1}H NMR ($CDCl_3$): δ 6.97 (s, 1 H), 6.63 (s, 1 H), 4.83 (s, 1 H), 4.54 (s, 2 H), 3.82 (s, 3 H), 3.79 (s, 3 H), 3.77 (s, 3 H). ^{13}C NMR (DMSO d_6): δ 153.07, 150.66, 144.19, 122.42, 115.08, 99.42, 59.94, 57.44, 56.78, 56.63. GCMS: (*m/z)* 198 $[M]^+$.

Synthesis of 2, 4, 5- trimethoxybenzyl chloride (**3**)

To compound **2** (10 g, 50 mmol) in dichloromethane (60 mL) at room temperature was added thionyl chloride (9 g, 75 mmol) dropwise for about 45 min. Stirred at same temperature for another 3 h, distilled off organic solvent under vacuum to give compound **3** as a dark green viscous mass (9.84 g, 90%). GCMS: (*m/z)* 216 $[M]^+$.

Synthesis of 2, 4, 5-trimethoxybenzyl phosphoniumchloride (**4**)

To compound **3** (10 g, 46 mmol) in toluene (60 mL) was added triphenylphosphine (12 g, 46 mmol) in one lot and stirred at room temperature for 30 min. Slowly raised the temperature to 85-90 °C and maintained at that temperature for another 5-6 h. Cooled the mass slowly to ambient temperature, filtered the solid and recrystalized from a mixture of ethyl acetate and chloroform to give compound **4** as off-white solid (17 g, 78%), mp 236-38 °C. ^{1}H NMR ($CDCl_3$): δ 7.78–7.63 (m, 15 H), 6.99 (s, 1 H), 6.26 (s, 1 H), 5.16 (d, *J* = 12.8 Hz, 2 H), 3.83 (s, 3 H), 3.57 (s, 3 H), 3.21 (s, 3 H). ^{13}C NMR ($CDCl_3$): δ 151.64, 149.92, 142.93, 134.68, 134.31, 129.90, 118.87, 118.02, 116.06, 105.68, 96.18, 56.46, 56.18, 55.11.

General procedure for the preparation of 2, 4, 5-trimethoxystilbene derivatives (6a-g)

To a solution of phosphonium salt **4** (6 g, 12.6 mmol) in dichloromethane (40 mL) at 25-30°C was added potassium t-butoxide (3.5 g, 31.2 mmol) and the resulting solution was stirred under nitrogen for 1 h. Appropriate aromatic aldehydes (**5a-g)** (12.6 mmol.) in dichloromethane (20 mL) was added dropwise over 30 min and the mixture was stirred for another 2-3 h at room temperature. Completion of reaction was monitored by TLC. After the completion of reaction, the resultant mass was quenched into water and extracted with dichloromethane. The organic phase was washed with water, dried over anhydrous sodium sulfate and evaporated. The residue obtained was purified by column chromatography using silica gel and EtOAc/Hexane mixture (0.5:9.5) as a mobile phase to obtain pure *trans*- stilbenes **6a-g**.

***(E)*-2, 4, 5-trimethoxystilbene (6a)**

Pale yellow viscous liquid **(**1.63 g, 48%). ^{1}H NMR ($CDCl_3$): δ 7.30–7.14 (m, 5 H), 6.72 (s, 1 H), 6.70 (d, *J* = 12.4 Hz, 1 H), 6.58 (d, *J* = 12.4 Hz, 1 H), 6.52 (s, 1 H), 3.90 (s, 3 H), 3.82 (s, 3 H), 3.46 (s, 3 H). ^{13}C NMR ($CDCl_3$): δ 151.75, 149.08, 142.44, 137.68, 128.82, 128.03, 126.76, 124.94, 117.43, 113.31, 97.38, 56.55, 55.92, 55.89. GCMS: (*m/z)* 270 $[M]^+$. HRMS calculated for $C_{17}H_{18}O_3$ $[M + Na]^+$ 293.1154, found 293.1154.

***(E)*- 2, 4, 4', 5 - Tetramethoxystilbene (6b)**

Off-white solid (1.58 g, 42%), mp 63-65 °C. ^{1}H NMR ($CDCl_3$): δ 7.21 (d, *J* = 8.8 Hz, 2 H), 6.77 (s, 1 H), 6.75 (d, *J* = 8.8 Hz, 2 H), 6.56 (d, *J* = 12.0 Hz, 1 H), 6.51 (s, 1 H), 6.50 (d, *J* = 12.0 Hz, 1 H), 3.89 (s, 3 H), 3.81 (s, 3 H), 3.76 (s, 3 H), 3.52 (s, 3 H). ^{13}C NMR ($CDCl_3$): δ 151.71, 148.99, 142.57, 130.08, 128.53, 127.46, 123.51, 120.97, 117.86, 113.45, 109.41, 97.53, 56.64, 56.10, 55.99, 55.20. GCMS: (*m/z)* 300 $[M]^+$. HRMS calculated for $C_{18}H_{20}O_4$ $[M + Na]^+$ 323.1259, found 323.1260.

***(E)*- 2, 3', 4, 5, 5' - Pentamethoxystilbene (6c)**

White solid **(**1.61 g, 39%), mp 90-92 °C. ^{1}H NMR ($CDCl_3$): δ 6.79 (s, 1 H), 6.67 (d, *J* = 12.0 Hz, 1 H), 6.51 (d, *J* = 12.0 Hz, 1 H), 6.50 (s, 1 H), 6.46 (d, *J* = 2.4 Hz, 2 H), 6.29 (dd, *J* = 2.4, 2.4 Hz, 1 H), 3.89 (s, 3 H), 3.82 (s, 3 H), 3.66 (s, 6H), 3.52 (s, 3 H). ^{13}C NMR ($CDCl_3$): δ 160.51, 151.80, 149.23, 142.48, 139.55, 128.74, 125.30, 117.33, 113.52, 106.73, 99.50, 97.33, 56.57, 56.12, 56.0, 55.21. GCMS: (*m/z)* 330 $[M]^+$. HRMS calculated for $C_{19}H_{22}O_5$ $[M + Na]^+$ 353.1365, found 353.1365.

***(E)*- 2, 3', 4, 4', 5 - Pentamethoxystilbene (6d)**

White solid **(**1.70 g, 41%), mp 118-20 °C. ^{1}H NMR ($CDCl_3$): δ 6.86 (s, 1 H), 6.83 (m, 2 H), 6.74 (d, *J* = 6.4 Hz, 1 H), 6.57 (d, *J* = 10.0 Hz, 1 H), 6.52 (s, 1 H), 6.49 (d, *J* = 10.0 Hz, 1 H), 3.89 (s, 3

H), 3.84 (s, 3 H), 3.82 (s, 3 H), 3.66 (s, 3 H), 3.54 (s, 3 H). ^{13}C NMR ($CDCl_3$): δ 151.68, 149.02, 148.29, 147.97, 142.51, 130.25, 128.69, 123.64, 121.84, 117.67, 112.77, 111.70, 110.73, 97.38, 56.53, 56.15, 56.09, 56.01, 55.90. GCMS: (*m/z)* 330 $[M]^+$. HRMS calculated for $C_{19}H_{22}O_5$ [M + Na] $^+$ 353.1365, found 353.1367.

***(E)*- 2, 2', 4, 4', 5 – Pentamethoxystilbene (6e)**

White solid (1.86 g, 45%), mp 98-100 °C. ^{1}H NMR ($CDCl_3$): δ 7.14 (d, *J* = 8.8 Hz, 1 H), 6.76 (s, 1 H), 6.65 (d, *J* = 12.0 Hz, 1 H), 6.60 (d, *J* = 12.0 Hz, 1 H), 6.49 (s 1 H), 6.44 (d, *J* = 2.4 Hz, 1 H), 6.29 (dd, *J* = 2.4, 8.4 Hz, 1 H), 3.87 (s, 3 H), 3.82 (s, 3 H), 3.81 (s, 3 H), 3.76 (s, 3 H), 3.47 (s, 3 H). ^{13}C NMR ($CDCl_3$): δ 160.06, 158.18, 151.65, 148.74, 142.42, 130.56, 126.91, 123.51, 119.18, 118.10, 113.15, 104.12, 98.18, 97.42, 56.66, 55.98, 55.93, 55.44, 55.30. GCMS: (*m/z)* 330$[M]^+$. HRMS calculated for $C_{19}H_{22}O_5$ [M + Na] $^+$ 353.1365, found 353.1364.

***(E)*- 2, 2', 4, 4', 5, 5' Hexamethoxystilbene (6f)**

White solid (1.96 g, 43%), mp 110-12 °C. ^{1}H NMR ($CDCl_3$): δ 6.82 (s, 2 H), 6.64 (s, 2 H), 6.50 (s, 2 H), 3.88 (s, 6 H), 3.82 (s, 6 H), 3.51 (s, 6 H). ^{13}C NMR ($CDCl_3$): δ 151.68, 148.92, 142.49, 123.37, 117.91, 113.28, 97.40, 56.52, 56.37, 56.34. GCMS: (*m/z)* 360 $[M]^+$. HRMS calculated for $C_{20}H_{24}O_6$ [M + Na] $^+$ 383.1471, found 383.1471.

***(E)*- 2, 4, 5 -Trimethoxy -3', 4'-methylene dioxystilbene (6g)**

White solid (1.66 g, 42%), mp 84-86 °C. ^{1}H NMR ($CDCl_3$): δ 6.78 – 6.76 (m, 3 H), 6.68 (d, *J* = 8.0 Hz, 1 H), 6.56 (d, *J* = 12.0 Hz, 1 H), 6.51 (s, 1 H), 6.46 (d, *J* = 12.0 Hz, 1 H), 5.88 (s, 2 H), 3.89 (s, 3 H), 3.81 (s, 3 H), 3.56 (s, 3 H). ^{13}C NMR ($CDCl_3$): δ 151.75, 149.15, 147.25, 146.34, 142.61, 131.60, 128.54, 124.02, 122.87, 117.50, 113.44, 108.96, 108.01, 100.80, 97.48, 56.58, 56.21, 55.98. GCMS: (*m/z)* 314 $[M]^+$. HRMS calculated for $C_{18}H_{18}O_5$ [M + Na] $^+$ 337.1052, found 337.1053.

Synthesis of *(E)* - 2, 4, 5 -Trimethoxy -4'-hydroxystilbene (6i)

To a mixture of phosphonium salt **4** (6 g, 12.6 mmol) in dichloromethane (40 mL) and potassium t-butoxide (3.5 g, 31.2 mmol) was added 4-Methoxymethyloxybenzaldehyde **(5h)** [18, 19] (12.6 mmol.) as described in general procedure. After the reaction was completed by TLC, the resultant mass was quenched into water and extracted with dichloromethane. The organic phase was washed with water, dried over anhydrous sodium sulfate and evaporated to obtain gummy mass **6h** as a crude material. The crude **6h** was then treated with a mixture of TEA (12.4 g, 123 mmol) and $AlCl_3$ (5.0 g, 37.5 mmol) in chlorobenzene (4 mL). The resultant mass was stirred at room temperature for 1-2 h. TLC was checked. Quenched the reaction mass into ice water, extracted with dichloromethane; The organic phase was washed with water, dried over anhydrous sodium sulfate

and concentrated under vacuum to obtain crude reaction mass **6i**. This was purified by column chromatography over silica gel using EtOAc/Hexane (0.5:9.5) to get **6i** as light brown solid (1.28 g, 35%), mp 148-50 °C. ^{1}H NMR ($CDCl_3$): δ 7.40 (d, *J* = 8.4 Hz, 2 H), 7.26 (d, *J* = 16.4 Hz, 1 H), 7.10 (s, 1 H), 6.90 (d, *J* = 16.4 Hz, 1 H), 6.80 (d, *J* = 8.4 Hz, 2 H), 6.53 (s, 1 H), 3.90 (s, 6 H), 3.86 (s, 3 H). ^{13}C NMR ($CDCl_3$): δ 154.94, 151.53, 149.32, 143.49, 130.32, 127.65, 126.51, 120.95, 115.52, 113.35, 109.46, 98.01, 56.65, 56.11. GCMS: (*m/z)* 286 $[M]^+$. HRMS calculated for $C_{17}H_{18}O_4$ $[M + Na]^+$ 309.1103, found 309.1103.

Antifungal assay:

Purified *trans*- stilbene derivatives have been subjected to *in vitro* antifungal activity against two phyto-pathogenic fungi by poison plate technique[20]. The plant pathogenic fungi viz., *Phytophthora capsici* and *Sclerotium rolfsii* were obtained from MTCC (Microbial Type Culture Collection), Chandigarh (Division of Microbiology), India. Bavistin was used as standard fungicide; β-Asarone was taken as secondary reference and DMSO as a negative control. The test compounds were dissolved in DMSO to get a concentration of 1000ppm. The fungicidal activity was performed over carrot agar media which was prepared by blending 200 g carrot tissue in 250 mL of distilled water. The juice was filtered and diluted with distilled water to make up to one litre; 15 g of agar (HiMedia, India) was then added. The medium was sterilized in 2 litre flasks for 20 min at 121°C. The test compounds of specified concentration in DMSO was added to molten carrot agar medium (20 mL) and poured into Petri plates. The inoculated plates were then incubated at 26 ± 1 °C for 3 days in case of *Sclerotium rolfsii* and 7 days for *Phytophthora capsici*. The mycelia growth of fungi was measured diametrically in three different directions and the average value was taken for expressing the zone of inhibition. The experiment was repeated thrice. The antifungal activity in terms of percentage inhibition (I %) was calculated by applying the expression:

$$I\ \% = \frac{C-T}{C} \times 100$$

Where

C = Diameter (in mm) of the fungal colony in control plate.

T = Diameter (in mm) of the fungal colony in test sample

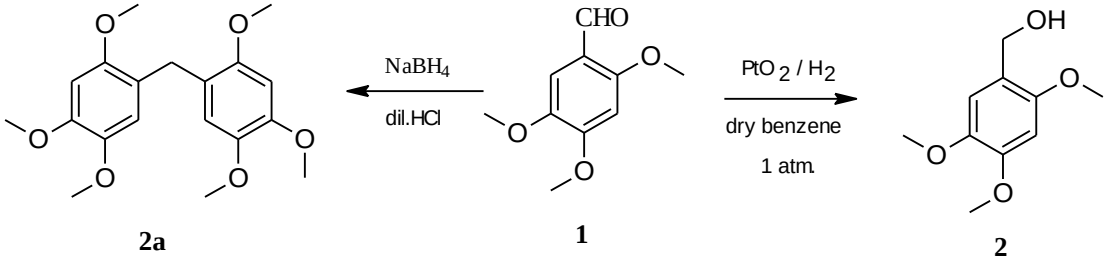
RESULTS AND DISCUSSION

Chemistry

β- Asarone was isolated from the fresh rhizomes of *Acorus calamus* L. as reported in the literature[7, 21]. This was oxidized with $KMnO_4$/ $NaHCO_3$ to get 2, 4, 5-trimethoxybenzaldehyde (**1**)

[22], a key starting material for our study which showed a molecular ion peak at *m/z* 196 in mass spectrum has a molecular formula $C_{10}H_{12}O_4$.

As shown in scheme 1, Anthony *et al*. [23] attempted the reduction of aldehyde **1** with sodium borohydride but ended up in the formation of bis derivative [bis-(2, 4, 5-trimethoxyphenyl) methane (**2a**)], which was not an expected product. Hence, they adopted catalytic hydrogenation in order to obtain desired product **2**. According to this method, the aldehyde **1** was hydrogenated at 1 atm. Pressure in dry benzene using platinum oxide as a catalyst to give 2, 4, 5-trimethoxybenzyl alcohol **(2**) as crystals with considerable yield.



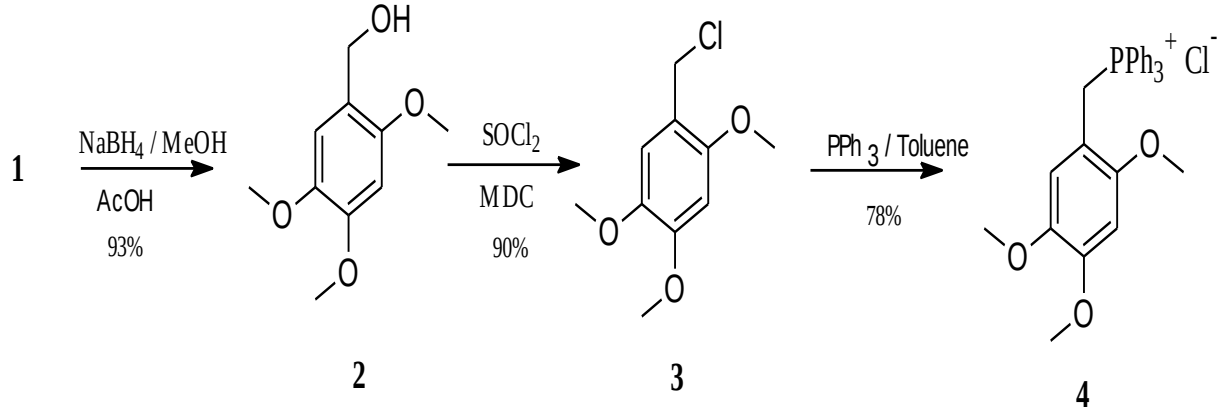
2a **1** **2**

Scheme 1: Synthesis of 2, 4, 5-trimethoxybenzyl alcohol (2)

Since platinum oxide is expensive and the process is cumbersome in bigger scale, we decided to use cheap and easily available sodium borohydride itself as a reducing agent but slightly modified the work up procedure. As we seen in scheme 1, Anthony *et al*. have used relatively strong protic acid such as dil.HCl during work up which probably cleave methoxy group on phenyl ring, this in turn, undergo rearrangement followed by coupling with another molecule to give bis compound **2a**. But as per our working procedure, we used mild organic acid for adjusting the pH. The successful reduction of compound **1** was achieved by taking stoichiometric quantity of sodium borohydide in methanol at room temperature followed by acidification using glacial acetic acid in the work up led to required alcohol **2**.

The procedure outlined in Scheme 2 illustrates the process of producing 2, 4, 5-trimethoxy benzyltriphenyl phosphonium chloride (**4**) and this is not reported so far, a key intermediate for Wittig reaction. The compound 2, 4, 5-trimehtoxybenzyl alcohol **(2**) thus obtained after $NaBH_4$ reduction of compound **1,** was further purified by passing through silica gel column chromatogram in order to obtain pure material. The obtained yield of **2** was about 93%. Further, compound **2** when treated with $SOCl_2$ in dichloromethane (MDC) at ambient temperature afforded corresponding benzyl chloride (**3)** as a dark green viscous mass which was relatively unstable. Hence compound **3** as such without purification was treated with equi-molar amounts of triphenylphosphine in toluene at 80-90º C to obtain compound **4** as off-white solid with over all

yield of 65%. The NMR and GCMS analysis of compound **2** confirmed the structure, similarly mass spectrum of compound **3** exhibited *m/z* peak at 216 which corresponds to the molecular formula $C_{10}H_{13}ClO_4$ confirming the formation of compound. The ^{1}H & ^{13}C NMR data of compound **4 s**howed the presence of triphenyl moiety in the structure.



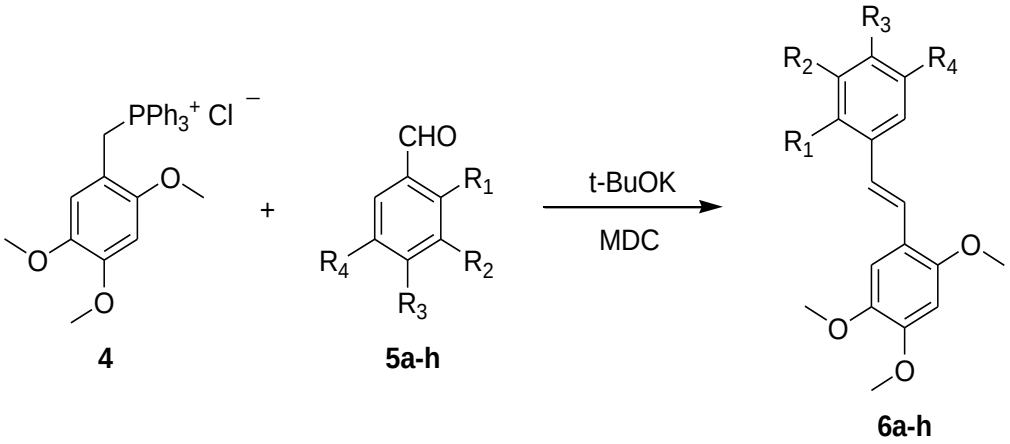
Scheme 2: Synthesis of 2, 4, 5 – trimethoxybenzyl phosphoniumchloride 4

Further, the Wittig reaction of compound **4** with various aromatic aldehydes **5a-h** in presence of potassium t-butoxide in dichloromethane at room temperature afforded crude mixtures, mainly *trans*-stilbenes (as per HPLC data) except in the case of **6a** where *cis*- and *trans*-isomers are in the ratio of 32: 68 (Table 1). This anomaly in case of **6a** could be due to the fact that phenyl ring is unsubstituted. But in the case of compounds **6c**, **6g** and **6h** only *trans*-geometry was observed.

Table 1 HPLC data of the crude mixtures 6a-h (*cis* / *trans*- ratio)

Compound	*cis*-isomer	*trans*- isomer
6a	32	68
6b	5	95
6c	–	100
6d	10	90
6e	4	96
6f	8	92
6g	–	100
6h	–	100

Since in **6h** the *para*-hydroxy group of phenyl ring was protected with methoxymethyl (MOM) moiety it was treated with TEA-$AlCl_3$ mixture at room temperature to obtain crude **6i**. All compounds **6a-g** and **6i** were purified by subjecting to silica gel column chromatography using ethyl acetate/hexane mixture as a mobile phase to obtain pure *trans*-stilbenes (Scheme 3) with isolated yields of up to 48%. ^{1}H & ^{13}C NMR and HRMS data of all the new *trans*-stilbenes were given in the experimental section.



5a, **6a** : R_1 R_2 R_3 R_4 = H

5b, **6b** : R_1 R_2 R_4 = H; R_3 = OMe

5c, **6c** : R_1 R_3 = H; R_2 R_4 = OMe

5d, **6d** : R_1 R_4 = H; R_2 R_3 = OMe

5e, **6e** : R_1 R_3 = OMe; R_2 R_4 = H

5f, **6f** : R_2 = H; R_1 R_3 R_4 = OMe

5g, **6g** : R_1 R_4 = H; R_2 R_3 = Methylene dioxy

5h : R_1 R_2 R_4 = H; R_3 = OMOM

6h : R_1 R_2 R_4 = H; R_3 = OMOM → TEA - $AlCl_3$

6i : R_1 R_2 R_4 = H; R_3 = OH

Scheme 3: Synthesis of *E*-stilbene derivatives 6a-i

Biological evaluation:

Antifungal activity (by poison plate method)

The percentage inhibition of all the compounds **6a-g** and **6i** has been summarized in Table 2. Results of *in vitro* antifungal activity demonstrated that compound **6f** showed good inhibition against both *P. capsici* and *S. rolfsii* comparable to β- asarone. The unusual substitution pattern of methoxy groups in both aromatic rings in **6f** coupled with structural symmetry perhaps play key role in inhibiting the growth of fungi. On the other hand, the compounds **6a, 6b, 6d, 6e, 6g** and **6i** exhibited lower to moderate fungicidal activity against **P.** *capsici* whereas compound **6c** was found to be almost inactive. Similarly, the compound **6c, 6d, 6e** and **6i** were inactive toward *S.rolfsii* but compound **6a, 6b** and **6g** exhibited mild antifungal property. This indicates that the compound **6f** may be taken as a lead molecule for the development of novel antifungal agents.

Table 2 The antifungal activity of *E*-stilbene derivatives 6a-g and 6i

Compound	Test fungi (% inhibition at 1000ppm)*	
	Phytophthora *capsici*	***Sclerotium rolfsii***
6a	38.29	24.4
6b	18.13	21.96
6c	NA	NA
6d	19.5	NA
6e	15.34	NA
6f	87.24	81.55
6g	23.71	8.8
6i	41.52	NA
β- Asarone (> 90%)	84.18	73.8
Bavistin**	100	100

* % inhibition calculated after nullifying the effect of DMSO

** Reference standard

NA – Not active

CONCLUSION

In summary, we have synthesized a series of novel *trans*-stilbene derivatives **6a-i** from 2, 4, 5-trimethoxy benzaldehyde obtained from β- asarone. The Wittig reaction of Phosphonium ylide **4 (**prepared for the first time) with substituted aromatic aldehydes **5a-h** followed by purification afforded pure *trans*- isomers. All the compounds were characterized by ^{1}H / ^{13}C-NMR and mass spectral analysis. The *in vitro* antifungal activity of compounds **6a-g** and **6i** was tested against two plant pathogenic fungi- *Phytophthora capsici* and *Sclerotium rolfsii*. The symmetrical *trans*-dimeric stilbene **6f** was found to exhibit better fungicidal property compared to others.

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