A facile synthesis of 2,6-dibenzoyl-5-methyl-3-(substituted styryl)-benzo[1,2-b; 5,4-b']difurans under phase transfer catalytic conditions and their antifeedant activity

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2,6-Dibenzoyl-5-methyl-3-(substituted styryl) benzodifurans 4a-i have been prepared by condensing 2-benzoyl-5-substituted cinnamoyl-6-hydroxy-3-methylbenzofurans 3a-i with 2-bromoacetophenone under phase transfer catalytic conditions. All the compounds 4a-i are screened for their antifeedant activity by the "Non-Choice test method" using 6 hr prestarved fourth instar larvae of Spodoptera litura F. Compounds 4g and 4h exhibit highest antifeedant activity.

A number of benzofuran derivatives have been shown to exhibit insecticidal\(^1\)-2, antiinflammatory\(^3\)-4, spasmylytic and vasodilatory\(^5\)-6, antibacterial\(^7\)-8, antifungal\(^9\), antiallergic\(^10\), antihistaminic\(^11\) as well as estrogenic and antiimplantation\(^11\)-12 properties. The aryl moieties at second position in benzodifurans play an important role in imparting various biological activities to benzodifuran nucleus. None of the aryl substituted benzofurans or benzodifurans has been screened for their antifeedant activity. Literature survey reveals that synthesis and antifeedant activity of the title compounds have not been reported so far. These considerations prompted us to take up the synthesis and study of 2,6-dibenzoyl-5-methyl-3-(substituted styryl)benzo[1,2-b;5,4-b']difurans as potential antifeedants.

The required starting materials, the cinnamoyl benzofurans 3a-i (cf. Scheme I) were prepared by the condensation of 4,6-diacetylresorcinol\(^13\) with 2-bromoacetophenone\(^14\) (1:1) in the presence of acetone-anhydrous K\(_2\)CO\(_3\) medium for 8 hr. Work-up of the reaction mixture yielded the corresponding 2,6-dibenzoyl-5-methyl-3-(substituted styryl)benzo[1,2-b;5,4-b']difurans 4a-i. As a representative case the spectral identification of 2,6-dibenzoyl-5-methyl-3-(p-methoxy styryl)benzo[1,2-b;5,4-b']difuran 4c, m.p. 200°C, C\(_{34}\)H\(_{24}\)O\(_5\), M\(^+\)512 has been discussed.

The IR spectrum of 4c shows a sharp peak at 1640 cm\(^{-1}\) (C=Ostr), and in UV spectrum, \(\lambda_{max}\) at 270 nm (log \(\varepsilon\) 4.05), 224 nm (log \(\varepsilon\) 3.81), 275 nm (log \(\varepsilon\) 3.24) were in agreement with the reported values for benzodifurans\(^16\). \(^1\)H NMR spectrum of 4c showed two sinlgets in the aliphatic region at \(\delta\) 2.73 and 3.86 integrating for three protons each, which were assigned to the C5-methyl and methoxyl protons, respectively. Two doublets (J=16 Hz) which appeared at \(\delta\) 6.9 and \(\delta\) 7.9 integrating for one proton each, were assigned to \(\beta\)-H and \(\alpha\)-H, respectively. A sharp singlet in the aromatic region at \(\delta\) 8.27 (1H) was assigned to C4 proton\(^19\). The spectrum also showed one doublet (J=9
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Scheme I

Table 1—Analytical and spectral data of the title compounds 4a-i

<table>
<thead>
<tr>
<th>Compd</th>
<th>Mol. formula</th>
<th>M⁺</th>
<th>mp °C</th>
<th>Yield %</th>
<th>IR(KBr) C=O (cm⁻¹)</th>
<th>UV(MeOH) λmax nm (log ε)</th>
<th>Antifeedant activity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4a</td>
<td>C₃,H₂,O₄</td>
<td>482</td>
<td>160</td>
<td>70</td>
<td>1638</td>
<td>360 (3.35)</td>
<td>82.48</td>
</tr>
<tr>
<td>4b</td>
<td>C₃,H₂,O₂Cl</td>
<td>516 &amp; 518 (3:1)</td>
<td>233</td>
<td>71</td>
<td>1640</td>
<td>359 (2.94)</td>
<td>83.26</td>
</tr>
<tr>
<td>4c</td>
<td>C₃,H₂,O₂</td>
<td>512</td>
<td>200</td>
<td>64</td>
<td>1640</td>
<td>275 (3.24)</td>
<td>72.56</td>
</tr>
<tr>
<td>4d</td>
<td>C₃,H₂,O₂</td>
<td>496</td>
<td>204</td>
<td>68</td>
<td>1640</td>
<td>363 (3.94)</td>
<td>74.76</td>
</tr>
<tr>
<td>4e</td>
<td>C₃,H₂,O₂Cl</td>
<td>516 &amp; 518 (3:1)</td>
<td>186</td>
<td>63</td>
<td>1640</td>
<td>361 (3.67)</td>
<td>59.88</td>
</tr>
<tr>
<td>4f</td>
<td>C₃,H₂,O₂,O₂Cl</td>
<td>550, 552 &amp; 554 (9:3:1)</td>
<td>202</td>
<td>73</td>
<td>1638</td>
<td>372 (3.46)</td>
<td>80.25</td>
</tr>
<tr>
<td>4g</td>
<td>C₃,H₂,O₂</td>
<td>542</td>
<td>194</td>
<td>69</td>
<td>1638</td>
<td>332 (3.72)</td>
<td>98.25</td>
</tr>
<tr>
<td>4h</td>
<td>C₃,H₂,O₂</td>
<td>526</td>
<td>172</td>
<td>74</td>
<td>1640</td>
<td>349 (3.66)</td>
<td>96.00</td>
</tr>
<tr>
<td>4i</td>
<td>C₃,H₂,O₂</td>
<td>472</td>
<td>182</td>
<td>75</td>
<td>1638</td>
<td>352 (3.12)</td>
<td>78.50</td>
</tr>
</tbody>
</table>

All the Compounds gave satisfactory elemental analysis.
Hz) in the aromatic region at δ 8.07 integrating for four protons due to C-2',2",6',6"^{19}, and also one multiplet appearing at δ 7.6 and integrating for 10 protons was assigned to remaining aromatic protons, of phenyl rings. In the aromatic region the spectrum also showed another singlet at δ 7.65 (1H) which was assigned to C8 proton^{19}. The mass spectrum of 4c showed the molecular ion peak at m/z 512 (35%), consistent with its molecular formula C34H24O5.

The above investigation revealed that phase transfer catalysis conditions possess several advantages over the Baker-Venkatraman transformation method. The yields are high, and the products are of excellent purity. At the same time, the need for anhydrous conditions can be dispensed with.

All the compounds 4a-i were tested for their antifeedant activity by “Non-Choice test method”^{20} using 6 hr prestarved fourth instar larvae of Spodoptera litura F. Approximately 10 cm diameter leaf disc was cut from fresh castor leaf and dipped in acetone solution of the compound containing 5% triton-X 100 as sticker. Then leaf disc was dried and kept in a petri-dish. Control disc of same diameter was dipped in acetone containing 5 % triton-X as sticker. Then leaf disc was dried and kept in a petri-dish. Control disc of same diameter, in each petri-dish a dropwise with stirring during a period of 15 min. To this emulsion 2-bromoacetophenone (1.5 g) was added and the mixture refluxed for a period of 10 min. The product was filtered, washed with water and dried.

Compounds 4g and 4h exhibited highest antifeedant activity. The present study revealed that introduction of substituents like 3,4-dimethoxy and 3,4-dimethylenedioxy in the phenyl group increased the antifeedant activity of benzodifurans.

**Experimental Section**

**General.** Melting points were taken in open capillary tubes in sulfuric acid-bath and are uncorrected. FT-IR spectra were obtained on a Perkin-Elmer 1605 spectrophotometer. UV spectra were obtained on a Hitachi U-3410 spectrometer. 1H NMR spectra were taken in CDCl3 on a Varian Gemini 200 MHz spectrometer with TMS as internal standard (chemical shifts in δ, ppm). El mass spectra were obtained on V G Micromass 7070H instrument.

**Cinnamoyl benzofurans 3a-i: General procedure.** A mixture of 1 and 2-bromoacetophenone (1:1 mole) was refluxed in the presence of acetone and anhydrous K2CO3 for 6 hr. After recovering excess acetone, the contents were poured over crushed ice. The solid separated was filtered, washed with water and extracted with hot 5% NaOH solution. The crude product obtained on neutralisation with dil HCl, on crystallisation from MeOH afforded the compound 2. A mixture of 2 (0.01 mole) and appropriate aldehyde (0.01 mole) in ethanol (40 mL) and aq KOH (60%, 20 mL) was kept at room temperature for 24 hr. The product obtained on dilution and acidification with dil HCl was subjected to column chromatography over silicagel (Acme, 200 mesh) using eluent benzene-chloroform (6:4 v/v) followed by concentration, afforded the compound 3.

**Synthesis of 2,6-dibenzoyl-5-methyl-3-(substituted styryl) benzofuran-[2,1-b;5,4-b']difurans 4: (a) By phase transfer catalytic condition.** To a stirred solution of substituted cinnamoyl benzofurans 3a-i (0.01 mole) in benzene (60 mL), and 20% of aqueous K2CO3 (60 mL), 150 mg of tetrabutyl ammonium hydrogen sulphate (TBAHSO4) in benzene (10 mL) was added dropwise with stirring during a period of 15 min. To this emulsion 2-bromoacetophenone (1.5 g) in 30 mL of benzene was added over a period of 20 min. Stirring was continued for 5-6 hr at room temperature. The organic layer was separated, washed with water and dried over anhydrous sodium sulphate. The solvent was removed under reduced pressure and the residue subjected to column chromatography over silica gel (Acme, 200 mesh) using eluent benzene-chloroform (1:1 v/v) followed by concentration afforded the compound 4, which was further crystallised from methanol.

**Limited Section**

**Cinnamoyl benzofurans 3a-i: General procedure.** A mixture of 1 and 2-bromoacetophenone (1:1 mole) was refluxed in the presence of acetone and anhydrous K2CO3 for 6 hr. After recovering excess acetone, the contents were poured over crushed ice. The solid separated was filtered, washed with water and extracted with hot 5% NaOH solution. The crude product obtained on neutralisation with dil HCl, on crystallisation from MeOH afforded the compound 2. A mixture of 2 (0.01 mole) and appropriate aldehyde (0.01 mole) in ethanol (40 mL) and aq KOH (60%, 20 mL) was kept at room temperature for 24 hr. The product obtained on dilution and acidification with dil HCl was subjected to column chromatography over silicagel (Acme, 200 mesh) using eluent benzene-chloroform (6:4 v/v) followed by concentration, afforded the compound 3.
concentration afforded the compound 4, which was further crystallised from methanol.

4a: $^1$H NMR (200 MHz, CDCl$_3$): $\delta$ 2.70 (3H, s, C$_5$-CH$_3$), 6.92 (1H, d, J = 14 Hz, $\beta$-H), 7.91 (1H, d, J = 14 Hz, $\alpha$-H), 8.26 (1H, s, C$_4$-H), 8.12 (4H, d, J = 9 Hz, H-2', 2'', 6', 6''), 7.55 (11H, m, aromatic protons), 7.68 (1H, s, C$_8$-H).

4b: $^1$H NMR (200 MHz, CDCl$_3$): $\delta$ 2.75 (3H, s, C$_3$-CH$_3$), 6.84 (1H, d, J = 16 Hz, $\beta$-H), 7.86 (1H, d, J = 16 Hz, $\alpha$-H), 8.05 (4H, d, J = 9 Hz, H-2', 2'', 6', 6''), 7.60 (10 H, m, aromatic protons), 7.74 (1H, s, C$_8$-H).

4d: $^1$H NMR (200 MHz, CDCl$_3$): $\delta$ 2.68 (3H, s, C$_5$-CH$_3$), 2.48 (3H, s, Ar-CH$_3$), 6.80 (1H, d, J = 14 Hz, $\beta$-H), 7.82 (1H, d, J = 14 Hz, $\alpha$-H), 8.20 (1H, s, C$_4$-H), 8.10 (4H, d, J = 9.2 Hz, H-2', 2'', 6', 6''), 7.52 (10H, m, aromatic protons), 7.70 (1H, s, C$_8$-H).

4f: $^1$H NMR (200 MHz, CDCl$_3$): $\delta$ 2.70 (3H, s, C$_5$-CH$_3$), 6.0 (2H, s, O-CH$_2$-O), 6.86 (1H, d, J = 15 Hz, $\beta$-H), 7.88 (1H, d, J = 15 Hz, $\alpha$-H), 8.20 (1H, s, C$_4$-H), 8.15 (4H, d, J = 9.2 Hz, H-2', 2'', 6', 6''), 7.64 (9H, m, aromatic protons), 7.70 (1H, s, C$_8$-H).

4g: $^1$H NMR (200 MHz, CDCl$_3$): $\delta$ 2.65 (3H, s, C$_5$-CH$_3$), 6.82 (1H, d, J = 16 Hz, $\beta$-H), 7.80 (1H, d, J = 16 Hz, $\alpha$-H), 8.26 (1H, s, C$_4$-H), 7.42 (9H, m, aromatic protons), 7.75 (1H, s, C$_8$-H), 8.10 (4H, d, J = 9 Hz, H-2', 2'', 6', 6'').

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References