

Note

A facile synthesis of 3-phenyl-4-(2-thienyl)- and 3, 4-di(2-thienyl)coumarins by phase transfer catalysis method

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Synthesis and characterization of 3-phenyl-4-(2-thienyl)coumarins, 4-(2-furyl)-3-phenylcoumarins and 3,4-di(2-thienyl)coumarins have been reported by phase transfer catalysis method in 75% yields. This method involves condensation of appropriate 2-thienyl or 2-furyl-2-hydroxyphenylmethanones with phenylacetyl chloride or 2-(2-thienyl)ethanoyl chloride using TABHSO₄ as PTC catalyst.

We report herein the synthesis of 3-phenyl-4-(2-thienyl)coumarins **4**, 4-(2-furyl)-3-phenylcoumarins **6** and 3,4-di(2-thienyl)coumarins **7** by PTC method. This method was used for the first time for the synthesis of these 3- and/or 4-heteryl substituted coumarins. The insect-antifeedant activity of the compounds was also assessed.

2-Hydroxyphenyl-2-thienylmethanones **3** were synthesized from the corresponding phenols **1**, through Fries migration *via* esters **2**. Condensation of **3** with phenylacetyl chloride, under PTC conditions,

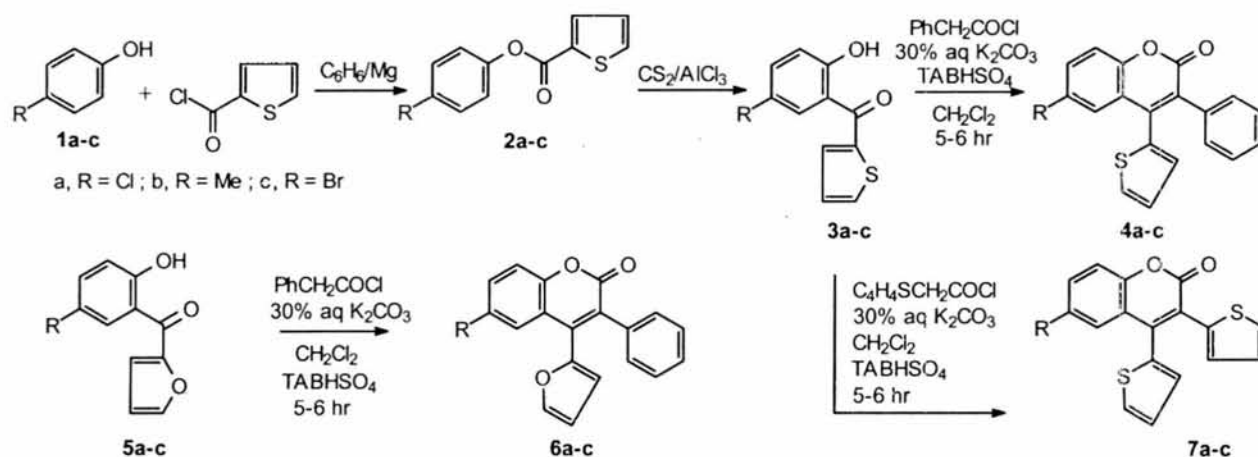
using catalytic amounts of tetrabutylammonium hydrogen sulphate (TABHSO₄) furnished 3-phenyl-4-(2-thienyl)coumarins **4** in yields around 88%. All the compounds are reported here for the first time by PTC method.

Likewise condensation of 2-hydroxyphenyl-2-furyl methanones **5** successively with phenylacetyl chloride under PTC conditions gave 4-(2-furyl)-3-phenylcoumarins **6** in high yields (~85%). These compounds were earlier synthesized by Perkins method¹ in lower yields (50-60%).

Similarly 3,4-di(2-thienyl)coumarins **7** were synthesized by the condensation of **3a-c**, successively, with 2-(2-thienyl)ethanoyl chloride under PTC conditions. The yields are high (~80 to 90%) and are reported here for the first time.

All the coumarins (**4**, **6** and **7**) were characterized by elemental analyses and spectral data. They exhibited characteristic carbonyl frequency of coumarins between 1710 and 1740 cm⁻¹. In UV three absorption bands were recorded in the regions 210-220, 270-280 and 338-370 nm which is characteristic of 3,4-disubstituted coumarins^{2,3}. The mass spectral and ¹H NMR data (experimental) were in agreement with the assigned structures.

The compounds **4**, **6** and **7** in 1000 ppm concentration in acetone were tested for their insect-antifeedant activity on 6-8 hr prestarved larva of fourth instar *Spodipetra litura* F., on fresh castor leaf disc, by non-



Scheme I

choice test method⁴. The percentage of antifeedant activity was calculated by the formula of Singh and Panth⁵. 6-Chloro-3, 4-di-(2-thienyl)coumarin **7a**, and 6-bromo-3,4-di-(2-thienyl)coumarin **7c** showed high insect-antifeedant activity, 85% and 80% respectively. Rest of the compounds showed moderate or poor antifeedant activity.

Experimental Section

General. Melting points were taken in open capillary tubes in sulfuric acid-bath and are uncorrected. IR spectra in solid KBr were recorded on infracord model 337 Perkin-Elmer instrument. UV spectra were recorded on a Shimadzu UV 200 spectrophotometer in MeOH. ¹H NMR were recorded in DMSO-*d*₆ on a Varian A90D or Varian EM 390 (90 MHz) machine with TMS as internal standard (chemical shifts in δ , ppm). Mass spectra were recorded on a Hitachi RMU-6L MS.30 instrument with D55 data system.

Synthesis of 5-chloro-2-hydroxyphenyl-2-thienylmethanone 3a. A mixture of 4-chlorophenol **1a** (1.6 g), anhydrous benzene (30 mL), magnesium (12 g) and 2-thiophenecarbonyl chloride (14.6 mL) was refluxed in a water-bath for 1 hr. The unreacted magnesium was filtered off, benzene removed under reduced pressure and the residue taken in ether, washed with 1% sodium hydroxide and then with water. The ether layer was dried over anhydrous sodium sulphate to give 4-chlorophenyl-2-thiophenecarboxylate **2a** as liquid (80% yield). The product was directly used in the next step.

Compound **2a** (3 g) was dissolved in carbon disulphide (180 mL) and anhydrous aluminium chloride (12 g) added to it slowly while cooling and stirring and then heated on a water-bath for 2 hr. Solvent was removed under reduced pressure and the residue heated for 2 hr in an oil-bath. It was cooled and decomposed by adding dil. hydrochloric acid to give **3a** as a solid. It recrystallized from methanol to give yellow needles, mp 82°C, yield 50%. Anal. Calcd for C₁₁H₇O₂ClS: C, 55.46; H, 2.94%. Found: C, 55.2; H, 2.7.

5-Methyl-2-hydroxyphenyl-2-thienylmethanone 3b. Similarly, 4-methylphenol **1b** on condensation with 2-thiophenecarbonyl chloride (14.6 g) gave 4-methylphenyl-2-thiophene carboxylate **2b** (5 g, 80% yield). This was directly subjected to Fries migration to yield **3b**. It recrystallised from methanol, mp 91°C (50% yield). It gave a violet coloration with metha-

nolic ferric chloride. Anal. Calcd for C₁₂H₁₀O₂: C, 66.04; H, 4.55%. Found: C, 66.0, H, 4.3%.

5-Bromo-2-hydroxyphenyl-2-thienylmethanone 3c. 4-Bromophenol **1c** (16 g), and 2-thiophenecarbonyl chloride (14.6 mL) on adopting the above procedure furnished 4-bromophenyl-2-thiophenecarboxylate **2c** (3 g, 90%) which was directly subjected to Fries migration as given above to give **3c**, mp 96°C (60% yield). It gave a violet coloration with methanolic ferric chloride. Anal. Calcd for C₁₁H₇O₂Br S: C, 46.8; H, 2.48%. Found: C, 46.7; H, 2.3%.

General procedure for the synthesis of 4-(2-thienyl)-3-phenylcoumarins 4, 4-(2-furyl)-3-phenyl coumarins 6 and 3,4-di-(2-thienyl)coumarins 7. A solution of 2-hydroxymethanone **3** or **5** (0.01 mole) in dichloromethane (30 mL), tetrabutylammonium hydrogen sulphate (50 mg, 0.0015 mole) and 30% aqueous potassium carbonate (30 mL) were placed in a flask equipped with a magnetic stirrer. Phenylacetyl chloride (1.5 mL) or 2-thiophenecarbonyl chloride (1.6 mL) in dichloromethane (10 mL) was added to it dropwise during 15-20 min. The mixture was stirred for 6 hr at room temperature. The organic layer was separated, washed with water (3×40 mL) and dried over sodium sulphate. The solvent was removed under reduced pressure and the residue recrystallised from appropriate solvent to furnish the title compounds.

6-Chloro-3-phenyl-4-(2-thienyl) coumarin 4a: Recrystallised from methanol as yellow needle, mp 147°C (3 g, 88% yield); IR: 1720 cm⁻¹; UV: 220 (log ϵ 4.78), 280 (4.23), 340 nm (4.30); ¹H NMR: 7.55 to 8.1 (m, 11H, aromatic protons); MS: m/z 338 (M⁺). Anal. Calcd for C₁₉H₁₁O₂ClS: C, 67.45; H, 3.25%. Found: C, 67.3; H, 3.2%.

6-Methyl-3-phenyl-4-(2-thienyl)coumarin 4b. Recrystallised from methanol as yellow coloured flakes, mp 178°C (2.8 g, 88%); IR: 1705 cm⁻¹; UV: 210 (log ϵ 4.44); 270 (3.97), 340 (4.05); ¹H NMR: 2.43 (s, 3H, H-6 CH₃), 6.83 (d, 1H, J_{8H, 7H} = 9Hz, H-8), 7.25 (s, 6H, H-3-phenyl and 7), 7.37 (m, 3H, H-5, 3' and 5'), 7.01 (dd, 1H, J_{4'H, 3'H} = 4.0Hz, J_{4'H, 5'H} = 5 Hz, H-4'), MS: m/z 318 (M⁺). Anal. Calcd for C₂₀H₁₄O₂S: C, 75.47; H, 4.40%. Found: C, 75.3, H, 4.3%.

6-Bromo-3-phenyl-4-(2-thienyl)coumarin 4c. Recrystallised from methanol as yellow coloured flakes, mp 150°C (3.0 g, 78% yield); IR: 1710 cm⁻¹;

UV: 210 (log ϵ 4.69), 280 (4.18), 340 nm (4.18); ^1H NMR: 7.01 (d, 1H, $J_{\text{8H}, 7\text{H}} = 9\text{ Hz}$, H-8), 7.07 (dd, 1H, $J_{4'\text{H}, 3'\text{H}} = 4.0\text{ Hz}$, $J_{4'\text{H}, 5'\text{H}} = 5\text{ Hz}$, H-4'), 7.25 (brm, 7H, H-3', 7 and 3-phenyl), 7.37 (d, 1H, $J_{5\text{H}, 7\text{H}} = 2\text{ Hz}$, H-5), 7.55 (d, 1H, $J_{5'\text{H}, 4'\text{H}} = 5\text{ Hz}$, H-5'). Anal. Calcd for $\text{C}_{19}\text{H}_{11}\text{O}_2\text{SBr}$: C, 59.6; H, 2.87. Found: C, 59.4 H, 2.7%.

6-Chloro-4-(2-furyl)-3-phenylcoumarin 6a. Recrystallised from methanol as yellow coloured needles, mp 139°C (2.9 g, 90% yield); lit.¹, mp 139°C .

6-Methyl-4-(2-furyl)-3-phenylcoumarin 6b. Recrystallised from methanol as light yellow needles, mp 114°C (2.7 g, 89% yield; lit.¹, mp 114°C).

6-Bromo-4-(2-furyl)-3-phenylcoumarin 6c. Recrystallised from methanol to give light yellow coloured needles, mp 148°C (3.1 g, 84% yield; lit. mp 148°C).

6-Chloro-3,4-di (2-thienyl)coumarin 7a. Recrystallised from methanol as yellow coloured needles, mp 170°C (2.8 g, yield 86%); IR: 1710 cm^{-1} ; UV: 210 (log ϵ 4.25), 270 (4.15), 370 nm (3.76); ^1H NMR: 6.81-7.5 (complex multiplets, 9H, Ar-H); MS: m/z 324 (M^+). Anal. Calcd for $\text{C}_{17}\text{H}_9\text{O}_2\text{S}_2\text{Cl}$: C, 62.96; H, 2.77. Found: C, 62.8, H, 2.6%.

6-Methyl-3, 4-di(2-thienyl)coumarin 7b. Recrystallised from methanol to give yellow coloured flakes, mp 185°C (2.8 g, 92% yield); IR: 1720 cm^{-1} ; UV: 215 (log ϵ 4.18), 270 (3.98), 370 nm (4.10), ^1H NMR: 2.38 (s, 3H, H-6 CH_3), 6.96 (d, 1H, $J_{\text{8H}, 7\text{H}} =$

9 Hz, H-8), 7.18 (m, 4H, H-3', 4' 3'', 4''), 7.38 (m, 3H, H-7, 5', 5''), 7.52 (d, 1H $J_{5\text{H}, 7\text{H}} = 2\text{ Hz}$, H-5) MS: m/z 304 (M^+). Anal. Calcd for $\text{C}_{18}\text{H}_{12}\text{O}_2\text{S}_2$: C, 71.05; H, 5.55. Found: C, 71.1; H, 5.6%.

6-Bromo-3,4-di (2-thienyl)coumarin 7c. Recrystallised from methanol to give yellow coloured flakes, mp 150°C (3 g, 81% Yield); IR: 1715 cm^{-1} ; UV: 215 (log ϵ 4.42), 270 (4.32), 370 nm (4.14); MS: m/z 368 (M^+). Anal. Calcd for $\text{C}_{17}\text{H}_9\text{O}_2\text{S}_2\text{Br}$: C, 55.43, H, 2.4. Found: C, 55.3; H, 2.3%.

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