

# Synthesis of Some 2-(2'-Thienoyl)Coumaran-3-Ones\*\*

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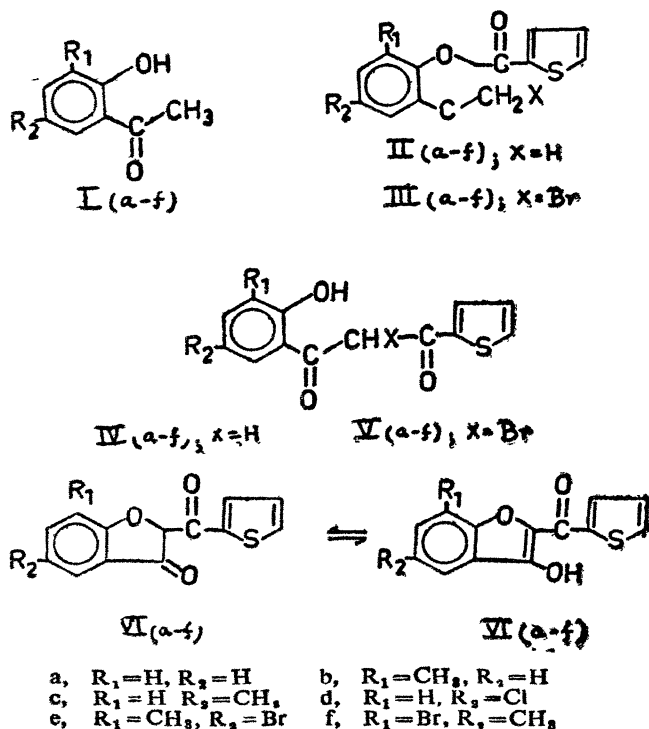
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Manuscript received 4 February 1980, revised 30 June 1980, accepted July 26, 1980

Synthesis of 2-(2'-Thienoyl)coumaran-3-one and its 7-methyl, 5-methyl, 5-chloro, 7-methyl-5-bromo, 5-methyl-7-bromo derivatives from two routes have been described. In one, the corresponding 2-(2'-thienoyloxy) acetophenones have been brominated using  $\text{CuBr}_2$  to obtain high yields of the  $\omega$ -bromoacetophenones, which on Baker-Venkataraman (B.V) transformation afforded the coumaran-3-ones. In the other, the thienoyloxy acetophenones have been first converted to the related 1:3 diketones by B. V. rearrangement. These ketones have then been converted to the coumaran-3-ones by careful bromination and cyclization.

THE synthesis of 2-acyl coumaranones do not appear to have received much attention<sup>1-11</sup> and in the reports published earlier, the acyl unit was invariably non-heterocyclic. A series of investigations leading to the synthesis of 2-heteroacylcoumaran-3-ones have, therefore, been currently undertaken in this laboratory (partly reported)<sup>12</sup>. In this communication the preparation of some 2-(2'-thienoyl) coumaran-3-ones has been described.

These coumaranones have been obtained by two routes. In one, the hydroxyacetophenones ( $\text{I}_{a-f}$ ) were converted to the O-acyl esters ( $\text{II}_{a-f}$ ) in 60 to 90% yield



by the direct condensation with thiophene-2-carboxylic acid using  $\text{POCl}_3$  as the condensing agent<sup>10,13</sup> and the esters were rearranged to the corresponding 1:3-diketones ( $\text{IV}_{a-f}$ ) by Baker-Venkataraman transformation. On careful bromination<sup>5</sup> of the  $\beta$ -diketones ( $\text{IV}_{a-f}$ ) and cyclization of the products the desired coumaranones ( $\text{VI}_{a-f}$ ) were obtained. Repeated crystallisation of the bromo compounds did not yield sharply melting products indicating partial cyclization during purification.

In the second procedure, the intermediate bromo compounds ( $\text{III}_{a-f}$ ) were obtained in high yields by employing dry  $\text{CuBr}_2$ <sup>10,13</sup> for bromination of the esters ( $\text{II}_{a-f}$ ) in conformity with Grover<sup>14</sup> and coworker's observation except, in the case of 3-methyl-2-(2'-thienoyloxy) acetophenone. Baker-Venkataraman rearrangement of these bromo-compounds with KOH in boiling dioxan afforded, (obviously through the unstable intermediate  $\text{V}_{a-f}$ ), the coumaranones identical with those obtained by the first procedure. The overall yields by the second procedure were slightly better than the first. All the coumaranones were soluble in dilute alkali and gave positive ferric reaction. The coumaranones gave the correct elemental analysis results. Their i.r. spectra agree with the assigned structure<sup>15,16</sup> and show distinct hydroxyl bands indicating enolisation to a degree. The PMR spectra of two representative coumaranones add further confirmation.

## Experimental

All mps are uncorrected. Nuclear brominated hydroxyacetophenones were obtained by the method of Buu-Hoi *et al*<sup>17</sup>.

### Preparation of the thienoyloxyacetophenones ( $\text{II}_{a-f}$ )<sup>1</sup>

A mixture of  $\text{I}_{a-f}$  (0.06 mole) and thiophene-2-carboxylic acid (0.07 mole) in dry pyridine (10 ml) was treated with  $\text{POCl}_3$  (2 ml) in drops with stirring (2 hrs)

\*\*Presented at the Annual Convention of Chemists, 1979 held at Kurukshetra University,

below 60°. It was left overnight and poured into ice-HCl mixture. The filtered solid was triturated with NaOH solution (2%), washed with water and recrystallised from ethanol. The m.ps and yields were as under :

II<sub>a</sub> 110°, 60%; II<sub>b</sub> 72-73°, 78% (Lit.<sup>18</sup> 55°); II<sub>c</sub> 91°, 75%; II<sub>d</sub> 84°, 65%; II<sub>e</sub> 89°, 90%; II<sub>f</sub> 82°, 80%.

(In several earlier lots II<sub>b</sub> was obtained as a viscous product. The solid analysed correctly for C & H).

#### Preparation of the 1:3 Diketones (IV<sub>a-f</sub>) :

II (0.01 mole) and powdered KOH (0.03 mole) in dry pyridine (15 ml) were stirred at 50° till the mixture turned into a thick yellow paste and left at room temperature for 2 hrs. Pouring into crushed ice containing HCl acid gave the crude diketone which was washed and recrystallised from ethanol. The m.ps and yields were as follows :

IV<sub>a</sub> 86-87°, 65%; IV<sub>b</sub> 79-80°, 80% (Lit.<sup>18</sup> 72-73°, 52%); IV<sub>c</sub> 80-81°, 78% (Lit.<sup>18</sup> 80°, 50%); IV<sub>d</sub> 106-07°, 60%; IV<sub>e</sub> 106°, 75%; IV<sub>f</sub> 99-100°, >0%.

#### Preparation of Coumaran-3-ones (VI<sub>a-f</sub>) :

A diketone (0.001 mole) in dry chloroform (15 ml) containing anhydrous K<sub>2</sub>CO<sub>3</sub> (1g) was treated with bromine (molar proportion) in dry chloroform (5 ml) at 0°. Stirring was continued till the disappearance of the colour due to bromine. The mixture was next

refluxed on a water bath (3 hrs) and acidified (dil.HCl). Removal of the chloroform layer, washing, drying (MgSO<sub>4</sub>) and distillation of the chloroform gave a solid which was crystallised from a proper solvent. The m ps, yields, solvent of crystallisation have been given in the table separately.

#### Preparation of ω-Bromo-thienoyloxyacetophenones (III<sub>a-f</sub>) :

Anhydrous CuBr<sub>2</sub> (0.01 mole) in dry dioxan (20 ml) was refluxed for ½ hr. with exclusion of moisture. An ester (II<sub>a-f</sub>) (0.005 mole) was next added and refluxing was continued for 2 hrs. The dioxan filtrate was concentrated under pump and diluted with ice-water. The solid which separated was washed and crystallised from alcohol. Viscous products were extracted with benzene, purified and directly used for the next experiment. M.ps and yields were : III<sub>a</sub> 93°, 82%; III<sub>b</sub> gummy mass; III<sub>c</sub> 81°, 60%; III<sub>d</sub> 90°, 61%; III<sub>e</sub> 132°, 60%; III<sub>f</sub> 97°, 62%.

#### Preparation of coumaran-3-ones (VI<sub>a-f</sub>) :

A ω-bromo ester (0.005 mole) in dry dioxan (15 ml) and powdered KOH (0.015 mole) was refluxed for ½ hr. After cooling, the mixture was poured over ice/dil. H<sub>2</sub>SO<sub>4</sub> and the resulting solid was filtered, washed with water and recrystallised.

These products showed no depression on admixture (1:1) with coumaran-3-ones obtained by the other route. The yields have been shown in the table.

TABLE

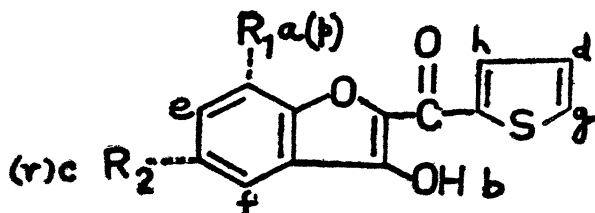
| S.N.            | Name  | M.P.    | % yield and solvent of crystallisation. | Mole formula                                      | Required |      | Found |     |
|-----------------|---|---------|---|---|----------|------|-------|-----|
|                 |   |         |   |   | C %      | H%   | C %   | H%  |
| VI <sub>a</sub> | (2-(2'-Thienoyl) coumaran-3-one                 | 108-09° | (i) 50<br>(ii) 80<br>Ethanol            | C <sub>11</sub> H <sub>8</sub> O <sub>2</sub> S   | 63.9     | 3.3  | 63.4  | 3.9 |
| VI <sub>b</sub> | 7-Methyl-2-(2'-thienoyl) coumaran-3-one         | 145-46° | (i) 45<br>(ii) 70<br>Ethanol            | C <sub>14</sub> H <sub>10</sub> O <sub>2</sub> S  | 65.1     | 3.9  | 65.0  | 4.0 |
| VI <sub>c</sub> | 5-Methyl-2-(2'-thienoyl) coumaran-3-one         | 140-41° | (i) 65<br>(ii) 70<br>Ethanol            | C <sub>14</sub> H <sub>10</sub> O <sub>2</sub> S  | 65.1     | 3.9  | 65.2  | 4.0 |
| VI <sub>d</sub> | 5-Chloro-2-(2'-thienoyl) coumaran-3-one         | 153-54° | (i) 60<br>(ii) 65<br>Ethanol            | C <sub>11</sub> H <sub>7</sub> O <sub>2</sub> ClS | 56.01    | 2.5  | 55.9  | 2.3 |
| VI <sub>e</sub> | 7-Methyl-5-bromo-2-(2'-thienoyl) coumaran-3-one | 174-75° | (i) 70<br>(ii) 60<br>Acetic acid        | C <sub>14</sub> H <sub>9</sub> O <sub>2</sub> BrS | 49.95    | 2.67 | 50.1  | 2.4 |
| VI <sub>f</sub> | 5-Methyl-7-bromo-2-(2'-thienoyl) coumaran-3-one | 193-94° | (i) 70<br>(ii) 75<br>Acetic acid        | C <sub>14</sub> H <sub>9</sub> O <sub>2</sub> BrS | 49.95    | 2.67 | 50.2  | 2.7 |

( i ) indicates yield by the first procedure & ( ii ) by the second )

*Ir. data (peaks at  $cm^{-1}$ ):*

Vib, 3150, 1600, 1550 1510, 1300, 1280, 724. Vlc, 3100, 1600, 1548, 1516, 1280, 728. Vid, 3440, 3100, 1600, 1550, 1505, 1315, 1295, 735. Vle, 3220, 3180, 1000, 1550, 1510, 1320, 730. Vlf, 3220, 1590, 1540, 1510, 1320, 720.

*PMR data*



Vib  $R_1 = CH_3$  (Proton labelled 'a')  
 $R_2 = H$  ( " " 'c')

Vlc  $R_1 = H$  ( " " 'p')  
 $R_2 = CH_3$  ( " " 'r')

The PMR spectra of Vib and Vlc show the proton resonances (in  $\delta$ ) as follows:

Vib  $a=2.59$ ,  $b=6.80$ ,  $c=7.15$ ,  $d=7.20$ ,  $e=7.31$ ,  $f=7.59$ ,  
 $g=7.73$ ,  $h=8.33$ .

Vlc  $r=2.49$ ,  $b=6.00$ ,  $d=7.23$ ,  $e=ca\ 7.36$ ,  $f=7.53$ ,  $g=7.73$ ,  
 $h=8.38$ ,  $p=ca\ 7.36$ .

In Vib, the enolic proton 'b' appears as a broad hump centering at 6.80  $\delta$ . The methyl protons (3H) show as a singlet at 2.59  $\delta$  while the six aromatic protons can be seen as multiplets in the region 7.15-8.33  $\delta$ . The proton 'h' comes at a low field centering at 8.33  $\delta$  under the influence of the *ortho* carbonyl group and is split into a slightly distorted doublets ( $J=6$ Hz). The proton 'c' signals at 7.15  $\delta$  as a doublet ( $J=6$ Hz).

The exact position of the peaks have been assigned by decoupling experiments (M/S Sadtler Research Laboratories).

#### Acknowledgement

The authors wish to express their thanks to Prof. J. N. Chatterjea (Patna University) and S. M. Osman (Aligarh Muslim University) for co-operation. M/S Sadtler Research Laboratories Inc., Philadelphia

(U.S.A.), have very kindly recorded the PMR spectra and assigned the protons (scanned on Varian CFT-20). They have also recorded the IR spectra of a few samples (scanned on Digilab FTS 1<sup>1</sup>) and the authors deeply appreciate the help. One of the authors (K R) gratefully acknowledges the grant of a Teacher Fellowship to him by the U.G.C., and to the authorities of the Bngalpur University for providing facilities.

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