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An Unusual Chromone Formation, and its Rearrangement to a Coumarin[1]

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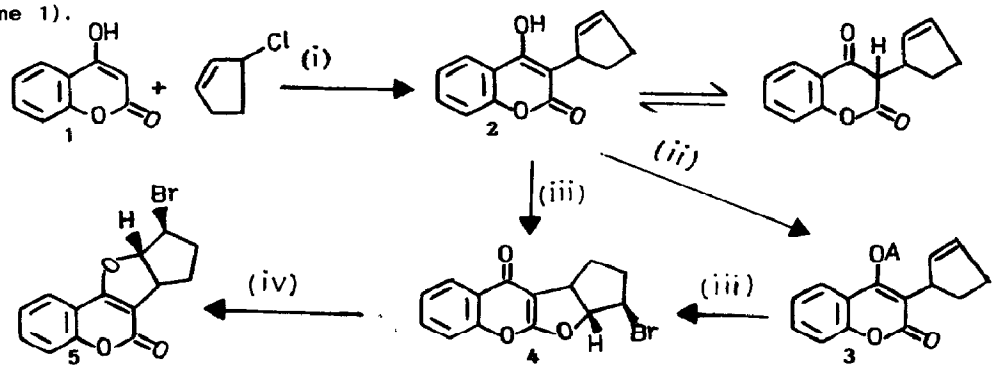
Abstract : 3-(2'-cyclopentenyl)-4-hydroxy[1]Benzopyran-2-one(**2**) or its acetate (**3**) reacts with pyridine hydrotribromide to give the fused furo chromone (**4**) in 90% yield, which on refluxing in 50% H_2SO_4 furnishes the fused furo coumarin (**5**) in 87% yield.

Coumarin derivatives are important for their well-known biological activity. There has been a continuous interest in the synthesis[3] of coumarin derivatives. During our work on the synthesis of fused bicyclic coumarins[4] we have made an interesting observation which we report here.

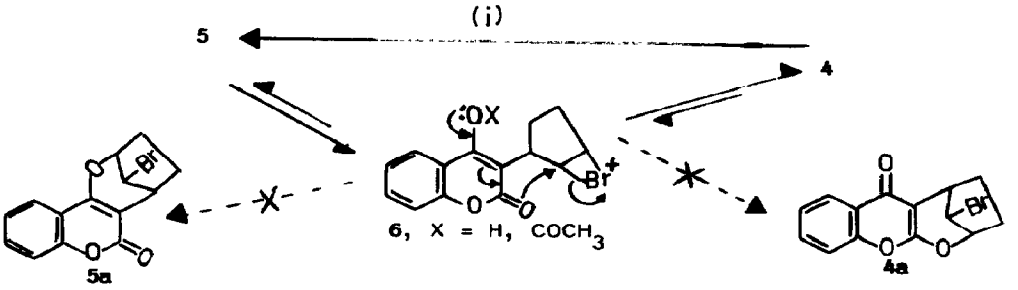
3-(2'-Cyclopentenyl)-4-hydroxy[1] benzopyran-2-one (**2**) a crystalline solid, m.p. 134°C, was obtained directly in 50% yield by refluxing a mixture of 4-hydroxycoumarin (**1**) and 3-chlorocyclopentene in acetone-potassium carbonate for 10 hr. Compound **2** was then converted to its acetate derivative **3**, yield 90%, m.p. 114°C. The acetate **3** was treated with pyridine hydrotribromide in dichloromethane at 0-5°C for 2hr. to give a white crystalline solid **4**, yield 90%, m.p. 129°C (Scheme 1).



Scheme 1 Reagents : (i) Me_2CO/K_2CO_3 (ii) Ac_2O/NaOAc (iii) $PyHBr_3/CH_2Cl_2$ (iv) 50% H_2SO_4

The formation of the chromone skeleton is clearly indicated by the i.r. absorption band at 1650 cm^{-1} and ^{1}H-n.m.r signal, a doublet of a doublet (1H) centred at δ 8.30. Compound **4** remains unchanged when refluxed in acetone with anhydrous potassium carbonate. The same compound **4** is also obtained in 89.6% yield

when 3-(2'-cyclopentenyl)-4-hydroxy [1] benzopyran-2-one is treated with pyridine hydrotribromide in dichloromethane under the same reaction conditions (Scheme 1). A possible pathway for the formation of **4** from **2** or **3** may involve formation of bromonium ion **6** followed by cyclisation to give the chromone derivative **4** (Scheme 2). Chromone **4** when refluxed in 50% sulphuric acid for 8hr. rearranges to the coumarin derivative **5**, yield 87%, m.p. 135°C. The i.r. absorption band in compound **5** is at 1720 cm^{-1} instead of 1650 cm^{-1} (in **4**) and the shift of the low field 1H (d,d) centred at δ 8.30 to relatively high field clearly indicates the conversion of chromone **4** to coumarin **5**.



Scheme 2 Reagents : (i) 50% H_2SO_4

There are two possible ways through which the intermediate bromonium ion **6**, can cyclise, viz. the nucleophilic attack by the oxygen at the C-2' of the cyclopentenyl side chain may provide the fused furo derivative (**4,5**) or the nucleophilic attack at the C-3' of the cyclopentenyl side chain would give the bridged bicyclic system (**4a,5a**). Unfortunately the assignments of structures for the products from the spectral data is not fully conclusive. Accordingly we have carried out single crystal X-ray analyses[5] of these compounds to definitely establish their structures. Alternative structures **4a** and **5a** for the products are discarded on the basis of the X-ray data. Figures 1 and 2 show the Pluto structures of products **4** and **5**. Product **4** is kinetically controlled and is formed exclusively. Thermodynamic product **5** is obtained only by acid catalysed rearrangement of **4**.

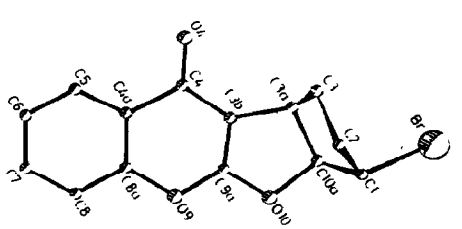


Fig. 1

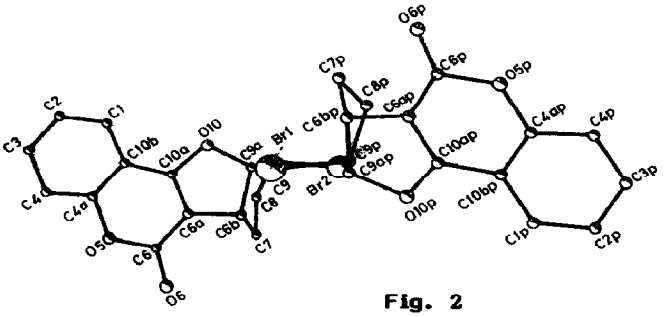
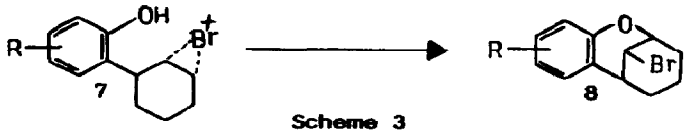


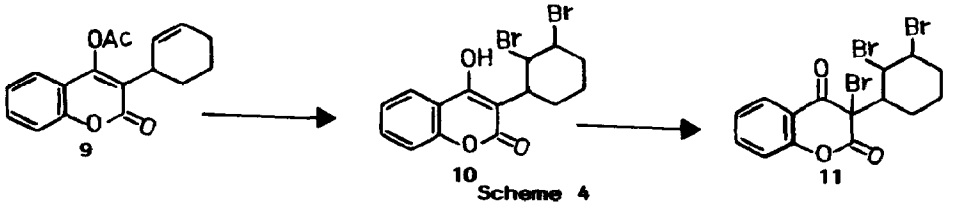
Fig. 2

It is relevant to mention here that the bromonium ion intermediates (7) derived from the reaction of o-cyclohexanylphenols and pyridine hydrotribromide cyclises exclusively to the bridged bicyclic products (8)[6] (Scheme 3).



Scheme 3

However the corresponding 3-(2'-cyclohexenyl)-4-acetoxy coumarin 9 shows the tendency[7] to form mostly the tribromo derivative 11 when treated with pyridine hydrotriboromide in dichloromethane at 0-5°C for 2 hr. (Scheme 4).



Scheme 4

The cyclisation of the proposed intermediate (6) is facile under such a mild condition perhaps due to favourable juxtaposition of reacting functionalities to provide a stable bicyclic compound 4. The failure of 9 to give the corresponding bicyclic derivative is at leastattributable to the fact that the preferred molecular conformation with bulky 3-coumarinyl moiety in equatorial orientation does not provide nucleophilic -OH group in proximity with carbon bearing the nucleophugic Br. We are currently working on the rearrangement and a full account will be reported later.

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5. **X-Ray Crystallographic Data :**

4. $C_{14}H_{14}O_3Br$: Mw=310.167, Monoclinic $P2_1/n$,a=7.000(1), b=18.619(4), c=9.399(3) Å, β=97.66(2), V=1214.1(5) $Å^3$, Z=4, D_c=1.697 g/cm^3, F(000) = 628, T=295K.

5 $C_{14}H_{14}O_3Br$: Mw=310.167, Monoclinic $P2_1/c$,a=13.375(6), b=9.327(2), c=20.692(2) Å, β =104.84(2°), V=2495(1) $Å^3$, Z=8, D_c=1.651 g/cm^3, F(000) = 1256, T=295K. For both the crystals MoK α radiation λ =0.7107A. Intensity data were collected on an Enraf Nonius CAD-4 Diffractometer using a crystal of 0.125x0.15x0.425 mm for **5** and for **4**, 0.3 x 0.175 x 0.1 mm in the ω/2 θ mode. A total of 4892 were measured and 4359 unique and 1970|FO| > 5.0 σ |FO| observed for **5** and for **4**, 2404 measured 2132 unique and 1195|FO| > 5.0σ|FO|. Both the structures were solved by direct methods[8] and a full matrix least squares refinement on FO's[9] with the non H-atoms anisotropic and H-atoms isotropic converged at 0.075 & WR=0.069 for **5** and R 0.059 & WR=0.061 for **4**. Atomic coordinates, bond lengths and angles, and thermal parameters and Fo/Fc have been deposited at the Cambridge Crystallographic Data Centre.

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All new compounds reported in this study gave satisfactory elemental analyses and exhibited characteristic u.v., i.r., ^{1}H-n.m.r and mass spectra.

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