HETEROCYCLES, Vol. 26, No 11, 1987

STUDIES ON HUTACAE : PART VII¹ - AN INTERESTING REARRANGEMENT OF THE RARE EPOXYCOUMARIN, MICROMELUM, TO THE LINEAR FURANOCOUMARIN, PSORALEN

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Abstract - Boron trifluoride etherate treatment of 7-methoxy-6-3'-methyl-3',4'-epoxycoumarin (micromelum), a constituent of Micromelum pubescens Blume (Rutaceae), afforded an interesting rearranged product, psoralen, in addition to 7-methoxycoumarinyl-6-tetronic acid derivative.

The presence of an epoxy-lactone system at C₆ in 7-methoxy-6-3'-methyl-3',4'-epoxycoumarin (micromelum) (1)²,³, a major constituent of Micromelum pubescens Blume (Rutaceae), afforded an interesting and rare system for study. This system was found to be extremely susceptible as a result of which products were formed, not only due to the opening up of the epoxide ring but also due to the degradation of the lactone system⁴,⁵.

On treatment with boron trifluoride in dry benzene at 50°C under a nitrogen atmosphere for 3 h (1) underwent an interesting rearrangement to give the linear furanocoumarin, psoralen (2) in addition to a new system, 7-methoxycoumarinyl-6-tetronic acid derivative (3) (Chart 1).

Psoralen (2), C₁₁H₆O₃ (M⁺ 186), mp 158°C (benzene), yield 57%, appears to have been formed by the demethylation of the C₇-methoxyl followed by the nucleophilic attack of the C₇-hydroxyl at C₄, with concomitant opening up of the oxirane ring. The intermediate species (4) underwent spontaneous 2-ring opening to give psoralen (Chart 1).

The second product (3), C₁₅H₁₂O₇ (M⁺ 288), mp 194°C (benzene) has been formed in 15% yield via the glycol (5) with subsequent dehydration. The glycol (5) could not be isolated under this reaction condition. It was obtained as the major product, C₁₅H₁₄O₇ (M⁺ 306), mp 240°C (acetone), yield 46%, on refluxing micromelum (1) with trifluoroacetic acid in benzene. With boron trifluoride
CHART-1

(1) → (2) → (3) → (4) → (5)

Reactions:
- TFA, C₆H₆, Reflux 20h
- BF₃·Et₂O, C₆H₆, 50°C, 3h
- BF₃·Et₂O, C₆H₆, 50°C, 3h
- Mercury vapor lamp, C₆H₆, 11 h
etherate (5) afforded product (3). The same tetronic acid derivative was also obtained by irradiating (1) with a medium pressure mercury vapour lamp in benzene for 11 h (Chart 1). The infrared spectrum of (3) showed the presence of hydroxyl (3400 cm⁻¹), a γ-lactone system (1710 cm⁻¹) and γ-butyrolactone unit (1760 cm⁻¹). The 80 MHz ¹H-nmr spectrum in CDCl₃ showed the signals for the coumarin C₃-H and C₄-H at 8 6.27 and 7.69 respectively (1H, d each, J = 9.7 Hz) and the aromatic C₂-H and C₅-H as singlets at 8 7.42 and 6.90 respectively. The C₇-methoxyl exhibited a singlet at 8 3.85. The C₅₁-H appeared at 8 5.67 (1H, s) and the vinyl methyl at 8 1.68 (3H, s). The hydroxyl at C₄₁ was observed at 8 10.48 (brs, exchangeable with D₂O).

**EXPERIMENTAL**

Melting points were recorded on a Kofler block apparatus and are uncorrected. The uv spectra (in 95% aldehyde free ethanol) were recorded in Varian 634 spectrophotometer, the ir spectra (KBr) in Perkin-Elmer 782, the ¹H-nmr spectra (in CDCl₃ using TMS as internal standard) in JNM (100 MHz) and Bruker WH-400 (400 MHz) spectrometers and the mass spectra in 70 eV. Hitachi RMU 6L mass spectrometer.

**Reaction of Microsalamin (1) with Boron Trifluoride Etherate**

To a solution of microsalamin (1) (500 mg) in dry benzene (50 ml) boron trifluoride etherate (1.5 ml) was added under a nitrogen atmosphere. The reaction mixture was stirred at 50°C for 3 h. The mixture was allowed to stand at room temperature overnight. This was poured over ice chips and extracted with ethyl acetate (3×50 ml). The extract was washed with 2%/ sodium bicarbonate solution (3×50 ml), water (3×50 ml) and dried. This was concentrated and the residue was chromatographed over silica gel. The benzene eluate afforded psoralen (2) which was crystallised from benzene (Found: C, 70.23; H, 3.56%. Calcd. for C₁₁H₆O₃: C, 70.96; H, 3.22%). mp 158°C, yield 57%; \( \lambda_{max} (\text{EtOH}) = 329, 291, 246 \\text{and} \ 212 \ \text{nm} \); (log \( E = 3.78, 4.02, 4.39 \text{ and } 4.24 \text{ respectively} \); \( \nu_{max} \) (KBr) = 1720, 1630, 1580, 1540, 1450, 1130, 820 cm⁻¹; \( \delta (\text{CDCl₃}) = 6.33 \ (1H, \ d, \ J = 9.5 \ Hz, \ C₃-H), \ 7.82 \ (1H, \ d, \ J = 9.5 \ Hz, \ C₄-H), \ 7.68 \ (1H, \ s, \ C₅-H), \ 7.48 \ (1H, \ s, \ C₆-H), \ 7.69 \ (1H, \ d, \ J = 2.2 \ Hz, \ C₇-H), \ 6.83 \ (1H, \ d, \ J = 2.2 \ Hz, \ C₈-H); m/z 186(M⁺), 158, 132, 130, 104, 102.

The benzene-ethyl acetate (4:1) eluate yielded the tetronic acid derivative (3).
crystallised from benzene (Found: C, 62.92; H, 4.35%). Calcd. for C_{15}H_{12}O_6: C, 62.50; H, 4.16%.

<table>
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<th>Compound</th>
<th>Formula</th>
<th>C (%)</th>
<th>H (%)</th>
<th>Found</th>
<th>Calcd.</th>
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<tbody>
<tr>
<td>C_{15}H_{12}O_6</td>
<td>C_{15}H_{12}O_6</td>
<td>62.92</td>
<td>4.35</td>
<td>62.50</td>
<td>4.16</td>
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Reaction of Micromelumin (1) with Trifluoro Acetic Acid

Micromelumin (1) (200 mg) was dissolved in dry benzene (25 ml) and to it trifluoroacetic acid (2 ml) in dry benzene (5 ml) was added dropwise under stirring at 0°C. The mixture was refluxed for 20 h and cooled. To the mixture ethyl acetate (50 ml) and water (100 ml) were added. This was extracted with ethyl acetate (3x50 ml). The organic layer was washed successively with 5% aqueous potassium bicarbonate (3x50 ml) and water (3x50 ml) and dried. This was concentrated. The residue was chromatographed over silica gel. The benzene - ethyl acetate (4:1) eluate afforded a white solid which on crystallisation from acetone yielded the glycol derivative (5) (Found: C, 58.34; H, 4.78%). Calcd. for C_{15}H_{14}O_7: C, 58.82; H, 4.57%.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Formula</th>
<th>C (%)</th>
<th>H (%)</th>
<th>Found</th>
<th>Calcd.</th>
</tr>
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<tbody>
<tr>
<td>C_{15}H_{14}O_7</td>
<td>C_{15}H_{14}O_7</td>
<td>58.34</td>
<td>4.78</td>
<td>58.82</td>
<td>4.57</td>
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</table>

Ultraviolet Irradiation of Micromelumin (1)

Micromelumin (1) (50 mg) dissolved in dry benzene (100 ml) was irradiated with a
medium pressure mercury vapour lamp (wave length 313 and 336 nm) for 11 h. The solution was concentrated. The concentrate on chromatographic resolution over silica gel afforded compound (3), mp 194°C (benzene), yield 24%.

ACKNOWLEDGMENT

Sincere thanks are accorded to Shri A.K. Acharya, Shri J. Ghosh and Shri P. Ghosh of the Organic Instrumentation Laboratory, Department of Chemistry, Calcutta University, for spectral measurements and to UGC (India) and OCRAS (India) for financial assistance.

REFERENCES


Received, 19th May, 1987