HETEROCYCLES, Vol. 26, No 11, 1987

STUDIES ON RUTACEAE : PART VII[1] - AN INTERESTING REARRANGEMENT OF THE RARE EPOXYCOUMARIN, MICROMELUMIN, TO THE LINEAR FURANOCOUMARIN, PSORALEN

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

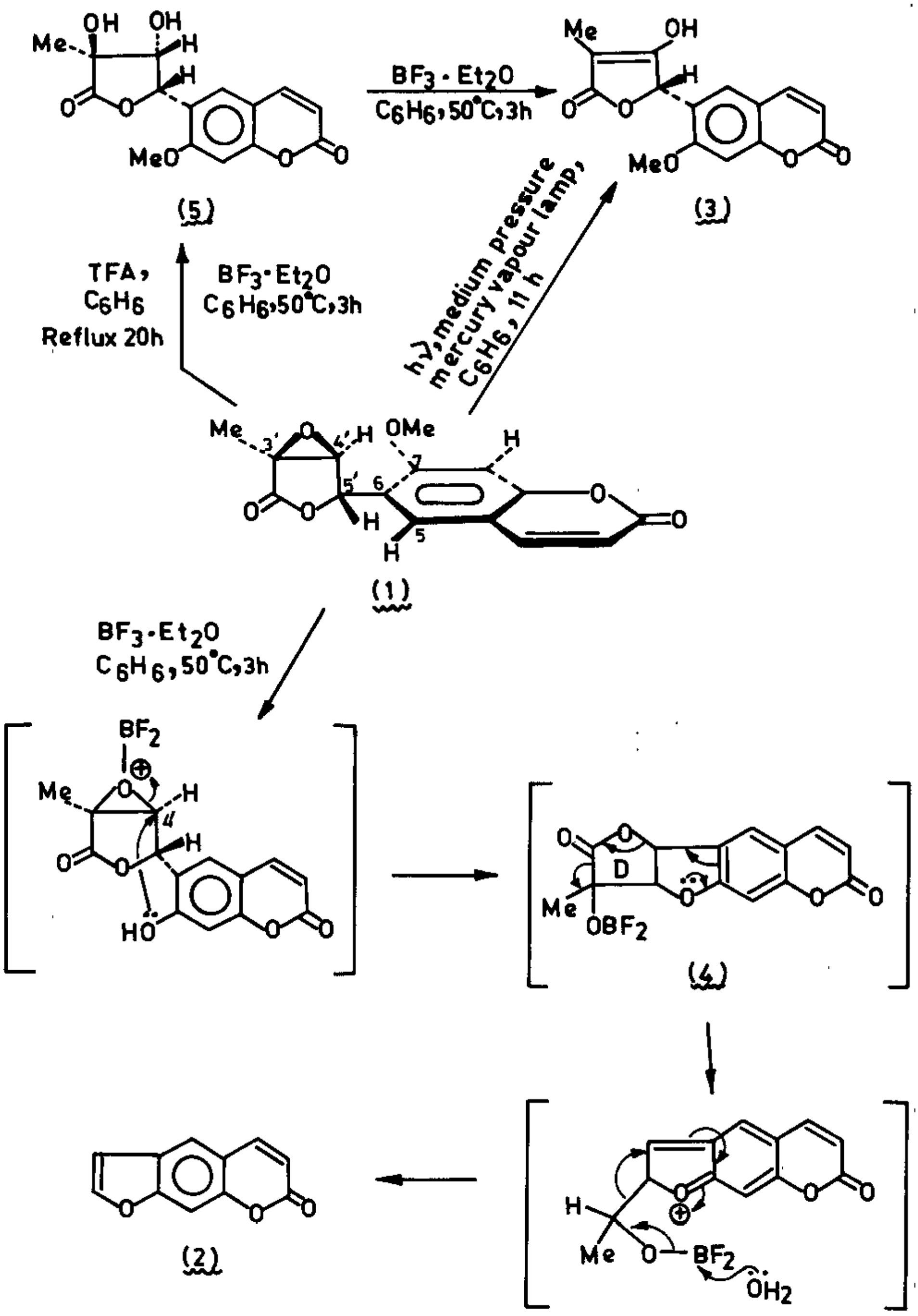
The presence of an epoxy-lactone system at C_6 in 7-methoxy-6-γ-butyrolactone-3'-methyl-3',4'-epoxycoumarin (micromelumin) (1)[2,3], a major constituent of *Micromelum pubescens* Blume (Rutaceae), afforded an interesting and rare system for study. This system was found to be extremely susceptible as 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 system[4,5].

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), $C_{11}H_6O_3$ (M^+ 186), mp 158°C (benzene), yield 57%, appears to have been formed by the demethylation of the C_7-methoxyl followed by the nucleophilic attack of the C_7-hydroxyl at $C_{4'}$ with concomitant opening up of the oxirane ring. The intermediate species (4) underwent spontaneous D-ring opening to give psoralen (Chart 1).

The second product (3), $C_{15}H_{12}O_6$ (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, $C_{15}H_{14}O_7$ (M^+ 306), mp 240°C (acetone), yield 46%, on refluxing micromelumin (1) with trifluoroacetic acid in benzene. With boron trifluoride

CHART-1


(5)
BF$_3$·Et$_2$O
C$_6$H$_6$,50°C,3h
(3)
TFA,
C$_6$H$_6$
Reflux 20h
BF$_3$·Et$_2$O
C$_6$H$_6$,50°C,3h
hν, medium pressure mercury vapour lamp, C$_6$H$_6$, 11 h
(1)
BF$_3$·Et$_2$O
C$_6$H$_6$,50°C,3h
(4)
(2)

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 δ-lactone system (1710 cm^{-1}) and γ-butyrolactone unit (1760 cm^{-1}). The 80 MHz ^{1}H-nmr spectrum in $CDCl_3$ showed the signals for the coumarin C_3-H and C_4-H at δ 6.27 and 7.69 respectively (1H, d each, J = 9.7 Hz) and the aromatic C_5-H and C_8-H as singlets at δ 7.42 and 6.90 respectively. The C_7-methoxyl exhibited a singlet at δ 3.85. The $C_{5'}$-H appeared at δ 5.67 (1H, s) and the vinyl methyl at δ 1.68 (3H, s). The hydroxyl at $C_{4'}$ was observed at δ 10.48 (brs, exchangeable with D_2O).

EXPERIMENTAL

Melting points were recorded on 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 ^{1}H-nmr spectra (in $CDCl_3$ using TMS as internal standard) in JEOL (100 MHz) and Bruker WH-400 (400 MHz) spectrometers and the mass spectra in 70 e.v. Hitachi RMU 6L mass spectrograph.

Reaction of Micromalumin (1) with Boron Trifluoride Etherate

To a solution of micromelumin (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 (3x50 ml). The extract was washed with 2% sodium bicarbonate solution (3x50 ml), water (3x50 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 $C_{11}H_6O_3$: C, 70.96; H, 3.22%), mp 158°C, yield 57%; λ_{max}(EtOH) : 329, 291, 246 and 212 nm (log ε = 3.78, 4.02, 4.39 and 4.24 respectively); ν_{max} (KBr) : 1720, 1630, 1580, 1540, 1450, 1130, 820 cm^{-1}; δ($CDCl_3$) : 6.38 (1H, d, J = 9.5 Hz, C_3-H), 7.82 (1H, d, J = 9.5 Hz, C_4-H), 7.68 (1H, s, C_5-H), 7.48 (1H, s, C_8-H), 7.69 (1H, d, J = 2.2 Hz, $C_{2'}$-H), 6.83 (1H, d, J = 2.2 Hz, $C_{3'}$-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%), mp 194°C, yield 15%; λ_{max}(EtOH) : 325, 254, 221 and 208 nm ($\log\varepsilon$ = 4.07, 3.85, 4.18 and 4.27 respectively), λ_{max}(EtOH+NaOH) : 332, 286 and 227 nm ($\log\varepsilon$ = 4.09, 3.87 and 3.93 respectively); ν_{max}(KBr) : 3400, 1760, 1710, 1620, 1560, 1130, 820 cm^{-1}; m/z : 288 (M^+), 260, 244, 204, 187, 176.

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 (1:1) 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%), mp 240°C, yield 46%; λ_{max}(EtOH) : 325, 222 and 207 nm ($\log\varepsilon$ = 4.08, 4.23 and 4.35 respectively); λ_{max}(EtOH+NaOH) : 327 and 226 nm ($\log\varepsilon$ = 4.04 and 4.16 respectively); ν_{max}(KBr) : 3400, 1770, 1720, 1620, 1560, 1500, 1130, 820 cm^{-1}; $\delta(CD_3COCD_3)$: 7.96 (1H, d, J = 9.5 Hz, C_4-H), 6.26 (1H, d, J = 9.5 Hz, C_3-H), 7.66 (1H, s, C_5-H), 7.01 (1H, s, C_8-H), 5.34 (1H, d, J = 6.9 Hz, $C_{5'}$-H), 4.48 (1H, d, J = 6.9 Hz, $C_{4'}$-H), 4.01 (3H, s, OCH_3), 2.83 (2H, brs, exchangeable with D_2O, -OH), 1.45 (3H, s, CH_3); m/z : 306 (M^+), 229, 206, 205, 189, 175.

Reaction of the Glycol Derivative (5) with Boron Trifluoride Etherate

The glycol derivate (5) (100 mg) in dry benzene (20 ml) was treated with boron trifluoride etherate (2 ml) at 50°C for 3 h under a nitrogen atmosphere. This was kept overnight. The reaction mixture was added onto ice-chips. The organic portion was taken up in ethyl acetate (3x50 ml), washed with 2% aqueous sodium bicarbonate (3x50 ml) and water (3x50 ml) and dried. The ethyl acetate concentrate upon chromatography over silica gel afforded the tetronic acid derivative (3) in the benzene - ethyl acetate (4:1) eluate, mp 194°C (benzene), yield 6.7%.

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%.

ACKNOWLEDGEMENT

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 CCRAS (India) for financial assitance.

REFERENCES

1. For Part VI : J. Banerji, K.P. Dhara, B. Das, A.K. Das and A. Chatterjee, Indian J. Chem. (in press), 1987.
2. A. Chatterjee, C.P. Dutta and S. Bhattacharya, Sci. Cult., 1967, 33, 371.
3. J.A. Lamberton, J.R. Price and A.H. Redcliffe, Aust. J. Chem., 1967, 20, 973.
4. J. Banerji, (Mrs) A. Chatterjee, N. Ghosal, A. Das, S. Sarkar, S. Bhattacharya and J.N. Shoolery, J. Indian Chem. Soc., 1982, 59, 145.
5. J.A. Lamberton and T.C. Morton, Aust. J. Chem., 1985, 38, 1025.

Received, 19th May, 1987