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GLYCOLONE, A QUINOLONE ALKALOID FROM *GLYCOSMIS PENTAPHYLLA*

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Key Word Index—*Glycosmis pentaphylla*; Rutaceae; leaves; glycolone; 2-quinolone alkaloid.

Abstract—Glycolone, a quinolone alkaloid has been isolated from the leaves of *Glycosmis pentaphylla*. The structure of the compound has been established as 4,8-dimethoxy-3-(3-methyl but-2-enyl)-2-quinolone from physical and chemical evidences.

INTRODUCTION

In continuation of our work on quinolone alkaloids of the Rutaceae [1] we now report structural studies of another quinolone alkaloid, glycolone, from the leaves of *Glycosmis pentaphylla*. Previously the structure of glycosolone, a quinolone alkaloid was reported from this plant [2].

RESULTS AND DISCUSSION

Glycolone (**1**) $C_{16}H_{19}NO_3$ ($[M]^+$ *m/z* 273), mp 118°, was found to be homogeneous by TLC and mass spectrometry. The UV spectrum of the compound in EtOH showed λ_{max} at 237 (log ε 4.32) 255 (4.46) 280 (3.95) 292 (3.91) 321 (3.55) 332 (3.62) and 346 nm (3.46). The IR spectrum (KBr) of the compound showed bands at 1640 (NHCO), 1600, 1565 (aromatic residue), 1220, 1208 (aromatic ether) and 840 cm^{-1} (substituted benzene derivative). This spectral behaviour is characteristic of a 2-quinolone skeleton [3, 4]. The ^1H NMR spectrum (60 MHz, $CDCl_3$) of the compound showed signals at δ7.88 (*br* s, 1H, NH, confirmed by D_2O exchange), δ7.55–7.0 (*m*, 3H, aromatic proton) δ5.25 (*t*, J = 8 Hz, 1H, vinylic) δ3.9 and δ3.8 (two singlets, 6H for two OMe) δ3.6 (*d*, J = 8 Hz, 2H, benzylic methylene) δ1.75, δ1.68 (*br* s, 6H, *gem* diMe). The two Me signals at δ1.78 and δ1.68, a benzylic methylene doublet at δ3.6, together with the singlet for a vinylic proton at δ5.25, suggested an isopentenyl chain in glycolone.

On heating glycolone with 6 N HCl, a cyclised product **2**, $C_{15}H_{17}NO_3$ ($[M]^+$ *m/z* 259), mp 131°, was obtained. The presence of a strong band at 1640 cm^{-1} in the IR spectrum of the compound indicated it to be a 2-quinolone compound. The ^1H NMR spectrum showed the presence of one OMe as singlet at δ3.85. Besides two symmetrical triplets at δ2.67 and δ1.84 (J = 7 Hz), the sharp singlet for six protons at δ1.4 indicate the presence of 2:2 dimethyl dihydro pyran ring in **2**. The cyclised product is formed by facile demethylation of the OMe at the C-4 position [5] and combination with the isopentenyl chain at the C-3 position.

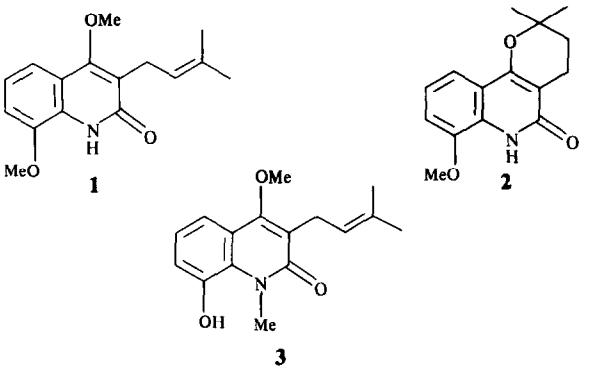
Most of quinolone alkaloids contain an isopentyl chain at the C-3 position and an oxygen function at the C-8 position. From biogenetic considerations the other OMe group was placed at the C-8 position and the structure of glycolone has thus been assigned as **1**.

Glycolone was found to be different from glycosolone **3**, mp 159°, in spectral properties. In the IR spectrum of **3** a band at 3130 cm^{-1} indicated the presence of hydrogen bonded OH which is absent from glycolone. Moreover, the ^1H NMR spectrum (60 MHz in $CDCl_3$) showed the presence of only one OMe group at δ4.12 and a phenolic OH group at δ11.95. These signals are absent in glycolone.

EXPERIMENTAL

All mps are uncorr. UV and IR spectra were recorded in EtOH and as KBr pellets, respectively.

Isolation of glycolone Air dried finely powdered leaves (2 kg) of *G pentaphylla* were first extracted with petrol for 48 hr. After extraction the leaves were dried and re-extracted with C_6H_6 for 48 hr. The C_6H_6 extract was concd and chromatographed over alumina (450 g). The column was successively eluted with petrol, petrol–C_6H_6 (1:1), C_6H_6–$CHCl_3$ (1:1), $CHCl_3$ and finally with MeOH. The residue from the $CHCl_3$ eluate showed three spots on TLC and was rechromatographed over alumina. Elution was carried out with C_6H_6, $CHCl_3$ and C_6H_6–EtOAc mixtures of increasing polarity. From C_6H_6–EtOAc (1:1) glycolone was obtained as a crystalline solid which was further crystallised from



Me_2CO–petrol, mp 118°. Yield 0.002%. TLC on silica gel (C_6H_6–EtOAc (9:1), R_f = 0.25) (Found: C, 70.20; H, 7.2; N, 5.4. Calc. for $C_{16}H_{19}NO_3$: C, 70.31; H, 7.01; N, 5.12%.)

Cyclisation of glycolone. Glycolone (200 mg) was refluxed with 6 N HCl (50 ml) for 6 hr. The reaction product was cooled, 10% aq NaOH added in excess and the mixture extracted with EtOAc. On evapn of solvent a solid was obtained which was crystallised from Me_2CO–petrol, mp 131°. Yield 90 mg. TLC on silica gel (C_6H_6–EtOAc (9.1), R_f = 0.38). (Found: C, 69.31; H, 6.72; N, 5.5. Calc. for $C_{15}H_{17}NO_3$: C, 69.48; H, 6.61; N, 5.40%)

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(+)-EPIMARITIDINE, AN ALKALOID FROM *ZEPHYRANTHES ROSEA**

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Key Word Index—*Zephyranthes rosea*; Amaryllidaceae; 5,10b-ethanophenanthridine alkaloid; (+)-epimaritidine; C-3 epimerization.

Abstract—The isolation and determination, by spectroscopic analyses and chemical correlation, of the structure and stereochemistry of (+)-epimaritidine, a new alkaloid from *Zephyranthes rosea*, is reported. A facile transformation of maritidine to (+)-epimaritidine is described and the mechanism is appraised in the light of the thermodynamic stability of the latter epimer. (+)-Epimaritidine comprises a missing link in the C-3 epimeric pairs of 5,10b-ethanophenanthridine alkaloids of the vittatine–haemanthamine type.

INTRODUCTION

In connection with our work on the reactive intermediates of Amaryllidaceae alkaloids [1–4], we have investigated the alkaloidal constituents of the fresh bulbs of *Zephyranthes rosea*, collected during flowering. The species grows abundantly in the upper Gangetic plain as well as in the Sikkim region of the Eastern Himalayas up to 1000 m, and is also grown in gardens as an ornamental flowering plant and for medicinal purposes. Extracts of its flowers and bulbs are used for a variety of therapeutic purposes which can be described in modern terms as immunomodulators. The species, of European origin, was previously reported [5] to contain only galanthamine. We report the isolation and characterization of four alkaloids from methanol extracts of fresh bulbs of this species. Additionally, a facile transformation of maritidine to (+)-epimaritidine is described and the mechanism of the epimerization is appraised.

*Part 9 in the series "Chemical Constituents of Amaryllidaceae" For Part 8 see ref. [1].

RESULTS AND DISCUSSION

Column chromatography of the chloroform-soluble fraction of the residue from methanol extracts of fresh bulbs of *Z. rosea*, collected during the first onset of flowers, afforded one new (compound **1**), and three known alkaloids, crinamine, haemanthamine and maritidine, in quantities sufficient for their complete characterization. Only the structural elucidation of the new alkaloid is described below.

The new compound, $C_{17}H_{21}O_3N$ (by accurate mass measurement), mp 214–215°, exhibited UV, IR and mass spectra similar to those of maritidine. The splitting pattern of the olefinic hydrogens in the 90 MHz ^1H NMR spectrum of the compound was, however, different from that of maritidine [4, 6]. It had the same HPLC R_t as a reference sample of (+)-epimaritidine. Maritidine, isolated from *Z. flava* Roem & Schult. [4], on oxidation with active manganese dioxide, in chloroform, gave (+)-oxomaritidine [6], which on reduction with sodium borohydride, in methanol, gave (+)-epimaritidine, referred to here as the reference sample The UV, IR,