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THE IDENTITY OF GLYCOPHYMINE AND GLYCOSMININE: AN ALKALOID OF GLYCOSMIS ARBOREA (ROXB.) DC.

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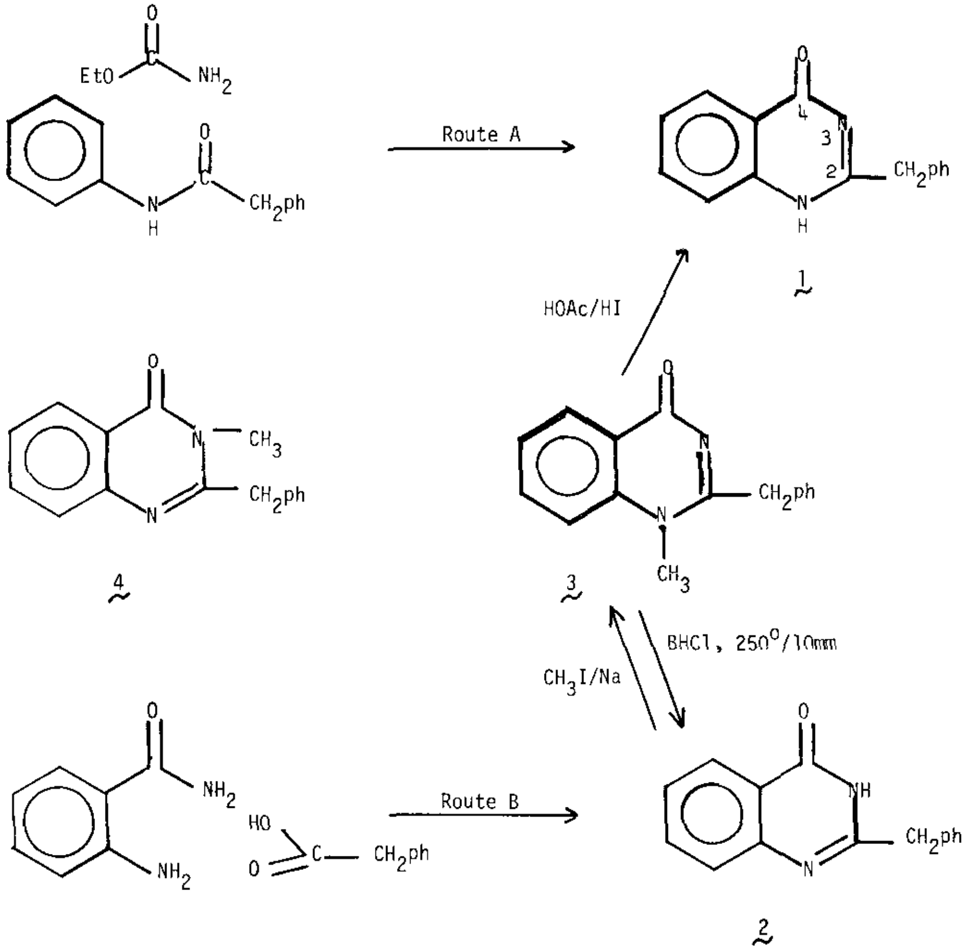
Abstract - Glycophymine, a new alkaloid reported from Glycosmis pentaphylla is shown to be identical to glycosminine isolated from the same plant earlier.

Recently, the isolation of a new 4-quinazolinone alkaloid, glycophymine, has been claimed by Sarkar and Chakraborty[1] from the flowers of a rutaceous plant alleged to be Glycosmis pentaphylla. The discoverers of glycophymine assigned structure (1) to the alkaloid having a double bond between C-2 and N-3 which they supported by its synthesis from the anilide of phenylacetic acid and ethyl carboxamate (route A, Scheme I).

While there is no doubt that the same species of Glycosmis was involved in all the investigations of this plant by the various groups of workers[1-4] in Calcutta, there has been much controversy over the correct identification and the authority of this species. Isolation of furoquinolines, acridine, carbazoles, and four 4-quinazolinone alkaloids including glycosminine[4] (2) and arborine[3] (3) were reported from this plant which was claimed by various workers as G. arborea Correa[4], G. pentaphylla (retz.) DC.,[1,2,5] and G. arborea (roxb.) DC[4]. However, we prefer the name, G. arborea (Roxb.) DC, based on the latest taxonomic work[6]. In this communication, we wish to report on the basis of chemical and spectral evidence that glycophymine is identical to glycosminine and it should be represented by (2).

Glycophymine is reported[1] to have a mp 254^0 while glycosminine melted at 249^0 which was confirmed by Kametani et. al.[7,8] who synthesized the alkaloid by various routes. Glycophymine was reported to show IR bands (in unspecified phase) at 3350, 1700, 1620, 1613, 1600 and 713cm^{-1}, while glycosminine showed IR bands in KBr at 3356, 1676, 1613, 1600 and 713cm^{-1}. Moreover, glycophymine was obtained by demethylation of arborine (3) with HOAc and HI, while, in our hands, glycosminine was obtained by demethylation of arborine hydrochloride by heating at 250^0 under vacuum[4]. Also, N-methylation of glycosminine with Na and CH_3I in absolute EtOH gave arborine as a minor product[9]. The reported UV and MS of glycophymine were identical with those of glycosminine. The existence of 4-quinazolinones in different tautomeric forms is well known. However, the reported[1] isolation of another tautomeric form of a compound from the same plant coupled with the great many similarities between glycophymine and glycosminine prompted us to investigate their

Scheme I



possible identity. Therefore, glycophymine was synthesized exactly following the procedure of Sarkar and Chakraborty[1]. It was found to be identical in all respects (mp, mmp, superimposible UV, IR and ^{1}H NMR) to glycosminine, synthesized via route B (Scheme I). The slight variation in the IR data taken in different phases of a compound capable of existing in tautomeric forms is not unlikely. Also, a difference in the mps between two synthetic samples of the same compound prepared in different laboratories is not an unambiguous evidence of their structural difference. Although an authentic sample of natural glycophymine was not available[10], the identity of synthetic glycophymine and synthetic glycosminine is thus established.

Although both the tautomeric structures (1) and (2) for glycosminine were taken into consideration[4], the overwhelming evidence in support of (2) as the predominent form cannot be overlooked. The broad one proton signal at 10.25 ppm in the ^1H NMR spectrum of glycosminine[4] can only be explained in terms of an intramolecularly hydrogen bonded (-N$\underline{H}$...O=C) proton as possible in (2). Also, the UV spectrum of glycosminine [λ_{max}^{EtOH} (log ε), 312(3.57), 303(3.66), 2.65(3.95), and 225 (4.44)] is much closer to that of 2-benzyl-3-methyl-4-quinazolinone [(4), λ_{max}^{EtOH} (log ε), 312 (3.61), 272 (3.55), 269(3.99), and 227(4.49)] than that of 2-benzyl-1-methyl-4-quinazolinone [(3), λ_{max}^{EtOH} (log ε), 315(3.87), 306(3.94), 277(3.72), 268(3.68), and 227(4.25)][9]. The prevelence of the thermodynamically more stable o-quinonoid form (2) rather than (1) for compounds of this type was also confirmed[11,12] by extensive UV, IR, ^1H NMR and chemical study.

Therefore, in view of its identity with glycosminine, the name glycophymine should be stricken from the literature.

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