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ALKALOIDS FROM *TINOSPORA CORDIFOLIA* MIERS

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Abstract

The details of isolation and spectral analysis of the protoberberine alkaloids, tetrahydropalmatin and jatrorrhizine, reported for the first time to occur in the roots of *Tinospora cordifolia* by the authors, are described.

Introduction

Tinospora cordifolia Miers (Menispermaceae) is widely used in the Indian system of medicine in the treatment of various ailments [1]. Categorized as a "Rasayana" in Ayurveda, it is used for its general adaptogenic and prohost immunomodulatory activity in fighting infections. A great deal of chemical investigation on this plant is already on record [1, 2] and a number of protoberberine and aporphine alkaloids have been reported to occur on it. Based on some spectral evidence, authors reported for the first time, the occurrence of tetrahydropalmatin [3] and jatrorrhizine [4] from the roots of this plant. More data has been collected since then and this paper describes the isolation procedure and detailed spectral investigation of these two alkaloids and some of their derivatives.

Isolation and Experimental

The root powder, in moderately coarse powder (3Kg) was extracted successively with petroleum ether (60-80ºC) in hot and rectified spirit in cold. The alcoholic extract concentrate was treated with aqueous citric acid (5%), free bases were regenerated from the acid extract by adding dilute ammonia, the liberated bases were extracted with chloroform, chloroform extract concentrated and chromatographed.

The water soluble bases were precipitated with Mayer's reagent and the Mayer's complex on treatment with anion exchange resin, Amberlite IRA-400 (Cl^- form) furnished alkaloids as chlorides, which were isolated and purified by chromatography over SiO_2. As a result one tertiary alkaloid (A) and two quaternary alkaloids (B & C) were obtained, the characterization and identity of which were established as follows:

Compound A; m.p 143-145º, soluble in acetone, chloroform and ethanol, insoluble in benzene, petroleum ether and water, did not give test for phenol; EIMS M^+ m/z 355; found (%) C 70.12, H 6.55, N 3.52, $C_{21}H_{25}O_4N$ requires (%) C 70.98, H 7.04, N 3.94, UV (ethanol), Max nm 228.282 (log ε 4.13,3.80), Min. nm 252 (log ε 2.70), spectrum remaining unaffected by the addition of alkali , acid or a reducing agent, suggesting compound to be related to tetrahydroprotoberberine group; IR (nujol) shows absence of any hydroxyl or a carbonyl function in the molecule. 60 MHz ^1H NMR spectrum ($CDCl_3$) shows signal at δ 3.92 (9H, s) for 3 Ar-OCH_3, δ 3.96 (3H,s) for one Ar-OCH_3; 6.73, 6.80 (1H, s each) for two isolated Ar-H, 6.98 (2H, s) for two equivalent Ar-H; ^1H NMR shows absence of any N-CH_3 group; compound gives a mono methiodide $C_{22}H_{28}O_4NI$, m.p 231-32° indicating the alkaloid to be tertiary in nature. All the above facts suggest the

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compound to be tetra cyclic in nature [5] with tertiary nitrogen at a junction of the two rings which is typical of tetrahydroprotoberberine nature of the compound A. EIMS recorded M^+ at m/z 355 (90 %) with other prominent fragment ions at m/z 354 (57 %), 340 (9.3 %),190 (32 %),164(100 %) & 149 (80 %). The compound is thus tetrahydropalmatin and its identity confirmed by its comparison with authentic sample (m.m.p,Co TLC & superimposible IR)

Compound B; m.p 216-217ºC, soluble in methanol, ethanol, water and insoluble in organic solvents; gives positive Dragendorff's test; blue color when its spot on paper is sprayed with phosphomolybic acid reagent and exposed to ammonia vapor, showing the compound to be phenolic in nature; UV in acidic & neutral conditions are similar, UV (ethanol), Max nm 225,264,345, Min. nm 210, 252, and 305; the absorption positions underwent bathochromic shifts following the addition of alkali, UV (ETOH/OH^-) max 245,281 and 385, UV(ETOH/OH^-) min 252 & 310, the addition of alkali resulted in the change in color from yellow to intense red; treatment with sodium borohydride decolorized the solution with change in UV characteristics, UV (ETOH/OH^-) max nm 207,282,337 and , UV(ETOH/OH^-) min 252 & 310. All the above facts are in agreement with the compound having a protoberberine skeleton with C-2, 3, 9, 10 substitution patterns [6]. IR (KBr) cm^{-1}3456 (-OH), 270 MHz ^1H NMR (CD_3OD) showed signals at δ 3.20 (4H, m, 2x-CH_2-); 4.01,4.09 & 4.18 (3H, s each 3x Ar-OCH_3); 6.84, 7.64(1H,s each, 2xAr-H); 8.00, 8.07(1H, d d each J= 10Hz each, 2x vicinal Ar-H) 8.75 & 9.72 (1H, s each, 2x Ar-H); 125 MHz ^{13}C NMR (CD_3OD), δc 152.7 s,152.5 s, 150.4 s, 149.6 s, 146.4 d,141.0 s,138.2 s,131.0 s, 128.8 d, 125.1 d, 123.9 s, 121.7 d, 116.7 d, 110.8 d, 63.3 q, 58.4 t,58.1 q, 57.7 q & 28.4 t; EIMS gave M^+ at m/z 341; with AC_2O/Et_3N furnished a mono acetate m.p 178-79 º;compound B was found to be distinguishable from an authentic sample of Jatrorrhizine (m.m.p,Co TLC & superimposible IR)

Compound C; m.p 244-245º, soluble in methanol, ethanol, water and insoluble in organic solvents; gave positive phenol & Dragendorff's test; UV (ETOH) max nm 221,270,312 (log ϵ 4.97, 3.76, 3.60) remaining unchanged upon the addition of alkali or sodium borohydride; but UV pattern changed upon the addition of $HClO_4$, UV (ETOH) max nm 223, 269, 303, suggesting it to be an aporphine alkaloid with C-1, 2, 10, 11 oxygenation pattern[7]; IR (KBr) cm^{-1} 3450 (phenolic-OH), picrate m.p 204-205 º; compound C was found to be indistinguishable from an authentic sample of Magnoflorine (m.m.p, Co TLC & superimposible IR)

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