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QUATERNARY ALKALOIDS OF *FUMARIA INDICA*

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Key Word Index—*Fumaria indica*; Fumariaceae; coptisine; dehydrocheilanthifoline.

Abstract—Dehydrocheilanthifoline, a phenolic protoberberine alkaloid has been isolated from the whole plant of *Fumaria indica* together with coptisine. This is the second report of the natural occurrence of dehydrocheilanthifoline and first from any *Fumaria* species.

INTRODUCTION

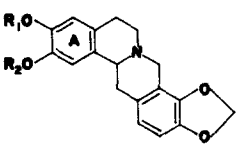
The isolation and characterisation of a number of tertiary alkaloids [1–3] and of a quaternary base, protopine methohydroxide [2] have so far been reported from *Fumaria indica* (Haussk) Pugsley, a plant distributed throughout India and locally known as "Pit-papra". The seeds of the plant have also been found [4] to be a rich source of alkaloids. Systematic investigation of the water-soluble base fraction of the whole plant of *F. indica* has resulted in the isolation of two other minor bases. The present communication discusses the isolation and characterisation of these alkaloids.

RESULTS AND DISCUSSION

The quaternary alkaloids were isolated as chlorides (see Experimental) and separated on silica gel. Elution of the column initially with EtOAc and subsequently with increasing amount of MeOH in EtOAc furnished two crystalline alkaloids: Alkaloid *A* as yellow needles and Alkaloid *B* as orange needles, both melting above 340°.

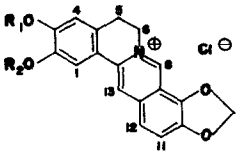
Alkaloid *A*, $C_{19}H_{14}NO_4Cl$, showed UV absorption maxima at 268, 362 and 465 nm (log ϵ, 4·03, 4·04 and 3·38) and a diagnostic [5] absorption minimum at 308 nm indicating the presence of a 2,3,9,10-tetraoxygenated protoberberine system [6] in the molecule. On borohydride reduction, it gave a colourless crystalline derivative, $C_{19}H_{17}NO_4$, mp 218°, the 60 MHz PMR spectrum of which showed proton signals ascribable to two methylenedioxy groups (δ, 6·03 and 6·06) and four aromatic protons (δ, 6·71–6·88). The MS of the compound showed in addition to the molecular ion peak at *m/e* 323, significant ion peaks at *m/e* 174, 149 and a base peak at *m/e* 148. The spectral data are in excellent agreement with stylopine or tetrahydrocoptisine (**1**) and in fact it was found to be indistinguishable from (±)-tetrahydrocoptisine [3] by direct comparison (mp, mmp, TLC, IR). Alkaloid *A* was thus coptisine chloride (**2**).

Alkaloid *B* crystallised from methanol as orange needles which turned red on drying. The UV spectral characteristics of *B* resembled coptisine chloride indicating similar chromophoric system in both alkaloids. The phenolic nature of the alkaloid was revealed from its positive phosphomolybdic acid test and from the



(1) R_1, R_2 = CH_2<

(3) R_1 = R_2 = Me



(2) R_1, R_2 = CH_2<

(4) R_1 = Me, R_2 = H

(5) R_1 = H, R_2 = Me

observed bathochromic shift in alkali in the UV spectrum of its borohydride reduction product, $C_{19}H_{19}NO_4$, mp 164°, λ_{max}^{EtOH} 285 nm (log ϵ, 3·70), $\lambda_{max}^{EtOH/OH^-}$ 293 nm (log ϵ, 3·74). The 60 MHz PMR spectrum of this compound was strikingly similar to that of tetrahydrocoptisine (**1**) and differed from the latter only by the presence of a methoxy (δ, 3·60) and a phenolic –OH (δ, 4·80, broad, exchangeable with D_2O) and by the absence of a methylenedioxy group. These data coupled with the fact that the molecular weight of the reduction product of *B* is 2 daltons higher than that of tetrahydrocoptisine (**1**) suggested that one of the methylenedioxy groups of the latter is replaced by a methoxy and a phenolic –OH in the former. The MS of this compound which showed molecular ion peak at *m/e* 325 and other important ions at *m/e* 176, 149 and 148 not only substantiated this view but also clarified that the two alkaloids differed in ring *A* substituents only [7]. Formation of (±)-sinactine (**3**) by methylation of the tetrahydroderivative of *B* by CH_2N_2 showed this was probably the case.

Alkaloid *B* therefore, was either dehydrocheilanthifoline (**4**) or its isomer (**5**). The Structure **5** was excluded from the observation that a methanolic solution of the alkaloid failed to develop a red colouration [8] on treatment with sodium bicarbonate and that its tetrahydroderivative failed to show a positive Gibb's test [9]. Alkaloid *B*, therefore, must be represented as (**4**) which was confirmed by establishing the identity of *B* and its borohydride reduction product with authentic dehydrocheilanthifoline (IR, Co-TLC, PMR) and (±)-cheilanthifoline (IR, mixed mp, Co-TLC, MS, PMR) respectively. The 90 MHz PMR spectrum of *B* in CF_3CO_2H was revealing

and accounted for all the protons on the basis of **4** [δ, 3·33, 4·90 (2 vicinal $-CH_2$, *t*), 4·08 (Ar-OMe, *s*), 6·42 (O-CH_2-O, *s*), 6·99 (C_4-H, *s*), 7·66 (C_1-H, *s*), 7·81 (C_{11} & C_{12}-H, *s*), 8·46 (C_{13}-H, *s*) and 9·35 (C_8-H, *s*)]. Dehydrocheilanthifoline was first isolated [10] from *Bocconia cordata* Willd. (*Papaveraceae*) and this is the first report of its isolation from a *Fumaria* species. Protopine, the major alkaloid of *F. indica*, contains only methylenedioxy groups. As protopines are known to be formed by oxidation of protoberberines [11] and methylenedioxy groups from *o*-methoxy phenols in nature [12], the presence of dehydrocheilanthifoline, a protoberberine alkaloid having an *o*-methoxy phenol grouping, in the plant is of biogenetic significance.

EXPERIMENTAL

Mps were determined in an open capillary and are uncorrected. UV were recorded in aldehyde-free EtOH. IR were determined in Nujol. PMR were taken in $CDCl_3$ or CF_3CO_2H. MS were determined by Dr. B. C. Das, Gif-sur-Yvette. France and by National Chemical Laboratory, Poona. The analytical samples were routinely dried over P_2O_5 *in vacuo*. Anhydrous Na_2SO_4 was used for drying organic solvents. Si gel was used for column chromatography. TLC was carried out on silica gel G (Merck) using mainly MeOH—HCl (9:1) (Solvent 1) and C_6H_6—EtOAc (7:1) (Solvent 2). Dragendorff's reagent was used for staining purposes. Amberlite IRA 400 (Cl^-) resin was used for regeneration of bases as chlorides from Mayer's complex.

Isolation of quaternary chlorides. Dried and powdered whole plant (4 kg) of *Fumaria indica* was extracted by cold percolation with EtOH (95%). The extract was concentrated to a dark brown syrup and stirred with aq. citric acid (7%) for 10 hr. The solution was basified with NH_4OH (pH ~ 9) and exhaustively extracted with $CHCl_3$. The aq. alkali left after $CHCl_3$ extraction was acidified with dil. HCl and treated with Mayer's reagent ($HgCl_2$ + KI) till precipitation was complete. The precipitate was washed free from excess reagent, suspended in ion-free water and stirred with IRA 400 (Cl^-) till exchange was complete. The aqueous solution was separated from the resin and concentrated under reduced pressure to a light brown gummy mass (0·75 g). It was chromatographed over Si gel (20 g) column and eluted first with EtOAc and subsequently with increasing percentage of MeOH in EtOAc.

Coptisine chloride (**2**). The EtOAc–MeOH (4:1) eluate on removal of solvent gave a yellow solid (160 mg) which on crystallisation from MeOH yielded yellow needles (90 mg), mp 340° UV; λ_{max} 268, 362, 465 nm (log ϵ, 4·03, 4·04, 3·38); R_f 0·53 (Solvent 1). (Found: C, 63·96, H, 4·21, N, 3·72. $C_{19}H_{14}NO_4Cl$ requires: C. 64·13, H, 3·93, N, 3·93%).

$NaBH_4$ reduction of coptisine chloride and work up in the usual way gave a solid which crystallised from MeOH as colourless needles, mp 217–18°; R_f 0·68 (solvent 2); PMR; δ, 6·03 (2H, *s*, O-CH_2-O), 6·06 (2H, *s*, O-CH_2-O), 6·71 (1H, *s*,), 6·78 (2H, *s*), 6·88 (1H, *s*); MS; *m/e* 323 (M^+, 42%), 174 (14), 149 (15), 148 (100); (Found: C, 70·5, 70·7, H, 5·59, 5·57, N, 3·92. $C_{19}H_{17}NO_4$ requires: C, 70·57, H, 5·30, N, 4·33). Mixed mp, Co-TLC and superimposable IR spectra indicated its identity with (±)-tetrahydrocoptisine.

Dehydrocheilanthifoline chloride (**4**). The EtOAc–MeOH (3:2) eluate on removal of solvent gave a red solid (60 mg) which crystallised from MeOH as orange needles, mp 340° (the crystals turned red on drying over boiling toluene in presence of P_2O_5 under vacuum); R_f 0·60 (Solvent 1); UV; λ_{max} 265, 361, 465 nm; IR: ν_{max} 3350, 1606 cm^{-1}; PMR (CF_3CO_2H): δ 3·33 (2H, *t*, C_5-methylene), 4·90 (2H, *t*, C_6-methylene), 4·08 (3H, *s*, Ar-OMe), 6·42 (2H, *s*, methylenedioxy), 6·99 (1H, *s*, C_4-H), 7·66 (1H, *s*, C_1-H), 7·81 (2H, *s*, C_{11} & C_{12}-H), 8·46 (1H, *s*, C_{13}-H), 9·35 (1H, *s*, C_8-H). Co-TLC, superimposable IR and PMR spectra indicated its identity with dehydrocheilanthifoline.

$NaBH_4$ reduction of dehydrocheilanthifoline chloride as before gave needles, mp [illegible] R_f 0·31 (Solvent 2); UV: λ_{max} 232 *sh*, 285 nm (log ϵ, [illegible]), ν_{max} 245 nm (in presence of alkali); PMR ($CDCl_3$): δ, 3·86 (3H, *s*, Ar-OMe), 5·95 (2H, *s*, O-CH_2-O), 6·63 (1H, *s*), 6·68 (2H, *s*), 6·85 (1H, *s*). MS: *m/e* 325 (M^+, 44%), 176 (22), 149 (96), 148 (100). Co-TLC and superimposable IR spectra indicated its identity with (±)-cheilanthifoline. Authentic sample of (±)-cheilanthifoline having reported mp 169–70° [13] melted in our hands at 164–65° and showed no depression on admixture with our sample. (Found: C, 69·87, H, 6·01, N, 4·15 $C_{19}H_{19}NO_4$ requires: C, 70·14, H, 5·89, N, 4·31%).

Methylation of (±)-cheilanthifoline with CH_2N_2 overnight afforded (±)-sinactine which was recrystallised from MeOH as needles, mp 168–69° (Lit. [14] mp 170°). Co-TLC with (–)-sinactine [15] showed identical spots in a variety of solvent systems.

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