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CELTINE, CELTISINE AND BREOGANINE, NEW PHENOLIC CULARINE ALKALOIDS FROM FUMARIACEAE

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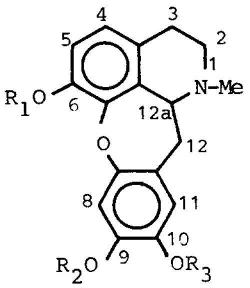
Abstract: Three new phenolic cularines have been isolated from Sarcocapnos and Corydalis species. Their structures have been elucidated on the basis of spectroscopic studies and chemical transformations.

In continuation of our study of alkaloids from Sarcocapnos and Corydalis species (Fumariaceae)[1] we have isolated and determined the structures of three new phenolic cularine alkaloids celtine (4a)[2], celtisine (5a)[3] and breoganine (6a)[4] the last two being the first examples of diphenolic cularines.

The cularine skeleton and oxygenated substitution pattern of these three new alkaloids was obtained from their conversion into cularine (1) by treatment with diazomethane. The placement of their phenolic groups was achieved by a pmr comparison of the chemical shifts of the OMe groups in cularine (1) with those of deuteromethylated 4b, 5b and 6b (Table I), which are easily obtained from celtine (4a), celtisine (5a) and breoganine (6a) by treatment with CD_2N_2[5]. The necessary previous assignment of the chemical shifts for the OMe groups in cularine (1) was achieved by a correlation of the pmr shifts of its OMe groups with those of deuteromethylated cularidine (2)[6] and synthetic cularine derivative (3)[1a] as shown in Table I.Celtine (4a) was found to be a monophenolic cularine having its phenolic group at the C-9 position as its O-deuteromethylated derivative (4b) lacks the OMe signal at 3.87 ppm. On the other hand, celtisine and breoganine were found to have diphenolic structures (5a) and (6a) respectively. Thus, deuteromethylated celtisine (5b) exhibited only one OMe group at 3.81 ppm while in deuteromethylated breoganine (6b) a single OMe group appeared at 3.89 ppm.

TABLE I. ^{1}H-NMR chemical shifts for -OMe groups of cularine derivatives in $CDCl_3$

Compound	C_6-OMe	C_9-OMe	C_{10}-OMe
1, $R_1=R_2=R_3=-CH_3$	3.85	3.87	3.79
2, $R_1=CD_3$; $R_2=R_3=-CH_3$	----	3.88	3.80
3, $R_1=R_2=-CH_3$; $R_3=-CD_3$	3.86	3.90	----
4b, $R_1=R_3=-CH_3$; $R_2=-CD_3$	3.85	----	3.80
5b, $R_1=R_2=-CD_3$; $R_3=-CH_3$	----	----	3.81
6b, $R_1=R_3=-CD_3$; $R_2=-CH_3$	----	3.89	----



4a, $R_1=R_3=-CH_3$; $R_2=-H$
5a, $R_1=R_2=-H$; $R_3=-CH_3$
6a, $R_1=R_3=-H$; $R_2=-CH_3$

Further support for the location of the OMe group at C-10 in celtine(4a) and celtisine(5a) was obtained from their mass spectra,which showed base peaks at respectively m/e 312(M^+-15) and m/e 298 (M^+-15), which are characteristic[7] of C-10 O-Methyl substituted cularines. Furthermore, in breoganine (6a), with a phenolic group at C-10, the base peak coincided with its molecular ion at m/e 313 (M^+).

The diphenolic breoganine (6a) has been reported[8] from the selective demethylation of cularine (1) under acidic conditions (48% HBr/AcOH, 135°C, 35 min.). However, in our experiments this reaction afforded a mixture of all possible demethylated compounds from which the diphenolic breoganine (6a) (37% yield) and celtisine (5a) (18% yield) were the main products isolated. On the other hand, by treating cularine (1) under nucleophilic conditions[9] (NaEtS, 3 mmoles, DMF, reflux, 40 min.) preferential attack at its C-9 rather than its C-10 methyl group was observed, giving celtine (4a) (33% yield) as the main product isolated. When this reaction was carried out under stronger conditions (NaEtS, 5mmoles, DMF, reflux, 4 h) a mixture of celtisine (5a) (43% yield) and breoganine (6a) (18% yield) was obtained.

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   b) J.M.Boente, L.Castedo, A.Rodríguez de Lera, J.M.Saá, R.Suau and M.C.Vidal, IBID, 24, 2295 (1983).
2. Celtine (4a), from Sarcocapnos enneaphylla, mp 94-96°C (EtOH), $|\alpha|_D$=+181 (c 0.08, MeOH), $C_{19}H_{21}NO_4$ |m/e 327.1483 (M^+, 45%)|; IR(KBr) 1280, 1510, 3350 cm^{-1}; UV λ_{max}(EtOH) (log ε) 216 (4.11), 228 (3.95, sh) and 282 (3.58); λ_{max}($EtOH-OH^-$) (log ε) 216 (4.59) and 298 (3.60); pmr (80MHz, $CDCl_3$, δ) 6.94 and 6.72 (AB_{dd}, J_{AB}=8.3Hz, 2H, H_4 and H_5 respectively) 6.82 and 6.48 (2s, 2H, H_8 and H_{11}) 4.44 (dd, J_{AX}= 11.3 and J_{BX}=4.2Hz, 1H, H_{12a}) 3.83 (s, 3H, -OMe) 3.80 (s, 3H, -OMe), 3.19-2.74 (m, 6H, 3x CH_2) and 2.58 (s, 3H, -NMe); MS, m/e (%) 327 (M^+, 45), 312 (100), 284 (9), 253 (8) and 174 (10).
3. Celtisine (5a), from S.enneaphylla, mp 158-160°C (EtOH), $|\alpha|_D$=+212 (c 0.025, MeOH); $C_{18}H_{19}NO_4$ |m/e 313.1328 (M^+)| UV λ_{max}(MeOH) (log ε) 225 (4.10) and 283 (3.85); λ_{max}($EtOH-OH^-$) (log ε) 225 (4.50) and 294 (3.91); pmr (80MHz, $CDCl_3$, δ) 6.78 (s, 3H, H_4, H_5 and H_{11}) 6.49 (s, 1H, H_8), 4.84 (bs, 2H, 2xOH), 4.27 (dd, J_{AX}=10.4Hz and J_{BX}=4.7Hz, 1H, H_{12a}), 3.77 (s, 3H, OMe), 3.16-2.76 (m, 6H, 3xCH_2) and 2.55 (s, 3H, NMe); MS, m/e (%) 313 (M^+, 54), 298 (100), 296 (12), 270 (9) and 161 (5). IR(KBr) 1305, 1510, 3400 cm^{-1}.
4. Breoganine (6a), from Corydalis claviculata and S.crassifolia, mp 249-250°C (EtOH), $|\alpha|_D$=+278 (c 0.057, MeOH); $C_{18}H_{19}NO_4$ m/e 313.1309; UV λ_{max}(EtOH) (log ε) 218 (4.18) and 284 (3.86); λ_{max}($EtOH-OH^-$) (log ε) 218 (4.34), 240 (4.19) and 300 (4.01); pmr (80MHz, $CDCl_3$, δ) 6.79 (s, 2H, H_4 and H_5), 6.70, 6.61 (2s, 2H, H_8 and H_{11}) 4.66 (bs, 2H, 2xOH), 4.24 (dd, J_{AX}=10 and J_{BX}=4.8 Hz, 1H, H_{12a}), 3.85 (s, 3H, OMe), 3.13-2.77 (m, 6H, 3xCH_2) and 2.54 (s, 3H, NMe); MS, m/e (%) 313 (100), 298 (70), 296 (40), 270 (15) and 161 (15), IR(KBr) 1300, 1510, 3300 cm^{-1}.
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