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DUGUESPIXINE, AN *N*-FORMYL 7-METHYL 6A,7-DEHYDRO-APORPHINE ISOMERIC WITH DUGUENAINE[1]

D. DEBOURGES, R. HOCQUEMILLER, A. CAVÉ,

Laboratoire de Pharmacognosie, ERA 317 CNRS, Faculté de Pharmacie, 92290 Châtenay-Malabry, France

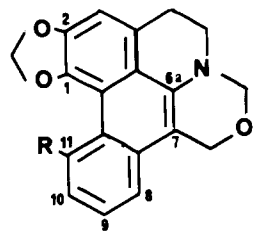
and J. LÉVY

Laboratoire des Substances Naturelles, ERA 319 CNRS, Faculté de Pharmacie 51000 Reims, France

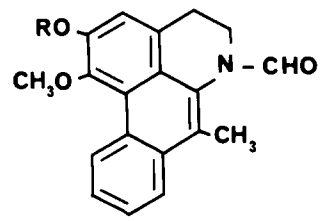
Aporphines are easily oxidized to 7-oxoaporphines via 6a,7-dehydroaporphines, a few examples of which have been encountered in nature (2-4). These highly reactive dehydroaporphines may suffer an oxidation or an alkylation on nucleophilic C-7. Such 7-alkylated aporphines have been isolated from various *Guatteria* species and seem to be characteristic of the genus (1, 5-8). Two further alkaloids from *Duguetia calycina*, i.e., duguecalyne (**1**) and duguenaine (**2**) (9), are related to the 7-alkylated aporphines, as their C-7 is involved in a supplementary oxazine ring. Furthermore, a 7-methyl dehydroaporphine has been isolated from a *Guatteria* species (1), and *N*-formylaporphines have been found in various *Duguetia* species (10).

We now wish to report on the isolation of a new *N*-formyl 7-methyl dehydroaporphine, duguespixine (**3**), from the bark of the Colombian tree *Duguetia spixiana* Mart. Examination of the available spectral data does not permit a clear choice between structures **3** and **4** for duguespixine.

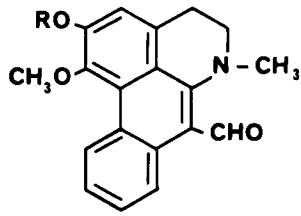
The methyl group resonates at a rather low field (δ=3.28 ppm) as compared with the *C*-methyl or *N*-methyl ^{1}H-nmr signals of 7-methyl 6a,7-dehydroaporphines ($\simeq$2.7 ppm) (1) and of the *N*-methyl of dehydroaporphines ($\simeq$ 3.0 ppm), respectively; the formyl proton resonates at 8.13 ppm, which could correspond to an *N*-formyl group (2-4). In order to clarify the question, duguespixine (**3**) was *O*-methylated while compound **6** was unambiguously prepared from nuciferine (11). Compound **6** and *O*-methylduguespixine are different; the



1 R=OCH_3
2 R=H



3 R=H
5 R=CH_3



4 R=H
6 R=CH_3

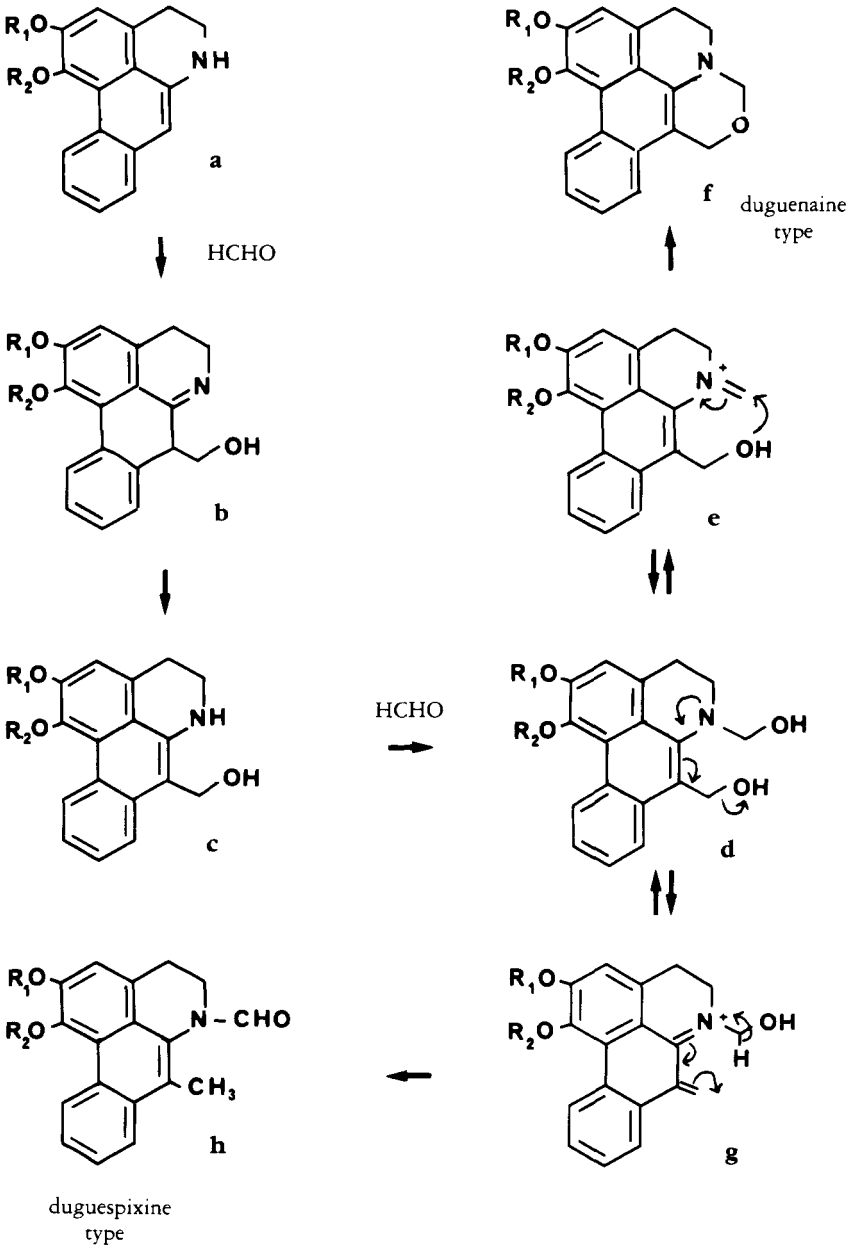
[1]Part LVII in the series "Alcaloïdes des Annonacées." For Part LVI, see Cortes *et. al.* (1).

latter must thus be **5**; and, hence, duguespixine is represented by formula **3**. The low field resonance of its methyl group is then due to the deshielding effect of the *N*-formyl group.

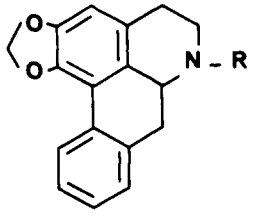
Of interest is the fact that, apart from the aromatic substitution pattern, such alkaloids as duguespixine (**3**) and duguenaine (**2**) are at the same oxidation level. Accordingly, they might originate from very similar precursors that are formulated as **d** (scheme 1).

Species **d** would result from the fixation of two molecules of formaldehyde onto dehydronoraporphine **a** (via **b** and **c**). Evolution of **d** would then lead to **f** (i.e., duguenaine) via **e** or to **h** (i.e., duguespixine) via **f**.

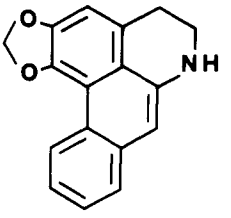
In order to check this mechanism, dehydroanonaine (**9**) was prepared from



SCHEME 1



7 R=H
8 R=Cl



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anonaine (**7**) via its chloramine and yielded a compound identical in all respects with natural duguenaine (**2**). However, no *N*-formylated derivative could be isolated from the reaction (12).

While this paper was in preparation, G.R. Lenz and F.J. Koszyk disclosed a total synthesis of duguenaine (**2**) along similar lines (13).

EXPERIMENTAL

PLANT MATERIAL.—*D. spixiana* was collected near San Luis, Antioquia, Colombia, by J. Brand in March 1982. A voucher sample is deposited at Medellin Herbarium (L.A.E. no. 202), University of Antioquia.

EXTRACTION AND ISOLATION OF DUGUESPIXINE (**3**).—Powdered plant material (7.2 kg) was extracted in a Soxhlet extractor with petroleum ether and then, after basification by dilute NH_3 solution, alkaloids were extracted with CH_2Cl_2. Separation of phenolic from nonphenolic bases gave 3.7 g of phenolic compounds from which duguespixine was isolated and purified by silica gel column chromatography (solvent=CH_2Cl_2-MeOH-NH_4OH, 95:5:0.5).

Duguespixine (300 mg, 0.004%) gave the following properties: ms ($M^{+\cdot}$ 307.1225); ir ν max (film) 1630 cm^{-1} (C=O); uv EtOH nm (log ϵ) 208 (4.19), 222 (4.16), 254 (4.17), 278 sh. (4.00), 430 (3.64); EtOH+OH^- 218 (4.23), 258 (4.25), 312 (3.90), 480 (3.42); ^{1}H nmr (90 MHz, $CDCl_3$, TMS) 3.28 (3H, s, 7-CH_3), 3.08 and 3.61 (2×2H, pseudotriplets, 4-H and 5-H), 3.70 (3H, s, 1-OCH_3), 6.80 (1H, s, 3-H), 7.43 (1H, td, J=7.5 and 1.5 Hz, 9-H), 7.63 (1H, td, J=7.5 and 1.5 Hz, 10-H), 8.13 (1H, s, N-CHO), 8.41 (1H, dd, J=7.5 and 1.5 Hz, 8-H), 8.98 (1H, dd, J=7.5 and 1.5 Hz, 11-H).

SYNTHESIS OF DUGUENAINE (**2**).—Dehydroanonaine (100 mg) was stirred at room temperature for 1 h with 50 mg of *N*-chlorosuccinimide to give the corresponding chloramine (80 mg). Sodium ethoxide was then added to the chloramine and the mixture stirred for 15 min at room temperature. The reaction mixture contained dehydroanonaine and several oxidation products but was not purified because of its instability. The crude mixture was refluxed under nitrogen for 30 min with 4 cc of HCHO, and the resulting solution was poured into H_2O and extracted several times with CH_2Cl_2. The combined extracts were dried and evaporated. Preparative tlc of the reaction mixture yielded 6 mg of duguenaine identical with the natural product (ms, ^{1}H nmr, ir, co-tlc).

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