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TWO NOVEL 1,4-DIHYDRONAPHTHALENE TYPE COMPOUNDS FROM CASSIA SEMICORDATA

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Abstract: Two new pigments have been isolated from the roots of Cassia semicordata and assigned the structures, 6,8-dihydroxy-7-acetyl-1-keto-3-methoxy-4,4-dimethyl-1,4-dihydronaphthalene (1) and di-2-(3,6,8-trihydroxy-7-acetyl-4,4-dimethyl-1,4-dihydro)naphthylmethane (2), respectively, on the basis of 2D NMR and mass spectral data.

The roots (1 Kg) of Cassia semicordata (Leguminosae), collected in Pernambuco state (Brazil), were initially extracted with cold MeOH and to this extract, H_2O and hexane were added. Separation of the latter afforded an extract which showed significant antimicrobial activity. Chromatography of the residue (6 g) on silica gel afforded, in addition to compounds normally found in this genus, two novel compounds 1 (160 mg, mp 191-2°C) and 2 (130 mg, mp 266-7°C). The high resolution mass spectrum of 1 (found 276.1003,calcd 276.0998) indicated a molecular formula, $C_{15}H_{16}O_5$, while the UV (λ_{max}^{MeOH} 254, 263, 310 and 343 nm) and IR ($\nu_{max}^{CHCl_3}$: 1630 and 1600 cm^{-1}) spectra showed the presence of at least two carbonyl groups as a part of a highly conjugated chromophore. The ^1H NMR spectrum displayed the signals for two strongly chelated hydroxy groups (at δ 14.0 and 15.8, respectively), two isolated protons in the olefinic/aromatic region (δ 6.48 and 5.62), a methoxy group (δ 3.86), a methyl group (downfield at δ 2.78), and two equivalent methyl groups on a quaternary carbon (6H at δ 1.51). These assignments were confirmed by the APT ^{13}C NMR spectrum (Table 1), but in spite of these data, the structure of the compound could not be assigned with certainty. Two dimensional NMR experiments (HETCOR[1] and LONG-RANGE HETCOR[2] (data summarized in Table 1) gave supplementary information about the carbon resonances in the ^{13}C NMR of 1. The lowest field carbon signal (δ 205.2) showed a long-range coupling with the methyl group protons at 2.78 ppm, thus establishing the presence of a COMe group. The resonance at 190.2 ppm can be assigned to another carbonyl, thereby accounting for the remaining oxygen atom, as required by the molecular formula, in view of the above noted data for two hydroxyl and one methoxy group. Initial inspection of the signal at 180.9 ppm (see Table 1), suggested the possible presence of still another carbonyl group but the long-range coupling with the methoxy group signal required that this center must be an oxygenated sp^2 carbon atom in close proximity to a highly substituted sp^3 carbon centre. Comparable examples[3,4] can be found in the literature. A series of selective INEPTL experiments[5,6], whose results are reported in the Table 2, allowed a complete correlation among the carbon signals.

Table 1

Carbon resonances and ^{13}C - ^{1}H connectivities of compound 1

	linked H	long range connected H
205.2	-	2.78
190.2	-	-
180.9	-	3.86, 1.51
168.7	-	13.99
167.8	-	15.76
157.6	-	1.51
108.5	-	6.48, 15.76, 13.99
106.4	-	6.48, 15.76, 5.62
105.9	6.48 (1H)	-
99.0	5.62 (1H)	-
56.4	3.86 (3H)	-
41.5	-	1.51, 5.62
33.4	2.78 (3H)	-
28.6	1.51 (6H)	-

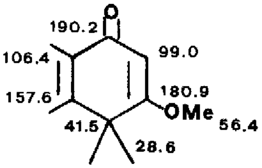
All the measurements were carried on a solution 0.15 M of 1 in $CDCl_3$.
The values of the first row were obtained by an APT ^{13}C NMR spectrum.
The ^{13}C - ^{1}H connectivities of the second and third row were displayed by HETCOR and LONG-RANGE HETCOR experiments, respectively.
The ^{1}H NMR spectrum is completed by two signals, exchangeable with D_2O, at 13.99 and 15.76 that were assigned to 6-OH and 8-OH, respectively.

Table 2

INEPTL experiments on compound 1

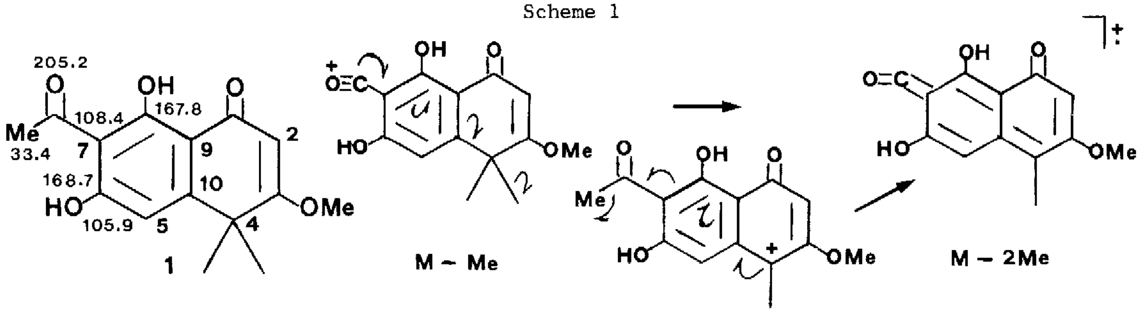
Selectively irradiated H	J^3 related C	J^2 related C	Minor effects
15.76	106.4, 108.4	167.8	99.0
13.99	105.9, 108.4	168.7	106.4
6.48	106.4, 108.4, 41.5	168.7	190.2
5.62	106.4, 41.5	180.9, 190.2	
3.86 OMe	180.9		
1.51 Me_2	157.6, 180.9	41.5	

In particular, the neighbouring carbons to the enolic methoxyl moiety (=C-OMe) were identified as a CH group (δ 99.0) and the $C(Me_2)$ group (δ 41.5). In summary, these data require a partial structure A, where are involved the carbonyl group at 190.2 ppm and two quaternary sp^2 carbons (at δ 106.4 and 157.6) connected through long-range coupling with the CH and the $C(Me_2)$ group, respectively. The proximity between the proton at C-2 and the OMe group was confirmed by the reciprocal NOE effect, as obtained by DIFNOE experiments.



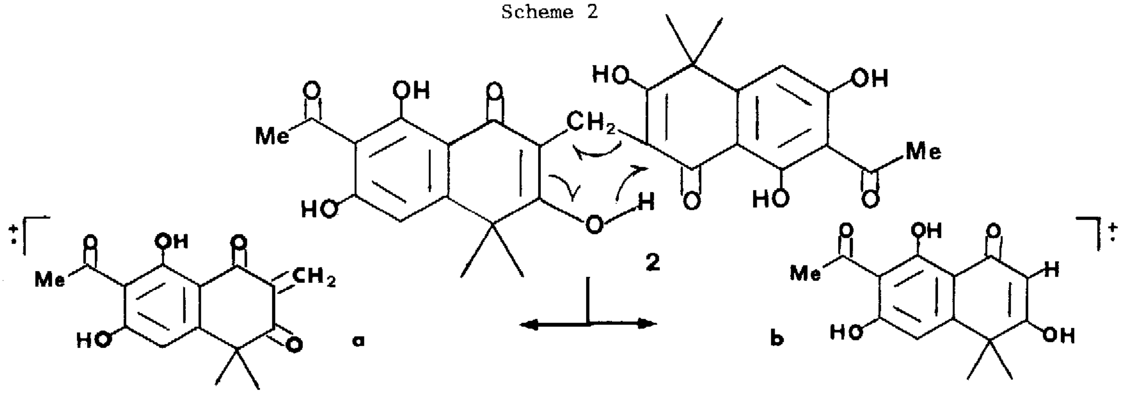
Once the resonances of the C-9 and C-10 carbons (see 1) had been identified the substitution pattern of the aromatic ring was inferred by the ^1H and ^{13}C connectivities (Tables 1 and 2). The mass spectral fragmentation[7] of 1 was characterized by a double loss of 15 mu. This pattern is expected for an acetophenone type system and for methyl group situated on a benzylic carbon (Scheme 1). Therefore, the structure 1 was assigned to the first pigment.

Scheme 1



The other isolated compound 2 ($C_{29}H_{28}O_{10}$ by HRMS: found 536.1694, calcd 536.1682); UV λ_{max}^{MeOH}: 255, 264, 320, 362 nm); IR ($\nu_{max}^{CHCl_3}$: 1625, 1600 cm^{-1}) showed spectral data very similar to those of 1. In addition the ^1H NMR spectrum[8] revealed many similar proton signals except that the resonances attributed to the C-2 and methoxyl protons were missing. Instead, new signals at δ 11.9 (1H) and 3.52 (1H) were now observed. The former signal, exchangeable with D_2O, was attributed to an hydroxyl, whereas the latter was correlated in the HETCOR spectrum with the carbon resonance of a methylene group, thus requiring the integration of all the other signals in the ^1H NMR spectrum to be doubled. Accordingly, the APT ^{13}C NMR spectrum[8] of 2 displayed only 15 signals. Moreover, the new OH and CH_2 groups showed mutual interference in DIFNOE experiments. These data suggest the structure 2, where two identical units are linked by a methylene bridge. Notably, in the mass spectrum of 2, two intense peaks at m/z 274 and 262 which analyzed for $C_{15}H_{14}O_5$ (HRMS: found 274.0832, calcd 274.0841) and $C_{14}H_{14}O_5$ (HRMS: found 262.0832, calcd 262.0841) were noted. These two fragments, whose formation can be rationalized through a six membered transition state, as in the Scheme 2, can now be assigned the structures a and b.

Scheme 2



The successive fragmentation[8] of ions a and b is in agreement with that of the analogous compound 1. In summary, the structure 2 for the second pigment is confirmed.

Compounds 1 and 2 are the first examples of a new class of natural compounds which represent an interesting oxygenation pattern of the fundamental naphthalene type structure. The biosynthetic pathway is likely to encompass a variation of the polyketide hypothesis although obviously experimental verification would be required.

Acknowledgements

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References and footnotes

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7) Mass spectrum of 1: m/z (rel. int.) 276 (M^+, 64), 261 (M - Me, 100), 246 (261 - Me, 15), 245 (M - OMe, 5), 233 (261 - CO, 12), 215 (233 - H_2O, 8), 130.5 (M - Me/2, 3), 124 (M - CO, 3); m* 246.8 (276 → 261), 231.8 (261 → 246).
8) Compound 2; ^{1}H NMR ($CDCl_3$): 14.86 (2H, s, 8-OH, 8'-OH), 14.02 (2H, s, 6-OH, 6'-OH), 11.89 (2H, s, 3-OH, 3'-OH), 6.55 (2H, s, H-5, H-5'), 3.52 (2H, s, CH_2), 2.79 (6H, s, 2x COMe), 1.61, 1.52 (6H each, s, 4-OMe, 4'-OMe); ^{13}C NMR ($CDCl_3$): 205.2 (s, 2x COMe), 190.1 (s, C-1, C-1'), 180.9 (s, C-3, C-3'), 169.0 (s, C-6, C-6'), 167.1 (s, C-8, C-8'), 157.8 (s, C-4a, C-4a'), 108.5 (s, C-7, C-7'), 105.7 (s, C-1a, C-1a'), 41.6 (s, C-4, C-4'), 33.5 (q, COMe), 29.3, 28.4 (q each, 4x Me), 16.6 (t, CH_2); m/z (rel. int.): 563 (M^+, 0.4), 274 (a^+, 63), 262 (b^+, 68), 259 (a - Me, 100), 247 (b - Me, 79), 245 (b - OH, 4), 244 (259 - Me, 7), 232 (247 - Me, 12), 231 (a - COMe, 43), 220 (a - $H_2C=C=CO$, 34), 219 (b - COMe, 23), 216 (244 - CO), 205 (220 - Me, 36), 203 (231 - CO, 11), 202 (220 - H_2O, 12), 187 (202 - Me, 12), 177 (205 - CO, 18); m* 244.8 (274 → 259), 232.8 (262 → 247), 229.1 (262 → 245), 217.9 (247 → 232), 191.2 (244 → 216), 185.5 (220 → 202).

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