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MOLECULAR STRUCTURE OF CRYPTOECHINULINE G, AN ISOPRENYLATED DEHYDROTRYPTOPHAN METABOLITE ISOLATED FROM *ASPERGILLUS RUBER*

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Neutral tryptophan metabolites which accompany echinuline[1] in *Aspergillus spp.* have recently received structural[2], biosynthetic[3], and synthetic[4] interest. We refer now on the spectroscopic evidences which allow to assign structural formula (3) to cryptoechinuline G, isolated from the fungal mat of *Aspergillus ruber*, grown on sugar beet molasses.

Cryptoechinuline G, $C_{29}H_{35}N_3O_2$ (by exact mass measurements), amorphous solid from the SiO_2 chromatography, optically inactive, showed in the ^{1}H-n.m.r. spectrum ($CDCl_3$, 270 MHz) the presence of two isopentenyl groups, of a reversed isoprenic moiety, of two aromatic hydrogens at δ 7.05 an 7.15, J_{AB} 8.2 Hz, typical of a tetrasubstituted benzene ring, of two amidic hydrogens at δ 9.75 and 8.34, of the signal due to the indolic NH at δ 7.38 and of three signals due to olefinic hydrogens at δ 7.22, 5.55 and 5.05, respectively. Comparison of the above evidences and of the mass spectroscopic behavior of (1)[2c] and related compounds indicated for cryptoechinuline G one of the two isomeric structures (3) and (4).

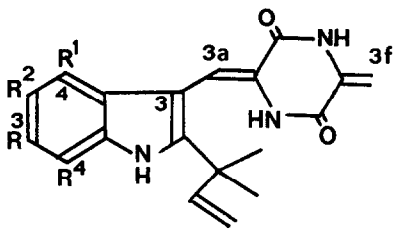
A preferential choice in favour of (3) is based on the following considerations.

a) In the ^{13}C-n.m.r. spectrum (22.63 MHz, d_6-DMSO) (the unsaturated region absorptions are reported in the Table) the signals at δ 123 and 109.5 (doublets in the single frequency off resonance) appear in a region typical for an indole nucleus without substituents at positions 6 and 7. In the other metabolites of this series[1,2] bearing substituents in positions 6 and 7, the resonances of these carbon atoms appear at about δ 134 and 123, respectively.

b) In cryptoechinuline G the carbon atom at position 3 absorbs at δ 101, whereas in other similar metabolites without a substituent in position 4, it appears at δ 103-104, the observed shift being possibly due to the shielding γ-effect of the CH_2 at position 4a.

c) Finally, in the ^{1}H-n.m.r. spectrum ($CDCl_3$, room temperature) one of the two CH_2 groups presents a line width considerably larger than the other. However, when the spectra are measured from -45°C to 100°C (d_5-pyridine) this signal splits in two separated components at lower temperature, which coalesce into a broad signal at 15°C. The latter becomes sharp at higher temperatures. The abovementioned influence of the temperature on the spectrum can be attributed to a reduction of the conformational mobility of one of the CH_2 groups.

Indeed, inspection of the steric models of (3) and (4) indicates that this happens for the isopentenyl chain at position 4 of (3), which appears in an extremly crowded situation.



(1) $R^1 = R^2 = R^4 = H$; $R^3 = -CH_2CH=C(Me)_2$

(2) $R^1 = R^3 = R^4 = H$; $R^2 = -CH_2CH=C(Me)_2$

(3) $R^1 = R^2 = -CH_2CH=C(Me)_2$; $R^3 = R^4 = H$

(4) $R^1 = R^2 = H$; $R^3 = R^4 = -CH_2CH=C(Me)_2$

TABLE: ^{13}C-n.m.r. Spectrum of Cryptoechinuline G (unsaturated region)

Chemical shift (assignement, multiplicity): 156.60 (C(3c)[†],s); 156.10 (C(3d)[†],s); 145.41 (C(2d),d); 142.16 (C(3b),s); 134.59 (C(3e), C(9),s); 130.32 (C(5),s); 130.23 (C(8), C(4c), C(5c),s); 128.89 (C(4),s); 126.61 (C(2),s); 124.99 (C(4b)[‡],d): 124.73 (C(5b)[‡],d); 123.00 (C(6),d); 114.59 (C(3a),d); 111.07 (C(2c),t); 109.54 (C(7),d); 101.30 (C(3),s); 100.43 (C(3f),t)

[†‡] assignements can be interchanged

In so far as the above evidences can be accepted in favour of structural formula (3), cryptoechinuline G represents a novelty from a chemotaxonomic point of view in the class of the isoprenylated tryptophan metabolites related to echinuline because of the presence of two adjacent isopentenyl chains, one of which at position 4, typical of the ergot alkaloids[5] and of cyclopiazonic acid . Feeding experiments with ^{3}H-labelled neoechinulineA and B[2b,h] and with isoechinuline A (2)[2g] designed to establish the metabolic significance of the α,β-desaturation of tryptophan to the timing of isoprenylation of the indole nucleus in the biosynthesis of (3) are in progress.

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