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^{13}C NMR ANALYSIS OF GEISSOSPERMINE AND ITS INDOLE ALKALOID MONOMER FRAGMENTS[1,2]

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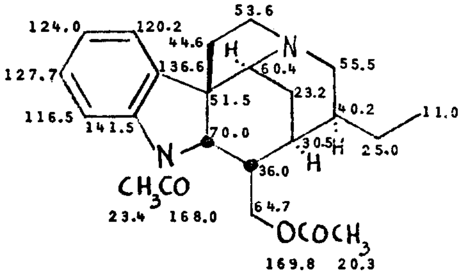
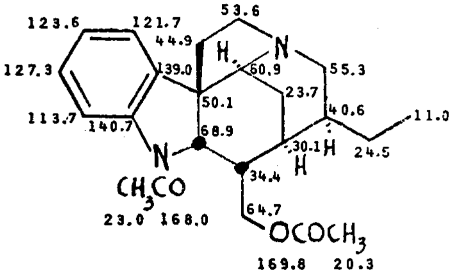
Recent studies of the ^{13}C NMR spectroscopy of alkaloids of the Strychnos[3] and corynanthoid[4,5] types have permitted the ^{13}C NMR analysis of the structurally complex alkaloid geissospermine (2) and its monomer components geissoschizoline and geissoschizine (3) and an assessment of their conformation. The chemical shifts of geissospermine (2), N,O-diacetyl-geissoschizoline (in the form of two amide rotamers, the major one 1a and minor one 1b) and geissoschizine (3) are listed on the formulas [starred numbers referring to interchangeable shifts; δ(TMS) = δ(CDCl$_3$) + 76.9 ppm].

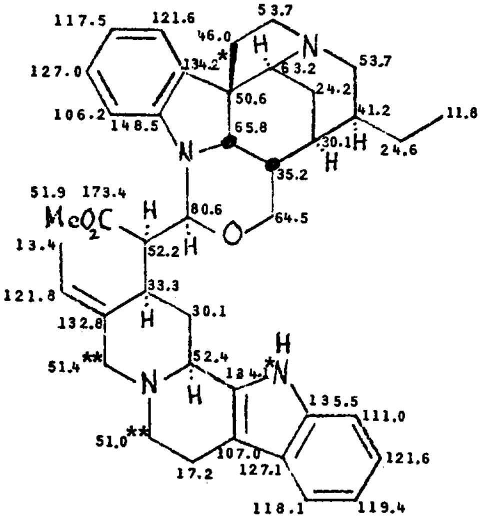


1a

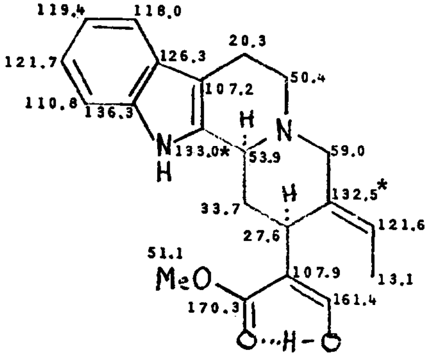


1b

Aside from the extra N-acetyl and acetoxy groups N,O-diacetylgeissoschizoline (1) differs from 16β-methyltubifolidine, a Strychnos alkaloid derivative previously inspected by ^{13}C NMR spectral means[3], by the stereochemistry of the methine holding the acetoxymethyl group. Two signal sets appear upfield in the spectra of 1 vs. those of the compound investigated earlier as a consequence of two new γ-interactions, i.e. those between the acetoxymethylated methine and the methylene of the ethyl group as well as the one-carbon bridge of the azabicyclo [3.3.1] -nonane system and the acetoxylated methyl group. The shift assignment of 1 makes that for the Strychnos skeleton part of geissospermine (2) a simple exercise.

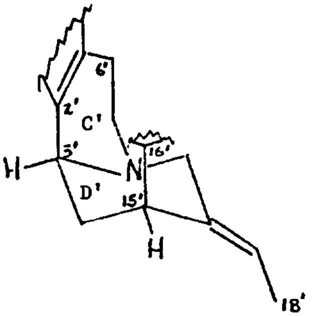


2



3

Whereas the cis H(3)-H(15) relationship in corynanthoid indole alkaloids leads normally to a trans-quinolizidine configuration and an equatorial conformation of the C(15) substituent, three carbon shifts reveal unambiguously that these features are not part of the geissospermine (2) structure. Thus the C(3') and C(6') shifts reflect clearly a cis-quinolizidine unit,[4,5] in conformity with infrared and ^{1}H NMR spectral data.[6] Furthermore, the C(18') shift is characteristic of that of C(4) in 2-methyl-2-butene[7] and that of C(18) of vobasine-like alkaloids[8] and hence indicative of a C(18')-H(15') γ-interaction in 2, ——— a situation incompatible with C(16') being disposed equatorially toward ring D'. The simplest explanation for these unusual results requires the assumption of the geissoschizine portion of geissospermine (2) adopting an all-chair conformation in which C(2') and C(16') are oriented axially toward ring D' (cf. 4). This relationship has been observed to be maintained also in the solid state.[6]



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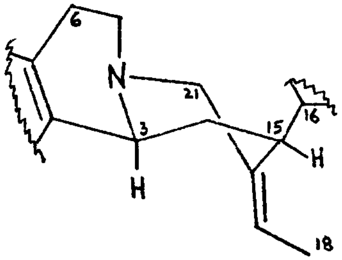

5

Geissoschizine (3) shows an even more unexpected shift pattern than geissospermine (2). Whereas the C(3) and C(18) shifts reflect a <u>cis</u>-quinolizidine and H(15)-C(18) <u>cis</u> coplanar relationship, respectively, the δ value of C(6) and the diminished shielding of C(21) support a <u>trans</u>-quinolizidine form. This apparent incompatibility is interpreted most readily on the basis of a boat ring D form within a second <u>cis</u>-quinolizidine configuration (cf. 5), a skeletal arrangement also favored from ^{1}H NMR data.[9,10] Thus the configuration of the ethylidene sidechain forces the formylacetic ester unit in both geissospermine (2) and geissoschizine (3) into an axial conformation, albeit with diverse consequences on the quinolizidine ring system.

In contrast with geissospermine the <u>cis</u>-quinolizidine form is not maintained in the crystal where geissoschizine adopts a trans-quinolizidine junction (11).

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