also oriented.[11] The nmr spectra of the solute species displays direct dipole–dipole interactions, chemical-shift anisotropies, and nuclear electric quadrupole interactions (if the resonant nucleus possesses an electric quadrupole moment), in addition to the interactions observed in an isotropic liquid.

In the present experiment CH_3F was dissolved in *p,p'*-di-*n*-hexyloxyazoxybenzene under a pressure of approximately 10 to 20 atm. The proton nmr spectrum at 100.000 Mcps in the isotropic phase at 140° consists of a doublet with $|J_{HF}| = 45 \pm 1$ cps, while the proton spectrum in the nematic phase at lower temperatures consists of two sets of triplets. The splitting between individual components of a triplet arises from H–H direct dipole interaction while the splitting between the two triplets is due to H–F direct dipole–dipole interaction *plus* H–F indirect spin–spin coupling. The ^{19}F spectrum at 94.0764 Mcps in the isotropic phase at 140° consists of a quartet with $|J_{HF}| = 45 \pm 1$ cps, while in the nematic phase the quartet remains but is split by the H–F direct dipole–dipole interaction in addition to the indirect H–F coupling. In addition, both the ^{19}F and proton spectra are shifted downfield (externally referenced) in the nematic phase as compared with the isotropic phase. These shifts arise from the anisotropic nature of the magnetic shielding which is expressed as $\Delta\sigma_i = \sigma_{\parallel} - \sigma_{\perp}$ for nucleus i where $\parallel$ and $\perp$ refer to components of the magnetic shielding tensor parallel and perpendicular to the threefold molecular symmetry axis. The anisotropic motion responsible for the above features can be expressed[12] in terms of the probability per unit solid angle that the symmetry axis of CH_3F makes an angle θ with the applied magnetic field.

$$P(\theta) = \frac{1}{4\pi} + C_{3z^2-r^2}\left(\frac{\sqrt{5}}{8\pi}\right)(3\cos^2\theta - 1) \tag{1}$$

The factor $C_{3z^2-r^2}$ is called a motional constant and takes values between $\sqrt{5}$ and $-\sqrt{5}/2$.

The determination of the absolute sign of one of the interactions, D_{ij}, J_{ij}, $\Delta\sigma_i$, and $C_{3z^2-r^2}$, determines the absolute sign of all the others. Measurements of the ^{19}F resonance of CH_3F trapped in a single crystal of β-quinol clathrate at 1.3°K show that $\Delta\sigma_F$ is negative.[13] This result makes possible the assignment of the absolute signs of D_{HH}, D_{HF}, J_{HF}, $C_{3z^2-r^2}$, and $\Delta\sigma_H$ in the following way. The average magnetic shielding, $\bar{\sigma}_{zz}$, of a nucleus in the semioriented molecule may be expressed[12] in terms of the isotropic magnetic shielding, $^1/_3(\sigma_{xx} + \sigma_{yy} + \sigma_{zz})$, and $\Delta\sigma$ as

$$\bar{\sigma}_{zz} = \frac{1}{3}(\sigma_{xx} + \sigma_{yy} + \sigma_{zz}) + C_{3z^2-r^2}\left(\frac{2}{3\sqrt{5}}\right)\Delta\sigma \tag{2}$$

with the z axis being identified with the molecular symmetry axis. Since σ_{zz} is less than $^1/_3(\sigma_{xx} + \sigma_{yy} + \sigma_{zz})$ for ^{19}F (downfield shift) in the nematic phase, and since $\Delta\sigma_F$ is negative, $C_{3z^2-r^2}$ must be positive. This means that the molecule tends to be oriented with the symmetry axis (which happens to be the longest geometrical dimension) parallel to the applied magnetic field and long axis of the nematic liquid crystal.[14]

Table I. Summary of the Interactions Obtained from the Analysis of the Proton and ^{19}F Nmr Spectra of CH_3F in the Nematic Liquid Crystal *p,p'*-Di-*n*-hexyloxyazoxybenzene at 80°[a]

Interaction	Splittings, cps	D_{HH}	D_{HF}	J_{HF}	$C_{3z^2-r^2}$
H–H	525	+350			+0.03910
H–F	234		−279	+45	+0.03873
H–F	234		−189	−45	+0.02623

[a] The positive value of J_{HF} results in the same motional constant as that obtained from the H–H interaction while a negative J_{HF} gives large disagreement.

A summary of the spectral analysis is given in Table I. It is seen that J_{HF} must be +45 cps in order that the motional constant obtained from the H–F interaction agree with that obtained from the H–H interaction.

The magnetic shielding anisotropy obtained for ^{19}F was $\Delta\sigma_F = -179 \pm 15$ ppm, which is about three times larger than the value of -66 ± 8 ppm obtained from the experiments on CH_3F trapped in a clathrate.[13] This discrepancy could be due to (a) incomplete alignment in the clathrate experiment or (b) a large difference in the effect of the matrix upon $\Delta\sigma$. We have observed a small solvent effect on $\Delta\sigma$ by repeating our measurement of the ^{19}F spectrum in *p*-*n*-hexyloxybenzoic acid where $\Delta\sigma_F = -211 \pm 12$ ppm. The magnetic shielding anisotropy for the protons in CH_3F is $\Delta\sigma_H = -28 \pm 4$ ppm, an unexpectedly large value.

From the knowledge of the relative signs of the coupling constants in $^{13}CHFCl_2$,[15] and if the absolute positive sign of $J_{gem\text{-}HF}$ determined in the present work holds for geminal H–F coupling in general, the absolute sign of $J_{^{13}CF}$ is found to be negative and the absolute sign of $J_{^{13}CH}$ is positive as predicted. The assignment of a positive sign to J_{HF} in CH_3F depends only upon the assumption that the sign of $\Delta\sigma_F$ is the same in *p,p'*-di-*n*-hexyloxyazoxybenzene solvent as it is in a β-quinol clathrate matrix.

The present results are also in agreement with a recent experiment[16] on $CHFCl_2$ in which the sign of J_{HF} was deduced from differences in the relaxation rates of the various magnetic resonance transitions.

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Biosynthesis of Gentiopicroside, a Novel Monoterpene

Sir:

The aglucone of gentiopicroside (**1**), a bitter principle glucoside,[1] possesses the same carbon skeleton, **6**, as the C_{10} moieties of *Yohimbé*, *Rauwolfia*, *Cinchona*, and *Strychnos* indole alkaloids. Moreover, within its chromophore is an enol ether grouping conjugated with a carboxyl, identical with that found in the cyclopentanoid monoterpenes or iridoids.[2]

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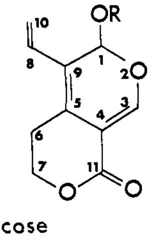
In previous studies on the biosynthesis of gentiopicroside[3] and a related compound, swertiamarin,[4] label from acetate-1-^{14}C was incorporated into these glucosides, but its location was not disclosed. The mevalonoid origin of both these nontryptophan-derived segments of the indole alkaloids[5,6] and the iridoid compounds[7] has been established. Furthermore, there is evidence that the cyclopentanoid monoterpene loganin is a precursor of the C_{10} units of certain alkaloids.[8] On the basis of its structural resemblance to these compounds, gentiopicroside has been postulated to be on this common biogenetic pathway,[9] and we wish to present evidence supporting this concept.

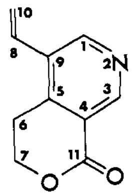
Gentiopicroside was found in relative abundance (2.5%) in the roots of *Swertia caroliniensis* (Walt) Kuntze. Ethyl acetate extraction afforded a mixture of predominantly polar compounds from which a hydrated amorphous gentiopicroside, mp 118–121°, could be isolated by silica gel chromatography with ethyl acetate–methanol (9:1) as eluent. Recrystallization from ethyl acetate–benzene–methanol (9:9:2) gave anhydrous crystals of gentiopicroside,[10] mp 181°, exhibiting the following spectral properties: $\lambda_{\max}^{\mathrm{EtOH}}$ 247 (sh), 255 (sh), and 270 mμ (log ϵ 3.84, 3.93, and 3.97, respectively); $[\alpha]$D −217.6° (*c* 1, MeOH); $\lambda_{\max}^{\mathrm{Nujol}}$ 2.90, 5.85, and 6.20 μ. Acetylation[1] of the hydrous or anhydrous forms of **1** yields gentiopicroside tetraacetate (**2**), mp 140°; optical rotation, $[\alpha]$D −159.5° (*c* 1, chloroform); ultraviolet: $\lambda_{\max}^{\mathrm{EtOH}}$ 248 (sh), 254 (sh), and 270 mμ (log ϵ 3.86, 3.89, and 3.94, respectively); infrared: $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.70, 5.80, and 6.18 μ; nmr:[11] δ 7.48 (singlet, 3 H).[2] Upon treatment of the tetraacetate **2** with methanolic ammonium hydroxide, followed by acid hydrolysis,[12] glucose is removed and the oxygen of the dihydropyran ring is replaced with nitrogen, affording gentianine (**3**), mp 81°; ultraviolet: $\lambda_{\max}^{\mathrm{EtOH}}$ 218, 245 (sh), and 285 (sh) mμ (log ϵ 4.42, 3.93, and 3.18, respectively); infrared: $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.80, 6.30, 6.35, and 6.75 μ; nmr: δ 3.10 (triplet, 6 H), 4.58 (triplet, 7 H), 5.5–6.0 (octet, 10 H, AB of ABX system), 6.6–7.0 (quartet, 8 H, X of ABX system), 8.91 (singlet, 3 H), and 9.23 (singlet, 1 H).[13]

Administration of DL-mevalonate-2-^{14}C (97.6 μcuries, 2.5 mg) by means of a cotton wick inserted through the stem of an intact *Swertia* plant resulted in the labeling of gentiopicroside (**1**) (0.04% incorporation). Crude gentiopicroside isolated as described above was converted directly to its tetraacetate (**2**) which was recrystallized to constant specific activity (0.13 μcurie/mmole). Conversion to gentianine (**3**) (0.13 μcurie/mmole) revealed that all of the radioactivity was present in the aglucone. Decarboxylation of the calcium salt[14] of gentianine afforded carbon dioxide representing the C-11 carbon. Measurements as $BaCO_3$ (0.026 μcurie/mmole) indicated it contained 20% of the total activity in gentianine (**3**).

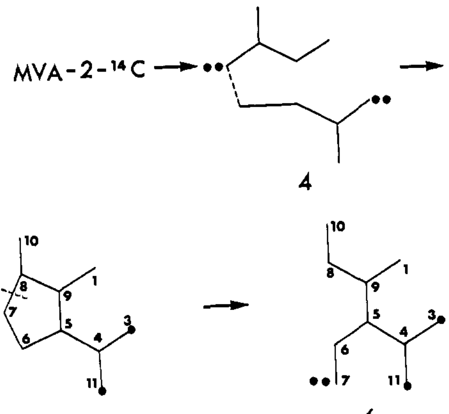
The similarity of the mevalonate-2-^{14}C labeling of gentiopicroside with that of the iridoid and indole alkaloid C_{10} moieties lends further support to a common pathway *via* a cyclopentanoid monoterpene **5**, possibly loganin,[8] as illustrated below. A compound having the skeleton of **6** may then serve as a precursor for either gentiopicroside and related glucosides or the above-mentioned indole alkaloids. Randomization of the original terminal dimethyl groups is characteristic of these monoterpenes.[5–7]



1, R = glucose
2, R = glucose tetraacetate



3



4

5

6

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The Addition of Sulfur Dioxide to *cis*-Hexatriene. Thiepin 1,1-Dioxide

Sir:

The nature of the conjugating properties of sulfones and the requirements for aromaticity in heterocycles render the properties of thiepin 1,1-dioxide of interest. We have prepared this compound by a reaction sequence utilizing the novel 1,6 addition of sulfur dioxide to *cis*-hexatriene.