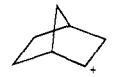
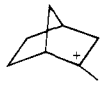
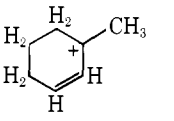
Table III. Hydride Affinities of Secondary and Tertiary Carbonium Ions

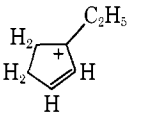
Tertiary		Secondary	
R^+	$D(R^+-H^-)$[a]	R^+	$D(R^+-H^-)$
	235.9		251.7
	232.5[b]		245.8
	232.1[b]		234.4
	231.1[b]		
	230.5[b]		
	229.5		
	228.4		

[a] All data in kcal/mol, $\Delta H^\circ_f(H^-) = 34.71$ kcal/mol. [b] Reference 4.

rangement of the ions can be made, although they do not permit one to draw an unequivocal conclusion about the probability of rearrangement or the lack thereof. (1) The reactions with which we are concerned are relatively gentle adiabatic processes with a maximum observed exothermicity of only 7.5 kcal/mol. (2) The values of ΔS°_{300} are consistent with the absence of rearrangement. ΔS°_{300} varies within only 3.6 eu of zero with an estimated uncertainty of ±2 eu. A negligible entropy change would be expected for the reaction of an acyclic ion with a cyclic neutral forming a cyclic product ion and an acyclic product neutral. An experimentally observed entropy change of small magnitude may be looked upon as a necessary, but not sufficient, condition for an absence of extensive rearrangement. (3) Ions with the same empirical formula as norbornyl ion ($C_7H_{11}^+$) but with different structures have approximately the same heats of formation as that found here for norbornyl (187.3 kcal/mol). Thus, using the group-equivalent method of calculating heats of formation and estimates of resonance energies, we obtain values of $\Delta H_f \simeq 182$ kcal/mol for A and $\Delta H_f \simeq 187$ kcal/mol for B. (4) Gas-phase hydrocarbon ions are



A



B

known to undergo rearrangements, but virtually all of the reactions involve ion formation by vertical ionization processes, such as electron ionization or photon ionization. For practical purposes, little is known about the proclivity toward isomerization of ions formed by low-energy adiabatic processes such as H^- transfer or about the relative proclivities for such isomerization in gas phase and in solution.

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Structure of Sarracenin. An Unusual Enol Diacetal Monoterpene from the Insectivorous Plant *Sarracenia flava*

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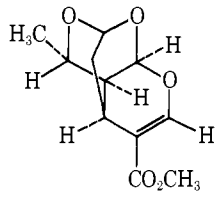
Abstract: The structure of an unusual enol diacetal monoterpene sarracenin ($C_{11}H_{14}O_5$, mp 127–128) from the insectivorous plant *Sarracenia flava* is reported. Confirmatory evidence includes x-ray crystallography and ^{13}C NMR data. A hypothesis is presented concerning the biogenetic role of sarracenin in the biosynthesis of monoterpenes and indole alkaloids.

Reports[2] that the ethanol (moonshine) extracts of the roots of *Sarracenia flava*[3] (golden trumpet) have been used as folk remedy by residents of the Okefenokee swamp region of Southeastern Georgia prompted the examination of this plant which entraps and digests insects.[4] We have recently confirmed the antitumor activity[5] of *S. flava* in the roots as well as the tops and reported[6] the presence of two amines which are responsible for paralyzing insects after they become entrapped in the pitcher. One of them, coniine,[7] is also one of the major alkaloids of the poisonous hemlock plant (*Conium maculatum*). We now wish to report the isolation and the structure of sarracenin as the

novel enol diacetal **1**. The structure was assigned on the basis of spectral evidence and biogenetic considerations and later confirmed by x-ray crystallography data.



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Experimental Section

Nuclear magnetic resonance spectra were obtained using a Jeolco Minimar spectrometer equipped with a spin decoupler. Tetramethylsilane was used as the internal standard and chloroform-*d*, 99.8% ($CDCl_3$), as solvent. The ^{13}C NMR data were recorded on a Varian CDF-20 in the Fourier Transfer Mode, using 38 210 transients with an acquisition time for each pulse of 0.8 s and a pulse delay of 0.5 s. Mass spectral data were obtained using a Perkin-Elmer Model 270 or a Hewlett-Packard Model 5930 mass spectrometer. Analytical GC–MS was done with a Hewlett-Packard 5930 quadrupole mass spectrometer interfaced with a 5700 gas chromatography from a 250 ft × 0.03 in. capillary gas chromatographic column coated with OV-17. The carrier gas flow was 8.0 ml/min N_2. The GLC was programmed from 120 to 160° at 1°/min rate. The final temperature was maintained for 20 min. Mass spectra were obtained at 70 eV. Infrared spectra were obtained using a Perkin-Elmer Model 137 G spectrophotometer. The spectra of solids were obtained by incorporating the sample into a pellet of potassium bromide. The band at 11.035 μ in a polystyrene film (0.05 mm) was used as a reference peak. Column chromatography (wet and dry column chromatography) was performed in glass columns with sintered glass using silica gel, alumina (neutral, Brockman Activity 1) of Fisher Scientific Co., and Florisil supplied by Applied Science Laboratory Inc. as the solid support. Thin layer chromatography (TLC) was performed using E. Merck (Darmstadt) silica gel G and GF-254 of Applied Science Laboratories Inc., coated (20 × 20 cm and 5 × 20 cm) glass plates. Chromatoplates were prepared by using Desaga spreader with thickness of 0.25 mm for identification and 0.5 and 0.75 mm for preparative TLC. The plates were activated at 110 °C for 1 h. The solvent system was acetone–benzene–$CHCl_3$ (1:2:17) unless otherwise stated. 2,7-Dichlorofluorescein, potassium dichromate in H_2SO_4, and 3% vanillin in 0.5% concentrated H_2SO_4 in MeOH and ultraviolet light were used as detecting agents. Melting points were obtained on a Fisher-Jones apparatus and are uncorrected. Elemental microanalyses were done by Galbraith Laboratories Inc., Knoxville, Tenn. Biological activities were performed by Cancer Chemotherapy National Service Center, Bethesda, Md.

Isolation of Sarracenin (1). The dry ground roots of *Sarracenia flava*[13] (4400 g) were extracted for 6 days in a Soxhlet extractor with *n*-hexane (24 l.). The hexane solution was removed from the extractor and evaporated in vacuo to yield 42 g of crude extract (fraction A). The plant material was then extracted with 95% ethyl alcohol (24 l.) for 6 days. Evaporation of the ethanol solution in vacuo yielded 727 g of crude extract, which was then distributed between $CHCl_3$ and water. Evaporation in vacuo of the $CHCl_3$ gave 412 g of crude material (fraction B). A portion of fraction B (206 g) gave 170 g of white needle crystals (fraction D) upon recrystallization from benzene–methanol (1:5). The filtrate after evaporation was labeled fraction E. Fifty grams of fraction E was extracted seven times with 250 ml of 20% benzene–petroleum ether. The solvent was removed in vacuo from the combined extracts to yield 11.2 g of 20% benzene–petroleum ether soluble material. The crude extract was dissolved in 50 ml of benzene and placed on a chromatography column (2.5 cm diameter × 55 cm long, neutral alumina activity 1, wet packing in petroleum ether). The column was eluted with petroleum ether, 5% benzene–petroleum ether, 20% benzene–petroleum ether, 40% benzene–petroleum ether, and pure benzene (200 ml per fraction). The separations were monitored by TLC, and the components were located by uv light and heating the developed plate after spraying with potassium dichromate–H_2SO_4. Fraction S (0.513 g) was obtained from fractions 1–5 of the 50% chloroform–benzene eluent. Fraction S (a mixture of a yellow oil and a white solid which had an R_f of 0.38 on TLC) was dissolved in a small volume of ether (5 ml) and separated by preparative TLC. The appropriate band (R_f 0.38) was cut out and removed from the silica gel by Soxhlet extraction with benzene. The solvent was removed in vacuo, and sarracenin (**1**) was crystallized from ether–benzene–petroleum ether to yield 0.143 g of a white crystalline material, mp 127–128 °C. Spectral properties of **1** were γ_{max} (KBr) 2970, 1707, 1640, 1440, 1380, 920, 860, and 818 cm^{-1}; NMR ($CDCl_3$) δ 1.33 (3 H, d, J = 6.5 Hz), 1.75 (2 H, m), 2.34 (1 H, m), 2.97 (1 H, m), 3.76 (3 H, s), 4.20 (1 H, q, J = 6.5 Hz), 4.96 (1 H, d, J = 3 Hz), 5.77 (t, J = 2 Hz), and 7.47 (1 H, s); ^{13}C NMR ($CDCl_3$) 18.72, 22.10, 32.39, 35.09, 51.40, 68.99, 81.14, 91.70, 112.33, 150.09, and 166.76 ppm; uv (ethanol) λ_{max} 232 mμ (ϵ 9660). Mass spectrum gave a parent ion at M^+ = 226 and fragmentation: *m/e* 41, 69, 96, 109, 121, 137, 148, 165, 180, 226, 227 % relative 60, 52, 48, 42, 94, 44, 56, 56, 68, 100, 16.

Anal. Calcd for $C_{11}H_{14}O_5$ (mol wt 226.23): C, 58.40; H, 6.24. Found: C, 58.30; H, 6.10.

X-Ray Data Collection and Structure Determination of Sarracenin (1). Sarracenin (**1**) was crystallized from chloroform as colorless plates which belong to the monoclinic system. Single crystals of the substances were sealed in thin-walled capillaries prior to x-ray examination. The unit cell parameters are a = 8.293 (4), b = 6.222 (4), c = 10.637 (4) Å, and β = 104.00 (4)°; the space group $P2_1$ is implied by systematic absences, density, and symmetry considerations (ρ_{calcd} = 1.41 g cm^{-3} for two molecules in the unit cell). A total of 659 independent observed reflections [$I \geq 3\sigma(I)$] were collected out to $2\theta \leq 50°$ using graphite-crystal monochromated Mo Kα radiation (0.71069 Å) on an Enraf-Nonius CAD-4-diffractometer. The structure was solved by direct methods using the program MULTAN[8] and refined by full-matrix least-squares techniques[9] to give discrepancy indexes of R_1 = 0.052 and R_2 = 0.055 where $R_1 = \Sigma(||F_o| - |F_c||)/\Sigma|F_o|$; $R_2 = \{\Sigma w(|F_o| - |F_c|)^2/\Sigma w|F_o|^2\}^{1/2}$. Carbon and oxygen atoms were refined with anisotropic thermal parameters (Table I); the contribution of the eight hydrogen atoms in hybridization fixed positions was included, but the methyl hydrogen atoms were not located. Bond lengths and angles agree well (esd's of 0.0008 Å and 0.5°, respectively) with generally accepted values.[10] The bond lengths and angles are given in Table II.

The diffracted intensities were collected by the ω–2θ scan technique with a takeoff angle of 3.0°. The scan rate was variable and was determined by a fast (20° min^{-1}) prescan. Calculated speeds based on the net intensity gathered in the prescan ranged from 7 to 0.2° min^{-1}. Moving-crystal moving-counter backgrounds were collected for 25% of the total scan width at each end of the scan range. For each intensity the scan width was determined by the equation

$$\text{scan range} = A + B \tan\theta$$

where A = 1.00° and B = 0.25°. Aperture settings were determined in a like manner with A = 4.0 mm and B = 0.87 mm. Other diffractometer parameters and the method of estimation of the standard deviations have been described previously.[11] As a check on the stability of the instrument and the crystal, three reflections were measured after every 25 reflections; the standards fluctuated within a range of ±2%.

One independent quadrant of data was measured out to 2θ = 50°; a slow scan was performed on a total of 659 unique reflections. Since these data were scanned at a speed which would yield a net count of 4000, the calculated standard deviations were all very nearly equal. No reflection was subjected to a slow scan unless a new count of 20 was obtained in the prescan. Based on these considerations, the data set of 659 reflections (used in the subsequent structure determination and refinement) was considered observed and consisted in the main of those for which $I > 3\sigma(I)$. The intensites were corrected for Lorentz and polarization effects but not for absorption (μ = 1.20). The final values of the positional and thermal parameters are given in Table I.[12]

Discussion

The finely ground dry roots of *S. flava*[13] were extracted first with hexane and then with 95% ethanol. The residue

Table I. Final Fractional Coordinates and Thermal Parameters[a] for Sarracenin

Atom	x/a	y/b	z/c	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
O(1)	0.6592 (7)	0.7562 (10)	0.4070 (6)	0.0220 (11)	0.0140 (15)	0.0118 (7)	0.0014 (12)	0.0043 (8)	−0.0010 (1)
O(2)	0.6800 (7)	0.3001 (12)	0.1370 (5)	0.0230 (12)	0.0355 (23)	0.0100 (7)	−0.0014 (16)	0.0035 (7)	−0.0040 (1)
O(3)	0.7834 (7)	0.6002 (10)	0.2579 (6)	0.0188 (11)	0.0221 (19)	0.0163 (8)	−0.0021 (12)	0.0090 (8)	0.0023 (1)
O(4)	0.8094 (7)	0.1490 (11)	0.6771 (5)	0.0220 (12)	0.0209 (18)	0.0127 (7)	−0.0029 (14)	0.0018 (7)	−0.0003 (1)
O(5)	0.8496 (7)	0.4812 (12)	0.7558 (5)	0.0261 (13)	0.0284 (21)	0.0098 (7)	−0.0017 (15)	0.0025 (8)	−0.0040 (1)
C(1)	0.7324 (10)	0.4418 (15)	0.5328 (8)	0.0125 (13)	0.0159 (21)	0.0109 (9)	0.0001 (15)	0.0047 (9)	0.0002 (1)
C(2)	0.7178 (10)	0.6524 (15)	0.5223 (8)	0.0135 (15)	0.0181 (25)	0.0125 (10)	−0.0001 (17)	0.0045 (10)	−0.0008 (1)
C(3)	0.6292 (10)	0.6291 (14)	0.2925 (8)	0.0181 (16)	0.0170 (23)	0.0121 (10)	0.0018 (18)	0.0052 (10)	0.0045 (1)
C(4)	0.5574 (10)	0.4096 (14)	0.3105 (8)	0.0143 (14)	0.0163 (23)	0.0115 (10)	−0.0008 (15)	0.0044 (9)	0.0001 (1)
C(5)	0.6866 (8)	0.2957 (13)	0.4156 (7)	0.0120 (12)	0.0131 (19)	0.0095 (8)	−0.0017 (14)	0.0019 (8)	0.0013 (1)
C(6)	0.8370 (10)	0.2496 (16)	0.3594 (7)	0.0189 (16)	0.0212 (24)	0.0096 (9)	0.0051 (19)	0.0038 (9)	0.0004 (1)
C(7)	0.8121 (12)	0.3757 (16)	0.2347 (10)	0.0170 (16)	0.0303 (31)	0.0150 (13)	0.0022 (20)	0.0085 (12)	−0.0021 (1)
C(8)	0.5306 (10)	0.2833 (17)	0.1843 (8)	0.0156 (15)	0.0276 (29)	0.0113 (10)	−0.0048 (20)	0.0037 (10)	−0.0043 (1)
C(9)	0.6170 (11)	0.8563 (18)	−0.0761 (8)	0.0198 (18)	0.0370 (38)	0.0108 (11)	−0.0016 (22)	−0.0013 (11)	−0.0010 (1)
C(10)	0.7995 (10)	0.3385 (16)	0.6590 (9)	0.0124 (14)	0.0230 (28)	0.0109 (10)	−0.0008 (17)	0.0035 (9)	0.0001 (1)
C(11)	0.9217 (13)	0.3918 (19)	0.8845 (9)	0.0361 (27)	0.0413 (46)	0.0089 (10)	0.0034 (31)	−0.0017 (13)	0.0014 (1)
H1(C2)	0.706	0.806	0.513	*b*					
H2(C3)	0.546	0.700	0.220						
H3(C4)	0.451	0.420	0.332						
H4(C5)	0.648	0.164	0.447						
H5(C6)	0.939	0.291	0.418						
H6(C6)	0.844	0.099	0.340						
H7(C7)	0.916	0.360	0.208						
H8(C8)	0.455	0.167	0.190						

[a] Anisotropic thermal parameters defined by $\exp[-(\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + 2\beta_{12}hk + 2\beta_{13}hl + 2\beta_{23}kl)]$. [b] Calculated positions 0.98 Å from the bonded carbon atom; isotropic thermal parameter set at 5.5 Å^2.

Table II. Bond Lengths (Å) and Angles (deg) for Sarracenin

	Bond Length[a]		
C(1)-C(2)	1.318 (10)	O(2)-C(7)	1.397 (9)
C(1)-C(5)	1.515 (10)	C(6)-C(7)	1.512 (11)
C(1)-C(10)	1.472 (8)	C(5)-C(6)	1.535 (10)
C(2)-O(1)	1.366 (8)	C(3)-O(3)	1.425 (8)
O(1)-C(3)	1.423 (8)	O(3)-C(7)	1.448 (9)
C(3)-C(4)	1.520 (10)	O(4)-C(10)	1.194 (9)
C(4)-C(5)	1.523 (10)	O(5)-C(10)	1.347 (8)
C(4)-C(8)	1.525 (10)	O(5)-C(11)	1.465 (10)
O(2)-C(8)	1.450 (8)	C(8)-C(9)	1.532 (10)
	Bond Angles		
C(2)-O(1)-C(3)	117.1 (5)	C(4)-C(5)-C(1)	108.5 (6)
C(7)-O(2)-C(8)	110.4 (5)	C(4)-C(5)-C(6)	107.2 (6)
C(3)-O(3)-C(7)	111.1 (6)	C(1)-C(5)-C(6)	111.5 (6)
C(10)-O(5)-C(11)	116.4 (6)	C(7)-C(6)-C(5)	107.0 (6)
C(2)-C(1)-C(10)	121.2 (8)	O(3)-C(7)-C(6)	110.1 (7)
C(2)-C(1)-C(5)	121.8 (7)	O(2)-C(7)-O(3)	108.7 (7)
C(5)-C(1)-C(10)	116.9 (6)	O(2)-C(7)-C(6)	113.2 (7)
C(1)-C(2)-O(1)	123.5 (8)	O(2)-C(8)-C(9)	108.2 (6)
O(1)-C(3)-C(4)	112.6 (6)	C(4)-C(8)-C(9)	115.4 (7)
O(1)-C(3)-O(3)	108.0 (6)	O(2)-C(8)-C(4)	108.3 (6)
O(3)-C(3)-C(4)	108.8 (6)	C(1)-C(10)-O(5)	112.9 (7)
C(3)-C(4)-C(5)	106.5 (6)	C(1)-C(10)-O(4)	125.0 (5)
C(3)-C(4)-C(8)	109.2 (6)	O(4)-C(10)-O(5)	122.1 (4)
C(5)-C(4)-C(8)	109.5 (6)		

[a] The nonbonded approaches are normal for a molecular compound of this type; the shortest is O(4)-O(3)′ $(2 - x, -\frac{1}{2} + y, 1 - z)$ = 3.293 (8) Å.

from the alcoholic fraction was partitioned between water and chloroform. Chromatography of the chloroform extract followed by crystallization yielded sarracenin, $C_{11}H_{14}O_5$ (M^+ 226), mp 127-128° dec, $[\alpha]^{22}D$ −68.8° ($CHCl_3$). Sarracenin, a neutral compound, upon catalytic hydrogenation gave a dihydro derivative with *m/e* 228 (M^+), indicating the presence of a reducible double bond. Alternatively, sarracenin (**1**) could be isolated[14] in a similar fashion from an extract (benzene) of the pitchers (leaves) of *S. flava* which showed significant activity (% T/C 150 at a dose of 50 mg/kg) against p-388 lymphocytic leukemia in BDF_1 mice.[15]

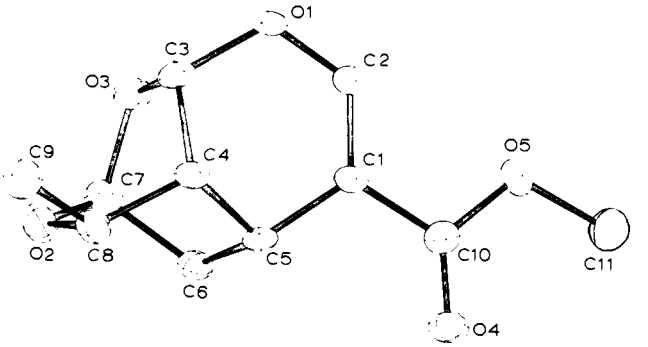


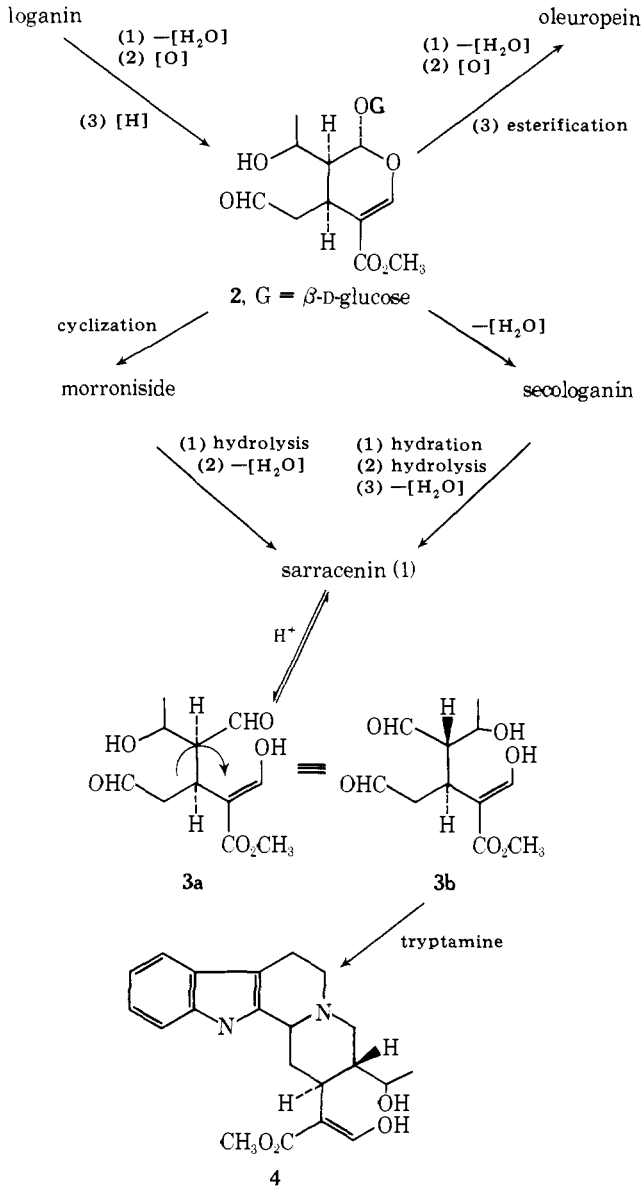
Figure 1. Molecular structure of sarracenin with the atoms displayed as 30% probability ellipsoids for thermal motion. Hydrogen atoms are not shown, and no absolute stereochemistry is implied.

Absorptions in the ir spectrum at 1710 (=$COOCH_3$) and 1640 cm^{-1} (-C=CO) and uv spectrum at λ_{max} 232 nm (ϵ 9660) indicated the presence of an ester enol-ether group ($CH_3OC(=O)C=CHO$) which is typically found in monoterpenes of the Iridoid group[17] and in ring E of many indole alkaloids.[18] The mass spectral fragmentation pattern[19] was also supportive of the presence of this functional group in an Iridoid-type monoterpene.[17]

The 100-MHz ^1H NMR spectrum of sarracenin (**1**) was obtained in chloroform-*d* using Me_4Si as an internal standard at δ 1.00. The spectrum showed the following absorptions: δ 1.33 [d, J = 6.5 Hz, 3 H, CH_3 (9)], 1.75 [m, 2 H, CH_2 (6)], 2.34 [m, 1 H, CH (4)], 2.97 [m, 1 H, CH (5)], 3.76 [s, 3 H, CH_3 (11)], 4.20 [q, J = 6.5 Hz, 1 H, CH (8)], 4.96 [d, J = 3 Hz, 1 H, CH (3)], 5.77 [t, J = 2 Hz, CH (7)], and 7.47[20] [s, 1 H, CH (2)]. The appearance of the C(8) methine proton as a quartet is consistent with the geometry of the molecule as shown in Figure 1. The C(7) H is coupled with the C(6) H's, the C(3) H with the C(4) H, and the C(8) H with the C(9) H's.

The decoupled ^{13}C NMR spectrum showed 11 signals, consistent with a compound with a molecular formula $C_{11}H_{14}O_5$, which were tentatively assigned as follows: (in ppm) 18.72 [primary carbon, C(9)], 22.10 [secondary car-

Scheme I



bon, C(6)], 32.39 [tertiary carbon, C(4) or C(5)], 35.09 [tertiary carbon, C(5) or C(4)], 51.40 [methoxy carbon, C(11)], 68.99 [tertiary carbon adjacent to oxygen, C(8)], 88.14 [tertiary carbon adjacent to two heteroatoms, C(3) or C(7)], 91.70 [tertiary carbon adjacent to two heteroatoms, C(7) or C(3)], 112.33 [vinyl carbon, C(1)], 150.09 [vinyl carbon, C(2)], 166.76 [carbonyl carbon, C(10)]. Speculation would lead one to predict that the C(1)-C(2) double bond would shield C(4) so that C(4) would appear upfield (32.25) as compared with C(5) (35.09). One would also predict that the C(3) carbon would be deshielded relative to the C(7) carbon through the influence of the C(1)-C(2) double bond.

The relative structure of **1** was confirmed by a single-crystal x-ray diffraction experiment. The molecular configuration is shown in Figure 1.

There is an abundance of literature[21-25] available concerning the role of loganin and secologanin in the biosynthesis of terpenoids and indole alkaloids; however, a number of other possible key intermediates have not been isolated or postulated. Furthermore, the intermediates postulated in the biogenetic sequence from loganin to secologanin have not been confirmed.[26] The molecular rotation of sarracenin (**1**) is one of the same sign and similar magnitude as loganin and other closely related monoterpenoids, such as morroniside[27] and secologanin. This result suggests identical configurations at C(4) and C(5). Since, sarracenin (**1**) can reasonably be derived from loganin, either directly through morroniside[27] or via secologanin, we propose the possible role of sarracenin (**1**) as an intermediate in the biogenesis of certain monoterpenes and indole alkaloids as illustrated in Scheme I. Acid-catalyzed cleavage of sarracenin (**1**) would presumably provide the novel enol aldehyde **3.** Compound **3** is significant because the simple rotation of a bond in **3a** would provide **3b** and thus explain the transformation from the cis ring junctures found in the monoterpenoid precursors to the trans stereochemistry found in a number of indole alkaloids. Also, the structure **3b** contains two aldehyde groups positioned for facile condensation with tryptamine which could possibly provide intermediate **4.** The postulation of **4** is in line with the presence of corynanthene aldehyde, ajmalicine, and geissochizine in nature and may also explain the recent observation[21] that corynanthene aldehyde and ajmalicine are not precursors of the Aspidosperma and Iboga types of alkaloids and thus lie beyond the branching point leading to rearranged systems.

Experimental test of these possibilities is in progress.

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Supplementary Material Available. A complete listing of structure factor amplitudes for sarracenin (11 pp). Ordering information is given on any current masthead page.

References and Notes

(1) (a) Mississippi State University; (b) The University of Alabama; (c) University of South Carolina.
(2) Private conversation with local resident.
(3) The plant material used was identified as *Sarracenia flava* (Sarraceniaceae) by Dr. Sidney McDaniel, Department of Botany, Mississippi State University. A voucher (preserved) specimen (SM-16, 702) representing material collected for this investigation is available for inspection at the Herbarium of the Department of Botany, Mississippi State University.
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Flow Nuclear Magnetic Resonance Study of the Dehydration of the Tetrahedral Intermediate Resulting from the Addition of Hydroxylamine to Acetaldehyde†

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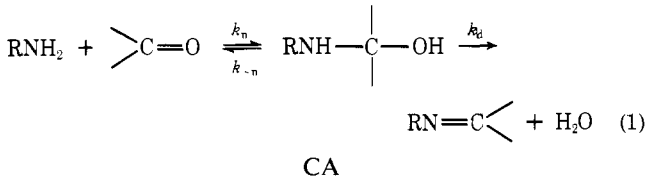
Abstract: The tetrahedral intermediate resulting from the nucleophilic addition of hydroxylamine to acetaldehyde in aqueous solution has been detected by means of NMR using flowing liquids. The rate of dehydration of the intermediate was measured as a function of pH and buffer concentration at 30°C. In addition, the rates of formation of syn and anti oximes were measured under the same conditions. It was found that the rate of dehydration of the intermediate is general acid catalyzed. The rate of appearance of the syn and anti oximes equals the rate of disappearance of the intermediate. However, the rate of formation of syn oxime is slower than the rate for the anti oxime. In addition, the rate of equilibration of syn and anti isomers is catalyzed by the buffer. The values for the rate constants for the various processes will be presented, and details of dehydration of the intermediate and equilibration of syn and anti oximes are discussed.

Introduction

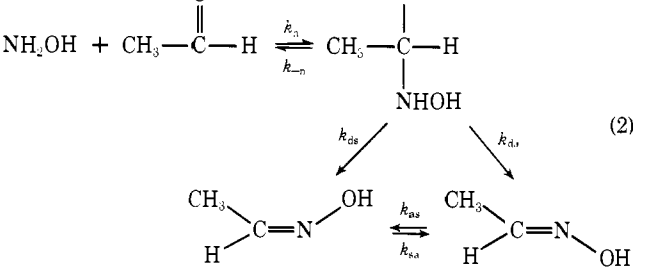
Kinetic studies of the addition of nitrogen nucleophiles to carbonyl compounds have been made by a number of workers.[1-4] The kinetic evidence supports strongly the conclusion that the reaction proceeds according to the mechanism



(1)

CA

in which k_n is the rate constant for nucleophilic addition and k_d is the rate constant for dehydration of the carbinolamine CA. According to this mechanism, the carbinolamine CA is an intermediate. In many of these studies, the kinetic measurements were made using uv-visible spectroscopy, and the spectrum of the carbinolamine was not observed.[5] Consequently, a detailed kinetic study of the dehydration step by direct observation of the decay of the carbinolamine intermediate has not been made. For this reason, we have undertaken a study of the nucleophilic addition of hydroxylamine to acetaldehyde using the nuclear magnetic resonance spectroscopy (NMR) of flowing liquids.[6] In this paper, we report part of the NMR spectrum of the carbinolamine intermediate and the measurement of its decay, as well as the growth of the oxime at a number of pH values and buffer concentrations for various buffers. The results can be discussed in terms of mechanism 2, in which the dehydration step involves the formation of the syn (k_{ds}) and the anti (k_{da}) isomers under kinetic controlled conditions,



(2)

followed by equilibration. Thus, our technique permits the direct observation of the properties of the intermediate and the various forms of the product.

Experimental Section

Flow NMR measurements were made using a suitably modified HA 100 spectrometer of which a detailed description will be given in a forthcoming publication.[7]

In brief, a system is used which includes two reservoirs to permit the protons of one or both of the reacting solutions to come to equilibrium in the applied magnetic field prior to mixing. Equal volumes are mixed in a high-pressure mixing chamber and flowed continuously through the measuring coils of the probe. There is some line broadening as a function of the flow rate, but at suitable flow rates the signal/noise ratio is appreciably better than for a stationary sample, as the nuclei are not saturated as readily by the

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