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The Geometric Structure of Spilanthol

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The structure of the pungent principle spilanthol isolated from the aerial part of *Spilanthes oleracea* Jacquin (Compositae) was elucidated as (2*E*,6*Z*,8*E*)-N-isobutyl-2,6,8-decatrienamide by comparing its proton and carbon-13 nuclear magnetic resonance spectra with those of all-*trans* spilanthol.

Keywords——*Spilanthes oleracea*; Compositae; pungent principle; spilanthol; (2*E*,6*Z*,8*E*)-N-isobutyl-2,6,8-decatrienamide; all-*trans* spilanthol; ^{13}C-NMR spectra

Spilanthol, a principal pungent constituent of *Spilanthes oleracea* Jacquin (Compositae), was isolated and its structure was determined as N-isobutyl-4,6-decadienamide by Asano.[2] Later, its structure was corrected to N-isobutyl-2,6,8-decatrienamide, in agreement with that of affinin,[3] by Jacobson.[4,5] He speculated that the structure contained a 6,8-*trans*, *cis*- or *cis*, *trans*-conjugated system on the basis of the reactivities in the Diels–Alder reaction and the infrared (IR) spectral data.[5] In this paper, we deal with the geometric structure of spilanthol isolated from *S. oleracea* and its carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectra. ^{13}C-NMR studies are effective for the structural elucidation of unsaturated aliphatic acid amides.

Table I. ^{13}C Chemical Shifts of Spilanthol and All-*trans* Spilanthol

Carbon No.	Spilanthol	All-*trans* spilanthol
C-1	166.3	166.2
C-2	124.5	124.5
C-3	143.4	143.5
C-4	32.2	32.0
C-5	26.5	31.3
C-6	127.8	127.7
C-7	129.6	131.5[a]
C-8	126.9	131.6[a]
C-9	130.0	130.1
C-10	18.3	18.0
C-1′	47.0	47.0
C-2′	28.7	28.7
C-3′	20.2	20.2

The measurements were made on a Varian NV-16 spectrometer (15.1 Hz) in $CDCl_3$ with TMS as an internal reference and are expressed in terms of ppm. The maximum experimental error of the chemical shift was within ± 0.1 ppm. The FT conditions were as follows; spectra with 3Kz, number of data points 8192, pulse repeat time 1.3 sec, number of pulses 5000—10000 and flipping angle 30°.
a) The assignments may be reversed.

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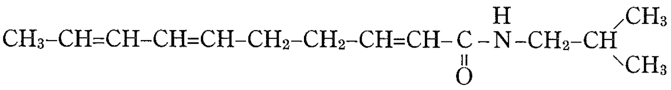
2) M. Asano and T. Kanematsu, *Yakugaku Zasshi*, **47**, 521 (1927); M. Asano and T. Kanematsu, *Ber. Dtsch. Chem. Ges.*, **65B**, 1602 (1932).
3) F. Acree, M. Jacobson, and H.L. Haller, *J. Org. Chem.*, **10**, 236, 449 (1945).
4) M. Jacobson, *J. Am. Chem. Soc.*, **78**, 5084 (1956).
5) M. Jacobson, *Chem. Ind.*, **1957**, 50.

The methanolic extract of the aerial part of *S. oleracea* was extracted with *n*-hexane. The *n*-hexane extract was subjected to silica gel column chromatography and the pungent fraction was followed up. Compound I was isolated from the principal pungent fraction as a colorless oil. Compound I corresponded to $C_{14}H_{23}NO$, with a base peak at *m/z* 81 in the mass spectrum (MS), and the other spectral data were consistent with the reported ultraviolet absorption (UV) and IR spectral data for spilanthol.[5,6] On the other hand, in the ^{13}C-NMR spectra of spilanthol and all-*trans* spilanthol, which was prepared from spilanthol according to the method of Jacobson,[5,6] the C–5 cabon signal at δ 31.3 in all-*trans* spilanthol was shifted upfield to δ 26.5 in spilanthol, as shown in Table I. Similarly, the C–8 carbon signal at δ 131.6 (or δ 131.5) was shifted upfield to δ 126.9 and virtually no difference in the chemical shifts of the other carbon-13 signals was observed. On the basis of these findings, it was assumed that the C-6 double bond in spilanthol was *cis*-form.[7,8] Further, we attempted to carry out experiments using $Eu(dpm)_3$ in order to confirm the assignments in Table I; it is generally known that lanthanide-induced shifts are observed in the NMR spectra of acid



$$CH_3\text{-}CH{=}CH\text{-}CH{=}CH\text{-}CH_2\text{-}CH_2\text{-}CH{=}CH\text{-}\underset{\underset{O}{\|}}{C}\text{-}\overset{H}{N}\text{-}CH_2\text{-}CH\begin{smallmatrix}\nearrow CH_3\\ \searrow CH_3\end{smallmatrix}$$

Fig. 1

spilanthol: 2*E*,6*Z*,8*E*
all-*trans* spilanthol: 2*E*,6*E*,8*E*

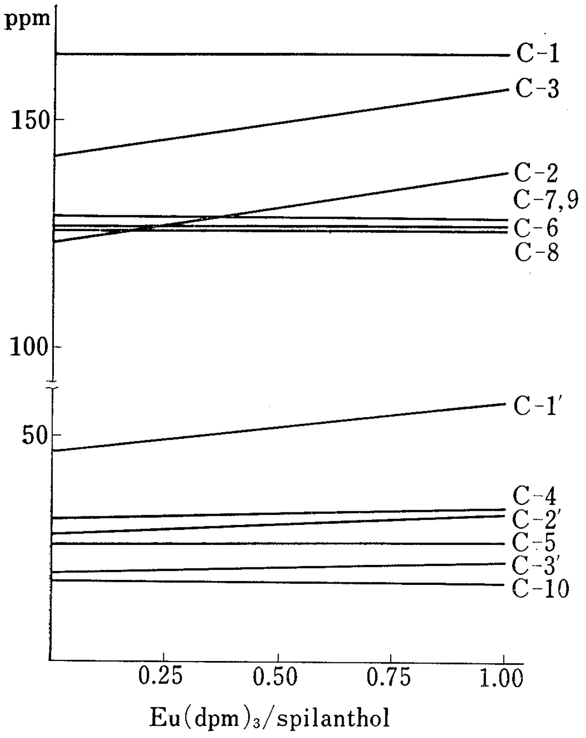


Fig. 2. The Effect of $Eu(dpm)_3$ on the ^{13}C Chemical Shifts of Spilanthol in $CDCl_3$ at 30±1°

The measurement conditions were the same as in Table I, except for the number of pulses (10000—100000).

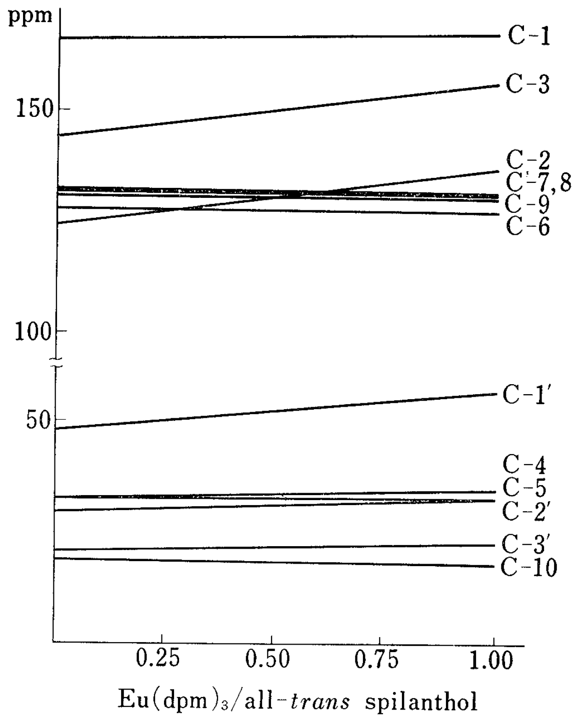


Fig. 3. The Effect of $Eu(dpm)_3$ on the ^{13}C Chemical Shifts of All-*trans* Spilanthol in $CDCl_3$ at 30±1°

The measurement conditions were the same as in Table I, except for the number of pulses (10000—100000).

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amides.[9] The results are shown in Fig. 2 and Fig. 3. These spectral data support the assignments in Table I. Consequently, it is evident that spilanthol (compound I) is (2*E*, 6*Z*,8*E*)-N-isobutyl-2,6,8-decatrienamide. The chemical shifts shown in Table I were established on the basis of comparison with generally known chemical shifts and single frequency off-resonance decoupling experiments with ^{1}H-NMR.

Unsaturated aliphatic acid amides are unstable in air, polymerize rapidly after isolation,[10] and are difficult to handle in degradation or synthesis reactions.[11] The structural elucidation of unsaturated aliphatic acid amides using ^{1}H-NMR spectra is often difficult due to the overlap of signals, but the ^{13}C-NMR signals show distinguishable chemical shifts for the geometrical isomers. As described above, the ^{13}C-NMR method is very effective for the structural elucidation of unsaturated aliphatic acid amides.

Experimental

Melting points were recorded on a Yanagimoto micro melting point apparatus and are uncorrected. UV measurements were made on a Hitachi EPS-3T, MS on a Shimadzu LKB-9000, high resolution MS on a JEOL D-300, and ^{1}H and ^{13}C-NMR on JEOL JNM-PS-100 and Varian NV-16 machines. Silica gel column chromatography was carried out using Kieselgel 60 (230—400 mesh, Merck).

Extraction and Isolation of Spilanthol——The aerial part of *S. oleracea* was collected at Tokyo Metropolitan Medicinal Plant Garden in Kodaira in November 1977. The aerial part (500 g) was cut into pieces, and extracted by homogenizing with MeOH (2 l) and allowing the homogenate to stand for three days. This extraction procedure was repeated three times. The extract was concentrated to 500 ml below 40° and dissolved in 500 ml of H_2O. The solution was transferred into a separatory funnel and extracted three times with 1 l of *n*-hexane. The *n*-hexane extract was applied to a silica gel column. Spilanthol was eluted with *n*-C_6H_{14}–Et_2O (1 : 1) : yield, 200 mg. The physical data for spilanthol are as follows: colorless oil, high resolution MS: Calcd for $C_{14}H_{23}NO$ 221.1779, Found: 221.1814, MS *m/z* (%): 221 (M^+, 6), 141 (61), 126 (17), 98 (18), 81 (100), 79 (19), 41 (31), ^{1}H-NMR ($CDCl_3$, δ, ppm): 0.94 (6H, d, $J=6.5$ Hz, 3′-$(CH_3)_2$), 1.78 (3H, d, $J=6.5$ Hz, 10-CH_3), 1.66—1.95 (1H, m, 2′-CH), 2.19—2.43 (4H, m, 4-CH_2 and 5-CH_2), 3.13 (2H, dd, $J=6.5$, 6.0 Hz, 1′-CH_2), 5.25 (1H, dt, $J=10$, 7 Hz, 6-CH), 5.65 (1H, dq, $J=15$, 6.5 Hz, 9-CH), 5.83 (1H, d, $J=15$ Hz, 2-CH), 5.94 (1H, dd, $J=10$, 10 Hz, 7-CH and 1H, m, NH), 6.28 (1H, dd, $J=15$, 10 Hz, 8-CH), 6.78 (1H, dt, $J=15$, 6.5 Hz, 3-CH). UV and IR spectral data were in agreement with those of Jacobson.[5,6] The ^{13}C-NMR spectral data are shown in Table I.

Preparation of All-*trans* Spilanthol——All-*trans* spilanthol was prepared according to the method of Jacobson[5,6] as follows, 100 mg of spilanthol was dissolved in 0.7 ml of *n*-hexane and irradiated in the presence of a little iodide with a high pressure mercury lamp (400 W) for two hours. The reaction mixture was applied to a silica gel column and 58 mg of all-*trans* spilanthol was isolated. The physical data for all-*trans* spilanthol purified by repeated recrystallization from *n*-hexane were as follows: colorless needles, mp 91.5°, high resolution MS: Calcd for $C_{14}H_{23}NO$ 221.1779, Found: 221.1811, MS *m/z* (%): 221 (M^+, 6), 141 (45), 126 (12), 98 (12), 81 (100), 79 (16), 41 (26), ^{1}H-NMR ($CDCl_3$, δ, ppm): 0.93 (6H, d, $J=6.5$ Hz, 3′-$(CH_3)_2$), 1.72 (3H, d, $J=6.5$ Hz, 10-CH_3), 1.65—1.90 (1H, m, 2′-CH), 2.12—2.34 (4H, m, 4-CH_2 and 5-CH_2), 3.12 (2H, dd, $J=6.5$, 6.0 Hz, 1′-CH_2), 5.26—6.22 (5H, m, 6-, 7-, 8-, 9-CH and NH), 5.79 (1H, d, $J=15$ Hz, 2-CH), 6.78 (1H, dt, $J=15$, 6.5 Hz, 3-CH). UV and IR spectral data were in agreement with those of Jacobson.[5,6] The ^{13}C-NMR spectral data are shown in Table I.

Lanthanide-induced ^{13}C-NMR Shifts of Spilanthol and All-*trans* Spilanthol——$Eu(dpm)_3$ was purchased from E. Merck Co., Ltd. The measurements were performed by complete proton decoupling. The spilanthol concentration was 0.40 mol/l in $CDCl_3$, while that of all-*trans* spilanthol was 0.18 mol/l in $CDCl_3$, and $Eu(dpm)_3$ was added in portions of 0.25 mol $Eu(dpm)_3$/mol sample in $CDCl_3$. The measurements were repeated until the $Eu(dpm)_3$/sample mol ratio reached unity. The results are shown in Fig. 2 and Fig. 3.

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