# SESQUITERPENE LACTONES FROM Inula japonica

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The sesquiterpene lactone inulicin has previously been isolated from Inula japonica (Japanese inula) [1]. In addition to inulicin, from this plant we have obtained a sesquiterpene lactone with the composition $C_{15}H_{22}O_4$, mp 174-176°C (from ethyl acetate), $[\alpha]_D^{20}$ +90.22° (c 2.66; ethanol). The NMR spectrum of the new lactone is extremely close to that of inulicin (Fig. 1).

With acetic anhydride in pyridine, the lactone forms an acetate identical with acetylinulicin. Consequently, the second lactone isolated from Japanese inula is deacetylinulicin.

In the preceding communication we gave the structure of inulicin. The results of a subsequent study of the NMR spectrum of inulicin and its NMR spectrum with the addition of the paramagnetic shift reagent $Eu(DPM)_3$ has enabled the conformation of the molecule of this lactone to be established.

By comparing the coupling constants $J_{4,5}$ in inulicin (8.5 Hz) and oxidized tetrahydroinulicin (6 Hz), we have deduced the cis addition of the lactone ring to the seven-membered ring. The small values of the coupling constants $J_{5,6'}$ and $J_{5,6}$ (2.1 and 4.0 Hz) show that the dihedral angles between the $H_5$, $H_6$, and the $H_5$, $H_{6'}$ protons are acute. In the spectrum of inulicin with the addition of the paramagnetic salt $Eu(DPM)_3$ (Fig. 2b), the signal of the $H_6$ protons ($J_{5,6}=4.0$ Hz) is greatly shifted, which shows the spatial propinquity of the hydroxy group and an $H_6$ proton (an $H_6$ proton and the hydroxy group occupy quasi-axial positions in the molecule). A large displacement is also observed for the signal of the methyl group at $C_2$ which shows the mutual cis arrangement of this methyl group and the hydroxyl. Also in favor of a quasi-axial arrangement of the $H_2$ proton is the value of the sum of $J_{8,2}+J_{8',2}$ (5 Hz), which is comparatively large for long-range constants.

The averaged values of the coupling constants of the protons of the methyl group at $C_7$ with the protons at $C_6$ are different. With the quasi-axial proton (at $C_6$) the value of the constant $J_{6,CH_3}$ is 1.5 Hz, while

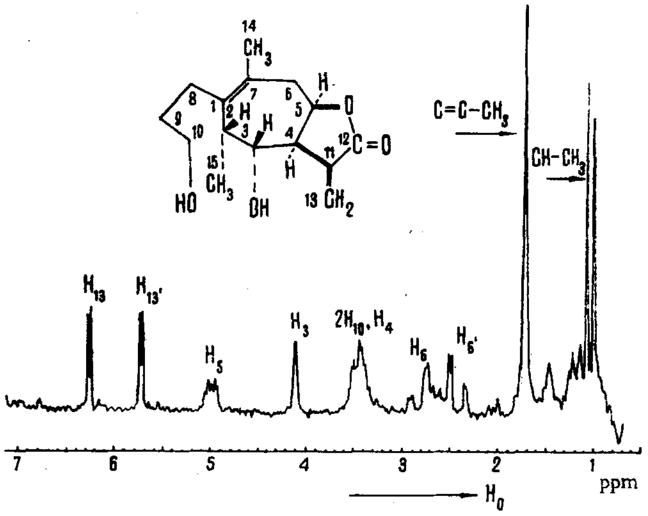

Fig. 1. NMR spectrum of deacetylinulicin in $CDCl_3$.

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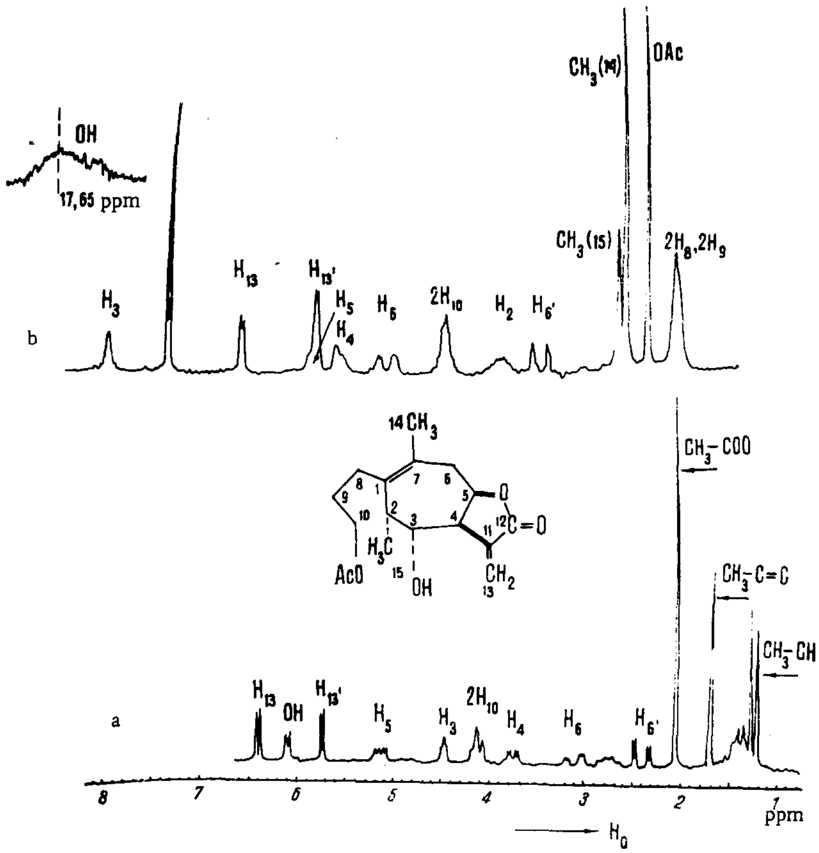
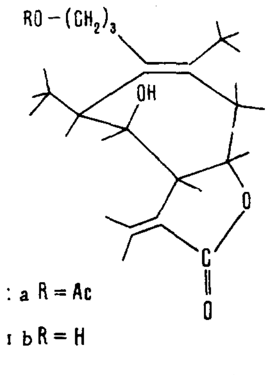


Fig. 2. Change of the chemical shifts in the NMR spectrum of inulicin on the addition of the reagent $Eu(DPM)_3$: a) NMR spectrum of inulicin; b) NMR spectrum of inulicin with the addition of $Eu(DPM)_3$.

with the quasi-equatorial proton it is less than 0.5 Hz. Since the hydrogen atoms at $C_8$ and $C_2$, and also at $C_{14}$ and $C_6$, occupy analogous positions in the molecule, large values of the coupling constants of the protons at $C_8$ with the proton at $C_2$, occupying the quasi-axial position, must be expected. This permits the following structural formulas (Ia and Ib, respectively) to be put forward for inulicin and deacetylinulicin:



EXPERIMENTAL

Isolation of Deacetylinulicin (Ib). The resin from the Japanese inula, after the precipitation of the inulicin [1] [according to TLC in silica gel in the benzene–methanol (9 : 1) system, two spots with $R_f$ 0.15 and 0.07] was chromatographed on silica gel and eluted with ether. The crystalline total lactones isolated were rechromatographed on silica gel and eluted with benzene. The first fraction gave a white crystalline substance with $R_f$ 0.16, identified as inulicin, and the subsequent fractions gave a white crystalline substance with $R_f$ 0.09, composition $C_{15}H_{22}O_4$ (from ethyl acetate), with mp 174-176°C, $[\alpha]_D^{20}$ +90.22 (c 2.66; ethanol), mol. wt. 266. IR spectrum (paraffin oil), $\nu_{max}$, $cm^{-1}$: 3530 (OH), 1730 and 1658 ($\alpha$-methylene in a $\gamma$-lactone). UV spectrum: $\lambda_{max}$ 203 nm ($\varepsilon$ 12,579).

Acetylation of Deacetylinulicin. Preparation of Acetylinulicin. A mixture of 0.1 g of deacetylinulicin, 1 ml of acetic anhydride, and 2 ml of pyridine was kept at room temperature for 12 h, diluted with water, and extracted with ether, and the extract was washed with 5% HCl solution and with water. After the solvent had been distilled off, crystals were obtained with mp 83-85°C (from ethanol), composition $C_{19}H_{26}O_6$. The IR and NMR spectra were identical with those for acetylinulicin. A mixture with acetylinulicin gave no depression of the melting point.

## SUMMARY

1. From Inula japonica a new sesquiterpene lactone – deacetylinulicin – has been isolated.

2. Spatial formulas have been put forward for inulicin and deacetylinulicin (Ia and Ib, respectively).

## LITERATURE CITED

1. E. Ya. Kiseleva, V. I. Sheichenko, K. S. Rybalko, G. A. Kalabin, and A. I. Ban'kovskii, Khim. Prirodn. Soedin., 263 (1971).