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N.M.R. and I.R. Spectra of Triterpenoids Isolated from Ginseng

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Recently we reported [1] that acid hydrolysis of individual ginseng glycosides—panaxosides A, B, and C—gives a mixture of at least 6 triterpenoids ("genins" A_1—A_6) that does not contain panaxadiol [2]. Chemical investigation of the principal substance of the mixture—the "genin" A_6, $C_{30}H_{49}O(OH)_3$, which we named panaxatriol—made it possible to establish that this triterpenoid has the carbon skeleton of panaxadiol, differing from the latter by the presence of an additional hydroxyl group [3]. According to preliminary N.M.R. data, the spectra of panaxatriol and panaxadiol are very similar [4]. In the present work the results of a more detailed study of "genin" A_5 and panaxatriol by N.M.R. and I.R. spectroscopy are discussed.

In the N.M.R. spectrum of panaxatriol (Fig. 1, *a*), lines 1, 2, 3, 4, 5, and 6 correspond to methyl groups, 7 and 8 to skeletal protons (CH_2 and CH groups), and 9 to hydroxyls not involved in intramolecular hydrogen bonds. The multiplet at 3-3.5 m.u. is given by the protons of carbon atoms C_3 and C_{12}; the shift to weaker field is due to the influence of the oxygen of the hydroxyl groups located at these same carbon atoms.

The lines at 4 and 6.2 m.u. are of greatest interest. The line at 6.2 corresponds to a hydroxyl involved in an intramolecular hydrogen bond (to prove that this is not a vinyl proton, a spectrum was taken in CD_3OD with ether oxygen). This follows from comparison with the N.M.R. spectrum of panaxadiol [4].

In the I.R. spectrum of panaxatriol (Fig. 3, *b*), the broad band with an absorption maximum at 3280 cm^{-1} ($CHBr_3$) is due to stretching vibrations of the hydroxyl at C_{12}, which has a hydrogen bond with the ether oxygen of the tetrahydropyran ring. The hydrogen bond hinders acetylation, and in the I.R. spectrum of the acetate this band is retained. The band at 1032 cm^{-1} (KBr) in the spectra of panaxatriol (Fig. 2, *b*) and its acetate behaves similarly. We assign it to vibrations of the C_{12}—OH bond. Both lines are absent in the spectra of panaxatriol oxidized and reduced by the Huang-Minlon method.

In the I.R. spectra of panaxatriol, panaxadiol, and their carbonyl analogs (panaxatrione and panaxadione), integral intensities of the hydroxyl (3600 cm^{-1}, $CHBr_3$) and carbonyl (1705-1715 cm^{-1}) groups were calculated [5]. Their ratio

Figure 1

Figure 1: Figure 1

Figure 2 and Figure 3: IR absorption spectra graphs

Figure 2: Figure 2 and Figure 3: IR absorption spectra graphs

makes it possible to assert the presence of two free hydroxyls in panaxatriol instead of one in panaxadiol. The absorption of the secondary equatorial hydroxyl at C_3 coincides with the corresponding absorption of panaxadiol in two regions of the spectrum: 1) OH stretching vibrations at 3600 cm^{-1} (Fig. 3, *a* and *b*); 2) vibrations of the C_3—OH bond, $\sim$ 1050 cm^{-1} (Fig. 2, *a* and *b*).

In the I.R. spectrum of panaxatriol, the band at 1050 cm^{-1} broadens with the appearance of a second peak around 1060 cm^{-1}. It probably corresponds to vibrations

C-OH bond of the third hydroxyl. Its valence vibrations have the same frequency as the OH vibrations at C_3. The position of the absorption band of the carbonyl group corresponding to this hydroxyl in the IR spectrum of panaxatrione (1712 cm^{-1}, $CHCl_3$) indicates that it belongs to a six-membered ring.

Fig. 1. NMR spectra of panaxatriol (*a*), its acetate (*b*), and "genin" A_5 (*c*)

In the NMR spectrum of panaxatriol, the line at 4 ppm (Fig. 1, *a*) is given by the proton of the carbon atom bonded to the hydroxyl. Its shift from the usual position–3.2 ppm to 4 ppm–can be explained by the fact that the hydroxyl is located in the tetrahydropyran ring in the axial position (^{6}). The splitting is explained by spin-spin interaction with neighboring methylene-

groups of the ring. The exact position of the third hydroxyl of panaxatriol is given by the study of the NMR spectra of panaxatrione (Fig. 4,) and panaxadione (Fig. 4,). The signals of the protons of methyl groups adjacent to the carbonyl appear at 2-2.5 ppm. Owing to spin-spin interaction with the nearest methyl groups of the ring or with angular protons, the protons of the CH_2 groups in positions 2 and 11 give split signals (Fig. 4,). If the third hydroxyl in panaxatriol were located in any of rings A, B, C, or D, an analogous picture would be obtained, with an increase in the intensity of the signals of methyl groups adjacent to the carbonyl by two proton units. However, in the spectrum of panaxatrione the methyl groups give a strong unsplit peak at 2.3 ppm, which indicates the location of the carbonyl at C_{23}, since only

Fig. 2. IR absorption spectra (KBr) of panaxadiol ( ), panaxatriol ( ), and "genin" A_5 ( )

Fig. 3. IR absorption spectra (solution in $CHBr_3$) of panaxadiol ( ), panaxatriol ( ), and "genin" A_5 ( )

in this case, next to the carbonyl, there are 2 equivalent methyl groups of the

Fig. 4. NMR spectra of panaxadiol (a) and panaxatriol (b)

Figure 3: Fig. 4. NMR spectra of panaxadiol (a) and panaxatriol (b)

ring with which there is nothing to interact. This is already indicated by the strong weakening of peak 5 (1.4 ppm) of the skeletal protons of panaxatrione in comparison with peak 4 in panaxadione.

Signal 10 (3.5 ppm) in the spectrum of panaxatrione is given by the proton at C_{13}, which interacts with the proton at C_{17}, as a result of which a doublet is obtained. The spin-spin coupling constant J = 9 Hz is identical with the spin-spin coupling constant of panaxadione, i.e., the mutual arrangement of the protons at C_{13} and C_{17} is the same in panaxatriol and panaxadiol ([7]). In the NMR spectrum of panaxatriol acetate (Fig. 1,), the intensity of the signal at 2 ppm corresponds to two acetoxy groups. The line at 6.2 ppm remains, i.e., the hydroxyl at C_{12} is not acetylated owing to hydrogen bonding with the ether oxygen. 10 (3.4 ppm) is the signal of the proton at C_{12}, 11 (4.35 ppm) is at C_3, and 12 (5.3 ppm) is at C_{23}. In the NMR spectrum of the more polar genin A_5–$C_{30}H_{49}(OH)_3(OCH_3)_2$ (Fig. 1,)–the signal at 5.8 ppm is given by a hydroxyl having a hydrogen bond different from the hydrogen bond of OH at C_{12} with the oxygen of the tetrahydropyran ring (panaxatriol), and there is a signal corresponding to two OCH_3 groups (3.2 ppm). Thus, in "genin" A_5 the tetrahydropyran ring is absent, and the hydroxyl at C_{12} apparently forms a hydrogen bond with the oxygen of OCH_3 at C_{20}. The hydroxyl line 8 (2 ppm) corresponds to the analogous line in the NMR spectrum of panaxatriol.

The IR spectrum of A_5 (Fig. 2, c) confirms the assumption that the tetrahydropyran ring is absent. The absorption bands at 1070 and 1120 cm^{-1} (KBr), due to vibrations of the cyclic oxygen in panaxatriol and panaxadiol ([2]), disappear in A_5. The absorption band at 3280 cm^{-1}, present in the spectra of panaxatriol and panaxadiol and corresponding to the hydrogen bond of OH at C_{12} with the oxygen of the pyran ring, is also absent. New lines appear in the spectrum–2827 cm^{-1} ($CHBr_3$) and 1085 cm^{-1} (KBr), indicating the presence of methoxy groups in the A_5 molecule ([8]). The absorption pattern in the region 1030-1060 cm^{-1} does not change. It may be assumed that all three hydroxyls remain at the same carbon atoms as in panaxatriol. The valence vibrations of two of them appear as a broadened band near 3600 cm^{-1}. The maximum of the absorption band of the third hydroxyl at 3310 cm^{-1} ($CHBr_3$) is shifted by 30 cm^{-1} toward higher frequencies than in panaxatriol. This makes it possible to suppose that the hydrogen bond in A_5 is weaker than in panaxatriol; consequently, the distance between the oxygen atoms is somewhat increased in comparison with panaxatriol, but remains less than 3.3 Å. This is natural if the hydroxyl at C_{12} is hydrogen-bonded to the oxygen of the methoxy group at C_{20}.

Fig. 4. NMR spectra of panaxadiol (*a*) and panaxatriol (*b*)

Further information can be obtained by studying the oxidation products of genin

A_5 and its acetate.

All NMR spectra were recorded on a JNM-C-60 spectrometer, and the IR spectra on a UR-10 spectrophotometer.

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Note: Figure translations are in progress. See original paper for figures.