# THE ISOLATION AND STRUCTURE OF NAHAGENIN

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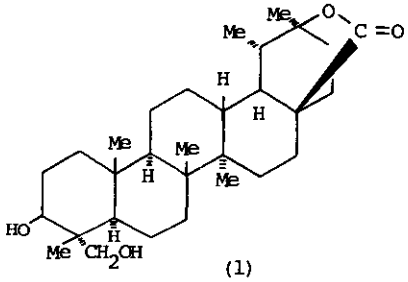
ABSTRACT: — The isolation and structure of a new sapogenin, nahagenin (1), from the medicinal plant *Fagonia indica* Linn is presented.

*Fagonia indica* Linn[1] (zygophyllaceae) is a small spiny undershrub which is widely distributed in Pakistan. An aqueous decoction of the leaves and young twigs is a popular remedy for the treatment of various skin lesions. The plant is claimed to be a remedy for cancer in its early stages and preliminary pharmacological tests of aqueous extracts on mice have shown some anti-cancer activity.[2] An Ames mutagenicity test has also indicated marginal activity.[3] Prior investigations have revealed triterpenoids,[4-6] carbohydrates, saponins,[7] alkaloids,[8] sapogenins,[9-13] fatty acids[14] and amino acids.[15] We now wish to report the isolation of a new sapogenin, nahagenin (1).




(1)

The crude saponins, obtained from the ethanolic extract of the aerial parts of the fresh plants, were hydrolysed with 20% ethanolic HCl to afford the corresponding sapogenins. Silica gel chromatography with elution by pet. ether, pet. ether-$CHCl_3$, $CHCl_3$, and finally $CHCl_3$-MeOH afforded two crystalline compounds which were further purifed by crystallization. The first of these nahagenin (1), m.p. 290°C, analyzed for $C_{30}H_{48}O_4$ and this was confirmed by high resolution mass spectrometry (m/z = 472.3540 meas, 472.3552 for $C_{30}H_{48}O_4$). Major peaks in the MS occurred at m/z of 454, 436, 424, 409, 395 and 261. The IR spectrum ($CHCl_3$) showed peaks at 1740 $cm^{-1}$ and 3460 $cm^{-1}$ suggesting a δ-lactone and hydroxy groups. The substance readily afforded a diacetate (m/z = 556) but was found to be remarkably inert to attempted hydrolysis of the lactone.

The $^1H$ NMR showed no olefinic protons. The $^{13}C$ NMR (100 MHz) confirmed the presence of thirty carbons and chemical shifts and multiplicities are given

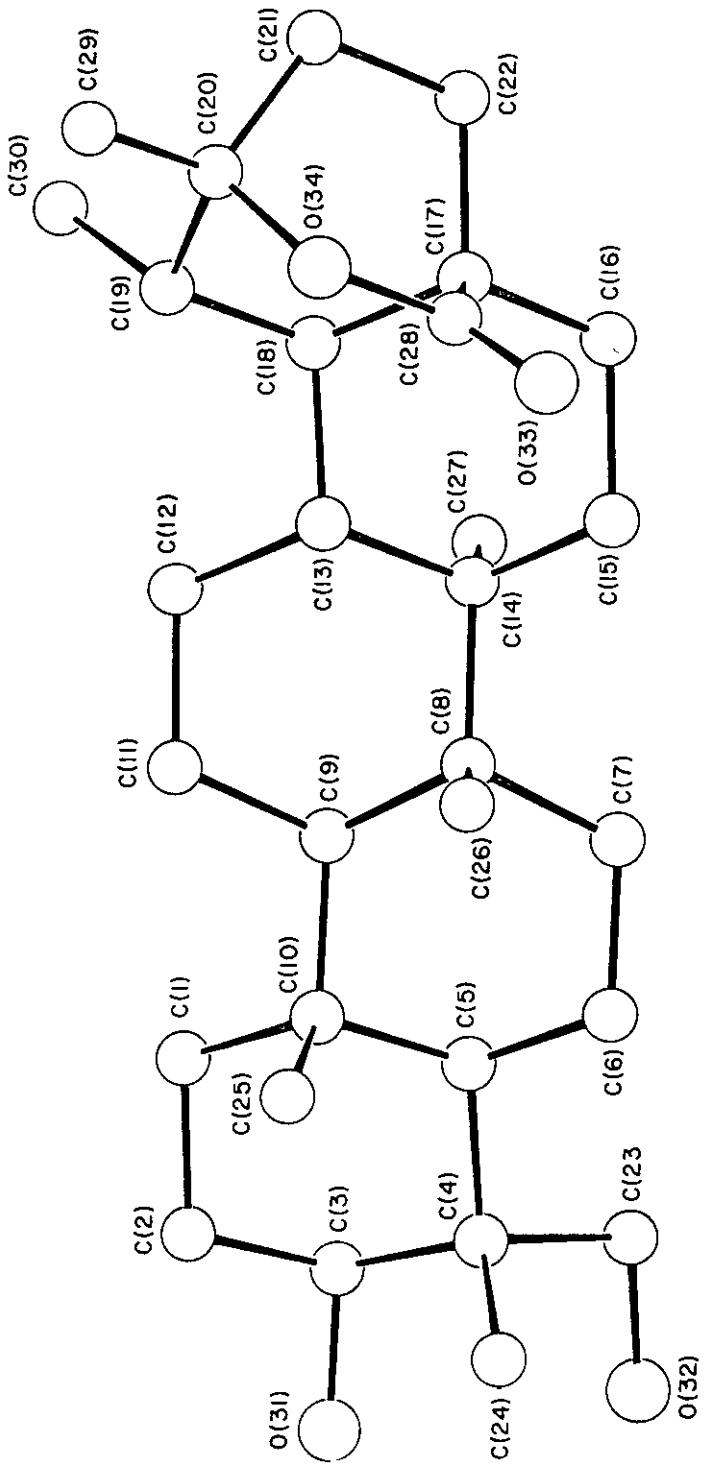



Figure 1. A computer generated perspective drawing of nahagenin. Hydrogens are omitted for clarity.

in Table 1. The carbon atoms in the A and B rings were readily recognized by comparison with corresponding signals of known pentacyclic triterpenoids.[16] Six quaternary centers and six methyl groups were also identified. The $^{13}C$ NMR displayed a resonance at $\delta$ 177.29 for the carbonyl carbon and three resonances at $\delta$ 84.27(s), 76.54(d ) and 71.92(dd) for the oxygen bearing carbons C(20), C(3) and C(23) respectively.

An unambiguous structure determination was carried out by a single crystal x-ray diffraction analysis. Crystals of nahagenin formed in the monoclinic system with a = 12.370(2), b = 6.7688(8), c = 15.832(2)Å and $\beta$ = 100.28(1)°. All unique diffraction maxima with $2\theta \leq 114°$ were collected on an automated four-circle diffractometer with variable speed, 1° $\omega$-scans. Of the 1972 reflections surveyed, 1509 (77%) were judged observed ($|F_o| \leq 3\sigma(F_o^2)$) after correction for Lorentz, polarization and background effects. The structure was solved by a multisolution weighted tangent formula approach with five special and one general reflection forming the variable starting set.[17] Fullmatrix least-squares refinements with anisotropic nonhydrogens and fixed isotropic hydrogens have converged to a standard crystallographic residual of 0.0585.[18] Figure 1 is a computer generated perspective drawing of the final x-ray model.

As expected nahagenin is a pentacyclic triterpene with a $\delta$-lactone added to the E ring. All of the carbocyclic rings are joined in a trans-anti fashion. In general bond distances and angles agree well with general accepted values.[18] Preliminary studies on the saponins present indicate that nahagenin is a genuine aglycone of the parent saponin, the structure of which is currently under investigation.

TABLE-I

| Carbon | Chemical Shift(s) | Multiplicity | Carbon | Chemical Shift(s) | Multiplicity |
|---|---|---|---|---|---|
| C(1) | 38.51 | d.d | C(16) | 25.15 | t |
| C(2) | 27.28 | t | C(17) | 42.06 | s |
| C(3) | 76.54 | d | C(18) | 50.51 | d |
| C(4) | 41.86 | s | C(19) | 48.37 | d |
| C(5) | 49.99 | d | C(20) | 84.27 | s |
| C(6) | 18.35 | t | C(21) | 41.98 | t(?) |
| C(7) | 32.22 | t | C(22) | 33.68 | t |
| C(8) | 40.51 | s | C(23) | 71.92 | d.d |
| C(9) | 42.83 | d | C(24) | 11.30 | q |
| C(10) | 37.05 | s | C(25) | 15.69 | q |
| C(11) | 20.96 | t | C(26) | 16.63 | q |
| C(12) | 27.05 | t | C(27) | 23.98 | q |
| C(13) | 27.59 | d | C(28) | 177.29 | s |
| C(14) | 41.08 | s | C(29) | 14.26 | q |
| C(15) | 26.87 | t | C(30) | 23.98 | q |

Acknowledgement: The authors (AR and AAA) wish to express their gratitude to Dr. David C.Lynn, Department of Chemistry, University of Virginia, U.S.A. for kindly providing $^{13}C$ NMR of nahagenin on a 100 MHz instrument and to Mr. T.Keller, Bruker Analytische Messtechnik GmbH, Silberstriefen, West Germany for providing $^{13}C$ NMR on a Bruker 400 MHz instrument. The authors (AR and AAA) are grateful to Professor Viqar Uddin Ahmad for stimulating discussions. Part of this work was supported by NIH grant CA-24487 to JC.

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Received, 30th September, 1981