

NIGELLIMINE N-OXIDE — A NEW ISOQUINOLINE ALKALOID FROM THE SEEDS OF
NIGELLA SATIVA

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Abstract — A new minor isoquinoline alkaloid, nigellimine N-oxide, has been isolated from the seeds of *Nigella sativa* and its structure has been determined on the basis of spectral studies.

Nigella sativa Linn. (Ranunculaceae), locally known as Kalonji is an indigenous herbaceous plant. It grows in mediterranean countries and is also cultivated in Pakistan. It is used as a spice as well as for the treatment of various diseases.¹⁻⁴ Little work has previously been carried out on its alkaloidal constituents.⁵⁻⁷ Recently we have reported a new unusual alkaloid, nigellicine from the seeds of this plant, the structure of which was confirmed by x-ray diffraction.⁸ In this communication we report the isolation and structure determination of a new minor alkaloid, nigellimine N-oxide, from the seeds of *Nigella sativa*.

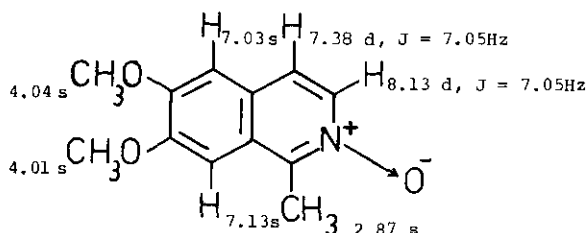
Nigella sativa seeds (20 kg) were soaked in ethanol (35 l), crushed, filtered and the solvent was evaporated. The concentrate thus obtained was treated with diethyl ether to remove fatty material. The defatted material thus obtained was basified with ammonia (conc.) to pH 8-9. This crude mixture was extracted with CHCl_3 , dried with anhydrous Na_2SO_4 and evaporated to dryness (2.45 g). This was subjected to column chromatography using an open column, packed with silica gel-60. Elution with increasing polarities of ethyl acetate-acetone and chloroform-methanol resulted in a number of fractions. The fractions obtained from 98% CHCl_3 : 2% MeOH and 96% CHCl_3 : 4% MeOH were combined and subjected to preparative tlc on 0.2 mm silica gel (GF-254) plates, using CHCl_3 : MeOH (8.8 : 1.2) as the solvent system. A faster running alkaloid ($R_f \approx 0.60$, ~3 mg) was thus obtained as an amorphous, brown optically inactive material.

The E.I. mass spectrum appeared to contain the molecular ion peak at m/z 203.0956 (calcd. for $C_{12}H_{13}NO_2$, 203.0946). Subsequent spectra recorded using a field desorption technique showed the true molecular ion peak at m/z 219. Other prominent peaks in the mass spectrum appeared at m/z (relative intensity) 203 (M^+-O , 100%), 188 (2.16), 172 (2.08), 160 (27.62), 145 (7.79), 131 (5.56), 117 (10.73), 97 (5.17), 85 (5.63) and 69 (8.26).

The uv spectrum showed absorptions at λ_{max}^{MeOH} 236 nm, 267, 278, 289 nm (shoulders), 310 nm and 324 nm. λ_{min}^{MeOH} 263 nm, 272 nm, 282 nm, 304 nm and 318 nm. The ir spectrum ($CHCl_3$) showed prominent absorptions at 2900, 2845 cm^{-1} (C-H), 1725 cm^{-1} ($-C=N^+$), 1600 cm^{-1} (aromatic C=C), 1318, ($\geq N^+O^-$), 1155 cm^{-1} (C-O) and 902 cm^{-1} (aromatic C-H).

The 1H -NMR ($CDCl_3$, 300 MHz) indicated a 3-protons singlet resonating at δ 2.87 for a methyl group attached to C-1. The downfield position of this signal is observed because of the charged nitrogen atom attached to C-1. Two singlets, each for 3 protons, at δ 4.01 and δ 4.04 indicated the presence of two methoxy groups attached to an aromatic system. The *ortho* disposition of these two methoxy groups was supported by the absence of meta-coupling between the two aromatic protons of the benzene moiety of the isoquinoline system. These two protons (C-5 H and C-8 H) appeared as singlets integrating for one proton each at δ 7.03 and δ 7.13. Two doublets each corresponding to one proton appeared at δ 7.38 and δ 8.13; these were mutually coupled with the same coupling constant, 7.05 Hz (J_{HH}^{ortho}) and were assigned to C-4 H and C-3 H respectively. This was further confirmed by carrying out homo-decoupling experiment for each doublet. The position of the C-3 H doublet at δ 8.13 is consistent with the presence of an adjacent quaternary nitrogen atom.

On the basis of the above spectral studies we have assigned structure (1) to nigellimine N-oxide.



A closely related isoquinoline alkaloid N-methyl-6,7-dimethoxyisoquinolone has earlier been reported from *Thalictrum alpinum*, a plant belonging to the same Ranunculaceae family.⁹

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3. R.N.Chopra, S.L.Nayar and I.C.Chopra, "Glossary of Indian Medicinal Plants", CSIR, New Delhi, 1956, p.176.
4. This plant has an extensive historical background, and according to Birdwood, it is the black cumin mentioned in Bible, the melanthion of Hippocrates and Dioscorides, and the gith of Pliny. The Prophet Mohammad (Peace be Upon Him) also mentioned its importance and called it a potent remedy for diseases.
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