

Brahol : A New Derivative of *allo*-Inositol from *Stocksia brahuica*

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Abstract – A new derivative of *allo*-inositol has been isolated from the aerial parts of *Stocksia brahuica* and named as brahol (**1**). The structure of **1** was elucidated with the help of extensive 2D-NMR spectroscopic techniques and identified as 5-O-methyl-*allo*-inositol. The structure was reconfirmed by acetate derivative (**2**).

Key words – Brahol, 5-O-Methyl-*allo*-inositol, *Stocksia brahuica*, Sapindaceae, acetate derivative.

Introduction

Stocksia brahuica belongs to the family Sapindaceae and grows well in the inner valleys of Pakistan (Abdulla, 1972). In view of the biologically active compounds isolated from various members of the family Sapindaceae, we decided to investigate the chemical constituents of *Stocksia brahuica*. No chemical work has been done so far on the plants belonging to genus *Stocksia*. However, the other genera of the same family show the presence of flavones (Sachdev *et al.*, 1982), diterpenes (Jefferies *et al.*, 1974), indoles (Payne *et al.*, 1973), and triterpenes (Kimata *et al.*, 1983).

Experimental

General – The IR spectrum was obtained on Shimadzu-460 spectrometer. The ¹H- and ¹³C NMR spectra were recorded on Bruker AM-300 spectrometer in D₂O. Mass spectra (positive and negative FAB) were measured on JMS HX-110 (Jeol). Purity of sample was

confirmed by HPTLC Silica gel 60 F₂₅₄ precoated glass plates (E. Merck).

Plant Material – Fresh plant material of *Stocksia brahuica* (13 kg) was collected in October, from Baluchistan and identified by Dr. Rasool Bakhsh Tareen, Department of Botany, Baluchistan University, Quetta, Pakistan. The plant was dried under the shade and finally chopped into small pieces.

Extraction and Isolation – The dried material of *Stocksia brahuica* was soaked in distilled methanol (10 L). The solvent was removed *in vacuo*. The methanolic extract obtained was diluted with water and partitioned between hexane, ethyl acetate and *n*-butanol. The butanol soluble portion was evaporated at reduced pressure and the gummy residue (170 g) was loaded on a silica gel column.

The column was eluted with CHCl₃, CHCl₃/MeOH and finally pure MeOH as mobile phase. The fraction eluted with CHCl₃/MeOH (7:3) was gummy in nature. This gummy material was dissolved in a small amount of methanol and left overnight. The compound **1** was settled down and purified by washing with methanol and **1** (16.0 mg)

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was isolated in colourless crystalline form.

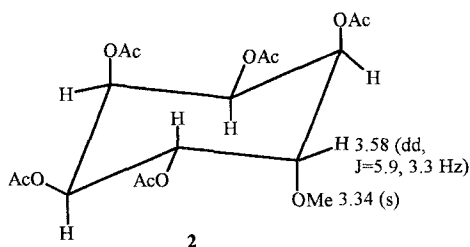
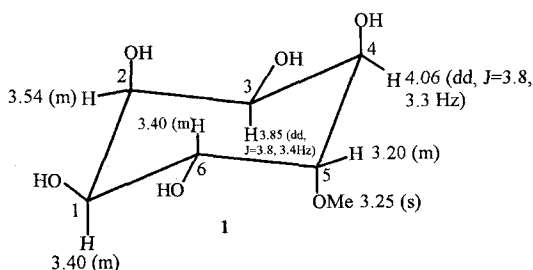
5-O-Methyl-*allo*-inositol (1)—IR (KBr) ν_{\max} 3200-3600 (OH) cm^{-1} ; ^1H NMR (300 MHz, D_2O): δ 4.06 (1H, dd, $J=3.8, 3.3$ Hz, H-4), 3.85 (1H, dd, $J=3.8, 3.4$ Hz, H-3), 3.54 (1H, m, H-2), 3.20 (1H, m, H-5), 3.25 (3H, s, OMe), 3.40 (2H, overlapped dd to give multiplet, H-1 and H-6); ^{13}C NMR (D_2O , 75 MHz): δ 75.3 (C-1), 72.9 (C-2), 73.9 (C-3), 69.7 (C-4), 82.7 (C-5), 74.4 (C-8), 59.4 (OMe); FAB-MS (-ve): m/z 193; FAB-MS (+ve): m/z 195; HRMS: $[\text{M}^+]$ m/z 194.0789 (calcd. For $\text{C}_7\text{H}_{14}\text{O}_6$ requires 194.0790).

Acetylation of Compound (1)—The compound **1** (10.0 mg) was dissolved in dry pyridine (1.5 ml) then acetic anhydride (3.0 ml) was added. After refluxing overnight, water was added and the organic material was recovered in ethyl acetate. The ethyl acetate soluble part yielded 6.10 mg of **2**.

^1H NMR (300 MHz, CDCl_3): δ 1.95, 1.99, 2.04, 2.13 and 2.14 (each 3H, s, OAc), 3.34 (OMe), 3.58 (1H, dd, $J=5.9, 3.3$ Hz, H-5), 5.19-5.42 (5H, m).

Results and Discussion

The compound **1** was obtained from the butanolic soluble portion of the methanolic extract of *S. brahuica*. It was eluted with



methanol-chloroform (3:7) showing the high polarity of **1**. The IR spectrum showed the strong absorption at 3200-3600 cm^{-1} due to the hydroxyl function, whereas no other functionality was concluded from this spectrum. The high resolution mass spectrum showed that the compound **1** has the molecular formula $\text{C}_7\text{H}_{14}\text{O}_6$. The negative and positive FAB mass spectra showed the molecular ion peaks at m/z 193 and 195, respectively, confirming the molecular weight 194 a.m.u.

The ^{13}C NMR spectrum of **1** showed the presence of seven carbon atoms in the molecule, out of them only one was found as a methyl signal. This was confirmed through DEPT experiment, the remaining six signals were present as methines. The chemical shifts of these methine signals show that each methine is directly attached to the oxygen atom. The absence of carbonylic absorption in the IR spectrum showed that these oxygen atoms are present in the molecule either in the form of ether bridge and/or hydroxyl function. The chemical shift values in the NMR spectra (^1H , ^{13}C) indicate that these oxygen atoms are present in the form of hydroxyl functions in the molecule. The only one oxygen atom was found to be attached directly with methyl and that methoxyl group appeared at δ 3.25 and 59.4 ppm in the NMR spectra.

In compound **1** the orientation of methoxyl group was found to be an axial position. This axial orientation of methoxyl group at C-5 was assigned with the help of literature values which shows the chemical shift of C-5 at 82.7 ppm in ^{13}C NMR spectrum when it is attached to methoxyl group provided the neighbouring carbon atoms contain axial proton on one side and equatorial proton on the other side (Angyal *et al.*, 1983). In compound **1** we have assigned axial proton, equatorial hydroxyl group at C-6 and axial hydroxyl group, equatorial proton at C-4. The coupling constant between H-4 and H-5

is 3.3 Hz, showing the di-equatorial arrangement. A double-doublet at δ 4.06 with the coupling constants 3.8 and 3.3 Hz. This double-doublet is coupled with another double-doublet at δ 3.85 and to the multiplet at δ 3.20 which was confirmed by decoupling experiments. With the help of coupling constants of double-doublet at δ 4.06 (H-4) confirms the stereochemistry of the substituents at C-5 and C-3, and are attested axial proton at C-3 and equatorial proton at C-5. The stereochemistry at C-2 was confirmed by the double-doublet at δ 3.85 showing the coupling constants 3.8 and 3.4 Hz. It has been proved above that this double-doublet is coupled with the double-doublet at δ 4.06 with the coupling constant 3.8 Hz, the remaining value (3.4 Hz), must be coupled with the multiplet at δ 3.54 (also confirmed by decoupling experiment). In this way the multiplet at δ 3.54 is assigned for H-2 and with equatorial arrangement. The remaining two protons at C-1 and C-6 appeared in the ^1H NMR spectrum at δ 3.40 as overlapped double-doublets, resulting in a multiplet. Due to this reason the coupling constants cannot be calculated properly. The axially oriented H-6 was confirmed with the help of literature value (Angyal *et al.*, 1983), and penta-acetate derivative **2**.

The stereochemistry at C-1 is assigned on the basis of molecular model and n.O.e experiment. The molecular model shows that the hydroxyl group at C-1 is equatorially oriented to give steric relief as compare to that when it is axially oriented. The stereochemistry of H-1 was further confirmed by n. O.e. experiment, when the methyl (δ 3.25) was irradiated. The maximum effects were observed at δ 3.20 (H-5, 7.5%), 3.40 (H-1, 28.7%), 3.85 (H-3, 28.7%) and at δ 4.06 (H-4, 10.2%). This experiment is enough to confirm that the protons at C-1 and C-3 are on the same side as the methoxyl group. The absence of any effect at H-6 by the irradiation of methoxyl group automatically

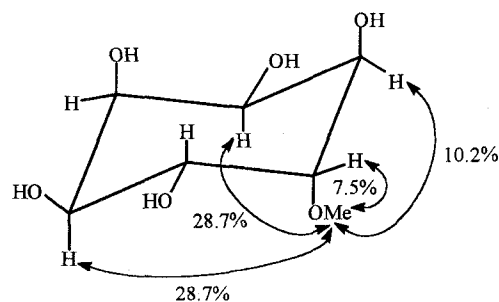


Fig. 1. n.O.e. interactions.

confirmed that H-6 has the reverse orientation with that of methoxyl group and both (OMe, H-6) are di-axially arranged.

The hetero-COSY experiment, carried out to reconfirm the relationship between carbon atoms and their respective protons.

The presence of five hydroxyl groups in **1** was confirmed by the formation of its penta-acetate derivative **2**. The signals of five acetate methyl groups were present in the ^1H NMR spectrum at δ 1.95, 1.99, 2.04, 2.13 and 2.14 as singlets. The methine protons associated with these five acetate groups appeared in the ^1H NMR spectrum as a multiplet for five protons integration at δ 5.19-5.42. The signal of H-5, geminal to the methoxyl group, could be observed at δ 3.58 as a double-doublet ($J=5.9, 3.2$ Hz). The multiplicity and the magnitude of coupling constants confirmed the stereochemistry of the hydroxyl functions attached to the C-4 and C-6. The coupling constant 3.2 Hz is due to the equatorial-equatorial coupling between H-4 and H-5 and the other coupling ($J=5.9$ Hz) is due to the axial-equatorial relationship between H-6 and H-5, respectively.

This is the first report on the isolation of *allo*-inositol or its methyl derivative. The numbering of **1** is given according to the literature (Commission, IUPAC, 1976).

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