

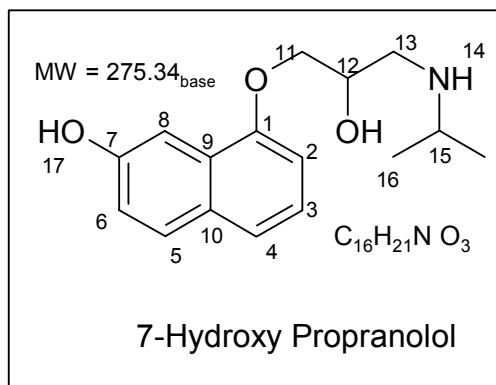


Certificate Of Analysis

Compound: 7-Hydroxy Propranolol

Molecular Formula: $C_{16}H_{21}NO_3$ ·(mw_{base} = 275.34)

Structure:



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Synonyms: (CA index name) 1-[(1-Methylethyl)amino]-3-(1-{7-hydroxy}-naphthalenyloxy)-2-Propanol

Summary of Analytical Results:

- 1H NMR proton data (DMSO- d_6):** The results of 1H NMR spectroscopic analysis are consistent with the structure of 1-[(1-Methylethyl)amino]-3-(1-{7-hydroxy}-naphthalenyloxy)-2-propanol. The aromatic region (8.4-6.6 ppm) of the 1H -NMR exhibits numerous proton resonances. These aromatic protons are consistent with a disubstituted naphthalenyl aromatic ring. Integration and proton-proton coupling reveals two separate spin systems; an ABX and an ABC. Aliphatic proton resonances are exhibited between 4.5 ppm and 1 ppm. These resonances reveal 12 protons separated into two isolated contiguously coupled spin systems. One spin system is an isopropyl and the second is a 1,2,3-tri-substituted propyl spin system. All features are consistent with the structure of 7-Hydroxy Propranolol.
- 1H NMR 2-D gCOSY data (DMSO- d_6):** The data developed from the 2-D COSY experiment reveal spin-spin 3-bond (vicinal) coupling via off axis contour correlations. The illustrated 2-D gCOSY is consistent with an isopropyl spin system, a 1,2,3-tri-substituted propyl spin system, an aromatic ABX and an ABC spin system.

- ¹H NMR 1-D GOCSY data (DMSO-d₆):** The data developed from the 1-D GOCSY experiment (eq. TOCSY exp) reveal isolated contiguously coupled spin systems. The illustrated portions of the 1-D GOCSY's are consistent with an isopropyl spin system, an aromatic ABX and an ABC spin system.

The 2-D gCOSY and 1-D GOCSY data are summarized

- ¹H NMR 1-D nOe difference experimental data (DMSO-d₆):** The results of ¹H NMR 1-D nOe difference spectroscopic analysis are consistent with the structure of 1-[(1-Methylethyl)amino]-3-(1-{7-hydroxy}-naphthalenyloxy)-2-propanol. These data reveal through space or proximal located spins. These data are based upon relaxation phenomenon. Thus, pre-irradiation of an isolated resonance reveals, via a difference spectrum, proximal protons.
- ¹³C NMR data (DMSO- d₆):** The data developed from the 1-D APT Carbon experiment modulate the carbon data based upon the one bond proton-carbon coupling (1J_{HC} –Hz). The data is expressed via up and down peak depending upon the magnitude of their one bond coupling. The data are consistent with the structure of 7-Hydroxy Propranolol
- ¹H - ¹³C NMR 2-D gHSQC data (DMSO-d₆):** The data developed from the 2-D gHSQC experiment reveal one bond cross correlations between protons and carbons in a two dimensional format. Assignments in either domain allow direct assignment of the opposite domain from their cross contours. The assignments are based upon data and conclusions obtained from earlier experiments, i.e. 2-D gCOSY, 1-D nOe difference data, 1-D APT carbon data, chemical shifts and coupling constant considerations. The data are consistent with the structure of 7-Hydroxy Propranolol .
- ¹H - ¹³C NMR 2-D HMBC data (DMSO-d₆):** The data developed from the 2-D HMBC experiment reveal 3-bond cross correlations between protons and carbons in a two dimensional format. The experiment is optimized with a time delay for 8 Hz coupling (³J_{HC} coupling). Occasionally a 2-bond correlation will appear. Furthermore, the suppression on 1-bond couplings also appears in the spectra due to non-optimal bird-pulse suppression.

Important 3-bond correlations are summarized in this structural illustration:

- IR (HCl salt in a KBr pellet):** The Infrared data are consistent with the structure of 7-Hydroxy Propranolol. The strongest absorbance is exhibited in the broad band between 3480 - 3000 cm⁻¹. This is consistent with hydroxyl moiety in the molecule. Asymmetric deformation modes of stretching for the naphthenyl ring occur as bands between 1628 and 1600 cm⁻¹, symmetric modes occur between 1540 and 1500 cm⁻¹. Aromatic character is also expressed in the area between 824 -751 cm⁻¹, the result of out-of-plane proton-carbon bending. Aliphatic character (2773, 2820 and 2861 cm⁻¹) is revealed in numerous areas of the spectrum and the strong bands at 1101 and 1263 cm⁻¹ are consistent with oxygen-carbon stretching.
- LC/UV/ESI/MS:** The sample was evaluated by HPLC/UV/ElectroSpray Ionization/MS. The results are consistent with the structure of 7-Hydroxy Propranolol. The molecular ion (M+H)⁺ is observed at 276 Daltons along with structurally related fragment ions. No unrelated ions were observed by mass spectrometry under the UV peak. The % Total Area of 7-Hydroxy Propranolol calculated at 220 nm is 99%.
- TLC Analysis:** via Thin Layer Chromatography via Analtech Uniplate - Silica Gel GHLF shows one spot (R.F. = 0.37; in methylene chloride : methanol : ammonia [90:10:1] and R.F. = 0.4; in ethyl acetate : methanol : ammonia [80 : 20 : 1]).

Fig 1. ¹H-NMR of Propranolol, structure and spectra

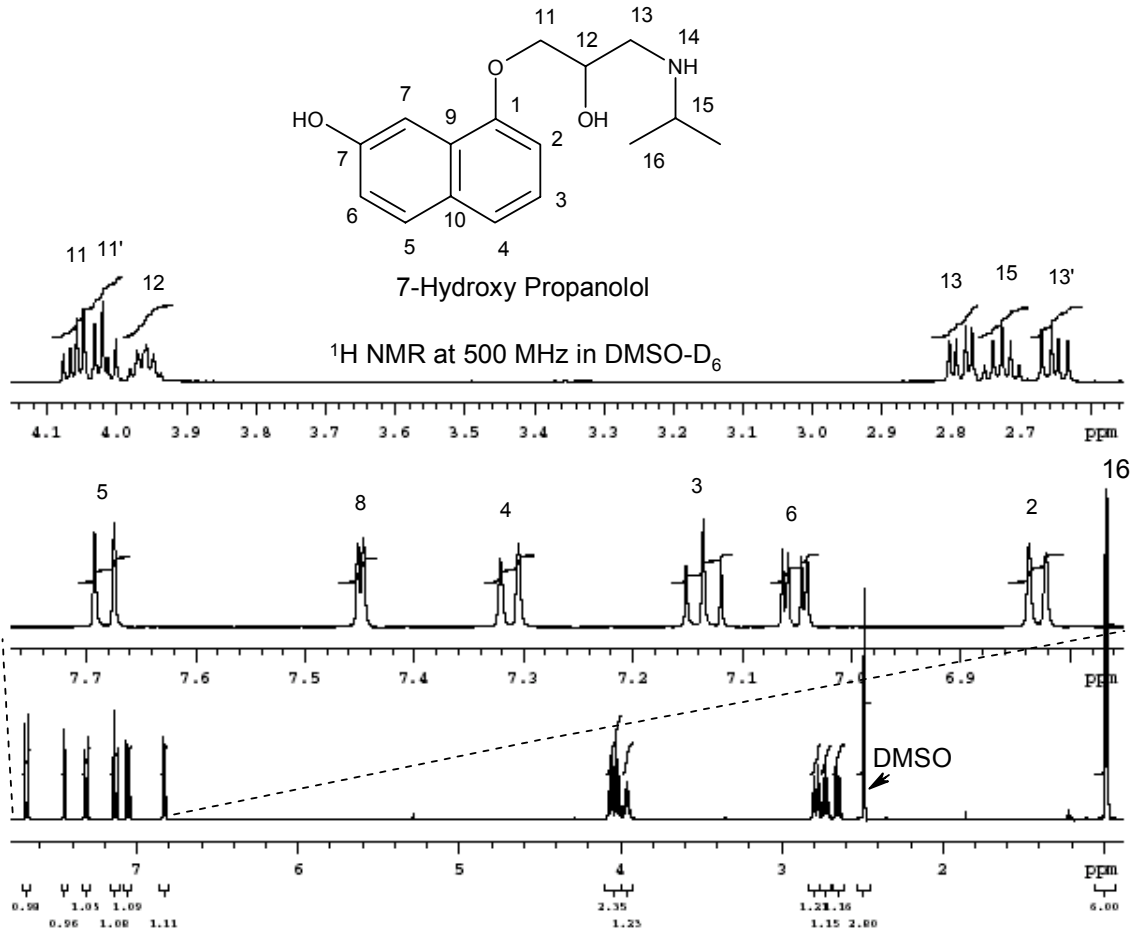


Fig 2. ¹H NMR 2-D gCOSY data (DMSO-d₆), structure and spectra

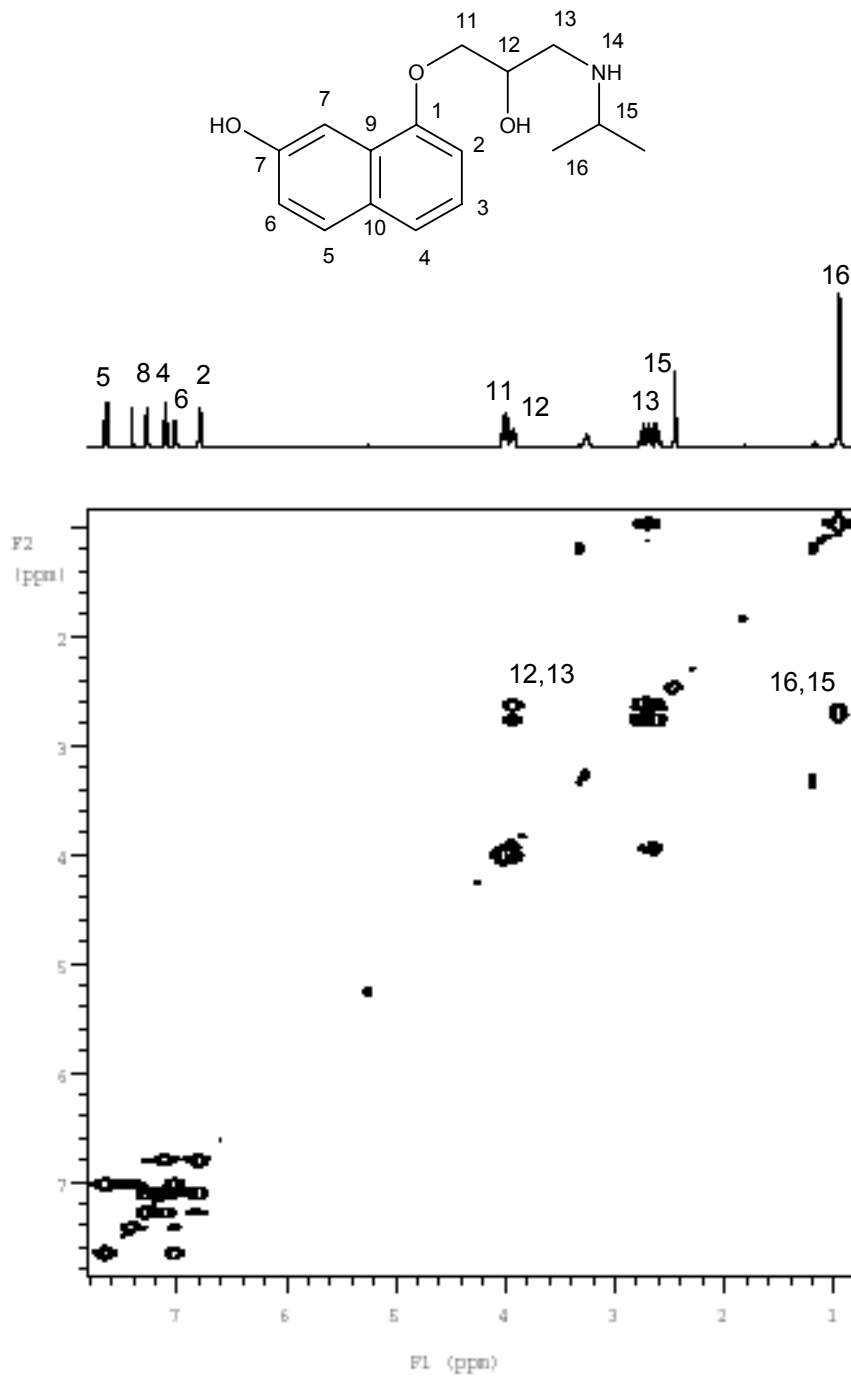


Fig 3. ¹H NMR 1-D GOCSY data (DMSO-d₆), structure and spectra

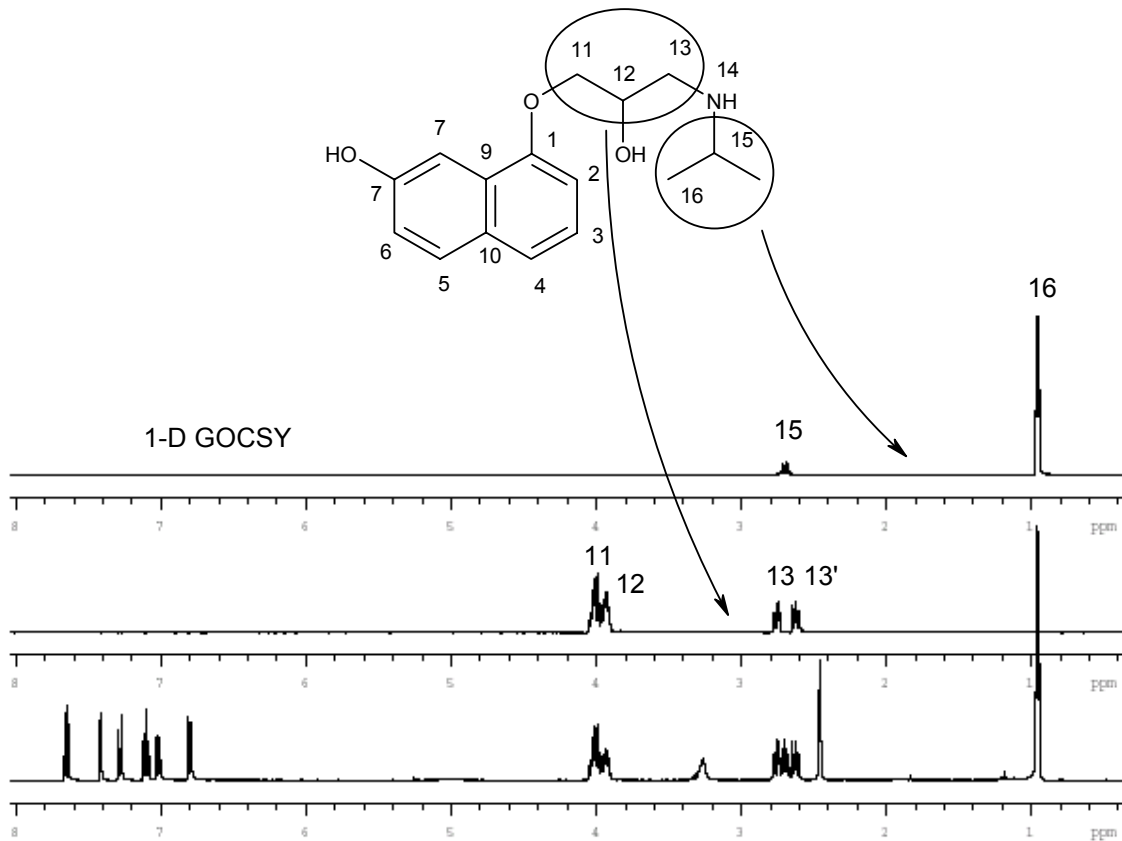


Fig 3B. 2-D gCOSY and 1-D gCOSY data are summarized

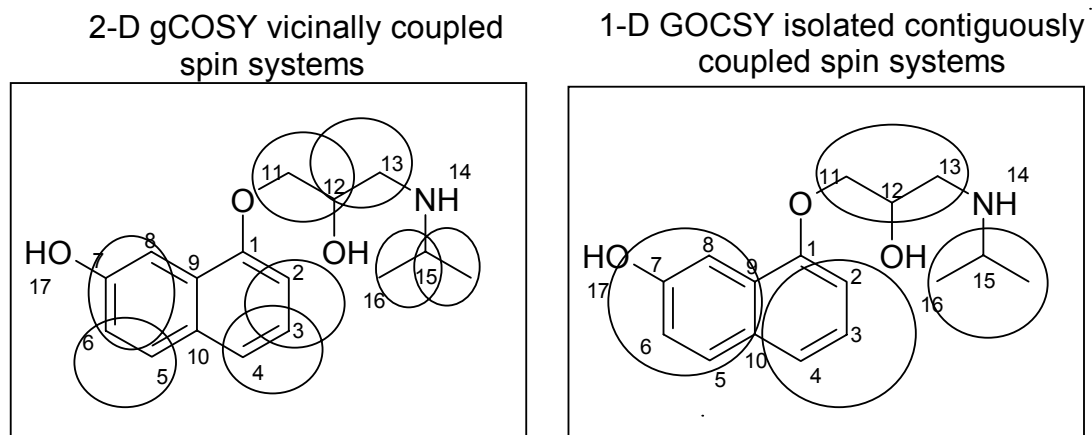


Fig 4. H^1 -NMR 1-D nOe, structure and spectra

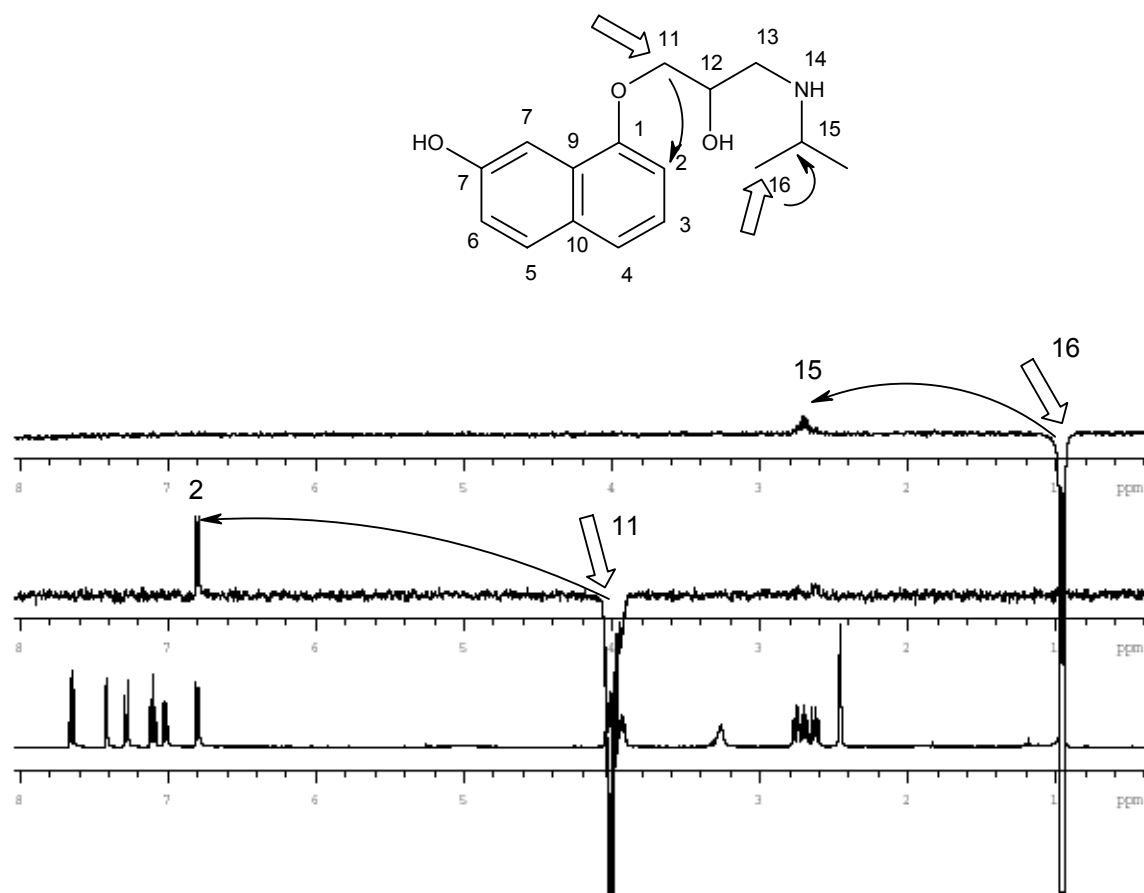
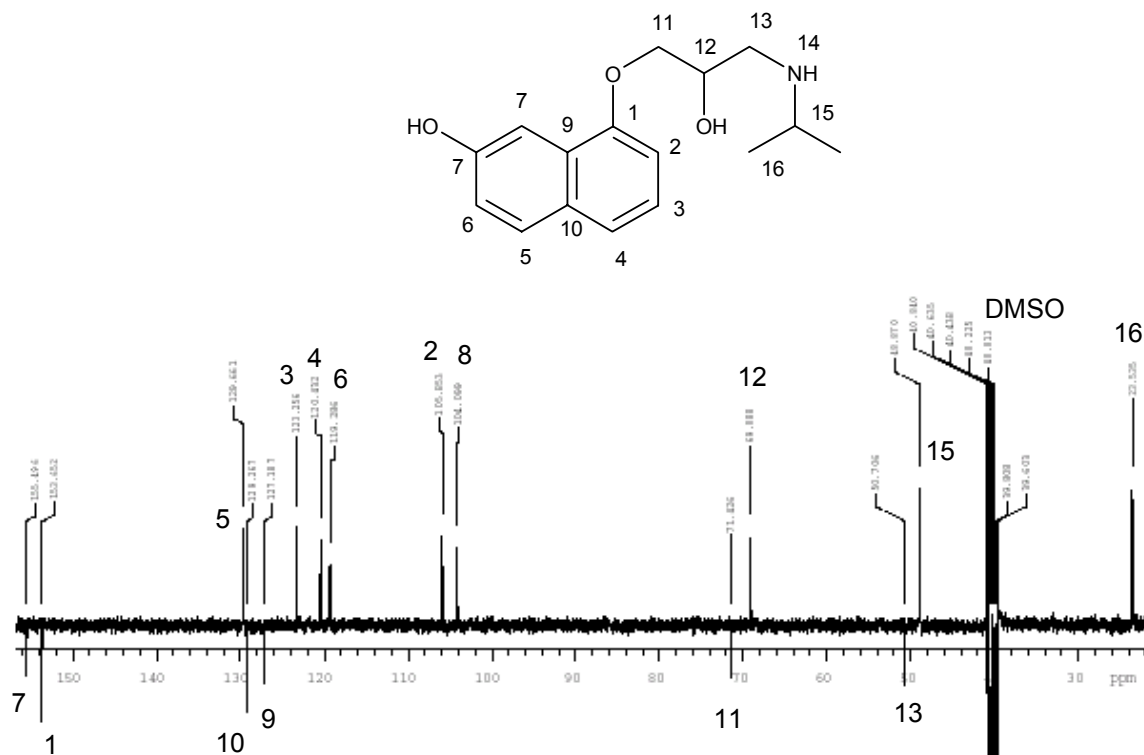


Fig 5. ¹³C NMR of 7-Hydroxy Propranolol, structure and spectra



APT (GASPE) J-modulated
13C data

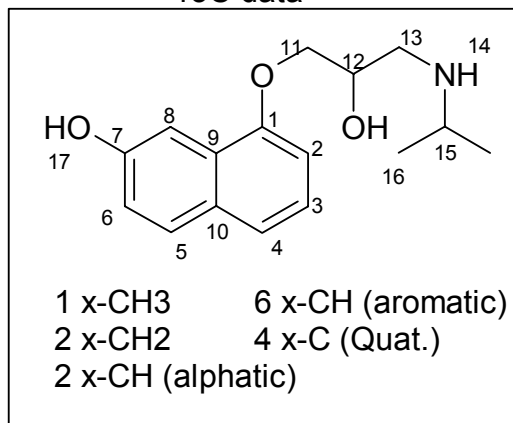


Fig 6. ^1H - ^{13}C NMR 2-D gHSQC data (DMSO- d_6), structure and spectra

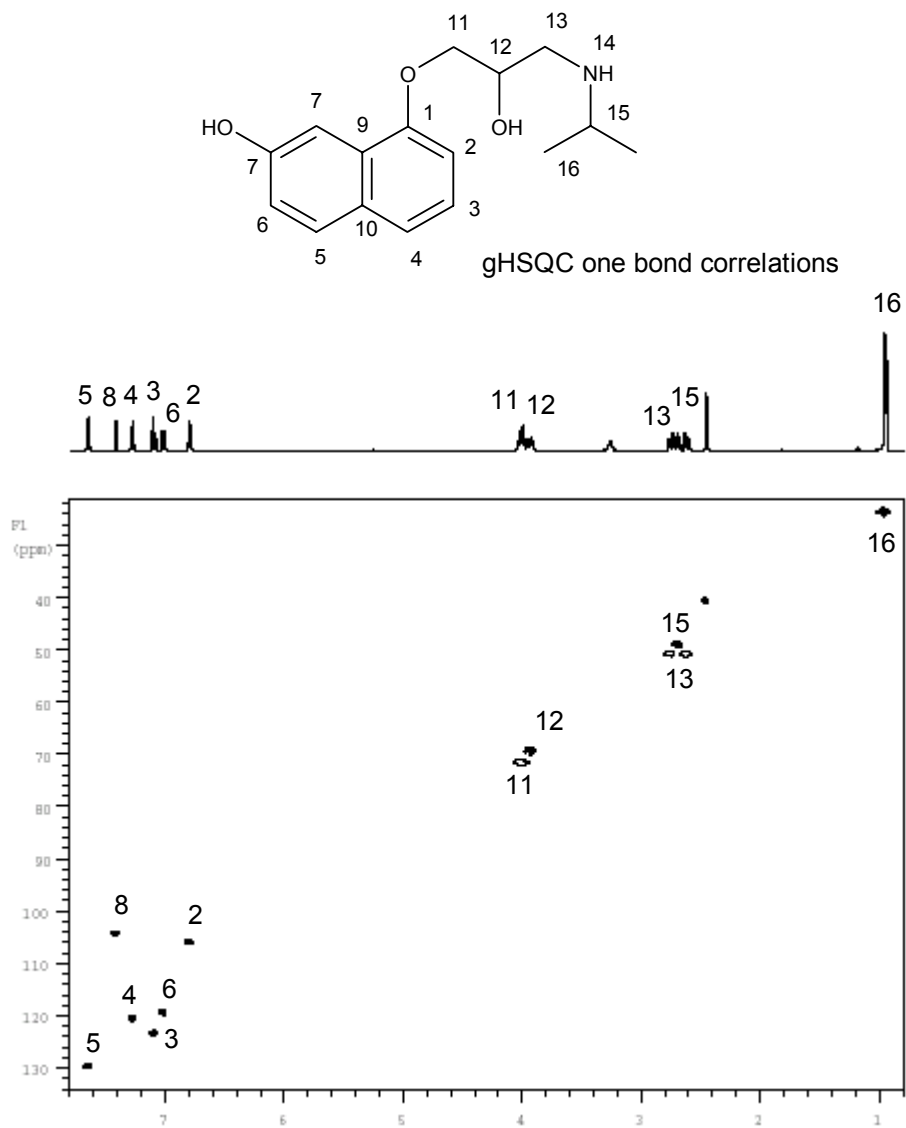


Fig 7. ^1H - ^{13}C NMR 2-D HMBC data (DMSO- d_6), structure and spectra

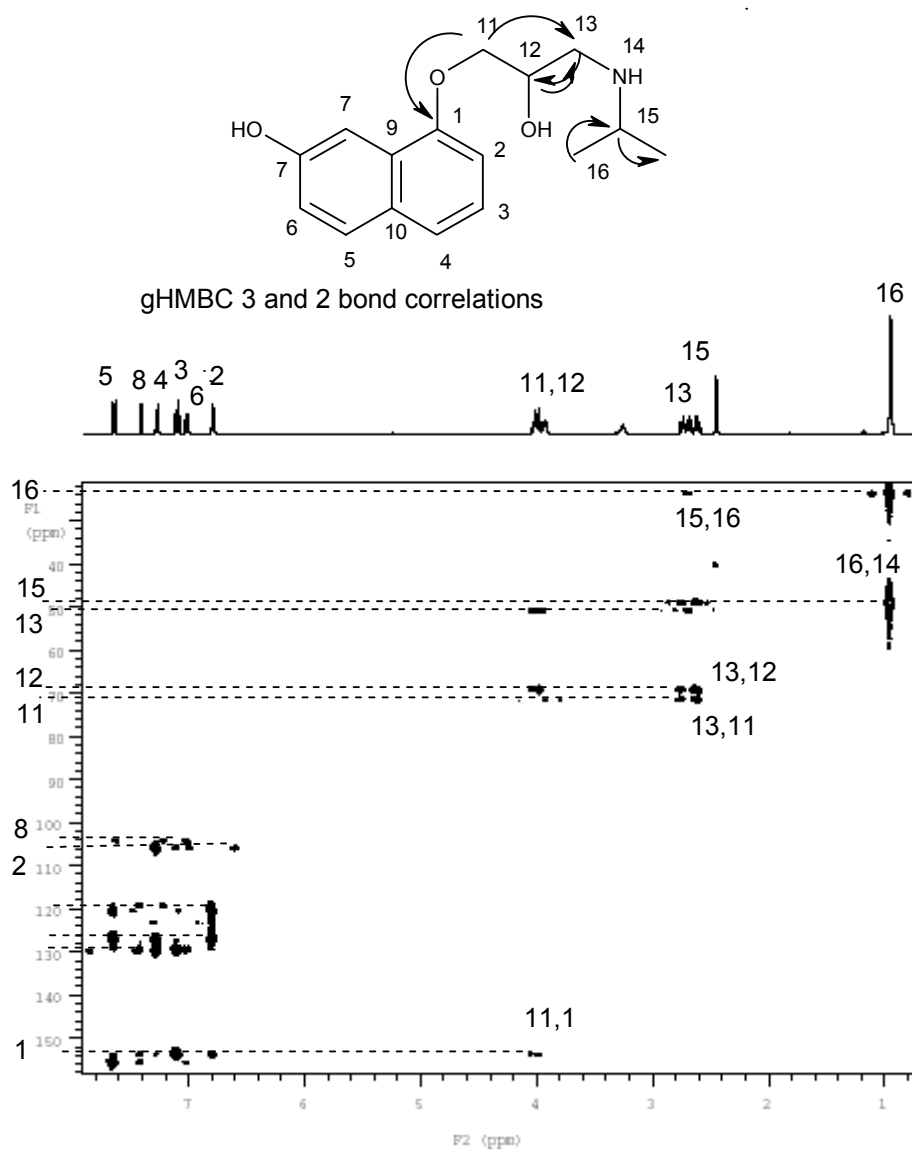


Fig 7B. Important 3-bond correlations are summarized in this structural illustration:

2-D HMBC experimental data
selected important correlations

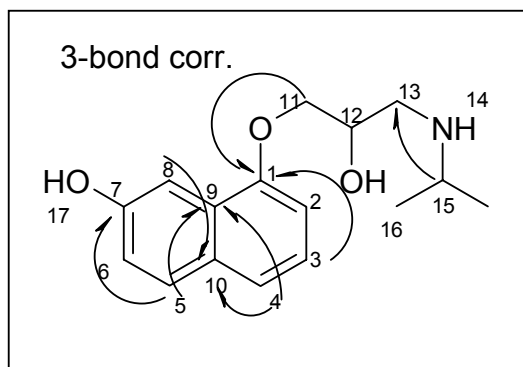


Fig 8. IR (HCl salt in a KBr pellet)

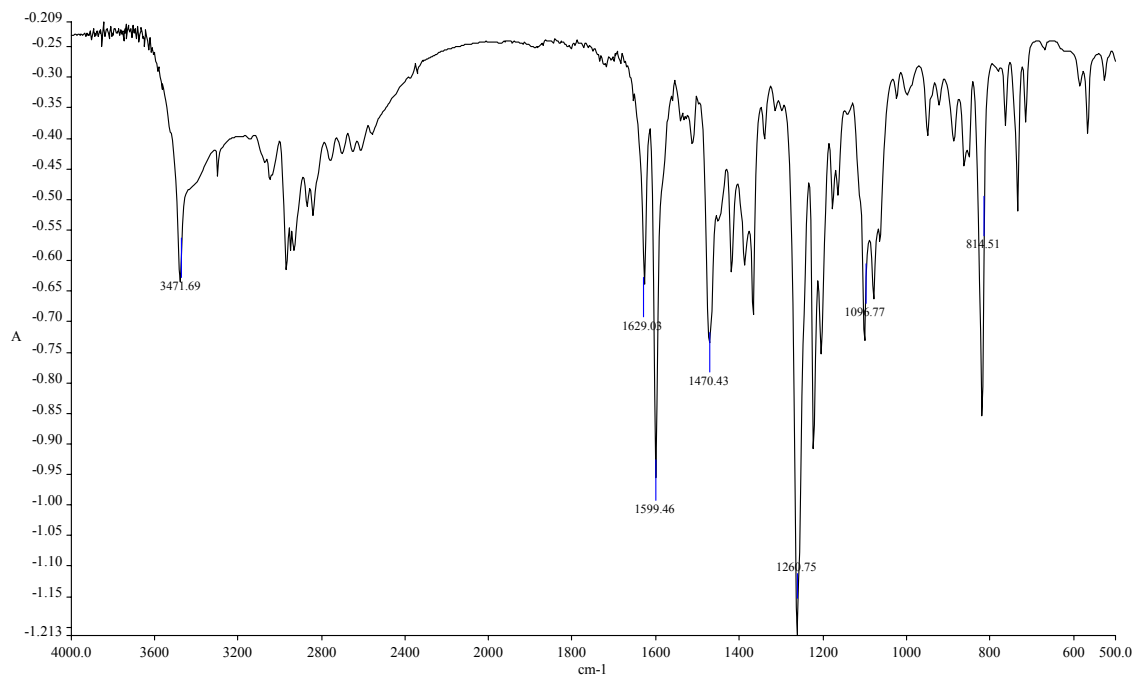


Fig 9. LC/UV/ESI/MS

