Journal of Molecular Structure 1160 (2018) 38–45

Contents lists available at ScienceDirect

Journal of Molecular Structure

journal homepage: http://www.elsevier.com/locate/molstruc

Polymorphism of a new Mannich base - [-4-methyl-2-((4-(4-nitrophenyl)piperazin-1-yl)methyl)phenol]

Ayowole O. Ayeni [a, b, *], Gareth M. Watkins [a], Eric C. Hosten [c]

[a] Department of Chemistry, Rhodes University, South Africa
[b] Department of Chemistry, Obafemi Awolowo University, Nigeria
[c] Department of Chemistry, Nelson Mandela Metropolitan University, South Africa

ARTICLE INFO

Article history:
Received 30 November 2017
Received in revised form
25 January 2018
Accepted 26 January 2018
Available online 2 February 2018

Keywords:
Polymorphism
Mannich base
DSC
PXRD

ABSTRACT

Two polymorphs (forms I and II) of a new Mannich base 4-methyl-2-((4-(4-nitrophenyl)piperazin-1-yl) methyl)phenol have been isolated and characterized by single crystal and powder (experimental and theoretical) X-ray diffraction, thermal analysis (differential scanning calorimetry), Fourier transform infrared spectroscopy. ^{1}H and ^{13}C nuclear magnetic resonance spectroscopy was employed in characterising the new Mannich base. Single crystal X-ray diffraction revealed that the two polymorphs contain different conformers of the Mannich base whose hydrogen bonding schemes and packing arrangements in their respective crystals are different. Thermal analysis led to the conclusion that the two polymorphs are enantiotropically related, with a transition temperature of 138.5 °C.

1. Introduction

Mannich reaction has over the years continuously afforded the formation of compounds from phenols for example that demonstrate great coordination chemistry and excellent biological properties [1–3].

One of the most active areas in solid state chemistry is the isolation, identification and characterization of different crystal forms (polymorphs, solvates, salts and co-crystals) of the same molecule or of aggregates of the same molecule with other molecules [4,5].

The importance of polymorphism lies in the fact that physical properties (melting point, colour, solubility, refractive index, hardness, conductivity, etc.) of a given compound vary between the polymorphic forms [6]. Of great significance as far as the application is concerned are the polymorphic forms of pharmaceutically active substances. Since the solubility and dissolution rates are different the bioavailability is affected [7,8].

The analytical strategy in approaching a polymorphism study will be dictated by the availability of instrumentation, time and material [9]. Searching through the literature revealed some of the methods employable in elucidating some of the distinguishing features of polymorphs and popular among such are Infrared spectroscopy Differential Scanning Calorimetry (DSC) and Powdered X-ray Diffraction (PXRD) amongst others [10,11]. Examples of polymorphism in organic compounds are not widely reported with few instances highlighted in the literature [12–14].

The need to expand the scope of polymorphism in Mannich bases led us to report two separate crystal structures a new Mannich base: 4-methyl-2-((4-(4-nitrophenyl)piperazin-1-yl)methyl) phenol in different space groups obtained by in different mixtures of solvents. These were characterized by nuclear magnetic resonance, infra-red spectroscopy, Differential Scanning Calorimetry (DSC) and single crystal and powdered diffraction techniques.

2. Experimental

Formaldehyde solution, p-cresol and 1-(4-nitrophenyl)piperazine were purchased from Sigma Aldrich and used without further preparation. Micro analytical determinations (C, H and N) were obtained using Elementar Analysensysteme VarioMICRO V1.62 GmbH analysis System. NMR spectra (^{1}H and ^{13}C NMR) were acquired in $CDCl_3$ using Bruker AMX 300 MHz spectrometer with tetramethylsilane (TMS) as an internal standard for ^{1}H. Attenuated total reflection Fourier transform infrared (ATR-FTIR) spectra for all the samples were recorded on a PerkinElmer Spectrum400

* Corresponding author.
E-mail address: aayeni@oauife.edu.ng (A.O. Ayeni).

https://doi.org/10.1016/j.molstruc.2018.01.068
0022-2860/

spectrophotometer in the range 4000 to 650 cm^{-1}. Electronic spectra were recorded for the solutions of the synthesized compounds in DMF on a Perkin Elmer UV–Vis spectrophotometer model Lamba 25. X-ray powder diffraction patterns were recorded on a Bruker D8 Discover (Billercica, MA, USA) equipped with a proportional counter, using Cu-Kα radiation (λ = 1.5405 Å, Nickel filter). Data were collected in the range from 2θ = 10° to 100°, scanning at 1.5° min^{-1} with a filter time constant of 0.38 s per step and a slit width of 6.0 mm samples were placed on a silicon slide. The x-ray diffraction data were treated using Eva (evaluation curve fitting) software. Baseline correction was performed on each diffraction pattern by subtracting a spline function fitted to the curved background.

Data for single crystal X-ray structure analyses of the two polymorphs were collected at 295(2) K on a Siemens P4 diffractometer. The crystal data were collected using a Bruker KAPPA APEX II single crystal X-ray diffractometer, with a 4-circle Kappa goniometer and sensitive CCD detector. The instrument used a Molybdenum fine focus sealed X-ray tube as an X-ray source and an Oxford Cryostream 700 system for sample temperature control. Bruker's APEX2 software [15] was used for instrument control. The structure was solved using SHELXT-2014 [16] and refined by least square procedures using SHELXL-2016 [17] with SHELXLE [18] as a graphical interface. Data were recorded for absorption effects using the numerical method implemented in SADABS [15].

Crystallographic data for the structures reported in this article have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication CCDC nos. 1585982 for polymorph I and 1554292 for polymorph II. Copy of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB1 1EZ, UK (Fax: t44-1223/336–033; e-mail: deposit@ccdc.cam.ac.uk).

2.1. Synthesis of -4-methyl-2-((4-(4-nitrophenyl)piperazin-1-yl) methyl)phenol

A mixture of p-cresol (0.006 mol, 0.6299 mL), 1-(4-nitrophenyl) piperazine (0.003 mol, 0.2584 g) and 3 mL of formaldehyde

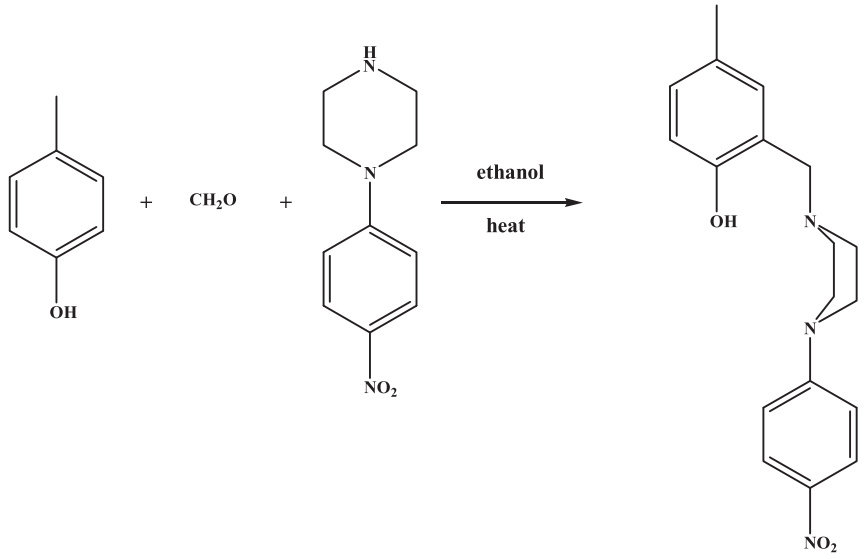

Fig. 1. Scheme depicting the synthesis of the Mannich base.

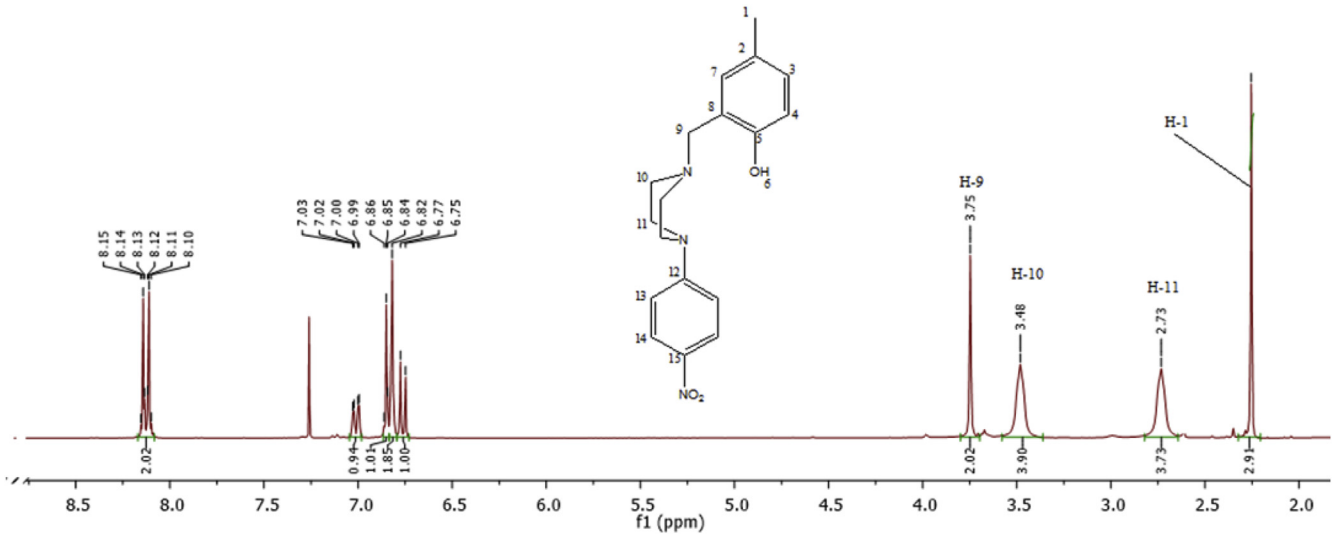

Fig. 2. ^1H spectrum of the Mannich base in $CDCl_3$.