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Synthesis, characterization and dynamic NMR studies of a novel chalcone based N-substituted morpholine derivative

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HIGHLIGHTS

- A novel chalcone based N-substituted morpholine derivative is synthesized.
- Complete assignments of ^{1}H and ^{13}C signals were made using modern 2D NMR techniques.
- The stereo dynamics of the morphline moiety have been examined by dynamic NMR spectroscopy.
- The energy barrier to morphline ring inversion is calculated.

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ABSTRACT

The synthesis of a novel chalcone based N-substituted morpholine derivative namely, (E)-1-(biphenyl-4-yl)-3-(4-(5-morpholinopentyloxy) phenyl) prop-2-en-1-one (BMPP), using a two step protocol is reported. The compound is characterized by FTIR, GC–MS and FTNMR spectroscopy techniques. Advanced 2D NMR techniques such as gradient enhanced COSY, HSQC, HMBC and NOESY were employed to establish through-bond and through-space correlations. Dynamic NMR measurements were carried out to obtain the energy barrier to ring inversion of the morpholine moiety.

1. Introduction

Chalcones are an important group of natural products belonging to the flavonoid family [1]. Chalcone derivatives are gaining much attention in the recent past because of their promising biological as well as pharmaceutical properties including antibacterial, anti inflammatory and anticancer activities [2]. Chalcone based anticancer drugs are reported to be devoid of the side effects often associated with genotoxic effects [3,4]. Ru(II)–DMSO–Cl–chalcone complexes have been shown recently to have significant effects on DNA binding and shows topoisomerase II inhibitory activity [5]. The presence of both electron-donating and electron withdrawing substituents attached to the aromatic ring of chalcone derivatives exhibits significant nonlinear optical responses [6]. Further, because of their high extinction coefficient of UV absorption, chalcone derivatives are reported to be good candidates for optical applications [7–9]. Chalcone–benzoxaborole hybrid molecules are found to be useful for antitrypanosomal therapies [10]. We have recently reported the use of chalcone derivatives as corrosion inhibitor of mild steel [11]. It has also been reported that chalcone derivatives attached by aliphatic spaced chain increases the antibacterial and antifungal activity [12]. Chalcone based morpholine derivatives are known to exhibit a broad spectrum of biological activities and present a great potential for pharmacological applications such as anti-ulcer, herbicidal, anti-bacterial, analgesic, sedative, anti-phlogistic, and virucidel agents [13]. Carbon substituted morpholines are reported to be effective for the treatment of panic disorder, deficit disorder, deficit hyperactivity disorder [14,15]. N-substituted morpholines are used in the treatment of inflammatory diseases, asthma and migraine [16]. N-substituted morpholines are also reported to show activity like anti-emetics, platelet aggregation inhibitors and bronchodialators [17]. Studies on the energetic of N-substituted morpholine derivatives are highly important in understanding the biological activities and designing new drugs. In the present study, we describe the synthesis and spectral characterization of a novel chalcone based, aliphatic chain spaced, morpholine derivative namely, (E)-1-(biphenyl-4-yl)-3-(4-(5-morpholinopentyloxy) phenyl) prop-2-en-1-one (abbreviated as BMPP, shown in Fig. 1).

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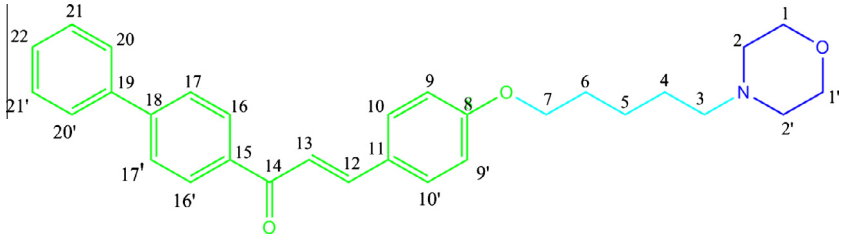
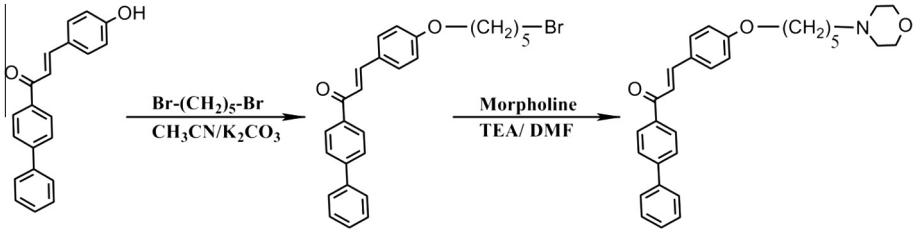


Fig. 1. Schematic drawing of BMPP (atom numbering is given for better understanding in discussions).



Scheme 1. Synthetic route to BMPP.

The stereo dynamics of the conformational interconversions of the morphline moiety have also been examined by means of dynamic NMR spectroscopy.

2. Experimental

2.1. Materials and methods

1,5-Dibromopentane, potassium carbonate, triethylamine, and morpholine were purchased from Merck, and used without further purification. Solvents were purified and dried according to standard procedure [18]. The starting material 4-[(1*E*)-3-(biphenyl-4-yl)buta-1,3-dien-1-yl]phenol is prepared from biphenyl using a two step protocol as described earlier [19].

2.2. Physical measurements

The infrared spectra were recorded on a Perkin Elmer Spectrum One instrument in the frequency range of 4000–450 cm^{-1}, using KBr pellet method. Mass spectra were recorded using JEOL GC MATE spectrometer in the EI mode. NMR spectra were recorded in $CDCl_3$ solvent on a Bruker Avance III 500 MHz instrument, using TMS as an internal reference standard. The DEPT135 spectrum was recorded on standard manner $\theta = 135$ pulse program. Gradient enhanced 2D COSY, HSQC, HMBC and NOESY spectra were recorded using the standard pulse programs from Bruker. Dynamic NMR measurements were carried out in CD_2Cl_2 solvent using Bruker B-VT 3200 model VT accessory with digital temperature controller. The temperature range of 298–223 K was used for the dynamic NMR investigations. The low temperature calibration was done using a solution of 4% CH_3OH in CD_3OD and the low temperature measurements were estimated to be accurate to ±0.2 K.

2.3. Synthesis

The Synthetic route to BMPP is provided in Scheme 1. The compound BMPP is synthesized from 4-[(1*E*)-3-(biphenyl-4-yl)buta-1,3-dien-1-yl] phenol, using a two step protocol (19). The details of each step are given in the following section.

2.3.1. (E)-1-(biphenyl-4-yl)-3-(4-(5-bromopentyloxy)phenyl)prop-2-en-1-one

In a 100 ml round-bottomed flask, 4-[(1*E*)-3-(biphenyl-4-yl)buta-1,3-dien-1-yl]phenol (1 g, 3.3 mmole), anhydrous potassium carbonate (.92 g, 6.6 mmole), freshly distilled acetonitrile (30 ml) and 1,5-dibromopentane (1.8 ml, 13.26 mmole) were placed. The mixture was refluxed at 70 °C for 12 h and the resulting solution was cooled down to room temperature, washed with large amount of water and then extracted using ethyl acetate. The organic layer was washed with brine solution and dried over anhydrous sodium sulfate. Solvents present in the resulting solution were removed through vacuum and further purified by column chromatography. The final product obtained was a pale yellow colored solid; Yield: 76%. m.p.: 110 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 1.67 (m, J = 7.5 Hz, 2H), 1.90 (m, J = 8.0 Hz, 2H), 1.98 (m, J = 7.0 Hz, 2H), 3.47 (t, J = 6.5 Hz, 2H), 4.05 (t, J = 6.5 Hz, 2H), 6.96 (d, J = 8.5 Hz, 2H), 7.43 (t, J = 7.5 Hz, 1H), 7.49 (d, J = 15.5 Hz, 1H), 7.50 (t, J = 7.5 Hz, 2H), 7.64 (d, J = 9.0 Hz, 2H), 7.65 (d, J = 7.0 Hz, 2H), 7.75 (d, J = 8.5 Hz, 2H), 7.84 (d, J = 16.0 Hz, 1H), 8.12 (d, J = 8.5 Hz, 2H), ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 24.81, 28.36, 32.45, 33.53, 67.77, 114.93, 119.66, 127.25, 127.30, 127.62, 128.16, 128.96,

Table 1
Infrared spectral data (cm^{-1}) for BMPP.

Vibrations	Wavenumber, ν^{-1} (cm^{-1})	Mode
C=O (α–β unsaturated)	1650 (s)	Stretching
C—H (aromatic)	3031 (w)	Stretching
C—O (morpholine)	1219 (m)	Stretching
C=C (α–β unsaturated)	1630 (m)	Stretching
C=C	1456 (m)	Stretching
C—H (aliphatic methyl)	2950, 2923, 2866 (s),	Stretching
	1376 (w)	Bending
C=O	3433 (m)	Overtone
C=C (vibration)		(Bending)
C—H (aliphatic methyl)	740–866	Out of bending
—C—O—C	1293	Stretching
—C—N—	1116 (s)	Stretching
	1570 (s)	Bending
—C—C	1253 (m)	Stretching
—C—O—	1176 (m)	Stretching
—O—C—	1033 (m)	Stretching

(s)-Strong; (m)-medium; (w)-weak.

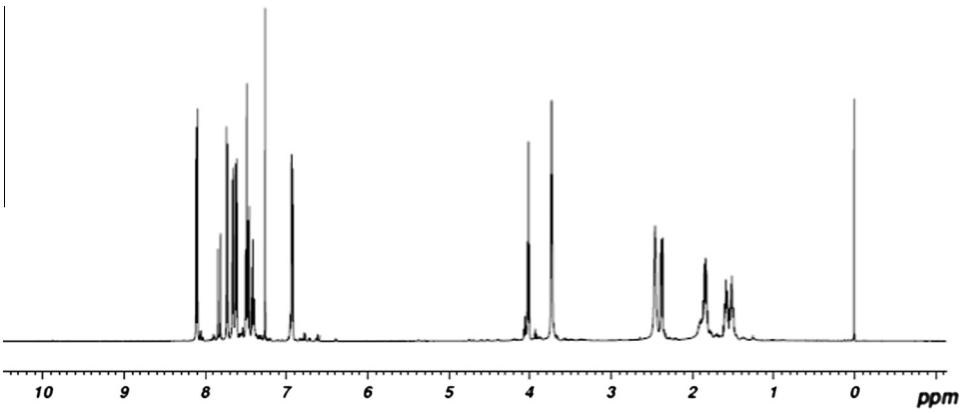


Fig. 2a. 500 MHz ^{1}H NMR spectrum of the compound in $CDCl_3$ at 298 K.

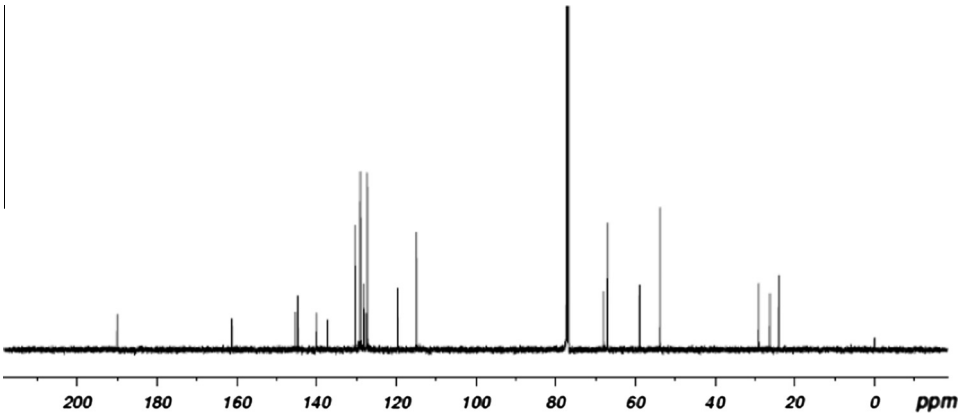


Fig. 2b. 125 MHz ^{13}C NMR spectrum of the compound in $CDCl_3$ at 298 K.

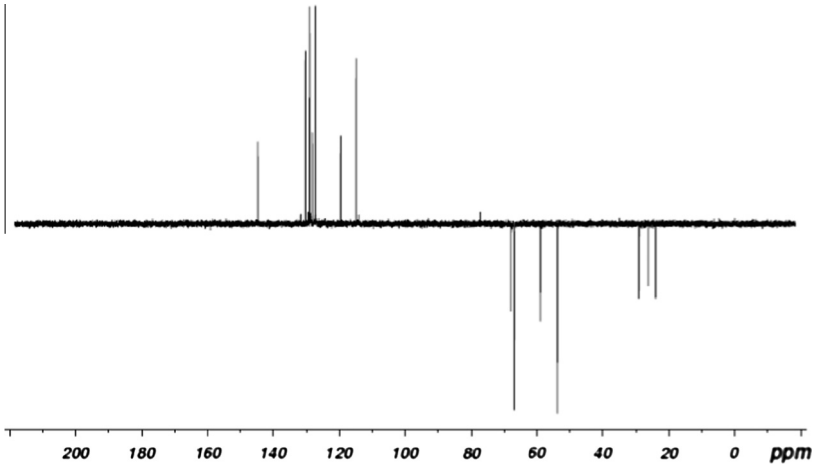


Fig. 2c. DEPT-135 spectrum of the compound in $CDCl_3$ at 298 K.

129.04, 130.28, 137.24, 140.03, 144.64, 145.311, 161.13, 189.97. IR (KBr, cm^{-1}) 732, 1029, 1170, 1216, 1422, 1474, 1601, 1647, 2857, 1942, 3055, 3440.

2.3.2. (E)-1-(biphenyl-4-yl)-3-(4-(5-morpholinopentyloxy)phenyl)prop-2-en-1-one (BMPP)

To a stirred solution of (E)-1-(biphenyl-4-yl)-3-(4-(5-bromopentyloxy)phenyl)prop-2-en-1-one (112 mg, 0.249 mmole) in N,N-dimethyformamide (15 ml) at room temperature, triethylamine (0.7 ml, 0.5 mmole) was added slowly followed by morpholine (0.21 ml, 0.249 mmole). Stirring was continued further for 48 h and the solution was poured in to beaker containing ice cold water. The yellow solid obtained was separated by filtration and purified by column chromatography. The final product obtained was a yellow colored solid; Yield: 72%. m.p.: 130 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 1.50 (m, J = 5.5 Hz, 2H, H_5), 1.58 (m, J = 7.0 Hz, 2H, H_4) 1.83 (m, J = 6.5 Hz, 2H, H_6), 2.37 (t, J = 8.0 Hz, 2H, H_3), 2.45 (s, 4H, H_2), 3.72 (t, J = 5.0 Hz, 4H, H_1), 4.01 (t,

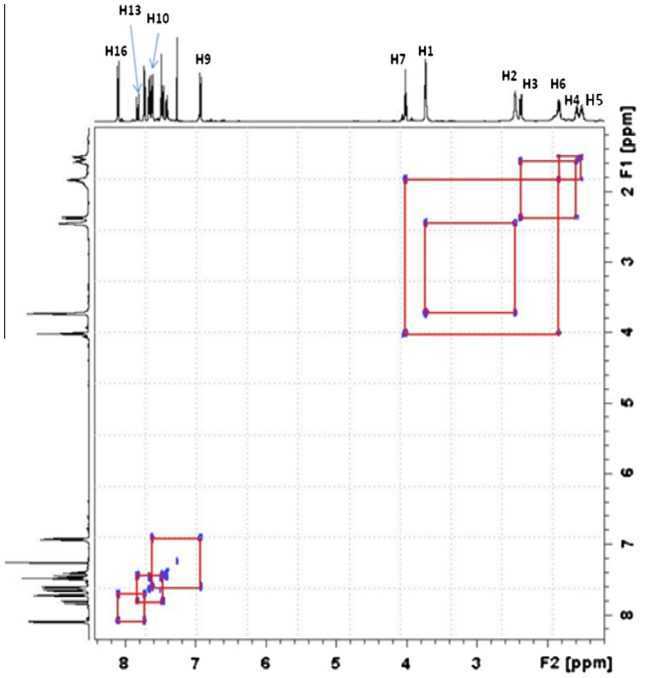


Fig. 3. $^{1}H—^{1}H$ COSY spectrum of BMPP in $CDCl_3$ at 298 K.

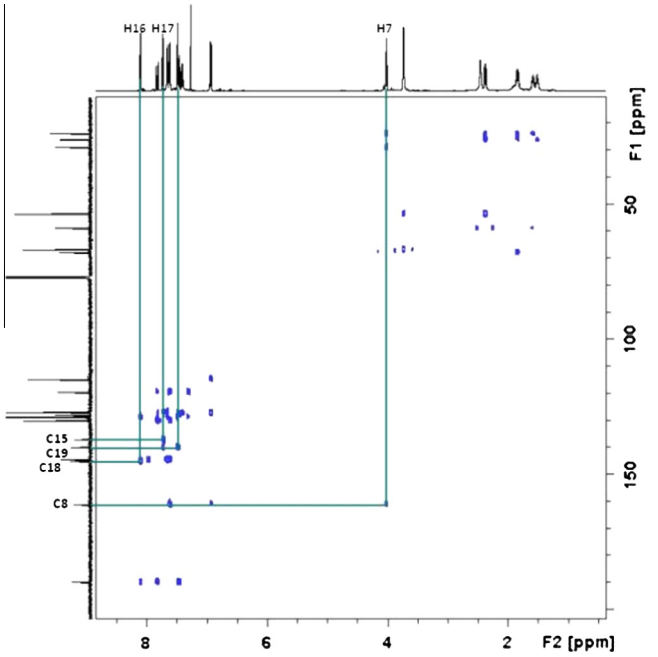


Fig. 5. Partial $^{1}H—^{13}C$ HMBC spectrum of BMPP in $CDCl_3$ at 298 K.

J = 6.5 Hz, 2H, H_7), 6.92 (d, J = 9.0 Hz, 2H, H_9), 7.40 (t, J = 7.5 Hz, 1H, H_{22}), 7.48 (d, J = 15.5 Hz, 1H, H_{12}), 7.49 (t, J = 7.5 Hz, 2H, H_{21}), 7.61 (d, J = 9.0 Hz, 2H, H_{10}), 7.65 (d, J = 7.0 Hz, 2H, H_{20}), 7.72 (d, J = 8.5 Hz, 2H, H_{17}), 7.82 (d, J = 15.5 Hz, 1H, H_{13}), 8.10 (d, J = 8.0 Hz, 2H, H_{16}), ^{13}C NMR (126 MHz, CDCl3) δ ppm 23.98 (C_5), 26.26 (C_4), 29.07 (C_6), 53.77 (C_2, $C_{2'}$), 58.94 (C_3), 66.96 (C_1, $C_{1'}$), 67.96 (C_7), 114.91 (C_9, $C_{9'}$), 119.61 (C_{12}), 127.25 (C_{17}, $C_{17'}$), 127.29 (C_{20}, $C_{20'}$), 127.52 (C_{11}), 128.16 (C_{22}), 128.96 (C_{21}, $C_{21'}$), 129.04 (C_{16}, $C_{16'}$), 130.27 (C_{10}, $C_{10'}$), 137.24 (C_{15}), 140.03 (C_{19}), 144.69 (C_{13}), 145.31 (C_{18}), 161.24 (C_8), 190.00 (C_{14}). IR (KBr, cm^{-1}) 740, 866, 1010, 1033, 1116, 1176, 1219, 1293, 1423, 1456, 1570, 1650, 2866, 2923, 2950, 2923, 2866, 3031, 3433.

3. Results and discussion

The purified compound was yellow in color and analytical data were in good agreement with molecular formula, $C_{30}H_{33}O_3N$. The melting point of the compound was 130 °C. The compound was found to be soluble in chloroform, dichloromethane, dimethyl sulfoxide, dimethyl formamide, ethyl acetate and acetone. The mass spectral data was in accordance with the calculated molecular weight of 455.6 amu.

3.1. IR spectral assignment

The important vibrational frequencies observed for BMPP are listed in Table 1. The characteristic carbonyl stretching vibration

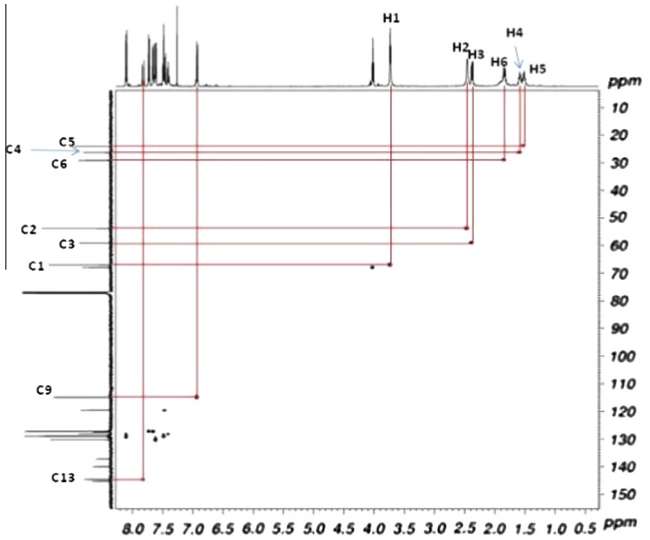


Fig. 4. $^{1}H—^{13}C$ HSQC spectrum of BMPP in $CDCl_3$ at 298 K.

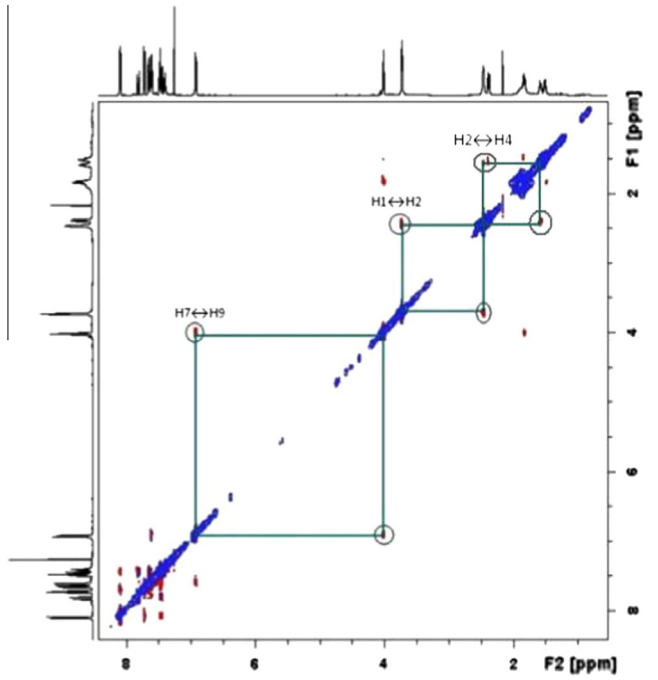


Fig. 6. NOESY spectrum of BMPP in $CDCl_3$ at 298 K with a mixing time of 300 ms.

Table 2
^{1}H and ^{13}C NMR data, $^{1}H—^{1}H$ COSY, $^{1}H—^{13}C$ HSQC and $^{1}H—^{13}C$ HMBC correlations of BMPP.

Carbon number	Chemical shift (ppm)		$^{1}H—^{1}H$ COSY	$^{1}H—^{13}C$ HSQC	$^{1}H—^{13}C$ HMBC
	δ_H	δ_C		(^{1}J)	(^{3}J)
C1,C1′	3.72 (t, *J* = 5.0 Hz, 4H)	66.96	H2	69.96	–
C2,C2′	2.45 (s, 4H)	53.77	H1	53.77	–
C3	2.37 (t, *J* = 8.0 Hz, 2H)	58.94	H4	58.94	–
C4	1.58 (m, *J* = 7.0 Hz, 2H)	26.26	H3	26.26	–
C5	1.50 (m, *J* = 5.5 Hz, 2H)	23.98	H6	23.98	–
C6	1.83 (m, *J* = 6.5 Hz, 2H)	29.07	H5,H7	29.07	–
C7	4.01 (t, *J* = 6.5 Hz, 2H)	67.96	H6	67.96	–
C8	–	161.24	–	–	67.96(C7) 130.27(C10)
C9,C9′	6.92 (d, *J* = 9.0 Hz, 2H)	114.91	C10	114.91	–
C10,C10′	7.61 (d, *J* = 9.0 Hz, 2H)	130.27	H9	130.27	–
C11	–	127.52	–	–	114.91(C9) 144.69(C13)
C12	7.48 (d, *J* = 15.5 Hz, 1H)	119.61	C13	119.61	–
C13	7.82 (d, *J* = 15.5 Hz, 1H)	144.69	C12	144.69	–
C14	–	190.00	–	–	119.61(C12) 129.04(C16)
C15	–	137.24	–	–	127.25(C17)
C16,C16′	8.10 (d, *J* = 8.0 Hz, 2H)	129.04	C17	129.04	–
C17,C17′	7.72 (d, *J* = 8.5 Hz, 2H)	127.25	C16	127.25	–
C18	–	145.31	–	–	129.04(C16) 127.29(C20)
C19	–	140.03	–	–	127.25(C17) 128.96(C21)
C20,C20′	7.65 (d, *J* = 7.0 Hz, 2H)	127.29	C21	127.29	–
C21,C21′	7.49 (t, *J* = 7.5 Hz, 2H)	128.96	C20	128.96	–
C22	7.40 (t, *J* = 7.5 Hz, 1H)	128.16	–	128.16	–

of α–β-unsaturated ester group occurred at 1650 cm^{-1}. The aromatic C—H stretching signal of the compound appeared at 3031 cm^{-1} while the aliphatic methyl stretching frequency appeared at 2923 cm^{-1}. The vibrational stretching frequency of C—O—C appeared at 1293 cm^{-1}. Alkyl C—H bending vibration appeared at 1423 cm^{-1}. The vibrational bands observed at regions between 820 cm^{-1} and 1010 cm^{-1} were assigned to be the characteristic C—H out of plane or wagging vibrations. The C—O stretching vibration of morpholine moiety is observed 1219 cm^{-1}, while the medium band at 3433 cm^{-1} is attributed to the C=O overtone of the chalcone moiety. The C—N stretching (1116 cm^{-1}) and C—N bending (1570 cm^{-1}) modes of vibrations were also identified.

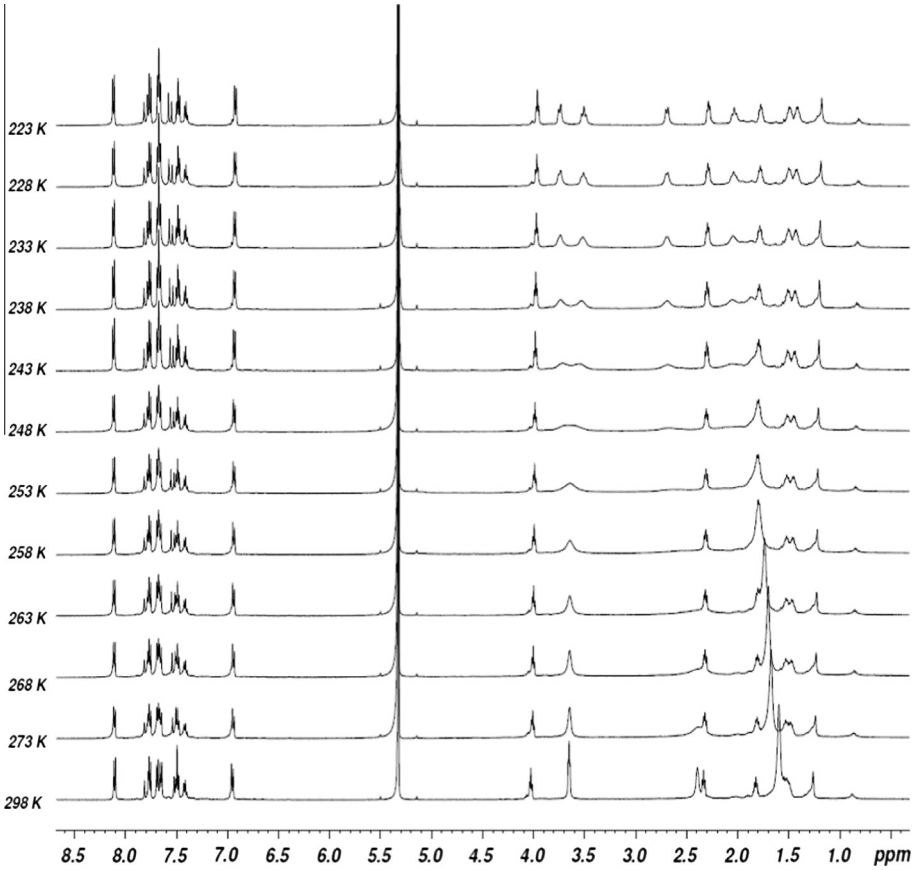


Fig. 7. Temperature-dependent ^{1}H NMR spectra of BMPP.

3.2. NMR spectral assignments

One dimensional ^{1}H, ^{13}C and DEPT-135 NMR spectra of the BMPP in $CDCl_3$ are shown in Figs. 2a, 2b and 2c respectively.

From these spectra, characteristic ^{1}H and ^{13}C resonances corresponding to the chalcone, alkyl spacer and morpholine moieties were identified, and further confirmed by advanced 2D NMR studies. Unequivocal assignment of assignments for these spin systems were obtained using Gradient enhanced COSY and HSQC experiments with additional data obtained from long-range $^{1}H—^{13}C$ correlation experiments and NOESY experiments. Two dimensional correlation spectroscopy (COSY) experiment is employed to establish connectivity between all directly coupled protons as illustrated in Fig. 3. The important through bond correlations derived from COSY are those between $H_1 \leftrightarrow H_2$, $H_3 \leftrightarrow H_4$, $H_4 \leftrightarrow H_5$, $H_5 \leftrightarrow H_6$, $H_6 \leftrightarrow H_7$, $H_9 \leftrightarrow H_{10}$, $H_{12} \leftrightarrow H_{13}$, $H_{16} \leftrightarrow H_{17}$, $H_{20} \leftrightarrow H_{21}$ and $H_{21} \leftrightarrow H_{22}$. The one bond $^{1}H—^{13}C$ connectivity between all carbons directly attached to protons was established from the heteronuclear single quantum coherence (HSQC) measurement using an evolution time of 17.2 ms (Fig. 4). Long range $^{1}H—^{13}C$ correlations were obtained from the heteronuclear multiple bond correlation (HMBC) experiment, employing an evolution time of 65 ms. HMBC

Table 3
Kinetic data of BMPP derived from dynamic NMR measurements.

T_c (K)	$\Delta\nu$ (Hz)	K_c ($^{s-1}$)	ΔG_c^* (Kcal mol^{-1})
248	405.6	884.43	11.08

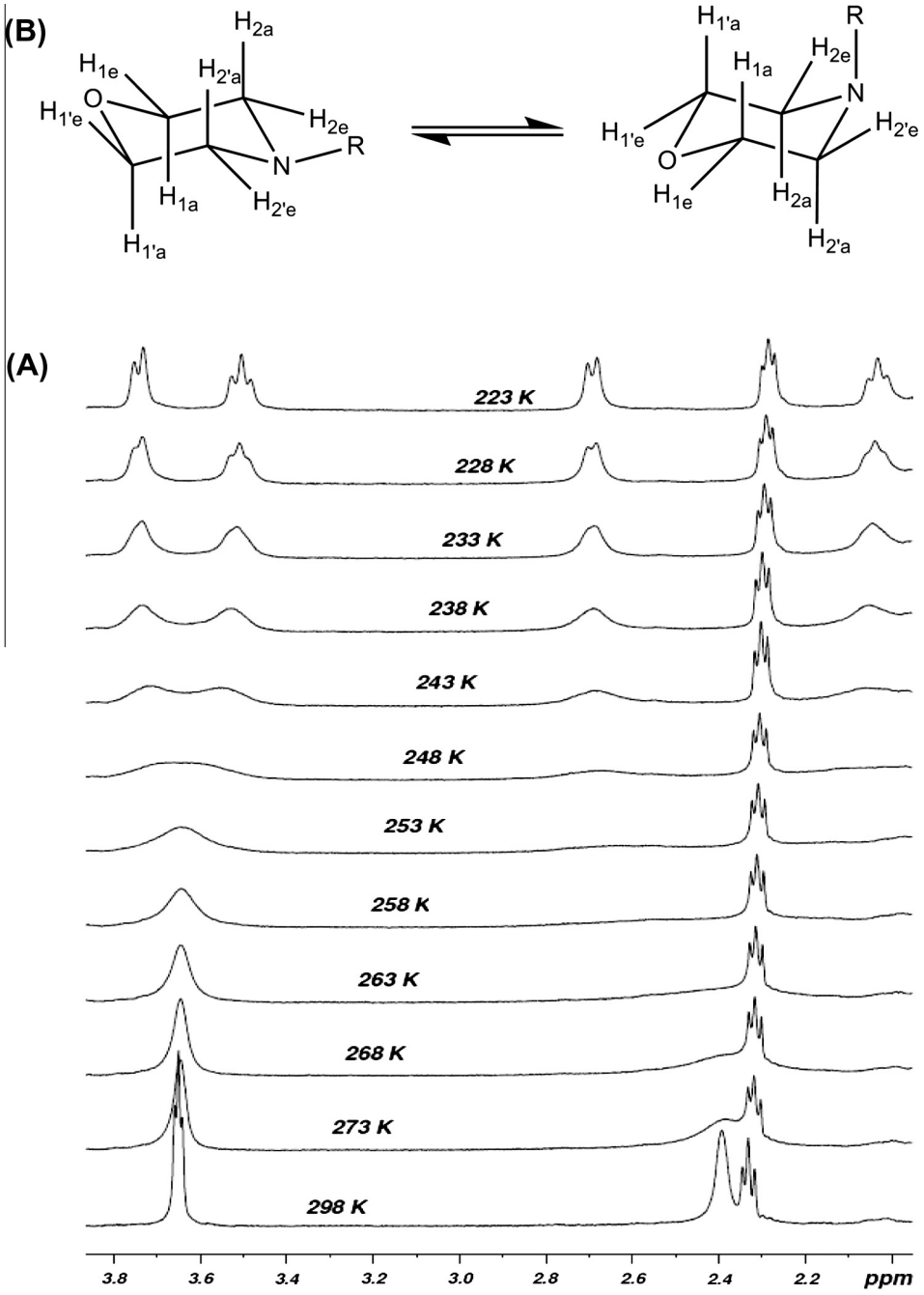


Fig. 8. (A) Expanded portion of dynamic NMR data of BMPP and (B) schematic of ring inversion of morpholine moiety.

was particularly useful for the assignments of —CO, —CN and the quaternary carbons, as illustrated in Fig. 5. The linkage between the chalcone moiety and the alkyl spacer and also between the alkyl spacer and the morpholine moiety were established from HMBC by deriving long range multiple bond correlation between $C_8 \leftrightarrow H_7$, $C_3 \leftrightarrow H_2$ and $C_2 \leftrightarrow H_3$. The NOESY correlation $H_9 \leftrightarrow H_7$, further conformed the linkage between the chalcone moiety and the alkyl spacer (Fig. 6).

The complete assignment of BMPP is given in Table 2. Important $^3J_{H—H}$ coupling constants derived are also given. The chair conformation of the morpholine moiety is established from the observation of through space NOE correlation between $H_2 \leftrightarrow H_4$ in the room temperature NOESY spectrum (Fig. 6) recorded with a mixing time of 300 ms.

3.3. Dynamic NMR studies

The conformational behavior of morpholine based systems has attracted special attention because of their occurrence in many complex natural and synthetic compounds of pharmacological interest [20]. Dynamic NMR spectroscopy has been employed as a vital tool in studying the stereo dynamics of the conformational interconversions of the morphline moiety [21]. In the chair conformation of the morpholine moiety, the axial and equatorial protons, being in slightly different chemical environments, are expected to resonate at different frequencies. Hence one should expect to see two signals each in the ^{1}H NMR spectrum. However, in the ^{1}H NMR recorded at room temperature (Fig. 1a), only one signal each is seen for protons attached to both C_1 and C_2 positions. This is because of the rapid ring interconversion of morpholine ring [21]. At room temperature, significant ring inversion of the morpholine moiety is occurring and as a result of this, the interconversion between the axial and equatorial protons (i.e., $H_{1a} \leftrightarrow H_{1e}$ and $H_{2a} \leftrightarrow H_{2e}$) becomes inaccessible in the NMR time scale. Hence only one signal each is observed for each site.

In order to find the stereo dynamic nature of the morpholine moiety in BMPP, ^{1}H NMR spectra of BMPP has been measured at temperatures sufficiently low for the ring-inversion process to appear slow. Since the solubility of BMPP in $CDCl_3$ solvent was very low as at lower temperatures, CD_2Cl_2 was used as solvent for the low temperature dynamic NMR measurements. The 500 MHz ^{1}H dynamic NMR spectra of BMPP recorded in CD_2Cl_2 solvent at different temperatures ranging from 298 K to 223 K are shown in Fig. 7.

At room temperature (298 K), the ring protons of the morpholine moiety (—NCH_2 and —OCH_2) appeared as two separate sets of signals, one broad triplet at δ 2.39 and a clear triplet at δ 3.6 with an intensity ratio of 4:4. The proton signals of the —NCH_2 protons are strongly broadened both pointing already to a dynamic process near to the slow exchange range. On gradual cooling, signals of the —NCH_2 and —OCH_2 protons of the morpholine ring gets broadened and decoalesced at 248 K into two broadened signals each. Apparently, on further cooling to 223 K, these signals formed pairs of clear doublets and triplets as shown in the expanded portion of the dynamic NMR spectra of BMPP in (Fig. 8A).

A schematic representation of the ring inversion of two chair conformations of morpholine moiety is presented in Fig. 8B. At room temperature (298 K), there is significant ring inversion of the morpholine moiety. As a result of this, interconversion between the axial and equatorial protons (i.e., $H_{1a} \leftrightarrow H_{1e}$ and $H_{2a} \leftrightarrow H_{2e}$) becomes inaccessible in the NMR time scale and only one signal is observed for each site (Fig. 8A). As the temperature is lowered, the rate of ring interconversion slows down, and signals corresponding to the axial and equatorial protons of the morpholine moiety are separated out. At about 248 K, the decoalescence temperature is observed. After the decoalescence temperature, the ring inversion approaches the slow exchange regime, resulting in well separated signals corresponding to non-equivalent protons (i.e., H_{1a}, H_{1e}, H_{2a} and H_{2e}). At 223 K, equatorial protons appeared as broad doublets at δ2.69 ($^2J_{ae}$ = 10.8 Hz) and 3.74 ($^2J_{ae}$ = 10.56 - Hz). The axial protons appeared at δ2.03 ($^3J_{aa}$ = 10.5 Hz) and 3.50 ($^3J_{aa}$ = 11.3 Hz). Thus, at lower temperature, the system is behaving like AB_2 rather than AA′XX′ (i.e., a triplet for axial proton and a doublet for equatorial proton). Similar dynamic behavior is reported earlier for other morpholine derivatives also [20].

The chemical shift difference ($\Delta\nu$) is obtained by taking the difference between the midpoint of the doublet and the middle point of a triplet. Barriers to ring inversion for the BMPP is calculated using the approximation equation $k_c = \pi\,\Delta\nu_c/\sqrt{2}$ and $\Delta G_c^{\neq}$ at T_c is determined by the Eyring equation at T_c [$(\Delta G_c^{\neq} = 19.14\ T_c\ (10.32 + \log\ T_c/k_c)$] [12]. Kinetic parameters estimated, based on dynamic NMR measurements, are given in Table 3. The calculated barriers to ring inversion of BMPP are found to be 11.08 Kcal mol^{-1} at 500 MHz frequency. The free energy of activation is in reasonable agreement with the values obtained [21].

The stereo dynamics of morphine ring inversion has been a very interesting topic of research in recent years [12]. When no substituent is present on the morpholine nitrogen, ring inversion is too fast to be monitored by dynamic NMR studies. However the barrier to ring inversion for N-methyl morpholine is reported to be 11.5 kcal mol^{-1}. From a study on the effect of substituents on the ring interconversion of morpholine compounds, it is documented that sterric phenomena slow down the conformational interconversion [21,22]. For example, bulkier group attached to nitrogen strongly increases the barrier to the ring inversion relative to an alkyl group [21]. The rate of conformational interconversion of morpholine ring also depends on the type of substituent. The equatorial and axial protons are observed even at room temperature, when bulkier substituents are present in morpholine ring [22].

It is also interesting to note that the even though slow, the interconversion is still occurring at temperature as low as 223 K. This is manifested by the NOESY spectrum recorded at 223 K. Generally, in the 2D NOESY spectrum, cross peaks arising from exchange phenomena have the same phase as the diagonal, while NOE cross peaks indicating spatial proximity have opposite phase

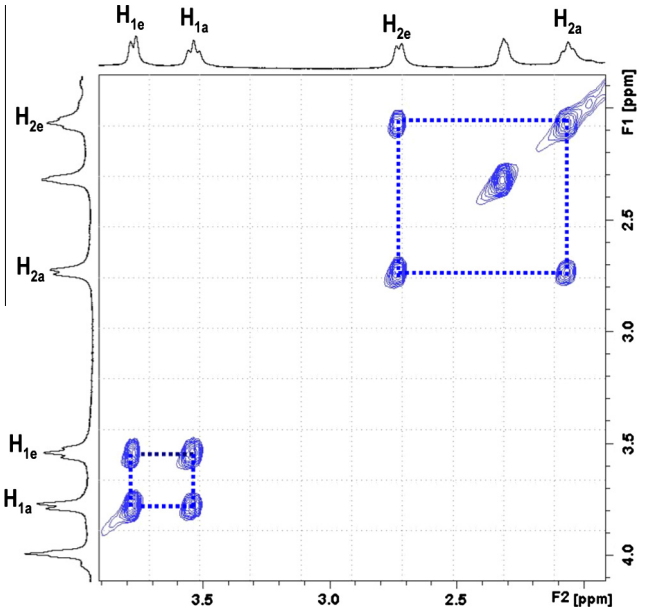


Fig. 9. Portion of the NOESY spectrum of BMPP. The spectrum was acquired at 233 K with a 300 ms mixing time. The exchange cross peak between $H_{1a} \leftrightarrow H_{1e}$, and between $H_{2a} \leftrightarrow H_{2e}$ are marked with corresponding one dimensional spectra at the top and to the left.

to the diagonal [20]. The existence of exchange cross peaks between the $H_{1a} \leftrightarrow H_{1e}$ and also $H_{2a} \leftrightarrow H_{2e}$, protons of the morpholine moiety in Fig. 9 illustrates that conformational interconversion occur even at 223 K. Exchange spectroscopy is often employed to establish the existence of equilibrium between two enantiomeric species [20].

Another interesting feature of dynamic NMR data is that neither the chemical shift nor the line width of signals other than those of the morpholine ring protons changes as the temperature is lowered. This means that the entire dynamics of the BMPP molecule depends on the stereodynamics of the morpholine moiety.

4. Conclusion

In this present study, we have synthesized a novel chalcone based N-substituted morpholine derivative, and their structure has been confirmed by different 1D and 2D NMR techniques. The ^{1}H NMR spectra of this compound as a function of temperature were investigated. The six membered heterocyclic ring of the morpholine moiety adopts a chair conformation and a process of rapid interconversion which averages the NMR signals at room temperature is observed. On freezing to 248 K, both proton signals in the morpholine moiety of BMPP show the expected decoalescence effects and well separated signals were observed at 223 K. The calculated free energy of activation is comparable with the literature data.

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