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Complementary hydrogen bonding of a carboxylato-barbiturate with urea and acetamide: Experimental and theoretical approach

Md. Amin Hasan[a], A. Seshaditya[a], Stanislav Záliš[b], Lallan Mishra[a,*]

[a] Department of Chemistry, Faculty of Science, Banaras Hindu University, Varanasi 221 005, India
[b] J. Heyrovský Institute of Physical Chemistry, Academy of Sciences of the Czech, Republic, Dolejškova 3, CZ-18223 Prague, Czech Republic

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ABSTRACT

A barbiturate derivative, 4-(2,4,6-trioxo-tetrahydro-pyrimidine-5-ylidenemethyl)-benzoic acid (L1) possessing functional complementarity to amides has been synthesized and characterized. Its binding separately with urea and acetamide was monitored using UV–vis, fluorescence and ^{1}H-NMR spectroscopic titrations. Experiments suggested stronger binding of L1 with urea as compared to acetamide. The solid adducts of L1 prepared separately with urea and acetamide were also characterized using IR, ^{1}H-NMR spectral and PXRD techniques. Theoretical studies on hydrogen bonded complexes of L1–urea and L1–acetamide in the gas phase, aqueous, and DMSO medium were carried out using density functional theory (DFT) at the B3LYP/6-31G** level. The theoretical calculations agreed to the experimental results.

1. Introduction

The design and synthesis of molecular and supramolecular receptors for the recognition of anionic [1–19], cationic [20] and neutral molecules [20–22] is a subject of contemporary research. However, development of thermodynamically stable and selective receptors of wider applications is still demanding more research in this area. In this construction, bringing of a substrate in contact with receptor through non-covalent interactions is more interesting as such interactions may tune the receptor in different conformations with little manipulations of external stimuli like light, heat as well as the polarity of the solvent [19].

In this context, urea being toxic [23–26] and chief constituent of metabolic product of nitrogenous compounds and a well-known protein denaturant even at micro molar concentration, caught our attention recently. Neutral hosts like pyrrole, urea or other amide groups [27–33] that bind guests exclusively through hydrogen bonding have recently been developed. Hamilton and Still have reported isophthalamide or urea derivatives as receptors for nucleotide bases, barbiturates, dicarboxylic acids, dicarboxylates, and peptides [34–42].

In this context, density functional theory (DFT) [43–45] which has emerged as a reliable and versatile computational method has been successfully used to study physical and chemical properties of molecules [46–50]. Moreover, its utility has been pointed out elsewhere [51–58] in the recent study of hydrogen bonding systems. We therefore set up a task of developing an adjustable probe molecule that forms complexes with amide analogues and would produce a differentiated UV–vis absorption band depending on the hydrogen-bonding sequence.

It was thought to investigate the donor–acceptor properties of a new barbiturate derivative, 4-(2,4,6-trioxo-tetrahydro-pyrimidine-5-ylidenemethyl) benzoic acid (L1) (Fig. 1) for the recognition of urea and acetamide using UV–vis, fluorescence and ^{1}H-NMR spectral titrations. The formation of stable supramolecular complexes of (L1) separately with urea and acetamide has also been isolated in solid state and characterized using their IR spectra and powder X-ray diffraction data. The complexes are also characterized in solution using their ^{1}H-NMR spectra in DMSO-d_6 solution. The formation of supramolecular composition of L1 separately with urea and acetamide is also investigated theoretically using density functional theory (DFT) calculations in gas phase, aqueous and DMSO medium. The selectivity of compound L1 as a receptor candidate is made owing to its easy preparation, stability towards air and moisture and bearing multiple binding sites being complementary to both urea and acetamide.

2. Experimental

2.1. Materials and methods

Urea and acetamide were purchased from Sigma–Aldrich Chem. Co. and were used as received without further purification. The solvents were purchased from E. Merck and were freshly distilled prior

* Corresponding author. Tel.: +91 542 6702449; fax: +91 542 2368174.
E-mail address: lmishrabhu@yahoo.co.in (L. Mishra).

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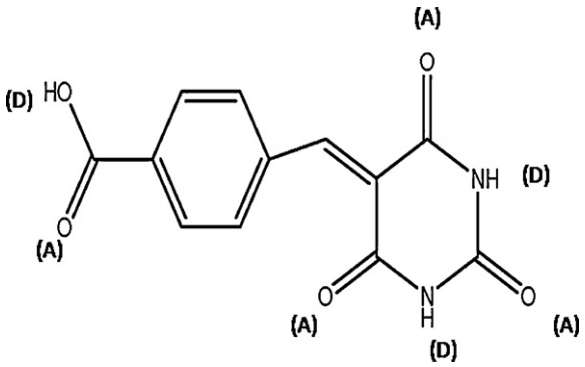


Fig. 1. Chemical structure of L1 showing H-donor and acceptor sites.

to their use. Elemental analyses (C, H and N) were carried out on a Perkin-Elmer CE-440 analyzer. IR spectra were recorded using KBr pellets on a Varian 3100 FT-IR in the 4000–400 cm^{-1} region. UV–vis spectra were recorded on a JASCO V-630 spectrometer in DMSO at room temperature. ^{1}H-NMR spectra were measured on a JEOL AL 300 FT-NMR spectrometer at room temperature. Fluorescence spectra were recorded on a Perkin Elmer LS45 Luminescence spectrometer.

2.2. Preparation of 4-(2,4,6-trioxo-tetrahydro-pyrimidine-5-ylidenemethyl)-benzoic acid (L1)

The compound (L1) was synthesized using reported method [59] by addition of a hot aqueous solution of barbituric acid (1.28 g, 10 mmol) to a solution of 4-carboxy-benzaldehyde (1.50 g, 10 mmol) in methanol. After stirring under reflux for 2.5 h, the reaction mixture was cooled at room temperature and filtered. The solid product thus obtained was washed with ethanol several times and dried *in vacuo*. Yield: 95%, M.P. > 250 °C, IR (KBr): ν_{max}/cm^{-1} 3448 (N–H, O–H), 1746, 1683, 1590 (>C=O, >COO), 1328 (C–O), 836 (C–H), ^{1}H-NMR (DMSO-d_6, δ ppm): 13.18 (s, 1H, COOH), 11.44 (s, 1H, NH), 11.27 (s, 1H, NH), 8.29 (s, 1H, CH), 7.99 (d, 2H, J = 6.6 MHz, Ar–H), 7.95 (d, 2H, J = 9 MHz, Ar–H). ^{13}C-NMR: δ_C (ppm) 193.0 (>C=O, carboxy), 166.6 and 166.5 (>C=O), 163.4 (C2), 15.3 (C14), 150.5 (C13), 149.5 (C11), 149.1 (C12), 129.2 (C10), 128.02 (C9), 125.5 (C8), 120.8 (C7), 116.4 (C6), 85.18 (C15), 53.28 (C4) and 33.6 (C5). ESI-MS, m/z 260 $[M]^+$.

2.3. Binding studies

2.3.1. UV–vis absorption titration

The absorption titrations of L1 separately with urea and acetamide were performed by monitoring the changes in the absorption spectrum of L1 (10^{-4} M) in DMSO by incremental addition of urea and acetamide within (0–325) × 10^{-6} M concentrations in DMSO. The absorption of free urea and acetamide was eliminated initially by keeping their equal quantities separately in host (L1) and reference solution. From the absorption data, the intrinsic association constant K_a was determined from a plot of [guest]/($\varepsilon_a - \varepsilon_f$) vs [guest] using Eq. (1).

$$\frac{[\text{guest}]}{(\varepsilon_a - \varepsilon_f)} = \frac{[\text{guest}]}{(\varepsilon_b - \varepsilon_f) + [K_a(\varepsilon_b - \varepsilon_f)]^{-1}} \quad (1)$$

where [guest] represents the concentration of urea or acetamide. The apparent absorption coefficients ε_a, ε_f, and ε_b correspond to A_{obsd}/[L1], the extinction coefficient of the free L1 and extinction coefficient of L1 in fully bound form, respectively [27–30]. The magnitude of K_a is given by the ratio of slope to the intercept.

2.3.2. Emission titration

Fluorescence spectra were recorded using a Perkin-Elmer LS-45 luminescence spectrometer. Luminescence titrations were performed by maintaining the concentration of L1 constant at 10^{-4} M in DMSO while the concentrations of the urea and acetamide were varied within (0–325) × 10^{-6} M and the fluorescence spectra were measured after incremental additions until fluorescence intensity reached minimum. The linear fit of the fluorescence intensity data at a particular wavelength for 1:3 complexation was obtained using [36] Eq. (2).

$$\frac{I_F^0}{I_F - I_F^0} = \left[\frac{a}{b-a}\right]\left[\frac{1}{(K_S[M])+1}\right] \quad (2)$$

where, I_F^0 and I_F are the fluorescence intensities of the free L1 and L1–guest (urea/acetamide) complex respectively; [M] is the concentration of the guest added for complexation. The K_S is obtained as intercept/slope ratio from the plot of $I_F^0/I_F - I_F^0$ against $[M]^{-1}$.The change in the absorption spectral data at a particular wavelength fitted in the above equation gives the value of K_S.

2.3.3. Structural characterization of composite solids

The samples were mechanically grinded and subjected to structural characterization using powder X-ray diffraction (XRD) Philips PW 1710 diffractometer with CuKα radiation λ = 1.5418 Å. The rating of X-ray generator (30 KV, 20 mA) and other diffractometer parameters such as scanning speed, were kept constant for all diffraction experiments performed on different samples.

2.4. DFT calculations

Molecular geometries of all systems were optimized using density functional theory (DFT) methods at B3LYP/6-31G(d,p) level of calculations using Gaussian09 (G09) program package. The calculations were performed in gas phase and in solution phases where solvents, water and DMSO, were modeled using polarizable continuum model (PCM) method. Geometries of L1 hydrogen bonded with one urea molecule in different positions were optimized and it was found that in the most stable optimized structure urea is hydrogen bonded to the carboxyl group of the L1. An inspection of the structures of these complexes indicates that more urea molecules may be complexed with L1. Therefore, the geometries of the hydrogen bonded complexes of L1 with two, three and four urea molecules were also optimized in gas and solution phases using same level of calculations. The complexes of L1 hydrogen bonded with one, two, and three acetamide molecules were also optimized at the same level of theory in gas and solution phases. The calculations for four acetamide molecules were also tried but it did not satisfy energy convergence criteria. In order to compare urea and acetamide bonding with possible L1 dimerization, hydrogen bonded dimer L1–L1 was also examined. The analyses of vibrational frequencies were performed at the B3LYP/6-31G(d,p) level of theory to ensure that total energy minimum had real vibrational frequencies and obtain zero-point energy (ZPE) corrections to total energies and corresponding thermal energy corrections giving enthalpies at 298.15 K. *In vacuo* bonding energies were calculated with basis set superposition error (BSSE) correction.

3. Results and discussion

Barbiturate derivative (Fig. 1) was prepared using reported procedure [59] and has been characterized using its elemental analysis, IR, NMR, UV–vis, mass spectra, and powder X-ray diffraction data. Its emission property is also studied. To evaluate its receptor property in solution, a titration was performed by the incremental addition of a solution of urea to a solution of L1 both in DMSO at

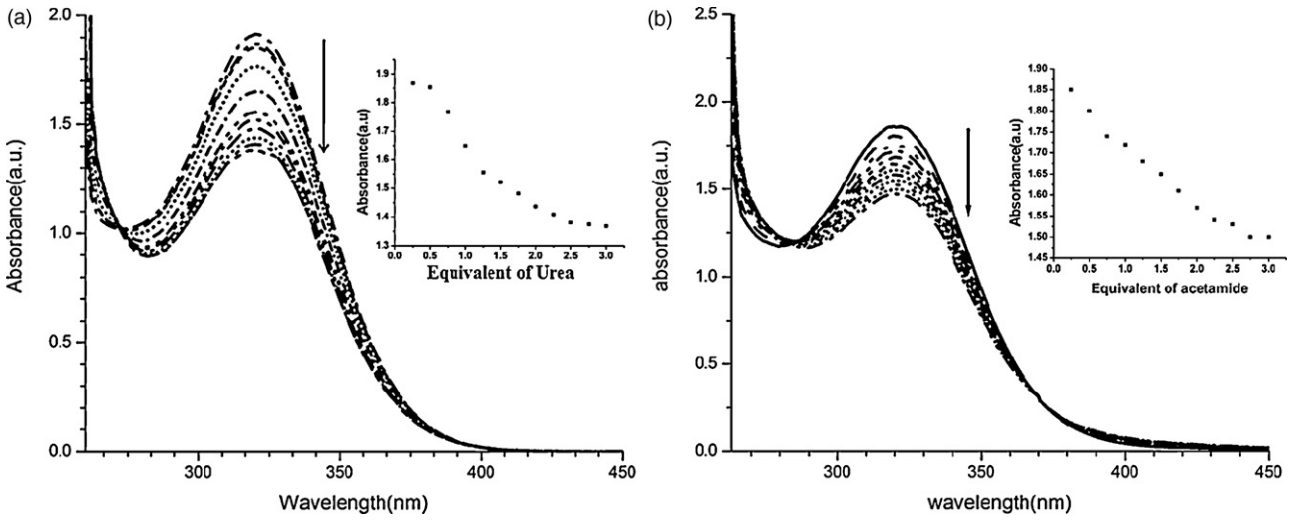
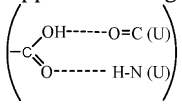
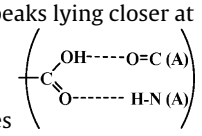


Fig. 2. (a) Absorption spectra of L1 = 10^{-4} M in the absence and in the presence of increasing concentrations of urea (0–325) × 10^{-6} M. Inset: absorbance changes upon increasing urea concentrations. (b) Absorption spectra of L1 = 10^{-4} M in the absence and in the presence of increasing concentrations of acetamide (0–325) × 10^{-6} M. Inset: absorbance changes upon increasing acetamide concentrations.

regular (~3 min.) interval of time. The spectroscopic (UV–vis and fluorescence) variations were recorded. The choice of the solvent was restricted owing to the solubility of L1 in it. A decrease in the absorbance (Fig. 2a) was observed upon increasing the concentrations of urea till 1:3 (L1: urea) stoichiometry was reached. Beyond this stoichiometry, no further significant change occurred in this peak position. An isobestic point is observed at λ_{max} 272 nm (Fig. 2a). Similar addition of acetamide to a solution of L1 showed isobestic point at λ_{max} 283 nm (Fig. 2b). Thus, this experiment supported the formation of L1–urea and L1–acetamide complexes in 1:3 molar ratio. Since no further enhancement in the intensity of the UV–vis absorption peak was observed beyond this stoichiometry, it indicates that complex formation is completed at this molar ratio. The corresponding Job plots (S1) provided additional support to the stoichiometric ratio, where the changes in absorbance ($A_o - A$) of L1 at λ_{max} 320 nm on incremental addition of urea/acetamide were plotted against molar fractions of L1. As a result, maxima were observed at molar fraction of [L1]/([L1]+[urea]) and [L1]/([L1]+[acetamide]) 0.25. It is in consistence with the earlier report [60].

The values of association constants ($K_a = 2.24 \times 10^7$ M^{-1} for urea and $K_a = 2.07 \times 10^7 M^{-1}$ for acetamide) suggest that compound L1 has more binding affinity with urea than for acetamide. This experiment also showed that binding of urea with L1 is ~8 times stronger than its binding with the receptor reported recently by us [61]. This could be considered owing to the presence of a carboxylic group appended in the structural frame of barbituric acid. Thus, L1 was found as a better receptor of urea than earlier reported barbiturate ligand. The presence of carboxyl group attached to phenyl ring enhanced the H-bond formation capability of L1 which is supported by the observation of substantial changes observed in the position of carboxyl proton in the ^{1}H-NMR spectral titration. The formation of extensive H-bonding of L1 separately with urea and acetamide is also expected to quench the fluorescence from free L1 as H-bonding provides a path for electron/energy travel. Thus, attempt was made to investigate the emission from L1. It emitted at λ_{emiss} 438 nm when it was excited at λ_{ex} 350 nm. But the emission from L1 gradually decreases upon incremental addition of either urea (Fig. 3a) or acetamide (Fig. 3b).

The decrease in the emission intensity is continued until addition of 3.0 equiv. of urea/acetamide was completed. Further addition of urea/acetamide did not change the spectrum significantly. The emission experiment supported the formation of H-bonded network using complementary groups present in the skeleton of both urea and acetamide. To investigate the host–guest display of L1 separately with urea and acetamide, ^{1}H-NMR spectroscopic titrations (Fig. 4) were carried out again with the incremental addition of urea and acetamide separately to a fixed concentration of L1 in DMSO-d_6. The corresponding changes were measured after complete (1:3) addition of urea or acetamide in the solution of L1. Being aware of the controversy [31] that exists on the signaling of amide, urea, thiourea or pyrrole-type receptors in organic solvents by barbiturate moieties, i.e. whether an actually hydrogen-bonded complex was formed or whether –OH deprotonates the ligand, the response of compound L1 upon addition of urea or acetamide was investigated. In a typical experiment, the concentration of L1 was kept constant at 10^{-2} M in DMSO-d_6 and aliquots of 4×10^{-1} M concentration of corresponding components (urea/acetamide) were added to it. The characteristic shifts of the –NH protons of both urea and acetamide together with barbiturate group were observed. Two additional peaks observed at δ 10.27 and 10.08 ppm were assigned to the formation of two new H-bonds of types 

. However, other two peaks observed at δ 6.87 and 7.28 ppm were assigned to (U) N–H···O=C (B) or (U) C=O···H–N (B), (U) and (B) represents urea and barbiturate group respectively. The peak observed at δ 5.66 ppm in the spectrum of L1 upon addition of urea is attributed to the –NH protons of free urea. Similarly, with addition of increasing concentration of acetamide to a fixed concentration of L1, new peaks lying closer at δ 10.17 ppm, were assigned to H-bonds of types 

. The peaks observed at δ 7.28, 6.67 and 1.75 ppm were tentatively assigned to H-bonds of types (A) N–H···O (B) or (B) C=O···H–N (A, acetamide) and $-CH_3$ protons of acetamide respectively. However, description of such complex spectra calls for deeper investigation using higher resolution NMR spectrometer. Since crystals of these H-bonded complexes could not be isolated, attempts were made to look into the spectral behaviour of the solid obtained after fine mechanical mixing of L1 separately with urea and acetamide in 1:3 stoichiometry. Corresponding composites were characterized by IR spectral data followed by PXRD studies and ^{1}H-NMR spectral data.

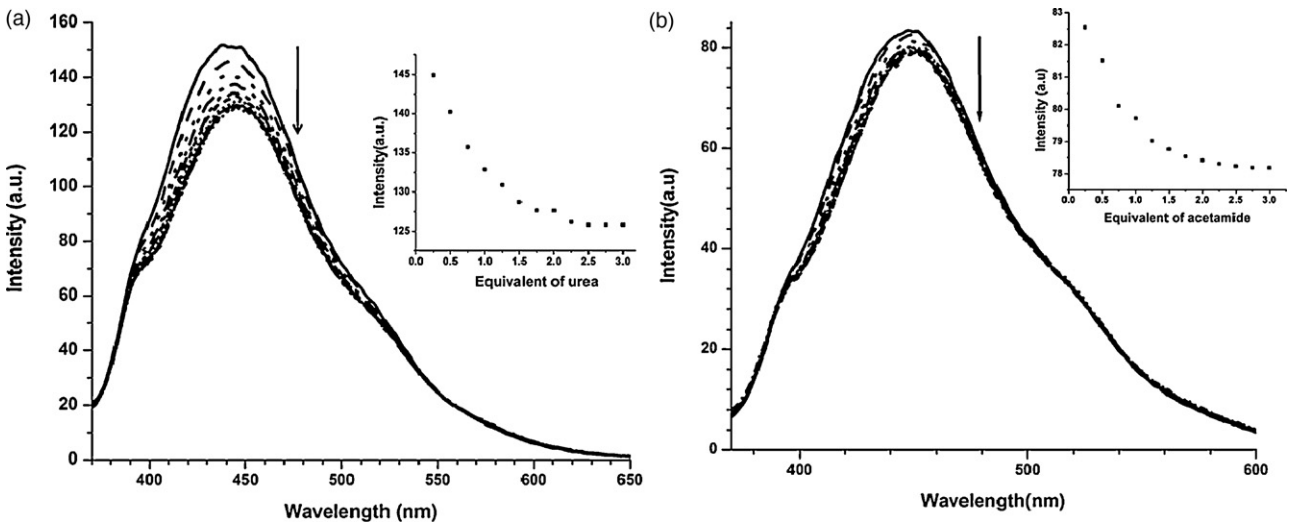


Fig. 3. (a) Emission spectra of L1 = 10^{-4} M in the absence and in the presence of increasing concentrations of urea (0–325) × 10^{-6} M. Inset: emission intensity changes upon increasing urea concentrations. (b) Emission spectra of L1 = 10^{-4} M in the absence and in the presence of increasing concentrations of acetamide (0–325) × 10^{-6} M. Inset: emission intensity changes upon increasing acetamide concentrations.

IR spectra of free L1, urea, acetamide, L1·urea and L1·acetamide adducts (S2) showed that ν(N–H) vibrations of free L1 (3192 cm^{-1}), urea (3445 cm^{-1}, 3360 cm^{-1}) and acetamide (3392 cm^{-1}) shifted to 3198 cm^{-1}, 3448 cm^{-1} and 3365 cm^{-1} as well as 3201 cm^{-1} and 3421 cm^{-1} respectively. Thus, shift in (N–H) vibrations of free components in their respective adducts supported that components interact with their complementary partners through corresponding NH groups. These adducts were further characterized by their ^{1}H-NMR spectral studies. Stronger binding of urea with L1 was again supported by the appearance of new peaks in the spectrum of L1·urea adduct apart from the original peaks of L1 and urea (S3).

The PXRD patterns of all components and their adducts were also recorded (S4). The grain size and the lattice strain of the samples can be calculated from the integral width of the physical broadening profile. Therefore, grain size has been calculated using Scherrer equation (3).

$$D = \frac{k\lambda}{\beta c \cos\theta} \tag{3}$$

where D is grain size, K is shape factor, λ is X-ray wavelength, β is HwHm (Half width at Half maximum) and θ is Bragg's angle. Crystallite sizes calculated using this equation was found to be 36.0 nm for urea, 9.2 nm for acetamide, 12.5 nm for L1, 15.2 nm for L1·urea adduct and 17.5 nm for L1·acetamide adduct.

The ZPE-corrected binding energies (ΔE), and the corresponding enthalpy changes (ΔH) at 298.15 K (kcal mol^{-1}) in gas phase, aqueous and DMSO media of free urea, acetamide, L1 and the all examined complexes are listed in Table 1. Depicts examined

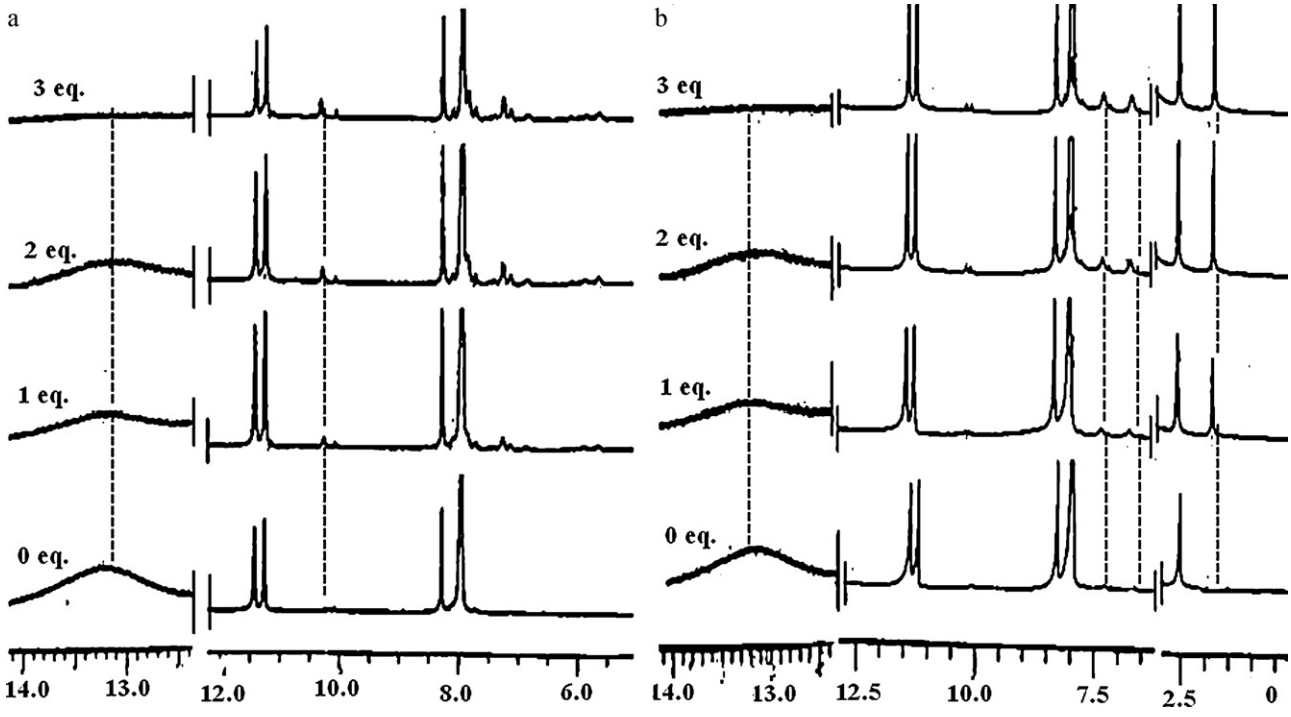


Fig. 4. ^{1}H-NMR spectra of L1 in DMSO-d_6 upon addition of different equivalents of (a) urea and (b) acetamide.

Table 1
Summary of data of DFT calculation.

Structures	Energy (ZEP cor.) (atomic units)	Enthalpies (atomic units)	Change in energies (ΔE) (kcal mol^{-1})	Change in enthalpies (ΔH) (kcal mol^{-1})
Urea				
Gas	−225.209785	−225.204469		
DMSO	−225.22304	−225.217639	–	–
Water	−225.223238	−225.217833		
Acetamide				
Gas	−209.150156	−209.145358		
DMSO	−209.165659	−209.159604	–	–
Water	−209.160219	−209.154636		
L1				
Gas	−947.60658	−947.590171		
DMSO	−947.623517	−947.606991	–	–
Water	−947.623742	−947.607217		
L1–one urea (conf. a in Fig. 5)				
Gas (BSSE cor.)	−1172.846323	−1172.824215	−14.925	−14.671
DMSO	−1172.870159	−1172.847774	−14.545	−14.523
Water	−1172.870505	−1172.848112	−14.762	−14.472
L1–one urea (conf. b in Fig. 5)				
Gas (BSSE cor.)	−1172.833614	−1172.811243	−10.824	−10.419
DMSO	−1172.863934	−1172.841401	−10.904	−10.524
Water	−1172.864317	−1172.841774	−10.879	−10.498
L1–one urea (conf. c in Fig. 5)				
Gas (BSSE cor.)	−1172.833479	−1172.81111	−10.739	−10.335
DMSO	−1172.863728	−1172.841084	−10.775	−10.325
Water	−1172.86410	−1172.841451	−10.743	−10.292
L1–one urea (conf. d in Fig. 5)				
Gas (BSSE cor.)	−1172.833249	−1172.810873	−10.595	−10.186
DMSO	−1172.864013	−1172.841414	−10.954	−10.532
Water	−1172.864395	−1172.841791	−10.928	−10.505
L1–one urea (conf. e in Fig. 5)				
Gas (BSSE cor.)	−1172.832314	−1172.809895	−10.008	−9.573
DMSO	−1172.863826	−1172.841414	−10.836	−10.442
Water	−1172.863827	−1172.841269	−10.572	−10.178
L1–two urea (Fig. 8a)				
Gas (BSSE cor.)	−1398.066858	−1398.038771	−25.545	−24.888
DMSO	−1398.110510	−1398.082087	−25.673	−24.986
Water	−1398.111009	−1398.082571	−25.597	−24.905
L1–three urea (Fig. 9a)				
Gas (BSSE cor.)	−1623.292159	−1623.25808	−35.281	−34.201
DMSO	−1623.35037	−1623.315802	−35.714	−34.567
Water	−1623.351056	−1623.316468	−36.145	−34.985
L1–four urea (Fig. 10)				
Gas (BSSE cor.)	−1848.512222	−1848.471739	−41.731	−39.967
DMSO	−1848.582429	−1848.542298	−41.249	−40.003
Water	−1848.581635	−1848.541535	−41.389	−40.153
L1–one acetamide (conf. [a]a)				
Gas (BSSE cor.)	−1156.779677	−1156.757028	−14.396	−13.491
DMSO	−1156.806136	−1156.784201	−14.088	−13.547
Water	−1156.806412	−1156.785421	−13.915	−13.496
L1–one acetamide (conf. [a]b)				
Gas (BSSE cor.)	−1156.772864	−1156.749901	−10.120	−9.019
DMSO	−1156.800269	−1156.777272	−14.466	−9.817
Water	−1156.800601	−1156.777601	−13.442	−9.789
L1–two acetamide (Fig. 8b)				
Gas (BSSE cor.)	−1365.946141	−1365.916963	−24.629	−22.638
DMSO	−1365.982616	−1365.953425	−24.442	−23.320
Water	−1365.983008	−1365.953804	−24.365	−23.230
L1–three acetamide (Fig. 9b)				
Gas (BSSE cor.)	−1575.111371	−1575.075559	−34.088	−30.945
DMSO	−1575.158825	−1575.12308	−34.153	−32.324
Water	−1575.159138	−1575.123493	−34.346	−32.583
L1–L1 (Fig. 7)				
Gas (BSSE cor.)	−1895.232481	−1895.198846	−12.124	−11.611
DMSO	−1895.266244	−1895.232574	−12.054	−11.383
Water	−1895.266651	−1895.232574	−12.027	−11.667

[a] Acetamide is attached in place of urea.

configurations of L1 hydrogen bonded with one urea molecule (Fig. 5).

It is evident from the B3LYP/6-31G(d,p) level calculation both *in vacuo* and employing polarizable-continuum model (PCM) that acid functional group is more reactive than the remaining part of (L1) ligand. As seen in Table 1 the conformation A is about 4.0 kcal mol^{-1} more stable than remaining conformations. The optimized structures of the most stable forms of complexes with one urea and acetamide are presented in Fig. 6. Each of the complexes of L1 involving one urea and one acetamide molecules is stabilized by two hydrogen bonds each, out of which one hydrogen bond is stronger than the other. The two hydrogen bonding distances in the complexes involving one urea molecule lie in the range 1.555–1.912 Å, while those in the complexes

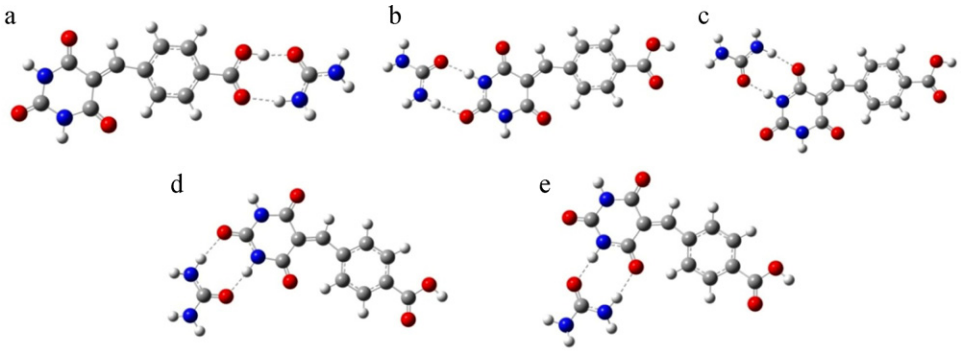


Fig. 5. Conformations of the complex of L1 with one urea optimized at the B3LYP/6-31G(d,p) level of theory.

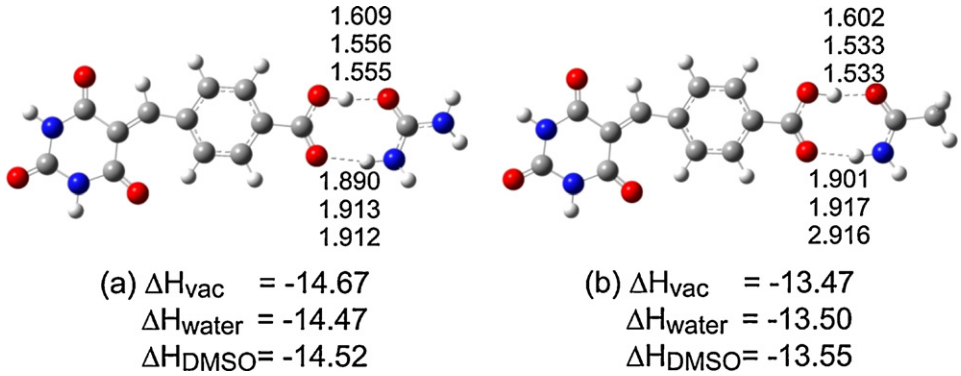


Fig. 6. Optimized structures of L1 with one urea (a) and acetamide (b). The enthalpy changes (ΔH) at 298.15 K (kcal mol^{-1}) of the complexes obtained at the B3LYP/6-31G(d,p) level of theory in gas phase, aqueous and DMSO media are given. Hydrogen bond lengths [Å] in gas phase, aqueous and DMSO media are given from top to bottom, respectively.

involving one acetamide molecule lie in the range 1.533–2.916 Å respectively.

The ΔH values for L1–L1 dimer (Fig. 7) listed in Table 1, indicate the lower stability of dimer than corresponding aggregates of L1 with one urea and one acetamide. The binding energies (ΔE) and the corresponding enthalpy changes (ΔH) of the all complexes showed stable structures in gas phase as well as in aqueous and DMSO medium.

The optimized structures and ΔH values of the complexes of L1 with two urea molecules and those of L1 with two acetamide molecules are presented in Fig. 8.

Similarly, the optimized structures and ΔH values of the complexes of L1 with three urea molecules and those of L1 with three acetamide molecules are presented in Fig. 9.

Further, the binding energies and the corresponding enthalpy changes of the complexes of L1 with one, two, and three urea molecules reveal that the magnitudes of ΔE and ΔH values increased in going from one urea to three urea molecules. The ΔH of the complex of L1 with three urea molecules is found to be 34.20, 34.98 and 34.57 kcal mol^{-1} in gas phase, aqueous and DMSO medium respectively. The ΔE of the complex of L1 with two urea molecules is found to be 24.89, 24.91 and 24.99 kcal mol^{-1} in gas phase, aqueous and DMSO medium (Table 1), respectively. The experimental values of binding constant were also found to increase from 1:1, 1:2, and 1:3 binding of L1 with urea and acetamide. The theoretical calculations agree to the experimental results. It appears that the binding of L1 with three urea molecules is favorable over the binding of L1 with one or two urea molecules. Similar observations were made theoretically for the binding of L1 with two and three acetamide molecules. A comparison of ΔE and ΔH values of the complexes of L1 with urea and those of the complexes of L1 with acetamide shows that the binding of

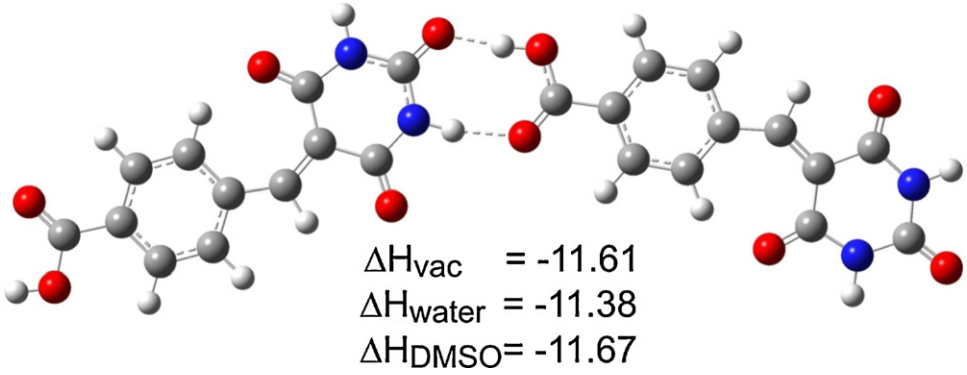


Fig. 7. Optimized structure of L1–L1 dimer. The enthalpy changes (ΔH) at 298.15 K (kcal mol^{-1}) of the complexes obtained at the B3LYP/6-31G(d,p) level of theory in gas phase, aqueous and DMSO media are given.

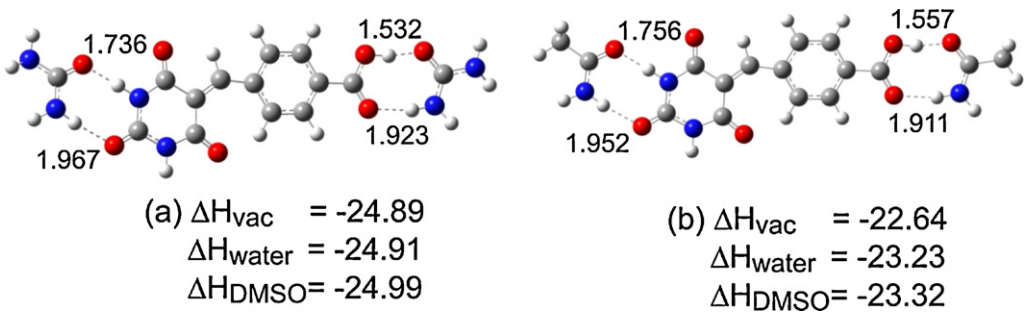


Fig. 8. Optimized structures of L1 with two urea (a) and acetamide (b). The enthalpy changes (ΔH) at 298.15 K (kcal mol^{-1}) of the complexes obtained at the B3LYP/6-31G(d,p) level of theory in gas phase, aqueous and DMSO media are given. Hydrogen bond lengths [Å] in aqueous media are given.

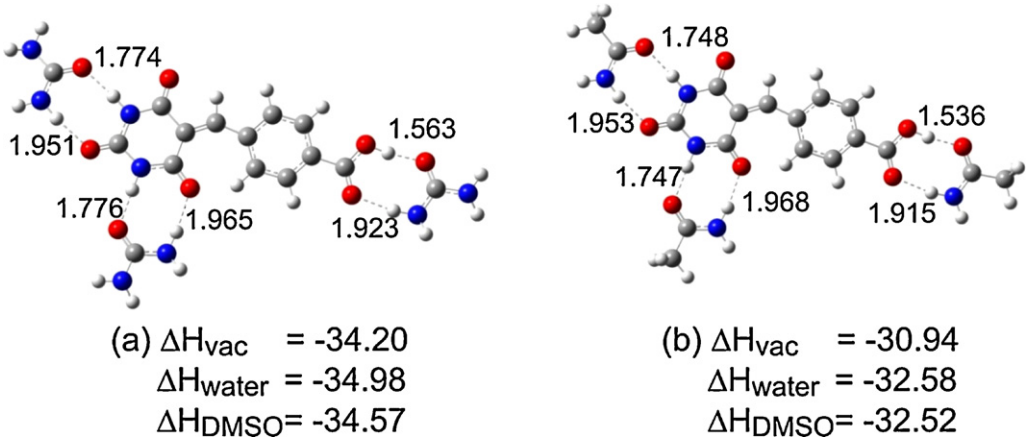


Fig. 9. Optimized structures of L1 with three urea (a) and acetamide (b). The enthalpy changes (ΔH) at 298.15 K (kcal mol^{-1}) of the complexes obtained at the B3LYP/6-31G(d,p) level of theory in gas phase, aqueous and DMSO media are given. Hydrogen bond lengths [Å] in aqueous media are given.

L1 with urea is stronger than that of L1 with acetamide. As the experiments were performed in DMSO medium, the ΔE and ΔH values of the complexes of L1 with three urea (Fig. 9a) and three acetamide (Fig. 9b) were also calculated in the DMSO medium at the B3LYP/6-31G(d,p) level using the polarizable-continuum model. The ΔE and ΔH values of the complexes were found to be similar in both the aqueous and DMSO medium. Thus, theoretical calculations strongly support our experimental findings that binding of L1 with urea molecules in DMSO medium is favorable over the binding with acetamide molecules. Although experimentally no significant change in the UV–vis spectrum was observed beyond 1:3 stoichiometry of L1 with urea, yet theoretically it was tried. As given in Table 1, data show that fourth bonding of urea to L1 (Fig. 10) is weaker since change of enthalpy is about 5.0 kcal mol^{-1} as compared to that obtained in 1:3 ratio in which enthalpy change is about 10.0 kcal mol^{-1} as compared to 1:2 ratio of L1 to urea. However, in case of in 1:4 ratio of L1 with acetamide, no convergence was obtained.

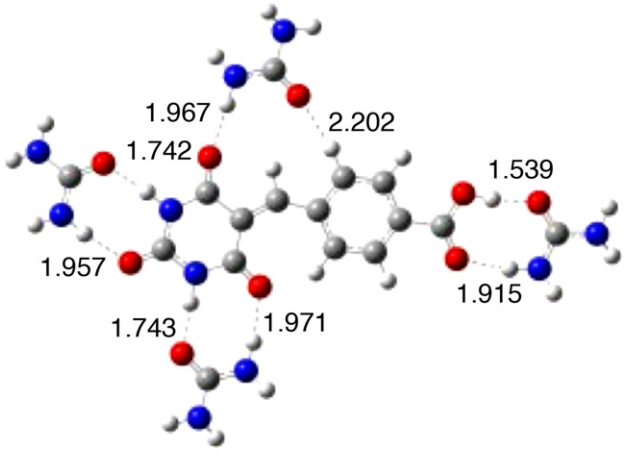


Fig. 10. Optimized structures of L1 with four urea at the B3LYP/6-31G(d,p) level of theory in gas phase, aqueous and DMSO media are given. Hydrogen bond lengths [Å] in aqueous media are given.

4. Conclusion

The designed barbiturate derivative L1 possessing H (D–A–D) binding sites is found very simple and interesting receptor for both urea and acetamide. The receptor molecule (L1) binds separately with three molecules of urea and acetamide in micro molar concentration range as monitored by their absorption, emission and ^{1}H-NMR spectroscopic measurements. The composite supramolecular adducts of L1 with urea and acetamide are prepared separately by grinding the components together. Theoretical calculations carried out at B3LYP/6-31G(d,p) level using the polarizable-continuum model in gas phase, aqueous, and DMSO medium support the experimental results. Thus, construction of a carboxyl group on the skeleton of a barbituric acid provides simple and novel receptor for urea and acetamide.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.saa.2011.08.079.

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