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Intra- versus intermolecular hydrogen bonding equilibrium in 2-hydroxy-*N,N*-diethylbenzamide†

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Complex studies of the intramolecular versus intermolecular hydrogen bond equilibrium and internal rotation of the *N,N*-diethylamine group in 2-hydroxy-*N,N*-diethylbenzamide were conducted. The intramolecular versus intermolecular process in 2-hydroxy-*N,N*-diethylbenzamide was studied by UV–Vis, NMR, IR and Vapour Pressure Osmometric (VPO) methods as a function of temperature and concentration in non-polar, basic and protic solvents. The unequal positions of the ethyl groups were analysed and the energy barrier to the re-orientation was defined by the NMR method. This paper presents a study into a complicated nature of competitive interaction 2-hydroxy-*N,N*-diethylbenzamide with the environment by means of the aforesaid methods. Copyright © 2008 John Wiley & Sons, Ltd.

Keywords: H bonds; amides; self-association; dynamic NMR; matrix-isolation

INTRODUCTION

Ortho-hydroxy benzamides are of great interest in research because of their application in the pharmaceutical industry.[1] Study of the proton transfer process in the excited state[2–8] seems worthy in view of the potential use of *ortho*-hydroxy benzamides as laser materials.[9] As to the ground state, the literature presents studies of the influence of substituents on the conformation of the benzamides in the amide fragment.[10–17] Thus, research on the ν(OH) stretching vibrational bands in IR spectra and quantum-mechanical calculations revealed that the intramolecular O—H···O hydrogen bond strength in *ortho*-hydroxy benzamides depends on the substituent in the *N,N*-dialkyl fragment according to the sequence $NHCH_3 < NH_2 < N(CH_3)_2 < N(CH_2CH_2)_2CH_2 < N(CH(CH_3)CH_2)_2CH_2$.[10–12]

However, this sequence is not fully consistent with the impact of alkyl substitution in the *N,N*-dialkyl fragment on the basicity of the oxygen atom in the amide group. According to papers [13,14], the inductive effect of the methyl substituent governs basicity more than the resonance effect and strengthens the oxygen atom basicity (e.g. $O{=}C(R)NH_2 < O{=}C(R)NHCH_3 < O{=}C(R)N(CH_3)_2$). Even so, Alkorta *et al.*,[15] examining *N,N*-diethyl formamide, *N*-formylaziridine and *N*-formylazirine, disclosed a dependence of the basicity of the oxygen and nitrogen atoms on the configuration (planar, pyramidal) of the amide fragment. Based on experimental and theoretical studies, Kim *et al.*[16] reported a phenomenon in which replacement of the methyl substituent by ethyl brought about a decrease in the intermolecular hydrogen bond strength between the thioacetamide and tertiary amides. This discrepancy can be explained by the steric effect actively operating on the configuration of the amide fragment and this indirectly changing the basicity of the oxygen atom.[17,18] The steric repulsion increase in *ortho*-hydroxy benzamides leads to a break of the intramolecular hydrogen bond in the solid state.[18–21] Another cause of the break is the weakening of the π-electronic coupling between the phenol ring and the amide group due to competitive resonance.[18,22,23]

2-Hydroxy-*N,N*-diethylbenzamide was selected for the study of environment influence on amides. In order to characterise the action of a solvent on *ortho*-hydroxy benzamides, we conducted the studies using IR, UV, NMR and VPO measurements as well as Density Functional Theory (DFT) calculations.

RESULTS AND DISCUSSION

Atypical bathochromic shift band in UV–Vis spectra

UV–Vis spectra of 2-hydroxy-*N,N*-diethylbenzamide recorded in different solvents revealed two π–π^* bands (Figure 1). The hypsochromic shifted band corresponds to the complex 2-hydroxy-*N,N*-diethylbenzamide with a protic or basic solvent and the shifted bathochromic band is assigned to a compound with intramolecular hydrogen bond. The two bands are similar in that the increase of the solvent polarity (the E_T parameter increase) causes a blue shift of both bands (Figure 2). Such a behaviour of the π–π^* band in electronic spectra of *ortho*-hydroxy aryl Schiff bases is observed in the proton transfer form[24,25] and is termed 'negative solvatochromy'. The negative solvatochromy characteristic of both bands of 2-hydroxy-*N,N*-diethylbenzamide shows equal amounts of *ortho*-quinoic and non-polar canonical structures in describing the tautomeric form (Scheme 1). The structural studies and calculations presented a clear difference between the resonance structures of the enol form for the *ortho*-hydroxy aryl Schiff bases and the

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† *Dedicated to Professor V.E. Borisenko on the occasion of his 70th birthday.*

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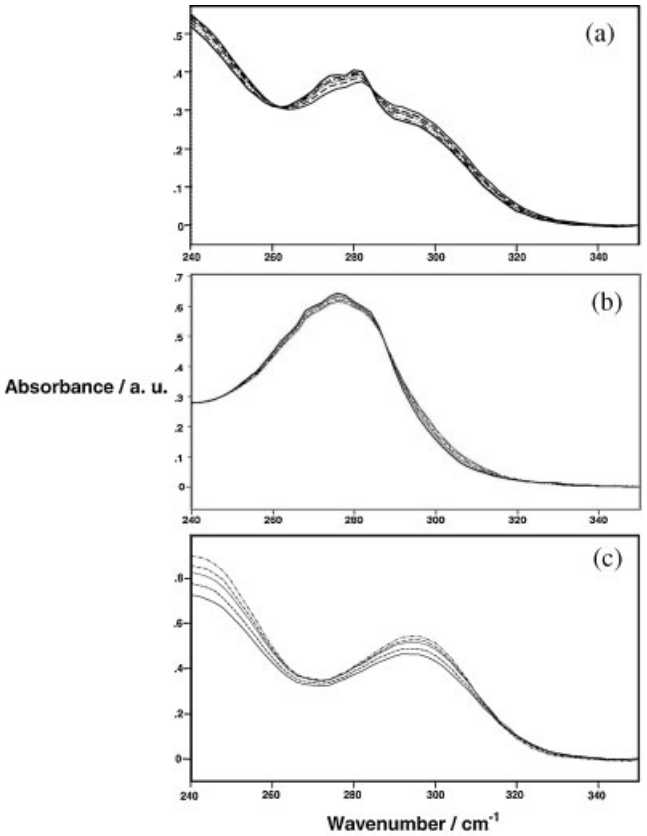


Figure 1. UV–Vis spectra of 2-hydroxy-*N,N*-diethylbenzamide in CH_3CN (a, $c = 10^{-5}$ M, d = 1 cm; from top to bottom 298 K, 275 K, 265 K, 256 K, 246 K, 236 K), C_4H_9OH (b, $c = 10^{-5}$ M, d = 1 cm; from top to bottom 296 K, 283 K, 274 K, 266 K, 257 K, 234 K) and CH_2Cl_2 (c, $c = 10^{-5}$ M, d = 1 cm; from top to bottom 216 K, 236 K, 256 K, 275 K, 297 K) as a function of temperature

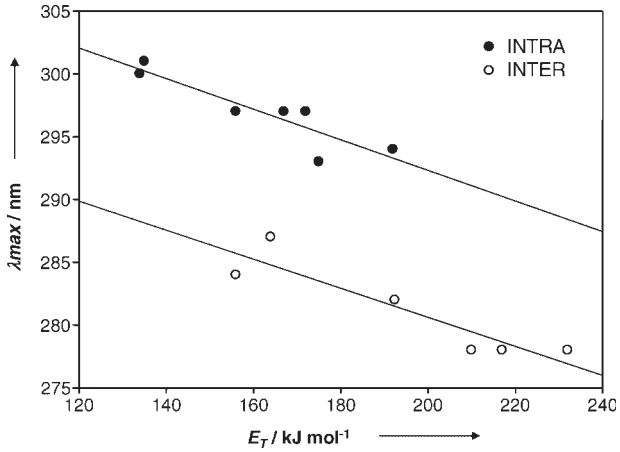
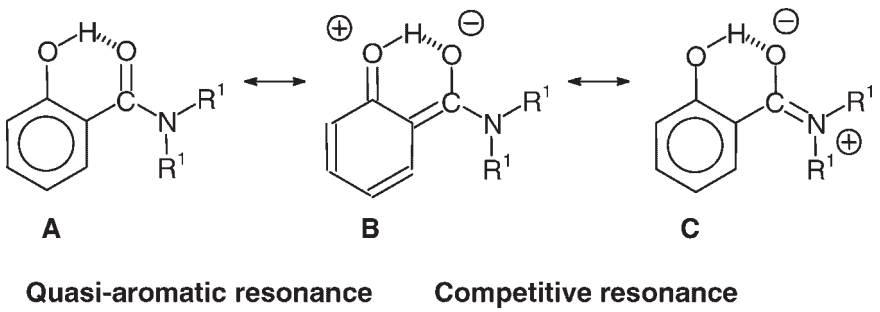


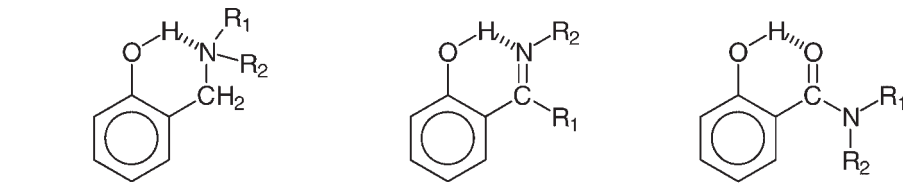
Figure 2. The correlations between the maximum of the π–π^* bands and ET (kJ mol^{-1}) for 2-hydroxy-*N,N*-diethylbenzamide

ortho-hydroxy benzamides.[18] Comparison of the bond lengths of *ortho*-hydroxy benzamides and *ortho*-hydroxy aryl Schiff bases (for e.g. *cf.* data of References 18 and 26) confirms that the degree of the *ortho*-quinoic form in the latter compound is visibly larger than in the former. The resonance is more active in the *ortho*-hydroxy aryl Schiff bases. A similar inference can be made upon collation of the electronic spectra. The negative solvatochromic effect is larger in *ortho*-hydroxy aryl Schiff bases ($\Delta\lambda_{max} \approx 25$ nm)[27] than in 2-hydroxy-*N,N*-diethylbenzamide ($\Delta\lambda_{max} < 10$ nm) (Figure 2).

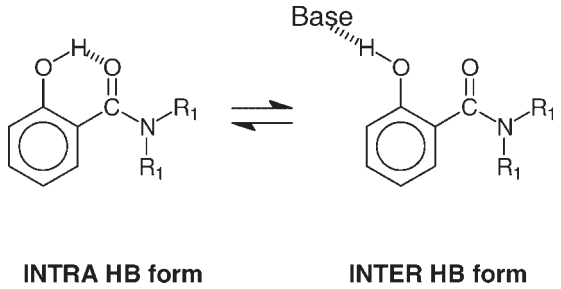
A marked difference between *ortho*-hydroxy aryl Schiff bases, *ortho*-hydroxy aryl Mannich bases and 2-hydroxy-*N,N*-diethylbenzamide (Scheme 2) is that the solvent polarity increase is accompanied by the following phenomena: (1) in *ortho*-hydroxy aryl Schiff bases the bathochromic shift of the π–π^* band is conditioned by the proton transfer process;[27,28] (2) in *ortho*-hydroxy aryl Mannich bases the same shift of the π–π^* band is also caused by the proton transfer form[29,30] and the subsequent break of the intramolecular hydrogen bond and the ionic pair formation;[31,32] (3) in the 2-hydroxy-*N,N*-diethylbenzamide the hypsochromic shift of the π–π^* band resulted from the intramolecular hydrogen bond breakage (Scheme 3). The phenomenon in 2-hydroxy-*N,N*-diethylbenzamide is not caused by the proton transfer process, as in *ortho*-hydroxy aryl Schiff bases, and not evoked by the formation of the intermolecular ionic pairs as in *ortho*-hydroxy aryl Mannich bases. The break of the intramolecular hydrogen bond in 2-hydroxy-*N,N*-diethylbenzamide is the result of strong steric squeezing of the ethyl groups (allylic strain) leading to the amide group turn and attenuated π-electronic coupling between the phenol and amide moieties.[18] Such disruption of the intramolecular hydrogen bond is likely to be caused by either additional impact of the crystal packing[18–21] or enhanced solvent competition by either donor or acceptor protic solvent.[33–36] However in the solid state, if the intramolecular hydrogen bond breaks, 2-hydroxy-*N,N*-diethylbenzamide forms a chain of intermolecular hydrogen bonds,[18] whereas *ortho*-hydroxy aryl Mannich bases develop dimers.[37] The similarity of 2-hydroxy-*N,N*-diethylbenzamide (according to DFT calculations, Figure 3, the torsional C2C1C8O9 and C2C1C8N10 angles equal −27.9 and 151.9°, respectively) and *ortho*-hydroxy aryl Mannich bases[37]



Scheme 1.



Scheme 2.



Scheme 3.

appears in the visible declination of the proton-acceptor atom from the phenol ring plane in the form with an intramolecular hydrogen bond.

According to the literature,[7,9,18–23] proton transfer is not observed in salicylamides in the ground state. To verify the phenomenon, we calculated the non-adiabatic potential curve to detect a local minimum in the vicinity of the amide oxygen.[26] However, a local minimum was not found for 2-hydroxy-*N,N*-diethylbenzamide, thus excluding the existence of proton transfer (Figure 4).

To define the thermodynamic characteristics of the transition from the form with an intramolecular hydrogen bond (INTRA form) to the form with an intermolecular hydrogen bond (INTER form) (Scheme 3), we studied the electronic spectra of 2-hydroxy-*N,N*-diethylbenzamide in the non-polar (CH_2Cl_2), basic (CH_3CN) and protic (C_4H_9OH) solvents as a function of temperature (Figure 2). In the non-polar solvent a single π–π^* band is observed, which indicates the presence of the INTRA form only. In the basic and protic solvents a new, hypsochromically shifted band (275 nm) appears with decreasing temperature and a reduction in the intensity of the bathochromically shifted band (295 nm) showing the presence of INTRA $\rightleftharpoons$ INTER equilibrium. The enthalpy of this process is 5.8 and 1.5 kJ mol^{-1} (1 kcal = 4.184 kJ) in CH_3CN and C_4H_9OH, respectively (Table 1). As for the difference in the energy values obtained for alcoholic and acetonitrile solutions, it is conditioned by a weaker interaction between 2-hydroxy-*N,N*-diethylbenzamide and acetonitrile and the necessity of a larger energy contribution than in butyl alcoholic solution.

N,N-diethylamine group rotation

The NMR spectroscopy method allows the estimation of the energetic barrier of internal rotation of the alkyl group and the proton exchange described in References 38–40. NMR spectra at different temperatures and in different solvents were recorded to investigate the processes in the molecule. A temperature-dependent splitting of the ethyl groups' bands emerges in the ^{1}H and ^{13}C spectra (Figure 5). The splitting of the ^{1}H and ^{13}C bands in different solvents as a function of temperature is conditioned by the unequal position (*trans* and *cis*) of the ethyl groups (according to DFT calculations, with the C1C8N10C11 and C1C8N10C13 angles equal to −20.5 and 177.0°, respectively) with respect to the carbonyl group (Figure 3). A comparison of the energetic barrier values for 2-hydroxy-*N,N*-diethylbenzamide ($\Delta G^{\#} = 48.8$ kJ mol^{-1}, Table 2) and *N,N*-diethylbenzamide ($\Delta G^{\#} = 62.6$ kJ mol^{-1})[41] discloses a significant reduction in the energy barrier ($\Delta G^{\#} = 13.8$ kJ mol^{-1}) related to the rotation

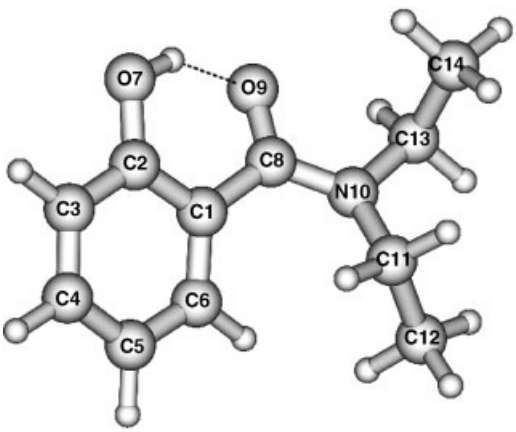


Figure 3. The calculated structure (B3LYP/6-311++G(d,p)) and the atom-labelling scheme of 2-hydroxy-*N,N*-diethylbenzamide

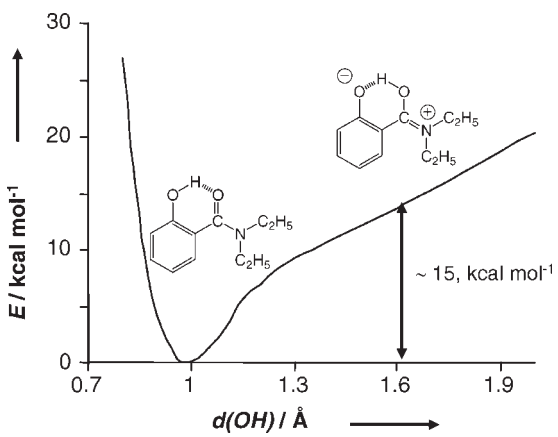


Figure 4. The non-adiabatic potential function for the proton displacement (B3LYP/6-31+G(d,p) calculation) for 2-hydroxy-*N, N*-diethylbenzamide

Table 1. The thermodynamic characteristics of INTRA ⇌ INTER hydrogen bonding equilibrium (from UV–Vis spectra) for 2-hydroxy-*N,N*-diethylbenzamide in CH_3CN and C_4H_9OH

Solvent	T (K)	$K_{intra\text{-}inter}$	$\Delta S^o_{intra-inter}$ (J mol^{-1} K^{-1})	$\Delta G^o_{intra-inter}$ (J mol^{-1})	$\Delta H^o_{intra-inter}$ (J mol^{-1})
CH_3CN	298	1.90	24.7 ± 2	−1584 ± 100	
	275	1.55	24.6 ± 2	−1003 ± 100	
	265	1.47	25.0 ± 2	−848 ± 100	5777 ± 500
	256	1.29	24.7 ± 2	−549 ± 100	
	246	1.14	24.6 ± 2	−273 ± 100	
	236	1.04	24.8 ± 2	−72 ± 100	
C_4H_9OH	298	0.76	7.3 ± 1	−678 ± 100	
	275	0.71	8.2 ± 1	−773 ± 100	
	265	0.71	8.5 ± 1	−763 ± 100	1503 ± 500
	256	0.68	9.0 ± 1	−809 ± 100	
	246	0.67	9.4 ± 1	−816 ± 100	
	236	0.64	10.0 ± 1	−862 ± 100	

of the *N,N*-diethylamine group in the studied compound. This can be explained as follows: with the substitution of the hydroxyl group in the *ortho* position, three factors influence the *N,N*-diethylamine group's rotation. First, resonance weighting of structure C competes with structure B which decreases the C—N bond order and leads to decreasing the energetic barrier. The next factor, steric repulsion between the oxygen atoms and between the ethyl group and phenol moiety (allylic strain), must increase the non-planarity of the molecule and the energetic barrier (*cf. ortho*-methoxy-*N,N*-dimethylbenzamide and *para*-methoxy-*N,N*-dimethylbenzamide, $\Delta G^{\#} = 76.9$ and 61.0 kJ mol^{-1},[36] respectively). However, intramolecular hydrogen bonding (the third factor) brings about flattening of the molecule and compensates the action of the steric effect and increases the resonance between the hydroxyl and amide groups.

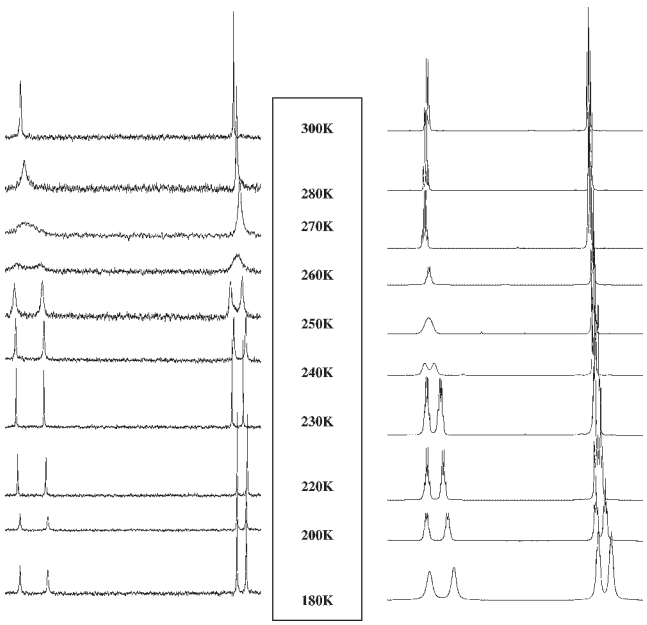


Figure 5. The temperature dependency on the position of the ^{1}H and ^{13}C bands of ethyl group of 2- hydroxy-*N,N*-diethylbenzamide in CD_2Cl_2

Gryff-Keller *et al.*[41] showed that a decrease in solvent polarity causes growth of the energetic barrier on the rotation of the *N,N*-diethylamine group in benzamide derivatives. However, the expected tendency of C_4H_8O ($\varepsilon = 7.6$) < CH_2Cl_2 ($\varepsilon = 8.9$) < C_5H_5N ($\varepsilon = 12.4$) < CH_3CN ($\varepsilon = 37.5$) for the energy barrier is not found for 2-hydroxy-*N,N*-diethylbenzamide due to the intramolecular hydrogen bond break in basic solvents and, as a consequence, we observe energy barrier growth according to the $C_4H_8O < CH_2Cl_2 < CH_3CN < C_5H_5N$ chain. The interpretation of these NMR data is quite difficult because of two phenomena that the molecule undergoes: rotation of the *N,N*-diethylamine fragment (in view of the unequal position of the alkyl groups) and INTRA ⇌ INTER equilibrium. Of course, the INTRA ⇌ INTER equilibrium influences the ethyl groups rotation and, consequently, a splitting of the bands in NMR spectra. Even so, the thermodynamic values obtained from NMR spectra define the rotation of ethyl group and cannot be directly interpreted as thermodynamic parameters of hydrogen bonding.

Interpretation of IR spectra

According to UV–Vis and NMR results there exists an intramolecular bond in the aprotic and non-basic solvents and an intermolecular bond in protic and basic solvents in the studied compound. Infrared study of 2-hydroxy-*N,N*-diethylbenzamide shows a marked difference in the spectra depending on environment. For discussion, we selected two of the most interesting ranges in the area of the stretching ν(OH) (3800–2400 cm^{-1}) and ν(C═O) (1700–1540 cm^{-1}) vibrations, (Figure 6). Two bands of equal intensity are observed in non-polar solvent (INTRA form) in the 1700–1540 cm^{-1} range. For assignments of these bands, the infrared spectrum of the compound was studied in an argon matrix (Figure 7) and quantum-mechanical calculations were completed (Table 3). According to the calculations, the bands at 1636 and 1598 cm^{-1} are assigned to the ν(C═O) and ν(C═C) stretching vibrations, respectively. The ν(C═O) vibration is strongly coupled with a deformational vibration mode of the hydroxyl group (δ(OH)) and the stretching vibration of carbon–carbon bonds of the aromatic ring (ν(C═C)). Markedly, the break of the intramolecular hydrogen bond by a basic solvent calls forth the emergence of two new bands in the

Table 2. NMR spectroscopic and thermodynamic characteristics of the rotation of the *N,N*-diethylamine group for 2-hydroxy-*N,N*-diethylbenzamide in C_4D_8O, CD_2Cl_2, CD_3CN and C_5D_5N

	T_c, ^{13}C NMR (K)		$\Delta\delta(^{13}C)$ (Hz)		Energy ^{13}C NMR (kJ mol^{-1})		T_c, ^1H NMR (K)		$\Delta\delta(^1H)$ (Hz)		Energy ^1H NMR (kJ mol^{-1})	
T (K)	CH_2	CH_3	CH_2	CH_3	CH_2	CH_3	CH_2	CH_3	CH_2	CH_3	CH_2	CH_3
						C_4D_8O						
260			278.67		48.74							
250			293.93	98.98	48.62	48.93						
240	260	250	292.33	101.99	48.63	48.87	240	240	65.77	14.21	47.71	50.77
230			291.92	100.78	48.64	48.90			71.56	26.83	47.54	49.50
220			291.13	97.98	48.64	48.95			76.82	30.52	47.40	49.24
						CD_2Cl_2						
260			253.43		48.94							
250			293.56	120.74	48.63	48.52						
240			301.90	124.72	48.56	48.45			34.76		48.98	
230	260	250	291.58	119.42	48.64	48.54	240	230	56.37	18.22	48.02	50.27
220			290.25	114.77	48.65	48.63			64.42	19.07	47.75	50.18
200			287.27	103.83	48.67	48.83			84.77	37.72	47.20	48.82
180			284.61	84.83	48.69	49.25			99.18	52.56	46.89	48.16
177			284.61	95.20	48.69	49.01			100.45	54.25	46.86	48.09
						CD_3CN						
260			299.55	71.08	48.58	51.69			57.35		52.15	
250			297.95	84.32	48.59	51.32			82.60	34.20	51.37	51.14
240	260	260	296.55	83.59	48.60	51.34	260	250	95.23	43.14	51.06	50.66
233			295.55	81.27	48.61	51.40			95.97	46.83	51.04	50.49
						C_5D_5N						
280			295.94	66.66	52.52	55.99			71.01	46.96	55.84	56.80
270			293.93	71.88	52.54	55.81			84.51	66.91	55.44	55.98
260	280	280	294.73	76.29	52.53	55.67	280	280	87.44	70.42	55.36	55.86
250			294.34	75.09	52.53	55.71			88.62	73.36	55.33	55.77
240			293.56	73.98	52.54	55.75			89.79	75.71	55.30	55.69

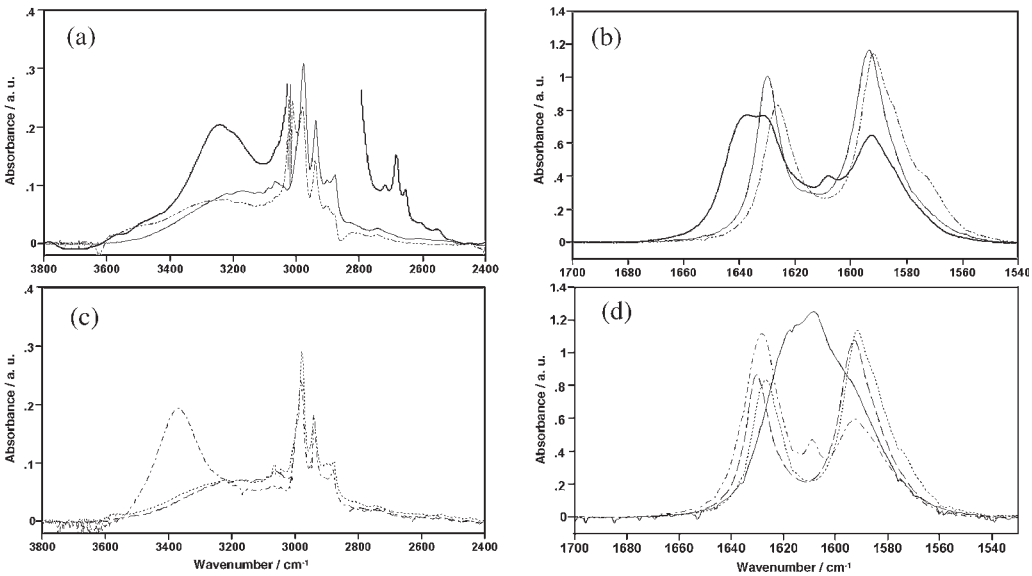


Figure 6. IR spectra in the region of the (ν(OH) (left side) and (ν(C=O) (right side) vibrations for 2-hydroxy-*N,N*-diethylbenzamide in KBr window: a, b) solid line—CCl_4, c = 0.1 M, d = 0.2 mm; - .. - line—$CHCl_3$, c = 0.1 M, d = 0.2 mm; bold line—C_4H_8O, c = 0.4 M, d = 0.054 mm. c) - - - line—C_4H_9Cl, c = 0.1 M, d = 0.2 mm;. .. line—CH_2Cl_2, c = 0.1 M, d = 0.2 mm; -.-.- line—CH_3CN, c = 0.1 M, d = 0.2 mm. d) - - - line—C_4H_9Cl, c = 0.1 M, d = 0.2 mm;. .. line—CH_2Cl_2, c = 0.1 M, d = 0.2 mm; -.-.- line—CH_3CN, c = 0.1 M, d = 0.2 mm; solid line—C_4H_9OH, c = 0.1 M, d = 0.2 mm

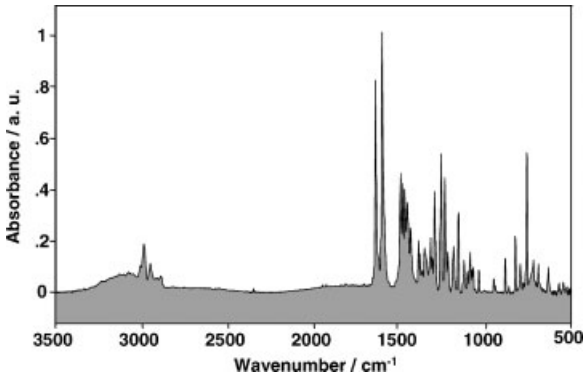


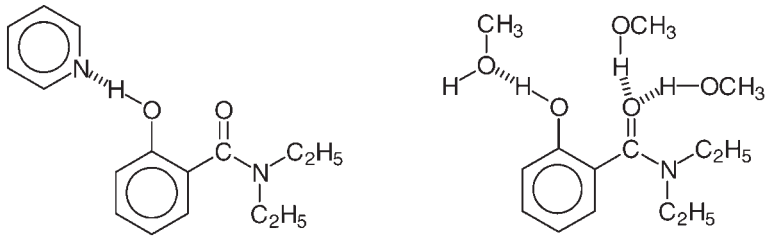
Figure 7. Matrix-isolated FT-IR spectrum of 2-hydroxy-*N, N*-diethylbenzamide

range between 1700 and 1540 cm^{-1}, shifted in the direction of higher wavenumbers (Figure 6). In C_4H_8O solution these bands are quite well resolved, whereas in a weaker proton-acceptor solvent (CH_3CN) the two bands of the ν(C═O) vibration overlap, where the large intensity of the band testifies to this fact. The shift of the ν(C═O) band of the proton-acceptor group in the direction of higher wavenumbers under the intramolecular hydrogen bond break is well grounded (the ν(C═O) band of the free C═O group (non-hydrogen-bonded))[33,34,42] and results from attenuation of the hydrogen bond. The fact of hydrogen bond weakening under the INTRA ⇌ INTER transition is verified by the ν(OH) band shift in the higher wavenumber range when replacing non-polar solvents (*cf.* Figure 6; $\nu_{cg} = 2976\ cm^{-1}$ (CCl_4), 3017 cm^{-1} ($CHCl_3$), 2908 cm^{-1} (C_4H_9Cl) and 2979 cm^{-1} (CH_2Cl_2)) by basic solvents ($\nu_{cg} = 3253\ cm^{-1}$ (C_4H_8O) and 3370 cm^{-1} (CH_3CN)). The chemical shift of the hydroxylic proton (8.7 ppm (CD_3CN) < 9.5 ppm (C_4D_8O) < 9.9 (CD_2Cl_2)) is consistent with IR results.

Table 3. The experimental (Ar matrix) and calculated (B3LYP/6-311++G**) IR spectral data for 2-hydroxy-*N,N*-diethylbenzamide

Exp. freq. (cm^{-1})	Calc. freq.[a] (cm^{-1})	Assignment	Exp. freq. (cm^{-1})	Calc. freq.[a] (cm^{-1})	Assignment
3100	3192	νOH	1293	1289	$\rho CH_2 + \delta$(CH)r
3071	3067	ν(CH)r	1258	1259	$\rho CH_2 + \nu$C2O7 + δ(CH)r
[b]	3053	ν(CH)r	1233	1229	δOH + δ(CH)r
—	3043	ν(CH)r	1217	1204	δO7H + δ(CH)r + νCN
—	3027	ν(CH)r	1186	1176	δO7H + δ(CH)r
3002	2991	$\nu^a CH_2 + \nu^a CH_3$	1155	1151	δ(CH)r
—	2990	$\nu^a CH_2 + \nu^a CH_3$	1124	1117	δ(CH)r + δOH
2980	2987	$\nu^a CH_2 + \nu^a CH_3$	1101	1091	ρCH_3
—	2965	$\nu^a CH_3$	1087	1076	$\rho CH_3 + \delta$r
—	2958	$\nu^a CH_3$	1077	1064	$\rho CH_3 + \delta$r
2945	2949	$\nu^a CH_3$	1071	1056	ρCH_3
—	2920	$\nu^s CH_2$	1037	1033	δr
2906	2895	$\nu^s CH_3$	[c]	981	νC11C12 + νC13C14
—	2893	$\nu^s CH_3$	—	971	γ(CH)r
2885	2885	$\nu^s CH_2$	950	947	γ(CH)r
1636	1632	νC8═O9 + δO7H + ν(CC)r	941	923	$\rho CH_3 + \nu$C11C12 + νC13C14
1598	1589	ν(CC)r + νC8═O9	884	868	δr + δC8═O9
1588[sh]	1579	δO7H + ν(CC)r	862	858	γ(CH)r
1491 {	1487	δO7H + νC8C1 + δCH_2	824	822	γO7H + δr
1491 }	1481	$\delta CH_2 + \delta CH_3$	795	806	γO7H
1477	1473	$\delta CH_3 + \delta CH_2$	778	780	$\tau CH_2 + \rho CH_3$
1468	1467	$\delta CH_3 + \delta CH_2$	758	768	$\tau CH_2 + \rho CH_3 + \gamma$O7H
1463	1461	$\delta CH_3 + \delta CH_2$	[c]	763	$\tau CH_2 + \rho CH_3 + \gamma$O7H + τC1C8
1456[sh]	1458	$\delta CH_3 + \delta CH_2$	721	752	γ(CH)r
1452	1452	$\delta CH_2 + \delta CH_3 + \delta$(CH)r	[c]	704	τC1C8 + τr
1450[sh]	1441	$\delta CH_2 + \delta CH_3 + \delta$(CH)r	689	683	τr
1435	1431	$\delta CH_2 + \nu$C8N10	635/627	629	δr + δC8═O9
1386	1386	$\delta CH_2 + \delta CH_3$	568	563	δr
1378 {	1380	δOH + δ(CH)r + δCH_2	548	545	τr + τC1C8N10
1378 }	1379	$\delta CH_3 + \delta CH_2 + \delta$O7H	[c]	526	τr
1351	1365	$\gamma CH_2 + \delta CH_3$	—	471	τC1C8N10
1346	1349	$\gamma CH_2 + \delta CH_3$	—	454	δC2O7
1317	1316	δ(CH)r + ρCH_2	—	429	τr
1308	1307	$\rho CH_2 + \delta$(CH)r	—	422	δC8═O9 + δC8N10C13

[a] Variable scaling factor were used: 0.95 for ν(XH), 0.98 for γ and τ, 0.975 for all other modes.
[b] Weak, unresolved absorption.
[c] Not observable in the experimental spectrum.



Basic intermolecular interactions **Protic intermolecular interactions**

Scheme 4.

It is interesting that the ν(C═O) band shifts toward lower wave numbers in an alcoholic solution. The reason for such behaviour is that breaking of the intramolecular hydrogen bond is different from the arrangements of the carbonyl bond in the basic and protic solutions (Scheme 4). A basic solvent makes the C═O bond free from hydrogen bonding (either attenuates it visibly in self-association agglomerates) thus strengthening the force constant, whereas an alcoholic solvent builds rather strong intermolecular hydrogen bonding where carbonyl oxygen weakens the force constant.

The above discussion shows that IR and DFT results corroborate UV–Vis data and also reflect the nature of the interactions of the compound with the environment (Scheme 4).

Self-association

To define the nature of the INTRA ⇌ INTER process, measurements of the average molecular weight in different solvents are made. Conceivably, 2-hydroxy-*N,N*-diethylbenzamide cannot form self-association in a non-polar solvent because of the strong intramolecular hydrogen bond or in a protic solvent due to the rather strong interaction with the solvent. It should be underlined that self-association is not observed for the *ortho*-hydroxy aryl Mannich and Schiff bases in alcohols.[27] In fact, in a non-polar solvent (CCl_4) the average molecular weight does not change as the solution's concentration increases (Figure 8), which means that the compound takes on an INTRA form. However, the average molecular weight does increase in a basic solvent, this growth being proof of self-association of the compound. This effect can consist of a few stages: interaction of the compound with a basic solvent which triggers the disruption of the intramolecular hydrogen bond and creation of a complex with the solvent molecules (Scheme 4, basic intermolecular interaction) with a consequent interaction of the hydroxyl group of complex (by means of bifurcate hydrogen bond) with a basic moiety of neighbouring complex (self-association). This result shows that the INTRA ⇌ INTER process needs to be stimulated by internal and external factors. It is noteworthy that the outside factors (protic and basic environment) act in different ways: protic solvent does not evoke self-association (Figure 8) due to a full block of the basic centres of the molecule. This phenomenon is supported by IR studies presented above.

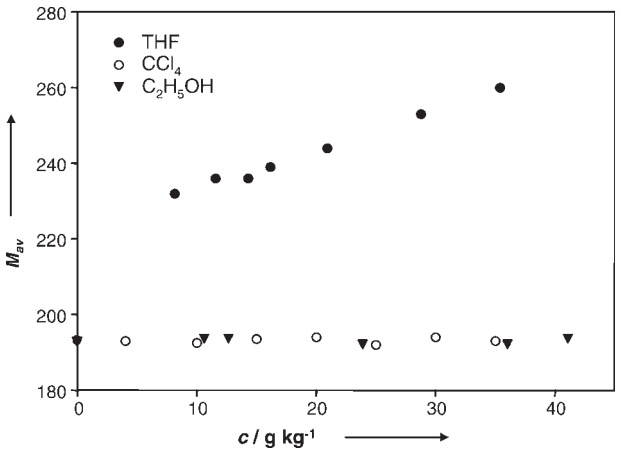


Figure 8. Dependence of average molecular weight (M_{av}) on concentration (c)

CONCLUSION

The most complete UV–Vis, NMR, IR, VPO and DFT studies of the thermodynamics and spectroscopic characteristics were carried out and the nature of the intra- versus intermolecular hydrogen bonding equilibrium in 2-hydroxy-*N,N*-diethylbenzamide was discussed.

The energy of the INTRA ⇌ INTER hydrogen bond equilibrium was estimated by means of UV–Vis spectra as a function of temperature.

Calculations of the non-adiabatic potential of the proton movement showed no presence of a second minimum.

NMR research of dynamic effect in 2-hydroxy-*N,N*-diethylbenzamide showed that the value of the energetic barrier on the amide group rotation cannot be directly interpreted as a thermodynamic parameter of the INTRA ⇌ INTER equilibrium.

It is shown that the changes in infrared spectral range of the ν(OH) and ν(C═O) vibrations are the most vivid indicator of the INTRA ⇌ INTER equilibrium. Besides, these changes reflect the differences between the molecule interaction with protic and basic solvents.

On the basis of the VPO results, we showed that the self-association process is observed in a basic solvent and is not detected in non-polar and protic solvents. A multi-stage mechanism of the self-association with the participation of the bifurcated hydrogen bond is suggested.

EXPERIMENTAL SECTION

2-Hydroxy-*N,N*-diethylbenzamide was purchased from Aldrich Co. and re-crystallised from methanol.

UV–Vis spectra were measured with a Cary 1 spectrophotometer in carbon tetrachloride (CCl_4), tetrachloroethylene (C_2Cl_4), methylene chloride (CH_2Cl_2), 1-chlorobutane (C_4H_9Cl), tetrahydrofurane (C_4H_8O), chloroform ($CHCl_3$), dichloroethane ($C_2H_2Cl_2$), butyl alcohol (C_4H_9OH), ethanol (C_2H_5OH), methanol (CH_3OH) and acetonitrile (CH_3CN) solutions at a concentration of 2.5×10^{-5} mol dm using 1 cm quartz cells. The constants ($K_{intra\text{-}inter}$) of intramolecular versus intermolecular (INTRA $\rightleftharpoons$ INTER) equilibrium were determined in CH_3CN, CH_2Cl_2 and C_4H_9OH solutions in the temperature range of 298–216 K using a UV–Vis spectroscopic technique with a two-beam cryostat made in this lab allowing measurements down to 143 K in quartz cells. The molar absorbance at peak maximum intensity was used to determine the concentration of the tautomeric forms. The numerical value of this parameter was taken from measurements in CH_2Cl_2. This value was corrected according to the temperature-dependent densities of the particular solvents.

The ^1H and ^{13}C spectra were recorded on a Bruker AMX 300 spectrometer. The measurements were performed in CD_3CN, C_4D_8O, CD_2Cl_2 and pyridine (C_5D_5N) solutions within the temperature range 300–180 K.

The experimental equipment for the IR-matrix experiment used for matrix sample preparation was described in Reference 43. Briefly, the solid compounds were evaporated from a mini-oven made in-house and placed in the cryostat. The vapour of the product with a large excess of Ar gas was deposited onto a cold CsI window (maintained at 10 K). The IR spectra of the matrices were scanned (32 interferograms) on a Bruker IFS-66 Fourier transform instrument with a resolution of 1 cm^{-1}. The routine IR spectra were measured on an FT-IR Nexus spectrophotometer with a resolution of 2 cm^{-1}.

The average molecular weight was measured in CCl_4, C_4H_8O and C_2H_5OH solutions at 40 °C by using the VPO method (Genotec 070 osmometer) within the concentration range of 3×10^{-3}–2×10^{-1} mol dm.

Ab initio molecular orbital calculations using DFT theory (B3LYP)[44,45] with the 6-311++G(d,p) basis set were performed for the full geometry optimisation with the GAUSSIAN 98 program.[46] In the calculations of the potential for proton transfer all parameters were fully optimised (B3LYP/6-31+G(d,p)) for each OH distance, changing gradually within the range of 0.8–2 Å.

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