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RESEARCH ARTICLE

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The unusual stability of H-bonded complexes in solvent caused by greater solvation energy of complex compared to those of isolated fragments

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Abstract

Here, the effect of solvent on the stability of non-covalent complexes, was studied. These complexes were from previously published S22, S66, and X40 datasets, which include hydrogen-, halogen- and dispersion-bonded complexes. It was shown that the charge transfer in the complex determines whether the complex is stabilized or destabilized in solvent.

KEYWORDS

binding energies, charge transfer, dispersion-bonded complexes, halogen-bonded complexes, hydrogen-bonded complexes

1 | INTRODUCTION

Solvation greatly influences the nature and stability of supramolecular systems. However, the complex nature of solvation makes effects sometimes difficult to predict.[1,2] A large number of studies have been published to resolve the effects of solvents on non-covalent interactions, including hydrogen bonds (H-bond),[1–8] halogen bonds (X-bond),[4,8–13] and dispersion interactions.[14,15] The studies show a variable response of the non-covalent complex stabilities to solvents, as shown, for example, in Robertson et al.[4] In this paper, the authors were able to control the competition between the hydrogen and halogen bond formations by changing the solvent properties and found that the studied systems prefer the formation of hydrogen bonds in nonpolar solvents. In contrast, halogen bonds are formed predominantly in more polar solvents.

Computational modeling of solvent is still a challenging task. Recently, possible computational approaches have been discussed by Menucci.[16] Explicit inclusion of solvent molecules using ab initio methods is limited by computational complexity. Modeling of solvent by empirical force fields is often questionable due to the use of reliable force field parameters. Another alternative that has proven to provide a reliable description of solvent effects is the use of the solvent model in its modeling by overlapping spheres, as done in the Polarized continuum model (PCM),[17,18] conductor like screening model (COSMO)[19,20] and solvent model (SM).[21]

The stability of covalent-bonded systems is thought to be only slightly affected by the solvent. However, in our recent study,[22] we found a surprising stabilization of covalent/dative bonding complexes that correlated with the increasing polarity of solvents. We explained this observation by transferring a charge (CT) between the donor and the acceptor of electrons which causes a significant dipole moment in the complex. As a result, the solvation of the complex is higher than that of the isolated fragments.

It is generally assumed that non-covalent complexes are destabilized as the polarity of solvent increases. The interactions of atomic cations and anions are typically strongly attractive in the gas

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Dedicated to Professor Gernot Frenking on the occasion of his 75th birthday.

phase (the interaction energies, Δ*E* are hundreds of kcal/mol) and decrease dramatically (Δ*E* are units of kcal/mol) in the solvent. Similarly, the stability of H-bond complexes is expected to decrease with the increasing polarity of the solvent.[3,4,7,11,23–25]

Unlike H-bond systems, the response of the X-bond complexes to the solvent seems to be more complicated.[12] While some authors of experimental studies predict that the strength of X-bond complexes is not sensitive to the solvent,[11] both stabilization[26] and destabilization[9] have been proposed by others. Also, computational studies[9,11,27,28] do not provide a definite answer. Controversial results raise the question of the properties that determine the response of non-covalent complexes to the solvents. It has been argued that its understanding cannot be achieved on the basis of a purely electrostatic description, and CT plays a significant role.[11,12,29,30] Shen et al. attributed the differences in the X-bond complex stabilities to different polarizabilities, which are suggested to be the most sensitive to solvent polarity.[12]

Following this discussion and in light of our previous results obtained for dative/covalent complexes, we performed studies of the solvent effect on the complex stabilities, considering H-bonded, X-bonded, and dispersion-bound systems of the previously published S22,[31] S66,[32] and X40[33] datasets (for more details, see the original papers). In the current study, we concentrated on the H-bond complexes. The results of calculated interaction energies and Gibbs free energies of the complexes are discussed with regard to their charge transfer (CT) character. The S22 and S66 data sets include complexes with a negligible CT character, while the halogen atoms present in the systems of the X40 dataset introduce a significant CT character in these complexes (for more details on the complex's specification, see original papers).

2 | METHODS

All complexes' equilibrium structures and electronic properties were optimized at the DFT-D level, employing the PBE0-D3 functional[34,35] with zero damping and def2-TZVPP basis set.[36] Thermodynamic characteristics at 298 K were evaluated with rigid rotor—harmonic oscillator—ideal gas approximation at the same computational level as geometry optimization. The solvent effects were described using the COSMO solvation model[19]; the solvent environments were characterized by their dielectric constants ε, using $\varepsilon = 1$ for the gas phase and $\varepsilon = 9.9$ for ortho-dichlorobenzene. All calculations were performed in Gaussian 16.[37] The COSMO solvation energies obtained for FH…methylamine, chloromethane…formaldehyde, and trifluoromethane…formaldehyde were compared with solvation energies determined by a more accurate PCM model developed by Tomasi et al.[38] The COSMO energies were systematically larger, with an average difference of about 13%. The small difference between COSMO and PCM models justifies the use of the COSMO method estimation of the solvation energies for all 128 complexes considered in the paper.

As noted in the following paragraph, charge transfer plays a critical role in altering the stability of complexes in solvents with different polarities. However, CT is not a physically well-defined characteristic, and its contribution to complex stabilizing energies poses a challenge to computational chemistry. The fundamental problem for CT calculation is the partitioning of the molecular complex into fragments. Řezáč et al.[39] proposed a method capable of defining CT with respect to the reference state free of charge transfer, a superposition of electron densities of isolated molecules. This method was recently successfully applied to the estimation of the charge transfer contributions to non-covalent complexes of the X40 data set.[40] Due to the computational demand of this approach, we used the CT values for the X40 dataset and compared them with those obtained from the less demanding NBO analyses.[41] Figure 1 shows a good correlation between these two data sets, justifying the use of the NBO approach for all other systems (S22, S66 data sets) considered in this study.

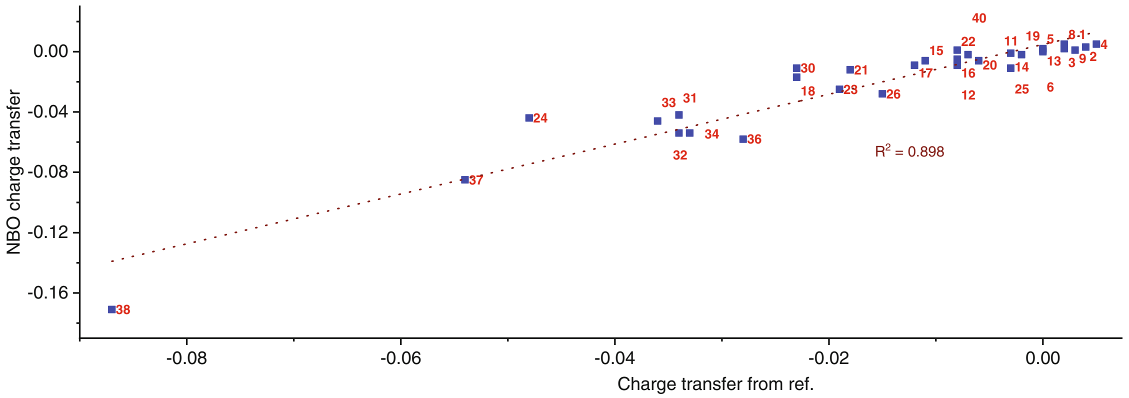
3 | RESULTS AND DISCUSSION

Tables S1, S2, and S3 show the results of the interaction energies (Δ*E*), binding free energies (Δ*G*), and transferred charge (*q*) calculated for datasets S22, S66, and X40 in the gas phase and ortho-dichlorobenzene. The tables also present the previously reported interaction energies obtained with the CCSD(T) method in the gas phase. A good agreement between CCSD(T) and PBE0-D3 interaction energies justifies the use of the DFT approach applied in the current study. As mentioned in the Introduction, the study concentrates primarily on the hydrogen bond systems, that is, complexes **1**–**7** from S22, **31**–**38** from X40, and **1**–**23** from the S66 datasets.

Tables 1 and 2 report the interaction energies (Δ*E*), binding free energies (Δ*G*), intermolecular H-bond distances (R_H), and transferred charge (*q*) between the fragments of the selected H-bond complexes from the S22 and X40 datasets.

In general, the hydrogen bond between the X—H donor and Y acceptor is characterized by an increase in the intramolecular X—H bond distance associated with the X—H frequency redshift. According to the IUPAC recommendation.[42] "There are, however, certain hydrogen bonds in which the X—H bond length decreases and a blue shift in the X—H stretching frequency are observed. It is conceivable that a hydrogen bond could exist without a red or a blue shift." Aquino et al. observed shortening of the stronger intermolecular X—H…Y distances upon increasing the solvent polarity[3] in all complexes. The results in Tables 1 and 2 show that, indeed, most of the intermolecular X—H…Y hydrogen bonds stabilize in terms of bond distances in polar environments. However, the opposite behavior was observed in some complexes (see Table 1, complexes **4**–**7**).

All complexes presented in Table 1 have relatively large Δ*E* values in the gas phase: Δ*E* = −3.9 and −6.0 kcal/mol for complexes **1** and **2**, respectively, and −16.0 to −20.0 kcal/mol for complexes **3**–**7**. In ortho-di-chlorobenzene, these values decrease to Δ*E* = −2.2 and −4.4 kcal/mol for complexes **1** and **2**, respectively, and in the range of −7.8 to −11.4 kcal/mol for complexes **3**–**7**. Δ*G* values predict the instability of **1** and **2**, while complexes **3**–**7** remain stable. Changing the dielectric constant from $\varepsilon = 1$ to $\varepsilon = 9.9$ destabilized all complexes



1: CH_4...F_2
2: CH_4...Cl_2
3: CH_4...Br_2
4: CH_4...I_2
5: CH_3F...CH_4
6: CH_3Cl...CH_4
7: CF_3H...CH_4
8: CCl_3H...CH_4
9: CH_3F... CH_3F
10: CH_3Cl... CH_3Cl
11: $C_6F_3H_3$...C_6H_6
12: C_6F_6...C_6H_6
13: CH_3Cl...HCHO
14: CH_3Br...HCHO
15: CH_3I...HCHO
16: CF_3Cl...HCHO
17: CF_3Br...HCHO
18: CF_3I...HCHO
19: C_6H_5Cl...CH_3COCH_3
20: C_6H_5Br...CH_3COCH_3
21: C_6H_5I...CH_3COCH_3
22: C_6H_5Cl...NMe_3
23: C_6H_5Br...NMe_3
24: C_6H_5I...NMe_3
25: C_6H_5Br...CH_3SH
26: C_6H_5I...CH_3SH
27: CH_3Br...C_6H_6
28: CH_3I...C_6H_6
29: CF_3Br...C_6H_6
30: CF_3I...C_6H_6
31: CF_3OH...H_2O
32: CCl_3OH...H_2O
33: HF...CH_3OH
34: HCl...CH_3OH
35: HBr...CH_3OH
36: HI...CH_3NH_2
37: HF...CH_3NH_2
38: HCl...CH_3NH_2
39: CH_3OH... CH_3F
40: CH_3OH... CH_3Cl

FIGURE 1 The correlation of charge transfer values for the X40 dataset from Řezáč and de la Lande[40] and NBO CT calculated in this study

TABLE 1 Interaction energies (Δ*E*, kcal/mol), binding free energies (Δ*G*, kcal/mol), intermolecular H-bond distances (R_H, Å), and total charge on one fragment (the first molecule in the complex) (q, e^-) for selected complexes of the S22 dataset[a]

	Δ*E*		Δ*G*		R_H		*q*	
Complex	**Gas**	**o-DCB**	**Gas**	**o-DCB**	**Gas**	**o-DCB**	**Gas**	**o-DCB**
1 Ammonium dimer	−3.90	−2.16	3.35	4.48	2.237	2.190	−0.010	−0.017
2 Water dimer	−6.02	−4.35	1.68	4.37	1.926	1.843	−0.016	−0.025
3 Formic acid dimer	−18.55	−11.44	−5.66	1.09	1.621	1.626	0.000	0.000
4 Formamide dimer	−16.19	−7.78	−2.87	4.20	1.814	1.881	0.000	0.000
5 Uracil dimer	−20.10	−10.03	−7.46	1.87	1.727	1.779	0.000	0.000
6 2-pyridoxine...2-aminopyridine	−17.49	−10.18	−6.24	0.92	1.795[b] 1.814[c]	1.889[b] 1.805[c]	−0.023	−0.036
7 Adenine...Thymine WC b.p.	−16.76	−9.87	−3.78	2.27	1.866[b] 1.753[c] 2.757[d]	1.888[b] 1.819[c] 2.831[d]	0.044	0.033

[a] Jurečka et al.[31]
[b] N—H...O bond.
[c] N—H...N.
[d] C—H...O.

in terms of both the interaction energies and binding free energies. In line with general expectations, the calculations predict that all complexes listed in Table 1 would not exist in ortho-dichlorobenzene. This behavior is explained by the interplay between the increased hydrogen binding force (in terms of the distances of the intermolecular hydrogen bond) in the polar solvent and the destabilizing effect of the solvent. This destabilization is due to two effects: (i) the frequently observed decrease in the dipole moment upon complexation; and (ii) a smaller solvent accessible area in the complex compared to that of the fragments.[3] The same results, that is, complex destabilization with the increasing solvent polarity of solvents, also show other complexes of the S22 dataset which is predominantly dispersive in nature.

The Δ*E* values of the S66 dataset complexes indicate destabilization in ortho-dichlorobenzene compared to the gas phase for the

TABLE 2 Interaction energies (ΔE, kcal/mol), binding free energies (ΔG, kcal/mol), intermolecular distances (R_H, Å), and total charge on one fragment (the first molecule in the complex) (q, e^-) for selected complexes from the X40 dataset[a]

	ΔE		ΔG		R_H		q	
Complex	Gas	o-DCB	Gas	o-DCB	Gas	o-DCB	Gas	o-DCB
31 Trifluoromethanol…water	−10.98	−8.82	−1.70	0.85	1.722	1.588	−0.042	−0.073
32 Trichloromethanol-water	−12.14	−9.51	−2.04	0.82	1.682	1.561	−0.054	−0.084
33 HF…methanol	−11.03	−10.34	−1.65	−0.64	1.643	1.522	−0.046	−0.080
34 HCl…methanol	−7.79	−7.81	0.99	1.32	1.740	1.443	−0.054	−0.142
35 HBr…methanol	−7.19	−10.32	1.50	1.03	1.736	1.091	−0.063	−0.300
36 HI…methanol	−5.49	−10.88	2.86	1.23	1.824	1.056	−0.058	−0.312
37 HF…methylamine	−15.73	−17.15	−5.70	−7.25	1.623	1.416	−0.085	−0.180
38 HCl…methylamine	−13.04	−29.63	−3.47	−16.59	1.503	1.064	−0.171	−0.447

[a] Řezáč and Riley.[33]

vast majority of systems. The exceptions are the dispersive complexes of cyclopentane…neopentane (**37**) and a cyclopentane dimer (**38**). However, the increase in interaction energies in **37** and **38** is negligible, less than 0.1 kcal/mol.

Summarizing the results obtained for the S22 and S66 datasets, an increased polarity of the solvent destabilized the complexes of all types, including those formed via hydrogen bonds, dispersion interactions, or their mixture. It is important to stress that *a negligible charge transfer characterizes all these complexes*.

Table 2 shows the selected hydrogen bonds systems from the X40 dataset. The presence of halogen atoms in these complexes results in their CT character, with a total charge transferred between the fragments in the range $q = (-0.042$ to $-0.171\ e^-)$ in the gas phase. As observed by Aquino et al.,[3] the intermolecular hydrogen bond distances decrease upon increasing environment polarity. Consequently, the charge transfer characters increase. While the CT in **31**–**33** is small, not larger than 0.03 e^-, significant changes show that complexes **35**–**38** range from 0.1 to 0.27 e^-. Differences in the CT in the gas phase and o-DCB are in line with the different responses of interaction energies and free binding energies to solvent polarity. The former complexes (**31**–**33**) show destabilization in terms of both ΔE and ΔG, while the complexes **35**–**38** significantly stabilize when the polarity increases. The substantial changes in bond distances of **35**, **36**, and **38** in o-DCB reflect the ion-pair $X^{-}\ldots(H{-}Y)^{+}$ formation and only **37** represents a neutral H-bond complex. Large stabilizations result from the ion-pair complex formation, showing increased absolute values of ΔE by up to 16 kcal/mol for **38**. However, even the neutral complex **37** stabilizes by 1.5 kcal/mol in o-DCB compared to the gas phase.

Inspection of the X40 dataset shows that the stabilization mentioned above is quite atypical. Indeed, except for complexes **2**, **5**–**7**, and **10**, all remaining complexes destabilize in terms of both ΔE and ΔG. However, note that interaction in **2**, **5**–**7**, **10** is of dispersion rather than hydrogen-bond character.

The results obtained for hydrogen-bond complexes in dataset X40, namely for **37**, show that the rationalization of stabilization/destabilization of the complex in the polar solvent *requires consideration of charge transfer character and its changes in the solvent*. In **37**, a sizable CT found already in the gas phase. This CT contributes to stabilizing by a polar solvent and outclasses a destabilizing effect due to the smaller accessible volume upon complexation, resulting in an overall solvent stabilization.

4 | CONCLUSIONS

The calculations of interaction and binding free energies of non-covalent complexes (S22, S66, and X40 datasets) obtained using the PBE0-D3/def2-TZVPP approach show that most complexes destabilize when the polarity of the environment increases. A smaller accessible volume of the complex than of isolated fragments explains the destabilization of hydrogen-bond complexes with a minor charge-transfer character, regardless of strengthening or weakening the intermolecular hydrogen bond. On the contrary, the hydrogen-bond complexes with a sizable charge transfer are more stable in the solvent than in the gas phase. The results show that the charge transfer character should be considered not only in the halogen-bond but also in the hydrogen-bond complexes.

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DATA AVAILABILITY STATEMENT

The data that supports the findings of this study are available in the supplementary material of this article.

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