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ORIGINAL PAPER

Interference of H-bonding and substituent effects in nitro- and hydroxy-substituted salicylaldehydes

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Abstract Two intramolecular interactions, i.e., (1) hydrogen bond and (2) substituent effect, were analyzed and compared. For this purpose, the geometry of 4- and 5-X-substituted salicylaldehyde derivatives (X=NO_2, H or OH) was optimized by means of B3LYP/6-311+G(d,p) and MP2/aug-cc-pVDZ methods. The results obtained allowed us to show that substituents (NO_2 or OH) in the para or meta position with respect to either OH or CHO in H-bonded systems interact more strongly than in the case of di-substituted species: 4- and 3-nitrophenol or 4- and 3-hydroxybenzaldehyde by ~31%. The substituent effect due to the intramolecular charge transfer from the para-counter substituent (NO_2) to the proton-donating group (OH) is ~35% greater than for the interaction of para-OH with the proton-accepting group (CHO). The total energy of H-bonding for salicylaldehyde, and its derivatives, is composed of two contributions: ~80% from the energy of H-bond formation and ~20% from the energy associated with reorganization of the electron structure of the systems in question.

Keywords Intramolecular hydrogen bond · H-bond energy · Homodesmotic reaction · DFT · MP2 · SESE

Dedicated to Professor Andrzej Górski, our friend and teacher, on the occasion of his 90th birthday.

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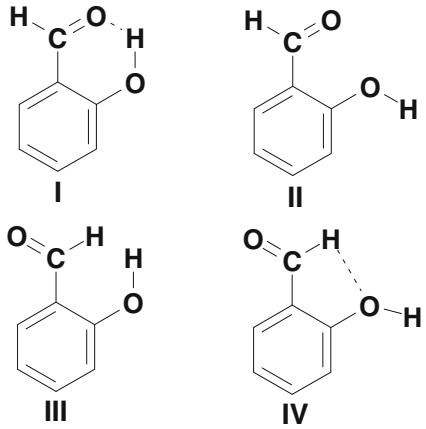
Introduction

Salicylaldehyde is a compound with well-recognized significance in many branches of chemistry. It undergoes a variety of chemical reactions, very often being a key precursor for new compounds exhibiting diverse molecular structures and properties [1–3]. It is worth mentioning that the salicylaldehyde moiety appears in many compounds exhibiting various biological activity, including reactants used in the design of new inhibitors of HIV-1 integrase [4], or compounds exhibiting antiviral activity [5], as well as in reactions resulting in new compounds with anticancer [6, 7] or antimicrobial activity [8]. It is also present during the synthesis of new products called "aspirin-like molecules" exhibiting anti-inflammatory activity [9]. In addition to its presence in many chemical reactions, salicylaldehyde has also found applications in molecular engineering [10].

Salicylaldehyde is also an interesting subject for various physico-chemical investigations; because it has four isomers, and due to internal reorganization, it can have more than one different hydrogen-bonded conformer [11]. The possible conformations of salicylaldehyde and hydrogen-bonded conformers are presented in Scheme 1.

The intramolecular hydrogen bond, spectroscopic signatures and geometric parameters of this compound have been of interest for the last several years. Many experimental as well as theoretical works on these issues have been



Scheme 1 Possible conformations of salicylaldehyde (taken from [11]). *Dashed line* Intramolecular hydrogen bond

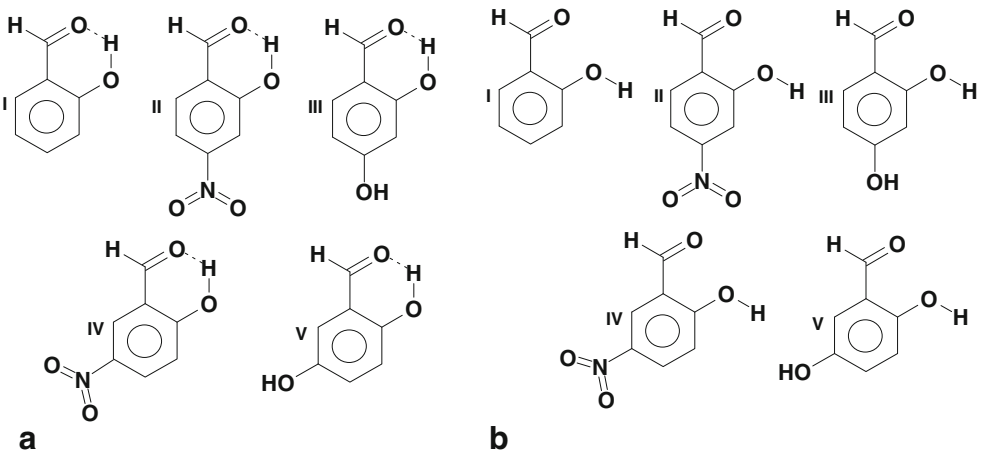
performed [12–19]. The intramolecular hydrogen bond present in salicylaldehyde can be classified as a resonance assisted hydrogen bond (RAHB) according to Gilli's concept [20]. The intramolecular hydrogen bond is of great importance in various aspects of chemistry, biology, and material science, as has been shown in selected examples [21–29]. An effort to understand and describe H-bonding can be observed in the literature, but there are still open questions related to the proton transfer phenomenon or the strength of the interaction, as well as environmental influences on it [30, 31]. The steric and inductive effects introduced by substituents can influence the strength of the intramolecular hydrogen bond significantly [32–40]. In the literature, one can find many papers dealing with the relationship between substituent effects and intramolecular H-bonding for acyclic systems [41, 42]. A very convenient system, malonaldehyde, has been used as a model for many studies [43–47]. One main conclusion from these studies is that the H-bond strength and π-electron delocalization in the OCCCO link in these systems depend on the type of substituent. All observed changes in the model systems are in agreement with Gilli's concept of RAHB [20, 48–50]; for further reading and review see [51, 52]. Concerning the intermolecular H-bond of para-substituted phenol/phenolate [53–55] or para-substituted aniline/anilide [56], the H-bonding and π-electron delocalization in the ring depend significantly on the kind of substituent.

In the study, we focus on salicylaldehyde and its derivatives presented in Scheme 2. The choice of these compounds was governed by substituent character (electron accepting or donating) and its position with respect to CHO and OH groups; it is always a para position with respect to one of them. Salicylaldehyde was used mostly as a reference structure to investigate changes in the molecular structure upon benzene ring substitution as well as changes in the intramolecular hydrogen bond strength.

It is worth mentioning that estimating intramolecular H-bond energy is not an easy task due to the possible implications of internal reorganization of bonds or steric effects. Recent decades have seen increased interest in this problem. Various approaches have been introduced to handle the issue. Here, a few of these are briefly reported.

Let us start with a short overview of the simplest method based on conformational analysis—the cis-trans method. In this method, the intramolecular hydrogen bond energy is calculated as the difference between the cis and trans conformers—with and without interaction by H-bonding. Another approach is the so-called ortho-para method, which is restricted to aromatic compounds where the hydrogen bond is present in two ortho substituents [57]. Cuma et al. [16, 58] calculated the H-bond energy as the energy required to rotate the bridged hydrogen 180° from its equilibrium position around the appropriate C–O single bond. Based on this method, Grabowski [43] distinguished two components that comprise the strength of the intramolecular interaction: "pure" H-bond energy and delocalization energy. The so-called "theoretical" energy (ΔE_T) was calculated using a thermodynamic cycle, which describes the partition of the intramolecular hydrogen bond energy. This approach is described in [59]. Another briefly reported approach is based on the approximate isolation of the energy contribution that occurs upon the transition from one structure to other conformers of the studied molecule. The estimated energy is thus associated strictly with changes in geometric parameters (bonds and valence angles). The method is restricted to molecules with a suitable number of conformers of specific form [60]. Another way to estimate intramolecular H-bond energy is the "Molecular Tailoring Approach" proposed by Deshmukh et al. [61] This method is based on compound partitioning and energy estimation of appropriate fragments, which yields the intramolecular hydrogen bond energy. The last reported approach here is based on a hydrogen bond making/breaking reaction. Isodesmotic/homodesmotic reactions are written in such a way that the number and type of bonds on both sides (reactants/products) is equal [62, 63]. Therefore, it is possible to estimate the stabilization energy.

The main goal of the current study was to investigate how the substituent effect acts on π-electron delocalization and H-bond strength in the case of aromatic systems with intramolecular H-bonding, i.e., salicylaldehyde and its derivatives, based on energetic characteristics. Another problem discussed is associated with the fact that, as a result of intramolecular H-bond formation, the proton donating group increases its electron donating power, and the proton accepting group increases its electron accepting power [47, 64]. A question arises: how does this effect



Scheme 2a,b Structures of studied compounds: *I* Salicylaldehyde, *II* 4-nitro-salicylaldehyde, *III* 4-hydroxy-salicylaldehyde, *IV* 5-nitro-salicylaldehyde and *V* 5-hydroxy-salicylaldehyde respectively. **a** Salicylaldehyde and its derivatives containing the intramolecular hydrogen bonds (*dashed lines*), **b** open conformations

affect relations between substituent and H-bonding in the studied systems?

It should be stressed that both interactions, i.e., (1) H-bonding and (2) substituent effect, are intramolecular in nature. Therefore another question arises: do they cooperate or act in opposite directions?

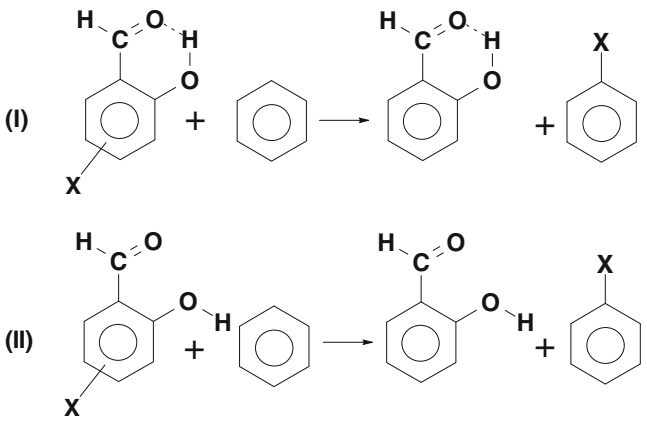
Computational methodology

The energy minimization of the studied set of compounds (see Scheme 2a,b; and Schemes 3, 4, 5, 6 and 7 for mono- and di-substituted benzene derivatives) was performed using density functional theory (DFT) [65, 66] and the second-order Møller-Plesset perturbation (MP2) method [67]. For DFT calculations, 6-311+G(d,p) basis sets were used [68], whereas MP2 simulations were performed using the aug-cc-pVDZ basis set [69]. Concerning the DFT method, the three parameter hybrid functional proposed by Becke [70] with correlation energy according to the Lee-Yang-Parr formula [71], denoted as B3LYP, was employed. Subsequently, harmonic frequencies were calculated to confirm that the geometries obtained correspond to the minimum on the potential energy surface (PES). Next, single point calculations were performed to build up an additional set of close conformers, with the intramolecular hydrogen bond using open structures (without H-bond) and rotation of the O–H bond 180° around the C–O single bond.

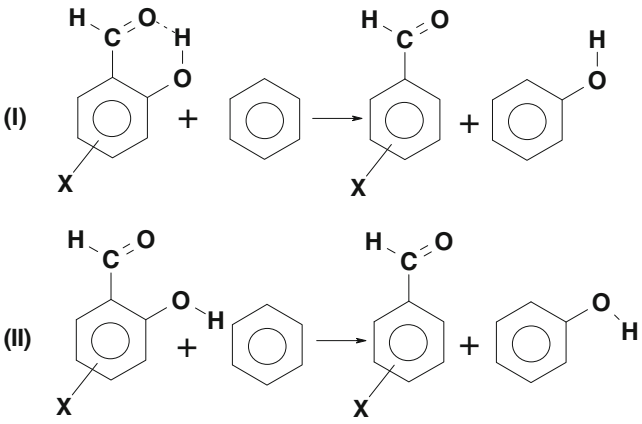
The estimation of the overall energy (E_{tot}) associated with the intramolecular H-bond formation was computed using the so-called cis-trans method, for details see Reference [72], as described below:

$$E_{tot} = E(\text{closed conformation}) - E(\text{open conformation}) \quad (1)$$

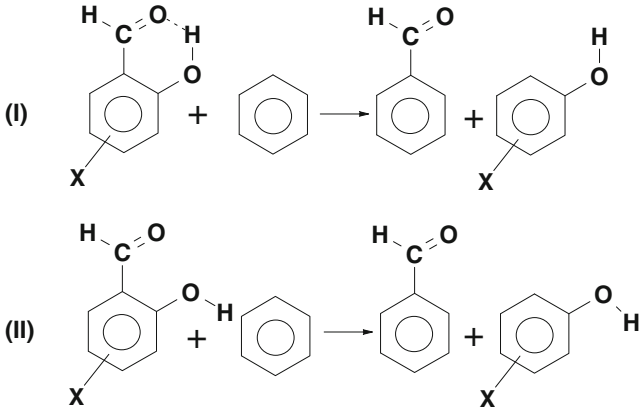
where E_{tot} indicates the total energy of the intramolecular hydrogen bond, whereas E(closed conformation) and E(open conformation) are the energies obtained after the geometry optimization procedures for closed and open conformations.



Scheme 3 Homodesmotic reactions (1) for closed and open conformations of 4- and 5-X substituted salicylaldehydes; X=NO_2 or OH



Scheme 4 Homodesmotic reaction (2) schemes for closed and open conformations of 4- and 5-X substituted salicylaldehydes; X=NO_2, H or OH



Scheme 5 Homodesmotic reaction (3) schemes for 4- and 5-X substituted salicylaldehydes; X=NO_2, H or OH

Two homodesmotic reaction schemes presented in Schemes 4 or 5 allow us to estimate the overall energy associated with intramolecular H-bond formation:

$$E_{\text{tot}} = \text{SESE(II)} - \text{SESE(I)} \tag{2}$$

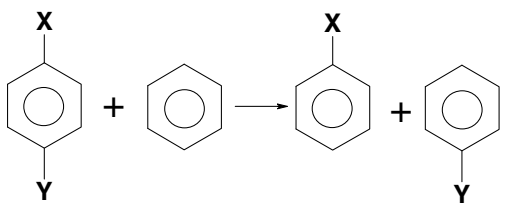
It is noteworthy that the final expression of the total energy, E_{tot}, could be transformed into the form of Eq. 1. In the case of substituted derivatives of salicylicaldehyde, the two homodesmotic reaction schemes presented in Schemes 4 and 5 can be proposed. These reactions differ in products only, but this leads to a change of meaning in their substituent effect stabilization energy (SESE) value.

Following Grabowski's method [43, 45], the "pure" energy of H-bonding, E_{HB}, can be obtained as:

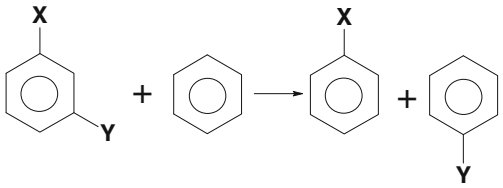
$$E_{\text{HB}} = E(\text{open conformation\_O-H rotated } 180^\circ) - E(\text{open conformation, optimized}) \tag{3}$$

where E(open conformation_O-H rotated 180°) means the energy of the single point calculation for the closed conformer formed from that obtained from the open one after the rotation of O–H around the C–O single bond. The difference between the total and above energies is the energy due to the changes in geometry, sometimes called the energy of delocalization, E_{deloc}:

$$E_{\text{deloc}} = E_{\text{tot}} - E_{\text{HB}}. \tag{4}$$



Scheme 6 Homodesmotic reaction scheme for para di-substituted benzene derivatives; X=OH or CHO, Y=NO_2 or OH



Scheme 7 Homodesmotic reaction scheme for meta di-substituted benzene derivatives; X=OH or CHO, Y=NO_2 or OH

Furthermore, the SESE [63] was computed on the basis of the designed reactions in Schemes 3, 4, 5, 6 and 7. All computations were performed within the framework of the Gaussian03 and Gaussian09 suite of programs [73, 74]. The reaction schemes were prepared using the ISIS Draw v2.3 program [75].

Results and discussion

The mutual interference of substituent effects and the intramolecular hydrogen bond in a set of 4- and 5-substituted salicylaldehyde derivatives (see Scheme 2) was analyzed. The energetic characteristics concerning the coupling of the substituent effect and the presence of intramolecular hydrogen bonds was performed using two approaches considered at two levels of computations (B3LYP/6-311+G(d,p) and MP2/aug-cc-pVDZ):

(1) Analysis of composition of the total energy of interaction, E_{tot}, for H-bonded systems perturbed by substituents.
(2) Analysis of SESE for homodesmotic reactions for substituted salicylaldehyde and appropriate disubstituted benzene derivatives: 4-substituted benzaldehyde and 4-substituted phenols (substituent: OH and NO_2).

Two of the four possible conformations of salicylaldehyde (see Scheme 1) and its derivatives were considered in the study. Conformation (**I**) presented in Scheme 1 was found to be the most stable in many studies, e.g., [11], whereas the open conformation, labelled (**II**) in Scheme 1, was necessary for the analysis presented in this study.

Table 1 summarises all the data concerning the strength of intramolecular H-bonding, where the studied systems are presented in sequence from the strongest down to the weakest, taking into account the overall energy of the H-bond, E_{tot}. Almost the same order was found in the case of "pure" H-bonding energy, E_{HB}. The only difference with respect to the sequence used in Table 1 concerns salicylaldehyde and its 5-nitro derivative, but the difference in the E_{HB} value was very small (amounts to 0.03 kcal mol^{-1}). The same was found for E_{tot}, so one can draw the conclusion that the nitro group in the meta position with respect to the CHO acts similarly to hydrogen.

Table 1 Intramolecular hydrogen bond energy profile for salicylaldehyde and its derivatives. E_{tot} Overall energy of the H-bond, E_{HB} "pure" H-bonding energy, E_{deloc} energy of delocalization

Level of theory	E_{tot} kcal/mol	E_{HB} kcal/mol	E_{del} kcal/mol	E_{del}/E_{tot} (%)
	4-hydroxy-salicylaldehyde			
B3LYP/6-311+G(d,p)	−11.88	−9.14	−2.74	23.1
MP2/aug-cc-pvdz	−10.82	−8.55	−2.27	21.0
	5-nitro-salicylaldehyde			
B3LYP/6-311+G(d,p)	−11.11	−8.91	−2.21	19.9
MP2/aug-cc-pvdz	−10.17	−8.28	−1.89	18.6
	Salicylaldehyde			
B3LYP/6-311+G(d,p)	−11.08	−8.94	−2.15	19.4
MP2/aug-cc-pvdz	−10.20	−8.37	−1.83	17.9
	5-hydroxy-salicylaldehyde			
B3LYP/6-311+G(d,p)	−10.82	−8.69	−2.13	19.7
MP2/aug-cc-pvdz	−10.02	−8.17	−1.84	18.4
	4-nitro-salicylaldehyde			
B3LYP/6-311+G(d,p)	−10.32	−8.16	−2.16	20.9
MP2/aug-cc-pvdz	−9.79	−7.91	−1.87	19.1

Note that E_{tot} indicates as the most stable systems those in which a strong through-resonance effect is present: the para positions of CHO/OH and OH/NO_2 (i.e., 4-OH- or 5-NO_2-salicylaldehyde, respectively). These systems are more stable by ∼1 kcal mol^{-1} than complexes with substituents of the same kind: para positions of OH/OH and CHO/NO_2 (i.e., 5-OH- and 4-NO_2-salicylaldehyde, respectively). This kind of regularity is also observed for H-bond energies, E_{HB}, but the difference between those with and without through-resonance is smaller, ∼0.6 kcal mol^{-1}. For the E_{del} the effect is even smaller, being equal to ∼0.3 kcal mol^{-1}. The above mentioned data are from B3LYP/6-311+G(d,p) computations, but a similar picture can be drawn from MP2/aug-cc-pVDZ calculations. It can be concluded from the data in Table 1 that the substituent effect on E_{tot}, E_{HB} and E_{del} is rather small. The variability of E_{HB} due to the substituent effect is also rather small (in the range of 0.98 kcal mol^{-1}), slightly smaller than that of E_{tot} (in the range of 1.56 kcal mol^{-1}), indicating resistance of H-bond interaction on perturbation stemming from substituents in the ring. Note that E_{del}, which is identified with changes in π-electron delocalization in the studied system, amounts to about 20% of E_{tot}.

A deeper insight into the intramolecular substituent effect gives an energetic characteristic of homodesmotic reactions (**1**), (**2**) and (**3**) (see Schemes 3, 4, 5, and Table 2).

Table 2 Substituent effect stabilization energy (SESE) of reactions (**1**), (**2**) and (**3**) calculated for salicylaldehyde and its 4-X- and 5-X- derivatives, X=NO_2 and OH; the homodesmotic reactions are shown in Schemes 3, 4, and 5, respectively. The sequence of the systems is the same as in Table 1 (from the strongest to the weakest in terms of H-bond overall energy)

Level of theory	SESE kcal/mol closed, I.1	SESE kcal/mol open, II.1	SESE kcal/mol closed, I.2	SESE kcal/mol open, II.2	SESE kcal/mol closed, I.3	SESE kcal/mol open, II.3
	4-OH					
B3LYP/6-311+G(d,p)	2.37	1.58	8.25	−3.62	9.45	−2.43
MP2/aug-cc-pvdz	1.49	0.86	7.20	−3.62	8.11	−2.71
	5-NO_2					
B3LYP/6-311+G(d,p)	−0.56	−0.59	8.75	−2.36	5.55	−5.56
MP2/aug-cc-pvdz	−1.25	−1.22	7.15	−3.02	4.97	−5.20
	H					
B3LYP/6-311+G(d,p)			7.36	−3.72		
MP2/aug-cc-pvdz			6.59	−3.61		
	5-OH					
B3LYP/6-311+G(d,p)	−2.40	−2.14	5.33	−5.49	6.82	−4.00
MP2/aug-cc-pvdz	−1.75	−1.57	4.86	−5.16	6.48	−3.53
	4-NO_2					
B3LYP/6-311+G(d,p)	−3.33	−2.57	6.51	−3.81	4.18	−6.14
MP2/aug-cc-pvdz	−1.26	−0.85	6.70	−3.08	4.93	−4.86

Table 3 SESE calculated for para-di-substituted benzene derivatives. The homodesmotic reactions are illustrated in Scheme 6. Energies of the reaction components are given in Hartree

Level of theory					SESE (kcal/mol)
	4-NO_2-C_6H_4-OH+C_6H_6→C_6H_5-OH+C_6H_5-NO_2				
	4-NO_2-C_6H_4-OH	Benzene	PhOH	$PhNO_2$	
B3LYP/6-311+G(d,p)	−512.124008	−232.311245	−307.558632	−436.874621	1.25
MP2/aug-cc-pVDZ	−510.689883	−231.540220	−306.610690	−435.618828	0.37
	4-OH-C_6H_4-OH+C_6H_6→C_6H_5-OH+C_6H_5-OH				
	4-OH-C_6H_4-OH	Benzene	PhOH	PhOH	
B3LYP/6-311+G(d,p)	−382.803057	−232.311245	−307.558632	−307.558632	−1.86
MP2/aug-cc-pVDZ	−381.678535	−231.540220	−306.610690	−306.610690	−1.65
	4-NO_2-C_6H_4-CHO+C_6H_6→C_6H_5-CHO+C_6H_5-NO_2				
	4-NO_2-C_6H_4-CHO	Benzene	PhCHO	$PhNO_2$	
B3LYP/6-311+G(d,p)	−550.228511	−232.311245	−345.669087	−436.874621	−2.48
MP2/aug-cc-pVDZ	−548.680014	−231.540220	−344.603603	−435.618828	−1.38
	4-OH-C_6H_4-CHO+C_6H_6→C_6H_5-CHO+C_6H_5-OH				
	4-OH-C_6H_4-CHO	Benzene	PhCHO	PhOH	
B3LYP/6-311+G(d,p)	−420.918827	−232.311245	−345.669087	−307.558632	1.48
MP2/aug-cc-pVDZ	−419.675466	−231.540220	−344.603603	−306.610690	0.87

The obtained SESE data are specified in the same sequence as in Table 1. Positive values of SESE indicate greater stability of substrates, whereas negative values are products of the homodesmotic reaction.

The influence of the substituent on the formyl and hydroxyl groups—participants in the intramolecular hydrogen bond—is seen in the first reaction (**1**; see Scheme 3 and data in the second and third column in Table 2). The greatest strengthening of the H-bond compared with that in salicylaldehyde, is caused by the OH group in the para position with respect to CHO [4-OH-salicylaldehyde, SESE (**I.1**)=2.37 kcal mol^{-1}], whereas the opposite situation occurs in the case of the NO_2 group in the same position [4-NO_2-salicylaldehyde, SESE(**I.1**) = −3.33 kcal mol^{-1}]. A similar variability in SESE values is also observed for "open" conformations (1.58 and −2.57 kcal mol^{-1}, respectively), indicating a strong through-resonance effect in the first case and its absence in the second.

The ranges of SESE variability for reaction (**1**), calculated for 4-X- and 5-X- salicylaldehyde derivatives, X=NO_2 and OH, are 5.70 kcal mol^{-1} and 4.15 kcal mol^{-1} for the closed and open forms, respectively. This data can

Table 4 SESE calculated for meta-di-substituted benzene derivatives. Energies of the reaction components are given in Hartree

Level of theory					SESE (kcal/mol)
	3-NO_2-C_6H_4-OH+C_6H_6→C_6H_5-OH+C_6H_5-NO_2				
	3-NO_2-C_6H_4-OH	Benzene	PhOH	$PhNO_2$	
B3LYP/6-311+G(d,p)	−512.121766	−232.311245	−307.558632	−436.874621	−0.15
MP2/aug-cc-pVDZ	−510.689934	−231.540220	−306.610690	−435.618828	0.40
	3-OH-C_6H_4-OH+C_6H_6→C_6H_5-OH+C_6H_5-OH				
	3-OH-C_6H_4-OH	Benzene	PhOH	PhOH	
B3LYP/6-311+G(d,p)	−382.806466	−232.311245	−307.558632	−307.558632	0.28
MP2/aug-cc-pVDZ	−381.681107	−231.540220	−306.610690	−306.610690	−0.03
	3-NO_2-C_6H_4-CHO+C_6H_6→C_6H_5-CHO+C_6H_5-NO_2				
	3-NO_2-C_6H_4-CHO	Benzene	PhCHO	$PhNO_2$	
B3LYP/6-311+G(d,p)	−550.229361	−232.311245	−345.669087	−436.874621	−1.95
MP2/aug-cc-pVDZ	−548.679327	−231.540220	−344.603603	−435.618828	−1.81
	3-OH-C_6H_4-CHO+C_6H_6→C_6H_5-CHO+C_6H_5-OH				
	3-OH-C_6H_4-CHO	Benzene	PhCHO	PhOH	
B3LYP/6-311+G(d,p)	−420.915883	−232.311245	−345.669087	−307.558632	−0.37
MP2/aug-cc-pVDZ	−419.674037	−231.540220	−344.603603	−306.610690	−0.02

be compared with SESE values for para and meta di-substituted benzene derivatives; X=OH or CHO and Y= NO_2 or OH of the appropriate reactions (see Schemes 6, 7). The relevant data are presented in Tables 3 and 4. The greatest SESE value was found for 4-OH-C_6H_4-CHO (1.48 kcal mol^{-1}), supporting the strong through-resonance effect mentioned above, whereas the smallest was found for 4-NO_2-C_6H_4-CHO (−2.48 kcal mol^{-1}). The ranges of SESE variability for these cases are 3.96 kcal mol^{-1} and 2.23 kcal mol^{-1} for the para and meta substituted systems, respectively. Energetically, it means that the overall substituent effect on intramolecular H-bond in 4-X- and 5-X- substituted salicylaldehyde is ~31% larger than that observed in 3-X- and 4-X- substituted benzaldehyde or 3-X- and 4-X- substituted phenol. It should be noted that for the "open" conformations the effects compared above are similar to those observed for di-substituted benzene derivatives.

When we compare the ranges of SESE values for H-bonded systems (Table 2, 5.70 kcal mol^{-1} for the closed system and 4.15 kcal mol^{-1} for the open one), those for hydroxy- and nitro- benzaldehyde and phenol (3.96 kcal mol^{-1} for para derivatives, Table 3; 2.23 kcal mol^{-1} for meta systems, Table 4) with the range of E_{tot} and E_{HB} (1.56 and 0.98 kcal mol^{-1}, respectively, Table 1) we find immediately that the substituent effect, which is energetically substantial, acts very weakly on the total energy of H-bond formation as well as on the H-bond energy itself.

Two remaining homodesmotic reactions for salicylaldehyde and its derivatives (presented in Schemes 4, 5, and S1–S5 in Supporting Information, and data in Table 2) show another aspect of the substituent effect on H-bond formation. The range of SESE values for the **I.2** reaction (closed) is 3.42 kcal mol^{-1}. In this case the substituent interacting via a through-resonance effect (OH group) is para in relation to the CHO group involved in H-bond formation. It may be compared with the range of SESE values for reaction **I.3** (closed) which is 5.27 kcal mol^{-1}. Note that, in this case, the substituent interacting via a through-resonance effect (NO_2 group) is para with respect to the OH group involved in H-bond formation as a proton donating group. Thus, energetically, the substituent effect due to the intramolecular charge transfer from the para-counter substituent (NO_2) to the proton-donating group (OH) is ~35% greater than for the interaction of the para-OH with the proton-accepting group (CHO). This may suggest that, due to intramolecular charge transfer, the proton-donating component of H-bonding is more sensitive to the substituent effect than the proton-accepting one. A weaker H-bonding in 5-nitro-salicylaldehyde than in 4-hydroxy-salicylaldehyde (Table 1) explains the obtained SESE value for meta-nitrobenzaldehyde (−1.95 kcal mol^{-1}, Table 4).

Conclusions

In the case of intramolecular H-bond formation, the proton donating group (OH) increases its electron donating power, and the proton-accepting group (CHO) increases its electron accepting power [47, 57]. As a result, counter substituents (NO_2 or OH) in the para position to them in H-bonded 4- or 5- substituted salicylaldehyde interact more strongly (by ~31%) than in the case of 4-nitrophenol or 4-hydroxybenzaldehyde. Despite this strengthening, this perturbation acts weakly on the total energy of H-bond formation, E_{tot}, as well as the H-bond energy itself, E_{HB}.

The substituent effect due to the intramolecular charge transfer from the para-counter substituent (NO_2) to the proton-donating group (OH) is ~35% greater than for the interaction of para-OH with the proton-accepting group, CHO.

The total energy of the intramolecular H-bonded system, E_{tot}, contains ~20% of the energy associated with electron redistribution of the whole system, E_{del}.

Computations carried out using B3LYP/6-311+G(d,p) and MP2/aug-cc-pVDZ levels of theory lead to equivalent results.

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