Cooperative effects in regular and bifurcated intramolecular OH···O C interactions: A computational study

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Cooperative effects in regular and bifurcated intramolecular OH···O=C interactions: A computational study

Ruben D. Parra *, Kristina Streu

Department of Chemistry, DePaul University, 1110 W. Belden Ave., Chicago, IL 60614, United States

ABSTRACT

Density functional theory calculations are performed to investigate the stabilizing or destabilizing cooperative effects in regular and bifurcated intramolecular OH···O=C hydrogen bond (H bond) interactions. Regular H bonds are examined in two model hydroxyketones: 1-hydroxy-3-butanone, and 5-hydroxy-4-quinolone. Bifurcated H bonds, OH···O(=C)···HO, are examined in two model systems: 1,5-dihydroxy-3-pentanone, and 1,8-dihydroxy-9-acridinone. Changes in the strength of the H bonds are examined upon extending the backbone of each model system with polyol chains of varying size. Stabilizing cooperative effects are seen in both the regular and the bifurcated H bonds. When compared with corresponding regular H bond counterparts, the bifurcated H bond model systems exhibit destabilizing cooperative effects with polyol addition. It is found that, for comparable systems, the OH···O=C interaction is strengthened more by stabilizing cooperative effects than it is weakened by destabilizing cooperative effects.

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1. Introduction

It is known that the strength of a given hydrogen bond (H bond) may be affected by its participation in additional H bonds [1]. For example, the H bond energy is increased if either of the following occurs on formation of another H bond: (i) the donor of the first H bond acts as H bond acceptor in the second H bond or (ii) the acceptor of the first H bond acts as H bond donor in the second H bond. A weakening of the H bond generally occurs, however, whenever the formation of the second H bond results in a double H bond donor, or in a double H bond acceptor. The term bifurcated is frequently used whenever a given H bond involves a H being shared by two H bond acceptors $A_1 \cdots H—(X) \cdots A_2$, or whenever an atom is acting as a double acceptor $H_1 \cdots A \cdots H_2$. The former case is referred to as bifurcated donor, while the latter case as bifurcated acceptor. Fundamental studies have shown that the enhancement or weakening of a given H bond results from three-body and higher order cooperative (non-pairwise) effects [2]. These cooperative effects can therefore be understood as stabilizing or destabilizing effects depending on whether they strengthen or weaken the H bond. For intermolecular systems, cooperativity is usually analyzed in terms of binding energies or H bond energies [1–3]. In contrast for intramolecular systems, cooperative effects are usually discussed in terms of parameters other than H bond energies. While suitable references, namely the non-interacting molecules, can be used for estimating the

energetics of intermolecular H bonds, the definition of similarly suitable references is less obvious when considering any intramolecular interaction. Consequently, intramolecular H bond cooperativity is normally studied by means of other H bond strength indicators such as geometries, vibrational spectroscopy, topological parameters, and Natural Bond Order (NBO) analysis [4]. It should be noted, however, that a number of interesting though somewhat debatable approaches have been used to estimate intramolecular H bond energies including isodesmic reactions, the ortho-para method, and conformational analysis [5–7]. Recently, Deshmukh et al. proposed the use of a systematic fragmentation scheme to estimate H bond energies in intramolecular systems [8–11]. The approach has been used in the estimation of OH···OH, and NH···O=C hydrogen bond energies in polyhydroxy compounds, and polypeptides respectively. Also recently, an analytic potential energy function was proposed to evaluate intramolecular H bond energies in α- and β-peptides conformers [12]. Additionally, the H bond energy for neutral OH···OH interactions has been estimated using the semiempirical Lippincott and Schroeder H bond (LS-HB) model [13–17].

Cooperative effects in intramolecular H bond interactions have been given a great deal of attention because of the role played by these interactions on the properties of a diverse group of molecules including polyols, carbohydrates, and proteins. Some recent publications include those showing the effect of cooperativity in the tautomerism of azo dyes [18]. Other studies have shown how intramolecular H bond cooperativity enhances the basicity in some cyclopropeneimines [19], and the acidity in polyols [20]. Also, Dashnau et al. reported that intramolecular H bond cooperativity

* Corresponding author. Tel.: +1 773 325 4343; fax: +1 773 325 7421.
E-mail address: rparra1@depaul.edu (R.D. Parra).

in carbohydrates can induce important changes in water structure in solution surrounding the aldohexopyranose stereoisomers [21]. Indeed, it was suggested by these authors that biological events such as protein carbohydrate recognition and cryoprotection by carbohydrates may be driven by intramolecular H bond cooperativity. The impact of polyols on water structure in solution has also been reported [22]. Furthermore, cooperativity in aliphatic and aromatic polyols has been published recently [23]. Cooperative strengthening of an intramolecular O—H···O═C H bond by a weak C—H···O counterpart was reported by Samanta et al. [24]. With regard to bifurcated (double donor/acceptor) intramolecular H bonds, examples of stabilizing and destabilizing effects have been reported [25–31]. Thus, in tandem with the noted importance of intramolecular H bonds, several methodical investigations of cooperative effects in systems containing the intramolecular NH···O═C, or OH···OH motif have been reported. In this paper, we further our knowledge of intramolecular H bonds by investigating the extent to which the strength of regular and bifurcated intramolecular OH···O═C bonds is altered upon formation of additional intramolecular H bonds. To accomplish this goal, some model polyol-containing hydroxyketones are chosen, and both aromatic and aliphatic polyol chains are considered. Cooperativity is determined by systematically increasing the size of the polyol chain. Additionally, the chosen models enable us to perform a direct comparison of the relative extent of destabilizing *vs.* stabilizing cooperative effects in comparable systems. The role of the backbone alone (without the hydroxy groups) in stabilizing or destabilizing a reference OH···O═C interaction is also investigated.

2. Computational details

Geometry optimizations and frequency calculations were carried out using the GAUSSIAN 09 program [32]. These calculations were performed with the 6-311G(d,p) basis set [33,34], and the B3LYP implementation of density functional theory [35–38]. The calculated harmonic vibrational frequencies confirmed that each optimized geometry corresponded to a minimum on the potential energy surface. The extent of cooperative effects is investigated by examining the H bond energy associated with the intramolecular OH···O═C interaction. The H bond energy is estimated using and equation based on the Lippincott and Schroeder H bond model (LS-HB). The actual equation used to estimate the H bond energy is discussed in detail by Gilli and Gilli [17] and for convenience is shown below:

$$E_{HB} = -43.8 + 0.38\theta \exp[-5.1(R - 2.40)] \qquad (1)$$

Energies are given in kcal/mol. Also in this equation, θ is the angle $A_{O-H\cdots O}$ in degrees, and R is the distance between the two oxygen atoms, $d_{O\cdots O}$, in angstroms. The impact of cooperative effects on the harmonic O—H stretching frequencies, and related geometrical parameters such as the hydrogen bond OH···O═C distance is also examined. Finally, the theory of atoms in molecules (AIM) of Bader [39] was employed to analyze topological features of electron density on wave functions obtained at the B3LYP/6-311++G(d,p) level using the AIM2000 software package [40].

3. Results and discussion

Two model hydroxyketones, 1-hydroxy-3-butanone and 5-hydroxy-4-quinolone [41,42], are considered here to study regular intramolecular OH···O═C interactions. The former system represents an aliphatic hydroxyketone, whereas the latter represents an aromatic hydroxyketone. For convenience, we will refer to the aliphatic system as AL_HK, and to the aromatic system as AR_HK. The bifurcated OH···O(═C)···HO interaction is investigated in

two model systems: 1,5-dihydroxy-3-pentanone, and 1,8-dihydroxy-9-acridinone [43,44,31]. Because the bifurcated systems are symmetric dihydroxyketones based on AL_HK, and AR_HK, we will refer to them as AL_DHK, and AR_DHK respectively. As shown in Fig. 1, each H bond in a given system is part of a six-membered ring. Some relevant parameters are summarized in Table 1. Inspection of Table 1 reveals that the H bond in AL_HK is much weaker than that in AR_HK. The weaker interaction in AL_HK is reflected, for example, in a significantly longer (by about 0.46 Å) H bond distance, and narrower (by about 20°) H bond angle. The weaker character of the H bond in AL_HK is also revealed by an H bond energy (0.63 kcal/mol) nine times smaller than that of the aromatic hydroxyketone. The superior strength of the hydrogen bond in AR_HK is expected since it benefits from extensive π-electron delocalization; this electron delocalization results in a completely planar system as indicated by the OH···O═C dihedral angle. In contrast, AL_HK is non-planar with corresponding dihedral angle that deviates substantially from 0°. Upon bifurcation, a given parent H bond interaction is weakened as seen in a sizeable elongation of the H bond, $d_{O\cdots H}$, along with a reduction of the covalent O—H bond, d_{O-H}. The destabilizing effects resulting from bifurcation are also seen in an important reduction in the estimated H bond energies.

In the following sections, we will discuss the extent of cooperativity resulting from extending the backbone of a parent hydroxyketone with polyol chains of varying sizes. Cooperative effects are many-body non-additive effects resulting primarily from three-body effects that influence the energies and other properties of a given structure. These cooperative effects are known to depend on the number, strength, and orientation of the H-bonds. Although usually understood as resulting in a non-additive increase of H bond energy, cooperative effects have also been shown to result in a decrease of H bond energy. In this paper, we will refer to the net, energetic cooperative effects for a given structure as stabilizing or destabilizing effects. Stabilizing effects will result in strengthening (increase of H bond energy) of a given reference H bond, while destabilizing effects will result in weakening (decrease of H bond energy) of a given reference H bond. Corresponding changes in structural parameters associated with (stabilizing/destabilizing) cooperative effects will also be discussed.
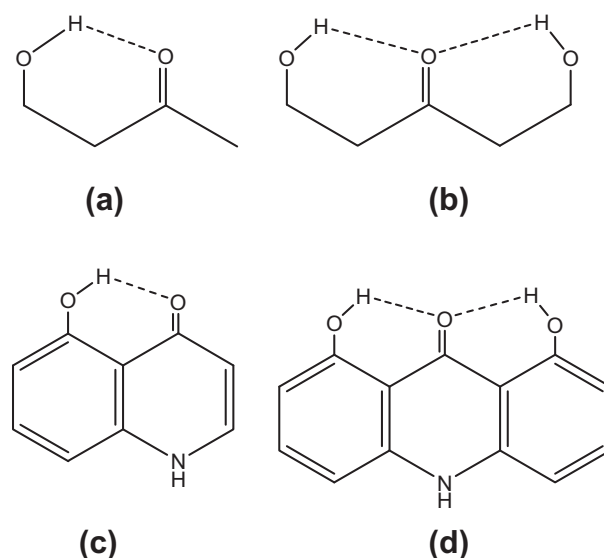

Fig. 1. Model systems used to investigate regular and bifurcated intramolecular O—H···O═C hydrogen bonding interactions: (a) 1-hydroxy-3-butanone; (b) 1,5-dihydroxy-3-pentanone; (c) 5-hydroxy-4-quinolone; (d) 1,8-dihydroxy-9-acridinone.

Table 1
H bond energies and geometrical parameters used as descriptors of H bond strength in the reference model systems.[*]

System	d_{H-O}	$d_{H\cdots O}$	$d_{O\cdots O}$	$d_{O=C}$	$A_{O-H\cdots O}$	$\tau_{O-H\cdots O=C}$	E_{HB}
AL_HK	0.966	2.111	2.833	1.215	130.3	14.2	0.63
AR_HK	0.997	1.653	2.566	1.248	150.2	0.0	5.69
AL_DHK	0.965	2.154	2.851	1.221	127.9	16.3	0.48
AR_DHK	0.988	1.688	2.580	1.266	148.1	0.0	4.97

[*] Distances in Å, angles in degrees, and E_{HB} in kcal/mol.

3.1. Stabilizing cooperative effects in regular OH···O=C H bonds

We examine the extent to which the H bond strength in each of the model systems AL_HK, and AR_HK is affected by the presence of additional intramolecular H bonds. To this end, we modified each model system by extending their backbones with the addition of polyol chains. Optimized geometries for the smallest and largest polyol chains added to AL_HK and AR_HK are shown in Fig. 2. Note that the hydroxyl oxygen of the parent hydroxyketone is now an H bond acceptor in an intramolecular H bond with the added polyol. Moreover, the hydroxyl groups in the polyols are themselves involved in a sequential OH···OH network. The primary focus of this work lies in the extent of cooperativity in internal OH···O=C interactions.

A summary of the various cooperativity indicators is presented in Table 2. Stabilizing effects for the AR_HK system upon polyol addition are revealed by considerable increases in the H bond energy. For instance, the estimated H bond energy in the largest system (13.17 kcal/mol) is more than twice that of the reference system AR_HK (5.69 kcal/mol); although it appears to be reaching convergence. Stabilizing effects for the AL_HK system upon addition of the smallest polyol result in a 0.41 kcal/mol increase in the H bond energy. Further stabilizing effects in AL_HK are negligible (within 0.10 kcal/mol) for polyol chains of larger size.

The stabilizing effects for the AR_HK system are accompanied by elongation of the O—H bond length and concomitant contraction of the H bond distance in the OH···O=C motif. Changes of these geometrical parameters as a function of polyol size, i.e.
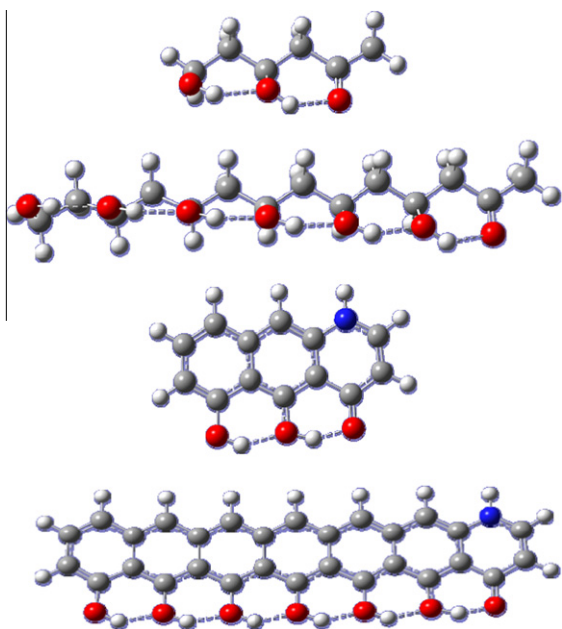

Fig. 2. B3LYP/6-311G(d,p) optimized geometries of the smallest ($n = 1$) and largest ($n = 5$) polyol-containing hydroxyketones studied in this work.

Table 2
Harmonic O—H frequencies (cm^{-1}), and H bond energies, E_{HB} (kcal/mol), based on $d_{O\cdots O}$ (Å), and $A_{O-H\cdots O}$ (°).

	E_{HB}	d_{H-O}	$d_{H\cdots O}$	$d_{O\cdots O}$	$A_{O-H\cdots O}$	ν_{O-H}
AR_HK						
0	5.69	0.997	1.653	2.566	150.24	3168
1	9.32	1.022	1.530	2.483	152.75	2715
2	11.11	1.038	1.479	2.454	153.71	2472
3	12.08	1.048	1.453	2.440	154.25	2342
4	12.73	1.056	1.435	2.432	154.63	2257
5	13.17	1.061	1.424	2.426	154.90	2204
AL_HK						
0	0.63	0.966	2.111	2.833	130.28	3772
1	1.04	0.968	2.013	2.766	133.02	3725
2	1.08	0.969	2.006	2.759	132.90	3727
3	1.14	0.969	1.995	2.751	133.22	3719
4	1.16	0.969	1.992	2.749	133.31	3717
5	1.14	0.969	1.994	2.750	133.21	3716

number of O—H groups in the added polyol chain, are shown in Fig. 3 for both model systems. The size of the polyols runs from $n = 0$ to $n = 5$, with $n = 0$ referring simply to the parent model systems. It is seen in Fig. 3 that the covalent O—H bond length in AL_HK is unaffected by the size of the polyol added. In the same system, a contraction of about 5% is observed for the H bond distance on addition of the smallest polyol, $n = 1$. The percentage change in this distance varies little with the size of the polyol, and reaches a maximum contraction of about 6% with the largest polyol, $n = 5$. Thus, the geometrical indicators are consistent with the weak stabilizing effects based on H bond energies noted previously. The more robust stabilizing effects in AR_HK are accompanied by larger O—H elongations, and H···O contractions. The percentage changes in these parameters increase with increasing size of the polyol, and appear to be slowly approaching convergence. As seen in Fig. 4, a quadratic correlation exists between the percentage change of the O—H bond length, and the reciprocal of the polyol size, $1/n$. Also shown in Fig. 4 is a quadratic correlation between $1/n$ and the percentage change of the H bond distance. These correlations enable us to obtain an estimated change, in the limit of $n = \infty$, of about 17% in the contraction of the H-bond distance, and of about 8% in the elongation of the O—H bond.

Vibrational frequencies are often used to gauge the extent of cooperativity in H bond interactions. In particular, the lengthening of the covalent O—H bond with increasing strength of the hydrogen bond OH···O=C results in a shift to lower frequencies of the corresponding O—H stretching mode. The O—H frequency shifts to the
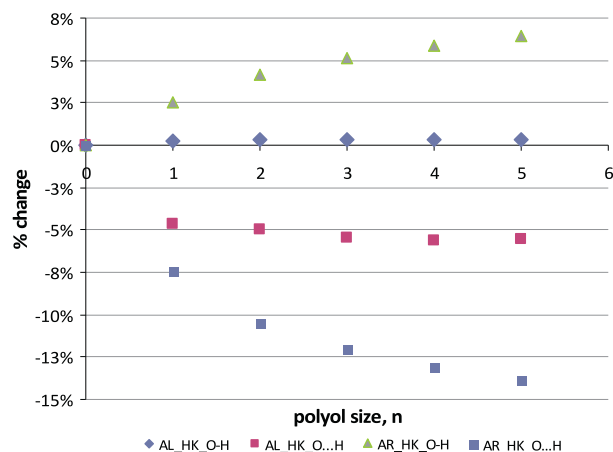

Fig. 3. Percentage changes of O—H and O···H distances as a function of polyol size.
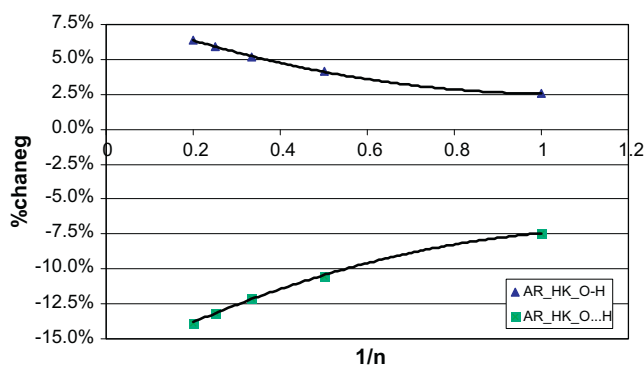
Fig. 4. Quadratic correlations between percentage change and reciprocal of polyol size for O—H and O···H distances in polyol-containing AR_HK systems: $\%\Delta d_{O-H} = -0.0546(1/n)^2 - 0.1132(1/n) + 0.0841$; $\%\Delta d_{O···H} = -0.0654(1/n)^2 + 0.1582(1/n) - 0.1672$. The correlation factor for each of the fitting lines is $r^2 = 1.00$.

red by 50 cm^{-1} for the smallest polyol, $n = 1$, and then no significant changes occur in the AL_HK system. The shifts to lower frequencies are significant in AR_HK, up to 30% when $n = 5$, in proportion to the O—H bond length changes mentioned previously for this system.

3.2. Stabilizing cooperative effects in bifurcated OH···O(=C)···HO hydrogen bonds

We examine the impact on the bifurcated H bond strength of adding simultaneously a polyol chain on each side of a given model system. The size of the added polyol, in terms of the number of O—H groups, varies from one to five. Optimized geometries for the smallest and largest polyol-containing model systems, AL_DHK and AR_DHK, are shown in Fig. 5. The parameters used to determine the extent of cooperativity are summarized in Table 3. As in the regular OH···O=C interactions, the cooperative enhancement of the bifurcated hydrogen bonds is corroborated by an increase in H bond energy. The aromatic model system exhibits considerable stabilizing effects revealed in larger H bond energies. The stabilizing effects in the aliphatic model system AL_DHK are relatively important upon addition of the smallest polyol chain, but then it becomes negligible for larger polyols. In general,
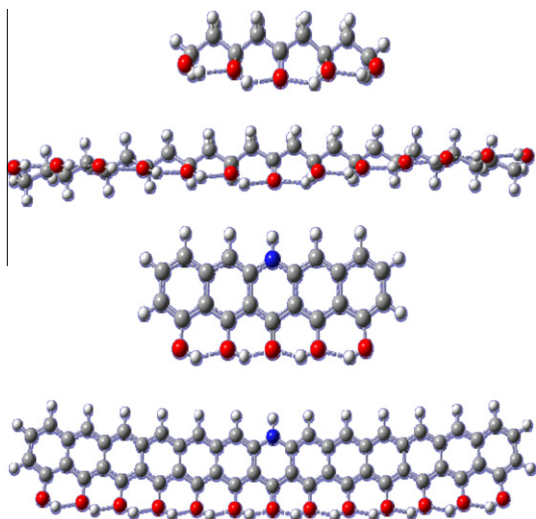

Fig. 5. B3LYP/6-311G(d,p) optimized geometries of the smallest ($n = 1$) and largest ($n = 5$) polyol-containing dihydroxyketones studied in this work.

Table 3
Harmonic O—H frequencies (cm^{-1}), and H bond energies, E_{HB} (kcal/mol), based on $d_{O···O}$ (Å), and $A_{O-H···O}$ (°).

	E_{HB}	d_{H-O}	$d_{H···O}$	$d_{O···O}$	$A_{O-H···O}$	v_{O-H}
AR_DHK						
0	4.97	0.988	1.688	2.580	148.10	3352
1	7.52	1.002	1.592	2.509	149.74	3103
2	8.45	1.008	1.563	2.489	150.34	2991
3	8.86	1.012	1.550	2.482	150.74	2930
4	9.06	1.014	1.544	2.479	150.99	2881
5	9.12	1.015	1.541	2.479	151.14	2853
AL_DHK						
0	0.48	0.965	2.154	2.851	127.91	3791
1	0.75	0.967	2.073	2.794	129.92	3770
2	0.78	0.967	2.063	2.783	129.75	3766
3	0.77	0.967	2.065	2.783	129.61	3765
4	0.77	0.967	2.065	2.782	129.46	3765
5	0.79	0.967	2.062	2.780	129.65	3765

changes in geometrical parameters mirror those in H bond energies. Cooperative enhancement of the bifurcated H bonds results in red shifts of the symmetric O—H stretching harmonic frequencies as seen in Table 3. Although no significant change in the O—H stretching mode occurs for polyols larger than $n = 2$ in AL_DHK, the red-shift extent in AR_DHK is substantial, and appears to be approaching saturation with the largest polyol.

It is noted that upon polyol addition, the percentage change in the O—H stretching harmonic vibrational frequency in both AR_HK, and AR_DHK varies linearly with percentage change in the corresponding O—H bond length:

$$\%\Delta v_{O-H} = -5.03\%\Delta d_{O-H} \tag{2}$$

The coefficient of determination, r^2, for the above regression is found to be 0.99, which means that 99% of the total variation in Δv_{O-H} can be explained by the linear relationship between $\%\Delta v_{O-H}$ and $\%\Delta d_{O-H}$ given by Eq. (2).

3.3. Destabilizing cooperative effects: regular vs. bifurcated hydrogen bonds

Although both the regular and the bifurcated H bond interactions are cooperatively enhanced by polyol addition, it is usually expected that the strength of the OH···O=C component of a bifurcated hydrogen bond be weaker than it is in the absence of the second H bond. We examine the weakening occurring in the bifurcated model systems relative to their regular two-center H bonding counterparts. The extent of weakening caused by destabilizing effects is monitored by considering the decrease in the H bond energy upon bifurcation of a given reference structure. Indeed, simultaneous inspection of Tables 2 and 3 shows that the H bonds in both AL_HK and AR_HK decrease upon bifurcation. The magnitude of the reduction tends to increase with increasing size of the system. Thus, the reduction in H bond energy, upon bifurcation, for the AR_HK ranges from 0.72 kcal/mol ($n = 0$) to 4.05 kcal/mol ($n = 5$). The corresponding reductions in the aliphatic systems are 0.24 and 0.35 kcal/mol respectively. Interestingly, the increase of the H bond energy in a regular OH···O(=C) interaction with the addition of a polyol chain of size n is more than the decrease resulting from the corresponding bifurcation. For example, extending the backbone of AR_HK with a polyol of size $n = 5$ increases the H bond energy by 7.48 kcal/mol, but the corresponding decrease in energy upon bifurcation is 4.05 kcal/mol. This is not surprising since both AR_HK and AR_DHK benefit from stabilizing cooperative effects with addition of the polyol chains.

Inspection of Tables 2 and 3 reveals that destabilizing cooperative effects result in shortening of the covalent O—H bond length

accompanied by lengthening of the H bond distance in the OH⋯O(=C) motif. The weakening of the OH⋯O=C interactions upon bifurcation is evident in both AL_DHK, and AR_DHK, with the effects being more prominent in the latter. For example, the lengthening of the H bond distance is about 8% in the largest polyol-containing AR_DHK system, compared to about 4% in the corresponding AL_DHK system. Also, the shortening of the O—H bond length is found to be between 2% and 4% for AR_DHK, while it is close to 0% for AL_DHK. The relative extent of the stabilizing and destabilizing cooperative effects, as reflected in H bond distances, are simultaneously shown in Fig. 6. Note that H bond enhancement brought about by stabilizing effects results in a decrease in the H bond distance in a polyol-containing hydroxyketone relative to the parent AL_HK or AR_HK. Similarly, H bond weakening caused by destabilizing effects results in an increase in the corresponding H bond distance. A salient feature in Fig. 6 is that the stabilizing effects give rise to larger contractions of H bond distances than the corresponding elongations resulting from the destabilizing effects. For instance, while the H bond distance is decreased by about 14% in the largest polyol-containing AR_HK, the H bond distance is increased by about 8% in the corresponding polyol-containing AR_DHK. Consistent with the noted geometrical changes, the weakening of the OH⋯O=C interaction produces a blue shift of the O—H stretching frequencies as seen in the frequencies of pertinent systems listed in Tables 2 and 3.

The stabilizing and destabilizing cooperative effects revealed in the energies, and in the geometrical parameters are mirrored in topological parameters such as the electron density at the H bond critical point, ρ_c. Examination of Table 4 shows that both AR_HK and AR_DHK exhibit sizeable strengthening of their respective H bonds as indicated by increases in the magnitudes of ρ_c, and the local electronic potential energies, V_c. On the other hand, cooperative effects are limited to just the smallest polyol ($n = 1$) in the aliphatic AL_HK, and AL_DHK systems. The weakening of a regular OH⋯O=C interaction upon bifurcation is reflected, for example, in a sizeable reduction in the magnitudes of both the electron density and the potential energy density at the H bond critical point. The topological results are thus in agreement with those presented previously based on geometry and energetic grounds. Finally, the nature, non-covalent or partly covalent, of a hydrogen bond may also be assessed. Previous studies have established that the ratio of the local kinetic (G_c) and the local potential (V_c) energies can be used to assess the nature of the H bond in a given system. If $-G_c/V_c > 1$, then the H bond is noncovalent in nature. On the other hand, if $0.5 < -G_c/V_c < 1$, then the interaction is partly covalent [45,46]. Examination of Table 4 indicates that the H bond in the aliphatic systems exhibits a noncovalent nature, whereas that in the

Fig. 6. Percentage changes in the O—H and O⋯H distances relative to the non-bifurcated systems as a function of polyol size.

Table 4
Relevant topological parameters of the hydroxyketone systems.[*]

AR_HK			AR_DHK		
n	ρ_c	V_c	$-G_c/V_c$	ρ_c	V_c	$-G_c/V_c$
0	0.054	−0.057	0.82	0.049	−0.050	0.86
1	0.074	−0.088	0.72	0.062	−0.069	0.79
2	0.084	−0.105	0.67	0.067	−0.076	0.76
3	0.091	−0.116	0.65	0.069	−0.080	0.75
4	0.095	−0.124	0.63	0.070	−0.081	0.75
5	0.098	−0.130	0.62	0.070	−0.082	0.74
AL_HK			AL_DHK		
0	0.020	−0.014	1.11	0.018	−0.013	1.14
1	0.024	−0.019	1.07	0.021	−0.016	1.11
2	0.024	−0.019	1.07	0.022	−0.016	1.10
3	0.025	−0.020	1.06	0.022	−0.016	1.10
4	0.025	−0.020	1.06	0.022	−0.016	1.10
5	0.025	−0.020	1.06	0.022	−0.016	1.10

The size of a polyol is given in terms of the number of O—H groups, n.
[*] Topological parameter is in atomic units.

aromatic systems exhibits a partly covalent nature. Upon polyol addition, the respective nature of the interactions remains unchanged.

One may trace down any changes in the strength of the H bond interaction in the hydroxyketone motif to changes in both H bond donor and acceptor abilities of the O—H and O=C groups respectively. In particular, the donor ability of the O—H group increases if the O—H group itself becomes part of a network of interlinked OH⋯OH bonds in which all OH⋯O bonds point in the same direction, that is, they form a homodromic H bond chain [3e,17,47]. A homodromic arrangement enables each O—H donor group to act simultaneously as acceptor. Here the H bonds are stronger than usual in part because of the mutual polarization brought on the O—H bond by the various H bonds present in the chain. Because of the induced polarization, the oxygen becomes more negative and the hydrogen becomes more positive making the O—H group better donor and acceptor when compared with an isolated O—H group. Thus, stabilizing cooperative effects due to mutual polarization of the O—H bonds enhances the donor ability of the O—H in the OH⋯O=C motif, and therefore strengthen the H bond interaction in AL_HK and AR_HK. As noted previously, cooperativity tends to increase to a saturation limit with the number of hydroxyl groups in the homodromic chain, a result consistent with the unidirectional orientation of the OH⋯O bonds. In contrast, each of the model dihydroxyketones AL_DHK, and AR_DHK has a homodromic chain that is broken into two antidromic half chains of OH⋯OH hydrogen bonds. The point of break is at the carbonyl oxygen that acts as a double acceptor forcing the half cooperative chains to point in opposite directions. Because cooperativity is a reflection of the overall effects of many different forces, including not only their magnitudes but also their directions, the net result of these cooperative effects running in opposite directions appears to be a weakening of the reference OH⋯O=C interaction (destabilizing cooperative effects). From a qualitative point of view, one may say that the formation of the reference OH⋯O=C H bond will transfer electron density from the O=C subunit to the O—H subunit. This electron redistribution is more pronounced the stronger the H bond interaction is to begin with. As a result, the O—H group becomes a better H bond acceptor, but the O=C subunit becomes a poorer acceptor. The weakening of the acceptor ability of the O=C group upon formation of the reference H bond in a hydroxyketone model renders the corresponding bifurcated interaction in a given dihydroyketone weaker than its non-bifurcated counterpart. Increasing the size of the backbone results in a stronger OH⋯O=C interaction in the model hydroxyketones, which in turn results in

Table 5
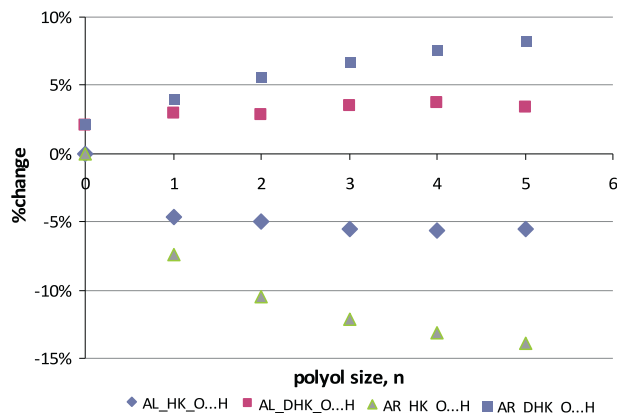Backbone effects on the O—H···O=C strength as revealed in H bond distances, (Å), and atomic charges (a.u.).[*]

System	Aliphatic					Aromatic					
	O···H	qO(H)	qH	qO(=C)	qC(=O)	System	O···H	qO(H)	qH	qO(=C)	qC(=O)
0_HK	2.111	−0.402	0.242	−0.321	0.194	0_HK	1.653	−0.354	0.264	−0.428	0.399
1_HK_b	2.043	−0.409	0.245	−0.324	0.198	1_HK_b	1.613	−0.356	0.269	−0.428	0.404
1_HK	2.013	−0.440	0.259	−0.326	0.199	1_HK	1.530	−0.454	0.290	−0.432	0.413
0_HK	2.111	−0.402	0.242	−0.321	0.194	0_HK	1.653	−0.354	0.264	−0.428	0.399
2_HK_b	2.044	−0.410	0.245	−0.324	0.198	2_HK_b	1.600	−0.353	0.270	−0.428	0.407
2_HK	2.006	−0.449	0.264	−0.326	0.200	2_HK	1.479	−0.477	0.296	−0.431	0.417

[*] 0_HK (reference hydroxyketone), n_HK_b (reference hydroxyketone with added backbone), and n_HK (reference hydroxyketone with added backbone including the O—H group); n = 1, or 2.

Table 6
Backbone effects on the O—H···O=C strength upon bifurcation as revealed in H bond distances, (Å), and atomic charges (a.u.).[*]

System	Aliphatic					Aromatic				
	O···H	qO(H)	qH	qO(=C)	qC(=O)	O···H	qO(H)	qH	qO(=C)	qC(=O)
0_HK	2.111	−0.402	0.242	−0.321	0.194	1.653	−0.354	0.264	−0.428	0.399
0_DHK_b	2.101	−0.402	0.241	−0.329	0.217	1.664	−0.350	0.265	−0.421	0.463
0_DHK	2.154	−0.400	0.242	−0.354	0.221	1.688	−0.349	0.272	−0.519	0.532
1_HK	2.013	−0.440	0.259	−0.326	0.199	1.530	−0.454	0.290	−0.432	0.413
1_DHK_b	2.002	−0.440	0.259	−0.336	0.219	1.544	−0.447	0.291	−0.427	0.480
1_DHK	2.073	−0.435	0.259	−0.364	0.226	1.592	−0.446	0.301	−0.551	0.563

[*] n_HK (reference hydroxyketone for bifurcation), n_DHK_b (reference hydroxyketone for bifurcation with added backbone), and n_DHK (bifurcated dihydroxketone based on n_HK), with n = 0, or 1.

an even poorer H bond acceptor power of the O=C group, and thus a more pronounced destabilizing cooperativity upon bifurcation.

Additional insight into the factors governing the strength of the OH···O=C interaction can be gained by examining the role played by the backbone itself, that is without the hydroxyl groups. We first investigated the backbone effects on the regular hydroxyketones whose extended backbone contains an additional O—H group. We replaced the O—H group with an H atom, and optimized the resulting systems. The results presented in Table 5 include H bond distances and relevant atomic charges. For consistency, we labeled the different systems as 0_HK (reference hydroxyketone), 1_HK_b (reference hydroxyketone with added backbone), and 1_HK (reference hydroxyketone with added backbone including the O—H group). One striking finding is that adding the backbone alone, without the O—H group, increases the strength of the interaction as seen in the important reduction in the H bond distances. Having the backbone alone brings about a slight increase in the magnitude of the atomic charges for most atoms listed in Table 5. Adding the backbone including the O—H group produces an additional strengthening of the OH···O=C interaction as seen in a further reduction of the H bond distances, and a further increase of the atomic charges, with a particular large increase in the O—H charges. The increase in the O—H charges is consistent with the mutual polarization on the O—H bonds discussed previously. We next examine the effects on the regular hydroxyketones whose extended backbone contains two additional O—H groups. We replaced the O—H groups with H atoms, and optimized the resulting systems. Inspection of the results presented in Table 5 indicates that for AL_HK the backbone effects (2_HK_b) are virtually identical to those in 1_HK_b suggesting that the ability of the aliphatic backbone alone to influence the H bond interaction is mostly limited to just the smallest size considered. For the aromatic systems, however, the influence of the larger backbone remains important producing an additional 0.013 Å reduction of the H bond distance. In short, it appears that both the backbone and the O—H groups act in the same direction and thus reinforce

each other. The effects of the backbone alone on the H bond appear to converge more quickly than those of the backbone with the O—H groups included; this highlights the importance of the mutual O—H polarization in the polyol network.

We examined the influence of the backbone on the strength of the OH···O=C interaction for the two smallest bifurcated systems. We replaced the O—H groups with H atoms, and optimized the resulting systems. The results are presented Table 6. We labeled the smallest systems listed in Table 6 as n_HK (reference hydroxyketone for bifurcation), n_DHK_b (reference hydroxyketone for bifurcation with added backbone), and n_DHK (bifurcated dihydroxketone based on n_HK), with n = 0, or 1. Table 6 shows that the aliphatic backbones strengthen the reference H bond interaction. It is apparent that extending the backbone results in negligible changes in the atomic charges for the atoms in the O—H subunit, and in a slight increase in the magnitude of the atomic charges for both the oxygen and the carbon atoms in the O=C subunit. Addition of the backbones with the O—H groups to form the bifurcated H bond systems, n_DHK weakens the OH···O=C H bond interaction. An additional increase in the magnitude of the O=C atomic charges is noted. In general, the increase in the atomic charge of the carbonyl oxygen should result in a more repulsive electrostatic interaction with the oxygen atom of the adjacent O—H groups, contributing then to weaken the OH···O=C interaction.

With regard to the two aromatic systems considered, inspection of Table 6 reveals that the aromatic backbones weaken the reference H bond interaction. It is worth mentioning that the magnitude of the atomic charge of the carbonyl oxygen decreases while that of the carbonyl carbon increases substantially. Thus, the aromatic backbone acts effectively as an electron withdrawing group that removes electron density from the O=C subunit. The reduced electron density makes the carbonyl oxygen a poorer H bond acceptor. Addition of the aromatic backbones with the O—H groups to form the bifurcated H bonded systems further weakens the reference H bond interactions.

4. Summary

Intramolecular H bonds containing the OH···O=C motif are cooperatively enhanced by a network of hydroxyl groups directionally arranged to act as an H bond donor to the hydroxyl group of the motif. Two model systems, AL_HK and AR_HK, were used to investigate cooperativity of the regular two-center H bonds. Of these two systems, AR_HK has the stronger OH···O=C H bond, and thus exhibits larger cooperative effects. Similarly, cooperative enhancement of bifurcated H bonds was investigated using two model systems AL_DHK and AR_DHK. The system with the stronger interaction, AR_DHK, also shows the larger extent of cooperativity. The relative extent of stabilizing *vs.* destabilizing effects was investigated. For comparable systems, the regular H bond is strengthened more by stabilizing effects than it is weakened by destabilizing effects.

Acknowledgments

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