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Density Functional Theory Study of the Hydrogen Bond Interaction between Lactones, Lactams, and Methanol

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The structure and relative stability of methanol complexes with various cyclic ketones, lactones, lactams, and *N*-methyl lactams from three- to seven-membered rings have been investigated using the density functional theory method. The geometries, harmonic frequencies, and energies were calculated at the B3LYP/6-311+G-(d,p) level. Three stable structures, cis-a, cis-b, and trans, with respect to the ring oxygen (nitrogen) atom, were found to be local minima of the potential energy surface. For lactones and *N*-methyl lactams, the most stable structure is trans; it is stabilized, as in cyclic ketones, through the conventional hydrogen bond (HB) interaction between the basic carbonyl oxygen and the acidic methanolic hydrogen and an unconventional HB interaction between the methanolic oxygen and the CH hydrogen, in the α position of the carbonyl group. For unsubstituted lactams, the cis-a structure, stabilized through a HB interaction between the NH group and the methanol oxygen in addition to the conventional HB interaction, is the most stable. The topological properties of the electron density ratify the existence of conventional (N,O−H···O) and unconventional (C−H···O) hydrogen bonding. A good correlation was found between the HB distances and the electron density at the HB critical point. The unsubstituted lactams yield more stable complexes with methanol than *N*-methyl lactams, lactones, and cyclic ketones. In the most stable complexes, both components behave simultaneously as a HB donor and as a HB acceptor.

Introduction

Hydrogen bonding is a fundamental component of chemical structure and reactivity. It plays a key role in many biological processes and can produce large changes in the kinetics of an enzymatic reaction.[1−3] The study of the nature of hydrogen bonds (HBs) is of particular interest, since it might help to elucidate the complex nature of biological processes.[4] Over the years, a large number of studies were devoted to the investigation of the HB of neutral species in the gas phase[5] as well as in solution and in the solid state.[6−12] In the same way, extensive theoretical studies have produced a lot of results obtained at a high level of calculations.[13−16] The understanding of hydrogen bonding has changed in the last two decades, since new types of HBs have been investigated.[17−19] In enzymatic catalysis, the conventional HBs, which are usually defined as X−H···Y where the group X−H is the donor and Y is the acceptor of the HB, have always been described as "short strong" or "low-barrier" HBs that stabilize enzyme-bound intermediates and/or transition states.[20−22] In recent years, other interactions known as unconventional HBs have been suggested in various organic and biological compounds.[23−27] Such interactions are of three types: HBs with unconventional donors, such as C−H bonds,[28−36] those with unconventional acceptors,[37] and those with unconventional donors and unconventional acceptors.[38] These unconventional HBs can be made and broken easily, facilitating rapid molecular recognition and chemical reaction because they are relatively weak.[23,24,31] The HB interaction was analyzed in terms of the HB basicity of the HB acceptor toward several alcohols used as reference acids. Taft et al.[39] have suggested the thermodynamic parameter pK_{HB} as a measure of the HB basicity toward 4-fluorophenol which was considered as a good reference acid. Later on, other acids such as 3-nitrophenol,[40] 3,5-dichlorophenol,[41] and 3,4-dinitrophenol[42] were used for similar studies. Other authors have used the spectroscopic parameter $\Delta\nu_{OH}$[43,44] to determine the basicity scale of several organic compounds toward OH donors.

In our experimental and theoretical work on the basicity of various organic bases, in particular cyclic ketones, lactones, and lactams,[45−47] we have focused our attention on the intrinsic basicities of these compounds toward protons, molecular iodine, and iodine monochloride. Quite recently, we have carried out a systematic investigation on electronic effects in charge-transfer complexes in the case of lactams.[47d] Lactones and lactams are chosen because (a) the lactone group is present in a wide range of pharmaceutical drugs,[48] (b) several lactams are used as antibiotics,[49] and (c) lactones and lactams could present more than one potentially basic or acid center. Because of the biological interest of these compounds and their HB capabilities in the living systems, and as a logical continuation of our long-standing interest in the complexation of these compounds, we report in this work a theoretical study of HB interactions between methanol and a large set of lactones and lactams. Methanol is chosen under its monomeric form because it is the

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smallest alcohol that can interact without significant steric constraints. One of the aims of this paper is to analyze the structures of the complexes formed via the following interaction types: O−H···O, N−H···O, and C−H···O. Inasmuch as methanol is an amphiprotic molecule, we face the analysis of whether lactones and lactams display basic and/or acidic behavior toward this alcohol. For the sake of completeness, we have included in this work the corresponding cyclic ketones. More precisely, we have investigated the following compounds: cyclopropanone (**1**), cyclobutanone (**2**), cyclopentanone (**3**), cyclohexanone (**4**), cycloheptanone (**5**), oxiran-2-one (**6**), β-propiolactone (**7**), γ-butyrolactone (**8**), δ-valerolactone (**9**), ϵ-caprolactone (**10**), aziridinone (**11**), azetidin-2-one (**12**), pyrrolidin-2-one (**13**), δ-valerolactam (**14**), and ϵ-caprolactam (**15**). To investigate the possible effect of *N*-methyl substitution on the characteristics of these HB interactions, the following derivatives were added to the previous set: 1-methylaziridinone (**16**), 1-methylazetidin-2-one (**17**), 1-methylpyrrolidin-2-one (**18**), 1-methyl-δ-valerolactam (**19**), and 1-methyl-ϵ-caprolactam (**20**).

Computational Details

All calculations were performed using the Gaussian 98 set of programs.[50] Geometry optimizations were carried out using the B3LYP[51,52] density functional theory (DFT) approach, with the 6-311+G(d,p) basis set.[53] The harmonic frequencies were calculated at the same level to characterize the stationary points found as minima of the potential energy surface and to evaluate the corresponding zero point vibrational energy (ZPE) that was scaled by the empirical factor 0.98,[54] as well as the thermal contributions to the energy. Basis set superposition error (BSSE) was calculated using the counterpoise method of Boys and Bernardi.[55] The topological properties of the electronic density were characterized using the atoms in molecules (AIM) theory.[56] The bond critical points (bcp's) and the ring critical points (rcp's) were located by means of the AIMPAC series of programs.[57] Charge distributions were obtained using the natural bond order (NBO) analysis of Weinhold et al.[58]

Results and Discussion

Geometries. As was found for protonation[45,46] and for charge-transfer complexation,[47] the carbonyl oxygen is the most favorable basic center for all considered compounds except for aziridinone (see later). Several orientations of methanol with respect to the carbonyl oxygen were examined. In the case of lactones and lactams, three stable structures were retained. The cis structures are complexes in which methanol approaches the carbonyl group from the same side of the ring oxygen (nitrogen) atom. When methanol approaches the opposite side of the ring oxygen (nitrogen), the structure is called trans. Two cis structures, namely, cis-a and cis-b, are identified. In cis-a complexes, the main interaction is between the OH hydrogen of methanol and the carbonyl oxygen of the base. In cis-b complexes, the dominant interaction is between the OH hydrogen of methanol and the ring ether-like oxygen for lactones and between the NH hydrogen and the methanol oxygen, that in this case behaves as a HB acceptor, for lactams and *N*-methyl lactams (see Figure 1). Fully optimized structures of complexes in their most stable conformations are reported in Figure 1.

The calculated total energies, ZPEs, thermal corrections, basis set superposition errors, and entropy values of the free and complexed compounds under investigation are summarized in Supporting Information Table S1.

In the investigated complexes, with the only exception of the cis-b complexes of lactones and some three-membered rings, both components behave simultaneously as a HB donor and as a HB acceptor. For instance, in complexes involving ketones and in all trans complexes of lactones and lactams, besides the OH···O HB between the OH group of methanol and the carbonyl oxygen of the base, an unconventional HB between the hydrogen in the α position to the carbonyl and the oxygen of methanol is observed. In cis-a complexes of lactones, this unconventional HB is replaced by a much weaker one between the methyl group of methanol and the ether-like oxygen of the lactones and by a quite strong NH···O HB in the case of both cis-a and cis-b complexes of lactams.

The fact that in all complexes the C=O group behaves as a HB acceptor leads to a sizable elongation of the bond. Accordingly, its bond length increases from 1.205 to 1.212 Å in the case of cyclic ketones, from 1.195 to 1.204 Å in the case of lactones, and from 1.213 to 1.223 Å in the case of lactams. Similarly, the O−H bond of methanol and the N−H bond of lactams when they behave as HB donors increase by about 0.010−0.015 and 0.010 Å, respectively. Interestingly, when the C−H bond in the α position to the carbonyl is involved in an unconventional HB, it is shortened by about 0.004−0.006 Å for cyclic ketones and lactones and very little in the case of *N*-methyl lactams. This behavior is in agreement with literature results.[7,59,60] As suggested by Hobza et al.,[24] this trend may be attributed to the electronic density transfer from the proton acceptor to the proton donor due to the dominant stabilizing role of the dispersion forces.[59,61]

The fact that most of the complexes are cyclic structures due to the aforementioned amphoteric behavior of both components has a significant effect on the O−H···O HB angles, which vary from 162 to about 172° for cyclic ketones and *N*-methyl lactams, from 152 to 162° for lactones, and from 149 to 153° for unsubstituted lactams. The smallest angles are found for unsubstituted lactams, reflecting the strength of the NH···O HB between the base and the molecule of methanol.

Vibrational Frequencies. Spectroscopy, in particular IR, was the most important method for the study of HB interaction. The shift to lower frequencies of the O−H, N−H, and C=O stretching bands, reflecting the lengthening of these bonds as a result of the HB formation, is a major indicator. In agreement with the elongation of the C=O bond discussed in previous sections, the C=O stretching band appears shifted upon complexation to lower frequency values (see Table 1). This red shifting is relatively small for the three-membered ring systems. In the others cases, it varies between 20 and 40 cm^{-1}. As expected, the OH and NH stretching frequencies vary more significantly. In fact, with the exception of three- and four-membered rings, the variation of ν_{OH} is about 153 cm^{-1} for cyclic ketones, 142 cm^{-1} for lactones, 246 cm^{-1} for lactams, and 210 cm^{-1} for *N*-methyl lactams. It can be observed that the variation regularly increases with the ring size, reflecting the increase of the HB strength. The last column of Table 1 shows the frequency shifts of the NH band associated with the acidic behavior of this group in lactams. The greatest shifting is found for aziridinone (164 cm^{-1}). In this case, the cis-b structure, where the main interaction is between the NH hydrogen and the methanol oxygen, is the most stable one, showing that this molecule acts as an acid rather than as a base toward methanol.

Electron Density Analysis. Different studies have pointed out that the formation of hydrogen bonds is associated with the appearance of a bond critical point between the hydrogen atom

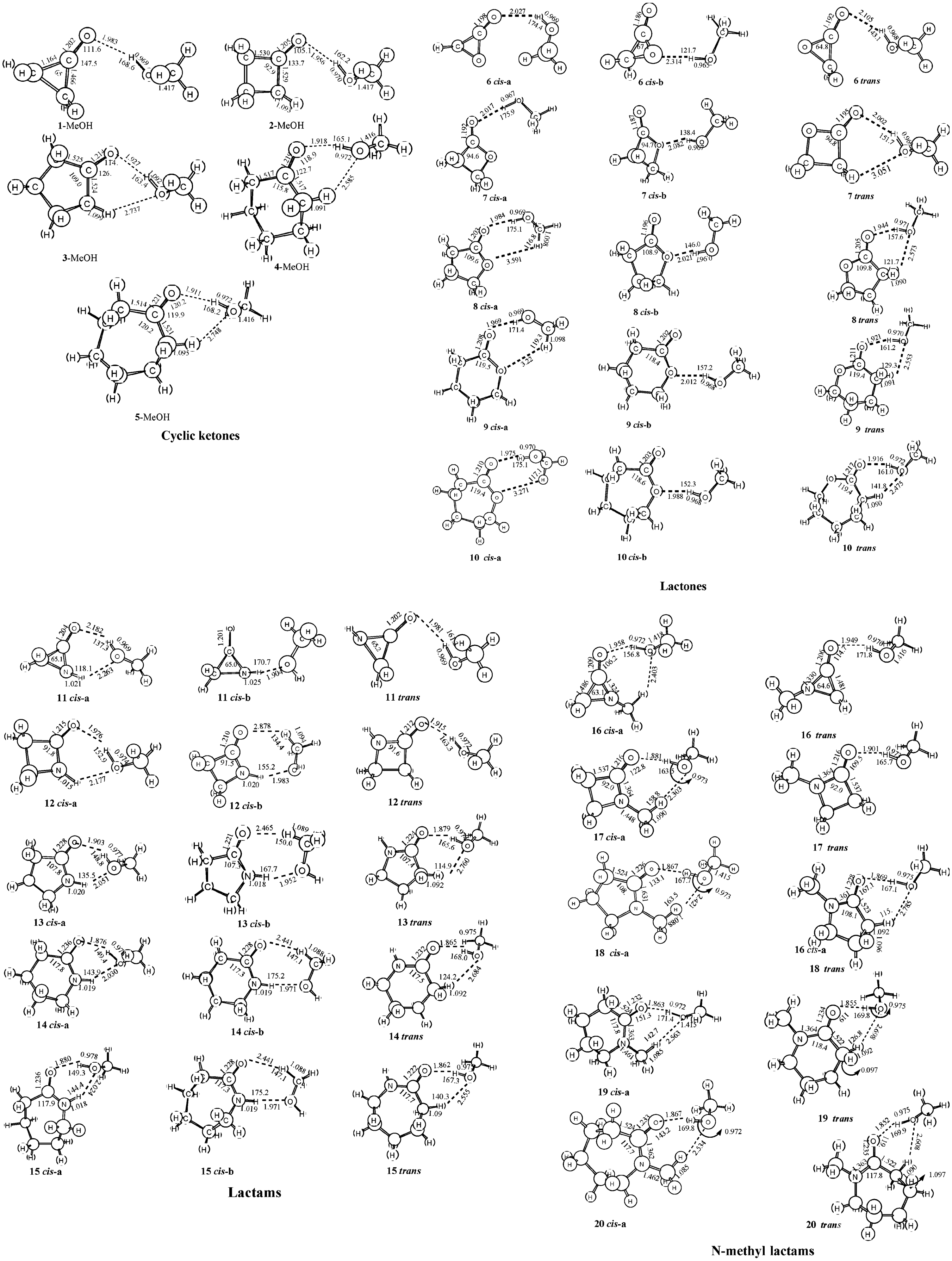

Figure 1. B3LYP/6-311+G* optimized geometries of the most stable complexes of cyclic ketones, lactones, lactams, and *N*-methyl lactams with methanol. For lactams, the most stable structure, in terms of free energies, is the cis-a structure, while, for lactones and for *N*-methyl lactams, it is the trans one.

TABLE 1: Frequencies ν_{O-H}, $\nu_{C=O}$, and ν_{NH} Evaluated at B3LYP/6-311+G* and Its Displacements (in cm^{-1})[a]

species	ν_{O-H}	$\Delta\nu_{O-H}$	$\nu_{C=O}$	$\Delta\nu_{C=O}$	ν_{N-H}	$\Delta\nu_{N-H}$
1			1890			
1−MeOH	3611	103	1878	12		
2			1823			
2−MeOH	3588	126	1799	24		
3			1775			
3−MeOH	3564	150	1751	24		
4			1746			
4−MeOH	3561	153	1725	21		
5			1733			
5−MeOH	3557	157	1708	25		
6			1967			
6 *cis*-a	3672	42	1955	12		
6 *cis*-b	3698	16	1948	4		
6 *trans*	3648	67	1963	19		
7			1875			
7 *cis*-a	3662	52	1856	19		
7 *cis*-b	3665	49	1877	−2		
7 *trans*	3615	99	1842	33		
8			1815			
8 *cis*-a	3630	84	1792	23		
8 *cis*-b	3657	57	1818	−3		
8 *trans*	3580	134	1781	34		
9			1772			
9 *cis*-a	3605	109	1744	28		
9 *cis*-b	3650	64	1775	−3		
9 *trans*	3568	146	1737	35		
10			1768			
10 *cis*-a	3607	107	1743	25		
10 *cis*-b	3643	72	1770	−2		
10 *trans*	3568	146	1736	32		
11			1917		3467	
11 *cis*-a	3611	103	1894	23	3434	33
11 *cis*-b	3723	9	1904	13	3303	164
11 *trans*	3632	82	1902	15	3474	−7
12			1820		3528	
12 *cis*-a	3530	184	1782	38	3480	48
12 *cis*-b	3718	4	1798	22	3389	139
12 *trans*	3555	158	1791	29	3529	−1
13			1753		3555	
13 *cis*-a	3480	234	1717	36	3437	118
13 *cis*-b	3731	17	1735	18	3513	142
13 *trans*	3517	196	1725	28	3554	1
14			1710		3518	
14 *cis*-a	3461	253	1689	21	3393	125
14 *cis*-b	3730	16	1698	12	3403	115
14 *trans*	3507	207	1684	26	3519	−1
15			1705		3535	
15 *cis*-a	3464	250	1686	19	3406	130
15 *cis*-b	3729	15	1695	10	3416	119
15 *trans*	3508	206	1681	24	3533	2
16			1908			
16 *cis*-a	3567	147	1894	14		
16 *trans*	3599	116	1897	11		
17			1797			
17 *cis*-a	3536	178	1771	26		
17 *trans*	3543	172	1769	28		
18			1730			
18 *cis*-a	3549	166	1707	23		
18 *trans*	3508	206	1698	32		
19			1681			
19 *cis*-a	3561	153	1660	21		
19 *trans*	3503	211	1649	32		
20			1682			
20 *cis*-a	3562	152	1659	23		
20 *trans*	3502	213	1650	32		

[a] The calculated values were scaled by the empirical factor 0.98.

and the acceptor atom, which are linked by the concomitant bond path.[52b] This critical point exhibits the typical properties of a closed-shell interaction, with a low value of the electron density, ρ_{bcp} (see Table 2).

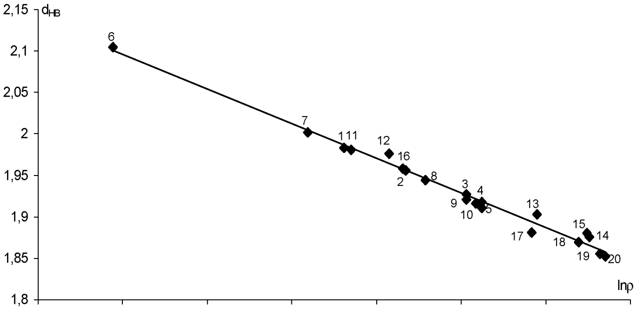

Figure 2. Correlation between the HB distances and the logarithm of the electron density at the OH· · ·O bcp.

The values of ρ_{bcp} reflect the strength of the bond, and they are larger for the OH· · ·O HB than for the NH· · ·O and CH· · ·O ones. Similarly, the density at the OH· · ·O bcp increases upon going from three- to seven-membered rings. This increment is consistent with the enhancement of the HB strength when progressing toward larger cycles (see Table 2). The same remark can be made as far as the NH· · ·O and CH· · ·O bcp's are concerned.

As described by Alkorta et al.,[62] the HB distances were found to correlate nicely with the logarithm of the electron density at the bcp (Figure 2).

The corresponding equation is

$$d_{HB} = (-0.42 \pm 0.02) \ln \rho_{bcp} + (0.42 \pm 0.04) \quad \text{with } r = 0.993, \text{ s.d.} = 0.007, \text{ and } n = 20 \quad (1)$$

The topological analysis of the charge density of the complexes considered reveals also the existence of ring critical points (rcp's), nicely indicating the existence of the unconventional HBs. Some previous studies[14a,63−64] indicate that the charge density at the rcp can be a reliable index of the strength of the HB interaction in cyclic systems. The values of the electron density at the rcp reported in Table 2 clearly show the stability enhancement of the complex with the ring size, in agreement with our previous arguments.

It is worth mentioning that, as expected, unconventional C−H· · ·O HBs exhibit rather large bond distances, typically greater than 2.2 Å. As a consequence, these interactions are not detected through a NBO analysis, although they are characterized by the existence of a bond critical point with charge densities in the range 0.005−0.009 au.

As we have mentioned in a previous work,[47d] the complexation energy and charge-transfer interactions constitute an example of synergy between them. In the case of a single HB, a charge transfer from the proton acceptor to the proton donor should be expected. In our case, where both components act as proton donors and as proton acceptors, the amount of electronic charge transferred from one monomer to the other does not follow a simple pattern. Nevertheless, it can be observed from the data of Table 2 that the charge transferred to methanol is relatively larger for larger rings. Concomitantly, the electron population of the methanol hydroxyl hydrogen decreases upon complexation, and this effect also increases with the ring size. Both effects are consistent with an enhancement of the strength of the interaction.

Thermodynamics of Hydrogen Bond Complexation. Table 3 gathers the computed thermodynamic values pertaining to the formation of the different structures of the complexes in the gas phase. The results include ZPE, BSSE, and $P\Delta V$ correc-

TABLE 2: Selected Geometrical Parameters of the HB (in Å), the Electron Density at the HB Critical Points, ρ, the Ring Critical Point (in au), and the Atomic Net Charges[a] of the Most Stable Complexes, in Terms of Free Energies

complex	$d_{OH\cdots O}$	$\rho_{OH\cdots O}$	$d_{XH\cdots O(X=C,N)}$	$\rho_{XH\cdots O(X=C,N)}$	rcp	Δq[b]	$\Delta q_{H(-O-CH_3)}$[c]	$q_{H(-C-C=O)}$
1−MeOH	1.983	0.0238				0.0168	0.0236	0.198 50
2−MeOH	1.956	0.0256				0.0186	0.0261	0.226 21
3−MeOH	1.927	0.0275	2.737	0.0054	0.0049	0.0184	0.0274	0.226 67
4−MeOH	1.918	0.0280	2.585	0.0066	0.0061	0.0199	0.0310	0.223 41
5−MeOH	1.911	0.0280	2.748	0.0061	0.0062	0.0178	0.0305	0.207 09
6 *trans*	2.105	0.0182				0.0078	0.0233	0.200 92
7 *trans*	2.202	0.0228	3.051	0.0048	0.0048	0.0125	0.0279	0.231 40
8 *trans*	1.944	0.0262	2.573	0.0073	0.0057	0.0159	0.0314	0.228 48
9 *trans*	1.921	0.0275	2.553	0.0074	0.0063	0.0162	0.0323	0.227 74
10 *trans*	1.916	0.0278	2.475	0.0082	0.0069	0.0165	0.0342	0.210 75
11 *cis*-a	2.182	0.0154	2.263	0.0139	0.0075	0.0050	0.0286	0.384 17
12 *cis*-a	1.976	0.0251	2.177	0.0158	0.0084	0.0140	0.0368	0.392 78
13 *cis*-a	1.903	0.0299	2.051	0.0204	0.0097	0.0148	0.0407	0.395 40
14 *cis*-a	1.876	0.0318	2.030	0.0215	0.0108	0.0149	0.0422	0.389 97
15 *cis*-a	1.880	0.0317	2.024	0.0217	0.0108	0.0139	0.0424	0.392 30
16 *cis*-a	1.958	0.0255	2.403	0.0105	0.0039	0.0170	0.0285	0.188 00
17 *cis*-a	1.881	0.0297	2.303	0.0117	0.0051	0.0222	0.0322	0.218 38
18 *trans*	1.869	0.0314	2.785	0.0050	0.0049	0.0229	0.0327	0.225 58
19 *trans*	1.855	0.0322	2.698	0.0058	0.0058	0.0245	0.0367	0.228 98
20 *trans*	1.852	0.0324	2.608	0.0068	0.0060	0.0236	0.0377	0.231 05

[a] Calculated using the NBO method. [b] Charge transferred from the proton acceptor. [c] The loss of the charge at the hydroxyl hydrogen.

tions(see Supporting Information Table S1). The values of $\Delta_r G°$ were obtained by means of the following equation:

$$\Delta_r G° = \Delta_r H° - T\Delta_r S° \qquad (2)$$

The first conspicuous fact is that for the lactones the trans complexes are the most stable, reflecting an additional stabilizing effect of the unconventional HB between the CH group α to the carbonyl group and the methanol oxygen, larger than that between the ether-like oxygen and the methyl methanol hydrogen, as in the cis-a conformer. As a matter of fact, the net atomic charge of the hydrogen in the α position of the carbonyl group for lactones (see Table 2) is greater than that of the CH_3 hydrogen of methanol (by about 0.1600), indicatingthat the first is more acidic than the second. Furthermore, the charge of the free methanol oxygen (−0.7254) is greater than that of the ether-like oxygen of lactones (about −0.540), and therefore, the former behaves as a better HB acceptor.

For unsubstituted lactams, on the contrary, the most stable complexes correspond to the cis-a arrangement, if one takes into account thermal corrections for relative energy calculations. This structure is clearly favored with respect to trans, because the NH···O HB in the former is stronger than the unconventional CH···O HB in the latter, reflecting the larger acidic character of the NH group of lactams (see Table 3). Similarly, the cis-a form is more stable than the cis-b one because in the latter the strong OH···O HB has been replaced by a rather weak unconventional hydrogen bond involving a methyl hydrogen of methanol.

The second important finding is that lactams (**11**−**15**) yield stronger complexes than lactones (**6**−**10**) and cyclic ketones (**1**−**5**) by more than 1 kcal/mol.

A priori, one should expect lactones to be poorer HB acceptors than cyclic ketones due to the presence of an ether-like oxygen in the ring. However, complexes with lactones, as well as those with ketones, are extrastabilized through the unconventional HB between the methanol oxygen and the hydrogen in the α position of the carbonyl group, and both families exhibit quite similar complexation energies. Lactams are in general more basic than lactones,[46] and they should be expected to be better HB acceptors. Besides, the stability of the corresponding complexes is enhanced through the formation of a quite strong NH···O HB that cannot be formed in the other systems.

The third important finding is that the trans and cis-a complexes are very closed in terms of free energies, and therefore, both should be present as an equilibrium mixture in the gas phase.

It is also worth noting that, in the case of aziridinone and according to our calculated $\Delta_r G°_{(MeOH)}$ value, the cis-b structure in which methanol hydrogen binds the ether-like oxygen only becomes the most stable complex, and therefore, this compound seems to behave as an acid rather than a base toward methanol.

Also, interestingly, our calculated enthalpies are in agreement with those of Gutmann[65] denoted “DN” (donor number) for which the reference acid is $SbCl_5$ and those of Maria and Gal[66] for which the reference acid is BF_3. The linear relationships in these two cases fulfilled eqs 3 and 4, respectively.

$$\Delta_r H°_{(MeOH)} = (-0.126 \pm 0.009)\mathrm{DN} - (4.626 \pm 0.215) \quad \text{with} \quad r = 0.991,\ \text{s.d.} = 0.098,\ \text{and}\ n = 5 \qquad (3)$$

$$\Delta_r H°_{(MeOH)} = (-0.0379 \pm 0.0047)\Delta_r H°_{(BF_3)} - (3.846 \pm 0.397) \quad \text{with} \quad r = 0.977,\ \text{s.d.} = 0.159,\ \text{and}\ n = 5 \qquad (4)$$

These correlations show that DN and $\Delta_r H°_{(BF_3)}$ scales are markedly more sensitive to structural effects than $\Delta_r H°_{(MeOH)}$. Although the complexation energies change significantly from quite small values when the reference acid is MeOH to much larger values when the reference acids are $SbCl_5$ or BF_3, the different basicity scales follow the same trends.

In the same way, it is of interest to compare our $\Delta_r G°_{(MeOH)}$ values and the calculated $\Delta_r G°_{(ICl)}$ values determined in a previous work,[47d] since the same acidic and basic sites of the carbonyl compounds interact with ICl and methanol. For this purpose, we have plotted in Figure 3 the data for all studied complexes. The overall plot exhibits a marked scatter (eq 5), showing that all of the data cannot be correlated by a single straight line.

$$\Delta_r G°_{(MeOH)} = (0.558 \pm 0.069)\Delta_r G°_{(ICl)} + (0.094 \pm 0.214) \quad \text{with} \quad r = 0.884,\ \text{s.d.} = 0.365\ \text{kcal/mol},\ \text{and}\ n = 20 \qquad (5)$$

However, a close examination of Figure 3 evidences that four

TABLE 3: Calculated Values (in kcal/mol) of Selected Thermodynamic State Functions at the B3LYP/6-311+G* Level for Cyclic Ketone−, Lactone−, and Lactam−Methanol Complexes

species	$\Delta_rH°$(MeOH)	$\Delta_rG°$(MeOH)
1		
1−MeOH	−5.77	−0.37
2		
2−MeOH	−6.30	−0.71
3		
3−MeOH	−6.78	−0.78
4		
4−MeOH	−6.85	−1.15
5		
5−MeOH	−6.92	−0.96
6		
6 *cis*-a	−5.47	−0.18
6 *trans*	−5.63	−0.35
6 *cis*-b	−4.93	0.59
7		
7 *cis*-a	−5.12	−0.76
7 *trans*	−6.39	−0.79
7 *cis*-b	−5.10	0.21
8		
8 *cis*-a	−5.82	−0.63
8 *trans*	−7.02	−0.87
8 *cis*-b	−5.34	−0.19
9		
9 *cis*-a	−6.52	−0.86
9 *trans*	−7.17	−1.07
9 *cis*-b	−5.90	−0.91
10		
10 *cis*-a	−6.22	−0.62
10 *trans*	−7.20	−1.08
10 *cis*-b	−6.06	−0.95
11		
11 *cis*-a	−7.29	−0.88
11 *trans*	−5.96	−1.05
11 *cis*-b	−6.84	−1.72
12		
12 *cis*-a	−8.90	−2.12
12 *trans*	−6.50	−1.49
12 *cis*-b	−6.00	0.27
13		
13 *cis*-a	−9.79	−2.45
13 *trans*	−7.89	−1.89
13 *cis*-b	−6.44	0.55
14		
14 *cis*-a	−9.99	−2.58
14 *trans*	−7.85	−1.80
14 *cis*-b	−6.1	0.77
15		
15 *cis*-a	−10.24	−2.53
15 *trans*	−7.95	−1.89
15 *cis*-b	−6.01	1.03
16		
16 *cis*-a	−7.34	−0.82
16 *trans*	−6.30	−1.63
17		
17 *cis*-a	−8.04	−1.95
17 *trans*	−7.51	−2.13
18		
18 *cis*-a	−7.68	−1.72
18 *trans*	−8.07	−2.24
19		
19 *cis*-a	−7.41	−1.79
19 *trans*	−8.10	−2.29
20		
20 *cis*-a	−7.39	−1.46
20 *trans*	−8.03	−2.16

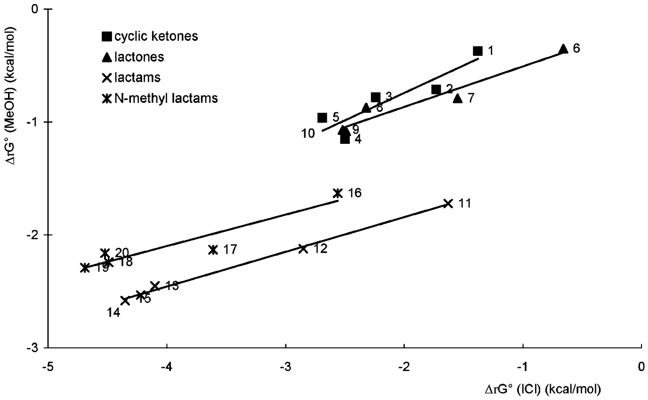

Figure 3. Correlation between $\Delta_rG°_{(\mathrm{MeOH})}$ and $\Delta_rG°_{(\mathrm{ICl})}$.

better correlations of different slopes can be obtained when cyclic ketones, lactones, lactams, and *N*-methyl lactams are considered separately:

$$\Delta_rG°_{(\mathrm{MeOH})} = (0.486 \pm 0.132)\Delta_rG°_{(\mathrm{ICl})} + (0.230 \pm 0.286)$$
$$\text{with } r = 0.905,\ \text{s.d.} = 0.144\ \text{kcal/mol, and } n = 5 \text{ for cyclic ketones} \quad (6)$$

$$\Delta_rG°_{(\mathrm{MeOH})} = (0.359 \pm 0.054)\Delta_rG°_{(\mathrm{ICl})} - (0.147 \pm 0.110)$$
$$\text{with } r = 0.967,\ \text{s.d.} = 0.087\ \text{kcal/mol, and } n = 5 \text{ for lactones} \quad (7)$$

$$\Delta_rG°_{(\mathrm{MeOH})} = (0.307 \pm 0.011)\Delta_rG°_{(\mathrm{ICl})} - (1.226 \pm 0.040)$$
$$\text{with } r = 0.998,\ \text{s.d.} = 0.026\ \text{kcal/mol, and } n = 5 \text{ for lactams} \quad (8)$$

$$\Delta_rG°_{(\mathrm{MeOH})} = (0.279 \pm 0.057)\Delta_rG°_{(\mathrm{ICl})} - (0.982 \pm 0.230)$$
$$\text{with } r = 0.943,\ \text{s.d.} = 0.102\ \text{kcal/mol, and } n = 5 \text{ for } N\text{-methyl lactams} \quad (9)$$

The quality of the correlations is remarkably good. This high degree of self-consistency supports the computational techniques used in this (and previous) work. Although the methanol complexes are significantly less stable than those with ICl, as indicated by the negative intercepts of these correlations, their linearity underlines the similarity of the involved interactions. The slopes of these equations, varying from about 0.5 for cyclic ketones to about 0.3 for *N*-methyl lactams, indicate that the HB interaction is at least a half less sensitive to structural effects than the complexation with ICl. These correlations exhibit that the interactions at work in charge-transfer and HB complexes are not fundamentally different in nature and can be interpreted in the same terms.

Conclusion

Our survey of the HB complexes between methanol and cyclic ketones, lactones, and lactams shows that, in the most stable conformation, both components behave simultaneously as a HB donor and as a HB acceptor. The dominant interaction for the most stable complexes is between the oxygen carbonyl and the OH hydrogen of methanol. However, the role of unconventional HBs, those between the CH group α to the carbonyl group and the oxygen of methanol, is important as far as the overall stability of the complex is concerned. The trans structure is the most stable in the case of lactones and *N*-methyl lactams, whereas the cis-a structure is the most stable one in the case of lactams. In the case of aziridinone, the interaction is principally between the NH hydrogen and the methanol oxygen, showing that this molecule acts as an acid rather than a base toward methanol. A good correlation was found between the charge density at the bond critical point and the O···H distances. For the majority of the complexes, the stabilities of the cis-a and trans forms as measured by the corresponding $\Delta_r G°$(MeOH) values are rather close and therefore both forms should be present as an equilibrium mixture in the gas phase. The red shift of the CO and OH stretching vibrational calculated frequencies provides information about the changes of these bonds after complexation and can be used as a fingerprint to identify these complexes. The shift is stronger in the case of lactams and at the larger cycles, indicating that the strength of the hydrogen bond increases with the ring size. The unsubstituted lactams yield more stable complexes with methanol than *N*-methyl lactams, lactones, and cyclic ketones. Finally, some correlations have been obtained between our calculated Gibbs energy for complexation with methanol and other basicity scales.

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Supporting Information Available: Table showing the calculated total energies, ZPEs, TCEs, BSSEs, and entropy values of the free and complexed compounds under investigation. This material is available free of charge via the Internet at http://pubs.acs.org.

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