

## Ab Initio SCF study of the barrier to internal rotation in simple amides

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Dedicated to Acad. Ivan Juchnovski on the occasion of his 80<sup>th</sup> birthday

The free energies of activation for rotation about the amide C-N bond in R-C(O)NR'<sub>2</sub> (R'=CH<sub>3</sub>, R = CN, N<sub>3</sub>, C≡C-H, C≡C-CH<sub>3</sub>; R'=H, R = C<sub>2</sub>H<sub>5</sub>, CH(CH<sub>3</sub>)<sub>2</sub>) were calculated at the MP2(fc)/6-31+G\*\*//6-31G\* and at the MP2(fc)/6-311++G\*\*//6-311++G\*\* levels of theory and compared with the NMR liquid and gas-phase data. On the basis of results from this and previous studies we generalize that in case of amides and thioamides the nonbonded interactions in ground state (GS) are mainly responsible for the differences in the rotational barriers and they prevail over the electronic effects of the substituents.

**Key words:** amides; barrier to internal rotation; ab initio SCF study

### INTRODUCTION

The great interest for the amide functional group in chemistry is mainly related to its occurrence as a building block in peptides and proteins. The internal rotation about the amide C-N bond in amides and thioamides has been intensively studied experimentally by NMR spectroscopy in the gas [1-7] and in the liquid phase [8]. The experimental results were used to judge theoretical methods of calculating barrier heights. The origin of the C-N rotational barrier and its relation to amide resonance has also received much attention in the last years [9-14].

Recently the electronic effect of polar substituents on the barrier of internal rotation around the amide carbon-nitrogen bond in p-substituted acetanilides [15, 16] and thioacetanilides [17] were studied at the B3LYP/6-31G(d,p) level. Several linear relationships were established linking the barrier heights with structural and electronic parameters that characterize the amide and thioamide grouping. The results obtained are consistent with the views for a classical amide resonance as being the origin of higher rotational barriers in thioamides than in amides.

Recently we presented *ab initio* calculations [18] of barrier to internal rotation about C-N bond in N,N-dimethylcinnamamides, which were studied by dynamic NMR spectroscopy [19,20]. On the other hand the interest to cinnamamides namely coumaric amides increases in the last years because

of potential antioxidant activity of these compounds [21,22]. The free energy of activation of substituted cinnamamides were reproduced very well using MP2(fc)/6-31+G\*\*//6-31G\* energies and PCM/6-31G\* energy change from gas phase to chloroform. For all studied compounds the anti transition state (*anti* TS) is more stable and determines the rotational barrier. The remote effect of phenyl substituents in the studied compound has pure electronic origin, which was demonstrated by the relationship between C-N bond order difference and calculated energy barrier [18].

In this paper we continue our investigation of effects of substituents on the height of rotational barriers in amides by *ab initio* studying at the MP2/6-31+G\*\*//6-31G\* and at the MP2(fc)/6-311++G\*\*//6-311++G\*\* levels of theory the amides R-C(O)N(CH<sub>3</sub>)<sub>2</sub> (R = CN, N<sub>3</sub>, C≡C-H, C≡C-CH<sub>3</sub>) and in H-C(O)NR<sub>2</sub> (R = C<sub>2</sub>H<sub>5</sub>, CH(CH<sub>3</sub>)<sub>2</sub>).

### METHODS

The *ab initio* SCF calculations were performed using the package GAMESS [23]. The complete geometry optimization was carried out using the 6-31G\* and 6-311++G\*\* basis sets. The molecules were assumed to have C<sub>1</sub> symmetry in the ground state (GS) and C<sub>s</sub> symmetry in the transition states (TS). The bond order analysis was done at the HF/6-31G\* level of theory as it is implemented in program GAMESS for closed shells by Giambiagi [24] and Mayer [25]. For recent review about bond orders see ref. [26]. The energies were

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then calculated at the MP2(fc)/6-31+G\*\*//6-31G\* and at the MP2(fc)/6-311++G\*\*//6-311++G\*\* levels of theory. In calculating the vibrational energies, the vibrational frequencies were scaled by 0.89[27]. In each case 7 (TS) or 8 (GS) scaled frequencies below 500 cm<sup>-1</sup> were treated as rotations ( $E=RT/2$ ) [27]. The imaginary frequency for the transition states is ignored in all thermodynamics calculations. The effect of solvent on the relative stabilities of the GS and TS was studied using the polarized continuum model (PCM) proposed by Tomasi et al. [28] with the built in parameters for solvents CCl<sub>4</sub> and toluene. In the case of 1,1,2,2-tetrachloroethane (TCE) and diethyl formamide we relied on the experimental data. The static dielectric constant was 8.20 for TCE and 29.02 for diethyl formamide, the dielectric constants at infinite frequency were calculated from the refractive indexes. The solvent radiuses, the solvent densities and the molar volumes were calculated from the tabulated densities and molar masses. In our investigations only the electrostatic contributions were taken into account utilizing single point PCM calculations at HF/6-311++G\*\* level of theory.

## RESULTS AND DISCUSSION

### *Geometry optimization*

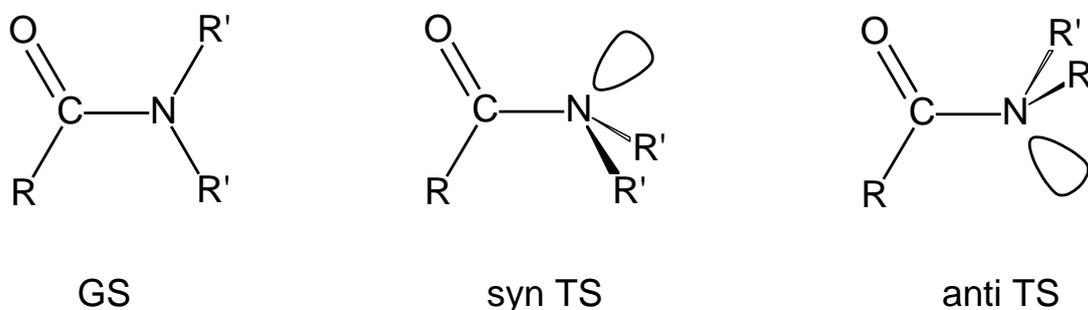
The heavy-atom framework of the studied molecules in the GS was found to be essentially planar and close to C<sub>s</sub> symmetry. The GS structures of H-C(O)NR<sub>2</sub> (R = C<sub>2</sub>H<sub>5</sub>, CH(CH<sub>3</sub>)<sub>2</sub>) are an exception (Figure 1 and S1). The two R substituents are not symmetrical [29]. The transition state geometries of studied amides (Figure 1 and 1S) were optimized in C<sub>s</sub> symmetry. This approach usually yields transition states, but for some of our structures additional refining of saddle point was necessary in order to locate TS structure with only

one imaginary frequency. Again the TS structures of H-C(O)NR<sub>2</sub> (R = C<sub>2</sub>H<sub>5</sub>, CH(CH<sub>3</sub>)<sub>2</sub>) were unsymmetrical (Figure 1S). The calculated energies for GS, *anti* and *syn* TS, are presented in Tables 1 and 1S. The *anti* TS is more stable in all cases. Therefore *anti* TS of studied compounds give the greatest contribution to the rotational barrier.

The most significant structural changes in the process of rotation towards the transition states are that the nitrogen is pyramidalized and the C-N bond lengthens from 1.34-1.35 to 1.40-1.42 Å (Table 2). However, the C=O bond length shortens by 0.01-0.02 Å only. This indicates that the carbonyl group is relatively unaffected by this rotation

### *Comparison of calculated activation parameters and experimental data*

Calculation of the vibrational frequencies confirmed the assignment of the *anti* and *syn* forms as transition states and allowed computation of the enthalpy, entropy and free energy changes at 298K. The thermodynamic results for the isomerisation of the studied amides are presented in Table 3. In present case,  $\Delta H^{298}$  is obtained from the sum of the changes in the electronic energy,  $\Delta E_e^0$ , the zero-point vibrational energy,  $\Delta E_v^0$ , and the thermal correction to the zero-point energy,  $\Delta \Delta E_v^{298}$ . The scaled frequencies were used also for the entropy calculation. In this case the two lowest real frequencies, which correspond to rotations of the methyl groups, need to be treated as hindered rotations. The resultant free energy,  $\Delta G^\ddagger(298K)$ , for the *anti* TS can be compared with the gas-phase NMR results.



**Fig. 1.** Ground state (GS) and two transition states (TS) of the studied amides: (R'=CH<sub>3</sub>, R = CN, N<sub>3</sub>, C=C-H, C≡C-CH<sub>3</sub>; R'=H, R = C<sub>2</sub>H<sub>5</sub>, CH(CH<sub>3</sub>)<sub>2</sub>).

**Table 1.** Calculated Electronic energies  $E_e^0$  for the studied amides  $R-C(O)NR'_2$  in Hartrees

R	R'	State	ZPE <sup>b</sup>	MP2(fc)/ 6-31+G**// 6-31G*	MP2(fc)/ 6-311++G**// 6-311++G**	PCM/311++G**
CH <sub>3</sub> C≡C	CH <sub>3</sub>	GS	84.20	-362.822927	-363.035250	-7.2 <sup>c</sup>
CH <sub>3</sub> C≡C	CH <sub>3</sub>	<i>anti</i> TS	83.98	-362.796311 <sup>a</sup>	-363.009445 <sup>a</sup>	-5.6 <sup>c</sup>
CH <sub>3</sub> C≡C	CH <sub>3</sub>	<i>syn</i> TS	83.92	-362.795327	-363.009209	-6.6 <sup>c</sup>
HC≡C	CH <sub>3</sub>	GS	67.31	-323.645785	-323.828466	-6.9 <sup>c</sup>
HC≡C	CH <sub>3</sub>	<i>anti</i> TS	67.05	-323.618149 <sup>a</sup>	-323.801902 <sup>a</sup>	-5.3 <sup>c</sup>
HC≡C	CH <sub>3</sub>	<i>syn</i> TS	66.98	-323.617324	-323.801782	-6.1 <sup>c</sup>
N≡C	CH <sub>3</sub>	GS	60.93	-339.732431	-339.915725	-7.2 <sup>c</sup>
N≡C	CH <sub>3</sub>	<i>anti</i> TS	60.60	-339.701189	-339.885634	-5.4 <sup>c</sup>
N≡C	CH <sub>3</sub>	<i>syn</i> TS	60.48	-339.701347 <sup>a</sup>	-339.886375 <sup>a</sup>	-6.0 <sup>c</sup>
N <sub>3</sub>	CH <sub>3</sub>	GS	63.94	-410.926097	-411.140548	-3.4 <sup>d</sup>
N <sub>3</sub>	CH <sub>3</sub>	<i>anti</i> TS	63.70	-410.901043 <sup>a</sup>	-411.116520 <sup>a</sup>	-3.9 <sup>d</sup>
N <sub>3</sub>	CH <sub>3</sub>	<i>syn</i> TS	63.67	-410.900286	-411.116026	-4.0 <sup>d</sup>
H	C <sub>2</sub> H <sub>5</sub>	GS	107.70	-326.070618	-326.287625	-7.3 <sup>e</sup>
H	C <sub>2</sub> H <sub>5</sub>	<i>anti</i> TS	106.95	-326.035407 <sup>a</sup>	-326.253552 <sup>a</sup>	-4.4 <sup>e</sup>
H	C <sub>2</sub> H <sub>5</sub>	<i>syn</i> TS	106.73	-326.033911	-326.252694	-6.4 <sup>e</sup>
H	i-C <sub>3</sub> H <sub>7</sub>	GS	129.54	-404.411288	-404.688025	-3.7 <sup>f</sup>
H	i-C <sub>3</sub> H <sub>7</sub>	<i>anti</i> TS	128.60	-404.373029 <sup>a</sup>	-404.650673 <sup>a</sup>	-2.3 <sup>f</sup>
H	i-C <sub>3</sub> H <sub>7</sub>	<i>syn</i> TS	128.51	-404.371845	-404.650225	-3.3 <sup>f</sup>
CH <sub>3</sub> C≡C	H	GS	50.16	-284.500681	-284.658790	
CH <sub>3</sub> C≡C	H	<i>anti</i> TS	50.04	-284.475042 <sup>a</sup>	-284.634549 <sup>a</sup>	
CH <sub>3</sub> C≡C	H	<i>syn</i> TS	50.03	-284.472365	-284.632523	
HC≡C	H	GS	33.31	-245.323182	-245.451906	
HC≡C	H	<i>anti</i> TS	33.09	-245.296724 <sup>a</sup>	-245.426980 <sup>a</sup>	
HC≡C	H	<i>syn</i> TS	33.06	-245.294253	-245.425100	
N≡C	H	GS	26.98	-261.407503	-261.536917	
N≡C	H	<i>anti</i> TS	26.60	-261.379307 <sup>a</sup>	-261.510356 <sup>a</sup>	
N≡C	H	<i>syn</i> TS	26.52	-261.376991	-261.508455	
N <sub>3</sub>	H	GS	29.92	-332.604377	-332.764778	
N <sub>3</sub>	H	<i>anti</i> TS	29.80	-332.579125 <sup>a</sup>	-332.741088 <sup>a</sup>	
N <sub>3</sub>	H	<i>syn</i> TS	29.76	-332.577935	-332.740094	

<sup>a</sup> more stable TS; <sup>b</sup> ZPE is reported in kcal/mol at the HF/6-31G\* level scaled by 0.89; <sup>c</sup> Energy change from gas phase to TCE in kcal/mol; <sup>d</sup> Energy change from gas phase to CCl<sub>4</sub> in kcal/mol; <sup>e</sup> Energy change from gas phase to diethyl formamide in kcal/mol; <sup>f</sup> Energy change from gas phase to toluene in kcal/mol.

**Table 2.** Selected bond lengths, bond orders and imaginary frequencies calculated at HF/6-311++G\*\* level of theory for the studied amides  $R-C(O)NR'_2$ .

R	R'	State	r <sub>C-N</sub> (Å)	r <sub>C=O</sub> (Å)	r <sub>C-C</sub> (Å)	r <sub>C-C</sub> (Å)	Bond Order C-N	iv(cm <sup>-1</sup> )
CH <sub>3</sub> C≡C	CH <sub>3</sub>	GS	1.353	1.197	1.185	1.468	0.985	
CH <sub>3</sub> C≡C	CH <sub>3</sub>	<i>anti</i> TS	1.425	1.182	1.186	1.456	0.849	102.9i
CH <sub>3</sub> C≡C	CH <sub>3</sub>	<i>syn</i> TS	1.421	1.178	1.186	1.468	1.171	80.3i
HC≡C	CH <sub>3</sub>	GS	1.349	1.195	1.193	1.472	1.018	
HC≡C	CH <sub>3</sub>	<i>anti</i> TS	1.421	1.180	1.184	1.462	0.961	108.6i
HC≡C	CH <sub>3</sub>	<i>syn</i> TS	1.417	1.177	1.184	1.474	1.211	82.1i
N≡C	CH <sub>3</sub>	GS	1.339	1.189		1.490	1.079	
N≡C	CH <sub>3</sub>	<i>anti</i> TS	1.409	1.174		1.484	0.938	114.9i
N≡C	CH <sub>3</sub>	<i>syn</i> TS	1.404	1.171		1.498	1.221	80.5i
N <sub>3</sub>	CH <sub>3</sub>	GS	1.346	1.199		1.410	1.139	
N <sub>3</sub>	CH <sub>3</sub>	<i>anti</i> TS	1.412	1.188		1.393	1.024	105.6i
N <sub>3</sub>	CH <sub>3</sub>	<i>syn</i> TS	1.409	1.182		1.408	1.074	97.3i
H	C <sub>2</sub> H <sub>5</sub>	GS	1.345	1.195			1.004	
H	C <sub>2</sub> H <sub>5</sub>	<i>anti</i> TS	1.421	1.180			0.843	252.8i
H	C <sub>2</sub> H <sub>5</sub>	<i>syn</i> TS	1.416	1.177			0.875	191.5i
H	i-C <sub>3</sub> H <sub>7</sub>	GS	1.346	1.196			1.019	
H	i-C <sub>3</sub> H <sub>7</sub>	<i>anti</i> TS	1.416	1.181			0.711	268.0i
H	i-C <sub>3</sub> H <sub>7</sub>	<i>syn</i> TS	1.413	1.179			0.741	201.2i

**Table 3.** Calculated barriers of the studied amides R-CONR<sub>2</sub> in the gas phase.

R	R'	Method <sup>a</sup>	TS	$\Delta H^\ddagger(298\text{K})$	$\Delta S^\ddagger(298\text{K})$	$\Delta G^\ddagger(298\text{K})$	$\Delta G_{\text{eff}}^\ddagger(298\text{K})^h$
CH <sub>3</sub> C≡C	CH <sub>3</sub>	1	<i>anti</i>	15.5	-10.5	18.6	18.1 (18.9)
			<i>syn</i>	16.0	-8.0	18.4	
		2	<i>anti</i>	14.0	-10.5	17.1	16.8 (17.8)
			<i>syn</i>	15.0	-8.0	17.4	
		3	<i>anti</i>	15.0	-10.5	18.1	17.3 (18.0)
			<i>syn</i>	15.1	-8.0	17.5	
exptl(TCE) <sup>b</sup>				19.8 ± 0.4	0.6 ± 1.2		19.6 ± 0.28
HC≡C	CH <sub>3</sub>	1	<i>anti</i>	16.1	-7.7	18.4	18.2 (19.4)
			<i>syn</i>	16.5	-7.5	18.8	
		2	<i>anti</i>	14.2	-7.7	16.5	16.4 (17.8)
			<i>syn</i>	15.2	-7.5	17.5	
		3	<i>anti</i>	15.4	-7.7	17.7	17.3 (18.4)
			<i>syn</i>	15.4	-7.5	17.6	
exptl(TCE) <sup>b</sup>							19.56
CN	CH <sub>3</sub>	1	<i>anti</i>	18.3	-6.8	20.3	19.7 (21.0)
			<i>syn</i>	18.0	-6.5	19.9	
		2	<i>anti</i>	15.5	-6.8	17.6	17.3 (18.8)
			<i>syn</i>	16.0	-6.5	18.0	
		3	<i>anti</i>	17.6	-6.8	19.6	18.7 (20.0)
			<i>syn</i>	16.9	-6.5	18.8	
exptl(gas) <sup>c</sup>							19.0 ± 0.1
exptl(TCE) <sup>c</sup>							21.4
N <sub>3</sub>	CH <sub>3</sub>	1	<i>anti</i>	14.5	-10.3	17.5	17.3 (16.7)
			<i>syn</i>	14.9	-9.9	17.8	
		2	<i>anti</i>	13.7	-10.3	16.7	16.6 (16.1)
			<i>syn</i>	14.7	-9.9	17.7	
		3	<i>anti</i>	13.8	-10.3	16.9	16.6 (16.0)
			<i>syn</i>	14.1	-9.9	17.0	
exptl(gas) <sup>c</sup>							16.5 ± 0.1
exptl(CCl <sub>4</sub> ) <sup>d</sup>							17.7
H	C <sub>2</sub> H <sub>5</sub>	1	<i>anti</i>	20.3	-3.5	19.0	21.1 (22.6)
			<i>syn</i>	20.9	-2.9	18.0	
		2	<i>anti</i>	18.8	-3.5	19.8	19.5 (21.0)
			<i>syn</i>	19.3	-2.9	20.1	
		3	<i>anti</i>	20.0	-3.5	20.1	20.7 (22.0)
			<i>syn</i>	20.3	-2.9	21.2	
exptl(gas) <sup>e</sup>				19.4 ± 0.9	0.8 ± 2.6		19.2 ± 0.1
exptl(neat) <sup>f</sup>							20.4
H	C <sub>3</sub> H <sub>7</sub>	1	<i>anti</i>	21.9	-1.2	22.2	22.0 (22.9)
			<i>syn</i>	22.4	-1.1	22.8	
		2	<i>anti</i>	19.5	-1.2	19.9	19.6 (20.3)
			<i>syn</i>	19.8	-1.1	20.1	
		3	<i>anti</i>	21.3	-1.2	21.7	21.3 (22.0)
			<i>syn</i>	21.4	-1.1	21.7	
4	<i>anti</i>			19.6			
	<i>syn</i>			21.3			
exptl(gas) <sup>e</sup>				18.8 ± 0.7	-0.6 ± 1.9		19.0 ± 0.1
exptl(toluene) <sup>g</sup>							19.8

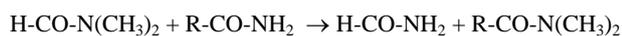
<sup>a</sup> 1 - MP2(fc)/6-31+G\*\*//6-31G\*, 2 - HF/6-311++G\*\*, 3 - MP2(fc)/6-311++G\*\*//6-311++G\*\*, 4 - QM/MM IMOMM (MP2:MM3) results from reference [29], <sup>b</sup> Reference [33], <sup>c</sup> Reference [34], <sup>d</sup> Reference [35], <sup>e</sup> Reference [36], <sup>f</sup> Reference [37], <sup>g</sup> Reference [38, 39], <sup>h</sup> Values in parenthesis include solvation correction of energy from Table 1.

$\Delta G_{\text{eff}}^\ddagger(298\text{K})$  is calculated by summing the rates through the two possible TS.

When the *syn* TS is slightly higher than *anti* TS, a part of reaction will proceed via the *syn* TS and to take this parallel reaction into account the effective free energy,  $\Delta G_{\text{eff}}^{\ddagger}(298\text{K})$ , was calculated by summing the rates through the two possible TS. The solvent effect was introduced by adding corrections to GS and both TS from single point PCM calculations given in Table 1. It is seen from Table 3 that the rotational barriers were reproduced very satisfactory. MP2(fc)/6-31+G\*\*//6-31G\* level of theory (Method 1) reproduce well  $\Delta G_{\text{eff}}^{\ddagger}(298\text{K})$  of studied amides with R = CH<sub>3</sub>C≡C and CH<sub>3</sub>C≡C, even the solvent effect was reproduced well. In case of R = CN and N<sub>3</sub> Method 1 overestimates  $\Delta G_{\text{eff}}^{\ddagger}(298\text{K})$  in gas phase compare to MP2(fc)/6-311++G\*\*//6-311++G\*\* (Method 3). In case of R = H, R' = C<sub>2</sub>H<sub>5</sub> or CH(CH<sub>3</sub>)<sub>2</sub> HF/6-311++G\*\* (Method 2) reproduce well  $\Delta G_{\text{eff}}^{\ddagger}(298\text{K})$  either in gas phase and in solution. Recently reported IMOMM (MP2:MM3) calculation [29] of R = H, R' = CH(CH<sub>3</sub>)<sub>2</sub> reproduce also well the barrier in gas phase. In general wider basis sets and addition of electron correlation effects is expecting to improve the calculation rotational barriers. In practice MP2(fc)/6-31+G\*\*//6-31G\* results are very often closer to experimental values than MP2(fc)/6-311++G\*\*//6-311++G\*\* results at a much lower computational price. Recently the barriers of rotation around C-N bond in gas phase of simple amides and tioamides were also well reproduced at MP2(fc)/6-31+G\*\*//6-31G\* level of theory, as well [30-32].

#### *Effect of the substituents on the rotational barrier*

In order to study the effect of substituents we considered two possible transition states and two rotational pathways and examined the following model reaction either in ground state or in the two possible transition states:



This approach was explored before to estimate the difference in repulsion between R and the CH<sub>3</sub> group, the difference in repulsion between R and the amide lone pair and the difference in repulsion between oxygen and amide lone pair [30-32]. The calculated enthalpy of the reaction for the ground state  $\Delta\Delta H^{\circ}(\text{GS})$  will be an estimate for the difference in repulsion between R and CH<sub>3</sub> group. The calculated enthalpy of the reaction for the *anti*

transition state  $\Delta\Delta H^{\circ}(\text{anti TS})$  will be an estimate for the difference in repulsion between R and amide lone pair, while the calculated enthalpy of the reaction for *syn* transition state  $\Delta\Delta H^{\circ}(\text{syn TS})$  will be an estimate for the difference in repulsion between oxygen and amide lone pair. The combined energy differences for both GS and *anti* TS [ $\Delta\Delta H^{\circ}(\text{anti TS}) - \Delta\Delta H^{\circ}(\text{GS})$ ] can be compared with the calculated differences in the calculated enthalpy of activation  $\Delta\Delta H^{\ddagger}(0\text{K})$  for the *anti* TS, while the combined energy differences for both GS and *syn* TS [ $\Delta\Delta H^{\circ}(\text{syn TS}) - \Delta\Delta H^{\circ}(\text{GS})$ ] can be compared with the calculated differences in the calculated enthalpy of activation  $\Delta\Delta H^{\ddagger}(0\text{K})$  for the *syn* TS. [ $\Delta\Delta H^{\circ}(\text{anti TS}) - \Delta\Delta H^{\circ}(\text{GS})$ ] and [ $\Delta\Delta H^{\circ}(\text{syn TS}) - \Delta\Delta H^{\circ}(\text{GS})$ ] can also be compared with the calculated change in free energy  $\Delta\Delta G_{\text{eff}}^{\ddagger}(298\text{K})$  and with the experimental change in free energy of activation  $\Delta\Delta G_{\text{exp}}^{\ddagger}(298\text{K})$ . All results of calculations for the model reaction are presented in Table 2S. The change in basis set leads to significant changes in  $\Delta\Delta G_{\text{eff}}^{\ddagger}(298\text{K})$  moreover in different directions, despite having a small influence on  $\Delta\Delta H$ . The explanation is hidden in the calculation scheme of  $\Delta G_{\text{eff}}^{\ddagger}(298\text{K})$ , which is sensitive to the relation of *syn*  $\Delta G^{\ddagger}(298\text{K})$  and *anti*  $\Delta G^{\ddagger}(298\text{K})$  values. In Table 4 the results of calculation for the model reaction obtained in this and previous papers are summarized. It is seen that the calculated  $\Delta\Delta H^{\circ}(\text{anti TS}) - \Delta\Delta H^{\circ}(\text{GS})$  values are a good estimation for the experimental change in free energy  $\Delta\Delta G_{\text{exp}}^{\ddagger}(298\text{K})$ . With a few exceptions the tendency to increase  $\Delta\Delta G_{\text{exp}}^{\ddagger}(298\text{K})$  absolute values from left to right column (decrease of the experimental barriers) is followed by the calculated  $\Delta\Delta H^{\circ}(\text{anti TS}) - \Delta\Delta H^{\circ}(\text{GS})$  values. This trend means that the difference in repulsion between R and CH<sub>3</sub> group in GS and difference in repulsion between R and amide lone pair in the preferred *anti* TS are mainly responsible for the decrease in the experimental rotation barriers around amide bond in simple amides. Further improvement in calculation of activation parameters either for rotational barriers or for modelling the effects of substituents require systematic increasing the level of theory (both basis set and method) and such calculations are in progress.

**Table 4.** Origin of the difference in the rotational barriers (kcal/mol) of the studied amides R-CON(CH<sub>3</sub>)<sub>2</sub> in the gas phase.

R	H-CO-N(CH <sub>3</sub> ) <sub>2</sub> + R-CO-NH <sub>2</sub> → H-CO-NH <sub>2</sub> + R-CO-N(CH <sub>3</sub> ) <sub>2</sub>											
	H	CN	CHF <sub>2</sub>	F	N <sub>3</sub>	CF <sub>3</sub>	Cl	CH <sub>3</sub>	CH <sub>2</sub> F	CCl <sub>3</sub>	Br	
$\Delta\Delta H^\circ(\text{anti TS})-\Delta\Delta H^\circ(\text{GS})$	0	-1.9	-4.3	-2.5	-3.5	-5.0	-4.8	-3.8	-7.4	-7.5	-5.5	
$\Delta G^\ddagger_{\text{exp}}(298\text{K})$	0	-0.4	-2.0	-2.3	-2.9	-3.3	-4.0	-4.1	-4.2	<-4	-5.3	

$\Delta\Delta H^\circ(\text{GS})$  and  $\Delta\Delta H^\circ(\text{anti TS})$  are the energy changes (they include ZPE correction) for the model reaction in the ground and *anti* transition state, respectively.  $\Delta\Delta G^\ddagger_{\text{exp}}(298\text{K})$  is the experimental change in free energy. The  $\Delta\Delta H^\circ(\text{anti TS})-\Delta\Delta H^\circ(\text{GS})$  values are compilation of data calculated at higher level of theory from this and previous studies

## CONCLUSION

The free energy of activation of studied amides were reproduces very well using MP2(fc)/6-31+G\*\*/6-31G\* energies and PCM/6-31G\* energy change from gas phase to solution. For all studied compounds the *anti* transition state (*anti* TS) is more stable and determines the rotational barrier. The nonbonded interactions in ground state (GS) and *anti* TS are mainly responsible for the differences in the rotational barriers in the studied amides

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Electronic Supplementary Data available here.

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## *Ab initio* SCF ИЗСЛЕДВАНЕ НА БАРИЕРА НА ВЪТРЕШНА РОТАЦИЯ В АМИДИ

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(Резюме)

Свободната енергия на активация за ротацията около amidната C-N връзка в R-C(O)NR'<sub>2</sub> (R'=CH<sub>3</sub>, R = CN, N<sub>3</sub>, C≡C-H, C≡C-CH<sub>3</sub>; R'=H, R = C<sub>2</sub>H<sub>5</sub>, CH(CH<sub>3</sub>)<sub>2</sub>) е изчислена на MP2(fc)/6-31+G\*//6-31G\* и на MP2(fc)/6-311++G\*\*//6-311++G\*\* нива на теорията и са сравнени с данните от ЯМР в течна и газова фаза. За всички изследвани съединения *анти* преходното състояние (*anti* TS) е по-стабилно и определя ротационния бариер. На база на резултатите от това и предишни изследвания ние обобщаваме, че в случая на амиди и тиоамиди несвързващите взаимодействия в основно състояние (GS) са основно отговорни за разликите в ротационните бариери и те преобладават над електронните ефекти на заместителите.