

# Relative Stability and Structure of Dihydro-1,2,4-triazines: A Theoretical Study

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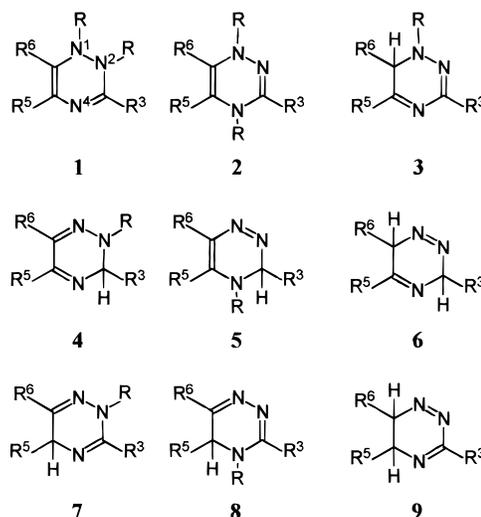
A brief survey is given on the synthesis and structure elucidation for dihydro-1,2,4-triazines. The relative stability of nine possible dihydro-1,2,4-triazines and three dihydrotriazinium cations is studied at HF, MP2, generalized gradient approximation DFT, and CBS-4 levels of theory. The structural consequences of the inclusion of the electron correlation are also given. We attempt to rationalize the experimental findings using high-quality theoretical results. The quantum chemical calculations support that the most stable isomer is the 2,5-dihydro-1,2,4-triazine and all the other relatively stable isomers have been experimentally identified correctly. Several experimental papers report structures that have been proved to be nonexistent. These structures have energy that is too high according to the best-quality calculations.

## 1. Introduction

Although dihydro-1,2,4-triazines have been known for a long time,<sup>1</sup> no thorough study on structures and tautomerism of dihydro-1,2,4-triazines is available. Good monographs<sup>2–4</sup> have been published in the last fifteen years, but structures of dihydro compounds were accepted without any critical review. There exist nine possible isomers of the dihydro-2,4,5-tri(alkyl or aryl)substituted-1,2,4-triazines (dihydrotriazines, **1–9**) (cf. Chart 1); however, only several (**1**, **2**, **3**, **4**, **7**, and **8**) of them have occurred in the earlier preparative works.

According to the experimental results, the most stable isomer proved to be the 2,5-dihydro-1,2,4-triazine (**7**). The ring closures,<sup>5–7</sup> the various reductions of aromatic triazines (**10**),<sup>8–12</sup> and the Grignard reaction<sup>12–15</sup> resulted in the formation of this isomer. The 4,5- (**8**),<sup>6,7,16–18</sup> and

Chart 1



R, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup> = H, alkyl, or aryl, or R<sup>3</sup> = S-alkyl

a R = H, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup> = Ph

b R = Me, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup> = Ph

c R = Ac, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup> = Ph

1,6-dihydro-1,2,4-triazines (**3**)<sup>8</sup> can only be prepared by the methods mentioned above starting from 4- or 1-substituted (e.g., **11**) compounds. The 2,3-dihydro-1,2,4-triazines (**4**) were obtained from electrocyclic reactions.<sup>19</sup>

Only a few representatives of 1,4-dihydrotriazines (**2**) have been prepared until now,<sup>9,18</sup> even though the

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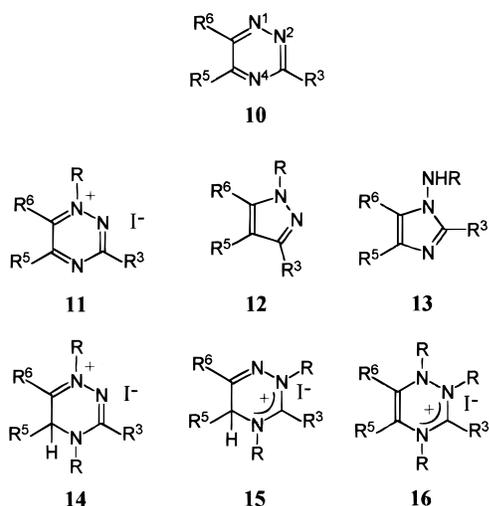
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Chart 2



R, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup> = H, alkyl, or aryl

a R = H, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup> = Ph

b R = Me, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup> = Ph

c R = Ac, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup> = Ph

electrochemical,<sup>20</sup> photochemical,<sup>8,16,21</sup> and Zn/acetic acid reduction<sup>9</sup> studies of the aromatic 1,2,4-triazine series (**10**) support the existence of the 1,4-dihydrotriazines (**2**) as intermediates.

The 1,2-dihydro-1,2,4-triazine (**1**) was not successfully prepared up to now; all papers claiming to prepare this compound proved to be erroneous and the reactions led to 2,5-dihydrotriazine (**7**),<sup>22</sup> (cf. refs 8 and 9) 1,4-dihydrotriazine (**2**),<sup>22</sup> (cf. ref 9) pyrazole (**12**),<sup>20</sup> (cf. ref 8) or aminoimidazole (**13**)<sup>23</sup> (cf. ref 19) (see in detail in the discussion) (Chart 2).

Three types of dihydrotriazinium salts (e.g., **14b**,<sup>18</sup> **15b**,<sup>8,9,16</sup> and **16b**<sup>22</sup>) are mentioned in the literature, although the correct structure for **16b** is **15b**.<sup>8</sup>

These experimental results raise several questions. Are the experimentally found structures the most stable ones? Why has the 1,2-dihydrotriazine not yet been found? How stable is the 1,4-dihydrotriazine? What is the relative energetic order of the selected triazinium cations? We attempt to answer these questions using the calculated relative stabilities and structural features of all possible parent dihydro-1,2,4-triazines (**1–9**, R, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup> = H) and the three dihydro-1,2,4-triazinium cations (**14–16**, R, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup> = H). The earlier quantum mechanical studies concentrated on the relative energy of several dihydro(mono and di)azines<sup>24–26</sup> (see also ref 3) and aromatic 1,2,4-triazines (see ref 4). To our knowledge the current study is the first systematic theoretical study on dihydro-1,2,4-triazines. We also apply the currently highest possible level of theory and include the basis set and electron correlation effects using the CBS-4 method (vide infra). The geometry optimiza-

tion of the phenyl-substituted molecules requires tremendous computational effort at the ab initio level; thus they were excluded from the present study.

## 2. Computational Methods

The geometries were optimized by the Hartree–Fock (HF), many-body perturbation theory using the Møller–Plesset partition to the second order (MP2)<sup>27,28</sup> and by the generalized gradient approximation density functional (GGA-DFT) methods using the Bery algorithm combined with redundant internal coordinates built into the GAUSSIAN 94 program.<sup>29</sup>

We employed the following combinations of the GGA-DFT functionals:

(i) BPW: The Becke 88 exchange functional<sup>30</sup> is combined with the correlation functionals of Perdew–Wang 91,<sup>31</sup> respectively.

(ii) B3PW: The hybrid method. It is a linear combination of various exchange and correlation functionals in the following form:

$$A\text{Ex}[\text{Exact}] + (1 - A)\text{Ex}[\text{S}] + B\Delta\text{Ex}[\text{B}] + \text{Ec}[\text{VWN5}] + C\Delta\text{Ec}[\text{PW}] \quad (1)$$

where Ex[Exact], Ex[S], and  $\Delta\text{Ex}[\text{B}]$  are the exact, Slater and Becke exchange functionals; and Ec[VWN] and  $\Delta\text{Ec}[\text{PW}]$  are the Vosko, Wilk, and Nussair<sup>5,32</sup> and Perdew–Wang correlation functionals, respectively. Note that  $\Delta\text{Ex}[\text{B}]$  is a gradient correction to the S + VWN or LSDA, for exchange, and that  $\Delta\text{Ec}[\text{PW}]$  is a gradient correction for correlation.

The constants *A*, *B*, and *C* are those determined by Becke by fitting heats of formation (*A* = 0.2, *B* = 0.72, *C* = 0.81).<sup>33</sup> Becke used the PW correlation functional for the determination of these parameters; however, the same parameters are generally used with the *P* correlation functional.

The HF and DFT optimized geometries were checked by frequency analysis. We used a fine grid for the calculation of DFT integrals. For the DFT basis set extension studies we performed a large basis set, 6-311+G(2d,p), single-point calculation using the 6-31G(d) geometries. This type of calculation is noted as X/6-311+G(2d,p)//6-31G(d), where X = BPW or B3PW. We use the standard basis sets developed by Pople's group.<sup>33</sup>

We use the Complete Basis Set (CBS) 4 method of Petersson et al.<sup>34</sup> for computing very accurate energies. This method uses the HF/3-21G geometry, zero point energy (ZPE) correction (scale factor: 0.91671), a HF component with 6-311+G-(2df,p) basis set, a CBS2/6-31+G<sup>††</sup> extrapolation based on five population localized pair natural orbitals, and a MP4(SDQ)/6-31G higher-order correlation estimation. It also includes a CBS interference correction term and 1- and 2-electron size-consistent higher-order and spin contamination corrections. This method has proven to be rather effective for energetic calculations. Enthalpy and Gibbs free energy were calculated after adding the necessary terms. Our Gibbs free energy results refer to 298.15 K and 1 bar of pressure in gas phase. All calculations were performed on Silicon Graphics computers.

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**Table 1. ZPE Corrected HF, MP2, GGA-DFT, and CBS-4 Energies for 2,5-Dihydro-1,2,4-triazine in Hartrees and Relative Energies for the Other Eight Isomers in kcal/mol Calculated with Various Methods<sup>a</sup>**

method	energy				relative energy				
	2,5-dihydro	4,5-dihydro	1,6-dihydro	1,4-dihydro	2,3-dihydro	1,2-dihydro	3,4-dihydro	3,6-dihydro	5,6-dihydro
HF/6-311+G(2df,p)//3-21G	-279.8017	7.36	7.98	10.46	10.59	13.31	18.55	16.04	17.89
MP2	-280.5785	8.87	8.56	13.74	9.13	20.44	14.24	12.73	15.50
BPW	-281.4170	8.21	6.90	12.65	7.85	17.96	11.19	11.60	15.41
BPW/6-311+G(2d,p)//6-31G(d)	-281.5033	8.19	7.17	8.37	7.96	15.38	11.17	13.80	18.17
B3PW	-281.3340	8.24	7.41	12.19	8.48	17.04	13.38	13.64	16.70
B3PW/6-311+G(2d,p)//6-31G(d)	-281.4178	8.34	7.76	8.14	8.73	14.62	13.39	15.67	19.37
ZPE	0.0863	-0.19	-0.02	-0.41	-0.07	-0.01	-0.42	-0.89	-0.67
CBS-4 (0 K)	-281.1088	9.51	9.15	9.57	10.32	14.40	14.95	16.17	18.28
free energy	-281.1371	8.89	9.33	9.46	10.39	14.48	15.13	16.08	18.39

<sup>a</sup> If no basis set is given the default 6-31G(d) basis set is used with the corresponding equilibrium molecular geometry. If different geometry is used for the energy calculations and the equilibrium geometry calculation the basis set used for the geometry optimization is shown after //; for example, HF/6-311+G(2df,p)//3-21G means that 6-311+G(2df,p) basis set is used for the energy calculation using the HF/3-21G equilibrium geometry.

**Table 2. ZPE Corrected HF, MP2, GGA-DFT, and CBS-4 Energies for 4,5-Dihydro-1,2,4-triazin-2-ium Cation in Hartrees and Relative Energies for the Other Two Isomers in kcal/mol Calculated with Various Methods<sup>a</sup>**

method	energy		relative energy	
	4,5-dihydro-2-ium	4,5-dihydro-1-ium	1,4-dihydro-2-ium	
HF/6-311+G(2df,p)//3-21G	-280.1706	9.32	12.20	
MP2	-280.9054	7.99	14.94	
BPW	-281.7525	5.96	14.58	
BPW/6-311+G(2d,p)//6-31G(d)	-281.8389	5.97	11.83	
B3PW	-281.6723	6.93	14.03	
B3PW/6-311+G(2d,p)//6-31G(d)	-281.7569	6.93	11.38	
ZPE	0.1005	-0.32	0.02	
CBS-4 (0 K)	-281.4619	8.98	10.39	
free energy	-281.4905	8.95	10.71	

<sup>a</sup> If no basis set is given the default 6-31G(d) basis set is used with the corresponding equilibrium molecular geometry. If different geometry is used for the energy calculations and the equilibrium geometry calculation the basis set used for the geometry optimization is shown after //; for example, HF/6-311+G(2df,p)//3-21G means that 6-311+G(2df,p) basis set is used for the energy calculation using the HF/3-21G equilibrium geometry.

The optimized 3D molecular structures are published on the Internet: <http://web.inc.bme.hu/mols/triazines/>.

### 3. Results and Discussion

**Energetic Order of the Nine Possible Dihydro-1,2,4-triazines.** Table 1 shows the HF, MP2, GGA-DFT, and CBS-4 energetic results in kilocalories per mole for the nine dihydro-1,2,4-triazines.

The ZPE corrected HF/6-311+G(2df,p)//3-21G method shows a quite balanced performance, appreciably better than the MP2 or GGA-DFT methods with the 6-31G(d) basis set (cf. Table 1). This observation is in agreement with the earlier experience that the HF method is capable of providing surprisingly good relative energies within a family of isomers or conformers.<sup>35</sup> Comparing HF/6-311+G(2df,p)//3-21G results to the CBS-4 (0 K) results shows the importance of the electron correlation (cf. Table 1). It might be concluded that the basis set effects are larger than the correlation effects. However, this is not uniformly true for all isomers. For example the electron correlation plays an important role for the 3,4-dihydro isomer (**5**) (cf. Table 1).

We show the CBS-4 0 K (ZPE corrected) and Gibbs free energies in Table 1; thus the importance of the thermal and other corrections necessary for the free-energy calculation can be followed. These corrections are fairly small except for the 4,5-dihydro isomer (**8**). Remember that the CBS-4 method uses the HF/3-21G equilibrium

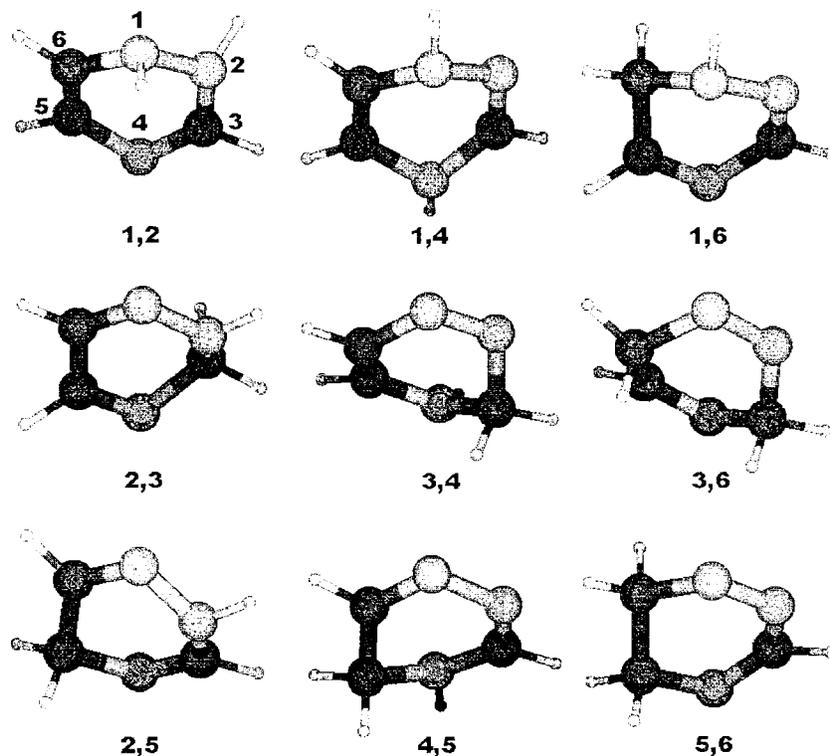
geometries. These geometries are in a better agreement with the MP2 or GGA-DFT equilibrium geometries than, for example, the HF/6-31G(d) equilibrium geometries for triazines (vide infra).

The B3PW/6-311+G(2d,p)//6-31G(d) results show the best agreement with the CBS-4 energetic order; the rms deviation is only 0.98 kcal/mol. The rms deviation for the second best BPW method is considerably larger (1.47 kcal/mol). The convergence between the B3PW and CBS-4 methods is quite encouraging, and this supports the use of the former, considerably less expensive method for relative stability studies of triazines.

Inspection of Table 1 reveals that the DFT basis set extension effects are below 0.4 kcal/mol for four isomers; however, they are very large for 1,4-dihydrotriazine (**2**) (more than 4 kcal/mol, cf. Table 1). It can be observed that the 6-31G(d) basis set considerably destabilizes the 1,4-dihydro isomer (**2**), and this feature is virtually method-independent. It seems that for this isomer the basis set error of the 6-31G(d) basis set is fairly large. We also note that the MP2/6-31G(d) method shows a rather poor performance for dihydrotriazines.

**Relative Energies of the Three Selected Dihydro-1,2,4-triazinium Cations.** The results in Table 2 show that there is a qualitative agreement between the CBS-4 and the highest-level correlated calculations for the relative energies of dihydro-1,2,4-triazinium cations. All methods provide that the most stable cation is the 4,5-dihydro-1,2,4-triazin-2-ium isomer (**15**) in agreement with the experimental expectations. The less stable cation is the 1,4-dihydro-2-ium isomer (**16**). The relative

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**Figure 1.** The nine MP2/6-31G(d) optimized dihydrotriazine structures. The atom numbering is shown in the upper left structure. The light and dark gray atoms are the N and C atoms, respectively.

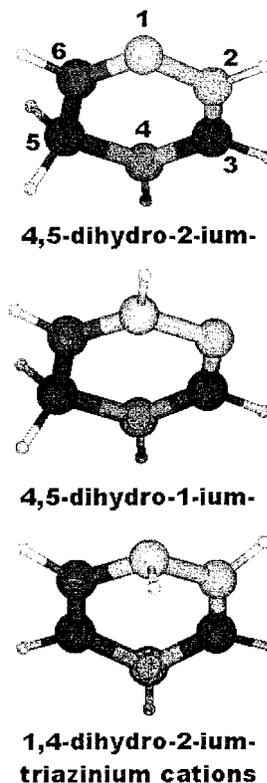
order is the same with any method; however there exists a surprisingly large quantitative difference between the best performing GGA-DFT and CBS-4 methods (2 and 1 kcal/mol, cf. Table 2).

We note that the expected standard deviations of the  $\Delta G$  and  $\Delta H$  values are about 1.5 kcal/mol and 3–6 kcal/mol for the CBS-4 and GGA-DFT methods with large basis sets, respectively. The MP2/6-31G(d) errors are expected to be considerably higher. We also note that within a series of molecules these methods perform considerably better; thus the above-mentioned errors are the worst case errors.

The GGA-DFT results are practically insensitive for the basis set extension effects for the 4,5-dihydro-1-ium isomer (**14**), while the relative energy of the 1,4-dihydro-2-ium isomer (**16**) shows a nearly 4 kcal/mol basis set effect (cf. Table 2). Comparing HF/6-311+G(2df,p)//3-21G and CBS-4 (0 K) results shows that the electron correlation has a minor energetic effect for 4,5-dihydro-1-ium (**14**) isomer and it is less than 2 kcal/mol for the 1,4-dihydro-2-ium (**16**) isomer. We checked the stability of the CBS-4 results with respect the localization scheme applied. Applying the Boys localization method instead of the standard population localization method did not change the calculated energies.

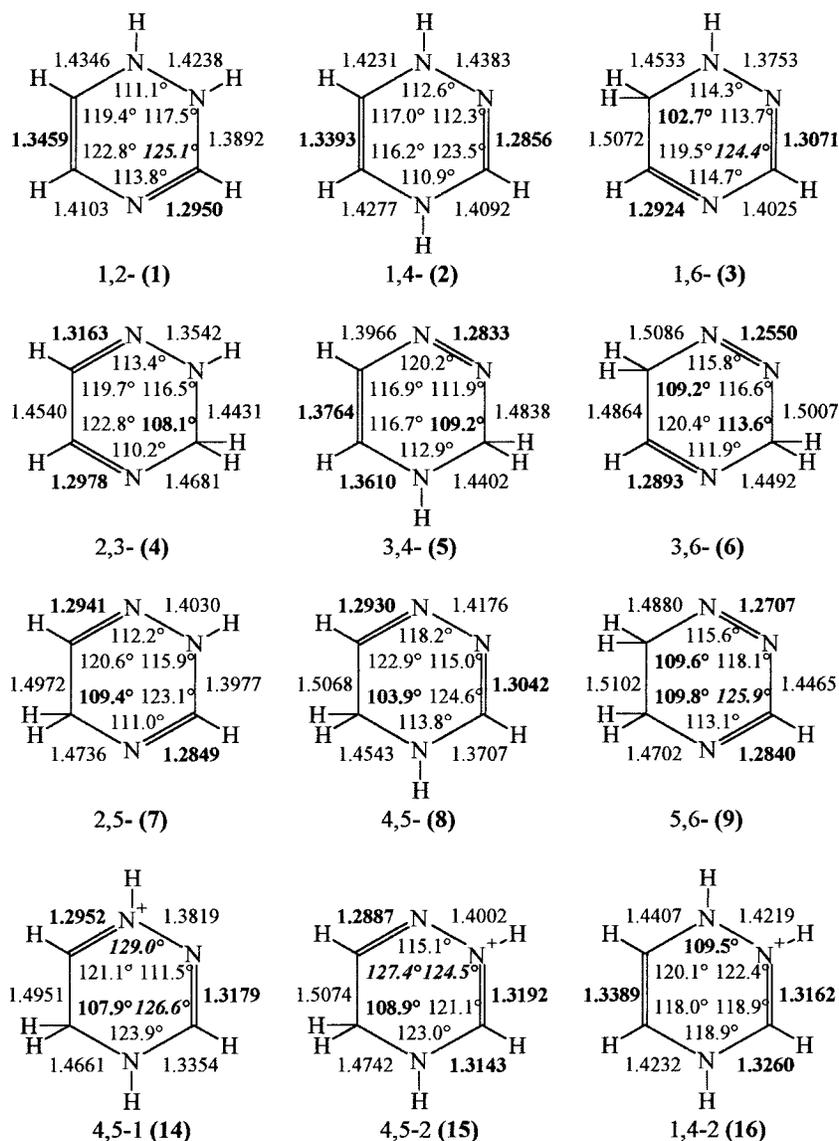
**Equilibrium Geometries.** The MP2/6-31G(d) equilibrium 3D structures are shown in Figures 1 and 2. Figure 3 shows the MP2/6-31G(d) equilibrium bond lengths and bond angles for the ring skeletons of the nine dihydrotriazines and of the three triazinium cations. Inspection of Figure 3 reveals immediately that the positions of the double bonds (short bond lengths) always correspond to the expectations.

The analysis of the difference between the MP2/6-31G(d) and other calculated ring skeleton bond lengths for the nine dihydro isomers shows that the following order



**Figure 2.** The structures of the three MP2/6-31G(d) optimized dihydro-1,2,4-triazinium cations. The atom numbering is shown in the upper structure. The light and dark gray atoms are the N and C atoms, respectively.

is valid:  $r(\text{HF}) \ll r(\text{B3PW}) < r(\text{MP2}) < r(\text{BPW})$ . This order is in good agreement with our earlier results with DFT methods for covalent bonds.<sup>36</sup> Good agreement can be found between the BPW and MP2 mean bond lengths.



**Figure 3.** The calculated MP2/6-31G(d) bond lengths in Å and bond angles in degrees for the ring skeleton of the nine dihydro-1,2,4-triazines and of the three dihydro-1,2,4-triazinium cations. The short bond lengths and small bond angles are bold; the large bond angles are bold italic. The label represents the dihydro- and the -ium positions.

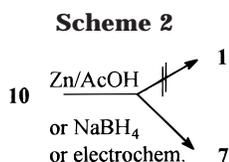
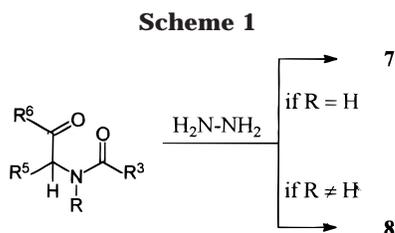
The BPW bond lengths are slightly longer than the MP2 bond lengths (by about 0.004 Å on average). The B3PW method provides slightly too short bond lengths, and the HF method provides largely too short bond lengths with the 6-31G(d) basis set. This is a well-known error of the HF method for covalent bonds.

The root-mean-square (rms) deviations from the MP2 bond lengths,  $\sigma$ , show the following order:  $\sigma(\text{B3PW}) \approx \sigma(\text{BPW}) \ll \sigma(\text{HF})$ . We should note that although the MP2/6-31G(d) geometries are usually far from being converged, and even the MP2 method is a rather crude approximation for the correlation effects, quite good agreement has been found between the experimental and MP2/6-31G(d) bond lengths. In this sense the relatively good agreement between the MP2, B3PW, and BPW bond lengths is encouraging. For the triazinium cations the agreement between the MP2, B3PW, and BPW geometries is even better than for the dihydrotriazines.

The bond angles in Figure 3 clearly show the typical bond angle changes due to the various protonations; for example, the bond angle changes to about 109.5° for the protonated carbon atoms. Because of the constraints in the ring skeletons, the method dependence of the bond angles is less systematic than that of the bond lengths. Our results show that the agreement between the MP2 and GGA-DFT results for the bond angles is quite reasonable (the difference is below 1°).

The analysis of the torsion angles provides that 1,4- (2), 2,5- (7), and 3,6-dihydrotriazines (6) with isolated double bonds show slightly distorted boat forms. The other six dihydro rings have distorted envelope forms with conjugated double bonds. For the 1,2- (1), 1,6- (3), 2,3- (4), 3,4- (5), 4,5- (8), and 5,6-dihydrotriazines (9) the atoms numbered 1, 6, 2, 3, 5, and 6 are above the ring plane, respectively (cf. Figure 1). The least stable triazinium cation has a considerably distorted envelope structure (cf. Figure 2). The more stable 4,5-dihydro-2-ium (15) and the 4,5-dihydro-1-ium (14) cations have planar rings. The method dependence of the torsion angles is considerable, showing that these angles are

(36) (a) Csonka, G. I.; Csizmadia, I. G. *Chem. Phys. Lett.* **1995**, *243*, 419. (b) Csonka, G. I.; Eliás, K.; Csizmadia, I. G. *J. Comput. Chem.* **1997**, *18*, 330. (c) Csonka, G. I.; Nguyen, N. A.; Kolossváry, I. *J. Comput. Chem.* **1997**, *18*, 1534.



sensitive measures of the quality of the method. The rms deviation between the MP2 and GGA-DFT methods is about  $2^\circ$ – $6^\circ$ . The GGA-DFT structures are systematically more planar than the MP2 structures. We constructed a small database and publish the structural data as a supplement (hypertext, chemscape readable).

The relative stabilities can be rationalized in terms of molecular structure. The more stable structures always contain two C=N double bonds. In the most stable boat structure (**7**) these two C=N bonds are possibly cross-conjugated over the  $\text{N}^2$  lone pair (cf. Figure 1). Two C=N bonds exist in **8**, **3**, and **4**; however, these conjugated structures are considerably less stable than **7** as the N lone pair is at the end of the conjugated system (not in the middle as in structure **7**). In the boat 1,4-dihydrotriazine (**2**) one C=N and one C=C double bond can be found. The situation is similar in the quasi envelope 1,2-dihydrotriazine (**1**). These two structures are considerably less stable than those with two C=N double bonds; however it should be noted that the double cross-conjugation present in **2** makes it considerably more stable than **1**. The three structures, **5**, **6**, and **9**, containing an N=N double bond are the least stable. The above-mentioned observations seem to be valid to the cationic systems too. For example the most stable 4,5-dihydro-2-ium (**15**) shows structure similar to those of **7** and **8**.

**Comparison of the Calculated Results with the Experimental Findings.** According to the first family of reactions considered here dihydrotriazines can be prepared by ring closure of  $\alpha$ -acylaminoketones, -aldehydes, or related compounds by hydrazine derivatives. In the first preparative papers 2,5- (**7**) or 4,5-dihydrotriazines (**8**) were reported as products.<sup>37,38</sup> The 2,5-dihydro isomer was identified using the  $^1\text{H}$  NMR spectrum;<sup>5</sup> however, it was shown in a subsequent publication<sup>13</sup> that the  $^1\text{H}$  NMR multiplicity of 5-H does not allow unambiguous assignment. The 2,5-dihydro-1,2,4-triazine (**7a**) was prepared from the following reaction<sup>6</sup> (cf. Scheme 1).

According to the UV spectroscopic results the tautomeric equilibrium between 2,5- (**7a**) and 4,5-dihydro (**8a**) isomers is shifted toward the more stable 2,5-dihydro form. To prepare the 4,5-dihydro isomer (**8**), which is the second isomer in the row of stability, alkyl or aryl substituents must be present on N-4.<sup>6,7,9,17,18</sup>

The second family of reactions to obtain various dihydro-1,2,4-triazines is the reduction of aromatic 1,2,4-triazines (**10**) (cf. Scheme 2).

Metze and Scherowsky<sup>22</sup> published a Zn/acetic acid reduction of several aromatic 1,2,4-triazines (**10**). It was supposed that the reactions go through 1,2-dihydrotriazine intermediates (**1**); however, it was shown in subsequent publications<sup>8,9</sup> by the reproduction of their reduction method that the dihydro intermediates have 2,5-dihydro structure, for example, **7a**.

By the sodium borohydride reduction of various 1,2,4-triazines (**10**) Sasaki et al.<sup>10</sup> and Boyle et al.<sup>11</sup> obtained the most stable 2,5-dihydro-compounds (**7**) as the predominant dihydro products. The sodium borohydride reduction of methylated aromatic triazine (**11b**)<sup>39</sup> resulted in the formation of the 1,6-dihydrotriazine (**3b**),<sup>8</sup> that is, the most stable isomer among the 1,2- (**1**), 1,4- (**2**), and 1,6-dihydrotriazines (**3**). Other 1,6-dihydrotriazines (**3**, R ≠ H) have been prepared in the presence of 1-aryl substituents.<sup>40</sup>

Pinson et al.<sup>20</sup> have studied the electrochemical reduction of the 3,5,6-triphenyl-1,2,4-triazine (**10a**) in acidic medium. They assumed the existence of a 1,4-dihydro intermediate (**2a**) which was rearranged into 1,2-dihydrotriazine (**1a**) and 4,5-dihydro derivative (**8a**). These structures were deduced from the corresponding  $^1\text{H}$  NMR spectra. Later it was unambiguously proven<sup>8</sup> that pyrazole (**12a**) and 2,5-dihydro compound (**7a**) were formed instead of 1,2-dihydrotriazine (**1a**) and 4,5-dihydro compound (**8a**), respectively. Moreover, the catalytic reduction of a triazine (**10**) also resulted in the isolation of the 2,5-dihydrotriazine (**7**, R = H) product.<sup>12</sup>

In the Grignard reactions of aromatic 1,2,4-triazines (**10**,  $\text{R}^5 = \text{H}$ ) the 2,5-dihydrotriazines (**7**, R = H) were obtained as main product.<sup>12–15</sup> If position 5 of aromatic triazine (**10**,  $\text{R}^5 \neq \text{H}$ ) was blocked by a substituent (like phenyl), then the 1,6-dihydrotriazine (**3**, R = H) was formed. If positions 5 and 6 of aromatic triazine (**10**,  $\text{R}^5$ ,  $\text{R}^6 \neq \text{H}$ ) were blocked by substituents, then probably the 2,3-dihydrotriazine (**4**, R = H) was formed.<sup>14</sup> These products (**3**, **4**, R = H) are unstable intermediates. The 1,6-dihydrotriazine (**3**, R = H) is the most stable isomer among the 1,6- (**3**), 3,6- (**6**), and 5,6-dihydrotriazines (**9**); the 2,3-dihydrotriazine (**4**, R = H) is the most stable isomer among the 2,3- (**4**), 3,4- (**5**), and 3,6-dihydrotriazines (**6**) according to our calculated relative stabilities. We note that these isomers are relatively unstable compared to the most stable 2,5-dihydrotriazines (**7**, R = H). It was found in these experiments that in aromatic triazines (**10**) the nucleophilic addition reactivity of the various positions decreases in the following order:  $5 > 6 > 3$ .<sup>14</sup>

The electrocyclic reactions of the 1,2,5-triazahexa-1,3,5-triene system produce 2,3-dihydrotriazines (**4**) and 1-aminoimidazoles (**13**).<sup>19</sup> The structures of the products (**4** and **13**) of the base-catalyzed ring-expansion/transformation of 1-alkyltriazolium salts were proven by X-ray. The latest paper that mentions the isolation of 1,2-dihydro isomer (**1**) was published in 1992.<sup>23</sup> The 1,2- (**1**) and 2,3-dihydrotriazine (**4**) structures for the products of the base-catalyzed ring contraction of several triazepines were supported only by  $^1\text{H}$  NMR spectroscopy. Probably the correct structure is 1-aminoimidazole (**13**) instead of

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(40) (a) Zhovtyak, V. N.; Dvorko, G. F. *Khim. Geterosykl. Soedin.* **1985**, *21*, 1431–1432. (b) Dvorko, G. F.; Zhovtyak, V. N. *Zh. Obshch. Khim.* **1988**, *58*, 165–183. (c) Dvorko, G. F.; Zhovtyak, V. N. *Zh. Obshch. Khim.* **1990**, *60*, 880–891.

(37) Metze, R. *Chem. Ber.* **1958**, *91*, 1863.

(38) Atkinson, C. M.; Cossey, H. D. *J. Chem. Soc.* **1962**, 1805.

1,2-dihydrotriazine (**1**). These two ring transformations must have a common intermediate.

The acetylation<sup>9</sup> of 2,5-dihydrotriazine (**7a**) by acetic anhydride using the method of Metze and Scherowsky<sup>22</sup> yielded the more stable 1,4-diacetyl-3,5,6-triphenyl-1,4-dihydro-1,2,4-triazine (**2c**) instead of 1,2-dihydro isomer (**1c**) proposed by Metze and Scherowsky.<sup>22</sup>

Moreover, the methylation<sup>8</sup> of 2,5-dihydrotriazine (**7a**) by methyl iodide using the method of Metze and Scherowsky<sup>22</sup> yielded the more stable 2,4-dimethyl-3,5,6-triphenyl-4,5-dihydro-1,2,4-triazin-2-ium iodide (**15b**) instead of 1,2,4-trimethyl-3,5,6-triphenyl-1,4-dihydro-1,2,4-triazin-2-ium iodide (**16b**) proposed by Metze and Scherowsky.<sup>22</sup>

#### 4. Conclusions

Comparisons with the reliable CBS-4 calculations show that the HF and the GGA-DFT methods perform quite well for the relative energetic order. The latter methods require sufficiently large, triple- $\zeta$  polarized basis sets for good relative energies. The GGA-DFT methods are able to reproduce the energetic and structural consequences of the electron correlation for dihydro-1,2,4-triazines.

Comparison of the calculated results with the experimental results is quite straightforward. All reliable theoretical methods are consistent in that the 2,5-dihydro isomer (**7**) is the most stable. This is in perfect agreement with the experimental observations. All of the synthetic methods mentioned above yielded the most stable 2,5-dihydrotriazine (**7**) isomer, if the structure of starting material and/or reaction mechanism allowed the formation of **7**. If the structure of starting material and/

or reaction mechanism did not allow the formation of **7**, then other possible reaction products were formed depending on their stability. In this sense the preparative experience agrees with the calculated stability order: the 4,5- (**8**), 1,6- (**3**), 1,4- (**2**), and 2,3-dihydro (**4**) isomers are increasingly less stable. It is quite probable that the preparation of 1,2- (**1**), 3,4- (**5**), 3,6- (**6**), and 5,6-dihydro (**9**) isomers is increasingly more difficult if it is possible at all.

The relative stabilities can be rationalized in terms of molecular structure. The more stable structures always contain two C=N double bonds, and a possible cross conjugation through a N lone pair between the two double bonds further stabilizes the structure. Replacing one or two C=N bonds by C=C and/or N=N bonds increasingly destabilizes the structure.

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**Supporting Information Available:** Table 3 showing the mean and the standard deviation between the relative energies of listed methods and Table 4 showing the rms and the mean deviations between ring skeleton bond lengths (2 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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