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Azide–Tetrazole Ring-Chain Isomerism in Polyazido-1,3,5-triazines, Triazido-*s*-heptazine, and Diazidotetrazines

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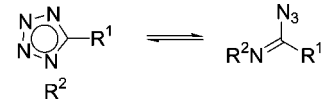
The azide–tetrazole isomerism in several polyazido-1,3,5-triazines, triazido-*sym*-heptazine, and some diazido-1,2,4,5-tetrazines was investigated by ab initio quantum chemical methods in order to determine whether the polyazides are suitable starting materials for the synthesis of the isomeric tetrazoles. The effects of solvation in CCl_4, DMSO and water on this isomerism were included using the self consistent reaction field (SCRF) method. The effect of amino- and nitro-substituents on the azide–tetrazole isomerism was also examined. In the gas phase all investigated polyazidoheterocycles do not cyclize to form tetrazoles. An electron-donating amino group favors the ring closure to tetrazoles, whereas an electron-withdrawing nitro group favors the azides. Solvation in polar solvents favors the formation of a tetrazole ring system due to higher charge separation in the tetrazole ring system, but for all polyazido-1,3,5-triazines, including triazido-*s*-heptazine, the effects of solvation are not strong enough to shift the equilibrium to the tetrazole side, which explains why several attempts to detect these compounds have failed. The monotetetrazoles of diazidotetrazine and bis(azido)azo-1,2,4,5-tetrazine and the ditetrazole of bis(azido)hydrazo-1,2,4,5-tetrazine are the minimum energy species in DMSO and water. Thus we predict that the diazidoazo- and hydrazotetrazines will readily cyclize to the tetrazoles in polar solvents.

Introduction

In recent years nitrogen-rich azidoheterocycles have been investigated as potential high energy density materials[1] and as precursors for carbon nitrides. Their clean and thermodynamically favorable decomposition, where only N_2 is released, makes them good precursors for nitrogen rich carbon nitrides, whose application is not only governed by texture and size of the particles,[2] but also by the relative nitrogen content. Nitrogen-rich carbon nitrides with the bulk formulas C_3N_4 and C_3N_5 have been prepared from cyanuric azide[3] as well as bis(azido)-1,2,4,5-tetrazine[4] and nitrides with the formulas C_2N_3 and C_3N_5 have been prepared from tetra(azido)azo-1,3,5-triazine.[5] Unfortunately, all described polyazides are very sensitive toward shock and friction and are classified as primary explosives. This makes the handling of these substances, especially in the amounts needed for commercial purposes, very difficult. The isomeric tetrazoles,[6] which are formed by an 1,5-dipolar cyclization[7] of the polyazides, are potential replacements for the hazardous polyazides. Even though we know of no precise data comparing the sensitivity of an azide to its isomeric tetrazole, the aromatic tetrazoles are, in general, less sensitive toward shock or friction than covalent azides. The nature of R^1 and R^2 determines whether the azide or the tetrazole isomer is dominant or whether both compounds are in equilibrium.[8] The open-ring azidoimine form is favored by electron-withdrawing groups and the tetrazole form is favored in the presence of electron-donating groups.[9] A wide series of fluoroalkyl-substituted imidoazyl azides is known that do not form a tetrazole.[10]



A key prerequisite for this cyclization is a *cis* orientation of the imino lone pair and the azide group. Therefore, electron-rich imidoazyl azides without the required conformation do not cyclize easily to the tetrazoles. Higher temperatures may help to overcome the activation barrier for tetrazole formation,[11] but higher temperatures generally favor the azide form.[12,13]

A decrease of solvent polarity shifts the equilibrium towards the azide form.[14] In the gas phase the reaction from the tetrazoles to the azides is exothermic.[15] Other reports indicate that the ring opening of the tetrazoles in the solid phase is endothermic.[16–18]

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In this investigation we address several points regarding the azide–tetrazole isomerism of the polyazidoheterocycles shown in Figure 1. Earlier investigations of the azide–tetrazole isomerism of cyanuric azide showed that the azide groups of cyanuric azide do not cyclize to form tetrazoles, but that the reaction of cyanuric acid with PPh_3 leads to triphenylphosphanimino compounds where an azide group is in equilibrium with the ring-closed tetrazole in solution and a tetrazole is formed upon precipitation.[19,20] While no tetrazole formed from a polyazido-1,3,5-triazine has yet been detected, the mono- and ditetrazoles of diazido-1,2,4,5-tetrazine were synthesized only very recently.[21] In order to better understand the effects of electron-donating and electron-withdrawing groups on the azide–tetrazole equilibrium of cyanuric azide, we replaced one azide group with an amino and a nitro group, respectively. We also investigated the recently synthesized azo- and hydrazo-bridged dimers[5,22] of bis(azido)-1,3,5-triazine as well as triazido-*s*-heptazine.[23] The same calculations were also performed for several polyazido-1,2,4,5-tetrazines: bis(azido)-tetrazine[4] and the yet unknown azo- and hydrazo- bridged dimers of azidotetrazine.

The differences in electronic energy in the gas phase were used to determine the favored side of the equilibrium in the gas phase. In order to understand the favorization of the azides at higher temperatures, the entropies of the involved species were compared.

The Mulliken charges of the molecules were analyzed to understand the effect of different solvent polarities. Three different continuum environments with the characteristics of CCl_4, DMSO, and water were calculated using the polarized continuum model to explore the influence of increasing

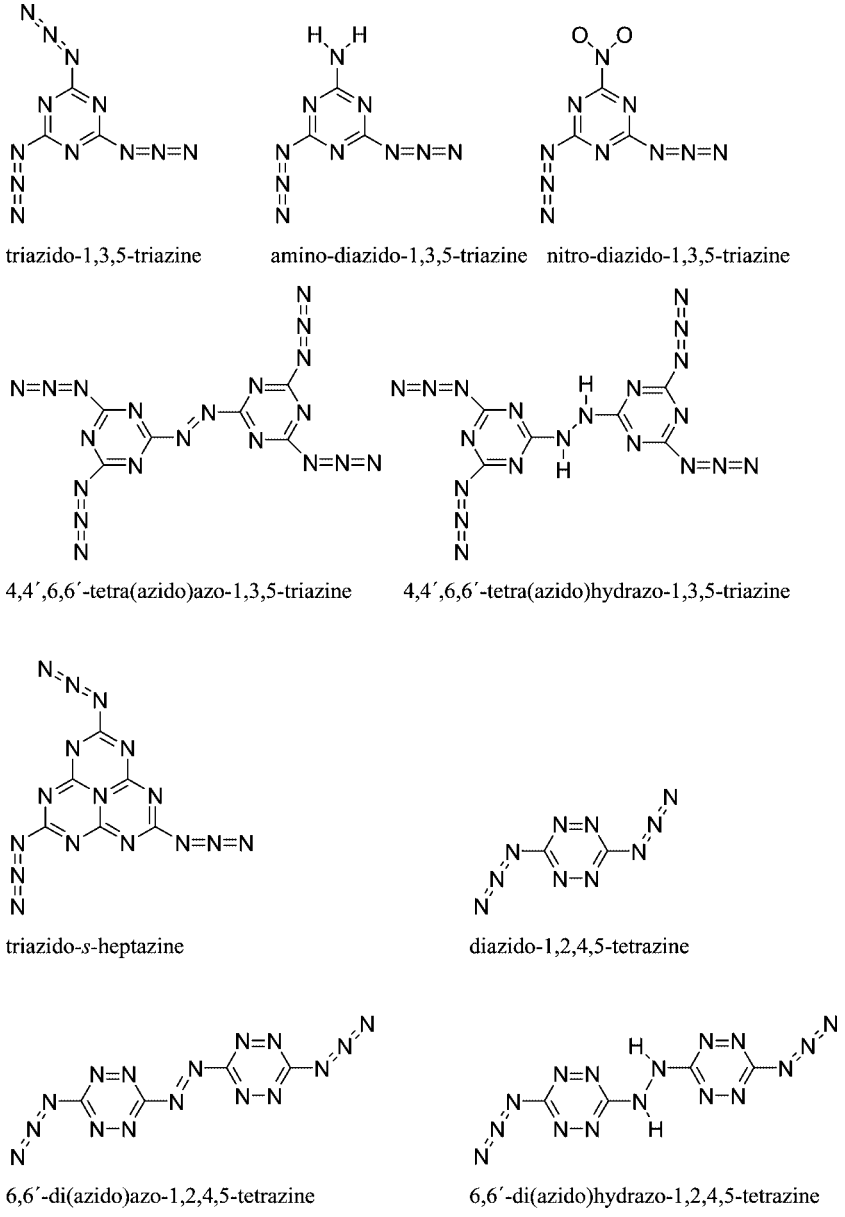
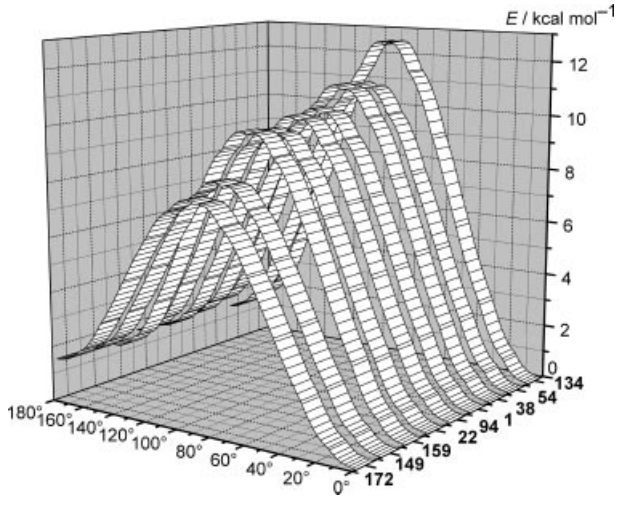


Figure 1. Investigated polyazidoheterocycles.

the dielectric permittivity on the potential energy of the investigated compounds.

Results and Discussion

The azide groups of the discussed compounds can rotate along the C–N σ bond. Scheme 1 shows the energy profile of the rotation of an azide group around the C–N single bond determined by single point energy calculations in 15° intervals. The azide groups prefer a planar configuration with a slight energy difference between the two possible planar configurations. The rotation profiles of the azo-bridged compounds show a slightly higher activation energy for a 180° rotation than for the hydrazo-bridged dimers.



Scheme 1. Energy profile for the rotation of an azide group around the N_α–C_{aryl} σ bond at the MP2 level. Single point energy calculations were performed at 15° intervals.

The minimum energy conformations for cyanuric azide and triazido-*s*-heptazine are the C_{3h} isomers **1** and **134**. The global minima **22** and **38** of amino- and nitro-1,3,5-triazine are derived from this structure by replacing one azide group with the respective substituent. The minimum energy structures **54** and **94** of the azo- and hydrazo-bridged dimers of bis(azido)-1,3,5-triazine are dimers of **1**. The global minimum for bis(azido)tetrazine is the C_{2h} conformer **149**. The global minima **159** and **172** of the azo- and hydrazo-bridged dimers of azidotetrazine also have a *trans* alignment of the azido groups.

Triazido-1,3,5-triazine (Cyanuric Azide)

Structures for all planar isomers and their possible intermediates for all three cyclization steps of cyanuric azide were calculated (Scheme 1). The calculated bonding parameters of **1** (see Supporting Information) are in good agreement with structural data.[19] The N_β–N_γ and bonding distances of the azide unit and the carbon–nitrogen bond of the azide unit are longer than in the X-ray structure.

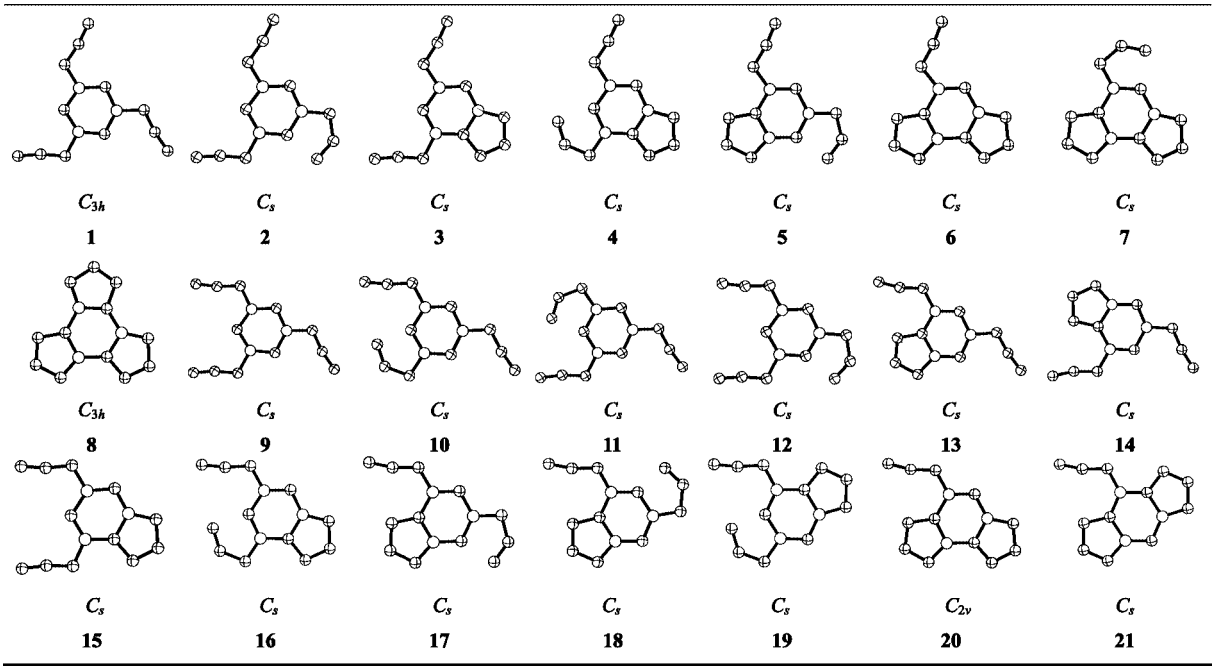
Two series of rotamers are formed based on the successive cyclization of the isomers **1** and **9**. The minimum energy reaction path (Scheme 2) is formed by cyclization of the C_{3h} isomer **1**, the less symmetric isomer **9** is about 0.5 kcal mol^{-1} higher in energy.

The energy difference calculated at the CCSD(T) level of theory are in good agreement with previously calculated values at the B3LYP level of theory (Table 1).[20] The MP2 energy differences are higher than the CCSD(T) values and increase for isomers with more tetrazole rings. The energy differences between the MP2 and CCSD(T) values are bigger for the transition states than for the ground states. At the CCSD(T) level, isomer **3** with one tetrazole ring system is 11.1 kcal mol^{-1} higher in energy than the triazide **1**, the ditetrazole **6** is 7.9 kcal mol^{-1} higher in energy than **3** and the tritetrazole **8** is 9.7 kcal mol^{-1} higher in energy than the ditetrazole **6**. The formation of the first tetrazole ring system has a CCSD(T) activation energy of 23.8 kcal mol^{-1}, the second cyclization requires an activation energy of 21.0 kcal mol^{-1} and the third cyclization requires an activation energy of 22.4 kcal mol^{-1} based on the respective azides. This shows that the formation of the first tetrazole ring system requires the most energy and consecutive ring formations are slightly easier.

The entropies slightly favor the azides over the ring-closed isomers. The entropy decreases with an increasing amount for every ring closure, in agreement with the loss of degrees of freedom upon cyclization. According to the equation $\Delta G = \Delta H - T\Delta S$ a temperature increase would therefore shift the equilibrium from the tetrazole to the azide in the long run. The slight entropy difference allow the use of heat to overcome the activation barrier for the formation of a tetrazole, but at higher temperatures the entropy favors the azides.

The sum of the positive and negative Mulliken charges is higher for the azide than for the tetrazole compounds (see Supporting Information). The individual charges of the atoms are higher in the tetrazoles. The positive charge is spread over more atoms in the azides. In the tetrazoles generally only the carbon atoms retain positive charges while in the azides the azide N_β atom is also positively charged. The charge in the tetrazoles is concentrated in the five-membered aromatic ring system, while in the azides the N_α and N_β atoms also retain a significant charge. The higher individual charges in the tetrazoles can be stabilized by more polar solvents, thus shifting the azide–tetrazole equilibrium to the tetrazole side. This explains the experimentally observed shift to the azide compounds with a decreasing solvent polarity, which was observed for example for thiazole[3,2-*d*]tetrazole[15] and diazidotetrazine.[21]

The PCM calculations for CCl_4, DMSO, and water also indicate that more polar solvents favor the tetrazoles. The ground states are influenced more by solvation than the ground states. Solvation in CCl_4 favors the monotetrazole **3** by 3.9 kcal mol^{-1}, the ditetrazole **6** by 6.5 kcal mol^{-1} and the tritetrazole **8** by 8.1 kcal mol^{-1}. The activation energy for the first cyclization is only slightly favored by 0.6 kcal mol^{-1}, the activation energy for the second cyclization is favored by 3.7 kcal mol^{-1} and the activation energy for the third cyclization is favored by 6.0 kcal mol^{-1} over the



Scheme 2. Calculated triazido-1,3,5-triazine isomers.

Table 1. Calculated energy differences between different triazido-1,3,5-triazine isomers. The gas-phase values include zero point energy corrections. The PCM values represent the differences in free energy of the various species.

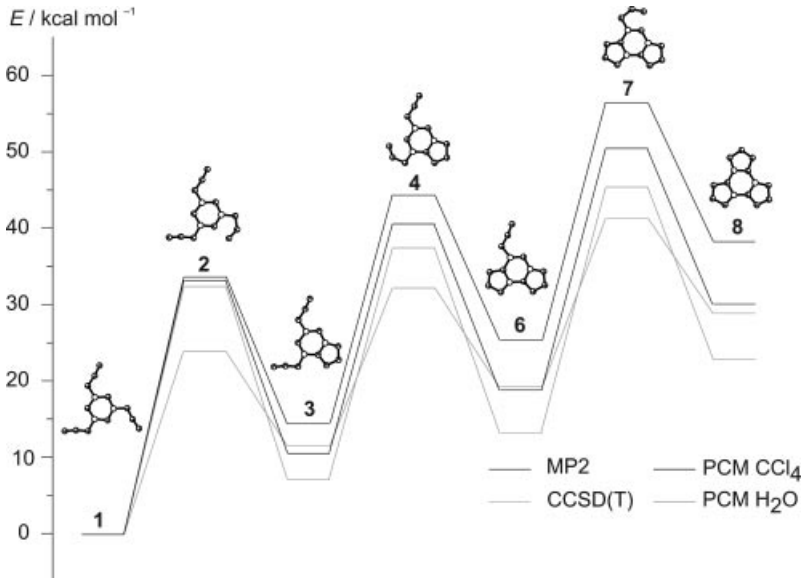
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**
E_{rel} (B3LYP/6-31G(d)) / kcal mol^{-1}	0	24.0	10.6	32.5	34.1	18.5	41.8	29.3	0.5	–	–
E_{rel} (MP2) / kcal mol^{-1}	0	33.4	14.5	44.3	46.3	25.4	56.5	38.2	0.3	34.4	35.2
E_{rel} (CCSD(T)) / kcal mol^{-1}	0	23.8	11.1	32.1	33.7	19.0	41.4	28.7	0.5	25.0	25.7
S / cal mol^{-1} K^{-1}	108.5	105.8	105.2	100.2	100.4	99.9	95.0	92.7	110.7	105.6	105.7
E_{rel} (MP2) / kcal mol^{-1} PCM H_2O	0	32.2	7.1	37.4	39.2	13.2	45.4	22.7	0.1	32.4	32.7
E_{rel} (MP2) / kcal mol^{-1} PCM DMSO	0	32.2	7.6	37.5	40.6	13.5	45.7	23.3	0	32.3	32.7
E_{rel} (MP2) / kcal mol^{-1} PCM CCl_4	0	32.8	10.6	40.6	42.5	18.9	50.5	30.1	0.2	33.4	34.1
	12	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	
E_{rel} (B3LYP/6-31G(d)) / kcal mol^{-1}	–	11.9	–	11.9	–	–	–	–	22.6	–	
E_{rel} (MP2) / kcal mol^{-1}	34.5	16.5	17.5	15.8	46.2	49.1	59.3	59.7	28.5	46.1	
E_{rel} (CCSD(T)) / kcal mol^{-1}	25.0	13.8	14.7	12.6	34.3	37.1	45.4	46.0	23.1	38.9	
S / cal mol^{-1} K^{-1}	105.9	105.2	105.2	105.3	100.2	100.7	99.8	99.8	100.4	99.1	
E_{rel} (MP2) / kcal mol^{-1} PCM H_2O	32.7	9.6	10.1	7.7	38.0	42.0	47.5	48.9	16.3	30.4	
E_{rel} (MP2) / kcal mol^{-1} PCM DMSO	32.6	9.7	10.3	11.7	38.2	42.2	47.8	49.2	16.6	30.8	
E_{rel} (MP2) / kcal mol^{-1} PCM CCl_4	33.8	12.9	13.7	7.9	42.0	45.4	53.9	54.7	22.1	38.7	

gas phase. The solvation in the more polar solvents water and DMSO also favors the tetrazoles. The differences between water and DMSO solvation are less than 0.4 kcal mol^{-1}, therefore only water solvatization is discussed here. In water the monotetrazole **3** is favored by 7.4 kcal mol^{-1}, the ditetrazole **6** by 12.2 kcal mol^{-1} and the tritetrazole **8** by 15.5 kcal mol^{-1} over the gas phase. The activation energy for the first cyclization is only slightly favored by 1.2 kcal mol^{-1}, the activation energy for the second cyclization is favored by 6.6 kcal mol^{-1} and the activation energy for the third cyclization is favored by 11.1 kcal mol^{-1} over the gas phase. While solvation in water favors the tritetrazole **8** to a great extent, it is still 22.7 kcal mol^{-1} higher in energy than **1** and has not yet been detected experimentally.[20,21] Thus cyanuric azide is not a suitable starting material for the synthesis of its tetrazole isomers.

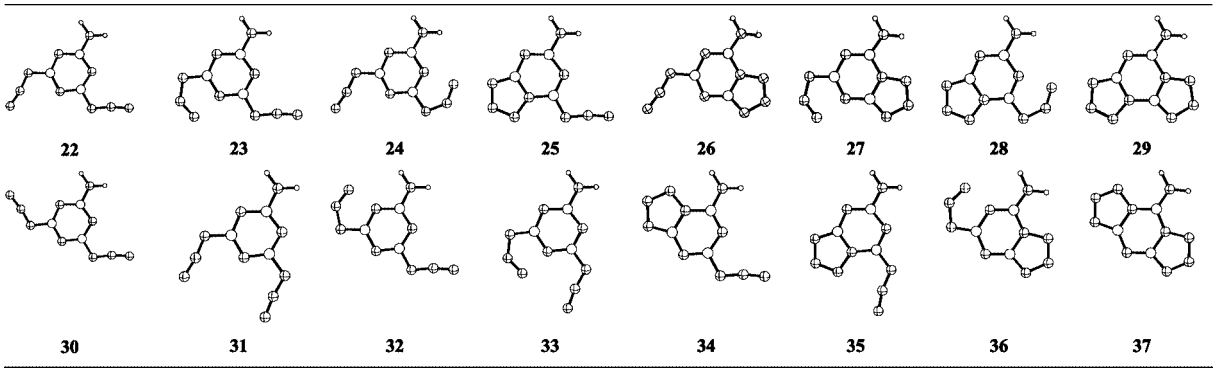
Amino- and Nitro-diazido-1,3,5-triazine

One azide substituent of cyanuric azide was replaced by the electron-donating amino group and the electron-withdrawing nitro group. As before, all possible planar conformations of the azide groups were considered (see Scheme 2 and Scheme 3).

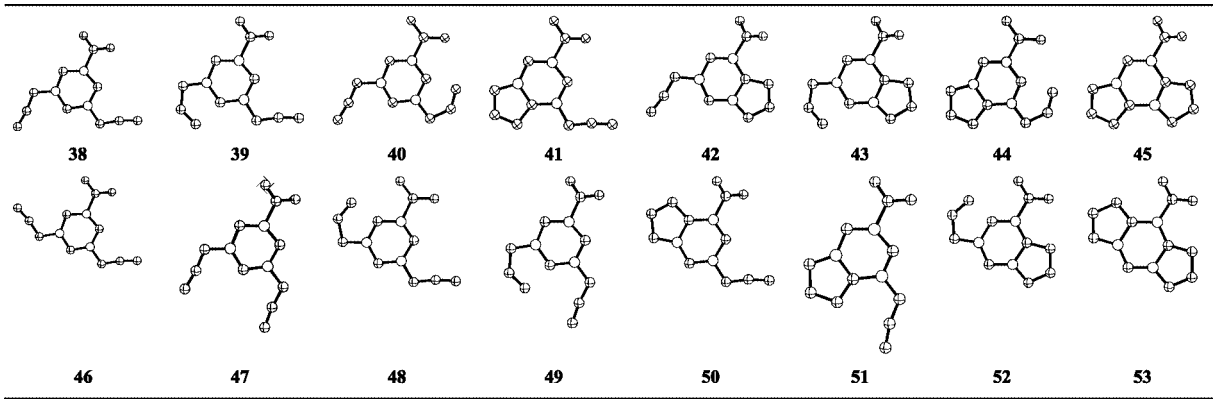
Both diazides have three planar isomers whose successive cyclization leads to the isomers shown in Scheme 4 and Scheme 5. The minimum energy reaction paths (Scheme 6 and Scheme 7) are formed by cyclization of the isomers **22** and **38**, which are derived from **1**. Isomers **30** and **31** as well as **40** and **41**, which are derived from **9**, have similar energies but their cyclization leads to tetrazoles with higher energies (Tables 2, 3). Interestingly, the amino compound first closes the tetrazole ring next to the amino group whereas



Scheme 3. Reaction profile for the ring closures in triazido-1,3,5-triazine.



Scheme 4. Calculated amino-diazido-1,3,5-triazine isomers, all isomers have C_1 symmetry.

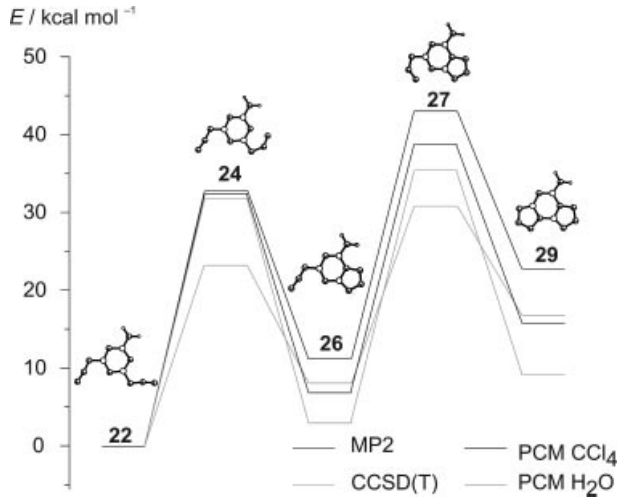


Scheme 5. Calculated diazido-nitro-1,3,5-triazine isomers, isomers have C_1 symmetry.

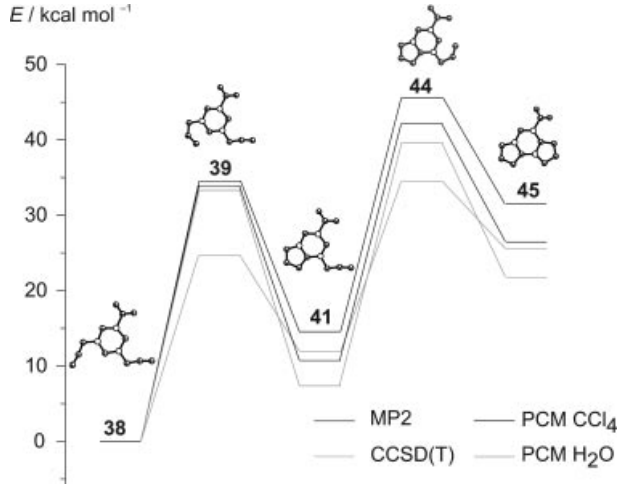
the nitro compound prefers to close the tetrazole ring farther away from the nitro group.

At the CCSD(T) level the amino derivative **26** with one tetrazole ring is 8.1 kcal mol^{-1} higher in energy than the azide **22** and the ditetrazole **29** is 8.5 kcal mol^{-1} higher in energy than the monotetrazole **26**. The activation energy for the cyclization of the amino compound **22** is 23.2 kcal mol^{-1} and the activation energy for the second cyclization is 22.7 kcal mol^{-1}. The nitro derivative **41** with one tetrazole group is 11.8 kcal mol^{-1} higher in energy than the azide **38** and the ditetrazole **45** is 13.8 kcal mol^{-1} higher in energy than the monotetrazole **41**. The activation energy for the cyclization of the nitro compound **41** is 24.6 kcal mol^{-1} and the activation energy for the second cyclization is

22.6 kcal mol^{-1}. As mentioned above for cyanuric azide, the MP2 energy differences for both compounds are larger and increase with the number of tetrazole rings.



Scheme 6. Reaction profile for the ring closures in 2-amino-4,6-diazido-1,3,5-triazine.



Scheme 7. Reaction profile for the ring closures in 4,6-diazido-2-nitro-1,3,5-triazine.

The formation of a tetrazole system leads to an entropy decrease for both amino- and nitro derivatives.

As observed for cyanuric azide, the sum of the positive and negative Mulliken charges is higher for the azide than for the tetrazole compounds (see Supporting Information) for both the amido and nitro derivatives, but the tetrazoles have higher individual charges. Similar to cyanuric azide, the ground states are influenced more by solvation in CCl_4, DMSO and water than the transition states.

Solvation of the amino derivatives in CCl_4 favors the monotetrazole **26** by 1.2 kcal mol^{-1} and the ditetrazole **29** by 7.0 kcal mol^{-1} over the gas phase. The activation energy for the first cyclization is only slightly favored by 0.9 kcal mol^{-1} and the activation energy for the second cyclization is favored by 4.2 kcal mol^{-1} over the gas phase. For the nitro derivatives solvation in CCl_4 decreases the energy difference to the diazide **1** by 3.6 kcal mol^{-1} for the monotetrazole **39** and by 4.9 kcal mol^{-1} for the ditetrazole **29** over the gas phase. The activation energies are lowered by 0.5 kcal mol^{-1} for the first cyclization and by 3.3 kcal mol^{-1} for the second cyclization compared to the gas phase. As observed for cyanuric azide, the effects of solvation in DMSO and water are similar. The amino-monotetrazole **26** is favored by 8.1 kcal mol^{-1} and the ditetrazole **29** by 13.4 kcal mol^{-1} over the gas phase. The activation energy for the first cyclization is lowered by 1.9 kcal mol^{-1} and the activation energy for the second cyclization by 7.6 kcal mol^{-1} over the gas phase. The nitro derivatives show a similar picture. Here the monotetrazole **41** is favored by 7 kcal mol^{-1} and the ditetrazole 45 by 9.5 kcal mol^{-1} in aqueous solution. The activation energies are lowered by 0.9 kcal mol^{-1} for the first cyclization and by 6.0 kcal mol^{-1} for the second cyclization.

In comparison to cyanuric azide, where the ditetrazole **16** is 19 kcal mol^{-1} higher in energy than the respective diazide **1**, the aminoditetrazole **29** is 16.6 kcal mol^{-1} higher in energy than the diazide **22** and the nitroditetrazole **45** is 25.6 kcal mol^{-1} higher in energy than the diazide **38** [CCDS(T) values]. This shows that substitution with an electron-donating group favors the tetrazole whereas substitution with an electron-withdrawing group favors the azide.

Table 2. Calculated energy differences between different amino-diazido-1,3,5-triazine isomers. The gas phase calculations include zero point energy corrections. The PCM values represent the differences in free energy of the various species.

	22	**23**	**24**	**25**	**26**	**27**	**28**	**29**
E_{rel} (MP2) / kcal mol^{-1}	0	33.5	32.7	14.4	11.1	43.0	44.5	22.7
E_{rel} (CCSD(T)) / kcal mol^{-1}	0	23.8	23.2	11.5	8.1	30.8	32.2	16.6
S / cal mol^{-1} K^{-1}	102.7	97.4	97.9	97.1	97.6	92.9	92.1	97.8
E_{rel} (MP2) / kcal mol^{-1} PCM H_2O	0	32.1	30.8	6.7	3.0	35.4	36.3	9.3
E_{rel} (MP2) / kcal mol^{-1} PCM DMSO	0	32.1	30.9	6.9	3.2	35.6	36.6	9.7
E_{rel} (MP2) / kcal mol^{-1} PCM CCl_4	0	32.8	31.8	10.9	6.9	38.8	40.3	15.7
	30	**31**	**32**	**33**	**34**	**35**	**36**	**37**
E_{rel} (MP2) / kcal mol^{-1}	0.3	–0.1	34.1	33.9	12.2	16.6	53.3	38.4
E_{rel} (CCSD(T)) / kcal mol^{-1}	0.5	–0.1	24.4	24.3	9.2	13.4	39.6	30.6
S / cal mol^{-1} K^{-1}	102.8	102.8	98.0	98.2	97.8	97.2	93.3	91.9
E_{rel} (MP2) / kcal mol^{-1} PCM H_2O	–0.1	0.2	30.9	32.2	3.2	9.3	40.0	18.9
E_{rel} (MP2) / kcal mol^{-1} PCM DMSO	–0.1	0.1	31.1	32.1	3.5	9.4	40.6	19.6
E_{rel} (MP2) / kcal mol^{-1} PCM CCl_4	0.2	–0.1	32.6	32.9	5.3	12.7	47.3	29.3

Table 3. Calculated energy differences between different diazido-nitro-1,3,5-triazine isomers. The gas phase calculations include zero point energy corrections. The PCM values represent the differences in free energy of the various species.

	38	**39**	**40**	**41**	**42**	**43**	**44**	**45**
E_{rel} (MP2) / kcal mol^{-1}	0	34.3	35.3	14.5	20.0	52.6	45.7	31.3
E_{rel} (CCSD(T)) / kcal mol^{-1}	0	24.6	25.9	11.8	17.0	40.1	34.4	25.6
S / cal mol^{-1} K^{-1}	111.9	107.0	108.4	106.3	106.1	101.5	101.9	100.6
E_{rel} (MP2) / kcal mol^{-1} PCM H_2O	0	33.4	35.1	7.5	15.0	48.4	39.7	21.8
E_{rel} (MP2) / kcal mol^{-1} PCM DMSO	0	33.4	34.5	7.7	15.1	48.5	39.8	22.1
E_{rel} (MP2) / kcal mol^{-1} PCM CCl_4	0	33.8	34.9	10.9	17.4	50.2	42.4	26.4
	46	**47**	**48**	**49**	**50**	**51**	**52**	**53**
E_{rel} (MP2) / kcal mol^{-1}	–0.1	0.4	36.1	35.6	20.7	16.8	67.4	54.0
E_{rel} (CCSD(T)) / kcal mol^{-1}	0	0.6	26.7	26.1	18.3	14.7	54.9	52.0
S / cal mol^{-1} K^{-1}	112.1	111.9	108.0	106.9	106.3	106.2	101.3	100.7
E_{rel} (MP2) / kcal mol^{-1} PCM H_2O	0.3	–0.2	35.4	33.6	16.0	9.7	60.4	44.1
E_{rel} (MP2) / kcal mol^{-1} PCM DMSO	0.4	–0.3	35.3	33.5	16.1	9.9	60.6	44.5
E_{rel} (MP2) / kcal mol^{-1} PCM CCl_4	0.1	0.2	35.8	34.6	18.6	13.2	64.3	49.3

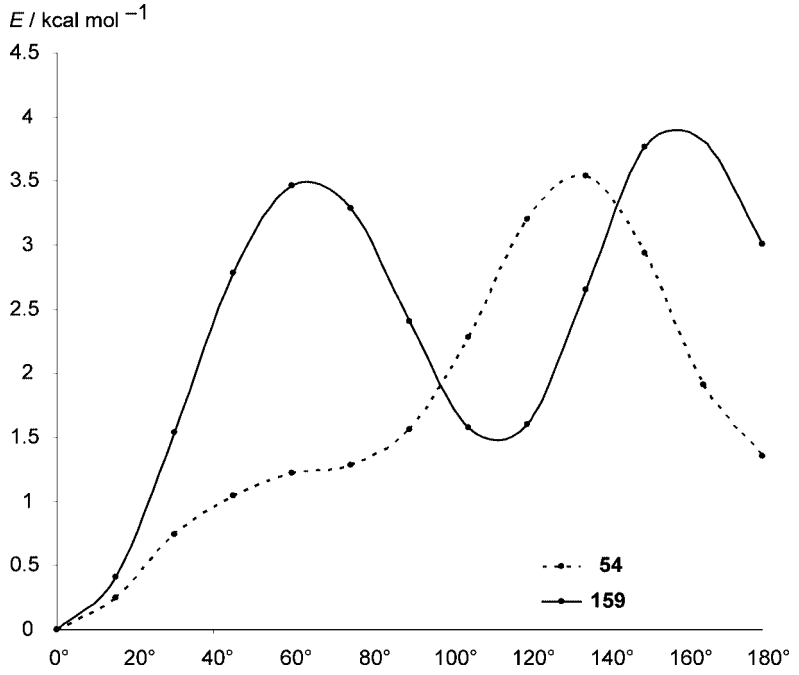
The activation energies for the first (23.8 kcal mol^{-1} for cyanuric azide, 23.8 kcal mol^{-1} for the amino derivative and 24.6 kcal mol^{-1} for the nitro derivative) and second cyclization (21.0 kcal mol^{-1} for cynuric azide, 22.7 kcal mol^{-1} for the amino derivative and 22.6 kcal mol^{-1} for the nitro derivative) are barely influenced by the substitution.

4,4′,6,6′-Tetra(azido)azo-1,3,5-triazine and 4,4′,6,6′-Tetra(azido)hydrazo-1,3,5-triazine

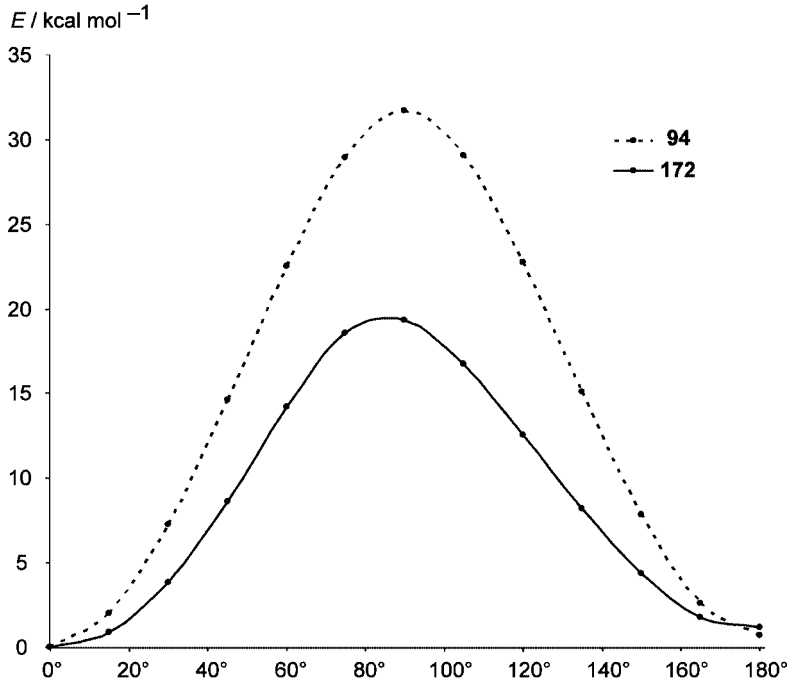
Here the size of the molecules prevented MP2 calculations due to computational cost. The good agreement between the B3LYP and CCSD(T) energy differences for cyanuric azide shows that these compounds could be investigated with density functional theory. Scheme 8, Scheme 9, and Scheme 10 show the rotation profiles around the C–N and N–N single bonds of the hydrazo-bridged **74** and the C–N bond of the azo-bridged dimer **54** with the minimum energy bonding angle set to zero. As expected, the C–N rotation barrier in the azo-bridged dimer is higher due to a partial double bond. The rotation around the N–N single bond in the hydrazo-bridged **94** is sterically hindered.

As there are too many possible routes for cyclization, not all possible isomers for the cyclization were calculated. Instead all possible tetraazides and tetratetrazoles were calculated. Then the isomers on the cyclization route linking the lowest energy tetraazide to the lowest energy tetratetrazole were calculated.

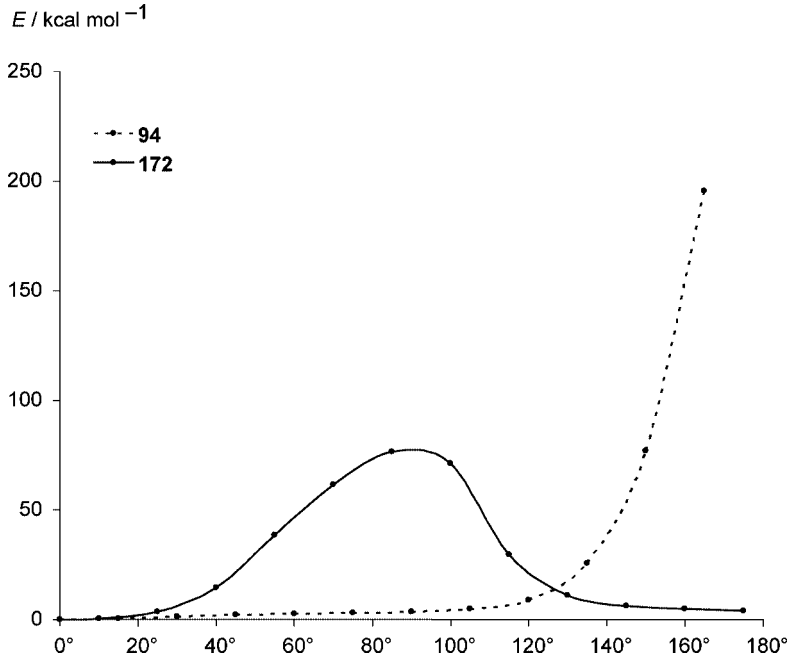
Two conformers of the azo-bridged tetraazide have already been found in the same crystal structure and yet another in a second crystal structure.[22] This confirms that the energy differences between the different tetraazide con-



Scheme 8. Energy profile for the rotation of **54** and **159** around the $N_{hydrazo}$–C_{aryl} σ bond with the minimum energy bonding angle set to zero at the MP2 level. Single point energy calculations were performed at 15° intervals.



Scheme 9. Energy profile for the rotation of **94** and **172** around the $N_{hydrazo}$–C_{aryl} σ bond with the minimum energy bonding angle set to zero at the MP2 level. Single point energy calculations were performed at 15° intervals.



Scheme 10. Energy profile for the rotation of **94** and **159** around the $N_{hydrazo}$–C_{aryl} σ bond with the minimum energy bonding angle set to zero at the MP2 level. Single point energy calculations were performed at 15° intervals.

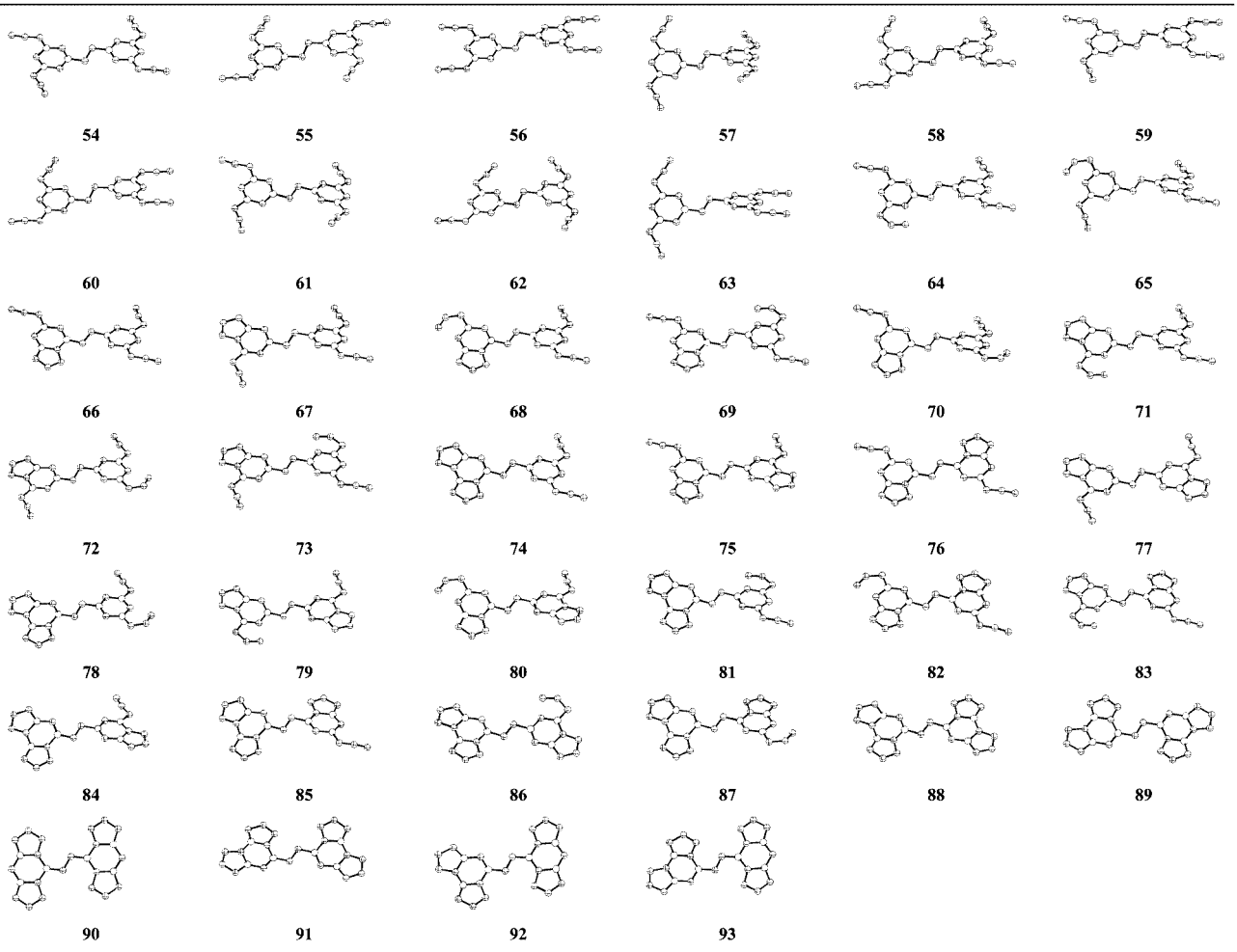
formers are only slight. For the azo-bridged dimers we find differences of only 1.3 kcal mol^{-1} between isomers **54**–**63**. Interestingly, the highest energy conformer **56** was found in a crystal structure together with conformer **55**. This is probably due to a better space filling in the crystal in the presence of both isomers. While isomer **54** does not have the lowest energy in the gas phase, it is the lowest energy isomer in solution and its cyclization product **88** is the lowest energy tetratetrazole. The tetratetrazoles have higher energy differences of up to 25.7 kcal mol^{-1}. Therefore, a cyclization route linking **54** to **88** was calculated. The hydrazo-bridged dimers **94**–**103** are also only separated by 1.5 kcal mol^{-1} in energy. Here the lowest energy tetraazide **94** was also found in the crystal structure[22] and no other conformers have yet been observed. The cyclization route linking **94** to the lowest energy tetratetrazole **128** was calculated. Similar to the

azo compounds the tetratetrazole isomers **128**–**133** have energy differences up to 27.0 kcal mol^{-1}. The lowest energy azo- and hydrazo-bridged tetraazides **54** and **94** and tetratetrazoles **88** and **128** have the same conformation of the azide groups and are, like the minimum energy amino- and nitro-diazido-1,3,5-triazines, derived from the minimum energy triazido-1,3,5-triazine **1**. The calculated bonding parameters of **55**, **56**, **57**, and **94** are in good agreement with the structural data.[22] The N_β-N_γ bond of the azide units is slightly longer than in the X-ray structures (see Supporting Information).

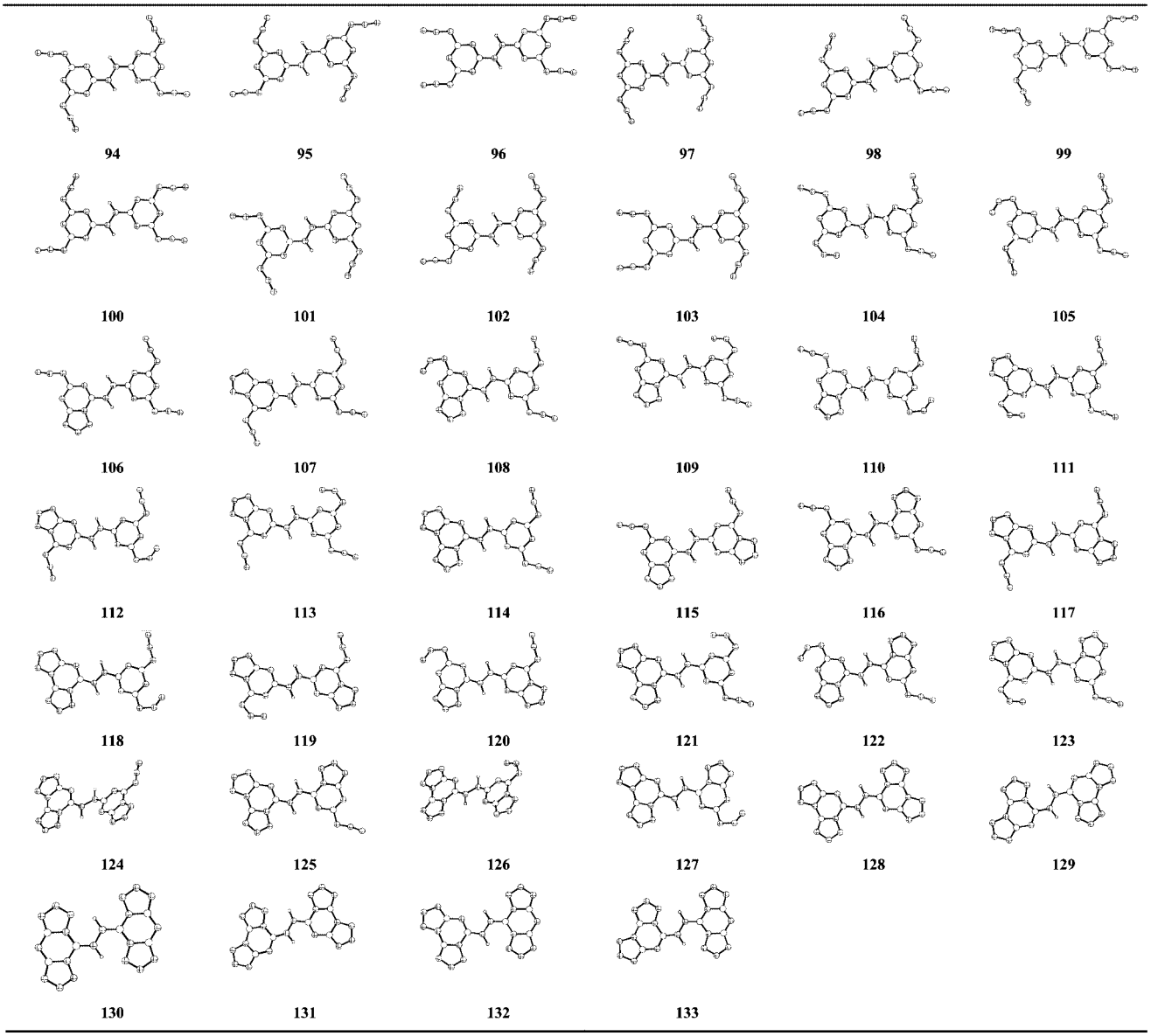
Scheme 11 and Scheme 12 show that the azo- and hydrazo-bridged dimers first cyclize both azide groups belonging to one triazine ring and then the azide groups of the second triazine unit.

The azo-bridged monotetrazole **67** is 11.2 kcal mol^{-1} higher in energy than the tetraazide **54**, the ditetrazole **74** 20.8 kcal mol^{-1}, the tritetrazole **84** 32.5 kcal mol^{-1} and the tetratetrazole **88** 44.3 kcal mol^{-1}, which translates to energy differences of 9.6 kcal mol^{-1} between the monotetrazole **67** and the ditetrazole **74**, 11.7 kcal mol^{-1} between the ditetrazole **74** and the tritetrazole **84** and 11.8 kcal mol^{-1} between the tritetrazole **84** and the tetratetrazole **88** (Scheme 13, Table 4). The ditetrazoles **75**–**77** with tetrazole rings at different triazine rings are about 3 kcal mol^{-1} less favored than **74**, where both tetrazole rings are bonded to the same triazine ring. The activation energies for the cyclizations are 23.5 kcal mol^{-1}, 21.4 kcal mol^{-1}, 23.9 kcal mol^{-1} and 22.5 kcal mol^{-1}. The third cyclization transition state **79**, which links ditratrazole **77** with tritetrazole **84**, is 0.6 kcal mol^{-1} lower than **78**, but the ditetrazole **77** is 1.7 kcal mol^{-1} higher in energy than ditetrazole **74**. The cyclization therefore should lead to ditetrazole **77**, which then requires a slightly higher activation energy to cyclize to tritetrazole **84**.

The hydrazo-bridged compounds have slightly lower energy differences than the azo-bridged compound to the tetraazide **94** for the mono- and ditetrazoles, while the tri- and tetratetrazoles have similar energies (Scheme 14, Table 5). The monotetrazole **106** is 10.7 kcal mol^{-1} higher in energy, the ditetrazole **114** 20.5 kcal mol^{-1}, the tritetrazole **124** 33.0 kcal mol^{-1} and the tetratetrazole **128** 44.3 kcal mol^{-1}. This translates to energy differences of 9.8 kcal mol^{-1} between one and two tetrazole rings, 12.5 kcal mol^{-1} between two and three tetrazole rings and 11.3 kcal mol^{-1} between three and four tetrazole rings. The ditetrazoles **115**–**117**



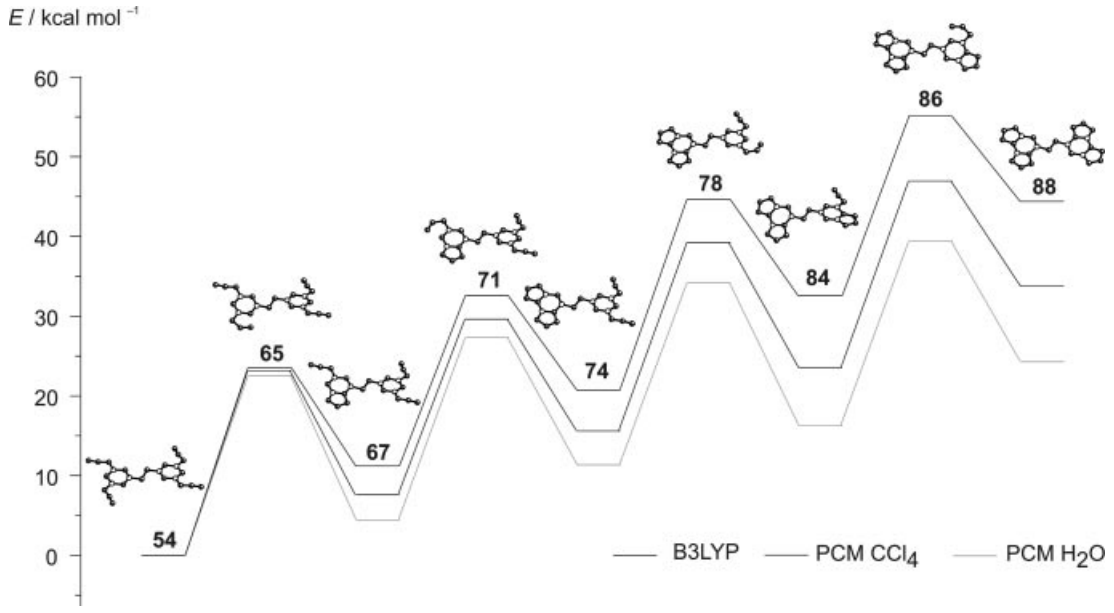
Scheme 11. Calculated isomers of 4,4′,6,6′-tetra(azido)azo-1,3,5-triazine.



Scheme 12. Calculated isomers of 4,4′,6,6′-tetra(azido)hydrazo-1,3,5-triazine.

with tetrazole rings at both triazine rings are about 2.5 kcal mol^{-1} less favored than **114**, where both tetrazole rings are bonded to the same triazine ring. The activation energies for the cyclizations are 23.4 kcal mol^{-1}, 22.3 kcal mol^{-1}, 23.0 kcal mol^{-1}, and 22.5 kcal mol^{-1}. Transition state **105** for the first cyclization, which links the tetraazide **94** with the monotetrazole **107**, is 0.7 kcal mol^{-1} lower than **104**, but the montetrazole **107** is 0.8 kcal mol^{-1} higher in energy than the monotetrazole **106**. The kinetic product **107** also requires a higher activation energy for a second cyclization, therefore the minimum energy cyclization route includes transition state **104** and monotetrazole **106**. As observed for all previous compounds, successive cyclization leads to a successive decrease of the entropy for both azo and hydrazo compounds. The sum of the positive and negative Mulliken charges is higher for the azides than for the tetrazole compounds (see Supporting Information) for both the azo- and hydrazo compounds, but the tetrazoles have higher individual charges.

Solvatization in CCl_4, DMSO and water has a higher influence on the ground states than on the transition states. Solvation in CCl_4 of the azo compound favors the monotetrazole **67** by 3.5 kcal mol^{-1}, the ditetrazole **74** by 5.2 kcal mol^{-1}, the tritetrazole **84** by 8.8 kcal mol^{-1} and the tetratetrazole **88** by 10.6 kcal mol^{-1} over the gas phase. The activation energy for the first cyclization is only slightly favored by 0.2 kcal mol^{-1}, the second cyclization is favored by 2.8 kcal mol^{-1}, the third cyclization by 5.5 kcal mol^{-1} and the final cyclization by 8.1 kcal mol^{-1} over the gas phase. The hydrazo compounds are favored by 3.1 kcal mol^{-1} for the monotetrazole **106**, by 5.8 kcal mol^{-1} for the ditetrazole **114**, by 10.3 kcal mol^{-1} for the tritetrazole **124**, and by



Scheme 13. Reaction profile for the ring closures in 4,4′,6,6′-tetra(azido)azo-1,3,5-triazine.

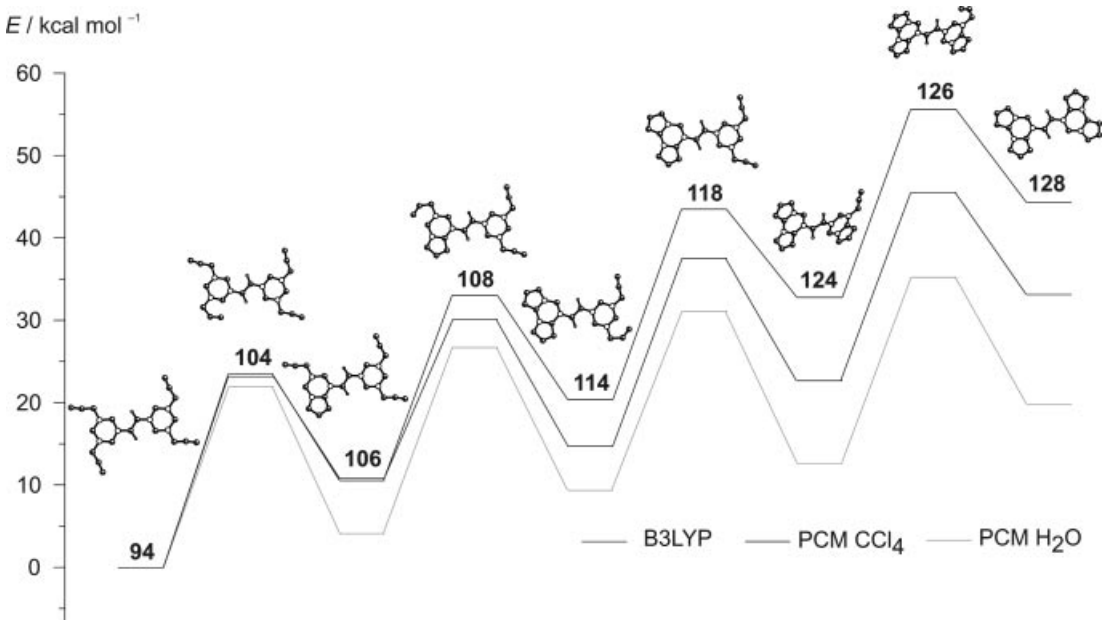
Table 4. Calculated energy differences between different 4,4′,6,6′-tetra(azido)azo-1,3,5-triazine. The gas phase calculations include zero point energy corrections. The PCM values represent the differences in free energy of the various species.

	54	**55**	**56**	**57**	**58**	**59**	**60**	**61**	**62**	**63**	**64**	**65**	**66**	**67**
E_{rel} (B3LYP) / kcal mol^{-1}	0	–0.2	0.9	–0.1	–0.1	0.5	0.3	–0.1	–0.2	0.4	23.8	23.5	12.1	11.2
S / cal mol^{-1} K^{-1}	160.5	160.5	160.6	160.7	160.2	160.4	160.3	160.2	160.3	160.4	155.6	155.4	154.7	154.5
E_{rel} (B3LYP) / kcal mol^{-1} PCM H_2O	0	0.2	0.5	0.3	0.1	0.2	0.3	0.1	0.3	0.4	23.5	22.7	6.8	4.6
E_{rel} (B3LYP) / kcal mol^{-1} PCM DMSO	0	0.5	0.3	0.7	0.2	0.1	0.4	0.3	0.6	0.5	23.5	22.7	7.0	4.9
E_{rel} (B3LYP) / kcal mol^{-1} PCM CCl_4	0	0.2	0.8	0.4	0.1	0.3	0.4	0.1	0.3	0.5	23.8	23.3	9.2	7.7
	68	**69**	**70**	**71**	**72**	**73**	**74**	**75**	**76**	**77**	**78**	**79**	**80**	**81**
E_{rel} (B3LYP) / kcal mol^{-1}	35.0	36.8	35.9	32.6	34.8	35.0	20.8	23.7	25.9	22.5	44.7	44.1	46.7	45.8
S / cal mol^{-1} K^{-1}	150.1	149.7	149.8	149.6	149.7	149.5	149.0	149.0	148.9	148.8	144.1	143.8	144.2	144.2
E_{rel} (B3LYP) / kcal mol^{-1} PCM H_2O	30.2	30.9	29.8	27.3	27.4	28.2	11.4	11.7	14.8	9.3	34.4	32.0	35.1	35.6
E_{rel} (B3LYP) / kcal mol^{-1} PCM DMSO	30.5	31.2	30.1	27.4	27.6	28.4	11.7	12.1	15.2	9.6	34.8	32.4	35.5	35.9
E_{rel} (B3LYP) / kcal mol^{-1} PCM CCl_4	32.5	33.9	32.8	29.8	31.1	31.7	15.6	17.3	20.1	15.4	39.2	37.8	40.6	40.5
	82	**83**	**84**	**85**	**86**	**87**	**88**	**89**	**90**	**91**	**92**	**93**		
E_{rel} (B3LYP) / kcal mol^{-1}	49.2	45.9	32.5	35.1	55.0	58.4	44.3	45.8	70.0	45.0	48.5	59.3		
S / cal mol^{-1} K^{-1}	144.4	144.0	143.2	143.4	138.4	138.8	137.8	137.9	138.7	137.7	137.8	137.4		
E_{rel} (B3LYP) / kcal mol^{-1} PCM H_2O	38.5	16.2	16.2	19.6	39.5	43.3	24.4	26.5	49.6	25.4	38.0	39.7		
E_{rel} (B3LYP) / kcal mol^{-1} PCM DMSO	38.9	16.8	16.8	20.2	40.1	44.0	25.1	27.4	50.7	27.4	39.0	40.1		
E_{rel} (B3LYP) / kcal mol^{-1} PCM CCl_4	43.7	23.7	23.7	26.7	46.9	50.6	33.7	35.6	60.6	34.6	48.5	49.5		

11.1 kcal mol^{-1} for the tetratetrazole **128** by solvation in CCl_4. The activation energy for the first cyclization is slightly increased by 0.2 kcal mol^{-1} while the activation energy for the second, third and fourth cyclization are favored by 2.9 kcal mol^{-1}, 6.0 kcal mol^{-1}, and 10.0 kcal mol^{-1}.

The difference between solvation in water and DMSO is more pronounced compared to the previous compounds, probably due to different displacement of solvent molecules. Still, the energy differences between DMSO and water solvation are within 1 kcal mol^{-1}. The azo-bridged mono- **67**, di- **74**, tri- **84**, and tetratetrazoles 88 are favored by 6.6, 9.4, 16.3, and 19.9 kcal mol^{-1} over the gas phase and the activation energy for the first, second, third, and fourth cyclization by 0.8, 5.3, 10.3, and 15.5 kcal mol^{-1}. Solvation of the hydrazo compounds in water leads to an even higher stabilization of the tetrazoles. The hydrazo-bridged mono- **106**, di- **114**, tri- **124**, and tetratetrazoles **128** are stabilized by 6.7, 11.2, 20.4, and 24.6 kcal mol^{-1} over the gas phase. The activation energy for the first, second, third, and fourth cyclizations are favored by 1.4, 6.3, 12.4, and 20.4 kcal mol^{-1} by solvation in water.

As a consequence, both 4,4′,6,6′-tetra(azido)azo-1,3,5-triazine and 4,4′,6,6′-tetra(azido)hydrazo-1,3,5-triazine do not form tetrazoles in gas phase or in solution. Solvation in polar solvents favors the tetrazoles, even more for the



Scheme 14. Reaction profile for the ring closures in 4,4′,6,6′-tetra(azido)hydrazo-1,3,5-triazine.

Table 5. Calculated energy differences between different4,4′,6,6′-Tetra(azido)hydrazo-1,3,5-triazine. The gas phase calculations include zero point energy corrections. The PCM values represent the differences in free energy of the various species.

	94	**95**	**96**	**97**	**98**	**99**	**100**	**101**	**102**	**103**	**104**	**105**	**106**	**107**
E_{rel} (B3LYP) / kcal mol^{-1}	0	1.0	0	1.9	0.6	0.0	0.5	1.0	1.5	0.9	23.4	22.7	10.7	11.5
S / cal mol^{-1} K^{-1}	163.6	165.0	162.9	166.4	164.2	163.6	163.4	164.3	164.6	165.9	160.9	158.6	157.1	158.9
E_{rel} (B3LYP) / kcal mol^{-1} PCM H_2O	0	2.0	0.2	2.6	1.2	0.3	1.2	1.3	2.3	1.3	22.0	21.8	4.0	4.0
E_{rel} (B3LYP) / kcal mol^{-1} PCM DMSO	0	3.7	0	4.7	2.0	0.0	1.9	2.2	4.0	2.1	23.3	21.7	5.2	4.2
E_{rel} (B3LYP) / kcal mol^{-1} PCM CCl_4	0	2.4	–0.2	3.6	1.3	–0.1	1.1	1.8	2.9	1.6	23.6	22.3	7.6	7.6
	108	**109**	**110**	**111**	**112**	**113**	**114**	**115**	**116**	**117**	**118**	**119**	**120**	**121**
E_{rel} (B3LYP) / kcal mol^{-1}	33.0	35.0	33.8	33.2	34.2	35.2	20.5	23.0	23.0	23.0	43.5	44.4	45.4	46.9
S / cal mol^{-1} K^{-1}	152.6	152.8	153.8	156.3	153.0	155.5	152.7	152.3	154.1	153.4	148.7	151.3	147.5	139.9
E_{rel} (B3LYP) / kcal mol^{-1} PCM H_2O	26.7	26.6	25.8	26.1	25.7	26.1	9.3	12.9	8.8	8.1	31.1	30.4	31.0	34.2
E_{rel} (B3LYP) / kcal mol^{-1} PCM DMSO	27.8	29.4	27.0	27.6	25.8	37.5	10.4	9.7	12.3	8.3	32.3	30.3	23.3	37.3
$37E_{rel}$ (B3LYP) / kcal mol^{-1} PCM CCl_4	30.1	32.3	30.3	30.3	29.8	31.5	14.7	16.0	17.3	15.1	37.5	38.2	23.6	42.3
	122	**123**	**124**	**125**	**126**	**127**	**128**	**129**	**130**	**131**	**132**	**133**		
E_{rel} (B3LYP) / kcal mol^{-1}	45.8	47.6	33.0	33.6	55.5	56.4	44.3	50.2	71.3	46.7	57.5	60.3		
S / cal mol^{-1} K^{-1}	148.9	140.1	144.8	151.0	140.0	149.6	146.6	139.2	137.6	141.7	140.7	138.3		
E_{rel} (B3LYP) / kcal mol^{-1} PCM H_2O	31.7	33.4	12.6	14.6	35.1	37.4	19.7	29.6	46.7	23.6	33.1	37.3		
E_{rel} (B3LYP) / kcal mol^{-1} PCM DMSO	35.2	37.1	13.9	17.9	36.3	40.8	23.6	30.7	47.7	25.1	35.1	38.4		
E_{rel} (B3LYP) / kcal mol^{-1} PCM CCl_4	40.2	42.6	22.7	25.2	45.5	48.1	33.2	39.2	60.1	35.0	46.1	49.0		

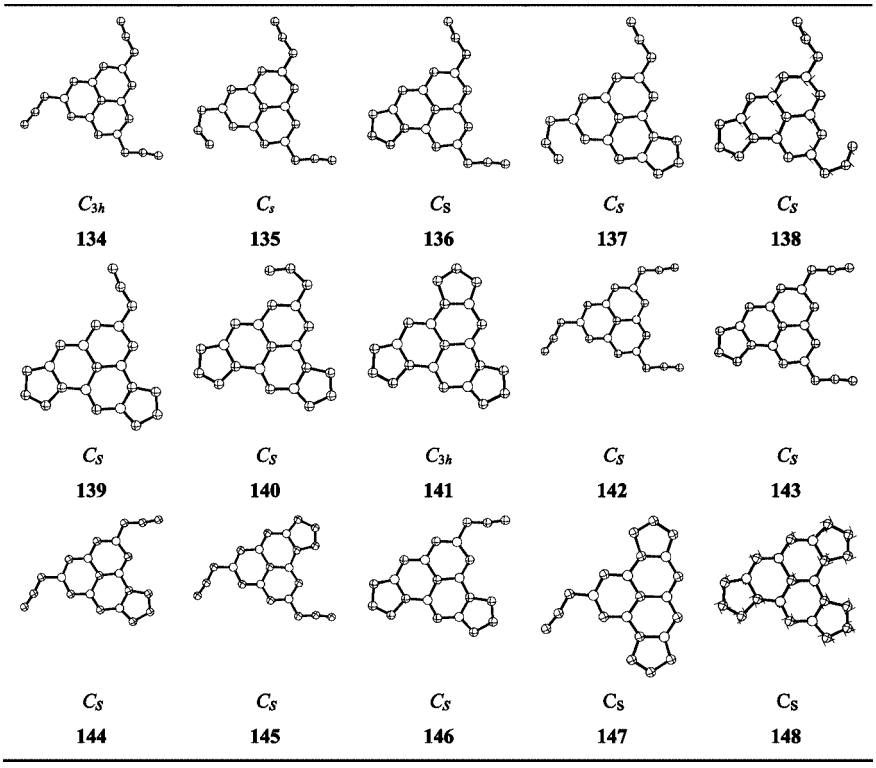
hydrazo compounds than the for the azo compounds. The solvation effect is not sufficient so that the detection of the tetrazoles in solution was not observed.[21]

Triazido-*s*-heptazine

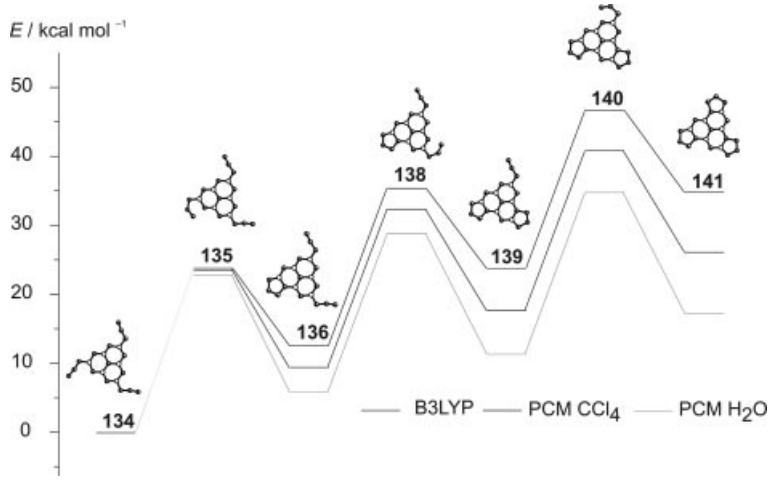
Triazido-*s*-heptazine behaves similarly to triazido-1,3,5-triazine. Two azide rotamers cyclize to different tetrazoles. To save computer time, we only calculated the ground states and the transition states linking the lowest ground states (Scheme 15).

The minimum energy C_{3h} isomer **139** is similar to the minimum energy cyanuric azide isomer **1**. The bonding parameters are in agreement with X-ray structural data,[23] with the same longer azide N_β–N_γ bond found for all previous compounds (Scheme 16, Table 6).

The reaction profile for the cyclization of the triazidoheptazine **139** is similar to the reaction profile of triazidotriazine **1**. The energy differences between the triazide **134** and monotetrazole **136**, the ditetrazole **139** and the tritetrazole **141** are 12.6, 23.8, and 34.9 kcal mol^{-1}. The ditetrazole **139** is therefore 11.2 kcal mol^{-1} higher in energy



Scheme 15. Calculated isomers of triazido-*s*-heptazine.



Scheme 16. Reaction profile for the ring closures in triazido-*s*-heptazine.

Table 6. Calculated energy differences between different triazido-*s*-heptazine isomers. The gas phase calculations include zero point energy corrections. The PCM values represent the differences in free energy of the various species.

	134	**135**	**136**	**137**	**138**	**139**	**140**	**141**	**142**	**143**	**144**	**145**	**146**	**147**	**148**
E_{rel} (B3LYP) / kcal mol^{-1}	0	23.5	12.6	35.4	35.4	23.8	46.5	34.9	0.1	13	13.2	13.0	24.5	31.7	55.3
S / cal mol^{-1} K^{-1}	127.8	125.4	124.9	120.5	120.4	119.8	115.3	112.5	130.0	125	125.0	125.0	119.9	120.3	116.3
E_{rel} (B3LYP) / kcal mol^{-1} PCM H_2O	0	23.1	5.9	29.0	29.0	11.4	34.7	17.1	0.0	6.0	6.4	6.4	11.9	16.6	36.3
E_{rel} (B3LYP) / kcal mol^{-1} PCM DMSO	0	23.0	6.1	29.2	29.3	11.8	35.1	17.8	–[a]	–[a]	6.7	6.6	12.4	17.2	37.0
E_{rel} (B3LYP) / kcal mol^{-1} PCM CCl_4	0	23.5	9.3	32.4	32.4	17.6	40.8	26.1	–[a]	–[a]	10.1	9.9	18.4	25.0	47.2

[a] Calculation did not converge.

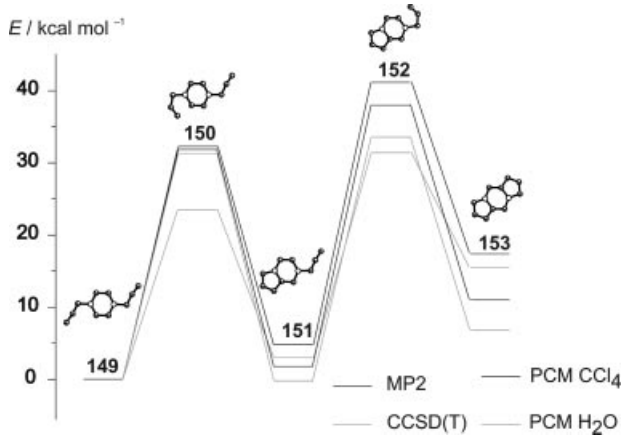
than the monotetrazole **136** and the tritetrazole **141** 11.1 kcal mol^{-1} higher than the ditetrazole **139**. The activation energies for the first, second and third cyclization are 23.5, 22.8, and 22.7 kcal mol^{-1}. The formation of the tetrazole rings is accompanied by a decrease of the entropy and a decrease of the sum of the positive and negative Mulliken charges. The tetrazoles have higher individual positive charges. Similar to cyanuric azide, the ground states are more influenced by solvation in CCl_4, DMSO, and water than the ground states.

Solvation in CCl_4 favors the monotetrazole **136** by 3.3 kcal mol^{-1} and the ditetrazole **139** by 6.2 kcal mol^{-1} and the tritetrazole **141** by 8.8 kcal mol^{-1} over the gas phase. The activation energy for the first cyclization is only slightly favored by 0.4 kcal mol^{-1} and the activation energy for the second and third cyclization are favored by 3.0 kcal mol^{-1} and 5.7 kcal mol^{-1} over the gas phase. The optimization of the solvation of **142** and **143** in DMSO and CCl_4 did not converge. Solvation in water and DMSO is only different by maximally 1 kcal mol^{-1}. Solvation lead to a favorization of 6.7 kcal mol^{-1} for the monotetrazole **136**, of 12.4 kcal mol^{-1} for the ditetrazole **139** and of 17.8 kcal mol^{-1} for the tritetrazole **141** over the gas phase. The activation energies for the cyclization are favored by 0.4, 6.4, and 11.8 kcal mol^{-1} for the first, second and third cyclization. Compared to triazido-1,3,5-triazine, triazido-*s*-heptazine is even less likely to form a tetrazole and it is therefore not surprising that the attempt to form a tetrazole isomer from triazido-*s*-heptazine have not been successful.[21]

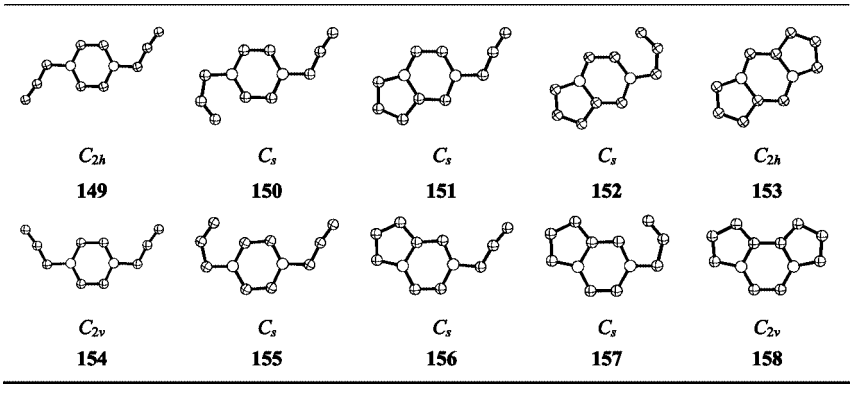
Diazidotetrazine

The rotation barriers of the azide unit around the C–N bonds of diazidotetrazine are slightly lower than those of the azido-1,3,5-triazines (see Scheme 1). Cyclization of diazidotetrazine in a *trans* **149** and a *cis* **154** conformation was investigated (Scheme 17). In the crystal structure only *trans* **149** was found.[4] Its bonding parameters are in agreement with the calculation. As observed for the triazines, the azide N_β–N_γ bond is shorter in the X-ray structure (see Supporting Information).

The *trans* and *cis* diazides **149** and **154** as well as the *trans* and *cis* monotetrazoles **151** and **156** are only separated at most 0.5 kcal mol^{-1} at the MP2 level and even less at the CCSD(T) level of theory (Scheme 18). The B3LYP values in Table 7 show the same tendency. Similar to the results for the triazines, the MP2 energy differences between azide and tetrazoles are larger. The *cis* ditetrazole **158** has an energy that is 5.2 kcal mol^{-1} higher than that of the *trans* ditetrazole **153** at the CCSD(T) level of theory. Therefore, the minimum energy cyclization path connects the *trans* diazide **149** with the *trans* ditetrazole **153**. The difference between the ditetrazole **153** and the monotetrazole **151** is with 12.6 kcal mol^{-1} much larger than the difference of 2.9 kcal mol^{-1} between diazide and monotetrazole. The cyclization of an azide group belonging to one of the previously mentioned 1,3,5-triazine derivatives resulted in relatively constant energy differences of 9 to 12 kcal mol^{-1} per tetrazole ring. Therefore the cyclization of an azide group, especially the first cyclization, is favored for the tetrazine ring system compared to the triazine ring system. The activation energies for the first and second cyclization are 23.6 and 28.6 kcal mol^{-1}. For comparison, the monotetrazoles of pyridazine diazides and triazides are favoured by about 3 kcal mol^{-1} over the all-azide and all-tetrazole isomers



Scheme 18. Reaction profile for the ring closures in diazidotetrazine.



Scheme 17. Calculated diazidotetrazine isomers.

Table 7. Calculated energy differences between different diazidotetrazine isomers. The gas phase calculations include zero point energy corrections.

	149	150	151	152	153	154	155	156	157	158
E_{rel} (B3LYP/aug-cc-pVTZ) / kcal mol^{-1}	0	24.9	5.9	34.5	19.7	0.1	–	5.9	–	26.9
E_{rel} (MP2) / kcal mol^{-1}	0	31.7	4.7	41.2	17.2	0.1	31.8	5.2	42.8	24.9
E_{rel} (CCSD(T)) / kcal mol^{-1}	0	23.6	2.9	31.5	15.5	0.1	23.6	3.2	31.9	20.7
S / cal mol^{-1} K^{-1}	96.4	92.8	90.7	85.5	82.9	96.4	92.8	90.7	86.2	83.9
E_{rel} (MP2) / kcal mol^{-1} PCM H_2O	0	31.6	–0.2	33.5	6.80	0.0	31.3	–0.2	37.7	15.1
E_{rel} (MP2) / kcal mol^{-1} PCM DMSO	0	31.5	0.9	36.1	7.2	0.0	31.4	–0.1	38.9	16.1
E_{rel} (MP2) / kcal mol^{-1} PCM CCl_4	0	31.6	2.0	37.9	10.9	0.1	31.6	2.1	40.0	19.9

with activation energies of about 20 kcal mol^{-1} for one cyclization.[24]

The formation of the tetrazole rings is accompanied by a decrease of the entropy and a decrease of the sum of the positive and negative Mulliken charges. Again the tetrazoles have higher individual positive charges. Solvation has a bigger effect on the ground states than on the transition states. In CCl_4 the monotetrazole **151** is favored by 2.7 kcal mol^{-1} and the ditetrazole **153** by 6.3 kcal mol^{-1}, while the first and second transition states are favored by 0.1 and 3.3 kcal mol^{-1}. As before, the results of DMSO and water are similar. Solvation in water leads to a stabilization of the monotetrazole **151** by 4.9 kcal mol^{-1} and of 10.4 kcal mol^{-1} for the ditetrazole **153**. The activation energies for the first and second cyclization are lowered by 0.1 and 6.7 kcal mol^{-1}. After solvation in water, the monotetrazole **151** is 0.2 kcal mol^{-1} lower in energy than the diazide **149**.

Very recently an equilibrium of diazidotetrazine with its monotetrazole in DMSO was observed with NMR spectroscopy.[21] Heating to 80 °C overcame the activation barrier and a ditetrazole was observed. The authors indicate that the ditetrazole **158** was formed. ^{13}C NMR spectroscopic data are not sufficient for this prediction. According to the energies caculated for the ditetrazole isomers **153** and **158**, we believe that ditetrazole **153** is formed in this reaction. For better identification of the diazide **149**, the monotetrazole **151** and the ditetrazole **153**, we included the calculated MP2 vibrational spectra in Figure 2 for easier assignment and positive identification of the respective isomers.

6,6′-Bis(azido)-azo-1,2,4,5-tetrazine and 6,6′-Bis(azido)-hydrazo-1,2,4,5-tetrazine

For comparison with the polyazidoazo- and hydrazo-1,3,5-triazines we also calculated the yet unknown bis(azido)azo- and bis(azido)hydrazo-1,2,4,5-tetrazines. In order to keep the computational costs low, all calculation were performed at the B3LYP level only. The rotation profiles along the C–N bond of the azo and hydrazo group are given in Scheme 11 and Scheme 12 and the rotation profile around the N–N bond of the hydrazo group in Scheme 13.

Both the azo- and hydrazotetrazines have the same *cis* and *trans* alignments of the azide groups found in bis(azido)-tetrazine. The hydrazo compound also has a third conformation due to the conformation of the hydrazo-hydrogen atoms.

The *trans* orientation of the azide groups is the lowest energy conformation of the azo- and hydrazo compounds, but the energy differences are negligible for the diazides and only very slight for the mono- and ditetrazoles. The azo-bridged monotetrazole **161** is 4.1 kcal mol^{-1} higher than the diazide **159** and the ditetrazole **163** 9.2 kcal mol^{-1} (Scheme 19, Table 8). The activation energies for the first

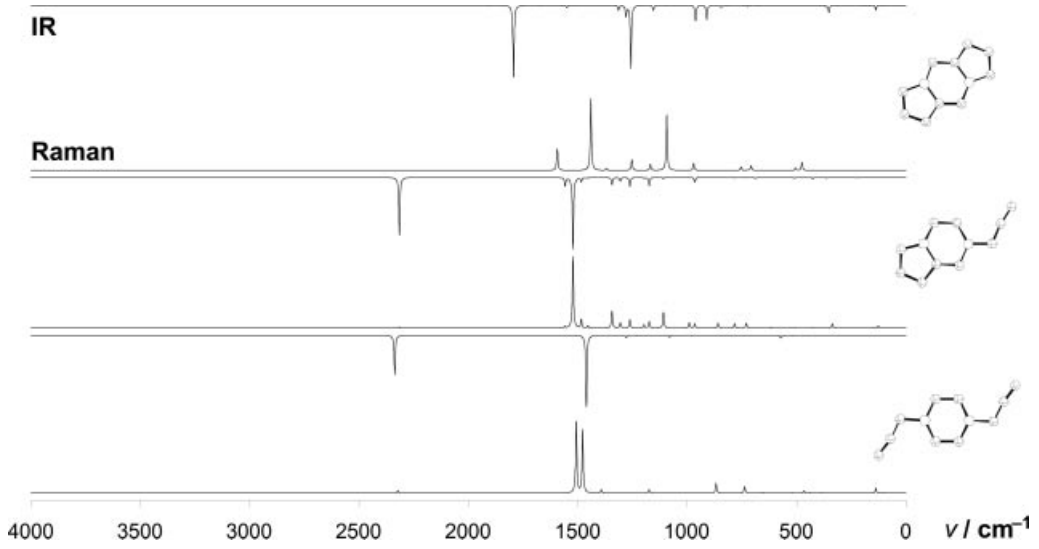
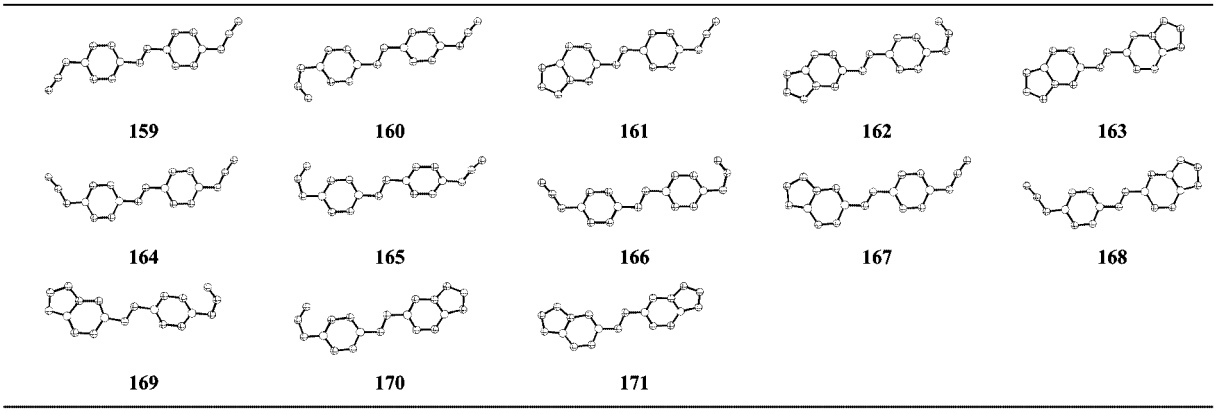


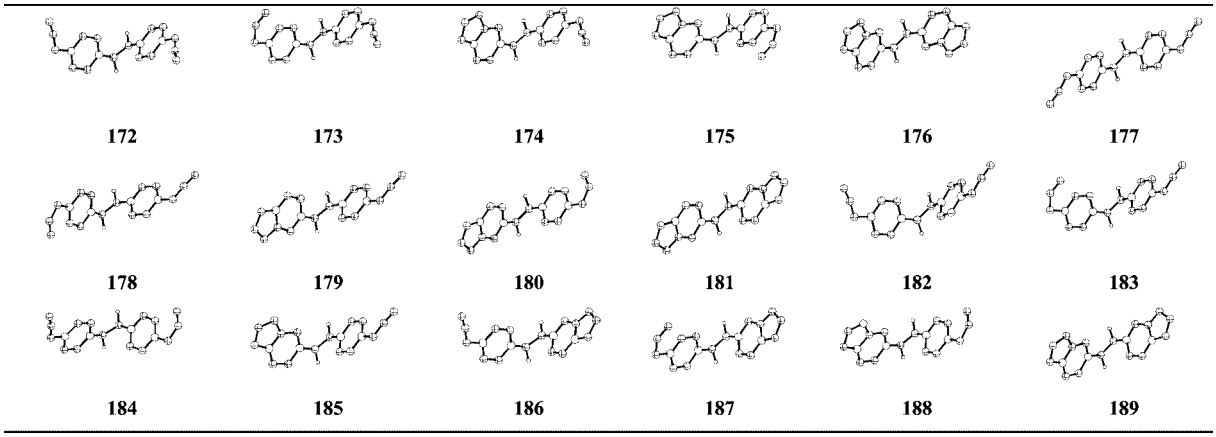
Figure 2. Vibrational spectra of diazidotetrazine isomers.



Scheme 19. Calculated isomers of bis(azido)azo-1,2,4,5-tetrazine.

Table 8. Calculated energy differences between different bis(azido)azo-1,2,4,5-tetrazine isomers. The gas phase calculations include zero point energy corrections.

	159	**160**	**161**	**162**	**163**	**164**	**165**	**166**	**167**	**168**	**169**	**170**	**171**
E_{rel} (B3LYP) / kcal mol^{-1}	0	20.95	4.1	25.4	9.2	0.0	21.0	21.0	4.2	4.35	26.5	25.5	9.2
S / cal mol^{-1} K^{-1}	133.5	127.9	127.5	121.7	122.3	133.6	128.0	127.7	127.9	127.2	121.3	121.2	119.5
E_{rel} (B3LYP) / kcal mol^{-1} PCM H_2O	0	21.63	–0.3	21.6	0.1	0.0	21.7	21.8	–0.2	0.1	21.8	21.8	0.7
E_{rel} (B3LYP) / kcal mol^{-1} PCM DMSO	0	21.65	–0.1	21.7	0.5	0.0	21.7	21.8	–0.1	0.2	21.8	22.0	6.9
E_{rel} (B3LYP) / kcal mol^{-1} PCM CCl_4	0	21.33	1.36	23.0	3.6	0.0	21.4	21.4	1.4	1.6	21.4	23.1	3.7



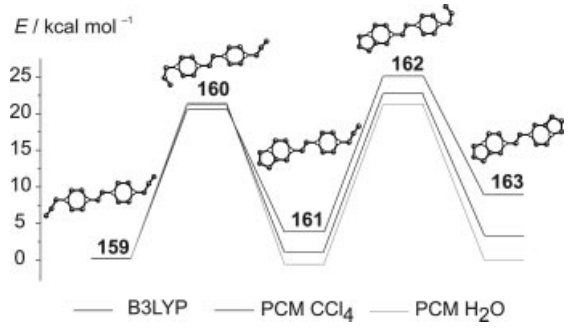
Scheme 20. Calculated isomers of bis(azido)hydrazo-1,2,4,5-tetrazine.

Table 9. Calculated energy differences between different bis(azido)azo-1,2,4,5-tetrazine isomers. The gas phase calculations include zero point energy corrections.

	172	**173**	**174**	**175**	**176**	**177**	**178**	**179**	**180**	**181**
E_{rel} (B3LYP) / kcal mol^{-1}	0	22.2	1.9	24.5	4.6	0.0	22.8	3.1	26.2	6.8
S / cal mol^{-1} K^{-1}	135.0	130.0	128.3	123.0	121.5	135.0	129.7	127.9	123.0	119.9
E_{rel} (B3LYP) / kcal mol^{-1} PCM H_2O	0	21.6	–4.2	17.6	–7.9	0.0	22.1	–2.7	19.9	–5.25
E_{rel} (B3LYP) / kcal mol^{-1} PCM DMSO	0	21.7	–3.7	18.1	–7.0	0.0	22.1	–2.5	19.5	–4.6
E_{rel} (B3LYP) / kcal mol^{-1} PCM CCl_4	0	22.2	–1.4	20.9	–2.3	0.0	22.6	–0.4	22.5	–0.2
	182	**183**	**184**	**185**	**186**	**187**	**188**	**189**		
E_{rel} (B3LYP) / kcal mol^{-1}	0.0	22.2	22.8	1.9	3.1	25.4	25.6	5.6		
S / cal mol^{-1} K^{-1}	134.9	129.7	129.5	128.1	128.0	123.8	122.7	121.1		
E_{rel} (B3LYP) / kcal mol^{-1} PCM H_2O	0	21.6	22.0	–4.1	–2.8	18.3	18.9	–6.6		
E_{rel} (B3LYP) / kcal mol^{-1} PCM DMSO	–0.1	21.8	22.2	–3.7	–2.5	18.8	19.4	–5.9		
E_{rel} (B3LYP) / kcal mol^{-1} PCM CCl_4	0.0	22.2	22.6	–1.5	–0.4	21.7	22.1	–1.3		

and second cyclization are 21.0 and 16.2 kcal mol^{-1}. The hydrazo-bridged monotetrazole **174** is only 1.9 kcal mol^{-1} higher than the diazide **172** and the ditetrazole **176** 4.6 kcal mol^{-1} (Scheme 20, Table 9). The activation energies for the first and second cyclization of the hydrazo-bridged compound are 22.2 and 19.9 kcal mol^{-1}. As observed before, the formation of the tetrazole rings is accompanied by a decrease of the entropy and a decrease of the sum of the positive and negative Mulliken charges with have higher individual charges for the tetrazoles.

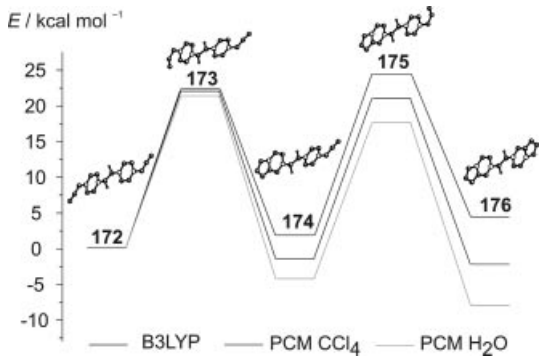
Solvation also leads to a stabilization of the tetrazoles. In CCl_4 the azo-bridged monotetrazole **160** is favored by 2.4 kcal mol^{-1} and the ditetrazole **163** by 9.1 kcal mol^{-1}. The activation energy for the first cyclization is increased by 0.3 kcal mol^{-1} and the activation energy for the second cyclization is decreased by 2.4 kcal mol^{-1}. The hydrazo-bridged monotetrazole **174** is favored by 3.3 kcal mol^{-1} and the ditetrazole **174** by 6.9 kcal mol^{-1} in CCl_4. The activation energy for the first cyclization of the hydrazoazide is not influenced by CCl_4 and the activation energy for the second cyclization is lowered by 3.6 kcal mol^{-1}. DMSO and water solvation give similar energy differences. The energy difference to the diazide **159** for the azo-bridged tetrazole is lowered by 4.4 kcal mol^{-1} and for the ditetrazole **163** by 9.1 kcal mol^{-1} (Scheme 21). The activation energies for the first cyclization is increased by 0.6 kcal mol^{-1} and the activation energy for the second cyclization is decreased by 3.8 kcal mol^{-1}. The solvation in water has a larger effect on the hydrazo-bridged compounds. Here the monotetrazole **174** is stabilized by 6.1 kcal mol^{-1} and the ditetrazole **176** is stabilized by 12.5 kcal mol^{-1} (Scheme 22). The activation energies for the first and second cyclization are lowered by 0.6 and 6.9 kcal mol^{-1}, respectively.



Scheme 21. Reaction profile for the ring closures in bis(azido)azo-1,2,4,5-tetrazine.

In absolute terms, the azo-bridged monotetrazole **161** is favored over the diazide **159** in the investigated solvents and the azo-bridged ditetrazole is only 0.1 kcal mol^{-1} above the diazide in aqueous solution. The hydrazo-bridged mono-**174** and ditetrazoles **176** are even more favored over the diazides in solution. The diazide **176** is the lowest energy diazo-bridged compound in all solvents and is favored by 7.9 kcal mol^{-1} over the diazide in aqueous solution.

For better experimental assignment, the calculated B3LYP vibrational spectra of the azo- and hydrazo-bridged



Scheme 22. Reaction profile for the ring closures in bis(azido)-hydrazo-1,2,4,5-tetrazine.

diazides, azidotetrazoles, and ditetrazoles are shown in Figure 3 and Figure 4.

Conclusions

The formation of a tetrazole ring requires a planar arrangement of the azide group. Both for polyazido-1,3,5-triazines and bis(azido)-1,2,4,5-tetrazines several planar orientations of the azide group are possible. The rotation barrier of the azide group is around 10 kcal mol^{-1} and the energy differences between the different planar conformers of the polyazides are slight. The ring closed polytetrazoles show larger energy differences. The minimum energy conformers derive from the C_{3h} isomer of triazido-1,3,5-triazine and from *trans* bis(azido)tetrazine.

The ring closure of an azide to a tetrazole in the 1,3,5-triazine systems increases the electronic energy by 9–12 kcal mol^{-1} per tetrazole ring, the activation energy for a tetrazole ring formation is around 20 kcal mol^{-1}. The electronic energy of the tetrazines increases by 2–5 kcal mol^{-1} for the first tetrazole ring and by another 3–10 kcal mol^{-1} for the second tetrazole ring. It was shown that the electron-donating amino group lowers the energy of a tetrazole ring relative to the azide by about 3 kcal mol^{-1} and the electron-withdrawing nitro group increases the relative energy of a tetrazole ring by about 6 kcal mol^{-1} relative to the azide. The entropy of the investigated compounds decreases slightly with every tetrazole ring closure due to the loss of degrees of freedom. Thus it is possible to overcome the activation barrier for the formation of some tetrazoles, e.g. diazidotetrazine, by heating, but at higher temperatures the azides are generally favored.

Taking into account solvent effects using a continuum of an uniform dielectric, the energy differences between the tetrazoles and the azides are lowered for both the polyazido-1,3,5-triazines and -tetrazines. This is explained by higher charges of individual atoms in the tetrazoles compared to the azides. Polar solvents stabilize these charges compared to the gas phase and lower the energy difference to the azides. The effect is smaller for the apolar CCl_4 with about 3 kcal mol^{-1} per tetrazole unit and larger for the more polar solvents DMSO and water with about 6 kcal mol^{-1}

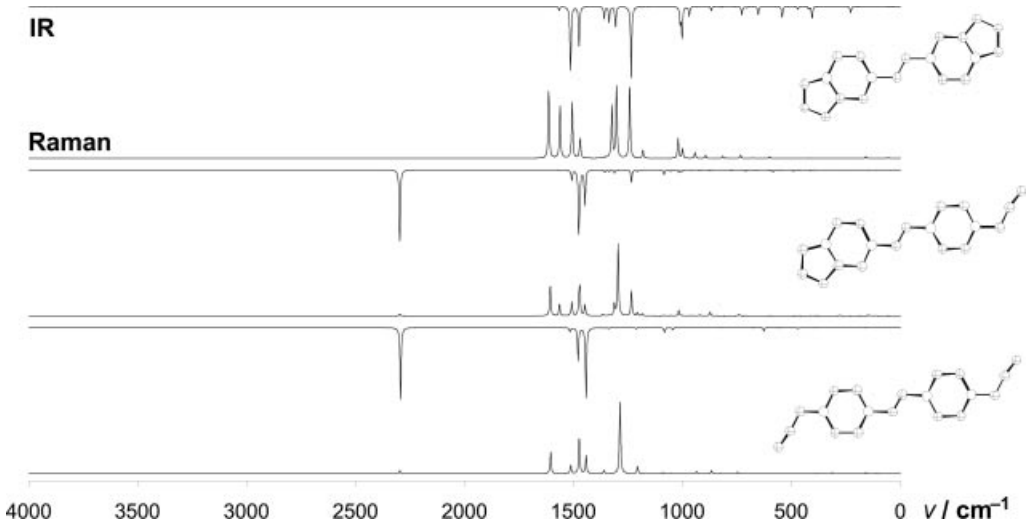


Figure 3. Vibrational spectra of bis(azido)azo-1,2,4,5-tetrazine isomers.

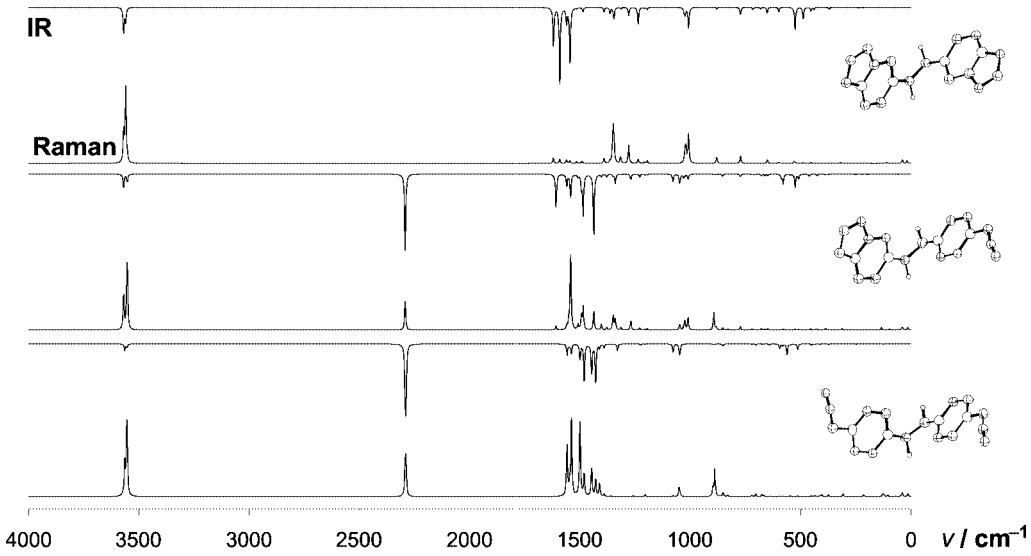


Figure 4. Vibrational spectra of bis(azido)hydrazo-1,2,4,5-tetrazine isomers.

per tetrazole unit. Solvation in DMSO has about the same effect as solvation in water. We conclude that solvation can change the equilibrium for the tetrazines. For the 1,3,5-triazines the energy differences are too large for the effects of the solvation to allow the formation of a tetrazole. For practical consequences two other effects have to be taken into account: hydrogen bonds to solvents like water which are not included in our treatment and the lattice energy of the respective azide and tetrazole species. Depending on lattice energy and therefore solubility, it is possible that both the ditetrazoles and the diazides of tetrazines can be isolated, while the energy differences of the 1,3,5-triazines suggest that the tetrazoles derivatives cannot be prepared from the corresponding azides. Solvation in DMSO and water makes the monotetrazoles **151** and **161** the minimum energy species for the bis(azido)-1,2,4,5-tetrazine and the bis(azido)azo-1,2,4,5-tetrazine system. The ditetrazole **176** is the minimum energy species in the bis(azido)hydrazo-1,2,4,5-tetrazine system.

The calculated data explain the experimental detection of the mono- and ditetrazole derivatives of diazidotetrazine. As the data supplied by the authors do not confirm the conformation of the ditetrazine, we believe that isomer **153**, which is 8.3 kcal mol^{-1} lower in energy, is formed in the reaction in contrast to the reported isomer **158**.

Computational Methods

The geometries of the triazido-1,3,5-triazine, aminodiazido-1,3,5-triazine, diazidonitro-1,3,5-triazine, and diazidotetrazine compounds were optimized at the MP2 level (full active orbital space) within the symmetry constraints stated in the respective Tables using a cc-pVDZ basis set.[25] Due to computational cost all other compounds were optimized on the B3LYP level of theory with the

same basis set. Comparison of the B3LYP energies from reference[20] for cyanuric azide and of values obtained for the diazidotetrazine isomers at the B3LYP/aug-cc-pVTZ level of theory shows good agreement with the energies obtained at the CCSD(T) level. The vibrational frequencies, which were computed at the optimized structures, show true minima on the potential energy surface with no imaginary frequencies for all azides and tetrazoles. The located transition states are of the first order, the Cartesian displacement coordinates of the imaginary frequency mode correspond to the ring opening of a tetrazole to an azide. For further validation single-point CCSD(T) calculations using a cc-pVDZ basis set were performed using the full orbital space for the triazido-1,3,5-triazine, aminodiazido-1,3,5-triazine, diazidonitro-1,3,5-triazine, and diazidotetrazine compounds. A Mulliken analysis was used for the charge discussion. For the discussion of solvent-induced changes, the solvent effects were introduced within the self-consistent reaction field (SCRF) formalism by means of the polarized continuum model (PCM) of Tomasi et al.[26] as implemented in GAUSSIAN 03. This method models the solvent as a continuum of uniform dielectric and therefore does not take into account explicit solvent–solute interactions such as hydrogen bonding. Three different continuum environments with the characteristics of CCl_4, DMSO and water were employed to explore the influence of an increasing dielectric permittivity on the potential energy of the investigated compounds. While the isomers of cyanuric azide, triazido-*s*-heptazine and diazidotetrazine were optimized within the PCM model, for all other compounds single point calculations were used due to computational cost. Coupled cluster single point calculations, for which the MP2 geometries were used, were performed with the MOLPRO program package,[27] all other calculations were performed with Gaussian03.[28]

Supporting Information (see also the footnote on the first page of this article): Computational details.

Acknowledgments

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