J Mol Model (2013) 19:5037–5043
DOI 10.1007/s00894-013-2003-9

ORIGINAL PAPER

Theoretical investigations on the synthesis mechanism of cyanuric acid from NH_3 and CO_2

Xueli Cheng · Yanyun Zhao · Weiqun Zhu · Yongjun Liu

Received: 4 July 2013 / Accepted: 8 September 2013 / Published online: 29 September 2013

Abstract In the synthesis of cyanuric acid from NH_3 and CO_2, urea and isocyanic acid OCNH are two pivotal intermediates. Based on density functional theory (DFT) calculations, the synthesis mechanism of cyanuric acid from NH_3 + CO_2 was investigated systematically. Urea can be synthesized from NH_3 and CO_2, and cyanuric acid can be obtained from urea or NH_3 + CO_2. In the stepwise mechanism of cyanuric acid from urea or NH_3 + CO_2, the energy barriers are relatively high, and the condition of high pressure and temperature does not decrease the energy barriers. Our theoretical model shows that cyanuric acid is actually acquired from OCNH via a one-step cycloaddition reaction.

Keywords Cyanuric acid · NH_3 and CO_2 · Urea · Density functional theory · Mechanism

Introduction

Since cyanuric acid and melamine were reported publicly to have been added illegally to dairy products and pet foods in China to increase the nitrogen content [1–5], they are almost regarded as detrimental and hazardous chemicals by the common Chinese populace. However, cyanuric acid, melamine and their derivatives are a class of representative heterocyclic compounds with unique physical and chemical properties [6–8]. Cyanuric acid is also an important chemical material and chemical intermediate [9]. Its most important feature is that it can be synthesized from small molecules such as ammonia and carbon dioxide with or without catalysts and solvents [10–13], and the products are cyanuric acid and water. It is well known that carbon dioxide is the main greenhouse gas (GHG) and the major contributing factor to recent global warming, so this green process also plays an important role in the efficient utilization of the abundant and renewable CO_2 resource in an environmentally friendly manner [14].

Urea can also be synthesized from NH_3 and CO_2 [11, 14–16], and then cyanuric acid synthesized from urea [3, 17]. Urea and isocyanic acid [10, 15, 18, 19] are key intermediates in the synthesis of cyanuric acid from NH_3 and CO_2. It has been reported that cyanuric acid can be acquired from urea $CO(NH_2)_2$ [20]. The Wöhler synthesis of urea from NH_3 and CO_2 is a chemical classic, and the pioneering work of Tsipis and Karipidis [11, 16] has reported systematical density functional theory (DFT) calculations on the formation of urea from NH_3 and CO_2 at B3LYP/6-31G(d,p) level. However, to the best of our knowledge, there are no experimental and theoretical mechanistic investigations on the formation of cyanuric acid from urea or NH_3 + CO_2. The synthetic mechanism of cyanuric acid from NH_3 and CO_2 in the absence of any catalysts or solvents needs further theoretical investigation, and the influence of high temperature and high pressure in the synthesis of cyanuric acid remain unknown. In the present work, we carried out a theoretical investigation on the gas-phase synthesis mechanisms of cyanuric acid from NH_3 and CO_2 free of any ligands, solvents and support effects with DFT methods, and consider the influence of temperature and pressure to confirm the reactivity of urea and isocyanic acid in this reaction system.

Electronic supplementary material The online version of this article (doi:10.1007/s00894-013-2003-9) contains supplementary material, which is available to authorized users.

X. Cheng · W. Zhu · Y. Liu (✉)
School of Chemistry and Chemical Engineering,
Shandong University, Jinan 250100, China
e-mail: yongjunliu_1@sdu.edu.cn

X. Cheng (✉) · Y. Zhao
School of Chemistry and Chemical Engineering, Taishan University,
Tai'an 271021, China
e-mail: ching108@sohu.com

Computational methods

The hybrid density functionals such as B3LYP are the most versatile theoretical methods, and have already been applied successfully to a variety of urea and ammonia systems [11, 16, 21–24]. The reactants, intermediates and products were fully optimized at B3LYP/6-311++G(d,p) level with the Gaussian 03 program package [25] in the present work. Frequency calculations were also performed at the same level to identify whether the stationary point is a local minimum or a transition state. Furthermore, the displacement vectors of the imaginary vibrational modes were used to identify real transition states and their connections [26]. Based on the optimized structures of intermediates or reactants, we adjusted the bond distances and bond angles to guess the initial structures of transition states, and then employed the opt=(calcfc,ts,noeigentest) keyword to request full optimization to transition states rather than a local minimum using the Berny algorithm and to specify that the force constants be computed at the first point [27]. The transition state structures all represent saddle points, characterized by one and only one negative eigenvalues of the Hessian matrix. Some key transition states were further checked by intrinsic reaction coordinate (IRC) calculations to confirm their connections between the corresponding intermediates [28, 29]. It is well known that cyanuric acid is synthesized from NH_3 and CO_2 under high pressure and temperature [11, 16]. To better simulate the reaction conditions, single-point energy (SPE) calculations with the keyword Freq=ReadIsotopes were carried out to recomputed the thermodynamic functions at 473.15 K and 100 atm. This temperature is much higher than the critical temperatures of NH_3 and CO_2 (132.4 and 31.0 °C, respectively), so the classical rigid rotator model and harmonic oscillator model were employed in this work.

Results and discussion

The lowest frequencies and their vibrational mode assignments as well as the differences of electronic and zero-point energies (ΔE), Gibbs free energies (ΔG) and thermal enthalpies (ΔH) at 473.15 K and 100 atm of all species involving this reaction system are listed in Table S1 of Supporting Information. High pressure and high temperature can alter the values of Gibbs free energies (G), thermal energies (U) and thermal enthalpies (H), so, in the present work, we used ΔG values to elucidate the reaction mechanisms.

To validate the reliability of the B3LYP method, the addition of NH_3 and CO_2 to form carbamic acid (NH_2COOH) was also fully optimized with the second order approximation of Møller-Plesset perturbation theory (MP2) at 6-311++G(d,p) basis set level, and we found that the MP2 energies and structural parameters are in excellent agreement with those of B3LYP. Based on the B3LYP-optimized structural parameters, for the addition of NH_3 and CO_2, the SPE calculations were carried out at CCSD(T)/aug-cc-pVDZ level with frequency calculations to obtain the thermodynamic functions at 473.15 K and 100 atm. Again, the CCSD(T) free energies are comparable with the B3LYP and MP2 values, but the barrier is lower than the B3LYP or MP2 barrier because the CCSD(T) relative energy of **IM1** is relatively higher, as shown in Fig. 1. We will now discuss the stepwise mechanism with the B3LYP results.

The initial step : $NH_3 + CO_2 \rightarrow OCNH + H_2O$

The reactions of $NH_3 + CO_2$ leading to $OCNH + H_2O$ are depicted in Fig. 1. Firstly, NH_3 bonds to CO_2 to form a weak van der Waals complex **IM1**. The interaction mode, which is similar to the bonding between methylenimine and isocyanic acid OCNH [30], was revealed by Tsipis and Karipidis [16]. The MP2 geometrical parameters of **IM1** [31] are also in excellent agreement with our results. **IM1** transforms to **IM2** via a hydrogen-shift transition state **TS1**, followed by an isomerization process and another H-shift process, ultimately leading to isocyanic acid OCNH and H_2O. These processes were investigated in the pioneering work of Tsipis and Karipidis [16], which agrees well with our calculation results. The ΔH values show that the formation of **IM3** is slightly endothermic, but the formation of $OCNH + H_2O$ requires a heat of 78.6 kJ/mol^{-1}, as shown in Table S1.

OCNH is a key intermediate, and its reactions with small molecules such as H_2O [31, 32], allenes [33], HCOOH [34] and NH_3 [11, 35] have been studied theoretically. Figure 1 shows that the free energy barrier of OCNH generation is as high as 222.3 kJ/mol^{-1}. Moreover, Tsipis and Karipidis [11] elucidated the reaction mechanism of $OCNH + NH_3$ to urea with a total barrier (ΔE) of 161.9 kJ/mol^{-1}.

We also investigated whether an additional NH_3 molecule can serve as a catalyst to decrease the free energy barrier of the addition reaction of NH_3 and CO_2 (Fig. 2). Two NH_3 molecules links to CO_2 via a six-membered ring to produce **IM1'**, and then a hydrogen atom on NH_3 transfers to O via **TS1'**. Although the barrier is reduced slightly to 195.1 kJ/mol^{-1}, the relative free energy of **TS1'** (225.2 kJ/mol^{-1}) does not decrease apparently compared with **TS1** (228.2 kJ/mol^{-1}). As a result, the influence of additional NH_3 molecules will not be considered further in the present work.

IM3 + NH_3 : Formation of rea and another channel producing OCNH

Then, another NH_3 molecule links to **IM3** and one hydrogen atom transfers from NH_3 to hydroxyl oxygen via **TS4** to produce urea by dehydration (Fig. 3*a*). From IRC scanning we obtain a quaint intermediate **IM4** before hydrogen transfer, as

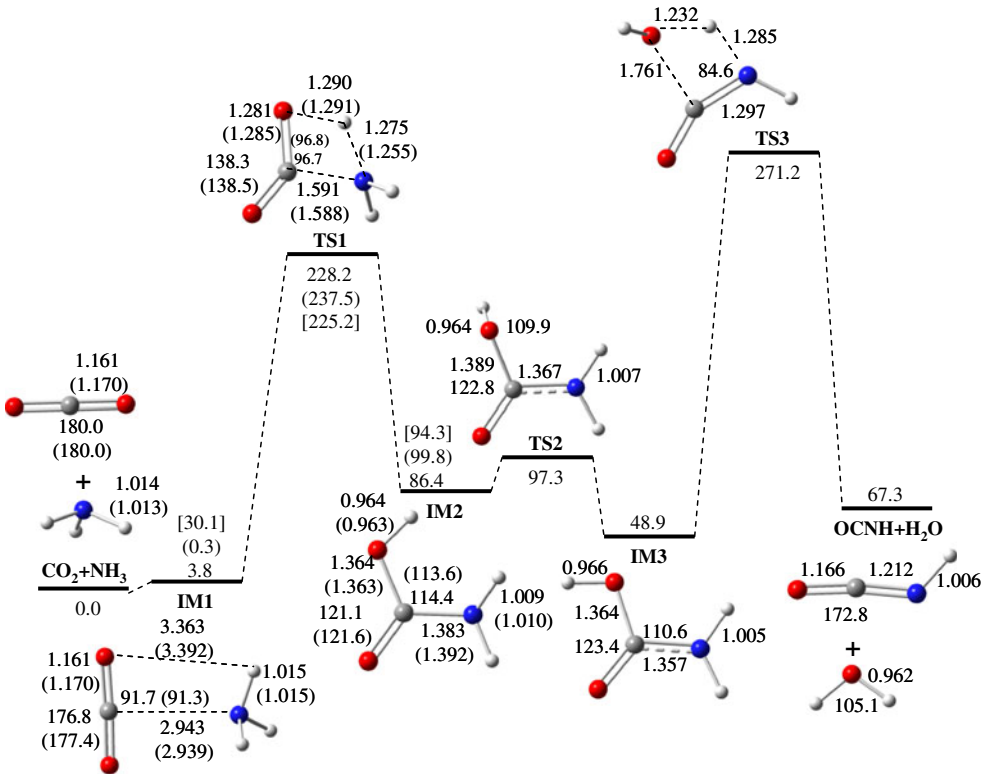


Fig. 1 Structural parameters and potential energy surface (PES) profiles of $NH_3 + CO_2 \rightarrow OCNH + H_2O$. *Red circles* Oxygen atoms, *blue circles* nitrogen atoms. Relative free energies (ΔG) are in kJ mol^{-1}, bond lengths are in Å and bond angles in degrees. Structural parameters and relative energies in brackets () are acquired from full optimization at MP2/6-311++G(d,p) level, and energies in square brackets [] are obtained by SPE calculations at CCSD(T)/aug-cc-pVDZ level. These units are employed uniformly in this work, and all energies are relative to the reactants ($3NH_3 + 3CO_2$) in all figures

reported by Tsipis and Karipidis [16]. The frontier orbitals reveal why ammonia nitrogen attacks the imine hydrogen via hydrogen bonding rather than the carbon atom, as shown in Fig. 3b. The hydrogen atom then transfers from NH_3 to the hydroxyl group via **TS4** with a barrier of 269.5 kJ/mol^{-1}, yielding **IM5**, which will decompose into urea and H_2O via a barrierless process.

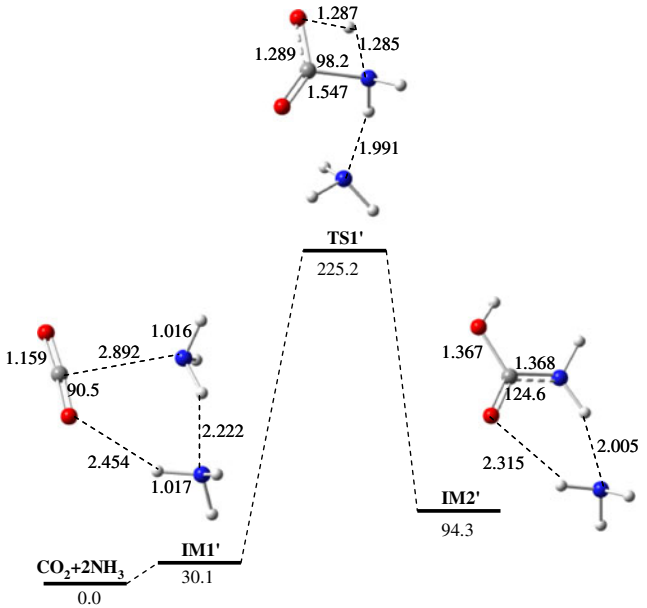


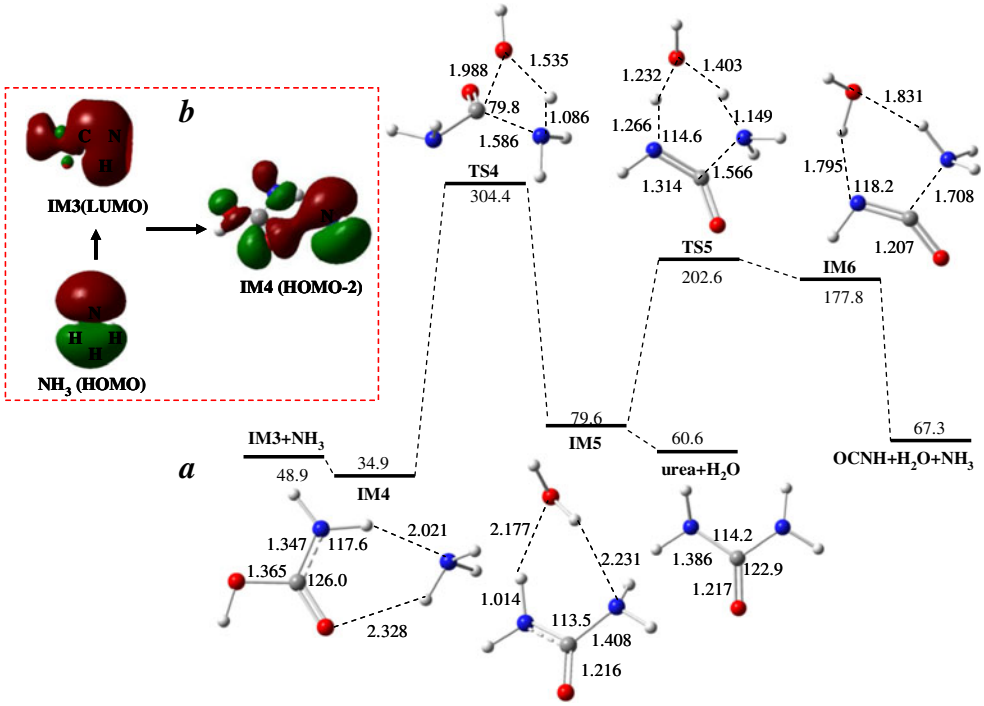
Fig. 2 Structural parameters and PES profile of $2NH_3 + CO_2 \rightarrow OCNH{\cdot}NH_3 + H_2O$

From **IM5**, there is another reaction channel generating OCNH, i.e., an imine hydrogen atom transfers to another imine group to d urea mediated by H_2O, as shown in Fig. 3. The free energy barrier is only 123.0 kJ/mol^{-1}, much lower than that of the IM3 dehydrating process producing OCNH. From Fig. 3 it can also be seen that urea can transform to OCNH with a relatively low barrier. Therefore, the generation of OCNH from urea and H_2O is energetically favorable.

Addition reaction of urea + CO_2

This addition reaction is very analogous to the reaction of $NH_3 + CO_2$, as shown in Fig. 4. CO_2 can be added to an amido group of urea to form **IM8**, but the bond distance of the newly formed C–N (3.233 Å) in **IM7** is much longer than that in **IM1** (2.943 Å). A hydrogen atom on the amino group then shifts to the oxygen atom of CO_2, and the carbon atom of CO_2 bonds simultaneously to the N atom via **TS6** to form **IM8**. The only imaginary frequency of **TS6** is assigned to the C–N–H asymmetrical stretch mode, and the bond lengths between the shifting hydrogen atom and O, N are 1.284 and 1.283 Å. The energy barrier of this addition reaction is relatively high (240.0 kJ/mol^{-1}).

There are two reaction pathways starting from **IM8**. We can add carbon dioxide to another imine group, or add NH_3 to the carboxyl group. Now we investigate the reaction mechanism of



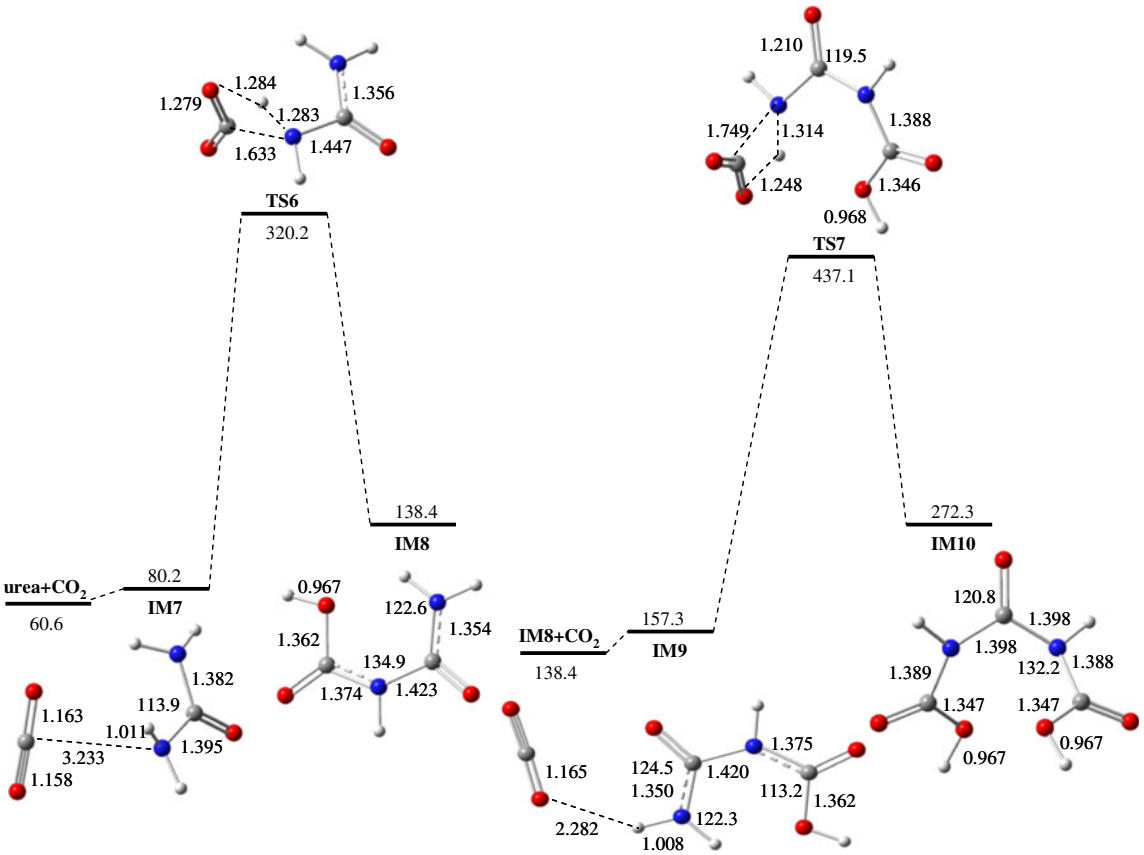


Fig. 3 **a** Structural parameters and PES profile of IM3+NH_3 → OCNH + H_2O +NH_3. **b** HOMO–LUMO interaction during the formation of complex IM3…NH_3 (IM4)

Fig. 4 PES profiles corresponding to urea + CO_2 and IM8 + CO_2 addition reactions

adding CO_2 to **IM8** to generate **IM10**, followed with adding NH_3 to **IM10** to produce cyanuric acid ultimately.

Reactions of **IM8** + CO_2→**IM10**,
and **IM10** + NH_3→**IM13**→cyanuric acid

As shown in Fig. 4, CO_2 adds to **IM8** to form intermediate **IM9**, and then the imine hydrogen transfers to CO_2 via **TS7** to produce **IM10** with a high barrier of 279.8 kJ/mol^{-1}. Similarly, the carboxyl group of **IM10** is amidated by adding CO_2 followed with H-transfer to form **IM12** via **TS8**. In **IM13**, an imine hydrogen atom bonds to the neighboring hydroxyl oxygen to form an eight-membered ring via a hydrogen bond (2.052 Å). The energy barrier is also high (274.0 kJ/mol^{-1}) as depicted in Fig. 5. Then **IM13** is cyclized and dehydrated via a hydrogen-shift transition state **TS9** to generate **IM14**, which has been proved by Rácz et al. [36]. The free energy barrier is 198.0 kJ/mol^{-1}. Subsequently, **IM14** decomposes into cyanuric acid and H_2O. From the PES profile it can be seen that the products are energetically stable species.

Our calculations predict that the overall reaction $3NH_3$ + $3CO_2$ → P + $3H_2O$ is endothermic with an enthalpic difference of 71.9 kJ/mol^{-1} at 473.15 K and 100 atm. However, the free energy difference ΔG (174.8 kJ/mol^{-1}) is relatively large, which is attributed to the entropic effect. We investigated whether the sequence of adding NH_3 and CO_2 can determine the potential energy surface (PES).

IM8 + NH_3→**IM17**, and **IM17** + CO_2→**IM19**

As shown in Fig. 6, the energy barriers of adding NH_3 to **IM8** and subsequently adding CO_2 to the generated **IM17** are 251.7 and 268.7 kJ/mol^{-1}, respectively. **IM19** is a trans isomer of **IM13**. It can transform to **IM13** via two group-rotation processes and increases its relative free energy by 32.0 kJ/mol^{-1}. Obviously, the sequence of adding NH_3 and CO_2 does not influence the free energy barriers.

Our theoretical model reveals that all reaction channels from urea to cyanuric acid bear high barriers. The high pressure and temperature do not decrease ΔG and ΔH markedly, so, for the formation of cyanuric acid, a one-step mechanism may exist. OCNH can be synthesized from urea [37], and cyanuric acid can be synthesized from OCNH. The dimerization mechanism of OCNH has been investigated [38], where

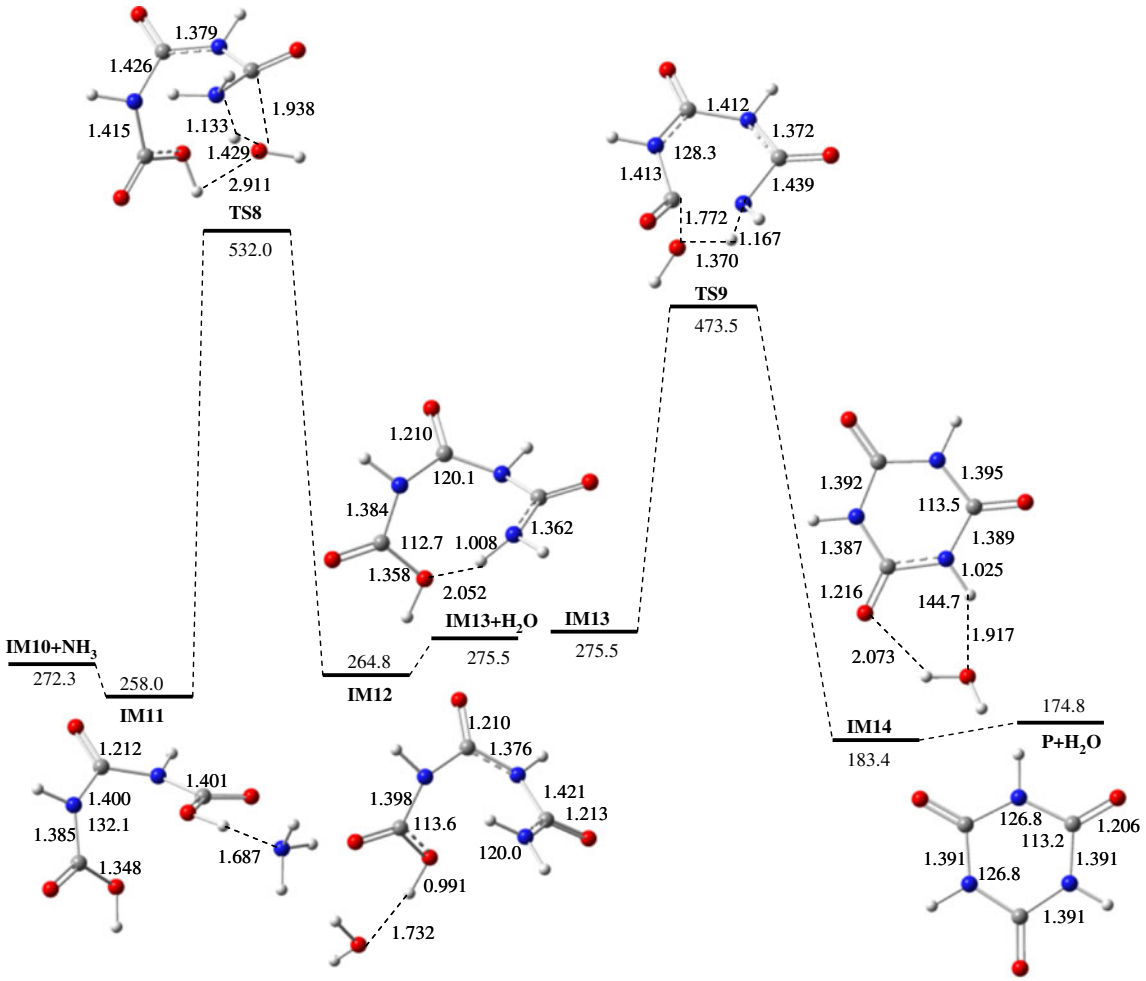


Fig. 5 Formation of cyanuric acid from IM10 via TS8 and TS9

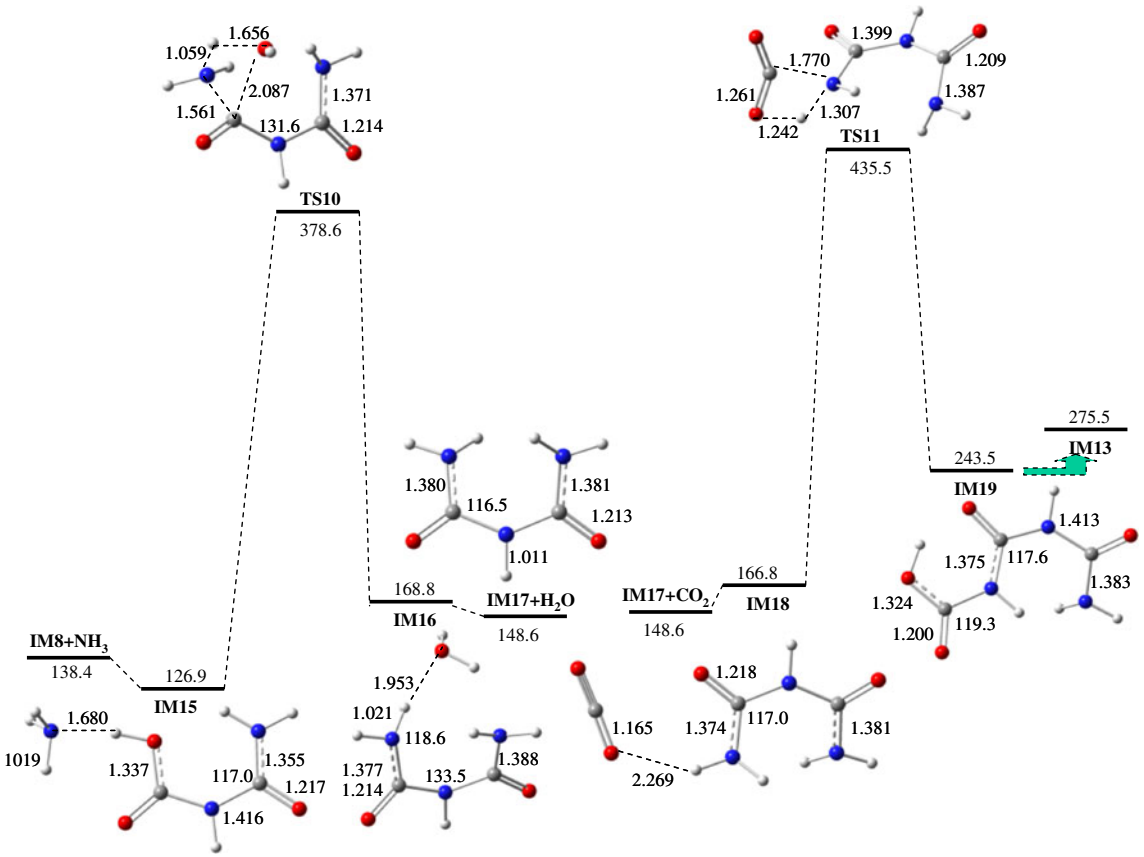


Fig. 6 Formation of IM19 by adding NH_3 and CO_2 to IM8

the stepwise reaction through the cyclic intermediates $(OCNH)_2$ is unfavorable. Moreover, a one-step synthesis mechanism from OCNH has been predicted [15, 19, 30]. We next investigated the cycloaddition reaction of OCNH producing cyanuric acid.

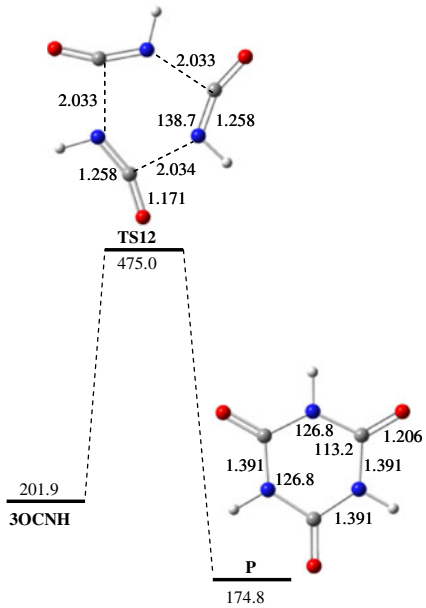


Fig. 7 One-step synthesis of cyanuric acid from OCNH

The one-step cycloaddition reaction of cyanuric acid from OCNH

Three OCNH molecules can be cyclized to cyanuric acid (**P**) via **TS12**, as depicted in Fig. 7. The smooth curve from IRC scanning shows that there is no intermediate between OCNH and **TS12**. The ΔE barrier of this one-step mechanism is only 168.0 kJ/mol^{-1}—much lower than those in the stepwise mechanism from urea to **P**—but the free energy barrier (273.1 kJ/mol^{-1}) does not decrease noticeably. Of course, a one-step synthetical channel with a relatively lower barrier will acquire a higher yield, so this process is energetically more favorable than the multi-step mechanism. Moreover, the relative enthalpies are low, and the high exothermicity may also drive this one-step cycloaddition reaction.

For the total reaction of $3NH_3 + 3CO_2 \rightarrow$ **P** $+ 3H_2O$, urea or OCNH is obtained from NH_3 and CO_2, and then cyanuric acid is cyclized from OCNH.

Conclusions

The synthesis mechanism of cyanuric acid from NH_3 and CO_2 was investigated at B3LYP/6-311++G(d,p) level, the condition of 473.15 K and 100 atm was considered with

thermodynamic function calculations in the rigid rotor and harmonic oscillator approximation. In the stepwise mechanism, the module molecules are linked together via weak van der Waals interactions, and then hydrogen transfers to the carboxyl oxygen to form new hydroxyl groups, or transfers to neighboring hydroxyl oxygen to dehydrate the hydroxyl groups; simultaneously new C–N bonds form to ultimately yield cyanuric acid. The addition reactions of NH_3 and CO_2 produce two key intermediates urea and OCNH. However, the energy barriers producing cyanuric acid are generally high in the stepwise mechanism, and the high pressure and temperature do not markedly decrease the thermodynamic values ΔG and ΔH. Therefore, cyanuric acid is obtained from the cycloaddition reaction of OCNH. In this one-step reaction, the free energy barrier is 273.1 kJ/mol^{-1}.

Acknowledgments This work was supported by the National Natural Science Foundation of China (No. 21173129 and 11174215), the Natural Science Foundation of Shandong Province, China (No. ZR2012BL10) and the University Science and Technology Project of Shandong Province (No. J13LD05).

References

1. Liang X, Zheng W, Wong N, Li J, Tian A (2004) J Mol Struc (Theochem) 672:151–159
2. Kobayashi T, Okada A, Fujii Y, Niimi K, Hamamoto S, Yasui T, Tozawa K, Kohri K (2010) Urol Res 38:117–125
3. Luo Y, Zhang L, Yang W, Liu W, Lu W, Li M (2011) J Labelled Compd Rad 54:171–172
4. Musumeci D, Ward MD (2011) CrystEngComm 13:1067–1069
5. Dorne JL, Doerge DR, Vandenbroeck M, Fink-Gremmels J, Mennes W, Knutsen HK, Vernazza F, Castle L, Edler L, Benford D (2013) Toxicol Appl Pharm 270:218–229
6. Pop F, Socaci C, Terec A, Condamine E, Varga RA, Raț CI, Roncali J, Grosu I (2012) Tetrahedron 68:8581–8588
7. Bahrami K, Khodaei MM, Sohrabnezhad S (2011) Tetrahedron Lett 52:6420–6423
8. Xue C, Zhu H, Zhang T, Cao D, Hu Z (2011) Colloids Surf A: Physicochem Eng Aspects 375:141–146
9. Hu A, Zhang F (2010) J Phys Condens Matter 22:505402
10. Ripka AS, Díaz DD, Sharpless KB, Finn MG (2003) Org Lett 5: 1531–1533
11. Tsipis CA, Karipidis PA (2003) J Am Chem Soc 125:2307–2318
12. Vinogradova EV, Fors BP, Buchwald SL (2012) J Am Chem Soc 134:11132–11135
13. Kanno E, Yamanoi K, Koya S, Azumaya I, Masu H, Yamasaki R, Saito S (2012) J Org Chem 77:2142–2148
14. Wu C, Cheng H, Liu R, Wang Q, Hao Y, Yu Y, Zhao F (2010) Green Chem 12:1811–1816
15. Seifer GB (2002) Russ J Coord Chem 28:301–324
16. Tsipis CA, Karipidis PA (2005) J Phys Chem A 109:8560–8567
17. She D, Yu H, Huang Q, Li F, Li C (2010) Molecules 15:1898–1902
18. Piazzesi G, Kröcher O, Elsener M, Wokaun A (2006) Appl Catal B: Environ 65:55–61
19. Geith J, Klapötke TM (2001) J Mol Struc (Theochem) 538:29–39
20. Bernhard AM, Peitz D, Elsener M, Wokaun A, Kröcher O (2012) Appl Catal B: Environ 115–116:129–137
21. Tang H, Doerksen RJ, Tew GN (2005) Chem Commun 12:1537–1539
22. Wells GM, Dudding T, Belding L, Frick JA, Nayek A, Huang J, Katz SJ, Bergmeier SC (2012) Tetrahedron 68:3980–3987
23. Li TH, Wang CM, Xie XG, Du GB (2012) J Phys Org Chem 25: 118–125
24. Nowacki A, Sikora K, Dmochowska B, Wiśniewski A (2013) J Mol Model. doi:10.1007/s00894-013-1835-7
25. Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, Zakrzewski VG, Montgomery JA, Stratmann RE, Burant JC, Dapprich S, Millam JM, Daniels AD, Kudin KN, Strain MC, Farkas O, Tomasi J, Barone V, Cossi M, Cammi R, Mennucci B, Pomelli C, Adamo C, Clifford S, Ochterski J, Petersson GA, Ayala PY, Cui Q, Morokuma K, Malick DK, Rabuck AD, Raghavachari K, Foresman JB, Cioslowski J, Oritz JV, Stefanov B, Liu G, Liashenko A, Piskorz P, Komaromi I, Gomperts R, Martin RL, Fox DJ, Keith T, Al-Laham MA, Peng CY, Nanayakkara A, Gonzalez C, Challacombe M, Gill PMW, Johnson BG, Chen W, Wong MW, Andres JL, Head-Gordon M, Replogle ES, Pople JA; Gaussian 03, revision C.02 (2004) Gaussian Inc; Wallingford CT
26. Cheng X, Chen D, Liu Y (2012) Chem Phys Chem 13:2392–2404
27. Head-Gordon M, Pople JA, Frisch M (1988) Chem Phys Lett 153: 503–506
28. Gonzalez C, Schlegel HB (1990) J Phys Chem 94:5523–5527
29. Gonzalez C, Schlegel HB (1989) J Chem Phys 90:2154–2161
30. Fang D, Fu X (1996) J Mol Struc (Theochem) 365:219–223
31. Wei X, Sun X, Wu X, Geng S, Ren Y, Wong N, Li W (2011) J Mol Model 17:2069–2082
32. Zabardasti A, Solimannejad M (2007) J Mol Struc (Theochem) 819: 52–59
33. Rode JE, Dobrowolski JC (2006) J Phys Chem A 110:3723–3737
34. Zhang X, Geng Z (2010) J Mol Struc (Theochem) 955:33–38
35. Zabardasti A, Amani S, Solimannejad M, Salehnassaj M (2009) Struct Chem 20:1087–1092
36. Rácz Á, Váradi A, Mazák K, Kökösi J, Noszál B (2013) J Mol Model. doi:10.1007/s00894-013-1905-x
37. Czekaj I, Kröcher O, Piazzesi G (2008) J Mol Catal A Chem 280: 68–80
38. Feng W, Wang Y, Zhang S (1995) J Mol Struc (Theochem) 342: 147–151