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The Degradation Pathway of 1,2,3,4-Tetrazine

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The potential energy surfaces of the degradations of 1,2,3,4-tetrazine (1a) to $C_2H_2+2N_2$ or $2HCN+N_2$ were obtained from semiempirical molecular orbital calculations using the AM1 method. It was suggested that the degradation of 1a to $2HCN+N_2$ occurred in a concerted fashion, whereas the decomposition to $C_2H_2+2N_2$ was demonstrated to proceed *via* a stepwise pathway. The latter process was more favorable than the former, and was analogous to the degradation process of 2-phenyl-2*H*-[1,2,3]triazolo[4,5-*e*][1,2,3,4]tetrazine (3), which is the only example of 1,2,3,4-tetrazine ring.

Keywords 1,2,3,4-tetrazine; molecular orbital calculation; AM1; potential energy surface; triazolotetrazine; degradation

1,2,3,4-Tetrazines **1** are among the basic 6-membered azaaromatics, and are of interest from the viewpoint of their physical and chemical properties.[1] We recently reported the synthesis of 2-phenyl-2*H*-[1,2,3]triazolo[4,5-*e*][1,2,3,4]-tetrazine (**3**) which is the only derivative of **1**, obtained by the oxidation of 4-amino-2,4-dihydro-2-phenyl[1,2,3]-triazolo[4,5-*d*][1,2,3]triazole (**2**) (Chart 1).[2] Compound **3** was degradated in solution to give a tetrazole **4** and a triazole **5**, which suggested that **3** was decomposed through stepwise N_2 eliminations (Chart 2).[2] These facts stimulated our interest in the properties of **1**, particularly the degradation process. We believed that **1** might have two types of degradation pathways, namely one that leads to two moles of nitriles and a nitrogen (path A), and an other that forms an acetylenes and two moles of nitrogen (path B). It was discussed that **1** may or may not exist as intermediates of the oxidation of aminotriazoles.[3] However, there has been no report that dealt with the degradation process of **1**, and it has remained unclarified which path (A or B) is more favorable. We investigated the degradation mechanisms of the two paths of **1a** by calculations of the potential energy surfaces of both reactions (Chart 3). We adopted the semiempirical Austin Model 1 (AM1) method[4] because it is known to afford better results for the calculation of heat of formation and activation energy than the modified neglect of diatomic overlap (MNDO) method,[5] and long-range potential surface can be appropriately calculated. Thus the AM1 method was believed most appropriate for our calculations.

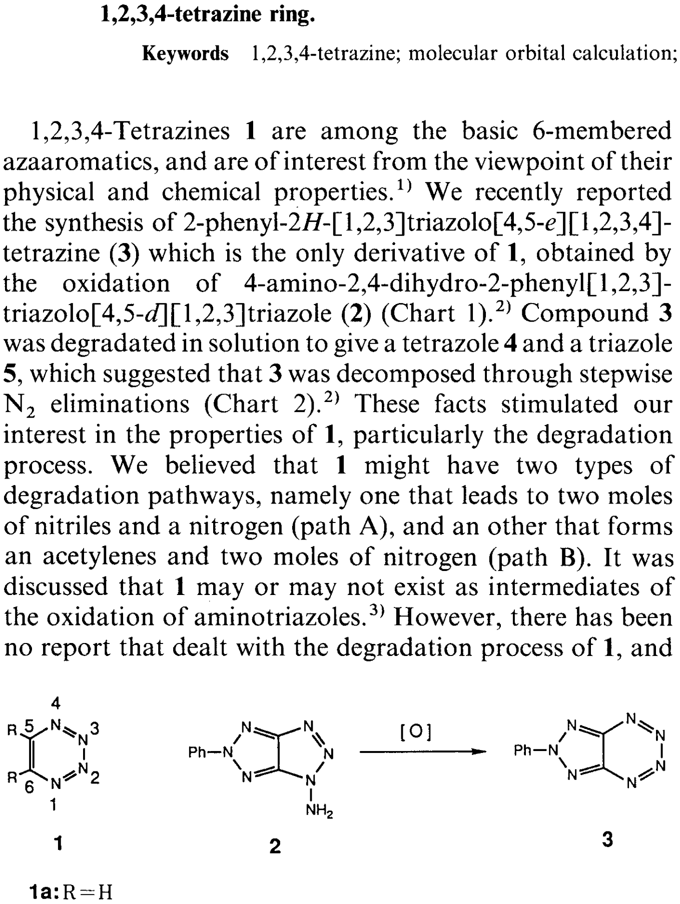

Chart 1

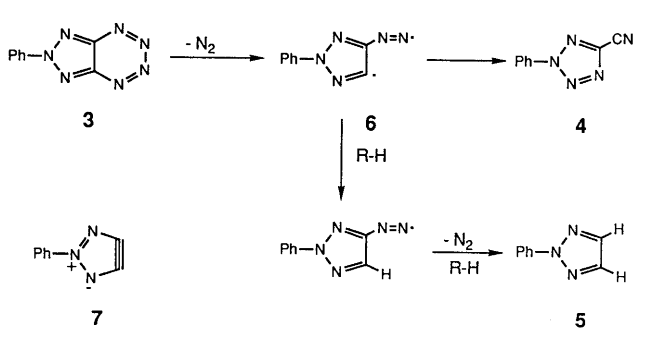

Chart 2

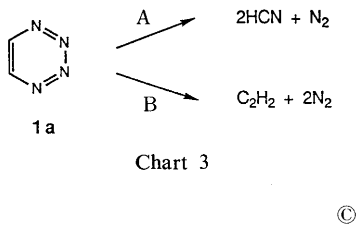

Chart 3

Procedure The calculations were carried out using the AM1 procedure[4] with the standard parameters, as implemented in the MOPAC program.[6] The geometries of stable species were found by minimizing the total enegy using the Broyden–Fletcher–Goldfarb–Shanno (BFGS) optimization procedure.[7] Transition states were located approximately by the reaction coordinate method[8] and then refined by minimizing the gradient norm.[9] Each transition state was characterized by calculating the force matrix.[9] Furthermore, it was confirmed that allowance for geometrical relaxation from the transition states after small geometrical distortions led to stable species.

Results

The calculations were carried out with AM1-RHF (Restricted Hartree–Fock) and AM1-UHF (Unrestricted Hartree–Fock) (singlet; charge $=0$, multiplicity $=1$, or triplet; charge $=0$, multiplicity $=3$). Use of the UHF method would give more pertinent results than that of RHF when the potential energy surface has a biradical character.[10] The structure and heat of formation of **1a** were exactly the same by both RHF and UHF-singlet calculations, whereas UHF-triplet gave higher heat of formation. Accordingly, the calculation was started adopting the singlet structure of **1a** as an initial coordinate. At the first stage for the calculation of the potential energy surfaces of paths A and B, a C_2 axis was assumed which went across C5–C6 and N2–N3.[11] The breaking bond lengths were adopted as two-dimensional reaction coordinates, and the rough appearances of the potential energy surfaces were obtained from a two-dimensional grid search. With the grids thus obtained, minimum energy reaction paths (MERP) and the initial geometries for the calculations of the stationary points were estimated. The obtained structures, energies, and other properties of the stationary points are shown in Figs. 1 to 3.

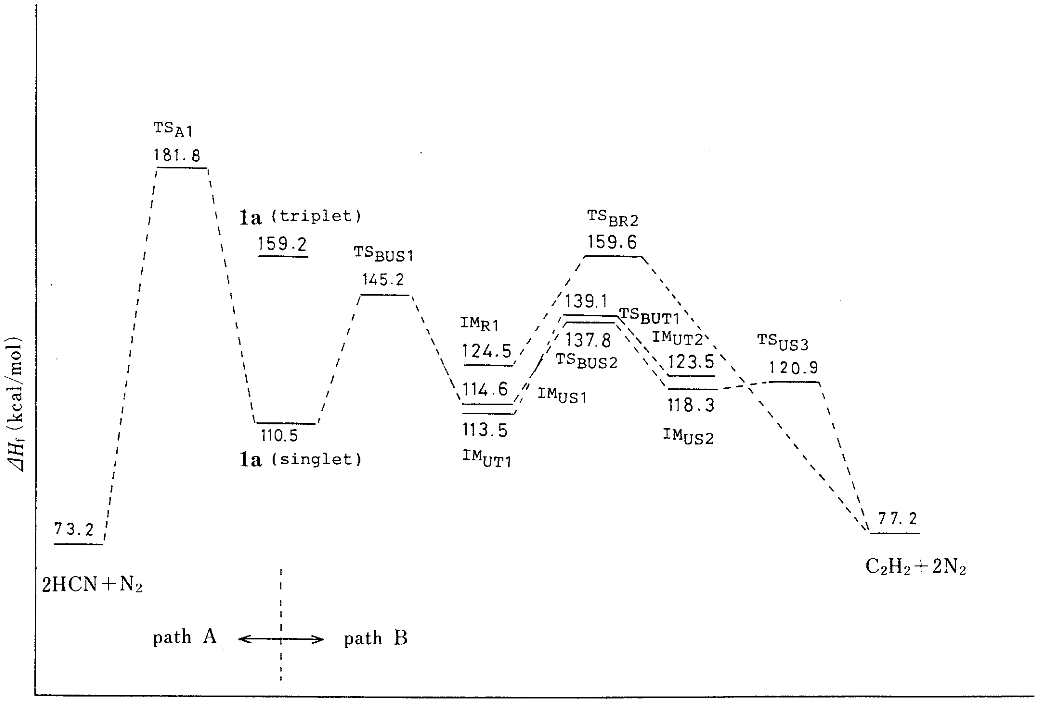

Fig. 1. Schematic Representation of Degradation Reactions of 1,2,3,4-Tetrazine (**1a**)

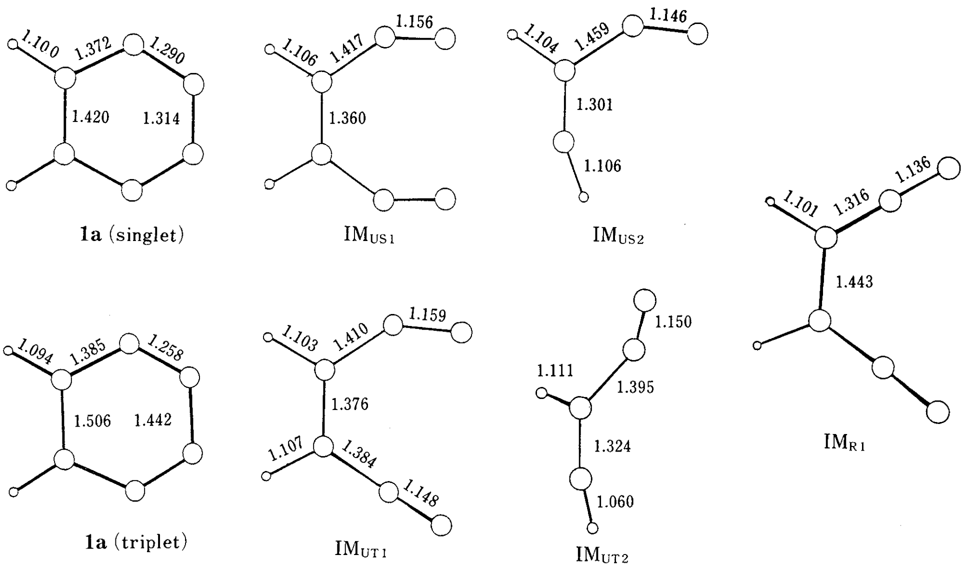

Fig. 2. Geometries of Stable Species Calculated for Degradation Reactions of 1,2,3,4-Tetrazine (**1a**) (Bond Length in Å)

Degradation to $2HCN+N_2$ (Path A) a) By the RHF method, the minimum energy pathway of **1a** (singlet) was calculated in the above described way using the atomic distances of C5–C6 and N1–N2 (N3–N4) as reaction coordinates, and it was shown that the reaction proceeded in a concerted fashion to give the products ($2HCN+N_2$) without going through any intermediates. The geometry of the transition state (TS_{A1}) was almost planar, and the lengths of C5–C6 and N1–N2 (N3–N4) were 2.095 and 1.623 Å, respectively; the heat of formation of TS_{A1} was 181.8 kcal/mol (activation enthalpy, 71.3 kcal/mol).

b) The same calculation was performed with the UHF method (singlet), which gave the similar potential surface and resulted in the same transition state as obtained by the RHF method. The reason for the same transition state by both RHF and UHF-singlet was believed to be the lack of biradical character of the MERP of path A.

Degradation to $C_2H_2+2N_2$ (Path B) The calculation of the potential energy surface of path B was carried out employing the distances of N2–N3 and N1–C6 (N4–C5) of **1a** (singlet) as two-dimensional coordinates.

a) The result of grid search with the RHF method showed that the cleavage of N2–N3 bond preceded that of N1–C6 (N4–C5) in this reaction. However, an appropriate transition state could not be obtained.[12)]

b) The grid search with UHF-singlet also showed the initial cleavage of the N2–N3 bond, and a transition state (TS_{BUS1}) and an intermediate (IM_{US1}) were found. These

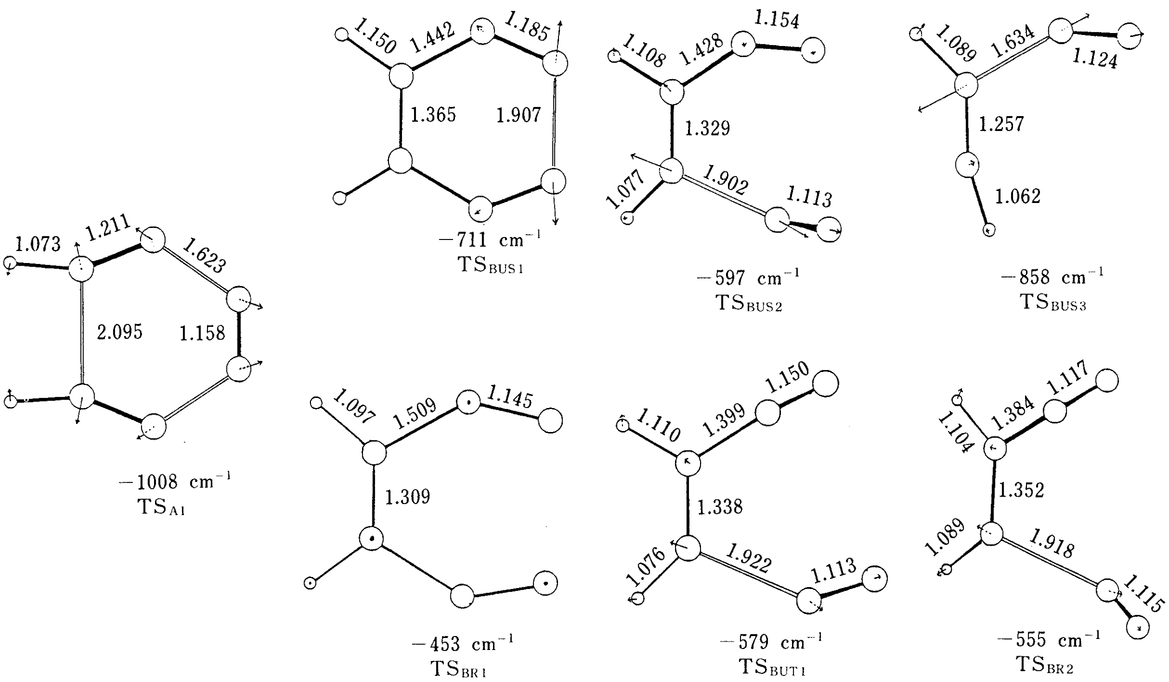

Fig. 3. Properties of Transition States for Degradation Reactions of **1a**; Bond Lengths (Å), Imaginary Frequencies Corresponding to the Negative Eigenvalues (cm^{-1})

Arrows represent the transition vectors.

facts suggested that the biradical character of the N2–N3 cleavage could not be appropriately recognized by the RHF method. The N2–N3 bond length in TS_{BUS1} was 1.907 Å, which showed a greater elongation than that of N1–C6 or N4–C5 (1.442 Å), as compared to the bond lengths of **1a**. The heat of formation of TS_{BUS1} and IM_{US1} was 145.2 and 114.6 kcal/mol, respectively, and the activation enthalpy was 34.7 kcal/mol. The degradation pathway from the intermediate (IM_{US1}) was calculated using C–N distance as a reaction coordinate.[13] The result showed that the first N_2 elimination from IM_{US1} afforded a transition state (TS_{BUS2}) (heat of formation, 137.8 kcal/mol; activation enthalpy, 23.2 kcal/mol) which led to the next intermediate (IM_{US2}: heat of formation, 118.3 kcal/mol), and IM_{US2} gave the products ($C_2H_2+2N_2$) *via* a transition state (TS_{BUS3} heat of formation, 120.9 kcal/mol; activation enthalpy, 2.6 kcal/mol). The calculation with UHF-triplet was carried out using the structure of IM_{UT1} (heat of formation, 113.5 kcal/mol) as an initial structure,[14] However, it was revealed that the pathway from IM_{UT1} to $C_2H_2+2N_2$ was energetically disadvantageous to the one that was calculated with UHF-singlet.[15] Hence path B was initiated by the cleavage of N2–N3, followed by the stepwise elimination of two nitrogens, and the activation enthalpy of its rate-determining step was estimated at 34.7 kcal/mol.

Discussion

The above calculations predicted the degradation mechanism of 1,2,3,4-tetrazines **1**. The results of the calculations of **1a** showed that path A (the degradation to $2HCN+N_2$) proceeded in a concerted manner with no intermediates, whereas path B (the degradation to $C_2H_2+2N_2$) went on stepwise *via* two intermediates. The activation enthalpy of path A was 71.3 kcal/mol, while the largest one of path B was that of the first breaking of N2–N3 (34.7 kcal/mol). Accordingly, **1a** was suggested to degrade more readily to $C_2H_2+2N_2$ than to $2HCN+N_2$. Based on these results, we are able to discuss the degradation of triazolotetrazine **3** as shown in Chart 2. At first, the N2–N3 bond of **3** was broken followed by the C–N bond cleavage accompanied by N_2 elimination. The release of N_2 from a biradical **6** thus obtained was expected to give triazolohetaryne **7**, however, this reaction could not proceed because of the instability of **7**. Thus a tetrazole **4** and a triazole **5** were obtained instead *via* the ring transformation of **6** and hydrogen abstraction of **6** from solvents, respectively. The degradation of **3** and the calculation results of **1a** both showed the ready N2–N3 bond cleavage of tetrazines, which is considered to be an important factor in the stability of **1**.

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11) Compound **1a** has C_{2V} symmetry.

12) A transition state (TS_{BR1}: heat of formation, 164.9 kcal/mol) was obtained, but its transition vectors showed that it could not lead to the starting structure, **1a**, while, a stable structure (IM_{R1}: heat of formation, 124.5 kcal/mol) which was derived from the N2–N3 bond cleavage was found by the grid. A transition state was not obtained when the 2 mol of nitrogen were eliminated from IM_{R1} under C_2 symmetry (force matrix had two negative eigenvalues). Using the distance of C1–N6 as a reaction coordinate, a transition state (TS_{BR2}: heat of formation, 159.6 kcal/mol; activation enthalpy, 34.9 kcal/mol), which led to $C_2H_2+2N_2$, was obtained.

13) Calculations were carried out on the reaction pathway from IM_{US1} to $C_2H_2+2N_2$ along with 2 molar denitrogenation under C_2 symmetry, but the transition state could not be obtained (the force matrix for calculated structure had two negative eigenvalues).

14) IM_{UT1} was calculated using IM_{US1} as the initial geometry.

15) The transition state TS_{BUT1}, which was calculated from IM_{UT1} using C–N bond length as a reaction coordinate, afforded 139.1 kcal/mol of the heat of formation, and 25.6 kcal/mol of the activation enthalpy. The intermediate IM_{UT2} which was formed *via* TS_{BUT1} had 123.5 kcal/mol of the heat of formation. These values are higher than those of TS_{BUS2} or IM_{US2}.