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Facile and Exclusive Formation of Aziridinofullerenes by Acid-catalyzed Denitrogenation of Triazolinofullerenes

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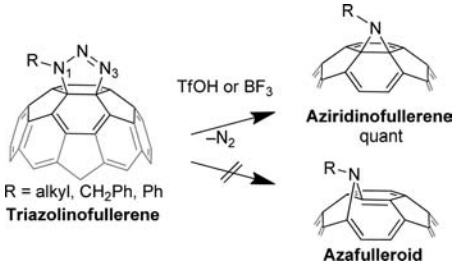
ABSTRACT



Variously substituted [6,6]closed aziridinofullerenes were exclusively obtained from acid-catalyzed denitrogenation of triazolinofullerenes without formation of relevant [5,6]open azafulleroids, which are the major products on noncatalyzed denitrogenation. The mechanistic consideration by DFT calculations suggested a reaction sequence involving initial pre-equilibrium protonation of the triazoline N_1 atom, generation of aminofullerenyl cation by nitrogen-extrusion, and final aziridination.

Aziridinofullerenes, bearing a strained aziridine ring, are useful synthetic intermediates for highly efficient and regioselective addition of spherical fullerene cages, such as acid-induced 1,4-bisaddition of aromatic compounds,[1,2] [2 + 2] cycloaddition with alkynes,[2] and isomerization to azafulleroids.[1b,3] The aziridinofullerenes have been hitherto widely prepared by 1,3-dipolar cycloaddition of azides to C_{60}, followed by thermal or photochemical denitrogenation of the triazolinofullerene adducts.[4] Although some new synthetic methods of certain aziridinofullerenes by nucleophilic addition of chloramines,[1] iminophenyliodinanes,[2] sulfilimines[3] and *N*,*N*-dihalosulfonamides[5] were recently reported, the classical denitrogenation of labile triazolinofullerenes is still a useful procedure for the introduction of various substituents and functional groups R at the triazoline N_1 position such as amino acids,[6] saccharides[7] and lipid substituents.[8] However, the thermal denitrogenation has some difficulty in controlling the reaction conditions and also preventing the formation of major concomitant [5,6]open azafulleroids.[4,9,10] In this context, it is eagerly desired to find an efficient aziridination reaction and hence

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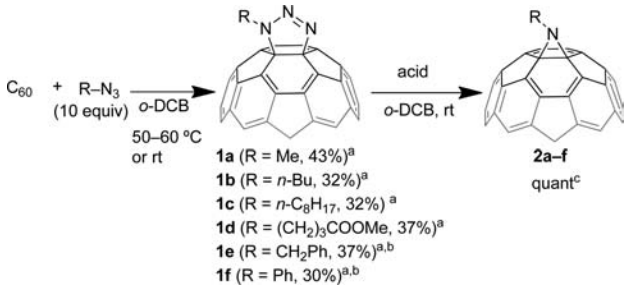
we have applied possible acid-catalyzed denitrogenation of usual triazoline compounds.[11] Here, we present the successful and exclusive formation of [6,6]closed aziridinofullerenes from simple Brønsted/Lewis acid-catalyzed denitrogenation of triazolinofullerenes.

The preparation of various triazolinofullerenes **1a**–**f** is described in Table 1. For the sake of safety, the employed alkyl azides were prepared from alkyl halides with sodium azide in acetonitrile, and then immediately used *in situ* for the subsequent 1,3-dipolar cycloaddition by adding C_{60} solution in *o*-dichlorobenzene (*o*-DCB) at elevated temperature (~50 °C). To reduce the multiaddition, the reaction was ceased at the 60–70% consumption of C_{60} (12–36 h) except for the syntheses of **1e** and **1f**, which were prepared at room temperature for the prolonged reaction time (96 h) to suppress the unfavorable thermal denitrogenation into the corresponding azafulleroids. The yields of **1a**–**f** were comparable with those of the previous syntheses of triazolinofullerenes.[4] All triazolinofullerenes were fully identified with $^1H/^{13}C$–NMR and HRMS spectrometry.

Table 1. Synthesis of Aziridinofullerenes **2a**–**f** via Acid-induced Denitrogenation of Triazolinofullerenes **1a**–**f**



entry	reactant	acid[d]	time (h)	conv (%)
1	**1a**	TfOH	<0.1	100
2	**1a**	CH_3SO_3H	0.5	100
3	**1a**	CF_3COOH	24	0
4	**1a**	BF_3	0.5	100
5	**1a**	BF_3[e]	3	81
6	**1a**	$B(C_6H_5)_3$	5	100
7	**1a**	$AlCl_3$	24	0
8	**1a**	$TiCl_4$	24	0
9	**1b**	TfOH	0.1	100
10	**1c**	TfOH	0.1	100
11	**1d**	TfOH	0.1	100
12	**1e**	TfOH (0.5 equiv)	0.1	100
13	**1f**	TfOH (1.0 equiv)	0.1	100

[a] Isolated yield. [b] At rt. [c] >95% isolated yield. [d] Unless otherwise noted, 0.1 equiv of acid was used. [e] Toluene solvent.

Acid-catalyzed denitrogenation of variously alkyl-substituted **1a**–**e** readily occurred on addition of catalytic ammounts (0.1–0.5 equiv) of superacid CF_3SO_3H (TfOH) and Lewis acid BF_3 (Table 1).[12] For phenyl-substituted **1f**, an equivalent amount of TfOH was needed to complete the denitrogenation (entry 13), probably because of the far more reduced basicity of the phenyl-sustituted N_1-atom than that of alkyl-substituted one. Noticeably, the [6,6]closed aziridinofullerenes **2a**–**f** were exclusively obtained with no appreciable amount of [5,6]open azafulleroids as exemplified for the denitrogenation of **1a** under BF_3 (Figure 1). The C_{2v} symmetric structures of **2a**–**f** were fully characterized by $^1H/^{13}C$–NMR spectroscopy (Supporting Information).

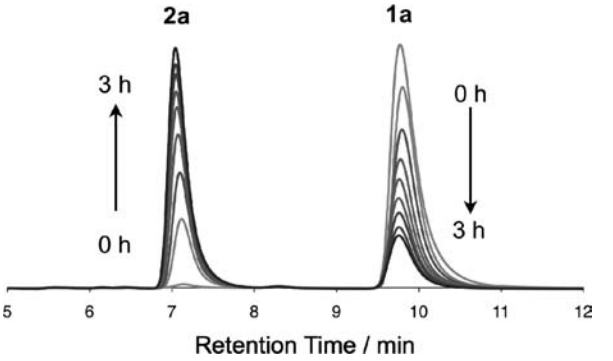


Figure 1. HPLC trace of denitrogenation of **1a** into **2a** by BF_3 in toluene (cf. Table 1, entry 5).

It was also found that the denitrogenation rates of triazolinofullerens **1a**–**f** by several Brønsted/Lewis acids depend on their acidities (Table 1). The weaker CH_3SO_3H needed longer reaction time (0.5h) than CF_3SO_3H (entries 1 and 2), and much weaker CF_3COOH was ineffective (entry 3). BF_3 was found to more efficiently cause the denitrogenation than $B(C_6F_5)_3$ (entries 4 and 6), but no reaction occurred with $AlCl_3$ and $TiCl_4$ (entries 7 and 8). These results suggest the protonation (or coordination of Lewis acids) at the basic triazoline N_1 atom would be a key step of the denitrogenation (*vide infra*). In fact, the reaction was accelerated with increasing solvent polarity as seen in a

(9) Although addition of nitrenes by denitrogenation of azides gave aziridinofullerenes with relatively high yields, their substituents were limited to carbonyl/sulfonyl compounds. See: (a) Banks, M.; Cadogan, J.; Gosney, I.; Hodgson, P.; Langridgesmith, P.; Millar, J.; Taylor, A. *Tetrahedron Lett.* **1994**, *35*, 9067–9070. (b) Smith, A. B.; Tokuyama, H. *Tetrahedron* **1996**, *52*, 5257–5262. (c) Ulmer, L.; Mattay, J. *Eur. J. Org. Chem.* **2003**, 2933–2940.

(10) Exceptionally, the reaction of hydrazoic acid with C_{60} gave aziridinofullerene, as recently reported by Akhmetov *et al.* In the light of our results and discussion in this paper, one can suppose that the excess amount of sulfuric acid used for *in situ* preparation of hydrazoic acid causes the formation of aziridinofullerene. See: Akhmetov, A. R.; Tuktarov, A. R.; Dzhemilev, U. M.; Yarullin, I. R.; Gabidullina, L. A. *Russ. Chem. Bull.* **2011**, *60*, 1885–1887.

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(12) An excess amount of acid in toluene led to further reaction, probably electrophilic arylation of aziridinofullerene as previously reported in refs 1b and 2.

plot of log k vs solvent polarity parameter E_T (Figure 2),[13,14] probably because of the stabilization of such polar acid–base complexes.

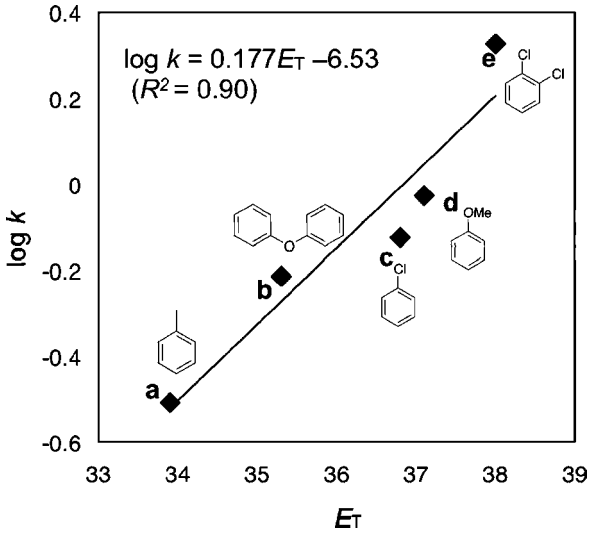

Figure 2. Plot of log k vs solvent polarity parameter E_T for the reaction of **1a** with BF_3[13]

Why does the present acid-catalyzed condition exclusively provide the [6,6]closed aziridinofullerene in contrast to the thermal denitrogenation? Thermal condition has been well-known to prefer the formation of [5,6]open azafulleroid via the possible three pathways: (1) concerted, (2) ionic stepwise and (3) radical stepwise.[4d,e,15] A DFT calculation (B3LYP/6-31G(d))[16] with solvent parameters (IEFPCM, *o*-dichlorobenzene) suggested a concerted-like transition state **1a**-TS (Scheme 1, path a, and Figure 3b) as previously reported for its carbon analog, pyrazolinofullerene.[17] The barrier energy (34.3 kcal/mol) for the denitrogenation of **1a** is lower than those of previously reported two types of ionic transition states (N_1–N_2 or N_3–C_1 cleavage) by AM1 calculations (46.8 and 45.2 kcal/mol, respectively).[15] Moreover, the calculation of inherent reaction coordinate (IRC) showed the sp^2-like N_1 atom considerably approached the C_2 atom (purple cross in Figure 3a), implying enhanced aza-bridging over the 5,6-conjunct bond. The optimization of the forward-edge structure of the IRC calculation showed transient [5,6]closed aziridinofullerene **3a** capable of undergoing labile valence isomerization to [5,6]open azafulleroid **4a** (Scheme 1 and Figure 3c). This computational result

(13) The 0.1 equiv of BF_3 was used (1.29×10^{-3} M). The k value in toluene is 0.310 M^{-1} s^{-1} and the relative k values in other solvents are 1.97 (**b**), 2.42 (**c**), 3.03 (**d**), and 6.84 (**e**), respectively.

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(16) All DFT calculations were carried out with *Gaussian 09* software. Its full citation is shown in Supporting Information.

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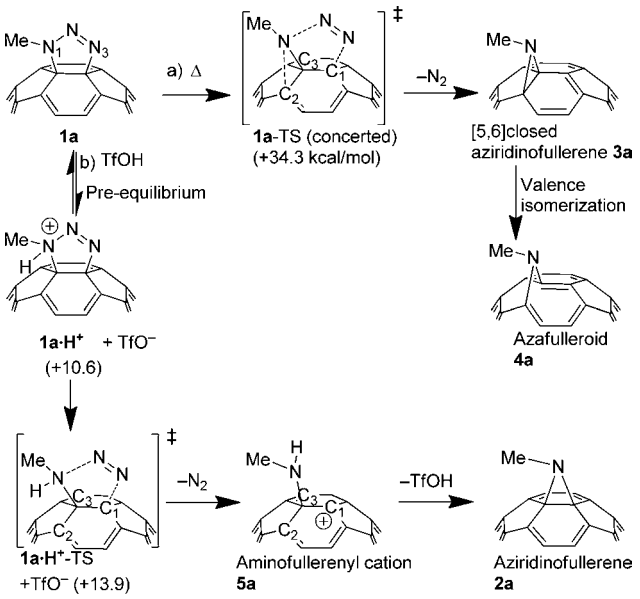
Scheme 1. Suggested (a) Thermal and (b) TfOH-catalytic Pathways with Calculated Energies (B3LYP/6-31G(d) with Solvent Parameter), which are Relative to the Heat of Formation of **1a** (for Thermal) and the Summation of Those of **1a** and TfOH (for Acid-catalyzed)



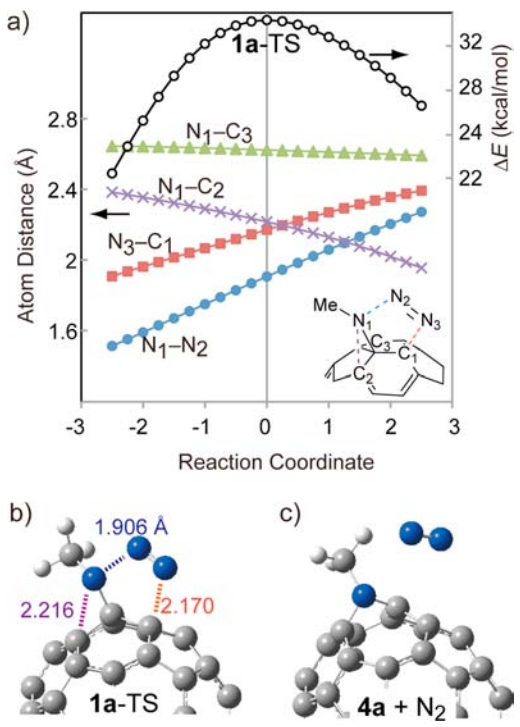


Figure 3. (a) Energies and atomic distances of IRC calculation (B3LYP/6-31G(d) with solvent parameters) for the thernal denitrogenation of **1a**. The energies are relative to the initial state **1a**. (b) Geometry of the concerted transition state **1a**-TS. (c) Geometry of [5,6]open **4a** (and N_2) derived from the optimization of the IRC forward-edge structure (s = 2.50).

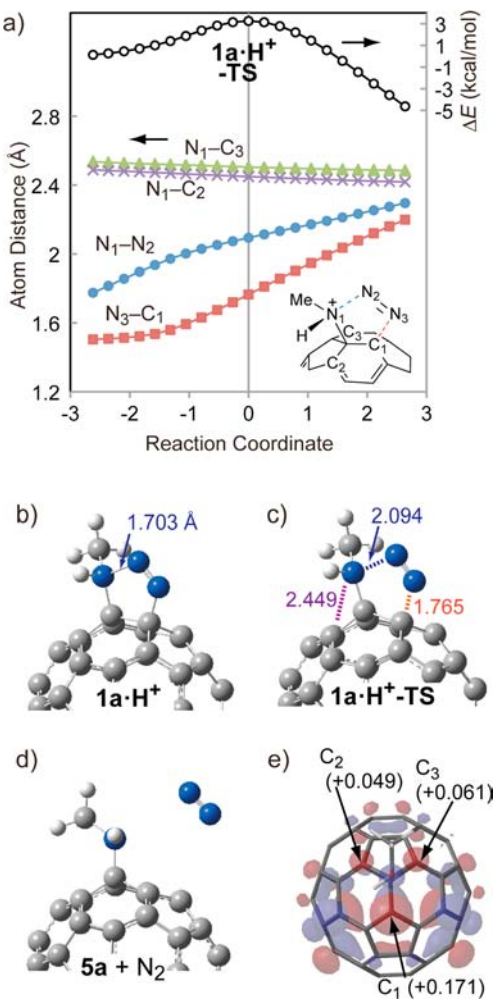


Figure 4. (a) Energies and atomic distances of IRC calculation (B3LYP/6-31G(d) with solvent parameters) for the acid-catatytic denitrogenation. The energies are relative to the initial state **1a·H**$^+$. (b) Geometry of N_1-acidified **1a·H**$^+$. (c) Transition state geometry (**1a·H**$^+$-TS) of denitrogenation of **1a·H**$^+$. (d) Geometry of aminofullerenyl cation **5a** (and N_2) derived from the optimization of the IRC forward-edge structure (s = 2.64). (e) LUMO orbital distribution and natural bonding orbital charge (in parentheses) of the ionic intermediate **5a**.

obviously conforms with the selective formation of azafulleroids on usual thermal conditions.

By contrast, TfOH can protonate an N_1 atom to give triazolinium intermediate **1a·H**$^+$ with a long N_1–N_2 distance (1.7 Å) (Scheme 1, path b, and Figure 4b).[18] A transition state calculation of denitrogenation of **1a·H**$^+$ showed far more lower barrier energy (3.3 kcal, Figure 4c) than that of the thermal reaction (34.3 kcal). In contrast to the case of thermal condition, the distance between the sp^3-like ammonium N_1 and C_2 (or C_3) is little changed by the IRC calculation, due to the absence of potential N_1 lone pair electrons (Figure 4a). Furthermore, the optimization of the IRC forward-edge structure resulted in aminofullerenyl cation **5a**, with N_1 being located almost perpendicular to the C_1–C_2–C_3 plane (Scheme 1 and Figure 4d). The higher LUMO coefficient and/or positive natural bonding charge on C_1 (relative to C_2 and C_3) by a DFT calculation would be responsible for the formation of [6,6]closed aziridinofullerene. The total barrier energy of the rate-determing protonation (10.6 kcal/mol) and the fast denitrogantation (3.3) is still less than the half of the thermal denitrogenation (34.3), so that the acid-catalyzed reaction seems to proceed very soomthly at room temperature and exclusively provide [6,6]closed aziridinofullerenes.

In conclusion, synthetically useful aziridinofullerenes were exclusively obtained from simple acid-catalyzed denitrogenation of triazolinofullerenes, and the DFT calculations suggested a possible mechanism involving the initial protonation at the N_1 atom, followed by denitrogenation into the aminofullerenyl cation, and the final aziridination. This effective synthetic method would open a way to more versatile and regioselective functionalization of fullerenes directed to photovoltaic materials[5,19] and biological applications.[7]

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Supporting Information Available. General procedure for the reaction and identification of compounds by ^{1}H, ^{13}C NMR spectra, and FAB/MALDI-MS of **1a–f** and **2a–f**, and calculational results (energy, imaginary frequency and coordinates). This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.

(18) Although the triazoline N_3 atom would be more easily protonated, such N_3-protonated species does not lead to the denitrogenation (see, ref 11b).

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