Tetrahedron Letters 51 (2010) 3266–3268

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

The generation of diazirinone: a computational study

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ARTICLE INFO

Article history:
Received 17 March 2010
Accepted 14 April 2010
Available online 18 April 2010

Keywords:
Diazirines
Calculations
Fluoride ion
Catalysis

ABSTRACT

Computational studies indicate that the reaction of *p*-nitrophenoxyfluorodiazirine with fluoride ion should generate diazirinone. However, fluoride ion also catalyzes the decomposition of diazirinone to carbon monoxide and nitrogen, so that the diazirinone is likely to be unstable to the conditions used to generate it.

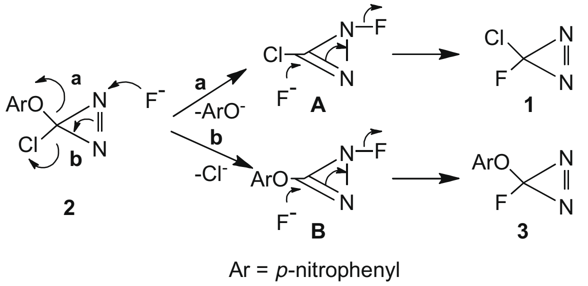
In 2005, we reported that chlorofluorodiazirine (**1**) results from the reaction of fluoride ion with *p*-nitrophenoxychlorodiazirine (**2**); cf. Scheme 1.[1] Fluoride, supplied as anhydrous tetrabutylammonium fluoride (TBAF), reacts with diazirine **2** via two competitive double S_N2' diazirine exchange reactions.[2–4] The first S_N2' fluoride attack on **2** displaces either *p*-nitrophenoxide (later protonated to *p*-nitrophenol, path **a**), affording isodiazirine intermediate **A** or chloride (path **b**), yielding isodiazirine **B**. Subsequent S_N2' reactions with fluoride then convert **A** to chlorofluorodiazirine (**1**) and **B** to *p*-nitrophenoxyfluorodiazirine (**3**).[1] *p*-Nitrophenol and diazirines **1** and **3** were each isolated and characterized.

However, the principal course of reaction between **2** and fluoride did not follow the channels of Scheme 1. The major non-volatile reaction product was *p*-nitrofluorobenzene (**4**), and its formation was accompanied by the evolution of carbon monoxide (and nitrogen).[1] The formation of **4** suggests a competitive *ipso* attack of fluoride on diazirine **2**; cf. Scheme 2. We proposed that this reaction led not only to **4** but also to diazirinone (diazacyclopropenone, **5**), which decomposed to CO (identified by IR spectroscopy) and, by necessity, to an equivalent of N_2.[1]

Diazirinone is believed to be the most stable of several isomers of N_2CO; for example, it is computed to be about 11 kcal/mol more stable than its known open-chain isomer nitrosyl cyanide.[5] Decomposition of diazirinone to CO + N_2 is computed to be exothermic by >90 kcal/mol,[5,6] but is opposed by a barrier of ~27 kcal/mol, so that diazirinone should be observable but metastable. Although the photochemistry and spectroscopy of several matrix-isolated N_2CO isomers have been described,[7] and triplet NNCO has apparently been generated from N_2CO^+ ions in a neutralization–reionization mass spectroscopy experiment,[8] diazirinone had not previously been prepared.

In our original experiments, combination of diazirine **2** and 'molten' TBAF in a small quantity of $CDCl_3$ or 1,2-dichloroethane in an IR cell at −10 to −15 °C led immediately to a strong absorption at 2150 cm^{-1}. This band gradually decayed over 3–5 min as the temperature rose toward 25 °C; simultaneously, absorptions of CO appeared at 2115 and 2173 cm^{-1}. We attributed the initial 2150 cm^{-1} absorption to diazirinone, formed as in Scheme 2, and the successor bands at 2115 and 2173 cm^{-1} to CO formed upon decomposition of the diazirinone.[1]

A very careful recent reinvestigation by Shaffer et al. confirmed the diazirine exchange chemistry described in Scheme 1, but casts doubt upon the generation of diazirinone (Scheme 2).[9] In particular, the immediately formed IR absorption at 2150 cm^{-1} was more reasonably ascribed to a broad, unresolved absorption of CO, supersaturated in solution, which subsequently afforded the R (2172 cm^{-1}) and P (2118 cm^{-1}) branches of the gas-phase CO spectrum as the CO degassed from solution with increasing tempera-



Scheme 1.

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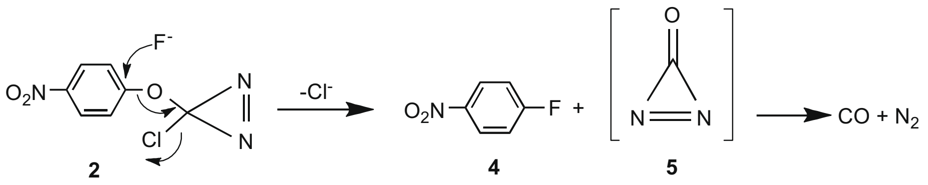
doi:10.1016/j.tetlet.2010.04.066



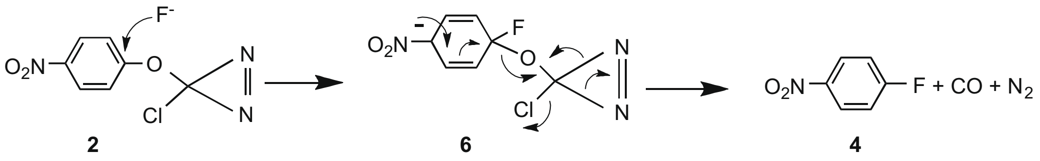
Scheme 2.

ture.[9] Moreover, high-level CCSD(T)/ANO2 calculations indicated that diazirinone should absorb at 2046 cm^{-1} (with an accuracy of 25 cm^{-1}),[9] rather than at 2150 cm^{-1}.[1]

Shaffer et al. highlight two key uncertainties.[9] (1) If diazirinone is indeed formed by the pathway of Scheme 2, it must either have a much shorter lifetime than anticipated from the 27 kcal/mol barrier calculated for its decomposition,[5,6] or be unstable to the reaction conditions used for its generation. Thus, although *p*-nitrofluorobenzene and CO certainly form in the reaction of F$^-$ and diazirine **2**, attempts to isolate the putative diazirinone in cold traps or in cryogenic matrices under reduced pressure were unsuccessful.[9] (2) Alternatively, the reaction of diazirine **2** and F$^-$ might bypass diazirinone entirely; cf. Scheme 3. Here, Meisenheimer complex **6** forms from **2** and F$^-$, but concertedly decomposes to **4**, CO, and N_2 *without* the intermediacy of diazirinone.[9]

Now we present a DFT computational study at the B3LYP/6-311+G(d) level of theory that enables us to evaluate these uncertainties. In the following, all computed structures are fully optimized by analytical gradient methods using the GAUSSIAN09 suite[10] and DFT calculations at the RB3LYP/6-311+G(d) level, the exchange functional of Becke[11] and the correlation functional of Lee et al.[12] Vibrational analyses establish the nature of all stationary points as either energy minima (no imaginary frequencies) or first order transition structures (one imaginary frequency). Intrinsic reaction coordinate (IRC) calculations verify that the TSs connect initial and product structures. Reported enthalpies (unscaled) are corrected for zero-point energy and temperature effects at 298.14 K. All solution optimizations are carried out in continuum acetonitrile medium ($\varepsilon = 36.34$) using the CPCM protocol.[13] Our calculations include acetonitrile as a solvent in order to mimic the experimental conditions of Shaffer et al., who use both MeCN and $CHCl_3$.[9]

Figure 1 summarizes our computational study of the reaction between F$^-$ and diazirine **2**; for a diagram that illustrates the relative energies of the intermediates, see Figure 1a in the Supplementary data. The results are fully consistent with the mechanism outlined in Scheme 2. Fluoride ion attacks the *ipso* carbon atom of **2** to give Meisenheimer complex **6** with an activation enthalpy of 10.4 kcal/mol and an endothermicity of 9.6 kcal/mol. Complex **6** resides in a very shallow enthalpy well; its decomposition to



Scheme 3.

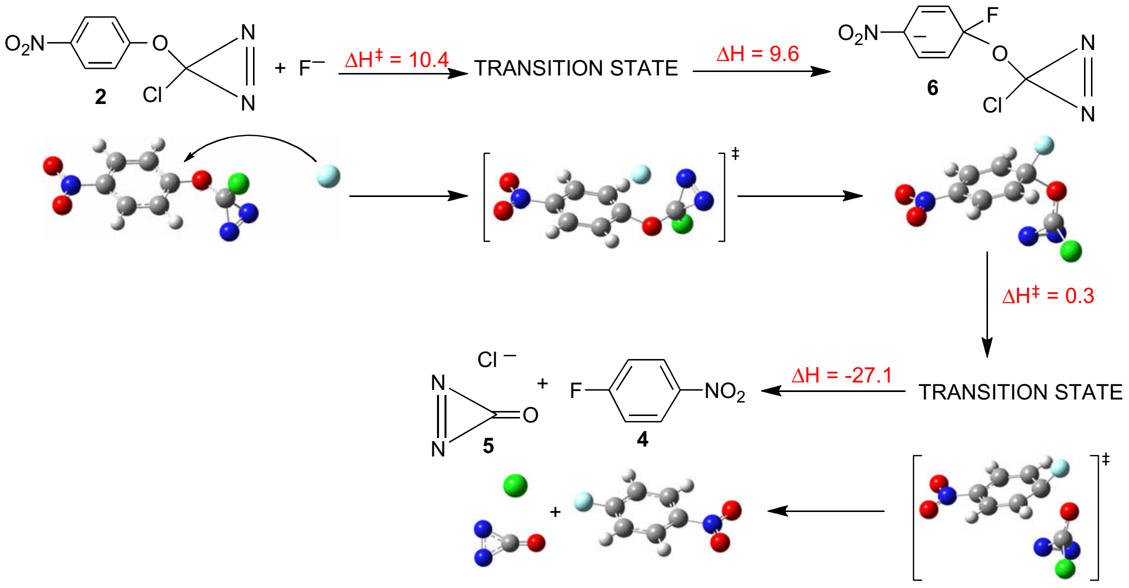


Figure 1. The generation of diazirinone (**5**) from *p*-nitrophenoxychlorodiazirine (**2**) via Meisenheimer complex **6**. Calculations are B3LYP/6-311+G(d)/CPCM in simulated MeCN; energies are in kcal/mol.

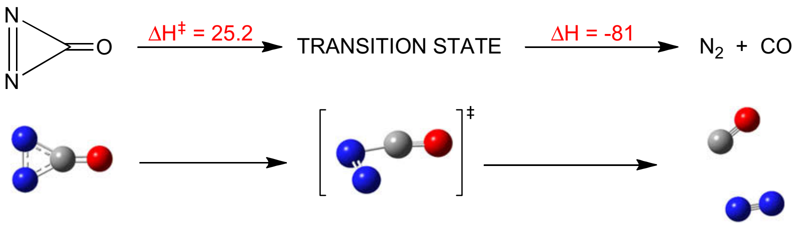


Figure 2. Computed decomposition of diazirinone in simulated MeCN. Calculations are B3LYP/6-311+G(d)/CPCM; energies are in kcal/mol.

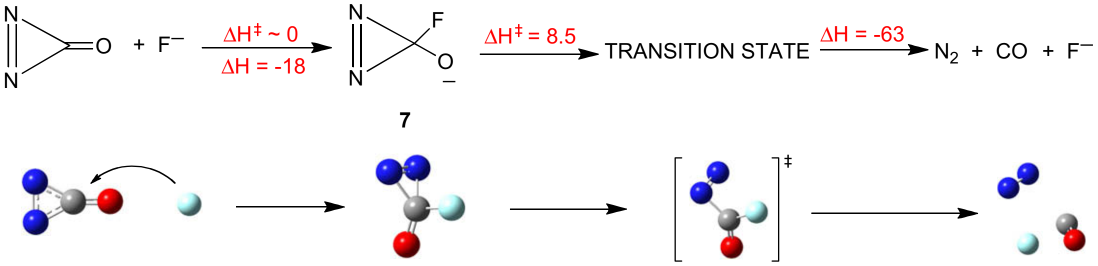


Figure 3. Fluoride-catalyzed decomposition of diazirinone in simulated MeCN. Calculations are B3LYP/6-311+G(d)/CPCM; energies are in kcal/mol.

diazirinone (**5**), *p*-nitrofluorobenzene (**4**), and chloride ion is opposed by a miniscule computed barrier of 0.3 kcal/mol and is driven by an exothermicity of 27.1 kcal/mol.

Given the low enthalpic barriers for the formation of complex **6**, and its subsequent breakdown to diazirinone, the conversion of diazirine **2** to diazirinone should be rapid, even at −15 °C. In resolution of uncertainty (2), above, the computational results suggest that diazirinone is *not* bypassed in the decomposition of **6**; the latter is formed and proceeds to diazirinone in accord with Scheme 2, avoiding the concerted process depicted in Scheme 3.

We consider next the lifetime of diazirinone and why it is not observed under the present reaction conditions.[9] Figure 2 presents our computational results for the decomposition of diazirinone in simulated MeCN.

These results are in good agreement with those of Korkin;[5] the enthalpic barrier to the decomposition of diazirinone is surprisingly high at 25 kcal/mol[14] and should suffice to permit the spectroscopic observation of diazirinone. Note the unsymmetrical, one-bond scission transition state for the conversion of **5** to CO + N_2.[14]

If the barrier to the decomposition of diazirinone is 25 kcal/mol, why was it not observed, given that its coproduct, *p*-nitrofluorobenzene was actually the major product of the reaction of diazirine **2** and fluoride? Why were Shaffer et al. unable to remove diazirinone from the reaction mixture under reduced pressure and condense it into an argon matrix at 25 K?[9] The answer to these questions is that diazirinone is very likely to be unstable to the reaction conditions used to generate it; *fluoride ion catalyzes the decomposition of diazirinone.*

As shown in Figure 3, there is essentially no enthalpic barrier for the addition of F^- to the carbonyl group of diazirinone, a process that is exothermic by 18 kcal/mol and affords adduct **7**. The ensuing decomposition of **7** to CO, N_2, and F^- confronts an activation barrier of only 8.5 kcal/mol and is exothermic by 63 kcal/mol. In other words, catalysis by fluoride is calculated to reduce the barrier to diazirinone decomposition from 25 kcal/mol (Fig. 2) to 8.5 kcal/mol (Fig. 3). Given that the experimental conditions used in the attempted generation of diazirinone involve an excess of fluoride,[1,9] it is not surprising that any diazirinone formed does not survive.

The computational studies provide reasonable resolutions for the uncertainties noted by Shaffer et al.[9] Diazirinone is very likely generated by the reaction of diazirine **2** and fluoride, but it is just as likely to be rapidly destroyed by fluoride-catalyzed decomposition to CO and N_2. Our calculations also suggest a possible way to finesse this difficulty: use a nucleophile in place of fluoride that generates diazirinone but that does not add to its carbonyl group. A possible candidate is chloride ion, which reacts with diazirine **2** to produce *p*-nitrochlorobenzene, *p*-nitrophenol, and dichlorodiazirine in processes that presumably parallel Schemes 1 and 2.[15] Calculations indicate, however, that chloride does *not* add to diazirinone to give the chloride analog of adduct **7**. Appropriate experiments are planned to explore these ideas.

Acknowledgment

We are grateful to the National Science Foundation and the Petroleum Research Fund for financial support.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.04.066.

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