Journal of Fluorine Chemistry 191 (2016) 103–109

Contents lists available at ScienceDirect

Journal of Fluorine Chemistry

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

Computational study of the reaction mechanism of vinyl ethers with hexafluorothioacetone

Stephen E. Burkhardt[a], Viacheslav A. Petrov[b,*], Stephen M. Manzo[a]

[a] DuPont Central Research and Development, Experimental Station, PO Box 80500, Wilmington, DE, 19880-0500, United States
[b] Chemours Co., Fluoroproducts, 200 Powder Mill Road, Experimental Station, E262/339, Wilmington DE, 19803, United States

ARTICLE INFO

Article history:
Received 12 April 2016
Received in revised form 26 September 2016
Accepted 27 September 2016
Available online 30 September 2016

Keywords:
2,2,4,4-Tetrakis(trifluoromethyl) dithienane-1,3
1,1-Dimethoxy ethylene
1-Methoxy ethylene
Ketene dimethylacetal
2,2-Bis(trifluoromethyl)-3,3-bis(methoxy) thietane
2,2-Bis(trifluoromethyl)-4,4-bis(methoxy) thietane
Computational chemistry
Density functional theory

ABSTRACT

A computational study was performed comparing two possible pathways for the fluoride ion catalyzed reaction of **1** with **2,** both proceeding through a zwitterion intermediate. The kinetic pathway corresponded to the initially observed product, **4**, with a low activation charge-controlled process resulting in a zwitterion intermediate. On the other hand, a thermodynamic pathway was also apparent, with a higher barrier towards zwitterion formation, corresponding to product **5**. A similar examination of the reaction pathway of vinyl ether, **6**, with **2**, demonstrated that the monomethoxy substitution was unable to stabilize the zwitterion intermediate in the proposed kinetic pathway, giving rise to only the thermodynamic pathway and the observed product, **7**. The calculated reaction pathways are used to support the hypothesized reaction mechanims leading to the unexpected product, **4**, while similar experimental studies of vinyl ethers are observed to only yield products analogous to **5**.

1. Introduction

In the preceding report, it was observed that the fluoride ion catalyzed reaction between 2,2,4,4-tetrakis(trifluoromethyl)-1,3-dithietane, **1**, and ketene dimethylacetal, **2**, led to the unexpected formation of thietane, **4** (Scheme 1) [1]. It is worth noting that reagents formed from the combination of fluoride salts (CsF, KF) and **1** are used as synthetic equivalents of **3** [2]. Compound **4** was isolated by distillation under reduced pressure, and the structure confirmed using ^{1}H, ^{13}C and ^{19}F NMR, IR-spectroscopy and mass spectrometry, while the structure of isomer **5** was firmly established by single crystal X-ray diffraction [1].

Interestingly, compound **4** subsequently underwent clean isomerization to form **5** over the course of several months in the dark. This interconversion suggested that **4** and **5** were kinetic and thermodynamic products, respectively. At this time, the mechanism of the reaction has not been sufficiently elucidated to explain the regioselectivity, however the formation of **5** from **4** does appear to involve generation of free hexafluorothioacetone (HFTA), **3**, as indicated by the reaction with an added quadricyclane trap. This may suggest that the reaction is, to some degree, reversible.

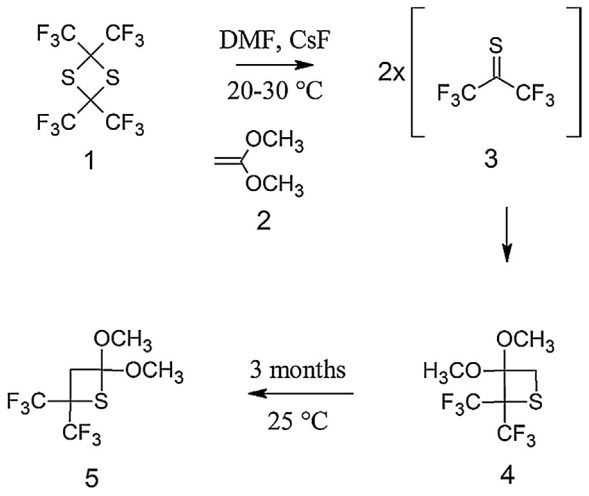
It has been postulated [1] that formation of **4** may take place through either (i) single electron transfer from **2** to **3** with subsequent coupling through radical termini, or (ii) direct nucleophilic attack of the $=CH_2$ terminus of **2** on the sulfur of compound **3**. Either of these routes would result in the same zwitterion intermediate. However, in both thermodynamic and kinetic pathways the proposed mechanisms involve initial formation of a zwitterion from reaction of **2** and **3**, followed by ring closure of the zwitterion to form the thietane.

Be that as it may, the formation of regioisomer **4** presents a problem when compared to the analogous reaction between vinyl ether, **6**, and **1** (Scheme 2). In the case of vinyl ethers, the only observed product corresponds to the route yielding 4-alkoxy-2,2-bis(trifluoromethyl)thietane, **7**, [3,4] which is structurally analogous to isomer **5.** While the structure of the thietane, e.g. **7** (alkoxy = OCH_3, OC_2H_5), was originally suggested based on mass-spectrometry data [5], recently the structure of a thietane product (alkoxy = *t*-Bu-O) was confirmed by single crystal diffraction [4].

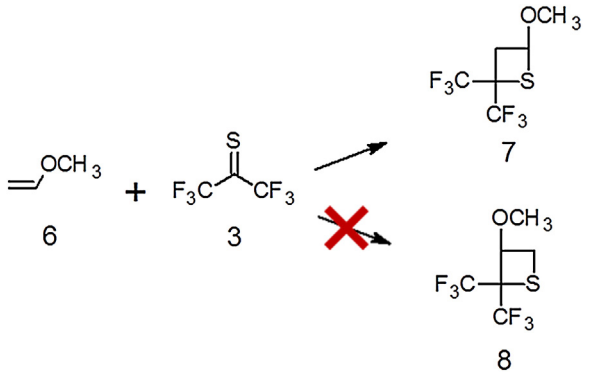
In this report, we have undertaken a density functional theory (DFT) study to evaluate the hypothesized mechanisms and

* Corresponding author.
E-mail address: viacheslav.petrov@chemours.com (V.A. Petrov).

http://dx.doi.org/10.1016/j.jfluchem.2016.09.018
0022-1139/



Scheme 1. Reported fluoride catalyzed reaction of 2,24,4-tetrakis(trifluoromethyl)-1,3-dithietane, 1, and ketene dimethylacetal, 2, to initially yield the kinetic thietane, 4, followed by conversion to thermodynamic thietane, 5.



Scheme 2. Depiction of vinyl ether reaction with 3, yeilding only the thermodynamic product, analogous to compound 5 in this study. The kinetic product, 8, is not observed.

elucidate the details that lead to the surprising formation of both kinetic and thermodynamic products when ketene dimethylacetal, **2**, is allowed to react with hexafluorothioacetone, **3**, generated in-situ from its dimer form by the action of fluoride anion. Comparisons to the experimental observations and proposed mechanism will guide the discussion.

2. Calculations

All calculations were performed at the level of density functional theory using Gaussian 09, Revision C.01 [6] Optimizations were performed using the B3LYP functional, employing Becke's 3-parameter exchange component (B3) in conjunction with the correlation component from Lee, Yang, Parr (LYP) [7,8] and the 6-311+g** basis set. Solvent effects were described by the polarizable continuum model (PCM) with the static and optical dielectric constant of dimethylformamide (DMF) as implemented in Gaussian09 [9,10]. The B3LYP hybrid functional was used based on the good agreement for enthalpies of formation [11], ionization potentials, and electron affinities [12]. Ionization energies were calculated as described in reference [13] with inclusion of solvent effects using the solvent model described above.

Additional optimizations were performed using the MPW1K functional, which has been optimized against a database of reaction barriers to yield data in close agreement with experiment [13]. Optimizations for all MPW1K calculations were performed in the gas phase, and utilized the 6-311+g**(d,p) basis set. Follow-up single point calculations were performed with the PCM model described above.

Vibrational analysis and thermodynamic properties such as enthalpy and Gibbs' free energy were computed at 298 K after geometric optimization. Stationary points were confirmed by the presence of zero imaginary frequencies (ground state) or a single imaginary frequency (transition state).

NMR chemical shifts were computed using the GIAO method with the solvent effects described by the PCM model using $CHCl_3$ parameters [14]. The absolute chemical shift of ^{19}F in $CFCl_3$ was taken as 155.5 ppm from predictions employing B3LYP/6-311++g(d,p) [15]. TMS absolute shielding for ^{13}C was taken as 177.2 ppm [16].

The natural bond orbital method was used to calculate atomic charges (NBO 3.1, as implemented in Gaussian09) [17–24]. The condensed-to-atom Fukui indices were calculated for the test set in an effort to understand the relative reactivity of atomic sites in the reactants [25,26]. The Fukui indices for electrophilic attack were calculated by taking the difference between NBO atomic charges for the cation radical, $(N-1)$, and neutral (N) species according to the equation:

$$f_{A-} = P(N) - P(N-1) \quad (1)$$

where f_{A-} is the susceptibility to electrophilic attack, $P(N)$ is the population (NBO atomic charge) on a specific atomic site in the neutral species, and $P(N-1)$ is the population on the same site of the cation radical species. These differences are taken with the geometry frozen in the geometry of the neutral species. The Fukui indices for nucleophilic attack, (f_{A+}) were generated in an analogous fashion using the charges of the anionic species $(P(N+1))$ in place of those of the cation.

Graphics were generated with the Avogadro program and rendered using POV-ray software [27]. Where possible, structures were first optimized using the MMFF94 molecular mechanics force field as implemented in Avogadro [28]. Molecular orbitals are displayed using an isodensity surface of 0.05.

3. Results and discussion

The ^{13}C and ^{19}F NMR chemical shifts of both products were calculated to provide a reference for determining agreement between the DFT and experimental data. Experimental and calculated chemical shifts are reported in Table 1, and the calculated data are in relative agreement with those observed experimentally (correlation is shown in Fig. S1). Notably, the observed upfield shift of the ^{19}F signal for the $-CF_3$ in **4**, and downfield shift in the ^{13}C signal for the same. The predicted ^{13}C shifts are in good agreement, and, while there is a large disparity in the predicted and observed ^{19}F chemical shifts, it should be noted that the *difference* between chemical shifts is approximately the same (15.9 vs. 17.3), i.e. the errors are systematic. The differences are likely attributable to errors of the method, as has been reported [15].

In order to examine the two mechanisms hypothesized for formation of **4** and **5**, the vertical ionization energies, partial atomic charges (condensed to atom), calculated Fukui functions, and ionization energy and electron affinity of ketene dimethylacetal (**2**), HFTA (**3**) and methyl vinyl ether (**6**) were calculated using the B3LYP method and are shown in Fig. 1.

The first proposed mechanism (electron transfer) is not consistent with the calculated ionization energy of **2** (6.4 eV) and electron affinity of **3** (−4.1 eV). According to the calculations, an energy deficit of 2.3 eV would need to be overcome in order for