JOC Note

Reactive Dications: The Superacid-Catalyzed Reactions of Alkynes Bearing Adjacent *N*-Heterocycles or Amine Groups

Douglas A. Klumpp,*,† Rendy Rendy, Yun Zhang,
Aaron McElrea, Alma Gomez, and Han Dang

Department of Chemistry and Biochemistry, Northern Illinois University, DeKalb, Illinois, 60115, and Department of Chemistry, California State Polytechnic University, 3801 West Temple Avenue, Pomona, California 91768

dklumpp@niu.edu

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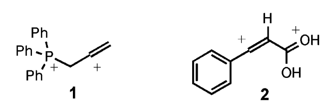
Abstract: A variety of aminoalkynes and related heterocycles are reacted in the Bronsted superacid CF_3SO_3H (triflic acid), and products are obtained in generally good yields (69−99%) from Friedel−Crafts-type reactions. The reactions are consistent with the formation of novel dicationic intermediates having a vinyl cationic site and an adjacent protonated *N*-heterocycle or ammonium cation.

Vinyl cations have been of general interest since the first report of these reactive intermediates and their chemistry has been extensively reviewed.[1] We recently described the reactions of propargyl-substituted phosphonium salts with superacidic triflic acid (CF_3SO_3H, TfOH) in benzene.[2] The results were consistent with the formation of a dicationic intermediate (**1**) composed of a vinylic cation center and an adjacent phosphonium cation center. In another recent paper, we proposed a dicationic intermediate (**2**) composed of a vinyl cation and protonated carboxylic acid group.[3] To our knowledge, these were the first reports to propose reactive, dicationic intermediates involving vinyl cation centers. Several earlier studies clearly involved these types of dicationic intermediates,[4] but either no mechanism was suggested,[4a−d] or the mechanistic proposal incorrectly employed monocationic intermediates.[4e] For example, the acid-catalyzed cyclizations of propargyl-substituted benzylamines have been reported (eqs 1 and 2) and dicationic intermediates (**3** and **4**) are likely involved.[4b,c]



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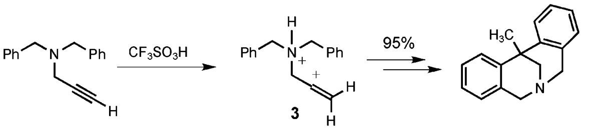

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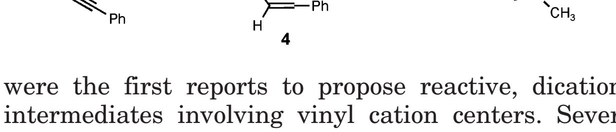

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(2)

Olah was the first to recognize the importance of reactive, dicationic electrophiles. Based on results from superacid-catalyzed reactions, superelectrophilic intermediates were proposed, like the protionitronium ion (NO_2H^{2+}) and the protioacetyl ion (CH_3COH^{2+}).[5] Superelectrophilic intermediates have since been proposed in a variety of acid-catalyzed conversions and studied by experimental and theoretical methods.[6] Superelectrophilic intermediates have been proposed in the conversions involving nitriles,[7] hydrogen cyanide,[7] diazonium salts,[8] and carbon monoxide.[9] However, there has been no systematic study of alkynes and their possible formation of dicationic electrophiles (or superelectrophiles). In the following report, we describe our studies of the superacid-catalyzed chemistry of alkynes bearing an adjacent *N*-heterocycle or amine functional groups. We propose a general mechanism that invokes reactive dicationic intermediates composed of vinylic cations and adjacent protonated *N*-base sites.

Alkynes with an adjacent *N*-heterocycle group are found to give the addition products from TfOH and C_6H_6. For example, the ethynyl-substituted imidazole (**5**) gives product **6**, while the propargyl-substituted benzotriazole (**7**) gives the addition product (**8**) in high yield (Figure 1). Both reactions give the *gem*-diphenyl group on the products suggesting that two reactive dications are generated. For the benzotriazole, the vinylic dication **10** and the benzylic dication **12** are the electrophilic intermediates leading the product **8**. Dication **10** is likely in equilibrium with the corresponding vinyl triflate (**11**).[4a] Although the arylation of alkynes with strong mineral acids has been known for many years,[10] these reports generally note the formation of significant amounts of polymeric "char." Dications such as **10** and **12** are probably more electrophilic than the analogous vinyl cations from protonation of simple alkynes (i.e., mono-

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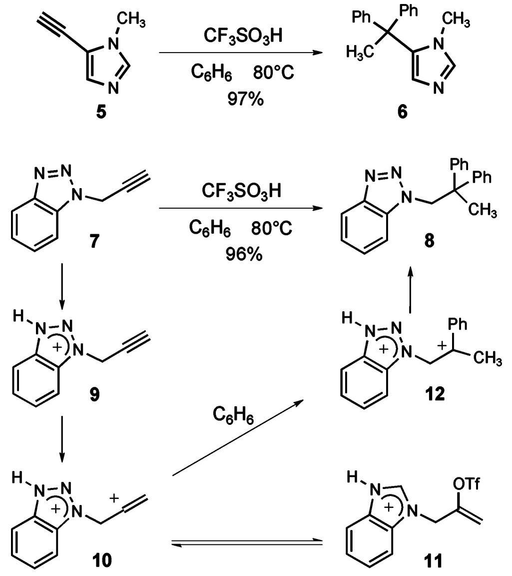
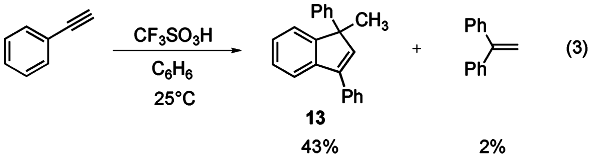


FIGURE 1. Conversions of alkynes **5** and **7** in CF_3SO_3H and C_6H_6, along with the proposed mechanism for the addition reaction.

cations), yet there is no evidence of oligomerization or polymerization with the reaction of **7** (or other alkynes in this study). Oligomerization reactions are suppressed by electrostatic repulsion between intermediates such as **9** and **10**. In contrast, the reaction of phenylacetylene under similar conditions gives a dimerization product (**13**) as the major product (eq 3).[11] The indene (**13**) likely arises from the formation of the 1,1-diphenylethyl cation followed by reaction steps including the electrophilic attack on a phenylacetylene and cyclization.



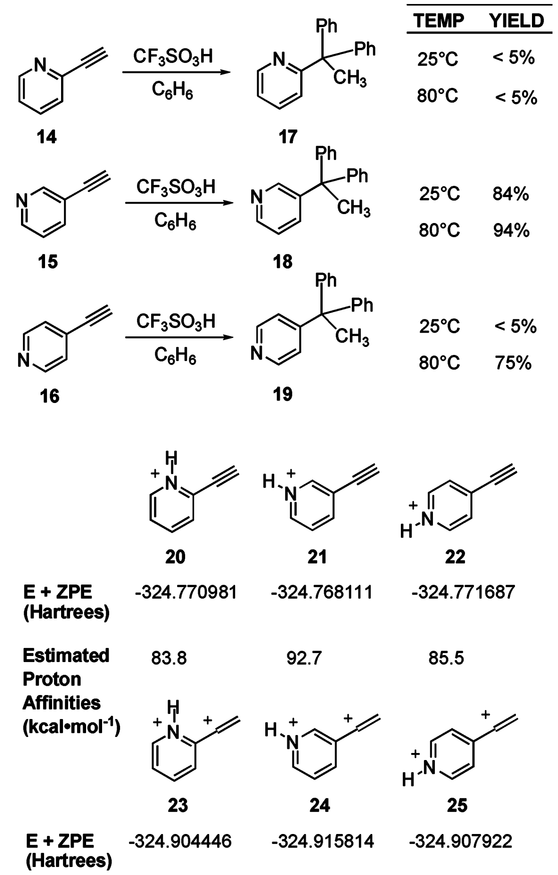
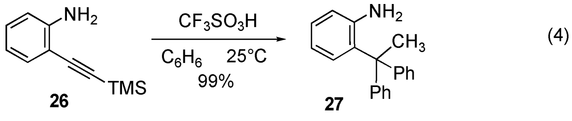
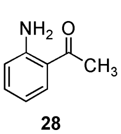


FIGURE 2. Yields from the reactions of ethynylpyridines (**14**–**16**) with CF_3SO_3H and C_6H_6 and the energies of proposed cationic intermediates.

When the regioisomers of ethynylpyridine (**14**–**16**) are reacted with TfOH and C_6H_6 at 25 °C (Figure 2), only the 3-ethynylpyridine (**15**) gives the addition product (**18**) in good yield. The conversion of **15** to **18** is also consistent with the formation of dicationic electrophiles, including one involving the vinyl cation. At 80 °C, 4-ethynylpyridine (**16**) is converted to the addition product (**19**) in higher yield, while at the same temperature, the 2-ethynylpyridine (**14**) is largely unreacted. Within the ethynylpyridine series, the 3-isomer is clearly the most reactive and the 2-isomer is the least reactive. This trend is in good agreement with the estimated gas-phase proton affinities of the monocationic intermediates (**20**–**22**). Ab initio calculations[12] were done and the results indicate that the 3-ethynylpyridinium cation (**21**) is the least stable monocationic species in the series, while the corresponding dication (**24**) is the most stable diprotonated species (Figure 2). Thus, ion **24** should be the most easily formed dication. In a similar respect, dication **23** from 2-ethynylpyridine is predicted to be the least favorable dication to be formed in the series, and this is in accord with the sluggish reactivity of 2-ethynylpyridine in TfOH.

The aniline derivative **26** gives the addition product (**27**) in quantitative yield (eq 4). Product **27** is the result of the addition reaction steps and the protolytic cleavage of the silyl group. Compound **26** was also reacted with less reactive arenes, chlorobenzene, and *o*-dichlorobenzene. In the reaction of **26**, C_6H_5Cl, and TfOH (80°C),

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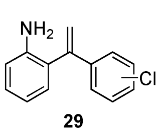
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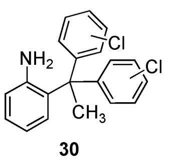
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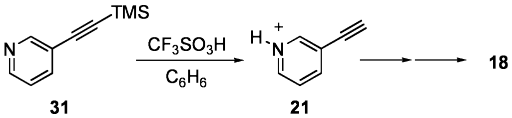
(11) ,1-diphenylethanol and acetophenone were also detected as minor products (<5% yield); a similar conversion was reported from H_3PO_4–BF_3; see: (a) Ryabov, V. D.; Korobkov, V. Yu. *Kinet. Katal.* **1979**, *20* (6), 1599. (b) Ryabov, V. D.; Korobkov, V. Yu. *Zh. Org. Khim.* **1980**, *16* (2), 377.

(12) Computations were done using *Gaussian 98W*, version 5.4, rev. A.9, Gaussian, Inc., Carnegie, PA. Geometry optimization and frequency calculations were done at the B3LYP 6-311G (d,p) level of theory and structures **20**–**25** were found at stationary points with zero imaginary frequencies. For details complete details of the calculations, see the Supporting Information.

three types of products are observed (**28**−**30**, ratio 1:4:1). Product **28** is simply from alkyne hydration (probably via the vinyl triflate), while **29**−**30** are the expected addition products. When **26** is reacted with o-$C_6H_4Cl_2$ in TfOH (80 °C), the monoaddition product (like **29**) is formed as only a minor product (ca. 20%) and the balance of starting material yields **28**.

When compounds **15** or **26** are reacted with C_6H_6 in H_2SO_4 at 80 °C, little or no addition products are formed. The 3-ethynylpyridine (**15**) gives primarily 3-acetylpyridine, while compound **25** is converted quantitatively to the ketone (**28**). These results suggest that the ethynyl groups of **15** and **26** are being protonated in H_2SO_4, but the transient vinylic dications are rapidly (and irreversibly) captured by the hydrogen sulfate anion. In contrast, the superacidic TfOH generates the vinylic dications in higher concentrations, or with longer lifetimes, enabling these electrophiles to react with benzene.

Although β-silyl stabilzation of vinyl cations has been demonstrated in other systems,[13] in this study the trimethylsilyl groups are rapidly cleaved from alkynes at 25 °C in superacidic CF_3SO_3H.[14] In comparing the reactivities of 3-ethynylpyridine (**15**) with 3-(trimethylsilylethynyl)-pyridine (**31**), the addition reactions occur at similar rates, and in the case of **31**, GC analysis shows that the TMS group is initially cleaved to give the ethynyl group and then the addition reaction occurs (eq 5).



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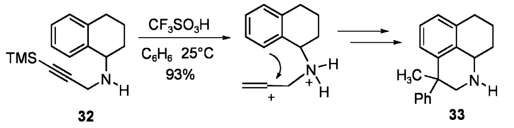
Propargyl-substituted benzylamines are known to undergo cyclization reactions in strong and superacidic solutions (eqs 1 and 2). When reacted with benzene and TfOH, both **32** and **34** give products which arise from cyclization and the addition of one benzene (eqs 6 and 7). According to ^1H NMR and GC analysis, product **33** is formed as a single diastereomer. Both of conversions likely involve dicationic intermediates having ammonium and vinylic cationic centers. Since no *gem*-diphenyl products are formed, this suggests cyclization occurs first, and phenylation occurs in a subsequent step (eq 6).

When the optically active amine (**36**) is reacted with TfOH and C_6H_6 at 80°C, the cyclization and addition give products **37a**,**b** in 85% overall yield (eq 8). Analysis of the products by NMR indicates the formation of diastereomeric structures (**37a**,**b**) in 29% diastereomeric excess. The two products are inseparable by column chromatography, so it is not presently clear which diastereomer is preferentially formed. Efforts to improve the stereoselectivity by conducting the reaction at lower temperatures (+25 and −15 °C) were not successful. At −15 °C, no cyclization is observed and the desilylated alkyne is recovered. Similar results were also obtained from the secondary amine **38**.



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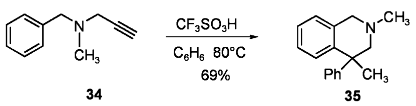

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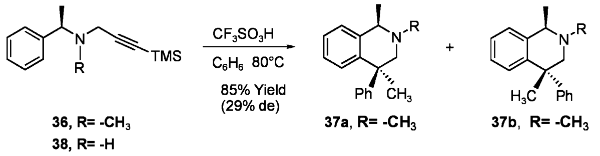

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In summary, aminoalkynes and related heterocyclic systems react with superacidic CF_3SO_3H to generate dicationic electrophiles that are capable of reacting with benzene and other arenes. These novel species are composed of vinyl cations with adjacent positive charge centers (pyridinium, ammonium, etc.) and can be used to prepare products in good yields (69−99%) from inter- and intramolecular reactions. With the present results involving *N*-heterocycles and amines, we further demonstrate the possibility of generating dicationic species having a vinyl cationic site and another adjacent cationic center.

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Supporting Information Available: Characterization data and spectra, representative experimental procedures, and computational data. This material is available free of charge via the Internet at http://pubs.acs.org.

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