

# Reactions of 1,5-Diaryl-3-(trifluoromethyl)pent-1-en-4-yn-3-yl Cations with Benzene in TfOH. Synthesis of CF<sub>3</sub>-“Helicopter”-Like Molecules

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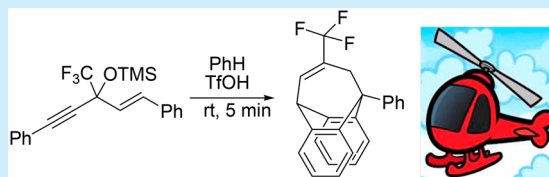
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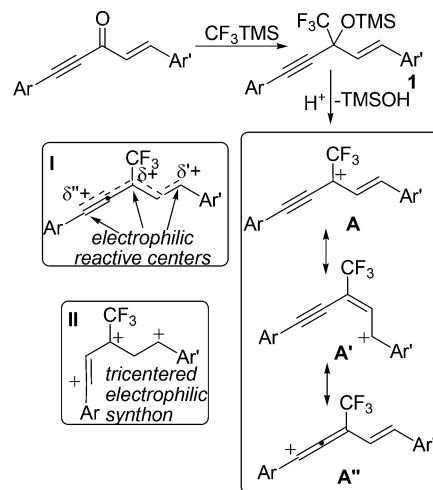
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## Supporting Information

**ABSTRACT:** Trimethylsilyl ethers of 1,5-diaryl-3-(trifluoromethyl)pent-1-en-4-yn-3-oles in superacid CF<sub>3</sub>SO<sub>3</sub>H (TfOH) give rise to the corresponding intermediate CF<sub>3</sub>-pentenynyl cations. These species react with benzene to afford conjugated CF<sub>3</sub>-pentenynes, which undergo subsequent cyclization, first, into CF<sub>3</sub>-cycloheptadienes and, finally, into unusual CF<sub>3</sub>-“helicopter”-like bicyclic structures.



**Scheme 1.** Synthesis of CF<sub>3</sub>-TMS Ethers **1** and Generation from Cations **A**



Fluoroorganics are of very great importance in chemistry, biology, medicine, physics, and material science. Because of the unique properties of fluorine-containing groups (high electronegativity and lipophilicity), these substances are widely used as drugs, monomers for polymerization, and components of molecular sensors, as evidenced by recent books and reviews on chemistry and the applications of organofluorine compounds.<sup>1–10</sup>

Based on our recent transformations<sup>11–14</sup> of trifluoromethyl-substituted carbocations generated from CF<sub>3</sub>-allyl alcohols in Brønsted superacids (CF<sub>3</sub>SO<sub>3</sub>H, FSO<sub>3</sub>H), or Lewis acids (FeCl<sub>3</sub>, AlCl<sub>3</sub>, AlBr<sub>3</sub>), we undertook a study of the reactions of TMS ethers of 1,5-diaryl-3-(trifluoromethyl)pent-1-en-4-yn-3-oles (**1**) in the superacid CF<sub>3</sub>SO<sub>3</sub>H (TfOH) (Scheme 1).

The starting compounds **1** were obtained from the corresponding ketones with the Ruppert–Prakash reagent CF<sub>3</sub>TMS (CF<sub>3</sub>SiMe<sub>3</sub>) according to the literature procedure.<sup>15,16</sup> Under the action of Brønsted acid, CF<sub>3</sub>-TMS ethers **1** gave rise to the CF<sub>3</sub>-enynyl cations **A**, which can be represented as mesomeric forms **A'** and **A''** with delocalization of positive charge in double and triple carbon–carbon bonds correspondingly. In general, these cations may be shown as structures **I** having three electrophilic centers (Scheme 1). From a synthon approach, compounds **1** are precursors of hypothetical tricationic species **II**, derived from protonation of TMSO group (followed by elimination of TMSOH) and  $\pi$ -bonds. Thus, cations **A** may act as multicentered electrophiles reacting with nucleophiles at different positions.

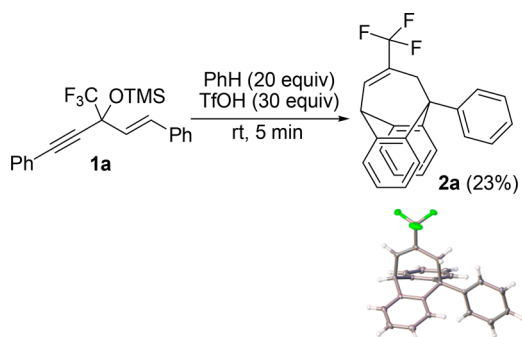
The main goal of this work was a study of reactivity of CF<sub>3</sub>-enynyl cations **A** in TfOH. This superacidic medium was chosen due to its high protonation ability and its low nucleophilicity, which would help to generate intermediate

species **A** and suppress reactions with the acid counteranion (triflate anion).<sup>17–19</sup>

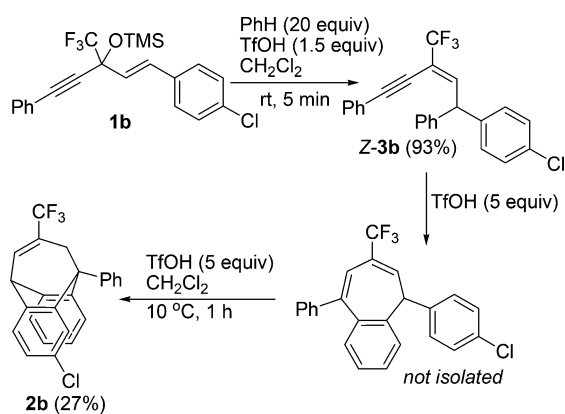
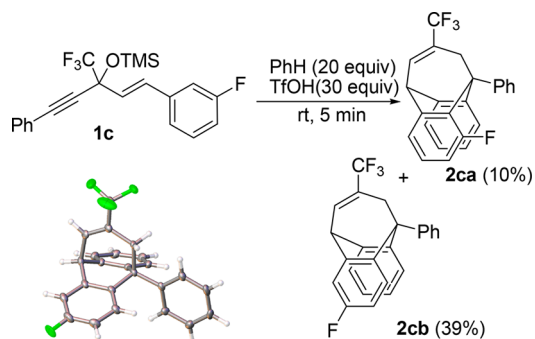
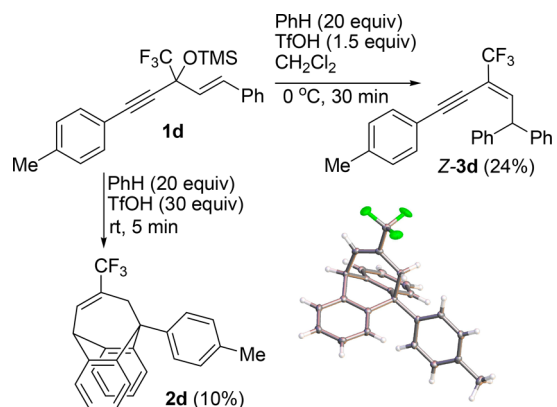
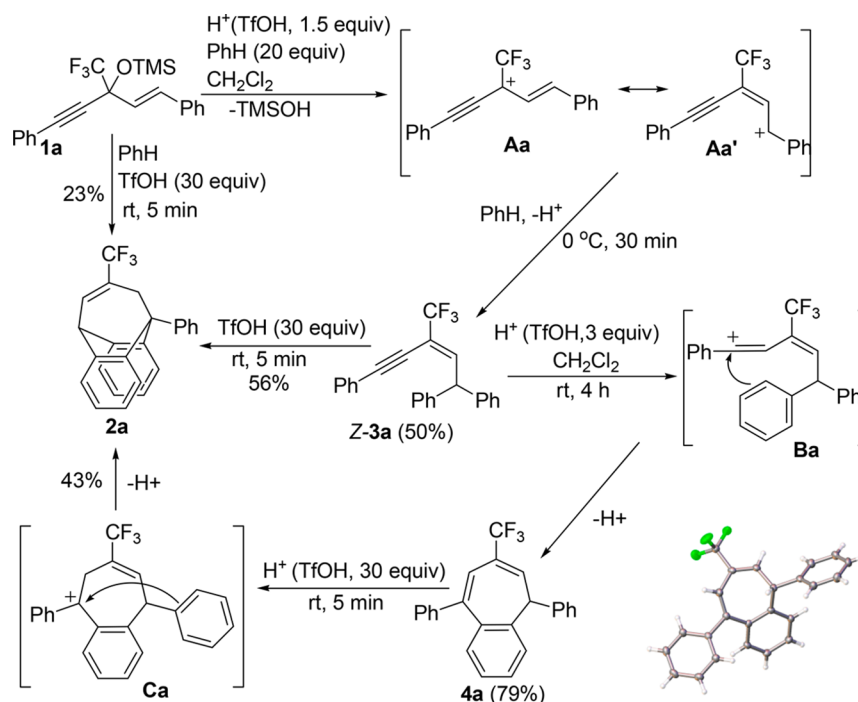
First, we checked a reaction of 3-(trifluoromethyl)-1,5-diphenyl pent-1-en-4-yn-3-ole (**1a**) in TfOH, which gave a complex mixture of oligomers. In contrast, the reaction of **1a** with 20 equiv of C<sub>6</sub>H<sub>6</sub> in TfOH (30 equiv) at room temperature for just 5 min resulted in the formation of unusual bicycle **2a** (Scheme 2), which may be viewed as a CF<sub>3</sub>-

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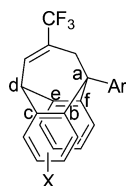
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Scheme 2. Transformation of **1a** and Benzene into "Helicopter"-like Molecule **2a** in TfOH<sup>a</sup><sup>a</sup>X-ray of **2a** (ellipsoid contours of probability levels are 50%).

Scheme 3. Synthesis of Z-3b and 2b from 1b

Scheme 5. Synthesis of **2ca** and **2cb** from **1c**<sup>a</sup><sup>a</sup>X-ray of **2cb** (ellipsoid contours of probability levels are 50%).Scheme 6. Synthesis of Z-3d and 2d from **1d**<sup>a</sup><sup>a</sup>X-ray of **2d** (ellipsoid contours of probability levels are 50%).Scheme 4. Consecutive Transformations of **1a** into Z-3a, **4a**, and **2a** in TfOH<sup>a</sup><sup>a</sup>X-ray of **4a** (ellipsoid contours of probability levels are 50%).

**Table 1.** Selected Geometric Parameters of Cyclohexane Boat Conformer a–b–c–d–e–f in “Helicopter”-like Structures 2



molecule	angles between planes (deg)	
	(cde)^(bcef)	(abf)^(bcef)
2a <sup>a</sup>	141.0 (1)	145.3 (2)
	142.2 (1)	145.4 (2)
2cb <sup>a</sup>	140.8 (1)	145.4 (2)
	141.9 (1)	146.0 (2)
2d	140.8(1)	145.5(2)

<sup>a</sup>Two symmetric independent molecules in the unit cell.

“helicopter”-like structure. The CF<sub>3</sub> group may be considered as a propeller, and the phenyl ring is a tail in “helicopter” 2a (see its X-ray structure in Scheme 2 and the Supporting Information). We also studied the reactions of other CF<sub>3</sub>-TMS ethers 1b–d (see Schemes 3, 5, and 6).

We decided to investigate this intriguing reaction deeper by changing reaction conditions (amount of TfOH, temperature, time), trying to catch intermediate compounds on the way of formation of 2a.

The use of 1.5 equiv of TfOH in CH<sub>2</sub>Cl<sub>2</sub>, as a solvent, at 0 °C for 30 min led to conjugated CF<sub>3</sub>-pentyne Z-3a in 50% yield (Scheme 4). In this case, the intermediate cation, as the mesomeric form Aa', reacted with benzene. The Z-configuration of 3a and other CF<sub>3</sub>-pentyne 3 (see below) was unambiguously determined by a NOESY correlation between vinyl proton and the CF<sub>3</sub> group. The isolated Z-3a was, in the next reaction, exposed to 3 equiv of TfOH in CH<sub>2</sub>Cl<sub>2</sub> at room temperature for 4 h, which afforded cycloheptadiene 4a (yield of 79%), through vinyl cation Ba (Scheme 4). The structure of 4a was confirmed by X-ray data (see Scheme 4).

It was found that when 4a was submitted to an excess of TfOH (30 equiv) at room temperature for just 5 min, 2a was obtained in a yield of 43%, through, most probably, the cation Ca (Scheme 4). When submitted to neat TfOH, enyne Z-3a gave 2a directly in 56% yield after 5 min at room temperature. This data clearly reveal that structures Z-3a and 4a lie on the route to 2a from 1a through intermediate cations Aa, Ba, and Ca (Scheme 4). One may stop the reaction at the any step by changing the amount of TfOH, the time and the temperature. The use of 1.5 equiv of TfOH in CH<sub>2</sub>Cl<sub>2</sub> and a short time allows one to stop this reaction at the stage of Z-3a, which further may be consequently converted into 4a and 2a. Conducting the reaction of 1a in excess of neat TfOH leads directly to 2a (Scheme 1). The formation of 2a is a cascade process involving several cationic species generated from 1a and products of its transformations in TfOH.

Chloro-substituted compound 1b reacted with benzene in the presence of 1.5 equiv of TfOH and gave, first, CF<sub>3</sub>-enyne Z-3b (in high yield of 93%), which then was converted into the “helicopter” 2b in the presence of excess of TfOH without isolation of the corresponding intermediate benzocycloheptadiene (Scheme 3).

Compound 1c, bearing a *meta*-fluorophenyl substituent at the double bond, reacted with benzene in neat TfOH to afford two regioisomeric bicycles 2ca and 2cb in an overall yield of 49% (Scheme 5). The structure of the latter was determined by X-ray analysis. These two isomers were formed by electrophilic substitution into different positions of the *m*-fluorophenyl ring at the last step of the reaction (see analogous transformation for Ca → 2a in the mechanism in Scheme 4).

The reaction of compound 1d, having an electron-donating *p*-methylphenyl (*p*-tolyl) ring at the acetylene bond, led to the corresponding products Z-3d and 2d in much lower yield (Scheme 6). In this case, protonation of the electron-rich acetylene bond may easily take place in intermediate structures, that help direct the reaction to other additional channels, leading to the formation of oligomeric materials.

It should be noted that compounds 2a–d have been obtained in a multistep process, that leads to low-moderate yields (10–49%).

The conformations of molecules of 2a, 2cb, 2d are practically equal (see SI). The central dibenzocyclohexa-1,4-diene exists in a boat conformation. The angles between the planes in this ring are given in Table 1. The edges (c–d–e and a–b–f) of the boat are bent to the base (b–c–e–f), and the difference between the slopes is not big (see angles in Table 1).

It is interesting to note that all aromatic protons in the “tail”-aryl (phenyl or *p*-tolyl) ring of compounds 2 give separate unequivalent signals in their <sup>1</sup>H NMR spectra, due to the restricted rotation of this ring between two other arene moieties in the bicyclic system.

Combination of both a pharmacophore CF<sub>3</sub> group and the rigid carcass in the structure of compounds 2 might make them very promising drugs. As an example, see our recent work on biological activity of CF<sub>3</sub>-indanes.<sup>20</sup>

In conclusion, we have found that TMS ethers of 1,5-diaryl-3-trifluoromethyl pent-1-en-4-yn-3-oles react with benzene in the superacid TfOH to give several novel CF<sub>3</sub>-containing compounds, including interesting bicyclic CF<sub>3</sub>-“helicopter”-like structures

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.7b03920.

Experimental procedures, characterization of compounds, and <sup>1</sup>H, <sup>13</sup>C, and <sup>19</sup>F NMR spectra (PDF)

## Accession Codes

CCDC 1575538, 1589555, and 1589960–1589961 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via [www.ccdc.cam.ac.uk/data\\_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif), or by emailing [data\\_request@ccdc.cam.ac.uk](mailto:data_request@ccdc.cam.ac.uk), or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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## Notes

The authors declare no competing financial interest.

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