TfOH-Promoted Reaction of 2,4-Diaryl-1,1,1-Trifluorobut-3-yn-2-oles with Arenes: Synthesis of 1,3-Diaryl-1-CF₃-Indenes and Versatility of the Reaction Mechanisms

Aleksey V. Zerov ¹, Anna N. Kazakova ¹, Irina A. Boyarskaya ¹, Taras L. Panikorovskii ², Vitalii V. Suslonov ³, Olesya V. Khoroshilova ³ and Aleksander V. Vasilyev ¹, 4, *

¹ Department of Organic Chemistry, Institute of Chemistry, Saint Petersburg State University, Universitetskaya nab., 7/9, Saint Petersburg 199034, Russia; lfdse@mail.ru (A.V.Z.); a.kazakova0@gmail.com (A.N.K.); iralbo@yahoo.com (I.A.B.)
² Department of Crystallography, Institute of Earth Sciences, Saint Petersburg State University, Universitetskaya nab., 7/9, Saint Petersburg 199034, Russia; taras.panikovskvy@spbu.ru
³ Center for X-ray Diffraction Studies, Research park, St. Petersburg State University, Universitetskiy pr. 26, Saint Petersburg, Petrodvoretz198504, Russia; v.suslonov@spbu.ru (V.V.S.); o_khoro@mail.ru (O.V.K.)
⁴ Department of Chemistry, Saint Petersburg State Forest Technical University, Institutsky per., 5, Saint Petersburg 194021, Russia

* Correspondence: aleksvasil@mail.ru; Tel.: +7-812-670-9352; Fax: +7-812-670-9390

Abstract: The TfOH-mediated reactions of 2,4-diaryl-1,1,1-trifluorobut-3-yn-2-oles (CF₃-substituted diaryl propargyl alcohols) with arenes in CH2Cl2 afford 1,3-diaryl-1-CF₃-indenes in yields up to 84%. This new process for synthesis of such CF₃-indenes is complete at room temperature within one hour. The synthetic potential, scope, and limitations of this reaction were illustrated by more than 70 examples. The proposed reaction mechanism invokes the formation of highly reactive CF₃-propargyl cation intermediates that can be trapped at the two mesomeric positions by the intermolecular nucleophilic attack of an arene partner with a subsequent intramolecular ring closure.

Keywords: trifluoromethyl propargyl alcohols; trifluoromethyl indenes; triflic acid; propargyl cations; cationic reaction mechanism

1. Introduction

Acetylene compounds are of great importance for chemistry, biology, medicine, materials science, and other fields of science and technology [1–11]. Fluorinated acetylene derivatives are useful building blocks in organic synthesis for the preparation of new substances and materials with valuable practical properties. The presence of fluorine atoms in organic compounds gives the compounds unique characteristics, such as high lipophilicity and biological activity, heat resistance, nonlinear optical and liquid crystal properties, and so forth [12–16]. Synthesis of new organofluorine derivatives is an actual goal of modern organic chemistry.

Among the variety of acetylene compounds, propargyl alcohols play an important role in the synthesis of miscellaneous substances. For instance, they have been widely used in Friedel-Crafts alkylation catalyzed by Brønsted [17–23] or Lewis [24–35] acids. However, reactions of trifloromethyl-substituted propargyl alcohols in electrophilic media have not been studied yet.

Based on our work on the electrophilic activation of unsaturated compounds (alkynes, alkenes, allenes) [36], we undertook a special study on the transformation of
trifluoromethyl-substituted propargyl alcohols. The main goal of this work was to investigate reactions of 2,4-diaryl-1,1,1-trifluorobut-3-yn-2-oles (CF₃-propargyl alcohols) with arenes under the action of various Brønsted and Lewis acids.

The starting diaryl-substituted CF₃-propargyl alcohols 1a–r bearing various substituents in aromatic rings are shown in Figure 1. They were obtained from the corresponding 1,3-diarylpropynones by trifluoromethylation-O-trimethylsilylation of the carbonyl group followed by a desilylation stage (see synthetic procedures in the Supplementary Materials).

![Figure 1. Starting CF₃-propargyl alcohols used in this study.](image)

**2. Results and Discussion**

One may propose several ways of conducting transformations of alcohols 1 in acidic media (Scheme 1). First, the protonation of the hydroxyl group takes place with the formation of cation A. Elimination of water from it gives the propargyl cation B, which may be presented as two mesomeric forms, B′↔B′′, having two electrophilic reactive centers on carbons C₂ and C₄, respectively. Species A and B′, with their electrophilic center on carbon C₂, may react with the arene, Ar′H, leading to alkyne 3 (way a). Protonation of the latter gives rise to the vinyl cation D, which may undergo cyclization into the aryl groups Ar′ or Ar′′, with the formation of indenes 4 or 7, respectively.

![Scheme 1. Plausible mechanisms of acid-promoted reactions of CF₃-alcohols 1 with arenes.](image)

Another reaction pathway is the reaction of the arene with species B′′ onto its electrophilic carbon C₄, which affords allene 2. Protonation of the latter gives the mesomeric allyl cation C″↔C‴. Species C‴
may be cyclized into both rings Ar" and Ar, leading to indenes 4 and 5, respectively (way b). One more possible pathway for this allyl cation is cyclization through its resonance form C", giving rise to indene 6 (way c).

To estimate the electronic characteristics of the initial intermediates A and B of these reactions, DFT (density functional theory) calculations of species Aa and Ba (B'a→B''a) derived at the protonation of alcohol 1a were carried out (Table 1). Energies of the HOMO (highest occupied molecular orbital) and LUMO (lowest unoccupied molecular orbital), charge distribution, the contribution of the atomic orbitals into the molecular orbital, and the global electrophilicity index \( \omega \) were calculated. The calculations show that species Ba should be a rather active electrophile, since it is characterized by a large value of the electrophilicity index \( \omega \), of 7.59 e, compared to species Aa, with \( \omega \) of 3.92 e. The cation Aa has a large positive charge of 1.00 e on carbon C2. This carbon gives a larger contribution into the LUMO of 28.5%. This proves that carbon C2 in the species Aa is an electrophilic reactive center according to both charge and orbital factors.

| Caption | \( E_{\text{HOMO}} \) eV | \( E_{\text{LUMO}} \) eV | \( \omega \), eV | \( q(C^2) \) b, e | \( k(C^2)\text{LUMO} \), % | \( k(C^2)\text{HOMO} \), % |
|---------|-----------------|-----------------|----------------|-----------------|-----------------|-----------------|
| Aa | -7.40 | -3.57 | 3.92 | 1.00 | -0.34 | 13.2 | 9.4 |
| Ba (B'a ↔ B''a) | -7.69 | -5.03 | 7.59 | 0.043 | 0.23 | 28.5 | 19.9 |

\( a \) Global electrophilicity index \( \omega = (E_{\text{HOMO}} + E_{\text{LUMO}})^2 / 8(E_{\text{LUMO}} - E_{\text{HOMO}}) \). \( b \) Natural charges. \( c \) Contribution of the atomic orbital into the molecular orbital.

Contrary to that, the cation Ba has a larger positive charge, of 0.23, on carbon C4. However, carbon C2 gives a larger contribution into the LUMO, of 28.5%. This suggests that in this species, the electrophilic reactivity of the atom C4 is ruled under charge control, but the reactivity of the atom C2 may be explained by orbital control.

Thus, there are three main pathways, a, b, and c, for the reactions of CF3-propargyl alcohols with arenes, proceeding through various cationic intermediates which may lead to various CF3-indenes (Scheme 1). A key point in this reaction mechanism is a possible dual reactivity of propargyl cations B (B'↔B''), which may finally lead to different indene structures.

To determine the dependence of the reaction pathway on the substituents in the aromatic rings in alcohols 1 and arenes, starting substrates containing various donor and acceptor substituents in aryl moieties were investigated in these reactions.

First, we conducted reactions of alcohol 1a with benzene under the action of different Brønsted and Lewis acids (Table 2). In all cases, indene 4aa was obtained. However, a better result with the highest yield of 4aa was achieved for the reaction with the use of 1.5 equivalents of trifluoromethanesulfonic acid CF3SO3H (triflic acid, TIOH) at room temperature for 1 h (entry 3, Table 2).
the phenyl one) at carbon C4 in cations (entries 9–11). Compounds 5a are formed at the cyclization into the electron-rich aryl ring (not into benzene). The highest yield of 4aa was achieved for the reaction with the use of 1.5 equivalents of TfOH, r.t., 1 h, and the reaction products 4a, 5a, and 6 were formed by means of TfOH-promoted reaction of alcohols.

Maintaining these conditions (1.5 equiv. of TfOH, r.t., 1 h), we conducted reactions of other alcohols 1 with various arenes, benzene (Table 3), ortho-xylene (Scheme 2), para-xylene (Table 4), meta-xylene (Table 5), pseudocumene (1,2,4-trimethylbenzene, Table 6), and veratrole (1,2-dimethoxybenzene, Table 7). These reactions led to compounds 3, 4, 5, and 6. Structures of these substances were determined by means of $^1$H, $^{13}$C, and $^{19}$F-NMR, HRMS, and X-ray single crystal structure analysis (see Figure 2).

Table 2. Acid-promoted reaction of 1a with benzene.

| Entry | Acid | Temperature, °C | Time, h | Yield of 4aa, b % |
|-------|------|-----------------|---------|------------------|
| 1     | TfOH (50 eq.) | r.t. | 1 | 30 |
| 2     | TfOH (50 eq. e) | −35 | 1 | 45 |
| 3     | TfOH (1.5 eq.) | r.t. | 1 | 57 |
| 4     | FSO$_2$H (86 eq. c) | −75 | 1 | 44 |
| 5     | H$_2$SO$_4$ (5 eq.) | r.t. | 1 | 40 |
| 6     | AlCl$_3$ (2 eq.) | r.t. | 1 | 33 |
| 7     | FeCl$_3$ (1 eq.) | r.t. | 1 | 40 |
| 8     | BF$_3$ × Et$_2$O (2 eq.) | r.t. | 72 | 27 d |
| 9     | Sc(OTf)$_3$ (0.1 eq. e) | 85 | 1 | 42 |
| 10    | Cu(OTf)$_2$ (0.1 eq. e) | 85 | 1 | 30 |

a Reaction conditions: acid, solvent CH$_2$Cl$_2$, molar ratio of 1:benzene = 1:50. b Complete conversion of 1a. c Cosolvent was CH$_2$Cl$_2$. d Conversion of 1a was 60%. e Cosolvent was 1,2-dichloroethane. r.t. room temperature.

Table 3. TfOH-promoted reaction of alcohols 1a–f with benzene; reaction conditions: TfOH, CH$_2$Cl$_2$, molar ratio of 1:benzene:TfOH = 1:50:1.5, room temperature, 1 h.

| Entry | Alcohol | Reaction Products 4a, 5a, and 6 (Yield, %, Ratio of Isomers) | Possible Reaction Way and Intermediates from Scheme 1 |
|-------|---------|-------------------------------------------------------------|-----------------------------------------------------|
| 1     | 1a      | 4aa (57%)                                                   | way a: A (or B'), D                                  |
| 2     | 1b      | 4ab (48%)                                                   | way b: B', C'                                       |
Table 3. Cont.

| Entry | Alcohol | Reaction Products 4a, 5a, and 6 (Yield, %, Ratio of Isomers) | Possible Reaction Way and Intermediates from Scheme 1 |
|-------|---------|---------------------------------------------------------------|--------------------------------------------------|
| 3     | HO Ph   |                                                               | way b: $B''$, $C'$                                 |
| 4     | HO Ph   |                                                               | 4ad—way b: $B''$, $C'$; 6a, 6b—way c: $B''$, $C''$       |
| 5     | HO Ph   |                                                               | way a: A (or $B'$), D; way b: $B''$, $C'$              |
| 6     | HO Ph   |                                                               | way a: A (or $B'$), D; way b: $B''$, $C'$              |
| 7     | HO Ph   |                                                               | way a: A (or $B'$), D; way b: $B''$, $C'$              |
| 8a    | HO Ph   |                                                               | way a: A (or $B'$), D; way b: $B''$, $C'$              |
| 9     | HO Ph   |                                                               | way a: A (or $B'$), D; way b: $B''$, $C'$              |
| 10    | HO Ph   |                                                               | way a: A (or $B'$), D; way b: $B''$, $C'$              |

Total yield of 47% ($4ad: 6a: 6b = 5:2:1$)

Total yield of 72% ($4ai: 5aa = 1:3.8$)

Total yield of 47% ($4aj: 5ab = 1:7$)
Table 3. Cont.

| Entry | Alcohol | Reaction Products 4a, 5a, and 6 (Yield, %, Ratio of Isomers) | Possible Reaction Way and Intermediates from Scheme 1 |
|-------|---------|-------------------------------------------------------------|-----------------------------------------------------|
| 11    | ![Structure](image1.png) | ![Structure](image2.png) 1k | way b: B″, C′ |
| 12    | ![Structure](image3.png) | ![Structure](image4.png) 1l | way a: A (or B′), D, way b: B″, C′ |
| 13    | ![Structure](image5.png) | ![Structure](image6.png) 1m | way a: A (or B′), D, way b: B″, C′ |
| 14 a  | ![Structure](image7.png) | ![Structure](image8.png) In | way a: A (or B′), D, way b: B″, C′ |
| 15    | ![Structure](image9.png) | Complex mixture of reaction products | - |
| 16    | ![Structure](image10.png) | Complex mixture of reaction products | - |
| 17    | ![Structure](image11.png) | ![Structure](image12.png) 1q | way a: A (or B′), D, way b: B″, C′ |
| 18    | ![Structure](image13.png) | ![Structure](image14.png) 1r | way a: A (or B′), D, way b: B″, C′ |

* Amount of TfOH was 2.5 equiv.
Table 4. TiOH-promoted reaction of 1 with p-xylene; reaction conditions: TiOH, CH₂Cl₂, molar ratio of 1:p-xylene:TiOH = 1:1:1.5, room temperature, 1 h.

![Diagram of reaction]

| Entry | Alcohol | Reaction Products 4 and 5 (Yield, %, Ratio of Isomers) | Possible Reaction Way and Intermediates from Scheme 1 |
|-------|---------|-------------------------------------------------------|----------------------------------------------------|
| 1     | 1a      | 4ba (75%)                                             | way a: A (or B'), D                                 |
|       |         |                                                       | way b: B″, C'                                      |
| 2     | 1b      | 4bb (66%)                                             | way b: B″, C'                                      |
| 3     | 1c      | 4bc (44%)                                             | way a: A (or B'), D                                 |
|       |         |                                                       | way b: B″, C'                                      |
| 4     | 1d      | 4bd (72%)                                             | way b: B″, C'                                      |
| 5     | 1e      | 4be (60%)                                             | way a: A (or B'), D                                 |
|       |         |                                                       | way b: B″, C'                                      |
| 6     | 1f      | 4bf (74%)                                             | way a: A (or B'), D                                 |
|       |         |                                                       | way b: B″, C'                                      |
| 7     | 1g      | 4bg (45%)                                             | way a: A (or B'), D                                 |
|       |         |                                                       | way b: B″, C'                                      |
| 8     | 1h      | 4bh (84%)                                             | way a: A (or B'), D                                 |
|       |         |                                                       | way b: B″, C'                                      |

*Table 4. TiOH-promoted reaction of 1 with p-xylene; reaction conditions: TiOH, CH₂Cl₂, molar ratio of 1:p-xylene:TiOH = 1:1:1.5, room temperature, 1 h.*
### Table 4. Cont.

| Entry | Alcohol | Reaction Products 4 and 5 (Yield, %, Ratio of Isomers) | Possible Reaction Way and Intermediates from Scheme 1 |
|-------|---------|-------------------------------------------------------|--------------------------------------------------|
| 9     | ![Image](image1) | ![Image](image2) (84%) | way a: A (or B′), D  
way b: B″, C′ |
| 10    | ![Image](image3) | ![Image](image4) total yield of 28% (4bj:5ba = 1.5:1) | way b: B″, C′ |
| 11    | ![Image](image5) | ![Image](image6) (68%) | way a: A (or B′), D  
way b: B″, C′ |
| 12    | ![Image](image7) | ![Image](image8) (59%) | way a: A (or B′), D  
way b: B″, C′ |
| 13a   | ![Image](image9) | ![Image](image10) (70%) | way a: A (or B′), D  
way b: B″, C′ |
| 14    | ![Image](image11) | ![Image](image12) (59%) | way a: A (or B′), D  
way b: B″, C′ |
Table 4. Cont.

| Entry | Alcohol | Reaction Products 4 and 5 (Yield, %, Ratio of Isomers) | Possible Reaction Way and Intermediates from Scheme 1 |
|-------|---------|-------------------------------------------------------|-----------------------------------------------------|
| 15    | ![Image](image1) | ![Image](image2) | ![Image](image3) | **way b**: B″, C′ |
| 16    | ![Image](image4) | ![Image](image5) | ![Image](image6) | **way a**: A (or B′), D Archer! **way b**: B″, C′ |
| 17    | ![Image](image7) | ![Image](image8) | ![Image](image9) | **way a**: A, B′, D Archer! **way b**: B″, C′ |

*a Amount of TfOH was 2.5 equiv.*

Table 5. TfOH-promoted reaction of 1 with m-xylene; reaction conditions: TfOH, CH2Cl2, molar ratio of 1:m-xylene:TfOH = 1:1.1:1.5, room temperature, 1 h.

| Entry | Alcohol | Reaction Products 4 and 5 (Yield, %, Ratio of Isomers) | Possible Reaction Way and Intermediates from Scheme 1 |
|-------|---------|-------------------------------------------------------|-----------------------------------------------------|
| 1     | ![Image](image10) | ![Image](image11) | ![Image](image12) | **way b**: B″, C′ |

total yield of 63% (4aj:5ab = 6:1)
Table 5. Cont.

| Entry | Alcohol | Reaction Products 4 and 5 (Yield, %, Ratio of Isomers) | Possible Reaction Way and Intermediates from Scheme 1 |
|-------|---------|------------------------------------------------------|--------------------------------------------------|
| 2     | ![Image](image1.png) | ![Image](image2.png) | way b: B″, C′ |
|       |         | total yield of 66% (4ca:5ca = 3:1)                   |                                                  |
| 3     | ![Image](image3.png) | ![Image](image4.png) | way b: B″, C′ |
|       |         | total yield of 69% (4cb:5cb = 6:1)                   |                                                  |
| 4     | ![Image](image5.png) | ![Image](image6.png) | way b: B″, C′ |
|       |         | total yield of 69% (4cc:5cc = 5.7:1)                 |                                                  |
| 5     | ![Image](image7.png) | ![Image](image8.png) | way b: B″, C′ |
|       |         | total yield of 60% (4cd:5cd = 4:1)                   |                                                  |
| 6     | ![Image](image9.png) | ![Image](image10.png) | way b: B″, C′ |
|       |         | total yield of 56% (4ce:5ce = 4.9:1)                 |                                                  |
| 7     | ![Image](image11.png) | ![Image](image12.png) | way b: B″, C′ |
| 8     | ![Image](image13.png) | ![Image](image14.png) | way b: B″, C′ |

*Note: Figure not included in text representation.*
Table 5. Cont.

| Entry | Alcohol | Reaction Products 4 and 5 (Yield, %, Ratio of Isomers) | Possible Reaction Way and Intermediates from Scheme 1 |
|-------|---------|-------------------------------------------------------|--------------------------------------------------|
| 9     | ![Alcohol Image](image1) | ![Reaction Products Image](image2) | way b: B′′, C′ |
|       |         | total yield of 56% (4ch:5cf = 2.8:1)                   |                                                  |
| 10    | ![Alcohol Image](image3) | ![Reaction Products Image](image4) | way b: B′′, C′ |
| 11    | ![Alcohol Image](image5) | ![Reaction Products Image](image6) | way b: B′′, C′ |
| 12 a  | ![Alcohol Image](image7) | ![Reaction Products Image](image8) | way b: B′′, C′ |
| 13    | ![Alcohol Image](image9) | Complex mixture of reaction products                  |                                                  |
| 14    | ![Alcohol Image](image10) | Complex mixture of reaction products                  |                                                  |
| 15    | ![Alcohol Image](image11) | ![Reaction Products Image](image12) | way b: B′′, C′ |
|       |         | 4cl (64%)                                             |                                                  |
| 16    | ![Alcohol Image](image13) | ![Reaction Products Image](image14) | way b: B′′, C′ |
|       |         | 4cm (50%)                                             |                                                  |

* Amount of TfOH was 2.5 equiv.
Table 6. TfOH-promoted reaction of 1 with pseudocumene; reaction conditions: TfOH, CH₂Cl₂, molar ratio of 1:pseudocumene:TfOH = 1:1:1:1.5, room temperature, 1 h.

| Entry | Alcohol | Reaction Products 4d and 4e (Yield, %, Ratio of Isomers) | Possible Reaction Way and Intermediates from Scheme 1 |
|-------|---------|----------------------------------------------------------|-------------------------------------------------|
| 1     | La      | ![Product Structure](image1)                              | 4da—way b: B″, C′                                 |
|       |         |                                                           | 4ea—way a: A (or B′), D                           |
|       |         | total yield of 75% (4da:4ea = 11.5:1)                     |                                                 |
| 2     | lb      | ![Product Structure](image2)                              | 4db—way b: B″, C′                                 |
|       |         |                                                           | 4eb—way a: A (or B′), D                           |
|       |         | total yield of 69% (4db:4eb = 11.5:1)                     |                                                 |
| 3     | lc      | ![Product Structure](image3)                              | 4dc—way b: B″, C′                                 |
|       |         |                                                           | 4ec—way a: A (or B′), D                           |
|       |         | total yield of 50% (4dc:4ec = 13:1)                       |                                                 |
| 4     | ld      | ![Product Structure](image4)                              | 4dd—way b: B″, C′                                 |
|       |         |                                                           | 4ed—way a: A (or B′), D                           |
|       |         | total yield of 67% (4dd:4ed = 15.7:1)                     |                                                 |
| 5     | le      | ![Product Structure](image5)                              | 4de—way b: B″, C′                                 |
|       |         |                                                           | 4ee—way a: A (or B′), D                           |
|       |         | total yield of 65% (4de:4ee = 11.5:1)                     |                                                 |
| 6     | lf      | ![Product Structure](image6)                              | 4df—way b: B″, C′                                 |
|       |         |                                                           | 4ef—way a: A (or B′), D                           |
|       |         | total yield of 80% (4df:4ef = 24:1)                       |                                                 |
| 7     | lg      | ![Product Structure](image7)                              | 4eg—way b: B″, C′                                 |
|       |         |                                                           | 4fg—way a: A (or B′), D                           |
|       |         | total yield of 70% (4dg:4eg = 2.7:1)                      |                                                 |
Table 6. Cont.

| Entry | Alcohol | Reaction Products 4d and 4e (Yield, %, Ratio of Isomers) | Possible Reaction Way and Intermediates from Scheme 1 |
|-------|---------|----------------------------------------------------------|--------------------------------------------------|
| 8 a   | ![Image](image) | ![Image](image) | 4dh—way b: B″, C′ 4eh—way a: A (or B′), D total yield of 58% (4dh:4eh = 1.8:1) |
| 9     | ![Image](image) | ![Image](image) | 4di—way b: B″, C′ 4ei—way a: A (or B′), D total yield of 51% (4di:4ei = 12:1) |
| 10    | Complex mixture of reaction products | - | |
| 11    | ![Image](image) | ![Image](image) | 4dj—way b: B″, C′ 4ej—way a: A (or B′), D total yield of 54% (4dj:4ej = 11.5:1) |
| 12    | ![Image](image) | ![Image](image) | 4dk—way b: B″, C′ 4ek—way a: A (or B′), D total yield of 49% (4dk:4ek = 10:1) |
| 13    | ![Image](image) | ![Image](image) | 4dl—way b: B″, C′ 4el—way a: A (or B′), D total yield of 66% (4dl:4el = 13:1) |
| 14    | ![Image](image) | ![Image](image) | 4dm—way b: B″, C′ 4em—way a: A (or B′), D total yield of 65% (4dm:4em = 6:1) |
| 15    | Complex mixture of reaction products | - | |
Table 6. Cont.

| Entry | Alcohol | Reaction Products 4d and 4e (Yield, %, Ratio of Isomers) | Possible Reaction Way and Intermediates from Scheme 1 |
|-------|---------|--------------------------------------------------------|-----------------------------------------------------|
| 16    | ![Alcohol Structure](image1) | ![Reaction Products](image2) | 4dn—way b: B″, C′ |
|       |         |                                                        | 4en—way a: A (or B′), D |
|       |         |                                                        | Total yield of 49% (4dn:4en = 10:1)                   |
| 17    | ![Alcohol Structure](image3) | ![Reaction Products](image4) | 4do—way b: B″, C′ |
|       |         |                                                        | 4eo—way a: A (or B′), D |
|       |         |                                                        | Total yield of 57% (4do:4eo = 11.5:1)                  |

*a Amount of TfOH was 2.5 equiv.

Table 7. TfOH-promoted reaction of 1 with veratrole; reaction conditions: TfOH, CH₂Cl₂, molar ratio of 1:veratrole:TfOH = 1:1.1:1.5, room temperature, 1 h.

| Entry | Alcohol | Reaction Products 4f and 3 (Yield, %, Ratio of Isomers) | Possible Reaction Way and Intermediates from Scheme 1 |
|-------|---------|--------------------------------------------------------|-----------------------------------------------------|
| 1     | ![Alcohol Structure](image5) | ![Reaction Products](image6) | way a: A (or B′), D |
|       |         |                                                        | Total yield of 60% (4fa:3a = 2.8:1)                   |
| 2     | ![Alcohol Structure](image7) | ![Reaction Products](image8) | way a: A (or B′), D |
|       |         |                                                        | Total yield of 49% (4gb:3b = 3.5:1)                   |
| Entry | Alcohol | Reaction Products 4f and 3 (Yield, %, Ratio of Isomers) | Possible Reaction Way and Intermediates from Scheme 1 |
|-------|---------|--------------------------------------------------------|--------------------------------------------------|
| 3     | ![Image](image1) | ![Image](image2) | way a: A (or B'), D |
|       |         |             | total yield of 98% (4fc:3c = 4.9:1) |
| 4     | ![Image](image3) | ![Image](image4) | way a: A (or B'), D |
|       |         |             | total yield of 70% (4ff:3f = 4:1) |
| 5     | ![Image](image5) | ![Image](image6) | way a: A (or B'), D |
|       |         |             | total yield of 44% (4fe:3e = 6:1) |
| 6     | ![Image](image7) | ![Image](image8) | way a: A (or B'), D |
|       |         |             | total yield of 70% (4ff:3f = 4:1) |
| 7a    | ![Image](image9) | ![Image](image10) | way a: A (or B'), D |
|       |         |             | way a: A (or B'), D |
| 8     | ![Image](image11) | Complex mixture of reaction products | - |
| 9     | ![Image](image12) | ![Image](image13) | way a: A (or B'), D |
|       |         |             | total yield of 54% (4fh:3g = 13:1) |
| 10a   | ![Image](image14) | ![Image](image15) | way a: A (or B'), D |
|       |         |             | way a: A (or B'), D |

*Table 7. Cont.*
| Entry | Alcohol | Reaction Products 4f and 3  
(Yield, %, Ratio of Isomers) | Possible Reaction Way and Intermediates from Scheme 1 |
|-------|---------|-----------------------------|--------------------------------------------------|
| 11 a  | ![Alcohol](image) | ![Reaction Products](image) (57%) | way a: A (or B′), D |
| 12    | ![Alcohol](image) | ![Reaction Products](image) total yield of 65% (4fk:3h = 10:1) | way a: A (or B′), D |
| 13    | ![Alcohol](image) | ![Reaction Products](image) total yield of 36% (4fl:3i = 7:1) | way a: A (or B′), D |
| 14    | ![Alcohol](image) | Complex mixture of reaction products | - |
| 15 a  | ![Alcohol](image) | ![Reaction Products](image) (69%) | way a: A (or B′), D |
| 16    | ![Alcohol](image) | Complex mixture of reaction products | - |
| 17    | ![Alcohol](image) | ![Reaction Products](image) total yield of 50% (4fn:3j = 2.8:1) | way a: A (or B′), D |
| 18    | ![Alcohol](image) | ![Reaction Products](image) total yield of 59% (4fo:3k = 2:1) | way a: A (or B′), D |

* Amount of TfOH was 2.5 equiv.
Figure 2. X-ray crystal structures of compounds 4bg (CCDC 1568593), 4ci (CCDC 1578216), 4dc (CCDC 1568602), 4de (CCDC 1568599), 4dg (CCDC 1568594), 4di (CCDC 1563374), 4dk (CCDC 1568596), 4dm (CCDC 1568600), 4fb (CCDC 1568595), 4fc (CCDC 1568597), 4fh (CCDC 1568603), 4fk (CCDC 1568598), and 5ac (CCDC 1568601) (ellipsoid contour of probability levels is 50%), Green sticks are fluorine atoms.
In principle, the structures of the target indenes 4, 5, and 6 reveal the reaction pathway of their formation (ways a, b, c in Scheme 1) and key intermediates of these transformations (A, B, C, and D in Scheme 1). These data are shown in Tables 3–7 for every reaction. In some cases, it is not possible to unequivocally distinguish the reaction pathways based only on the structures of the compounds obtained. However, many reactions clearly point out the mechanism of the formation of the final products.

The data in Table 3 show that for alcohols 1 having phenyl or aryl rings with acceptor groups at the acetylene bond, the only reaction products are indenes of the general structure 4a, obtained as a result of cyclization into a phenyl ring (entries 1–3, 5–8, 12–14, 17, and 18). These compounds may be formed via pathways a or b (Scheme 1).

Alcohols 1 bearing donor methyl groups in the aryl substituent at the triple bond react with benzene to form a mixture of indenes of types 4a and 5a. The latter is the main reaction product (entries 9–11). Compounds 5a are formed at the cyclization into the electron-rich aryl ring (not into the phenyl one) at carbon C^4 in cations C (way a, Scheme 1).

Alcohol 1d, with a 3,4-dimethylphenyl ring at carbon C^2, additionally gave indenes 6a and 6b, which were formed by way c only (see Scheme 1).

Alcohol 1a in reaction with o-xylene afforded indene 5ac (Scheme 2). Again, one may propose two possible directions for the formation of this compound: way a or b (see Scheme 1).

In almost all cases for the reactions of alcohols 1 with p-xylene, indenes of the general structure 4b were obtained (Table 4). These compounds may be formed by way a through the vinyl cation D or way b through the cation C' (Scheme 1).

Additional proof for the proceeding of the reaction of alcohol 1n with p-xylene in way b was the isolation of allene 2a, which then was transformed into indene 4bm in TfOH (Scheme 3).

Based on the structure of the reaction products 4c and 5c obtained from alcohols 1 and m-xylene (Table 5), one may assume that in all cases, the m-xylene molecule is attacked by the electrophilic center C^4 of species B'', which leads to the formation of the corresponding indenes in way b (Scheme 1). The presence of electron-withdrawing substituents in the aryl ring at the atom C^4 prevents electrophilic substitution into this ring, and only indenes 4ci–4cm were isolated (entries 10–12, 15, 16).

Reactions of alcohols 1 with electron-rich pseudocumene afforded two types of indene structures, 4d and 4e, formed by electrophilic substitution onto the pseudocumene moiety only (Table 6). Taking into account that the most active position for electrophilic attack in the pseudocumene molecule is the atom C^5 and that the first reaction occurs in this particular position, one may propose that indenes 4da–4do are formed in way b through cations B'' and C', and indenes 4ea–4eo in way a through cations A (or B') and D (see Scheme 1). The structures of compounds 4d and 4e and positions of the methyl
groups in the indene core were determined by H,H and H,F NOESY correlations between the methyl substituents, CF$_3$ group, and aromatic indene protons (see the Supporting Information).

Surprisingly, reactions of alcohols 1 with veratrole yielded mixtures of alkyne 3 and indene 4f. Moreover, treatment of alkyne 3 with TfOH (1.5 eq.) in CH$_2$Cl$_2$ at room temperature for 1 h gave indene 4f. This data unambiguously proves that reactions with veratrole proceed in way a with the participation of cations A (or B') and D (see Scheme 1).

Summarizing the data obtained on the TfOH-promoted reactions of CF$_3$-propargyl alcohols 1 with different arenes, leading to CF$_3$-indenes (Tables 3–7), one may conclude that these indenes may be formed in several reaction pathways (Scheme 1), depending on the structures of the starting alcohol 1 and the nucleophilicity of the arene. Key intermediates of these reactions are o-protonated forms A of the alcohols and the mesomeric propargyl cations B (B' ↔ B'') generated from alcohols 1 in acidic media (see Scheme 1). Most probably, reactions with electron-rich arenes, pseudocumene (Table 6), and veratrole (Table 7) may proceed through cations A (way a in Scheme 1), which are sufficiently electrophilic (see data on DFT calculations in Table 2) to react with such donating arenes. Reactions with other less nucleophilic arenes, benzene, and xylenes (Tables 3–5) may go both in way a and b (Scheme 1) due to the dual reactivity of the propargyl cation B. However, way b through the allenyl resonance form B'' may be more preferable; see the reactions with m-xylene that proceed mainly in this way (Table 5). Construction of the indene core at the final stages of the reaction depends on the nucleophilicity of the aryl rings Ar, Ar', and Ar'' in the intermediate species C and D. Electrophilic cyclization takes place in the more-donating aromatic moiety.

It should be noted that many of the reactions studied lead to the exclusive formation of only one of CF$_3$-indene 4 or 5 in good yields. Such CF$_3$-indenes are rather rare substrates, and there are only a few reports on their synthesis [39–44].

3. Conclusions

We have studied, for the first time, reactions of diaryl-substituted CF$_3$-propargyl alcohols with arenes under the action of the superacid TfOH. The reaction proceeds through the intermediate formation of several cationic species, which finally lead to the formation of the synthetically hardly available 1,3-diaryl-1-CF$_3$-indenes.

Supplementary Materials: The following are available online. Experimental procedures, characterization of compounds, copies of NMR spectra, and data on DFT calculations.

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References
1. Trost, B.M.; Li, C.J. Modern Alkyne Chemistry: Catalytic and Atom-Economic Transformations, 1st ed.; John Wiley & Sons: Weinheim, Germany, 2014.
2. Stang, P.J.; Diederich, F. Modern Acetylene Chemistry; John Wiley & Sons: Weinheim, Germany, 2008.
3. Diederich, F.; Stang, P.J.; Tykwinski, R.R. Acetylene Chemistry; John Wiley & Sons: Weinheim, Germany, 2005.
4. Xie, J.; Zhang, T.; Mehrkens, N.; Rudolph, M.; Hashmi, A.S.K. A highly efficient gold-catalyzed photoredox α-C(sp$^3$)-H alkynylation of tertiary aliphatic amines with sunlight. Angew. Chem. Int. Ed. 2015, 54, 6046–6050. [CrossRef] [PubMed]
5. Asiri, A.M.; Hashmi, A.S.K. Gold-catalyzed reactions of diynes. Chem. Soc. Rev. 2016, 45, 4471–4503. [CrossRef] [PubMed]
6. Ledovskaya, M.S.; Voronin, V.V.; Rodygin, K.S. Methods for the synthesis of O-, S- and N-vinyl derivatives. *Russ. Chem. Rev.* **2018**, *87*, 167–191. [CrossRef]

7. Voronin, V.V.; Ledovskaya, M.S.; Bogachenkov, A.S.; Rodygin, K.S.; Ananikov, V.P. Acetylene in organic synthesis: Recent progress and new uses. *Molecules* **2018**, *23*, 2442. [CrossRef]

8. Zakharova, E.A.; Shmatova, O.I.; Nenajdenko, V.G. Acetylene-azide click macrocyclization of peptides. *Russ. Chem. Rev.* **2018**, *87*, 619–635. [CrossRef]

9. Larson, G.L. Some aspects of the chemistry of alkynylsilanes. *Synthesis* **2018**, *50*, 2433–2462. [CrossRef]

10. Lewis, D.E. Intramolecular pericyclic reactions of acetylene derivatives leading to dehydroaromatic and related species. *Mini-Rev. Org. Chem.* **2017**, *14*, 107–121. [CrossRef]

11. Trofimov, B.A.; Schmidt, E.Y. Reactions of acetylenes in superbasic media. *Russ. Chem. Rev.* **2014**, *83*, 600–619. [CrossRef]

12. Begue, J.P.; Bonnet-Delpont, D. Bioorganic and Medicinal Chemistry of Fluorine; Published simultaneously in Canada; Wiley: Hoboken, NJ, USA, 2008.

13. Tressaud, A.; Haufe, G. (Eds.) *Fluorine and Health: Molecular Imaging, Biomedical Materials and Pharmaceuticals*, 1st ed.; Elsevier: Amsterdam, The Netherlands, 2008.

14. Petrov, V.A. (Ed.) *Fluorinated Heterocyclic Compounds: Synthesis, Chemistry, and Applications*; Published Simultaneously in Canada; Wiley: Hoboken, NJ, USA, 2009.

15. Nenajdenko, V.G. (Ed.) *Fluorine in Heterocyclic Chemistry*; Springer: Berlin, Germany, 2014.

16. Prakash, R.V. *Organofluorine Compounds in Biology and Medicine*; Elsevier: Amsterdam, The Netherlands, 2015.

17. Ikekame, Y.; Tanayama, M.; Yamauchi, T.; Higashiyama, K. Bronsted Acid Catalyzed Friedel-Crafts Alkylation Reactions of Trifluoromethyl-α,β-ynes with Indoles. *Synlett* **2012**, *23*, 2699–2703. [CrossRef]

18. Kumar, G.G.K.S.N.; Laali, K.K. Condensation of propargylic alcohols with C-, O-, S- and N-centered nucleophiles. *Adv. Synth. Catal.* **2013**, *54*, 965–969. [CrossRef]

19. Sanz, R.; Martínez, A.; Alvarez-Gutiérrez, J.M.; Rodríguez, F. Metal-Free Catalytic Nucleophilic Substitution of Propargylic Alcohols. *Eur. J. Org. Chem.* **2006**, *2006*, 1383–1386. [CrossRef]

20. Sanz, R.; Miguel, D.; Martínez, A.; Gohain, M.; García-Garcia, P.; Fernandez-Rodriguez, M.A.; Alvarez, E.; Rodríguez, F. Bronsted Acid Catalyzed Alkylation of Indoles with Tertiary Propargyl Alcohols: Scope and Limitations. *Eur. J. Org. Chem.* **2010**, *2010*, 7027–7039. [CrossRef]

21. Savarimuthu, S.A.; Prakash, D.G.L.; Thomas, S.A. Nucleophilic substitution of propargyl alcohols with aliphatic alcohols, aliphatic amines and heterocycles catalyzed by 4-nitrobenzenesulfonic acid: A scalable and metal-free process. *Tetrahedron Lett.* **2014**, *55*, 3213–3217. [CrossRef]

22. Gujarathi, S.; Hendrickson, H.P.; Zheng, G. Amberlite IR-120H as an efficient and versatile solid phase catalyst for nucleophilic substitution of propargyl alcohols. *Eur. J. Org. Chem.* **2006**, *2006*, 1383–1386. [CrossRef]

23. Sasaki, S.; Ikekame, Y.; Tanayama, M.; Yamauchi, T.; Higashiyama, K. Bronsted Acid Catalyzed Friedel-Crafts Alkylation Reactions of Trifluoromethyl-α,β-ynes with Indoles. *Synlett* **2012**, *23*, 2699–2703. [CrossRef]

24. Zhan, Z.P.; Yu, J.L.; Liu, H.J.; Cui, Y.Y.; Yang, R.F.; Yang, W.Z.; Li, J.P. A General and Efficient FeCl₃-Catalyzed Propargylic Substitution of Propargylic Alcohols. *J. Org. Chem.* **2006**, *71*, 8289–8301. [CrossRef] [PubMed]

25. Liu, J.; Muth, E.; Flörke, U.; Henkel, G.; Merz, K.; Sauvageau, J.; Schwake, E.; Dyker, G. Alkylation of Arenes with Benzylc and Propargylic Alcohols—Classical versus Fancy Catalysts. *Adv. Synth. Catal.* **2006**, *348*, 456–462. [CrossRef]

26. Georgy, M.; Boucard, V.; Campagne, J.M. Gold(III)-Catalyzed Nucleophilic Substitution of Propargylic Alcohols. *J. Am. Chem. Soc.* **2005**, *127*, 14180–14181. [CrossRef] [PubMed]

27. Yadan, J.S.; Reddy, B.V.S.; Rao, K.V.R.; Narayana Kumar, G.G.K.S. Indium(III) Bromide Catalyzed Rapid Propargylation of Heteroaromatic Systems by α-Aryl-Substituted Propargyl Alcohols. *Synthesis* **2007**, *20*, 3205–3210.

28. Masuyama, Y.; Hayashi, M.; Suzuki, N. SnCl₂-Catalyzed Propargylic Substitution of Propargylic Alcohols with Carbon and Nitrogen Nucleophiles. *Eur. J. Org. Chem.* **2013**, *2013*, 2914–2921. [CrossRef]

29. Zhan, Z.P.; Yang, W.F.; Yu, J.L.; Li, J.P.; Liu, H.J. BiCl₃-Catalyzed propargylic substitution reaction of propargylic alcohols with C-, O-, S- and N-centered nucleophiles. *Chem. Commun.* **2006**, *31*, 3352–3354. [CrossRef] [PubMed]
30. Gohain, M.; Marais, C.; Beузidenhoudt, B.C.B. Al(OTf)₃: An efficient recyclable catalyst for direct nucleophilic substitution of the hydroxy group of propargylic alcohols with carbon- and heteroatom-centered nucleophiles to construct C-C, C-O, C-N and C-S bonds. Tetrahedron Lett. 2012, 53, 1048–1050. [CrossRef]

31. Gohain, M.; Marais, C.; Beузidenhoudt, B.C.B. An Al(OTf)₃-catalyzed environmentally benign process for the propargylation of indoles. Tetrahedron Lett. 2012, 53, 4704–4707. [CrossRef]

32. Yadav, J.S.; Reddy, B.V.S.; Rao, K.V.R.; Narayana Kumar, G.G.K.S.N. Sc(OTf)₃-catalyzed alkylation of indoles. Tetrahedron Lett. 2007, 48, 5573–5576. [CrossRef]

33. Zhang, L.; Zhu, Y.; Lu, P.; Wang, Y. 3-Alkenylation or 3-Alkylation of Indole with Propargylic Alcohols: Construction of 3,4-Dihydrocyclopenta[b]indole and 1,4-Dihydrocyclopenta[b]indole in the Presence of Different Catalysts. J. Org. Chem. 2012, 77, 9510–9520. [CrossRef] [PubMed]

34. Silveira, C.C.; Mendes, S.R.; Martins, G.M. Propargylation of aromatic compounds using Ce(OTf)₃ as catalyst. Tetrahedron Lett. 2012, 53, 1567–1570. [CrossRef]

35. Hashmi, A.S.K.; Schwarz, L.; Rubenbauer, P.; M. Blanco, C. The Condensation of Carbonyl Compounds with Electron-Rich Arenes: Mercury, Thallium, Gold or a Proton? Adv. Synth. Catal. 2006, 348, 705–708. [CrossRef]

36. Vasilyev, A.V. Superelectrophilic activation of alkynes, alkenes, and allenes. Adv. Org. Synth. 2018, 8, 81–120.

37. Chattaraj, P.K.; Giri, S.; Duley, S. Update 2 of: Electrophilicity Index. Chem. Rev. 2011, 111, 43–75. [CrossRef]

38. Radix-Large, S.; Kucharski, S.; Langlois, B.R. Trifluoromethylated Vinlyc and Aromatic Compounds from α-(Trifluoromethyl)allyl Alcohols. Synthesis 2004, 456–465.

39. Boreux, A.; Lonca, G.H.; Riant, O.; Gagosz, F. Synthesis of Trifluoromethyl-allenes by Gold-Catalyzed Rearrangement of Propargyl Benzyl Ethers. Org. Lett. 2016, 18, 5162–5165. [CrossRef] [PubMed]

40. Ghavtadze, N.; Roland, F.; Wuerthwein, E.U. Acid-Mediated Electrocyclic Domino Transformations of 5,5-Disubstituted 1-Amino-1-azapenta-1,4-dien-3-ones into Dihydrospiroindenepyrazole and Dihydroindenodiazepine Derivatives. J. Org. Chem. 2009, 74, 4584–4591. [CrossRef] [PubMed]

41. Allen, A.D.; Fujio, M.; Mohammed, N.; Tidwell, T.; Tsuji, Y. 3-(Trifluoromethyl)indenyl Cation: Ion Pair Return in the Formation of an Antiaromatic and Electron-Deficient Doubly Destabilized Carbocation. J. Org. Chem. 1997, 62, 246-252. [CrossRef] [PubMed]

42. Gassman, P.G.; Ray, J.A.; Wenthold, P.G.; Mickelson, J.W. Synthesis of perfluoroalkylated indenes. J. Org. Chem. 1991, 56, 5143–5146. [CrossRef]

43. Martynov, M.Y.; Iakovenko, R.O.; Kazakova, A.N.; Boyarskaya, I.A.; Vasilyev, A.V. Acid-promoted cyclization of 2,4-diaryl-1,1,1-trifluorobut-3-en-2-oles and their TMS-ethers into CF₃-indenes. Org. Biomol. Chem. 2017, 12, 2541–2550. [CrossRef] [PubMed]

Sample Availability: Samples of the compounds are available from the authors.