

Article

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

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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 indenenes; 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 trifluoromethyl-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-ols (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).

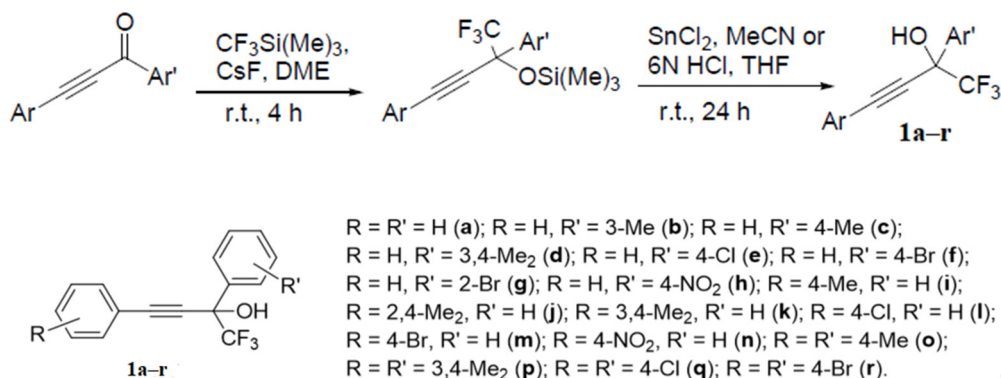
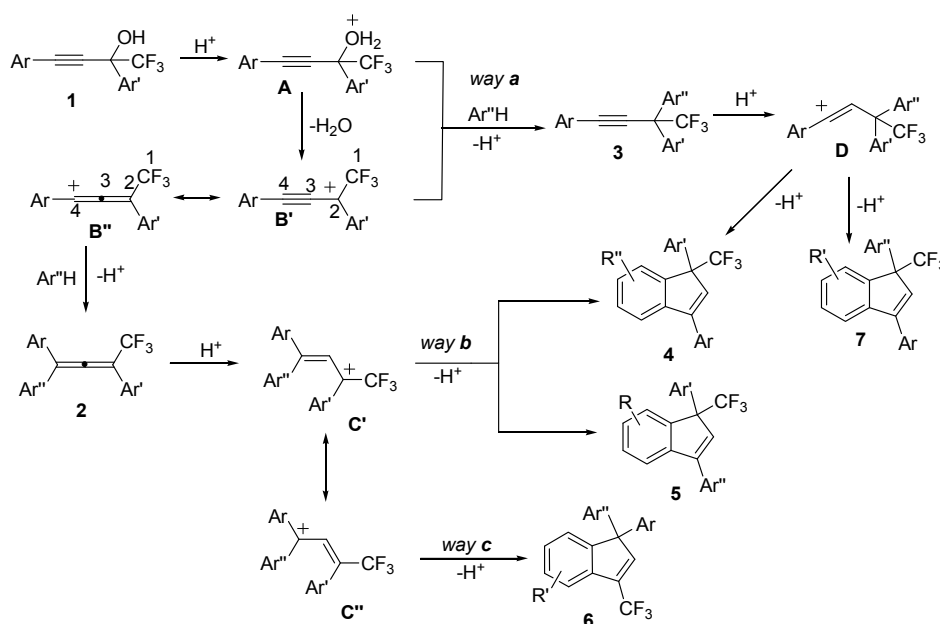


Figure 1. Starting CF₃-propargyl alcohols used in this study.

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 indenenes **4** or **7**, respectively.



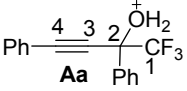
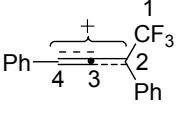
Scheme 1. Plausible mechanisms of acid-promoted reactions of CF₃-alcohols **1** with arenes.

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 indenenes **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 ω [37,38] 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 ω , of 7.59 e, compared to species **Aa**, with ω of 3.92 e. The cation **Aa** has a large positive charge of 1.00 e on carbon C². This carbon gives a large contribution into the LUMO of 13.2%. This proves that carbon C² in the species **Aa** is an electrophilic reactive center according to both charge and orbital factors.

Table 1. Selected electronic characteristics (DFT calculations) of cations **Aa** and **Ba** (**B'a** ↔ **B''a**) derived at the protonation of alcohol **1a**.

Caption	E _{HOMO} , eV	E _{LUMO} , eV	ω^a , eV	q(C ²) ^b , e	q(C ⁴) ^b , e	k(C ²) _{LUMO} ^c , %	k(C ⁴) _{LUMO} ^c , %
 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

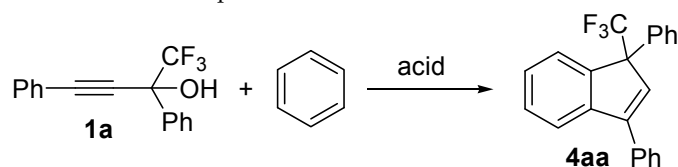
^a Global electrophilicity index $\omega = (E_{\text{HOMO}} + E_{\text{LUMO}})^2 / 8(E_{\text{LUMO}} - E_{\text{HOMO}})$. ^b Natural charges. ^c Contribution of the atomic orbital into the molecular orbital.

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-indenenes (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.

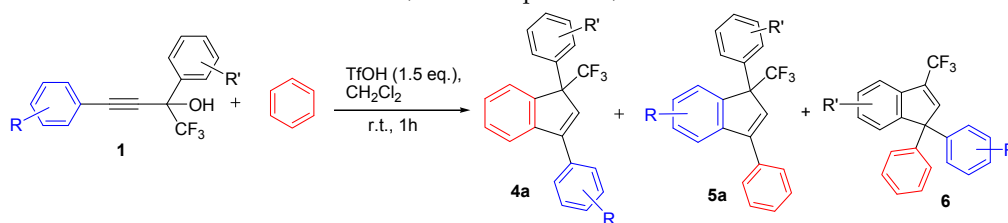
First, we conducted reactions of alcohol **1a** with benzene under the action of different Brønsted and Lewis acids (Table 2). In all cases, indene **4aa** was obtained. However, a better result with the highest yield of **4aa** was achieved for the reaction with the use of 1.5 equivalents of trifluoromethanesulfonic acid CF₃SO₃H (triflic acid, TfOH) at room temperature for 1 h (entry 3, Table 2).

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

Entry	Reaction Conditions ^a			Yield of 4aa , ^b %
	Acid	Temperature, °C	Time, h	
1	TfOH (50 eq.)	r.t.	1	30
2	TfOH (50 eq.) ^c	−35	1	45
3	TfOH (1.5 eq.)	r.t.	1	57
4	FSO ₃ 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 (1eq.)	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 CH₂Cl₂, molar ratio of **1**:benzene = 1:50. ^b Complete conversion of **1a**. ^c Cosolvent was CH₂Cl₂. ^d Conversion of **1a** was 60%. ^e Cosolvent was 1,2-dichloroethane. ^{r.t.} room temperature.

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 ¹H, ¹³C, and ¹⁹F-NMR, HRMS, and X-ray single crystal structure analysis (see Figure 2).

Table 3. TfOH-promoted reaction of alcohols **1a–f** with benzene; reaction conditions: TfOH, CH₂Cl₂, 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		 4aa (57%)	way a: A (or B'), D way b: B'' , C'
2		 4ab (48%)	way b: B'' , C'

Table 3. Cont.

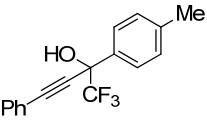
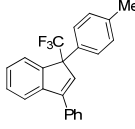
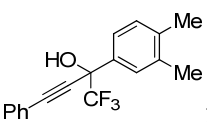
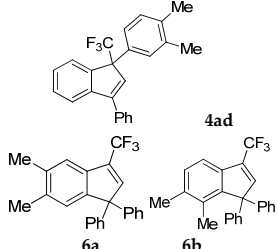
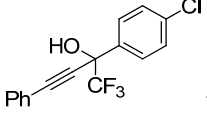
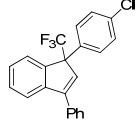
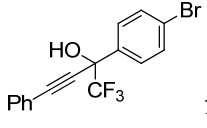
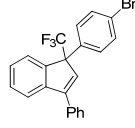
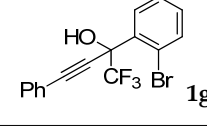
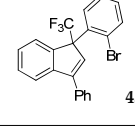
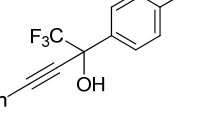
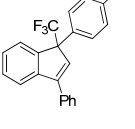
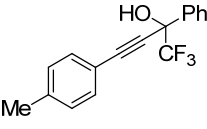
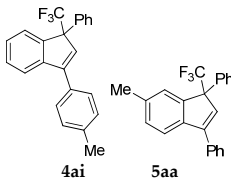
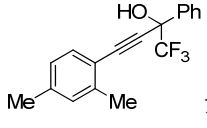
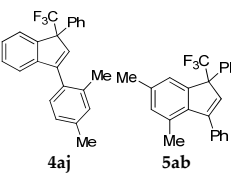
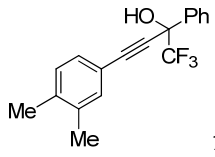
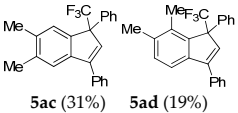
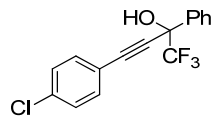
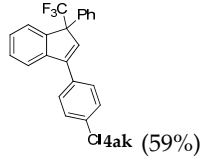
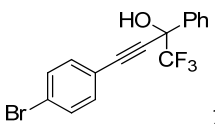
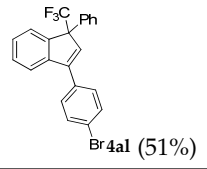
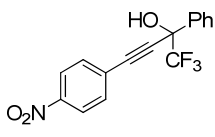
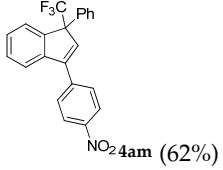
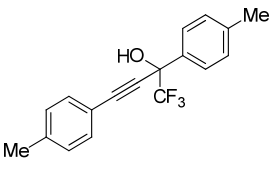
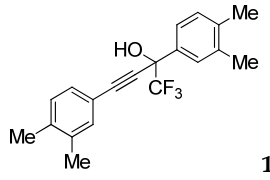
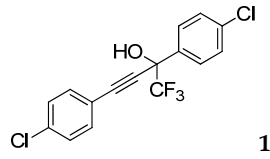
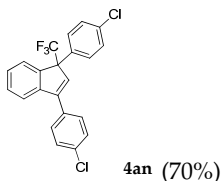
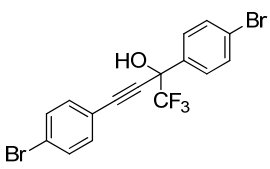
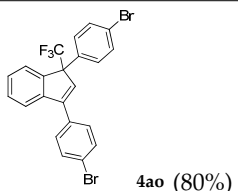
Entry	Alcohol	Reaction Products 4a, 5a, and 6 (Yield, %, Ratio of Isomers)	Possible Reaction Way and Intermediates from Scheme 1
3	 1c	 4ac (69%)	<i>way b: B'', C'</i>
4	 1d	 4ad 6a 6b	4ad — <i>way b: B'', C'</i> 6a, 6b — <i>way c: B'', C''</i>
total yield of 47% (4ad:6a:6b = 5:2:1)			
5	 1e	 4ae (73%)	<i>way a: A (or B'), D</i> <i>way b: B'', C'</i>
6	 1f	 4af (80%)	<i>way a: A (or B'), D</i> <i>way b: B'', C'</i>
7	 1g	 4ag (66%)	<i>way a: A (or B'), D</i> <i>way b: B'', C'</i>
8 a	 1h	 4ah (70%)	<i>way a: A (or B'), D</i> <i>way b: B'', C'</i>
9	 1i	 4ai 5aa	<i>way a: A (or B'), D</i> <i>way b: B'', C'</i>
total yield of 72% (4ai:5aa = 1:3.8)			
10	 1j	 4aj 5ab	<i>way a: A (or B'), D</i> <i>way b: B'', C'</i>
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	 1k	 5ac (31%) 5ad (19%)	<i>way b: B'', C'</i>
12	 1l	 4lak (59%)	<i>way a: A (or B'), D</i> <i>way b: B'', C'</i>
13	 1m	 4al (51%)	<i>way a: A (or B'), D</i> <i>way b: B'', C'</i>
14 ^a	 1n	 4am (62%)	<i>way a: A (or B'), D</i> <i>way b: B'', C'</i>
15	 1o	Complex mixture of reaction products	-
16	 1p	Complex mixture of reaction products	-
17	 1q	 4an (70%)	<i>way a: A (or B'), D</i> <i>way b: B'', C'</i>
18	 1r	 4ao (80%)	<i>way a: A (or B'), D</i> <i>way b: B'', C'</i>

^a Amount of TfOH was 2.5 equiv.

Table 4. TfOH-promoted reaction of **1** with *p*-xylene; reaction conditions: TfOH, CH₂Cl₂, molar ratio of **1**:*p*-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		 4ba (75%)	way a: A (or B'), D way b: B'', C'
2		 4bb (66%)	way b: B'', C'
3		 4bc (44%)	way a: A (or B'), D way b: B'', C'
4		 4bd (72%)	way b: B'', C'
5		 4be (60%)	way a: A (or B'), D way b: B'', C'
6		 4bf (74%)	way a: A (or B'), D way b: B'', C'
7		 4bg (45%)	way a: A (or B'), D way b: B'', C'
8 a		 4bh (84%)	way a: A (or B'), D way b: B'', C'

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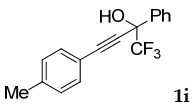
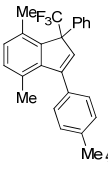
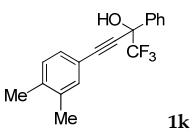
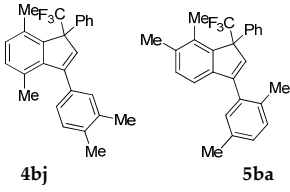
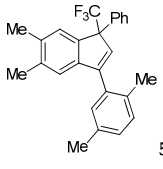
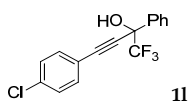
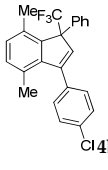
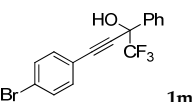
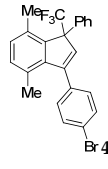
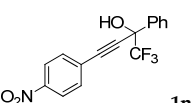
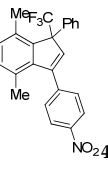
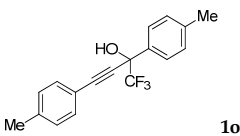
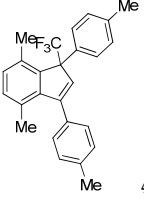
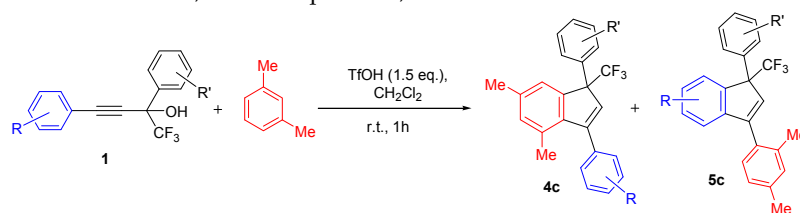
Entry	Alcohol	Reaction Products 4 and 5 (Yield, %, Ratio of Isomers)	Possible Reaction Way and Intermediates from Scheme 1
9	 1i	 Me 4bi (71%)	way a: A (or B'), D way b: B'', C'
10	 1k	 4bj 5ba total yield of 28% (4bj:5ba = 1.5:1)	way b: B'', C'
		 5bb (34%)	
11	 1l	 Cl 4lk (68%)	way a: A (or B'), D way b: B'', C'
12	 1m	 Br 4bl (58%)	way a: A (or B'), D way b: B'', C'
13 ^a	 1n	 NO ₂ 4bn (70%)	way a: A (or B'), D way b: B'', C'
14	 1o	 Me 4bn (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		 4bo 5bc total yield of 25% (4bo:5bc = 1.4:1)	way b: B'', C'
16		 4bp (74%)	way a: A (or B'), D way b: B'', C'
17		 4bq (78%)	way a: A, B', D 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		 4aj 5ab total yield of 63% (4aj:5ab = 6:1)	way b: B'', C'

Table 5. Cont.

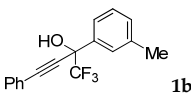
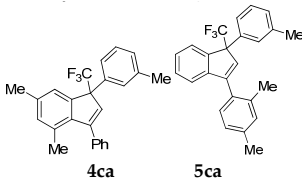
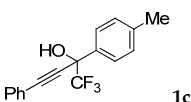
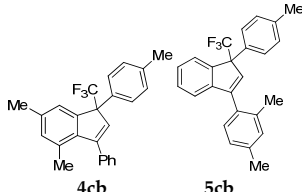
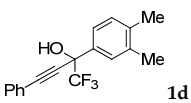
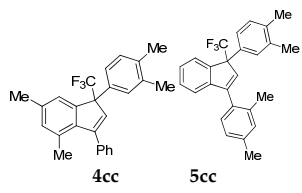
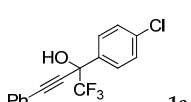
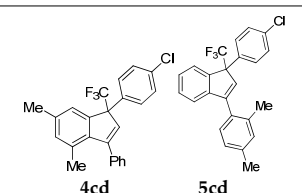
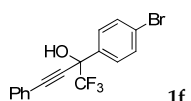
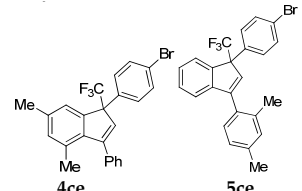
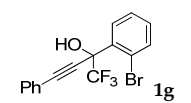
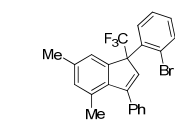
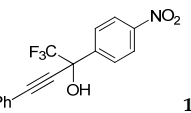
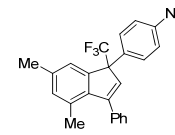
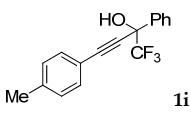
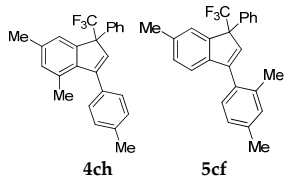
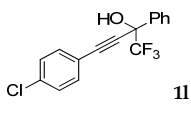
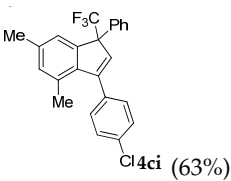
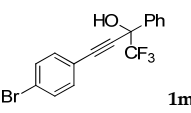
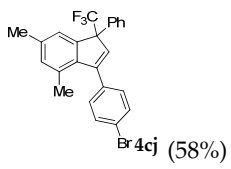
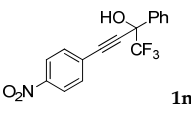
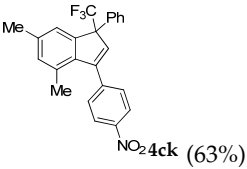
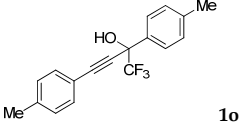
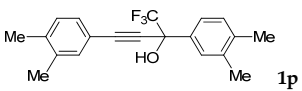
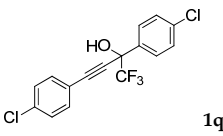
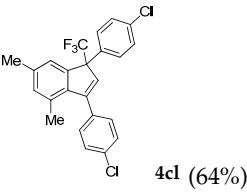
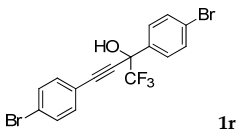
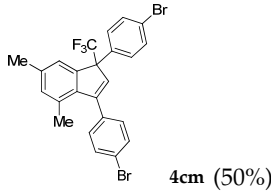
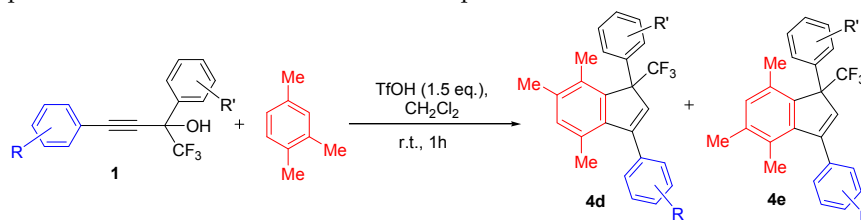
Entry	Alcohol	Reaction Products 4 and 5 (Yield, %, Ratio of Isomers)	Possible Reaction Way and Intermediates from Scheme 1
2	 1b	 4ca 5ca total yield of 66% (4ca:5ca = 3:1)	<i>way b: B'', C'</i>
3	 1c	 4cb 5cb total yield of 69% (4cb:5cb = 6:1)	<i>way b: B'', C'</i>
4	 1d	 4cc 5cc total yield of 69% (4cc:5cc = 5.7:1)	<i>way b: B'', C'</i>
5	 1e	 4cd 5cd total yield of 60% (4cd:5cd = 4:1)	<i>way b: B'', C'</i>
6	 1f	 4ce 5ce total yield of 56% (4ce:5ce = 4.9:1)	<i>way b: B'', C'</i>
7	 1g	 4cf (40%)	<i>way b: B'', C'</i>
8 ^a	 1h	 4cg (54%)	<i>way b: B'', C'</i>

Table 5. Cont.

Entry	Alcohol	Reaction Products 4 and 5 (Yield, %, Ratio of Isomers)	Possible Reaction Way and Intermediates from Scheme 1
9	 1i	 4ch 5cf total yield of 56% (4ch:5cf = 2.8:1)	way b: B'', C'
10	 1l	 Cl4ci (63%)	way b: B'', C'
11	 1m	 Br4cj (58%)	way b: B'', C'
12 ^a	 1n	 NO ₂ 4ck (63%)	way b: B'', C'
13	 1o	Complex mixture of reaction products	-
14	 1p	Complex mixture of reaction products	-
15	 1q	 4cl (64%)	way b: B'', C'
16	 1r	 4cm (50%)	way b: B'', C'

^a 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		 total yield of 75% (4da:4ea = 11.5:1)	4da —way b: B'', C' 4ea —way a: A (or B'), D
2		 total yield of 69% (4db:4eb = 11.5:1)	4db —way b: B'', C' 4eb —way a: A (or B'), D
3		 total yield of 50% (4dc:4ec = 13:1)	4dc —way b: B'', C' 4ec —way a: A (or B'), D
4		 total yield of 67% (4dd:4ed = 15.7:1)	4dd —way b: B'', C' 4ed —way a: A (or B'), D
5		 total yield of 66% (4de:4ee = 11.5:1)	4de —way b: B'', C' 4ee —way a: A (or B'), D
6		 total yield of 80% (4df:4ef = 24:1)	4df —way b: B'', C' 4ef —way a: A (or B'), D
7		 total yield of 70% (4dg:4eg = 2.7:1)	4eg —way b: B'', C' 4fg —way a: A (or B'), D

Table 6. Cont.

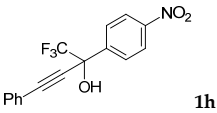
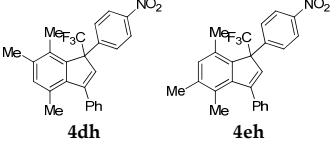
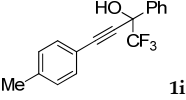
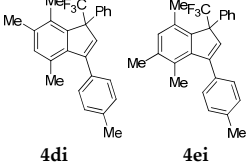
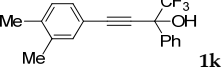
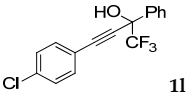
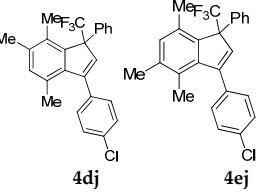
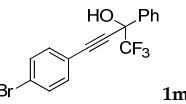
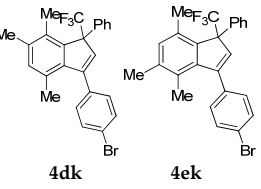
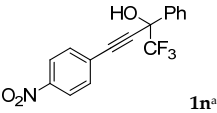
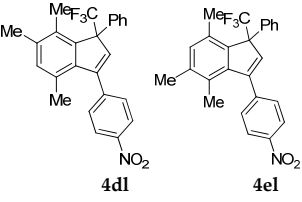
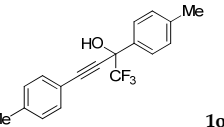
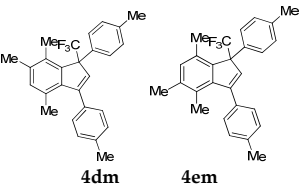
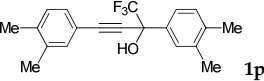
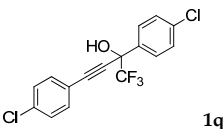
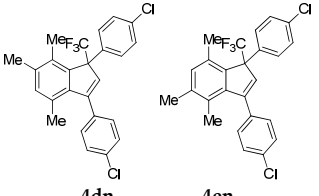
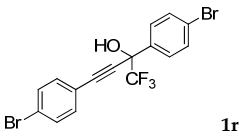
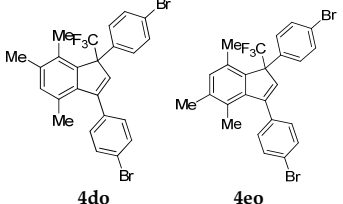
Entry	Alcohol	Reaction Products 4d and 4e (Yield, %, Ratio of Isomers)	Possible Reaction Way and Intermediates from Scheme 1
8 a	 1h	 4dh 4eh total yield of 58% (4dh:4eh = 1.8:1)	4dh —way b: B'' , C' 4eh —way a: A (or B'), D
9	 1i	 4di 4ei total yield of 51% (4di:4ei = 12:1)	4di —way b: B'' , C' 4ei —way a: A (or B'), D
10	 1k	Complex mixture of reaction products	-
11	 1l	 4dj 4ej total yield of 54% (4dj:4ej = 11.5:1)	4dj —way b: B'' , C' 4ej —way a: A (or B'), D
12	 1m	 4dk 4ek total yield of 49% (4dk:4ek = 10:1)	4dk —way b: B'' , C' 4ek —way a: A (or B'), D
13	 1n^a	 4dl 4el total yield of 66% (4dl:4el = 13:1)	4dl —way b: B'' , C' 4el —way a: A (or B'), D
14	 1o	 4dm 4em total yield of 65% (4dm:4em = 6:1)	4dm —way b: B'' , C' 4em —way a: A (or B'), D
15	 1p	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		 4dn 4en total yield of 49% (4dn:4en = 10:1)	4dn—way b: B'', C' 4en—way a: A (or B'), D
17		 4do 4eo total yield of 57% (4do:4eo = 11.5:1)	4do—way b: B'', C' 4eo—way a: A (or B'), D

^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.

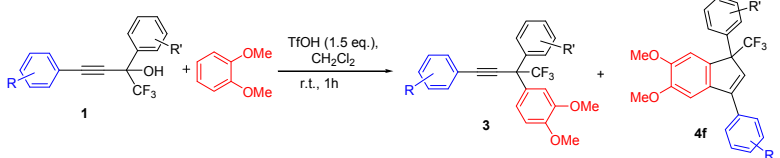
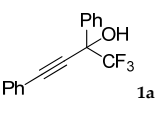
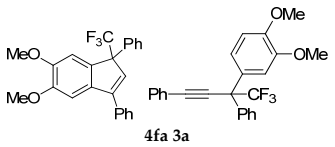
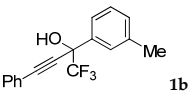
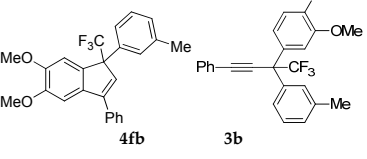
			
Entry	Alcohol	Reaction Products 4f and 3 (Yield, %, Ratio of Isomers)	Possible Reaction Way and Intermediates from Scheme 1
1 ^a		 4fa 3a total yield of 60% (4fa:3a = 2.8:1)	way a: A (or B'), D
2		 4fb 3b total yield of 49% (4fb:3b = 3.5:1)	way a: A (or B'), D

Table 7. Cont.

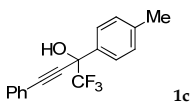
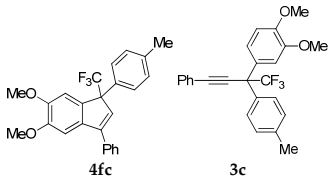
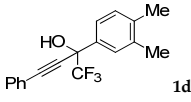
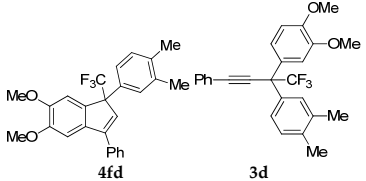
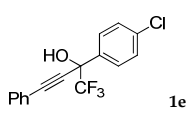
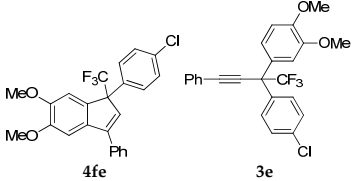
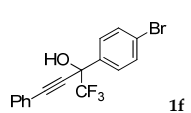
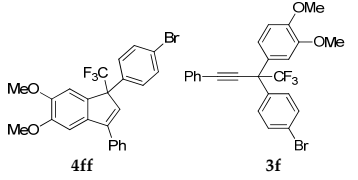
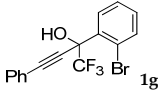
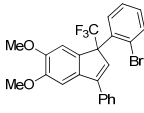
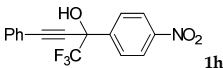
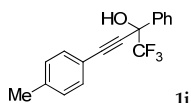
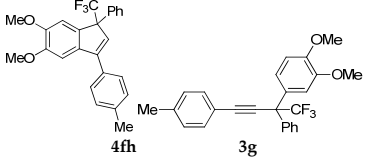
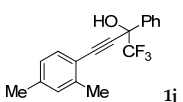
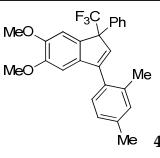
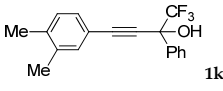
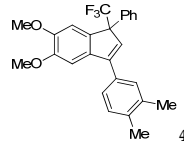
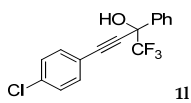
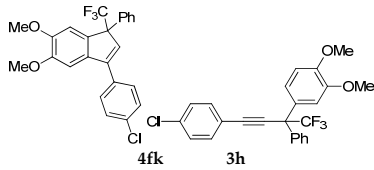
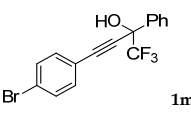
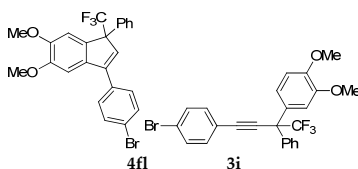
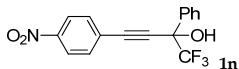
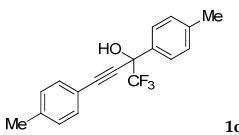
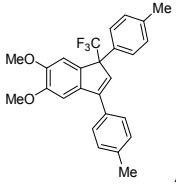
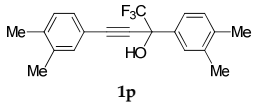
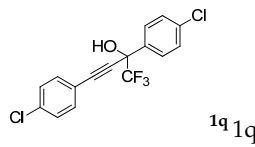
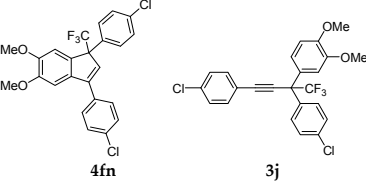
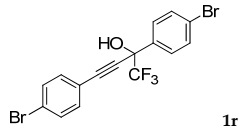
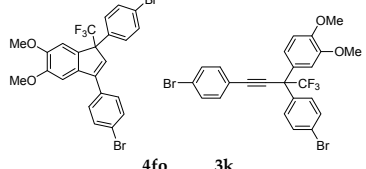
Entry	Alcohol	Reaction Products 4f and 3 (Yield, %, Ratio of Isomers)	Possible Reaction Way and Intermediates from Scheme 1
3		 total yield of 98% (4fc:3c = 4.9:1)	way a: A (or B'), D
4		 total yield of 76% (4fd:3d = 5:1)	way a: A (or B'), D
5		 total yield of 44% (4fe:3e = 6:1)	way a: A (or B'), D
6		 total yield of 70% (4ff:3f = 4:1)	way a: A (or B'), D
7 ^a		 4fg (82%)	way a: A (or B'), D
8		Complex mixture of reaction products	-
9		 total yield of 54% (4fh:3g = 13:1)	way a: A (or B'), D
10 ^a		 4fi (67%)	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	 1k	 4fj (57%)	<i>way a</i> : A (or B'), D
12	 1l	 4fk 3h total yield of 65% (4fk:3h = 10:1)	<i>way a</i> : A (or B'), D
13	 1m	 4fl 3i total yield of 36% (4fl:3i = 7:1)	<i>way a</i> : A (or B'), D
14	 1n	Complex mixture of reaction products	-
15 ^a	 1o	 4fm (69%)	<i>way a</i> : A (or B'), D
16	 1p	Complex mixture of reaction products	-
17	 1q 1q	 4fn 3j total yield of 50% (4fn:3j = 2.8:1)	<i>way a</i> : A (or B'), D
18	 1r	 4fo 3k total yield of 59% (4fo:3k = 2:1)	<i>way a</i> : A (or B'), D

^a Amount of TfOH was 2.5 equiv.

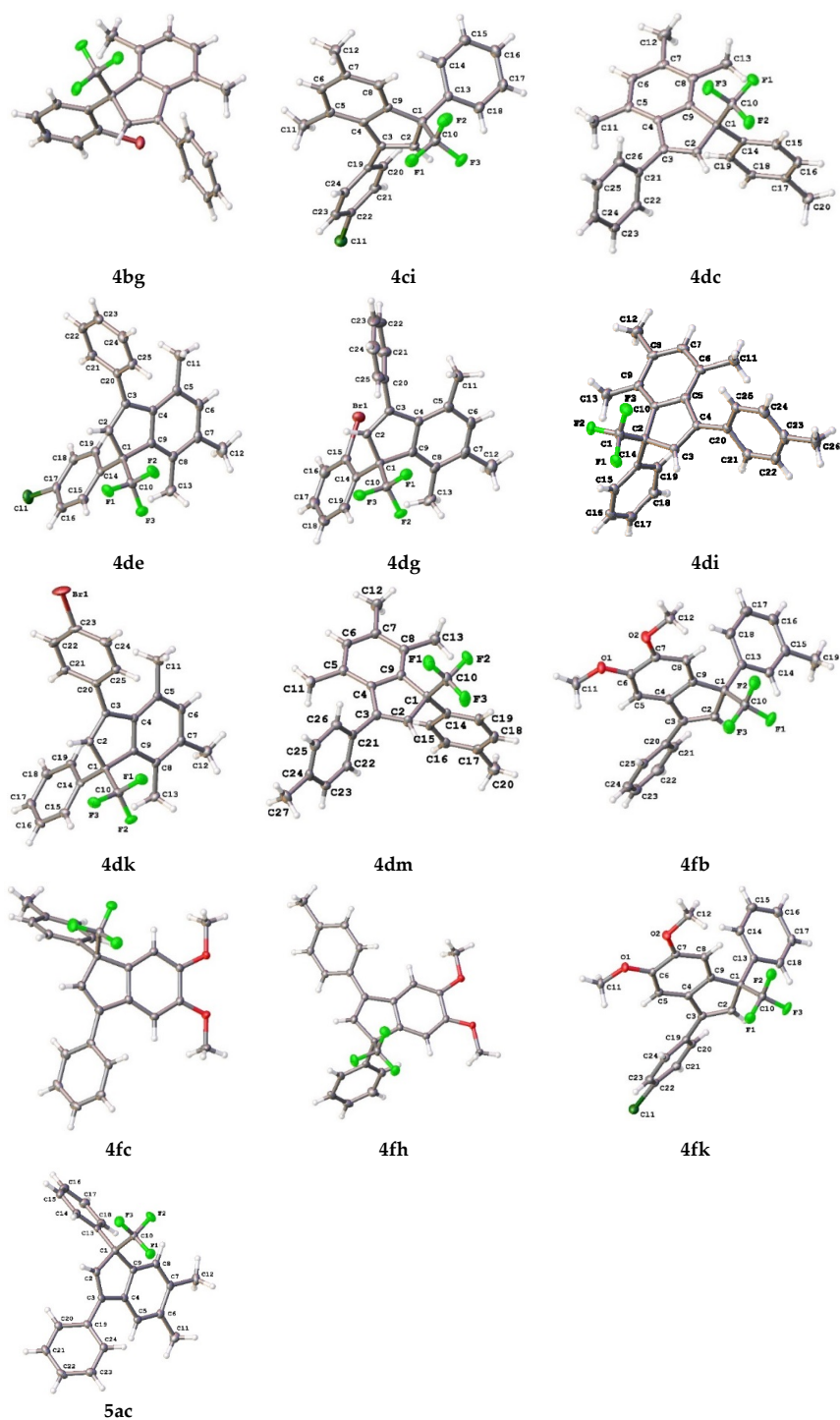
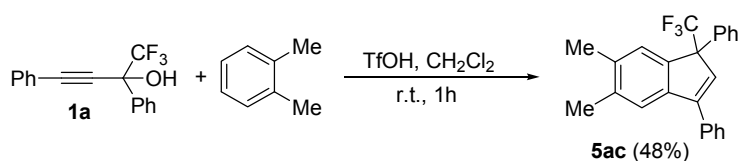


Figure 2. X-ray crystal structures of compounds **4bg** (CCDC 1568593), **4ci** (CCDC 1578216), **4dc** (CCDC 1568602), **4de** (CCDC 1568599), **4dg** (CCDC 1568594), **4di** (CCDC 1563374), **4dk** (CCDC 1568596), **4dm** (CCDC 1568600), **4fb** (CCDC 1568595), **4fc** (CCDC 1568597), **4fh** (CCDC 1568603), **4fk** (CCDC 1568598), and **5ac** (CCDC 1568601) (ellipsoid contour of probability levels is 50%), Green sticks are fluorine atoms.



Scheme 2. TfOH-promoted reaction of **1** with *o*-xylene in TfOH; reaction conditions: TfOH, CH₂Cl₂, molar ratio of **1**:benzene:TfOH = 1:1.1:1.5, room temperature, 1 h.

In principle, the structures of the target indenenes **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 indenenes 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 *pathway a* or **b** (Scheme 1).

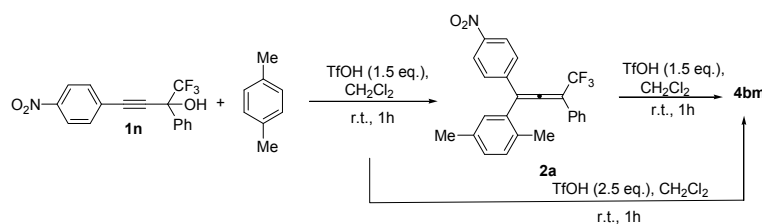
Alcohols **1** bearing donor methyl groups in the aryl substituent at the triple bond react with benzene to form a mixture of indenenes of types of **4a** and **5a**. The latter is the main reaction product (entries 9–11). Compounds **5a** are formed at the cyclization into the electron-rich aryl ring (not into the phenyl one) at carbon C⁴ in cations **C** (*way a*, Scheme 1).

Alcohol **1d**, with a 3,4-dimethylphenyl ring at carbon C², additionally gave indenenes **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, indenenes 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).



Scheme 3. TfOH-promoted reaction of **1n** with *p*-xylene in TfOH.

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 C⁴ of species **B''**, which leads to the formation of the corresponding indenenes in *way b* (Scheme 1). The presence of electron-withdrawing substituents in the aryl ring at the atom C⁴ prevents electrophilic substitution into this ring, and only indenenes **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 C⁵ and that the first reaction occurs in this particular position, one may propose that indenenes **4da**–**4do** are formed in *way b* through cations **B''** and **C'**, and indenenes **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, CF₃ 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 CH₂Cl₂ 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 CF₃-propargyl alcohols **1** with different arenes, leading to CF₃-indenenes (Tables 3–7), one may conclude that these indenenes 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 CF₃-indene **4** or **5** in good yields. Such CF₃-indenenes 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 CF₃-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-CF₃-indenenes.

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

Author Contributions: Conceptualization, A.V.V.; Synthesis of Starting Compounds and Study on Their Electrophilic Reactions, A.V.Z. and A.N.K.; DFT Study, I.A.B.; X-Ray Study, T.L.P., V.V.S. and O.V.K.; Writing-Original Draft Preparation, A.V.V.

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Conflicts of Interest: The authors declare no conflict of interest.

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



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