



Trifluoromethylated allyl alcohols: acid-promoted reactions with arenes and unusual ‘dimerization’



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ABSTRACT

An unusual ‘dimerization’ of CF₃-allyl alcohols [ArCH=CHCH(OH)CF₃] under the action of anhydrous FeCl₃ was found to give fluorinated indanes in 62–90% yields via the formation of intermediate allyl cations. Reactions of CF₃-allyl alcohols with arenes (Ar'H) led to CF₃-alkenes [Ar(Ar')CHCH=CHCF₃] in 48–75% yields. The mechanisms of the transformations are discussed.

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Fluorinated organic compounds have significant theoretical and practical value in chemistry, biology, medicine, and materials science.^{1,2} Incorporation of a fluorinated moiety into a molecule often changes important parameters such as lipophilicity, metabolic activity, and bioavailability. The electron-withdrawing character of fluorinated groups is another advantage, which allows one to control transformations of fluorinated compounds. Examples of CF₃-substituted carbocations are very promising, but are still a rare type of fluorinated species exhibiting high electrophilicity and selectivity.³

The present work is a continuation of our investigations on the electrophilic activation of alkenes⁴ and alkynes.⁵ The reactions of CF₃-substituted allyl alcohols **1** promoted by Brønsted or Lewis acids were investigated. Dehydroxylation of **1** can lead to allyl cations having resonance forms **A** and **B** (Table 1). However, due to the strong electron-withdrawing character of the CF₃-group, form **A** is destabilized significantly. As a result, very selective reaction can be expected of such cations at position 4 of form **B**. To confirm this hypothesis we performed DFT calculations on CF₃-allyl cations bearing various substituents on the arene ring and the CH₃-substituted allyl cation **C1**.⁶ The global electrophilicity indices, ω (14.1–

16.6 eV) for the CF₃-cations **B1–B5** are significantly higher than the ω value (13.4 eV) for the cation **C1**, therefore cations **B1–B5** are much more electrophilic. Due to the electron-withdrawing effect of the CF₃-group, cation **B1** has a greater charge on C-4 and a lower charge on C-2, in comparison with **C1** having similar charges for both C-2 and C-4. As a result, the DFT calculations predict highly selective reactions for trifluoromethylated allyl cations **B1–B5**.

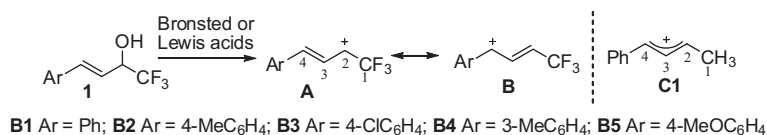
One of the most important transformations of substituted allyl cations⁷ is their participation in new carbon–carbon bond forming reactions by reactions with arenes,⁸ heteroarenes,⁹ alkenes,¹⁰ alkynes,¹¹ or carbonyl compounds.¹² To our surprise, reactions of trifluoromethylated allyl cations with C-nucleophiles have not been described to date.

To start our investigation, a series of CF₃-allyl alcohols were prepared by reduction of α,β -unsaturated trifluoromethyl ketones¹³ using a literature procedure.¹⁴ Initially, we studied the reaction of **1a** with benzene under treatment with various Brønsted and Lewis acids (Table 2). Indeed, the expected alkene **2a** was obtained through formation of the corresponding cation **B** in protic acids (H₂SO₄; CF₃CO₂H was too weak) and superacids (FSO₃H, TfOH) (entries 1–5). The reaction is highly diastereoselective forming only the *E*-isomer of **2a**. Moreover, unusual ‘dimeric’ diastereomeric indane derivatives **3a,a'** were also isolated. Yields of the compounds **2a** (21–33%) and **3a,a'** (22–44%) are roughly equal (entries 1, 3, 4, 7, and 10, Table 1), which reflects an

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Table 1
Formation of CF₃-allyl cations and selected characteristics of the cations **B1–B5**, and **C1**

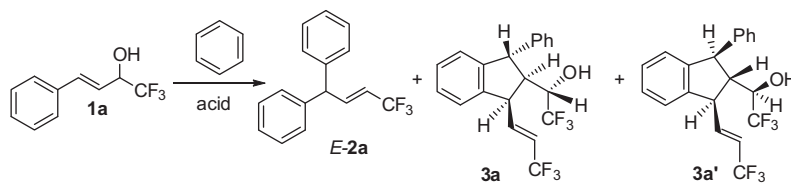


Cation	E_{HOMO} (eV)	E_{LUMO} (eV)	ω^{a} (eV)	$q(\text{C-2})^{\text{b}}$ (e)	$q(\text{C-4})^{\text{b}}$ (e)
C1	-11.54	-7.97	13.4	0.10	0.08
B1	-12.18	-8.75	16.0	-0.05	0.09
B2	-11.89	-8.43	14.9	-0.07	0.08
B3	-11.88	-8.66	16.4	-0.06	0.08
B4	-11.71	-8.60	16.6	-0.06	0.10
B5	-11.88	-8.01	14.1	-0.09	0.04

^a Global electrophilicity index.

^b Natural charges.

Table 2
Acid-promoted reactions of **1a** with benzene



Entry	Reaction conditions				Yield (%)	
	Acid	1a /PhH/acid ratio	T (°C)	Time (h)	2a	3a+a'
1	TfOH ^a	1:3:50	-35	1	33	22
2	TfOH	1:15:50	20	1	Oligomers	—
3	FSO ₃ H ^b	1:3:86	-75	1	24	—
4	H ₂ SO ₄	1:16:268	20	1	22	38
5	CF ₃ CO ₂ H	1:50:5	20	1	No reaction	—
6	FeCl₃ ^c	1:50:1 ^c	20 ^c	1 ^c	65 ^c	—
7	FeCl ₃ ^a	1:1.1:1	20	1	32	40
8	AlCl ₃	1:50:1	20	1	21	—
9	AlBr ₃	1:50:2	20	1	Oligomers	—
10	BF ₃ ·Et ₂ O	1:50:1	20	72	32	44
11	BBr ₃	1:50:1	20	1	Oligomers	—
12	TiCl ₄ ^d	1:50:1	20	1	30	—
13	GaCl ₃	1:50:1	20	1	No reaction	—
14	InCl ₃	1:50:1	20	1	No reaction	—
15	CuBr ₂	1:50:1	20	1	No reaction	—
16	SnCl ₄	1:50:1	20	1	No reaction	—
17	ZnCl ₂	1:50:1	20	1	No reaction	—
18	ZnBr ₂	1:50:1	20	1	No reaction	—
19	Sc(OTf) ₃	1:50:1	20	1	No reaction	—
20	In(OTf) ₃	1:50:1	20	1	No reaction	—
21	Fe(OTf) ₂	1:50:1	20	1	No reaction	—
22	Cu(OTf) ₂	1:50:1	20	1	No reaction	—

^a Solvent = CH₂Cl₂.

^b Solvent = SO₂.

^c The best result for preparation of *E*-**2a**.

^d The main reaction product (yield 45%) was compound *E*-**4a**, PhCH=CHCH(Cl)CF₃.

approximately equal probability of reaction of intermediate cation **B1** in two different pathways under these particular reaction conditions.

The formed dimer is a result of the domino reaction of two molecules of **1a** to form two new C–C bonds. Among the Lewis acids (entries 6–22), the highest yield of compound **2a** was obtained with anhydrous FeCl₃. In this case alcohol **1a** gave *E*-**2a** as the only reaction product with excess benzene (entry 6). Reaction of equimolar amounts of **1a** and benzene afforded preferentially **3a,a'** (Entry 7). The other Lewis acids tested were found to be less effective giving lower yields of **2a**. Moreover, in most cases, no reaction took place (entries 13–22). FeCl₃ seems to be more 'oxophilic'

Table 3
Transformation of **1a** into **3a,a'**

Entry	Acid	1a :acid ratio	T (°C)	Time (h)	3a+a' (%) / a : a' ratio
1	FeCl ₃ ^a	1:1	20	1	62/1:1
2	FeCl ₃ ^a	1:0.5	20	1	60/1.2:1
3	BF ₃ ·Et ₂ O ^a	1:1	20	48	45/1.2:1
4	TiCl ₄ ^{a,b}	1:1	20	1	11/1:2.7
5	TfOH	1:50	-35	1	30/1.1:1

^a Solvent = CH₂Cl₂.

^b *E*-**4a** was obtained as the major product in 51% yield (see structure in footnote 'c' in Table 1, entry 12).

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