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CHEMISTRY

Synthesis and Unusual [2 + 2] Cycloaddition Reactions of 1-Trifluoroacetyl-2-haloacetylenes

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Acetylenic dienophiles and enophiles containing two activating substituents, one of which is a halogen, are of great interest not only for theory but also as substrates in the synthesis of biologically active compounds [1, 2]. Previously, we obtained certain trifluoroacetylacetylenes and studied their Diels–Alder reactions with various 1,3-dienes [3, 4]. The consideration of the structure of 1-trifluoroacetyl-2-haloacetylenes allowed one to suppose that these compounds should exhibit high reactivity in different addition reactions; therefore, we attempted to develop a general method for the synthesis of these acetylenes.

Readily available [5] bis(trimethylstannyl)acetylene was found to react exothermically with trifluoroacetic anhydride to form 1-trifluoroacetyl-2-(trimethylstannyl)acetylene (**1**), which is a stable compound distillable in a vacuum:

$$\mathrm{Me_3Sn{-}C{\equiv}C{-}SnMe_3 + (CF_3CO)_2O}$$
$$\longrightarrow \underset{\mathbf{1}}{\mathrm{Me_2Sn{-}C{\equiv}C{-}COCF_3}} + \mathrm{CF_3CO_2SnMe_3}.$$

The halogenation of acetylene **1** readily proceeds even in the cold to give the corresponding 1-trifluoroacetyl-2-haloacetylenes (**2a**–**2c**) in high yields:

$$\mathbf{1} + \mathrm{X_2} \xrightarrow{\text{from }-30\text{ to }0^\circ\mathrm{C}} \mathrm{X{-}C{\equiv}C{-}COCF_3 + Me_3SnX},$$
$$\mathrm{X = Cl}\ (\mathbf{2a}),\ \mathrm{Br}\ (\mathbf{2b}),\ \mathrm{I}\ (\mathbf{2c}).$$

Chloroacetylene **2a** and bromoacetylene **2b** are stable compounds distillable without decomposition even at atmospheric pressure, whereas iodoacetylene **2c** gradually becomes dark and undergoes resinification in storage.

In the course of ^{1}H NMR study of the reaction of bromide **2b** with isoprene, which yielded a complex mixture of products, we noticed that one product resulted not from the Diels–Alder reaction. Taking into account this observation, we supposed that bromide **2b** could react with simple alkenes. Even the first experiments not only confirmed this assumption but also gave striking results: compound **2b** was found to react with alkenes to form [2 + 2] cycloaddition products **3** without illumination and in the absence of a catalyst. The reaction of 1,1-disubstituted alkenes is exothermic even at 20°C, while the addition of 1,2-disubstituted alkenes requires heating to 70–80°C. Ene reaction products **4** are formed simultaneously, and their quantity depends on the nature of the alkene.

As yet, we have studied chloride **2a** only in its reaction with isobutene. Although the addition reaction proceeds somewhat more slowly than in the case of bromide **2b**, the corresponding cyclobutene **3a** is formed more selectively.

We failed to separate cyclobutenes and their isomers, ene adducts, by rectification or chromatography. However, we found that the ene adducts readily underwent bromine addition across the nonconjugated C=C bond, whereas cyclobutenes **3** did not react even at 20°C. Thus, after vacuum distillation of the isomer mixture (Table 1) and the determination of the isomer ratio therein by ^{1}H NMR, the mixture was treated with bromine in an amount equivalent to that of the ene adduct and then redistilled. This technique enabled us to isolate pure cyclobutenes **3** in high yields except the adduct with methylenecyclopentane **3d**, which gave rise to the decomposition of the mixture in the course of distillation:

$$\mathbf{3} + \mathbf{4} \xrightarrow[-4]{\mathrm{Br_2}} \mathbf{3}.$$

Concerted thermal [2 + 2] cycloaddition with the participation of two alkene molecules or alkene and acetylene is known to be symmetry-forbidden according to the Woodward–Hoffmann rules [6]. Notice that [2 + 2] cycloaddition for ketenes, ketiminium salts, and other heterocumulenes is not forbidden, and such reactions are well known [7]. Alkenes containing strong electron-donating substituents (NR$_2$, OR) at the C=C bond react with electron-withdrawing alkenes and acetylenes to form cyclobutanes and cyclobutenes [8, 9]; however, these reactions proceed with a considerable asymmetry of the transition state and cannot be considered as concerted processes.

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Table 1

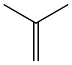
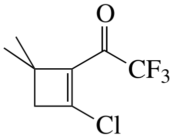
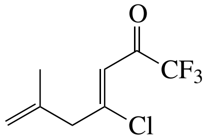
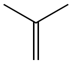
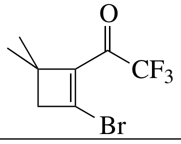
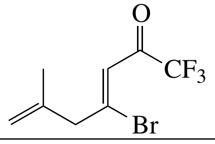
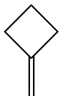
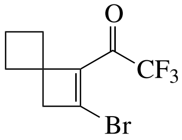
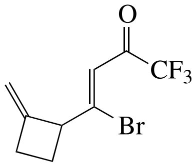
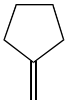
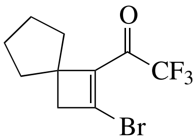
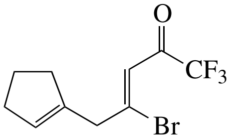
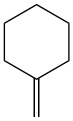
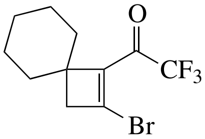
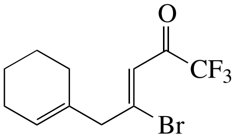
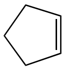
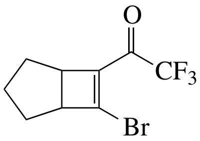
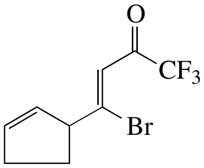
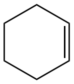
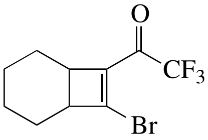
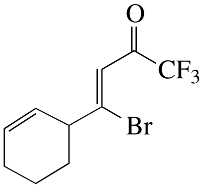
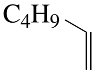
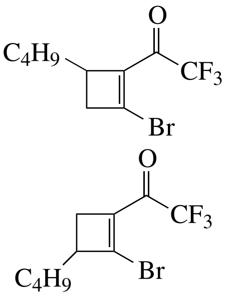
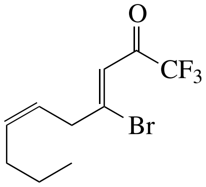
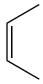
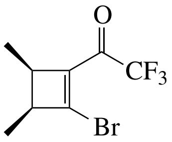
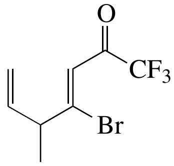
Compound index	Alkene, conditions	[2 + 2] Cycloaddition product **3**	Ene reaction product **4**	Total yield, %; product ratio	T_b of mixture, °C; pressure, mmHg
a	 20°C 72 h			60 80 : 20	41–60 8
b	 20°C 36 h			81 65 : 35	55–70 7
c	 20°C 24 h			81 75 : 25	45–50 1
d	 20°C 18 h			70 35 : 65	53–60 1
e	 20°C 18 h			79 90 : 10	53–57 1
f	 78°C 18 h			66 95 : 5	40–44 1
g	 78°C 24 h			78 95 : 5	55–56 1
h	 80°C 45 h			50 90 : 10	52–63 1
i	 80°C 24 h			79 95 : 5	64–67 10

Table 2

T_b, °C; pressure, mmHg	Cyclobutene **3**	Yield, %
41–42/8	**3a**	45
50–51/7	**3b**	50
45–46/1	**3c**	60
–	**3d**	0
55–56/1	**3e**	61
40/1	**3f**	60
55/1	**3g**	65
63/1	**3h**	41
66–67/10	**3i**	67

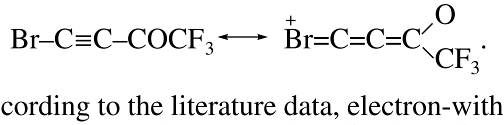
In certain cases, the addition of acetylenes to alkenes is catalyzed by aluminum chloride and ethylaluminum dichloride [10, 11], as well as by transition metal complexes [12, 13]. Polyhalogenated alkenes were also reported to participate in [2 + 2] cycloaddition reactions, which occurred under severe conditions via a radical mechanism [14].

The unusualness of the revealed addition reaction is that it falls into none of the above cases. The reaction requires neither illumination nor a catalyst. It was also found that the addition of radical scavengers has no effect on the rate or direction of the reaction.

Polar solvents are known to accelerate considerably the rate of [2 + 2] dipolar addition reactions; however, the addition of acetonitrile provided no discernible acceleration of the studied reactions. The formation of two regioisomers in a 1 : 1 ratio in the reaction of acetylene **2b** with hexene-1 is also contradictory to both the polar and the radical mechanisms.

The above circumstances allow us to suppose that acetylenes **2a** and **2b** undergo addition to alkenes by a concerted mechanism, although it is symmetry-forbidden.

To overcome this contradiction, we supposed that the double bond index of the terminal carbon atom and the halogen atom in the molecules of compounds **2a** and **2b** is sharply increased owing to the strong negative mesomeric effect of the trifluoroacetyl group. The resonance structure describing such a redistribution of electron density has a ketenium structure, which enables concerted [2 + 2] cycloaddition:



$$\mathrm{Br{-}C{\equiv}C{-}COCF_3} \longleftrightarrow \mathrm{\overset{+}{Br}{=}C{=}C{=}C(\overset{-}{O})CF_3}.$$

According to the literature data, electron-withdrawing acetylenes such as acetylenedicarboxylic esters, hexafluorobutyne-2, 1,1,1-trifluoropropyne, and propiolic esters, whose molecules are devoid of a mesomeric electron-donating substituent at the C≡C bond, react with simple alkenes under severe conditions to give only ene addition products [15].

EXPERIMENTAL

All manipulations with trimethylstannylacetylenes were carried out in an argon atmosphere with the use of anhydrous solvents. Trifluoroacetic anhydride was distilled over P_2O_5 prior to use. The structure of the compounds obtained was confirmed by elemental analysis data, ^{1}H and ^{13}C NMR spectra, and IR spectroscopy. The yields and boiling points of isomer mixtures and pure cyclobutenes **3** are given in Tables 1 and 2.

Trimethylstannyltrifluoroacetylacetylene (1). Trifluoroacetic anhydride (42.4 mL, 63 g, 0.30 mol) was added in one portion with stirring to a solution of 100 g (0.28 mol) of bis(trimethylstannyl)acetylene in 200 mL of tetrahydrofuran using a powerful magnetic stirrer; after an exothermic reaction was completed, the reaction mixture was allowed to stand overnight. The major portion of the tetrahydrofuran was distilled off in the vacuum of a water-jet pump over a water bath at 20°C. The reflux condenser was replaced with a distilling column fitted with a descending condenser and a receiver adapter equipped with a trap cooled with dry ice. In a vacuum of 10–15 mmHg, the water bath temperature was gradually increased to 90–95°C while the reaction mixture was vigorously stirred until the distillation of a product within 45–65°C was completed (the distillation residue, accumulating trimethylstannyl trifluoroacetate, quickly solidified and partly sublimed, and the stirring became difficult; however, the distillation was continued). An additional amount of the product was distilled off from the reaction mixture in the vacuum of an oil pump at 1–2 mmHg after replacement of the receiver. Repeated distillation afforded 72.7 g (90%) of acetylene **1**, bp 53–56°C (8 mmHg).

1-Trifluoroacetyl-2-chloroacetylene (2a) and 1-trifluoroacetyl-2-bromoacetylene (2b). A solution of 4.0 g (0.056 mol) of chlorine (for preparing compound **2a**) or 8.4 g (0.052 mol) of bromine (for preparing compound **2b**) in 10 mL of ethyl benzoate was added dropwise with stirring and cooling to –20°C to a solution of 15 g (0.052 mol) of acetylene **1** in 10 mL of ethyl benzoate. The solution was stirred for 5 min at 20°C, and then the halogenation product was short-path distilled on gradual heating in a vacuum of 15–20 mmHg into a trap cooled with dry ice. The distillation was terminated after the vapor temperature rose to 40°C, and the distillate was redistilled to give 6.9 g (85%) of chloroacetylene **2a**, bp 64–66°C, or 9.2 g (87%) of bromoacetylene **2b**, bp 89–91°C.

1-Trifluoroacetyl-2-iodoacetylene (2c). Crystalline iodine (3.3 g, 0.013 mol) was added in small portions to a solution of 2.5 mL (3.72 g, 0.013 mol) of acetylene **1** in 10 mL of methylene chloride. The solution was stirred for 10 min at 20°C, concentrated in a vacuum, and distilled to give 1.6 g (50%) of iodoacetylene **2c**, bp 40–45°C (15 mmHg).

General procedure for the synthesis of cyclobutenes 3a–3i. Acetylene **2a** or **2b** (0.01 mol) was mixed with a 30 mol % excess of alkene (the reaction was carried out in a sealed ampoule in the case of gaseous alkenes or when heating was necessary). The reaction mixture was kept for the required time at the prescribed temperature and then distilled in a vacuum collecting a fraction within the specified temperature range (Table 1). The distillate was dissolved in 5 mL of methylene chloride and a solution of bromine in an amount equivalent to the ene adduct in 2 mL of methylene chloride was added dropwise with stirring and cooling to –20°C (Table 1). After warming to 0°C, the solution was concentrated in a vacuum and redistilled to give pure cyclobutenes **3a**–**3i** (Table 2).

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