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Synthesis and Properties of 1-Trifluoroacetylacetylene

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The Diels–Alder reaction is one of the most general methods for the synthesis of different six-membered heterocyclic compounds containing functional groups [1–3]. The presence of the trifluoroacetyl group in a dienophile should result in its considerable activation in cycloaddition reactions and open a simple way to the synthesis of complex fluorine-containing compounds showing biological activity [4, 5].

In recent years, our research group has developed methods of preparing halogen-substituted trifluoroacetylacetylenes and studied their reactions with different dienes and alkenes [6–9]. There is a sole report in the literature on the synthesis of 1-trifluoroacetylacetylene, the parent compound of this series; however, the compound was obtained only in trace amounts in a low yield after separation of an isomer mixture using a liquid chromatograph [10].

In the present paper, we describe a preparative method for the synthesis of trifluoroacetylacetylene and report the results of studying its properties. As a starting compound, we used 1-trimethylstannyl-2-trifluoroacetylacetylene **1**, readily obtainable from bis(trimethylstannyl)acetylene and trifluoroacetic anhydride [8].

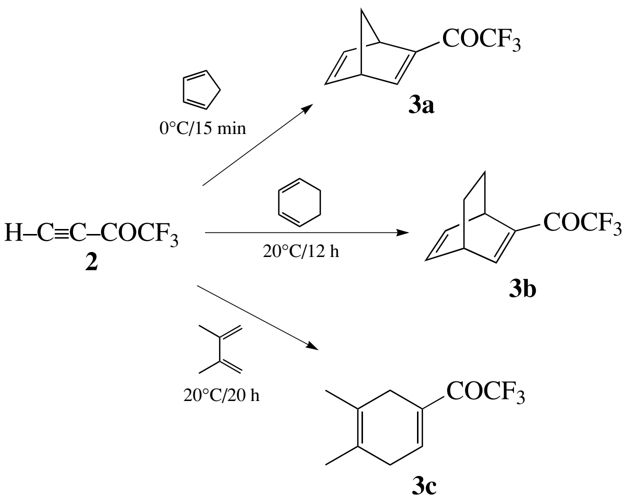
$$\mathrm{Me_3Sn{-}C{\equiv}C{-}SnMe_3 + (CF_3CO)_2O}$$
$$\longrightarrow \underset{\mathbf{1},\ 90\%}{\mathrm{Me_3Sn{-}C{\equiv}C{-}COCF_3}} + \mathrm{CF_3CO_2SnMe_3}$$

The trimethylstannyl substituent in compound **1** is known to undergo electrophilic substitution by a halogen atom under mild conditions [8]. Taking into account this feature, we supposed that the electrophilic substitution of a proton for this residue could proceed similarly.

Indeed, the treatment of acetylene **1** with trifluoroacetic acid was found to result in trifluoroacetylacetylene **2** in high yield; the second reaction product, trimethylstannyl trifluoroacetate, is precipitated. The use of high-boiling ethyl benzoate as a solvent makes it possible to isolate the target compound by distillation from the reaction mixture.

$$\mathrm{Me_3Sn{-}\underset{\mathbf{1}}{C}{\equiv}C{-}COCF_3 + CF_3CO_2H}$$
$$\longrightarrow \underset{\mathbf{2},\ 85\%}{\mathrm{H{-}C{\equiv}C{-}COCF_3}} + \mathrm{CF_3CO_2SnMe_3}$$

Acetylene **2** is a low-boiling compound (bp 31°C) stable upon storage in the absence of moisture and showing high reactivity in the Diels–Alder reaction with different dienes. Thus, the addition reaction to cyclopentadiene is completed in several minutes at 0°C, whereas the reaction with less reactive cyclohexadiene and 2,3-dimethylbutadiene requires several hours at 20°C.



Although cycloadducts **3a**, **3b**, and **3c** can be distilled in a vacuum, we revealed an unusual dimerization reaction for bicyclic compounds **3a** and **3b**, which is completed in the case of cycloadduct **3a** at 20°C in the

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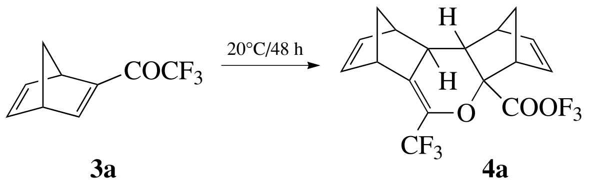
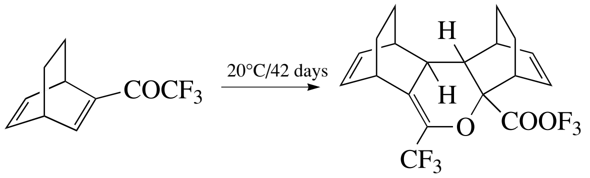
absence of a solvent over 48 h, while cycloadduct **3b** undergoes complete dimerization during six weeks.

Therefore, the latter compound can be purified by vacuum distillation, but bicyclic compound **3a** should be used immediately after the cycloaddition reaction is completed because the distillation is accompanied by fast dimerization.

Cycloadducts **3a** and **3b** were shown to undergo dimerization via the Diels–Alder reaction where the conjugated C=C bond of one molecule behaves as the dienophile component, while the conjugated C=C–C=O system of the other reacts as the diene component.



3a **4a**



3b **4b**

Dimers **4a** and **4b** are stable crystalline solids. At present, we are studying the reasons for such easy dimerization of cycloadducts **3a** and **3b**, as well as the mutual spatial arrangement of bicycles in **4a** and **4b** molecules.

EXPERIMENTAL

All manipulations with trimethylstannyltrifluoroacetylacetylene were performed 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, ^1H and ^{13}C NMR spectra, and IR spectroscopy.

Trimethylstannyltrifluoroacetylacetylene 1. Trifluoroacetic anhydride (42.4 mL, 63 g, 0.30 mol) was added in one portion to a solution of 100 g (0.28 mol) of bis(trimethylstannyl)acetylene in 200 mL of tetrahydrofuran under stirring with a powerful magnetic stirrer; after the exothermic reaction was completed, the mixture was allowed to stand overnight. The main portion of the tetrahydrofuran was removed in a vacuum of a water-jet pump on a water bath at 20°C. A reflux condenser was replaced by a distilling column with a descending condenser and an adapter with a receiver cooled with dry ice. The temperature of the water bath was gradually increased to 90–95°C while the reaction mixture was vigorously stirred under a vacuum of 10–15 mmHg until the distillation of the product within 45–65°C ceased (the distillation residue accumulating trimethylstannyl trifluoroacetate quickly solidified and partially sublimed, and the stirring was hampered, but the distillation should not be stopped). An additional portion of the product was distilled off from the reaction mixture in a vacuum of an oil pump at 1–2 mmHg after the receiver was replaced. The product was redistilled to give 72.7 g (90%) of acetylene **1**, bp 53–56°C/8 mmHg.

1-Trifluoroacetylacetylene 2. A solution of 6.0 g (3.9 mL, 0.052 mol) of trifluoroacetic acid in 5 mL of ethyl benzoate was added dropwise to a solution of 15 g (0.052 mol) of acetylene **1** in 10 mL of ethyl benzoate with stirring and cooling to –20°C. The solution was stirred for 15 min at 20°C, then the mixture was gradually heated to distill the product off through a short distilling column into a trap with a receiver cooled with dry ice. The product was redistilled to give 5.4 g (85%) of acetylene **2**, bp 31°C.

General procedure for the synthesis of cycloadducts 3. An appropriate diene (0.0052 mol) was added to a solution of 0.64 g (0.0052 mol) of acetylene **2** in 2.5 mL of anhydrous diethyl ether (deuteriochloroform was used as the solvent when ^1H NMR monitoring of the reaction course was necessary). When cyclopentadiene was used, the reagents were mixed at –15°C and kept for 1 h at 0°C to bring about the quantitative formation of cycloadduct **3a** as shown by ^1H NMR data. For the reaction of cyclohexadiene and 2,3-dimethylbutadiene, the reaction mixture was kept for the required time at a prescribed temperature and then distilled in a vacuum to give 0.76 g (72%) of adduct **3b**, bp 90–92°C (20 mmHg), and 0.9 g (84%) of adduct **3c**, bp 80–90°C (15 mmHg).

Synthesis of dimers 4a and 4b. A solution of cycloadduct **3a** in anhydrous diethyl ether was concentrated in a vacuum at 20°C, and the residue was kept for 48 h at 20°C. The resulting dimer **4a** was recrystallized from hexane, mp 81–83°C. Cycloadduct **3b** was kept for 42 days at 20°C. The resulting dimer **4b** was recrystallized from hexane, mp 81–82°C.

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