1-Trifluoroacetyl-2-trimethylstannyl- and 1-trifluoroacetyl-2-bromoacetylenes as new dienophiles in the Diels–Alder reactions

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Trifluoroacetic anhydride exotermically reacts with bis(trimethylstannyl)acetylene to form previously unknown 1-trifluoroacetyl-2-trimethylstannylacetylene, which interacts with bromine to produce 1-trifluoroacetyl-2-bromoacetylene.

Diels–Alder reactions with the participation of acetylene dienophiles activated with electron-withdrawing groups are widely employed in organic synthesis.[1,2] The strong electron-withdrawing trifluoroacetyl group can impart both activating and regiocontrolled effects on cycloaddition reactions and provide further useful transformations of cycloadducts. Trifluoromethylketones are of great interest to synthetic, physical and medicine chemists because of their unique properties.[3,4] The synthesis of trifluoroacetyl ketones with the acetylene moiety was described.[4,5] However, only 1-phenyl-2-trifluoroacetylacetylene[6] and 1-chloromethyl-2-trifluoroacetylacetylene[7] were investigated in Diels–Alder reactions.

Here, we report the preparation of 1,1,1-trifluoro-4-trimethylstannylbut-3-yn-2-one **1** and 4-bromo-1,1,1-trifluourobut-3-yn-2-one **2**, new versatile dienophiles, and their application to [4 + 2]-cycloaddition reactions.

It was found that trifluoroacetic anhydride exotermically reacts with easily available bis(trimethylstannyl)acetylenes[8] in THF to form acetylene **1** and trimethylstannyltrifluoroacetate, which can be readily separated.

$$Me_3SnC{\equiv}CSnMe_3 + (CF_3CO)_2O \xrightarrow{\text{THF, 20 °C}}$$
$$CF_3COC{\equiv}CSnMe_3 + CF_3COOSnMe_3$$
1 (98%)
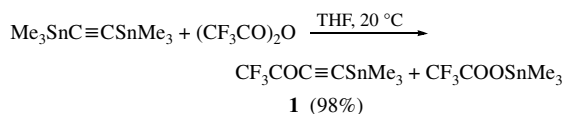
Acetylene **1** can be distilled *in vacuo*, and it is stable at room temperature in the absence of air. It is an active dienophile affording cycloadducts **3**[†] (Table 1). Thus, the reaction of **1** with cyclopentadiene proceeds even at 10°. The reaction with

spiro-(2,4)-hepta-4,6-diene occurs when refluxing in CH_2Cl_2. However, with less active dienes such as cyclohexadiene, 2,3-dimethylbutadiene and 1,3-butadiene it is necessary to reflux the components in THF. Note that cycloaddition reactions of trimethylstannylacetylenes activated with cyano, acetyl or alkoxy-carbonyl groups proceeded under more severe conditions to form cycloadducts in moderate yields, and in the case of cyclohexadiene aromatization takes place as a result of ethylene extrusion.[9]

We found that acetylene **1** reacts with bromine in CH_2Cl_2 at –30 °C to afford previously unknown 1-trifluoroacetyl-2-bromoacetylene **2** in almost 100% yield:

$$Me_3SnC{\equiv}CCOCF_3 \xrightarrow[\text{CH}_2\text{Cl}_2,\ -30\ °C]{Br_2} BrC{\equiv}CCOCF_3 + Me_3SnBr$$
1　　　　　　　　　　　　　　　**2**
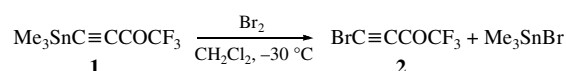
[†] *Characteristics and spectroscopic data.* ¹H NMR spectra were recorded on a Bruker AMX-400 spectrometer (400.13 MHz) in CDCl₃, TMS was used as an internal standard. IR spectra were measured on a 'Nicolett' FT spectrometer.

1: bp 50–52 °C (10 Torr). ¹H NMR, δ: 0.05 (s, 9H, SnMe₃). IR, ν/cm⁻¹: 2140 (C≡C), 1705 (C=O). Found (%): C, 29.81; H, 3.49; Sn, 40.53; F, 19.45. Calc. for C₇H₉F₃OSn (%): C, 29.53; H, 3.19; Sn, 41.64; F, 20.01.

2: bp 39–42 °C (100 Torr). IR, ν/cm⁻¹: 2180 (C≡C), 1700 (C=O). Found (%): C, 29.43. Calc. for C₄BrF₃O (%): C 23.91.

3a: bp 68–69 °C (1 Torr). ¹H NMR, δ: 0.25 (s, 9H, SnMe₃), 2.09 (d, 1H, H-7, ²J 12 Hz), 2.20 (d, 1H, H-7, ²J 12 Hz), 4.11 (d, 2H, H-1, H-4, ²J 10 Hz), 6.63 (m, 1H, H-5), 6.87 (m, 1H, H-6). Found (%): C, 41.34; H, 4.56; F, 15.93; Sn, 33.01. Calc. for C₁₂H₁₅F₃OSn (%): C, 41.08; H, 4.31; F, 16.25; Sn, 33.80.

3b: bp 88–89 °C (2 Torr). ¹H NMR, δ: 0.21 (s, 9H, SnMe₃), 0.45–0.65 (m, 4H, CH₂CH₂), 3.50 (d, 2H, H-1, H-4, ²J 11 Hz), 6.90 (m, 1H, H-6). Found (%): C, 44.08; H, 4.21; F, 15.40; Sn, 31.74. Calc. for C₁₄H₁₇F₃OSn (%): C, 44.62; H, 4.55; F, 15.12; Sn, 31.47.

3c: bp 70–71 °C (1 Torr). ¹H NMR, δ: 0.25 (s, 9H, SnMe₃), 1.05–1.51 (m, 4H, CH₂CH₂), 4.23 (d, 2H, H-1, H-4, ²J 11 Hz), 6.23 (d, 1H, H-6), 6.40 (d, 1H, H-6). Found (%): C, 43.01; H, 4.92; F, 15.93; Sn, 31.87. Calc. for C₁₃H₁₇F₃OSn (%): C, 42.79; H, 4.70; F, 15.62; Sn, 32.50.

3d: bp 80–81 °C (1.5 Torr). ¹H NMR, δ: 0.18 (s, 9H, SnMe₃), 1.63 (s, 3H, Me), 1.68 (s, 3H, Me), 3.05 (d, 2H, H₂C-3, ²J 8 Hz), 3.12 (d, 2H, H₂C-6, ²J 8 Hz). Found (%): C, 42.85; H, 5.36; F, 15.27; Sn, 32.01. Calc. for C₁₃H₁₉F₃OSn (%): C, 42.56; H, 5.22; F, 15.54; Sn, 32.33.

3e: bp 64–66 °C (1 Torr). ¹H NMR, δ: 0.21 (s, SnMe₃), 3.04 (d, 2H, H₂C-3, ²J 8 Hz), 3.08 (d, 2H, H₂C-6, ²J 8 Hz), 5.70–5.85 (m, 2H, CH=CH). Found (%): C, 38.53; H, 4.27; F, 17.05; Sn, 35.32. Calc. for C₁₁H₁₅F₃OSn (%): C, 38.99; H, 4.46; F, 16.82; Sn, 35.00.

4a: bp 65–67 °C (2 Torr). ¹H NMR, δ: 2.23 (d, 1H, H-7, ²J 10 Hz), 2.36 (d, 1H, H-7, ²J 10 Hz), 3.69 (s, 1H, H-4), 4.10 (s, 1H, H-1), 6.85 (m, 1H, CH=CH), 6.89 (m, 1H, CH=CH). Found (%): C, 40.61; H, 2.42. Calc. for C₉H₆BrF₃O (%): C, 40.48; H, 2.26.

4b: bp 75–76 °C (1 Torr). ¹H NMR, δ: 0.50–0.72 (m, 4H, CH₂CH₂), 3.30 (d, 1H, H-4, ²J 11 Hz), 3.59 (d, 1H, H-1, ²J 11 Hz), 6.88 (m, 1H, H-6), 6.95 (m, 1H, H-5). Found (%): C, 45.24; H, 3.08. Calc. for C₁₁H₈BrF₃O (%): C, 45.08; H, 2.75.

4c: bp 69–70 °C (1 Torr). ¹H NMR, δ: 1.40–1.70 (m, 4H, CH₂CH₂), 4.05 (m, 1H, H-1), 4.41 (m, 1H, H-4), 6.30–6.48 (m, 2H, CH=CH). Found (%): C, 42.48; H, 2.44. Calc. for C₁₀H₈BrF₃O (%): C, 42.73; H, 2.87.

4d: bp 68–69 °C (1 Torr). ¹H NMR, δ: 1.63 (s, 6H, 2Me), 2.91 (dd, 2H, H₂C-6), 3.24 (dd, 2H, H₂C-3). Found (%): C, 42.63; H, 3.77. Calc. for C₁₀H₁₀BrF₃O (%): C, 42.43; H, 3.56.
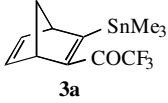
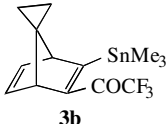**Table 1** Diels–Alder reactions of **1**.
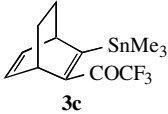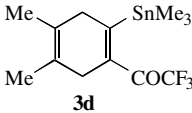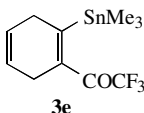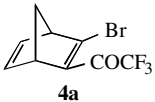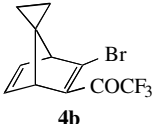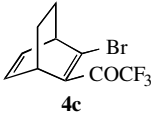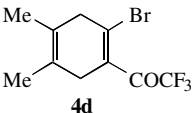
Entry	Diene	Reaction conditions	Product	Yield (%)
a	(cyclopentadiene)	Et₂O, 24 h, 20 °C	**3a**	78
b	(spiro diene)	CH₂Cl₂, 6 h, 50 °C	**3b**	69
c	(cyclohexadiene)	THF, 6 h, 60 °C	**3c**	63
d	Me / Me butadiene	THF, 8 h, 65 °C	**3d**	60
e	(butadiene)	THF, 8 h, 80 °C	**3e**	52

Table 2 Diels–Alder reactions of **2**.

Entry	Diene	Reaction conditions	Product	Yield (%)
a		CH$_2$Cl$_2$, 15 min, −30–20 °C	Br, COCF$_3$ **4a**	77
b		CH$_2$Cl$_2$, 15 min, −30–20 °C	Br, COCF$_3$ **4b**	83
c		CH$_2$Cl$_2$, 6 h, 0–20 °C	Br, COCF$_3$ **4c**	84
d	Me, Me	CH$_2$Cl$_2$, 6 h, 20 °C	Me, Br, Me, COCF$_3$ **4d**	72

Acetylene **2** exibits high reactivity in Diels–Alder reactions (Table 2). With active dienes sush as cyclopentadiene and spiro-(2,4)-hepta-4,6-diene, an exothermic reaction takes place even at −30 °C, while less active dienes exothermically react at 0–20 °C.

Note that the isolation of **2** is not necessary when cyclo-adducts **4**† and trimethylstannyl bromide can be easily separated by distillation. In such cases, a diene can be added to the reaction mixture when the colour of bromine disappears.

Unfortunately, the reactions of **2** with isoprene and 1,3-buta-diene give a mixture of products.

In conclusion we developed the preparation of two acetylenic dienophiles activated by trifluoroacetyl group. Their cycloaddition reactions afford α,β-unsaturated trifluoromethyl ketones containing trimethylstannyl substituents or bromine in the β-position, which open a wide range of further transformations.

References

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