# Synthesis and Photochemical Reaction of 1,4-Dialkyl-7-oxa-2,3,5,6-tetrakis(trifluoromethyl)bicyclohepta-2,5-diene

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Diels-Alder reaction of 2,5-dialkyl-3,4-bis(trifluoromethyl)furan with hexafluoro-2-butyne gave 1,4-dialkyl-7-oxa-2,3,5,6-tetrakis(trifluoromethyl)bicyclohepta-2,5-diene. Irradiation (uv) of 1,4-diethyl-7-oxa-2,3,5,6-tetrakis(trifluoromethyl)bicyclohepta-2,5-diene afforded 1-ethyl-2,3,4,5-tetrakis(trifluoromethyl)-1,4-cyclopentadiene, ethyl 3-[1-ethyl-2,3,4,5-tetrakis(trifluoromethyl)-1,4-cyclopentadienyl] ketone, and 2,7-diethyl-3,4,5,6-tetrakis(trifluoromethyl)oxepin.

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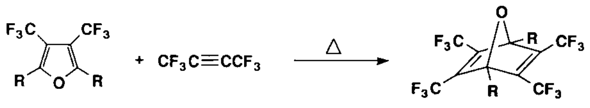
Much attention has been focused on the synthesis of heterocycles containing trifluoromethyl groups, because they can be used as medicinal and agricultural chemicals, *etc.* The Diels-Alder reaction is one of the most useful methods to synthesize heterocylic compounds [1-3]. Recently, we have reported the $\gamma$-ray induced addition reaction of propionaldehyde with hexafluoro-2-butyne to give 2,5-diethyl-3,4-bis(trifluoromethyl)furan [4]. We report here the synthesis and photochemical reaction of 1,4-diethyl-7-oxa-2,3,5,6-tetrakis(trifluoromethyl)bicyclohepta-2,5-diene.

The Diels-Alder reaction of 2,5-diethyl-3,4-bis(trifluoromethyl)furan (**1a**) with hexafluoro-2-butyne (**2**) gave 1,4-diethyl-7-oxa-2,3,5,6-tetrakis(trifluoromethyl)bicyclohepta-2,5-diene (**3a**) (Scheme 1). The best yield (*ca.* 35%) of **3a** was obtained in the molar ratio of **1a** to **2** = 1:1 at 160°. The same reaction of 2,5-dimethyl-3,4-bis(trifluoromethyl)furan (**1b**) with **2** gave 1,4-dimethyl-7-oxa-2,3,5,6-tetrakis(trifluoromethyl)bicyclohepta-2,5-diene (**3b**) in 38% yield.

Scheme 1



1 2 3

a: R = $C_2H_5$
b: R = $CH_3$

The uv irradiation of **3a** afforded 1-ethyl-2,3,4,5-tetrakis(trifluoromethyl)-1,4-cyclopentadiene (**5**), ethyl 3-[1-ethyl-2,3,4,5-tetrakis(trifluoromethyl)-1,4-cyclopentadienyl] ketone (**6**), and 2,7-diethyl-3,4,5,6-tetrakis(trifluoromethyl)oxepin (**7**) (Scheme 2). The products were isolated by using a preparative gas chromatograph and identified on the basis of their spectral data. The cyclopentadiene **5** showed four $CF_3$, one $C_2H_5$, one CH, and two C=C groups and molecular ion peak at m/z 336. The ketone **6** showed four $CF_3$, two $C_2H_5$, two C=C, and one C=O groups and molecular ion peak at m/z 422. The oxepin **7** had a highly symmetrical structure and showed two sets of two $CF_3$ and one $C_2H_5$ groups and molecular ion peak at m/z 422.

Scheme 2

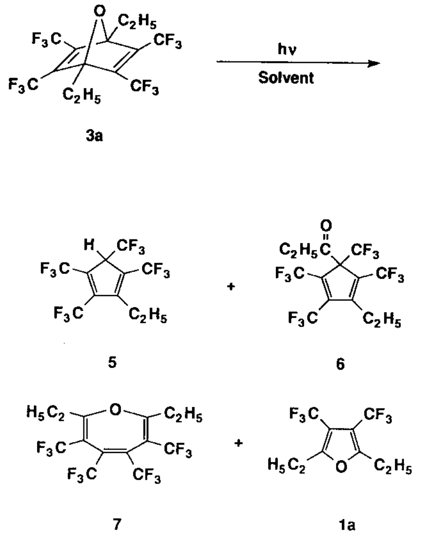


Table 1

UV Irradiation of 7-Oxabicycloheptadiene **3a**

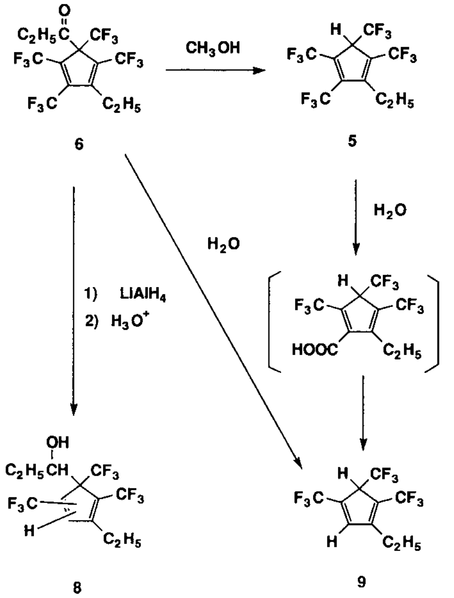
| Solvent | Reaction Time, hours | Yield [a] (%) | | | | |
|---|---|---|---|---|---|---|
| | | **1a** | **3a** | **5** | **6** | **7** |
| ether [b] | 173 | 0 | 75 | 14 | 3 | 8 |
| ether | 184 | 0 | 59 | 14 | 23 | 4 |
| ether | 337 | 0 | 32 | 9 | 57 | 2 |
| carbon tetrachloride | 142 | 10 | 64 | 0 | 8 | 16 |

[a] Determined by gc analysis. [b] A small amount of water was added.

The results of uv irradiation of **3a** are summarized in Table 1. The reaction in ether gave **6** as the main product accompanied by **5** and **7**. The longer was the irradiation time, the greater the yield of **6**. Addition of a small amount of water to the solution decreased the yield of **6**. While the reaction in carbon tetrachloride gave **7** as the main product accompanied by **1a**.

In order to confirm the structures of the products, a few reactions of **5** and **6** were conducted (Scheme 3). The uv irradiation of **6** gave **5** in 20% yield. Since the ketone **6** had high reactivity for nucleophiles, it was converted easily into **5** in methanol. The hydrolysis of **5** provided 1-ethyl-2,3,4-tris(trifluoromethyl)-1,4-cyclopentadiene (**9**), which may be formed *via* the corresponding carboxylic acid. The hydrolysis of **6** also gave **9**. The reduction of **6** with lithium aluminum hydride afforded two regioisomers of 3-[1-ethyltris(trifluoromethyl)-1,4-cyclopentadienyl]-1-propanol (**8**).

Scheme 3



A plausible mechanism for the formation of ketone **6** and oxepin **7** is shown in Scheme 4. The uv irradiation of **3a** can give the corresponding oxaquadricyclane **4**. Though several oxaquadricyclanes have been isolated in the literature [1,3,5-7], the oxaquadricyclane **4** could not be isolated. Rearrangement of two $\sigma$-bonds of **4** into $\pi$-bonds gives oxepin **7** [1,8]. Cleavage of the C-O bond of **4** gives **6**. In carbon tetrachloride, the reverse Diels-Alder reaction of **3a** affords **1a**.

## EXPERIMENTAL

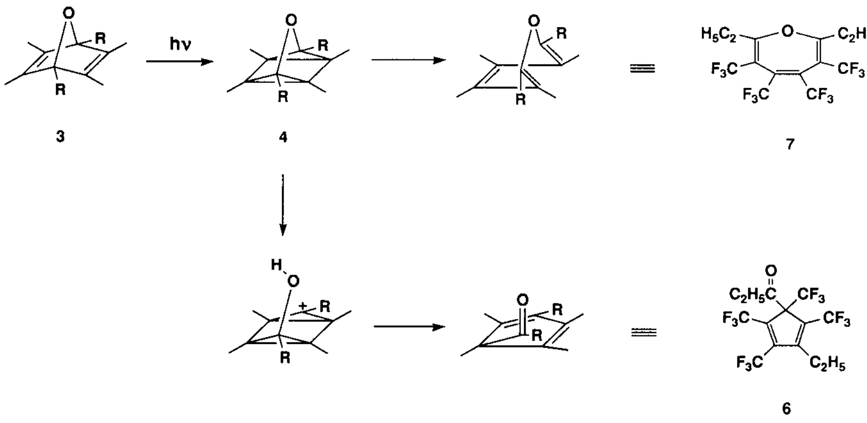
All boiling points are uncorrected. The ir spectra were recorded on a EPI-2 infrared spectrophotometer. The $^1$H nmr spectra were measured in carbon tetrachloride with a Hitachi R-22 (90 MHz) spectrometer. The $^{19}$F nmr spectra were measured in carbon tetrachloride with a Hitachi R-20B (56.45 MHz) and positive $\delta$ value are downfield from trifluoroacetic acid as an external reference. Preparative gc was performed on a Varian model 700 instrument, using aluminum column (5 mm x 300 cm) packed with 10% OV-17 on Chromosorb WAW DMCS (60-80 mesh). Mass spectra were measured with a Hitachi RMU-7 spectrometer.

### 2,5-Dimethyl-3,4-bis(trifluoromethyl)furan (**1b**).

2,5-Dimethyl-3,4-bis(trifluoromethyl)furan (**1b**) was prepared by a procedure similar to that for 2,5-diethyl-3,4-bis(trifluoromethyl)furan [4].

In a stainless steel autoclave (500 ml) were placed acetaldehyde (57.9 g, 1.31 moles, prepared by heating paraldehyde in the presence of a small amount of sulfuric acid) and 1,1,2-trichloro-1,2,2-trifluoroethane (147.9 g). The autoclave was cooled by liquid nitrogen. Hexafluoro-2-butyne (75.2 g, 0.464 mole) was introduced into the solution under reduced pressure. The $\gamma$-ray irradiation was performed at 2.0 x $10^5$ r $h^{-1}$ by a $^{60}$Co source for 150 hours (total irradiation 30 Mr) at ambient temperature. After the irradiation, volatile products were removed. Distillation of the residue provided 5,5,5-trifluoro-3-trifluoromethyl-3-penten-2-one (12.31 g, 13% yield) and 3,4-bis(trifluoromethyl)-2,4-hexanedione (8.49 g, 7.3% yield). To 3,4-bis(trifluoromethyl)-2,4-hexanedione (14.00 g, 56.0 mmoles) was added dropwise sulfuric acid (100 ml).

Scheme 4



The mixture was stirred for 15 minutes and poured into a mixture of ice and ether. After stirring for several minutes, the product was extracted with ether (3 x 100 ml), dried over sodium sulfate, and distilled under reduced pressure to give **1b** in 68% yield.

Compound **1b** had bp 77-78°/88 mm Hg; $n_d^{20}$ 1.3686; $d_4^{20}$ 1.384; $^1$H nmr: $\delta$ 2.35 (s, $CH_3$); $^{19}$F nmr: $\delta$ 20.5.

*Anal.* Calcd. for $C_8H_6F_6O$: C, 41.39; H, 2.61. Found: C, 41.22; H, 2.65.

### Diels-Alder Reaction of 2,5-Dialkyl-3,4-bis(trifluoromethyl)furan (1) with Hexafluoro-2-butyne (2).

In a stainless steel cylinder (200 ml) equipped with a magnetic stirrer was placed **1a** (57.02 g, 0.219 mole). Into the cylinder cooled by liquid nitrogen was introduced **2** (38.5 g, 0.238 mole) under reduced pressure. The cylinder was heated at 140° for 80 hours and then cooled to room temperature. After unreacted **2** was recovered, a mixture of 1,4-diethyl-7-oxa-2,3,5,6-tetrakis(trifluoromethyl)bicyclohepta-2,5-diene (**3a**, 32% gc yield) and **1a** was obtained. The oxabicycloheptadiene **3a** was isolated by using a gas chromatograph (24.66 g, 27% yield).

Compound **3a** had bp 153-157°; $n_d^{20}$ 1.3603; $d_4^{20}$ 1.463; ir: $\nu$ (cm$^{-1}$) 1664 (C=C); $^1$H nmr: $\delta$ 1.06 (t, J = 7.2 Hz, $CH_3$), 2.57 (q, J = 7.2 Hz, $CH_2$); $^{19}$F nmr: $\delta$ 17.9; ms: m/z 422 ($M^+$).

*Anal.* Calcd. for $C_{14}H_{10}F_{12}O$: C, 39.83; H, 2.39. Found: C, 39.35; H, 2.33.

In a procedure similar to that for **3a**, the Diels-Alder reaction of **1b** with **2** provided 1,4-dimethyl-7-oxa-2,3,5,6-tetrakis(trifluoromethyl)bicyclohepta-2,5-diene (**3b**) (10.36 g, 23% yield).

Compound **3b** had bp 143-146°; $n_d^{20}$ 1.3437; $d_4^{20}$ 1.526; ir: $\nu$ (cm$^{-1}$) 1677 (C=C); $^1$H nmr: $\delta$ 1.92 (s); $^{19}$F nmr: $\delta$ 18.2.

*Anal.* Calcd. for $C_{12}H_6F_{12}O$: C, 36.57; H, 1.57. Found: C, 36.93; H, 1.77.

### UV Irradiation of 1,4-Diethyl-7-oxa-2,3,5,6-tetrakis(trifluoromethyl)bicyclohepta-2,5-diene (3a).

An anhydrous ether solution of **3a** (13.23 g, 31.35 mmoles) sealed under an argon atmosphere in a quartz ampoule (50 ml) was irradiated with a 1 kW high pressure mercury lamp at a distance of about 10-15 cm for 184 hours at room temperature. Products were analyzed by a gas chromatograph. Three products, 1-ethyl-2,3,4,5-tetrakis(trifluoromethyl)-1,4-cyclopentadiene (**5**, 14% gc yield), ethyl 3-[1-ethyl-2,3,4,5-tetrakis(trifluoromethyl)-1,4-cyclopentadienyl] ketone (**6**, 23% gc yield), and 2,7-diethyl-3,4,5,6-tetrakis(trifluoromethyl)oxepin (**7**, 4% gc yield) were isolated by using a preparative gas chromatograph.

Compound **5** had bp 152-153°; $n_d^{20}$ 1.3542; $d_4^{20}$ 1.551; ir: $\nu$ (cm$^{-1}$) 1660, 1601 (C=C); $^1$H nmr: $\delta$ 1.19 (t, J = 7.5 Hz, $CH_3$), 2.52 (q, J = 7.5 Hz, $CH_2$), 4.32 (q, J = 6.0 Hz, CH); $^{19}$F nmr: $\delta$ 21.0, 20.3, 17.4, 14.7; ms: m/z 336 ($M^+$).

*Anal.* Calcd. for $C_{11}H_6F_{12}$: C, 36.08; H, 1.65. Found: C, 36.37; H, 1.93.

Compound **6** had bp 81-82°/12 mm Hg; $n_d^{20}$ 1.3822; $d_4^{20}$ 1.496; ir: $\nu$ (cm$^{-1}$) 1754 (C=O), 1648, 1592 (C=C); $^1$H nmr: $\delta$ 1.05 (t, $CH_3$), 1.21 (t, $CH_3$), 2.17 (q, $CH_2$), 2.68 (q, $CH_2$); $^{19}$F nmr: $\delta$ 22.9, 21.9, 17.9, 14.1; ms: m/z 422 ($M^+$).

*Anal.* Calcd. for $C_{14}H_{10}F_{12}O$: C, 39.83; H, 2.39. Found: C, 39.74; H, 2.53.

Compound **7** had $n_d^{20}$ 1.3841; $d_4^{20}$ 1.482; ir: $\nu$ (cm$^{-1}$) 1653, 1607 (C=C); $^1$H nmr: $\delta$ 1.23 (t, J = 7.5 Hz, $CH_3$), 2.50 (q, J = 7.5 Hz, $CH_2$); $^{19}$F nmr: $\delta$ 22.5, 20.6; ms: m/z 422 ($M^+$).

*Anal.* Calcd. for $C_{14}H_{10}F_{12}O$: C, 39.83; H, 2.39. Found: C, 40.49; H, 2.70.

### Reaction of Ethyl 3-[1-Ethyl-2,3,4,5-tetrakis(trifluoromethyl)-1,4-cyclopentadienyl] Ketone (6).

#### 1) UV Irradiation.

An anhydrous ether solution (180 ml) of the ketone **6** (3.83 g) sealed under argon atmosphere in a quartz ampoule (200 ml) was irradiated using a 1 kW high pressure mercury lamp at a distance of about 12 cm for 256 hours at room temperature. After evaporation of the solvent, residual crude **5** was purified by a preparative gas chromatograph (20% yield).

#### 2) With Methanol.

A methanol solution (0.513 g, 16.0 mmoles) of the ketone **6** (5.64 g, 13.4 mmoles) was stirred for 4.5 hours at room temperature. The dark yellow reaction mixture was distilled under reduced pressure to give **5** (3.19 g, 65% yield).

#### 3) With Water.

To an ether solution (2 ml) of the ketone **6** (0.188 g) was added 2 drops of water. The reaction mixture was stirred for 2.5 hours and allowed to stand overnight. The reaction afforded a mixture of **5** and 1-ethyl-2,3,4-tris(trifluoromethyl)-1,4-cyclopentadiene (**9**).

#### 4) With Lithium Aluminum Hydride.

To an ether solution (80 ml) of the ketone **6** (5.58 g, 13.2 mmoles) was added lithium aluminum hydride (1.50 g, 39.6 mmoles). After refluxing the solution for 90 minutes, the solution was poured into dilute sulfuric acid solution. The product was extracted, distilled, and purified by a preparative gas chromatograph to give 3-[1-ethyl-tris(trifluoromethyl)-1,4-cyclopentadienyl]-1-propanol (**8**, 0.44 g, 9.4%).

Compound **8** (regioisomer) had ir: $\nu$ (cm$^{-1}$) 3640, 3475 (OH), 1693, 1644 (C=C); $^1$H nmr: $\delta$ 0.9-1.4 ($CH_3$), 2.0-3.2 ($CH_2$), 3.9-4.3 (CH), 6.35 (s, =CH-), 7.70 (s, =CH-); $^{19}$F nmr: $\delta$ 23.1, 13.7, 11.5, 22.0, 14.1, 12.5.

*Anal.* Calcd. for $C_{13}H_{13}F_9O$: C, 43.83; H, 3.68. Found: C, 43.91; H, 3.95.

### Hydrolysis of 1-Ethyl-2,3,4,5-tetrakis(trifluoromethyl)-1,4-cyclopentadiene (5).

To an ether solution (5 ml) of cyclopentadiene **5** (3.61 g, 9.86 mmoles) was added water (0.45 g, 25.1 mmoles) with stirring. After stirring the solution for 5 hours, the product was distilled and purified by using a preparative gas chromatograph to give 1-ethyl-2,3,4-tris(trifluoromethyl)-1,4-cyclopentadiene (**9**, 1.11 g, 38%).

Compound **9** (regioisomer) had ir: $\nu$ (cm$^{-1}$) 1649, 1597 (C=C); $^1$H nmr: $\delta$ 1.16 (t, J = 7.5 Hz, $CH_3$), 2.54 (q, J = 7.5 Hz, $CH_2$), 4.18 (q, J = 7.5 Hz, CH), 6.80 (s, =CH-); $^{19}$F nmr: $\delta$ 20.1, 16.2, 12.8; ms: m/z 298 ($M^+$).

*Anal.* Calcd. for $C_{10}H_7F_9$: C, 40.29; H, 2.37. Found: C, 40.43; H, 2.32.

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