A Facile and Convenient Synthesis of 5,5-Dialkylthio- and 5-Alkyl(or Aryl)thio-2,4-pentadienoic Acids

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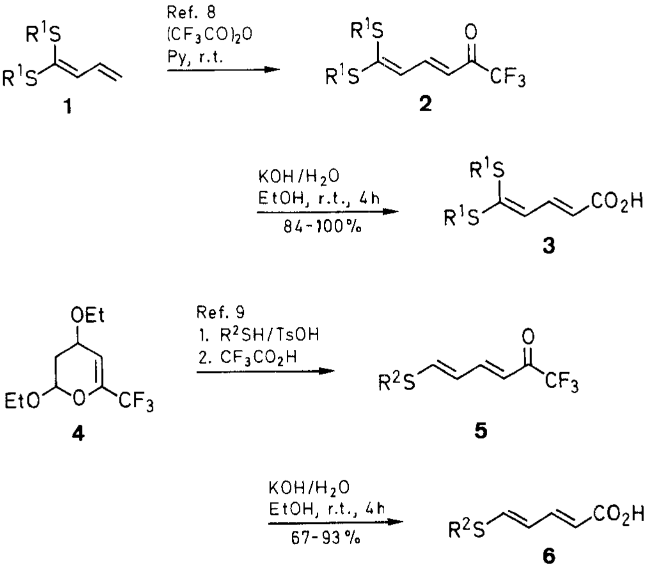
The hydrolysis of 6,6-dialkylthio- and 6-alkyl(or aryl)thio-1,1,1-trifluoro-3,5-hexadien-2-ones **2**, **5** with potassium hydroxide in ethanol proceeds quite easily to give the corresponding 2,4-pentadienoic acids **3**, **6**, respectively, in excellent yields. Bistrifluoroacetyl compounds **8**, **10a**, **b** give corresponding monocarboxylic acids **6a**, **3a**, **b** in high yields, with accompanied monodecarboxylation.

In our earlier communication we reported that β-trifluoroacetylvinyl ethers, readily prepared from commercial vinyl ethers[1] are hydrolyzed by wet potassium hydroxide in boiling benzene to give β-alkyl(or aryl)oxyacrylic acids in excellent yields.[2] This two-step process, a combination of trifluoroacetylation and subsequent hydrolysis, provided the most accessible route to this type of unsaturated aliphatic carboxylic acids. We have now extended this work to the synthesis of 5,5-dialkylthio-2,4-pentadienoic acids **3** and 5-alkyl(or aryl)thio-2,4-pentadienoic acids **6** by hydrolysis of the corresponding 1,1,1-trifluoro- or 1,1,1-trifluoro-3(or 5)-trifluoroacetyl-3,5-hexadien-2-ones **2**, **5**, **8**, **10**. Although there are some reports[3-7] of the synthesis of 5,5-dialkylthio- and 5-alkylthio-2,4-pentadienoic acids, yields are not generally high and the starting materials are not readily available. In addition, these methods are concerned with the synthesis of variously substituted **3** and **6**, and not suitable for the parent compounds **3** and **6**. We now wish to present here a convenient and versatile synthetic method for 2,4-pentadienoic acids **3** and **6**.

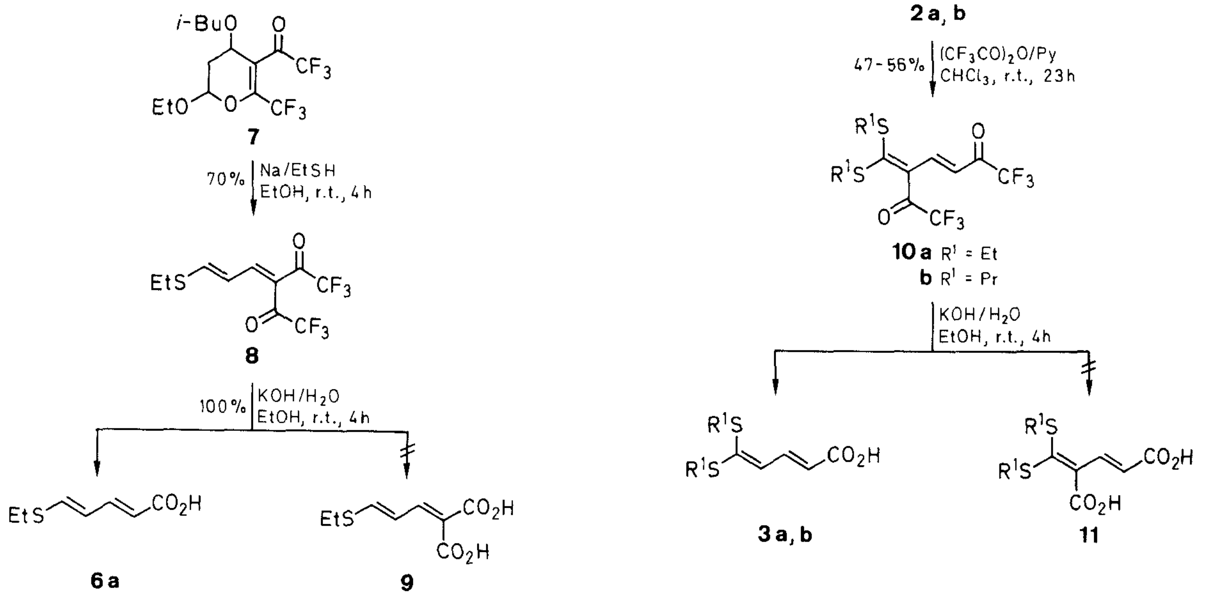


1-3	R^1	5, 6	R^2
a	Et	**a**	Et
b	Pr	**b**	Pr
c	$-CH_2-$	**c**	CH_2Ph
		d	Ph

Scheme A

6,6-Dialkylthio-1,1,1-trifluoro-3,5-hexadien-2-ones **2a–c** were readily obtained from 1,1-dialkylthio-1,3-butadienes **1a–c** with trifluoroacetic anhydride in satisfactory yields.[8] The hydrolysis of **2a–c** with saturated aqueous potassium hydroxide was performed in ethanol as solvent at room temperature for 4 hours and the corresponding 2,4-pentadienoic acids **3a–c** were obtained in 84–100% yield. Similarly, 6-alkyl(or aryl)thio-1.1.1-trifluoro-3.5-hexadien-2-ones **5a–d**, were hydrolyzed under the same conditions to afford 5-alkyl(or aryl)thio-2,4-pentadienoic acids **6a–d** in 67–93% yields (Scheme A). Since **5a–d** can be prepared in excellent yields by treatment of 2,4-diethoxy-6-trifluoromethyl-3,4-dihydro-2*H*-pyran (**4**) with thiols[9] and **4** are easily obtainable from vinyl ethers,[10] this method is especially useful for the synthesis of **6a–d** starting from vinyl ethers. In the case of β-trifluoroacetylvinyl ethers attempted hydrolysis by potassium hydroxide in ethanol resulted in the formation of β-alkoxyacrylic acids only in meager yields, presumably due to extensive concurrence of Michael-type addition.[2] In contrast, the hydrolysis of the present butadiene system proceeded cleanly without any such side reaction.

The present procedure could be applicable to 6-ethylthio-1,1,1-trifluoro-3-trifluoroacetyl-3,5-hexadien-2-one (**8**), which is prepared in 70% yield by treatment of 2-ethoxy-4-isobutoxy-5-trifluoroacetyl-6-trifluoromethyl-3,4-di-hydro-2*H*-pyran (**7**)[11] with sodium ethylthiolate. In this case 2,4-pentadienoic acid **6a** was obtained quantitatively without any formation of the expected 2-carboxy-2,4-pentadienoic acid **9**. Likewise, the hydrolysis



Scheme **B**

Table. 5,5-Dialkylthio- and 5-Alkyl(or Aryl)thio-2,4-pentadienoic Acids **3a–c**, **6a–d** Prepared

Product	Substrate	Yield[a] (%)	mp (°C) (solvent) or bp (°C)/ mbar[b]	Molecular Formula[c]	IR (KBr) (cm^{-1}) ν_{OH}, $\nu_{C=O}$	^{1}H-NMR (CDCl$_3$/TMS) δ, *J* (Hz)
3a	**2a** **10a**	90 98	99–100 (CHCl$_3$)	$C_9H_{14}O_2S_2$ (218.3)	3550–1918, 1674	1.27 (t, 3H, *J* = 7, CH$_3$), 1.32 (t, 3H, *J* = 7, CH$_3$), 2.88 (q, 4H, *J* = 7, CH$_2$), 5.75 (d, 1H, *J* = 15, H-2), 6.38 (d, 1H, *J* = 11, H-4), 7.88 (dd, 1H, *J* = 11, 15, H-3), 10.3–11.0 (br, 1H, OH)
3b	**2b** **10b**	84 100	250/0.3	$C_{11}H_{18}O_2S_2$ (246.4)	3525–2300, 1673	1.00 (br t, 6H, *J* = 7, CH$_3$), 1.43–1.83 (m, 4H, $C\underline{H}_2CH_3$), 2.83 (t, 4H, *J* = 7, SCH$_2$), 5.73 (d, 1H, *J* = 15, H-2), 6.37 (d, 1H, *J* = 11, H-4), 7.88 (dd, 1H, *J* = 11, 15, H-3), 8.9–9.7 (br, 1H, OH)
3c	**2c**	100	186–187 (EtOAc)	$C_7H_8O_2S_2$ (188.3)	3575–2100, 1673	3.43 (s, 4H, CH$_2$), 5.51 (d, 1H, *J* = 15, H-2), 6.18 (d, 1H, *J* = 11, H-4), 7.20 (dd, 1H, *J* = 11, 15, H-3), 8.0–9.0 (br, 1H, OH)[d]
6a	**5a** **8**	67 100	115–116 (CHCl$_3$)	$C_7H_{10}O_2S$ (158.2)	3575–2110, 1690	1.32 (t, 3H, *J* = 7, CH$_3$), 2.78 (q, 2H, *J* = 7, CH$_2$), 5.57 (d, 1H, *J* = 15, H-2), 6.07 (dd, 1H, *J* = 10, 14, H-4), 6.72 (d, 1H, *J* = 14, H-5), 7.20 (dd, 1H, *J* = 10, 15, H-3), 8.7–9.3 (br, 1H, OH)
6b	**5b**	93	82–83 (CHCl$_3$)	$C_8H_{12}O_2S$ (172.2)	3600–2245, 1658	1.02 (t, 6H, *J* = 7, CH$_3$), 1.3–2.0 (m, 4H, $C\underline{H}_2CH_3$), 2.74 (t, 4H, *J* = 7, SCH$_2$), 5.58 (d, 1H, *J* = 15, H-2), 6.07 (dd, 1H, *J* = 10, 14, H-4), 6.72 (d, 1H, *J* = 14, H-5), 7.23 (dd, 1H, *J* = 10, 15, H-3), 10.1–10.8 (br, 1H, OH)
6c	**5c**	92	143–144 (EtOAc)	$C_{12}H_{12}O_2S$ (220.3)	3520–2280, 1665	4.0 (s, 2H, CH$_2$), 5.2–5.7 (br, 1H, OH), 5.58 (d, 1H, *J* = 15, H-2), 6.18 (dd, 1H, *J* = 11, 14, H-4), 6.85 (d, 1H, *J* = 14, H-5), 6.9–7.3 (m, 6H, H-3 and 5H$_{arom}$)[e]
6d	**5d**	90	100–101 (CHCl$_3$)	$C_{11}H_{10}O_2S$ (206.3)	3600–2040, 1685	5.58 (d, 1H, *J* = 15, H-2), 6.10 (dd, 1H, *J* = 11, 14, H-4), 6.83 (d, 1H, *J* = 14, H-5), 7.0–7.5 (m, 6H, H-3 and 5H$_{arom}$), 10.1–10.7 (br, 1H, OH)

[a] Yield of isolated products.

[b] Oven temperature of Kugelrohr distillation.

[c] Satisfactory microanalyses obtained: C ±0.43, H ±0.26, S ±0.21; exception: **3c**, S −0.52.

[d] Solvent: CDCl$_3$/DMSO-d_6.

[e] Solvent: CD$_3$CN/DMSO-d_6.

of 1,1,1-trifluoro-5-trifluoroacetyl compounds **10a, b**, which are obtainable by diacylation of monoacylated compounds **2a, b** with trifluoroacetic anhydride in 47–56% yields, proceeded quite easily at room temperature to give 2,4-pentadienoic acids **3a, b** in almost quantitative yields (Scheme **B**). None of 4-carboxy-2,4-pentadienoic acids **11** and 2-vinylacrylic acids were produced. Probably the decarboxylation occurred preferentially at the 4-position of the diacid so as to give the more stable product with longer conjugated system.

IR spectra were recorded on a Hitachi EGI-G3 spectrophotometer. ^{1}H-NMR spectra were measured using a JEOL PMX-60SI spectrometer.

5,5-Dialkylthio- and 5-(Alkyl(or Aryl)thio-2,4-pentadienoic Acids (3, 6); General Procedure:

To a stirred solution of **2**[8] or **4**[10] (5.66 mmol) in EtOH (20 mL) is added sat. aq solution of KOH (10 mL) and stirring is continued at r.t. for 4 h. The basic solution is acidified with 2N HCl (100 mL) in an ice bath. Most of the solvent is removed under reduced pressure and the resulting mixture is extracted with CH_2Cl_2 (200 mL), and dried (Na_2SO_4). The solvent is evaporated to give the product **3** or **6** (Table).

6-Ethylthio-1,1,1-trifluoro-3-trifluoroacetyl-3,5-hexadien-2-one (8):

Sodium (138 mg, 6 mmol) is added to anhydrous EtOH (20 mL) and stirred under N_2 until complete dissolution. After addition of ethanethiol (0.44 mL, 6 mmol), **7**[11] (1.10 g, 3 mmol) is added to the mixture and stirred at r.t. for 4 h. The solution is acidified with 2N HCl (5 mL) and most of the solvent is evaporated under reduced pressure. The residue is washed with water (200 mL), extracted with CH_2Cl_2 (200 mL), and dried (Na_2SO_4). Evaporation of the solvent gives a crude mixture, which is distilled *in vacuo* to afford pure **8**; yield: 643 mg (70%); bp 90 °C/5 mbar (oven temperature).

$C_{10}H_8F_6O_2S$	calc.	C 39.22	H 2.63	F 37.22
(306.2)	found	39.52	2.77	37.70

IR (film): ν = 1685 (C=O), 1555 cm^{-1} (C=C).

^{1}H-NMR (CDCl$_3$/TMS): δ = 1.37 (t, 3H, J = 7 Hz, CH$_3$), 2.88 (q, 2H, J = 7 Hz, CH$_2$), 6.43 (dd, 1H, J = 11, 14 Hz, H-5), 7.36 (d, 1H, J = 11 Hz, H-4), 7.47 (d, 1H, J = 14 Hz, H-6).

6,6-Diethylthio-1,1,1-trifluoro-5-trifluoroacetyl-3,5-hexadien-2-one (10a); Typical Procedure:

To a stirred mixture of **2a**[8] (1.35 g, 5 mmol), pyridine (0.79 g, 10 mmol), and $CHCl_3$ (35 mL) is added dropwise trifluoroacetic anhydride (4.20 g, 20 mmol) at r.t. and the solution is allowed to stand for 23 h. The mixture is then poured into aq. 10% Na_2CO_3 (200 mL), and CH_2Cl_2 (200 mL) is added. The organic layer is separated, washed with 2N HCl (200 mL), water (200 mL), and dried (Na_2SO_4). The solvent is evaporated, and the crude mixture is chromatographed on silica gel column (5 × 15 cm; 200 mesh) using hexane/benzene (3:2) as eluent to give **10a**; yield: 1.02 g (56%); mp 55–56 °C (hexane).

$C_{12}H_{12}F_6O_2S_2$	calc.	C 39.34	H 3.30	F 31.12
(366.3)	found	39.57	3.11	30.87

IR (KBr): ν = 1723 (C=O), 1710 (C=O), 1572 cm^{-1} (C=C).

^{1}H-NMR (CDCl$_3$/TMS): δ = 1.33 (t, 6H, J = 7 Hz, CH$_3$), 3.02 (q, 4H, J = 7 Hz, CH$_2$), 6.10 (d, 1H, J = 16 Hz, H-3), 8.03 (d, 1H, J = 16 Hz, H-4).

10b; yield: 47%; eluent: hexane/benzene (4:1); mp 30–31 °C (hexane).

$C_{14}H_{16}F_6O_2S_2$	calc.	C 42.64	H 4.09	F 28.90
(394.4)	found	42.74	4.09	28.84

IR (KBr): ν = 1710 (C=O), 1565 cm^{-1} (C=C).

^{1}H-NMR (CDCl$_3$/TMS): δ = 1.03 (t, 6H, J = 7 Hz, CH$_3$), 1.40–1.97 (m, 4H, C$\underline{H}_2$CH$_3$), 2.98 (t, 4H, J = 7 Hz, SCH$_2$), 6.03 (d, 1H, J = 16 Hz, H-3), 7.98 (d, 1H, J = 16 Hz, H-4).

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