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A Facile and Convenient Synthesis of (E,E)-4-Trifluoroacetyl-1,3-butadienyl Sulfides by Acid Catalyzed Reaction of 2,4-Diethoxy-6-trifluoromethyl-3,4-dihydro-2H-pyran with Thiols

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(E,E)-4-Trifluoroacetyl-1,3-butadienyl sulfides are prepared from 2,4-diethoxy-6-trifluoromethyl-3,4-dihydro-2H-pyran with thiols in the presence of acid catalysts.

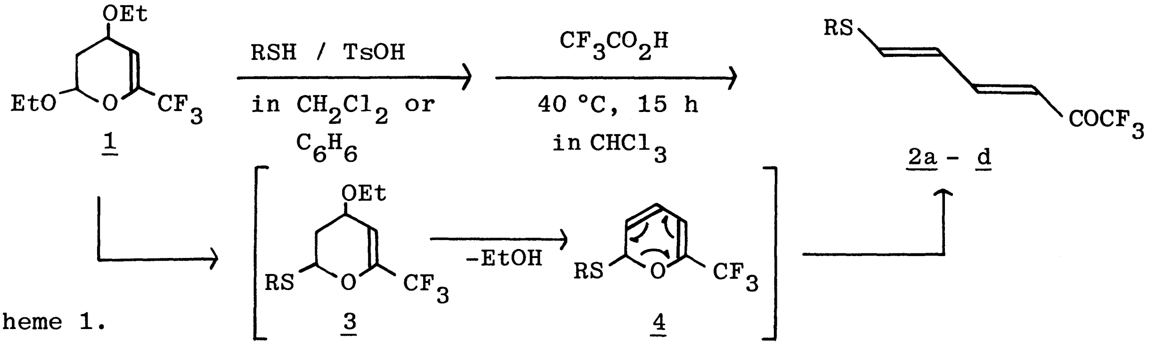
In the course of our investigations on the nucleophilic substitutions at olefinic carbon atoms activated by trifluoroacetyl group,[1)] it became necessary to prepare 2-trifluoroacetylvinylketene dithioacetals and their analogous 4-trifluoroacetyl-1,3-butadienyl sulfides. Although the former compounds could be easily obtained by acylation of vinylketene dithioacetals with trifluoroacetic anhydride,[2)] the latter ones were not accessible efficiently from 1,3-butadienyl sulfides in a similar method. Recently, we presented a useful synthetic method for 2,4-dialkoxy-6-trifluoromethyl-3,4-dihydro-2H-pyrans by hetero-Diels-Alder reaction of 2-trifluoroacetylvinyl ethers with vinyl ethers.[3)] On this occasion, we attempted to utilize these new CF_3-containing dihydropyrans, for example, 2,4-diethoxy derivative 1, as a building block for the syntheses of various 4-trifluoroacetyl-1,3-butadienes and found that the captioned compounds 2 can be prepared by acid catalyzed reaction of 1 with thiols. We now wish to communicate the results.

Reaction of dihydropyran 1 with ethanethiol in the presence of p-toluenesulfonic acid[4)] and the subsequent treatment of the resulted mixtures with trifluoroacetic acid gave the desired butadienyl sulfide 2a in 74% yield. Similarly, some aliphatic and aromatic thiols underwent the present acid catalyzed reaction (Table 1). In some cases, after work-up at earlier stage of the reaction, dihydropyrans 3 were obtained as a main product together with a small amount of 2. On treatment with trifluoroacetic acid, the mixtures were completely converted into butadienyl sulfides 2. So, trifluoroacetic acid was found to be much superior to p-toluenesulfonic acid for the conversion of 3 to 2.

A possible pathway for the formation of 2 is depicted in Scheme 1. An intermediate 2H-pyran 4 via 3 formed by acid catalyzed O-S exchange of 1 with thiol, would undergo an electrocyclic ring-opening reaction to give 2.

The stereochemistry of butadienyl sulfides 2 was confirmed by ^1H-NMR. The large value of the coupling constant $J_{CH=CH}$ (14-15 Hz) suggests all E configuration.

Further works regarding this direction are now undertaken in our laboratory, together with an attempt to utilize these new compounds 1 and 2 as synthetic tools for constructing fluorine-containing heterocycles, which are now widely recognized



Scheme 1.

Table 1. Synthesis of (E,E)-4-Trifluoroacetyl-1,3-butadienyl Sulfides 2a-d

Run	R	Reaction Conditions[a)]			Method[b)]	Product	Yield[c)]	Bp θ_b/°C
		Temp/°C	Time/h	Solv.			%	(mbar)[d)]
1	Et	50	5	CH_2Cl_2	A	2a	74	90(1.3)
2	n-Pr	reflux	5	CH_2Cl_2	B	2b	75	110(1.3)
3	$PhCH_2$	reflux	0.5	C_6H_6	B	2c	70	185(1.3)
4	$PhCH_2$	reflux	0.5	C_6H_6	C	2c	78	185(1.3)
5	Ph	reflux	0.5	C_6H_6	B	2d	81	170(1.3)

a) Reaction conditions of the first step are shown. b) See experimental section. c) Isolated yields of products purified by distillation. d) Oven temperature.

as important materials for the medicinal and agricultural use.[5)]

Typical procedure is as follows: Method A; A mixture of 1 (408 mg, 1.7 mmol), ethanethiol (118 mg, 1.9 mmol), CH_2Cl_2 (3 ml) and p-toluenesulfonic acid (86 mg, 0.5 mmol) was sealed in a tube and heated at 50 °C for 5 h. The mixture was washed with aq. 20% Na_2CO_3, extracted with CH_2Cl_2 and dried over Na_2SO_4. The solvent was evaporated and the resulting mixture was dissolved in $CHCl_3$ (1 ml). To this mixture, trifluoroacetic acid (0.3 ml) was added. After stirring at 40 °C for 15 h, the same work-up mentioned above gave a crude mixture, which was distilled in vacuo to afford 265 mg (74%) of 2a, bp 90 °C/1.3 mbar (oven temp); NMR (δ, $CDCl_3$): 7.47 (dd, 1H, J=11, 15 Hz), 7.10 (d, 1H, J=15 Hz), 6.23 (dd, 1H, J=11, 15 Hz), 6.20 (d, 1H, J=15 Hz), 2.85 (q, 2H, J=7 Hz), 1.33 (t, 3H, J=7 Hz): IR (film, cm^{-1}): $\nu_{C=O}$ 1675, $\nu_{C=C}$ 1558; Anal (%): Calcd for $C_8H_9F_3SO$: C, 45.71; H, 4.32; F, 27.11: Found: C, 45.47; H, 4.31; F, 26.84. Method B; This is essentially the same as Method A except that the first step of the reaction was carried out in an open vessel. Method C; This is almost the same as Mehtod B except that the second step was carried out without work-up after the first step.

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