TRIFLUOROMETHYL-CONTAINING CUMULATED 1,3-OXATHIOLS AND 1,4-OXATHIANS

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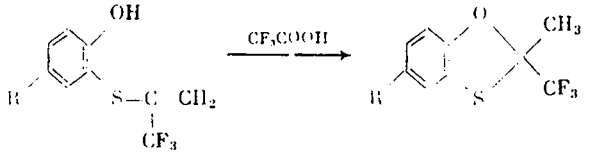
In the course of acid catalysis, ortho-(1-trifluoromethylvinylthio)phenols cyclize into benzo-1,3-oxathiols, and on treatment with aqueous alkali — into benzo-1,4-oxathians. The characteristic features of these transformations and the oxidative reactions of oxathians were studied.

The previously described [1] ortho-(1-trifluoromethyl-2-chloroethylthio)- and ortho-(1-trifluoromethylvinylthio)phenols were found to be effective precursors of cumulated fluorine-containing 1,3-oxathiols and 1,4-oxathians. Thus, heating of ortho-(1-trifluoromethylvinylthio)phenols in CF_3COOH at 120°C produces 2-methyl-2-trifluoromethylbenzo-1,3-oxathiols (I)-(III) in a yield of 60%.

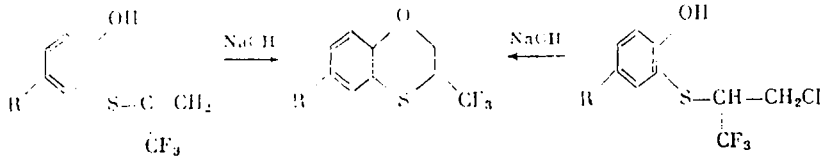


(I)—(III)

R = H (I), CH_3 (II), C_2H_5 (III).

Under milder conditions (35-40°C), oxathiols (I)-(III) are formed in the presence of strong acids (4-$CH_3C_6H_4SO_3H$, H_2SO_4, FSO_3H). However, in this case, the reaction is accompanied by strong resinification and the yield of the desired end compounds is reduced to 20-30%.

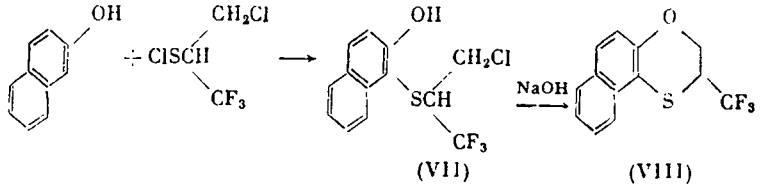
Heating of ortho-(1-trifluoromethylvinylthio)phenols with aqueous alkali gives 3-trifluoromethylbenzo-1,4-oxathians (IV)-(VI), which are also formed in high yield by heating ortho-(1-trifluoromethyl-2-chloroethylthio)phenols with an excess of aqueous alkali.



(IV)—(VI)

R = H (IV), C_2H_5 (V), t-C_4H_9 (VI).

Compounds (VII), (IX), which are obtained by thiolation of 2-naphthol and 3,4-methylenedioxyphenol by means of 1-trifluoromethyl-2-chloroethylsulfenyl chloride, are similarly smoothly converted into tricyclic compounds (VIII), (X).



(VII) (VIII)

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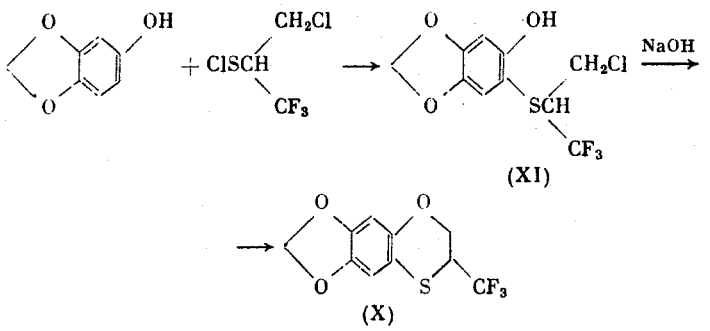
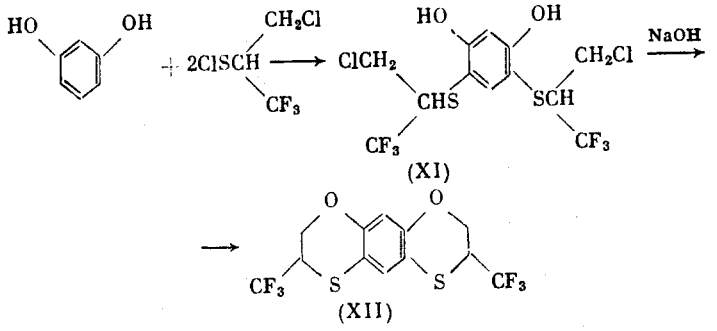


(XI)

(X)

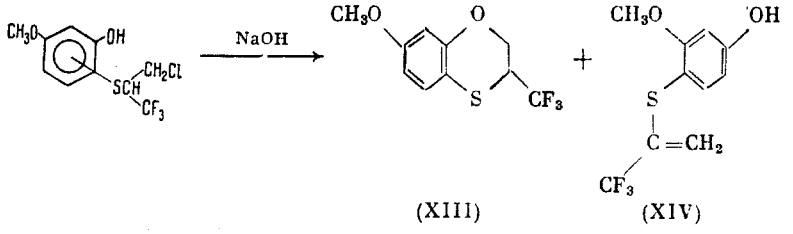
The bisthiolation product of resorcinol (XI) was converted in the same way into the tricyclic compound (XII) containing two 1,4-oxathian rings.



(XI)

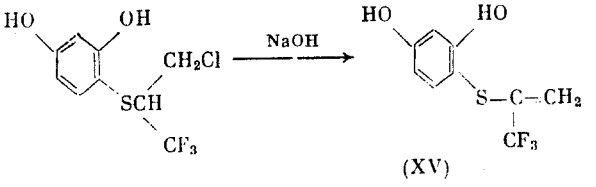
(XII)

On treating a mixture of 2- and 4-(1-trifluoromethyl-2-chloroethylthio)-5-methoxyphenols with aqueous alkali, a mixture of cyclization (XIII) and dehydrochlorination (XIV) products was obtained, which can be readily separated.



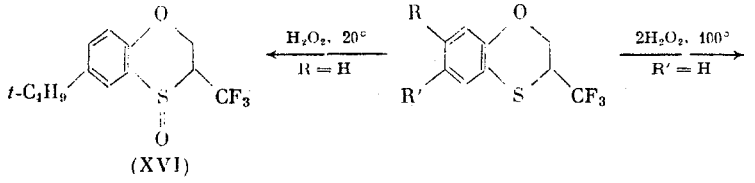
(XIII) (XIV)

The synthesis of oxathians (IV)-(VI), (VIII), (X), (XII), and (XIII) was found to be possible because of their low solubility in an aqueous-alkaline medium and removal from the reaction sphere after their formation. Water soluble oxathians are not formed under these conditions. For example, the product of thiolation of resorcinol by 1-trifluoromethyl-2-chloroethylsulfenyl chloride in aqueous alkali media is converted only into a dehydrochlorination product (XV).

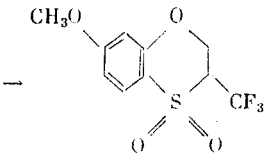


(XV)

The benzo-1,4-oxathians are readily oxidized by hydrogen peroxide in acetic acid. For example, sulfoxide (XVI) was obtained by oxidation at ~20°C and sulfone (XVII) by heating to 100°C.



(XVI)



(XVII)

EXPERIMENTAL

The ^1H and ^{19}F NMR spectra of the synthesized compounds were run on a Bruker WR-200SY spectrometer with working frequencies of 200 and 188 MHz, respectively. The chemical shifts (δ, ppm) were determined with reference to HMDS (internal standard) and CF_3COOH (external standard). The R_f values of the compound obtained are given for Silufol UV-254 plates in acetone–CCl_4 or pure CCl_4 systems. The compounds were identified according to their absorption in UV light. 1-Trifluoromethyl-2-chloroethylsulfenyl chloride was obtained according to [2].

2-Methyl-2-trifluoromethylbenzo-1,3-oxathiols (general procedure). A solution of 0.05 mole of the corresponding 2-(1-trifluoromethylvinylthio)phenol in 10 ml of CF_3COOH was heated for 5 h in a sealed glass ampul at 120°C. The ampul was opened and the contents were poured into cold water. The product was extracted with ether, the extract was dried over Na_2SO_4 and fractionated. 2-Methyl-2-trifluoromethylbenzo-1,3-oxathiol (I), 2-methyl-2-trifluoromethyl-5-methylbenzo-1,3-oxathiol (II), and 2-methyl-2-trifluoromethyl-5-ethylbenzo-1,3-oxathiol (III) were obtained by this method.

3-Trifluoromethylbenzo-1,4-oxathians (general procedure). A 0.05 mole portion of the corresponding 2-(1-trifluoromethyl-2-chloroethylthio)phenol or 2-(1-trifluoromethylvinylthio)phenol was added to 30 ml of a 20% of aqueous NaOH solution. The mixture was heated for 1 h at 80°C, cooled to 20°C, the oil that separated out was extracted with ether, and the extract was dried over Na_2SO_4. The solvent was evaporated under vacuum and the residue was fractionated or crystallized from hexane. 3-Trifluoromethylbenzo- (IV), 3-trifluoromethyl-6-ethylbenzo- (V), 3-trifluoromethyl-6-tert-butylbenzo- (VI), 3-trifluoromethylnaphtho[2,1-b]- (VIII), 3-trifluoromethyl-6,7-methylenedioxybenzo- (X), 3,7-bis(trifluoromethyl)-1,4-oxathoano[3,2-g]benzo-1,4-oxathians (XII) were obtained by this method.

1,(1-Trifluoromethyl-2-chloroethylthio)-2-naphthol (VII). A 4.0 g (0.02 mole) portion of 1-trifluoromethyl-2-chloroethylsulfenyl chloride was added to a solution of 2.5 g (0.02 mole) of 2-naphthol in 10 ml of $CHCl_3$. The mixture was allowed to stand until HCl ceased to evolve (20 h), the solvent was evaporated in vacuo and the residue was crystallized from hexane. Yield, 5.0 g of compound (VII).

2-(1-Trifluoromethyl-2-chloroethylthio)-4,5-methylenedioxyphenol (IX). A 4.0 g portion (0.02 mole) of 1-trifluoromethyl-2-chloroethylsulfenyl chloride was added to a solution of 2.8 g (0.02 mole) of 3,4-methylenedioxyphenol in 10 ml of $CHCl_3$. The mixture was held until HCl ceased to evolve (10 h), the solution was evaporated under vacuum, and the residue was crystallized from hexane. Yield, 5.2 g of compound (IX).

3-Trifluoromethyl-7-methoxybenzo-1,4-oxathian (XIII) and 3-Methoxy-4-(1-trifluoromethylvinylthio)phenol (XIV). A 14.3 g portion (0.05 mole) of a mixture of 2- and 4-(1-trifluoromethyl-2-chloroethylthio)-5-methoxyphenol (ratio ortho:para 1:5) was added to 30 ml of a 20% aqueous solution of NaOH. The mixture was heated for 1 h at 80°C, cooled to 20°C, and the oil that separated out was extracted with ether. The ether solution was dried over Na_2SO_4 and fractionated. Yield, 1.7 g of compound (XIII). The aqueous solution was acidified by hydrochloric acid and the oil that separated out was extracted with ether. The ether solution was dried over Na_2SO_4 and fractionated. Yield, 7.7 g of compound XIV.

2-(1-Trifluoromethylvinylthio)-5-hydroxyphenol (XV). A 13.6 g portion (0.05 mole) of 2-(1-trifluoromethyl-2-chloroethylthio)-5-hydroxyphenol was added to 30 ml of 20% aqueous solution of NaOH. The mixture was heated for 1 h at 80°C, cooled to 20°C, acidified with hydrochloric acid, and the oil that separated out was extracted with ether. The ether solution was dried over Na_2SO_4 and fractionated. Yield, 9.3 g of compound (XV).

TABLE 1. Physicochemical Properties of Compounds (I)-(XVII)

Compound	Yield, %	R^f (CCl_4: acetone)	Bp, °C (p, mm Hg) mp, °C	n_D^{25}	Found/Calculated, %		Empirical formula
					C	H	
(I)	56	0,69 (10 : 1)	65(7)	1,4960	49,17 49,09	3,15 3,18	$C_9H_7F_3OS$
(II)	59	0,73 (10 : 1)	74(7)	1,4995	51,40 51,28	3,87 3,85	$C_{10}H_9F_3OS$
(III)	57	0,89 (5 : 1)	52(1)	1,5035	53,42 53,23	4,40 4,44	$C_{11}H_{11}F_3OS$
(IV)	81	0,53 (CCl_4)	110(13)	1,5235	49,25 49,09	3,22 3,18	$C_9H_7F_3OS$
(V)	78	0,47 (CCl_4)	95(1)	1,5130	53,37 53,23	4,49 4,44	$C_{11}H_{11}F_3OS$
(VI)	83	0,70 (CCl_4)	56–57	–	56,41 56,52	5,39 5,43	$C_{13}H_{15}F_3OS$
(VII)	84	0,86 (6 : 1)	82–83	–	50,73 50,90	3,23 3,26	$C_{13}H_{10}ClF_3OS$
(VIII)	83	0,67 (CCl_4)	51–52	–	57,64 57,78	3,27 3,33	$C_{13}H_9F_3OS$
(IX)	86	0,50 (10 : 1)	31–32	–	40,07 39,93	2,61 2,66	$C_{10}H_8ClF_3OS$
(X)	77	0,78 (10 : 1)	57–58	–	45,31 45,45	2,62 2,65	$C_{10}H_7F_3O_3S$
(XI)	75	0,58 (4 : 1)	78–80	–	33,35 33,10	2,24 2,30	$C_{12}H_{10}Cl_2F_6O_2S_2$
(XII)	72	0,88 (4 : 1)	193–194	–	39,68 39,80	2,19 2,21	$C_{12}H_8F_6O_2S_2$
(XIII)	14	0,83 (5 : 1)	103(1)	1,5240	48,11 48,00	3,54 3,60	$C_{10}H_9F_3O_2S$
(XIV)	62	0,75 (5 : 1)	86(1)	1,5125	47,88 48,00	3,56 3,60	$C_{10}H_9F_3O_2S$
(XV)	79	0,37 (4 : 1)	77–78	–	45,60 45,76	2,94 2,97	$C_9H_7F_3O_2S$
(XVI)	90	0,30 (10 : 1)	111–112	–	53,49 53,42	5,15 5,14	$C_{13}H_{15}F_3O_2S$
(XVII)	92	0,36 (5 : 1)	132–134	–	42,67 42,55	3,22 3,19	$C_{10}H_9F_3O_4S$

3-Trifluoromethyl-6-tert-butylbenzo-1,4-oxathian Oxide (XVI). A 2 ml portion of 30% hydrogen peroxide was added to a solution of 5.5 g (0.02 mole) of 3-trifluoromethyl-6-tert-butylbenzo-1,4-oxathian in 15 ml of glacial acetic acid. The mixture was held for 20 h at 20°C, poured into 100 ml of cold (0°C) water, the crystals that separated out were filtered off and recrystallized from an alcohol–water mixture. Yield, 5.2 g of compound (XVI).

3-Trifluoromethyl-7-methoxybenzo-1,4-oxathian 4,4-Dioxide (XVII). A 5 ml portion of 30% hydrogen peroxide was added to a solution of 5.0 g (0.02 mole) of 3-trifluoromethyl-7-methoxybenzo-1,4-oxathian in 30 ml of glacial acetic acid. The mixture was heated for 5 h at 100°C, then was cooled to 20°C, poured into 100 ml of cold (0°C) water, the crystals that separated out were filtered off and recrystallized from an alcohol–water mixture. Yield, 5.2 g of compound (XVII).

TABLE 2. NMR Spectra of Compounds (I)-(XVII)* [δ, ppm (J, Hz)]

Compound	^{19}F NMR spectrum δ(J_{H-F})	PMR Spectra δ (J)
(I) **	5,4 s	7,26 d.d (1H, 1,8 & 7,8); 7,15m (1H); 7,01 m (1H); 6,88 m (1H); 2,05 s (3H)
(II)	5,6 s	7,09 d (1H, 1,5); 6,92 d.d (1H, 1,5 & 8,5); 6,80 d (1H, 8,5); 2,26 s (3H); 2,01 s (3H)
(III)	5,3 s	7,14 d (1H, 1,5); 6,93 d.d (1H, 1,5 & 8,5); 6,80 d (1H, 8,5); 2,58 q (2H, 7,5); 2,01 s (3H); 1,18 t (3H, 7,5)
(IV) **	−8,6 d.d (2,1 & 8,7)	7,11 m (2H); 6,92 m (2H); 4,76 d.d (1H, 2,8 and 12,5); 4,22 d.p (1H, 2,1 & 12,5); 4,05 q. t (1H, 2,8 & 8,7)
(V)	−8,6 d.d (2,0 & 8,6)	6,93 m (2H); 6,81 d (1H, 8,2); 4,80 d.d (1H, 2,1 and 12,0); 4,29 m (2H); 2,55 q (2H, 7,5); 1,19 t (3H, 7,5)
(VI)	−8,6 d.d (1,9 & 8,4)	7,13 m (2H); 6,83 d (1H, 8,0); 4,82 d.d (1H, 2,7 and 12,4); 4,30 m (2H); 1,30 s (9H)
(VII)	−10,5 d (8,6)	9,10 s (1H); 8,50 d (1H, 8,5); 7,88 m (2H); 7,59 m (1H); 7,34 m (2H); 4,09 m (3H)
(VIII)	−8,7 d.d (2,0 & 8,3)	7,88 m (2H); 7,40–7,68 m (3H); 7,12 d (1H, 8,5); 4,94 d. d (1H, 3,0 & 12,5); 4,56 d. p (1H, 2,0 and 12,5); 4,40 q. t (1H, 3,0 & 8,3)
(IX)	−10,4 d (8,3)	8,41 s (1H); 6,92 s (1H); 6,56 s (1H); 5,97 s (2H); 4,03 m (3H)
(X)	−8,4 d. d (1,9 & 8,4)	6,63 s (1H); 6,48 s (1H); 5,94 s (2H); 4,78 d.d (1H, 2,7 & 12,0); 4,28 m (2H)
(XI) **	−10,4 d (8,0)	7,68 s (1H); 7,64 s (2H); 6,59 s (1H); 3,91 m (6H)
(XII) **	−8,6 d. d (8,7 & 2,1)	6,90 s (1H); 6,51 s (1H); 4,77 d.d (2H, 3,0 and 12,5); 4,20 d.d (2H, 2,1 & 12,5); 4,04 q. t (2H, 3,0 & 8,7)
(XIII) **	−8,6 d.d (8,6 & 2,0)	7,04 d (1H, 8,5); 6,57 m (2H); 4,81 d.d (1H, 3,0 & 12,5); 4,28 d.d (1H, 2,0 & 12,5); 4,09 q. t (1H, 3,0 & 8,6); 3,78 s (3H)
(XIV) **	−13,2 s	7,40 d.d (1H, 2,5 & 9,0); 7,28 s (1H); 6,60 m (2H); 5,93 m (1H); 5,12 m (1H); 3,83 s (3H)
(XV)	−13,1 s	8,90 s (1H); 8,63 s (1H); 7,30 d (1H, 8,2); 6,55 d (1H, 2,5); 6,46 d.d (1H, 2,5 & 8,2); 5,86 m (1H); 5,05 m (1H)
(XVI)	−11,6 d.d (1,5 & 8,0)	7,73 d (1H, 2,2); 7,65 d.d (1H, 2,2 & 8,5); 7,05 d (1H, 8,5); 4,62 m (2H); 4,17 m (1H); 1,35 s (9H)
(XVII)	−14,0 d.d (1,5 & 8,4)	7,65 d (1H, 9,0); 6,78 d.d (1H, 2,5 & 9,0); 6,54 d (1H, 2,5); 5,05 m (2H); 4,68 m (1H); 3,84 s (3H)

*The spectra were run in acetone-d_6.
**The spectra were run in acetonitrile-d_3.

The yields, properties and analysis results of compounds (I)-(XVII) are listed in Tables 1 and 2.

LITERATURE CITED

1. A. Yu. Sizov, A. F. Kolomiets, and A. V. Fokin, Izv. Akad. Nauk SSSR, Ser. Khim., No. 4, 832 (1990).
2. R. A. Bekker, V. Ya. Popkova, and I. L. Knunyants, Izv. Akad. Nauk SSSR, Ser. Khim., No. 7, 1688 (1983).