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REACTION OF TRIFLUOROMETHYL-CONTAINING ENONES WITH THIOPHENOL DERIVATIVES

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The reaction of trifluoromethyl-containing enones with thiophenol derivatives has been studied. Reactions with 4-methylthiophenol proceed with the formation of either ketosulfides or a pyran derivative. Reactions of trifluoromethyl-containing enones with 2-mercaptobenzaldehyde lead to 3-trifluoroacetyl-substituted 2H-thiochromenes.

Fluorine-containing heterocyclic compounds are the subject of numerous investigations [1,2] as a result of their high physiological activity [3]. Trifluoromethyl-containing enones are convenient and promising starting materials for the synthesis of heterocycles containing a CF_3 group. Methods for the synthesis of such enones have been developed intensively during the last decade [4,5].

The addition of thiols to an unsaturated ketone is a standard method of synthesizing ketosulfides by the Michael reaction. The products of addition of thiophenol and its derivatives to an α,β-unsaturated ketone, *viz.* S-aryl-substituted β-ketosulfides, are cyclized under the action of acids ($HClO_4$, polyphosphoric acid) with the formation of thiochromanes or thiochromylium salts [6] depending on the reaction conditions and the structure of the initial ketone.

When studying the reaction of CF_3-enones with 4-methylthiophenol (I) it was established that β-trifluoroacetylstyrene (II) reacts with 4-methylthiophenol in ethanol at room temperature in the presence of catalytic amounts of triethylamine with the formation of two compounds. One of them was the usual product of Michael addition, the β-ketosulfide III and the second was the pyran derivative IV, the product of the reaction of two molecules of enone II with one molecule of 4-methylthiophenol and one molecule of water.

The ratio of the reaction products depends on the reaction conditions. A change in the order of addition and in the reactant ratio enables the predominant formation of one of the substances to be achieved. For example, addition of 4-methylthiophenol to a solution of enone II using a 2.5-fold excess of the latter enables the yield of pyran IV to be increased to 68%. On the other hand β-ketosulfide III was isolated in 61% yield on slow addition (during 1 h) of ketone to a small (10%) excess of 4-methylthiophenol.

We suggest the following route for the formation of pyran IV. An enolate anion is formed by the addition of 4-methylthiophenol anion to enone II, protonation of which leads to the β-ketosulfide III. Reaction of this enolate anion with another molecule of enone and subsequent cyclization of the intermediate with addition of a molecule of water (solvent is 90% ethanol) leads to the formation of pyran IV. The latter is a stable compound due to stabilization of the hemiacetal fragments by the presence of the trifluoromethyl groups.

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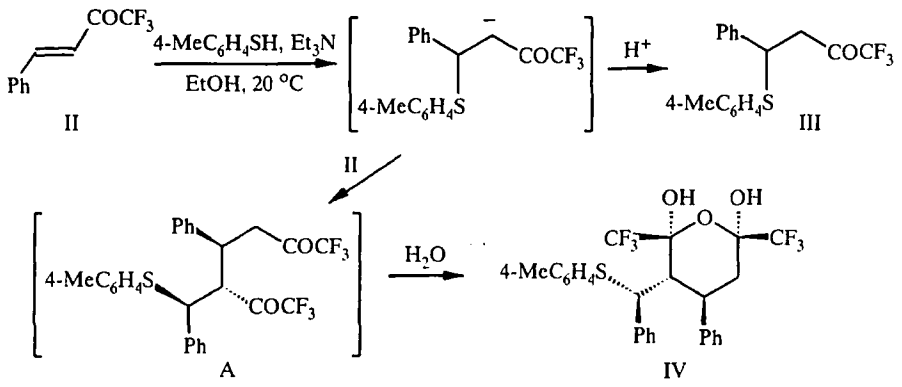


According to the data of ^{1}H and ^{13}C NMR compound IV is formed as a single diastereomer out of the 16 possible (there are 5 asymmetric centers in the molecule). Its configuration was established unequivocally by X-ray structural analysis (Fig. 1). It turned out that the most bulky substituents [Ph, CF_3, (4-phenylthio)phenylmethyl] occupy equatorial positions [7,8]. It is also remarkable that the relative configuration of the carbon atom carrying phenyl and methylphenylthio substituents proved to be fixed. An efficient asymmetric 1,2-induction has taken place. Examenation of molecular models suggested that such a disposition of substituents is probably most favored in the intermediate A and is retained in the reaction product, pyran IV.

According to the X-ray crystallographic data there are two crystallographically independent enantiomeric molecules (see Fig. 1) in the structure of compound IV. They have extremely close geometric parameters however conformational differences lead to their crystallographic independence. These molecules are linked into a dimer by hydrogen bonds between the atoms $H_{(1A)}$–H–$O_{(12)}$ (2.062 Å) and $H_{(11A)}$–H–$O_{(2)}$ (2.021 Å) (Tables 1 and 2).

We have studied the cyclization of β-ketosulfide III under the action of perchloric and trifluoromethanesulfonic acids in order to obtain a thiochromane derivative. It turned out that in the first case the reaction did not occur at room temperature but did on heating (100°C). The reaction proceeded at room temperature under the action of trifluoromethanesulfonic acid, in both cases forming a mixture of products difficult to identify. This is probably linked with the fact that protonation of the oxygen atom of the carbonyl group with the formation of a carbocation, an intermediate in the cyclization reaction, is hindered by the presence of the electron-withdrawing CF_3 group.

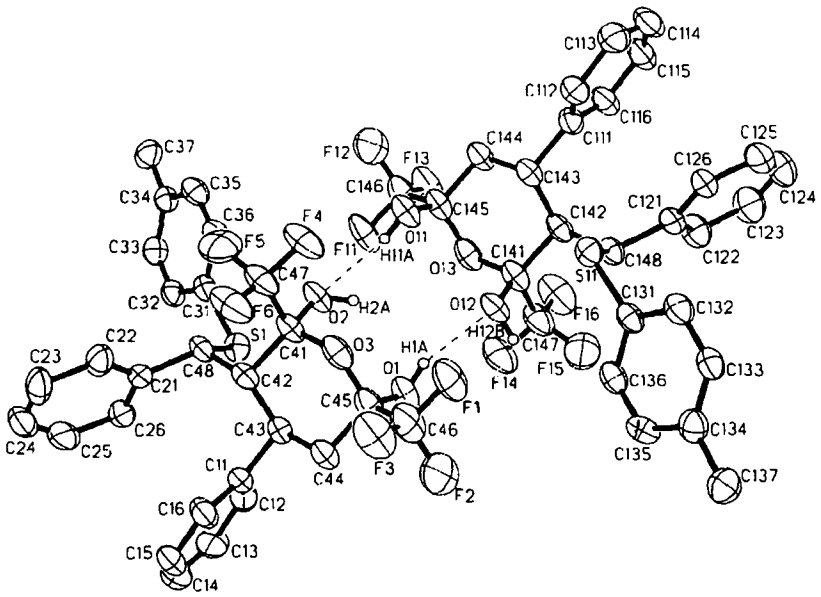


Fig. 1. Structure of compound IV.

TABLE 1. Selected Bond Lengths in Molecule of Compound IV

Bond	*d*, Å	Bond	*d*, Å
$S_{(1)}$–$C_{(31)}$	1,766(9)	$S_{(11)}$–$C_{(131)}$	1,778(8)
$S_{(1)}$–$C_{(48)}$	1,845(7)	$S_{(11)}$–$C_{(148)}$	1,839(7)
$O_{(1)}$–$C_{(45)}$	1,394(10)	$O_{(11)}$–$C_{(145)}$	1,387(10)
$O_{(2)}$–$C_{(41)}$	1,412(8)	$O_{(12)}$–$C_{(141)}$	1,392(9)
$O_{(3)}$–$C_{(45)}$	1,420(13)	$O_{(13)}$–$C_{(141)}$	1,410(11)
$O_{(3)}$–$C_{(41)}$	1,421(10)	$O_{(13)}$–$C_{(145)}$	1,419(12)
$F_{(1)}$–$C_{(46)}$	1,339(12)	$F_{(11)}$–$C_{(146)}$	1,343(11)
$F_{(2)}$–$C_{(46)}$	1,32(2)	$F_{(12)}$–$C_{(146)}$	1,350(14)
$F_{(3)}$–$C_{(46)}$	1,33(2)	$F_{(13)}$–$C_{(146)}$	1,321(13)
$F_{(4)}$–$C_{(47)}$	1,323(9)	$F_{(14)}$–$C_{(147)}$	1,326(11)
$F_{(5)}$–$C_{(47)}$	1,329(14)	$F_{(15)}$–$C_{(147)}$	1,33(2)
$F_{(6)}$–$C_{(47)}$	1,344(12)	$F_{(16)}$–$C_{(147)}$	1,31(2)
$C_{(41)}$–$C_{(47)}$	1,52(2)	$C_{(141)}$–$C_{(147)}$	1,54(2)
$C_{(41)}$–$C_{(42)}$	1,549(9)	$C_{(141)}$–$C_{(142)}$	1,554(10)
$C_{(42)}$–$C_{(43)}$	1,550(11)	$C_{(142)}$–$C_{(143)}$	1,531(12)
$C_{(42)}$–$C_{(48)}$	1,556(11)	$C_{(142)}$–$C_{(148)}$	1,558(11)
$C_{(43)}$–$C_{(44)}$	1,530(11)	$C_{(143)}$–$C_{(144)}$	1,537(11)
$C_{(44)}$–$C_{(45)}$	1,530(11)	$C_{(144)}$–$C_{(145)}$	1,512(11)
$C_{(45)}$–$C_{(46)}$	1,504(14)	$C_{(145)}$–$C_{(146)}$	1,500(14)

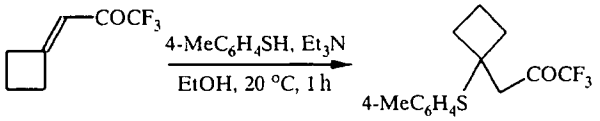
Enone V reacts with 4-methylthiophenol in the presence of catalytic amounts of triethylamine leading to β-ketosulfide VI in good yield. A change in the order of reactant addition or their ratio leads to the formation of a complex mixture of compounds. Probably partial oligomerization occurs in the basic medium as a result of the condensation of compound VI with the initial enone, as well as selfcondensation of ketone V. Consequently the introduction of an excess of enone V into the reaction does not lead to the selective formation of a double addition product analogous to the pyran IV.

TABLE 2. Valence Angles in Molecule of Compound IV

Angle	ω, deg.	Angle	ω, deg.
$C_{(31)}$–$S_{(1)}$–$C_{(48)}$	101,8(4)	$C_{(131)}$–$S_{(11)}$–$C_{(148)}$	102,4(3)
$C_{(41)}$–$O_{(3)}$–$C_{(45)}$	119,3(6)	$C_{(141)}$–$O_{(13)}$–$C_{(145)}$	119,8(6)
$O_{(2)}$–$C_{(41)}$–$O_{(3)}$	109,2(6)	$O_{(12)}$–$C_{(141)}$–$O_{(13)}$	109,2(7)
$O_{(2)}$–$C_{(41)}$–$C_{(47)}$	105,6(7)	$O_{(12)}$–$C_{(141)}$–$C_{(147)}$	106,9(8)
$O_{(3)}$–$C_{(41)}$–$C_{(47)}$	100,2(7)	$O_{(13)}$–$C_{(141)}$–$C_{(147)}$	100,5(8)
$O_{(2)}$–$C_{(41)}$–$C_{(42)}$	113,4(6)	$O_{(12)}$–$C_{(141)}$–$C_{(142)}$	112,9(6)
$O_{(3)}$–$C_{(41)}$–$C_{(42)}$	113,5(6)	$O_{(13)}$–$C_{(141)}$–$C_{(142)}$	112,6(7)
$C_{(47)}$–$C_{(41)}$–$C_{(42)}$	113,9(7)	$C_{(147)}$–$C_{(141)}$–$C_{(142)}$	113,8(7)
$C_{(41)}$–$C_{(42)}$–$C_{(43)}$	109,8(6)	$C_{(143)}$–$C_{(142)}$–$C_{(141)}$	111,8(6)
$C_{(41)}$–$C_{(42)}$–$C_{(48)}$	110,9(6)	$C_{(143)}$–$C_{(142)}$–$C_{(148)}$	114,2(6)
$C_{(43)}$–$C_{(42)}$–$C_{(48)}$	115,2(6)	$C_{(141)}$–$C_{(142)}$–$C_{(148)}$	112,0(6)
$C_{(11)}$–$C_{(43)}$–$C_{(44)}$	108,5(6)	$C_{(111)}$–$C_{(143)}$–$C_{(142)}$	114,0(6)
$C_{(11)}$–$C_{(43)}$–$C_{(42)}$	114,3(6)	$C_{(111)}$–$C_{(143)}$–$C_{(144)}$	109,5(6)
$C_{(44)}$–$C_{(43)}$–$C_{(42)}$	111,0(6)	$C_{(142)}$–$C_{(143)}$–$C_{(144)}$	109,7(6)
$C_{(45)}$–$C_{(44)}$–$C_{(43)}$	110,5(7)	$C_{(145)}$–$C_{(144)}$–$C_{(143)}$	110,8(7)
$O_{(1)}$–$C_{(45)}$–$O_{(3)}$	113,4(7)	$O_{(11)}$–$C_{(145)}$–$O_{(13)}$	113,3(7)
$O_{(1)}$–$C_{(45)}$–$C_{(46)}$	110,2(9)	$O_{(11)}$–$C_{(145)}$–$C_{(146)}$	110,4(8)
$O_{(3)}$–$C_{(45)}$–$C_{(46)}$	103,1(9)	$O_{(13)}$–$C_{(145)}$–$C_{(146)}$	102,9(8)
$O_{(1)}$–$C_{(45)}$–$C_{(44)}$	107,1(7)	$O_{(11)}$–$C_{(145)}$–$C_{(144)}$	108,0(7)
$O_{(3)}$–$C_{(45)}$–$C_{(44)}$	111,5(7)	$O_{(13)}$–$C_{(145)}$–$C_{(144)}$	110,8(7)
$C_{(46)}$–$C_{(45)}$–$C_{(44)}$	111,6(8)	$C_{(146)}$–$C_{(145)}$–$C_{(144)}$	111,5(8)
$C_{(21)}$–$C_{(48)}$–$C_{(42)}$	113,7(6)	$C_{(121)}$–$C_{(148)}$–$C_{(142)}$	113,7(6)
$C_{(21)}$–$C_{(48)}$–$S_{(1)}$	114,5(5)	$C_{(121)}$–$C_{(148)}$–$S_{(11)}$	114,8(5)
$C_{(42)}$–$C_{(48)}$–$S_{(1)}$	109,8(5)	$C_{(142)}$–$C_{(148)}$–$S_{(11)}$	109,2(5)

Crystallographic Data, Unit Cell Parameters, and Structural Refinement for Compound IV

Molecular formula	$C_{27}H_{24}F_6O_3S_1$
Molecular weight	542,52
Size of crystal	0,6×0,4×0,4
Color, form	Colorless parallelopipeds
Crystal system	Orthorhombic
Space group	$Pn2_1a$
a (*E*)	19,560(4)
b (*E*)	26,039(5)
c (*E*)	10,367(2)
V (E^3)	5280(2)
Z	8
Calculated density (g/cm^3)	1,365
F(000)	2240
Absorption coefficient (mm^{-1})	1,714
Scanning region (deg)	$3,39 < q < 74,95$
Scanning type	*w*
Breadth of scanning	1,47 + 0,15 tan*q*
Ranges of reflection indexes	$-1 < h < 24$ $-1 < k < 32$ $-1 < l < 12$
Reflections collected	5458
Number of reflections with $I > 2\sigma(I)$	3402
Number of refinement variables	675
R-factors [$I > 2\ \sigma(I)$]	$R_1 = 0,0766$, $wR_2 = 0,1895$
R-factors (all reflections)	$R_1 = 0,1057$, $wR_2 = 0,2224$
Weighting scheme, w^{-1}	$s^2(F_o^2) + (0,157IP)^2$, where $P = (F_o^2 + F_c^2)/3$
Quality on F^2	1,038
Flak parameter	0,32(8)
Extinction coefficient	0,0030(4)
Residual electron density, min/max ($e \cdot E^{-3}$)	-0,331 / 0,909



V VI 60%

In contrast to enones II and V the trifluoromethyl-containing enone VII does not react with 4-methylthiophenol either at room temperature or on heating, or on using other basic catalysts (such as EtONa) or in their absence. The presence of a methyl group in position 4 of enone VII cases the formation of an adduct with 4-methylthiophenol to be thermodynamically unfavored due to steric difficulties.

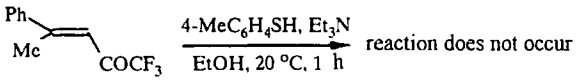
TABLE 3. Characteristics of the Synthesized Compounds

Compound	Empirical formula	Found, % / Calculated, %		mp, °C	Yield, %
		C	H		
X	$C_{17}H_{13}F_3O_2S$	60,19 / 60,35	3,79 / 3,87	154...155 (dec.)	65
XIa	$C_{17}H_{11}F_3OS$	63,86 / 63,74	3,55 / 3,46	45	86
XIb	$C_{14}H_{11}F_3OS$	59,13 / 59,15	3,85 / 3,90	69...70	69
XIc	$C_{16}H_{12}F_3NOS$	59,37 / 59,44	3,67 / 3,74	111...112	64
XId	$C_{15}H_9F_3OS_2$	55,39 / 55,21	2,82 / 2,78	53...54	70

TABLE 4. IR and ^{1}H and ^{13}C NMR Spectra of Thiochromane X and 2H-Thiochromenes XIa-d

Compound	IR spectrum, ν, cm^{-1}	^{1}H NMR spectrum, δ, ppm	^{13}C NMR spectrum, δ, ppm
X	1710 (CO); 3300...3500 (OH)	7,72-7,68 (1H, m, 5-H or 8-H) 7,45-7,12 (m, 8H, 5H Ph, 3H arom. thiochromane) 5,57 (1H, d, ^{3}J = 8,0 Hz, 2-H) 5,15 (1H, d d, ^{3}J = 8,0, ^{3}J = 10,0 Hz, 3-H) 4,94 (1H, d, ^{3}J = 11,2 Hz, OH) 4,08 (1H, t, ^{3}J = 10,6 Hz, 4-H)*	195,39 (q, CO, $^{2}J_{C-F}$ = 35,4 Hz); 138,22; 137,75; 133,48 ($C_{(1a)}$, $C_{(4a)}$, $C_{(1)}$, Ph) 129,69 (3C); 129,54; 129,18 (2C); 128,69; 125,71; 125,49 ($C_{(5)}$ to $C_{(8)}$, 5C Ph) 115,43 (q, CF_3, $^{1}J_{C-F}$ = 289 Hz); 73,42; 56,04; 47,57 ($C_{(2)}$ to $C_{(4)}$)*
XIa	1700 (CO)	7,95 (1H, d, ^{4}J = 1,6 Hz, 4-H) 7,43-7,40 (1H, m, 5-H or 8-H) 7,28-7,16 (8H, m, 5H Ph, 3H arom. thiochromane) 5,36 (1H, s, 2-H)	179,34 (q, CO, $^{2}J_{C-F}$ = 34,3 Hz); 142,90 ($C_{(4)}$, q, $^{4}J_{C-F}$ = 3,6 Hz); 140,95 ($C_{(1)}$, Ph) 133,84 ($C_{(1a)}$); 132,77 and 132,42 ($C_{(5)}$, $C_{(7)}$); 129,56 ($C_{(3)}$); 128,84 (2C Ph) 128,16 and 127,93 ($C_{(6)}$, $C_{(8)}$); 126,88 ($C_{(4a)}$); 126,53 (2C, Ph); 126,17 ($C_{(4)}$, Ph) 116,84 (q, CF_3, $^{1}J_{C-F}$ = 292 Hz); 38,96 ($C_{(2)}$)
XIb	1700 (CO)	7,44 (1H, s, 4-H); 7,19-7,40 (4H, m, 5-H to 8-H) 3,03-2,92 (2H, m, CH_2 cyclobut.) 2,35-2,13 (3H, m, CH_2 cyclobut.) 2,13-1,98 (1H, m, CH_2 cyclobut.)	180,04 (q, CO, $^{2}J_{C-F}$ = 34,4 Hz); 140,50 ($C_{(4)}$); 135,94 ($C_{(1a)}$); 132,00 ($C_{(4a)}$) 131,62 and 131,40 ($C_{(5)}$, $C_{(7)}$); 130,16 ($C_{(3)}$); 127,52; 125,91 ($C_{(6)}$, $C_{(8)}$) 116,27 (q, CF_3, $^{1}J_{C-F}$ = 291 Hz); 47,31 ($C_{(2)}$); 34,96 ($2CH_2$ cyclobut.) 15,62 (CH_2 cyclobut.)
XIc	1700 (CO)	7,97 (1H, s, 4-H); 7,53-7,56 (1H, m, 5-H) 7,37-7,32 (1H, m, 7-H); 7,23-7,32 (2H, m, 6-H and 8-H); 6,64 (1H, d, ^{3}J = 3,0 Hz, 5-H pyrrole) 5,89 (1H, t, ^{3}J = 3,0 Hz, 4-H pyrrole) 5,75 (1H, d, ^{3}J = 3,0 Hz, 3-H pyrrole) 5,44 (1H, s, 2-H); 3,80 (3H, s, CH_3)	179,06 (q, CO, $^{2}J_{C-F}$ = 34,3 Hz); 142,32 ($C_{(4)}$); 132,81 ($C_{(1a)}$); 132,28 132,09 ($C_{(5)}$, $C_{(7)}$); 129,76 ($C_{(4a)}$); 128,54 ($C_{(6)}$ or $C_{(8)}$); 128,16 ($C_{(3)}$) 126,09 ($C_{(8)}$ or $C_{(6)}$ and $C_{(2)}$ pyrrole); 124,25 ($C_{(5)}$ pyrrole) 116,68 (q, CF_3, $^{1}J_{C-F}$ = 290 Hz); 109,21; 106,80 ($C_{(3)}$, $C_{(4)}$ pyrrole); 33,83 (CH_3) 31,36 ($C_{(2)}$)
XId	1700 (CO)	7,85 (1H, s, 4-H); 7,47 (1H, d, ^{3}J = 7,2 Hz, 5-H) 7,38-7,32 (2H, m, 6-H and 8-H); 7,22-7,27 (1H, m, 7-H) 7,05 (1H, d, ^{3}J = 5,2 Hz, 5-H thiophene) 6,85 (1H, d, ^{3}J = 3,6 Hz, 3-H thiophene) 6,79 (1H, dd, ^{3}J = 5,2, ^{3}J = 3,6 Hz, 4-H thiophene) 5,61 (1H, s, 2-H)	178,92 (q, CO, $^{2}J_{C-F}$ = 34,9 Hz); 143,87 ($C_{(2)}$ thiophene) 142,07 (q, $C_{(4)}$, $^{4}J_{C-F}$ = 3,5 Hz); 133,43 ($C_{(1a)}$); 132,65; 132,35 ($C_{(5)}$, $C_{(7)}$) 129,27 ($C_{(4a)}$); 128,15 ($C_{(5)}$ thiophene); 127,35 ($C_{(3)}$); 126,58; 126,26 ($C_{(6)}$, $C_{(8)}$) 125,17; 125,05 ($C_{(3)}$, $C_{(4)}$ thiophene); 116,61 (q, CF_3, $^{1}J_{C-F}$ = 290 Hz); 34,47 ($C_{(2)}$)

* In acetone-d_6.

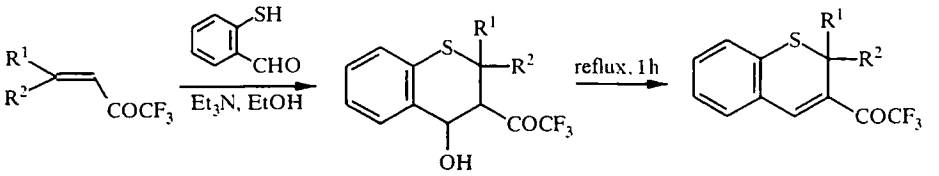


VII

Study of the reaction of a series of trifluoromethyl-containing enones with 2-mercaptobenzaldehyde showed that compounds having a HSC=CCHO fragment are rather promising synthons for the synthesis of sulfur-containing heterocycles, since both nucleophilic and electrophilic centers are contained in the molecule. However similar reactions of 2-mercaptobenzaldehyde with unsaturated ketones were not studied previously probably since a convenient method of obtaining this compound by the reaction of the dilithium derivative of thiophenol with DMF was only developed quite recently [9].

The reaction of enones with 3-mercapto-3-trifluoromethylacrolein [10] has been studied to obtain trifluoromethyl-containing thiopyrans. The reaction proceeds as a Michael addition with a subsequent crotonate condensation.

We found that enones II, VII, VIII, and IX, containing a CF3 group, react with 2-mercaptobenzaldehyde at room temperature in ethanol in the presence of triethylamine as basic catalyst. A mixture of two compounds was formed as a result, *viz.* a thiochromane X and its dehydration product – 2H-thiochromene XI. Boiling the reaction mixture for 1 h leads to the formation of the latter in good yield. The intermediate thiochromane was isolated only in the case of enone II.



II, VII, VIII, IX X XIa–d

II, X, XI a R^1 = Ph, R^2 = H; VII, XI b R^1 = thienyl-2, R^2 = H;
VIII, XI c R^1 = N-methyl-2-pyrrolyl, R^2 = H; IX, XI d R^1, R^2 = $-(CH_2)_3-$

According to the data of ^1H and ^{13}C NMR spectra thiochromane X is formed as a diastereomer with equatorial disposition of all substituents. Refluxing in benzene in the presence of toluene-*p*-sulfonic acid with azeotropic distillation of water or in alcohol in the presence of triethylamine leads to 2H-thiochromene XIa in practically quantitative yield.

The reaction of trifluoromethyl-containing enones with thiophenol derivatives therefore proceeds as a Michael addition reaction. In the case of 2-formylthiophenol the reaction proceeds with a subsequent intramolecular aldol condensation with the formation of thiochromanes, which are readily converted into 2H-thiochromenes. By reacting β-trifluoroacetylstyrene with 4-methylthiophenol the β-ketosulfide III or pyran IV are formed and the formation of the latter proceeds stereospecifically.

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were recorded on Varian VXR 400 and Bruker AMX 400 spectrometers (operating frequency for ^{13}C nuclei 100 MHz) in $CDCl_3$, CD_3COCD_3, and C_6D_6, TMS was used as internal standard. The IR spectra were obtained on a UR 20 spectrometer in Nujol. Analysis by TLC was carried out on Silufol UV 254 plates, visualization with acidified $KMnO_4$ solution or with iodine vapor. The trifluoromethyl-containing enones were obtained by known procedures [11-15].

The X-ray structural investigation of compound IV was carried out on a RIGAKU AFC6S automatic four-circle diffractometer at room temperature [λCu Kα (1.54184 Å), graphite monochromator].

Interpretation of the structure was carried out by direct statistical methods [16]. All non-hydrogen atoms were refined by the full-matrix anisotropic least squares method on F^2 [17]. All hydrogen atoms were placed in calculated positions (d_{O-H} = 0.82 Å; d_{C-H} = 0.93 Å for aromatic H; d_{C-H} = 0.97 for all others) and refined with a 'rider' scheme allowing for rotation of methyl (AFIX 137) and hydroxyl (AFIX 147) groups. The investigated crystal of compound IV was a racemic pair and on refinement (SHELXL-93) the instruction TWIN was used.

β-Ketosulfides. A solution of the enone (5.0 mmol) in ethanol (10 ml) was added dropwise with stirring during 1 h to a solution of 4-methylthiophenol (0.68 g, 5.5 mmol) and Et_3N (0.10 g, 1 mmol) in ethanol (15 ml). The solution was left for 1 h at room temperature, then evaporated in vacuum. The reaction product was separated by column chromatography on silica gel (20 g), the excess of 4-methylthiophenol was eluted with hexane and the reaction product with benzene, R_f 0.30-0.35 (hexane–EtOAc, 9 : 1). Ketosulfide III was crystallized from hexane on cooling to -20°C, ketosulfide V was redistilled in vacuum.

4-[(4-Methylphenyl)thio]-4-phenyl-1,1,1-trifluoro-2-butanone (III). Yield 1.0 g (61%); mp 56-57°C. IR spectrum: 1765 cm^{-1} (CO). ^1H NMR spectrum (acetone-d_6): 7.29 (2H, d, ^3J = 8.0 Hz, 4-MeC_6H_4); 7.25-7.16 (5H, m, Ph); 7.04 (2H, d, ^3J = 8.0 Hz, 4-MeC_6H_4); 4.72 (1H, dd, ^3J = 7.8, ^3J = 6.7 Hz, 1-H); 3.55 (1H, dd, ^2J = 18.8, ^3J = 7.8 Hz, 2-H); 3.47 (1H, dd, ^2J = 18.8, ^3J = 6.7 Hz, 2-H); 2.21 ppm (3H, s, CH_3). ^{13}C NMR spectrum (acetone-d_6): 189.35 (q, CO, $^2J_{C-F}$ = 36.1 Hz); 141.08 and 139.01 ($C_{(1)}$ and $C_{(4)}$, 4-MeC_6H_4); 134.37 (2C, 4-MeC_6H_4); 130.54 (2C, 4-MeC_6H_4); 129.26 ($C_{(1)}$, Ph); 129.21 (2C, Ph); 128.52 (2C, Ph); 128.38 ($C_{(4)}$, Ph); 118.07 (q, CF_3, $^1J_{C-F}$ = 286 Hz); 47.78 ($C_{(1)}$); 43.17 ($C_{(2)}$); 21.06 ppm (CH_3). Found, %: C 62.88; H 4.56. $C_{17}H_{15}F_3OS$. Calculated, %: C 62.95; H 4.66.

4[(4-Methylphenyl)thio]-1,1,1-trifluoro-4,4-trimethylene-2-butanone (VI). Yield 0.86 g (60%), bp 99-101°C (1 mm Hg). IR spectrum: 1770 cm^{-1} (CO). ^1H NMR spectrum ($CDCl_3$): 7.37 (2H, d, ^3J = 8.0 Hz, 4-MeC_6H_4); 7.17 (2H, d, ^3J = 8.0 Hz, 4-MeC_6H_4); 3.09 (2H, s, 2-H); 2.39-2.18 (5H, m, $3CH_2$ cyclobut.); 2.37 (3H, s, CH_3); 2.01-1.94 ppm (1H, m, CH_2 cyclobut.). ^{13}C NMR spectrum ($CDCl_3$); 188.54 (q, CO, $^2J_{C-F}$ = 34.5 Hz); 139.03 ($C_{(1)}$ or $C_{(4)}$, 4-MeC_6H_4); 135.72 (2C, 4-MeC_6H_4); 129.73 (2C, 4-MeC_6H_4); 128.65 ($C_{(4)}$ or $C_{(1)}$, 4-MeC_6H_4); 115.06 (q, CF_3, $^1J_{C-F}$ = 291 Hz); 49.39 ($C_{(1)}$); 45.17 ($C_{(2)}$); 33.94 ($2CH_2$ cyclobut.); 21.04 (CH_3); 16.46 ppm (CH_2 cyclobut.). Found, %: C 58.17; H 5.31. $C_{14}H_{15}F_3OS$. Calculated, %: C 58.32; H 5.24.

3-{[(4-Methylphenyl)thio](phenyl)methyl}-4-phenyl-2,6-bis(trifluoromethyl)tetrahydro-2H-pyran-2,6-diol (IV). A solution of 4-methylthiophenol (0.62 g, 5.0 mmol) in ethanol (10 ml) was added dropwise with stirring to a solution of enone II (2.5 g, 12.5 mmol) and Et_3N (0.10 g, 1.0 mmol) in ethanol (15 ml). The solution was left for 1 h at room temperature and then evaporated in vacuum. The reaction product was separated by column chromatography on silica gel (20 g). The excess of enone II was eluted with hexane and the reaction product with benzene (R_f 0.18, hexane–EtOAc, 9 : 1). The product was then crystallized from hexane. Yield 1.8 g (68%); mp 156-157°C (with decomposition). IR spectrum: 2800-3500 cm^{-1} (OH). ^1H NMR spectrum (benzene-d_6): 7.17 (2H, d, ^3J = 8.0 Hz, 4-MeC_6H_4); 6.94-6.67 (8H, m, 2Ph); 6.55 (2H, d, ^3J = 8.0 Hz, 4-MeC_6H_4); 6.48 (2H, d, ^3J = 7.0 Hz, Ph); 5.18 (1H, s, –SCH); 4.27 (2H, br. s, 2OH); 3.88 (1H, dt, ^3J = 12.2, ^3J = 3.9 Hz, 4-H); 3.17 (1H, d, ^3J = 11.9 Hz, 3-H); 1.98 (1H, dd, ^2J = 13.5, ^3J = 3.9 Hz, 5-H_{eq}); 1.86 (1H, t, ^2J = ^3J = 12.9 Hz, 5-H_{ax}); 1.77 ppm (3H, s, CH_3). ^{13}C NMR spectrum (acetone-d_6): 142.18; 141.20 ($C_{(1)}$ and $C_{(4)}$, 4-MeC_6H_4); 137.87 ($C_{(1)}$, Ph); 132.98 ($C_{(1)}$, Ph'); 131.58 (2C, 4-MeC_6H_4); 130.54 (2C, 4-MeC_6H_4); 129.54; 128.97; 128.55; 128.11 (4 × 2C, Ph); 127.82 ($C_{(4)}$, Ph); 126.65 ($C_{(4)}$, Ph'); 124.33 (q, CF_3, $^1J_{C-F}$ = 287 Hz); 123.33 (q, CF_3, $^1J_{C-F}$ = 283 Hz); 98.84 (q, $C_{(2)}$ or $C_{(6)}$, $^2J_{C-F}$ = 29.4 Hz); 95.18 (q, $C_{(6)}$ or $C_{(2)}$, $^2J_{C-F}$ = 32.5 Hz); 54.75 (–SCH–); 49.64 ($C_{(4)}$); 37.85 ($C_{(3)}$); 36.03 ($C_{(5)}$; 20.88 ppm (CH_3). Found, %: C 59.57; H 4.46. $C_{27}H_{24}F_6O_3S$. Calculated, %: C 59.77; H 4.46.

2H-Thiochromenes (XI). The appropriate enone (5.0 mmol) and Et_3N (0.10 g, 1.0 mmol) were added to a solution of 2-mercaptobenzaldehyde (0.69 g, 5.0 mmol,) in ethanol (25 ml). The solution was boiled for 1 h and then evaporated in vacuum. Hexane (10 ml) was added to the residue and the mixture was passed through a short column of silica gel (~10 g), and the reaction product was eluted with hexane (30 ml). The solvent was evaporated in vacuum and the 2H-thiochromenes XI were crystallized from hexane by cooling to -20°C.

The intermediate thiochromane X was isolated in the case of reaction with enone II by maintaining the reaction mixture at room temperature for 15 min, after which water (15 ml) was added. The precipitated solid [compound X] was filtered off, washed with water, and dried in vacuum. Characteristics of the synthesized compounds X and XI are given in Tables 3 and 4.

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