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Synthesis and Properties of 2,2-Dichlorovinyl Trifluoromethyl Ketone

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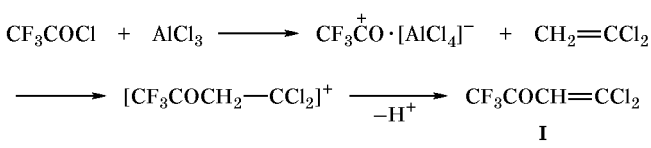
Abstract—Highly reactive 2,2-dichlorovinyl trifluoromethyl ketone was synthesized. Its reactions with N,N- and N,S-nucleophiles gave 1,3-thiazine, pyrazole, and imidazole derivatives containing a trifluoromethyl substituent.

Compounds containing a trifluoromethyl group, especially those belonging to the heterocyclic series, exhibit high biological activity. Some representatives have found application as drugs and herbicides [1]. With the goal of obtaining heteroatomic and heterocyclic compounds having a CF_3 group we synthesized previously unknown 2,2-dichlorovinyl trifluoromethyl ketone and studied its reactions with N,N- and N,S-nucleophiles.

2,2-Dichlorovinyl trifluoromethyl ketone (**I**) was synthesized by the known procedure which is used for preparation of 2,2-dichlorovinyl ketones: by reaction of trifluoroacetyl chloride with 1,1-dichloroethene in the presence of $AlCl_3$ [2, 3]. The reaction was performed with equimolar amounts of the reactants and the catalyst at –50 to –60°C. It should be noted that the process was not accompanied by formation of a saturated product, trichloroethyl trifluoromethyl ketone, though alkanoyl and benzoyl chlorides are known to react with 1,1-dichloroethene, yielding the corresponding 2,2,2-trichloroethyl ketones which are converted into 2,2-dichlorovinyl ketones by thermolysis, treatment with bases, or steam distillation [3]. Presumably, intermediate carbocation formed in the reaction of 1,1,-dichloroethene with trifluoroacetyl chloride is stabilized through elimination of proton to give the final product, rather than through addition of chloride ion with formation of 2,2,2-trichloroethyl trifluoromethyl ketone (Scheme 1).

Scheme 1.



Ketone **I** is a slightly colored volatile liquid with a strong specific odor. Unlike alkyl dichlorovinyl ketones, 2,2-dichlorovinyl trifluoromethyl ketone is stable to storage and is incapable of undergoing crotonization to form pyranones [2, 3]. The structure of ketone **I** and other compounds derived therefrom was proved by spectral data and elemental analyses (Tables 1, 2). The IR spectrum of **I** contains a number of absorption bands typical of the C=O group and C=C, =C–H, and CF_2–F bonds [4] (Table 1). In the ^{1}H NMR spectrum of ketone **I**, as well as in the ^{1}H NMR spectra of alkyl and aryl 2,2-dichlorovinyl ketones (the spectra of these compounds were not reported previously), we observed only one olefinic proton signal (Table 2). As a rule, the olefinic proton signal in the spectra of alkyl (or aryl) 2,2-dichlorovinyl ketones shifts downfield as the electron-acceptor power of the substituent at the carbonyl group rises. The olefinic proton signal of ketone **I** is located in a weaker field than those of alkyl 2,2-dichlorovinyl ketones and chloromethyl 2,2-dichlorovinyl ketone but in a stronger field than the corresponding signal of dichloromethyl, trichloromethyl, and aryl 2,2-dichlorovinyl ketones.

By reaction of ketone **I** with 2,4-dinitrophenylhydrazine we obtained the corresponding hydrazone **II** which underwent intramolecular cyclization to to 5-chloro-1-(2,4-dinitrophenyl)-3-trifluoromethyl-

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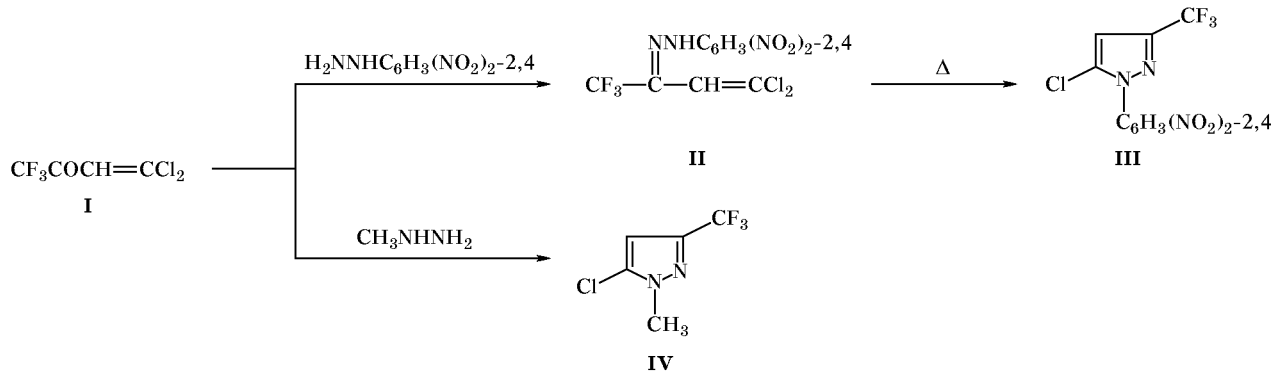
Scheme 2.



pyrazole (**III**) on heating above the melting point or on treatment with triethylamine (Scheme 2). The cyclization was accompanied by liberation of HCl. An analogous transformation was reported for 2,2-dichlorovinyl phenyl ketone dinitrophenylhydrazone [7]. As is known [7], alkyl 2,2-dichlorovinyl ketone 2,4-dinitrophenylhydrazones do not undergo cyclization to pyrazoles on treatment with bases or on heating.

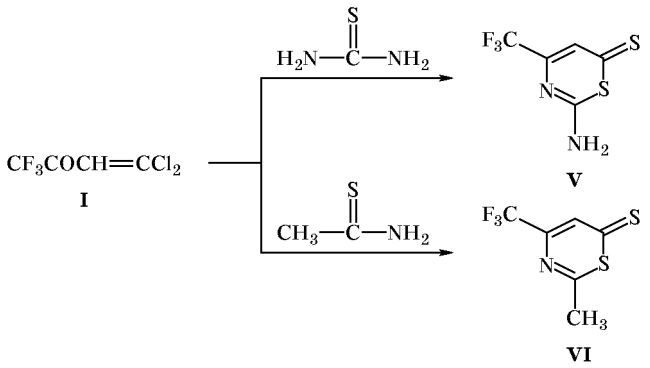
The reaction of ketone **I** with methylhydrazine in the presence of triethylamine (equimolar amounts of the reactants) resulted in formation of only cyclic product, 5-chloro-1-methyl-3-trifluoromethylpyrazole (**IV**) (Scheme 2). Pyrazole **IV** was also formed from equimolar amounts of ketone **I** and methylhydrazine in the absence of dehydrochlorinating agent, but in this case the conversion of **I** was not complete and the yield of the product was lower. We succeeded in increasing the yield of **IV** by reacting ketone **I** with 2 equiv of methylhydrazine. Compounds **II** and **III** are strongly colored crystalline substances. Pyrazole **IV** is a liquid with a pungent odor.

The presence of a halogen atom in 3-trifluoromethylpyrazoles **III** and **IV** provides the possibility for synthesizing promising biologically active substances, herbicides, dyes, and fluorescent compounds [1, 8, 9].

The IR spectrum of 2,4-dinitrophenylhydrazone **II** contains an absorption band of the NH group, which is absent in the spectrum of cyclization product **III**. Instead, a band from the C–H bond appears at at 3110 cm^{-1}. A similar band is present in the IR spectrum of pyrazole **IV**. Its frequency is higher than the C–H vibration frequency in the spectrum of initial hydrazone **II** (Table 1). Pyrazoles **III** and **IV** also showed in the IR spectra absorption bands belonging to the C–C and C–N bonds. In the ^1H NMR spectrum of **IV** we observed signals from the CH and NCH_3 protons.

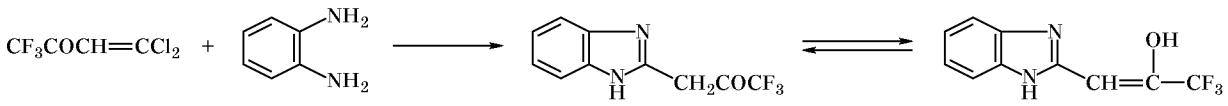
2,2-Dichlorovinyl ketones are known to react with thiourea and *N*-acetylthiourea to afford, respectively, 2-amino- and 2-acetylamino-1,3-thiazine-6-thiones [10]. We performed analogous reactions of triluoromethyl ketone **I** with thiourea and thioacetamide in alcohol. These reactions involved replacement of both chlorine atoms with simultaneous heterocyclization to give 2-amino-4-trifluoromethyl-1,3-thiazine-6-thione (**V**) and 2-methyl-4-trifluoromethyl-1,3-thiazine-6-thione (**VI**), respectively (Scheme 3).

Scheme 3.



Compounds **V** and **VI** are colored solids with a specific odor. The IR spectra of **V** and **VI** contained absorption bands typical of C=C, C–N, and C=S bonds, which were located at shorter frequencies than the corresponding bands of known 4-alkyl(aryl)-2-amino-1,3-thiazine-6-thiones [10]. In the ^1H NMR spectra of compounds **V** and **VI** we observed only signals from the olefinic proton (Table 2) and methyl group for thiazine **VI**. The 5-H signal of **VI** appears in a weaker field (δ 7.23 ppm) than those of compound **V** and 4-alkyl(aryl)-2-amino-1,3-thiazine-6-thiones [10] (Table 1). This fact may be explained by increase of electron density in the thiazine ring of 2-amino-thiazinethiones due to effect of lone electron pair on

Scheme 4.



VII

the amino nitrogen atom, which is transmitted through the conjugated bond system.

2-(3,3,3-Trifluoroacetonyl)benzimidazole was previously synthesized [11, 12] by reaction of 2,2-diethoxyvinyl triflurometyl ketone or ethyl trifluoroacetoacetate with *o*-phenylenediamine (yield 70 and 15%, respectively). We have found that the reaction of ketone **I** with *o*-phenylenediamine also leads to formation of 2-(3,3,3-trifluoroacetonyl)benzimidazole (**VII**) in 70% yield (Scheme 4, Table 1).

According to the IR and NMR spectra, trifluoroacetonylbenzimidazole **VII** exists in different tautomeric forms. The ketone tautomer predominates in the crystalline state. The IR spectrum of benzimidazole **VII** in KBr contains absorption bands of the C=O, N–H, C=C, and C–H (alkyl and aryl) bonds. It should be noted that the carbonyl vibration frequency of trifluoroacetonylbenzimidazole **VII** is appreciably lower than the carbonyl frequency of initial trifluoromethyl ketone **I**.

Compound **VII** showed in the ^{1}H NMR spectrum signals from four aromatic proton, a one-proton signal at δ 5.41 (DMSO-d_6) or 5.5 ppm (CD_3OD), and a broadened downfield signal from the NH proton at δ 12–13 ppm. Likewise, in the ^{1}H NMR spectrum of **VII**, recorded in $CDCl_3$, only one olefinic proton signal was observed at δ 6.1 ppm [11]. According to [11], the NH proton signal is overlapped by signals from the imidazole ring protons, and the broadened downfield signal at δ 9.1 ppm was assigned to the OH group. We observed no hydroxy proton signal in the ^{1}H NMR spectra of benzimidazole **VII** in DMSO-d_6 and CD_3OD. This fact may be explained by H–D exchange with the solvent, as well as by formation of intramolecular hydrogen bond =C–O–H···N=.

Obviously, the formation of intramolecular hydrogen bond –C=O···H–N like that proposed in [13] for 2-phenacylbenzimidazole is also typical of the ketone tautomer of compound **VII** in the crystalline state. As a result, the carbonyl absorption frequency in the IR spectrum of **VII** is anomalously low.

Thus, the chemical properties of 2,2-dichlorovinyl trifluoromethyl ketone are determined by the presence of two labile chlorine atoms and highly electrophilic carbonyl group. In reactions with S,N-dinucleophiles and hydrazines both chlorine atoms and the carbonyl oxygen atom are replaced simultaneously, leading to formation of 1,3-thiazine and pyrazole derivatives, respectively; the reaction with *o*-phenylenediamine involves only the halogen atoms and yields 2-(trifluoroacetonyl)benzimidazole.

EXPERIMENTAL

The ^{1}H and ^{19}F NMR spectra were obtained on Bruker DPX-400 (400 and 376.3 MHz, respectively) and Jeol FX-90Q spectrometers (90 and 84 MHz, respectively). Hexamethyldisiloxane was used as internal reference (for ^{1}H). The IR spectra were recorded on a Specord IR75 instrument from samples prepared as KBr pellets or thin films.

2,2-Dichlorovinyl trifluoromethyl ketone (I). Trifluoroacetyl chloride, 48 g (0.36 mol), was added through a gas-inlet tube into a suspension of 48 g (0.36 mol) of $AlCl_3$ in 50 ml of anhydrous chloroform or methylene chloride, stirred at –50 to –60°C. 1,1-Dichloroethene, 35 g (0.36 mol), was then added dropwise, and the mixture was stirred for 2 h, gradually raising the temperature to ambient. The mixture was treated with ice, the organic layer was separated, the aqueous layer was extracted with chloroform, and the combined organic layers were dried over $CaCl_2$ and evaporated. The residue was distilled, a fraction with bp 103–110°C being collected. Repeated distillation gave 40.6 g of pure product **I**, bp 108–110°C, n_D^{20} 1.4210; d_4^{20} 1.6523. Found, %: C 25.15; H 0.52. $C_4HCl_2F_3O$. Calculated, %: C 24.87; H 0.52.

2,2-Dichlorovinyl trifluoromethyl ketone 2,4-dinitrophenylhydrazone (II). 2,2-Dichlorovinyl trifluoromethyl ketone (**I**), 1.93 g (0.01 mol), was added with stirring to a solution of 1.76 g (0.01 mol) of 2,4-dinitrophenylhydrazine in 15 ml of anhydrous methanol containing 0.5 ml of concentrated sulfuric acid. When the exothermic reaction was complete, the mixture was stirred for 15 min at 60°C. The precipitate was filtered off and dried in a vacuum desiccator. Yield 2.30 g. Found, %: C 31.89; H 1.31; Cl 19.31; N 15.05. $C_{10}H_5Cl_2F_3N_4O_4$. Calculated, % C 32.19; H 1.35; Cl 19.00; N 15.02.

Table 1. Yields, melting points, and IR and NMR spectral parameters of compounds **I**–**VII**

Comp. no.	Yield, %	mp, °C	IR spectrum (KBr), ν, cm^{-1}	^1H and ^{19}F NMR spectra, δ or δ_F, ppm
I	58	108–110[a]	1050–1330 (CF_3) [4], 1575 (C=C), 1720 (C=O), 3070 (=C−H)[b]	$CDCl_3$: 7.00 (=CH); –80.30 (CF_3)[c]
II	62	182–183	1310, 1350, 1510, 1545 (NO_2); 1610, 1620 (C=N), 3100 (=C−H); 3265, 3300 (NH)	DMSO-d_6: 6.39 s (=CH), 9.46 (NH), 7.52 d, 8.34 d, 9.34 d (J = 10 Hz) (C_6H_3)
III	68	84–86	1330, 1350, 1510, 1550 (NO_2); 1600, 1625 (C=N, C=C); 3110 (=C−H)	
IV	56	140–141[a]	790 (C−Cl), 1280 (CF_2−F) [4], 1480 (C=C), 2960 (CH_3), 3150 (=C−H)[b]	CD_3Cl: 3.88 s (NCH_3), 6.47 s (=CH); –63.40 s (CF_3)[c]
V	50	177–178	1300 (C=S); 1500, 1570 (C=C); 1635 (C=N); 3100 (=C−H); 3295 (NH_2)	CD_3OD: 6.85 s (=CH), –70.15 s (CF_3)[c]
VI	50	53–55	1300 (C=S); 1510, 1590 (C=C, C=N); 2930, 2970 (CH_3); 3045 (=C−H)	CD_3OD: 7.23 s (=CH), 2.61 s (CH_3); –69.93 s (CF_3)[c]
VII	70	289–291	1483 (C=C); 1603 (C=N); 1632 (C=O); 2653–2923 (N−H···, C−H); 3040, 3080 (=C−H); 3250 (N−H)	DMSO-d_6: 7.49 m, 7.21 m (C_7H_5), 5.414 s (=CH), 13–12 (NH)

[a] Boiling point.
[b] The IR spectrum was recorded from thin film.
[c] Relative to CCl_3F.

5-Chloro-1-(2,4-dinitrophenyl)-3-trifluoromethylpyrazole (III). 2,2-Dichlorovinyl trifluoromethyl ketone 2,4-dinitrophenylhydrazone (**II**), 1.58 g (0.005 mol), was heated at 185°C. Evolution of HCl was observed over a period of 5 min. The product was recrystallized from alcohol. Yield 1.08 g (68%). Found, %: C 35.18; H 1.24; Cl 10.38; N 16.09. $C_{10}H_4ClF_3N_4O_4$. Calculated, % C 35.68; H 1.20; Cl 10.00; N 16.64.

5-Chloro-1-methyl-3-trifluoromethylpyrazole (IV). *a*. Methylhydrazine sulfate, 1.46 g (0.01 mol), was mixed with 15 ml of anhydrous ethanol, and a solution of 1.45 g (0.0075 mol) of ketone **I** in 5 ml of anhydrous ethanol was added dropwise with stirring. Triethylamine, 1.95 g (0.03 mol), was then added, and the mixture was stirred for 2 h. The precipitate of triethylamine sulfate and hydrochloride was filtered off, and the filtrate was evaporated to isolate 5.46 g of pyrazole **IV**. Found, %: C 35.18; H 1.24; Cl 10.38; N 16.09. $C_{10}H_4ClF_3N_4O_4$. Calculated, %: C 35.68; H 1.20; Cl 10.00; N 16.64.

b. Ketone **I**, 10.97 g (0.0619 mol), was slowly added (dropwise) to a solution of 0.1238 mol of methylhydrazine in 40–50 ml of anhydrous acetonitrile. The mixture warmed up, and methylhydrazine hydrochloride precipitated. When the exothermic reaction was complete, the mixture was stirred for 1–2 h. The precipitate was filtered off, and the filtrate was evaporated to isolate 5.45 g (56%) of product **IV**.

When the reaction of 2,2-dichlorovinyl trifluoromethyl ketone with methylhydrazine was performed at a reactant ratio of 1:2 in ether, hexane, benzene, and lower alcohols (methanol, ethanol, or 2-propanol), other conditions being equal, pyrazole **IV** was obtained in 50–60% yield.

2-Amino-4-trifluoromethyl-6*H*-1,3-thiazine-6-thione (V). 2,2-Dichlorovinyl trifluoromethyl ketone (**I**), 3.06 g (0.016 mol), was added dropwise with stirring to a solution of 2.44 g (0.032 mol) of thiourea in 50 ml of ethanol. When the exothermic reaction was complete, the mixture was stirred for 4 h at 40°C and poured into cold water. The yellow flaky precipitate was filtered off and dried in a vacuum desiccator. Yield 1.7 g. Found, %: C 27.79; H 1.72; N 13.25; S 29.60. $C_5H_3F_3N_2S_2$. Calculated, %: C 28.29; H 1.41; N 13.20; S 30.17.

2-Methyl-4-trifluoromethyl-6*H*-1,3-thiazine-6-thione (VI). 2,2-Dichlorovinyl trifluoromethyl ketone (**I**), 1.93 g (0.01 mol), was added dropwise with stirring to a solution of 1.5 g (0.02 mol) of thioacetamide in 32 ml of methanol. When the exothermic reaction was complete, the mixture was stirred for

Table 2. Chemical shifts of the dichlorovinyl group proton in the ^{1}H NMR spectra of 2,2-dichlorovinyl trifluoromethyl ketone (**I**) and ketones $RCOCH{=}CCl_2$ (**Ia**–**In**) in dilute solutions in CCl_4 and $CDCl_3$[a]

Comp. no.	R	δ, ppm	σ* [5], (σ*) [6]	σ_I [5], (σ_I) [6]	σ [5]	σ^p [5]	σ_C [6]
Ia	CH_3	6.45	0.00 (0.0)	–0.05 (–0.08)		–0.129	–0.15
Ib	C_2H_5	6.54	–0.10 (–0.10)	–0.05 (–0.09)		–0.117	–0.14
Ic	C_3H_7	6.53	–0.15 (–0.115)			–	
Id	*iso*-C_3H_7	6.59	–0.19	–0.07 (–0.11)		–0.098	–0.15
Ie	CH_2Cl	6.95	1.05 (–1.09)	0.17 (0.14)		–	–0.03
I[b]	CF_3	7.00		0.42		0.532	
If	$CHCl_2$	7.09	(1.94)	–		–	
Ig	CCl_3	7.20	–	2.65 [6]			0.32
Ih	4-$CH_3OC_6H_4$	7.08		0.26 (0.29)	–0.268	–0.111	–0.52
Ii	4-$CH_3C_6H_4$	7.12		–0.05 (–0.08)	–0.17	–0.129	–0.17 (–0.12 [5])
Ij	C_6H_5	7.17		0.0	0.0	0.0	0.0
Ik	4-BrC_6H_4	7.11		0.45 (0.44)	0.232	0.265	–0.22
Il	4-ClC_6H_4	7.12		0.47 (0.47)	0.227	0.238	–0.24
Im	4-$NO_2C_6H_4$	7.20		0.63 (0.60)	0.778	0.778	0.15
In	3-$NO_2C_6H_4$	7.24		0.63 (0.60)	0.710	0.710	0.08

[a] σ is the Hammett constant, σ* is the Taft constant, σ_I is the inductive constant, σ^p is the substituent constant [5], and σ_C is the conjugation constant.

[b] In $CDCl_3$.

3 h at 50°C and poured into water. The precipitate was filtered off and dried in a vacuum desiccator. Yield 1.05 g. Found, %: C 34.24; H 1.82; N 5.80; S 29.50. $C_6H_4F_3NS_2$. Calculated, %: C 34.12; H 1.91; N 6.63; S 30.36.

2-(Trifluoroacetonyl)benzimidazole (VII). 2,2-Dichlorovinyl trifluoromethyl ketone, 2 g (0.01034 mol), was added dropwise with stirring to a solution of 1.12 g (0.01034 mol) of *o*-phenylenediamine in 60 ml of dry diethyl ether. When the exothermic reaction was complete, the mixture was stirred for 3 h. The precipitate of 2-(trifluoroacetonyl)benzimidazole hydrochloride, mp 166–169°C, was filtered off, dried in a vacuum desiccator, and treated with a solution of sodium carbonate. The precipitate of **VII** was filtered off and dried. Yield 1.65 g, mp 289–291°C. Found, %: C 52.37; H 3.42; N 12.14. $C_{10}H_7F_3N_2O$. Calculated, %: C 52.46; H 3.09; N 12.28.

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