ISSN 1070-4280, Russian Journal of Organic Chemistry, 2007, Vol. 43, No. 4, pp. 553–558. © Pleiades Publishing, Ltd., 2007.
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Heterocyclizations of Functionalized Heterocumulenes with C,N-, C,O-, and C,S-Binucleophiles: VII.* Reaction of 1-Chloroalkyl Isocyanates with N,N-Disubstituted Cyanothioacetamides. A New Synthetic Route to 6-Dialkylamino-4-oxo-3,4-dihydro-2*H*-1,3-thiazine-5-carbonitriles

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Received May 4, 2006

Abstract—Reactions of α-chlorobenzyl isocyanates and 1-aryl-2,2,2-trifluoro-1-chloroethyl isocyanates with N,N-disubstituted cyanothioacetamides gave 3,4-dihydro-2*H*-1,3-thiazin-4-ones and 3-aryl-2-cyano-4,4,4-trifluorobut-2-enethioamides. The effect of substituents in the reactant molecules on the reaction course and product ratio was studied.

DOI: 10.1134/S1070428007040112

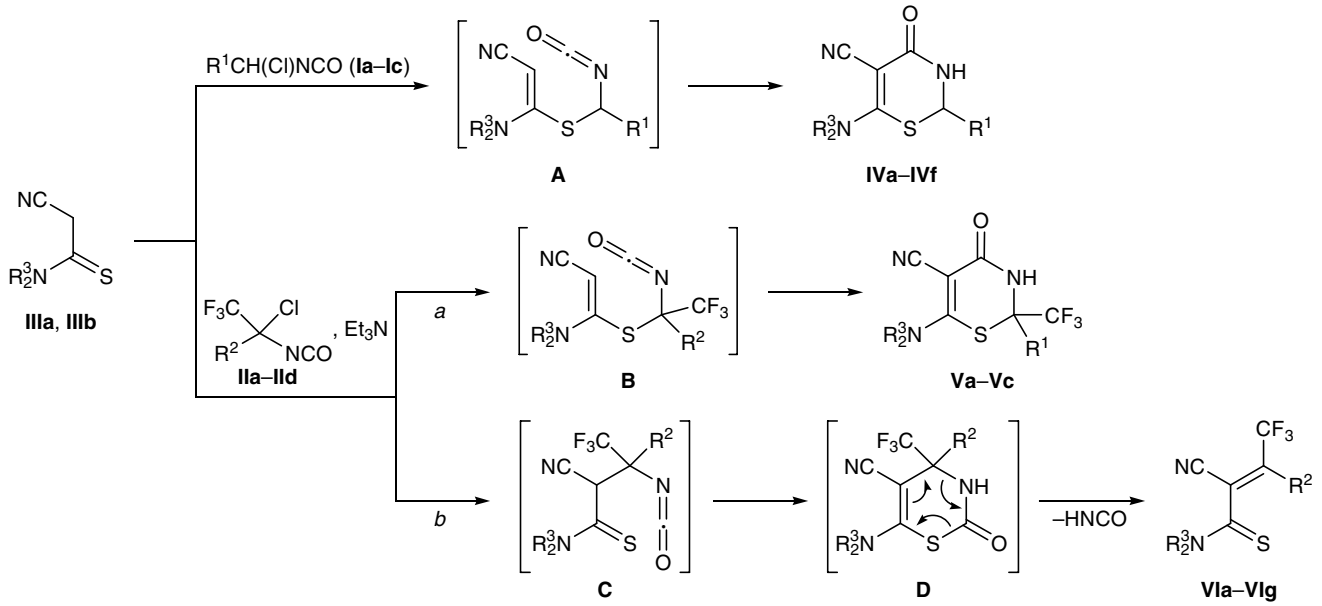
We previously performed a detailed study on the cyclocondensation of 1-chloroalkyl isocyanates with N-substituted β-aminocrotonates [2, 3] and β-diketones [1, 4] and developed new methods for the synthesis of isomeric 2,3- and 3,4-dihydro-1,3-azine (pyrimidine and oxazine) systems. The revealed general relations holding in these reactions prompted us to involve in analogous transformations C,S-binucleophiles with a view to obtain compounds of the 1,3-thiazine series. As C,S-binucleophiles we selected accessible (from the preparative viewpoint) cyanothioacetamides having a cyclic amine fragment. It should be noted that, depending on the substituents on the nitrogen atom and methyl carbon atom, thioacetamides are capable of acting as both N,S- [6], and C,S-binucleophiles [7]. In particular, we showed in [8] that N-monosubstituted alkanethioamides behave as N,S-binucleophiles in reactions with 1-chloroalkyl isocyanates and that the products of these reactions are 1,3,5-thiadiazine derivatives.

Taking into account different regioselectivities in the reactions of 1-chloroalkyl isocyanates with aminocrotonates [3] and β-diketones [4], as starting compounds we used both α-chlorobenzyl isocyanates **Ia**–**Ic** and 2,2,2-trifluoro-1-chloroethyl isocyanates **IIa**–**IId**. We found that α-chlorobenzyl isocyanates **Ia**–**Ic** react with N,N-disubstituted cyanothioacetamides **IIIa** and **IIIb** on heating in methylene chloride to give 6-(pyrrolidin-1-yl or morpholino)-4-oxo-3,4-dihydro-2*H*-1,3-thiazine-5-carbonitriles **IVa**–**IVf** in 31–52% yield. The most probable reaction scheme includes initial nucleophilic substitution of the chlorine atom in **I** by the S-nucleophilic center of thioamide **III** with formation of intermediate **A** which undergoes spontaneous cyclization to final product **IV** (Scheme 1). Less electrophilic α-chlorobenzyl isocyanates **I** (R^1 = Ph, 4-BrC_6H_4) are incapable of effectively alkylating the sulfur atom in **III**, and they give rise to mixtures of unidentified products. 3,4-Dihydro-1,3-thiazin-4-ones **IV** thus obtained are structural analogs of 6-alkyl(aryl)-amino-5-cyano-3,4-dihydro-2*H*-1,3-thiazin-4-ones which were synthesized by us previously via [5+1]-cyclocondensation of 2-alkyl(aryl)amino-2-sulfanyl-1-cyanoacrylamides with aldehydes and ketones [9]. We can state that the proposed alternative approach on the basis of [3+3]-cyclocondensation of difunctional nucleophiles **III** and bielectrophilic isocyanates **I** opens a way to difficultly accessible derivatives of the dihydro-1,3-thiazine system.

The structure of 3,4-dihydro-2*H*-1,3-thiazin-4-ones **IVa**–**IVf** was proved by IR and ^{1}H and ^{13}C NMR spectroscopy. The IR spectra of **IVa**–**IVf** contained

* For communication VI, see [1].

Scheme 1.



I, R^1 = 3-$O_2NC_6H_4$ (**a**), 4-$O_2NC_6H_4$ (**b**), 3,4-$Cl_2C_6H_3$ (**c**); **II**, R^2 = Ph (**a**), 4-MeC_6H_4 (**b**), 4-$MeOC_6H_4$ (**c**), 4-$F_3CC_6H_4$ (**d**); **III**, R^3R^3 = $(CH_2)_4$ (**a**), $(CH_2)_2O(CH_2)_2$ (**b**); **IV**, R^3R^3 = $(CH_2)_4$, R^1 = 3-$O_2NC_6H_4$ (**a**), 4-$O_2NC_6H_4$ (**b**), 3,4-$Cl_2C_6H_3$ (**c**); R^3R^3 = $(CH_2)_2O(CH_2)_2$, R^1 = 3-$O_2NC_6H_4$ (**d**), 4-$O_2NC_6H_4$ (**e**), 3,4-$Cl_2C_6H_3$ (**f**); **V**, R^3R^3 = $(CH_2)_4$, R^2 = Ph (**a**), 4-$F_3CC_6H_4$ (**b**); R^3R^3 = $(CH_2)_2O(CH_2)_2$, R^2 = 4-$F_3CC_6H_4$ (**c**); **VI**, R^3R^3 = $(CH_2)_4$, R^2 = 4-MeC_6H_4 (**a**), 4-$MeOC_6H_4$ (**b**), 4-$F_3CC_6H_4$ (**c**); R^3R^3 = $(CH_2)_2O(CH_2)_2$, R^2 = Ph (**d**), 4-MeC_6H_4 (**e**), 4-$MeOC_6H_4$ (**f**), 4-$F_3CC_6H_4$ (**g**).

absorption bands due to stretching vibrations of the carbonyl and cyano groups at 1640–1650 and 2220–2230 cm^{-1}, respectively, and the endocyclic NH group gave rise to absorption in the region 3160–3180 cm^{-1}. Compounds **IVa–IVf** showed in the ^1H NMR spectra doublet signals at δ 6.06–6.26 and 8.38–8.77 ppm (J = 3.0–4.2 Hz) from the 2-H and NH protons, respectively. In the ^{13}C NMR spectra of these compounds, the C^2 signal was located in the δ_C range from 56.22 to 56.32 ppm, which is also typical of N-monosubstituted dihydrothiazines [9] due to the presence of an $SCH(R^1)NR^2$ fragment in their molecules.

Trifluoromethyl-substituted thiazine derivatives were synthesized using 1-aryl-1-chloro-2,2,2-trifluoroethyl isocyanates **IIa–IId**. Compounds **IIa** and **IIIa** reacted in toluene at room temperature only in the presence of an organic base (triethylamine) to give 6-(pyrrolidin-1-yl)-4-oxo-3,4-dihydro-2*H*-1,3-thiazine-5-carbonitrile (**Va**). Unexpectedly, the reaction of **IIa** with morpholide **IIIb** afforded 2-cyano-4,4,4-trifluoro-3-phenylbut-2-enethioamide **VIa**. Analysis of the reaction mixture by ^{19}F NMR spectroscopy showed that in both cases the reaction gives a mixture of two products of type **V** and **VI**, but only the major product can be isolated. We examined the effect of the substituents in reactants **II** and **III** on the reaction course in more detail and found that the main factor is the nature of the aryl group in initial isocyanate **II**. *p*-Tolyl and *p*-methoxyphenyl derivatives **IIb** and **IIc** give rise to only acyclic 3-aryl-2-cyano-4,4,4-trifluorobut-2-enethioamides **VIb–VIe** and cyanuric acid, the latter being formed as a result of trimerization of isocyanic acid. In the reactions with the most electrophilic isocyanate **IId** having an additional trifluoromethyl group in the *para* position of the benzene ring, depending on the thioamide **III**, we obtained mixtures of compounds **Vb** and **VIf** and **Vc** and **VIg**, their molar ratios being 1:2.4 and 1:3.3, respectively. Each product was isolated as individual substance and characterized by a set of spectral methods. We can conclude that increased nucleophilicity of the sulfur atom in thioamides **III** in combination with reduced electrophilicity of isocyanates **II** favors formation of acyclic products like **VI**. Compounds **VIb–VIe** are additionally stabilized due to the presence of a methyl or methoxy group in the *para* position of the phenyl substituent. Our conclusions are consistent with the mechanism shown in Scheme 1. Compounds **V** are formed via initial alkylation of the sulfur atom in **III** through intermediate **B** (path *a*), whereas the formation of products **VI** involves alkylation of the methylene carbon atom to give intermediate **C** (path *b*). Triethylamine used as catalyst is likely to

enhance the reactivity of thioamides **III** via abstraction of proton therefrom with generation of a strongly nucleophilic C,S-ambident carbanion. We believe that elimination of isocyanic acid from intermediate **C** is assisted by the neighboring thioamide group through intermediate thiazine **D** and that the elimination process follows a concerted mechanism leading to stable compound **VI**.

The structure of compounds **Va**–**Vc** and **VIa**–**VIg** was confirmed by the IR and NMR data. The IR spectra of thiazines **Va**–**Vc** contained absorption bands due to stretching vibrations of the C=O (1640–1650 cm^{-1}), CN (2220–2240 cm^{-1}), and NH groups (3150–3190 cm^{-1}). In the ^1H NMR spectra of these compounds we observed a singlet at δ 9.72–10.26 ppm from the NH proton and two multiplets belonging to the methylene protons of the pyrrolidine or morpholine fragment. In the ^{13}C NMR spectra, quartets from the CF_3 groups (δ_C 123.30–123.39, 123.61–123.64 ppm) and C^2 (δ_C 69.40–69.44 ppm) were present with the following coupling constants: $^1J_{CF}$ = 270–287, $^2J_{CF}$ = 31–33 Hz. Fluorine nuclei in the trifluoromethyl group directly attached to the thiazine ring resonated in the ^{19}F NMR spectra at δ_F –73.66 to –73.06 ppm. Comparison of the ^{13}C and ^{19}F chemical shifts in the spectra of **V** and 1,3,5-thiadiazines [8] provides an additional support to the presence of an $SCH(R^1)NR^2$ fragment in molecules **V**.

Acyclic products **VIa**–**VIg** displayed in the IR spectra absorption bands at 2230–2240 and 1610–1620 cm^{-1}, belonging to stretching vibrations of the C≡N and C=S groups, respectively, while no NH absorption at 3100–3200 cm^{-1} was observed. Unlike heterocyclic compounds **IV** and **V**, the ^1H NMR spectra of **VI** are characterized by complex multiplet signals from protons in the morpholine and pyrrolidine moieties as a result of restricted rotation about the thioamide C–N bond. In the ^{13}C NMR spectra of **VI**, signals from carbon atoms in the trifluoromethyl groups and C^3 appeared as quartets at δ_C 121–122 and 137–138 ppm, respectively; $^1J_{CF}$ = 273–277, $^2J_{CF}$ = 30–32 Hz. The fluorine nuclei in **VI** resonated in the ^{19}F NMR spectra at δ_F –60.94 to –60.93 and –62.94 to –62.92 ppm, i.e., in the region typical of trifluoromethyl groups attached to an aromatic ring or a double-bonded carbon atom.

EXPERIMENTAL

The IR spectra were recorded in KBr on a UR-20 spectrometer. The ^1H, ^{13}C, and ^{19}F NMR spectra were measured from solutions in DMSO-d_6 on a Varian Gemini instrument (299.95, 75.4, and 282.2 MHz, respectively) using tetramethylsilane (^1H, ^{13}C) and CCl_3F (^{19}F) as internal standards. 1-Aryl-1-chloro-2,2,2-trifluoroethyl isocyanates **IIa**–**IId** [10], α-chlorobenzyl isocyanates **Ia**–**If** [3], and N,N-disubstituted cyanothioacetamides **IIIa** and **IIIb** [5] were synthesized by known methods.

2-Aryl-6-amino-4-oxo-3,4-dihydro-2*H*-1,3-thiazine-5-carbonitriles IVa–IVf (*general procedure*). Thioamide **IIIa** or **IIIb**, 5 mmol, was added to a solution of 5 mmol of isocyanate **Ia**–**If** in 20 ml of anhydrous methylene chloride, the mixture was heated for 4 h under reflux, and the precipitate was filtered off, washed with methylene chloride, dried, and recrystallized from ethanol.

2-(3-Nitrophenyl)-4-oxo-6-(pyrrolidin-1-yl)-3,4-dihydro-2*H*-1,3-thiazine-5-carbonitrile (IVa). Yield 41%, mp 180–185°C. IR spectrum, ν, cm^{-1}: 3180 (NH), 2220 (CN), 1640 (C=O). ^1H NMR spectrum, δ, ppm: 1.94 s (4H, CH_2), 3.67 s (4H, CH_2), 6.22 d (1H, CH, *J* = 3.0 Hz), 7.71 t (1H, H_{arom}, *J* = 7.8 Hz), 7.90 d (1H, H_{arom}, *J* = 7.8 Hz), 8.22 d (1H, H_{arom}, *J* = 7.8 Hz), 8.34 s (1H, H_{arom}), 8.53 d (1H, NH, *J* = 3.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 24.96 (CH_2); 52.40 (CH_2); 56.32 (CH); 73.81 (C^5); 118.54 (CN); 121.88, 123.60, 130.15, 133.47 (CH_{arom}); 139.86, 147.66 (C_{arom}); 162.70, 166.28 (C=O, C^6). Found, %: C 54.31; H 4.32; N 16.83. $C_{15}H_{14}N_4O_3S$. Calculated, %: C 54.54; H 4.27; N 16.96.

2-(4-Nitrophenyl)-4-oxo-6-(pyrrolidin-1-yl)-3,4-dihydro-2*H*-1,3-thiazine-5-carbonitrile (IVb). Yield 58%, mp 210–215°C. IR spectrum, ν, cm^{-1}: 3170 (NH), 2220 (CN), 1650 (C=O). ^1H NMR spectrum, δ, ppm: 1.94 s (4H, CH_2), 3.66 s (4H, CH_2), 6.19 d (1H, CH, *J* = 4.2 Hz), 7.73 d (2H, H_{arom}, *J* = 8.7 Hz), 8.25 d (2H, H_{arom}, *J* = 8.7 Hz), 8.52 d (1H, NH, *J* = 4.2 Hz). ^{13}C NMR spectrum, δ_C, ppm: 25.03 (CH_2); 52.46 (CH_2); 56.35 (CH); 73.85 (C^5); 118.65 (CN); 123.67, 128.42 (CH_{arom}); 145.21, 147.49 (C_{arom}); 162.67, 166.32 (C=O, C^6). Found, %: C 54.66; H 4.24; N 17.08. $C_{15}H_{14}N_4O_3S$. Calculated, %: C 54.54; H 4.27; N 16.96.

2-(3,4-Dichlorophenyl)-4-oxo-6-(pyrrolidin-1-yl)-3,4-dihydro-2*H*-1,3-thiazine-5-carbonitrile (IVc). Yield 34%, mp 230–233°C. IR spectrum, ν, cm^{-1}: 3170 (NH), 2230 (CN), 1650 (C=O). ^1H NMR spectrum, δ, ppm: 1.94 s (4H, CH_2), 3.66 s (4H, CH_2), 6.06 d (1H, CH, *J* = 3.0 Hz), 7.43 d (1H, H_{arom}, *J* = 8.0 Hz), 7.62 d (1H, H_{arom}, *J* = 8.0 Hz), 7.66 s (1H, H_{arom}), 8.38 d (1H, NH, *J* = 3.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 25.02

(CH_2); 52.46 (CH_2); 56.27 (CH); 73.68 (C^5); 118.66 (CN); 127.45, 129.22, 130.80 (CH_{arom}); 131.18, 131.53, 138.31 (C_{arom}); 162.93, 166.43 (C=O, C^6). Found, %: C 50.70; H 3.68; N 11.77. $C_{15}H_{13}Cl_2N_3OS$. Calculated, %: C 50.86; H 3.70; N 11.86.

6-Morpholino-2-(3-nitrophenyl)-4-oxo-3,4-dihydro-2*H*-1,3-thiazine-5-carbonitrile (IVd). Yield 50%, mp 225–230°C. IR spectrum, ν, cm^{-1}: 3190 (NH), 2230 (CN), 1640 (C=O). ^1H NMR spectrum, δ, ppm: 3.71 m (8H, CH_2), 6.26 d (1H, CH, J = 3.6 Hz), 7.72 t (1H, H_{arom}, J = 8.4 Hz), 7.91 d (1H, H_{arom}, J 8.6 Hz), 8.23 d (1H, H_{arom}, J = 8.6 Hz), 8.35 s (1H, H_{arom}), 8.76 d (1H, NH, J = 3.6 Hz). ^{13}C NMR spectrum, δ_C, ppm: 51.78 (CH_2); 56.22 (CH); 65.93 (CH_2); 77.53 (C^5); 117.66 (CN); 121.99, 123.87, 130.33, 133.59 (CH_{arom}); 139.16, 147.70 (C_{arom}); 166.07, 167.62 (C=O, C^6). Found, %: C 52.18; H 4.01; N 16.25. $C_{15}H_{14}N_4O_4S$. Calculated, %: C 52.02; H 4.07; N 16.18.

6-Morpholino-2-(4-nitrophenyl)-4-oxo-3,4-dihydro-2*H*-1,3-thiazine-5-carbonitrile (IVe). Yield 52%, mp 245–250°C. IR spectrum, ν, cm^{-1}: 3180 (NH), 2230 (CN), 1650 (C=O). ^1H NMR spectrum, δ, ppm: 3.69 m (8H, CH_2), 6.25 d (1H, CH, J = 3.6 Hz), 7.73 d (1H, H_{arom}, J = 8.7 Hz), 8.25 d (1H, H_{arom}, J = 8.7 Hz), 8.77 d (1H, NH, J = 3.6 Hz). ^{13}C NMR spectrum, δ_C, ppm: 51.65 (CH_2); 56.30 (CH); 65.87 (CH_2); 78.07 (C^5); 117.20 (CN); 123.43, 128.36 (CH_{arom}); 144.20, 147.46 (C_{arom}); 165.71, 167.37 (C=O, C^6). Found, %: C 51.89; H 4.05; N 16.10. $C_{15}H_{14}N_4O_4S$. Calculated, %: C 52.02; H 4.07; N 16.18.

2-(3,4-Dichlorophenyl)-6-morpholino-4-oxo-3,4-dihydro-2*H*-1,3-thiazine-5-carbonitrile (IVf). Yield 31%, mp 212–214°C. IR spectrum, ν, cm^{-1}: 3160 (NH), 2230 (CN), 1650 (C=O). ^1H NMR spectrum, δ, ppm: 3.68 m (8H, CH_2), 6.10 d (1H, CH, J = 3.3 Hz), 7.44 d (1H, H_{arom}, J = 8.0 Hz), 7.63 d (1H, H_{arom}, J = 8.0 Hz), 7.69 s (1H, H_{arom}), 8.63 d (1H, NH, J = 3.3 Hz). ^{13}C NMR spectrum, δ_C, ppm: 51.77 (CH_2); 56.12 (CH); 65.93 (CH_2); 77.38 (C^5); 117.70 (CN); 127.51, 129.29, 130.87 (CH_{arom}); 131.26, 131.70, 137.62 (C_{arom}); 166.09, 167.79 (C=O, C^6). Found, %: C 48.82; H 3.48; N 11.26. $C_{15}H_{13}Cl_2N_3O_2S$. Calculated, %: C 48.66; H 3.54; N 11.35.

4-Oxo-2-phenyl-6-(pyrrolidin-1-yl)-2-trifluoromethyl-3,4-dihydro-2*H*-1,3-thiazine-5-carbonitrile (Va). Thioamide **IIIa**, 0.77 g (5 mmol), was added to a solution of 1.17 g (5 mmol) of isocyanate **IIa** in 20 ml of anhydrous toluene, and a solution of 0.7 ml (5 mmol) of triethylamine in 10 ml of anhydrous toluene was then added over a period of 0.5 h under stirring. The mixture was stirred for 6 h, the precipitate was filtered off, the filtrate was evaporated, and the residue was recrystallized from ethanol. Yield 32%, mp 165–170°C. IR spectrum, ν, cm^{-1}: 3180 (NH), 2210 (CN), 1680 (C=O). ^1H NMR spectrum, δ, ppm: 1.94 m (4H, CH_2), 3.62 m (4H, CH_2), 7.46 m (5H, H_{arom}), 10.26 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 23.38, 25.42 (CH_2); 52.58 (C^2); 112.52, 118.14 (CN, C^5); 121.43 q (CH_3, J = 275.0 Hz); 128.23 (CH_{arom}); 128.53 (C_{arom}); 128.76, 130.89 (CH_{arom}); 138.30, 138.55 (C=O, C^6). ^{19}F NMR spectrum: δ_F –73.66 ppm. Found, %: C 54.22; H 4.03; N 11.80. $C_{16}H_{14}F_3N_3OS$. Calculated, %: C 54.38; H 3.99; N 11.89.

3-Aryl-2-cyano-4,4,4-trifluorobut-2-enethioamides VIa–VIe were synthesized from isocyanates **IIa–IIc** and thioamides **IIIa** and **IIIb** according to a similar procedure.

4,4,4-Trifluoro-3-(4-methylphenyl)-2-(pyrrolidin-1-ylcarbonothioyl)but-2-enenitrile (VIa). Yield 68%, mp 95–97°C. IR spectrum, ν, cm^{-1}: 2240 (CN), 1620 (C=S). ^1H NMR spectrum, δ, ppm: 1.66 m (2H, CH_2), 1.94 m (2H, CH_2), 2.35 s (3H, CH_3), 3.26 m (2H, CH_2), 3.67 m (2H, CH_2), 7.26 d (2H, H_{arom}, J = 8.1 Hz), 7.31 d (2H, H_{arom}, J = 8.1 Hz). ^{13}C NMR spectrum, δ_C, ppm: 20.90 (CH_3); 23.39, 25.42, 52.55, 52.57 (CH_2); 112.62 (CN); 117.74 (C^2); 121.49 q (CF_3, J = 275.0 Hz); 125.70 (C_{arom}); 128.12, 129.30 (CH_{arom}); 138.63 q (C^3, J = 31.2 Hz); 149.89 (C_{arom}); 182.99 (C=S). ^{19}F NMR spectrum: δ_F –60.90 ppm. Found, %: C 59.21; H 4.60; N 8.66. $C_{16}H_{15}F_3N_2S$. Calculated, %: C 59.25; H 4.66; N 8.64.

4,4,4-Trifluoro-3-(4-methoxyphenyl)-2-(pyrrolidin-1-ylcarbonothioyl)but-2-enenitrile (VIb). Yield 70%, mp 79–81°C. IR spectrum, ν, cm^{-1}: 2240 (CN), 1610 (C=S). ^1H NMR spectrum, δ, ppm: 1.66 m (2H, CH_2), 1.94 m (2H, CH_2), 3.22 m (2H, CH_2), 3.67 m (2H, CH_2), 3.80 s (3H, OCH_3), 6.99 d (2H, H_{arom}, J = 9.0 Hz), 7.37 d (2H, H_{arom}, J = 9.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 23.42, 25.41, 52.48, 52.61 (CH_2); 55.36 (OCH_3); 112.81 (CN); 114.28 (CH_{arom}); 117.13 (C^2); 120.49 (C_{arom}); 121.65 q (CF_3, J = 276.5 Hz); 130.04 (CH_{arom}); 138.34 q (C^3, J = 30.5 Hz); 160.98 (C_{arom}); 180.72 (C=S). ^{19}F NMR spectrum: δ_F –60.88 ppm. Found, %: C 56.35; H 4.36; N 8.20. $C_{16}H_{15}F_3N_2OS$. Calculated, %: C 56.46; H 4.44; N 8.23.

4,4,4-Trifluoro-2-(morpholin-4-ylcarbonothioyl)-3-phenylbut-2-enenitrile (VIc). Yield 53%, mp 165–170°C. IR spectrum, ν, cm^{-1}: 2230 (CN), 1620 (C=S). ^1H NMR spectrum, δ, ppm: 2.89 m (1H, CH_2), 3.22 m (1H, CH_2), 3.60 m (3H, CH_2), 3.78 m (3H, CH_2), 7.50 m (5H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm:

48.28, 51.94, 65.03, 65.38 (CH_2); 112.70 (CN); 118.09 (C^2); 121.32 q (CF_3, J = 277.5 Hz); 128.34 (CH_{arom}); 128.49 (C_{arom}); 128.82, 130.92 (CH_{arom}); 137.35 q (C^3, J = 30.0 Hz); 149.89 (C_{arom}); 182.99 (C=S). ^{19}F NMR spectrum: δ_F –60.89 ppm. Found, %: C 55.15; H 4.06; N 8.63. $C_{15}H_{13}F_3N_2OS$. Calculated, %: C 55.21; H 4.02; N 8.58.

4,4,4-Trifluoro-3-(4-methylphenyl)-2-(morpholin-4-ylcarbonothioyl)but-2-enenitrile (VId). Yield 65%, mp 99–101°C. IR spectrum, ν, cm^{-1}: 2240 (CN), 1620 (C=S). ^1H NMR spectrum, δ, ppm: 2.38 s (3H, CH_3), 2.96 m (1H, CH_2), 3.24 m (1H, CH_2), 3.55 m (2H, CH_2), 3.64 m (1H, CH_2), 3.80 m (1H, CH_2), 3.92 m (2H, CH_2), 7.31 s (4H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 20.81 (CH_3); 48.20, 51.85, 64.97, 65.32 (CH_2); 112.69 (CN); 116.41 (C^2); 121.31 q (CF_3, J = 275.0 Hz); 125.58 (C_{arom}); 128.14, 129.23 (CH_{arom}); 137.56 q (C^3, J = 31.2 Hz); 140.88 (C_{arom}); 183.26 (C=S). ^{19}F NMR spectrum: δ_F –60.90 ppm. Found, %: C 56.56; H 4.38; N 8.21. $C_{16}H_{15}F_3N_2OS$. Calculated, %: C 56.46; H 4.44; N 8.23.

4,4,4-Trifluoro-3-(4-methoxyphenyl)-2-(morpholin-4-ylcarbonothioyl)but-2-enenitrile (VIe). Yield 67%, mp 114–116°C. IR spectrum, ν, cm^{-1}: 2240 (CN), 1610 (C=S). ^1H NMR spectrum, δ, ppm: 2.87 m (1H, CH_2), 3.25 m (1H, CH_2), 3.51 m (2H, CH_2), 3.60 m (1H, CH_2), 3.73 m (1H, CH_2), 3.81 s (3H, OCH_3), 3.93 m (2H, CH_2), 7.02 d (2H, H_{arom}, J = 8.7 Hz), 7.37 d (2H, H_{arom}, J = 8.7 Hz). ^{13}C NMR spectrum, δ_C, ppm: 48.23, 51.82, 55.35 (CH_2); 64.03 (OCH_3); 112.88 (CN); 114.28 (CH_{arom}); 115.85 (C^2); 120.42 (C_{arom}); 121.38 q (CF_3, J = 275.0 Hz); 130.04 (CH_{arom}); 137.44 q (C^3, J = 31.2 Hz); 161.03 (C_{arom}); 183.55 (C=S). ^{19}F NMR spectrum: δ_F –60.91 ppm. Found, %: C 53.79; H 4.33; N 7.95. $C_{16}H_{15}F_3N_2O_2S$. Calculated, %: C 53.93; H 4.24; N 7.86.

6-Amino-4-oxo-2-trifluoromethyl-2-(4-trifluoromethylphenyl)-3,4-dihydro-2*H*-1,3-thiazine-5-carbonitriles Vb and Vc and 2-cyano-4,4,4-trifluoro-3-(4-trifluoromethylphenyl)but-2-enethioamides VIf and VIg (*general procedure*). Thioamide **IIIa** or **IIIb**, 5 mmol, was added to a solution of 1.52 g (5 mmol) of isocyanate **IId** in 20 ml of anhydrous toluene, and a solution of 0.7 ml (5 mmol) of triethylamine in 10 ml of anhydrous toluene was then added over a period of 0.5 h under stirring. The mixture was stirred for 6 h, and the precipitate was filtered off, washed with hexane and water, dried, and recrystallized from ethanol. We thus isolated compounds **Vb** and **Vc**. The filtrate was evaporated, and the residue was recrystallized from ethanol to obtain compounds **VIf** and **VIg**.

4-Oxo-6-(pyrrolidin-1-yl)-2-trifluoromethyl-2-(4-trifluoromethylphenyl)-3,4-dihydro-2*H*-1,3-thiazine-5-carbonitrile (Vb). Yield 18%, mp 242–244°C. IR spectrum, ν, cm^{-1}: 3160 (NH), 2230 (CN), 1660 (C=O). ^1H NMR spectrum, δ, ppm: 1.93 s (4H, CH_2), 3.73 s (4H, CH_2), 7.94 s (4H, H_{arom}), 9.72 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 25.01 (CH_2); 52.74 (CH_2); 69.52 q (C^2, J = 30.0 Hz); 73.05 (C^5); 117.63 (CN); 123.60 q (CF_3, J = 287.5 Hz); 123.66 q (CF_3, J = 271.2 Hz); 125.99 (CH_{arom}); 128.53 (CH_{arom}); 130.54 q (C_{arom}, J = 32.5 Hz); 138.66 (C_{arom}); 158.67, 165.27 (C^6, C=O). ^{19}F NMR spectrum, δ_F, ppm: –73.09, –62.40. Found, %: C 48.33; H 3.08; N 10.02. $C_{17}H_{13}F_6N_3OS$. Calculated, %: C 48.46; H 3.11; N 9.97.

6-Morpholino-4-oxo-2-trifluoromethyl-2-(4-trifluoromethylphenyl)-3,4-dihydro-2*H*-1,3-thiazine-5-carbonitrile (Vc). Yield 15%, mp 191–193°C. IR spectrum, ν, cm^{-1}: 3170 (NH), 2230 (CN), 1670 (C=O). ^1H NMR spectrum, δ, ppm: 3.67 m (4H, CH_2), 3.77 m (4H, CH_2), 7.86 d (2H, H_{arom}, J = 8.7 Hz), 7.90 d (2H, H_{arom}, J = 8.7 Hz), 9.97 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 51.94, 65.88 (CH_2); 69.42 q (C^2, J = 31.3 Hz); 77.26 (C^5); 116.58 (CN); 123.39 q (CF_3, J = 283.7 Hz); 123.64 q (CF_3, J = 270 Hz); 126.03, 128.57 (CH_{arom}); 130.70 q (C_{arom}, J = 31.2 Hz); 138.46 (C_{arom}); 163.18, 165.05 (C^6, C=O). ^{19}F NMR spectrum, δ_F, ppm: –73.07, –62.38. Found, %: C 46.77; H 2.94; N 9.58. $C_{17}H_{13}F_6N_3O_2S$. Calculated, %: C 46.69; H 3.00; N 9.61.

4,4,4-Trifluoro-2-(pyrrolidin-1-ylcarbonothioyl)-3-(4-trifluoromethylphenyl)but-2-enenitrile (VIf). Yield 44%, mp 134–136°C. IR spectrum, ν, cm^{-1}: 2240 (CN), 1620 (C=S). ^1H NMR spectrum, δ, ppm: 1.70 m (2H, CH_2), 1.93 m (2H, CH_2), 3.25 m (1H, CH_2), 3.59 m (2H, CH_2), 3.74 m (1H, CH_2), 3.93 m (2H, CH_2), 7.68 d (2H, H_{arom}, J = 8.1 Hz), 7.90 d (2H, H_{arom}, J = 8.1 Hz). ^{13}C NMR spectrum, δ_C, ppm: 23.36, 25.48, 52.66, 52.79 (CH_2); 112.03 (CN); 119.25 (C^2); 121.12 q (CF_3, J = 273.7 Hz); 123.50 q (CF_3, J = 271.2 Hz); 125.68, 129.53 (CH_{arom}); 130.85 q (C_{arom}, J = 32.5 Hz); 132.57 (C_{arom}); 137.64 q (C^3, J = 31.2 Hz); 179.43 (C=S). ^{19}F NMR spectrum, δ_F, ppm: –62.94, –60.93. Found, %: C 50.73; H 3.21; N 7.34. $C_{16}H_{12}F_6N_2S$. Calculated, %: C 50.79; H 3.20; N 7.40.

4,4,4-Trifluoro-2-(morpholin-4-ylcarbonothioyl)-3-(4-trifluoromethylphenyl)but-2-enenitrile (VIg). Yield 49%, mp 115–117°C. IR spectrum, ν, cm^{-1}: 2230 (CN), 1620 (C=S). ^1H NMR spectrum, δ, ppm: 3.22 m (2H, CH_2), 3.63 m (3H, CH_2), 3.85 m (3H, CH_2), 7.63 d (2H, H_{arom}, J = 8.4 Hz), 7.90 d (2H, H_{arom}, J =

8.4 Hz). ^{13}C NMR spectrum, δ_C, ppm: 48.28, 52.00, 65.12, 65.51 (CH_2); 112.23 (CN); 117.72 (C^2); 121.01 q (CF_3, J = 275.0 Hz); 123.59 q (CF_3, J = 272.5 Hz); 125.78, 129.61 (CH_{arom}); 130.94 q (C_{arom}, J = 32.0 Hz); 132.46 (C_{arom}); 136.53 q (C^2, J = 31.4 Hz); 182.38 (C=S). ^{19}F NMR spectrum, δ_F, ppm: –62.92, –60.94. Found, %: C 48.80; H 3.01; N 7.13. $C_{16}H_{12}F_6N_2OS$. Calculated, %: C 48.73; H 3.07; N 7.10.

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