

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-2H-1,3-thiazine-5-carbonitriles

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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-2H-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.

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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.

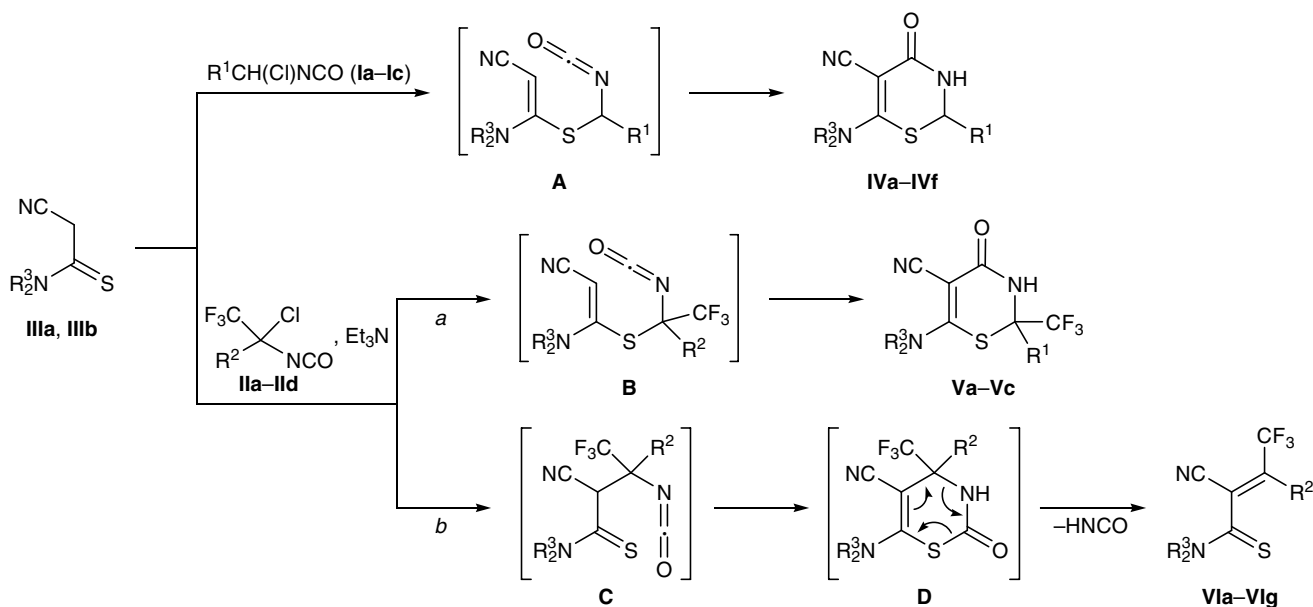
Taking into account different regioselectivities in the reactions of 1-chloroalkyl isocyanates with aminocrotonates [3] and β -diketones [4], as starting compounds we used both α -chlorobenzyl isocyanates **Ia–Ic** and 2,2,2-trifluoro-1-chloroethyl isocyanates **IIa–IIId**.

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-2H-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** ($R^1 = \text{Ph}$, 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-2H-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-2H-1,3-thiazin-4-ones **IVa–IVf** was proved by IR and ^1H and ^{13}C NMR spectroscopy. The IR spectra of **IVa–IVf** contained

* For communication VI, see [1].

Scheme 1.



I, R¹ = 3-O₂NC₆H₄ (**a**), 4-O₂NC₆H₄ (**b**), 3,4-Cl₂C₆H₃ (**c**); **II**, R² = Ph (**a**), 4-MeC₆H₄ (**b**), 4-MeOC₆H₄ (**c**), 4-F₃CC₆H₄ (**d**); **III**, R³R³ = (CH₂)₄ (**a**), (CH₂)₂O(CH₂)₂ (**b**); **IV**, R³R³ = (CH₂)₄, R¹ = 3-O₂NC₆H₄ (**a**), 4-O₂NC₆H₄ (**b**), 3,4-Cl₂C₆H₃ (**c**); R³R³ = (CH₂)₂O(CH₂)₂, R¹ = 3-O₂NC₆H₄ (**d**), 4-O₂NC₆H₄ (**e**), 3,4-Cl₂C₆H₃ (**f**); **V**, R³R³ = (CH₂)₄, R² = Ph (**a**), 4-F₃CC₆H₄ (**b**); R³R³ = (CH₂)₂O(CH₂)₂, R² = 4-F₃CC₆H₄ (**c**); **VI**, R³R³ = (CH₂)₄, R² = 4-MeC₆H₄ (**a**), 4-MeOC₆H₄ (**b**), 4-F₃CC₆H₄ (**c**); R³R³ = (CH₂)₂O(CH₂)₂, R² = Ph (**d**), 4-MeC₆H₄ (**e**), 4-MeOC₆H₄ (**f**), 4-F₃CC₆H₄ (**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 ¹³C NMR spectra of these compounds, the C² 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(R¹)NR² 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 ¹⁹F 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-ene-thioamides **VIIb–VIIe** and cyanuric acid, the latter being formed as a result of trimerization of isocyanic acid. In the reactions with the most electrophilic isocyanate **IIId** 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 **VIIb–VIIe** 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 ¹³C NMR spectra, quartets from the CF₃ groups (δ_C 123.30–123.39, 123.61–123.64 ppm) and C² (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 ¹⁹F NMR spectra at δ_F –73.66 to –73.06 ppm. Comparison of the ¹³C and ¹⁹F chemical shifts in the spectra of **V** and 1,3,5-thiadiazines [8] provides an additional support to the presence of an SCH(R¹)NR² 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 ¹³C NMR spectra of **VI**, signals from carbon atoms in the trifluoromethyl groups and C³ 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 ¹⁹F 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, ¹³C, and ¹⁹F 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, ¹³C) and CCl₃F (¹⁹F) as internal standards. 1-Aryl-1-chloro-2,2,2-trifluoroethyl isocyanates **IIa–IIId** [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-2H-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-2H-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, CH₂), 3.67 s (4H, CH₂), 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). ¹³C NMR spectrum, δ_C , ppm: 24.96 (CH₂); 52.40 (CH₂); 56.32 (CH); 73.81 (C⁵); 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, C⁶). Found, %: C 54.31; H 4.32; N 16.83. C₁₅H₁₄N₄O₃S. Calculated, %: C 54.54; H 4.27; N 16.96.

2-(4-Nitrophenyl)-4-oxo-6-(pyrrolidin-1-yl)-3,4-dihydro-2H-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, CH₂), 3.66 s (4H, CH₂), 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). ¹³C NMR spectrum, δ_C , ppm: 25.03 (CH₂); 52.46 (CH₂); 56.35 (CH); 73.85 (C⁵); 118.65 (CN); 123.67, 128.42 (CH_{arom}); 145.21, 147.49 (C_{arom}); 162.67, 166.32 (C=O, C⁶). Found, %: C 54.66; H 4.24; N 17.08. C₁₅H₁₄N₄O₃S. Calculated, %: C 54.54; H 4.27; N 16.96.

2-(3,4-Dichlorophenyl)-4-oxo-6-(pyrrolidin-1-yl)-3,4-dihydro-2H-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, CH₂), 3.66 s (4H, CH₂), 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). ¹³C NMR spectrum, δ_C , ppm: 25.02

(CH₂); 52.46 (CH₂); 56.27 (CH); 73.68 (C⁵); 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, C⁶). Found, %: C 50.70; H 3.68; N 11.77. C₁₅H₁₃Cl₂N₃OS. Calculated, %: C 50.86; H 3.70; N 11.86.

6-Morpholino-2-(3-nitrophenyl)-4-oxo-3,4-dihydro-2H-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, CH₂), 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). ¹³C NMR spectrum, δ _C, ppm: 51.78 (CH₂); 56.22 (CH); 65.93 (CH₂); 77.53 (C⁵); 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, C⁶). Found, %: C 52.18; H 4.01; N 16.25. C₁₅H₁₄N₄O₄S. Calculated, %: C 52.02; H 4.07; N 16.18.

6-Morpholino-2-(4-nitrophenyl)-4-oxo-3,4-dihydro-2H-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, CH₂), 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). ¹³C NMR spectrum, δ _C, ppm: 51.65 (CH₂); 56.30 (CH); 65.87 (CH₂); 78.07 (C⁵); 117.20 (CN); 123.43, 128.36 (CH_{arom}); 144.20, 147.46 (C_{arom}); 165.71, 167.37 (C=O, C⁶). Found, %: C 51.89; H 4.05; N 16.10. C₁₅H₁₄N₄O₄S. Calculated, %: C 52.02; H 4.07; N 16.18.

2-(3,4-Dichlorophenyl)-6-morpholino-4-oxo-3,4-dihydro-2H-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, CH₂), 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). ¹³C NMR spectrum, δ _C, ppm: 51.77 (CH₂); 56.12 (CH); 65.93 (CH₂); 77.38 (C⁵); 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, C⁶). Found, %: C 48.82; H 3.48; N 11.26. C₁₅H₁₃Cl₂N₃O₂S. Calculated, %: C 48.66; H 3.54; N 11.35.

4-Oxo-2-phenyl-6-(pyrrolidin-1-yl)-2-trifluoromethyl-3,4-dihydro-2H-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, CH₂), 3.62 m (4H, CH₂), 7.46 m (5H, H_{arom}), 10.26 s (1H, NH). ¹³C NMR spectrum, δ _C, ppm: 23.38, 25.42 (CH₂); 52.58 (C²); 112.52, 118.14 (CN, C⁵); 121.43 q (CH₃, J = 275.0 Hz); 128.23 (CH_{arom}); 128.53 (C_{arom}); 128.76, 130.89 (CH_{arom}); 138.30, 138.55 (C=O, C⁶). ¹⁹F NMR spectrum: δ _F –73.66 ppm. Found, %: C 54.22; H 4.03; N 11.80. C₁₆H₁₄F₃N₃OS. 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, CH₂), 1.94 m (2H, CH₂), 2.35 s (3H, CH₃), 3.26 m (2H, CH₂), 3.67 m (2H, CH₂), 7.26 d (2H, H_{arom}, J = 8.1 Hz), 7.31 d (2H, H_{arom}, J = 8.1 Hz). ¹³C NMR spectrum, δ _C, ppm: 20.90 (CH₃); 23.39, 25.42, 52.55, 52.57 (CH₂); 112.62 (CN); 117.74 (C²); 121.49 q (CF₃, J = 275.0 Hz); 125.70 (C_{arom}); 128.12, 129.30 (CH_{arom}); 138.63 q (C³, J = 31.2 Hz); 149.89 (C_{arom}); 182.99 (C=S). ¹⁹F NMR spectrum: δ _F –60.90 ppm. Found, %: C 59.21; H 4.60; N 8.66. C₁₆H₁₅F₃N₂S. 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, CH₂), 1.94 m (2H, CH₂), 3.22 m (2H, CH₂), 3.67 m (2H, CH₂), 3.80 s (3H, OCH₃), 6.99 d (2H, H_{arom}, J = 9.0 Hz), 7.37 d (2H, H_{arom}, J = 9.0 Hz). ¹³C NMR spectrum, δ _C, ppm: 23.42, 25.41, 52.48, 52.61 (CH₂); 55.36 (OCH₃); 112.81 (CN); 114.28 (CH_{arom}); 117.13 (C²); 120.49 (C_{arom}); 121.65 q (CF₃, J = 276.5 Hz); 130.04 (CH_{arom}); 138.34 q (C³, J = 30.5 Hz); 160.98 (C_{arom}); 180.72 (C=S). ¹⁹F NMR spectrum: δ _F –60.88 ppm. Found, %: C 56.35; H 4.36; N 8.20. C₁₆H₁₅F₃N₂OS. 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, CH₂), 3.22 m (1H, CH₂), 3.60 m (3H, CH₂), 3.78 m (3H, CH₂), 7.50 m (5H, H_{arom}). ¹³C NMR spectrum, δ _C, ppm:

48.28, 51.94, 65.03, 65.38 (CH₂); 112.70 (CN); 118.09 (C²); 121.32 q (CF₃, *J* = 277.5 Hz); 128.34 (CH_{arom}); 128.49 (C_{arom}); 128.82, 130.92 (CH_{arom}); 137.35 q (C³, *J* = 30.0 Hz); 149.89 (C_{arom}); 182.99 (C=S). ¹⁹F NMR spectrum: δ_F –60.89 ppm. Found, %: C 55.15; H 4.06; N 8.63. C₁₅H₁₃F₃N₂OS. Calculated, %: C 55.21; H 4.02; N 8.58.

4,4,4-Trifluoro-3-(4-methylphenyl)-2-(morpholin-4-ylcarbonothioyl)but-2-enenitrile (VIId). 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, CH₃), 2.96 m (1H, CH₂), 3.24 m (1H, CH₂), 3.55 m (2H, CH₂), 3.64 m (1H, CH₂), 3.80 m (1H, CH₂), 3.92 m (2H, CH₂), 7.31 s (4H, H_{arom}). ¹³C NMR spectrum, δ_C, ppm: 20.81 (CH₃); 48.20, 51.85, 64.97, 65.32 (CH₂); 112.69 (CN); 116.41 (C²); 121.31 q (CF₃, *J* = 275.0 Hz); 125.58 (C_{arom}); 128.14, 129.23 (CH_{arom}); 137.56 q (C³, *J* = 31.2 Hz); 140.88 (C_{arom}); 183.26 (C=S). ¹⁹F NMR spectrum: δ_F –60.90 ppm. Found, %: C 56.56; H 4.38; N 8.21. C₁₆H₁₅F₃N₂OS. 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, CH₂), 3.25 m (1H, CH₂), 3.51 m (2H, CH₂), 3.60 m (1H, CH₂), 3.73 m (1H, CH₂), 3.81 s (3H, OCH₃), 3.93 m (2H, CH₂), 7.02 d (2H, H_{arom}, *J* = 8.7 Hz), 7.37 d (2H, H_{arom}, *J* = 8.7 Hz). ¹³C NMR spectrum, δ_C, ppm: 48.23, 51.82, 55.35 (CH₂); 64.03 (OCH₃); 112.88 (CN); 114.28 (CH_{arom}); 115.85 (C²); 120.42 (C_{arom}); 121.38 q (CF₃, *J* = 275.0 Hz); 130.04 (CH_{arom}); 137.44 q (C³, *J* = 31.2 Hz); 161.03 (C_{arom}); 183.55 (C=S). ¹⁹F NMR spectrum: δ_F –60.91 ppm. Found, %: C 53.79; H 4.33; N 7.95. C₁₆H₁₅F₃N₂O₂S. Calculated, %: C 53.93; H 4.24; N 7.86.

6-Amino-4-oxo-2-trifluoromethyl-2-(4-trifluoromethylphenyl)-3,4-dihydro-2H-1,3-thiazine-5-carbonitriles Vb and Vc and 2-cyano-4,4,4-trifluoro-3-(4-trifluoromethylphenyl)but-2-enethioamides VIg and VIg (general procedure). Thioamide IIIa or IIIb, 5 mmol, was added to a solution of 1.52 g (5 mmol) of isocyanate IIId 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 VIg and VIg.

4-Oxo-6-(pyrrolidin-1-yl)-2-trifluoromethyl-2-(4-trifluoromethylphenyl)-3,4-dihydro-2H-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, CH₂), 3.73 s (4H, CH₂), 7.94 s (4H, H_{arom}), 9.72 s (1H, NH). ¹³C NMR spectrum, δ_C, ppm: 25.01 (CH₂); 52.74 (CH₂); 69.52 q (C², *J* = 30.0 Hz); 73.05 (C⁵); 117.63 (CN); 123.60 q (CF₃, *J* = 287.5 Hz); 123.66 q (CF₃, *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 (C⁶, C=O). ¹⁹F NMR spectrum, δ_F, ppm: –73.09, –62.40. Found, %: C 48.33; H 3.08; N 10.02. C₁₇H₁₃F₆N₃OS. Calculated, %: C 48.46; H 3.11; N 9.97.

6-Morpholino-4-oxo-2-trifluoromethyl-2-(4-trifluoromethylphenyl)-3,4-dihydro-2H-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, CH₂), 3.77 m (4H, CH₂), 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). ¹³C NMR spectrum, δ_C, ppm: 51.94, 65.88 (CH₂); 69.42 q (C², *J* = 31.3 Hz); 77.26 (C⁵); 116.58 (CN); 123.39 q (CF₃, *J* = 283.7 Hz); 123.64 q (CF₃, *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 (C⁶, C=O). ¹⁹F NMR spectrum, δ_F, ppm: –73.07, –62.38. Found, %: C 46.77; H 2.94; N 9.58. C₁₇H₁₃F₆N₃O₂S. Calculated, %: C 46.69; H 3.00; N 9.61.

4,4,4-Trifluoro-2-(pyrrolidin-1-ylcarbonothioyl)-3-(4-trifluoromethylphenyl)but-2-enenitrile (VIg). 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, CH₂), 1.93 m (2H, CH₂), 3.25 m (1H, CH₂), 3.59 m (2H, CH₂), 3.74 m (1H, CH₂), 3.93 m (2H, CH₂), 7.68 d (2H, H_{arom}, *J* = 8.1 Hz), 7.90 d (2H, H_{arom}, *J* = 8.1 Hz). ¹³C NMR spectrum, δ_C, ppm: 23.36, 25.48, 52.66, 52.79 (CH₂); 112.03 (CN); 119.25 (C²); 121.12 q (CF₃, *J* = 273.7 Hz); 123.50 q (CF₃, *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 (C³, *J* = 31.2 Hz); 179.43 (C=S). ¹⁹F NMR spectrum, δ_F, ppm: –62.94, –60.93. Found, %: C 50.73; H 3.21; N 7.34. C₁₆H₁₂F₆N₂S. 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, CH₂), 3.63 m (3H, CH₂), 3.85 m (3H, CH₂), 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. $\text{C}_{16}\text{H}_{12}\text{F}_6\text{N}_2\text{OS}$. Calculated, %: C 48.73; H 3.07; N 7.10.

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