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Recyclization of morpholinium 3,4-*trans*-4-aryl-5-cyano-2-hydroxy-3-nitro-1,2,3,4-tetrahydropyridine-6-thiolates to 2-acylamino-5-amino-4-aryl-3-cyanothiophenes. Molecular and crystal structures of 5-amino-3-cyano-2-(4-methylbenzamido)-4-(2-thienyl)-thiophene

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Abstract—2-Acylamino-5-amino-4-aryl-3-cyanothiophenes were synthesized by the reaction of arylidenecyanothioacetamides with α-nitroketones or by the three-component reaction of aromatic aldehydes, α-nitroketones, and cyanothioacetamide, or the reaction of 3-(4-chlorophenyl)-2-nitro-1-phenyl-2-propen-1-one with cyanothioacetamide in the presence of morpholine. These diaminothiophenes are formed via the recyclization stage of the primarily formed tetrahydropyridines, morpholinium 3,4-*trans*-4-aryl-5-cyano-2-hydroxy-3-nitro-1,2,3,4-tetrahydropyridine-6-thiolates.

1. Introduction

α-Nitrocarbonyl compounds are known as reagents participating in syntheses of various heterocycles.[1–9] However, reactions of α-nitrocarbonyl compounds with α,β-unsaturated thioamides have not been studied up to presently. It is known that the reactions of α,β-unsaturated thioamides with α-methylenecarbonyl compounds and 1,3-dicarbonyl compounds result in the formation of 4-aryl-3-cyanopyridine-2(1*H*)-thiones and 5-carbonyl-substituted 4-aryl-3-cyano-2(1*H*)-dihydropyridinethiones and 1,2,3,4-tetrahydropyridine-6-thiolates.[10–14]

2. Results and discussion

We studied the possibility of the formation of nitro-substituted pyridines from α-nitrocarbonyl compounds and α,β-unsaturated thioamides. It is established that the three-component condensation of benzaldehyde (**1**), cyanothioacetamide (**2**), and α-nitroacetophenone (**3a**) in ethanol at 40–55°C in the presence of an equimolar amount of morpholine affords morpholinium 3,4-*trans*-5-cyano-2,4-diphenyl-2-hydroxy-3-nitro-1,2,3,4-tetrahydropyridine-6-thiolate (**4a**). When the reaction is performed in absolute ethanol or methanol at 30–35°C, the noncyclic Michael adducts 1-amino-2-cyano-3,5-diphenyl-4-nitro-5-oxo-1,2-pentene-1-thiolates (**5a**, **b**) was isolated in 70 and 75% yield.

The treatment of compounds **4a** and **5** or their mixture with concentrated hydrochloric acid at 20°C proceeds selectively to form 3,4-*trans*-4,5-*trans*-5-cyano-2,4-diphenyl-2-hydroxy-3-nitrohexahydropyridine-6(1*H*)-thione (**6**). Note that there is little data on hexahydropyridinethiones because compounds of this class are unstable. Therefore, the preparation of thione **6** containing several reactive functional groups is of undoubted interest (Scheme 1).

When α-nitroacetone **3b** is used in this reaction, morpholinium 3,4-*trans*-5-cyano-2-hydroxy-3-methyl-3-nitro-4-phenyl-1,2,3,4-tetrahydropyridine-6-thiolate (**4b**) is selectively formed. In this case, we failed to isolate the corresponding noncyclic Michael adduct and hexahydropyridine-6(1*H*)-thione.

It is most likely that in solutions the Michael adduct **5** and its cyclic form **4** are in equilibrium, and the equilibrium is shifted toward acyclic adduct **5** with decreasing temperature and toward cyclic form **4** with increasing temperature, which allowed us to obtain purposefully either compound **4a** or compound **5** by the variation of the temperature regime of the reaction. The presence of this ring-chain tautomerism is favored by the fact that thiolate **4a** is transformed into isomer **5** 30–40 min after the beginning of recording NMR spectra in DMSO-d_6 solution.

When the reaction time of the three-component condensation

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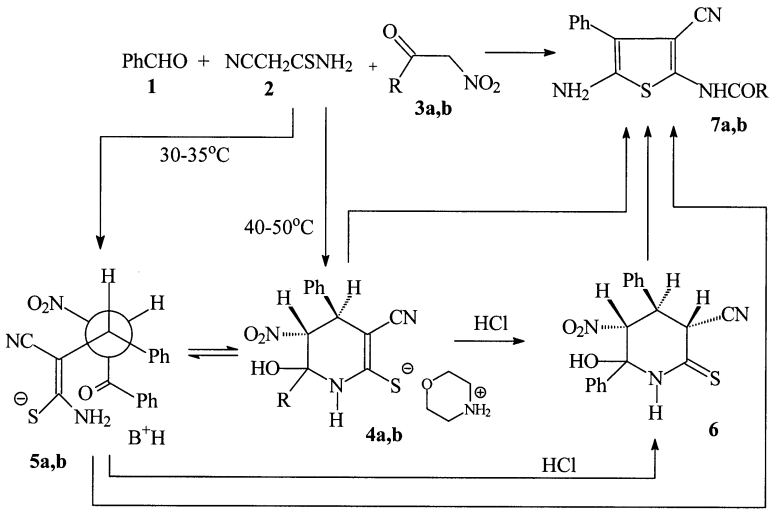


Scheme 1. **3**, **4**, **7** R=C_6H_5 (a), CH_3 (b). **5a** B=morpholine, **5b** B=*N*,*N*-tetramethylethylenediamine.

of α-nitroketones **3a**, **b**, benzaldehyde **1**, and cyanothioacetamide **2** was increased to 40–60 min or the reaction temperature increased to 58–60°C, the process occurred to completion and 2-acylamino-5-amino-4-aryl-3-cyanothiophenes (**7a**) or (**7b**), respectively, were obtained as the reaction products. On heating in ethanol in the presence of a base, each of the obtained reaction intermediates **4a**, **b**, **5a**, **b** and **6** is also irreversibly transformed into the corresponding thiophene **7a** or **7b**.

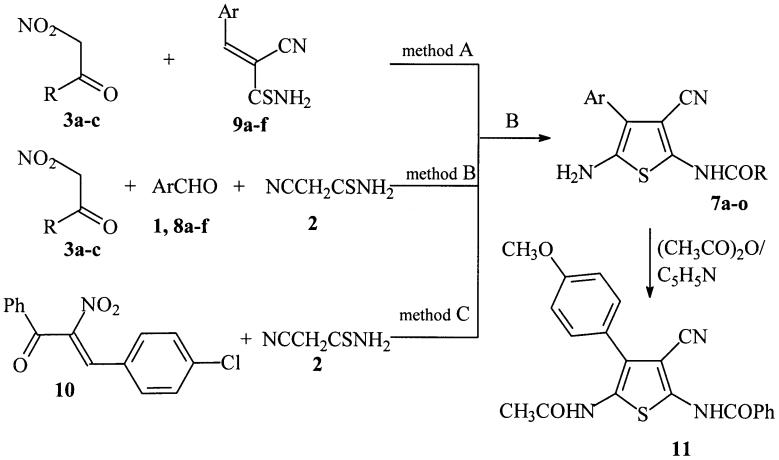
This rather unexpected result forced us to study the reaction in detail. We found that short heating in ethanol in the presence of organic bases (morpholine, triethylamine, *N*,*N*-tetramethylethylenediamine) of α-nitroketones **3a**–**c**, various aromatic aldehydes (**8**, and cyanothioacetamide **2** affords the corresponding 2-acylamino-5-amino-4-aryl-3-cyanothiophenes **7**. The same compounds **7** were prepared by the reaction of α-nitroketones **3a**–**c** and unsaturated thioamides (**9**). The reaction of ketonitrostyrene (**10**) with thioamide **2** gave the corresponding aminothiophene **7h**.

Note that although the class of 2,5-diaminothiophenes is described in literature, methods for preparation of similar compounds are rather restricted and labor-consuming.[15] Therefore, the synthesis of 2-acylamino-5-amino-4-aryl-3-cyanothiophenes **7** is of independent synthetic interest. Compounds **7** are readily acylated at the free amino group to form 2,5-diacylaminothiophenes, which we showed for the synthesis of thiophene (**11**).

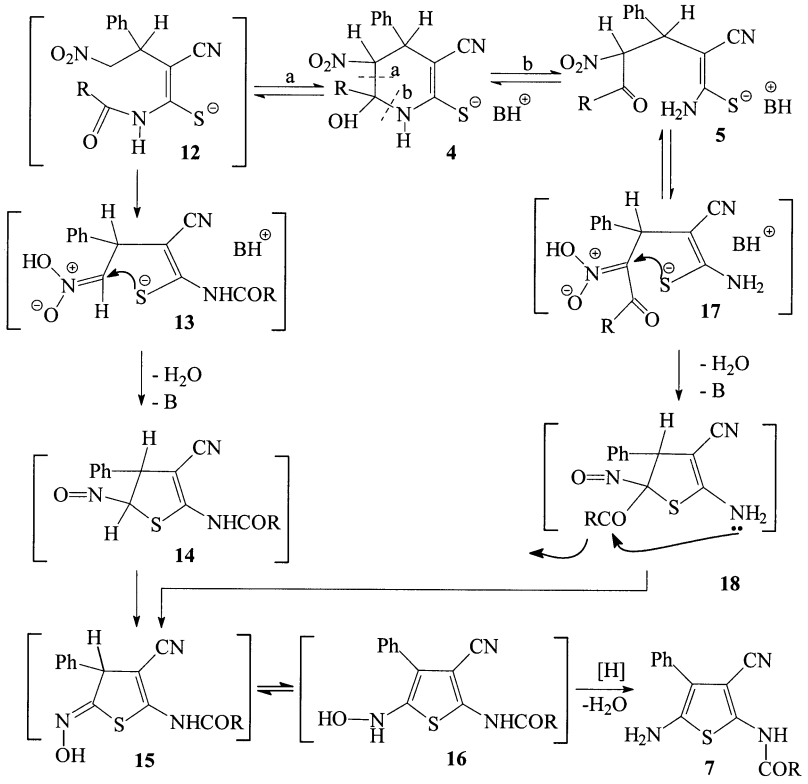
The obtained results allowed us to discuss the discovery of the recyclization of 3,4-*trans*-5-cyano-2-hydroxy-3-nitro-4-phenyl-1,2,3,4-tetrahydropyridine-6-thiolates **4** to 2-acylamino-5-amino-4-aryl-3-cyanothiophenes **7** (Scheme 2).

The most probable reaction mechanism includes the primary formation of the Michael adduct **5**, cyclization of acyclic adduct **5** to form tetrahydropyridinethiolate **4**, and subsequent recyclization of **4** to thiophene **7** with the simultaneous transformation of the nitro group into the amino group (pathway a) (Scheme 3).

Recyclization occurs with the cycle opening of tetrahydropyridinethiolate **7** at the C_5–C_6 bond (**12**) and closure of the new cycle due to the attack of thiolate sulfur to the carbon



Scheme 2. B=morpholine. R=C_6H_5 (**3a**; **7a**, **c**–**h**), 4-CH_3–C_6H_4 (**3c**; **7i**–**k**), CH_3 (**3b**; **7b**, **l**–**o**). Ar=C_6H_5 (**1**; **7a**, **b**, **i**), 4-Cl–C_6H_4 (**7h**, **l**; **8a**; **9a**), 4-CH_3O–C_6H_4 (**7c**, **j**, **m**; **8b**; **9b**), 2-NO_2–C_6H_4 (**7d**, **n**; **8c**; **9c**), 3-Br–C_6H_4 (**7e**; **8d**; **9d**), 2-C_4H_3S (**7f**, **k**; **8e**; **9e**), 3-C_5H_4N (**7g**, **o**; **8f**; **9f**).



Scheme 3.

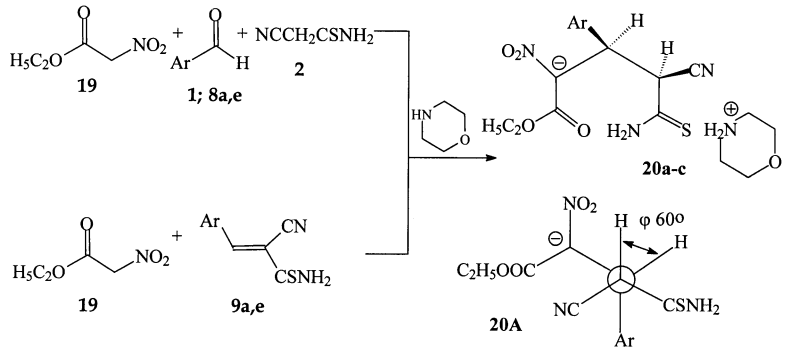
atom of at the double bond of the aci form of the nitro group (**13**). Our mechanism of pyridine cycle recyclization to diaminothiophenes **7** agrees well with published data on the retro-Henry reaction.[16] When the thiophene cycle is formed, the nitro groups is simultaneously transformed. The ability of the nitro group to such an easy and fast reduction is a distinctive feature of this reaction. Since the yield of the reaction products is only 30–35% when equimolar amounts of reactants are used, it is reasonable to assume that the thioamide group of compounds **2** or **9** acts as a reducing agent at one of the stages of the process. The use excess of thioamide or the addition of 0.5 equiv. of sodium thiosulfate allowed us to almost double the yield of thiophenes **7**.

Other reaction schemes cannot be excluded. As an alternative scheme, we can propose the scheme (pathway b) in which the transformation of Michael adduct **5** proceeds through the closure of the thiophene cycle (**17**) with the simultaneous rearrangement of a sufficiently stable acyl group (**18**).

Another confirmation of the reaction mechanism proposed by us is the fact that it is impossible to obtain similar thiophenes when ethyl nitroacetate (**19**) is used instead of nitroketones.

The three-component condensation of the corresponding aromatic aldehyde **1**, compound **8a**, **e**, cyanothioacetamide **2**, and ester **19** affords the Michael adducts (**20**) in the individual state with negative charge localization on the $C_{(1)}$ carbon atom at the nitro group. Morpholinium 2-aryl-3-cyano-1-ethoxycarbonyl-1-nitro-3-thiocarbamoylpropyl-1-ates **20b**, **c** were also prepared by the reaction of arylidenecyanothioacetamides **9a**, **e** with ester **19**. The salts of Michael adducts **20** are rather stable. On boiling salts **20** in ethanol we failed to transform them (Scheme 4). Probably, this inertness is related, on the one hand, to the specific negative charge localization and, on the other hand, unfavorable steric arrangement of the $CSNH_2$ and $COOC_2H_5$ reaction centers, for example, antiperiplanar (**20A**). This is confirmed, to a certain extent, by the data of IR and NMR spectroscopy.

The structure of all obtained compounds was confirmed by the data of physicochemical studies. As a whole, the spectral parameters of compounds **5a**, **b** indicate the acyclic structure of these compounds. In the IR spectra of these compounds, the frequency of vibrations of the nitrile group is much decreased (to 2162–2185 cm^{-1}) with a simultaneous increase in its intensity compared to the spectra of 3-cyanopyridine-2(1*H*)-thiones, which can be explained by an increase in the degree of conjugation in the NC═C(R)═C(NH_2)S– fragment due to salt formation.[13,14,17] The absorption bands at 1591 and 3064–3353 cm^{-1} indicate that compounds **5a**, **b** in the solid state (pellets with KBr) contain the NH^+ and NH_2 groups and can be in the keto-enol equilibrium. This is indicated by the IR spectrum of thiolate **5b** recorded in a THF solution. Probably, in a solution the equilibrium is shifted toward ketone[18] (the absorption band of the C═O group appears at 1776 cm^{-1}) with simultaneous charge transfer to the NO_2 group (an increase in the frequency of vibrations of the CN group to 2212 cm^{-1}). The absorption bands of the NH and NH_2 groups at 3190 and 3480 cm^{-1} remain broadened, which is characteristic of salts.

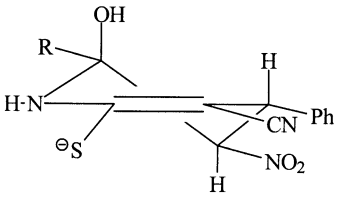


Scheme 4. Ar=C_6H_5 (**1**; **20a**); 4-ClC_6H_4 (**8a**; **9a**; **20b**); 2-C_4H_3S (**8e**; **9e**; **20c**).

The NMR spectra also confirm the linear structure of thiolates **5a**, **b**. The ^{1}H NMR spectra contain singlets of protons of the NH_2 group at 7.16 and 7.15 ppm, respectively. The signals of the 3-H and 4-H protons, which appear as two doublets at 4.75 and 5.22 ppm, respectively, with the SSC constant ^3J=3.7 Hz, are characteristic. The torsion angle φ $C_{(3)}H–C_{(4)}H$ calculated by the Karplus–Conroy equation[19] from these constants is equal to 62°, which indicates the synclinal arrangement of these hydrogen atoms (Michael *cis*-adduct).

In the ^{13}C NMR spectrum of compounds **5a**, **b** presents the characteristic signals of the carbon atoms of the $C_{(5)}$=O group at 193.03 and 193.05 ppm and of the $C_{(1)}$ atoms bound to the formally negatively charged sulfur atom at 161.18 and 161.25 ppm.

The physicochemical parameters of tetrahydropyridinethiolates **4a**, **b** confirm their cyclic form and also represent their spatial structure. The IR spectra of compounds **4** contain the characteristic intense signal of the conjugated CN group at 2170 and signals of the NH or OH groups at 3058 and 3349 cm^{-1}.The ^{1}H NMR spectra of compounds **4a**, **b** contain the characteristic signals from the OH group as a singlet at 5.67 and 6.46 ppm, respectively. The signals from the 4-H and 3-H protons are also characteristic, they appear as two doublets in the regions of 4.23–4.43 and 4.71–4.90 ppm, respectively, with the SSC constant ^3J=11.5 Hz for compound **4a** and 11.7 Hz for compound **4b**. The torsion angles φ $C_{(3)}H–C_{(4)}H$ calculated using the Karplus–Conroy equation[19] from these constants are equal to 158 and 160°, respectively, which indicates the *trans*-pseudo-axial arrangement of the hydrogen atoms.[13,14] Pyridinethiolates **4**, similarly to cyclohexene[20] and tetrahydropyridine-2-thiolates,[21] exist in the 'half-chair' conformation.



The ^{13}C NMR spectrum of compound **4a** contains the signal from the $C_{(6)}$ atom linked to the formally negative sulfur atom at 165.34 ppm.

The IR spectrum of compound **6** contains the absorption band at 2278 cm^{-1} characteristic of the nonconjugated CN group.[22,23] The ^{1}H NMR spectra contain singlet signals from the proton of the OH group at 7.92 ppm and NH group at 11.50 ppm. The signal from the 4-H proton appears as a triplet at 4.44 ppm, that from the 5-H proton as a doublet at 4.96 ppm with the SSC constant $^3J_{5\text{-H},4\text{-H}}$=11.5 Hz, and that from the 3-H proton as a doublet at 5.79 ppm with the SSC constant $^3J_{4\text{-H},3\text{-H}}$=12.6 Hz. The torsion angles φ $C_{(5)}H–C_{(4)}H$ and φ $C_{(3)}H–C_{(4)}H$ calculated as before are equal to 158° and 169°, which indicates the *trans-trans*-pseudo-axial arrangement of the hydrogen atoms of the pyridine cycle. The ^{13}C NMR spectrum of compound **6** contains the signal from the $C_{(2)}$ atom of the pyridine cycle appears at 191.98 ppm, which is characteristic of pyridines containing the C=S fragment with the exocyclic double bond.

The mass spectra of compounds **4**, and **5** contain no peak of molecular ions, however, the spectra of the decomposition products of the molecules under electron impact ionisation contain peaks due to elimination of the organic base and H_2O molecules. Peaks characteristic of nitro compound decomposition appeared produced when one or two oxygen atoms are eliminated from the nitro group.[24] In the mass spectrum of compound **6** the intensity of the peak of the molecular ion (353 *m/z*) is very low.

The spectral parameters of highly stable Michael adducts **20** differ considerably from those of Michael adducts **5**, which confirms their different reactivities.

The IR spectra of compounds **20** contain the characteristic low-intensity signals of the nonconjugated CN group in the region of 2248–2250 cm^{-1}. These data indicate that the negative charge in molecules of compounds **20** exists in the $[O_2NCCOOC_2H_5]^-$ rather than in the $[NCCCSNH_2]^-$ fragment as it was observed for compounds **5**. The ^{1}H NMR spectra of compounds **20a**–**c**, along with other characteristic signals of protons, contain singlets from protons of the NH_2 group at 7.27–7.33 ppm and signals from the 3-H and 2-H protons, which appear as doublets in the regions of 4.28–4.31 and 4.54–4.85 ppm, respectively, with the SSC constant ^3J=4 Hz. The torsion angle φ $C_{(2)}H–C_{(3)}H$ calculated is equal to 60°, which indicates the synclinal arrangement of the hydrogen atoms (Michael *cis*-adduct). The ^{13}C NMR spectrum of compound **20b** exhibits the characteristic signals of the carbonyl carbon atom (C=S) at 169.93 ppm and thione carbon atom (C=O) at

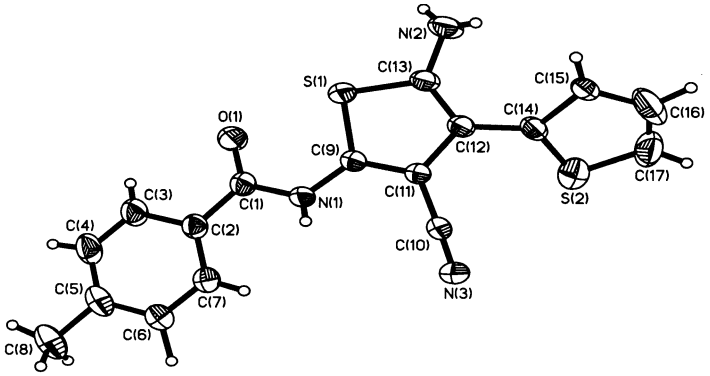
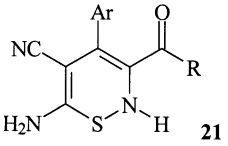


Figure 1. Molecular structure of 5-amino-3-cyano-2-(4-methylbenzamido)-4-(2-thienyl)-thiophene (**7k**).

162.09 ppm. The mass spectra of compounds **20a**, **b** are characterized by the absence of peaks of molecular ions but contain the characteristic peaks appeared when morpholine and ethanol or the nitro group are eliminated.

Since the preparation of thiophenes **7** was not a predicted result of the reactions under study, it was especially important to establish the structure of these compounds.

The studied reactions occur unexpectedly, and the IR and NMR spectroscopy and mass spectrometry data only do not contradict the structure of aminothiophenes **7** and do not rule out the possibility of formation of alternative structures, for example, thiazines (**21**).



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With the purpose for the final establishment of the structure of the reaction products, we carried out the X-ray diffraction study of 5-amino-3-cyano-2-(4-methylbenzamido)-4-(2-thienyl)-thiophene (**7k**).

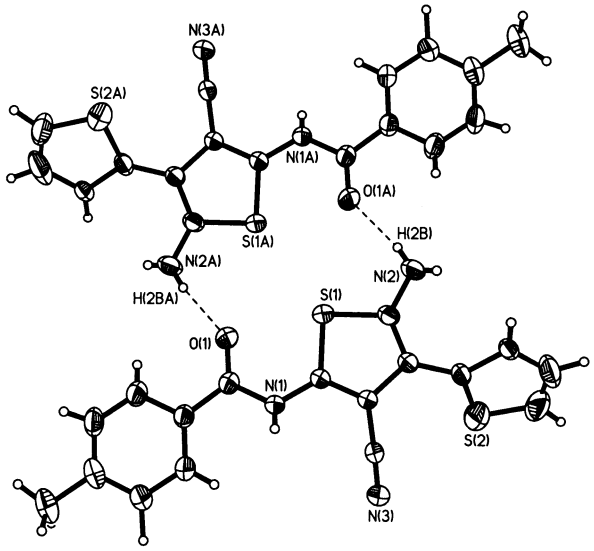

Figure 2. Structure of the center-symmetric dimer of 5-amino-3-cyano-2-(4-methylbenzamido)-4-(2-thienyl)-thiophene (**7k**) formed by two hydrogen bonds. d (O(1)–N(2A))=2.96 Å.

According to the data of X-ray diffraction analysis of compound **7k**, the substituted thiophene cycle lies in the same plane with the amino group, acylamino group, and nitrile group, whereas the nonsubstituted thiophene cycle is shifted from the plane of the substituted cycle (Fig. 1). For nonhydrogen atoms lying in the plane of the substituted thiophene cycle, the mean deviation from the cycle plane is 0.0642 Å, whereas the $C_{(4)}$–$C_{(5)}$ bond lengths is equal to 1.315 Å. Molecules of compound **3k** in the crystalline packing form center-symmetric dimers by hydrogen bonds between the hydrogen atoms of the amino groups and oxygen atoms of the acylamino groups of the dimer with the distance d (O(1)–N(2A))=2.96 Å. The dimer of compound **7k** is presented in Fig. 2.

Thus, in this report, we present the results of studying the reactions of α-nitrocarbonyl compounds with unsaturated thioamides or their precursors (cyanothioacetamide and aromatic aldehydes). Despite the variety of the formed reaction products, general regularities of the reactions can be distinguished. For example, the primary stage of the reactions under study is the formation of noncyclic Michael adducts. In the case of using α-nitroesters, the reaction is ceased at this stage, and when α-nitroketones are used the Michael adduct are further transformed with cyclization into derivatives of hydrogenated pyridines and then recyclization to aminothiophenes occurs. We observed the specific redox transformation of hydrogenated pyridine derivatives to aminothiophenes, which is a distinctive feature of the reactions of α-nitroketones with unsaturated thioamides unlike the widely studied reactions of α-methyl, methylenecarbonyl compounds.

2.1. X-Ray structure determination (Tables 1–3)

X-Ray diffraction study of 5-amino-3-cyano-2-(4-methylbenzamido)-4-(2-thienyl)-thiophene (**7k**) was carried out on an Enraf-Nonius CAD-4 automated diffractometer at room temperature using Mo Kα radiation (λ=0.71073 Å, graphite monochromator). The crystals ($C_{17}H_{13}N_3OS_2$, M=339.42) are triclinic, space group $P1$, a=8.298 (3), b=9.155 (4), c=10.917 (3) Å, α=90.54 (3), β=105.59 (2), γ=95.67 (3)°, V=794.4 (5) Å^3, Z=2, D_{calcd}=1.419 g/

Table 1. Coordinates of nonhydrogen atoms (Å×10^4) and their isotropic equivalent temperature parameters U_{eq} (Å×10^3) for 5-amino-3-cyano-2-(4-methylbenzamido)-4-(2-thienyl)-thiophene (**7k**)

Atom	x	y	z	U_{eq}, E^2
S(1)	538 (1)	3131 (1)	5085 (1)	49 (1)
S(2)	2955 (2)	−49 (2)	8932 (1)	89 (1)
O(1)	2226 (4)	4818 (3)	3755 (3)	70 (1)
N(1)	3487 (4)	2845 (3)	4491 (3)	46 (1)
N(2)	−1447 (5)	2096 (5)	6499 (5)	70 (1)
N(3)	5273 (4)	−31 (4)	6560 (4)	69 (1)
C(1)	3362 (4)	4053 (4)	3777 (3)	47 (1)
C(2)	4619 (4)	4386 (3)	3051 (3)	46 (1)
C(3)	4407 (6)	5547 (4)	2231 (4)	60 (1)
C(4)	5539 (6)	5936 (5)	1560 (4)	66 (1)
C(5)	6927 (5)	5215 (5)	1657 (4)	59 (1)
C(6)	7162 (5)	4036 (5)	2463 (4)	64 (1)
C(7)	6018 (5)	3637 (5)	3149 (4)	61 (1)
C(8)	8219 (6)	5656 (6)	950 (5)	81 (1)
C(9)	2403 (4)	2389 (3)	5220 (3)	41 (1)
C(10)	4081 (4)	548 (4)	6361 (3)	48 (1)
C(11)	2615 (4)	1297 (3)	6079 (3)	40 (1)
C(12)	1242 (4)	1046 (3)	6674 (3)	42 (1)
C(13)	39 (4)	1954 (4)	6195 (3)	45 (1)
C(14)	1234 (4)	58 (4)	7711 (3)	47 (1)
C(15)	−226 (4)	−867 (3)	7962 (3)	41 (1)
C(16)	371 (9)	−1527 (5)	9124 (6)	100 (2)
C(17)	1971 (9)	−1193 (6)	9718 (5)	97 (2)

cm^3, μ(Mo K$_\alpha$)=0.342 mm^{-1}, F(000)=352. Intensities of 3565 reflections (of them 2775 independent, R_{int}=0.0141) were measured using ω scan mode in the interval $2.24<\theta<24.97°$ ($-9<h<9$, $-10<k<10$, $-2<l<12$). Experimental data were corrected taking into account the Lorentz and polarization factors.[25] The structure was solved by the direction method (SHELXL-86[26]). All nonhydrogen atoms were refined in the full-matrix anisotropic least-squares method by F^2 (SHELXL-93[27]). All hydrogen atoms were placed to the calculated positions; H atoms of the amine and amide groups and the benzene ring were refined isotropically, and all other atoms were refined by the 'rider' scheme. The resulting value of the divergence factor was R_1=0.0544, R_ω=0.1783 for 2035 reflections with $i>2\sigma(I)$ and 238 refinement parameters. The X-ray diffraction study was performed by Doct. Sci. (Chem.) V. S. Sergienko at the N. S. Kurnakov Institute of General and Inorganic Chemistry. The coordinates of nonhydrogen atoms and their isotropic equivalent temperature parameters are presented in Table 1 bond lengths and their angles are presented in Table 2 and Table 3.

Table 2. Bond lengths (d) in a molecule of 5-amino-3-cyano-2-(4-methylbenzamido)-4-(2-thienyl)-thiophene (**7k**)

Bond	d/E	Bond	d/E
S(1)–C(9)	1.722 (3)	C(4)–C(5)	1.364 (6)
S(1)–C(13)	1.734 (3)	C(5)–C(6)	1.394 (6)
S(2)–C(17)	1.651 (5)	C(5)–C(8)	1.508 (5)
S(2)–C(14)	1.683 (4)	C(6)–C(7)	1.384 (5)
O(1)–C(1)	1.224 (4)	C(9)–C(11)	1.369 (4)
N(1)–C(1)	1.355 (4)	C(10)–C(11)	1.419 (4)
N(1)–C(9)	1.390 (4)	C(11)–C(12)	1.456 (4)
N(2)–C(13)	1.378 (5)	C(12)–C(13)	1.361 (4)
N(3)–C(10)	1.139 (4)	C(12)–C(14)	1.457 (4)
C(1)–C(2)	1.481 (5)	C(14)–C(15)	1.496 (4)
C(2)–C(7)	1.386 (5)	C(15)–C(16)	1.398 (7)
C(2)–C(3)	1.390 (5)	C(16)–C(17)	1.315 (8)
C(3)–C(4)	1.361 (6)		

Table 3. Bond angles (ω) in a molecule of 5-amino-3-cyano-2-(4-methylbenzamido)-4-(2-thienyl)-thiophene (**7k**)

Angle	ω	Angle	ω
C(9)–S(1)–C(13)	91.4 (2)	N(1)–C(9)–S(1)	122.3 (2)
C(17)–S(2)–C(14)	94.1 (3)	N(3)–C(10)–C(11)	178.0 (3)
C(1)–N(1)–C(9)	124.7 (3)	C(9)–C(11)–C(10)	121.3 (3)
O(1)–C(1)–N(1)	119.2 (3)	C(9)–C(11)–C(12)	113.5 (3)
O(1)–C(1)–C(2)	122.8 (3)	C(10)–C(11)–C(12)	125.2 (3)
N(1)–C(1)–C(2)	118.0 (3)	C(13)–C(12)–C(11)	110.2 (3)
C(7)–C(2)–C(3)	117.3 (3)	C(13)–C(12)–C(14)	124.9 (3)
C(7)–C(2)–C(1)	124.6 (3)	C(11)–C(12)–C(14)	124.6 (3)
C(3)–C(2)–C(1)	118.1 (3)	C(12)–C(13)–N(2)	129.5 (3)
C(4)–C(3)–C(2)	121.1 (4)	C(12)–C(13)–S(1)	113.3 (2)
C(3)–C(4)–C(5)	122.0 (4)	N(2)–C(13)–S(1)	117.1 (3)
C(4)–C(5)–C(6)	118.1 (3)	C(12)–C(14)–C(15)	128.5 (3)
C(4)–C(5)–C(8)	122.8 (4)	C(12)–C(14)–S(2)	121.9 (2)
C(6)–C(5)–C(8)	119.1 (4)	C(15)–C(14)–S(2)	109.4 (2)
C(7)–C(6)–C(5)	120.2 (4)	C(16)–C(15)–C(14)	107.1 (4)
C(6)–C(7)–C(2)	121.3 (4)	C(17)–C(16)–C(15)	116.5 (4)
C(11)–C(9)–N(1)	126.2 (3)	C(16)–C(17)–S(2)	112.9 (4)
C(11)–C(9)–S(1)	111.5 (2)		

Crystallographic data (excluding structure factor) for the structure **7k** in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 174909.

3. Experimental

3.1. General

Melting temperatures of the compounds were determined on the Kofler stage. Infrared spectral measurements were obtained for KBr molds using a Perkin–Elmer 577 instrument. ^{1}H and ^{13}C NMR spectra were measured using a Bruker WM-250 instrument (250 and 63 MHz, respectively) for DMSO-d_6 solutions. Mass spectra were obtained on a MAT INCOS-50 instrument (Finnigan) (ionizing energy 70 eV). Elemental analysis was carried out on a Perkin–Elmer C, H, N analyzer.

3.1.1. Morpholinium 3,4-*trans*-5-cyano-2,4-diphenyl-2-hydroxy-3-nitro-1,2,3,4-tetrahydropyridine-6-thiolate (4a). Morpholine (0.01 ml) was added to a suspension of nitroketone **3a** (1.01 g, 6 mmol), cyanothioacetamide **2** (0.61 g, 6.1 mmol), and benzaldehyde **1** (0.65 g, 6 mmol) in absolute ethanol (15 ml). The mixture was stored at 40–55°C until the starting substances were dissolved, and then morpholine (0.63 ml, 7.2 mmol) was added. The crystallization of a precipitate was evoked in 4–5 min by rubbing with a glass rod. The white precipitate that formed was filtered off and title compound **4a** (1.76 g, 65%) as a white solid, mp 144–145°C; [Found: C, 59.6; H, 5.6; N, 12.5; S, 7.1. $C_{22}H_{24}N_4O_4S$ requires C, 59.98; H, 5.49; N, 12.72; S, 7.28%]; ν_{max} (KBr), 3349, 3058, 2170, 1553, 1372 cm^{-1}; δ_H (250 MHz DMSO-d_6) 3.08 (4H, m, N(CH_2)$_2$), 3.74 (4H, m, O(CH_2)$_2$), 4.43 (1H, d, $^3J_{4,3}$=11.5 Hz, C(4)H), 4.90 (1H, d, $^3J_{3,4}$=11.5 Hz, C(3)H), 5.67 (1H, s, OH), 7.15–7.68 (10H, m, Ph); δ_c (63 MHz DMSO-d_6) 42.97, 63.62 (C$_{(morpholine)}$), 44.09

(*C*(4)), 95.55 (*C*(2)), 101.29 (*C*(3)), 111.77 (*C*(5)H), 115.38 (*C*≡N), 124.43, 126.82, 127.49, 128.17, 128.77, 132.29, 133.71, 143.27 (C_{Ph}), 165.34 (C(6)), *m/z* 335 (18, $M-H_2O$, morpholine), 319 (25), 304 (34), 273 (45), 187 (20), 105 (70), 87 (65), 77 (100%).

3.1.2. Morpholinium 3,4-*trans*-5-cyano-2-hydroxy-2-methyl-3-nitro-4-phenyl-1,2,3,4-tetrahydropyridine-6-thiolate (4b). The title compound was prepared similarly to compound **4a** using nitroacetone **3b** instead of nitroacetophenone **3a**, to give the title compound **4b** as white solid (45%), mp 144–145°C; [Found: C, 54.2; H, 6.2; N, 14.00; S, 8.5. $C_{17}H_{22}N_4O_4S$ requires C, 53.95; H, 5.86; N, 14.80; S, 8.47%]; ν_{max} (KBr), 3349, 3058, 2170, 1554, 1372 cm^{-1}; δ_H (250 MHz DMSO-d_6) 1.35 (3H, s, CH_3), 3.06 (4H, m, N(CH_2)$_2$), 3.72 (4H, m, O(CH_2)$_2$), 4.23 (1H, d, $^3J_{4,3}$=11.7 Hz, C(4)*H*), 4.71 (1H, d, $^3J_{3,4}$=11.7 Hz, C(3)*H*), 6.46 (1H, s, O*H*), 7.05–7.38 (5H, m, Ph); *m/z* 291 (15, M^+−morpholine), 271 (15), 257 (40), 226 (28), 201 (10), 187 (30), 128 (60), 87 (100), 77 (97), 57 (80%).

3.1.3. Morpholinium 1-amino-2-cyano-3,5-diphenyl-4-nitro-5-oxo-1,2-pentene-1-thiolate (5a). Morpholine (0.01 ml) and nitroketone **3a** (1.01 g, 6 mmol) were added to a suspension of benzaldehyde **1** (0.65 g, 6.1 mmol) and cyanothioacetamide **2** (0.61 g, 6.1 mmol) in absolute ethanol (15 ml). The mixture was stored at 30–35°C until a solution was formed, and then morpholine (0.63 ml, 7.2 mmol) was added. The crystallization of a precipitate was evoked in 4–5 min by rubbing with a glass rod. The white precipitate that formed was filtered off to give title compound **5a** (1.84 g, 70%) as white solid, mp 124–125°C; [Found: C, 59.9; H, 5.6; N, 12.4; S, 7.0. $C_{22}H_{24}N_4O_4S$ requires C, 59.98; H, 5.49; N, 12.72; S, 7.28%]; ν_{max} (KBr), 3353, 3064, 2162, 1591, 1557, 1370 cm^{-1}; δ_H (250 MHz DMSO-d_6) 3.03 (4H, m, N(CH_2)$_2$), 3.72 (4H, m, O(CH_2)$_2$), 4.75 (1H, d, $^3J_{3,4}$=3.7 Hz, C(3)*H*), 5.22 (1H, d, $^3J_{4,3}$=3.7 Hz, C(4)*H*), 7.16 (2H, s, NH_2), 7.30–7.60 (8H, m, Ph), 7.90 (2H, d, *J*=8.2 Hz, Ph); δ_c (63 MHz DMSO-d_6) 43.17, 64.07 ($C_{(morpholine)}$); 50.85 (*C*(3)), d, $^1J_{C,H}$=136 Hz), 56.03 (*C*(4), dd, $^1J_{C,H}$=147 Hz, $^3J_{C,H}$=3.8 Hz), 70.99 (*C*(2)), 118.26 (*C*≡N), 126.35, 126.54, 127.40, 127.94, 128.05, 128.20, 128.34, 128.65, 128.83, 133.62, 134.50, 141.82 (C_{Ph}), 161.18 (*C*(1)), 193.03 (*C*=O); *m/z* 335 (12, M^+-H_2O, morpholine), 319 (25), 304 (34), 289 (45), 273 (20), 187 (50), 105 (90), 87 (100), 77 (100%).

3.1.4. *N,N*-Tetramethylethylenediammonium 1-amino-2-cyano-3,5-diphenyl-4-nitro-5-oxo-1,2-pentene-1-thiolate (5b). This was obtained similarly to compound **5a** using TMEDA instead of morpholine to give title compound **5b** as white solid (2.03 g, 75%), mp 123–124°C; [Found: C, 61.2; H, 5.5; N, 13.4; S, 7.5. $C_{21}H_{23}N_4O_3S$ ($C_{18}H_{15}N_3O_3S\cdot 1/2C_6H_{16}N_2$) requires C, 61.30; H, 5.63; N, 13.62; S, 7.79%]; ν_{max} (KBr), 3250, 2185, 1555, 1370 cm^{-1}; ν_{max} (THF), 3480, 3190, 2212, 1776, 1680, 1590, 1555, 1370 cm^{-1}; δ_H (250 MHz DMSO-d_6) 2.45 (6H, s, N(CH_3)$_2$-TMEDA), 3.44 (2H, s, CH_2-TMEDA), 4.75 (1H, d, $^3J_{3,4}$=3.7 Hz, C(3)*H*), 5.22 (1H, d, $^3J_{4,3}$=3.7 Hz, C(4)*H*), 7.15 (2H, s, NH_2), 7.30–7.65 (8H, m, Ph), 7.95 (2H, d, *J*=8.2 Hz, Ph); δ_c (63 MHz DMSO-d_6) 43.69 14 ($C_{(TMEDA)}$), 53.14 ($C_{(TMEDA)}$), 50.81 (*C*(3)), 56.05 (*C*(4)), 70.92 (*C*(2)), 118.39 (*C*≡N), 126.42, 127.9, 127.75, 128.04, 128.58, 128.74, 128.92, 129.30, 130.23, 133.71, 134.53, 141.90 (C_{Ph}), 161.25 (*C*(1)), 193.05 (*C*=O); *m/z* 319 (20, M^+-20, TMEDA), 304 (30), 273 (30), 187 (20), 116 (50), 105 (95), 77 (100), 58 (80%).

3.1.5. 3,4-*trans*-4,5-*trans*-5-Cyano-2,4-diphenyl-2-hydroxy-3-nitrohexahydropyridine-6(1*H*)-thione (6). Concentrated hydrochloric acid (4 ml) was added dropwise with stirring to a suspension of salt **4a** (1.82 g, 4.14 mmol) in ethanol (10 ml). After 4 h, the white precipitate was filtered off and washed subsequently with water, ethanol, and hexane to give title compound **6** (1.32 g, 90%), mp 154–155°C (decomp.); Compound **6** was obtained similarly from salt **5a** in 89% yield; [Found: C, 61.2; H, 4.0; N, 11.9; S, 9.0. $C_{18}H_{15}N_3O_3S$ requires C, 61.18; H, 4.28; N, 11.89; S, 9.07%]; ν_{max} (KBr), 3280, 3130, 2278, 1563, 1360 cm^{-1}; δ_H (250 MHz DMSO-d_6) 4.44 (1H, t, $^3J_{4,5}$=11.5 Hz, $^3J_{4\text{-}H,3\text{-}H}$=12.6 Hz, C(4)*H*), 4.96 (1H, d, $^3J_{5,4}$=11.5 Hz, C(5)*H*), 5.79 (1H, d, $^3J_{3,4}$=12.6 Hz, C(3)*H*), 7.92 (1H, s, C*H*), 7.34–7.61 (10H, m, Ph), 11.50 (1H, s, N*H*); δ_c (63 MHz DMSO-d_6) 42.02 (*C*(4)), 49.41 (*C*(5)), 83.66 (*C*(4)), 95.45 (*C*(2)), 116.83 (*C*≡N), 126.34, 127.99, 128.22, 128.56, 128.91, 136.03, 136.88 (C_{Ph}); *m/z* 353 (30, M^+), 335 (40), 319 (50), 307 (20), 273 (30), 187 (70), 105 (100), 77 (100%).

3.2. 2-Acylamino-5-amino-4-aryl-3-cyanothiophenes (7). General procedure

Method (A): Morpholine (0.11 ml, 1.25 mmol) was added dropwise to a suspension of arylidenecyanothioacetamide **9** (1 mmol), nitroketone **3** (1 mmol), and sodium thiosulfate $Na_2S_2O_3\cdot 5H_2O$ (0.12 g, 0.5 mmol) in ethanol (2.5 ml) heated at 35–40°C. The reaction mixture was refluxed for 3–5 min. After 20–30 min, a crystalline precipitate was isolated, subsequently washed with ethanol and hexane, and crystallized from ethanol to give title compounds **7a–o**.

Method (B): Morpholine (0.11 ml, 1.25 mmol) was added to a suspension of nitroketone **3** (1 mmol), corresponding aldehyde **1**, **8** (1 mmol), and cyanothioacetamide **2** (0.15 g, 1.5 mmol) in ethanol (2.5 ml). The reaction mixture was refluxed for 3–5 min. After 20–30 min, a crystalline precipitate was isolated, subsequently washed with ethanol and hexane, and crystallized from ethanol.

Method (C): Morpholine (0.11 ml, 1.25 mmol) was added dropwise to a suspension of cyanothioacetamide **2** (0.11 g, 1.1 mmol), sodium thiosulfate $Na_2S_2O_3\cdot 5H_2O$ (0.12 g, 0.5 mmol), and 2-nitro-1-phenyl-3-(4-chlorophenyl)-2-propen-1-one **10** (0.28 g, 1 mmol) obtained by a described procedure[1] in ethanol (2.5 ml). The mixture was refluxed for 3 min. Compound **7h** was isolated similarly to method A.

3.2.1. 5-Amino-2-benzamido-3-cyano-4-phenylthiophene (7a). 45%, mp 242–243; [Found: C, 67.6; H, 4.0; N, 13.0; S, 9.9. $C_{18}H_{13}N_3OS$ requires C, 67.69; H, 4.10; N, 13.16; S, 10.04%]; ν_{max} (KBr), 3392, 3320, 2208, 1652 cm^{-1}; δ_H (250 MHz DMSO-d_6) 11.35 (1H, s, N*H*), 5.65 (2H, s, NH_2), 7.31–7.52 (5H, m, Ph), 7.65 (3H, m, Ar), 7.96 (2H, d, *J*=8.2 Hz, Ph); δ_c (63 MHz DMSO-d_6) 135.38 (C(2)); 111.89 (C(3)); 97.44 (C(4)); 143.34 (C(5)); 115.00 (CN);

165.10 (CO); (R, Ar): 126.70; 127.9; 128.38; 128.61; 132.19; 132.54; 132.90; *m/z* 319 (29, M^+), 214 (5, M^+-PhCO), 105 (100%).

3.2.2. 2-Acetamido-5-amino-3-cyano-4-phenylthiophene (7b). 23%, mp 215–216; [Found: C, 60.5; H, 4.4; N, 16.1; S, 12.3. $C_{13}H_{11}N_3OS$ requires C, 60.68; H, 4.31; N, 16.33; S, 12.46%]; ν_{max} (KBr), 3400, 3228, 2216, 1672 cm^{-1}; δ_H (250 MHz DMSO-d_6) 11.21 (1H, s, N*H*), 5.42 (2H, s, NH_2), 2.17 (3H, s, CH_3), 7.26–7.52 (5H, m, Ph); δ_c (63 MHz DMSO-d_6) 36.72 (C(2)), 110.87 (C(3)), 92.20 (C(4)), 141.42 (C(5)), 115.31 (CN), 167.94 (CO), (R, Ar): 22.33 (*C*H_3), 126.64, 128.62, 128.73, 133.08; *m/z* 257 (22, M^+), 212 (60), 45 (100%).

3.2.3. 5-Amino-2-benzamido-3-cyano-4-(4-methoxyphenyl)thiophene (7c). 68%, mp 268–269; [Found: C, 65.4; H, 4.5; N, 12.1; S, 8.9. $C_{19}H_{15}N_3O_2S$ requires C, 65.31; H, 4.33; N, 12.03; S, 9.18%]; ν_{max} (KBr), 3304, 3120, 2208, 1648 cm^{-1}; δ_H (250 MHz DMSO-d_6) 10.32 (1H, s, N*H*), 4.95 (2H, s, NH_2), 7.65 (3H, m, Ar), 7.96 (2H, d, *J*=8.2 Hz, Ph), 3.85 (3H, s, CH_3O), 7.07 (2H, d, *J*=7.9 Hz, Ar), 7.40 (2H, d, *J*=7.9 Hz, Ar); δ_c (63 MHz DMSO-d_6) 135.14 (*C*(2)), 112.08 (*C*(3)), 97.77 (*C*(4)), 142.66 (*C*(5)), 114.14 (*C*N), 165.14 (*C*O), (R, Ar): 55.11 (O*C*H_3), 125.08, 127.99, 128.40, 130.00, 132.19, 158.10; *m/z* 349 (44, M^+), 244 (14, M^+-PhCO), 217 (10), 105 (100), 77 (38%).

3.2.4. 5-Amino-2-benzamido-3-cyano-4-(2-nitrophenyl) thiophene (7d). 60%, mp 272–273; [Found: C, 59.3; H, 3.3; N, 15.6; S, 8.6. $C_{18}H_{12}N_4O_3S$ requires C, 59.33; H, 3.32; N, 15.38; S, 8.80%]; ν_{max} (KBr) 3424, 3336, 3224, 2216, 1648 cm^{-1}; δ_H (250 MHz DMSO-d_6) 11.25 (1H, s, N*H*), 5.42 (2H, s, NH_2), 7.96 (2H, d, *J*=8.2 Hz, Ar), 7.61 (3H, m, Ar), 7.51 (1H, d, *J*=8.0 Hz, Ar), 7.61 (1H, d, *J*=8.0 Hz), 7.80 (1H, t, *J*=8.0, 8.2 Hz, Ar), 8.12 (1H, d, *J*=8.2 Hz, Ar); *m/z* 364 (12, M^+), 259 (2, M^+-PhCO), 105 (100), 77 (50%).

3.2.5. 5-Amino-2-benzamido-4-(3-bromophenyl)-3-cyanothiophene (7e). 65%, mp 269–270; [Found: C, 54.5; H, 2.7; N, 10.2; S, 7.7. $C_{18}H_{12}BrN_3OS$ requires C, 54.28; H, 3.04; N, 10.55; S, 8.05%]; ν_{max} (KBr), 3420, 3323, 3245, 2224, 1648 cm^{-1}; δ_H (250 MHz DMSO-d_6) 11.20 (1H, s, N*H*); 5.51 (2H, s, NH_2); 7.3–7.96 (9H, m, Ar); δ_c (63 MHz DMSO-d_6) 135.70 (C(2)), 109.93 (C(3)), 96.71 (C(4)), 144.26 (C(5)), 114.87 (CN), 165.17 (CO), (R, Ar): 121.92, 127.99, 128.44, 129.00, 132.27, 132.51; *m/z* 398 (16, M^+), 293 (2, M^+-PhCO), 212 (5), 105 (100), 77 (45%).

3.2.6. 5-Amino-2-benzamido-3-cyano-4-(2-thienyl)-thiophene (7f). 62%, mp 262–263; [Found: C, 58.9; H, 3.5; N, 12.7; S, 19.7. $C_{16}H_{11}N_3OS_2$ requires C, 59.06; H, 3.41; N, 12.91; S, 19.70%]; ν_{max} (KBr), 3408, 3344, 2216, 1652 cm^{-1}; δ_H (250 MHz DMSO-d_6) 11.35 (1H, s, N*H*), 5.65 (2H, s, NH_2), 7.02–7.96 (8H, m, Ar); *m/z* 325 (6, M^+), 220 (3, M^+-PhCO), 105 (100), 77 (47%).

3.2.7. 5-Amino-2-benzamido-3-cyano-4-(3-pyridyl)-thiophene (7g). 65%, mp 270–271; [Found: C, 63.7; H, 4.1; N, 17.3; S, 9.7. $C_{17}H_{12}N_4OS$ requires C, 63.74; H, 3.78; N, 17.49; S, 10.01%]; ν_{max} (KBr), 3360, 3384, 2216, 1640 cm^{-1}; δ_H (250 MHz DMSO-d_6) 11.25 (1H s, N*H*), 5.60 (2H, s, NH_2), 7.96 (2H, d, *J*=8.2 Hz, Ar), 7.65 (3H, m, Ar), 7.46 (1H, t, *J*=8.1, 8.2 Hz, Ar), 7.69 (1H, d, *J*=8.1 Hz, Ar), 8.45 (1H, d, *J*=8.1 Hz, Ar), 8.60 (1H, s, Ar); *m/z* 320 (35, M^+), 215 (2, M^+-PhCO), 105 (100), 77 (44%).

3.2.8. 5-Amino-2-benzamido-4-(4-chlorophenyl)-3-cyanothiophene (7h). 65% (A), 60% (B), 23% (C), mp 265–266; [Found: C, 61.1; H, 3.4; N, 11.5; S, 8.8. $C_{18}H_{12}ClN_3OS$ requires C, 61.10; H, 3.42; N, 11.88; S, 9.06%]; ν_{max} (KBr), 3392, 3312, 3256, 2224, 1648 cm^{-1}; δ_H (250 MHz DMSO-d_6) 11.10 (1H, s, N*H*), 5.49 (2H, s, NH_2), 7.95 (2H, d, *J*=8.2 Hz, Ar), 7.65 (3H, m, Ar); 7.45 (4H, dd, *J*=8.2 Hz, Ar); δ_c (63 MHz DMSO-d_6) 135.73 (C(2)), 110.46 (C(3)), 96.92 (C(4)), 143.94 (C(5)), 115.06 (CN), 165.28 (CO), (R, Ar): 128.17, 128.51, 128.73, 130.63, 131.45, 132.34; 132.65; *m/z* 353 (10, M^+), 338 (5), 320 (2), 255 (42), 224 (28), 215 (16), 105 (100), 77 (48%).

3.2.9. 5-Amino-3-cyano-2-(4-methylbenzamido)-4-phenylthiophene (7i). 52%, mp 245–246; [Found: C, 68.3; H, 4.7; N, 12.4; S, 9.5. $C_{19}H_{15}N_3OS$ requires C, 68.45; H, 4.53; N, 12.60; S, 9.62%]; ν_{max} (KBr), 3318, 3424, 2204, 1648 cm^{-1}; δ_H (250 MHz DMSO-d_6) 11.08 (1H, s, N*H*), 5.35 (2H, s, NH_2), 2.36 (3H, s, CH_3), 7.85 (2H, d, *J*=8.0 Hz, Ar), 7.23 (2H, d, *J*=8.0 Hz, Ar), 7.31–7.52 (5H, m, Ph); *m/z* 333 (18, M^+), 119 (90%, $CH_3-C_6H_4CO^+$).

3.2.10. 5-Amino-3-cyano-4-(4-methoxyphenyl)-2-(4-methylbenzamido)-thiophene (7j). 63%, mp 264–265; [Found: C, 66.4; H, 4.6; N, 11.4; S, 8.7. $C_{20}H_{17}N_3O_2S$ requires C, 66.10; H, 4.71; N, 11.56; S, 8.82%]; ν_{max} (KBr), 3308, 3424, 2204, 1648 cm^{-1}; δ_H (250 MHz DMSO-d_6) 11.09 (1H, s, N*H*), 5.39 (2H, s, NH_2), 2.37 (3H s, CH_3), 7.12 (2H, d, *J*=8.0 Hz, Ar), 7.88 (2H, d, *J*=8.0 Hz, Ar), 3.81 (3H, s, Me), 7.45 (4H, dd, *J*=8.0 Hz, Ar); δ_c (63 MHz DMSO-d_6) 135.36 (C(2)), 111.94 (C(3)), 97.46 (C(4)), 142.65 (C(5)), 114.47 (CN), 164.99 (CO), (R, Ar): 21.14 (*C*H_3), 55.16 (O*C*H_3), 125.19, 131.45, 158.18; *m/z* 363 (19, M^+), 119 (88%, $CH_3-C_6H_4CO^+$).

3.2.11. 5-Amino-3-cyano-2-(4-methylbenzamido)-4-(2-thienyl)-thiophene (7k). Yield 67%, mp 265–267; [Found: C, 59.9;H, 3.9; N, 12.3; S, 18.9. $C_{17}H_{13}N_3OS_2$ requires C, 60.16; H, 3.86; N, 12.38; S, 18.89%]; ν_{max} (KBr), 3424, 3308, 3208, 2204, 1646 cm^{-1}; δ_H (250 MHz DMSO-d_6) 11.13 (1H, s, N*H*), 5.75 (2H, s, NH_2), 2.35 (3H, s, CH_3), 7.32 (2H, d, *J*=8.0 Hz, Ar), 7.88 (2H, d, *J*=8.0 Hz, Ar), 7.16 (1H, m, C_4H_3S), 7.29 (1H, m, C_4H_3S), 7.54 (1H, m, C_4H_3S); δ_c (63 MHz DMSO-d_6) 135.94 (C(2)), 104.66 (C(3)), 96.36 (C(4)), 142.71 (C(5)), 115.10 (CN), 165.07 (CO), (R, Ar): 21.16 (*C*H_3), 125.14, 125.91, 127.44, 128.22, 129.11, 129.59, 133.97, 144.24; *m/z* 339 (16, M^+), 119 (95%, $CH_3-C_6H_4CO^+$).

3.2.12. 2-Acetamido-5-amino-4-(4-chlorophenyl)-3-cyanothiophene (7l). 25%, mp 225–226; [Found: C, 53.5; H, 3.5; N, 14.6; S, 10.9. $C_{13}H_{10}ClN_3OS$ requires C, 53.52; H, 3.45; N, 14.40; S, 10.99%]; ν_{max} (KBr), 3416, 3336, 3272, 2216, 1680 cm^{-1}; δ_H (250 MHz DMSO-d_6) 11.25 (1H, s, N*H*); 5.51 (2H, s, NH_2); 2.15 (3H, s, CH_3); 7.40–7.60 (4H, s, 4-Cl–C_6H_4); *m/z* 291 (25, M^+), 246 (4%, M^+-CH_3CO).

3.2.13. 2-Acetamido-5-amino-3-cyano-4-(4-methoxyphenyl)-thiophene (7m). 25%, mp 223–224; [Found: C, 58.4; H, 4.6;N, 14.2; S, 10.9. $C_{14}H_{13}N_3O_2S$ requires C, 58.52; H, 4.56; N, 14.62; S, 11.16%]; ν_{max} (KBr), 3400, 3360, 3228, 2216, 1672 cm^{-1}; δ_H (250 MHz DMSO-d_6) 11.18 (1H, s, N*H*), 5.26 (2H, s, NH_2), 2.14 (3H, s, CH_3), 3.87 (3H, s, CH_3O), 7.07 (2H, d, *J*=7.8 Hz, Ar), 7.42 (2H, d, *J*=7.8 Hz, Ar); δ_c (63 MHz DMSO-d_6) 136.51 (C(2)), 111.36 (C(3)), 92.76 (C(4)), 140.73 (C(5)), 114.17 (CN), 167.95 (CO), (R, Ar): 22.40 (*C*H_3), 55.20 (O*C*H_3), 125.31, 130.01, 131.45, 158.15; *m/z* 287 (33, M^+), 245 (16%, M^+-CH_3CO).

3.2.14. 2-Acetamido-5-amino-3-cyano-4-(2-nitrophenyl)-thiophene (7n). 22%, mp 233–235; [Found: C, 51.4; H, 3.5; N, 18.8; S, 10.5. $C_{13}H_{10}N_4O_3S$ requires C, 51.65; H, 3.33; N, 18.53; S, 10.61%]; ν_{max} (KBr), 3492, 3319, 3206, 2216, 1672 cm^{-1}; δ_H (250 MHz DMSO-d_6) 11.25 (1H, s, N*H*), 5.42 (2H, s, NH_2), 2.17 (3H, s, CH_3), 7.51 (1H, d, *J*=8.0 Hz, Ar), 7.61 (1H, d, *J*=8.1 Hz, Ar), 7.80 (1H, t, *J*=8.1, 8.0 Hz, Ar), 8.12 (1H, d, *J*=8.1 Hz, Ar); *m/z* 302 (29, M^+), 257 (7%, M^+-CH_3CO).

3.2.15. 2-Acetamido-5-amino-3-cyano-4-(3-pyridyl)-thiophene (7o). 24%, mp 228–229; [Found: C, 55.7; H, 4.1; N, 21.9; S, 12.5. $C_{12}H_{10}N_4OS$ requires C, 55.80; H, 3.90; N, 21.69; S, 12.41%]; ν_{max} (KBr), 3380, 3320, 3210, 2216, 1664 cm^{-1}; δ_H (250 MHz DMSO-d_6) 11.25 (1H, s, N*H*), 5.62 (2H, s, NH_2), 2.13 (3H, s, CH_3), 7.46 (1H, t, *J*=7.9 Hz, C_5H_4N), 7.69 (1H, d, *J*=7.9 Hz), 8.45 (1H, d, *J*=7.9 Hz), 8.60 (s, 1H, C_5H_4N); *m/z* 258 (35, M^+), 213 (9, M^+-CH_3CO).

3.2.16. 2-Acetamido-5-benzamido-3-cyano-4-(4-methoxyphenyl)-thiophene (1l). Pyridine (0.2 ml) was added dropwise to a suspension of compound **7c** (0.1 g, 0.29 mmol) in acetic anhydride (1 ml). The mixture was heated to 70°C. Immediately after dissolution, heating was stopped. The reaction mixture was stored at room temperature for 1 h and diluted with water (1 ml). The precipitate that formed was filtered off to give title compound **11** (0.1 g, 89%) as white solid, mp 226–227°C; [Found: C, 64.6; H, 4.4; N, 10.6; S, 8.1. $C_{21}H_{17}N_3O_3S$ requires C, 64.44; H, 4.38; N, 10.73; S, 8.19%]; ν_{max} (KBr), 3336, 2224, 1680, 1664 cm^{-1}; δ_H (250 MHz DMSO-d_6) 1.95 (3H, s, CH_3CO), 3.87 (3H, s, CH_3O), 7.08 (2H, d, 7.7 Hz, Ar), 7.35 (2H, d, *J*=7.7 Hz, Ar), 7.61 (3H, m, Ar), 8.01 (2H, d, *J*=7.7 Hz), 10.00 (1H, s, N*H*), 11.42 (1H, s, N*H*).

3.3. Morpholinium 2-aryl-3-cyano-1-ethoxycarbonyl-1-nitro-3-thiocarbamoylpropyl-1-ates (20a–c). General procedure

(A) Ethyl nitroacetate **19** (0.12 ml, 1.1 mmol) and then morpholine (0.11 ml, 1.25 mmol) were added dropwise to a suspension of the corresponding aldehyde **1**, **8a**, **e** (1 mmol) and cyanothioacetamide **2** (0.1 g, 1 mmol) in absolute ethanol (3 ml). The reaction mixture was stirred at 40–45°C until the starting substances were dissolved. After 10 min, colorless crystals of product **20a–c** were isolated and filtered off.

(B) Compounds **20b**, **c** were prepared as described in procedure A from the corresponding arylidenecyanothioacetamides **9a**, **e** and ethyl nitroacetate **19**. The yields of products by methods A and B differ insignificantly.

3.3.1. Morpholinium 3-cyano-1-ethoxycarbonyl-1-nitro-2-phenyl-3-thiocarbamoylpropyl-1-ate (20a). 45%, mp 114–115°C; [Found: C, 52.8; H, 5.8; N, 13.5; S, 7.6. $C_{18}H_{24}N_4O_5S$ requires C, 52.93; H, 5.92; N, 13.72; S, 7.85%]; ν_{max} (KBr), 3340, 3080, 2248, 1672, 1655, 1583 (as, NO_2), 1385 (s, NO_2) cm^{-1}; δ_H (250 MHz DMSO-d_6) 1.19 (3H, t, *J*=7.8 Hz, CH_3); 3.02 (4H, m, N(CH_2)$_2$), 3.72 (4H, m, O(CH_2)$_2$), 4.15 (2H, q, *J*=7.8 Hz, CH_2), 4.28 (1H, d, $^3J_{3,2}$=4.0 Hz, C(3)*H*), 4.54 (1H, d, $^3J_{2,3}$=4.0 Hz, C(2)*H*), 7.27 (2H, s, NH_2), 7.32–7.37 (5H, m, Ph); *m/z* 275 (35), 241 (55), 229 (48), 201 (27), 187 (22), 155 (32), 128 (42), 115 (53), 102 (21), 87 (100), 77 (100), 57 (78), 46 (70%).

3.3.2. Morpholinium 2-(4-chlorophenyl)-3-cyano-1-ethoxycarbonyl-1-nitro-2-phenyl-3-thiocarbamoylpropyl-1-ate (20b). 65%, mp 126–127°C; [Found: C, 48.8; H, 5.3; Cl, 7.8; N, 12.8; S, 7.0 $C_{18}H_{23}ClN_4O_5S$ requires C, 48.81; H, 5.23; Cl, 8.00; N, 12.65; S, 7.24%]; ν_{max} (KBr), 3367, 3310, 2248, 1677, 1649, 1582, 1385 cm^{-1}; δ_H (250 MHz DMSO-d_6) 1.19 (3H, t, *J*=7.8 Hz, CH_3), 3.03 (4H, m, N(CH_2)$_2$), 3.71 (4H, m, O(CH_2)$_2$), 4.15 (2H, q, *J*=7.8 Hz, CH_2), 4.31 (1H, d, $^3J_{3,2}$=4.4 Hz, C(3)*H*), 4.55 (1H, d, $^3J_{2,3}$=4.4 Hz, C(2)*H*), 7.27 (2H, s, NH_2), 7.33 (2H, d, *J*=7.8 Hz, C_6H_4Cl), 7.43 (2H, d, *J*=7.8 Hz, C_6H_4Cl); δ_c (63 MHz DMSO-d_6) 13.92 (*C*H_3), 42.61, 63.59 ($C_{(morpholine)}$), 52.40 (*C*(2)), 54.41 (*C*(3)), 61.70 (*C*H_2CH$_3$), 69.54 (*C*(1)), 118.04 (*C*≡N), 128.67, 129.28, 132.14, 140.43 (C_6H_4Cl), 162.09 (*C*=O), 169.93 (*C*=S); *m/z* 357 (6, M^+−morpholine), 354 (15), 310 (23), 308 (12), 281 (45), 234 (30), 225 (40), 200 (67), 189 (80), 174 (30), 165 (60), 155 (20), 140 (32), 125 (40), 112 (54), 100 (80), 87 (100), 57 (75), 46 (80), 45 (55%).

3.3.3. Morpholinium 3-cyano-1-ethoxycarbonyl-1-nitro-2-thienyl-3-thiocarbamoylpropyl-1-ate (20c). 50%, mp 122–123°C; [Found: C, 46.5; H, 5.4; N, 13.2; S, 15.3. $C_{16}H_{22}N_4O_5S_2$ requires C, 46.36; H, 5.35; N, 13.52; S, 15.47%]; ν_{max} (KBr), 3359, 3090, 2250, 1673, 1655, 1580, 1390 cm^{-1}; δ_H (250 MHz DMSO-d_6) 1.20 (3H, t, *J*=7.8 Hz, CH_3), 3.01 (4H, m, N(CH_2)$_2$), 3.71 (4H, m, O(CH_2)$_2$), 4.15 (2H, q, *J*=7.8 Hz, CH_2), 4.28 (1H, d, $^3J_{3,2}$=3.9 Hz, C(3)*H*), 4.84 (1H, d, $^3J_{2,3}$=3.9 Hz, C(2)*H*), 7.33 (2H, s, NH_2), 7.44 (1H, d, *J*=8 Hz, thiophene), 7.04 (1H, d, *J*=7.5 Hz, thiophene), 6.99 (1H, t, *J*=8, 7.5 Hz, thiophene).

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