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# STUDY OF THE THREE-COMPONENT REACTION OF α-NITROCARBONYL COMPOUNDS, AROMATIC ALDEHYDES, AND CYANOTHIOACETAMIDE

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*The reaction of benzaldehyde, α-nitro ketone, and cyanothioacetamide in the presence of morpholine has given the novel 3,4-trans-2-R-5-cyano-2-hydroxy-3-nitro-4-phenyl-1,2,3,4-tetrahydropyridine-6-thiolates. It was found that the reaction occurs via the formation of 1-amino-2-cyano-4-nitro-5-oxo-3-phenyl-1,2-pentene-1-thiolate. In the case of α-nitroacetophenone, 3,4-trans-4,5-trans-5-cyano-2-hydroxy-3-nitro-2,4-diphenylhexahydropyridine-6(1H)-thione was also obtained. The use of α-nitroesters in place of the nitro ketones in the reaction leads to morpholinium 2-aryl-1-carbethoxy-3-cyano-1-nitro-3-thiocarbamoylpropyl-1-ates as the single product.*

**Keywords:** Michael adducts, arylidenecyanothioacetamides, 3,4-*trans*-4,5-*trans*-5-cyano-2-hydroxy-3-nitro-2,4-diphenylhexahydropyridine-6(1H)-thione, α-nitro ketones, 3,4-*trans*-1,2,3,4-tetrahydropyridine-6-thiolates, cyanothioacetamide, ethyl nitroacetate.

The reaction of α,β-unsaturated thioamides with α-methylenecarbonyl compounds and with 1,3-dicarbonyl compounds, which leads to 4-aryl-3-cyanopyridine-2(1H)-thiones and to 5-carbonyl-substituted 4-aryl-3-cyano-2-(1H)-dihydropyridinethiones respectively, has been studied before [1]. In our work we have for the first time shown [2] the possibility of using α-nitro ketones in analogous reactions and this broadens the potential synthesis of functionally substituted pyridinethiones.

It has been found that the three component condensation of benzaldehyde (**1**), cyanothioacetamide (**2**), and α-nitroacetophenone (**3**) in ethanol at 40-55°C in the presence of an equimolar amount of morpholine occurs to give morpholinium 3,4-*trans*-5-cyano-2-hydroxy-3-nitro-2,4-diphenyl-1,2,3,4-tetrahydropyridine-6-thiolate (**4**). Carrying out this reaction in absolute ethanol or in methanol at 30-35°C gives the noncyclic Michael adduct morpholinium 1-amino-2-cyano-4-nitro-5-oxo-3,5-diphenyl-1,2-pentene-1-thiolate (**5a**) in 70°C yield. The use of N,N,N',N'-tetramethylethylenediamine (TMEDA) gave the analogous adduct **5b** in 75% yield.

The process of formation of the thiolate **4** is similar to that of forming 3-pyridino-1,2,3,4-tetrahydropyridine-6-thiolates from carbonyl containing pyridinium ylids and arylidenecyanothioacetamides [3-6]. However, the use of the α-nitroacetophenone in place of the ylids permitted one, for the first time and dependent upon the reaction conditions, to obtain either the nitrogroup-containing tetrahydropyridinethiolate **4** or the corresponding noncyclic Michael adduct **5**.

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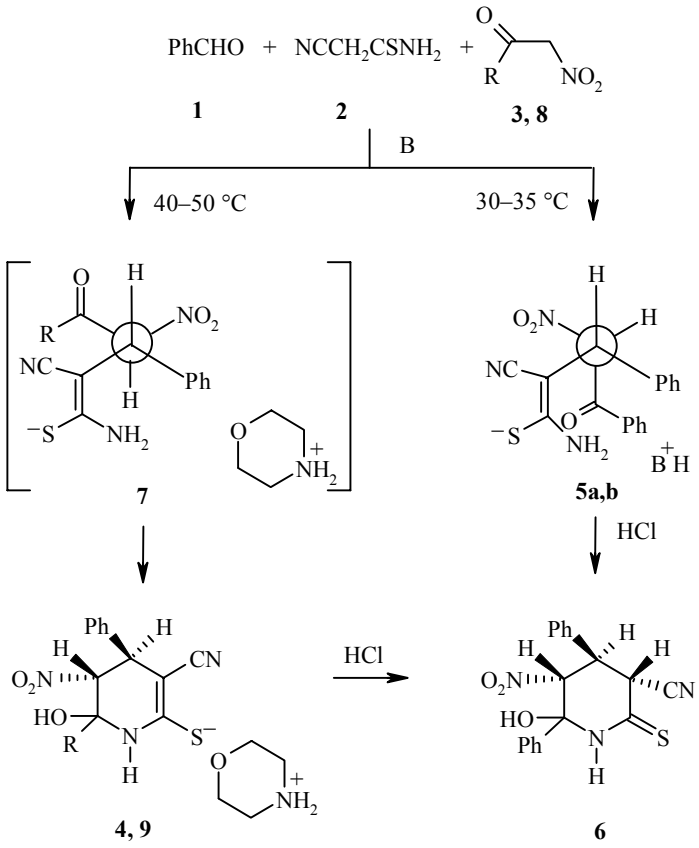


**3, 4** R = Ph; **8, 9** R = Me; **5 a** B = morpholine, **b** B = TMEDA

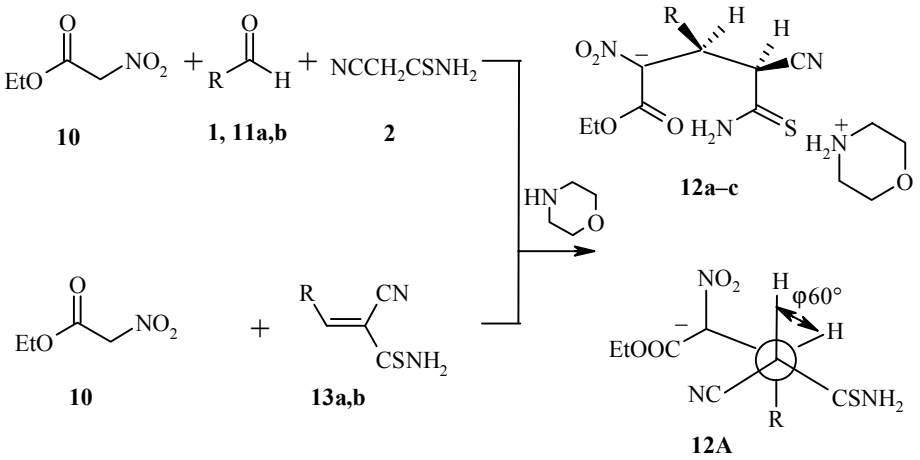
Compounds **4** and **5** probably exist in solutions as a mixture of tautomers. Hence, when the NMR spectra are recorded for DMSO-$d_6$ solutions, after 30-40 min the thiolate **4** is converted to isomer **5** thus indicating the occurrence of such a ring-chain type tautomerism.

Treatment of compounds **4** and **5** or their mixture with concentrated hydrochloric acid at 20°C occurs selectively to give the 3,4-*trans*-4,5-*trans*-5-cyano-2-hydroxy-3-nitro-2,4-diphenylhexahydropyridine-6(1H)-thione (**6**).

The selectivity of the process is evidently determined at the stage of formation of the Michael adducts. It is likely that compound **5** is formed as the kinetically controlled product in the first stage of the reaction with a synclinal positioning of the atoms 3-H and 4-H (*cis*-adduct). Upon increasing the reaction temperature or the time of standing the *cis*-adduct **5** is isomerized to compound **7** with an *anti*-periplanar positioning of atoms 3-H and 4-H (*trans*-adduct) and with subsequent intramolecular cyclization of the latter to the *trans*-adduct **4**.

When the nitroacetone **8** is used in the discussed reaction, the 3,4-*trans*-5-cyano-2-hydroxy-2-methyl-3-nitro-4-phenyl-1,2,3,4-tetrahydropyridine-6-thiolate (**9**) is formed and identification of the corresponding non cyclic Michael adduct did not prove possible in that case.

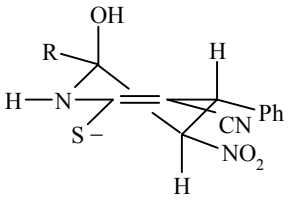
We have also investigated the possible synthesis of 3-nitropyridine derivatives from ethyl nitroacetate (**10**). A three component condensation of the corresponding aromatic aldehyde **1, 11a,b,** cyanothioacetamide **2** and ester **10** gives the fairy stable Michael adduct **12** which has the negative charge localized on atom $C_{(1)}$ bonded to the nitro group.




**1, 12a** R = Ph; **11a, 12b, 13a** R = 4-$ClC_6H_4$; **11b, 12c, 13b** R = 2-$C_4H_3S$

The morpholinium 2-aryl-1-carbethoxy-3-cyano-1-nitro-3-thiocarbamoylpropyl-1-ates **12b,c** were also prepared by the reaction of the arylidenecyanothioacetamides **13a,b** with the ester **10**. Salts of the adducts **12** were quite stable. Thus we were unable to prepare the expected substituted tetrahydropyridines, even by refluxing the Michael adduct salts **12** in ethanol. It is likely that this inertness is connected with the unfavorable (e.g. the antiperiplanar **12A**) steric disposition of the $CSNH_2$ and the $COOC_2H_5$ reaction centers. To a certain extent this is also supported by the physico-chemical analysis of compound **12**.

The structure of the obtained compounds was confirmed by physico-chemical investigation (see Experimental section). The IR spectra of compounds **4** and **9** show absorption bands for all of the functional groups. We note the presence of a characteristically strong signal for the conjugated CN group at 2170 $cm^{-1}$ and signals for the NH or OH groups at 3058 and 3349 $cm^{-1}$. The $^1H$ NMR spectra of compounds **4** and **9** show a signal for the OH group as a singlet at 5.67 and 6.46 ppm respectively. The signals for the 4-H and 3-H protons are characteristic and appear as two doublets at 4.23-4.43 ppm ($^3J$ = 11.7 Hz) for compound **4** and 4.71-4.90 ppm ($^3J$ = 11.5 Hz) for compound **9**. The torsional angles $C_{(3)}H–C_{(4)}H$, calculated from the Karplus–Conroy equation [7] for compounds **4** and **9** with these constants (Φ = 158° and 160° respectively), point to a *trans* pseudoaxial positioning of the hydrogen atoms of the hydrogenated pyridine ring [5, 6]. The pyridinethiolates **4, 9** are similar to cyclohexene [8] and hydrogenated pyridine-2-thiolates [9] and are found in a half chair conformation.




**4, 9**

The $^{13}C$ NMR spectrum also confirms the structure of compound **4**. In the pentad of carbon atoms the signal for $C_{(4)}$ appears at 44.09 and the $C_{(2)}$, $C_{(3)}$, and $C_{(5)}$ at 95.55 101.29, and 111.77 ppm respectively. The characteristic signal for $C_{(6)}$, bonded to the formally negatively charged sulfur atom is at 165.34 ppm.

In the IR spectra, compounds **5a,b** show a significantly lower frequency for the nitrile group absorption (to 2162-2185 $cm^{-1}$) with a simultaneous increase in strength compared with the spectra of 3-cyanopyridine-2(1H)-thiones and this can be rationalized in terms of the increased degree of conjugation in the fragment $NC–C(R)=C(NH_2)S^-$ due to salt formation [5, 6, 10]. In the solid state (KBr tablets) compound **5** contains the

$NH^+$, and $NH_2$ groups and exists in a keto-enol tautomeric equilibrium as indicated by the absorption bands at 1591 and 3064, 3353 $cm^{-1}$ and also the IR spectrum of the thiolate **5b** recorded in THF solution. It is likely that the equilibrium is shifted in solution to ketone [11] (shown by the absorption for the C=O group at 1776 $cm^{-1}$) with a simultaneous charge transfer to the $NO_2$ group (increasing the frequency of the CN group vibration to 2212 $cm^{-1}$). Moreover, the absorption bands for the NH and $NH_2$ groups at 3190 and 3480 $cm^{-1}$ remain broad, which is typical of salts. Overall, to some extent, the IR spectra of compounds **5a,b** point to an acyclic structure for these compounds

The NMR spectra also confirm the linear structure of the thiolates **5a,b**. The $^1H$ NMR spectra show both the multiplets for the phenyl group protons and singlets for the $NH_2$ group protons at 7.16 and 7.15 ppm respectively. The signals for the 3-H and 4-H protons are diagnostic since they appear as two doublets at 4.75 and 5.22 ppm respectively with a spin-spin coupling of $^3J$ = 3.7 Hz. The torsional angle $C_{(3)}H–C_{(4)}H$, calculated from the Karplus–Conroy equation [7] for compounds with this constant (φ = 62°) points to a synclinal positioning of these hydrogen atoms (*cis* Michael adduct).

Among the pentad of carbon atoms in the $^{13}C$ NMR spectrum of compound **5a** the signal for $C_{(3)}$ appears at 50.85 ppm as a doublet with spin spin coupling $^1J_{^{13}C,^1H}$ = 136 Hz (the $^{13}C$ NMR spectrum without suppression of the protons was recorded using the GATE program), that of $C_{(4)}$ at 56.03 ppm as a double doublet with spin-spin coupling $^1J_{^{13}C,^1H}$ = 147 and $^3J_{^{13}C,^1H}$ = 3.8 Hz. The carbon atom signals for the $C_{(5)}$=O at 193.03 ppm and the $C_{(1)}$ atom bonded to the formally negatively charged sulfur atom at 161.18 ppm are diagnostic.

Along with other signals in the IR spectrum of compound **6** there is observed an absorption band at 2278 $cm^{-1}$ which is typical of the nonconjugated CN group [12, 13]. The $^1H$ NMR spectra show both a multiplet for the phenyl protons and singlet signals for the protons of the OH and NH groups at 7.92 and 11.50 ppm respectively. The signals for the protons of the hydrogenated pyridine ring are an important feature since the signal for the 4-H proton appears as a triplet at 4.44 ppm, the 5-H is a doublet at 4.96 ppm with spin-spin coupling $^3J_{5,4}$ = 11.5 Hz, and the 3-H is a doublet at 5.79 ppm with $^3J_{4,3}$ = 12.6 Hz. The torsional angles $C_{(5)}H–C_{(4)}H$ and $C_{(3)}H–C_{(4)}H$, calculated from the Karplus–Conroy equation [7] based on these constants (φ = 158 and 169° respectively) point to a *trans,trans*-pseudoaxial positioning of the hydrogen atoms in the pyridine ring. The $^{13}C$ NMR spectra also confirm the structure of compound **6** and indicate that this compound exists in the thione tautomeric form. The signal for the $C_{(2)}$ atom in the pyridine ring is at 191.98 ppm which is typical of a pyridine ring containing the C=S fragment with an exocyclic double bond. In addition, the positions of the signals for the $C_{(4)}$, $C_{(5)}$, and $C_{(3)}$ atoms of the hydrogenated pyridine ring at 42.02, 49.44, and 83.66 ppm respectively are typical.

Molecular ion peaks for compounds **4**, **5**, and **9** are absent in their mass spectra. However, they show the presence of a peak at *m/z* 335 in the product of molecular fission under electron impact arising from loss of morpholine and water and also a peak characteristic for fission of a nitro compound peak arising from the loss of one (*m/z* 319) or two (*m/z* 304) oxygen atoms from the nitro group [14]. The mass spectra for compound **9** are similar and contain peaks which are formed after elimination of morpholine (*m/z* 291) and water (*m/z* 271) from the molecule as well as peaks which typify the decomposition a nitro compound arising from the loss of a molecule of water and an oxygen atom from the nitro group (*m/z* 257). In the mass spectrum of compound **6** the intensity of the molecular ion peak (*m/z* 353) is very low and there are also present characteristic peaks at *m/z* 335 and 319.

Physicochemical analytical data for the salts of the adducts **12** confirms their linear structure and, to some extent, their stability towards cyclization reactions. In the IR spectra of compound **12** there are present characteristic, low intensity signals for the nonconjugated CN group in the region 2248-2250, broad signals for the $NH_2$ group in the region 3340-3367 and 3080-3110, and bending vibrations signals for the $NH_2$ group at 1649-1655 $cm^{-1}$ as well as signals for a carbonyl group at 1672-1677 $cm^{-1}$. The data indicates that the negative charge in the molecule of compound **12** is found in the fragment $[O_2NCCOOC_2H_5]^-$ and not in the $[NCCCSNH_2]$ fragment as observed for compound **5**.

The $^1$H NMR spectra of compound **12a-c** show singlet signals for the protons of the $NH_2$ group protons in the region 7.27-7.33 ppm. The signals for the 3-H and 2-H protons, which are observed as doublets in the regions 4.28-4.31 and 4.54-4.85 ppm with a spin-spin coupling $^3J$ = 4 Hz are characteristic. The torsional angle $C_{(2)}H–C_{(3)}H$, calculated from the Karplus–Conroy equation [7] based on these constants (φ = 60°) point to a synclinal positioning of the hydrogen atoms (*cis* Michael adduct).

The $^{13}$C NMR spectrum of compound **12b** shows a typical carbonyl carbon atom signal (C=O) at 169.93 and a thione carbon atom (C=S) at 162.09 ppm. The signal for $C_{(2)}$ appears at 52.40, $C_{(3)}$ at 54.41, and $C_{(1)}$ bearing the negative charge at 69.54 ppm.

In the mass spectra of compounds **12a,b**, the molecular ion peaks are absent but typical peaks are seen which arise from fission of morpholine (*m/z* 357 from compound **12b**) and ethanol or a nitro group (*m/z* 275 and 310 respectively).

## EXPERIMENTAL

Melting points were determined on a Koffler stage. IR spectra were taken on a Perkin-Elmer 577 spectrometer for KBr tablets and $^1$H and $^{13}$C NMR spectra on a Bruker WM-250 (250 and 63 MHz respectively) for solutions in DMSO-$d_6$. Mass spectra were obtained on a Finnigan MAT INCOS-50 instrument (ionization energy 70 eV). Elemental analysis was performed on a Perkin-Elmer C, H, N analyser.

**Morpholinium 3,4-*trans*-5-Cyano-2-hydroxy-3-nitro-2,4-diphenyl-1,2,3,4-tetrahydropyridine-6-thiolate (4).** Morpholine (0.01 ml) was added to a suspension of the nitro ketone **3** (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 held at 40-55°C until solution of the starting materials, and then more morpholine (0.63 ml, 7.2 mmol) was added. After 4-5 min stirring with a glass rod gave a crystalline precipitate. The white solid produced was filtered off to give the product **4** (1.76 g, 65%); mp 144-145°C. IR spectrum, ν, cm$^{-1}$: 2170 (CN), 1553 (as, $NO_2$), 1372 (s, $NO_2$), 3058, 3349 (br, OH, NH). $^1$H NMR spectrum, δ, ppm, *J* (Hz): 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, 4-H); 4.90 (1H, d, $^3J_{3,4}$ = 11.5, 3-H); 5.67 (1H, s, OH); 7.15-7.68 (10H, m, $H_{Ph}$). $^{13}$C NMR spectrum, δ, ppm: 42.97 and 63.62 ($C_{morpholine}$); 44.09 ($C_{(4)}$); 95.5 ($C_{(2)}$); 101.29 ($C_{(3)}$); 111.77 ($C_{(5)}$); 115.38 (C≡N); 124.43; 126.82; 127.49; 128.17; 128.55; 128.77; 132.29; 133.71; 143.27 ($C_{Ph}$); 165.34 ($C_6$). Mass spectrum, *m/z*: 335, 319, 304, 273, 187, 105, 87, 77. Found, %: C 59.62; H 5.61; N 12.56; S 6.52. $C_{18}H_{15}N_3O_3S·C_4H_9NO$. Calculated, %: C 59.98; H 5.49; N 12.72; S 7.28.

**Morpholinium 1-Amino-2-cyano-4-nitro-5-oxo-3,5-diphenyl-1,2-pentene-1-thiolate (5a).** Morpholine (0.01 ml) and the nitro ketone **3** (1.01 g, 6 mmol) were added to a suspension of benzaldehyde **1** (0.65 g, 6.1 mmol) and cyanothioacetamide **2** (0.61g, 6.1 mmol) in absolute ethanol (15 ml), the mixture was held at 30-35°C until a solution was formed, and then morpholine (0.63 ml, 7.2 mmol) was added. After 4-5 min stirring with a glass rod gave a crystalline precipitate. The white solid produced was filtered off to give the product **5a** (1.84 g, 70%); mp 124-125°C. IR spectrum, ν, cm$^{-1}$ : 2162 (CN), 1557 (as, $NO_2$), 1370 (s, $NO_2$), 3064, 3353 (br, OH, $NH_2$), 1591 (δ, $NH_2$). $^1$H NMR spectrum, δ, ppm, *J* (Hz): 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, 3-H); 5.22 (1H, d, $^3J_{4,3}$ = 3.7, 4-H); 7.16 (2H, s, $NH_2$); 7.30-7.60 (8H, m, $H_{Ph}$); 7.90 (2H, d, *J* = 7.6, $H_{Ph}$). $^{13}$C NMR spectrum δ, ppm, *J* (Hz): 43.17 and 64.07 ($C_{morpholine}$); 50.85 ($C_{(3)}$, d, $^1J_{^{13}C,^1H}$ = 136); 56.03 ($C_{(4)}$, dd, $^1J_{^{13}C,^1H}$ = 147, $^3J_{^{13}C,^1H}$ = 3.8); 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). Mass spectrum, *m/z*: 335, 319, 304, 289, 273, 187, 105, 87,77. Found, %: C 59.92; H 5.56; N 12.12; 2. S 6.73. $C_{18}H_{15}N_3O_3S·C_4H_9NO$. Calculated, %: C 59.98; H 5.49; N 12.72; S 7.28.

**N,N-Tetramethylethylenediaminium 1-Amino-2-cyano-4-nitro-5-oxo-3,5-diphenyl-1,2-pentene-1-thiolate (5b)** was prepared similarly to compound **5a** as a white product with mp 123-124°C using TMEDA in place of morpholine in a yield of 2.03 g (75%). IR spectrum (KBr), ν, cm$^{-1}$: 2185 (CN), 1555 (as, $NO_2$), 1370 (s,

$NO_2$), 3250 (br, OH, NH). IR spectrum (THF solution), ν, $cm^{-1}$: 2212 (CN), 1555 (as, $NO_2$), 1370 (s, $NO_2$), 3190 and 3480 (br, OH, NH), 1776 (C=O), 1590 and 1680 sh (δ, $NH_2$). $^1$H NMR spectrum, δ, ppm, *J* (Hz): 2.45 (12H, s, 2 $N(CH_3)_2$); 3.44 (4H, m, $CH_2CH_2$); 4.75 (1H, d, $^3J_{3,4}$ = 3.7, 3-H); 5.22 (1H, d, $^3J_{4,3}$ = 3.7, 4-H); 7.15 (2H, s, $NH_2$); 7.30-7.65 (8H, m, $H_{Ph}$); 7.95 (2H, d, *J* = 7.7, $H_{Ph}$). $^{13}$C NMR spectrum, δ, ppm: 43.69 and 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). Mass spectrum, *m/z*: 319, 304, 273, 187, 116, 105, 77. Found, %: C 61.35; H 6.52; N 14.43; S 6.37. $C_{18}H_{15}N_3O_3S.C_6H_{16}N_2$. Calculated, %: C 61.38; H 6.65; N 14.91; S 6.83.

**3,4-*trans*-4,5-*trans*-5-Cyano-2-hydroxy-3-nitro-2,4-diphenylhexahydropyridine-6(1H)-thione (6).** Concentrated hydrochloric acid (4 ml, 4.14 mmol) was added dropwise with stirring to a suspension of the salt **4** (1.82 g, 4.14 mmol) in ethanol (10 ml). After 4 h the white precipitate was filtered off and washed successively with water, ethanol, and hexane to give the product **6** (1.32 g, 90%); mp 154-155°C (decomp.). IR spectrum, ν, $cm^{-1}$: 2278 (CN), 1563 (as, $NO_2$), 1360 (s, $NO_2$), 3130, 3280 (br, OH, NH). $^1$H NMR spectrum, δ, ppm, *J* (Hz): 4.44 (1H, t, $^3J_{4,5}$ = 11.5, $^3J_{4H,3H}$ = 12.6, 5-H); 4.96 (1H, d, $^3J_{5,4}$ = 11.5, 5-H); 5.79 (1H, d, $^3J_{3,4}$ = 12.6, 3-H); 7.92 (1H, s, OH); 7.34-7.61 (10H, m, $H_{Ph}$); 11.50 (1H, s, NH). $^{13}$C NMR spectrum, δ, ppm: 42.02 ($C_{(4)}$); 49.41 ($C_{(5)}$); 83.66 ($C_{(3)}$); 95.45 ($C_{(2)}$); 116.83 (C≡N); 126.34; 127.99; 128.22; 128.56; 128.91; 136.03; 136.88 ($C_{Ph}$); 191.98 (C=S). Mass spectrum: 352, 335, 319, 307, 273, 187, 105, 77. Found, %: C 61.18; H 4.04; N 11.91; S 9.02. $C_{18}H_{15}N_3O_3S$. Calculated, %: C 61.18; H 4.28; N 11.89; S 9.07.

Compound **6** was prepared similarly from salt **5a** in 89% yield.

**Morpholinium 3,4-*trans*-5-Cyano-2-hydroxy-2-methyl-3-nitro-4-phenyl-1,2,3,4-tetrahydropyridine-6-thiolate (9)** was prepared similarly to compound **4** using the nitroacetone **8** instead of the nitroacetophenone **3** and was obtained in 45% yield as a white product; mp 144-145°C. IR spectrum, ν, $cm^{-1}$: 2170 (CN), 1554 (as, $NO_2$), 1372 (s, $NO_2$), 3058, 3349 (br, OH, NH). $^1$H NMR spectrum, δ, ppm, *J* (Hz): 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, 4-H); 4.71 (1H, d, $^3J_{3,4}$ = 11.7, 3-H); 6.46 (1H, s, OH); 7.05-7.38 (5H, m, $H_{Ph}$). Mass spectrum, *m/z*: 291, 271, 257, 226, 201, 187, 128, 87, 77, 57, 43. Found, %: C 54.23; H 6.19; N 13.98; S 8.5. $C_{13}H_{13}N_3O_3S.C_4H_9O$. Calculated, %: C 53.95; H 5.86; N 14.80; S 8.47.

**Morpholinium 2-Aryl-3-carbamoyl-1-carbethoxy-3-cyano-1-nitropropyl-1-ates (12a-c). (General Method).** A. Ethyl nitroacetate (**10**, 0.12 ml, 1.1 mmol) was added dropwise to a suspension of the corresponding aldehyde **1, 11a,b** (1 mmol) in absolute ethanol (3 ml) followed by morpholine (0.11 ml, 1.25 mmol). The reaction mixture was stirred at 40-55°C until the starting materials had dissolved. After 10 min the colorless crystalline product **12a-c** was filtered off.

B. Compounds **12b,c** were obtained by method A from the corresponding arylidenecyanothioacetamides **13a,b** and ethyl nitroacetate **10**. The yields of the products using methods A and B differed little.

**Compound 12a.** Yield 45%; mp 114-115°C. IR spectrum, ν, $cm^{-1}$: 2248 (CN), 3340, 3080 ($NH_2$), 1672 (C=O), 1655 sh (δ, $NH_2$), 1583 (as, $NO_2$), 1385 (s, $NO_2$). $^1$H NMR spectrum, δ, ppm, *J* (Hz): 1.19 (3H, t, $^3J$ = 6.6, $CH_3$); 3.02 (4H, m, $N(CH_2)_2$); 3.72 (4H, m, $O(CH_2)_2$); 4.15 (2H, q, $^3J$ = 6.6, $CH_2$); 4.28 (1H, d, $^3J_{3,2}$ = 4.0, 3-H); 4.54 (1H, d, $^3J_{2,3}$ = 4.0, 2-H); 7.27 (2H, s, $NH_2$); 7.32-7.37 (5H, m, Ph). Mass spectrum, *m/z*: 275, 241, 229, 201, 187, 155, 128, 115, 102, 87, 77, 57, 46. Found, %: C 52,83; H 5.75; N 13.52; S 7.55. $C_{14}H_{15}N_3O_4S.C_4H_9O$. Calculated, %: C 52.93; H 5.92; N 13.72; S 7.85.

**Compound 12b.** Yield 65%; mp 126-127°C. IR spectrum, ν, $cm^{-1}$: 2248 (CN), 3367, 3310 ($NH_2$), 1677 (C=O), 1649 sh (δ, $NH_2$), 1582 (as, $NO_2$), 1385 (s, $NO_2$). $^1$H NMR spectrum, δ, ppm, *J* (Hz): 1.19 (3H, t, $^3J$ = 7.1, $CH_3$); 3.03 (4H, t, *J* = 5.0, *J* = 4.4, $N(CH_2)_2$); 3.71 (4H, t, *J* = 5.0, *J* = 4.4, $O(CH_2)_2$); 4.15 (2H, q, $^3J$ = 7.1, $CH_2$); 4.31 (1H, d, $^3J_{3,2}$ = 4.4, 3-H); 4.55 (1H, d, $^3J_{2,3}$ = 4.4, 2-H); 7.27 (2H, s, $NH_2$); 7.33 (2H, d, $^3J$ = 8.2, $C_6H_4Cl$); 7.43 (2H, d, $^3J$ = 8.2, $C_6H_4Cl$). $^{13}$C NMR spectrum, δ, ppm: 13.92 ($CH_3$); 42.61 and 63.59 ($C_{morpholine}$); 52.40 ($C_{(2)}$); 54.41 ($C_{(3)}$); 61.70 ($\underline{C}H_2CH_3$); 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). Mass spectrum, *m/z*: 357, 354, 310, 308, 281, 234, 225, 200, 189, 174, 165, 155, 140, 125, 112, 100, 75, 57, 46, 45. Found, %: C 48.81; H 5.27; Cl 7.79; N 12.75; S 7.04. $C_{14}H_{14}ClN_3O_4S.C_4H_9NO$. Calculated, %: C 48.81; H 5.23; Cl 8.00; N 12.65; S 7.24.

**Compound 12c.** Yield 50%; mp 122-123°C. IR spectrum, ν, $cm^{-1}$: 2250 (CN), 3359, 3090 ($NH_2$), 1673 (C=O), 1655 sh (δ, $NH_2$), 1580 (as, $NO_2$), 1390 (s, $NO_2$). $^1H$ NMR spectrum, δ, ppm, *J* (Hz): 1.20 (3H, t, $^3J = 7.2$, $CH_3$); 3.01 (4H, t, $J = 5.0$, $J = 4.4$, $N(CH_2)_2$); 3.71 (4H, t, $J = 5.0$, $J = 4.4$, $(OCH_2)_2$); 4.15 (2H, q, $J = 7.2$, $CH_2$); 4.28 (2H, d, $^3J_{3,2} = 3.9$, 3-H); 4.84 (1H, d, $^3J_{2,3} = 3.9$, 2-H); 7.33 (2H, s, $NH_2$); 7.44 (1H, d, $^3J_{3,4} = 4.4$, thiophene); 7.04 (1H, d, $^3J_{5,4} = 3.7$, thiophene); 6.99 (1H, t, $^3J_{4,3} = 4.4$, $^3J_{4,5} = 3.8$, thiophene). Found, %: C 46.47; H 5.44; N 13.21; S 15.27. $C_{12}H_{13}N_3O_4S_2.C_4H_9NO$. Calculated, %: C 46.36; H 5.35; N 13.52; S 15.47.

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