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# RING TRANSFORMATION REACTIONS STARTING FROM 6-IMINO-6*H*-1,3-THIAZINES

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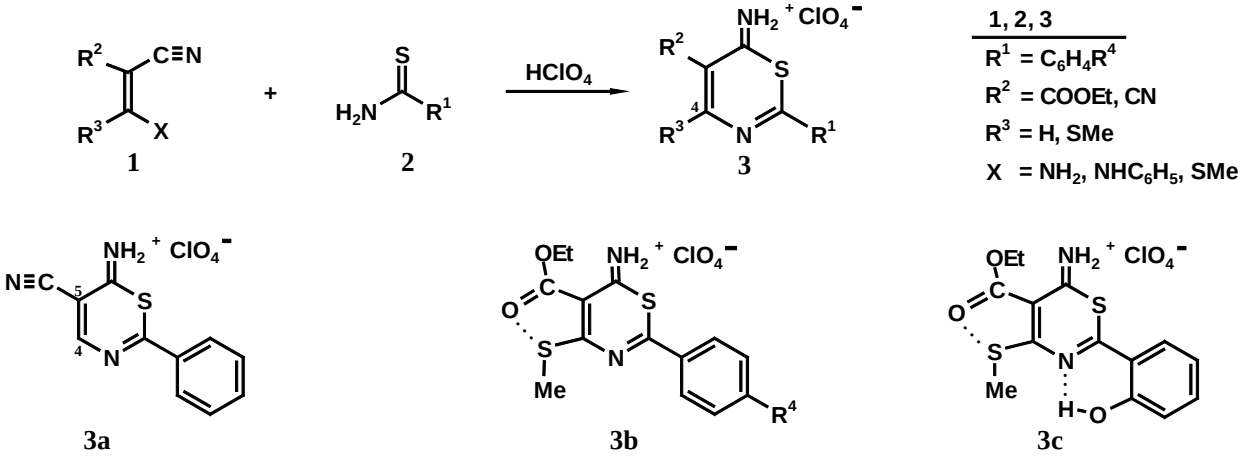
**Abstract** - Ring transformation reactions of 6-imino-*6H*-1,3-thiazines (**4**), 6-imino-*6H*-1,3-thiazine hydroperchlorates (**3**), respectively, are initiated under basic conditions by a ring opening of the thiazine nucleous. Two possibilities exist, either intramolecular elimination occurs to give acrylonitriles (**5**), or addition of a nucleophile (YH) results in the formation of substituted acrylthioamides (**6**). The way by which stable products were formed depends on both the functionality of the thiazine, and the reaction conditions. The way **4** → **5** produce 1,3-benzoxazines (**8**), or 1,2,4-dithiazoles (**14**), respectively. The way **4** → **6** gives pyrimidinethiones (**7**), or 1,2-dithioles (**17**), respectively. Upon treatment of thiazine perchlorates (**3**) with alkylhalides under basic conditions, acrylonitriles (**18**) are formed by the way **4** → **5**. Compounds (**18**) can be transformed to 1,2,4-triazoles (**19**).

## INTRODUCTION

*6H*-1,3-Thiazines bearing an oxo-[1-5] or thioxo function[4-8] at position 6 are known as starting materials for the preparation of heterocycles *via* ring transformations.[7,9] Both 6-oxo- and 6-thioxo-*6H*-1,3-thiazines are stable and well characterized,[1,4-13] whereas 6-imino derivatives readily undergo further transformations[14-19] and could be isolated only in exceptional cases, e.g. the preparation of bicyclic 6-imino-*6H*-1,3-thiazines, such as benzo-,[20,21] pyrazolo-,[22,23] and thienothiazines,[11] as well as tricyclic thiazines[20,24-29] which have been described. Typically, these thiazines underwent a Dimroth rearrangement to 6-thioxopyrimidine derivatives.[11,20-28] However, certain fused 6-imino-*6H*-1,3-thiazines did not undergo a Dimroth rearrangement in the present of bases, but were transformed by a ring opening reaction to 3-thioaroylaminoacrylonitriles. Such acrylonitrile derivatives could be converted to thiazines by

recyclization reactions.[11,24,25,27]

Similar reactivity of monocyclic thiazines has also been described. Thus, thioxopyrimidines (**7**) have been prepared from 3-thioaroylaminoacrylonitriles (**5**) *via* 6-imino-*6H*-1,3-thiazines (**4**), thioamides (**6**) (Scheme 2).[7,14,30] In this transformation, thiazines (**4**) were not isolated. The isolation of mono- cyclic 6-imino-*6H*-1,3-thiazines could only be achieved in certain situations, e.g. in cases in which a special functionalization resulted in a favored formation of a tautomeric 6-amino structure,[6,31,32] or in cases in which substitution at the exocyclic nitrogen inhibited rearrangement to thioxopyrimidines.[32,33] There is only one general method described so far, that allows for the synthesis of the reactive, monosubstituted 6-imino-*6H*-1,3-thiazines: Acrylonitrile derivatives (**1**) (Scheme 1) were reacted with aromatic thioamides (**2**) under acidic conditions to obtain 6-imino-*6H*-1,3-thiazines as stable hydroperchlorates (**3**). Additional stabilization can be achieved with methylthio ($R^3$) as donor substituent at position 4 of the thiazine ring (push-pull-effect), to allow for the isolation of the corresponding thiazine bases.[34] Iminothiazine hydroperchlorates (**3a**-**c**) were used as starting compounds for the present investigations. Since these substrates are differently functionalized, diverse reaction mechanism are possible. **3a** (Scheme 1) was found to be highly reactive; an attempt to wash the crystals with water immediately led to hydrolysis. Thiazine salts (**3b**) and (**3c**) are less reactive. After preparation, the crystals could be washed with water and the compounds were found to be stable during storage. Compared to **3a**, the different substitution at positions 4 and 5 lead to an increased electron density in the thiazine ring of **3b** and **3c**. Furthermore, in **3b** and **3c**, a nonbonded polar interaction between the exocyclic sulfur and the carbonyl oxygen accounts for the increased stability.[34] Additionally, the formation of a hydrogen bond in **3c** is likely.




Scheme 1

It was considered that thiazine perchlorates (**3**), upon treatment with bases might undergo two alternative ring opening reactions and that the competing steps might be both reversible (Scheme 2):

Attack of a nucleophile at the thiazine C-2 atom leads to the formation of thioamides (**6**), whereas

elimination results in the formation of nitriles (**5**). Preference to the one or the other transformation should depend on the reaction conditions as well as the substitution at the thiazine. Investigations on such thiazine transformations provide informations that are helpful to utilize 6-imino-*6H*-1,3-thiazines as substrates to prepare heterocycles via ring transformation reactions.

## RESULTS AND DISCUSSION

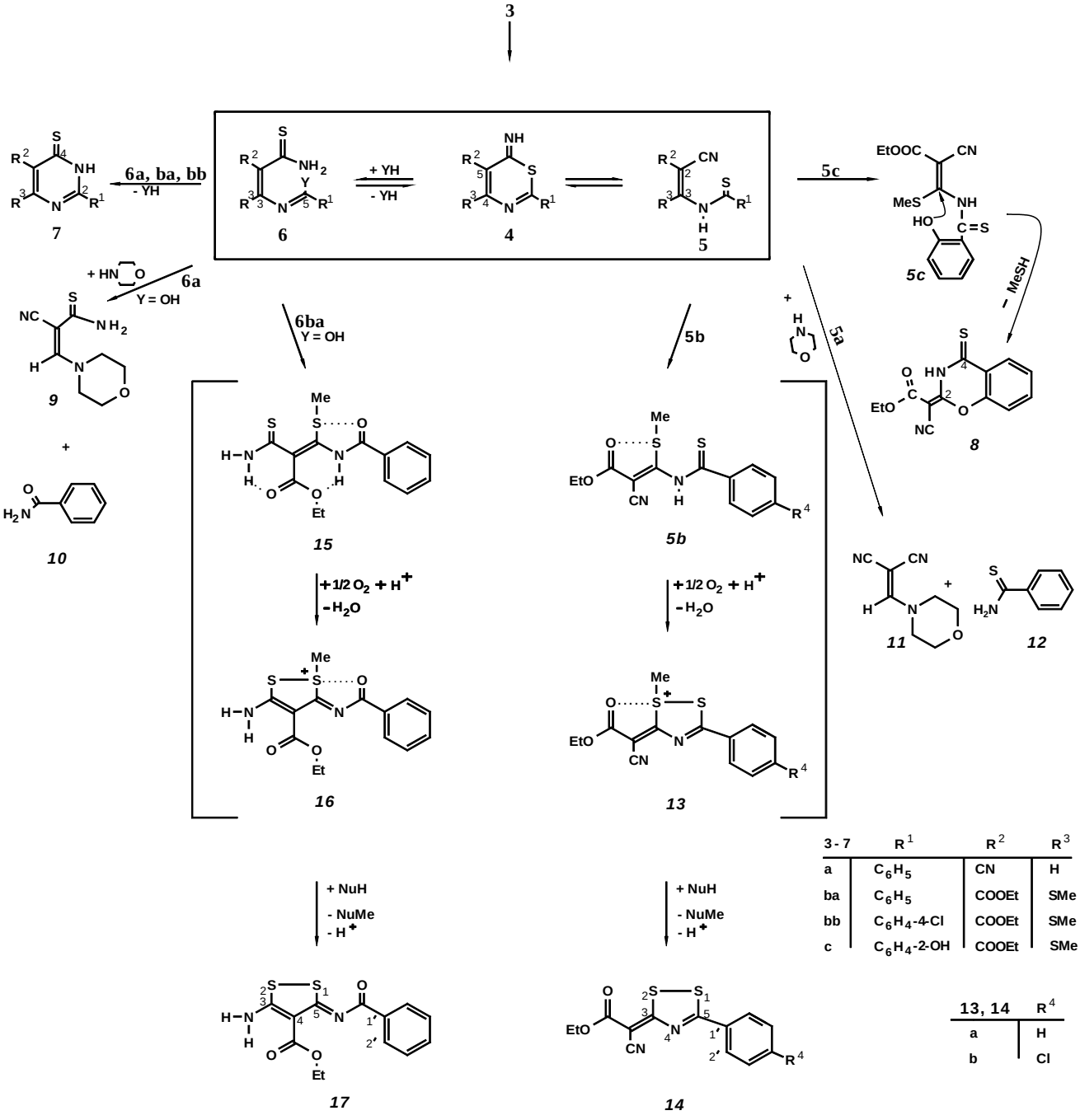
Hydrolysis of **3a** (Scheme 2) gave the thioamide (**6a**) (Y = OH), which was isolated quantitatively. When **6a** was dissolved in aqueous sodium hydroxide (1 mol/L), cyclocondensation led to the thioxopyrimidine (**7a**). Treatment of **6a** with morpholine, instead of hydroxide, resulted in a cleavage reaction to produce the morpholinothioamide (**9**) and benzamide (**10**). Thus, in **6a**, the thioamide carbon C-3 was found to be more reactive towards morpholine compared to the competing intramolecular reaction of the carbon C-5 with the thioamide moiety.

When thiazine perchlorate (**3a**) was treated with morpholine, instead of hydroxide, the morpholinonitrile (**11**) together with thiobenzamide (**12**) were isolated. Thus, the alternative pathway *via* **5** was operative in this transformation. The reaction of the initially formed nitrile (**5**) with morpholine was similar to those of the thioamide (**6**); the (thio)aroylamino residue at C-3 was displaced by morpholine in both cases.

The reaction of the 2-phenyl-1,3-thiazine (**3ba**) with morpholine did not involve a cleavage reaction, but followed the route **3** → **4** → **6** → **7** to furnish the corresponding (**7ba**). The same product was also obtained in 92% yield when **3ba** was reacted with hydroxide instead of morpholine. Reaction of the 2-(4-chlorophenyl)-*6H*-1,3-thiazine (**3bb**) with sodium hydroxide or morpholine also afforded the corresponding thioxopyrimidine (**7bb**). The yield, however, was considerably lower (24% in the reaction with sodium hydroxide) and the 1,2,4-dithiazole (**14b**) was isolated as an unexpected byproduct. The formation of **14b** from **3bb** is assumed to be initialized by an eliminating ring cleavage of the substrate to the nitrile (**5**), followed by an oxidation step and displacement of a methyl group. It is known, that in substituted enamino esters the free rotation around the C-3–N bond is hindered leading to corresponding rotamers.[35] Since two enolizable sulfur atoms are required for the formation of **14b**, it was assumed that the intermediate (**5b**) might be transformed into the intermediate (**13**) under the influence of air oxygen. Subsequently, the methyl group of **13** might be transferred to a nucleophile (NuH, possibly another molecule **5b**) of the reaction mixture. However, an alternative mechanism to produce **14**, by which another molecule (**5b**) would act as sulfur donor is possible.

A *Z*-configuration around the C-2–C-3 double bond in nitriles (**5**) is assumed to be stabilizyd by non-bonding S···O=C interaction, as reported for similar structures.[36,37] Since **14** exhibit the same configuration, a participation of the S···O=C interaction is also assumed for the intermediates leading to **14**. When

**3bb** was treated with an equimolar excess of sodium acetate in DMSO at room temperature, the dithiazole (**14b**) was isolated as the main product. Under such mild conditions, also **3ba** gave the corresponding dithiazole (**14a**), together with the thioxopyrimidine (**7ba**). The crystal structure analysis of **14a** showed, except for the ethyl rest, a planar orientation of the molecule. The distance between the sulfur S-2 and the carbonyl oxygen, being 2.526 Å, indicated a polar interaction between both atoms.[34,36,37,38] MS of **14a**, **14b** are characterized by [$R_4$-$C_6H_4$-C≡$NH^+$], [$R_4$-$C_6H_4$-C≡$N^+$], and [$R_4$-$C_6H_4$-C≡$S^+$] fragment ions, besides the corresponding molpeaks. Base peaks in the mass spectra of **14a** (*m/z* = 105), **14b** (*m/z* = 139), respectively, were considered as [$R_4$-$C_6H_4$-CH=$NH^+$] or [$R^4$-$C_6H_4$-C≡$O^+$] ions. However, high-resolution mass spectra revealed the formation of [$R_4$-$C_6H_4$-C≡$O^+$] ions.




Scheme 2

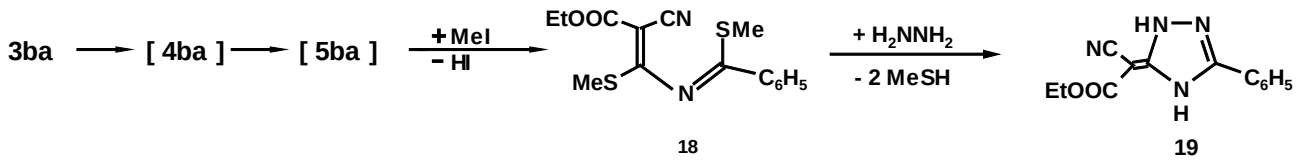
Likely, rearrangement reactions, involving the participation of the ester oxygen, are responsible for these fragmentations.

An alternative pathway was observed to be dominant in the absence of a base. Thus, thiazine (**4ba**) was treated with aqueous DMF at room temperature for three weeks to give the 1,2-dithiole (**17**). The crystal structure of **17** indicated a polar interaction between the sulfur atom S-1 and the carboxamide oxygen; the distance was only 2.324 Å. The C-5–S-1 distance (1.774 Å) within the dithiole ring showed the expected value for a single bond. The S-2–C-3 distance, being 1.728 Å was shorter than expected for a single bond, thus indicating a partial double bond character. Furthermore, planar orientation of the molecule was observed and a hydrogen bond between the ester carbonyl oxygen and the amino group was concluded.

Likely, the formation of **17** involves the hydrolytic ring cleavage to the thioamide (**6**), and the formation of an isomeric form, that allows for the oxidative S–S-coupling and demethylation. Thus, the mechanism is similar to the formation of **14**. Compared to the conversion to **14**, in the formation of **17**, additional a *E/Z*-isomerization had to be occurred. In structures with a similarly delocalized $\pi$ electron system,[7,30,39,40] the corresponding energy barrier is relatively low.

When thiazine salt (**3c**) was treated with morpholine, the formation of a thioxopyrimidine was not observed, but benzoxazine (**8**) was isolated in 47% yield. This conversion is thought to involve the intermediates (**5**) and (**5c**) which cyclized under elimination of methyl mercaptane. The transformation revealed the preferred pathway **4** $\rightarrow$ **5**, compared to **4** $\rightarrow$ **6**. Similar reactions of intermediate (hetero)-Salicoylaminoacrylonitriles have been reported.[39] The ortho hydroxy group strongly influenced the reaction course and alternative cyclization did not occur. On optimizing the preparation, **8** was obtained in 76% yield by using triethylamine instead of morpholine.

The potential of 6-imino-*6H*-1,3-thiazines as starting materials for ring transformations was extended by alkylating the corresponding intermediates (Scheme 3). Compound (**3ba**) was dissolved in a mixture of MeOH and triethylamine and treated with methyl iodide. Nitrile (**18**) was obtained quantitatively as *E/Z*-mixtures (approximately 1:1). The possibility of further syntheses of heterocycles by reacting nitriles (**18**) with nitrogen nucleophiles was investigated. Thus, **18** was treated with hydrazine to yield the triazole (**19**).




18 19

**Scheme 3**

## EXPERIMENTAL

Melting points are uncorrected. IR spectra were measured with a Perkin Elmer 16 PC FTIR spectrophotometer. $^{1}$H-NMR spectra and $^{13}$C-NMR spectra were recorded on a Varian Gemini 300. MS were recorded on a JEOL JMS-D 100 spectrometer. For details in X-Ray structure analysis, see ref.[41]

### 5-Ethoxycarbonyl-2-(2-hydroxyphenyl)-6-imino-4-methylsulfanyl-6*H*-1,3-thiazine hydroperchlorate (3c)

Salicylic acid thioamide[43] (1.4 g, 9.2 mmol) was added to a stirred solution of ethyl 2-cyano-3,3-bis-(methylsulfanyl)acrylate[42] (2.0 g, 9.2 mmol) in a solution of $HClO_4$ in AcOH (8 mL, 2.3 mol/L). The mixture was heated at 60 °C for 30 min. The mixture was filtered off to yield **3c** (2.6 g, 67%) as yellow crystals, mp 211-216 °C (AcOH).

IR (KBr): ν = 3270, 3200, 3140 (OH, NH), 1685 (C=O), 1600 cm$^{-1}$.

$^{1}$H-NMR (DMSO-$d_6$, 250 MHz): δ = 1.35 (t, 3H, J= 7.1 Hz, $CH_2C\underline{H}_3$), 2.74 (s, 3H, $SCH_3$), 4.42 (q, 2H, J= 7.1 Hz, $CH_2$), 7.09 (t, 1H, J= 8.1 Hz, phenyl-5-H), 7.12 (d, 1H, J= 8.1 Hz, phenyl-3-H), 7.64 (t, 1H, J= 8.2 Hz, phenyl-4-H), 8.31 (d, 1H, J= 8.2 Hz, phenyl-6-H), 9.5-11.1 (br, 3H, NH, OH).

MS (EI, 70 eV): *m/z* (%) = 322 (1, $[M\text{-}HClO_4]^+$); 274 (39, $[M\text{-}HClO_4\text{-}HSCH_3]^+$); 228 (88, $[M\text{-}HClO_4\text{-}94]^+$); 137 (100, $[HOC_6H_4CS]^+$); 136 (98, $[OC_6H_4CS]^+$); 121 (62, $[HOC_6H_4CO]^+$); 120 (95, $[OC_6H_4CO]^+$ resp. $[HOC_6H_4CNH]^+$).

Anal. Calcd for $C_{14}H_{14}N_2O_3S_2 \cdot HClO_4$: C 39.76, H 3.58, N 6.26, S 15.17, Cl 8,38; Found: C 39.72, H 3.60, N 6.46, S 15.08, Cl 8.45.

### 3-Benzoylamino-2-cyanothioacrylamide (6a, Y = OH)

Compound **(3a**) (0.6 g, 1.9 mmol, freshly synthetized crude product[34]) was triturated with 5 mL $H_2O$, filtered off and dried on air to yield **6a** (Y = OH) (0.37 g, 94%) as yellow needles, mp 191-203 °C (AcOH); lit.,[34] mp 187-203 °C.

### 3,4-Dihydro-2-phenyl-4-thioxopyrimidine-5-carbonitrile (7a)

Compound (**6a**) (0.5 g, 2.2 mmol) was dissolved in 5 mL NaOH (1 mol/L). The mixture was stirred at rt for 2 min and was then acidified with HCl (1 mol/L). The solid residue was filtered off and recrystallized from $CH_3CN$ to yield **7a** (0.45 g, 96%) as yellow needles,
mp 217-230 °C (MeCN); lit.,[34] mp 217-230 °C.

### Ethyl 3,4-Dihydro-6-methylsulfanyl-2-phenyl-4-thioxopyrimidine-5-carboxylate (7ba)

For preparation as main product from the thiazine (**3ba**), see ref.[34]

For preparation as byproduct, see compound (**14a**).

**Ethyl 3,4-Dihydro-6-methylsulfanyl-2-(4-chlorphenyl)-4-thioxopyrimidine-5-carboxylate (7bb)**

For preparation, see compound (**14b**).

**Ethyl Cyano(3,4-dihydro-4-thioxo-1,3-benzoxazin-2-ylidene)acetate (8)**

A) Compound (**3c**) (1.65 g, 3.9 mmol) was treated with EtOH (15 mL) and morpholine (1.4 mL, 16 mmol). The mixture was refluxed for 3 min and poured into $H_2O$ (30 mL). The precipitated material was separated and triturated with $H_2O$ to yield **8** (0.5 g, 47%).

B) Compound (**3c**) (1.65 g, 3.9 mmol) was treated with EtOH (30 mL) and $Et_3N$ (1.6 mL, 11.4 mmol). The mixture was heated under reflux for 20 min and poured into 20 mL HCl (1 mol/L). The precipitate was filtered off and recrystallized from methylglycol to yield **8** (0.8 g, 76%) as yellow crystals; mp 215-219 $^oC$ (methylglycol).

IR (KBr): $\nu$ = 2220 (C≡N), 1665 (C=O) $cm^{-1}$ .

$^1$H-NMR (DMSO-$d_6$, 250 MHz): $\delta$= 1.26 (t, 3H, J= 7.0 Hz, $COOCH_2C\underline{H}_3$) , 4.28 (q, 2H, J= 7.1 Hz, $COOC\underline{H}_2CH_3$), 7.50-8.28 (m, 4H, aromat), 13.06 (br s, 1H, NH).

$^{13}$C-NMR (DMSO-$d_6$, 50 MHz): $\delta$= 14.07 ($CH_2\underline{C}H_3$), 61.82 ($\underline{C}H_2CH_3$), 63.26 (C=$\underline{C}$-COO), 113.80 (C≡N), 116.91 (C-8), 120.92 (C-4a), 127.20 (C-6), 129.71 (C-5), 137.73 (C-7), 147.99 (C-8a), 160.39 (COO), 166.75 (C-2), 184.27 (CS).

MS (EI, 70 eV): *m/z* (%) = 274 (31, $M^+$); 136 (63, $[OC_6H_4CS]^+$); 108 (100, $[C_5H_4CS]^+$).

Anal. Calcd for $C_{13}H_{10}N_2O_3S$: C 56.92, H 3.67, N 10.21, S 11.69; Found: C 57.30, H 3.88, N 10.30, S 11.55.

**3-Morpholino-2-thiocarbamoyl-acrylonitrile (9) and Benzamide (10)**

Compound (**6a**) (Y=OH) (1.0 g, 4.3 mmol) was added to morpholine (5 mL)**.** The mixture was refluxed for 1 min and was then acidified with 5 mL HCl (1mol/L). The precipitated material was filtered off and recrystallized from methylglycol to yield **9**. The filtrate concentrated in vacuo. The residue was extracted with NaOH (1 mol/L). The insoluble material was purified by recrystallization from $H_2O$ to yield benzamide (**10**) (0.177 g, 34%) as colourless crystals; mp 113-115 $^oC$ ($H_2O$); lit.,[44] mp 115-116 $^oC$.

**9**: yield 0.3g (35%); light beige crystals; mp 228-235 $^oC$ (methylglycol).

IR (KBr): $\nu$ = 3380, 3310, 3210 (NH), 2200 (C≡N), 1610 $cm^{-1}$ .

$^1$H-NMR (DMSO-$d_6$, 250 MHz): $\delta$ = 3.60-3.90 (m, 8H, $CH_2$), 8.00 (s, 1H, NH), 8.38 (s, 1H, CH), 8.87 (s, 1H, NH).

$^{13}$C-NMR (DMSO-$d_6$, 50 MHz): $\delta$ = 46.72, 55.24 ($NCH_2$), 65.31, 65.62 ($OCH_2$), 78.45 [$\underline{C}$(CN)$CSNH_2$), 118.26 (C≡N), 158.14 (CH), 193.07 (CS).

MS (EI, 70 eV): *m/z* (%) = 197 (100, $M^+$); 86 (100, $[O(C_2H_4)_2N]^+$).

Anal. Calcd for $C_8H_{11}N_3OS$: C 48.71, H 5.62, N 21.30, S 16.25; Found: C 48.79, H 5.52, N 21.16, S 16.10.

**Morpholinomethylenemalononitrile (11) and Thiobenzamide (12)**

Compound **(3a)** (3.0 g, 9.5 mmol, freshly synthetized crude product[34]) was treated with EtOH (26 mL) and 4.0 mL (46 mmol) morpholine. The mixture was refluxed for 10 min. The solvent was removed under reduced pressure. The residue was poured into DMF (2 mL) and then into $H_2O$ (10 mL). Filtration and recrystallization from $H_2O$ afforded **11**. The filtrate was poured into $H_2O$ (60 mL). The resulting precipitate was collected and recrystallized from $C_6H_6$ and then from $H_2O$ to yield **12** (0.19 g, 15%) as light yellow needles, mp 115-116 $^oC$ ($H_2O$), lit.,[45] mp 116-116.5 $^oC$.

**11**: yield 0.46g (30%); light beige crystals; mp 147-150$^oC$ ($H_2O$).

IR (KBr): $\nu$ = 2200, 2210 (C≡N), 1535 $cm^{-1}$ .

$^1$H-NMR (DMSO-$d_6$, 250 MHz): $\delta$= 3.55-3.80 (m, 8H, $CH_2$), 7.73 (s, 1H, CH).

$^{13}$C-NMR (DMSO-$d_6$, 50 MHz): $\delta$= 46.08, 54.47 ($NCH_2$), 64.84, 66.08 ($OCH_2$), 116.08 [$\underline{C}(CN)_2$], 117.85 (C≡N), 157.58 (=CH).

MS (EI, 70 eV): *m/z* (%) = 163 (100, $M^+$).

Anal. Calcd for $C_8H_9N_3O$: C 58.88, H 5.56, N 25.75; Found: C 58.61, H 5.58, N 25.65.

**Ethyl Cyano(5-phenyl-3*H*-1,2,4-dithiazol-3-ylidene)acetate (14a) and**

**Ethyl 3,4-Dihydro-6-methylsulfanyl-2-phenyl-4-thioxopyrimidine-5-carboxylate (7ba)**

A mixture of **3ba**[34] (1.0 g, 2.5 mmol) and NaAc (0.4 g, 0.5 mmol) in DMSO (4 mL) was stirred at rt for 3 days. $H_2O$ (1 mL) was added. The precipitate was filtered off to yield **14a**. $H_2O$ (10 mL) was added to the filtrate. The precipitate was collected and recrystallized from MeOH to yield **7ba** (0.25 g, 33%) as yellow crystals; mp 162-170 $^oC$ (EtOH), lit.,[34] mp 163-174 $^oC$. **14a**: yield 0.1g (14%); yellow crystals; mp 150-151$^oC$ ($C_6H_6$).

IR (KBr): $\nu$ = 2215 (C≡N), 1640 $cm^{-1}$ (C=O).

$^1$H-NMR (DMSO-$d_6$, 250 MHz): $\delta$ = 1.31(t, 3H, J= 7.1 Hz, $COOCH_2C\underline{H}_3$), 4.30 (q, 2H, J= 7.1 Hz, $COOC\underline{H}_2CH_3$), 7.37-8.16(m, 5H, phenyl).

MS (EI, 70 eV): *m/z* (%) = 290 (29, $M^+$); 261.9859 (6, [M-$C_2H_4$]$^+$) ($C_{11}H_6N_2O_2S_2$ calcd: 261.9871); 244.9804 (9, [M-$C_2H_5OH$]$^+$) ($C_{11}H_4N_2OS_2$ calcd: 244.9766); 218.0004 (22, [M-$C_2H_4$-$CO_2$]$^+$) ($C_{10}H_6N_2S_2$ calcd: 217.9937; 153.0456 (16) ($C_{10}H_5N_2$ calcd:153.0453); 121.0101 (41, [$C_6H_5$-CS]$^+$) ($C_7H_5S$ calcd:121.0112); 105.0325 (100, [$C_6H_5$-CO]$^+$) ($C_7H_5O$ calcd: 105.0340); 104.0477 (32, [$C_6H_5$-CNH]$^+$) ($C_7H_6N$ calcd: 104.0900); 103.0402 (8, [$C_6H_5$-CN]$^+$) ($C_7H_5N$ calcd: 103.0422). Anal. Calcd for $C_{13}H_{10}N_2O_2S_2$: C 53.77, H 3.47, N 9.65, S 22.09; Found: C 53.69, H 3.45, N 9.66, S 21.75.

X-Ray Crystal Structure Analysis (for details, see ref[41]):

Intramolecular Distances (C) (standard deviation)

| | | | |
|---|---|---|---|
| S1 – S2 | 2.061(1) | O – $CH_2CH_3$ | 1.462(3) |
| S2 – C3 | 1.759(3) | $CH_3$ – $CH_2$ | 1.500(5) |
| C3 – N4 | 1.369(3) | Cyano: C - N | 1.144(3) |
| N4 – C5 | 1.289(3) | C5 – phenylC1 | 1.485(3) |
| C5 – S1 | 1.747(3) | phenylC1-phenylC2 | 1.395(4) |
| S2 - $CH_3CH_2OCO$ | 2.526(2) | phenylC2-phenylC3 | 1.396(3) |
| C3 – C(CN) | 1.368(3) | phenylC3-phenylC4 | 1.368(4) |
| $CH_3CH_2O$ – CO | 1.333(3) | phenylC4-phenylC5 | 1.377(4) |
| $CH_3CH_2OC$ – O | 1.215(3) | phenylC5-phenylC6 | 1.390(3) |
| C(CN) – $COOCH_2CH_3$ | 1.463(3) | phenylC1-phenylC6 | 1.385(4) |
| $CH_2CH_3O(CO)C$ – CN | 1.424(4) | | |

Selected Bond Angles (deg) (standard deviation)

| | | | |
|---|---|---|---|
| S1 – S2 – C3 | 93.0(0.1) | CO – O – $CH_2CH_3$ | 115.9(0.2) |
| S2 – C3 – N4 | 117.3(0.2) | $CH_3CH_2O$ – C – O | 124.9(0.2) |
| C3 – N4 – C5 | 116.6(0.2) | $CH_3$ – $CH_2$ – O | 110.1(0.3) |
| N4 – C5 – S1 | 119.5(0.2) | S1 – C5 – phenylC1 | 117.8(0.2) |
| C5 – S1 – S2 | 93.6(0.1) | N4 - C5 – phenylC1 | 122.6(0.2) |
| S2 – C3 – C(CN) | 121.0(0.2) | C5-phenylC1-phenylC2 | 118.9(0.3) |
| N4 – C3 – C(CN) | 121.7(0.2) | C5 – phenylC1 – phenylC6 | 121.3(0.3) |
| C3 – C – CN | 120.9(0.2) | phenylC1-phenylC2-phenylC3 | 118.8(0.3) |
| C3 – C(CN) - $CO(OCH_2CH_3)$ | 118.9(0.2) | phenylC2-phenylC3-phenylC4 | 120.9(0.3) |
| CN – C – $CO(OCH_2CH_3)$ | 120.2(0.2) | phenylC3-phenylC4-phenylC5 | 120.6(0.3) |
| C(CN) – CO – $OCH_2CH_3$ | 113.3(0.2) | phenylC4-phenylC5-phenylC6 | 119.3(0.3) |
| C(CN) – $C(OCH_2CH_3)$ – O | 121.8(0.2) | phenylC5-phenylC6-phenylC1 | 120.7(0.3) |
| (C3)C($COOCH_2CH_3$) - C - N | 177.8(0.3) | phenylC6-phenylC1-phenylC2 | 119.8(0.2) |

**Ethyl Cyano[5-(4-chlorphenyl)-3*H*-1,2,4-dithiazol-3-ylidene]acetate (14b) and**
**Ethyl 3,4-Dihydro-6-methylsulfanyl-2-(4-chlorphenyl)-4-thioxopyrimidine-5-carboxylate (7bb)**

A) A mixture of **3bb**[34] (1.6 g , 3.6 mmol), 1 mL NaOH (10 mol/L) and DMSO (4 mL) was heated at 100 $^{o}$C for 2 min and was then acidified with HCl (1 mol/L). The mixture was concentrated in vacuo. The residue was triturated with brine (5 mL). The solid residue was extracted with a solution of NaOH in MeOH (3 mol/L). The insoluble material was recrystallized from $C_6H_6$/hexane to yield **14b** (47 mg, 4%). The solution of NaOH in MeOH was acidified with HCl (1 mol/L). The precipitated material was filtered

off to yield **7bb** (0.3 g, 24%).

B) A mixture of **3bb** (1.6 g, 3.6 mmol) and anhydrous NaAc (0.6 g, 7.2 mmol) in DMSO ( 6 mL) was stirred at rt overnight. Then, $H_2O$ (2 mL) was added. The precipitate was filtered off, washed with $H_2O$ and with MeOH to yield **14b** (0.3 g). The filtrate was treated with $H_2O$ (5 mL). The precipitate was collected to yield **14b** (65 mg). The filtrate was poured into $H_2O$ (20 mL). The precipitated material was separated and dissolved in NaOH in MeOH (3 mol/L). The NaOH solution was acidified with HCl (1 mol/L). The precipitated material was filtered off to give **7bb (**61 mg, 5%) as yellow crystals; mp 133-136 $^oC$ (EtOH); lit.,[34] mp 133-136 $^oC$.

**14b**: yield 0.362 g (31%); yellow crystals; mp 203-204 $^oC$ (DMSO/$H_2O$).

IR (KBr): ν = 2230 (C≡N), 1630 $cm^{-1}$ (C=O).

$^1$H-NMR (DMSO-$d_6$, 250 MHz): δ = 1.30 (t, 3H, J= 7.1 Hz, $COOCH_2C\underline{H}_3$), 4.30( q, 2H, J= 7.0 Hz, $COOC\underline{H}_2CH_3$), 7.70-8.12 (m, 4H, phenyl).

MS (EI, 70 eV): *m/z* (%) = 324 (92, $M^+$); 296 (14, $[M-C_2H_4]^+$); 279 (17, $[M-C_2H_5OH]^+$); 270,2* (2, $296^2/324 = 270,42$); 252 (28, $[M-C_2H_4-CO_2]^+$); 187 (25, $C_{10}H_4ClN_2$); 155 (33, $[ClC_6H_4-CS]^+$); 139 (100, $[ClC_6H_4-CO]^+$); 138 (22, $[ClC_6H_4-CNH]^+$); 137 (11, $[ClC_6H_4-CN]^+$).

Anal. Calcd for $C_{13}H_9N_2O_2ClS_2$: C 48.07, H 2.79, N 8.63, S 19.74, Cl 10.91; Found: C 47.93, H 2.95, N 8.48, S 20.08, Cl 10.96.

**Ethyl 3-Amino-5-benzoylimino-5*H*-1,2-dithiol-4-carboxylate (17)**

$H_2O$ (0.1 mL) was added to a solution of **4ba**[34] (0.5 g, 1.63 mmol) in DMF (2 mL). The solution was kept at rt for 14 d. Then, the mixture was concentrated in vacuo. The precipitated crystals was collected and dried to yield **17** (0.17 g, 34%) as light yellow crystals; mp 151-165 $^oC$ (DMF).

IR (KBr): ν = 1645 (C=O Ester), 1635 $cm^{-1}$ (C=O Benzoyl).

$^1$H-NMR (DMSO-$d_6$, 250 MHz): δ= 1.32 (t, 3H, J= 7.0 Hz, $COOCH_2C\underline{H}_3$), 4.21 (q, 2H, J= 7.1 Hz, $COOC\underline{H}_2CH_3$), 7.60-8.40 (m, 5H, phenyl), 9.10 (brs, 2H, NH).

X-Ray Crystal Structure Analysis (for details, see ref[41]):

Intramolecular Distances (C) (standard deviation)

| | | | |
|---|---|---|---|
| S1 - S2 | 2.101(3) | C4 – CO($OCH_2CH_3$) | 1.508(9) |
| S2 – C3 | 1.728(7) | $CH_3CH_2OC$ – O | 1.216(8) |
| C3 – C4 | 1.394(8) | $CH_3CH_2O$ – C | 1.312(8) |
| C4 – C5 | 1.424(8) | $CH_3CH_2$ – O | 1.462(7) |
| C5 - S1 | 1.774(6) | $CH_2$ – $CH_3$ | 1.48(1) |
| S1 - O$C_6H_5$ | 2.324(5) | $CH_3CH_2OCO$ – HN | 1.68(8) |
| C5 – N$COC_6H_5$ | 1.320(7) | $CH_3CH_2OCO$ – $NH_2$ | 2.62(1) |
| N(C5) – CO($C_6H_5$) | 1.356(8) | phenylC1 – phenylC2 | 1.394(8) |

| | | | |
|---|---|---|---|
| $C_6H_5C - O$ | 1.240(7) | phenylC2 – phenylC3 | 1.369(9) |
| $C_6H_5 - CO$ | 1.480(9) | phenylC3 – phenylC4 | 1.362(9) |
| $NCOC_6H_5 - OCH_2CH_3$ | 2.704(8) | phenylC4 – phenylC5 | 1.361(9) |
| $C3 - NH_2$ | 1.331(8) | phenylC5 – phenylC6 | 1.370(9) |
| | | phenylC1 – phenylC6 | 1.390(8) |

Selected Bond Angles (deg) (standard deviation) .

| | | | |
|---|---|---|---|
| S1 – S2 – C3 | 96.0(0.3) | S1 – C5 – N($COC_6H_5$) | 119.6(0.5) |
| S2 – C3 – C4 | 117.1(0.6) | C4 – C5 – N(COC6H5) | 124.5(0.6) |
| C3 – C4 – C5 | 117.1(0.7) | C5 – N – $COC_6H_5$ | 117.5(0.6) |
| C4 – C5 – S1 | 115.9(0.6) | O – C($C_6H_5$) – N(C5) | 122.5(0.7) |
| C5 – S1 – S2 | 93.9(0.3) | phenylC1 – C –N | 116.1(0.6) |
| S2 – C3 – $NH_2$ | 117.9(0.6) | phenylC1 – C – O | 121.4(0.7) |
| C4 – C3 – $NH_2$ | 125.0(0.7) | phenylC2–phenylC1 – CO | 122.0(0.7) |
| C3 – C4 – $COCH_2CH_3$ | 118.8(0.7) | phenylC6-phenylC1-CO | 120.1(0.7) |
| C4 – C($OCH_2CH_3$) – O | 121.1(0.8) | phenylC1-phenylC2-phenylC3 | 120.2(0.7) |
| $CH_3CH_2OC$ – C4 – C5 | 124.1(0.7) | phenylC2–phenylC3–phenylC4 | 121.1(0.7) |
| $CH_3CH_2$ – O – CO | 117.2(0.6) | phenylC3-phenylC4-phenylC5 | 119.5(0.8) |
| $CH_3CH_2O$ – C – O | 123.2(0.6) | phenylC4–phenylC5–phenylC6 | 120.8(0.8) |
| $CH_3CH_2O$ – CO – C4 | 115.8(0.7) | phenylC5-phenylC6-phenylC1 | 120.5(0.7) |
| $CH_3$ – $CH_2$ – O | 111.0(0.7) | phenylC6–phenylC1–phenylC2 | 117.9(0.7) |

Anal. Calcd for $C_{13}H_{12}N_2O_3S_2$: C 50.63, H 3.92, N 9.09, S 20.79; Found: C 50.63, H 4.02, N 8.92, S 20.85.

**Ethyl 2-Cyano-3-methylsulfanyl-3-(methylsulfanylphenylmethyleneamino)acrylate (18)**

$Et_3N$ (2 mL, 15 mmol) and MeI (1 mL, 15mmol) were added to a stirred suspension of **3ba** (2.04 g, 5 mmol) in 20 mL MeOH at 10-15 $^oC$. The mixture was stirred at rt overnight. The precipitate was collected and washed with $H_2O$ to yield **18** (1.54 g, 96%) as light yellow crystals; mp 114-118 $^oC$ (MeOH).

IR (KBr): ν = 2220 (C≡N), 1690 $cm^{-1}$ (C=O).

$^1$H-NMR (DMSO-$d_6$, 250 MHz): δ= 1.13 t, 1.18 t (3H, J= 7.1 Hz, $COOCH_2CH_3$); 2.37 (s, 3H, $SCH_3$), 2.39 (s, 3H, $SCH_3$), 4.03 q, 4.10 q (2H, J= 7.1 Hz, $COOCH_2CH_3$), 7.52-7.62 (m, 5H, aromat).

$^{13}$C-NMR (DMSO-$d_6$, 50 MHz): δ= 14.07 ($CH_2CH_3$), 14.49 ($C_6H_5CSCH_3$), 15.28 ($NCCCSCH_3$), 60.61 ($OCH_2$), 80.73 ($CCOOCH_2CH_3$), 115.61 (CN), 126.77, 129.09, 132.15, 134.20 (C-phenyl), 163.09 ($C_6H_5CSCH_2$), 171.92 ($COOCH_2CH_3$), 181.41($NCCCSCH_3$).

MS (EI, 70eV): *m/z* (%) = 320 (3, $M^+$), 98 (100).

Anal. Calcd for $C_{15}H_{16}N_2O_2S_2$: C 56.22, H 5.03, N 8.74; Found: C 56.44, H 5.16, N 8.80.

**Ethyl Cyano(5-phenyl-2,4-dihydro-[1,2,4]triazol-3-ylidene)acetate (19)**

Compound (**18**) (0.96 g, 3 mmol) was treated with MeOH (1 mL) and $N_2H_4 \cdot H_2O$ (1 mL, 22 mmol). The mixture was refluxed for 2 min. The precipitate was collected and washed with $H_2O$ to yield **19** (0.69 g, 90%) as colourless crystals; mp 236-250 $^oC$ (pyridine).

IR (KBr): ν = 3230, 3225 (N-H), 2215 (C≡N), 1660 $cm^{-1}$ (C=O).

$^1$H-NMR (DMSO-$d_6$, 250 MHz): δ= 1.23 (t, 3H, J= 7.0 Hz, $COOCH_2C\underline{H}_3$), 4.12 (q, 2H, J= 7.0 Hz, $COOC\underline{H}_2CH_3$), 7.53-8.04 (m, 5H, phenyl), 13.53 (s, 2H, NH).

$^{13}$C-NMR (DMSO-$d_6$, 50 MHz): δ= 14.70($OCH_2\underline{C}H_3$), 48.42 ($\underline{C}COOCH_2CH_3$), 58.73 ($O\underline{C}H_2CH_3$), 119.10 (C≡N), 125.06-130.83 (C-phenyl), 149.49 (C-3), 153.53 (C-5), 166.82 ($\underline{C}OOCH_2CH_3$).

MS (EI, 70eV): *m/z* (%)= 256 (78, $M^+$); 210 (100, $[M-C_2H_5OH]^+$).

Anal. Calcd for $C_{13}H_{12}N_4O_2$: C 60.93, H 4.72, N 21.86; Found: C 60.82, H 4.76, N 21.63.

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