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[4+2] CYCLOADDITION REACTIONS BETWEEN 2,4-DIAMINO-1-THIA-3-AZABUTADIENES AND KETENE. SYNTHESIS OF NEW 1,3-THIAZIN-6-ONES, 1,3-THIAZINE-6-THIONES AND 2-THIOXOPYRIMIDIN-4-ONES

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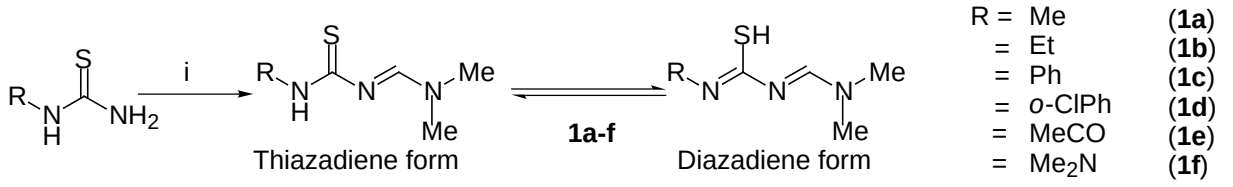
Abstract – The reaction of 2,4-diamino-1-thia-3-azabutadienes with an excess of ketene afforded 2-amino-1,3-thiazin-6-ones and 2-thioxopyrimidin-4-ones by [4+2] cycloaddition reaction. Reaction between thiazabutadienes and ketene gave rise to aminothiazinones, which were sulfured by action of phosphorus pentasulfide leading to aminothiazinethiones. Furthermore, synthesis of thioxopyrimidinones starting from S-methyl salts of thiazadienes is described.

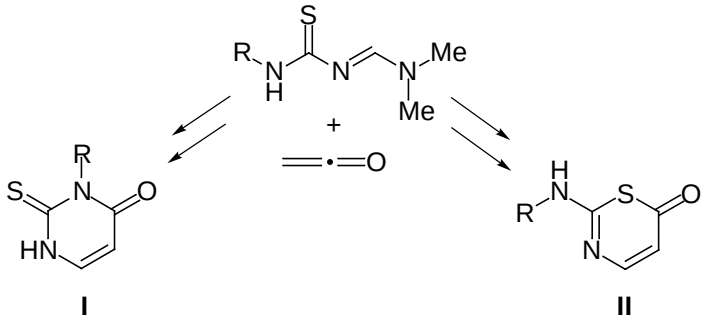
Many synthesis of heterocyclic compounds containing sulfur and nitrogen have been reported and have demonstrated utility in pharmaceutical and agrochemical research.[1-4] In particular, 1,3-thiazinones, 1,3-thiazinethiones and pyrimidinethiones have been explored as antitumor, antibacterial agents, as well as antiviral agents for human immunodeficiency virus (HIV).[5-10]

We are herein reporting an efficient synthesis of substituted 1,3-thiazinones (and 1,3-thiazinethiones) and of thioxopyrimidinones starting from common precursors, the 2,4-diamino-1-thia-3-azabutadienes (**1a-f**). These compounds, which derive from monosubstituted thioureas,[11] are powerful tools in organic synthesis, particularly in the construction of heterocyclic rings. We have recently shown that these compounds could react either as thiazadienes or as diazadienes, giving rise to 1,3-thiazines or tetrahydropyrimidines.[12]



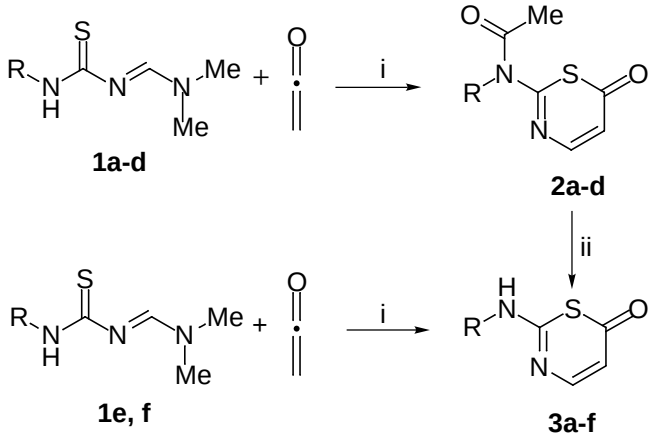
Scheme 1 Synthesis of 2,4-diamino-1-thia-3-azabutadiene ; (i) $(Me)_2N\text{-}CH(OMe)_2$, CH_2Cl_2, reflux

In this paper, we report a divergent synthesis of two isomeric heterocyclic compounds (thioxopyrimidinones (I) and thiazinones (II)) starting from 2,4-diamino-1-thia-3-azabutadienes and ketene (Scheme 2).



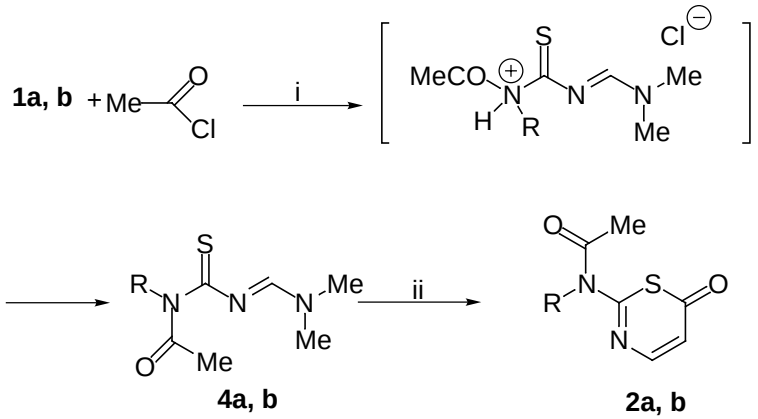
Scheme 2 2-Thioxo-1,2,3,4-tetrahydropyrimidin-4-one (I), 2-amino-6*H*-1,3-thiazin-6-one (II)

We previously showed[13] that the diazadiene tautomeric form of compounds (**1a-d**) reacted with acrylic dienophiles to provide 1,2,3,4-tetrahydropyrimidine-2-thiones. We are herein reporting a different behaviour of compounds (**1 a-f**) with ketene. In this case, only thiazadiene form reacted, and we obtained compounds (**3a-f**) (Scheme 3).



Scheme 3 (i) CH_2Cl_2, rt, 20 min ; (ii) CH_2Cl_2, Me_2NH, rt, 18 h

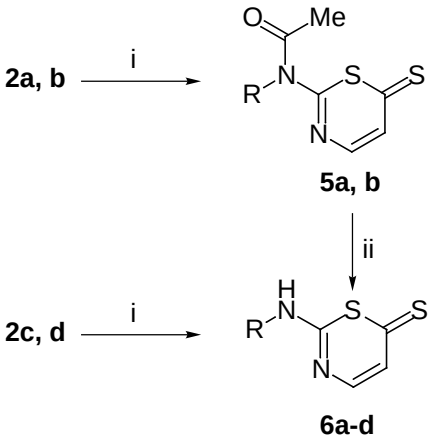
The reaction between thiazabutadienes (**1a-d**) and ketene, formed by cracking of acetone, yielded 2-aminothiazinones (**3a-d**) in good yields. During this reaction, we observed the acetylation of compounds (**1a-d**) which affected the nitrogen atom, providing the *N*-acetylated compounds (**2a-d**). These intermediates were deacylated by reaction of equimolar amount of dimethylamine to afford aminothiazine (**3a-d**). We thought that the first reaction was the *N*-acylation and that the resulting compounds reacted as thiazadiene chain to afford the corresponding thiazinones. These sequence have been proved by treatment of compounds (**1a, b**) with acetylchloride affording *N*-acetylated compounds (**4a, b**), which were subjected to [4+2] cycloaddition reaction with ketene leading to substrats (**2a, b**). This reaction was carried out in presence of triethylamine in order to eliminate hydrochloric acid formed (Scheme 4).



Scheme 4 (i) Et_3N, rt, 20 h ; (ii) CH_2Cl_2, CH_2CO, rt, 18 h

When the reaction was performed between thiazabutadienes (**1e, f**) and ketene, in dichloromethane at room temperature for twenty minutes, thiazinones (**3e, f**) were directly isolated. In this case, the acetylated intermediates were never observed (Scheme 3). The cyclisation occurred with loss of dimethylamine, also we supposed that thiazinones (**3e, f**) were obtained by deacylation thanks to the amine present in the mixture. For the compounds (**2a-d**), the dimethylamine was losted in the cyclisation reacted with the excess of ketene because no deacetylated compounds were formed. The presence of an electron-withdrawing group on the nitrogen atom increased the instability of the intermediates (**2e, f**) and explained that acetylated compounds were not observed.

Our next target was to obtain thiazinethiones starting from thiazinones. The 2-amino-1,3-thiazine-6-thiones (**6a-d**) were prepared from (**2a-d**) and phosphorus pentasulfide by heating at 80°C in dry toluene for six hours (Scheme 5). For compounds (**2a, b**) the reaction afforded compounds (**5a, b**) which were deacylated by reaction with dimethylamine to give rise to corresponding thiazinethiones.

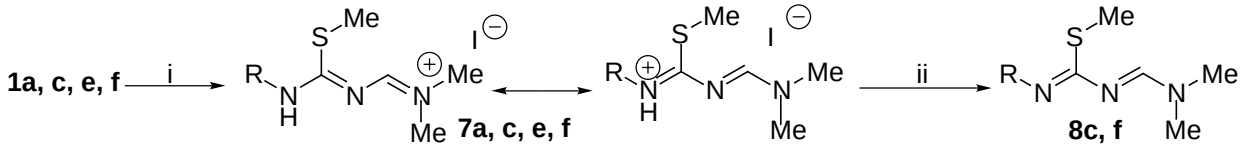


Scheme 5 (i) Toluene, P_4S_{10}, 80°C, 6 h ; (ii) CH_2Cl_2, Et_3N, rt, 18 h

On the other hand, reaction between (**2c, d**) and phosphorus pentasulfide provided directly compounds (**6c, d**) with loss of the acetyl group. Hydrogen sulfide present in the mixture reacted with unstable

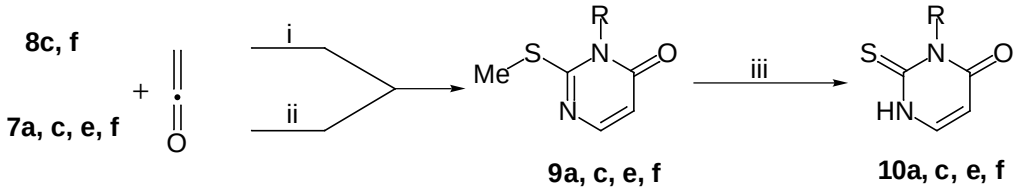
thiazinethiones (**5c, d**) and accounted for this result. In contrast, sulfuration of deacylated compounds (**3a-f**) did not proceed under the same conditions. By increasing reaction time and using excess of P_4S_{10}, we only observed the formation of a complex mixture of products.

As we have already reported, 2,4-diamino-1-thia-3-azabutadienes could react as diazadienes giving rise to tetrahydropyrimidines.[14] Alkylation of compounds (**1a, c, e, f**) using methyl iodide afforded as the sole products the corresponding *S*-methyl salts (**7a, c, e, f**) which present only the diazadiene chain. Only for (**7c, f**) we observed a dehydrohalogenation with potassium hydrogencarbonate to afford methylthioimines (**8c, f**) (Scheme 6). In the other cases, the expected products were not stable enough to be isolated.



Scheme 6 (i) MeI, rt, 24 h ; (ii) Et_2O, $KHCO_3$, rt, 4 h

The derivates (**9a, c, e, f**) were relatively easily obtained by operating at room temperature, starting from corresponding *S*-methyl salts or methylthioimines (for **8c, f**) and ketene. The [4+2] cycloaddition was carried out in presence of triethylamine in order to eliminate hydroiodic acid formed. Furthermore, the treatment of methylsulfanylimine group with hydrogen sulfide furnished thioxotetrahydropyrimidinones (**10a, c, e, f**) by loss of methanethiol (Scheme 7).



Scheme 7 (i) CH_2Cl_2, rt, 20 min ; (ii) CH_2Cl_2, Et_3N, rt, 15 min ; (iii) Et_3N, C_5H_5N, H_2S, rt, 4 h

Then, we synthesized the two heterocyclic compounds isomers (**3** and **10**) which showed similar ^1H NMR spectra, so by a sequence of protection-deprotection of sulfur atom we were able to assign the respective structures of these heterocycles.

In this work, we have shown that 2,4-diamino-1-thia-3-azabutadienes can react either as diazadienes or as thiazadienes with ketene and afford two isomeric heterocyclic compounds by Diels-Alder cycloaddition reaction. Moreover, the method described here offers a new access to 2-thioxotetrahydropyrimidin-4-ones, 2-aminothiazine-6-thiones and 2-aminothiazin-6-ones. The pharmacological activities of these new compounds are investigated and will be reported in due course.

EXPERIMENTAL SECTION

All reagents were purchased from Acros Organics and Aldrich. The chemical analyses were performed by the C.N.R.S. Analysis Laboratory (Vernaison). Column chromatography was conducted on silica gel 60 (40-63 μm), available from E. Merck. Thin layer chromatography was performed on 0.5 mm x 20 cm x 20 cm E. Merck silica gel plate (60 F-254). Melting points were taken using a Reichert microscope and are uncorrected. NMR spectra were recorded at room temperature using a BRUKER AC 200 at 50 and 200 MHz. Chemical shifts (δ) are given in ppm downfield from tetramethylsilane as internal standard. MS spectra were determined with a Hewlett Packard 5989 spectrometer. IR spectra were obtained using a BRUKER Vector 22 spectrophotometer. Ketene,[15] 1,1-dimethylthiosemicarbazide,[16] **1a**, **c**, **e**,[12] **4a**,[12] **7a**, **c**, **e**,[12] **8c**,[12] **9a**, **c**, **e**,[13] **10a**, **c**, **e**[13] were prepared according to literature procedures.

General Procedure for the Preparation of Thiazabutadienes (1): *N*,*N*-Dimethylformamide dimethyl acetal (1.55 g, 13 mmol) was added to a suspension of substituted thiourea (10 mmol) in dichloromethane (10 mL). The mixture was heated under reflux for 4 h. The solvent was removed and the residue was crystallized from ether.

4-Dimethylamino-2-ethylamino-1-thia-3-azabuta-1,3-diene (1b): 84% yield, white solid (mp 87°C) ; ^{1}H NMR ($CDCl_3$): δ = 1.26 (t, *J* = 7.2 Hz, 3 H, CH_2CH_3), 3.04, 3.14 [2 s, 6 H, $N(CH_3)_2$], 3.72 (qd, 2 H, *J* = 5.6 Hz, *J* = 7.2 Hz, CH_2CH_3), 6.75 (br s, 1 H, N*H*), 8.89 (s, 1 H, C*H*) ; ^{13}C NMR ($CDCl_3$): δ = 13.7 (CH_2CH_3), 35.3 (NCH_2), 39.6, 41.1 [$N(CH_3)_2$], 161.9 (*C*H), 192.8 (*C*S) ; IR (KBr): ν = 3216, 1624, 1548, 1338, 1197, 1101 cm^{-1} ; MS (EI); *m/z* (%): 159 (100) [M^+], 115 (77) [M^+ - $N(CH_3)_2$] ; *Anal.* Calcd for $C_6H_{13}N_3S$: C; 45.25, H; 8.23, N; 26.39. Found: C; 45.25, H; 8.32, N; 26.27.

2-(2-Chlorophenylamino)-4-dimethylamino-1-thia-3-azabuta-1,3-diene (1d): 93% yield, white solid (mp 124°C) ; ^{1}H NMR ($CDCl_3$): δ = 3.12, 3.22 [2 s, 6 H, $N(CH_3)_2$], 7.02–7.41 (m, 4 H, Ar*H*), 8.62 (br s, 1 H, N*H*), 8.91 (s, 1 H, C*H*) ; ^{13}C NMR ($CDCl_3$): δ = 36.1, 41.6 [$N(CH_3)_2$], 125.3, 126.6, 129.1, 135.6 (4 *C*H, 2 q*C*, Ar), 163.3 (*C*H), 192.2 (*C*S) ; IR (KBr): ν = 3238, 1623, 1520, 1338, 1116 cm^{-1} ; MS (CI, NH_3): *m/z* (%): 242 (100) [M^+ + H] ; *Anal.* Calcd for $C_{10}H_{12}N_3ClS$: C; 49.69, H; 5.00, N; 17.38. Found: C; 49.51, H; 4.91, N; 17.11.

4-Dimethylamino-2-(*N*',*N*'-dimethylhydrazino)-1-thia-3-azabuta-1,3-diene (1f): 97% yield, white solid (mp 109°C) ; ^{1}H NMR ($CDCl_3$): δ = 2.69 [s, 6 H, $NN(CH_3)_2$], 3.04, 3.14 [2 s, 6 H, $CN(CH_3)_2$], 7.25 (br s, 1 H, N*H*), 8.91 (s, 1 H, C*H*) ; ^{13}C NMR ($CDCl_3$): δ = 35.6, 41.4 [$CN(CH_3)_2$], 47.1 [$NN(CH_3)_2$], 162.6 (*C*H), 180.2 (*C*S) ; IR (KBr): ν = 3164, 1625, 1524, 1364, 1102 cm^{-1} ; MS (EI); *m/z* (%): 174 (17) [M^+], 115 (93) [M^+ - $NHN(CH_3)_2$], 97 (41) ; *Anal.* Calcd for $C_6H_{14}N_4S$: C; 41.35, H; 8.10, N; 32.15. Found: C; 41.55, H; 8.18, N; 32.11.

General Procedure for the Reaction of Ketene with Thiazabutadienes (1) and Diazabutadiene (8f). Synthesis of Thiazinones (2) and (3) and Pyrimidinone (9f): Ketene (HIGHLY TOXIC) was passed through a solution of **1** or **8f** (4 mmol) in anhydrous dichloromethane (150 mL) until starting product had disappeared. The mixture was cautiously evaporated and the residue was purified twice by flash chromatography (silica gel, dichloromethane/ethyl acetate 9/1). Crystallization from ether afforded the pure product.

2-*N*-Methylacetamido-6*H*-1,3-thiazin-6-one (2a): 57% yield, white solid (mp 124°C) ; ^{1}H NMR ($CDCl_3$): δ = 2.43 (s, 3 H, COC*H*$_3$), 3.54 (s, 3 H, NC*H*$_3$), 6.02 (d, *J* = 7.9 Hz, 1 H, C*H*CO), 7.96 (d, *J* = 7.9 Hz, 1 H, NC*H*) ; ^{13}C NMR ($CDCl_3$): δ = 25.3 (CO*C*H$_3$), 35.6 (N*C*H$_3$), 110.6 (*C*HCO), 152.0 (N*C*H), 165.3 (S*C*N), 172.6 (N*C*O), 183.0 (S*C*O) ; IR (KBr): ν = 1692, 1641, 1492, 1241 cm^{-1} ; MS (EI); *m/z* (%): 184 (9) [M$^+$], 156 (23), 114 (100) ; *Anal.* Calcd for $C_7H_8N_2O_2S$: C; 45.64, H; 4.38, N; 15.21. Found: C; 45.81, H; 4.49, N; 15.02.

2-*N*-Ethylacetamido-6*H*-1,3-thiazin-6-one (2b): 55% yield, white solid (mp 105°C) ; ^{1}H NMR ($CDCl_3$): δ = 1.31 (t, *J* = 7.0 Hz, 3 H, CH$_2$C*H*$_3$), 2.42 (s, 3 H, C*H*$_3$), 4.09 (q, *J* = 7.0 Hz, 2 H, C*H*$_2$CH$_3$), 6.03 (d, *J* = 7.9 Hz, 1 H, C*H*CO), 7.97 (d, *J* = 7.9 Hz, 1 H, NC*H*) ; ^{13}C NMR ($CDCl_3$): δ = 13.7 (CH$_2$*C*H$_3$), 24.7 (*C*H$_3$), 43.4 (*C*H$_2$CH$_3$), 110.7 (*C*HCO), 152.1 (N*C*H), 164.7 (S*C*N), 172.2 (N*C*O), 183.0 (S*C*O) ; IR (KBr): ν = 1689, 1643, 1497, 1229 cm^{-1} ; MS (EI); *m/z* (%): 198 (5) [M$^+$], 170 (19), 128 (100) ; *Anal.* Calcd for $C_8H_{10}N_2O_2S$: C; 48.47, H; 5.08, N; 14.13. Found: C; 48.51, H; 5.31, N; 14.23.

2-*N*-Phenylacetamido-6*H*-1,3-thiazin-6-one (2c): 64% yield, white solid (mp 165°C) ; ^{1}H NMR ($CDCl_3$): δ = 2.08 (s, 3 H, C*H*$_3$), 5.96 (d, *J* = 7.8 Hz, 1 H, C*H*CO), 7.20–7.59 (m, 5 H, Ar*H*), 7.77 (d, *J* = 7.8 Hz, 1 H, NC*H*) ; ^{13}C NMR ($CDCl_3$): δ = 25.9 (*C*H$_3$), 110.6 (*C*HCO), 128.9, 129.5, 130.1 (5 *C*H, Ar), 139.7 (q*C*, Ar), 152.1 (N*C*H), 166.0 (S*C*N), 172.3 (N*C*O), 182.3 (S*C*O) ; IR (KBr): ν = 1703, 1652, 1461, 1228 cm^{-1} ; MS (EI); *m/z* (%): 246 (15) [M$^+$], 204 (100), 176 (38), 135 (40) ; *Anal.* Calcd for $C_{12}H_{10}N_2O_2S$: C; 58.52, H; 4.09, N; 11.37. Found: C; 58.39, H; 3.99, N; 11.09.

2-*N*-(2-Chlorophenyl)acetamido-6*H*-1,3-thiazin-6-one (2d): 67% yield, white solid (mp 146°C) ; ^{1}H NMR ($CDCl_3$): δ = 2.06 (s, 3 H, C*H*$_3$), 5.97 (d, *J* = 7.9 Hz, 1 H, C*H*CO), 7.26–7.61 (m, 4 H, Ar*H*), 7.74 (d, *J* = 7.9 Hz, 1 H, NC*H*) ; ^{13}C NMR ($CDCl_3$): δ = 25.3 (*C*H$_3$), 110.8 (*C*HCO), 128.5, 130.7, 130.8, 131.0 (4 *C*H, Ar), 133.3, 137.3 (2 q*C*, Ar), 152.1 (N*C*H), 165.0 (S*C*N), 171.8 (N*C*O), 182.3 (S*C*O) ; IR (KBr): ν = 1705, 1661, 1473, 1240 cm^{-1} ; MS (EI); *m/z* (%): 280 (5) [M$^+$], 238 (22), 203 (100) ; *Anal.* Calcd for $C_{12}H_9N_2O_2ClS$: C; 51.34, H; 3.23, N; 12.63. Found: C; 51.44, H; 3.21, N; 12.55.

2-Acetamido-6*H*-1,3-thiazin-6-one (3e): 38% yield, pink solid (mp 195°C) ; ^{1}H NMR ($CDCl_3$): δ = 2.14 (s, 3 H, C*H*$_3$), 6.07 (d, *J* = 7.8 Hz, 1 H, C*H*CO), 8.02 (d, *J* = 7.8 Hz, 1 H, NC*H*), 9.44 (br s, 1 H, N*H*) ; ^{13}C NMR (DMSO-d$_6$): δ = 23.4 (*C*H3), 109.8 (*C*HCO), 154.0 (N*C*H), 164.3 (S*C*N), 171.0

(N*C*O), 180.6 (S*C*O) ; IR (KBr): ν = 3171, 1708, 1622, 1521, 1242 cm^{-1} ; MS (EI); *m/z* (%): 170 (12) [M^+], 142 (32), 100 (100) ; *Anal.* Calcd for $C_6H_6N_2O_2S$: C; 42.35, H; 3.55, N; 16.46. Found: C; 41.99, H; 3.57, N; 16.51.

2-(*N'*,*N'*-Dimethylhydrazino)-6*H*-1,3-thiazin-6-one (3f): 53% yield, pink solid (mp 175°C) ; ^1H NMR ($CDCl_3$): δ = 2.63 [s, 6 H, N(C*H*$_3$)$_2$], 5.68 (d, *J* = 7.8 Hz, 1 H, C*H*CO), 7.54 (d, *J* = 7.8 Hz, 1 H, NC*H*) ; ^{13}C NMR ($CDCl_3$): δ = 47.1 [N(*C*H$_3$)$_2$], 104.8 (*C*HCO), 153.1 (N*C*H), 171.2 (S*C*N), 182.4 (S*C*O) ; IR (KBr): ν = 2827, 1652, 1592, 1547, 1455, 1438, 1399 cm^{-1} ; MS (EI); *m/z* (%): 171 (8) [M^+], 129 (43), 112 (22), 101 (17), 59 (100) ; *Anal.* Calcd for $C_6H_9N_3OS$: C; 42.09, H; 5.30, N; 24.54. Found: C; 41.81, H; 5.28, N; 24.24.

3-Dimethylamino-2-methylsulfanylpyrimidin-4(3*H*)-one (9f): 84% yield, white solid (mp 64°C) ; ^1H NMR ($CDCl_3$): δ = 2.26 (s, 3 H, SC*H*$_3$), 2.92 [s, 6 H, N(C*H*$_3$)$_2$], 6.03 (d, *J* = 6.4 Hz, 1 H, C*H*CO), 7.60 (d, *J* = 6.4 Hz, 1 H, NC*H*) ; ^{13}C NMR ($CDCl_3$): δ = 14.7 (S*C*H$_3$), 42.6 [N(*C*H$_3$)$_2$], 111.6 (*C*HCO), 151.7 (N*C*H), 162.0, 168.0 (S*C*N, *C*O) ; IR (KBr): ν = 1684, 1487, 1327 cm^{-1} ; MS (EI); *m/z* (%): 142 (10) [M^+ - H_2C=N–CH_3], 112 (13), 95 (24) ; *Anal.* Calcd for $C_7H_{11}N_3OS$: C; 45.39, H; 5.99, N; 22.68. Found: C; 45.55, H; 6.04, N; 22.73.

General Procedure for the Desacylation of Compounds (2) and (5). Synthesis of Thiazinones (3), Thiazinethiones (6a) and (6b): A solution of compounds (**2**) or (**7**) (2 mmol) in dichloromethane (5 mL) and dimethylamine (100 mg, 2.4 mmol) was stirred for 18 h at rt. The mixture was concentrated in *vacuo* and the residue was chromatographied (silica gel, dichloromethane/ethyl acetate 8/2). The product was crystallized from ether (dichloromethane for **6a**).

2-Methylamino-6*H*-1,3-thiazin-6-one (3a): 75% yield, white solid (mp 121°C) ; ^1H NMR ($CDCl_3$): δ = 3.04 (s, 3 H, C*H*$_3$), 5.71 (d, *J* = 7.9 Hz, 1 H, C*H*CO), 7.74 (d, *J* = 7.9 Hz, 1 H, NC*H*) ; ^{13}C NMR ($CDCl_3$): δ = 29.6 (*C*H$_3$), 103.5 (*C*HCO), 156.3 (N*C*H), 169.0 (S*C*N), 179.3 (S*C*O) ; IR (KBr): ν = 3255, 1641, 1563, 1495, 1391 cm^{-1} ; MS (EI); *m/z* (%): 142 (37) [M^+], 114 (100), 86 (39), 74 (30) ; *Anal.* Calcd for $C_5H_6N_2OS$: C; 42.24, H; 4.25, N; 19.70. Found: C; 42.01, H; 4.23, N; 19.88.

2-Ethylamino-6*H*-1,3-thiazin-6-one (3b): 72% yield, white solid (mp 98°C) ; ^1H NMR ($CDCl_3$): δ = 1.29 (t, *J* = 7.2 Hz, 3 H, CH_2C*H*$_3$), 3.45 (q, *J* = 7.2 Hz, 2 H, C*H*$_2$CH$_3$), 5.69 (d, *J* = 7.9 Hz, 1 H, C*H*CO), 6.58 (br s, 1 H, N*H*), 7.72 (d, *J* = 7.9 Hz, 1 H, NC*H*) ; ^{13}C NMR ($CDCl_3$): δ = 14.2 (CH_2*C*H$_3$), 38.0 (*C*H$_2$CH$_3$), 103.5 (*C*HCO), 156.4 (N*C*H), 168.0 (S*C*N), 179.5 (S*C*O) ; IR (KBr): ν = 3173, 1652, 1576, 1533, 1439, 1334 cm^{-1} ; MS (EI); *m/z* (%): 156 (21) [M^+], 128 (100), 113 (59), 100 (37) ; *Anal.* Calcd for $C_6H_8N_2OS$: C; 46.14, H; 5.16, N; 17.93. Found: C; 46.21, H; 5.07, N; 18.03.

2-Phenylamino-6*H*-1,3-thiazin-6-one (3c): 65% yield, pale yellow solid (mp 141°C) ; ^1H NMR (DMSO-d_6): δ = 5.72 (d, *J* = 8.1 Hz, 1 H, C*H*CO), 7.09–7.51 (m, 5 H, Ar*H*), 7.80 (d, *J* = 8.1 Hz, 1 H,

NC*H*), 10.93 (br s, 1 H, N*H*) ; ^{13}C NMR (DMSO-d_6): δ = 103.3 (*C*HCO), 121.4, 124.6, 129.0 (5 *C*H, Ar), 140.0 (q*C*, Ar), 153.9 (N*C*H), 160.8 (S*C*N), 178.7 (S*C*O) ; IR (KBr): ν = 3287, 1644, 1479, 1443 cm^{-1} ; MS (EI); *m/z* (%): 204 (20) [M$^+$], 176 (100), 135 (17), 112 (38) ; *Anal.* Calcd for $C_{10}H_8N_2OS$: C; 58.81, H; 3.95, N; 13.72. Found: C; 58.92, H; 3.88, N; 13.60.

2-(2-Chlorophenylamino)-6*H*-1,3-thiazin-6-one (3d): 97% yield, white solid (mp 135°C) ; ^{1}H NMR ($CDCl_3$): δ = 5.68 (d, *J* = 8.4 Hz, 1 H, C*H*CO), 7.12–7.60 (m, 4 H, Ar*H*), 7.44 (d, *J* = 8.4 Hz, 1 H, NC*H*) ; ^{13}C NMR ($CDCl_3$): δ = 103.0 (*C*HCO), 124.3, 127.1, 128.1, 130.4, 139.3 (4 *C*H, 2 q*C*, Ar), 147.6 (N*C*H), 160.4 (S*C*N), 178.6 (S*C*O) ; IR (KBr): ν = 2894, 1667, 1598, 1578, 1333 cm^{-1} ; MS (EI); *m/z* (%): 238 (19) [M$^+$], 210 (47), 203 (100), 175 (93), 112 (62) ; *Anal.* Calcd for $C_{10}H_7N_2OClS$: C; 50.32, H; 2.96, N; 11.74. Found: C; 50.18, H; 3.04, N; 11.68.

2-Methylamino-6*H*-1,3-thiazine-6-thione (6a): 84% yield, ochre solid (mp 221°C) ; ^{1}H NMR (DMSO-d_6): δ = 2.93 (s, 3 H, CH_3), 6.60 (d, *J* = 6.9 Hz, 1 H, C*H*CS), 7.68 (d, *J* = 6.9 Hz, 1 H, NC*H*), 9.48 (br s, 1 H, N*H*) ; ^{13}C NMR (DMSO-d_6): δ = 29.1 (*C*H_3), 117.6 (*C*HCS), 151.3 (N*C*H), 168.4 (S*C*N), 199.1 (*C*S) ; IR (KBr): ν = 3202, 1567, 1538, 1490, 1439, 1391, 1331, 1241, 1139 cm^{-1} ; MS (EI); *m/z* (%): 158 (100) [M$^+$], 128 (8), 114 (48) ; *Anal*. Calcd for $C_5H_6N_2S_2$: C; 37.95, H; 3.82, N; 17.70. Found: C; 38.01, H; 3.72, N; 17.85.

2-Ethylamino-6*H*-1,3-thiazine-6-thione (6b): 94% yield, orange solid (mp 150°C) ; ^{1}H NMR (DMSO-d_6): δ = 1.25 (t, *J* = 7.2 Hz, 3 H, CH_2C*H*$_3$), 3.46 (m, 2 H, C*H*$_2$$CH_3$), 6.65 (d, *J* = 7.0 Hz, 1 H, C*H*CS), 7.55 (d, *J* = 7.0 Hz, 1 H, NC*H*), 8.75 (br s, 1 H, N*H*) ; ^{13}C NMR (DMSO-d_6): δ = 13.3 (CH_2*C*H_3), 37.2 (*C*H_2CH_3), 117.7 (*C*HCS), 150.2 (N*C*H), 167.8 (S*C*N), 212.1 (*C*S) ; IR (KBr): ν = 3174, 1589, 1505, 1419, 1326, 1243, 1174, 1079 cm^{-1} ; MS (EI); *m/z* (%): 172 (100) [M+], 139 (15), 128 (35), 113 (17) ; *Anal.* Calcd for $C_6H_8N_2S_2$: C; 41.83, H; 4.68, N; 16.26. Found: C; 42.01, H; 4.55, N; 16.23.

2-*N*-Ethylacetamido-4-dimethylamino-1-thia-3-azabuta-1,3-diene (4b): Triethylamine (223 mg, 2.2 mmol) and acetyl chloride (157 mg, 2 mmol) were successively added to a solution of **1b** (318 mg, 2 mmol) in dichloromethane (5 mL). After stirring for 4 h at rt, these additions were repeated in the same proportions. The mixture was then stirred for 20 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (dichloromethane/ethyl acetate 19/1) to give **4b** (277.4 mg, 69%) as a red oil ; ^{1}H NMR ($CDCl_3$): δ = 1.23 (t, *J* = 7.0 Hz, 3 H, CH_2C*H*$_3$), 2.51 (s, 3 H, C*H*$_3$), 3.12, 3.25 [2 s, 6 H, N(C*H*$_3$)$_2$], 4.26 (q, *J* = 7.0 Hz, 2 H, C*H*$_2$$CH_3$), 8.67 (s, 1 H, C*H*) ; ^{13}C NMR ($CDCl_3$): δ = 13.0 (CH_2*C*H_3), 28.2 (*C*H_3), 35.9 (N*C*H_2), 41.5, 44.7 [N(*C*H_3)$_2$], 161.0 (*C*H), 173.7 (*C*O), 197.2 (*C*S) ; IR (film): ν = 1684, 1622, 1525, 1423, 1339, 1233 cm^{-1} ; MS (EI); *m/z* (%): 201 (33) [M$^+$], 158 (8), 115 (100) [M$^+$ - N(COCH_3)(C_2H_5)].

General Procedure for the Sulfuration of Thiazinones (2). Synthesis of Thiazinethiones (5a), (5b), (6c) and (6d): To a suspension of compounds (**2**) or (**6**) (2 mmol) in dry toluene (30 mL) was added phosphorus pentasulfide (178 mg, 0.4 mmol). The mixture was heated for 6 h at 80°C then allowed to cool and evaporated. The residue was purified by flash chromatography (silica gel, dichloromethane/ethyl acetate 8/2) followed by recrystallization from ether.

2-*N*-Methylacetamido-6*H*-1,3-thiazine-6-thione (5a): 65% yield, orange solid (mp 182°C) ; ^{1}H NMR ($CDCl_3$): δ = 2.43 (s, 3 H, COC*H*$_3$), 3.55 (s, 3 H, NC*H*$_3$), 6.89 (d, *J* = 7.2 Hz, 1 H, C*H*CO), 7.69 (d, *J* = 7.2 Hz, 1 H, NC*H*) ; ^{13}C NMR ($CDCl_3$): δ = 25.1 (CO*C*H$_3$), 35.5 (N*C*H$_3$), 124.4 (*C*HCS), 144.3 (N*C*H), 166.2 (S*C*N), 172.9 (N*C*O), 207.7 (*C*S) ; IR (KBr): ν = 1693, 1548, 1486, 1399, 1250 cm^{-1} ; MS (EI); *m/z* (%): 200 (69) [M$^+$], 158 (100), 125 (26), 114 (56) ; *Anal*. Calcd for $C_7H_8N_2OS_2$: C; 41.98, H; 4.03, N; 13.99. Found: C; 41.82, H; 4.03, N; 14.01.

2-*N*-Ethylacetamido-6*H*-1,3-thiazine-6-thione (5b): 70% yield, ochre solid (mp 120°C) ; ^{1}H NMR ($CDCl_3$): δ = 1.32 (t, *J* = 7.0 Hz, 3 H, CH$_2$C*H*$_3$), 2.44 (s, 3 H, C*H*$_3$), 4.11 (q, *J* = 7.0 Hz, 2 H, C*H*$_2$CH$_3$), 6.90 (d, *J* = 7.0 Hz, 1 H, C*H*CS), 7.70 (d, *J* = 7.0 Hz, 1 H, NC*H*) ; ^{13}C NMR ($CDCl_3$): δ = 13.6 (CH$_2$*C*H$_3$), 24.4 (*C*H$_3$), 43.4 (*C*H$_2$CH$_3$), 124.1 (*C*HCS), 144.6 (N*C*H), 165.5 (S*C*N), 172.7 (N*C*O), 207.6 (*C*S) ; IR (KBr): ν = 1685, 1545, 1488, 1408, 1369, 1357, 1234, 1200, 1141, 1115 cm^{-1} ; MS (EI); *m/z* (%): 214 (64) [M$^+$], 172 (100), 139 (41), 128 (44) ; *Anal*. Calcd for $C_8H_{10}N_2OS_2$: C; 44.84, H; 4.70, N; 13.07. Found: C; 45.01, H; 4.72, N; 13.11.

2-Phenylamino-6*H*-1,3-thiazine-6-thione (6c): 67% yield, yellow solid (mp 174°C) ; ^{1}H NMR (DMSO-d_6): δ = 6.68 (d, *J* = 7.2 Hz, 1 H, C*H*CS), 7.16–7.57 (m, 5 H, Ar*H*), 7.70 (d, *J* = 7.2 Hz, 1 H, NC*H*), 10.33 (br s, 1 H, N*H*) ; ^{13}C NMR (DMSO-d_6): δ = 118.4 (*C*HCS), 122.0, 125.4, 129.1 (5 *C*H, Ar), 138.4 (q*C*, Ar), 149.0 (N*C*H), 163.9 (S*C*N), 200.6 (*C*S) ; IR (KBr): ν = 3447, 1517, 1402, 1357, 1242, 1157, 1099 cm^{-1} ; MS (EI); *m/z* (%): 220 (100) [M$^+$], 176 (37), 128 (55) ; *Anal*. Calcd for $C_{10}H_8N_2S_2$: C; 54.52, H; 3.66, N; 12.72. Found: C; 54.65, H; 3.61, N; 12.79.

2-(2-Chlorophenylamino)-6*H*-1,3-thiazine-6-thione (6d): 70% yield, ochre solid (mp 140°C) ; ^{1}H NMR ($CDCl_3$): δ = 5.77 (br s, 1 H, N*H*), 6.67 (d, *J* = 7.5 Hz, 1 H, C*H*CS), 7.18–7.72 (m, 4 H, Ar*H*), 7.42 (d, *J* = 7.5 Hz, 1 H, NC*H*) ; ^{13}C NMR ($CDCl_3$): δ = 118.7 (*C*HCS), 125.3, 128.0, 128.3, 130.6, 136.4 (4 *C*H, 2 q*C*, Ar), 142.9 (N*C*H), 163.0 (S*C*N), 202.3 (*C*S) ; IR (KBr): ν = 2839, 1638, 1570, 1502, 1399, 1353, 1240, 1145, 1098 cm^{-1} ; MS (EI); *m/z* (%): 254 (42) [M$^+$], 219 (100), 175 (23), 128 (67) ; *Anal*. Calcd for $C_{10}H_7N_2OClS$: C; 47.15, H; 2.77, N; 11.00. Found: C; 47.01, H; 2.83, N; 10.82.

1,1,6,6-Tetramethyl-3-methylsulfanyl-1,2,4,6-tetraazahexadienium iodide (7f): A suspension of **1e** (346 mg, 2 mmol) in methyl iodide (4 mL, 64,2 mmol) was stirred for 24 h at rt. Addition of ether achieved to precipitate compound (**7f**) which was collected by filtration to afford in 95% yield a pale yellow solid (mp 146°C) ; ^{1}H NMR ($CDCl_3$): δ = 2.41 (s, 3 H, SC*H*$_3$), 3.11 [s, 6 H,

NN(CH_3)$_2$], 3.19, 3.42 [2 s, 6 H, CN(CH_3)$_2$], 7.89 (s, 1 H, C*H*), 10.81 (br s, 1 H, N*H*) ; ^{13}C NMR ($CDCl_3$): δ = 13.9 (S*C*H$_3$), 38.2, 42.1 [CN(*C*H$_3$)$_2$], 46.9 [NN(*C*H$_3$)$_2$], 156.6 (*C*H), 178.7 (*C*S) ; IR (KBr): ν = 3000, 1644, 1521, 1355 cm^{-1} ; MS (EI); *m/z* (%): 188 (61) [M$^+$ - HI], 141 (29), 115 (35), 98 (100) ; *Anal.* Calcd for $C_7H_{17}N_4IS$: C; 26.59, H; 5.42, N; 17.72. Found: C; 26.72, H; 5.47, N; 17.64.

1,4-Bisdimethylamino-2-methylsulfanyl-1,3-diazabuta-1,3-diene (8f): To a suspension of **7f** (950 mg, 3 mmol) in ether (10 mL) was added 50 mL of a saturated solution of potassium hydrogencarbonate. The mixture was stirred at rt for 4 h. After extraction with ethyl acetate (2 x 20 mL), the combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated in *vacuo* to give **8f** (440 mg, 78%) as a pale yellow oil ; ^{1}H NMR ($CDCl_3$): δ = 2.29 (s, 3 H, SC*H*$_3$), 2.50 [s, 6 H, NN(C*H*$_3$)$_2$], 2.99, 3.05 [2 s, 6 H, CN(C*H*$_3$)$_2$], 7.87 (s, 1 H, C*H*) ; ^{13}C NMR ($CDCl_3$): δ = 13.5 (S*C*H$_3$), 34.1, 40.2 [CN(*C*H$_3$)$_2$], 47.0 [NN(*C*H$_3$)$_2$], 152.2 (*C*H), 169.0 (*C*S) ; IR (KBr): ν = 1747, 1634, 1541, 1374, 1255, 1101, 1046 cm^{-1} ; MS (EI); *m/z* (%): 188 (40) [M$^+$], 141 (24), 115 (34), 98 (100).

3-Dimethylamino-2-thioxo-1,2,3,4-tetrahydropyrimidin-4-one (10f): Hydrogen sulfide was passed at rt for 4 h through a solution of methylsulfanylpyrimidinone **(9f)** (185 mg, 1 mmol) in triethylamine (5 mL) and pyridine (5 mL). The solvents were removed and the residue was purified by flash chromatography (silica gel, dichloromethane/ethyl acetate 9/1). The product was crystallized from dichloromethane to provide **10f** (83,8 mg, 49%) as a white solid (mp >300°C) ; ^{1}H NMR (DMSO-d_6): δ = 2.84 [s, 6 H, N(C*H*$_3$)$_2$], 5.84 (d, *J* = 7.5 Hz, 1 H, C*H*CO), 7.30 (d, *J* = 7.5 Hz, 1 H, NC*H*), 9.26 (br s, 1 H, N*H*) ; ^{13}C NMR (DMSO-d_6): δ = 41.7 [N(*C*H$_3$)$_2$], 105.0 (*C*HCO), 140.3 (N*C*H), 161.0 (*C*O), 178.0 (*C*S) ; IR (KBr): ν = 1713, 1681, 1366, 1243 cm^{-1} ; MS (EI); *m/z* (%): 171 (10) [M$^+$], 129 (100), 112 (21), 101 (39) ; *Anal.* Calcd for $C_6H_9N_3OS$: C; 42.09, H; 5.30, N; 24.54. Found: C; 42.13, H; 5.21, N; 24.32.

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