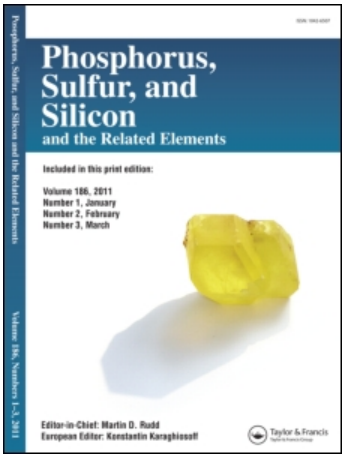

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2,4-DIAMINO-1-THIA-3-AZABUTADIENES, INTERMEDIATES IN HETEROCYCLIC SYNTHESIS

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2,4-DIAMINO-1-THIA-3-AZABUTADIENES, INTERMEDIATES IN HETEROCYCLIC SYNTHESIS

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(Received April 13, 1999)

2,4-Diamino-1-thia-3-azabutadienes **1** were studied. Methylation occured at sulfur and acylation at nitrogen bound to the 2 position. Alkylation by α-bromoketones gave rise to 2-amino-5-acylthiazoles. Upon treatment with acrylic dienophiles compounds **1** reacted either as diazadiene or as thiazadiene yielding tetrahydropyrimidinethiones or 6H-1,3-thiazines respectively.

Keywords: 2,4-Diamino-1-thia-3-azabutadienes; 2-amino-5-acylthiazoles; 1,2,3,4-tetrahydropyrimidinethiones; 2-amino-6H- 1,3-thiazines

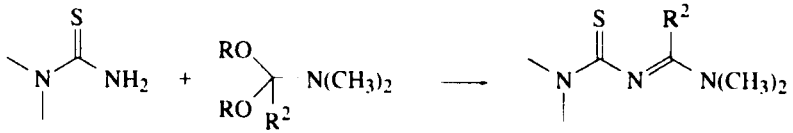
INTRODUCTION

During past years different types of 4-amino-1-thia-3-azabutadienes have been studied in our laboratory. These compounds are mainly used in heterocyclic synthesis. They allowed the access to various heterocycles containing sulfur and nitrogen: thiazoles[1,2], thiazolines[3], 6H-1,3-thiazines[1,2,4], 2H-1,3-thiazines[5,6] and cephems.[7–10]

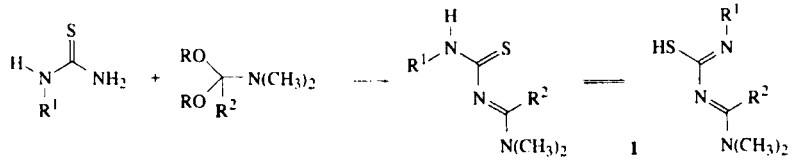
We display here our first results in the study of 2,4-diamino-1-thia-3-azabutadienes.

These compounds were prepared by condensation of an amide acetal with thioureas:

* Correspondance Author.



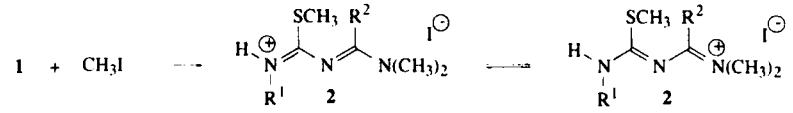
On one hand the N,N-disubstituted thioureas gave rise to compounds without any interesting properties[11]. On the other hand products **1** obtained from monosubstituted thioureas (N-methyl, N-phenyl and N-acetyl) present two nucleophilic centers : sulfur and nitrogen at the 2 position. They can have two tautomeric forms either thiazadiene or diazadiene and thus probably possess a wide reactivity.



RESULTS

With the aim to investigate the reactivity of these compounds we have first realized the alkylation reaction using methyl iodide and the acylation reaction upon treatment with acetyl chloride or benzoyl chloride.

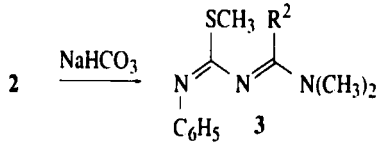
Obviously the methylation of compounds **1** afforded as the sole products the corresponding S-methyl iodides **2** due to the nucleophily of the sufur:



compounds	**1a, 2a**	**1b, 2b**	**1c**[12]**, 2c**	**1d**[12]**, 2d**	**1e, 2e**
R^1	CH_3	CH_3	C_6H_5	C_6H_5	CH_3CO
R^2	H	CH_3	H	CH_3	H

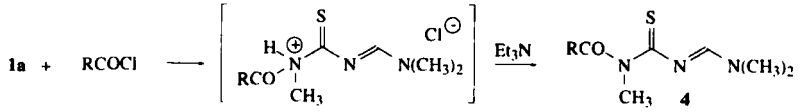
The iodides **2c,d** derived from N-phenylthiourea ($R^1 = C_6H_5$) were dehydrohalogenated using sodium hydrogencarbonate giving rise to aro-

matic methylthioimines **3**. In the other cases, the expected products were not stable enough to be isolated.



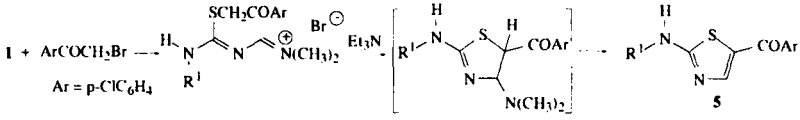
compounds	**3a**[13]	**3b**
R^2	H	CH_3

By reaction with acid chlorides the acylation of compounds **1** affected the nitrogen atom providing the N-acylated compounds **4**. The reaction was carried out in presence of triethylamine in order to eliminate hydrochloric acid. The intermediate salt was never isolated.



compounds	**4a**	**4b**
R	CH_3	C_6H_5

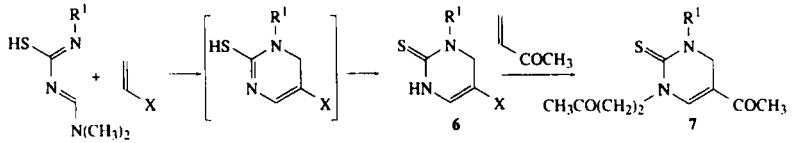
Interaction of p-chlorophenacylbromide with compounds **1** gave rise to 2-amino-5-p-chlorophenylthiazoles **5**. By comparison with the methylation reaction we suppose that the reaction began by alkylation of sulfur. The intermediate salt was deprotonated by triethylamine and cyclisation occurred with loss of dimethylamine. The imidazole that would correspond to the alkylation of nitrogen was not observed.



compounds	**5a**	**5b**	**5c**
R^1	CH_3	C_6H_5	CH_3CO

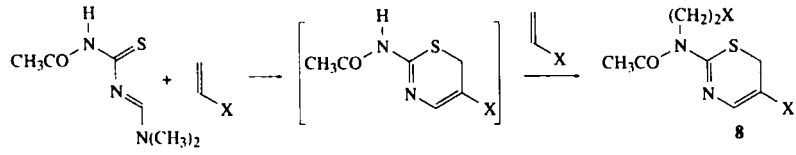
During the reaction with acrylic dienophiles, the behaviour of heterodienes **1** depends on the nature of the amino group close to the thiocarbo-

nyl. Compounds **1a,c** reacted according to the diazadiene tautomeric form and gave 1,2,3,4-tetrahydropyrimidinethiones **6** upon treatment with methylacrylate or ethylacrylate. With methylvinylketone the reaction was followed by a second addition of the dienophile on nitrogen at the **1** position and tetrahydropyrimidines **7** were obtained:



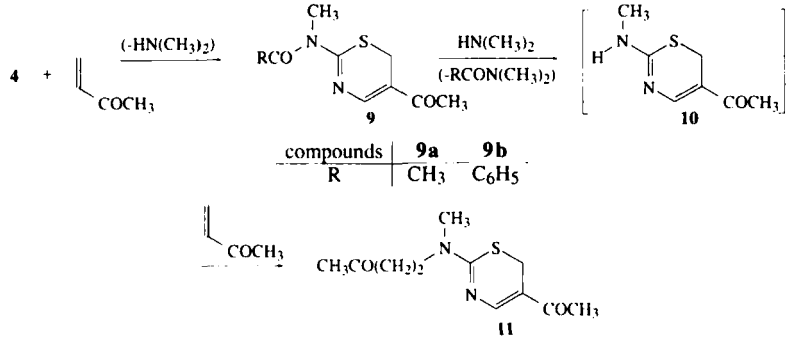
compounds	**6a**	**6b**	**6c**	**6d**	**7a**	**7b**
R^1	CH_3	CH_3	C_6H_5	C_6H_5	CH_3	C_6H_5
X	$COOCH_3$	$COOC_2H_5$	$COOCH_3$	$COOC_2H_5$		

Compound **1e** showed a different behaviour. The acetyl group penalizes the imine-thiol tautomeric form and in this case the thiazadiene chain reacted affording compound **8** which results from a second condensation of the dienophile with the expected 1,3-thiazine:



compounds	**8a**	**8b**
X	$COCH_3$	$COOC_2H_5$

This reaction was also realized starting with compounds **4** for which only the thiazadiene form is possible. Opposed to methylvinylketone they first gave thiazine **9** (minor). The major product was thiazine **11** obtained by deacylation of **9** by dimethylamine present in the mixture and by condensation of a second equivalent of the dienophile on intermediate **10**. We checked that compound **9b** treated with dimethylamine gives **10** which easily reacts with methylvinylketone yielding **11**:



CONCLUSION

2,4-Diamino- 1-thia-3-azabutadienes derived from monosubstituted thioureas possess two nucleophilic atoms; they are alkylated on sulfur and acylated on nitrogen in position 2. Opposed to dienophiles, they can react either as diazadiene or as thiazadiene and give rise to tetrahydropyrimidines or to 1,3-thiazines. Further work will consist in investigating more selectively the reactivity of these compounds.

EXPERIMENTAL

All reagents were purchased from Jansen Chimica Co. Kieselgel 60 (70–230 mesh) from E. Merck was used for silica gel column chromatography. Melting points were taken using Reichert microscope and are uncorrected. ^{1}H and ^{13}C NMR spectra were obtained using a BRUKER AC200 (200MHz) spectrometer in $CDCl_3$ (compounds **1–4,6–11**) or DMSO-D_6 (compounds **5**) and TMS as an internal standard. Mass spectra were obtained using a Hewlett Packard 5989 spectrometer. IR spectra were obtained using a BRUKER IFS 85 spectrometer.

Preparation of the 2-amino-4-dimethylamino-1-thia-3-azabutadienes 1

N,N-dimethylformamide dimethylacetal (0.023 mol) (for **1a,c,e**) or N,N-dimethylacetamide dimethylacetal (0.023 mol) (for **1b, 1d**) was added to a suspension of N-substituted thiourea (0.02 mol) in chloroform

(20 ml) (for **1a,b**) or dichloromethane (10 ml) (for **1c,d,e**). The reaction mixture was refluxed for 4 h. After removal of the solvent compounds **1** were crystallized from Et_2O.

2-N-methylamino-4-N,N-dimethylamino-1-thia-3-azabutadiene 1a

Colourless solid, m.p. 109°C, yield 98%. ^1H NMR δ : 3.04 and 3.15 (2s, 6H, $N(CH_3)_2$), 3.19 (d, 3H, ^3J=5.0 Hz, NCH_3), 7.12 (br.s, 1H, NH), 8.86 (s, 1H, CH). ^{13}C NMR δ : 31.8 (NCH_3), 35.5 and 41.3 ($N(CH_3)_2$), 162.1 (NCH), 194.3 (CS). MS 145 (100, M^+), 129 (10), 112 (22), 99 (38), 83 (11), 74 (23). IR (KBr) ν cm^{-1} : 3214, 3041, 2958, 1646, 1624, 1542, 1491, 1426, 1259, 1204, 1104, 1038, 744. Anal. calcd. for $C_5H_{11}N_3S$: C, 41.35; H, 7.63; N, 28.94. Found : C, 41.22; H, 7.58; N, 29.08.

2-N-methylamino-4-N,N-dimethylamino-1-thia-3-azapenta-1,3-diene 1b

Colourless solid, m.p. 64°C, yield 84%. ^1H NMR δ : 2.32 (s, 3H, CH_3-C), 3.08 (s, 6H, $N(CH_3)_2$), 3.13 (d, 3H, ^3J=5.0 Hz, CH_3NH), 6.57 (br.s, 1H, CH_3NH). ^{13}C NMR δ : 16.6 (CH_3-C), 31.0 (CH_3NH), 38.1 ($N(CH_3)_2$), 160.5 (CH_3-C), 189.2 (CS). MS 159 (100, M^+), 158 (12), 129 (51), 126 (67), 97 (23), 86 (10), 85 (21), 75 (21), 74 (35). IR (KBr) ν cm^{-1} : 3234, 2932, 1597, 1529, 1418, 1398, 1338, 1195, 1120. Anal. calcd. for $C_6H_{13}N_3S$: C, 45.25; H, 8.23; N, 26.39. Found : C, 45.06; H, 8.35; N, 26.25.

***4-N,N-dimethylamino-2-N-phenylamino-1-thia-3-azabutadiene 1c*[12]**

Colourless solid, m.p. 156°C, yield 94%. ^1H NMR δ : 3.10 and 3.21 (2s, 6H, $N(CH_3)_2$), 7.06 – 7.78 (m, 5H, C_6H_5), 8.71 (s, 1H, NH), 8.90 (s, 1H, CH). ^{13}C NMR δ : 36.3 and 41.6 ($N(CH_3)_2$), 122.3 and 128.5 (5CH), 138.9 (C), 163.8 (NCH), 191.0 (CS). MS 207 (28, M^+), 118 (10), 115 (100), 77 (16). IR (KBr) ν cm^{-1} : 3200, 3177, 3030, 1625, 1595, 1542, 1479, 1372, 1313, 1254, 1122.

***4-N,N-dimethylamino-N-phenylamino-1-thia-3-azapenta-1,3-diene 1d*[12]**

Colourless solid, m.p. 141°C, yield 91%. ^1H NMR δ : 2.48 (s, 3H, CH_3-C), 3.09 (s, 6H, $N(CH_3)_2$), 7.02 – 7.29 (m, 5H, C_6H_5), 8.48 (s, 1H, NH). ^{13}C NMR δ : 17.8 (CH_3-C), 38.2, 38.5 ($N(CH_3)_2$), 121.0, 123.7, 128.3 (5CH), 139.2 (C), 163.8 (C-CH_3), 185.7 (CS). MS 221 (48, M^+), 188 (11), 136 (18), 135 (82), 130 (13), 129 (100), 86 (23), 77 (59). IR (KBr) ν cm^{-1} : 3165, 1592, 1575, 1371.

2-N-acetylamino-4-N,N-dimethylamino-1-thia-3-azabutadiene 1e

Yellow solid, m.p. 139°C, yield 96%. ^{1}H NMR δ : 3.00 (s, 3H, CH_3CO), 3.15 and 3.29 (2s, 6H, $N(CH_3)_2$), 8.71 (s, 1H, CH), 8.82 (br.s, 1H, NH). ^{13}C NMR δ : 25.6 (CH_3CO), 35.9 and 41.2 ($N(CH_3)_2$), 162.0 (NCH), 169.0 (CO), 192.9 (CS). MS 173 (100, M^+), 140 (10), 130 (27), 115 (51), 114 (27), 99 (15), 98 (71). IR (KBr) ν cm^{-1}: 3176, 3143, 2925, 1688, 1626, 1477, 1440, 1375, 1351, 1273, 1245, 1157, 1120, 1038, 1038, 867. Anal. calcd. for $C_6H_{11}N_3OS$: C, 41.60; H, 6.40; N, 24.26. Found : C, 41.80; H, 6.25; N, 24.14.

Preparation of the 1,1-dimethyl-4-methylthio-1,3,5-triazapentadienium iodides 2

Methyl iodide (0. 1 mol) was added to a suspension of dimethylamino-1-thia-3-azabutadiene **1** (0.01 mol) in THF (5ml). The reaction mixture was stirred at room temp. for 24 h. After removal of the solvent, compounds **2** were precipitated by addition of Et_2O.

1,1,5-Trimethyl-4-methylthio-1,3,5-triazapentadienium iodide 2a

Colourless solid, m.p. 143°C, yield 98%. ^{1}H NMR δ : 2.52 (s. 3H, SCH_3), 3.07, 3.20 and 3.40 (3s, 9H, $N(CH_3)_2$ and NCH_3), 8.90 (s, 1H, CH), 9.50 (br.s. 1H, NH). ^{13}C NMR δ : 16.4 (SCH_3), 30.3 (NCH_3), 36.2 and 42.5 ($N(CH_3)_2$), 158.4 (NCH), 173.3 (C-SCH_3). MS 145 (20, M^+- CH_3I), 142 (28), 128 (16), 127 (22), 115 (10), 112 (100). IR (KBr) ν cm^{-1}: 3193, 2976, 2913, 1646, 1564, 1492, 1388, 1341. Anal. calcd. for $C_6H_{14}IN_3S$: C. 25.10; H, 4.91; N, 14.63. Found : C, 25.25; H. 5.02; N, 14.51.

1,1,2,5-Tetramethyl-4-methylthio-1,3,5-triazapentadienium iodide 2b

Colourless solid, m.p. 126°C, yield 96%. ^{1}H NMR δ : 2.41 (s, 3H, SCH_3), 2.51 (s, 3H, CH_3-C), 3.00 (d, 3H, ^{3}J=5.0 Hz, CH_3NH), 3.24 (d, 6H, $N(CH_3)_2$), 9.23 (br.s, 1H, NH). ^{13}C NMR δ : 14.1 (SCH_3), 20.2 (CH_3-C), 29.8 (CH_3-NH), 39.8 et 40.3 ($N(CH_3)_2$), 166.0 (CH_3-C), 172.0 (C-SCH_3). MS 173 (53, M^+-HI), 159 (36), 158 (13), 142 (64), 141 (10), 129 (27), 128 (42), 127 (56), 126 (100). IR (KBr) ν cm^{-1} : 2991, 2927, 1582, 1437, 1369, 1038. Anal. calcd. for $C_7H_{16}IN_3S$: C, 27.92; H, 5.35; N, 13.95. Found : C, 28.05; H, 5.49; N, 13.72.

1,1-Dimethyl-4-methylthio-5-phenyl-1,3,5-triazapentadienium iodide 2c

Colourless solid, m.p. 151°C, yield 98%. ^{1}H NMR δ : 2.49 (s, 3H, SCH_3), 3.22 and 3.41 (2s, 6H, $N(CH_3)_2$), 7.37–7.49 (m, 5H, C_6H_5), 8.99 (s, 1H, NCH), 10.06 (br.s, 1H, NH). ^{13}C NMR δ : 15.1 (SCH_3), 36.4 and 42.8 ($N(CH_3)_2$), 125.5, 127.9 and 128.7 (5CH), 134.9 (C), 157.1 (NCH), 176.7 (*C*-SCH_3). MS 221 (62, M^+-HI), 207 (20, M^+-CH_3I), 175 (64), 174 (100), 150 (20), 142 (22), 135 (21), 128 (62), 127 (43). IR (KBr) ν cm^{-1} : 3080, 2982, 2877, 2835, 1646, 1536, 1457, 1422, 1390, 1342. Anal. calcd. for $C_{11}H_{16}IN_3S$: C, 37.83; H, 4.62; N, 12.03. Found : C, 37.60; H, 4.48; N, 12.20.

1,1,2-trimethyl-4-methylthio-5-phenyl-1,3,5-triazapentadienium iodide 2d

Colourless solid, m.p. 145°C, yield 98%. ^{1}H NMR δ : 2.36 (s, 3H, SCH_3), 2.64 (s, 3H, CH_3-C), 3.30 (d, 6H, $N(CH_3)_2$), 7.30–7.51 (m, 5H, C_6H_5), 10.71 (s, 1H, NH). ^{13}C NMR δ : 14.6 (SCH_3), 20.51 (*C*H_3-C), 40.3, 40.7 ($N(CH_3)_2$), 125.4, 127.6, 128.9 (5CH), 135.3 (C), 167.0 (CH_3-*C*), 169.8 (*C*-SCH_3). MS 235 (15, M^+-HI), 189 (23), 188 (100), 142 (24), 135 (28), 129 (11), 128 (14), 127 (15). IR (KBr) ν cm^{-1} : 2886, 1602, 1592, 1568, 1487. Anal. calcd. for $C_{12}H_{18}IN_3S$: C, 39.68; H, 4.99; N, 11.57. Found : C, 39.75; H, 4.82; N, 11.42.

5-Acetyl-1,1-dimethyl-4-methylthio-1,3,5-triazapentadienium iodide 2e

Colourless solid, m.p. 124°C, yield 98%. ^{1}H NMR δ : 2.50 (s, 3H, SCH_3), 2.57 (s, 3H, CH_3CO), 3.29 and 3.52 (2s, 6H, $N(CH_3)_2$), 9.00 (s, 1H, CH), 11.70 (br.s, 1H, NH). ^{13}C NMR δ : 15.4 (SCH_3), 26.8 (CH_3CO), 37.1 and 43.6 ($N(CH_3)_2$), 156.1 (NCH), 169.7 and 176.0 (*C*-SCH_3 and CO). MS 173 (3, M^+- CH_3I), 140 (29), 12 (25), 127 (12), 98 (100). IR (KBr) ν cm^{-1} : 3176, 3143, 2925, 1688, 1626, 1477, 1440, 1375, 1351, 1273, 1245, 1157, 1120, 1030, 867. Anal. calcd. for $C_7H_{14}IN_3OS$: C, 26.28; H, 4.48; N, 13.33. Found : C, 26.11; H, 4.53; N, 13.51.

Preparation of the 4-N, N-dimethylamino-2-methylthio-1-phenyl-1,3-diazabutadienes 3

A saturated solution of sodium hydrogencarbonate (100 ml) was added to a suspension of the iodide **2c** or **2d** (0.01 mol) in Et_2O (50 ml). The reac-

tion mixture was stirred at room temp. for 3 h and extracted with AcOEt (2 × 70 ml). The organic layer was dried with $MgSO_4$ and the solvent was removed. Compounds **3** were isolated as oils.

4-N,N-dimethylamino-2-methylthio-1-phenyl-1,3-diazabutadiene 3a[13]

Yellow oil, Rf 0.3 (CH_2Cl_2/AcOEt 80/20), yield 98%. ^1H NMR δ : 2.40 (s, 3H, SCH_3), 3.10 (s, 6H, $N(CH_3)_2$), 6.91–7.31 (m, 5H, C_6H_5), 8.25 (s, 1H, NCH). ^{13}C NMR δ : 14.9 (SCH_3), 34.6 and 40.6 ($N(CH_3)_2$), 121.7, 122.9 and 128.6 (5 CH), 128.8 (C), 150.1 and 154.0 (NCH and *C*-SCH_3). MS 221 (11, M^+), 175 (15), 174 (100). IR (KBr) ν cm^{-1}: 3056, 3024, 2924, 1628, 1557, 1429, 1090.

4-Methyl-4-N,N-dimethylamino-2-methylthio-1-phenyl-1,3-diazapenta-1,3-diene 3b

Yellow oil, Rf 0.3 (CH_2Cl_2/AcOEt 80/20), yield 98%. ^1H NMR δ : 2.28 (s, 3H, CH_3-C), 2.43 (s, 3H, SCH_3), 2.84 (s, 6H, $N(CH_3)_2$), 7.15–7.28 (m, 5H, C_6H_5). ^{13}C NMR δ : 14.8 (SCH_3), 16.8 (*C*H_3-C), 37.7 ($N(CH_3)_2$), 121.6, 121.9, 122.0 (5CH), 123.1 (C), 149.7 (CH_3-*C*), 156.6 (*C*-SCH_3). MS 235 (23, M^+), 189 (33), 188 (100), 147 (13), 104 (47). IR (KBr) ν cm^{-1} : 3058, 3023, 2923, 1575, 1486, 1417 1399, 1285, 1220, 1124, 952, 695.

Preparation of the 2-(N-acyl-N-methylamino)-4-N,N-dimethylamino-1-thia-3-azabutadienes 4

Triethylamine (0.009 mol) and acid chloride (0.008 mol) (acetyl chloride for **4a** or benzoyl chloride for **4b**) were successively added to a suspension of compound **1a** (0.08 mol) in CH_2Cl_2 (10 ml). After 4 h stirring at room temp. the same amounts of triethylamine and acid chloride were added and the solution mixture was stirred 20 h. The solvent was removed and the residue was purified by flash chromatography using CH_2Cl_2/AcOEt (19/1) as eluent. Compounds **4** were crystallized from Et_2O.

2-(N-acetyl-N-methylamino)-4-N,N-dimethylamino-1-thia-3-azabutadiene 4a

Yellow solid, m.p. 48°C, yield 69%. ^1H NMR δ : 2.51 (s, 3H, CH_3CO), 3.13 and 3.26 (2s, 6H, $N(CH_3)_2$), 3.58 (s, 3H, NCH_3), 8.65 (s, 1H, CH).

^{13}C NMR δ : 28.4 (CH_3CO), 36.1 (NCH_3), 37.5 and 41.7 ($N(CH_3)_2$), 161.2 (NCH), 174.0 (CO), 198.2 (CS), MS 187 (76, M^+), 144 (12), 115 (100), 112 (36). Anal. calcd. for $C_7H_{13}N_3OS$: C, 44.90; H, 7.00; N, 22.44. Found : C, 50.05; H. 7.13; N, 22.30.

2-(N-benzoyl-N-methylamino)-4-N,N-dimethylamino-1-thia-3-azabutadiene 4b

Yellow solid, m.p. 93°C. yield 70%. ^1H NMR δ : 2.37 and 3.00 (2s, 6H, $N(CH_3)_2$), 3.72 (s, 3H, CH_3N), 7.33–7.65 (m. 5H, C_6H_5), 8.41 (s, 1H, CH). ^{13}C NMR δ : 35.3 (CH_3N), 38.0 and 41.2 ($N(CH_3)_2$), 127.8, 127.9 and 130.9 (5 CH). 167.9 (C), 160.2 (CH), 174.9 (CO), 196.9 (CS), MS 249 (53, M^+), 248 (27), 115 (100), 112 (83). Anal. calcd. for $C_{12}H_{15}N_3OS$: C, 57.81; H, 6.06; N, 16.85. Found : C, 58.01; H, 5.88; N. 16.65.

Preparation of the 2 -amino-5-p-chlorobenzoylthiazoles 5

p-Chlorophenacyl bromide (0.002 mol) was added to a suspension of **1a,c,e** (0.002 mol) in CH_2Cl_2 (5 ml). After 1 h stirring at room temp. triethylamine (0.006 mol) was added and the mixture was stirred 20 h. The solvent was removed and the residue was purified by flash chromatography using CH_2Cl_2/AcOEt (1/1) as eluent. Compounds **5** were crystallized from AcOEt.

5-p-Chlorobenzoyl-2-N-methylaminothiazole 5a

Yellow solid, m.p. 181°C, yield 95% ^1H NMR δ : 2.90 (s, 3H, NCH_3), 7.57 and 7.77 (2d, J = 8.5 Hz, 4H, C_6H_4), 7.76 (s, 1H, NCH), 8.80 (s.e., 1H, NH). ^{13}C NMR δ : 31.0 (NCH_3), 126.2 (*C*-CO), 128.5, 129.9 (4CH), 136.4, 136.8 (2C), 151.1 (NCH), 175.1 (CN), 183.8 (CO). MS 254/252 (38/100, M^+), 224 (35), 141 (88), 138 (38), 113 (53), 111 (44). Anal. calcd. for $C_{11}H_9ClN_2OS$: C, 52.28; H, 3.59; N, 11.08. Found : C, 52.35; H, 3.70; N, 10.94.

5-p-Chlorobenzoyl-2-N-phenylaminothiazole 5b

Yellow solid, m.p. 233°C, yield 97%. ^1H NMR δ : 7.05-7.85 (m, 9H, C_6H_4 and C_6H_5), 7.92 (s, 1H, NCH). MS 316/314 (40/100, M^+), 203 (21), 175 (37), 139 (29), 111 (27). Anal. calcd. for $C_{16}H_{11}ClN_2OS$: C, 61.05; H, 3.52; N, 8.90. Found : C, 61.18; H, 3.65; N, 9.01.

2-N-acetylamino-5-p-chlorobenzoylthiazole 5c

Yellow solid, m.p. 261°C, yield 94%. ^{1}H NMR δ : 2.22 (s, 3H, CH_3CO), 7.62 and 7.87 (2d, J=8.6 Hz, 4H, C_6H_4), 8.11 (s, 1H, NCH), 12.65 (s.e., 1H, NH). ^{13}C NMR δ : 22.5 (*C*H_3CO), 127.7, 130.4 (4CH), 130.9 (*C*-CO), 136.2, 137.3 (2C), 146.9 (NCH), 163.7 (NCO), 169.3 (CN), 185.8 (CO). MS 282/280 (8/19, M^+), 240 (38), 238 (100), 203 (11), 139 (23), 127 (40), 111 (22). Anal. calcd. for $C_{12}H_9ClN_2O_2S$: C, 51.34; H, 3.23; N, 9.98. Found : C, 51.20; H, 3.12; N, 9.75.

Preparation of the 1,2,3,4-tetrahydropyrimidine-2-thiones 6 and 7

A solution of **1a** or **1c** (0.003 mol) in methyl or ethylacrylate (10 ml) for compounds **6** or methylvinylketone (3 ml) for compounds **7** was refluxed (4 days for compounds **6**, 24 h for compounds **7**). The solvent was removed and the residue was purified by flash chromatography using CH_2Cl_2/AcOEt (4/1) as eluent. Compounds **6** and **7** were crystallized from AcOEt/Et_2O.

5-Methoxycarbonyl-3-methyl-1,2,3,4-tetrahydropyrimidine-2-thione 6a

Yellow solid, m.p. 205°C, yield 68%. ^{1}H NMR δ : 3.39 (s, 3H, NCH_3), 3.75 (s, 3H, OCH_3), 4.20 (d, 2H, ^{4}J=0.9 Hz, NCH_2), 7.05 (dt, 1H, ^{3}J=5.5 Hz, ^{4}J=0.9 Hz, NCH), 8.07 (d, 1H, ^{3}J=5.5 Hz, NH). ^{13}C NMR δ : 40.8 (NCH_3), 47.8 (NCH_2), 51.1 (OCH_3), 99.6 (*C*-$COOCH_3$), 132.6 (NCH), 164.8 (CO). 175.1 (CS). MS 186 (100, M^+), 185 (17), 171 (53), 153 (11), 127 (15). IR (KBr) ν cm^{-1} : 2893, 1619, 1532, 1315, 1293, 1204, 1065, 1022, 874, 739, 725, 701, 694, 670. Anal. calcd. for $C_7H_{10}N_2O_2S$: C, 45.15; H, 5.41; N, 15.04; S, 17.22. Found : C, 45.10; H, 5.42; N, 15.12; S, 16.98.

5-Ethoxycarbonyl-3-methyl-1,2,3,4-tetrahydropyrimidine-2-thione 6b

Colorless solid, m.p. 136°C, yield 57%. ^{1}H NMR δ : 1.28 (t,3H, ^{3}J=7.2 Hz, C*H*$_3$CH$_2$O), 3.40 (s, 3H, NCH_3), 4.20 (d, 2H, ^{4}J=0.9 Hz, NCH_2), 4.21 (q, 2H, ^{3}J=7.2 Hz, CH_3CH_2O), 7.05 (dt, 1H, ^{3}J=5.5 Hz, ^{4}J=0.9 Hz, NCH), 8.70 (d, 1H, ^{3}J=5.5 Hz, NH). ^{13}C NMR δ : 14.3 (*C*H_3CH$_2$), 41.7 (NCH_3), 48.8 (NCH_2), 60.5 (*C*H_2CH$_3$), 101.1 (*C*-$COOCH_2CH_3$), 132.4 (NCH), 165.0 (CO), 175.5 (CS). MS 200 (95, M^+), 199 (10), 171 (100), 155 (10), 153 (15), 127 (19), 112 (14). IR (KBr)

ν cm^{-1} : 2893, 1619, 1532, 1315, 1293, 1204, 1065, 1022, 874, 739, 725, 701, 694, 670. Anal. calcd. for $C_8H_{12}N_2O_2S$: C, 47.98; H, 6.04; N, 13.99; S, 16.01. Found : C, 47.88; H, 6.11; N, 14.00; S, 16.08.

5-Methoxycarbonyl-3-phenyl-1,2,3,4-tetrahydropyrimidine-2-thione 6c

Colorless solid, m.p. 207°C, yield 85%. ^1H NMR δ : 3.73 (s. 3H, CH_3), 4.48 (s, 2H, CH_2), 7.12 (d, 1H, ^3J=5.4 Hz, NCH), 7.30–7.54 (m, 5H, C_6H_5), 8.88 (d, 1H, ^3J=5.4 Hz, NH). ^{13}C NMR δ : 50.9 (CH_2), 51.8 (CH_3), 102.4 (*C*-$COOCH_3$). 126.8, 128.5, 130.0 (5CH), 132.5 (NCH), 144.8 (C), 165.2 (CO), 177.1 (CS). MS 248 (96, M^+), 247 (100), 233 (28), 215 (15), 136 (11), 135 (78). IR (KBr) ν cm^{-1} : 2893, 1619, 1532, 1315, 1293, 1204, 1065, 1022, 874, 739, 725, 701, 694, 670.

5-Ethoxycarbonyl-3-phenyl-1,2,3,4-tetrahydropyrimidine-2-thione 6d

Colorless solid, m.p. 185°C, yield 77%. ^1H NMR δ: 1.26 (t. 3H, ^3J=7.3 Hz, CH_3), 4.19 (q, 2H, ^3J=7.3 Hz, OCH_2), 4.46 (s, 2H, NCH_2), 7.11 (d. 1H, ^3J=5.0 Hz, NCH), 7.31–7.48 (m, 5H C_6H_5), 8.86 (d, 1H, ^3J=5.0 Hz. NH). ^{13}C NMR δ : 14.1 (CH_3), 50.7 (NCH_2), 60.5 (OCH_2), 102.4 (*C*-$COOCH_2CH_3$). 126.6, 128.2, 129.7 (5CH), 132.1 (NCH). 144.6 (C), 164.5 (CO), 176.9 (CS), MS 262 (100, M^+). 261 (81). 234 (16), 233 (76). 217 (11), 215 (16), 189 (15), 137 (10), 136 (22), 135 (91). IR (KBr) ν cm^{-1} : 2893, 1619, 1532, 1315, 1293, 1204, 1065, 1022, 874, 739, 725, 701, 694, 670. Anal. calcd. for $C_{13}H_{14}N_2O_2S$: C, 59.52; H, 5.38; N, 10.68. Found : C, 59.22; H, 5.41; N, 10.54.

5-Acetyl-1-(3-oxobut-1-yl)-3-methyl-1,2,3,4-tetrahydropyrimidine-2-thione 7a

colorless solid, m.p 128°C, yield 78%. ^1H NMR δ : 2.18 and 2.28 (2s,6H, $COCH_3$), 3.08 (t, 2H, ^3J=5.7 Hz, CH_2CO), 3.37 (s, 3H, NCH_3), 4.15 (d, 2H,^4J=0.7 Hz, NCH_2), 4.27 (t, 2H, ^3J=5.7 Hz, NCH_2CH_2), 7.48 (t, 1H, ^4J=0.7 Hz, NCH). ^{13}C NMR δ : 24.2 and 30.1 ($COCH_3$), 42.9 (CH_2CO), 43.4 (NCH_3), 48.4 (NCH_2CH_2), 49.6 (NCH_2), 110.5 (*C*-$COCH_3$), 139.8 (NCH), 177.1 (CS), 193.6 and 207.1 (2CO). MS 240 (33, M^+), 124 (32), 112 (12). IR (KBr) ν cm^{-1} : 3062, 2963, 1706, 1670, 1621, 11423, 1389, 1339, 1253, 1209. Anal. calcd. for $C_{11}H_{16}N_2O_2S$: C, 54.98; H, 6.71; N, 11.66; S, 12.34. Found : C, 54.69; H, 6.64; N, 11.57; S, 12.98.

5-Acetyl-1-(3-oxobut-1-yl)-3-phenyl-1,2,3,4-tetrahydropyrimidine-2-thione 7b

Colorless solid, m.p. 145°C, yield 90%. ^{1}H NMR δ : 2.22 and 2.35 (2s,6H, $2CH_3$), 3.14 (t, 2H, ^{3}J=5.6 Hz, CH_2CO), 4.33 (t, 2H,^{3}J=5.6 Hz, NCH_2CH_2), 4.40 (s, 2H, NCH_2), 7.22–7.49 (m, 5H, C_6H_5), 7.60 (s, 1H, NCH). ^{13}C NMR δ : 24.4 and 30.2 ($COCH_3$), 42.8 (CH_2CO), 49.5 (NCH_2CH_2), 50.1 (NCH_2), 112.0 (*C*-$COCH_3$), 126.6, 127.9 and 129.7 (5 CH), 139.5 (NCH), 146.3 (C), 178.5 (CS), 193.8 and 207.6 (2CO). MS 302 (76, M^+), 301 (24), 259 (20), 257 (15), 232 (16), 231 (44), 174 (10), 136 (10), 135 (19), 124 (84). IR (KBr) ν cm^{-1} : 3139, 2963, 1705, 1664, 1628, 1538, 1478, 1406, 1329, 1271, 1198, 1124, 697. Anal. calcd. for $C_{16}H_{18}N_2O_2S$: C, 63.55; H, 6.00; N, 9.26; S, 10.60. Found : C, 63.66; H, 5.83; N, 9.51; S, 10.95.

Preparation of the 2-N-acetylamino-6H-1,3-thiazines 8

A solution of **4a** (0.003 mol) in methylvinylketone for **8a** (3 ml) or in methylacrylate for **8b** (5 ml) was refluxed 20 h or 5 days respectively. The solvent was removed and the residue was purified by flash chromatography using CH_2Cl_2/AcOEt (4/1) as eluent. Compounds **8** were isolated as oils.

5-Acetyl-2-(N-acetyl-N-3-oxobut-1-ylamino)-6H-1,3-thiazine 8a

Colorless oil, Rf 0.40 (CH_2Cl_2/AcOEt : 4/1), yield 75%. ^{1}H NMR δ : 2.19, 2.24 and 2.36 (3s, 9H, $3COCH_3$), 2.98 (t, 2H, ^{3}J=6.0 Hz, CH_2CO), 3.53 (d, 2H,^{4}J=0.6 Hz, SCH_2), 4.10 (t, 2H, ^{3}J=6.0 Hz, NCH_2), 7.60 (t, 1H, ^{4}J=0.6 Hz, NCH). ^{13}C NMR δ : 21.1 (SCH_2), 24.4, 26.2 and 29.8 ($3COCH_3$), 41.6 (CH_2CO), 47.8 (NCH_2), 114.0 (*C*-CO), 143.0 (NCH), 157.3 (CN), 181.4 (NCO), 193.4 and 206.6 (2CO), MS 268 (5, M^+), 225 (20), 183 (11).

2-[N-acetyl-N-(2-methoxycarbonyl)ethylamino]-5-methoxycarbonyl-6H-1,3-thiazine 8b

Colorless oil, Rf 0.55 (CH_2Cl_2/AcOEt : 4/1), yield 67%. ^{1}H NMR δ : 2.25 (s, 3H, $COCH_3$), 2.80 (t, 2H, ^{3}J=6.0 Hz, CH_2CO), 3.55 (d, 2H,^{4}J=0.7 Hz, SCH_2), 3.70 and 3.81 (2s, 6H, OCH_3), 4.14 (t, 2H, ^{3}J=6.0 Hz, NCH_2), 7.47 (t, 1H, ^{4}J=0.7 Hz, NCH). ^{13}C NMR δ : 22.6 (SCH_2), 26.4 ($COCH_3$),

32.7 (CH_2CO), 49.1 (NCH_2), 51.8 and 51.9 ($2CH_3O$), 104.4 (*C*-CO), 141.1 (NCH), 157.7 (CN), 165.2 and 171.6 ($2COOCH_3$), 181.6 (NCO). MS 300 (27, M^+), 285 (44), 241 (45), 200 (69), 168 (35), 140 (25), 126 (57).

Preparation of the 5-acetyl-2-(N-acyl-N-methylamino)-6H-1,3-thiazines 9 and 5-acetyl-2-(N-3-oxobut-1-yl-N-methylamino)-6H-1,3-thiazine 11

A solution of **4** (0.003 mol) in methylvinylketone (5 ml) was refluxed 48 h. The solvent was removed and the residue was purified by flash chromatography. Compounds **9** were isolated after elution by CH_2Cl_2/AcOEt (9/1) and compound **11** after elution by CH_2Cl_2/AcOEt (4/1).

5-Acetyl-2-(N-methylacetamido)-6H-1,3-thiazine 9a

Yellow oil, Rf 0.4 (CH_2Cl_2/AcOEt 9/1), yield 12%. ^{1}H NMR δ : 2.36 and 2.39 (2s, 6H, $2COCH_3$), 3.48 (s, 3H, NCH_3), 3.50 (s, 2H, SCH_2), 7.75 (s, 1H, NCH). MS 212 (10, M^+), 170 (20), 169 (29), 127 (74).

5-Acetyl-2-(N-methylbenzamido)-6H-1,3-thiazine 9b

Yellow solid (Et_2O), m.p. 144°C, yield 44%. ^{1}H NMR δ : 2.38 (s, 3H, $COCH_3$), 3.47 (s, 2H, SCH_2), 3.52 (s, 3H, NCH_3), 7.39–7.65 (m, 5H, C_6H_5), 7.75 (s, 1H, NCH), ^{13}C NMR δ : 22.6 (SCH_2), 25.3 ($COCH_3$), 37.5 (NCH_3), 116.9 (*C*-CO), 128.6, 128.6 and 131.9 (5CH), 134.8 (C), 146.3 (NCH), 160.9 (CN), 171.7 (NCO), 195.3 (CO), MS 274 (7, M^+), 231 (43), 105 (100).

5-Acetyl-2-(N-3-oxobut-1-yl-N-methylamino)-6H-1,3-thiazine 11

Yellow oil. Rf 0.2 (CH_2Cl_2/AcOEt 9/1), yield 60% from **4a**, 51% from **4b**. ^{1}H NMR δ : 2.19 and 2.32 (2s, 6H, $2COCH_3$), 2.83 (t, 2H. ^{3}J=6.8 Hz, CH_2CO), 3.22 (s, 3H, NCH_3), 3.67 (s. 2H, SCH_2), 3.86 (t, 2H, ^{3}J=6.8 Hz, NCH_2), 7.81 (s, 1H, NCH). ^{13}C NMR δ : 22.4 (SCH_2), 24.6 and 30.2 ($2COCH_3$), 38.0 (NCH_3), 41.7 (CH_2-CO), 46.5 (NCH_2), 10.3 (*C*-CO), 151.3 (NCH), 160.7 (CN), 195.1 and 207.3 (2CO). MS 240 (15, M^+), 197 (64), 127 (32).

Preparation of the 5-acetyl-2-(N-methylamino)-6H-1,3-thiazine 10

A solution of dimethylamine (0.0012 mol) in CH_2Cl_2(ml) was added to a solution of **9b** (0.001 mol) in CH_2Cl_2 (5 ml). The mixture was stirred 24 h at room temp..The solvent was removed and the residue was purified by flash chromatography. Compound **10** was isolated after elution by CH_2Cl_2/AcOEt (7/3) and crystallized from AcOEt.

Yellow solid, m.p. 141°C, yield 68%. ^{1}H NMR δ : 2.34 (s, 3H, $COCH_3$), 3.08 (s, 3H, NCH_3), 3.68 (s, 2H, SCH_2), 5.60 (s, 1H, NH), 7.84 (s, 1H, NCH). ^{13}C NMR δ : 22.2 (SCH_2), 24.7 ($COCH_3$), 38.2 (NCH_3), 109.9 (*C*-CO), 151.5 (NCH), 160.0 (CN), 195.6 (CO). MS 170 (16, M^+), 127 (100), 86 (23). Anal. calcd. for $C_7H_{10}N_2OS$: C, 49.39; H, 5.92; N, 16.41. Found : C, 49.51; H, 6.03; N, 16.56.

References

1. J.C. Meslin, H. Quiniou, *Synthesis*, **4**, 298–300 (1974).
2. J.C. Meslin, H. Quiniou, *Tetrahedron*, **31**, 3055–3058 (1975).
3. A. Reliquet, J. C. Meslin, F. Reliquet, D. Benhadda, B. Bossard, *Sulfur Lett.*, **7(2)**, 49–54, (1987).
4. J.C. Meslin, H. Quiniou, *Bull. Soc. Chim. Fr.*, **II**, 347–349 (1979).
5. A. Reliquet, F. Reliquet, J. C. Meslin, H. Quiniou, *Phosphorus and Sulfur*, **15**, 143–153, (1983).
6. F. Reliquet, J. C. Meslin, A. Reliquet, B. Bossard, D. Benhadda, *Sulfur Lett.*, **7(2)**, 55–60, (1987).
7. J.C. Meslin, A. Reliquet, F. Reliquet, H. Quiniou, *Synthesis*, **6**, 453–454 (1980).
8. A. Reliquet, J.C. Meslin, F. Reliquet, H. Quiniou, *Tetrahedron*, **44 (4)**, 1107–1115 (1988).
9. M. Bakasse, A. Reliquet, F. Reliquet, G. Duguay, H. Quiniou, *J. Org. Chem.*, **54**, 2889–2893 (1989).
10. C. Friot, A. Reliquet, J. C. Meslin, *Phosphorus Sulfur and Silicon*, **131**, 147–160, (1997).
11. M. Chehna, J.P. Pradère, A. Guingant, *Syn. Commun.*, 1971–1976 (1987).
12. Y-I Lin, S.A. Lang Jr., S.R. Petty, *J. Org. Chem.*, **45**, 3750–3753 (1980).
13. S.N. Mazumdar and M.P. Mahajan, *Synthesis*, 417–419 (1990).