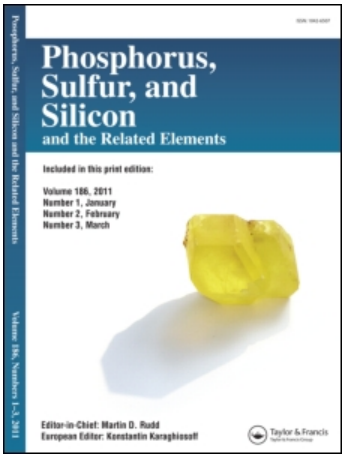

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STABLE α-HYDRAZONOTHIOACETOPHENONES USED AS HETERODIENES

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STABLE α-HYDRAZONOTHIOACETOPHENONES USED AS HETERODIENES

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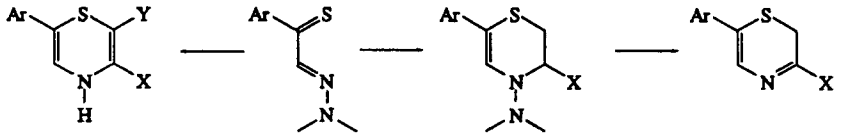
Preparation of three stable α-dimethylhydrazonothioacetophenones containing an aromatic cycle substituted by strongly electron withdrawing groups (*o*-fluoro, *o*- or *p*-nitro) is described. By [4 + 2] cycloaddition, these compounds react with acrylic dienophiles (acrolein, methylvinylketone, methylacrylate, acrylonitrile) or with cyclic dienophiles (N-methyl or N-phenylmaleimide) to lead to 3,4-dihydro-2H-1,4-thiazines, 2H-1,4-thiazines or 4H-1,4-thiazines in good yields.

Key words: α-Dimethylhydrazonothioacetophenones, 3,4-dihydro-2H-1,4-thiazines, 2H-1,4-thiazines, 4H-1,4-thiazines.

INTRODUCTION

We have recently reported the synthesis of α-hydrazonothioacetophenones **5**, compounds containing an original heterodiene chain, and their properties. These compounds constitute potential precursors for heterocyclic synthesis. They allow the access to dihydro-1,4-thiazines and to 1,4-thiazines[1,2]:



4H-1,4-thiazines **5** 3,4-dihydro-2H-1,4-thiazines 2H-1,4-thiazines

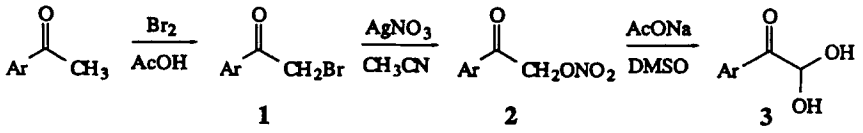
The great unstability of the α-hydrazonothioacetophenones has limited their use and led to an important fall in the yields of the considered reactions.

Carrying out the study of these compounds, we noted an appreciable increase of stability when the aromatic cycle is substituted by strongly electron withdrawing groups (*o*-fluoro, *o*- or *p*-nitro).

We report here the preparation of these compounds and the results obtained about their reactivity.

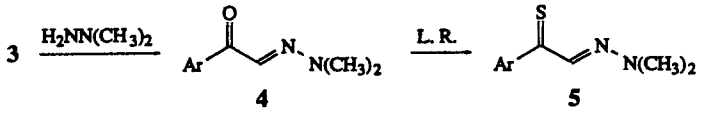
RESULTS

The synthesis of the compounds **5** starts with arylacylbromides. These compounds, apart *p*-nitrophenacylbromide which is commercially available, are obtained by the action of bromine in acetic acid on the corresponding acetophenones.[3] Then, the



bromides **1** are easily converted into arylglyoxal hydrates **3** via the synthesis of the nitric esters **2** (silver nitrate in acetonitrile) and the reaction of the latter with sodium acetate in DMSO.[4]

The subsequent addition of N,N-dimethylhydrazine on **3** leads to the hydrazones **4** which afford the desired α-hydrazonothioacetophenones **5** in the presence of Lawesson's Reagent[5]:



compounds					Ar
1a	**2a**	**3a**	**4a**	**5a**	o-F-C_6H_4
1b	**2b**	**3b**	**4b**	**5b**	o-NO_2-C_6H_4
1c	**2c**	**3c**	**4c**	**5c**	p-NO_2-C_6H_4

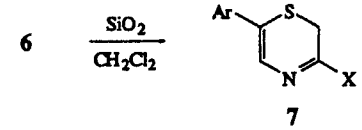
The compounds **5** thus obtained are stable and can be kept for days at r.t. The compound **5c** (Ar = *p*-$NO_2C_6H_4$) is even well crystallised.

The reaction of α-hydrazonothioacetophenones **5** with acrylic dienophiles be-

compounds	**6a**	**6b**	**6c**	**6d**	**6e**
Ar	o-F-C_6H_4	o-F-C_6H_4	o-F-C_6H_4	o-NO_2-C_6H_4	o-NO_2-C_6H_4
X	CN	$COCH_3$	$COOCH_3$	CN	$COCH_3$
compounds	**6f**	**6g**	**6h**	**6i**	**6j**
Ar	o-NO_2-C_6H_4	p-NO_2-C_6H_4	p-NO_2-C_6H_4	p-NO_2-C_6H_4	p-NO_2-C_6H_4
X	$COOCH_3$	CN	CHO	$COCH_3$	$COOCH_3$

haves like heterodienes and leads to the expected [4 + 2] cycloaddition products. 3,4-Dihydro-2H-1,4-thiazines **6** are then isolated in excellent yields.

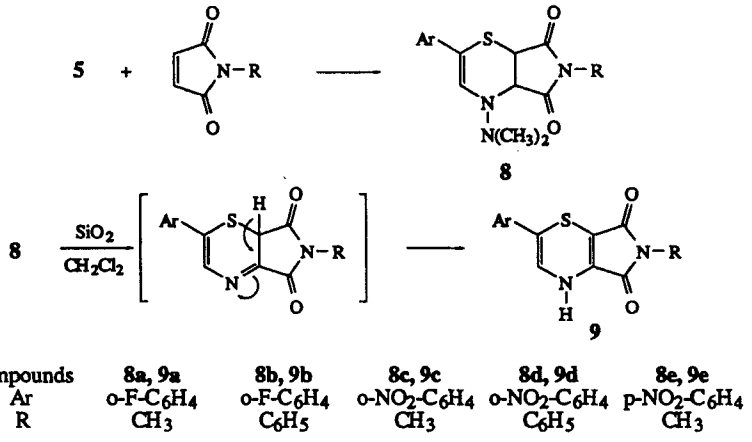
The dihydrothiazines are usually purified on silica column chromatography, except the compound **6h** which must be directly crystallised. Indeed, after chroma-



compounds	**7b**	**7e**	**7h**	**7i**
Ar	o-F-C_6H_4	o-NO_2-C_6H_4	p-NO_2-C_6H_4	p-NO_2-C_6H_4
X	$COCH_3$	$COCH_3$	CHO	$COCH_3$

tography, a little amount of 2H-1,4-thiazine **7h** resulting from elimination of dimethylamine is still present. This reaction of elimination of amine by silica gel is known[6–8] and we tried to apply it to the other prepared compounds. Only dihydrothiazines **6b**, **6e** and **6i** bearing an acetyl group in 3 position, stirred in methylene chloride containing a silica suspension, lead to the corresponding 2H-1,4-thiazines. The hydrogen atom near the methylcarboxylate group or the cyano group in the other compounds is probably not acidic enough to lead to the elimination of amine.

The yields of these reactions are good, except for the compound **7h**, which is not very stable.



compounds	**8a, 9a**	**8b, 9b**	**8c, 9c**	**8d, 9d**	**8e, 9e**
Ar	o-F-C_6H_4	o-F-C_6H_4	o-NO_2-C_6H_4	o-NO_2-C_6H_4	p-NO_2-C_6H_4
R	CH_3	C_6H_5	CH_3	C_6H_5	CH_3

α-Hydrazonothioacetophenones **5** behave similarly when the N-methylmaleimide or the N-phenylmaleimide is used as a dienophile. After [4 + 2] cycloaddition, the bicyclic 4-dimethylamino-3,4-dihydro-2H-1,4 thiazines **8** are isolated. Treated with a silica suspension in methylene chloride, they give the 4H-1,4-thiazines **9** which are probably more stable than the tautomer intermediates 2H-1,4-thiazines.

CONCLUSION

α-Hydrazonothioacetophenones prepared from acetophenones whose aromatic cycle is substituted by an electron withdrawing group (*o*-fluoro, *o*- or *p*-nitro), present a satisfactory stability. By [4 + 2] cycloaddition with acrylic dienophiles (acrolein, methylvinylketone, methylacrylate or acrylonitrile) or with cyclic dienophiles (N-methyl or N-phenylmaleimide), they allow the preparation of 3,4-dihydro-2H-1,4-thiazines, 2H-1,4-thiazines and 4H-1,4-thiazines in good yields.

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. ^1H and ^{13}C NMR spectra were obtained using a JEOL FX90Q (90 MHz) spectrometer or a BRUCKER AC200 (200 MHz) spectrometer. Mass spectra were obtained using a Hewlett Packard 5989 spectrometer.

α-Hydrazonoacetophenones **4**. N,N-dimethylhydrazine (20 mmol) in EtOH (20 ml) is added dropwise to a solution of arylglyoxal hydrate **3** (20 mmol) in EtOH (20 ml). After 24 h stirring at r.t., EtOH is evaporated. The residue is then diluted with CH_2Cl_2 and fractionated by silica gel chromatography. After elution using CH_2Cl_2/EtOAc (90:10), compound **4a** is isolated as yellow oil, compound **4b** or **4c** is crystallized in EtOH and isolated as orange crystals.

Compound **4a**: oil; 74% yield; NMR ^1H ($CDCl_3$) 3.18 (s, 6H, $N(CH_3)_2$), 7.00 (s, 1H, CH), 7.03–7.62 (m, $4H_{arom}$); NMR ^{13}C 42.84 (q, $N(CH_3)_2$), 115.87 (dd, $^2J_{C-F}$ = 22.8 Hz, CH_{arom}), 123.86 (dd, $^4J_{C-F}$ = 3.4 Hz CH_{arom}), 126.51 (dd, $^4J_{C-F}$ = 2.5 Hz, CH=N) 128.02 (d, $^2J_{C-F}$ = 15.4 Hz, C_{arom}), 130.67 (dd, $^3J_{C-F}$ = 3.5 Hz, CH_{arom}), 132.05 (dd, $^3J_{C-F}$ = 8.4 Hz, CH_{arom}), 160.13 (d, $^1J_{C-F}$ = 250.5 Hz, C_{arom}), 188.62 (d, $^3J_{C-F}$ = 2.1 Hz, C=O); MS $C_{10}H_{11}FN_2O$ 194 (M^+).

Compound **4b**: mp 119°C; 57% yield; NMR ^1H ($CDCl_3$) 3.07 (s, 6H, $N(CH_3)_2$), 6.82 (s, 1H, CH), 7.44–7.72 (m, $3H_{arom}$), 7.97 (d, ΣJ = 8.70 Hz, $1H_{arom}$); NMR ^{13}C 42.66 (q, $N(CH_3)_2$), 125.99 (d, CH=N), 123.18, 129.55, 129.75 and 133.28 (4d, CH_{arom}), 135.85 and 148.32 (2s, C_{arom}), 190.38 (s, C=O); MS $C_{10}H_{11}N_3O_3$ 221 (M^+).

Compound **4c**: mp 139°C; 70% yield; NMR ^1H ($CDCl_3$) 3.23 (s, 6H, $N(CH_3)_2$), 6.98 (s, 1H, CH), 8.05 and 8.25 (2d, ΣJ = 9.10 Hz, $4H_{arom}$); NMR ^{13}C 42.65 (q, $N(CH_3)_2$), 122.71 (d, CH_{arom}), 126.22 (d, CH=N), 130.55 (d, CH_{arom}), 143.85 and 149.06 (2s, C_{arom}), 188.06 (s, C=O); MS $C_{10}H_{11}N_3O_3$ 221 (M^+).

α-Hydrazonothioacetophenones **5**. Lawesson's Reagent (6 mmol) is added to a solution of α-hydrazonoacetophenone **4** (10 mmol) in benzene (25 ml) under inert atmosphere (N_2). After 1 h stirring at 20°C for **5a**, 90 min at 50°C for **5b** or 20 min at 40°C for **5c**, the solution is fractionated by silica gel chromatography. After elution using CH_2Cl_2, compound **5a** or **5b** is isolated as a brown oil, compound **5c** is crystallized in Et_2O and isolated as brown crystals.

Compound **5a**: oil; 56% yield; NMR ^1H ($CDCl_3$) 3.18 (s, 6H, $N(CH_3)_2$), 6.94–7.47 (m, $4H_{arom}$), 7.74 (s, 1H, CH); NMR ^{13}C 43.75 (q, $N(CH_3)_2$), 115.23 (dd, $^2J_{C-F}$ = 22.9 Hz, CH_{arom}), 123.66 (dd, $^3J_{C-F}$ = 3.4 Hz, CH_{arom}), 130.39 (dd, $^3J_{C-F}$ = 8.4 Hz, CH_{arom}), 130.65 (dd, $^4J_{C-F}$ = 3.0 Hz, CH_{arom}), 134.95 (d, $^2J_{C-F}$ = 15.3 Hz, C_{arom}), 138.89 (dd, $^4J_{C-F}$ = 1.1 Hz, CH=N), 157.34 (d, $^1J_{C-F}$ = 249.1 Hz, C_{arom}), 218.61 (d, $^3J_{C-F}$ = 1.5 Hz, C=S); MS $C_{10}H_{11}FN_2S$ 210 (M^+).

Compound **5b**: oil; 60% yield; NMR ^1H ($CDCl_3$) 3.08 (s, 6H, $N(CH_3)_2$), 7.41–7.50 (m, $3H_{arom}$), 7.61 (s, 1H, CH), 7.87 (d, ΣJ = 8.70 Hz, $1H_{arom}$); NMR ^{13}C 43.12 (q, $N(CH_3)_2$), 123.12, 128.92, 130.89 and 132.58 (4d, CH_{arom}), 137.99 (d, CH=N), 141.11 and 147.53 (2s, C_{arom}), 219.01 (s, C=S); MS $C_{10}H_{11}N_3O_2S$ 237 (M^+); Anal. Calcd.: C, 50.62; H, 4.67; Found: C, 50.71; H, 4.58.

Compound **5c**: mp 112°C; 66% yield; NMR ^1H ($CDCl_3$) 3.23 (s, 6H, $N(CH_3)_2$), 7.82 (s, 1H, CH), 7.71 and 8.16 (2d, ΣJ = 9.10 Hz, $4H_{arom}$); NMR ^{13}C 43.69 (q, $N(CH_3)_2$), 122.58 and 129.83 (2d, CH_{arom}), 138.61 (d, CH=N), 148.05 and 151.53 (2s, C_{arom}), 219.55 (s, C=S); MS $C_{10}H_{11}N_3O_2S$ 237 (M^+).

3-Cyano-4-dimethylamino-3,4-dihydro-2H-1,4-thiazines **6a**, **d**, **g** *and 3-methoxycarbonyl-4-dimethylamino-3,4-dihydro-2H-1,4-thiazines* **6c**, **f**, **j**. A solution of **5** (5 mmol) in methylacrylate or acrylonitrile (50 ml) containing some hydroquinone crystals is stirred 24 h at r.t.. The mixture is then evaporated under reduced pressure, diluted with CH_2Cl_2 and fractionated by silica gel column chromatography. After elution using CH_2Cl_2, compounds **6a**, **c** are isolated as yellow oil. Compounds **6d**, **f**, **g**, **j** are crystallized in Et_2O and isolated as brown crystals (**6d**), red crystals (**6f** and **6j**), orange crystals (**6g**).

3-Acetyl-4-dimethylamino-3,4-dihydro-2H-1,4-thiazines **6b**, **e**, **i** *and 3-formyl-4-dimethylamino-3,4-dihydro-2H-1,4-thiazines* **6h**. Acrolein (10 mmol) or methylvinylketone (20 mmol) is added to a solution of **5** (5 mmol) in benzene (5 ml) containing some hydroquinone crystals. After 10 h stirring at r.t., the mixture is evaporated under reduced pressure. Compound **6h** is then obtained by precipitation with Et_2O and isolated as orange crystals. In the other cases, the residue is diluted in CH_2Cl_2 and treated as above. Compound **6b** is isolated as red oil, **6e** as yellow oil and **6i** is crystallised in Et_2O and isolated as red crystals.

Compound **6a**: oil; 62% yield; NMR ^1H.($CDCl_3$) 2.63 (s, 6H, $N(CH_3)_2$), 3.22 (2d, 2H, J = 3.96 Hz and J = 3.51 Hz, CH_2S), 4.75 (dd, 1H, J = 3.96 Hz and J = 3.51 Hz, N—CH—CH_2), 6.88 (s, 1H, =CH—N), 6.96–7.51 (m, $4H_{arom}$); NMR ^{13}C 28.93 (t, CH_2S), 43.89 (q, $N(CH_3)_2$), 48.65 (d, N—CH—CH_2), 97.93 (d, $^3J_{C-F}$ = 3.2 Hz, C—S), 115.75 (dd, $^2J_{C-F}$ = 23.2 Hz, CH_{arom}), 120.51 (s, CN), 124.04 (dd, $^4J_{C-F}$ = 3.5 Hz, CH_{arom}), 125.44 (d, $^2J_{C-F}$ = 11.8 Hz, C_{arom}), 126.34 (dd, $^3J_{C-F}$ = 11.1 Hz, CH_{arom}), 127.26 (dd, $^3J_{C-F}$ = 8.5 Hz, CH_{arom}), 128.77 (dd, $^4J_{C-F}$ = 3.3 Hz, =CH—N), 159.18 (d, $^1J_{C-F}$ = 247.6 Hz, C_{arom}); MS $C_{13}H_{14}FN_3S$ 263 (M^+); Anal. Calcd.: C, 59.29; H, 5.36; Found: C, 59.12; H, 5.40.

Compound **6b**: oil; 75% yield; NMR ^1H ($CDCl_3$) 2.28 (s, 3H, CH_3), 2.57 (s, 6H, $N(CH_3)_2$), 2.61 and 3.33 (2dd, 2H, J = 12.60 Hz, J = 4.32 Hz and J = 3.66 Hz, CH_2S), 4.30 (dd, 1H, J = 4.32 Hz and J = 3.66 Hz, N—CH—CH_2), 6.98–7.48 (m, $4H_{arom}$), 7.12 (s, 1H, =CH—N); NMR ^{13}C 26.61 (t, CH_2S), 27.50 (t, CH_3), 44.23 (q, $N(CH_3)_2$), 65.42 (d, N—CH—CH_2), 97.36 (d, $^3J_{C-F}$ = 3.0 Hz, C—S), 115.70 (dd, $^2J_{C-F}$ = 23.5 Hz, CH_{arom}), 123.96 (dd, $^4J_{C-F}$ = 3.5 Hz, CH_{arom}), 126.26 (d, $^2J_{C-F}$ = 11.5 Hz, C_{arom}), 126.64 (dd, $^3J_{C-F}$ = 8.6 Hz, CH_{arom}), 128.11 (dd, $^3J_{C-F}$ = 11.3 Hz, CH_{arom}), 128.80 (dd, $^4J_{C-F}$ = 3.5 Hz, =CH—N), 159.21 (d, $^1J_{C-F}$ = 247.1 Hz, C_{arom}), 208.54 (s, C=O); MS $C_{14}H_{17}FN_2OS$ 280 (M^+).

Compound **6c**: oil; 72% yield; NMR ^1H ($CDCl_3$) 2.60 (s, 6H, $N(CH_3)_2$), 2.80 and 3.38 (2dd, 2H, J = 12.69 Hz, J = 4.17 Hz and J = 3.75 Hz, CH_2S), 3.78 (s, 3H, CH_3), 4.54 (dd, 1H, J = 4.17 Hz and J = 3.75 Hz, N—CH—CH_2), 7.12 (s, 1H, =CH—N), 6.92–7.47 (m, $4H_{arom}$); NMR ^{13}C 27.62 (t, CH_2S), 44.04 (q, $N(CH_3)_2$), 52.56 (q, CH_3), 60.38 (d, N—CH—CH_2), 94.89 (d, $^3J_{C-F}$ = 3.2 Hz, C—S), 115.74 (dd, $^2J_{C-F}$ = 23.5 Hz, CH_{arom}), 124.03 (dd, $^4J_{C-F}$ = 3.4 Hz, CH_{arom}), 126.16 (dd, $^3J_{C-F}$ = 8.5 Hz, CH_{arom}), 126.45 (d, $^2J_{C-F}$ = 11.4 Hz, C_{arom}), 127.92 (dd, $^3J_{C-F}$ = 12.7 Hz, CH_{arom}), 128.46 (dd, $^4J_{C-F}$ = 3.7 Hz, =CH—N), 159.22 (d, $^1J_{C-F}$ = 246.9 Hz, C_{arom}), 170.79 (s, C=O); MS $C_{14}H_{17}FN_2O_2S$ 296 (M^+).

Compound **6d**: mp 99°C; 67% yield; NMR ^1H ($CDCl_3$) 2.63 (s, 6H, $N(CH_3)_2$), 3.08 and 3.23 (2dd, 2H, J = 12.81 Hz and J = 3.45 Hz, CH_2S), 4.83 (t, 1H, J = 3.45 Hz, N—CH—CH_2), 6.52 (s, 1H, =CH—N), 7.37–7.75 (m, $4H_{arom}$); NMR ^{13}C 29.28 (t, CH_2S), 44.12 (q, $N(CH_3)_2$), 48.98 (d, N—CH—CH_2), 100.29 (s, C—S), 117.98 (s, CN), 126.01 (d, =CH—N), 124.40, 128.22, 132.07 and 132.48 (4d, CH_{arom}), 133.16 and 149.49 (2s, C_{arom}); MS $C_{13}H_{14}N_4O_2S$ 290 (M^+).

Compound **6e**: oil; 61% yield; NMR ^1H ($CDCl_3$) 2.27 (s, 3H, CH_3), 2.47 and 3.30 (2dd, 2H, J = 12.45 Hz and J = 3.66 Hz, CH_2S), 2.54 (s, 6H, $N(CH_3)_2$), 4.33 (t, 1H, J = 3.66 Hz, N—CH—CH_2), 6.63 (s, 1H, =CH—N), 7.20–7.60 (m, $4H_{arom}$); NMR ^{13}C 26.55 (t, CH_2S), 28.00 (q, CH_3), 43.40 (q, $N(CH_3)_2$), 65.21 (d, N—CH—CH_2), 99.11 (s, C—S), 127.64 (d, =CH—N), 124.06, 127.34, 131.85 and 131.87 (4d, CH_{arom}), 133.81 and 149.64 (2s, C_{arom}), 208.76 (s, C=O); MS $C_{14}H_{17}N_3O_3S$ 307 (M^+).

Compound **6f**: mp 108°C; 71% yield; NMR ^1H ($CDCl_3$) 2.58 (s, 6H, $N(CH_3)_2$), 2.72 and 3.33 (2dd, 2H, J = 12.60 Hz and J = 3.66 Hz, CH_2S), 3.78 (s, 3H, CH_3), 4.58 (t, 1H, J = 3.66 Hz, N—CH—CH_2), 6.64 (s, 1H, =CH—N), 7.24–7.68 (m, $4H_{arom}$); NMR ^{13}C 27.66 (t, CH_2S), 44.00 (q, $N(CH_3)_2$), 52.61 (q, CH_3), 59.92 (d, N—CH—CH_2), 96.66 (s, C—S), 127.42 (d, =CH—N), 124.10, 127.06, 131.75 and 131.96 (4d, CH_{arom}), 134.11 and 149.38 (2s, C_{arom}), 170.61 (s, C=O); MS $C_{14}H_{17}N_3O_4S$ 323 (M^+).

Compound **6g**: mp 136°C; 68% yield; NMR ^1H ($CDCl_3$) 2.68 (s, 6H, $N(CH_3)_2$), 3.04 and 3.31 (2dd, 2H, J = 13.20 Hz and J = 3.40 Hz, CH_2S), 4.87 (t, 1H, J = 3.40 Hz, N—CH—CH_2), 7.04 (s, 1H, =CH—N), 7.46 and 8.10 (2d, ΣJ = 9.00 Hz, $4H_{arom}$); NMR ^{13}C 28.62 (t, CH_2S), 44.24 (q, $N(CH_3)_2$), 47.39 (d, N—CH—CH_2), 102.17 (s, C—S), 117.53 (s, CN), 127.25 (d, =CH—N), 124.00 and 124.48 (2d, CH_{arom}), 144.79 and 145.50 (2s, C_{arom}); MS $C_{13}H_{14}N_4O_2S$ 290 (M^+).

Compound **6h**: mp 86°C; 80% yield; NMR ^1H ($CDCl_3$) 2.63 (s, 6H, $N(CH_3)_2$), 2.70 and 3.41 (2dd, 2H, J = 12.90 Hz and J = 3.50 Hz, CH_2S), 4.43 (t, 1H, J = 3.50 Hz, N—CH—CH_2), 7.27 (s, 1H, =CH—N), 7.47 and 8.12 (2d, ΣJ = 8.90 Hz, $4H_{arom}$), 9.51 (s, 1H, CHO); NMR ^{13}C 24.98 (t, CH_2S), 44.17 (q, $N(CH_3)_2$), 62.58 (d, N—CH—CH_2), 90.38 (s, C—S), 124.07 (d, CH_{arom}), 128.46 (d, =CH—N), 144.80 and 145.15 (2s, C_{arom}), 197.55 (d, CHO); MS $C_{13}H_{15}N_3O_3S$ 293 (M^+).

Compound **6i**: mp 120°C; 78% yield; NMR ^1H ($CDCl_3$) 2.25 (s, 3H, CH_3), 2.57 and 3.37 (2dd, 2H, J = 12.70 Hz and J = 3.50 Hz, CH_2S), 2.67 (s, 6H, $N(CH_3)_2$), 4.47 (t, 1H, J = 3.50 Hz, N—CH—CH_2), 7.30 (s, 1H, =CH—N), 7.50 and 8.12 (2d, ΣJ = 8.60 Hz, $4H_{arom}$); NMR ^{13}C 26.35 (t, CH_2S), 27.26 (q, CH_3), 43.85 (q, $N(CH_3)_2$), 64.54 (d, N—CH—CH_2), 107.71 (s, C—S), 129.30 (d, =CH—N), 123.97 (d, CH_{arom}), 144.89 and 145.70 (2s, C_{arom}), 206.19 (s, C=O); MS $C_{14}H_{17}N_3O_3S$ 307 (M^+).

Compound **6j**: mp 146°C; 83% yield; NMR ^1H ($CDCl_3$) 2.63 (s, 6H, $N(CH_3)_2$), 2.73 and 3.42 (2dd, 2H, J = 12.90 Hz and J = 3.50 Hz, CH_2S), 3.79 (s, 3H, CH_3), 4.67 (t, 1H, J = 3.50 Hz, N—CH—CH_2), 7.27 (s, 1H, =CH—N), 7.46 and 8.10 (2d, ΣJ = 9.00 Hz, $4H_{arom}$); NMR ^{13}C 27.16 (t, CH_2S), 44.24 (q, $N(CH_3)_2$), 52.76 (q, CH_3), 58.62 (d, N—CH—CH_2), 92.95 (s, C—S), 123.55 and 123.97 (2d, CH_{arom}), 129.11 (d, =CH—N), 144.56 and 145.83 (2s, C_{arom}) 169.90 (s, C=O); MS $C_{14}H_{17}N_3O_4S$ 323 (M^+).

2H-1,4-Thiazines **7**. Solution of **6b**, **e** or **i** (0.8 mmol) in CH_2Cl_2 (10 ml) containing silica (0.5 g) is stirred 10 h at r.t. The solution is then fractionated by silica gel column chromatography. After elution using CH_2Cl_2, compounds **7b**, **e**, and **i** are crystallized in Et_2O and isolated as yellow crystals. Compound **7h** is obtained with low yield if the corresponding 3,4-dihydro-2H,1-4-thiazine **6h** is chromatographied on silica gel column.

Compound **7b**: mp 52°C; 95% yield; NMR ^1H ($CDCl_3$) 2.64 (s, 3H, CH_3), 3.46 (s, 2H, CH_2S), 7.09–7.66 (m, $4H_{arom}$), 7.91 (s, 1H, =CH—N); NMR ^{13}C 19.89 (t, CH_2S), 25.11 (q, CH_3), 116.36 (dd, $^2J_{C-F}$

= 22.8 Hz, CH_{arom}), 123.10 (d, $^2J_{C-F}$ = 11.8 Hz, C_{arom}), 124.42 (dd, $^4J_{C-F}$ = 3.8 Hz, CH_{arom}), 126.29 (dd, $^3J_{C-F}$ = 3.0 Hz, C—S), 130.94 (dd, $^3J_{C-F}$ = 8.6 Hz, CH_{arom}), 132.10 (dd, $^4J_{C-F}$ = 2.3 Hz, =CH—N), 135.63 (dd, $^3J_{C-F}$ = 8.3 Hz, CH_{arom}), 142.59 (s, C=N), 159.83 (dd, $^1J_{C-F}$ = 252.4 Hz, C_{arom}), 198.35 (s, C=O); MS $C_{12}H_{10}FNOS$ 235 (M^+).

Compound **7e**: mp 103°C; 78% yield; NMR ^1H ($CDCl_3$) 2.59 (s, 3H, CH_3), 3.48 (s, 2H, CH_2S), 7.58 (s, 1H, =CH—N), 7.49–7.96 (m, $4H_{arom}$); NMR ^{13}C 20.10 (t, CH_2S), 25.12 (q, CH_3), 124.77, 130.45, 132.15 and 132.68 (4d, CH_{arom}), 134.69 (d, =CH—N), 127.91 and 150.45 (2s, C_{arom}), 143.87 (s, C—S and C=N), 198.27 (s, C=O); MS $C_{12}H_{10}N_2O_3S$ 262 (M^+).

Compound **7h**: mp 147°C; 8% yield; NMR ^1H ($CDCl_3$) 3.44 (s, 2H, CH_2S), 7.82–8.30 (2d, ΣJ = 9.40 Hz, $4H_{arom}$), 8.08 (s, 1H, =CH—N), 9.77 (s, 1H, CHO); NMR ^{13}C 24.55 (t, CH_2S), 129.01 (d, =CH—N), 124.07 and 129.10 (2d, CH_{arom}), 133.24 and 151.97 (2s, C_{arom}), 141.57 (s, C—S), 144.90 (s, C=N), 190.44 (d, C=O); MS $C_{11}H_8N_2O_3S$ 248 (M^+).

Compound **7i**: mp 140°C; 88% yield; NMR ^1H ($CDCl_3$) 2.58 (s, 3H, CH_3), 3.47 (s, 2H, CH_2S), 7.76 (s, 1H, =CH—N), 7.91 and 8.29 (2d, ΣJ = 9.40 Hz, $4H_{arom}$); NMR ^{13}C 20.00 (t, CH_2S), 25.08 (q, CH_3), 124.03 and 129.27 (2d, CH_{arom}), 134.12 (d, =CH—N), 130.06 and 148.46 (2s, C_{arom}), 141.34 (s, C—S), 144.33 (s, C=N), 197.84 (s, C=O); MS $C_{12}H_{10}N_2O_3S$ 262 (M^+); Anal. Calcd.: C, 54.95; H, 3.84; Found: C, 55.08; H, 3.70.

4-Dimethylamino-3,4-dihydro-2H-1,4-thiazines **8**. N-methylmaleimide or N-phenylmaleimide (6 mmol) is added to a solution of **5** (5 mmol) in benzene (8 ml). After stirring at r.t. (4 h for **8a**, **b**, 48 h for **8c**, **d** or 16 h for **8e**), compounds **8** are precipitated in Et_2O and isolated as orange crystals.

Compound **8a**: mp 99°C; 76% yield; NMR ^1H ($CDCl_3$) 2.73 (s, 6H, $N(CH_3)_2$), 3.06 (s, 3H, NCH_3), 3.79 (d, 1H, J = 6.10 Hz, S—CH), 4.65 (d, 1H, J = 6.10 Hz, N—CH), 6.89–7.38 (m, $4H_{arom}$), 7.32 (s, 1H, =CH—N); NMR ^{13}C 25.10 (q, NCH_3), 38.53 (d, S—CH), 44.07 (q, $N(CH_3)_2$), 61.24 (d, N—CH), 95.15 (s, C—S), 115.85 (dd, $^2J_{C-F}$ = 23.3 Hz, CH_{arom}), 124.22 (d, CH_{arom}), 125.33 (d, $^2J_{C-F}$ = 11.5 Hz, C_{arom}), 127.28 (dd, $^3J_{C-F}$ = 8.4 Hz, CH_{arom}), 128.86 (d, =CH—N), 129.43 (dd, $^3J_{C-F}$ = 11.1 Hz, CH_{arom}), 159.27 (d, $^1J_{C-F}$ = 247.6 Hz, C_{arom}), 172.10 and 173.95 (2s, C=O); MS $C_{15}H_{16}FN_3O_2S$ 321 (M^+); Anal. Calcd.: C, 56.06; H, 5.02; Found: C, 55.91; H, 5.15.

Compound **8b**: mp 137°C; 75% yield; NMR ^1H ($CDCl_3$) 2.77 (s, 6H, $N(CH_3)_2$), 3.90 (d, 1H, J = 6.10 Hz, S—CH), 4.90 (d, 1H, J = 6.10 Hz, N—CH), 7.08–7.58 (m, $9H_{arom}$), 7.42 (s, 1H, =CH—N); NMR ^{13}C 38.46 (d, S—CH), 44.25 (q, $N(CH_3)_2$), 61.56 (d, N—CH), 94.66 (s, C—S), 115.96 (dd, $^2J_{C-F}$ = 22.9 Hz, CH_{arom}), 124.29 (dd, $^4J_{C-F}$ = 3.4 Hz, CH_{arom}), 125.28 (d, $^2J_{C-F}$ = 11.6 Hz, C_{arom}), 126.27 (d, CH_{arom}), 127.38 (dd, $^3J_{C-F}$ = 8.4 Hz, CH_{arom}), 128.89 (d, CH_{arom}), 129.05 (dd, $^3J_{C-F}$ = 9.5 Hz, CH_{arom}), 129.08 (d, =CH—N), 129.29 (d, CH_{arom}), 131.26 (s, C_{arom}), 159.36 (d, $^1J_{C-F}$ = 247.6 Hz, C_{arom}), 170.99 and 173.03 (2s, C=O); MS $C_{20}H_{18}FN_3O_2S$ 383 (M^+).

Compound **8c**: mp 99°C; 84% yield; NMR ^1H ($CDCl_3$) 2.72 (s, 6H, $N(CH_3)_2$), 3.06 (s, 3H, NCH_3), 3.78 (d, 1H, J = 6.08 Hz, S—CH), 4.69 (d, 1H, J = 6.08 Hz, N—CH), 6.92 (s, 1H, =CH—N), 7.34–7.82 (m, $4H_{arom}$); NMR ^{13}C 26.26 (q, NCH_3), 38.92 (d, S—CH), 44.20 (q, $N(CH_3)_2$), 61.50 (d, N—CH), 97.72 (s, C—S), 124.75, 128.16, 132.02 and 132.70 (4d, CH_{arom}), 129.46 (d, =CH—N), 132.91 and 148.93 (2s, C_{arom}), 171.84 and 174.04 (2s, C=O); MS $C_{15}H_{16}N_4O_4S$ 348 (M^+).

Compound **8d**: mp 128°C; 76% yield; NMR ^1H ($CDCl_3$) 2.74 (s, 6H, $N(CH_3)_2$), 3.87 (d, 1H, J = 5.95 Hz, S—CH), 4.95 (d, 1H, J = 5.95 Hz, N—CH), 6.96 (s, 1H, =CH—N), 7.25–7.83 (m, $4H_{arom}$); NMR ^{13}C 38.55 (d, S—CH), 44.34 (q, $N(CH_3)_2$), 61.76 (d, N—CH), 96.97 (s, C—S), 124.86, 126.42, 128.28, 129.04, 129.42, 132.18 and 132.81 (7d, CH_{arom}), 129.13 (d, =CH—N), 131.37, 133.00 and 149.33 (3s, C_{arom}), 170.75 and 173.08 (2s, C=O); MS $C_{20}H_{18}N_4O_4S$ 410 (M^+).

Compound **8e**: mp 144°C; 78% yield; NMR ^1H ($CDCl_3$) 2.76 (s, 6H, $N(CH_3)_2$), 3.08 (s, 3H, NCH_3), 3.79 (d, 1H, J = 6.15 Hz, S—CH), 4.76 (d, 1H, J = 6.15 Hz, N—CH), 7.37 (s, 1H, =CH—N), 7.50 and 8.14 (2d, ΣJ = 9.10 Hz, $4H_{arom}$); NMR ^{13}C 25.15 (q, NCH_3), 37.87 (d, S—CH), 44.30 (q, $N(CH_3)_2$), 60.90 (d, N—CH), 97.92 (s, C—S), 124.68 and 124.89 (2d, CH_{arom}), 131.92 (d, =CH—N), 145.63 (s, C_{arom}), 172.62 and 174.76 (2s, C=O); MS $C_{15}H_{16}N_4O_4S$ 348 (M^+).

4H-1,4-Thiazines **9**. Solution of dihydrothiazine **8** (0.5 mmol) in CH_2Cl_2 (10 ml) containing silica (0.6 g) is stirred 3 h at r.t. The solution is then fractionated by silica gel column chromatography. After elution using CH_2Cl_2/EtOAc (19/1 for **9a**, **c**, **e** or 9/1 for **9b**, **d**), compounds **9** are precipitated in Et_2O and isolated as green crystals (**9a**, **c**, **e**) or blue crystals (**9b**, **d**).

Compound **9a**: mp 165°C; 64% yield; NMR ^1H (CD_3COCD_3) 2.86 (s, 3H, NCH_3), 6.31 (d, 1H, J = 5.19 Hz, =CH—N), 7.08–7.42 (m, $4H_{arom}$), 7.64 (s.e., 1H, NH); NMR ^{13}C 23.72 (q, NCH_3), 100.51 (s, S—C—CO), 101.12 (d, $^3J_{C-F}$ = 2.7 Hz, Ar—C—S), 116.78 (dd, $^2J_{C-F}$ = 22.5 Hz, CH_{arom}), 124.22 (d, $^2J_{C-F}$ = 12.2 Hz, C_{arom}), 125.52 (dd, $^4J_{C-F}$ = 3.8 Hz, CH_{arom}), 128.60 (dd, $^3J_{C-F}$ = 6.5 Hz, CH_{arom}),

128.72 (d, =CH—N), 130.37 (dd, $^3J_{C-F}$ = 8.8 Hz, CH_{arom}), 142.66 (s, N—C—CO), 160.74 (d, $^1J_{C-F}$ = 248.0 Hz, C_{arom}), 164.01 and 167.46 (2s, C=O); MS $C_{13}H_9FN_2O_2S$ 276 (M^+).

Compound **9b**: mp 179°C; 75% yield; NMR ^1H (CD_3COCD_3) 6.36 (d, 1H, J = 5.19 Hz, =CH—N), 7.11–7.49 (m, $9H_{arom}$), 7.81 (s.e., 1H, NH); NMR ^{13}C 101.03 (s, S—C—CO), 101.47 (d, $^3J_{C-F}$ = 2.7 Hz, Ar—C—S), 116.84 (dd, $^2J_{C-F}$ = 22.9 Hz, CH_{arom}), 124.12 (d, $^2J_{C-F}$ = 12.2 Hz, C_{arom}), 125.56 (dd, $^4J_{C-F}$ = 3.8 Hz, CH_{arom}), 127.14, 128.15 and 129.53 (3d, CH_{arom}), 128.45 (dd, $^3J_{C-F}$ = 9.5 Hz, CH_{arom}), 128.70 (dd, $^4J_{C-F}$ = 2.7 Hz, =CH—N), 130.50 (dd, $^3J_{C-F}$ = 8.4 Hz, CH_{arom}), 132.82 (s, C_{arom}), 142.66 (s, N—C—CO), 160.74 (d, $^1J_{C-F}$ = 248.3 Hz, C_{arom}), 162.77 and 166.21 (2s, C=O); MS $C_{18}H_{11}FN_2O_2S$ 338 (M^+).

Compound **9c**: mp 168°C; 60% yield; NMR ^1H (CD_3COCD_3) 2.87 (s, 3H, NCH_3), 5.95 (d, 1H, J = 5.04 Hz, =CH—N), 7.55–7.92 (m, $4H_{arom}$ and NH); NMR ^{13}C 23.75 (q, NCH_3), 100.28 (s, S—C—CO), 103.87 (s, Ar—C—S), 125.44, 130.70, 132.35 and 134.30 (4d, CH_{arom}), 127.48 (d, =CH—N), 131.50 and 149.94 (2s, C_{arom}), 143.22 (s, N—C—CO), 163.89 and 167.20 (2s, C=O); MS $C_{13}H_9N_3O_4S$ 303 (M^+).

Compound **9d**: mp 160°C; 62% yield; NMR ^1H (CD_3COCD_3) 5.99 (d, 1H, J = 4.27 Hz, =CH—N), 7.30–7.72 and 7.84–7.94 (2m, $9H_{arom}$), 7.79 (s.e., 1H, NH); NMR ^{13}C 100.78 (s, S—C—CO), 104.28 (s, Ar—C—S), 125.49, 127.19, 128.22, 129.56, 130.82, and 132.31 and 134.38 (7d, CH_{arom}), 127.27 (d, =CH—N), 131.33, 132.78 and 149.99 (3s, C_{arom}), 143.18 (s, N—C—CO), 162.71 and 165.97 (2s, C=O); MS $C_{18}H_{11}N_3O_4S$ 365 (M^+).

Compound **9e**: mp 223°C; 57% yield; NMR ^1H (CD_3COCD_3) 2.89 (s, 3H, NCH_3), 6.74 (d, 1H, J = 5.12 Hz, =CH—N), 7.61 and 8.21 (2d, ΣJ = 9.00 Hz, $4H_{arom}$), 7.62 (s.e., 1H, NH); MS $C_{13}H_9N_3O_4S$ 303 (M^+); Anal. Calcd.: C, 51.48; H, 2.99; Found: C, 51.37; H, 3.09.

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