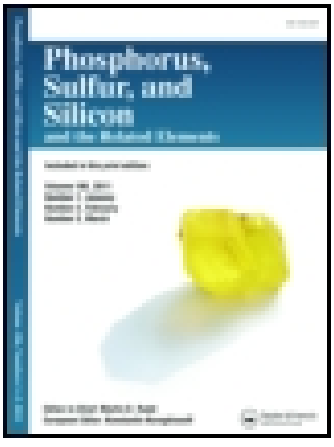


Phosphorus, Sulfur, and Silicon and the Related Elements

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gpss20

NEW 2-HYDRAZONOPHENYLTHIOACETAMIDES INTERMEDIATES IN THE SYNTHESIS OF 6-ACYLAMINO-3,6- DIHYDRO-2H-1,3,4-THIADIAZINES

M. J. Gil [a] , A. Reliquet [a] & J. C. Meslin [a]

[a] Laboratoire de Synthése Organique, U. A. C.N.R.S. 475 , 2, rue de la Houssiniére, 44072, Nantes Cedex, France

Published online: 04 Oct 2006.

To cite this article: M. J. Gil , A. Reliquet & J. C. Meslin (1997) NEW 2-HYDRAZONOPHENYLTHIOACETAMIDES INTERMEDIATES IN THE SYNTHESIS OF 6-ACYLAMINO-3,6-DIHYDRO-2H-1,3,4-THIADIAZINES, Phosphorus, Sulfur, and Silicon and the Related Elements, 126:1, 39-52, DOI: 10.1080/10426509708043544

To link to this article: http://dx.doi.org/10.1080/10426509708043544

Phosphorus, Sulfur, and Silicon, 1997, Vol. 126, pp. 39-52
Reprints available directly from the publisher
Photocopying permitted by license only

NEW 2-HYDRAZONOPHENYLTHIOACETAMIDES INTERMEDIATES IN THE SYNTHESIS OF 6-ACYLAMINO-3,6-DIHYDRO-2H-1,3,4-THIADIAZINES

M. J. GIL, A. RELIQUET and J. C. MESLIN

Laboratoire de Synthèse Organique, U. A. C.N.R.S. 475, 2, rue de la Houssinière, 44072 Nantes Cedex (France)

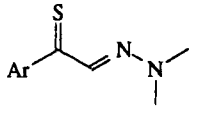
(Received 10 December, 1996)

The three steps synthesis of new 2-hydrazonophenylthioacetamides having a N-monosubstitued thioamide group is described. The selective acylation of the thioamide nitrogen atom involves an intramolecular cyclisation affording 3,6-dihydro-2H-1,3,4-thiadiazines with good yields.

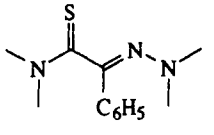
Keywords: 2-hydrazonophenylacetamides; 2-hydrazonophenylthioacetamides; 3,6-dihydro-2H-1,3,4-thiadiazines

INTRODUCTION

We have recently reported the synthesis and some properties of 2-hydrazonophenylthioacetamides[1-3] (2,4-diamino-3-phenyl-1-thia-4-azabutadienes) the molecular structure of which presents an original heteroatomic chain. These compounds were obtained later than 2-hydrazonothioacetophenones which have been used in heterocyclic synthesis to build thiazoles, Δ^4-thiazolines,[4] 3,4-dihydro-1,4-thiazines and 1,4-thiazines.[5]



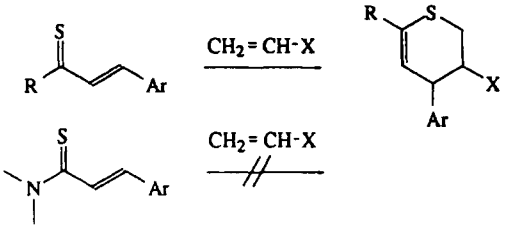
2-hydrazonothioacetophenones



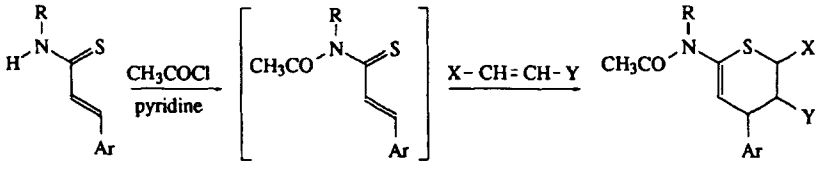
2-hydrazonophenylthioacetamides

The 2-hydrazonophenylthioacetamides present the advantage of a greater stability than the former compounds but their reactivity is quite different. Particularly, the dienic chain does not allow the [4 + 2] cycloaddition reaction.

I. T. Barnish had already observed the same difference between α,β-ethylenic thioketones[6-8] and thioamides analogs,[9] the latter being inefficient as dienes in Diels-Alder cycloadditions.



In 1989 this author has described the dihydrothiopyranes synthesis starting from α,β-ethylenic thioamides which react with dienophile reagents only if acetyl chloride and pyridine are added to the reaction mixture.[9] It is likely that the in-situ acylation of the nitrogen of the thioamide thus bearing an electron withdrawing group enhances the reactivity of the dienophile.

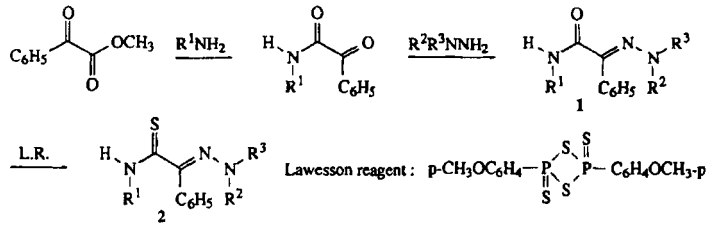


In this paper we report firstly on the preparation of new 2-hydrazonophenylthioacetamides with a N-monosubstituted thioamide group and secondly the substitution of the nitrogen atom by electron withdrawing groups with the aim to get closer to the Barnish models. The synthetized molecules do not even react with dienophiles but they lead to 3,6-dihydro-2H-1,3,4-thiadiazines. The aim of this paper is to present this new way of synthesis of these compounds.

RESULTS

2-Hydrazonophenylthioacetamides **2** are obtained in three steps starting from methylbenzoylformate which reacts with primary amines to give benzoylformamides. Condensation of substituted hydrazines leads to the 2-hydrazonophenyl-

acetamides **1.** Then the latter are thionated using Lawesson reagent affording compounds **2.**

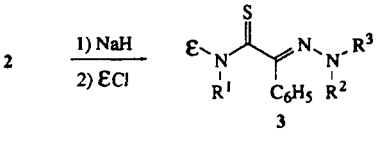


1,2	a	b[2,3]	c	d[3]	e	f
R^1	CH_3	CH_3	CH_3	CH_3	CH_3	CH_3
NR^2R^3				NHC_6H_5		$N(CH_3)C_6H_5$

1,2	g	h	i	j	k
R^1	CH_3	$(CH_3)_2CH$	$(CH_3)_2CH$	$C_6H_5CH_2$	$C_6H_5CH_2$
NR^2R^3	$N(C_6H_5)_2$				

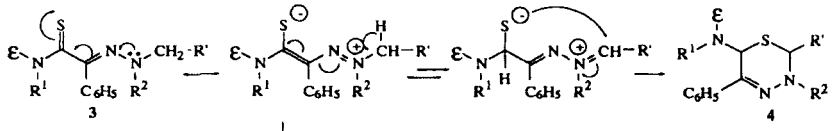
The isolated compound **1f** presents two diastereoisomeric forms. The determination of the corresponding geometries has been already discussed in a previous paper.[3]

Deprotonation of compounds **2** by sodium hydride followed by substitution of the anion using acid chlorides, methylchloroformate or mesyl chloride yields the corresponding N-substituted compounds **3.**



3	R^1	NR^2R^3	E
a	CH_3		CH_3OCO
b	CH_3	$N(CH_3)C_6H_5$	CH_3SO_2
c	CH_3	$N(CH_3)C_6H_5$	CH_3OCO
d	CH_3	$N(CH_3)C_6H_5$	C_6H_5CO
e	CH_3	$N(C_6H_5)_2$	CH_3SO_2
f	CH_3	$N(C_6H_5)_2$	CH_3CO
g	CH_3	$N(C_6H_5)_2$	CH_3OCO
h	$C_6H_5CH_2$		CH_3OCO

In most of the cases compounds **3** are not isolated. In fact the substitution reaction is spontaneously followed by an intramolecular cyclisation to give 6-acylamino-3,6-dihydro-2H-1,3,4-thiadiazines **4.** This annelation proceeds probably through the zwitterionic form of compound **3** which isomerises to a tautomer. In the latter the thiolate is added to the iminium carbon.



4	R^1	R^2	R'	ε
a	CH_3		$-(CH_2)_2-O-CH_2-$	CH_3SO_2
b	CH_3		$-(CH_2)_4-$	CH_3SO_2
c	CH_3		$-(CH_2)_3-$	CH_3CO
d	CH_3		$-(CH_2)_2-O-CH_2-$	CH_3CO
e	CH_3		$-(CH_2)_4-$	CH_3CO
f	CH_3		$-(CH_2)_2-O-CH_2-$	CF_3CO[a]
g	CH_3		$-(CH_2)_2-O-CH_2-$	CH_3OCO
h	CH_3		$-(CH_2)_4-$	CH_3OCO
i	CH_3		$-(CH_2)_3-$	C_6H_5CO
j	CH_3		$-(CH_2)_2-O-CH_2-$	C_6H_5CO
k	CH_3		$-(CH_2)_4-$	C_6H_5CO
l	CH_3		$-(CH_2)_5-$	C_6H_5CO
m	CH_3	C_6H_5	H	C_6H_5CO
n	$(CH_3)_2CH$		$-(CH_2)_4-$	CH_3OCO
o	$(CH_3)_2CH$		$-(CH_2)_2-O-CH_2-$	C_6H_5CO
p	$(CH_3)_2CH$		$-(CH_2)_4-$	C_6H_5CO
q	$C_6H_5CH_2$		$-(CH_2)_2-O-CH_2-$	CH_3CO
r	$C_6H_5CH_2$		$-(CH_2)_2-O-CH_2-$	CH_3OCO
s	$C_6H_5CH_2$		$-(CH_2)_4-$	CH_3OCO

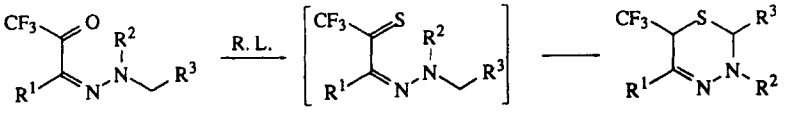
(a) compound **4f** is obtained using trifluoroacetyl anhydride as acylating agent.

NMR spectra of the compounds **4** allow to observe only one diastereomer signal. The relative configuration of both carbons in the 2 and 6 position can be determinated observing **4m** ^1H spectrum. This compound bears a methylen group in the 2 position and only one of the two hydrogens is coupled (J = 1.0 Hz) with the proton in 6 position. According to Karplus, it is reasonable to think that both coupled protons are on the same side of the ring. In all the other cases, hydrogens at the 2 and 6 positions are not coupled. Thus, relative configuration of the corresponding carbons is probably 2RS, 6RS. Compounds **3** which can be isolated give easily the corresponding dihydrothiadiazines **4** in quantitative yields when they are heated in benzene.

The proposed mecanism needs an hydrogen atom in the α position of the nitrogen of the hydrazono group. Compounds **3** bearing a diphenylhydrazono group are quite stable. Surprisingly, such stable compounds **3** treated with dienophile reagents do not react as thiazadienes and we have never obtained the desired 1,4-thiazines.

CONCLUSION

The mode of synthesis of the 1,3,4-thiadiazine ring system described in this work is quite different relatively to the methods already described in the litterature.[10] However Hojo[11] has obtained 1,3,4-thiadiazines by sulfuration of C-trifluoroalkylketones α-dialkylhydrazones using Lawesson reagent.



This author supposes thiocarbonyl compounds as intermediates but never isolates them. This result shows like in our case that an electron withdrawing group α to the β-group is an important factor in the cyclisation process. Many 1,3,4-thiadiazines are used particularly in therapeutic area.[12] Thus a new way to synthetise this ring system is interesting.

EXPERIMENTAL

Melting points were measured using a Reichert microscope and are uncorrected. Kieselgel 60 (70-230 mesh) from Merck was used for silica gel chromatography. TLC was done on Merck silica gel 60 F_{254} precoated plates. ^1H and ^{13}C NMR spectra were recorded on Bruker AC 200 NMR spectrometer operating at 200 MHz and 50.3 MHz respectively. Chemical shifts were reported as δ value in part per million relative to tetramethylsilane as an internal standard. All samples were dissolved in $CDCl_3$. Mass spectra were measured on a Hewlett Packard 5989A at an ionizing voltage of 70 eV. Microanalysis were performed by the analyses central service of CNRS.

2-Hydrazonophenylacetamides 1 general procedure: substituted hydrazine (3.10^{-2} mol) (or the corresponding chlorhydrate (10^{-2} mol) for **1a** and **1g**) was added to an ethanolic solution (20mL) of benzoylformamide (10^{-2} mol) and acetic acid (4.10^{-2} mol) (or sodium acetate (10^{-2} mol) for **1a** and **1g**). After refluxing (7 h for **1a, i, j**, 24 h for **1c, e-h, k**) the solvent was removed and the residue, diluted with CH_2Cl_2, was chromatographed. After elution by CH_2Cl_2/AcOEt (19/1 for **1a** and F_1 of **1f**, 9/1 for **1c, e, i, k** and 7/3 for F_2 of **1f**, **1g**, **h**, **j**) compounds **1** were crystallised from Et_2O.

Compound **1a**: yield 70%; mp 149°C; ^1H NMR δ1.63-1.82 (4H, m, $2CH_2$), 2.88 (3H, d, J = 5.1 Hz, CH_3), 2.98-3.11 (4H, m, $2NCH_2$), 7.00 (1H, br.s, NH),

7.30 (5H, br.s, C_6H_5); ^{13}C NMR δ 23.9 (t, $2CH_2$), 25.6 (q, CH_3N), 54.9 (t, $2NCH_2$), 126.8, 127.3, 129.8 (3d, CH_{arom}), 133.8 (s, C_{arom}), 134.4 (s, C=N), 166.0 (s, C=O); MS $C_{13}H_{17}N_3O$ 231 (M^+). Anal. calcd: C, 67.50; H,7.41, N,18.17. Found: C, 67.41; H, 7.52; N, 18.09.

Compound **1c**: yield 70%; mp 112°C; ^1H NMR δ 1.43-1.51 (6H, m, $3CH_2$), 2.88 (3H, d, J = 5.1 Hz, CH_3), 2.92-3.00 (4H, m, $2NCH_2$), 7.13 (1H, br.s, NH), 7.37 (5H, br.s, C_6H_5); ^{13}C NMR δ 23.8 (t, CH_2), 24.8 (t, $2CH_2$), 25.9 (q, CH_3N), 54.8 (t, $2NCH_2$), 127.8, 128.3, 128.7 (3d, CH_{arom}), 134.1 (s, C_{arom}), 139.7 (s, C=N). 165,7 (s, C=O); MS $C_{14}H_{19}N_3O$ 245 (M^+).

Compound **1e**: yield 88%; mp 71°C; ^1H NMR δ 1.44-1.53 (8H, m, $4CH_2$), 2.87 (3H, d, J = 5.0 Hz, CH_3), 3.12-3.23 (4H, m, $2NCH_2$), 7.01 (1H, br.s, NH), 7.28 (5H, br.s, C_6H_5); ^{13}C NMR δ 25.9 (q, CH_3N), 27.2 (t, $2CH_2$), 27.4 (t, $2CH_2$), 56.5 (t, $2NCH_2$), 127.1, 127.6, 129.8 (3d, CH_{arom}), 131.4 (s, C_{arom}), 135.3 (s, C=N), 166.5 (s, C=O); MS $C_{15}H_{21}N_3O$ 259 (M^+).

Compound **1f**: yield 88%

F_1: mp 105°C; ^1H NMR δ 2.92 (3H, d, J = 5.0 Hz, $C\mathbf{H}_3NH$), 3.42 (3H, s, $N(C\mathbf{H}_3)C_6H_5$), 6.11 (1H, br.s, NH), 6.97-7.68 (10H, m, $2C_6H_5$); ^{13}C NMR δ 26.2 (q, CH_3NH), 41.0 (q, $N(\mathbf{C}H_3)C_6H_5$), 115.9, 121.9, 127.7, 128.5, 128.9, 129.6 (6d, CH_{arom}), 134.2, 138.9 (2s, C_{arom}), 148.6 (s, C=N), 165.9 (s, C=O). F_2: mp 150°C; ^1H NMR δ 2.94 (3H, d, J = 5.0 Hz, $C\mathbf{H}_3NH$), 2.95 (3H, s, $N(C\mathbf{H}_3)C_6H_5$), 6.03 (1H, br.s, NH), 7.21-7.42 (10H, m, $2C_6H_5$); ^{13}C NMR δ 25.8 (q, CH_3NH), 39.3 (q, $N(\mathbf{C}H_3)C_6H_5$), 115.5, 120.8, 126.3, 128.3, 128.8, 129.2 (6d, CH_{arom}), 136.1, 142.6 (2s, C_{arom}), 149.5 (s, C=N), 168.1 (s, C=O) MS $C_{16}H_{17}N_3O$ 267 (M^+).

Compound **1g**: yield 82%; mp 140°C; ^1H NMR δ 2.42 (3H, d, J = 4.8 Hz, CH_3), 5.38 (1H, br.s, NH), 7.06-7.82 (15H, m, $3C_6H_5$); ^{13}C NMR δ 25.3 (q, CH_3N), 122.9, 124.5, 126.5, 128.4, 129.0 (9d, CH_{arom}), 129.1, 135.7, 145.9 (3s, C_{arom}), 147.0 (s, C=N), 165.7 (s, C=O); MS $C_{21}H_{19}N_3O$ 329 (M^+). Anal. calcd: C, 76.57; H, 5.81; N, 12.76. Found: C, 76.63; H, 5.96; N, 12.59.

Compound **1h**: 73%; mp 146°C; ^1H NMR δ 1.27 (6H, d, J = 6.6 Hz, $(C\mathbf{H}_3)_2CH$), 3.01-3.06 (4H, m, $2NCH_2$), 3.78-3.83 (4H, m, $2OCH_2$), 4.31 (1H, h.d, J = 6.6 Hz and J = 8.2 Hz, $(CH_3)_2C\mathbf{H}$), 6.14 (1H, d, J = 8.2 Hz, NH), 7.32-7.41 and 7.70-7.77 (5H, 2m, C_6H_5); ^{13}C NMR δ 22.5 (q, $(\mathbf{C}H_3)_2CH$), 41.3 (d, $(CH_3)_2\mathbf{C}H$), 55.7 (t, $2NCH_2$), 66,2 (t, $2OCH_2$), 127.1, 128.4, 130.3 (3d, CH_{arom}), 133.9 (s, C_{arom}), 158.2 (s, C=N), 164.7 (s, C=O); MS $C_{15}H_{21}N_3O_2$ 275 (M^+).

Compound **1i**: yield 86%: mp 83°C; ^1H NMR δ 1.19 (6H, d, J = 6.6 Hz, $(C\mathbf{H}_3)_2CH$), 1.34-1.53 (6H, m, $3CH_2$), 2.91-2.99 (4H, m, $2NCH_2$), 4.08 (1H, h.d, J = 6.6 Hz and J = 8.2 Hz, $(CH_3)_2C\mathbf{H}$), 7.01 (1H, d, J = 8.2 Hz, NH), 7.26-7.72 (5H, m, C_6H_5); ^{13}C NMR δ 22.9 (q, $(\mathbf{C}H_3)_2CH$), 23.9 and 25,0 (2t, $3CH_2$), 41.3

(d, $(CH_3)_2CH$), 54.9 (t, $2NCH_2$), 127.9, 128.4, 128.9 (3d, CH_{arom}), 134.2 (s, C_{arom}), 139.6 (s, C=N), 164.2 (s, C=O); MS $C_{16}H_{23}N_3O$ 273 (M^+).

Compound **1j**: yield 80%; mp 158°C; ^1H NMR δ 2.92-2.97 (4H, m, $2NCH_2$), 3.59-3.64 (4H, m, $2OCH_2$), 4.62 (2H, d, J = 6.0 Hz, $C_6H_5CH_2$), 6.71 (1H, br.s, NH), 7.29-7.81 (10H, m, $2C_6H_5$); ^{13}C NMR δ 43.2 (t, $C_6H_5CH_2$), 55.8 (t, $2NCH_2$), 66.0 (t, $2OCH_2$), 127.3, 127.8, 128.2, 128.5, 128.8, 130.5 (6d, CH_{arom}), 133.8, 137.7 (2s, C_{arom}), 158.2 (s, C=N), 165.4 (s, C=O); MS $C_{19}H_{21}N_3O_2$323 (M^+).

Compound **1k**: yield 62%; mp 80°C; ^1H NMR δ 1.42-1.47 (6H, m, $3CH_2$), 2.90-3.01 (4H, m, $2NCH_2$), 4.53 (2H, d, J = 6.1 Hz, $C_6H_5CH_2$), 7.32-7.53 (11H, m, $2C_6H_5$ and NH buried); ^{13}C NMR δ 23.9 and 24.9 (2t, $3CH_2$), 43.4 (t, $C_6H_5CH_2$), 54.9 (t, $2NCH_2$), 127.2, 127.7, 127.9, 128.4, 128.5, 128.9 (6d, CH_{arom}), 134.2, 138.6 (2s, C_{arom}), 139.1 (s, C=N), 165.1 (s, C=O); MS $C_{20}H_{23}N_3O$ 321 (M^+).

2-Hydrazonophenylthioacetamides 2 general procedure: Lawesson reagent ($2.6\ 10^{-3}$ mol) was added to a benzenic solution (5mL) of 2-hydrazonophenylacetamide **1** ($4\ 10^{-3}$mol) under a N_2 atmosphere. After refluxing (5 h for **2a, e-h,** 18 h for **2i-k)** the solvent was removed and the residue diluted with CH_2Cl_2 and chromatographed. After elution by CH_2Cl_2 (for **2c, f, g, i, j**) or by CH_2Cl_2/AcOEt (19/1) (for **2a, e, h, k**) compounds **2** were crystallised from Et_2O or isolated as a yellow oil (**2i, j**).

Compound **2a**: yield 67%; mp 108°C; ^1H NMR δ 1.61-1.82 (4H, m, $2CH_2$), 2.94-3.16 (4H, m, $2NCH_2$), 3.25 (3H, d, J = 5.0 Hz, CH_3), 7.28 (5H, br.s, C_6H_5), 8.86 (1H, br.s, NH); ^{13}C NMR δ 23,8 (t, $2CH_2$), 32.0 (q, CH_3), 54.4 (t, $2NCH_2$), 126.5, 127.4, 130.9 (3d, CH_{arom}), 136.3 (s, C_{arom}), 136.5 (s, C=N), 193.0 (s, C=S); MS $C_{13}H_{17}N_3S$ 247 (M^+).

Compound **2c**: yield 65%; mp 85°C; ^1H NMR δ 1.42-1.59 (6H, m, $3CH_2$), 2.86-3.03 (4H, m, $2NCH_2$), 3.26 (3H, d, J = 5.0 Hz, CH_3), 7.33 (5H, br.s, C_6H_5), 9.06 (1H, br.s, NH); ^{13}C NMR δ 23.8 and 25.0 (2t, $3CH_2$), 32.8 (q, CH_3N), 54.8 (t, $2NCH_2$), 127.6, 128.2, 129.4 (3d, CH_{arom}), 136.4 (s, C_{arom}), 140.7 (s, C=N), 193.3 (s, C=S); MS $C_{14}H_{19}N_3S$ 261 (M^+). Anal. calcd: C, 67.33; H, 7.33; N, 16.08; S, 12.27. Found: C, 67.15; H, 7.45; N, 15.97; S; 12.35.

Compound **2e**: yield 62%; mp 90°C; ^1H NMR δ 1.29-1.61 (8H, m, $4CH_2$), 3.11-3.27 (4H, m, $2NCH_2$), 3.23 (3H, d, J = 5.0 Hz, CH_3), 7.27 (5H, br.s, C_6H_5), 8.91 (1H, br.s, NH); ^{13}C NMR δ 27.2 and 27.6 (2t, $4CH_2$), 32.3 (q, CH_3N), 56.4 (t, $2NCH_2$), 127.0, 127.6, 130.5 (3d, CH_{arom}), 134.1 (s, C_{arom}), 137.2 (s, C=N), 193.6 (s, C=S); MS $C_{15}H_{21}N_3S$ 275 (M^+).

Compound **2f**: yield 89%; mp 125°C; ^1H NMR δ 2.86 (3H, s, $N(CH_3)C_6H_5$), 3.22 (3H, d, J = 5.0 Hz, CH_3NH), 7.26 (10H, br.s, $2C_6H_5$), 8.95 (1H, br.s, NH); ^{13}C NMR δ 32.6 (q, CH_3NH), 40.5 (q, $N(CH_3)C_6H_5$), 116.3, 122.0, 127.3,

128.9, 130.2 (6d, CH_{arom}), 136.1, 142.2 (2s, C_{arom}), 148.5 (s, C=N), 193.4 (s, C=S); MS $C_{16}H_{17}N_3S$ 283 (M^+).

Compound **2g**: yield 80%; mp 134°C; ^1H NMR δ 3.33 (3H, d, J = 5.0 Hz, CH_3), 6.82-7.36 (15H, m, $3C_6H_5$), 9.26 (1H, br.s, NH); ^{13}C NMR δ 32.8 (q, CH_3N), 122.9, 124.7, 127.0, 129.0, 129.0, 129.6 (9d, CH_{arom}), 135.5, 138.9, 147.2 (3s, C_{arom}), 146.3 (s, C=N), 193.0 (s, C=S); MS $C_{21}H_{19}N_3S$ 345 (M^+). Anal. calcd: C, 73.01; H, 5.54; N, 12.16; S, 9.28. Found: C, 73.17; H, 5.63; N, 12.33; S, 9.45.

Compound **2h**: yield 78%; mp 100°C; ^1H NMR δ 1.33 (6H, d, J = 6.6 Hz, $(\mathbf{CH_3})_2CH$), 2.89-2.94 (4H, m, $2NCH_2$), 3.57-3.62 (4H, m, $2OCH_2$), 4.67 (1H, h.d, J = 6.6 Hz and J = 8.2 Hz, $(CH_3)_2\mathbf{CH}$), 7.26-7.36 (5H, m, C_6H_5); ^{13}C NMR δ 21.4 (q, $(\mathbf{CH_3})_2CH$), 46.8 (d, $(CH_3)_2\mathbf{CH}$), 54.2 (t, $2NCH_2$), 66.2 (t, $2OCH_2$), 127.8, 128.6, 129.3 (3d, CH_{arom}), 135.6 (s, C_{arom}), 145.1 (s, C=N), 190.2 (s, C=S); MS $C_{15}H_{21}N_3OS$ 291 (M^+).

Compound **2i**: yield 88%; Rf (CH_2Cl_2) 0.75; ^1H NMR δ 1.24 (6H, d, J = 6.6 Hz, $(\mathbf{CH_3})_2CH$), 1.29-1.48 (6H, m, $3CH_2$), 2.78-2.97 (4H, m, $2NCH_2$), 4.61 (1H, h.d, J = 6.6 Hz and J = 8.1 Hz, $(CH_3)_2\mathbf{CH}$), 7.14-7.39 (5H, m, C_6H_5), 8.77 (1H, br.s, NH); ^{13}C NMR δ 21.6 (q, $(\mathbf{CH_3})_2CH$), 23.9 and 25.2 (2t, $3CH_2$), 46.6 (d, $(CH_3)_2\mathbf{CH}$), 54.9 (t, $2NCH_2$), 127.7, 128.2, 129.5 (3d, CH_{arom}), 136.5 (s, C_{arom}), 140.5 (s, C=N), 190.7 (s, C=S); MS $C_{16}H_{23}N_3S$ 289 (M^+).

Compound **2j**: yield 95%; Rf (CH_2Cl_2) 0.45; ^1H NMR δ 2.89-2.92 (4H, m, $2NCH_2$), 3.54-3.59 (4H, m, $2OCH_2$), 4.93 (2H, d, J = 5.5 Hz, $C_6H_5\mathbf{CH_2}$), 7.27-7.50 (10H, m, $2C_6H_5$), 9.17 (1H, br.s, NH); ^{13}C NMR δ 49.5 (t, $C_6H_5\mathbf{CH_2}$), 54.1 (t, $2NCH_2$), 66.0 (t, $2OCH_2$), 127.7, 127.8, 127.9, 128.6, 128.7, 129.3 (6d, CH_{arom}), 135.5, 136.8 (2s, C_{arom}), 144.1 (s, C=N), 192.0 (s, C=S); MS $C_{19}H_{21}N_3OS$ 339 (M^+).

Compound **2k**: yield 78%; mp 127°C; ^1H NMR δ 1.44-1.62 (6H, m, $3CH_2$), 2.92-2.97 (4H, m, $2NCH_2$), 5.00 (2H, d, J = 6.1 Hz, $C_6H_5\mathbf{CH_2}$), 7.35-7.70 (10H, m, $2C_6H_5$), 8.46 (1H, br.s, NH); ^{13}C NMR δ 23.8 and 25.2 (2t, $3CH_2$), 49.2 (t, $C_6H_5\mathbf{CH_2}$), 56.2 (t, $2NCH_2$), 127.9, 128.2, 128.3, 128.6, 129.0, 129.7 (6d, CH_{arom}), 136.0, 137.5 (2s, C_{arom}), 157.8 (s, C=N), 195.9 (s, C=S); MS $C_{20}H_{23}N_3S$ 337 (M^+).

2-Acyl (and 2-mesyl)amino-4-amino-1-thia-4-azabutadienes 3 general procedure: Sodium hydride ($1.65\ 10^{-3}$ mol) was added to a solution of 2-hydrazonophenylthioacetamide **2** ($1.5\ 10^{-3}$ mol) in THF (5mL) cooled at 0°C. After 1h at room temperature the mixture was cooled again and acylating reagent (acetyl chloride, benzoyl chloride methylchloroformate or mesyl chloride) ($1.8\ 10^{-3}$ mol) was added. After 20 h stirring at room temperature the mixture was diluted in AcOEt, whashed with brine and dried. The solvent was removed and the residue, diluted with CH_2Cl_2, was chromatographed. After elution by CH_2Cl_2 (for

3b-h) or by CH_2Cl_2/AcOEt (4/1) (for **3a**) compounds **3** were crystallised from Et_2O (**3c-e, g**) or isolated as a red oil (**3a, b, f, h**).

Compound **3a**: yield 65%; Rf (CH_2Cl_2/AcOEt: 4/1) 0.66; ^{1}H NMR δ 2.54-2.64 and 2.79-2.89 (4H, 2m, $2NCH_2$), 3.61-3.79 (4H, m, $2OCH_2$), 3.73 (3H, s, CH_3N), 3.74 (3H, s, CH_3O), 7.24-7.41 and 7.70-7.81 (5H, 2m, C_6H_5); ^{13}C NMR δ 36.2 (q, CH_3N), 54.2 (q, CH_3O), 54.5 (t, $2NCH_2$), 65.8 (t, $2OCH_2$), 127.6, 127.9, 130.0 (3d, CH_{arom})(134.3 (s, C_{arom}), 152.8 (s, C=N), 166.5 (s, C=O), 203.8 (s, C=S); MS $C_{15}H_{19}N_3O_3S$ 321 (M^+).

Compound **3b**: yield 70%; Rf (CH_2Cl_2) 0.63; ^{1}H NMR δ 2.62 (3H, s, CH_3SO_2), 3.24 (3H, s, $N(CH_3)C_6H_5$), 3.60 (3H, s, CH_3N), 6.84-7.78 (10H, m, $2C_6H_5$); ^{13}C NMR δ 38.5 (q, CH_3N), 39.7 (q, CH_3SO_2), 42.0 (q, $N(CH_3)C_6H_5$), 116.3, 121.54, 127.6, 128.2, 129.0, 129.4 (6d, CH_{arom}), 136.4, 150.0 (2s, C_{arom}), 153.2 (s, C=N), 201.9 (s, C=S); MS $C_{17}H_{19}N_3O_2S_2$ 361 (M^+).

Compound **3c**: yield 65%; mp 88°C; ^{1}H NMR δ 3.16 (3H, s, $N(CH_3)C_6H_5$), 3.58 (3H, s, CH_3N), 3.65 (3H, s, CH_3O), 6.89-7.71 (10H, m, $2C_6H_5$); ^{13}C NMR δ 36.9 (q, CH_3N), 42.4 (q, $N(CH_3)C_6H_5$), 54.6 (q, CH_3O), 116.5, 120.9, 127.4, 128.3, 128.6, 129.6 (6d, CH_{arom}), 135.7, 150.7 (2s, C_{arom}), 153.0 (s, C=N), 158.7 (s, C=O), 203.7 (s, C=S); MS $C_{18}H_{19}N_3O_2S$ 341 (M^+).

Compound **3d**: yield 57%; mp 145°C; ^{1}H NMR δ 3.26 (3H, s, $N(CH_3)C_6H_5$), 3.94 (3H, s, CH_3N), 6.89-7.64 (15H, m, $3C_6H_5$); ^{13}C NMR δ 40.6 (q, CH_3N), 42.0 (q, $N(CH_3)C_6H_5$), 115.6, 122.7, 126.9, 127.1, 127.5, 128.1, 128.5, 128.7, 129.0 (9d, CH_{arom}), 131.0, 136.7, 138.1 (3s, C_{arom}), 149.3 (s, C=N), 173.8 (s, C=O), 201.6 (s, C=S); MS $C_{23}H_{21}N_3OS$ 387 (M^+).

Compound **3e**: yield 59%; mp 137°C; ^{1}H NMR δ 2.79 (3H, s, CH_3SO_2), 3.18 (3H, s, CH_3N), 7.02-7.45 and 7.61-7.79 (15H, 2m, $3C_6H_5$); ^{13}C NMR δ 38.2 (q, CH_3N), 40.2 (q, CH_3SO_2), 123.3, 123.5, 123.6, 127.3, 129.2, 129.3 (9d, CH_{arom}), 128.6, 129.0, 129.5 (3s, C_{arom}), 146.7 (s, C=N), 198.8 (s, C=S); MS $C_{22}H_{21}N_3O_2S_2$ 423 (M^+).

Compound **3f**: yield 67%; Rf (CH_2Cl_2/ligroin: 9/1) 0.60; ^{1}H NMR δ 1.92 (3H, s, CH_3CO), 3.29 (3H, s, CH_3N), 6.81-7.40 and 7.68-7.80 (15H, 2m, $3C_6H_5$); ^{13}C NMR δ 24.1 (q, CH_3CO), 37.0 (q, CH_3N), 122.7, 122.8, 122.9, 123.8, 124.8, 127.0 ,128.2, 128.8, 128.9 (9d, CH_{arom}), 129.1, 129.5, 129.6 (3s, C_{arom}),146.8 (s, C=N), 166.1 (s, C=O), 202.1 (s, C=S); MS $C_{23}H_{21}N_3OS$ 387 (M^+).

Compound **3g**: yield 81%; mp 112°C; ^{1}H NMR δ 3.29 (3H, s, CH_3N), 3.47 (3H, s, CH_3O), 6.91-7.42 and 7.67-7.81 (15H, 2m, $3C_6H_5$); ^{13}C NMR δ 36.3 (q, CH_3N), 54.3 (q, CH_3O), 122.7, 122.8, 123.9, 126.7, 128.1, 128.5, 128.7 (9d, CH_{arom}), 129.3, 136.2, 151.7 (3s, C_{arom}), 146.9 (s, C=N), 159.0 (s, C=O), 201.9 (s, C=S); MS $C_{23}H_{21}N_3O_2S$ 403 (M^+). Anal. calcd: C, 68.46; H, 5.25; N, 10.41. Found: C, 68.59; H, 5.12; N, 10.28.

Compound **3h**: yield 73%; Rf (CH_2Cl_2/AcOEt: 9/1) 0.52; ^1H NMR δ 2.57-2.67 and 2.85-2.95 (4H, 2m, $2NCH_2$), 3.62-3.66 (4H, m, $2OCH_2$), 3.70 (3H, s, CH_3), 5.44 and 5.86 (2H, 2d, J = 15.1 Hz, $C_6H_5C\mathbf{H}_2$), 7.33-7.76 (10H, m, $2C_6H_5$); ^{13}C NMR δ 51.4 (t, $C_6H_5CH_2$), 54.8 (q, CH_3O), 54.9 (t, $2NCH_2$), 65.9 (t, $2NCH_2$), 127.8, 127.9, 128.0, 128.1, 128.4, 128.6 (6d, CH_{arom}), 130.6, 135.7 (2s, C_{arom}), 153.0 (s, C=N), 167.5 (s, C=O), 204.1 (s, C=S); MS $C_{21}H_{23}N_3O_3S$ 397 (M^+).

6-Acyl (and 6-mesyl)amino-3,6-dihydro-2H-1,3,4-thiadiazines 4: In most of the cases the compounds **3** were not isolated and compounds **4** were obtained using the same procedure starting from 2-hydrazonophenylthioacetamides **2.** After removal of the solvent and chromatography, elution by CH_2Cl_2 (for **4a, b, e, f, i, l, s),** by CH_2Cl_2/AcOEt (9/1) (for **4d, g, h, j, k, m, n, r)** or by CH_2Cl_2/AcOEt (4/1) (for **4c, o-q**) affords compounds **4** which were crystallised from Et_2O **(4a-g, i-m, o, p, r, s)** or isolated as a colorless oil **(4h, n, q).** Compound **4f** is obtained using trifluoroacetyl anhydride as acylating reagent. When compounds **2** were isolated, they gave easily the corresponding compounds **4** after heating 20 h in benzenic solution **(4g, m, r** from **3a, d, h).** The yields were in all the cases calculated using compounds **2** as starting products.

Compound **4a**: yield 31%; mp 153°C; ^1H NMR δ 2.77 (3H, s, CH_3SO_2), 2.88 (3H, s, CH_3N) 3.12-4.18 (7H, m, ($3CH_2$ and CH, 2-H buried), 6.25 (1H, s, CH, 6-H), 7.24-7.41 and 7.61-7.75 (5H, 2m, C_6H_5); ^{13}C NMR δ 31.0 (q, CH_3N), 39.0 (q, CH_3SO_2), 50.7 (d, CH, 6-C), 53.3 (d, CH, 2-C), 55.8 (t, NCH_2), 67.6, 68.8 (2t, $2CH_2O$), 126.5, 128.4, 128.9 (3d, CH_{arom}), 136.6 (s, C_{arom}), 138,4 (s, C=N); MS $C_{14}H_{19}N_3O_3S_2$ 341 (M^+).

Compound **4b**: yield 33%; mp 120°C; ^1H NMR δ 1.38-2.21, 2.82-3.13 and 3.69-3.96 (9H, 3m, $4CH_2$ and CH, 2-H buried), 2.76 (3H, s, CH_3SO_2), 2.89 (3H, s, CH_3N), 6.17 (1H, s, CH, 6-H), 7.21-7.43 and 7.60-7.82 (5H, 2m, C_6H_5); ^{13}C NMR δ 23.3 (t, $NCH_2CH_2\mathbf{C}H_2CH_2$), 25.5 (t, $NCH_2CH_2CH_2\mathbf{C}H_2$), 31.0 (q, CH_3N), 31.3 (t, $NCH_2\mathbf{C}H_2CH_2CH_2$), 38.9 (q, CH_3SO_2), 51.7 (d, CH, 6-C), 54.2 (d, CH, 2-C), 57.1 (t, $N\mathbf{C}H_2CH_2CH_2CH_2$), 126.3, 126.5, 128.3 (3d, CH_{arom}), 136.5 (s, C_{arom}), 137.0 (s, C=N); MS $C_{15}H_{21}N_3O_2S_2$ 339 (M^+).

Compound **4c**: yield 42%; mp 140°C; ^1H NMR δ 1.75-2.08, 2.31-2.83 and 3.46-4.00 (6H, 3m, $3CH_2$), 2.10 (3H, s, CH_3CO), 2.86 (3H, s, CH_3N), 4.49-4.68 (1H, m, CH, 2-H), 6.62 (1H, s, CH, 6-H), 7.21-7.42 and 7.51-7.70 (5H, 2m, C_6H_5); ^{13}C NMR δ 21.4 (t, $NCH_2CH_2\mathbf{C}H_2$), 22.3 (q, CH_3CO), 32.0 (t, $NCH_2\mathbf{C}H_2CH_2$), 34.6 (q, CH_3N), 48.4 (d, CH, 6-C), 53.0 (d, CH, 2-C), 53.8 (t, $N\mathbf{C}H_2CH_2CH_2$), 124.2, 127.4, 128.4 (3d, CH_{arom}), 133.6 (s, C_{arom}), 137.4 (s, C=N), 170.4 (s, C=O); MS $C_{15}H_{19}N_3OS$ 289 (M^+).

Compound **4d**: yield 51%; mp 206; ^1H NMR δ 2.04 (3H, s, CH_3CO), 2.87 (3H, s, CH_3N), 3.19-4.09 (7H, m, $3CH_2$and CH, 2-H buried), 6.80 (1H, s, CH, 6-H), 7.30-7.34 and 7.52-7.57 (5H, 2m, C_6H_5); ^{13}C NMR δ 22.1 (q, $\mathbf{C}H_3CO$), 32.7 (q,

CH_3N), 45.8 (d, CH, 6-C), 53.3 (d, CH, 2-C), 55.7 (t, NCH_2), 67.5, 68.8 (2t, $2CH_2O$), 125.6, 128.4, 128.8 (3d, CH_{arom}), 136.7 (s, C_{arom}), 139.6 (s, C=N), 170.7 (s, C=O); MS $C_{15}H_{19}N_3O_2S$ 305 (M^+). Anal. calcd: C, 58.99; H, 6.27; N, 13.76; S, 10.50. Found: C, 58.76; H, 6.35; N, 13.91; S, 10.68.

Compound **4e**: yield 56%; mp 122°C; ^1H NMR δ 1.37-1.98, 2.72-3.10 and 3.73-3.98 (9H, 3m, $4CH_2$ and CH, 2-H buried), 2.03 (3H, s, CH_3CO), 2.87 (3H, s, CH_3N), 6.72 (1H, s, CH, 6-H), 7.21-7.38 and 7.47-7.62 (5H, 2m, C_6H_5); ^{13}C NMR δ 22.0 (q, CH_3CO), 24,0 (t, $NCH_2CH_2CH_2CH_2$), 25,5 (t, $NCH_2CH_2CH_2CH_2$), 31,2 (t, $NCH_2CH_2CH_2CH_2$), 32.7 (q, CH_3N), 46,7 (d, CH, 6-C), 54.0 (d, CH, 2-C), 57.0 (t, $NCH_2CH_2CH_2CH_2$), 125.3, 128.1, 128.2 (3d, CH_{arom}), 137.1 (s, C_{arom}), 137.8 (s, C=N), 170.4 (s, C=O); MS $C_{16}H_{21}N_3OS$ 303 (M^+).

Compound **4f**: yield 58%; mp 137°C; ^1H NMR δ 2.99 (3H, s, CH_3N), 3.23-4.09 (7H, m, $3CH_2$ and CH, 2-H buried), 6.62 (1H, s, CH, 6-H), 7.32-7.38 and 7.46-7.51 (5H, 2m, C_6H_5); ^{13}C NMR δ 31.6 (qq, CH_3N, $^4J_{CF}$ = 4.2 Hz), 47.7 (d, CH, 6-C), 53.0 (d, CH, 2-C), 55.7 (t, NCH_2, 67.6, 68.7 (2t, $2CH_2O$), 116.0 (q, CF_3, $^1J_{CF}$ = 288.0 Hz), 125.4, 128.7 129.3 (3d, CH_{arom}), 136.0 (s, C_{arom}), 137.4 (s, C=N), 157.0 (q, C=O, $^2J_{CF}$= 36.6 Hz); MS $C_{15}H_{16}F_3N_3O_2S$ 359 (M^+).

Compound **4g**: yield 52%; mp 143°C; ^1H NMR δ 2.79 (3H, s, CH_3N), 3.11-4.19 (7H, m, $3CH_2$ and CH, 2-H buried), 3.73 (3H, CH_3O), 6.40 (1H, s, CH, 6-H), 7.22-7.43 and 7.49-7.61 (5H, 2m, C_6H_5); ^{13}C NMR δ 31.0 (q, CH_3N), 49.4 (d, CH, 6-C), 53.3 (q, CH_3O and d, CH, 2-C), 55.5 (t, NCH_2), 67.6, 68.9 (2t, $2CH_2O$), 125.7, 128.5, 128.7 (3d, CH_{arom}), 137.0 (s, C_{arom}), 138.9 (s, C=N), 156.3 (s, C=O); MS $C_{15}H_{19}N_3O_3S$ 321 (M^+).

Compound **4h**: yield 49%; Rf (CH_2Cl_2) 0.39; ^1H NMR δ 1.36-2.18, 2.77-3.15 and 3.31-3.85 (9H, 3m, $4CH_2$ and CH, 2-H buried), 2.77 (3H, s, CH_3N), 3.70 (3H, s, CH_3O), 6.32 (1H, s, CH, 6-H), 7.19-7.38 and 7.50-7.71 (5H, 2m, C_6H_5); ^{13}C NMR δ 23.8 (t, $NCH_2CH_2CH_2CH_2$), 25.4 (t, $NCH_2CH_2CH_2CH_2$), 31.0 (t, $NCH_2CH_2CH_2CH_2$), 31.1 (q, CH_3N), 50.0 (d, CH, 6-C), 52.9 (q, CH_3O), 53.8 (d, CH, 2-C), 56,6 (t, $NCH_2CH_2CH_2CH_2$), 125.2, 127.9, 128.1 (3d, CH_{arom}), 136.9 (s, C_{arom}), 137.2 (s, C=N), 156,0 (s, C=O); MS $C_{16}H_{21}N_3O_2S$ 319 (M^+).

Compound **4i**: yield 63%; mp 123°C; ^1H NMR δ 1.62-2.18, 2.41-2.63 and 3.50-3.97 (6H, 3m, $3CH_2$), 2.82 (3H, s, CH_3), 4.46-4.75 (1H, m, CH, 2-H), 7.23-7.72 (10H, m, $2C_6H_5$); ^{13}C NMR δ 21.3 (t, $NCH_2CH_2CH_2$), 31.9 (t, $NCH_2CH_2CH_2$), 35.4 (q, CH_3), 48.5 (d, CH, 6-C), 53.2 (d, CH, 2-C), 53.7 (t, $NCH_2CH_2CH_2$), 124.6, 126.7, 127.6, 128.4, 128.5, 129.8 (6d, CH_{arom}), 134.2, 135.8 (2s, C_{arom}), 137.6 (s, C=N), 171.3 (s, C=O); MS $C_{20}H_{21}N_3OS$ 351 (M^+).

Compound **4j**: yield 49%; mp 198°C; ^1H NMR δ 2.81 (3H, s, CH_3), 3.09-4.18 (7H, m, $3CH_2$ and CH, 2-H buried), 6.92 (1H, s, CH, 6-H), 7.01-7.68 (10H, m, $2C_6H_5$); ^{13}C NMR δ 33.9 (q, CH_3), 46.4 (d, CH, 6-C), 54.0 (d, CH, 2-C), 56.0 (t,

NCH_2), 67.7, 69.0 (2t, $2CH_2O$), 126.2, 126.9, 128.6, 129.1, 130.2 (6d, CH_{arom}), 135.4, 137.0 (2s, C_{arom}), 140.7 (s, C=N), 171.6 (s, C=O); MS $C_{20}H_{21}N_3O_2S$ 334 (M^+ - SH). Anal. calcd: C, 65.37; H, 5.76, N; 11.43; S, 8.73. Found: C, 65.51; H, 5.61; N, 11.58; S, 8.88.

Compound **4k**: yield 67%; mp 113°C; ^1H NMR δ 1.52-2.12, 2.81-3.17 and 3.73-3.99 (9H, 3m, $4CH_2$ and CH, 2-H buried), 2.78 (3H, s, CH_3), 6.87 (1H, s, CH, 6-H), 7.12-7.70 (10H, m, $2C_6H_5$); ^{13}C NMR δ 24.1 (t, $NCH_2CH_2\mathbf{C}H_2CH_2$), 25.6 (t, $NCH_2CH_2CH_2\mathbf{C}H_2$), 31.3 (t, $NCH_2\mathbf{C}H_2CH_2CH_2$), 33.9 (q, CH_3), 47.1 (d, CH, 6-C), 54.7 (d, CH, 2-C), 57.3 (t, $N\mathbf{C}H_2CH_2CH_2CH_2$), 125.9, 126.7, 128.3, 128.5, 129.9 (6d, CH_{arom}), 135.6, 137.4 (2s, C_{arom}), 138.7 (s, C=N), 171.6 (s, C=O); MS $C_{21}H_{23}N_3OS$ 332 (M^+ - SH).

Compound **4l**: yield 45%; mp 110°C; ^1H NMR δ 1.50-2.26, 3.70-3.91 and 4.49-4.68 (11H, 3m, $5CH_2$ and CH, 2-H), 2.79 (3H, s, CH_3N), 6.90 (1H, s, CH, 6-H), 7.13-7.71 (10H, m, $2C_6H_5$); ^{13}C NMR δ 25.3 (t, $NCH_2CH_2CH_2\mathbf{C}H_2CH_2$), 29.3, 29.8 (2t, $NCH_2CH_2\mathbf{C}H_2CH_2CH_2$), 32.5 (t, $NCH_2\mathbf{C}H_2CH_2CH_2CH_2$), 34.8 (q, CH_3), 49.7 (d, CH, 6-C), 57.0 (d, CH, 2-C), 58.3 (t, $N\mathbf{C}H_2CH_2CH_2CH_2CH_2$), 125.2, 126.9, 127.6, 128.5, 128.6, 129.9 (6d, CH_{arom}), 133.0, 136.0 (2s, C_{arom}), 138.2 (s, C=N), 171.5 (s, C=O); MS $C_{22}H_{25}N_3OS$ (M^+).

Compound **4m**: yield 38%; mp 163°C; ^1H NMR δ 2.84 (3H, s, CH_3), 4.68 and 5,03 (2H, d and dd, J = 1.0 Hz and J = 12.7 Hz, CH_2), 6.88-7.80 (16H, m, $3C_6H_5$ and CH, 6-H buried); ^{13}C NMR δ 34.9 (q, CH_3), 41.8 (t, CH_2), 46.4 (d, CH), 115.9, 122.3, 125.6, 126.9, 128.6, 129.3, 130.1 (9d, CH_{arom}), 135.5, 137.0, 146.5 (3s, C_{arom}), 137.5 (s, C=N), 171.6 (s, C=O); MS $C_{23}H_{21}N_3OS$ 387 (M^+).

Compound **4n**: yield 51%; Rf (CH_2Cl_2) 0.44; ^1H NMR δ 0.73 and 1.34 (6H, 2d, J = 6.6 Hz, $(C\mathbf{H}_3)_2CH$), 1.45-2.07, 2.91-3.04 and 3.81-3.87 (9H, 3m, $4CH_2$ and CH, 2-H buried), 3.51-3.65 (1H, m, $(CH_3)_2C\mathbf{H}$), 3.76 (3H, s, CH_3O), 6.21 (1H, s, CH, 6-H), 7.22-7.39 and 7.51-7.69 (5H, 2m, C_6H_5); ^{13}C NMR δ 20.9 (q, $(\mathbf{C}H_3)_2CH$), 24.2 (t, $NCH_2CH_2\mathbf{C}H_2CH_2$), 25.8 (t, $NCH_2CH_2CH_2\mathbf{C}H_2$), 31.4 (t, $NCH_2\mathbf{C}H_2CH_2CH_2$), 49.2 (d, $(CH_3)_2\mathbf{C}H$), 51.1 (d, CH, 6-C), 52.5 (d, CH, 2-C), 53.6 (q, CH_3O), 57.0 (t, $N\mathbf{C}H_2CH_2CH_2CH_2$), 126.0, 128.3 (3d, CH_{arom}), 136.3 (s, C_{arom}), 137.8 (s, C=N), 156.2 (s, C=O); MS $C_{18}H_{25}N_3O_2S$ 347 (M^+).

Compound **4o**: yield 38%; mp 152°C; ^1H NMR δ 0.83-0.86 and 1.18-1.29 (6H, 2m, $(C\mathbf{H}_3)_2CH$), 3.52-4.10 (7H, m, $3CH_2$ and CH, 2-H buried), 3.24-3.50 (1H, m, $(CH_3)_2C\mathbf{H}$), 6.97 (1H, s, CH, 6-H), 7.35 (10H, br.s, $2C_6H_5$); ^{13}C NMR δ 20.8 (q, $(\mathbf{C}H_3)_2CH$, 50.6 (d, $(CH_3)_2\mathbf{C}H$), 51.3 (d, CH, 6-C), 53.8 (d, CH, 2-C), 55.9 (t, NCH_2), 67.8, 69.1 (2t, $2CH_2O$), 126.2, 127.7, 128.3, 128.7, 129.8 (6d, CH_{arom}), 130.4, 137.0 (2s, C_{arom}), 138.3 (s, C=N), 171.9 (s, C=O); MS $C_{22}H_{25}N_3O_2S$ 395 (M^+).

Compound **4p**: yield 53%; 135°C; ^1H NMR δ 0.83 and 1.56 (6H, 2d, J = 6.7 Hz, $(C\mathbf{H}_3)_2CH$), 1.15-2.02, 2.93-3.07 and 3.73-3.81 (9H, 3m, $4CH_2$ and CH, 2-H

buried), 3.66-3.72 (1H, m, $(CH_3)_2CH$), 7.06 (1H, s, CH, 6-H), 7.37 (10H, br.s, $2C_6H_5$); ^{13}C NMR δ 20.6 (q, $(CH_3)_2CH$), 24.1 (t, $NCH_2CH_2CH_2CH_2$), 25.8 (t, $NCH_2CH_2CH_2CH_2$), 31.3 (t, $NCH_2CH_2CH_2CH_2$), 47.3 (d, $(CH_3)_2CH$), 51.0 (d, CH, 6-C), 54.4 (d, CH, 2-C), 57.1 (t, $NCH_2CH_2CH_2CH_2$), 126.0, 128.1, 128.3, 128.5, 129.5 (6d, CH_{arom}), 126.9, 128.6 (2s, C_{arom}), 137.2 (s, C=N), 171.6 (s, C=O); MS $C_{23}H_{27}N_3OS$ 393 (M^+).

Compound **4q**: yield 55%; Rf (CH_2Cl_2) 0.42; ^1H NMR δ 1.97 (3H, s, CH_3), 2.97-4.54 (7H, m, $3CH_2$ and CH, 2-H buried), 4.37 and 4.48 (2H, 2d, J = 14.2 Hz, $C_6H_5CH_2$), 6.85 (1H, s, CH, 6-H), 7.21-7.53 (10H, m, $2C_6H_5$); ^{13}C NMR δ 22.0 (q, CH_3), 46.8 (t, $C_6H_5CH_2$), 50.0 (d, CH, 6-C), 52.6 (d, CH, 2-C), 54.9 (t, NCH_2), 67.2, 68.2 (2t, $2CH_2O$), 125.3, 126.1, 127.6, 128.1, 128.2 (6d, CH_{arom}), 133.2, 136.4 (2s, C_{arom}), 137.8 (s, C=N), 171.5 (s, C=O); MS $C_{21}H_{23}N_3O_2S$ 381 M^+).

Compound **4r**: yield 48%; mp 155°C; ^1H NMR δ 3.02-4.12 (7H, m, $3CH_2$ and CH, 2-H buried), 3.77 (3H, s, CH_3), 4.60 and 4.79 (2H, 2d, J = 14.1 Hz, $C_6H_5CH_2$), 6.28 (1H, s, CH, 6-H), 7.12-7.48 (10H, m, $2C_6H_5$); ^{13}C NMR δ 49.0 (t, $C_6H_5CH_2$), 50.0 (d, CH, 6-C), 52.8 (d, CH, 2-C), 53.6 (q, CH_3), 55.1 (t, NCH_2), 67.7, 68.7 (2t, $2CH_2O$), 125.7, 127.6, 128.0, 128.6, 128.7 (6d, CH_{arom}), 127.4, 128.9 (2s, C_{arom}), 137.7 (s, C=N), 156.7 (s, C=O); MS $C_{21}H_{23}N_3O_3S$ 397 (M^+).

Compound **4s**: yield 48%; Rf (CH_2Cl_2) 0.46; ^1H NMR δ 1.18-1.86, 2.57-2.94 and 3.66-3.83 (9H, 3m, $4CH_2$ and CH, 2-H buried), 3.77 (3H, s, CH_3), 4.65 and 4.83 (2H, 2d, J = 14.3 Hz, $C_6H_5CH_2$), 6.19 (1H, s, CH, 6-H), 7.10-7.62 (10H, m, $2C_6H_5$); ^{13}C NMR δ 21.1 (q, CH_3), 23.8 (t, $NCH_2CH_2CH_2CH_2$), 25.6 (t, $NCH_2CH_2CH_2CH_2$), 30.6 (t, $NCH_2CH_2CH_2CH_2$), 48.7 (t, $C_6H_5CH_2$), 50.8 (d, CH, 6-C), 53.4 (d, CH, 2-C), 56.3 (t, $NCH_2CH_2CH_2CH_2$), 125.2, 127.5, 128.1, 128.3, 128.5 (6d, CH_{arom}), 128.7, 130.7 (2s, C_{arom}), 137.7 (s, C=N), 156.6 (s, C=O); MS $C_{22}H_{25}N_3O_2S$ 395 (M^+).

References

[1] A. Reliquet, M. J. Gil, F. Reliquet and J. C. Meslin, *Sulfur Lett.*, **16**, 1, (1993).

[2] M. J. Gil, A. Reliquet, F. Reliquet and J. C. Meslin, *Phosphorus, Sulfur and Silicon*, **97**, 89, (1994).

[3] M. J. Gil, A. Reliquet, F. Reliquet and J. C. Meslin, *Phosphorus, Sulfur and Silicon*, in press.

[4] A. Reliquet, R. Besbes, F. Reliquet and J.C. Meslin, *Sulfur Lett.*, **14**, 189, (1992).

[5] A. Reliquet, R. Besbes, F. Reliquet and J.C. Meslin, *Synthesis*, **7**, 543, (1991).

[6] J. P. Pradère, G. Bouet and H. Quiniou, *Tetrahedron Lett.*, **33**, 3471, (1972).

[7] T. Karakasa and S. Motoki, *J. Org. Chem.*, **43**, 4147, (1978).

[8] J. P. Guémas, A. Reliquet, F. Reliquet and H. Quiniou, *C. R. Acad. Sc. Paris*, **288(C)**, 89, (1979).

[9] I. T. Barnish, C. W. G. Fishwick, D. R. Hill and C. Jr. Szantay, *Tetrahedron Lett.*, **33**, 4449, (1989).

[10] S. V. Usoltseva, G. P. Andronnikova and V. S. Mokrushin, *Khimiya Geterotsiklicheskikh Soedinii*, **4**, 435, (1991), (Engl. Transl.: *Chem. Heterocycl. Comp.*, (1991)); P. K. Bose, *Quart.*

J. Indian Chem. Soc,. **1**, 51, (1924); H. Beyer, *Quart. rep. Sulfur Chem.*, **5**, 177, (1970); A. Neugebauer and H. Fischer, *Chem. Ber.*, **107**, 717, (1974); H. Beyer, *Chem. Ber.*, **89**, 107, (1956); Y. V. Zachinaev, M. L. Petrov, A. N. Frolkov, V. N. Chistokletov and A. A. Petrov, *Zhurnal Organicheskoi Khimii*, **16**, 938, (1980), (Engl. Transl.: *Jl of Organic Chem. of USSR*, 818, (1980)); R. M. Mohareb, A. Habashi, E. A. Hafez and S. M. Sherif, *Arch. Pharm. (Weinheim, Ger.)*, **320**, 776, (1987); D. L. Trepanier, P. E. Krieger, J. H. Mennear and J. N. Eble, *J. Med. Chem.*, **10**, 1085, (1967); S. Tadashi and O. Masaki, *Yakugaku Zasshi*, **75**, 1535, (1955), (Engl. Transl.: *Jl of the pharmaceutical society of Japan*, (1955)); A. E. Baydar, G. V. Boyd and P. F. Lindley, *J. Chem. Soc., Chem. Commun.*, 1003, (1981); D. L. Trepanier, W. Reifschneider, W. Shumaker and D. S. Tharpe, *J. Org. Chem.*, **30**, 2228, (1965); H. Kristinsson, T. Winkler and M. Mollenkopf, *Helv. Chim. Acta*, **66**, 2714, (1983); D. M. Evans, D. R. Taylor and M. Myers, *J. Chem. Soc., Chem. Commun.*, 1444, (1984); K. Hirai and T. Ishiba, *J. Chem. Soc., Chem. Commun.*, 1318, (1971); P. Molina, A. Arques, I. Cartagena and J. M. Olmos, *Synthesis*, 518, (1989); G. Seitz, R. Mohr, W. Overheu, R. Allmann and M. Nagel, *Angew. Chem. Int. Ed. Engl.*, **11**, 890, (1984); G. Hesse and I. Jorder, *Chem. Ber.*, **85**, 924, (1952).

[11] Y. Kamitori, M. Hojo, R. Masuda, Y. Kawamura and T. Numai, *Synthesis*, 491, (1990).

[12] A. P. Novikova, N. M. Perova and O. N. Chupakhin, *Khimiya Geterotsiklicheskikh Soedinii*, **11**, 1443, (1991), (Engl. Transl.: *Chem. Heterocycl. Comp.*, (1991)); D. Brown, R. B. Hargreaves, B. J. Mc Loughlin and S. D. Mills, Eur. Pat. 80,296, *CA*, **100**, 22672, (1984); N. Yoshida, K. Tanaka, Y. Iizuka, K. Wachi, T. Nishimura and H. Yasuda, (Sankyo Co., Ltd), Jpn. Kokai Tokkyo Koho JP 7,488,889, *CA*, **82**, 57744, (1975); J. Dizon and D. H. Robinson, (Fisons PLC), Brit. UK Pat. Appl. GB 2,179,655, *CA*, **108**, 37839, (1988); W. Thorwart, U. Gebert, R. Schleyerbach and R. Bartlett, (Hoechst A.-G.), Ger. Offen. DE. 3,702,757, *CA*, **110**, 8223, (1988); W. Thorwart, U. Gebert, R. Schleyerbach and R. Barlett, (Hoechst A.-G.), Ger. Offen. DE. 3,702,756, *CA*, **109**, 170466, (1988); W. D. Jones and F. P. Miller, (Richardson-Merrell Inc.), Ger. Offen. DE. 3,031,703, *CA*, **95**, 81033, (1981); F. P. Miller and W. D. Jones, (Richardson-Merrell Inc.), Belgian Pat. 884,990, *CA*, **95**, 62276, (1981).