

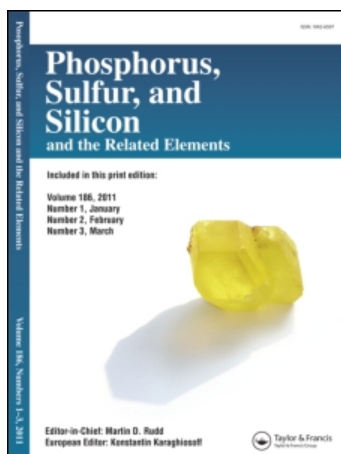
This article was downloaded by:

On: 28 January 2011

Access details: *Access Details: Free Access*

Publisher *Taylor & Francis*

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Phosphorus, Sulfur, and Silicon and the Related Elements

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t713618290>

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 Synthèse Organique, U. A. C.N.R.S. 475, Nantes Cedex, France

To cite this Article Gil, M. J. , Reliquet, A. and Meslin, J. C.(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

To link to this Article: DOI: 10.1080/10426509708043544

URL: <http://dx.doi.org/10.1080/10426509708043544>

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <http://www.informaworld.com/terms-and-conditions-of-access.pdf>

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

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)*

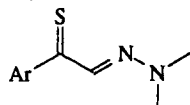
(Received 10 December, 1996)

The three steps synthesis of new 2-hydrazonophenylthioacetamides having a N-monosubstituted 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.

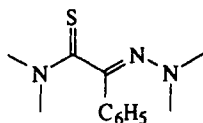
Keywords: 2-hydrazonophenylacetamides; 2-hydrazonophenylthioacetamides; 3,6-dihydro-2H-1,3,4-thiadiazines

INTRODUCTION

We have recently reported the synthesis and some properties of 2-hydrazonophenylthioacetamides¹⁻³ (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



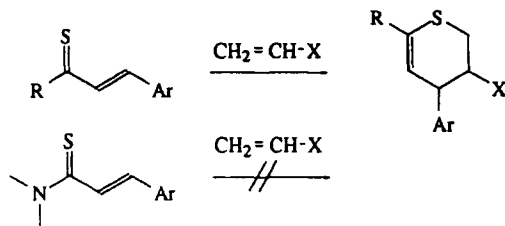
2-hydrazonothioacetophenones



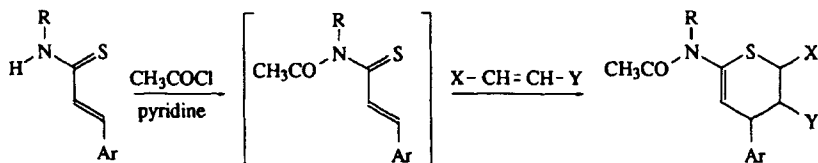
2-hydrazonophenylthioacetamides

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 thioketones⁶⁻⁸ 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.

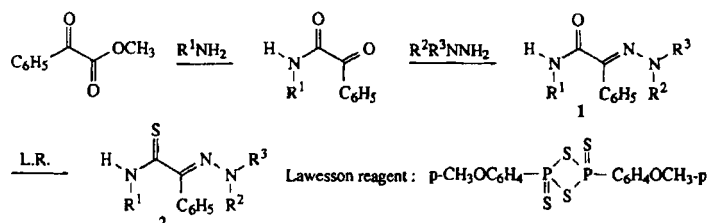


In this paper we report firstly on the preparation of new 2-hydrazonophenylthioacetamides with a N-monosubstituted thioamide group and secondly the substitution of the nitrogen atom by electron withdrawing groups with the aim to get closer to the Barnish models. The synthesized molecules do not even 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-

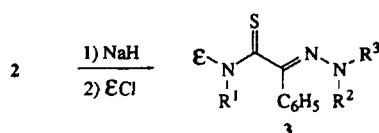
acetamides **1**. Then the latter are thionated using Lawesson reagent affording compounds **2**.



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 ² R ³				NHC ₆ H ₅		N(CH ₃)C ₆ H ₅
1,2	g	h	i	j	k	
R ¹	CH ₃	(CH ₃) ₂ CH	(CH ₃) ₂ CH	C ₆ H ₅ CH ₂	C ₆ H ₅ CH ₂	
NR ² R ³	N(C ₆ H ₅) ₂					

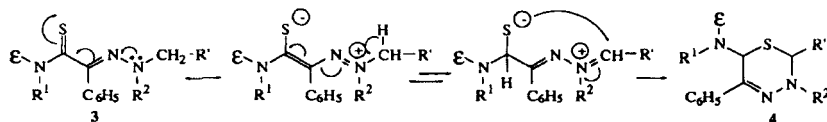
The isolated compound **1f** presents two diastereoisomeric forms. The determination of the corresponding geometries has been already discussed in a previous paper.³

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 ² R ³	E
a	CH ₃		CH ₃ OCO
b	CH ₃	N(CH ₃)C ₆ H ₅	CH ₃ SO ₂
c	CH ₃	N(CH ₃)C ₆ H ₅	CH ₃ OCO
d	CH ₃	N(CH ₃)C ₆ H ₅	C ₆ H ₅ CO
e	CH ₃	N(C ₆ H ₅) ₂	CH ₃ SO ₂
f	CH ₃	N(C ₆ H ₅) ₂	CH ₃ CO
g	CH ₃	N(C ₆ H ₅) ₂	CH ₃ OCO
h	C ₆ H ₅ CH ₂		CH ₃ OCO

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'	E
a	CH ₃	-(CH ₂) ₂ -O-CH ₂ -		CH ₃ SO ₂
b	CH ₃	-(CH ₂) ₄ -		CH ₃ SO ₂
c	CH ₃	-(CH ₂) ₃ -		CH ₃ CO
d	CH ₃	-(CH ₂) ₂ -O-CH ₂ -		CH ₃ CO
e	CH ₃	-(CH ₂) ₄ -		CH ₃ CO
f	CH ₃	-(CH ₂) ₂ -O-CH ₂ -		CF ₃ CO ^(a)
g	CH ₃	-(CH ₂) ₂ -O-CH ₂ -		CH ₃ OCO
h	CH ₃	-(CH ₂) ₄ -		CH ₃ OCO
i	CH ₃	-(CH ₂) ₃ -		C ₆ H ₅ CO
j	CH ₃	-(CH ₂) ₂ -O-CH ₂ -		C ₆ H ₅ CO
k	CH ₃	-(CH ₂) ₄ -		C ₆ H ₅ CO
l	CH ₃	-(CH ₂) ₅ -		C ₆ H ₅ CO
m	CH ₃	C ₆ H ₅	H	C ₆ H ₅ CO
n	(CH ₃) ₂ CH	-(CH ₂) ₄ -		CH ₃ OCO
o	(CH ₃) ₂ CH	-(CH ₂) ₂ -O-CH ₂ -		C ₆ H ₅ CO
p	(CH ₃) ₂ CH	-(CH ₂) ₄ -		C ₆ H ₅ CO
q	C ₆ H ₅ CH ₂	-(CH ₂) ₂ -O-CH ₂ -		CH ₃ CO
r	C ₆ H ₅ CH ₂	-(CH ₂) ₂ -O-CH ₂ -		CH ₃ OCO
s	C ₆ H ₅ CH ₂	-(CH ₂) ₄ -		CH ₃ OCO

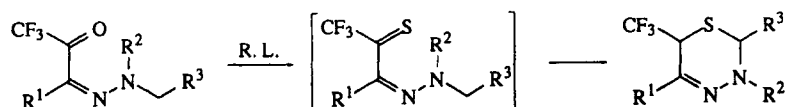
(a) compound **4f** is obtained using trifluoroacetyl anhydride as acylating agent.

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 determined observing **4m** ¹H spectrum. This compound bears a methylene 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 2*RS*, 6*RS*. Compounds **3** which can be isolated give easily the corresponding dihydrothiadiazines **4** in quantitative yields when they are heated in benzene.

The proposed mechanism 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 literature.¹⁰ However Hojo¹¹ 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 synthesise 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 F₂₅₄ precoated plates. ¹H and ¹³C 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 CDCl₃. 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 ($3 \cdot 10^{-2}$ mol) (or the corresponding chlorhydrate (10^{-2} mol) for **1a** and **1g**) was added to an ethanolic solution (20 mL) of benzoylformamide (10^{-2} mol) and acetic acid ($4 \cdot 10^{-2}$ 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 CH₂Cl₂, was chromatographed. After elution by CH₂Cl₂/AcOEt (19/1 for **1a** and F₁ of **1f**, 9/1 for **1c**, **e**, **i**, **k** and 7/3 for F₂ of **1f**, **1g**, **h**, **j**) compounds **1** were crystallised from Et₂O.

Compound 1a: yield 70%; mp 149°C; ¹H NMR δ 1.63-1.82 (4H, m, 2CH₂), 2.88 (3H, d, J = 5.1 Hz, CH₃), 2.98-3.11 (4H, m, 2NCH₂), 7.00 (1H, br.s, NH),

7.30 (5H, br.s, C₆H₅); ¹³C NMR δ 23.9 (t, 2CH₂), 25.6 (q, CH₃N), 54.9 (t, 2NCH₂), 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 C₁₃H₁₇N₃O 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, 3CH₂), 2.88 (3H, d, J = 5.1 Hz, CH₃), 2.92-3.00 (4H, m, 2NCH₂), 7.13 (1H, br.s, NH), 7.37 (5H, br.s, C₆H₅); ¹³C NMR δ 23.8 (t, CH₂), 24.8 (t, 2CH₂), 25.9 (q, CH₃N), 54.8 (t, 2NCH₂), 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 C₁₄H₁₉N₃O 245 (M⁺).

Compound 1e: yield 88%; mp 71°C; ¹H NMR δ 1.44-1.53 (8H, m, 4CH₂), 2.87 (3H, d, J = 5.0 Hz, CH₃), 3.12-3.23 (4H, m, 2NCH₂), 7.01 (1H, br.s, NH), 7.28 (5H, br.s, C₆H₅); ¹³C NMR δ 25.9 (q, CH₃N), 27.2 (t, 2CH₂), 27.4 (t, 2CH₂), 56.5 (t, 2NCH₂), 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 C₁₅H₂₁N₃O 259 (M⁺).

Compound 1f: yield 88%

F₁: mp 105°C; ¹H NMR δ 2.92 (3H, d, J = 5.0 Hz, CH₃NH), 3.42 (3H, s, N(CH₃)C₆H₅), 6.11 (1H, br.s, NH), 6.97-7.68 (10H, m, 2C₆H₅); ¹³C NMR δ 26.2 (q, CH₃NH), 41.0 (q, N(CH₃)C₆H₅), 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). F₂: mp 150°C; ¹H NMR δ 2.94 (3H, d, J = 5.0 Hz, CH₃NH), 2.95 (3H, s, N(CH₃)C₆H₅), 6.03 (1H, br.s, NH), 7.21-7.42 (10H, m, 2C₆H₅); ¹³C NMR δ 25.8 (q, CH₃NH), 39.3 (q, N(CH₃)C₆H₅), 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 C₁₆H₁₇N₃O 267 (M⁺).

Compound 1g: yield 82%; mp 140°C; ¹H NMR δ 2.42 (3H, d, J = 4.8 Hz, CH₃), 5.38 (1H, br.s, NH), 7.06-7.82 (15H, m, 3C₆H₅); ¹³C NMR δ 25.3 (q, CH₃N), 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 C₂₁H₁₉N₃O 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, (CH₃)₂CH), 3.01-3.06 (4H, m, 2NCH₂), 3.78-3.83 (4H, m, 2OCH₂), 4.31 (1H, h.d, J = 6.6 Hz and J = 8.2 Hz, (CH₃)₂CH), 6.14 (1H, d, J = 8.2 Hz, NH), 7.32-7.41 and 7.70-7.77 (5H, 2m, C₆H₅); ¹³C NMR δ 22.5 (q, (CH₃)₂CH), 41.3 (d, (CH₃)₂CH), 55.7 (t, 2NCH₂), 66.2 (t, 2OCH₂), 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 C₁₅H₂₁N₃O₂ 275 (M⁺).

Compound 1i: yield 86%; mp 83°C; ¹H NMR δ 1.19 (6H, d, J = 6.6 Hz, (CH₃)₂CH), 1.34-1.53 (6H, m, 3CH₂), 2.91-2.99 (4H, m, 2NCH₂), 4.08 (1H, h.d, J = 6.6 Hz and J = 8.2 Hz, (CH₃)₂CH), 7.01 (1H, d, J = 8.2 Hz, NH), 7.26-7.72 (5H, m, C₆H₅); ¹³C NMR δ 22.9 (q, (CH₃)₂CH), 23.9 and 25.0 (2t, 3CH₂), 41.3

(d, $(\text{CH}_3)_2\text{CH}$), 54.9 (t, 2NCH_2), 127.9, 128.4, 128.9 (3d, CH_{arom}), 134.2 (s, C_{arom}), 139.6 (s, $\text{C}=\text{N}$), 164.2 (s, $\text{C}=\text{O}$); MS $\text{C}_{16}\text{H}_{23}\text{N}_3\text{O}$ 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, $\text{C}_6\text{H}_5\text{CH}_2$), 6.71 (1H, br.s, NH), 7.29-7.81 (10H, m, $2\text{C}_6\text{H}_5$); ^{13}C NMR δ 43.2 (t, $\text{C}_6\text{H}_5\text{CH}_2$), 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, $\text{C}=\text{N}$), 165.4 (s, $\text{C}=\text{O}$); MS $\text{C}_{19}\text{H}_{21}\text{N}_3\text{O}_2$ 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, $\text{C}_6\text{H}_5\text{CH}_2$), 7.32-7.53 (11H, m, $2\text{C}_6\text{H}_5$ and NH buried); ^{13}C NMR δ 23.9 and 24.9 (2t, 3CH_2), 43.4 (t, $\text{C}_6\text{H}_5\text{CH}_2$), 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, $\text{C}=\text{N}$), 165.1 (s, $\text{C}=\text{O}$); MS $\text{C}_{20}\text{H}_{23}\text{N}_3\text{O}$ 321 (M^+).

2-Hydrazonophenylthioacetamides 2 general procedure: Lawesson reagent (2.6×10^{-3} mol) was added to a benzenic solution (5 mL) 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 $\text{CH}_2\text{Cl}_2/\text{AcOEt}$ (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, $\text{C}=\text{N}$), 193.0 (s, $\text{C}=\text{S}$); MS $\text{C}_{13}\text{H}_{17}\text{N}_3\text{S}$ 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, $\text{C}=\text{N}$), 193.3 (s, $\text{C}=\text{S}$); MS $\text{C}_{14}\text{H}_{19}\text{N}_3\text{S}$ 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, $\text{C}=\text{N}$), 193.6 (s, $\text{C}=\text{S}$); MS $\text{C}_{15}\text{H}_{21}\text{N}_3\text{S}$ 275 (M^+).

Compound 2f: yield 89%; mp 125°C ; ^1H NMR δ 2.86 (3H, s, $\text{N}(\text{CH}_3)\text{C}_6\text{H}_5$), 3.22 (3H, d, $J = 5.0$ Hz, CH_3NH), 7.26 (10H, br.s, $2\text{C}_6\text{H}_5$), 8.95 (1H, br.s, NH); ^{13}C NMR δ 32.6 (q, CH_3NH), 40.5 (q, $\text{N}(\text{CH}_3)\text{C}_6\text{H}_5$), 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 C₁₆H₁₇N₃S 283 (M⁺).

Compound 2g: yield 80%; mp 134°C; ¹H NMR δ 3.33 (3H, d, J = 5.0 Hz, CH₃), 6.82-7.36 (15H, m, 3C₆H₅), 9.26 (1H, br.s, NH); ¹³C NMR δ 32.8 (q, CH₃N), 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 C₂₁H₁₉N₃S 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, (CH₃)₂CH), 2.89-2.94 (4H, m, 2NCH₂), 3.57-3.62 (4H, m, 2OCH₂), 4.67 (1H, h.d, J = 6.6 Hz and J = 8.2 Hz, (CH₃)₂CH), 7.26-7.36 (5H, m, C₆H₅); ¹³C NMR δ 21.4 (q, (CH₃)₂CH), 46.8 (d, (CH₃)₂CH), 54.2 (t, 2NCH₂), 66.2 (t, 2OCH₂), 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 C₁₅H₂₁N₃OS 291 (M⁺).

Compound 2i: yield 88%; R_f (CH₂Cl₂) 0.75; ¹H NMR δ 1.24 (6H, d, J = 6.6 Hz, (CH₃)₂CH), 1.29-1.48 (6H, m, 3CH₂), 2.78-2.97 (4H, m, 2NCH₂), 4.61 (1H, h.d, J = 6.6 Hz and J = 8.1 Hz, (CH₃)₂CH), 7.14-7.39 (5H, m, C₆H₅), 8.77 (1H, br.s, NH); ¹³C NMR δ 21.6 (q, (CH₃)₂CH), 23.9 and 25.2 (2t, 3CH₂), 46.6 (d, (CH₃)₂CH), 54.9 (t, 2NCH₂), 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 C₁₆H₂₃N₃S 289 (M⁺).

Compound 2j: yield 95%; R_f (CH₂Cl₂) 0.45; ¹H NMR δ 2.89-2.92 (4H, m, 2NCH₂), 3.54-3.59 (4H, m, 2OCH₂), 4.93 (2H, d, J = 5.5 Hz, C₆H₅CH₂), 7.27-7.50 (10H, m, 2C₆H₅), 9.17 (1H, br.s, NH); ¹³C NMR δ 49.5 (t, C₆H₅CH₂), 54.1 (t, 2NCH₂), 66.0 (t, 2OCH₂), 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 C₁₉H₂₁N₃OS 339 (M⁺).

Compound 2k: yield 78%; mp 127°C; ¹H NMR δ 1.44-1.62 (6H, m, 3CH₂), 2.92-2.97 (4H, m, 2NCH₂), 5.00 (2H, d, J = 6.1 Hz, C₆H₅CH₂), 7.35-7.70 (10H, m, 2C₆H₅), 8.46 (1H, br.s, NH); ¹³C NMR δ 23.8 and 25.2 (2t, 3CH₂), 49.2 (t, C₆H₅CH₂), 56.2 (t, 2NCH₂), 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 C₂₀H₂₃N₃S 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, washed with brine and dried. The solvent was removed and the residue, diluted with CH₂Cl₂, was chromatographed. After elution by CH₂Cl₂ (for

3b-h) or by $\text{CH}_2\text{Cl}_2/\text{AcOEt}$ (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 ($\text{CH}_2\text{Cl}_2/\text{AcOEt}$: 4/1) 0.66; ^1H 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, $\text{C}=\text{N}$), 166.5 (s, $\text{C}=\text{O}$), 203.8 (s, $\text{C}=\text{S}$); MS $\text{C}_{15}\text{H}_{19}\text{N}_3\text{O}_3\text{S}$ 321 (M^+).

Compound 3b: yield 70%; Rf (CH_2Cl_2) 0.63; ^1H NMR δ 2.62 (3H, s, CH_3SO_2), 3.24 (3H, s, $\text{N}(\text{CH}_3)\text{C}_6\text{H}_5$), 3.60 (3H, s, CH_3N), 6.84-7.78 (10H, m, $2\text{C}_6\text{H}_5$); ^{13}C NMR δ 38.5 (q, CH_3N), 39.7 (q, CH_3SO_2), 42.0 (q, $\text{N}(\text{CH}_3)\text{C}_6\text{H}_5$), 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, $\text{C}=\text{N}$), 201.9 (s, $\text{C}=\text{S}$); MS $\text{C}_{17}\text{H}_{19}\text{N}_3\text{O}_2\text{S}_2$ 361 (M^+).

Compound 3c: yield 65%; mp 88°C ; ^1H NMR δ 3.16 (3H, s, $\text{N}(\text{CH}_3)\text{C}_6\text{H}_5$), 3.58 (3H, s, CH_3N), 3.65 (3H, s, CH_3O), 6.89-7.71 (10H, m, $2\text{C}_6\text{H}_5$); ^{13}C NMR δ 36.9 (q, CH_3N), 42.4 (q, $\text{N}(\text{CH}_3)\text{C}_6\text{H}_5$), 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, $\text{C}=\text{N}$), 158.7 (s, $\text{C}=\text{O}$), 203.7 (s, $\text{C}=\text{S}$); MS $\text{C}_{18}\text{H}_{19}\text{N}_3\text{O}_2\text{S}$ 341 (M^+).

Compound 3d: yield 57%; mp 145°C ; ^1H NMR δ 3.26 (3H, s, $\text{N}(\text{CH}_3)\text{C}_6\text{H}_5$), 3.94 (3H, s, CH_3N), 6.89-7.64 (15H, m, $3\text{C}_6\text{H}_5$); ^{13}C NMR δ 40.6 (q, CH_3N), 42.0 (q, $\text{N}(\text{CH}_3)\text{C}_6\text{H}_5$), 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, $\text{C}=\text{N}$), 173.8 (s, $\text{C}=\text{O}$), 201.6 (s, $\text{C}=\text{S}$); MS $\text{C}_{23}\text{H}_{21}\text{N}_3\text{OS}$ 387 (M^+).

Compound 3e: yield 59%; mp 137°C ; ^1H 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, $3\text{C}_6\text{H}_5$); ^{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, $\text{C}=\text{N}$), 198.8 (s, $\text{C}=\text{S}$); MS $\text{C}_{22}\text{H}_{21}\text{N}_3\text{O}_2\text{S}_2$ 423 (M^+).

Compound 3f: yield 67%; Rf ($\text{CH}_2\text{Cl}_2/\text{ligroin}$: 9/1) 0.60; ^1H 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, $3\text{C}_6\text{H}_5$); ^{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, $\text{C}=\text{N}$), 166.1 (s, $\text{C}=\text{O}$), 202.1 (s, $\text{C}=\text{S}$); MS $\text{C}_{23}\text{H}_{21}\text{N}_3\text{OS}$ 387 (M^+).

Compound 3g: yield 81%; mp 112°C ; ^1H 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, $3\text{C}_6\text{H}_5$); ^{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, $\text{C}=\text{N}$), 159.0 (s, $\text{C}=\text{O}$), 201.9 (s, $\text{C}=\text{S}$); MS $\text{C}_{23}\text{H}_{21}\text{N}_3\text{O}_2\text{S}$ 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 (CH₂Cl₂/AcOEt: 9/1) 0.52; ¹H NMR δ 2.57-2.67 and 2.85-2.95 (4H, 2m, 2NCH₂), 3.62-3.66 (4H, m, 2OCH₂), 3.70 (3H, s, CH₃), 5.44 and 5.86 (2H, 2d, J = 15.1 Hz, C₆H₅CH₂), 7.33-7.76 (10H, m, 2C₆H₅); ¹³C NMR δ 51.4 (t, C₆H₅CH₂), 54.8 (q, CH₃O), 54.9 (t, 2NCH₂), 65.9 (t, 2NCH₂), 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 C₂₁H₂₃N₃O₃S 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 CH₂Cl₂ (for **4a, b, e, f, i, l, s**), by CH₂Cl₂/AcOEt (9/1) (for **4d, g, h, j, k, m, n, r**) or by CH₂Cl₂/AcOEt (4/1) (for **4c, o-q**) affords compounds **4** which were crystallised from Et₂O (**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, CH₃SO₂), 2.88 (3H, s, CH₃N), 3.12-4.18 (7H, m, (3CH₂ and CH, 2-H buried), 6.25 (1H, s, CH, 6-H), 7.24-7.41 and 7.61-7.75 (5H, 2m, C₆H₅); ¹³C NMR δ 31.0 (q, CH₃N), 39.0 (q, CH₃SO₂), 50.7 (d, CH, 6-C), 53.3 (d, CH, 2-C), 55.8 (t, NCH₂), 67.6, 68.8 (2t, 2CH₂O), 126.5, 128.4, 128.9 (3d, CH_{arom}), 136.6 (s, C_{arom}), 138.4 (s, C=N); MS C₁₄H₁₉N₃O₃S₂ 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, 4CH₂ and CH, 2-H buried), 2.76 (3H, s, CH₃SO₂), 2.89 (3H, s, CH₃N), 6.17 (1H, s, CH, 6-H), 7.21-7.43 and 7.60-7.82 (5H, 2m, C₆H₅); ¹³C NMR δ 23.3 (t, NCH₂CH₂CH₂CH₂), 25.5 (t, NCH₂CH₂CH₂CH₂), 31.0 (q, CH₃N), 31.3 (t, NCH₂CH₂CH₂CH₂), 38.9 (q, CH₃SO₂), 51.7 (d, CH, 6-C), 54.2 (d, CH, 2-C), 57.1 (t, NCH₂CH₂CH₂CH₂), 126.3, 126.5, 128.3 (3d, CH_{arom}), 136.5 (s, C_{arom}), 137.0 (s, C=N); MS C₁₅H₂₁N₃O₂S₂ 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, 3CH₂), 2.10 (3H, s, CH₃CO), 2.86 (3H, s, CH₃N), 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, C₆H₅); ¹³C NMR δ 21.4 (t, NCH₂CH₂CH₂), 22.3 (q, CH₃CO), 32.0 (t, NCH₂CH₂CH₂), 34.6 (q, CH₃N), 48.4 (d, CH, 6-C), 53.0 (d, CH, 2-C), 53.8 (t, NCH₂CH₂CH₂), 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 C₁₅H₁₉N₃OS 289 (M⁺).

Compound 4d: yield 51%; mp 206; ¹H NMR δ 2.04 (3H, s, CH₃CO), 2.87 (3H, s, CH₃N), 3.19-4.09 (7H, m, 3CH₂ and CH, 2-H buried), 6.80 (1H, s, CH, 6-H), 7.30-7.34 and 7.52-7.57 (5H, 2m, C₆H₅); ¹³C NMR δ 22.1 (q, CH₃CO), 32.7 (q,

CH₃N), 45.8 (d, CH, 6-C), 53.3 (d, CH, 2-C), 55.7 (t, NCH₂), 67.5, 68.8 (2t, 2CH₂O), 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 C₁₅H₁₉N₃O₂S 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, 4CH₂ and CH, 2-H buried), 2.03 (3H, s, CH₃CO), 2.87 (3H, s, CH₃N), 6.72 (1H, s, CH, 6-H), 7.21-7.38 and 7.47-7.62 (5H, 2m, C₆H₅); ¹³C NMR δ 22.0 (q, CH₃CO), 24.0 (t, NCH₂CH₂CH₂CH₂), 25.5 (t, NCH₂CH₂CH₂CH₂), 31.2 (t, NCH₂CH₂CH₂CH₂), 32.7 (q, CH₃N), 46.7 (d, CH, 6-C), 54.0 (d, CH, 2-C), 57.0 (t, NCH₂CH₂CH₂CH₂), 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 C₁₆H₂₁N₃OS 303 (M⁺).

Compound 4f: yield 58%; mp 137°C; ¹H NMR δ 2.99 (3H, s, CH₃N), 3.23-4.09 (7H, m, 3CH₂ and CH, 2-H buried), 6.62 (1H, s, CH, 6-H), 7.32-7.38 and 7.46-7.51 (5H, 2m, C₆H₅); ¹³C NMR δ 31.6 (qq, CH₃N, ⁴J_{CF} = 4.2 Hz), 47.7 (d, CH, 6-C), 53.0 (d, CH, 2-C), 55.7 (t, NCH₂), 67.6, 68.7 (2t, 2CH₂O), 116.0 (q, CF₃, 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 C₁₅H₁₆F₃N₃O₂S 359 (M⁺).

Compound 4g: yield 52%; mp 143°C; ¹H NMR δ 2.79 (3H, s, CH₃N), 3.11-4.19 (7H, m, 3CH₂ and CH, 2-H buried), 3.73 (3H, CH₃O), 6.40 (1H, s, CH, 6-H), 7.22-7.43 and 7.49-7.61 (5H, 2m, C₆H₅); ¹³C NMR δ 31.0 (q, CH₃N), 49.4 (d, CH, 6-C), 53.3 (q, CH₃O and d, CH, 2-C), 55.5 (t, NCH₂), 67.6, 68.9 (2t, 2CH₂O), 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 C₁₅H₁₉N₃O₃S 321 (M⁺).

Compound 4h: yield 49%; Rf (CH₂Cl₂) 0.39; ¹H NMR δ 1.36-2.18, 2.77-3.15 and 3.31-3.85 (9H, 3m, 4CH₂ and CH, 2-H buried), 2.77 (3H, s, CH₃N), 3.70 (3H, s, CH₃O), 6.32 (1H, s, CH, 6-H), 7.19-7.38 and 7.50-7.71 (5H, 2m, C₆H₅); ¹³C NMR δ 23.8 (t, NCH₂CH₂CH₂CH₂), 25.4 (t, NCH₂CH₂CH₂CH₂), 31.0 (t, NCH₂CH₂CH₂CH₂), 31.1 (q, CH₃N), 50.0 (d, CH, 6-C), 52.9 (q, CH₃O), 53.8 (d, CH, 2-C), 56.6 (t, NCH₂CH₂CH₂CH₂), 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 C₁₆H₂₁N₃O₂S 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, 3CH₂), 2.82 (3H, s, CH₃), 4.46-4.75 (1H, m, CH, 2-H), 7.23-7.72 (10H, m, 2C₆H₅); ¹³C NMR δ 21.3 (t, NCH₂CH₂CH₂), 31.9 (t, NCH₂CH₂CH₂), 35.4 (q, CH₃), 48.5 (d, CH, 6-C), 53.2 (d, CH, 2-C), 53.7 (t, NCH₂CH₂CH₂), 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 C₂₀H₂₁N₃OS 351 (M⁺).

Compound 4j: yield 49%; mp 198°C; ¹H NMR δ 2.81 (3H, s, CH₃), 3.09-4.18 (7H, m, 3CH₂ and CH, 2-H buried), 6.92 (1H, s, CH, 6-H), 7.01-7.68 (10H, m, 2C₆H₅); ¹³C NMR δ 33.9 (q, CH₃), 46.4 (d, CH, 6-C), 54.0 (d, CH, 2-C), 56.0 (t,

NCH₂), 67.7, 69.0 (2t, 2CH₂O), 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 C₂₀H₂₁N₃O₂S 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, 4CH₂ and CH, 2-H buried), 2.78 (3H, s, CH₃), 6.87 (1H, s, CH, 6-H), 7.12-7.70 (10H, m, 2C₆H₅); ¹³C NMR δ 24.1 (t, NCH₂CH₂CH₂CH₂), 25.6 (t, NCH₂CH₂CH₂CH₂), 31.3 (t, NCH₂CH₂CH₂CH₂), 33.9 (q, CH₃), 47.1 (d, CH, 6-C), 54.7 (d, CH, 2-C), 57.3 (t, NCH₂CH₂CH₂CH₂), 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 C₂₁H₂₃N₃OS 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, 5CH₂ and CH, 2-H), 2.79 (3H, s, CH₃N), 6.90 (1H, s, CH, 6-H), 7.13-7.71 (10H, m, 2C₆H₅); ¹³C NMR δ 25.3 (t, NCH₂CH₂CH₂CH₂CH₂), 29.3, 29.8 (2t, NCH₂CH₂CH₂CH₂CH₂), 32.5 (t, NCH₂CH₂CH₂CH₂CH₂), 34.8 (q, CH₃), 49.7 (d, CH, 6-C), 57.0 (d, CH, 2-C), 58.3 (t, NCH₂CH₂CH₂CH₂CH₂), 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 C₂₂H₂₅N₃OS (M⁺).

Compound 4m: yield 38%; mp 163°C; ¹H NMR δ 2.84 (3H, s, CH₃), 4.68 and 5.03 (2H, d and dd, J = 1.0 Hz and J = 12.7 Hz, CH₂), 6.88-7.80 (16H, m, 3C₆H₅ and CH, 6-H buried); ¹³C NMR δ 34.9 (q, CH₃), 41.8 (t, CH₂), 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 C₂₃H₂₁N₃OS 387 (M⁺).

Compound 4n: yield 51%; R_f (CH₂Cl₂) 0.44; ¹H NMR δ 0.73 and 1.34 (6H, 2d, J = 6.6 Hz, (CH₃)₂CH), 1.45-2.07, 2.91-3.04 and 3.81-3.87 (9H, 3m, 4CH₂ and CH, 2-H buried), 3.51-3.65 (1H, m, (CH₃)₂CH), 3.76 (3H, s, CH₃O), 6.21 (1H, s, CH, 6-H), 7.22-7.39 and 7.51-7.69 (5H, 2m, C₆H₅); ¹³C NMR δ 20.9 (q, (CH₃)₂CH), 24.2 (t, NCH₂CH₂CH₂CH₂), 25.8 (t, NCH₂CH₂CH₂CH₂), 31.4 (t, NCH₂CH₂CH₂CH₂), 49.2 (d, (CH₃)₂CH), 51.1 (d, CH, 6-C), 52.5 (d, CH, 2-C), 53.6 (q, CH₃O), 57.0 (t, NCH₂CH₂CH₂CH₂), 126.0, 128.3 (3d, CH_{arom}), 136.3 (s, C_{arom}), 137.8 (s, C=N), 156.2 (s, C=O); MS C₁₈H₂₅N₃O₂S 347 (M⁺).

Compound 4o: yield 38%; mp 152°C; ¹H NMR δ 0.83-0.86 and 1.18-1.29 (6H, 2m, (CH₃)₂CH), 3.52-4.10 (7H, m, 3CH₂ and CH, 2-H buried), 3.24-3.50 (1H, m, (CH₃)₂CH), 6.97 (1H, s, CH, 6-H), 7.35 (10H, br.s, 2C₆H₅); ¹³C NMR δ 20.8 (q, (CH₃)₂CH), 50.6 (d, (CH₃)₂CH), 51.3 (d, CH, 6-C), 53.8 (d, CH, 2-C), 55.9 (t, NCH₂), 67.8, 69.1 (2t, 2CH₂O), 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 C₂₂H₂₅N₃O₂S 395 (M⁺).

Compound 4p: yield 53%; 135°C; ¹H NMR δ 0.83 and 1.56 (6H, 2d, J = 6.7 Hz, (CH₃)₂CH), 1.15-2.02, 2.93-3.07 and 3.73-3.81 (9H, 3m, 4CH₂ and CH, 2-H

buried), 3.66-3.72 (1H, m, (CH₃)₂CH), 7.06 (1H, s, CH, 6-H), 7.37 (10H, br.s, 2C₆H₅); ¹³C NMR δ 20.6 (q, (CH₃)₂CH), 24.1 (t, NCH₂CH₂CH₂CH₂), 25.8 (t, NCH₂CH₂CH₂CH₂), 31.3 (t, NCH₂CH₂CH₂CH₂), 47.3 (d, (CH₃)₂CH), 51.0 (d, CH, 6-C), 54.4 (d, CH, 2-C), 57.1 (t, NCH₂CH₂CH₂CH₂), 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 C₂₃H₂₇N₃OS 393 (M⁺).

Compound 4q: yield 55%; Rf (CH₂Cl₂) 0.42; ¹H NMR δ 1.97 (3H, s, CH₃), 2.97-4.54 (7H, m, 3CH₂ and CH, 2-H buried), 4.37 and 4.48 (2H, 2d, J = 14.2 Hz, C₆H₅CH₂), 6.85 (1H, s, CH, 6-H), 7.21-7.53 (10H, m, 2C₆H₅); ¹³C NMR δ 22.0 (q, CH₃), 46.8 (t, C₆H₅CH₂), 50.0 (d, CH, 6-C), 52.6 (d, CH, 2-C), 54.9 (t, NCH₂), 67.2, 68.2 (2t, 2CH₂O), 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 C₂₁H₂₃N₃O₂S 381 (M⁺).

Compound 4r: yield 48%; mp 155°C; ¹H NMR δ 3.02-4.12 (7H, m, 3CH₂ and CH, 2-H buried), 3.77 (3H, s, CH₃), 4.60 and 4.79 (2H, 2d, J = 14.1 Hz, C₆H₅CH₂), 6.28 (1H, s, CH, 6-H), 7.12-7.48 (10H, m, 2C₆H₅); ¹³C NMR δ 49.0 (t, C₆H₅CH₂), 50.0 (d, CH, 6-C), 52.8 (d, CH, 2-C), 53.6 (q, CH₃), 55.1 (t, NCH₂), 67.7, 68.7 (2t, 2CH₂O), 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 C₂₁H₂₃N₃O₃S 397 (M⁺).

Compound 4s: yield 48%; Rf (CH₂Cl₂) 0.46; ¹H NMR δ 1.18-1.86, 2.57-2.94 and 3.66-3.83 (9H, 3m, 4CH₂ and CH, 2-H buried), 3.77 (3H, s, CH₃), 4.65 and 4.83 (2H, 2d, J = 14.3 Hz, C₆H₅CH₂), 6.19 (1H, s, CH, 6-H), 7.10-7.62 (10H, m, 2C₆H₅); ¹³C NMR δ 21.1 (q, CH₃), 23.8 (t, NCH₂CH₂CH₂CH₂), 25.6 (t, NCH₂CH₂CH₂CH₂), 30.6 (t, NCH₂CH₂CH₂CH₂), 48.7 (t, C₆H₅CH₂), 50.8 (d, CH, 6-C), 53.4 (d, CH, 2-C), 56.3 (t, NCH₂CH₂CH₂CH₂), 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 C₂₂H₂₅N₃O₂S 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 Soediniy*, **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. Bartlett, (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).