Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron
Tetrahedron 64 (2008) 3837–3858
www.elsevier.com/locate/tet

Simple construction of fused and spiro nitrogen/sulfur containing heterocycles by addition of thioamides or thioureas on cycloalkenyl-diazenes: examples of click chemistry

Orazio A. Attanasi [a], Lucia De Crescentini [a], Gianfranco Favi [a], Paolino Filippone [a], Gianluca Giorgi [b], Fabio Mantellini [a,*], Francesca R. Perrulli [a], Domenico Spinelli [c]

[a] *Istituto di Chimica Organica, Università degli Studi di Urbino 'Carlo Bo', Via I Maggetti 24, 61029 Urbino, Italy*
[b] *Dipartimento di Chimica, Università degli Studi di Siena, Via Aldo Moro, 53100 Siena, Italy*
[c] *Dipartimento di Chimica Organica 'A. Mangini', Università di Bologna, Via San Giacomo 11, 40126 Bologna, Italy*

Received 2 October 2007; received in revised form 17 December 2007; accepted 25 January 2008
Available online 31 January 2008

Abstract

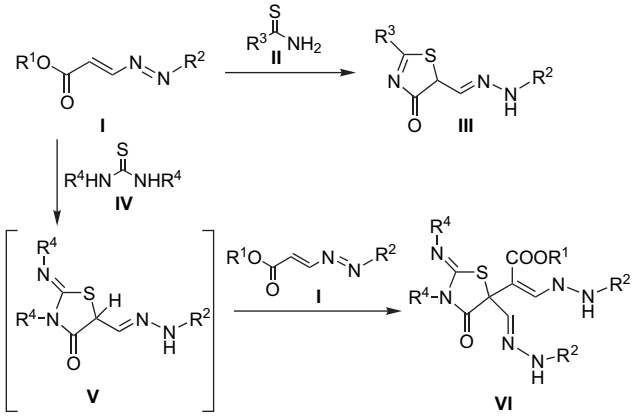
New 1-cycloalkenyl-1-diazenes have been obtained in good yields from cyclic β-ketoesters and hydrazine derivatives. They furnished new cycloalkyl[*d*][1,3]thiazolines with thioamides or new spirocycloalkyl-thiazolinones with thioureas. Moreover they gave, with imidazolidine-2-thione and tetrahydropyrimidine-2-thione, new and interesting spiro[cycloalkyl-1,2′-imidazo[2,1-*b*][1,3]thiazole] or spiro[cycloalkyl-1,2′-[1,3]thiazolo[3,2-*a*]pyrimidine] derivatives, respectively. Cycloalkyl[*d*][1,3]thiazolines were useful for the further preparation of unknown thia-triaza-tricyclo derivatives. Novel hexahydro-1,3-benzothiazoles have been achieved by reaction of *N*,*N*′-dialkylthioureas on *N*-1-phenyl-2-(1-cyclohexenyl)-1-diazene-1-carboxyamide. The acidic hydrolysis of spirocycloalkyl-thiazolinones produced 2-imino-5-(ω-carboxyalkyl)-4-thiazolidinones.

1. Introduction

Thiazoline derivatives represent a family of compounds with great industrial interest, which have found applications in food and flavour chemistry.[1,2] Thiazolines have also attracted very significant biochemical interest, owing to the presence of the thiazoline moiety in the structures of several naturally occurring molecules with important pharmacological properties such as antibiotic,[3] antihelmintic,[4] antifungal,[3a] or antitumour drugs.[5] Recently, new metabolites derived from aminoacids containing thiazole rings have been isolated from marine species: they exhibit antineoplastic and cytotoxic activity.[6] The aminothiazole system has found applications in drug development for the treatment of allergies, hypertension, inflammation, schizophrenia, bacterial and HIV infections.[7] Based on these properties, it can be reasonably supposed that the development of synthetic strategies for new cycloalkyl[*d*][1,3]thiazolines, spirocycloalkyl-thiazolinones, spirocycloalkane-1,2′-imidazo[2,1-*b*][1,3]thiazoles, spirocycloalkane-1,2′-[1,3]thiazolo[3,2-*a*]pyrimidines might provide additional lead molecules for drug discovery. Usually, the synthesis of the thiazole core involves the condensation of aminothiols with either nitrile,[8] carboxylic acid,[9] or ester,[10] as well as by intramolecular dehydration of β-hydroxythioamides under Mitsunobu conditions,[11] or with Burgess reagent.[12] Other methods exploit intramolecular cyclization of β-hydroxyamides with P_2S_5[13] or Lawesson's reagent,[14] by the reaction of amino sugar derivatives with aryl isothiocyanates,[15] or by deselenylation of thioamido selenides.[16] We previously reported the synthesis of substituted 2-thiazolin-4-ones **III**[17] and 5,5-disubstituted 3-alkyl-2-(alkylimino)-thiazolidin-4-ones **VI**[18] from 1,2-diaza-1,3-butadienes **I** and thioamides **II** or thioureas **IV**, respectively (Scheme 1).

* Corresponding author. Tel.: +39 0722 303445; fax: +39 0722 303441.
E-mail address: fabio.mantellini@uniurb.it (F. Mantellini).

0040-4020/$ - see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2008.01.102



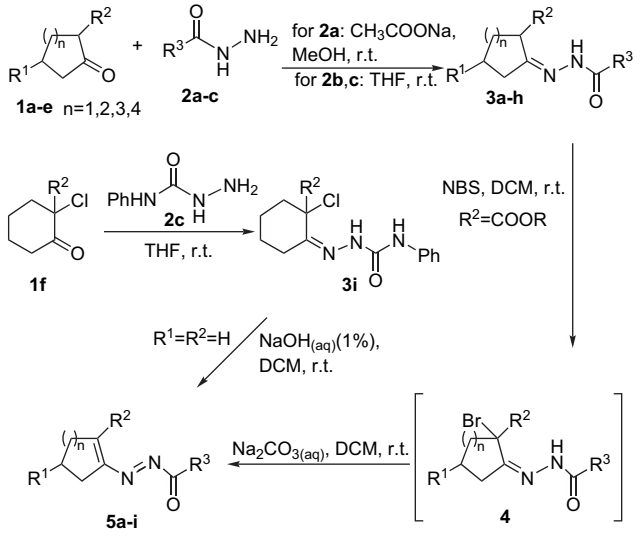
Scheme 1.

More recently,[19] we observed a different regioselectivity leading to new cycloalkyl-thiazolines when this synthetic methodology was applied to cyclopentenyl- or cyclohexenyl-1-diazenes. Herein, we enlarge the scope of previous syntheses by using new cycloheptenyl- and cyclooctenyl-1-diazenes, which are able to give the corresponding cycloalkyl[*d*][1,3]-thiazoline derivatives, that, in turn, can be further converted into interesting thia-triaza-tricyclo derivatives. We also describe an efficient strategy for the preparation of unknown spirocycloalkyl-thiazolinones of different sizes using cycloalkyl-1-diazenes and thioureas. This methodology proceeds rapidly to completion, is very selective and wide in scope, produces the compounds in high yields, generates only inoffensive by-products (alcohols), requires simple and mild reaction conditions, uses readily available starting materials and offers a simple product isolation by crystallization in the reaction medium, fulfilling the click chemistry criteria.[20] Finally, in this work we investigate the acidic hydrolysis and the ring-opening process of cycloalkyl-thiazoline derivatives and 1-thia-3-azaspiro compounds.

2. Results and discussion

1-Cycloalkenyl-1-diazenes **5a–h** were prepared from cyclic β-ketoesters **1a–e** and hydrazine derivatives **2a–c** (1 equiv), in methanol (MeOH) or tetrahydrofuran (THF), at room temperature to achieve the corresponding hydrazones **3a–h**. These latter were subjected to bromination by the action of *N*-bromosuccinimide (NBS, 1 equiv) in dichloromethane (DCM) at room temperature to obtain the respective brominated hydrazones **4**. Treatment of **4** with aqueous saturated solution of sodium carbonate at room temperature provided the new cycloalkenyl-1-diazenes **5a–h** in good yields (Scheme 2, Table 1).[21]

N-1-Phenyl-2-(1-cyclohexenyl)-1-diazene-1-carboxamide **5i** was prepared by reaction at room temperature of 2-chlorocyclohexanone **1f** with 4-phenylsemicarbazide **2c** affording the relevant halogenated hydrazone **3i** that was then treated at room temperature with sodium hydroxide (1%) (Scheme 2, Table 1).



Scheme 2.

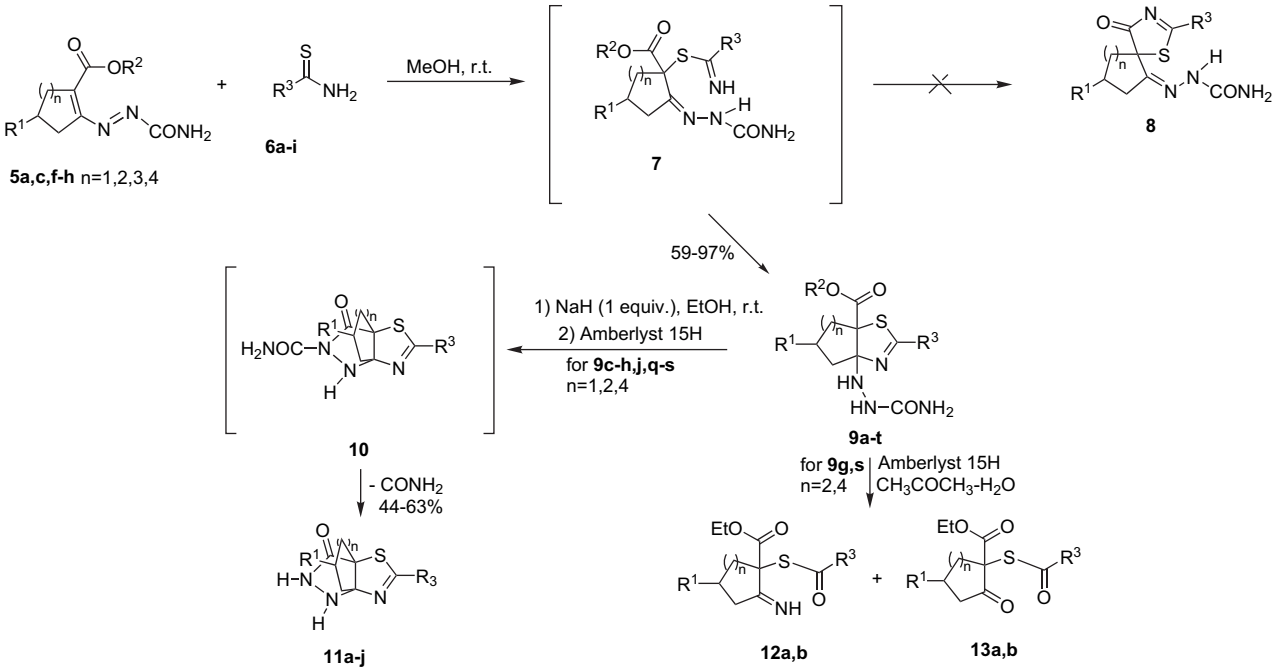
Table 1
Yields of hydrazones **3a–i** and 1-cycloalkenyl-1-diazenes **5a–i**

1	*n*	R^1	R^2	2	R^3	3	Yield[a] (%)	5	Yield[b] (%)
1a	1	H	CO_2Et	**2a**	NH_2	**3a**	89	**5a**	78
1a	1	H	CO_2Et	**2b**	O*t*-Bu	**3b**	86	**5b**	63
1b	2	H	CO_2Et	**2a**	NH_2	**3c**	91	**5c**	76
1b	2	H	CO_2Et	**2b**	O*t*-Bu	**3d**	90	**5d**	60
1b	2	H	CO_2Et	**2c**	NHPh	**3e**	86	**5e**	63
1c	2	Me	CO_2Et	**2a**	NH_2	**3f**	93	**5f**	74
1d	3	H	CO_2Me	**2a**	NH_2	**3g**	87	**5g**	82
1e	4	H	CO_2Et	**2a**	NH_2	**3h**	83	**5h**	92
1f	2	H	H	**2c**	NHPh	**3i**	95	**5i**	65

[a] Yields of the pure products **3a–i** based on the carbonyl compounds **1a–f**.
[b] Yields of the pure isolated products **5a–i** based on the hydrazone compounds **3a–i**.

Thioamides **6a–i** easily added to cycloalkenyl-1-diazenes **5a**,**c**,**f–h** in methanol at room temperature affording new tetrahydro-cyclopenta[*d*][1,3]thiazolines **9a–d** (*n*=1), hexahydro-1,3-benzothiazolines **9e–m** (*n*=2), hexahydro-cyclohepta[*d*][1,3]thiazolines **9n–p** (*n*=3) and octahydrocycloocta[*d*][1,3]thiazolines **9q–t** (*n*=4) in good yields (Scheme 3, Table 2). The reaction occurs by a preliminary nucleophilic attack by the sulfur of thioamides **6a–i** at the terminal carbon atom of the azo–ene system[17,18] of **5** with formation of the respective 1,4-adduct (Michael-type) cycloalkyl-hydrazones intermediates **7**. They immediately undergo the thiazole ring closure by regioselective internal nucleophilic attack from the imino nitrogen of the thioamides at the hydrazono moiety, producing interesting cycloalkyl[*d*][1,3]thiazoline derivatives **9**. Their structure, proposed on the basis of spectrometric (^1H and ^{13}C NMR as well as MS) data, was definitively confirmed by X-ray diffraction determination on **9k** (Fig. 1).[22]

Significant differences in the regioselectivity were observed in the previous reaction of thioamides on 1,2-diaza-1,3-butadienes under the same experimental conditions.[17] In such a case, the second nucleophilic attack of the imino nitrogen occurs only at the ester function on the terminal carbon of the azo–ene system leading to the corresponding 2-thiazolin-4-ones **III**



Scheme 3.

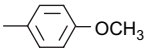
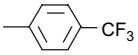
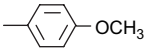
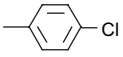
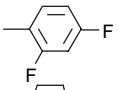
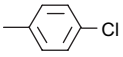
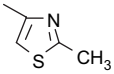
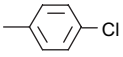
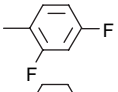
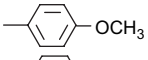
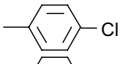
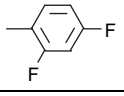
(Scheme 1). By using cycloalkenyl-1-diazenes, no formation of spirocycloalkyl-thiazolinones **8** by means of the internal nucleophilic attack of the imino nitrogen on the ester function was observed (Scheme 3). The presence in **9** of both ester and semicarbazide groups makes them able to be further modified. In fact, by treatment of compounds **9c–h,j,q–s** in ethanol at room temperature with a stoichiometric amount of sodium hydride, the internal nucleophilic attack of the semicarbazide nitrogen at the ester function caused the second ring closure giving the intermediates **10** (Scheme 3). The spontaneous loss of the carbamic residue produced the new 6-thia-2,3,8-triaza-tricyclo[3.3.3.$0^{1,5}$]undec-7-en-4-ones **11a,b** (n=1), 10-thia-7,8,12-triaza-tricyclo[4.3.3.$0^{1,6}$]dodec-11-en-9-ones **11c–g** (n=2) and 12-thia-9,10,14-triaza-tricyclo[6.3.3.$0^{1,8}$]tetradec-13-en-11-ones **11h–j** (n=4) (Scheme 3, Table 2). In order to avoid the formation of decomposition products, it was necessary to neutralize the reaction mixture by addition of Amberlyst 15H (2 equiv) immediately after the disappearance of the starting thiazoles **9**.

We have also investigated the reactivity of ethyl 3*a*-[2-(aminocarbonyl)hydrazino]-2-(4-chlorophenyl)-3*a*,4,5,6,7,7*a*-hexahydro-1,3-benzothiazole-7*a*-carboxylate **9g** and of ethyl 3*a*-[2-(aminocarbonyl)hydrazino]-2-(4-chlorophenyl)-3*a*,4,5,6,7,8,9,9*a*-octahydrocycloocta[*d*][1,3]thiazoline-9*a*-carboxylate **9s** with 4 equiv of Amberlyst 15H in a mixture of acetone–water (9:1) at room temperature (Scheme 3, Table 2).[23] In these cases we observed the hydrolytic thiazoline ring-opening with formation of mixtures of imino- (**12a,b**) and keto-cycloalkyl (**13a,b**) derivatives in different ratios.

The reaction of thiourea **14a**, *N*,*N*′-dimethylthiourea **14b** and *N*,*N*′-diethylthiourea **14c** on the same cycloalkenyl-1-diazenes **5a–h** in methanol at room temperature was parallelly investigated (Scheme 4). The reaction proceeds by means of the 1,4-conjugate addition (Michael-type) of thioureas to the heterodiene system of diazenes by a sulfur nucleophilic attack affording the hydrazone intermediates **15**. The further cyclization process occurred by regioselective internal nucleophilic attack of the second NH group of thioureas at the ester function giving 2-imino-4-oxo-1-thia-3-azaspiro[4.4]non-6-ylidenes **16a–d** (n=1), 2-imino-4-oxo-1-thia-3-azaspiro[4.5]dec-6-ylidenes **16e–n** (n=2), 2-imino-4-oxo-1-thia-3-azaspiro[4.6]undec-6-ylidenes **16o–q** (n=3) and 2-imino-4-oxo-1-thia-3-azaspiro[4.7]dodec-6-ylidenes **16r–t** (n=4) in very good yields (Scheme 4, Table 3). It has been reported that molecules with structures similar to **16** exhibit antipsychotic activity.[24] The peculiar regioselectivity observed in the ring closure process of these reactions could depend on the different nucleophilicity of thioamides and thioureas together with the diverse nucleophilic affinity of ester and hydrazone groups. Also the typical strain of cyclic azadienes compared with that of open-chain ones could play an important role.

In the case of the reaction of thiourea **14a** or *N*,*N*′-dialkylthioureas **14b,c** on cycloalkenyl-1-diazenes **5a–h** we observed the same regioselectivity of the second internal nucleophilic attack as for 1,2-diaza-1,3-butadienes **I** with the same thiourea derivatives **IV** (Scheme 1).[18] However, thiourea derivatives added to 1,2-diaza-1,3-butadienes with a 2:1 molar ratio thus giving 5,5-disubstituted 3-alkyl-2-(alkylimino)-thiazolidin-4-ones **VI**. This can be related to the presence of the strongly acidic hydrogen on the carbon in α-position with respect to the sulfur and to the ester group of the thiazolinone **V**, which makes possible a further addition on another 1,2-diaza-1,3-butadiene molecule even in neutral conditions (Scheme 1). Cycloalkenyl-1-diazenes **5** lack the above hydrogen and this makes possible the direct isolation of the spirocycloalkyl-thiazolinone **16** without the formation of further products of reaction.

Table 2
Yields of cycloalkyl[*d*][1,3]thiazolines **9a–t**, thia-triaza-tricyclo derivatives **11a–j**, iminocycloalkyl derivatives **12a**,**b** and keto-cycloalkyl derivatives **13a**,**b**

5	*n*	R^1	6	R^3	9	Yield[a] (%)	11	Yield[b] (%)	12	Yield[c] (%)	13	Yield[c] (%)
5a	1	H	**6a**		**9a**	68						
5a	1	H	**6b**		**9b**	59						
5a	1	H	**6c**		**9c**	91	**11a**	54				
5a	1	H	**6d**		**9d**	86	**11b**	44				
5c	2	H	**6a**		**9e**	93	**11c**	63				
5c	2	H	**6c**		**9f**	97	**11d**	56				
5c	2	H	**6e**		**9g**	64	**11e**	59	**12a**	67	**13a**	12
5c	2	H	**6f**		**9h**	96	**11f**	63				
5c	2	H	**6g**		**9i**	92						
5f	2	Me	**6a**		**9j**	92	**11g**	62				
5f	2	Me	**6e**		**9k**	69						
5f	2	Me	**6h**		**9l**	84						
5f	2	Me	**6i**		**9m**	77						
5g	3	H	**6a**		**9n**	72						
5g	3	H	**6e**		**9o**	82						
5g	3	H	**6f**		**9p**	76						
5h	4	H	**6a**		**9q**	81	**11h**	43				
5h	4	H	**6c**		**9r**	82	**11i**	36				
5h	4	H	**6e**		**9s**	78	**11j**	45	**12b**	8	**13b**	58
5h	4	H	**6f**		**9t**	83						

[a] Yields of the pure isolated products **9a–t** based on the cycloalkenyl-1-diazenes **5a**,**c**,**f–h**.
[b] Yields of the pure isolated products **11a–j** based on the thiazolines **9c–h**,**j**,**q–s**.
[c] Yields of the pure isolated products **12a**,**b** and **13a**,**b** based on the thiazolines **9g**,**s**.

In order to obtain the corresponding ketone derivatives, we have also investigated the hydrolysis of the hydrazono moiety of compounds **16b**,**c**,**e–h**,**l**,**n–p**,**s** by treatment with 4 equiv of Amberlyst 15H in a mixture of acetone–water (9:1) at room temperature (Scheme 4, Table 3).[23]

Only the treatment of 4-oxo-1-thia-3-azaspiro[4.6]undec-6-ylidenes **16o**,**p** (n=3) or of 4-oxo-1-thia-3-azaspiro[4.7]dodec-6-ylidene **16s** (n=4) led to the formation of the stable 1-thia-3-azaspiro[4.6]undecan-4,6-diones **17b**,**c** or of 1-thia-3-azaspiro[4.7]dodecan-4,6-dione **17d**, respectively.

Surprisingly enough, we achieved the 2-imino-5-(ω-carboxyalkyl)-4-thiazolidinone compounds **18a–f** from 4-oxo-1-thia-3-azaspiro[4.4]non-6-ylidenes **16b**,**c** (n=1) or 4-oxo-1-thia-3-azaspiro[4.5]dec-6-ylidenes **16e–h**,**l**,**n** (n=2). Only from **16g** it was possible to isolate the ketone **17a** by flash chromatography.

To obtain the corresponding carboxylic acids **18g–i** (n=3,4) the reaction mixture was refluxed for 3–4 h in the presence of Amberlyst 15H (Scheme 4, Table 3). It has been reported that molecules similar to **18** exhibit antitubercular

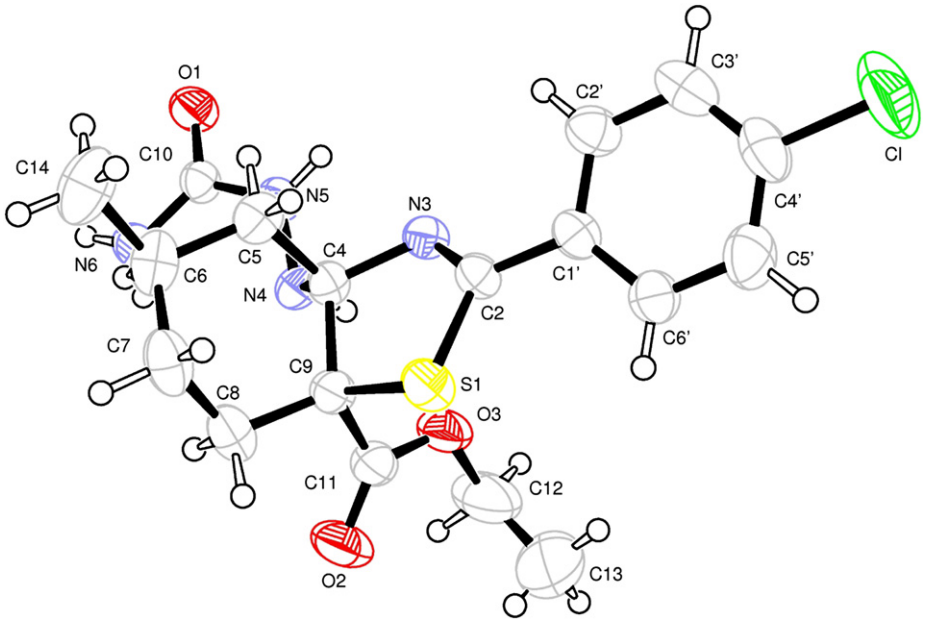
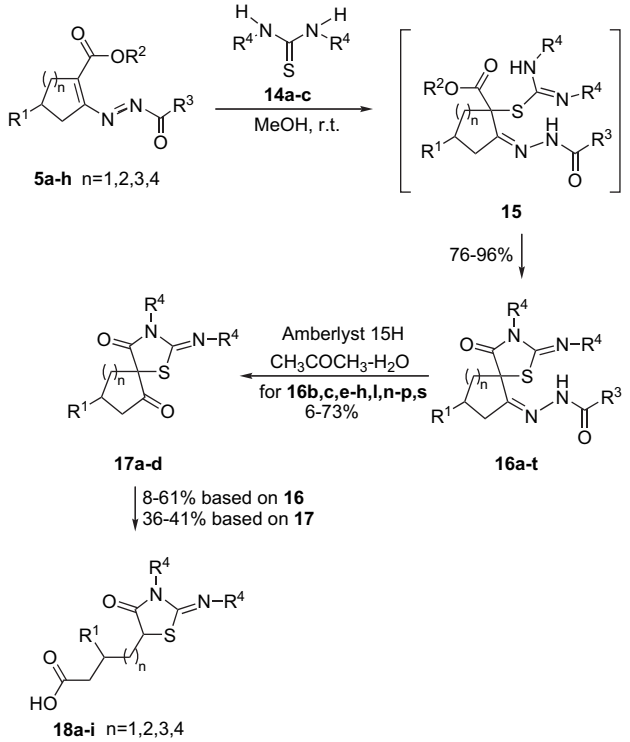


Figure 1. Crystal structure of compound **9k**. Ellipsoids enclose 50% probability.

activity.[25] Concerning the formation of **18**, they can be derived from the preliminary hydrolysis of the semicarbazono moiety of **16** to give rise to the ketones **17**, which by a retro-Claisen reaction occurring with a ring-opening process afford 2-imino-5-(ω-carboxyalkyl)-4-thiazolidinone derivatives **18a–i**. Their structure, proposed on the basis of spectrometric (^{1}H and ^{13}C NMR as well as MS) data, was definitively confirmed by X-ray diffraction determination on **18d** (Fig. 2).[26]



Scheme 4.

Lastly, we have also investigated the reactivity of two cyclic thioureas (five-member ring: imidazolidine-2-thione **19a**; or six-member ring: tetrahydropyrimidine-2-thione **19b**) in methanol at room temperature with cycloalkenyl-1-diazenes **5a**,**c**,**g**,**h**: the new 5′,6′-dihydro-2*H*-spiro[cycloalkyl-1,2′-imidazo[2,1-*b*][1,3]thiazole]-2,3′-dione 2-semicarbazones **21a**,**c**,**f**

Table 3
Yields of spirocycloalkyl-thiazolinones **16a–t**, ketones **17a–d** and 2-imino-5(ω-carboxyalkyl)-4-thiazolidinones **18a–i**

5	*n*	R^1	R^2	R^3	**14**	R^4	**16**	Yield[a] (%)	**17**	Yield[b] (%)	**18**	Yield[b] (%)	Yield[c] (%)
5a	1	H	Et	NH_2	**14a**	H	**16a**	96					
5a	1	H	Et	NH_2	**14b**	Me	**16b**	87			**18a**	54	
5a	1	H	Et	NH_2	**14c**	Et	**16c**	83			**18b**	61	
5b	1	H	Et	O*t*-Bu	**14a**	H	**16d**	78					
5c	2	H	Et	NH_2	**14a**	H	**16e**	79			**18c**	52	
5c	2	H	Et	NH_2	**14b**	Me	**16f**	82			**18d**	49	
5c	2	H	Et	NH_2	**14c**	Et	**16g**	83	**17a**	6	**18e**	48	
5d	2	H	Et	O*t*-Bu	**14b**	Me	**16h**	76			**18d**	61	
5e	2	H	Et	NHPh	**14a**	H	**16i**	85					
5e	2	H	Et	NHPh	**14b**	Me	**16j**	92					
5e	2	H	Et	NHPh	**14c**	Et	**16k**	81					
5f	2	Me	Et	NH_2	**14a**	H	**16l**	89			**18f**	52	
5f	2	Me	Et	NH_2	**14b**	Me	**16m**	76					
5f	2	Me	Et	NH_2	**14c**	Et	**16n**	79			**18g**	45	
5g	3	H	Me	NH_2	**14a**	H	**16o**	85	**17b**	69	**18h**	12	41
5g	3	H	Me	NH_2	**14b**	Me	**16p**	79	**17c**	65	**18i**	8	40
5g	3	H	Me	NH_2	**14c**	Et	**16q**	84					
5h	4	H	Et	NH_2	**14a**	H	**16r**	89					
5h	4	H	Et	NH_2	**14b**	Me	**16s**	92	**17d**	73	**18j**	11	36
5h	4	H	Et	NH_2	**14c**	Et	**16t**	94					

[a] Yields of the pure isolated products **16a–t** based on the cycloalkenyl-1-diazenes **5a–h**.

[b] Yields of the pure isolated **17a–d** and **18a–i** based on the spiro compounds **16**.

[c] Yields of the pure isolated products **18g–i** based on the compounds **17b–d**.

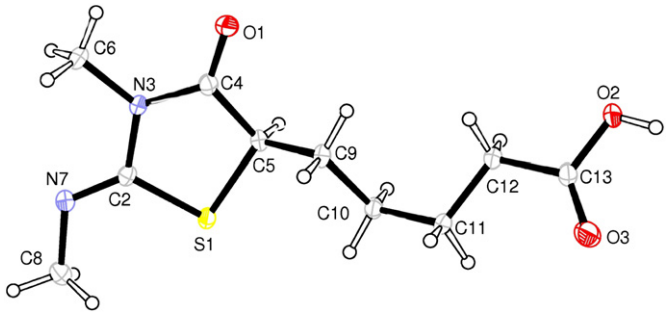
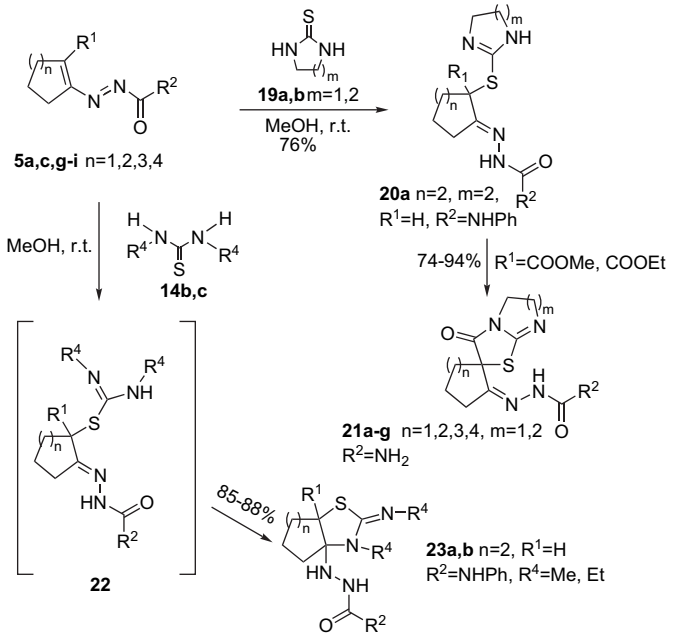


Figure 2. Ortep drawing of **18d**. Ellipsoids of non-hydrogen atoms enclose 50% probability.

(m=1) or the 6′,7′-dihydro-2*H*,5′*H*-spiro[cycloalkyl-1,2′-[1,3]thiazolo[3,2-*a*]pyrimidine]-2,3′-dione 2-semicarbazones **21b**,**d**,**e**,**g** (m=2) were obtained in good yields (Scheme 5, Table 4). Interestingly, compounds **21** represent the spiro-tricyclic counterpart of the relevant spiro-bicyclic **16** previously obtained (Scheme 4).



Scheme 5.

Under the same experimental conditions, the cyclic thiourea tetrahydropyrimidine-2-thione **19b** reacted with the *N*1-phenyl-2-(1-cyclohexenyl)-1-diazene-1-carboxyamide **5i**, but the reaction stopped with the formation of 2-(1,4,5,6-tetrahydropyrimidin-2-ylthio)cyclohexan-1-one *N*-phenylsemicarbazone **20a**. As a matter of fact the absence of the ester group on the terminal carbon of the heterodiene system prevents the formation of the thiazolinone system (Scheme 5, Table 4). On the other hand, the treatment of **5i** with **14b**,**c** gave the usual α-thiohydrazone 1,4-adduct intermediates **22**, which by further internal nucleophilic attack of the NH of the thioureic group at the hydrazono double bond determines the closure to the hexahydro-1,3-benzothiazol-3a(4*H*)-yl-*N*-phenylhydrazinecarboxamides **23a**,**b** in good yields (Scheme 5, Table 4). The further cyclization as for compounds **22** does not proceed in the case of **20a** probably because of the three fused strained rings.

3. Conclusion

The present investigation has evidenced a different behaviour in the reactions of thioamides and thioureas on 1,2-diaza-1,3-butadienes (**I**) or cycloalkyl-1-diazenes (**5**) and demonstrates that the use of these cyclic azoalkenes provides straightforward access to new classes of interesting heterocycles. As a matter of fact in the whole the syntheses realized indicate that **5** can react with different sulfur activated nucleophiles showing an interesting variegate reactivity: (1) with thioamides the bicyclic thiazolines **9** and the tricyclic pyrazolinones **11** can be obtained; (2) with open-chain thioureas **14** the spirothiazolines **16** and **17** or the bicyclothiazolines **23** can be synthesized; (3) with cyclic thioureas **19** (containing a five- or a six-member ring) the tricyclic **21** can be obtained. These one-pot synthetic methodologies proceed under very mild reaction conditions using easily available starting materials and provide interesting new products in high yields without complicated work-up procedures. In particular, the reactions of thioureas with cycloalkyl-1-diazenes furnish crude products (**16**, **17**, **21**) at a high purity degree by direct precipitation from the reaction mixture. Moreover, the acidic hydrolysis with ring-opening of **17** furnishes the acids **18** with a core structure similar to that of some antitubercular drugs. In conclusion, we described the syntheses of different

Table 4
Yields of 2-(1,4,5,6-tetrahydropyrimidin-2-ylthio)cyclohexan-1-one *N*-phenylsemicarbazone **20a**, spiro-cycloalkyl-1,2′-imidazo[2,1-*b*][1,3]thiazoles **21a**,**c**,**f**, spiro-cycloalkyl-1,2′-[1,3]thiazolo[3,2-*a*]pyrimidines **21b**,**d**,**e**,**g** and hexahydro-1,3-benzothiazoles **23a**,**b**

5	n	R^1	R^2	**14**	R^4	**19**	m	**20**	Yield[a] (%)	**21**	Yield[a] (%)	**23**	Yield[a] (%)
5a	1	CO_2Et	NH_2			**19a**	1			**21a**	85		
5a	1	CO_2Et	NH_2			**19b**	2			**21b**	88		
5c	2	CO_2Et	NH_2			**19a**	1			**21c**	76		
5c	2	CO_2Et	NH_2			**19b**	2			**21d**	79		
5g	3	CO_2Me	NH_2			**19b**	2			**21e**	74		
5h	4	CO_2Et	NH_2			**19a**	1			**21f**	88		
5h	4	CO_2Et	NH_2			**19b**	2			**21g**	94		
5i	2	H	NHPh			**19b**	2	**20a**	76				
5i	2	H	NHPh	**14a**	Me							**23a**	85
5i	2	H	NHPh	**14b**	Et							**23b**	88

[a] Yields of the pure isolated products **20a**, **21a–g** and **23a**,**b** based on cycloalkenyl-1-diazenes **5a**,**b**,**g–i**.

new classes of polyheterocyclics of interest as targets in organic, biological, medicinal and agricultural chemistry: all the examined syntheses usually occur with excellent yields (82–97%).

4. Experimental

4.1. General experimental section

Ethyl 2-oxocyclopentanecarboxylate, ethyl 2-oxocyclohexanecarboxylate, ethyl 4-methyl-2-oxocyclohexanecarboxylate, methyl 2-oxocycloeptanecarboxylate, ethyl 2-oxocyclooctanecarboxylate, 2-chlorocycloesanone, semicarbazide hydrochloride, 4-phenylsemicarbazide, *tert*-butyl carbazate, *N*-bromosuccinimide, thiobenzamide, thionicotinamide, 4-methoxythiobenzamide, 4-(trifluoromethyl)thiobenzamide, 4-chloro-thiobenzamide, 2,4-difluorothiobenzamide, thiophene-2-thiocarboxyamide, 2-methylthiazole-4-thiocarboxyamide, thioisonicotinamide, sodium hydride, Amberlyst 15H, thiourea, *N*,*N*′-dimethylthiourea, *N*,*N*′-diethylthiourea, imidazolidine-2-thione, tetrahydropyrimidine-2-thione were commercial materials and were used without further purification. Solvents were purchased and used without further purification with the exception of THF, which was distilled over sodium hydroxide. Melting points were determined in open capillary tubes and are uncorrected. FTIR spectra were obtained as Nujol mulls. Mass spectra (MS) were carried out by electron impact (EI) at an ionizing voltage of 70 eV. ^{1}H (400 MHz) and ^{13}C (100 MHz) spectra were recorded in $CDCl_3$ or in DMSO-d_6, as specified below. Chemical shifts (δ_H) are reported in parts per million (ppm), relative to TMS as internal standard. All coupling constant (J) values are given in hertz. Chemical shifts (δ_C) are reported in parts per million (ppm), relative to $CDCl_3$ or DMSO-d_6, as internal standard in a broad band decoupled mode; the multiplicities were obtained using 135° and 90° DEPT experiments to aid in assignment (q=methyl, t=methylene, d=methine, s=quaternary). The abbreviations used are as follows: s, singlet; d, doublet; dd, double-doublet; t, triplet; q, quartet; qui, quintet; oc, octet; m, multiplet; br, broad; cy, cycloalkylic; alk, alkyl; Ar, aromatic. All the NH and NH_2 exchanged with D_2O. Precoated silica gel plates 0.25 mm were employed for analytical thin layer chromatography and silica gel 35–70 μm for column chromatography. All new compounds showed satisfactory elemental analysis (C ±0.35; H ±0.30; N ±0.30). The nomenclature was generated using ACD/IUPAC Name (version 3.50, 5 Apr. 1998), Advanced Chemistry Development Inc., Toronto, ON (Canada).

4.2. General procedure for the synthesis of cycloalkenyl-1-diazenes **5a–i**

Semicarbazide hydrochloride **2a** (1.0 mmol) or *tert*-butyl carbazate **2b** (1.0 mmol) or 4-phenylsemicarbazide **2c** (1.0 mmol) was added at room temperature to a magnetically stirred solution of cyclic β-dicarbonyl compounds **1a–e** (1.0 mmol) in methanol (30 mL) in the case of **2a**, or in tetrahydrofuran (30 mL) in the cases of **2b**,**c**. The semicarbazide hydrochloride **2a** was pretreated with an equimolecular amount of sodium acetate. The reaction was allowed to stand under magnetic stirring at room temperature (4 h) until the disappearance of the reagents (monitored by TLC chromatography). The reaction solvent was then evaporated under reduced pressure and the products **3a–h** were crystallized by adding ethyl acetate–cyclohexane to the crude. To a magnetically stirred solution of hydrazones **3a–h** in dichloromethane (150 mL), *N*-bromosuccinimide (1.0 equiv) was added portion-wise at room temperature obtaining α-bromohydrazones **4** that were treated with aqueous saturated solution of sodium carbonate (20 mL×3). Then, the mixture was dried on sodium sulfate. Dichloromethane was evaporated under reduced pressure and the final cycloalkenyl-1-diazenes **5a–h** were purified by chromatography on silica gel column (elution mixtures: ethyl acetate–cyclohexane). In the synthesis of *N*-1-phenyl-2-(1-cyclohexenyl)-1-diazene-1-carboxyamide **5i**, 4-phenylsemicarbazide **2c** (1.0 mmol) was added at room temperature to solution of 2-chloro-cyclohexanone **1f** (1.0 mmol) in tetrahydrofuran (25 mL). The reaction was allowed to stand under magnetic stirring at room temperature (14.0 h) until the disappearance of the reagents (monitored by TLC chromatography). The reaction solvent was then evaporated under reduced pressure, the crude was dissolved in dichloromethane (80 mL) and treated with an aqueous solution of sodium hydroxide (1%, 20 mL×3). Dichloromethane was evaporated under reduced pressure and the final product **5i** was crystallized from diethyl ether–light petroleum ether (at 40–60 °C).

4.2.1. Ethyl 2-[2-(aminocarbonyl)-1-diazenyl]-1-cyclopentene-1-carboxylate (**5a**)

Red powder, mp 106–108 °C; IR (Nujol) ν_{max} 3402, 3237, 1718, 1694 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28 (t, 3H, ^3J=7.2 Hz, OCH_2CH_3), 2.02 (qui, 2H, ^3J=7.2 Hz, cy), 2.67–2.72 (m, 2H, cy), 2.90–2.95 (m, 2H, cy), 4.26 (q, 2H, ^3J=7.2 Hz, OCH_2CH_3), 6.46 (br s, 2H, NH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0 (q), 20.1 (t), 29.5 (t), 34.7 (t), 61.2 (t), 145.6 (s), 159.0 (s), 162.4 (s), 164.2 (s); MS (EI) *m*/*z* (%) 213 (5) [M$^+$+2], 211 (4) [M$^+$], 167 (46), 140 (36), 122 (100). Anal. Calcd for $C_9H_{13}N_3O_3$: C, 51.18; H, 6.20; N, 19.89. Found: C, 51.10; H, 6.13; N, 19.96.

4.2.2. tert-Butyl 2-[2-(ethoxycarbonyl)-1-cyclopentenyl]-1-diazene-1-carboxylate (**5b**)

Red oil; IR (Nujol) ν_{max} 3376, 3200, 1717, 1703 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.30 (t, 3H, ^3J=7.2 Hz, OCH_2CH_3), 1.60 (s, 9H, $C(CH_3)_3$), 2.01 (qui, 2H, ^3J=7.8 Hz, cy), 2.63–2.69 (m, 2H, cy), 2.90–2.97 (m, 2H, cy), 4.29 (q, 2H, ^3J=7.2 Hz, OCH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0 (q), 20.2 (t), 27.7 (q), 29.3 (t), 34.7 (t), 61.1 (t), 84.8 (s), 144.7 (s), 159.3 (s), 161.2 (s), 164.6 (s); MS (EI) *m*/*z* (%) 270 (6) [M$^+$+2], 268 (4) [M$^+$], 211 (13), 195 (45), 168 (100), 136 (17), 122 (36). Anal. Calcd for $C_{13}H_{20}N_2O_4$: C, 58.19; H, 7.51; N, 10.44. Found: C, 58.24; H, 7.53; N, 10.36.

4.2.3. Ethyl 2-[2-(aminocarbonyl)-1-diazenyl]-1-cyclohexene-1-carboxylate (**5c**)

Red powder, mp 110–112 °C; IR (Nujol) ν_{max} 3358, 3220, 1721, 1695 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32 (t, 3H,

^3J=7.2 Hz, OCH_2CH_3), 1.67–1.80 (m, 4H, cy), 2.36–2.39 (m, 2H, cy), 2.66–2.69 (m, 2H, cy), 4.30 (q, 2H, ^3J=7.2 Hz, OCH_2CH_3), 5.37 and 6.14 (2br s, 2H, NH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2 (q), 20.9 (t), 21.2 (t), 21.7 (t), 28.0 (t), 61.4 (t), 148.0 (s), 151.5 (s), 162.5 (s), 168.6 (s); MS (EI) *m/z* (%) 225 (14) [M^+], 208 (2), 197 (5), 154 (37), 137 (71), 125 (100), 109 (100). Anal. Calcd for $C_{10}H_{15}N_3O_3$: C, 53.32; H, 6.71; N, 18.66. Found: C, 53.42; H, 6.67; N, 18.59.

*4.2.4. tert-Butyl 2-[2-(ethoxycarbonyl)-1-cyclohexenyl]-1-diazene-1-carboxylate (**5d**)*

Red oil; IR (Nujol) ν_{max} 3407, 3196, 1734, 1689 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28 (t, 3H, ^3J=7.2 Hz, OCH_2CH_3), 1.55 (s, 9H, $C(CH_3)_3$), 1.68–1.74 (m, 4H, cy), 2.18–2.27 (m, 2H, cy), 2.57–2.63 (m, 2H, cy), 4.27 (q, 2H, ^3J=7.2 Hz, OCH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1 (q), 21.0 (t), 21.2 (t), 27.6 (q), 38.7 (t), 40.4 (t), 62.7 (t), 84.2 (s), 147.2 (s), 151.3 (s), 161.3 (s), 169.0 (s); MS (EI) *m/z* (%) 284 (3) [M^++2], 282 (1) [M^+], 225 (21), 209 (36), 180 (100), 153 (42), 136 (79). Anal. Calcd for $C_{14}H_{22}N_2O_4$: C, 59.56; H, 7.85; N, 9.92. Found: C, 59.43; H, 7.81; N, 9.96.

*4.2.5. Ethyl 2-[2-(anilinocarbonyl)-1-diazenyl]-1-cyclohexene-1-carboxylate (**5e**)*

Red powder, mp 90–92 °C with decomposition; IR (Nujol) ν_{max} 3365, 3172, 1718, 1674 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (t, 3H, ^3J=7.2 Hz, OCH_2CH_3), 1.74–1.79 (m, 4H, cy), 2.35–2.39 (m, 2H, cy), 2.67–2.71 (m, 2H, cy), 4.32 (q, 2H, ^3J=7.2 Hz, OCH_2CH_3), 7.14 (t, 1H, ^3J=7.2 Hz, Ar), 7.35 (t, 2H, ^3J=8.4 Hz, Ar), 7.62 (d, 2H, ^3J=8.4 Hz, Ar), 8.31 (br s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2 (q), 20.9 (t), 21.2 (t), 21.9 (t), 28.1 (t), 61.5 (t), 119.4 (d), 124.7 (d), 129.1 (d), 136.6 (s), 148.1 (s), 151.5 (s), 157.3 (s), 168.4 (s); MS (EI) *m/z* (%) 303 (3) [M^++2], 301 (11) [M^+], 272 (17), 256 (37), 228 (100), 209 (46), 180 (17), 165 (15), 109 (64). Anal. Calcd for $C_{16}H_{19}N_3O_3$: C, 63.77; H, 6.35; N, 13.94. Found: C, 63.65; H, 6.27; N, 13.99.

*4.2.6. Ethyl 2-[2-(aminocarbonyl)-1-diazenyl]-4-methyl-1-cyclohexene-1-carboxylate (**5f**)*

Red powder, mp 72–74 °C; IR (Nujol) ν_{max} 3399, 3180, 1729, 1686 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.03 (d, 3H, ^3J=6.0 Hz, $CHCH_3$), 1.31 (t, 3H, ^3J=7.2 Hz, OCH_2CH_3), 1.34–1.42 (m, 1H, cy), 1.76–1.85 (m, 3H, cy), 2.54–2.74 (m, 3H, cy), 4.27 (q, 2H, ^3J=7.2 Hz, OCH_2CH_3), 6.12 and 6.17 (2br s, 2H, NH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2 (q), 21.2 (t), 27.5 (d), 28.0 (t), 29.3 (t), 29.8 (t), 61.4 (t), 146.7 (s), 151.2 (s), 162.4 (s), 168.6 (s); MS (EI) *m/z* (%) 239 (4) [M^+], 224 (4), 208 (1), 168 (27), 151 (45), 139 (92), 123 (100), 111 (52). Anal. Calcd for $C_{11}H_{17}N_3O_3$: C, 55.22; H, 7.16; N, 17.56. Found: C, 55.31; H, 7.25; N, 17.50.

*4.2.7. Methyl 2-[2-(aminocarbonyl)-1-diazenyl]-1-cycloheptene-1-carboxylate (**5g**)*

Red powder, mp 86–89 °C; IR (Nujol) ν_{max} 3365, 3218, 1726, 1695 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.54–1.67 (m, 2H, cy), 1.77–1.88 (m, 4H, cy), 2.63–2.72 (m, 4H, cy), 3.82 (s, 3H, OCH_3), 5.40 and 6.10 (2br s, 2H, NH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.4 (t), 24.3 (t), 26.0 (t), 31.2 (t), 31.3 (t), 52.3 (q), 152.9 (s), 157.2 (s), 161.9 (s), 169.9 (s); MS (EI) *m/z* (%) 227 (2) [M^++2], 225 (4) [M^+], 195 (2), 182 (7), 168 (8), 154 (100), 139 (38), 122 (100), 109 (81). Anal. Calcd for $C_{10}H_{15}N_3O_3$: C, 53.32; H, 6.71; N, 18.66. Found: C, 53.26; H, 6.69; N, 18.72.

*4.2.8. Ethyl 2-[2-(aminocarbonyl)-1-diazenyl]-1-cyclooctene-1-carboxylate (**5h**)*

Red powder, mp 72–74 °C; IR (Nujol) ν_{max} 3385, 3154, 1721, 1659 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.13 (t, 3H, ^3J=7.2 Hz, OCH_2CH_3), 1.25–1.41 (m, 6H, cy), 1.67–1.73 (m, 2H, cy), 2.43–2.48 (m, 2H, cy), 2.52–2.60 (m, 2H, cy), 4.13 (q, 2H, ^3J=7.2 Hz, OCH_2CH_3), 6.21 and 6.67 (2br s, 2H, NH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9 (q), 21.7 (t), 25.8 (t), 25.9 (t), 27.6 (t), 29.6 (t), 29.9 (t), 60.9 (t), 150.4 (s), 153.6 (s), 162.7 (s), 168.9 (s); MS (EI) *m/z* (%) 254 (3) [M^++1], 211 (5), 182 (33), 165 (100), 153 (100), 135 (92), 107 (100). Anal. Calcd for $C_{12}H_{19}N_3O_3$: C, 56.90; H, 7.56; N, 16.59. Found: C, 56.92; H, 7.63; N, 16.54.

*4.2.9. N1-Phenyl-2-(1-cyclohexenyl)-1-diazene-1-carboxyamide (**5i**)*

Red powder, mp 86–88 °C; IR (Nujol) ν_{max} 3257, 3165, 1704, 1679 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.68–1.78 (m, 4H, cy), 2.30–2.41 (m, 2H, cy), 2.46–2.55 (m, 2H, cy), 7.16 (t, 1H, ^3J=7.2 Hz, Ar), 7.28–7.40 (m, 3H, Ar and C=CH), 7.70 (d, 2H, ^3J=8.4 Hz, Ar), 8.46 (s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4 (t), 21.7 (t), 22.4 (t), 27.1 (t), 119.4 (d), 124.6 (d), 129.0 (d), 137.0 (s), 151.5 (d), 155.5 (s), 157.8 (s); MS (EI) *m/z* (%) 229 (18) [M^+], 152 (73), 137 (100), 109 (100). Anal. Calcd for $C_{13}H_{15}N_3O$: C, 68.10; H, 6.59; N, 18.33. Found: C, 68.22; H, 6.54; N, 18.42.

*4.3. General procedure for the synthesis of tetrahydrocyclopenta[d][1,3]thiazolines **9a–d**, hexahydro-1,3-benzothiazolines **9e–m**, hexahydrocyclohepta[d]-[1,3]thiazolines **9n–p** and octahydrocycloocta[d]-[1,3]thiazolines **9q–t***

Cycloalkenyl-1-diazenes **5a**,**c**,**f–h** (1.0 mmol) were added at room temperature to a magnetically stirred solution of aryl thioamides **6a–i** (1.0 mmol) in methanol (10 mL). The reaction was allowed to stand under magnetic stirring at room temperature (0.5–1.5 h) until the disappearance of the reagents (monitored by TLC chromatography). The compounds **9c–e**,**g**,**k**,**l** crystallized directly from the reaction medium and were collected as pure products by filtration. In the other cases, the reaction solvent was evaporated under reduced pressure and the final cycloalkyl[*d*][1,3]thiazolines **9a**,**b**,**h–j**,**m–t** were purified by chromatography on silica gel column (elution mixtures: ethyl acetate–cyclohexane) and crystallized from ethyl acetate–cyclohexane.

*4.3.1. Ethyl 3a-[2-(aminocarbonyl)hydrazino]-2-phenyl-4,5,6,6a-tetrahydro-3aH-cyclopenta[d][1,3]thiazoline-6a-carboxylate (**9a**)*

Colourless powder, mp 141–143 °C with decomposition; IR (Nujol) ν_{max} 3474, 3375, 3216, 3176, 1708, 1684, 1555 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.27 (t, 3H, ^3J=7.2 Hz, OCH_2CH_3), 1.73–1.85 (m, 2H, cy), 2.09–2.28 (m, 3H, cy), 2.73–2.81 (m, 1H, cy), 4.24 (q, 2H, ^3J=7.2 Hz, OCH_2CH_3), 4.91 (br s, 1H, NH), 5.67 (br s, 2H, NH_2), 6.60 (s, 1H, NH), 7.46 (t, 2H, ^3J=7.6 Hz, Ar), 7.52 (t, 1H, ^3J=6.4 Hz, Ar), 7.78 (d, 2H, ^3J=7.6 Hz, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0 (q), 22.8 (t), 37.6 (t), 40.0 (t), 62.5 (t), 71.4 (s), 110.8 (s), 128.4 (d), 128.6 (d), 131.8 (d), 132.1 (s), 160.8 (s), 166.7 (s), 171.1 (s); MS (EI) *m/z* (%) 348 (8) [M^+], 319 (42), 303 (67), 275 (100), 275 (64), 259 (43), 231 (100), 203 (86), 183(49), 126 (72). Anal. Calcd for $C_{16}H_{20}N_4O_3S$: C, 55.16; H, 5.79; N, 16.08. Found: C, 55.04; H, 5.84; N, 16.00.

*4.3.2. Ethyl 3a-[2-(aminocarbonyl)hydrazino]-2-(3-pyridyl)-4,5,6,6a-tetrahydro-3aH-cyclopenta[d][1,3]thiazoline-6a-carboxylate (**9b**)*

Colourless powder, mp 144–146 °C; IR (Nujol) ν_{max} 3476, 3354, 3243, 3165, 1735, 1691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.28 (t, 3H, ^3J=6.8 Hz, OCH_2CH_3), 1.70–1.87 (m, 2H, cy), 2.11–2.29 (m, 3H, cy), 2.77–2.82 (m, 1H, cy), 4.26 (q, 2H, ^3J=6.8 Hz, OCH_2CH_3), 4.93 (br s, 1H, NH), 5.62 (br s, 2H, NH_2), 6.73 (s, 1H, NH), 7.38 (ddd, 1H, ^3J=7.6 Hz, ^3J=4.8 Hz, ^5J=0.4 Hz, Ar), 8.10 (ddd, 1H, ^3J=8.0 Hz, ^4J=2.4 Hz, ^4J=2.0 Hz, Ar), 8.70 (dd, 1H, ^3J=4.8 Hz, ^4J=1.6 Hz, Ar), 8.70 (d, 1H, ^4J=1.2 Hz, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0 (q), 22.8 (t), 37.6 (t), 40.0 (t), 62.6 (t), 72.0 (s), 111.3 (s), 123.5 (d), 128.4 (d), 135.9 (s), 149.0 (s), 152.0 (s), 160.8 (s), 163.1 (s), 170.9 (s); MS (EI) *m/z* (%) 349 (5) [M^+], 304 (85), 276 (100), 232 (69), 204 (26), 157 (48), 110 (78). Anal. Calcd for $C_{15}H_{19}N_5O_3S$: C, 51.56; H, 5.48; N, 20.04. Found: C, 51.55; H, 5.51; N, 20.13.

*4.3.3. Ethyl 3a-[2-(aminocarbonyl)hydrazino]-2-(4-methoxyphenyl)-4,5,6,6a-tetrahydro-3aH-cyclopenta[d][1,3]thiazoline-6a-carboxylate (**9c**)*

Colourless powder, mp 148–150 °C; IR (Nujol) ν_{max} 3465, 3286, 1742, 1676, 1686, 1585 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.20 (t, 3H, ^3J=7.2 Hz, OCH_2CH_3), 1.52–1.63 (m, 1H, cy), 1.77–1.83 (m, 1H, cy), 2.00–2.11 (m, 3H, cy), 2.72–2.80 (m, 1H, cy), 3.82 (s, 3H, OCH_3), 4.16 (q, 2H, ^3J=7.2 Hz, OCH_2CH_3), 5.43 (s, 1H, NH), 5.86 (br s, 2H, NH_2), 6.76 (br s, 1H, NH), 7.02 (d, 2H, ^3J=6.8 Hz, Ar), 7.72 (d, 2H, ^3J=6.8 Hz, Ar); ^{13}C NMR (100 MHz, DMSO-d_6) δ 14.5 (q), 23.2 (t), 37.8 (t), 41.3 (t), 56.2 (q), 62.6 (t), 72.7 (s), 112.5 (s), 114.8 (d), 125.4 (s), 130.6 (d), 160.8 (s), 162.7 (s), 163.3 (s), 171.6 (s); MS (EI) *m/z* (%) 378 (1) [M^+], 304 (25), 289 (100), 260 (13), 232 (75), 198 (25), 156 (61). Anal. Calcd for $C_{17}H_{22}N_4O_4S$: C, 53.95; H, 5.86; N, 14.80. Found: C, 53.87; H, 5.94; N, 14.71.

*4.3.4. Ethyl 3a-[2-(aminocarbonyl)hydrazino]-2-[4-(trifluoromethyl)phenyl]-4,5,6,6a-tetrahydro-3aH-cyclopenta[d][1,3]thiazoline-6a-carboxylate (**9d**)*

Colourless powder, mp 146–148 °C; IR (Nujol) ν_{max} 3472, 3391, 3243, 3114, 1714, 1700, 1564 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.23 (t, 3H, ^3J=7.2 Hz, OCH_2CH_3), 1.54–1.64 (m, 1H, cy), 1.78–1.85 (m, 1H, cy), 2.00–2.19 (m, 3H, cy), 2.71–2.87 (m, 1H, cy), 4.18 (q, 2H, ^3J=7.2 Hz, OCH_2CH_3), 5.58 (s, 1H, NH), 5.87 (br s, 2H, NH_2), 6.89 (s, 1H, NH), 7.87 (d, 2H, ^3J=8.4 Hz, Ar), 8.00 (d, 2H, ^3J=8.4 Hz, Ar); ^{13}C NMR (100 MHz, DMSO-d_6) δ 13.7 (q), 22.6 (t), 37.0 (t), 40.9 (t), 62.0 (t), 72.5 (s), 111.9 (s), 121.8 (s, $^1J_{CF}$=271.6 Hz), 125.7 (d, $^3J_{CF}$=3.0 Hz), 128.9 (d), 131.5 (s, $^2J_{CF}$=31.9 Hz), 131.8 (s), 160.1 (s), 162.4 (s), 170.6 (s); MS (EI) *m/z* (%) 416 (2) [M^+], 399 (2), 342 (46), 327 (100), 298 (64), 270 (100), 156 (97). Anal. Calcd for $C_{17}H_{19}F_3N_4O_3S$: C, 49.03; H, 4.60; N, 13.45. Found: C, 49.09; H, 4.53; N, 13.51.

*4.3.5. Ethyl 3a-[2-(aminocarbonyl)hydrazino]-2-phenyl-3a,4,5,6,7,7a-hexahydro-1,3-benzothiazole-7a-carboxylate (**9e**)*

Colourless powder, mp 133–135 °C with decomposition; IR (Nujol) ν_{max} 3473, 3256, 3156, 1732, 1682 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.27 (t, 3H, ^3J=6.8 Hz, OCH_2CH_3), 1.40–1.52 (m, 1H, cy), 1.53–1.56 (m, 1H, cy), 1.59–1.66 (m, 2H, cy), 1.90–1.98 (m, 1H, cy), 2.07–2.11 (m, 1H, cy), 2.18–2.26 (m, 2H, cy), 4.17 (q, 2H, ^3J=6.8 Hz, OCH_2CH_3), 5.18 (br s, 1H, NH), 5.72 (br s, 2H, NH_2), 6.56 (br s, 1H, NH), 7.36 (dt, 2H, ^3J=6.8 Hz, ^4J=1.2 Hz, Ar), 7.43 (dt, 1H, ^3J=7.2 Hz, ^4J=1.2 Hz, Ar), 7.76 (dt, 2H, ^3J=7.2 Hz, ^4J=1.2 Hz, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8 (q), 20.3 (t), 20.9 (t), 29.0 (t), 35.3 (t), 61.9 (t), 68.1 (s), 93.5 (s), 128.0 (d), 128.4 (d), 131.8 (d), 132.7 (s), 161.2 (s), 167.4 (s), 170.4 (s); MS (EI) *m/z* (%) 362 (1) [M^+], 317 (2), 288 (65), 273 (67), 244 (42), 216 (46), 170 (100), 141 (53). Anal. Calcd for $C_{17}H_{22}N_4O_3S$: C, 56.38; H, 6.12; N, 15.46. Found: C, 56.38; H, 6.12; N, 15.38.

*4.3.6. Ethyl 3a-[2-(aminocarbonyl)hydrazino]-2-(4-methoxyphenyl)-3a,4,5,6,7,7a-hexahydro-1,3-benzothiazole-7a-carboxylate (**9f**)*

Colourless powder, mp 144–146 °C; IR (Nujol) ν_{max} 3463, 3253, 1737, 1694, 1653, 1604 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.20 (t, 3H, ^3J=6.8 Hz, OCH_2CH_3), 1.30–1.38 (m, 1H, cy), 1.44–1.53 (m, 1H, cy), 1.52–1.68 (m, 2H, cy), 1.71–1.83 (m, 1H, cy), 1.89–2.00 (m, 1H, cy), 2.01–2.13 (m, 1H, cy), 2.29–2.36 (m, 1H, cy), 3.81 (s, 3H, OCH_3), 4.13 (q, 2H, ^3J=6.8 Hz, OCH_2CH_3), 5.41 (s, 1H, NH), 5.83 (br s, 2H, NH_2), 6.77 (br s, 1H, NH), 7.01 (d, 2H, ^3J=6.8 Hz, Ar), 7.73 (d, 2H, ^3J=6.8 Hz, Ar); ^{13}C NMR (100 MHz, DMSO-d_6) δ 13.8 (q), 20.1 (t), 20.9 (t), 29.6 (t), 35.6 (t), 55.4 (q), 61.5 (t), 68.8 (s), 93.6 (s), 124.0 (d), 125.6 (d), 129.7 (d), 160.2 (s), 162.0 (s), 164.7 (s), 170.4 (s); MS (EI) *m/z* (%) 392 (12) [M^+], 318 (4), 303 (61), 274 (9), 252 (14), 261 (5), 245 (29), 170 (81), 133 (100), 110 (73). Anal.

Calcd for $C_{18}H_{24}N_4O_4S$: C, 55.09; H, 6.16; N, 14.28. Found: C, 55.15; H, 6.11; N, 14.16.

4.3.7. Ethyl 3a-[2-(aminocarbonyl)hydrazino]-2-(4-chlorophenyl)-3a,4,5,6,7,7a-hexahydro-1,3-benzothiazole-7a-carboxylate (**9g**)

Colourless powder, mp 163–165 °C; IR (Nujol) ν_{max} 3473, 3314, 3256, 3156, 1732, 1682 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.18 (t, 3H, ^3J=7.2 Hz, OCH_2CH_3), 1.27–1.35 (m, 1H, cy), 1.43–1.53 (m, 1H, cy), 1.55–1.67 (m, 2H, cy), 1.71–1.81 (m, 1H, cy), 1.89–1.98 (m, 1H, cy), 2.07–2.19 (m, 1H, cy), 2.29–2.38 (m, 1H, cy), 4.14 (q, 2H, ^3J=7.2 Hz, OCH_2CH_3), 5.48 (s, 1H, NH), 5.80 (br s, 2H, NH_2), 6.88 (br s, 1H, NH), 7.53 (d, 2H, ^3J=8.8 Hz, Ar), 7.78 (d, 2H, ^3J=8.8 Hz, Ar); ^{13}C NMR (100 MHz, DMSO-d_6) δ 13.8 (q), 20.0 (t), 20.9 (t), 29.5 (t), 35.8 (t), 61.7 (t), 69.4 (s), 93.8 (s), 128.8 (d), 129.7 (d), 131.9 (s), 136.5 (s), 160.3 (s), 164.6 (s), 170.2 (s); MS (EI) *m/z* (%) 324 (12), 322 (37), 309 (5), 307 (14), 278 (12), 252 (14), 250 (43), 205 (100), 189 (6), 167 (21), 137 (82), 111 (87). Anal. Calcd for $C_{17}H_{21}ClN_4O_3S$: C, 51.45; H, 5.33; N, 14.12. Found: C, 51.43; H, 5.37; N, 14.15.

4.3.8. Ethyl 3a-[2-(aminocarbonyl)hydrazino]-2-(2,4-difluorophenyl)-3a,4,5,6,7,7a-hexahydro-1,3-benzothiazole-7a-carboxylate (**9h**)

Colourless powder, mp 119–122 °C; IR (Nujol) ν_{max} 3423, 3278, 3169, 1724, 1691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.13 (t, 3H, ^3J=7.2 Hz, OCH_2CH_3), 1.16–1.46 (m, 4H, cy), 1.51–1.60 (m, 1H, cy), 1.76–2.19 (m, 3H, cy), 4.08 (q, 2H, ^3J=7.2 Hz, OCH_2CH_3), 5.10 (br s, 1H, NH), 5.85 (br s, 2H, NH_2), 6.74 (dt, 1H, ^3J=8.8 Hz, ^4J=2.4 Hz, Ar), 6.76–6.87 (m, 2H, NH and Ar), 7.83–7.91 (m, 1H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.6 (q), 20.0 (t), 20.6 (t), 28.7 (t), 34.6 (t), 61.7 (t), 67.7 (s), 92.1 (s), 104.1 (d, $^2J_{CF}$=25.8 Hz, $^3J_{CF}$=5.3 Hz), 111.6 (d, $^2J_{CF}$=21.2 Hz), 117.4 (s, $^3J_{CF}$=10.7 Hz, $^4J_{CF}$=3.1 Hz), 131.6 (s, $^3J_{CF}$=9.1 Hz), 160.8 (s, $^1J_{CF}$=256.5 Hz, $^3J_{CF}$=12.1 Hz), 161.0 (s, $^3J_{CF}$=4.4 Hz), 161.4 (s), 164.4 (s, $^1J_{CF}$=253.4 Hz, $^3J_{CF}$=11.3 Hz), 170.2 (s); MS (EI) *m/z* (%) 398 (7) [M^+], 369 (31), 353 (65), 325 (100), 309 (58), 281 (37), 239 (67), 179 (15), 211 (42), 167 (26), 152 (14). Anal. Calcd for $C_{17}H_{20}F_2N_4O_3S$: C, 51.25; H, 5.06; N, 14.06. Found: C, 51.21; H, 5.11; N, 14.11.

4.3.9. Ethyl 3a-[2-(aminocarbonyl)hydrazino]-2-(2-thienyl)-3a,4,5,6,7,7a-hexahydro-1,3-benzothiazole-7a-carboxylate (**9i**)

Colourless powder, mp 47–49 °C; IR (Nujol) ν_{max} 3458, 3402, 3264, 3136, 1716, 1702, 1587 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.30 (t, 3H, ^3J=7.2 Hz, OCH_2CH_3), 1.44–1.76 (m, 4H, cy), 1.94–2.17 (m, 2H, cy), 2.24–2.38 (m, 2H, cy), 4.24 (q, 2H, ^3J=7.2 Hz, OCH_2CH_3), 5.08 (br s, 3H, NH_2 and NH), 6.13 (br s, 1H, NH), 7.08 (dd, 1H, ^3J=5.2 Hz, ^3J=3.6 Hz, Ar), 7.46 (dd, 1H, ^3J=4.0 Hz, ^4J=1.2 Hz, Ar), 7.51 (dd, 1H, ^3J=5.2 Hz, ^4J=1.2 Hz, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0 (q), 20.5 (t), 21.2 (t), 29.1 (t), 35.9 (t), 62.2 (t), 68.8 (s), 93.4 (s), 127.7 (d), 131.1 (d), 131.3 (d), 136.7 (s), 160.7 (s), 161.0 (s), 170.3 (s); MS (EI) *m/z* (%) 368 (1) [M^+], 323 (22), 294 (81), 279 (46), 250 (42), 237 (11), 220 (100), 204 (100), 193 (21), 165 (100). Anal. Calcd for $C_{15}H_{20}N_4O_3S_2$: C, 48.90; H, 5.47; N, 15.21. Found: C, 48.78; H, 5.54; N, 15.13.

4.3.10. Ethyl 3a-[2-(aminocarbonyl)hydrazino]-5-methyl-2-phenyl-3a,4,5,6,7,7a-hexahydro-1,3-benzothiazole-7a-carboxylate (**9j**)

Colourless powder, mp 138–140 °C; IR (Nujol) ν_{max} 3484, 3364, 3269, 3148, 1737, 1676 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.87 (d, 3H, ^3J=6.4 Hz, $CHCH_3$), 1.20 (t, 3H, ^3J=7.2 Hz, OCH_2CH_3), 1.30–1.38 (m, 1H, cy), 1.41–1.68 (m, 2H, cy), 1.91–2.03 (m, 2H, cy), 2.26–2.34 (m, 1H, cy), 2.40–2.50 (m, 1H, cy), 4.00–4.14 (m, 2H, OCH_2CH_3), 4.89 (br s, 1H, NH), 5.66 and 5.87 (2br s, 2H, NH_2), 6.59 (s, 1H, NH), 7.30–7.45 (m, 3H, Ar), 7.70 (d, 2H, ^3J=6.8 Hz, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.6 (q), 21.2 (q), 26.6 (d), 27.0 (t), 29.2 (t), 37.2 (t), 61.7 (t), 66.4 (s), 95.2 (s), 127.7 (d), 128.4 (d), 131.6 (d), 132.8 (s), 161.1 (s), 162.5 (s), 171.6 (s); MS (EI) *m/z* (%) 376 (1) [M^+], 302 (100), 287 (8), 258 (43), 230 (75), 184 (27), 169 (3), 152 (14). Anal. Calcd for $C_{18}H_{24}N_4O_3S$: C, 57.43; H, 6.43; N, 14.88. Found: C, 57.34; H, 6.49; N, 14.96.

4.3.11. Ethyl 3a-[2-(aminocarbonyl)hydrazino]-2-(4-chlorophenyl)-5-methyl-3a,4,5,6,7,7a-hexahydro-1,3-benzothiazole-7a-carboxylate (**9k**)

Colourless powder, mp 156–158 °C; IR (Nujol) ν_{max} 3477, 3254, 1738, 1639, 1612, 1586 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.92 (d, 3H, ^3J=6.4 Hz, $CHCH_3$), 1.06–1.18 (m, 3H, OCH_2CH_3), 1.24–1.44 (m, 2H, cy), 1.54–1.73 (m, 2H, cy), 1.93–2.06 (m, 1H, cy), 2.27–2.36 (m, 1H, cy), 2.41–2.53 (m, 1H, cy), 4.06–4.22 (m, 2H, OCH_2CH_3), 4.97 (br s, 1H, NH), 5.68 (br s, 2H, NH_2), 6.50 (s, 1H, NH), 7.35 (d, 2H, ^3J=9.2 Hz, Ar), 7.66 (d, 2H, ^3J=9.2 Hz, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.6 (q), 21.3 (q), 26.7 (d), 27.0 (t), 29.2 (t), 37.2 (t), 61.9 (t), 66.4 (s), 95.4 (s), 128.7 (d), 129.0 (d), 131.3 (s), 137.8 (s), 160.9 (s), 161.4 (s), 171.6 (s); MS (EI) *m/z* (%) 338 (15), 336 (38), 323 (34), 321 (90), 294 (13), 292 (36), 266 (23), 264 (64), 223 (26), 221 (71), 184 (100), 151 (61). Anal. Calcd for $C_{18}H_{23}ClN_4O_3S$: C, 52.61; H, 5.64; N, 13.63. Found: C, 52.53; H, 5.68; N, 13.71.

4.3.12. Ethyl 3a-[2-(aminocarbonyl)hydrazino]-5-methyl-2-(2-methyl-1,3-thiazol-4-yl)-3a,4,5,6,7,7a-hexahydro-1,3-benzothiazole-7a-carboxylate (**9l**)

Colourless powder, mp 97–99 °C; IR (Nujol) ν_{max} 3458, 3384, 3251, 3134, 1717, 1703, 1625 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.92 (d, 3H, ^3J=6.4 Hz, $CHCH_3$), 1.24 (t, 3H, ^3J=6.4 Hz, OCH_2CH_3), 1.33–1.42 (m, 1H, cy), 1.55–1.71 (m, 2H, cy), 1.84–1.99 (m, 2H, cy), 2.26–2.35 (m, 1H, cy), 2.41–2.51 (m, 1H, cy), 2.73 (s, 3H, N=CCH_3), 4.10–4.20 (m, 2H, OCH_2CH_3), 4.81 (br s, 1H, NH), 5.76 (br s, 2H, NH_2), 6.36 (br s, 1H, NH), 7.81 (br s, 1H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7 (q), 19.08 (q), 21.3 (q), 26.6 (d), 27.0 (t), 29.2 (t), 37.4 (t), 62.0 (t), 65.4

(s), 95.2 (s), 120.0 (d), 148.2 (s), 158.7 (s), 160.8 (s), 166.6 (s), 171.7 (s); MS (EI) *m/z* (%) 396 (1) [M^+-1], 323 (100), 308 (4), 279 (15), 264 (1), 251 (100), 224 (3), 210 (12), 184 (10), 167 (5). Anal. Calcd for $C_{16}H_{23}N_5O_3S_2$: C, 48.35; H, 5.83; N, 17.62. Found: C, 48.33; H, 5.88; N, 17.57.

*4.3.13. Ethyl 3a-[2-(aminocarbonyl)hydrazino]-5-methyl-2-(pyridyl)-3a,4,5,6,7,7a-hexahydro-1,3-benzothiazole-7a-carboxylate (**9m**)*

Colourless powder, mp 112–114 °C; IR (Nujol) ν_{max} 3453, 3261, 3143, 1718, 1701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.86 (d, 3H, ^3J=6.4 Hz, $CHCH_3$), 1.14–1.21 (m, 3H, OCH_2CH_3), 1.32–1.42 (m, 1H, cy), 1.55–1.73 (m, 2H, cy), 1.89–1.99 (m, 2H, cy), 2.26–2.35 (m, 1H, cy), 2.39–2.49 (m, 1H, cy), 4.00–4.16 (m, 2H, OCH_2CH_3), 5.71 and 5.76 (2br s, 3H, NH_2 and NH), 6.58 (s, 1H, NH), 7.54 (d, 2H, ^3J=4.4 Hz, Ar), 8.65 (d, 2H, ^3J=4.4 Hz, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.6 (q), 21.2 (q), 26.5 (d), 26.9 (t), 29.2 (t), 37.0 (t), 62.0 (t), 66.7 (s), 95.7 (s), 121.3 (d), 139.8 (d), 150.1 (s), 160.8 (s), 161.1 (s), 171.4 (s); MS (EI) *m/z* (%) 377 (4) [M^+], 348 (19), 332 (28), 304 (100), 287 (17), 260 (39), 231 (56), 210 (11), 183 (23), 152 (4). Anal. Calcd for $C_{17}H_{23}N_5O_3S$: C, 54.10; H, 6.14; N, 18.55. Found: C, 54.03; H, 6.19; N, 18.58.

*4.3.14. Methyl 3a-[2-(aminocarbonyl)hydrazino]-2-phenyl-4,5,6,7,8,8a-hexahydro-3aH-cyclohepta[d][1,3]thiazoline-8a-carboxylate (**9n**)*

Colourless powder, mp 149–152 °C; IR (Nujol) ν_{max} 3465, 3318, 3262, 3196, 1724, 1678 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.03–1.12 (m, 1H, cy), 1.27–1.38 (m, 1H, cy), 1.56–1.73 (m, 4H, cy), 1.91–2.02 (m, 1H, cy), 2.07–2.15 (m, 1H, cy), 2.30–2.42 (m, 2H, cy), 3.72 (s, 3H, OCH_3), 5.25 and 5.74 (2br s, 3H, NH_2 and NH), 6.66 (s, 1H, NH), 7.45–7.61 (m, 3H, Ar), 7.83 (d, 2H, ^3J=7.6 Hz, Ar); ^{13}C NMR (100 MHz, DMSO-d_6) δ 23.0 (t), 23.1 (t), 30.3 (t), 31.0 (t), 39.8 (t), 53.0 (q), 75.8 (s), 100.5 (s), 128.0 (d), 128.7 (d), 131.7 (d), 132.6 (s), 160.2 (s), 164.7 (s), 171.5 (s); MS (EI) *m/z* (%) 363 (1) [M^++1], 287 (21), 270 (1), 254 (3), 229 (16), 224 (3), 184 (16), 152 (40), 123 (43), 103 (100). Anal. Calcd for $C_{17}H_{22}N_4O_3S$: C, 56.43; H, 6.12; N, 15.46. Found: C, 56.48; H, 6.03; N, 15.46.

*4.3.15. Methyl 3a-[2-(aminocarbonyl)hydrazino]-2-(4-chlorophenyl)-4,5,6,7,8,8a-hexahydro-3aH-cyclohepta[d][1,3]thiazoline-8a-carboxylate (**9o**)*

Colourless powder, mp 139–143 °C; IR (Nujol) ν_{max} 3483, 3347, 3223, 3165, 1738, 1659 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.03–1.14 (m, 1H, cy), 1.30–1.39 (m, 1H, cy), 1.50–1.69 (m, 4H, cy), 1.91–2.02 (m, 1H, cy), 2.09–2.17 (m, 1H, cy), 2.30–2.41 (m, 2H, cy), 3.72 (s, 3H, OCH_3), 5.27 and 5.72 (2br s, 3H, NH_2 and NH), 6.71 (s, 1H, NH), 7.56 (d, 2H, ^3J=7.2 Hz, Ar), 7.84 (d, 2H, ^3J=7.2 Hz, Ar); ^{13}C NMR (100 MHz, DMSO-d_6) δ 23.8 (t), 31.0 (t), 32.2 (t), 53.7 (q), 76.8 (s), 101.3 (s), 129.4 (d), 130.0 (d), 132.1 (s), 137.1 (s), 161.0 (s), 164.3 (s), 172.1 (s); MS (EI) *m/z* (%) 397 (2) [M^++1], 368 (4), 366 (14), 339 (24), 337 (69), 295 (36), 293 (100), 265 (3), 263 (10), 255 (8), 227 (39), 183 (74), 144 (62). Anal. Calcd for $C_{17}H_{21}ClN_4O_3S$: C, 51.45; H, 5.33; N, 14.12. Found: C, 51.38; H, 5.39; N, 14.16.

*4.3.16. Methyl 3a-[2-(aminocarbonyl)hydrazino]-2-(2,4-difluorophenyl)-4,5,6,7,8,8a-hexahydro-3aH-cyclohepta[d][1,3]thiazoline-8a-carboxylate (**9p**)*

Colourless powder, mp 108–110 °C; IR (Nujol) ν_{max} 3478, 3272, 1734, 1681, 1641, 1598 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.07–1.15 (m, 1H, cy), 1.25–1.34 (m, 1H, cy), 1.52–1.78 (m, 4H, cy), 1.87–1.97 (m, 1H, cy), 2.01–2.11 (m, 1H, cy), 2.26–2.38 (m, 2H, cy), 3.70 (s, 3H, OCH_3), 5.71 (br s, 3H, NH_2 and NH), 6.70 (br s, 1H, NH), 7.20 (t, 1H, ^3J=7.6 Hz, Ar), 7.40 (t, 1H, ^3J=7.6 Hz, Ar), 7.96–8.07 (m, 1H, Ar); ^{13}C NMR (100 MHz, DMSO-d_6) δ 23.0 (t), 23.1 (t), 30.3 (t), 30.9 (t), 39.6 (t), 53.0 (q), 75.6 (s), 98.9 (s), 104.8 (d, $^2J_{CF}$=26.5 Hz), 112.3 (d, $^2J_{CF}$=22.0 Hz), 117.3 (s, $^3J_{CF}$=8.3 Hz), 132.4 (d, $^3J_{CF}$=9.8 Hz), 159.0 (s), 160.1 (s), 160.5 (s, $^1J_{CF}$=254.2 Hz, $^3J_{CF}$=12.9 Hz), 164.1 (s, $^1J_{CF}$=251.1 Hz, $^3J_{CF}$=12.1 Hz), 171.4 (s); MS (EI) *m/z* (%) 323 (40), 265 (38), 211 (7), 184 (36), 139 (100). Anal. Calcd for $C_{17}H_{20}F_2N_4O_3S$: C, 51.25; H, 5.06; N, 14.06. Found: C, 51.19; H, 5.13; N, 14.12.

*4.3.17. Ethyl 3a-[2-(aminocarbonyl)hydrazino]-2-phenyl-3a,4,5,6,7,8,9,9a-octahydrocycloocta[d][1,3]thiazoline-9a-carboxylate (**9q**)*

Colourless powder, mp 148–150 °C; IR (Nujol) ν_{max} 3452, 3333, 3251, 3231, 1729, 1684 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.10–1.78 (m, 7H, cy), 1.22 (t, 3H, ^3J=7.2 Hz, OCH_2CH_3), 1.86–1.94 (m, 1H, cy), 2.03–2.12 (m, 1H, cy), 2.41–2.55 (m, 3H, cy), 4.10–4.22 (m, 2H, OCH_2CH_3), 5.25 (s, 1H, NH), 5.38 (br s, 2H, NH_2), 6.66 (br s, 1H, NH), 7.47 (t, 2H, ^3J=7.6 Hz, Ar), 7.54 (t, 1H, ^3J=7.2 Hz, Ar), 7.82 (d, 2H, ^3J=7.2 Hz, Ar); ^{13}C NMR (100 MHz, DMSO-d_6) δ 13.9 (q), 21.8 (t), 23.2 (t), 24.9 (t), 25.8 (t), 30.2 (t), 33.6 (t), 61.7 (t), 75.9 (s), 98.7 (s), 128.0 (d), 128.7 (d), 131.7 (d), 132.9 (s), 160.2 (s), 165.3 (s), 170.9 (s); MS (EI) *m/z* (%) 390 (9) [M^+], 361 (53), 345 (79), 317 (100), 301 (38), 273 (56), 244 (31), 224 (75), 196 (38), 166 (63). Anal. Calcd for $C_{19}H_{26}N_4O_3S$: C, 58.44; H, 6.71; N, 14.35. Found: C, 58.51; H, 6.76; N, 14.27.

*4.3.18. Ethyl 3a-[2-(aminocarbonyl)hydrazino]-2-(4-methoxyphenyl)-3a,4,5,6,7,8,9,9a-octahydrocycloocta[d][1,3]thiazoline-9a-carboxylate (**9r**)*

Colourless powder, mp 164–166 °C; IR (Nujol) ν_{max} 3432, 3268, 3204, 1737, 1678 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.13–1.24 (m, 1H, cy), 1.28 (t, 3H, ^3J=7.2 Hz, OCH_2CH_3), 1.30–1.70 (m, 6H, cy), 1.91–2.02 (m, 1H, cy), 2.10–2.22 (m, 1H, cy), 2.46–2.58 (m, 3H, cy), 3.88 (s, 3H, OCH_3), 4.19–4.27 (m, 2H, OCH_2CH_3), 5.26 (s, 1H, NH), 5.71 (br s, 2H, NH_2), 6.71 (br s, 1H, NH), 7.09 (d, 2H, ^3J=8.8 Hz, Ar), 7.85 (d, 2H, ^3J=8.8 Hz, Ar); ^{13}C NMR (100 MHz, DMSO-d_6) δ 14.5 (q), 22.5 (t), 23.9 (t), 25.6 (t), 26.5 (t), 30.3 (t), 34.4 (t), 56.2 (q), 62.4 (t), 76.4 (s), 99.2 (s), 114.7 (d), 126.2 (s), 130.5 (d), 160.9 (s), 162.7 (s),

165.2 (s), 171.7 (s); MS (EI) *m/z* (%) 420 (4) [M^+], 397 (14), 375 (57), 347 (100), 331 (47), 303 (25), 271 (81), 177 (58). Anal. Calcd for $C_{20}H_{28}N_4O_4S$: C, 57.12; H, 6.71; N, 13.32. Found: C, 57.23; H, 6.72; N, 13.21.

*4.3.19. Ethyl 3a-[2-(aminocarbonyl)hydrazino]-2-(4-chlorophenyl)-3a,4,5,6,7,8,9,9a-octahydrocycloocta[d][1,3]-thiazoline-9a-carboxylate (**9s**)*

Colourless powder, mp 160–162 °C with decomposition; IR (Nujol) ν_{max} 3465, 3395, 3255, 3124, 1725, 1708, 1590 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.07–1.16 (m, 1H, cy), 1.23 (t, 3H, ^3J=7.2 Hz, OCH_2CH_3), 1.29–1.74 (m, 6H, cy), 1.86–1.94 (m, 1H, cy), 2.01–2.12 (m, 1H, cy), 2.40–2.51 (m, 3H, cy), 4.10–4.24 (m, 2H, OCH_2CH_3), 5.27 (s, 1H, NH), 5.72 (br s, 2H, NH_2), 6.73 (br s, 1H, NH), 7.54 (d, 2H, ^3J=8.0 Hz, Ar), 7.84 (d, 2H, ^3J=8.0 Hz, Ar); ^{13}C NMR (100 MHz, DMSO-d_6) δ 13.8 (q), 21.8 (t), 23.3 (t), 24.9 (t), 25.8 (t), 30.1 (t), 34.6 (t), 61.8 (t), 76.3 (s), 98.8 (s), 128.8 (d), 129.8 (d), 131.7 (s), 136.5 (s), 160.2 (s), 164.2 (s), 170.8 (s); MS (EI) *m/z* (%) 422 (2) [M^+−2], 276 (3), 274 (10), 224 (2), 222 (6), 198 (17), 166 (100). Anal. Calcd for $C_{19}H_{25}ClN_4O_3S$: C, 53.70; H, 5.93; N, 13.18. Found: C, 53.79; H, 5.86; N, 13.13.

*4.3.20. Ethyl 3a-[2-(aminocarbonyl)hydrazino]-2-(2,4-difluorophenyl)-3a,4,5,6,7,8,9,9a-octahydrocycloocta-[d][1,3]thiazoline-9a-carboxylate (**9t**)*

Colourless powder, mp 171–174 °C with decomposition; IR (Nujol) ν_{max} 3434, 3206, 3116, 1728, 1696 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.10–1.20 (m, 1H, cy), 1.22 (t, 3H, ^3J=7.2 Hz, OCH_2CH_3), 1.25–1.73 (m, 6H, cy), 1.84–1.93 (m, 1H, cy), 2.01–2.11 (m, 1H, cy), 2.40–2.49 (m, 3H, cy), 4.09–4.20 (m, 2H, OCH_2CH_3), 5.30 (s, 1H, NH), 5.73 (br s, 2H, NH_2), 6.70 (br s, 1H, NH), 7.22 (t, 1H, ^3J=8.0 Hz, Ar), 7.40 (t, 1H, ^3J=7.6 Hz, Ar), 8.00–8.10 (m, 1H, Ar); ^{13}C NMR (100 MHz, DMSO-d_6) δ 13.8 (q), 21.8 (t), 23.2 (t), 25.0 (t), 25.8 (t), 30.0 (t), 33.5 (t), 61.8 (t), 75.6 (s), 97.1 (s), 104.8 (d, $^2J_{CF}$=25.8 Hz), 112.3 (d, $^2J_{CF}$=20.5 Hz), 117.7 (s, $^3J_{CF}$=9.3 Hz), 132.4 (s), 159.5 (s), 160.2 (s), 160.5 (s, $^1J_{CF}$=254.1 Hz, $^3J_{CF}$=12.8 Hz), 164.0 (s, $^1J_{CF}$=250.4 Hz, $^3J_{CF}$=12.2 Hz), 170.8 (s); MS (EI) *m/z* (%) 426 (14) [M^+], 396 (45), 381 (86), 331 (100), 309 (12), 280 (5), 167 (14). Anal. Calcd for $C_{19}H_{24}F_2N_4O_3S$: C, 53.51; H, 5.67; N, 13.14. Found: C, 53.64; H, 5.73; N, 13.11.

*4.4. General procedure for the synthesis of 6-thia-2,3,8-triaza-tricyclo[3.3.3.0^{1,5}]undec-7-en-4-ones **11a**,**b**, 10-thia-7,8,12-triaza-tricyclo[4.3.3.0^{1,6}]dodec-11-en-9-ones **11c**–**g** and 12-thia-9,10,14-triaza-tricyclo[6.3.3.0^{1,8}]tetradec-13-en-11-ones **11h**–**j***

To a magnetically stirred solution of aryl-4,5,6,6a-tetrahydro-3a*H*-cyclopenta[*d*][1,3]thiazolines **9c**,**d** (1.0 mmol), or aryl-3a,4,5,6,7,7a-hexahydro-1,3-benzothiazolines **9e**–**h**,**j** (1.0 mmol) or aryl-3a,4,5,6,7,8,9,9a-octahydrocycloocta[*d*][1,3]thiazolines **9q**–**s** (1.0 mmol) in tetrahydrofuran (30 mL) a stoichiometric amount of sodium hydride (1.0 mmol) was added at room temperature. The reaction easily took place (0.5–1.0 min) at room temperature (monitored by TLC chromatography). Then, on the disappearance of **9**, 2 equiv of Amberlyst 15H was added under magnetic stirring to the crude and the reaction was allowed to stand at room temperature for 2 min. The mixture was filtered and the solvent was evaporated under reduced pressure. The products **11a**–**j** were obtained pure by chromatography on silica gel column (elution mixtures: ethyl acetate–cyclohexane).

*4.4.1. 7-(4-Methoxyphenyl)-6-thia-2,3,8-triaza-tricyclo-[3.3.3.0^{1,5}]undec-7-en-4-one (**11a**)*

Colourless oil; IR (Nujol) ν_{max} 3426, 3257, 3143, 1694 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.81–1.91 (m, 2H, cy), 2.19–2.24 (m, 2H, cy), 2.44–2.48 (m, 1H, cy), 2.65–2.70 (m, 1H, cy), 3.85 (s, 3H, OCH_3), 4.90 (br s, 1H, NH), 6.90 (d, 2H, ^3J=8.8 Hz, Ar), 7.77 (d, 2H, ^3J=8.8 Hz, Ar), 8.12 (br s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.5 (t), 29.7 (t), 39.0 (t), 40.4 (q), 55.4 (s), 68.9 (s), 114.0 (s), 124.4 (d), 130.6 (d), 162.9 (s), 168.7 (s), 174.0 (s); MS (EI) *m/z* (%) 289 (66) [M^+], 261 (47), 229 (42), 182 (100), 154 (16), 124 (32). Anal. Calcd for $C_{14}H_{15}N_3O_2S$: C, 58.11; H, 5.22; N, 14.52. Found: C, 58.03; H, 5.29; N, 14.43.

*4.4.2. 7-(4-Trifluoromethyl-phenyl)-6-thia-2,3,8-triaza-tricyclo[3.3.3.0^{1,5}]undec-7-en-4-one (**11b**)*

Colourless oil; IR (Nujol) ν_{max} 3443, 3324, 3232, 3157, 1697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.76–2.05 (m, 2H, cy), 2.17–2.32 (m, 2H, cy), 2.53–2.59 (m, 1H, cy), 2.69–2.76 (m, 1H, cy), 4.77 (br s, 1H, NH), 7.68 (d, 2H, ^3J=8.4 Hz, Ar), 7.93 (d, 2H, ^3J=8.4 Hz, Ar), 8.31 (br s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.6 (t), 27.0 (t), 39.3 (t), 61.4 (s), 69.6 (s), 123.8 (s, $^1J_{CF}$=271.0 Hz), 125.9 (d, $^3J_{CF}$=3.8 Hz), 129.3 (d), 134.0 (s, $^2J_{CF}$=32.6 Hz), 135.4 (s), 168.1 (s), 173.8 (s); MS (EI) *m/z* (%) 327 (100) [M^+], 298 (47), 269 (35), 181 (86), 154 (24), 124 (36). Anal. Calcd for $C_{14}H_{12}F_3N_3OS$: C, 51.37; H, 3.70; N, 12.84. Found: C, 51.29; H, 3.75; N, 12.90.

*4.4.3. 11-Phenyl-10-thia-7,8,12-triaza-tricyclo-[4.3.3.0^{1,6}]dodec-11-en-9-one (**11c**)*

Colourless oil; IR (Nujol) ν_{max} 3428, 3219, 3160, 1687 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.37–1.56 (m, 3H, cy), 1.59–1.66 (m, 1H, cy), 1.86–1.93 (m, 1H, cy), 1.98–2.04 (m, 1H, cy), 2.06–2.22 (m, 2H, cy), 5.92 (br s, 1H, NH), 6.21 (br s, 1H, NH), 7.47 (dt, 2H, ^3J=8.0 Hz, ^4J=1.6 Hz, Ar), 7.51 (dt, 1H, ^3J=7.2 Hz, ^4J=1.4 Hz, Ar), 7.84 (dt, 2H, ^3J=7.2 Hz, ^4J=1.6 Hz, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.1 (t), 20.5 (t), 28.7 (t), 31.0 (t), 63.7 (s), 99.0 (s), 128.6 (d), 129.0 (d), 131.8 (d), 132.4 (s), 169.4 (s), 175.3 (s); MS (EI) *m/z* (%) 273 (91) [M^+], 245 (58), 215 (72), 195 (100), 167 (42), 139 (13). Anal. Calcd for $C_{14}H_{15}N_3OS$: C, 61.51; H, 5.53; N, 15.37. Found: C, 61.59; H, 5.44; N, 15.29.

*4.4.4. 11-(4-Methoxy-phenyl)-10-thia-7,8,12-triaza-tricyclo-[4.3.3.0^{1,6}]dodec-11-en-9-one (**11d**)*

Colourless oil; IR (Nujol) ν_{max} 3443, 3354, 3232, 3178, 1693 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 1.15–1.31 (m,

2H, cy), 1.43–1.71 (m, 3H, cy), 1.91–2.20 (m, 3H, cy), 3.85 (s, 3H, OCH_3), 5.21 (br s, 1H, NH), 6.91 (d, 2H, ^3J=7.2 Hz, Ar), 7.83 (d, 2H, ^3J=7.2 Hz, Ar), 8.79 (br s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.3 (t), 20.7 (t), 29.1 (t), 31.3 (t), 55.5 (q), 63.6 (s), 98.9 (s), 114.0 (d), 124.4 (s), 130.6 (d), 136.1 (s), 169.2 (s), 175.4 (s); MS (EI) *m/z* (%) 303 (69) [M^+], 275 (38), 244 (21), 196 (100), 169 (72), 138 (66). Anal. Calcd for $C_{15}H_{17}N_3O_2S$: C, 59.39; H, 5.65; N, 13.85. Found: C, 59.47; H, 5.71; N, 13.77.

*4.4.5. 11-(4-Chloro-phenyl)-10-thia-7,8,12-triaza-tricyclo-[4.3.3.0^{1,6}]dodec-11-en-9-one (**11e**)*

Colourless oil; IR (Nujol) ν_{max} 3426, 3211, 3154, 1703, 1649 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.45–1.66 (m, 4H, cy), 1.81–1.88 (m, 1H, cy), 1.95–2.05 (m, 1H, cy), 2.05–2.24 (m, 2H, cy), 5.17 (br s, 1H, NH), 7.40 (d, 2H, ^3J=7.8 Hz, Ar), 7.78 (d, 2H, ^3J=7.8 Hz, Ar), 9.02 (br s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.0 (t), 20.5 (t), 28.6 (t), 31.0 (t), 64.0 (s), 99.2 (s), 128.9 (d), 129.8 (d), 130.4 (s), 138.6 (s), 167.9 (s), 175.4 (s); MS (EI) *m/z* (%) 309 (16) [M^++2], 307 (46) [M^+], 281 (2), 283 (8), 250 (16), 248 (46), 196 (100), 168 (39), 167 (54). Anal. Calcd for $C_{14}H_{14}ClN_3OS$: C, 54.63; H, 4.58; N, 13.65. Found: C, 54.71; H, 4.52; N, 13.71.

*4.4.6. 11-(2,4-Difluoro-phenyl)10-thia-7,8,12-triaza-tricyclo[4.3.3.0^{1,6}]dodec-11-en-9-one (**11f**)*

Colourless oil; IR (Nujol) ν_{max} 3428, 3369, 3219, 3160, 1687 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.40–1.63 (m, 4H, cy), 1.69–1.75 (m, 1H, cy), 1.85–1.91 (m, 1H, cy), 2.09–2.21 (m, 2H, cy), 5.12 (br s, 1H, NH), 6.81–6.92 (m, 2H, Ar), 7.90–7.98 (m, 1H, Ar), 8.01 (br s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.8 (t), 20.2 (t), 28.0 (t), 30.8 (t), 63.2 (s), 97.6 (s), 104.5 (d, $^2J_{CF}$=25.8 Hz), 111.9 (d, $^2J_{CF}$=21.3 Hz), 116.8 (s, $^2J_{CF}$=10.6 Hz), 132.0 (d, $^3J_{CF}$=10.7 Hz), 161.2 (s, $^1J_{CF}$=245.0 Hz, $^3J_{CF}$=12.2 Hz), 162.1 (s), 164.9 (s, $^1J_{CF}$=254.0 Hz, $^3J_{CF}$=12.2 Hz), 175.4 (s); MS (EI) *m/z* (%) 309 (100) [M^+], 281 (43), 231 (57), 195 (100), 137 (21). Anal. Calcd for $C_{14}H_{13}F_2N_3OS$: C, 54.36; H, 4.24; N, 13.58. Found: C, 54.29; H, 4.21; N, 13.65.

*4.4.7. 4-Methyl-11-phenyl-10-thia-7,8,12-triaza-tricyclo-[4.3.3.0^{1,6}]dodec-11-en-9-one (**11g**)*

Colourless oil; IR (Nujol) ν_{max} 3430, 3394, 3256, 3104, 1683 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.96 (d, 3H, ^3J=6.4 Hz, CHCH_3), 1.08–1.29 (m, 2H, cy), 1.46–1.52 (m, 1H, cy), 1.67–1.72 (m, 2H, cy), 2.22 (d, 1H, ^3J=14.4 Hz, cy), 2.45 (d, 1H, ^3J=11.6 Hz, cy), 4.90 (br s, 1H, NH), 7.40 (t, 2H, ^3J=7.6 Hz, Ar), 7.46 (t, 1H, ^3J=7.6 Hz, Ar), 7.82 (d, 2H, ^3J=7.2 Hz, Ar), 8.62 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$) δ 21.5 (q), 26.9 (t), 27.2 (d), 28.1 (t), 38.9 (t), 63.0 (s), 99.5 (s), 128.4 (d), 128.5 (d), 132.0 (d), 132.2 (s), 166.0 (s), 176.1 (s); MS (EI) *m/z* (%) 287 (100) [M^+], 231 (18), 211 (3). Anal. Calcd for $C_{15}H_{17}N_3OS$: C, 62.69; H, 5.96; N, 14.62. Found: C, 62.60; H, 5.91; N, 14.67.

*4.4.8. 13-Phenyl-12-thia-9,10,14-triaza-tricyclo-[6.3.3.0^{1,8}]tetradec-13-en-11-one (**11h**)*

Colourless oil; IR (Nujol) ν_{max} 3445, 3234, 3168, 1701 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26–1.46 (m, 4H, cy), 1.52–1.83 (m, 4H, cy), 1.97–2.09 (m, 2H, cy), 2.26–2.33 (m, 1H, cy), 2.41–2.47 (m, 1H, cy), 5.20 (br s, 1H, NH), 7.43 (t, 2H, ^3J=7.2 Hz, Ar), 7.51 (t, 1H, ^3J=7.2 Hz, Ar), 7.88 (d, 2H, ^3J=8.0 Hz, Ar), 8.1 (br s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.0 (t), 25.0 (t), 25.4 (t), 28.3 (t), 29.7 (t), 32.8 (t), 69.8 (s), 104.1 (s), 128.5 (d), 128.6 (d), 132.0 (d), 132.4 (s), 166.7 (s), 177.2 (s); MS (EI) *m/z* (%) 301 (100) [M^+], 273 (75), 243 (92), 223 (58), 195 (34), 166 (60). Anal. Calcd for $C_{16}H_{19}N_3OS$: C, 63.76; H, 6.35; N, 13.94. Found: C, 63.82; H, 6.36; N, 13.89.

*4.4.9. 13-(4-Methoxy-phenyl)-12-thia-9,10,14-triaza-tricyclo[6.3.3.0^{1,8}]tetradec-13-en-11-one (**11i**)*

Colourless oil; IR (Nujol) ν_{max} 3424, 3356, 3224, 3176, 1694 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26–1.36 (m, 3H, cy), 1.48–1.82 (m, 3H, cy), 2.03–2.16 (m, 2H, cy), 2.21–2.31 (m, 2H, cy), 2.35–2.41 (m, 1H, cy), 2.45–2.56 (m, 1H, cy), 3.86 (s, 3H, OCH_3), 5.13 (br s, 1H, NH), 6.92 (d, 2H, ^3J=6.8 Hz, Ar), 7.77 (d, 2H, ^3J=6.8 Hz, Ar), 8.41 (br s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.1 (t), 25.1 (t), 25.5 (t), 27.1 (t), 29.1 (t), 32.6 (t), 55.2 (q), 70.3 (s), 102.3 (s), 114.1 (d), 125.7 (s), 129.8 (d), 160.3 (s), 167.6 (d), 178.3 (s); MS (EI) *m/z* (%) 331 (84) [M^+], 303 (54), 273 (100), 195 (53), 165 (37). Anal. Calcd for $C_{17}H_{21}N_3O_2S$: C, 61.61; H, 6.39; N, 12.68. Found: C, 61.71; H, 6.32; N, 12.73.

*4.4.10. 13-(4-Chloro-phenyl)-12-thia-9,10,14-triaza-tricyclo[6.3.3.0^{1,8}]tetradec-13-en-11-one (**11j**)*

Colourless oil; IR (Nujol) ν_{max} 3431, 3232, 3143, 1698 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26–1.35 (m, 2H, cy), 1.46–1.58 (m, 2H, cy), 1.59–1.70 (m, 2H, cy), 1.71–1.81 (m, 2H, cy), 1.95–2.05 (m, 2H, cy), 2.24–2.28 (m, 1H, cy), 2.40–2.44 (m, 1H, cy), 4.58 (br s, 1H, NH), 7.39 (d, 2H, ^3J=8.4 Hz, Ar), 7.80 (d, 2H, ^3J=8.4 Hz, Ar), 7.94 (br s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.8 (t), 24.9 (t), 25.3 (t), 26.0 (t), 28.2 (t), 32.5 (t), 70.4 (s), 103.8 (s), 128.8 (d), 129.8 (d), 130.8 (s), 138.2 (s), 165.1 (s), 177.0 (s); MS (EI) *m/z* (%) 337 (36) [M^++2], 335 (100) [M^+], 309 (13), 307 (42), 223 (67), 195 (38), 165 (69). Anal. Calcd for $C_{16}H_{18}ClN_3OS$: C, 57.22; H, 5.40; N, 12.51. Found: C, 57.32; H, 5.46; N, 12.53.

*4.5. General procedure for the syntheses of ethyl 1[(4-chlorobenzoyl)thio]-2-iminocycloalkylcarboxylates **12a**,**b** and ethyl 1[(4-chlorobenzoyl)thio]-2-oxocycloalkylcarboxylates **13a**,**b***

To a magnetically stirred solution of ethyl 3a-[2-(aminocarbonyl)hydrazino]-2-(4-chlorophenyl)-3a,4,5,6,7,7a-hexahydro-1,3-benzothiazole-7a-carboxylate **9g** (1.0 mmol) or ethyl 3a-[2-(aminocarbonyl)hydrazino]-2-(4-chlorophenyl)-3a,4,5,6,7,8,9,9a-octahydrocycloocta[*d*][1,3]thiazoline-9a-carboxylate **9s** (1.0 mmol) in acetone–water=9:1 (30 mL) 4 equiv of Amberlyst 15H was

added at room temperature. The mixture was allowed to stand at room temperature under magnetic stirring (6.0–15.0 h) until the disappearance of the reagents (monitored by TLC chromatography). The resin was removed by filtration and the reaction solvent was evaporated under reduced pressure. Then the crude was chromatographed on silica gel column (elution mixtures: ethyl acetate–cyclohexane) to obtain pure products **12a**,**b** and **13a**,**b** that were crystallized from ethyl acetate–cyclohexane.

*4.5.1. Ethyl 1[(4-chlorobenzoyl)thio]-2-iminocyclohexane-carboxylate (**12a**)*

Colourless powder, mp 142–145 °C; IR (Nujol) ν_{max} 3252, 1758, 1738, 1674 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.22–1.30 (m, 3H, OCH_2CH_3), 1.84–1.98 (m, 4H, cy), 2.22–2.32 (m, 1H, cy), 2.65–2.78 (m, 3H, cy), 4.17–4.31 (m, 2H, OCH_2CH_3), 5.32 (br s, 1H, NH), 7.37 (d, 2H, ^3J=8.4 Hz, Ar), 7.73 (d, 2H, ^3J=8.4 Hz, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8 (q), 22.2 (t), 26.1 (t), 36.7 (t), 40.4 (t), 62.5 (t), 67.5 (s), 104.4 (s), 128.5 (d), 128.8 (d), 134.4 (s), 140.0 (s), 168.2 (s), 188.4 (s); MS (EI) *m/z* (%) 341 (9) [M^++2], 339 (31) [M^+], 296 (23), 294 (67), 267 (31), 265 (100), 225 (42), 199 (31), 182 (58), 154 (26). Anal. Calcd for $C_{16}H_{18}ClNO_3S$: C, 56.55; H, 5.34; N, 4.12. Found: C, 56.43; H, 5.39; N, 4.23.

*4.5.2. Ethyl 1[(4-chlorobenzoyl)thio]-2-iminocyclooctane-carboxylate (**12b**)*

Colourless powder, mp 151–154 °C; IR (Nujol) ν_{max} 3247, 1765, 1724, 1658 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.22–1.35 (m, 3H, OCH_2CH_3), 1.40–1.50 (m, 2H, cy), 1.54–1.64 (m, 2H, cy), 1.67–1.75 (m, 3H, cy), 1.87–1.94 (m, 1H, cy), 2.06–2.13 (m, 1H, cy), 2.20–2.30 (m, 2H, cy), 2.50–2.59 (m, 1H, cy), 4.17–4.32 (m, 2H, OCH_2CH_3), 5.04 (br s, 1H, NH), 7.37 (d, 2H, ^3J=8.4 Hz, Ar), 7.73 (d, 2H, ^3J=8.4 Hz, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9 (q), 22.8 (t), 23.1 (t), 24.4 (t), 25.7 (t), 29.1 (t), 34.7 (t), 62.1 (t), 71.2 (s), 107.8 (s), 128.7 (d), 129.3 (d), 131.2 (s), 137.9 (s), 161.8 (s), 173.0 (s); MS (EI) *m/z* (%) 369 (13) [M^++2], 367 (43) [M^+], 340 (9), 338 (32), 322 (56), 295 (27), 293 (100), 183 (7), 168 (4). Anal. Calcd for $C_{18}H_{22}ClNO_3S$: C, 58.77; H, 6.03; N, 3.81. Found: C, 58.61; H, 5.96; N, 3.77.

*4.5.3. Ethyl 1[(4-chlorobenzoyl)thio]-2-oxocyclohexane-carboxylate (**13a**)*

Colourless powder, mp 127–129 °C; IR (Nujol) ν_{max}1756, 1725, 1713, 1628 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.24 (t, 3H, ^3J=7.2 Hz, OCH_2CH_3), 1.84–1.99 (m, 4H, cy), 2.27–2.29 (m, 1H, cy), 2.65–2.76 (m, 3H, cy), 4.23 (q, 2H, ^3J=7.2 Hz, OCH_2CH_3), 7.38 (d, 2H, ^3J=8.4 Hz, Ar), 7.81 (d, 2H, ^3J=8.4 Hz, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8 (q), 22.2 (t), 26.1 (t), 36.7 (t), 40.4 (t), 62.5 (t), 67.5 (s), 128.5 (d), 128.8 (d), 134.4 (s), 140.0 (s), 168.2 (s), 188.4 (s), 201.0 (s); MS (EI) *m/z* (%) 342 (2) [M^++2], 340 (9) [M^+], 156 (6), 139 (100), 127 (3). Anal. Calcd for $C_{16}H_{17}ClO_4S$: C, 56.38; H, 5.03; S, 9.41. Found: C, 56.41; H, 5.12; S, 9.50.

*4.5.4. Ethyl 1[(4-chlorobenzoyl)thio]-2-oxocyclooctane-carboxylate (**13b**)*

Colourless powder, mp 118–121 °C; IR (Nujol) ν_{max} 3198, 1746, 1731, 1647 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.86–0.92 (m, 1H, cy), 1.19 (t, 3H, ^3J=7.2 Hz, OCH_2CH_3), 1.17–1.25 (m, 2H, cy), 1.55–1.80 (m, 3H, cy), 2.00–2.07 (m, 2H, cy), 2.31–2.44 (m, 2H, cy), 2.71–2.81 (m, 2H, cy), 4.14 (t, 2H, ^3J=7.2 Hz, OCH_2CH_3), 7.31 (d, 2H, ^3J=8.4 Hz, Ar), 7.64 (d, 2H, ^3J=8.4 Hz, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1 (q), 23.7 (t), 25.4 (t), 25.8 (t), 28.8 (t), 38.1 (t), 39.7 (t), 62.1 (t), 67.6 (s), 127.4 (d), 132.0 (d), 133.8 (s), 140.9 (s), 166.2 (s), 189.6 (s), 202.3 (s); MS (EI) *m/z* (%) 370 (29) [M^++2], 368 (100) [M^+], 324 (3), 322 (8), 296 (24), 294 (77), 256 (23), 211 (37), 183 (27), 155 (23). Anal. Calcd for $C_{18}H_{21}ClO_4S$: C, 58.61; H, 5.74; S, 8.69. Found: C, 58.50; H, 5.69; S, 8.79.

*4.6. General procedure for the syntheses of 4-oxo-1-thia-3-azaspiro[4.4]non-6-ylidenes **16a–d**, 4-oxo-1-thia-3-azaspiro[4.5]dec-6-ylidenes **16e–n**, 4-oxo-1-thia-3-azaspiro[4.6]undec-6-ylidenes **16o–q** and 4-oxo-1-thia-3-azaspiro[4.7]dodec-6-ylidenes **16r–t***

Cycloalkenyl-1-diazenes **5a–h** (1.0 mmol) were added to a magnetically stirred solution of thioureas **14a–c** (1.0 mmol) in methanol (4 mL) at room temperature. The reaction was allowed to stand under magnetic stirring at room temperature (0.1–1.5 h) until the disappearance of the reagents (monitored by TLC chromatography). Compounds **16** crystallized directly from the reaction medium and were collected as pure products by filtration.

*4.6.1. 2-(2-Imino-4-oxo-1-thia-3-azaspiro[4.4]non-6-yliden)-1-hydrazinecarboxamide (**16a**)*

Colourless powder, mp 233–236 °C with decomposition; IR (Nujol) ν_{max} 3457, 3185, 3158, 1728, 1705, 1650, 1586 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.66–1.75 (m, 1H, cy), 2.10–2.17 (m, 2H, cy), 2.30–2.48 (m, 3H, cy), 6.04 (br s, 2H, NH_2), 8.84 (s, 1H, NH), 9.08 (s, 1H, NH), 9.21 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 22.8 (t), 27.9 (t), 38.6 (t), 71.0 (s), 156.1 (s), 156.4 (s), 180.4 (s), 189.0 (s); MS (EI) *m/z* (%) 241 (9) [M^+], 224 (17), 198 (42), 182 (90), 156 (23), 143 (43), 129 (100), 114 (86). Anal. Calcd for $C_8H_{11}N_5O_2S$: C, 39.83; H, 4.60; N, 29.03. Found: C, 39.76; H, 4.68; N, 29.08.

*4.6.2. 2-[3-Methyl-2-(methylimino)-4-oxo-1-thia-3-azaspiro[4.4]non-6-yliden]-1-hydrazinecarboxamide (**16b**)*

Colourless powder, mp 201–204 °C with decomposition; IR (Nujol) ν_{max} 3387, 3191, 1731, 1708, 1653, 1632 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.74–1.81 (m, 1H, cy), 2.01–2.20 (m, 2H, cy), 2.29–2.49 (m, 3H, cy), 3.02 (s, 3H, NCH_3), 3.07 (s, 3H, NCH_3), 6.08 (br s, 2H, NH_2), 9.14 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 22.4 (t), 27.6 (t), 29.3 (q), 38.1 (q), 62.7 (s), 151.7 (s), 155.2 (s), 156.3 (s), 173.7 (s); MS (EI) *m/z* (%) 269 (52) [M^+], 252 (4), 225 (4), 210 (6), 196 (6), 170 (42), 157 (100), 127 (22), 112

(22). Anal. Calcd for $C_{10}H_{15}N_5O_2S$: C, 44.60; H, 5.61; N, 26.00. Found: C, 44.66; H, 5.65; N, 26.03.

4.6.3. 2-[3-Ethyl-2-(ethylimino)-4-oxo-1-thia-3-aza-spiro[4.4]non-6-yliden]-1-hydrazinecarboxamide (**16c**)

Colourless powder, mp 192–193 °C; IR (Nujol) ν_{max} 3392, 3258, 3138, 1720, 1698, 1644 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.08 (t, 3H, ^3J=7.2 Hz, NCH_2CH_3), 1.16 (t, 3H, ^3J=7.2 Hz, NCH_2CH_3), 1.71–1.91 (m, 1H, cy), 2.01–2.12 (m, 2H, cy), 2.18–2.40 (m, 3H, cy), 3.10 (q, 2H, ^3J=7.2 Hz, NCH_2CH_3), 3.67 (q, 2H, ^3J=7.2 Hz, NCH_2CH_3), 6.06 (br s, 2H, NH_2), 9.36 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 12.3 (q), 15.7 (q), 22.5 (t), 27.6 (t), 37.3 (t), 38.2 (t), 46.3 (t), 62.3 (s), 148.9 (s), 155.8 (s), 156.3 (s), 173.5 (s); MS (EI) *m/z* (%) 297 (67) [M^+], 280 (1), 253 (4), 238 (12), 224 (6), 198 (38), 185 (100), 157 (15), 112 (20). Anal. Calcd for $C_{12}H_{19}N_5O_2S$: C, 48.47; H, 6.44; N, 23.55. Found: C, 48.39; H, 6.45; N, 23.42.

4.6.4. tert-Butyl 2-(2-imino-4-oxo-1-thia-3-aza-spiro[4.4]non-6-yliden)-1-hydrazinecarboxylate (**16d**)

Colourless powder, mp 167–169 °C with decomposition; IR (Nujol) ν_{max} 3429, 3203, 3136, 1724, 1711, 1685, 1594 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.42 (s, 9H, $C(CH_3)_3$), 1.72–1.81 (m, 1H, cy), 2.16–2.28 (m, 2H, cy), 2.38–2.44 (m, 2H, cy), 2.45–2.60 (m, 1H, cy), 5.07 (br s, 1H, NH), 8.13 (br s, 1H, NH), 8.80 (br s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.2 (t), 27.7 (t), 28.2 (q), 39.3 (t), 70.5 (s), 81.2 (s), 153.1 (s), 159.6 (s), 181.5 (s), 189.9 (s); MS (EI) *m/z* (%) 298 (2) [M^+], 242 (100), 225 (35), 198 (65), 182 (41), 169 (44), 156 (16), 129 (100), 114 (87). Anal. Calcd for $C_{12}H_{18}N_4O_3S$: C, 48.31; H, 6.08; N, 18.78. Found: C, 48.28; H, 6.11; N, 18.84.

4.6.5. 2-(2-Imino-4-oxo-1-thia-3-azaspiro[4.5]dec-6-yliden)-1-hydrazinecarboxamide (**16e**)

Colourless powder, mp 186–189 °C with decomposition; IR (Nujol) ν_{max} 3404, 3216, 3176, 1735, 1712, 1675 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.34–1.40 (m, 2H, cy), 1.75–1.97 (m, 4H, cy), 2.17–2.27 (m, 1H, cy), 2.95–3.06 (m, 1H, cy), 5.69 and 6.39 (2br s, 2H, NH_2), 8.73 (s, 1H, NH), 8.95 (s, 1H, NH), 9.54 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 23.8 (t), 24.0 (t), 25.3 (t), 37.1 (t), 72.9 (s), 149.0 (s), 157.2 (s), 179.9 (s), 187.9 (s); MS (EI) *m/z* (%) 256 (3) [M^++1], 226 (14), 167 (22), 153 (100), 111 (77). Anal. Calcd for $C_9H_{13}N_5O_2S$: C, 42.34; H, 5.13; N, 27.43. Found: C, 42.26; H, 5.06; N, 27.49.

4.6.6. 2-[3-Methyl-2-(methylimino)-4-oxo-1-thia-3-aza-spiro[4.5]dec-6-yliden]-1-hydrazinecarboxamide (**16f**)

Colourless powder, mp 191–194 °C with decomposition; IR (Nujol) ν_{max} 3465, 3244, 3191, 3142, 1722, 1696, 1652 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.39–1.48 (m, 2H, cy), 1.81–2.10 (m, 4H, cy), 2.29–2.38 (m, 1H, cy), 2.95–3.03 (m, 1H, cy), 3.04 (s, 3H, NCH_3), 3.10 (s, 3H, NCH_3), 5.94 (br s, 2H, NH_2), 9.48 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 22.2 (t), 23.7 (t), 24.1 (t), 29.0 (q), 36.5 (t), 38.3 (q), 63.6 (s), 148.2 (s), 151.0 (s), 156.9 (s), 173.0 (s); MS (EI) *m/z* (%) 283 (21) [M^+], 266 (13), 240 (2), 224 (96), 210 (9), 170 (7), 157 (100), 141 (14). Anal. Calcd for $C_{11}H_{17}N_5O_2S$: C, 46.63; H, 6.05; N, 24.72. Found: C, 46.67; H, 6.09; N, 24.68.

4.6.7. 2-[3-Ethyl-2-(ethylimino)-4-oxo-1-thia-3-aza-spiro[4.5]dec-6-yliden]-1-hydrazinecarboxamide (**16g**)

Colourless powder, mp 200–202 °C; IR (Nujol) ν_{max} 3436, 3165, 1713, 1703, 1643, 1591 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.09 (t, 3H, ^3J=7.2 Hz, NCH_2CH_3), 1.15 (t, 3H, ^3J=7.2 Hz, NCH_2CH_3), 1.39–1.48 (m, 2H, cy), 1.79–2.06 (m, 4H, cy), 2.27–2.38 (m, 1H, cy), 3.01 (d, 1H, ^3J=15.6 Hz, cy), 3.14–3.28 (m, 2H, NCH_2CH_3), 3.69 (q, 2H, ^3J=7.2 Hz, NCH_2CH_3), 5.84 and 6.17 (2br s, 2H, NH_2), 9.59 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ 12.4 (q), 15.8 (q), 22.2 (t), 23.7 (t), 24.1 (t), 36.4 (t), 37.1 (t), 46.3 (t), 63.2 (s), 148.2 (s), 148.5 (s), 156.9 (s), 172.6 (s); MS (EI) *m/z* (%) 311 (25) [M^+], 294 (9), 252 (100), 238 (5), 153 (2), 110 (11). Anal. Calcd for $C_{13}H_{21}N_5O_2S$: C, 50.14; H, 6.80; N, 22.49. Found: C, 50.19; H, 6.75; N, 22.55.

4.6.8. tert-Butyl 2-[3-methyl-2-(methylimino)-4-oxo-1-thia-3-azaspiro[4.5]dec-6-yliden]-1-hydrazinecarboxylate (**16h**)

Colourless powder, mp 152–154 °C; IR (Nujol) ν_{max} 3296, 3175, 1718, 1704, 1678, 1629 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.45 (s, 9H, $C(CH_3)_3$), 1.54–1.63 (m, 2H, cy), 1.97–2.14 (m, 4H, cy), 2.52–2.59 (m, 1H, cy), 2.74–2.81 (m, 1H, cy), 3.10 (s, 3H, NCH_3), 3.20 (s, 3H, NCH_3), 7.98 (br s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.5 (t), 23.6 (t), 23.9 (t), 28.1 (t), 29.2 (q), 37.0 (q), 38.6 (q), 63.4 (s), 81.2 (s), 150.8 (s), 151.8 (s), 152.9 (s), 173.4 (s); MS (EI) *m/z* (%) 341 (1) [M^++1], 284 (56), 267 (4), 240 (3), 224 (20), 211 (9), 184 (4), 170 (7), 157 (100), 116 (13). Anal. Calcd for $C_{15}H_{24}N_4O_3S$: C, 52.92; H, 7.11; N, 16.46. Found: C, 52.86; H, 7.14; N, 16.40.

4.6.9. N1-Phenyl-2-(2-imino-4-oxo-1-thia-3-aza-spiro[4.5]dec-6-yliden)-1-hydrazinecarboxamide (**16i**)

Colourless powder, mp 196–198 °C with decomposition; IR (Nujol) ν_{max} 3405, 3206, 3163, 1732, 1716, 1637, 1564 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.39–1.50 (m, 2H, cy), 1.79–2.03 (m, 4H, cy), 2.23–2.34 (m, 1H, cy), 3.00–3.07 (m, 1H, cy), 7.02 (t, 1H, ^3J=7.2 Hz, Ar), 7.33 (d, 2H, ^3J=7.2 Hz, Ar), 7.38 (d, 2H, ^3J=7.6 Hz, Ar), 8.28 (s, 1H, NH), 8.81 (s, 1H, NH), 9.07 (s, 1H, NH), 10.14 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 23.9 (t), 25.6 (t), 37.0 (t), 72.9 (s), 118.1 (d), 122.5 (d), 129.0 (d), 138.5 (s), 150.6 (s), 153.2 (s), 179.1 (s), 188.0 (s); MS (EI) *m/z* (%) 331 (1) [M^+], 284 (1), 256 (12), 212 (21), 196 (17), 182 (14), 153 (81), 129 (64), 119 (100). Anal. Calcd for $C_{15}H_{17}N_5O_2S$: C, 54.37; H, 5.17; N, 21.13. Found: C, 54.34; H, 5.12; N, 21.15.

4.6.10. N1-Phenyl-2-[3-methyl-2-(methylimino)-4-oxo-1-thia-3-azaspiro[4.5]dec-6-yliden]-1-hydrazinecarboxamide (**16j**)

Colourless powder, mp 206–208 °C; IR (Nujol) ν_{max} 3368, 3188, 1720, 1699, 1646, 1598 cm^{-1}; ^1H NMR (400 MHz,

DMSO-d_6) δ 1.44–1.52 (m, 2H, cy), 1.80–1.93 (m, 2H, cy), 1.98–2.14 (m, 2H, cy), 2.30–2.41 (m, 1H, cy), 3.01–3.12 (m, 1H, cy), 3.04 (s, 3H, NCH_3), 3.18 (s, 3H, NCH_3), 7.03 (t, 1H, ^3J=7.2 Hz, Ar), 7.32 (t, 2H, ^3J=7.2 Hz, Ar), 7.40 (d, 2H, ^3J=7.6 Hz, Ar), 8.10 (s, 1H, NH), 10.17 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 22.2 (t), 23.8 (t), 24.4 (t), 29.1 (q), 36.5 (t), 38.3 (q), 63.7 (s), 118.2 (d), 122.6 (d), 129.0 (d), 138.4 (s), 149.9 (s), 150.8 (s), 153.0 (s), 173.0 (s); MS (EI) *m/z* (%) 359 (28) [M^+], 267 (96), 240 (18), 224 (52), 211 (23), 185 (8), 157 (80). Anal. Calcd for $C_{17}H_{21}N_5O_2S$: C, 56.81; H, 5.89; N, 19.48. Found: C, 56.78; H, 5.96; N, 19.44.

*4.6.11. N1-Phenyl-2-[3-ethyl-2-(ethylimino)-4-oxo-1-thia-3-azaspiro[4.5]dec-6-yliden]-1-hydrazinecarboxamide (**16k**)*

Colourless powder, mp 186–188 °C; IR (Nujol) ν_{max} 3454, 3179, 1721, 1708, 1664, 1584 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.09–1.20 (m, 6H, $2NCH_2CH_3$), 1.42–1.51 (m, 2H, cy), 1.81–1.91 (m, 2H, cy), 1.98–2.09 (m, 2H, cy), 2.30–2.40 (m, 1H, cy), 3.01–3.09 (m, 1H, cy), 3.16–3.34 (m, 2H, NCH_2CH_3), 3.70–3.82 (m, 2H, NCH_2CH_3), 7.02 (t, 1H, ^3J=7.2 Hz, Ar), 7.31 (t, 2H, ^3J=7.2 Hz, Ar), 7.38 (d, 2H, ^3J=7.6 Hz, Ar), 8.05 (s, 1H, NH), 10.16 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 15.5 (q), 15.8 (q), 22.2 (t), 23.8 (t), 24.6 (t), 36.6 (t), 37.3 (t), 46.4 (t), 63.4 (s), 118.3 (d), 122.7 (d), 129.0 (d), 138.3 (s), 148.0 (s), 150.3 (s), 153.0 (s), 172.7 (s); MS (EI) *m/z* (%) 387 (27) [M^+], 295 (100), 266 (12), 252 (37), 239 (19), 185 (42). Anal. Calcd for $C_{19}H_{25}N_5O_2S$: C, 58.89; H, 6.50; N, 18.07. Found: C, 58.93; H, 6.46; N, 18.00.

*4.6.12. 2-(2-Imino-8-methyl-4-oxo-1-thia-3-azaspiro-[4.5]dec-6-yliden)-1-hydrazinecarboxamide (**16l**)*

Colourless powder, mp 212–215 °C with decomposition; IR (Nujol) ν_{max} 3354, 3162, 3139, 1721, 1698, 1608 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 0.96 (d, 3H, ^3J=6.4 Hz, $CHCH_3$), 0.98–1.13 (m, 1H, cy), 1.40–1.50 (m, 1H, cy), 1.56–1.63 (m, 1H, cy), 1.85–1.96 (m, 2H, cy), 2.20–2.30 (m, 1H, cy), 3.08–3.17 (m, 1H, cy), 5.60 and 6.17 (2br s, 2H, NH_2), 8.72 (s, 1H, NH), 8.94 (s, 1H, NH), 9.50 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 21.9 (q), 31.1 (q), 32.7 (t), 33.4 (t), 36.6 (t), 72.5 (s), 148.9 (s), 157.1 (s), 178.9 (s), 187.8 (s); MS (EI) *m/z* (%) 269 (2) [M^+], 252 (5), 226 (11), 210 (42), 196 (11), 184 (12), 167 (15), 152 (75), 129 (43), 110 (100). Anal. Calcd for $C_{10}H_{15}N_5O_2S$: C, 44.60; H, 5.61; N, 26.00. Found: C, 44.27; H, 5.76; N, 26.05.

*4.6.13. 2-[3,8-Dimethyl-2-(methylimino)-4-oxo-1-thia-3-azaspiro[4.5]dec-6-yliden]-1-hydrazinecarboxamide (**16m**)*

Colourless powder, mp 201–203 °C; IR (Nujol) ν_{max} 3419, 3214, 1716, 1703, 1665, 1587 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 0.96 (d, 3H, ^3J=6.4 Hz, $CHCH_3$), 1.10–1.21 (m, 1H, cy), 1.51–1.63 (m, 2H, cy), 1.81–1.89 (m, 1H, cy), 2.00–2.09 (m, 1H, cy), 2.29–2.39 (m, 1H, cy), 3.01–3.10 (m, 1H, cy), 3.03 (s, 3H, NCH_3), 3.07 (s, 3H, NCH_3), 5.81 and 6.15 (2br s, 2H, NH_2), 9.55 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 21.8 (q), 29.0 (t), 31.0 (d), 32.0 (q), 36.0 (t), 38.2 (t), 38.3 (q), 63.1 (s), 148.2 (s), 150.9 (s), 156.8 (s), 172.9 (s); MS (EI) *m/z* (%) 297 (10) [M^+], 280 (6), 238 (47), 225 (5), 157 (70), 104 (100). Anal. Calcd for $C_{12}H_{19}N_5O_2S$: C, 48.47; H, 6.44; N, 23.55. Found: C, 48.54; H, 6.39; N, 23.61.

*4.6.14. 2-[3-Ethyl-2-(ethylimino)-8-methyl-4-oxo-1-thia-3-azaspiro[4.5]dec-6-yliden]-1-hydrazinecarboxamide (**16n**)*

Colourless powder, mp 193–196 °C with decomposition; IR (Nujol) ν_{max} 3382, 3246, 3176, 1717, 1704, 1663 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 0.96 (d, 3H, ^3J=6.0 Hz, $CHCH_3$), 1.01–1.11 (m, 4H, cy and NCH_2CH_3), 1.15 (t, 3H, ^3J=7.6 Hz, NCH_2CH_3), 1.50–1.69 (m, 2H, cy), 1.81–1.90 (m, 1H, cy), 1.97–2.05 (m, 1H, cy), 2.26–2.38 (m, 1H, cy), 3.06–3.13 (m, 1H, cy), 3.14–3.30 (m, 2H, NCH_2CH_3), 3.70 (q, 2H, ^3J=7.6 Hz, NCH_2CH_3), 5.56 and 6.41 (2br s, 2H, NH_2), 9.58 and 9.63 (2s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 13.1 (q), 16.5 (q), 22.5 (q), 28.8 (t), 31.5 (d), 31.7 (t), 36.6 (t), 37.8 (t), 47.1 (t), 63.4 (s), 148.8 (s), 149.2 (s), 157.5 (s), 173.3 (s); MS (EI) *m/z* (%) 325 (11) [M^+], 308 (3), 293 (5), 279 (9), 266 (33), 252 (4), 237 (3), 220 (30), 185 (30), 167 (34), 149 (100). Anal. Calcd for $C_{14}H_{23}N_5O_2S$: C, 51.67; H, 7.12; N, 21.52. Found: C, 51.58; H, 7.17; N, 21.57.

*4.6.15. 2-(2-Imino-4-oxo-1-thia-3-azaspiro[4.6]undec-6-yliden)-1-hydrazinecarboxamide (**16o**)*

Colourless powder, mp 185–187 °C; IR (Nujol) ν_{max} 3416, 3220, 3168, 1719, 1701, 1641, 1564 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.36–1.57 (m, 5H, cy), 1.81–1.90 (m, 1H, cy), 1.97–2.07 (m, 1H, cy), 2.24–2.31 (m, 1H, cy), 3.11–3.18 (m, 2H, cy), 5.67 and 6.43 (2br s, 2H, NH_2), 8.74 (s, 1H, NH), 8.96 (s, 1H, NH), 9.50 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 25.1 (t), 26.6 (t), 27.5 (t), 29.6 (t), 37.4 (t), 74.2 (s), 150.6 (s), 156.9 (s), 179.1 (s), 189.0 (s); MS (EI) *m/z* (%) 269 (5) [M^+], 253 (17), 227 (66), 210 (100), 195 (100), 183 (17), 168 (35), 152 (100). Anal. Calcd for $C_{10}H_{15}N_5O_2S$: C, 44.60; H, 5.61; N, 26.00. Found: C, 44.53; H, 5.68; N, 26.13.

*4.6.16. 2-[3-Methyl-2-(methylimino)-4-oxo-1-thia-3-aza-spiro[4.6]undec-6-yliden]-1-hydrazinecarboxamide (**16p**)*

Colourless powder, mp 199–201 °C; IR (Nujol) ν_{max} 3374, 3192, 1716, 1694, 1657, 1625 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.38–1.61 (m, 5H, cy), 1.74–1.81 (m, 1H, cy), 1.98–2.08 (m, 1H, cy), 2.28–2.40 (m, 2H, cy), 2.70–2.78 (m, 1H, cy), 3.02 (s, 3H, NCH_3), 3.06 (s, 3H, NCH_3), 5.59 and 6.45 (2br s, 2H, NH_2), 9.58 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 25.0 (t), 25.6 (t), 27.2 (t), 28.9 (q), 29.6 (t), 37.0 (q), 38.2 (t), 64.2 (s), 150.5 (s), 151.1 (s), 156.7 (s), 174.3 (s); MS (EI) *m/z* (%) 297 (28) [M^+], 280 (3), 254 (3), 238 (42), 225 (4), 199 (23), 157 (100), 141 (30). Anal. Calcd for $C_{12}H_{19}N_5O_2S$: C, 48.47; H, 6.44; N, 23.55. Found: C, 48.55; H, 6.39; N, 23.42.

*4.6.17. 2-[3-Ethyl-2-(ethylimino)-4-oxo-1-thia-3-aza-spiro[4.6]undec-6-yliden]-1-hydrazinecarboxamide (**16q**)*

Colourless powder, mp 204–207 °C; IR (Nujol) ν_{max} 3416, 3296, 3095, 1717, 1695, 1658 cm^{-1}; ^{1}H NMR (400 MHz,

DMSO-d_6) δ 1.05 (t, 3H, ^3J=7.2 Hz, NCH_2CH_3), 1.14 (t, 3H, ^3J=7.2 Hz, NCH_2CH_3), 1.38–1.59 (m, 5H, cy), 1.70–1.81 (m, 1H, cy), 1.91–2.02 (m, 1H, cy), 2.27–2.38 (m, 2H, cy), 2.65–2.75 (m, 1H, cy), 3.11–3.26 (m, 2H, NCH_2CH_3), 3.64 (q, 2H, ^3J=7.2 Hz, NCH_2CH_3), 5.46 and 6.51 (2br s, 2H, NH_2), 9.57 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 12.4 (q), 15.9 (q), 25.0 (t), 25.6 (t), 27.3 (t), 29.6 (t), 36.9 (t), 37.1 (t), 46.3 (t), 63.8 (s), 148.4 (s), 150.8 (s), 156.7 (s), 174.1 (s); MS (EI) *m/z* (%) 325 (23) [M^+], 282 (3), 266 (25), 227 (13), 185 (100). Anal. Calcd for $C_{14}H_{23}N_5O_2S$: C, 51.67; H, 7.12; N, 21.52. Found: C, 51.78; H, 7.16; N, 21.49.

*4.6.18. 2-(2-Imino-4-oxo-1-thia-3-azaspiro[4.7]dodec-6-yliden)-1-hydrazinecarboxamide (**16r**)*

Colourless powder, mp 218–220 °C with decomposition; IR (Nujol) ν_{max} 3404, 3162, 3114, 1719, 1701, 1663, 1592 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.04–1.13 (m, 1H, cy), 1.30–1.61 (m, 6H, cy), 1.65–1.78 (m, 1H, cy), 1.88–1.97 (m, 1H, cy), 2.53–2.61 (m, 2H, cy), 2.64–2.74 (m, 1H, cy), 5.39 and 6.39 (2br s, 2H, NH_2), 8.80 (s, 1H, NH), 8.99 (s, 1H, NH), 9.44 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 24.3 (t), 24.8 (t), 25.2 (t), 25.7 (t), 26.6 (t), 33.8 (t), 74.8 (s), 149.0 (s), 156.9 (s), 179.9 (s), 187.9 (s); MS (EI) *m/z* (%) 283 (14) [M^+], 266 (8), 241 (78), 224 (53), 209 (100), 198 (28), 185 (40), 155 (35), 129 (100), 111 (67). Anal. Calcd for $C_{11}H_{17}N_5O_2S$: C, 46.63; H, 6.05; N, 24.72. Found: C, 46.74; H, 5.97; N, 24.65.

*4.6.19. 2-[3-Methyl-2-(methylimino)-4-oxo-1-thia-3-azaspiro[4.7]dodec-6-yliden]-1-hydrazinecarboxamide (**16s**)*

Colourless powder, mp 196–198 °C; IR (Nujol) ν_{max} 3362, 3164, 1732, 1721, 1692, 1649, 1576 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.21–1.30 (m, 1H, cy), 1.33–1.59 (m, 6H, cy), 1.92–2.01 (m, 1H, cy), 2.18–2.24 (m, 1H, cy), 2.40–2.53 (m, 2H, cy), 2.68–2.80 (m, 1H, cy), 3.02 (s, 3H, NCH_3), 3.04 (s, 3H, NCH_3), 5.68 and 6.45 (2br s, 2H, NH_2), 9.55 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 24.2 (t), 24.8 (t), 25.0 (t), 25.1 (t), 25.8 (t), 28.9 (q), 33.5 (t), 38.2 (q), 65.2 (s), 148.9 (s), 151.3 (s), 156.8 (s), 173.0 (s); MS (EI) *m/z* (%) 311 (7) [M^+], 295 (3), 267 (53), 252 (100), 238 (56), 212 (43), 184 (13), 157 (85). Anal. Calcd for $C_{13}H_{21}N_5O_2S$: C, 50.14; H, 6.80; N, 22.49. Found: C, 50.06; H, 6.85; N, 22.58.

*4.6.20. 2-[3-Ethyl-2-(ethylimino)-4-oxo-1-thia-3-azaspiro[4.7]dodec-6-yliden]-1-hydrazinecarboxamide (**16t**)*

Colourless powder, mp 201–204 °C; IR (Nujol) ν_{max} 3385, 3275, 3142, 1715, 1693, 1640 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.05 (t, 3H, ^3J=7.2 Hz, NCH_2CH_3), 1.15 (t, 3H, ^3J=7.2 Hz, NCH_2CH_3), 1.16–1.23 (m, 1H, cy), 1.28–1.63 (m, 6H, cy), 1.86–1.95 (m, 1H, cy), 2.36–2.46 (m, 2H, cy), 2.71–2.83 (m, 2H, cy), 3.16–3.32 (m, 2H, NCH_2CH_3), 3.63 (q, 2H, ^3J=7.2 Hz, NCH_2CH_3), 5.84 and 6.53 (2br s, 2H, NH_2), 9.54 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 12.3 (q), 15.8 (q), 24.3 (t), 24.8 (t), 24.9 (t), 25.0 (t), 25.8 (t), 33.5 (t), 36.9 (t), 46.2 (t), 64.6 (s), 148.5 (s), 149.2 (s), 156.7 (s), 172.7 (s); MS (EI) *m/z* (%) 339 (20) [M^+], 322 (1), 280 (15), 256 (2), 241 (18), 213 (8), 185 (100), 157 (18). Anal. Calcd for $C_{15}H_{25}N_5O_2S$: C, 53.07; H, 7.42; N, 20.63. Found: C, 53.01; H, 7.39; N, 20.52.

*4.7. General procedure for the syntheses of 3-ethyl-2-(ethylimino)-1-thia-3-azaspiro[4.5]decane-4,6-dione **17a**, 1-thia-3-azaspiro[4.6]undecan-4,6-diones **17b**,**c**, 3-methyl-2-(methylimino)-1-thia-3-azaspiro[4.7]dodecan-4,6-dione **17d** and 2-imino-5-(ω-carboxyalkyl)-4-thiazolidinones **18a–i***

To a magnetically stirred solution of 4-oxo-1-thia-3-azaspiro[4.4]non-6-ylidenes **16b**,**c** (1.0 mmol) or 4-oxo-1-thia-3-azaspiro[4.5]dec-6-ylidenes **16e–h**,**l**,**n** (1.0 mmol) or 4-oxo-1-thia-3-azaspiro[4.6]undec-6-ylidenes **16o**,**p** (1.0 mmol) or 4-oxo-1-thia-3-azaspiro[4.7]dodec-6-ylidene **16s** (1.0 mmol) in acetone–water=9:1 (30 mL) 4 equiv of Amberlyst 15H was added at room temperature. The mixture was allowed to stand at room temperature under magnetic stirring (6–15 h) until the disappearance of the reagents (monitored by TLC chromatography). The resin was removed by filtration, the reaction solvent was evaporated under reduced pressure. Then the crude was chromatographed on silica gel column (elution mixtures: ethyl acetate–cyclohexane) to obtain pure products **18a–f** that were crystallized from ethyl acetate–cyclohexane. In the case of the reaction of **16g** along with **18e**, product **17a** was isolated and crystallized from ethyl acetate–cyclohexane. In the case of the reactions of **16o**,**p** and **16s** only products **17b–d** were isolated. To obtain the pertinent 2-imino-5-(ω-carboxyalkyl)-4-thiazolidinones **18g–i**, compounds **16o**,**p**,**s**, or pure **17b–d** were refluxed under magnetic stirring in acetone–water=9:1 (30 mL) in the presence of 4 equiv of Amberlyst 15H. At the disappearance of the reagents (4.0–9.0 h) (monitored by TLC chromatography) the resin was removed, the reaction solvent was evaporated under reduced pressure, products **18g–i** were purified by flash chromatography on a silica gel column (elution mixtures: ethyl acetate–cyclohexane) and crystallized from diethyl ether–light petroleum ether (40–60 °C).

*4.7.1. 3-Ethyl-2-(ethylimino)-1-thia-3-azaspiro[4.5]decane-4,6-dione (**17a**)*

Colourless powder, mp 90–92 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.19–1.26 (m, 6H, $2NCH_2CH_3$), 1.64–1.71 (m, 1H, cy), 1.79–1.85 (m, 1H, cy), 2.00–2.10 (m, 2H, cy), 2.18–2.23 (m, 1H, cy), 2.49–2.76 (m, 3H, cy), 3.29–3.35 (m, 2H, NCH_2CH_3), 3.79 (q, 2H, ^3J=7.2 Hz, NCH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.5 (q), 15.7 (q), 22.4 (t), 25.7 (t), 29.7 (t), 38.2 (t), 38.7 (t), 47.3 (t), 65.3 (s), 147.2 (s), 171.6 (s), 202.0 (s). Its low stability does not allow a more complete characterization.

*4.7.2. 2-Imino-1-thia-3-azaspiro[4.6]undecan-4,6-dione (**17b**)*

Colourless powder, mp 112–114 °C; IR (Nujol) ν_{max} 1735, 1669, 1632 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 1.24–1.43 (m, 2H, cy), 1.50–1.60 (m, 1H, cy), 1.69–1.81 (m, 1H, cy), 1.95–2.13 (m, 3H, cy), 2.45–2.56 (m, 2H, cy), 2.81–2.93 (m, 1H, cy),

8.98 (s, 1H, NH), 9.21 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ 25.0 (t), 27.6 (t), 29.4 (t), 35.9 (t), 42.2 (t), 78.1 (s), 180.7 (s), 186.6 (s), 206.0 (s); MS (EI) *m/z* (%) 212 (41) [M^+], 184 (59), 155 (56), 150 (43), 129 (100), 109 (30). Anal. Calcd for $C_9H_{12}N_2O_2S$: C, 50.92; H, 5.70; N, 13.20. Found: C, 50.78; H, 5.81; N, 13.32.

*4.7.3. 3-Methyl-2-(methylimino)-1-thia-3-azaspiro[4.6]-undecan-4,6-dione (**17c**)*

Colourless powder, mp 84–87 °C; IR (Nujol) ν_{max} 1709, 1663, 1654 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01–1.15 (m, 1H, cy), 1.61–1.88 (m, 4H, cy), 2.03–2.17 (m, 2H, cy), 2.58–2.74 (m, 2H, cy), 2.84–2.91 (m, 1H, cy), 3.16 (s, 6H, $2NCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.5 (t), 26.6 (t), 26.8 (t), 30.1 (t), 35.8 (t), 38.7 (q), 42.2 (q), 68.0 (s), 151.0 (s), 172.7 (s), 204.7 (s); MS (EI) *m/z* (%) 240 (100) [M^+], 225 (5), 212 (11), 183 (36), 167 (2), 138 (6). Anal. Calcd for $C_{11}H_{16}N_2O_2S$: C, 54.98; H, 6.71; N, 11.66. Found: C, 55.08; H, 6.63; N, 11.62.

*4.7.4. 3-Methyl-2-(methylimino)-1-thia-3-azaspiro[4.7]-dodecan-4,6-dione (**17d**)*

Colourless powder, mp 60–62 °C; IR (Nujol) ν_{max} 1743, 1732, 1621, 1504 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.96–1.06 (m, 1H, cy), 1.45–1.53 (m, 1H, cy), 1.60–1.83 (m, 6H, cy), 1.90–1.97 (m, 1H, cy), 2.15–2.23 (m, 1H, cy), 2.43–2.49 (m, 1H, cy), 2.98–3.05 (m, 1H, cy), 3.10 (s, 3H, NCH_3), 3.18 (s, 3H, NCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.0 (t), 25.4 (t), 25.6 (t), 26.8 (t), 29.3 (q), 30.2 (t), 34.4 (q), 38.1 (q), 71.3 (s), 151.4 (s), 171.1 (s), 206.4 (s); MS (EI) *m/z* (%) 254 (100) [M^+], 225 (52), 210 (2), 196 (36), 153 (42), 124 (16). Anal. Calcd for $C_{12}H_{18}N_2O_2S$: C, 56.67; H, 7.13; N, 11.01. Found: C, 56.72; H, 7.21; N, 11.20.

*4.7.5. 4-[3-Methyl-2-(methylimino)-4-oxo-1,3-thiazolidin-5yl]butanoic acid (**18a**)*

Colourless powder, mp 153–155 °C; IR (Nujol) ν_{max} 2682, 1705, 1653, 1457 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.68–1.89 (m, 3H, alk), 2.13–2.24 (m, 1H, alk), 2.38 (t, 2H, ^3J=7.2 Hz, alk), 3.13 (s, 3H, NCH_3), 3.15 (s, 3H, NCH_3), 4.07 and 4.09 (2d, 1H, ^3J=4.4 Hz, ^3J=4.0 Hz, cy), 9.20 (br s, 1H, OH); ^{13}C NMR ($CDCl_3$) δ 21.8 (t), 29.3 (q), 32.7 (t), 33.2 (t), 38.3 (q), 48.1 (d), 154.5 (s), 174.0 (s), 177.7 (s); MS (EI) *m/z* (%) 230 (31) [M^+], 212 (100), 184 (6), 171 (1), 157 (60). Anal. Calcd for $C_9H_{14}N_2O_3S$: C, 46.94; H, 6.13; N, 12.16. Found: C, 46.99; H, 6.18; N, 12.04.

*4.7.6. 4-[3-Ethyl-2-(ethylimino)-4-oxo-1,3-thiazolidin-5yl]-butanoic acid (**18b**)*

Colourless powder, mp 80–82 °C; IR (Nujol) ν_{max} 3119, 1704, 1649, 1459 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.12 (t, 3H, ^3J=7.2 Hz, NCH_2CH_3), 1.19 (t, 3H, ^3J=7.2 Hz, NCH_2CH_3), 1.61–1.84 (m, 3H, alk), 2.08–2.19 (m, 1H, alk), 2.36 (t, 2H, ^3J=6.8 Hz, alk), 3.31 (q, 2H, ^3J=7.2 Hz, NCH_2CH_3), 3.71 (q, 2H, ^3J=7.2 Hz, NCH_2CH_3), 4.00 and 4.03 (2d, 1H, ^3J=4.0 Hz, ^3J=4.0 Hz, cy), 10.63 (br s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.6 (q), 15.6 (q), 22.0 (t), 33.0 (t), 33.5 (t), 38.1 (t), 47.1 (t), 48.0 (d), 151.4 (s), 174.2 (s), 178.0 (s); MS (EI) *m/z* (%) 258 (90) [M^+], 240 (31), 225 (26), 215 (20), 185 (26), 157 (100). Anal. Calcd for $C_{11}H_{18}N_2O_3S$: C, 51.14; H, 7.02; N, 10.84. Found: C, 51.05; H, 7.08; N, 10.97.

*4.7.7. 5-(2-Imino-4-oxo-1,3-thiazolidin-5yl)pentanoic acid (**18c**)*

Colourless powder, mp 97–100 °C; IR (Nujol) ν_{max} 3212, 2987, 3178, 1708, 1665, 1606 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.17–1.28 (m, 1H, alk), 1.35–1.54 (m, 3H, alk), 1.59–1.68 (m, 1H, alk), 1.84–2.01 (m, 1H, alk), 2.20 (t, 2H, ^3J=7.2 Hz, alk), 4.21 and 4.24 (2d, 1H, ^3J=4.0 Hz, ^3J=3.6 Hz, cy), 8.76 (s, 1H, NH), 8.78 (s, 1H, NH), 11.80 (br s, 1H, OH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 24.1 (t), 26.5 (t), 32.5 (t), 33.5 (t), 56.4 (d), 174.4 (s), 181.4 (s), 189.6 (s); MS (EI) *m/z* (%) 216 (26) [M^+], 200 (100), 171 (34), 143 (16), 113 (8). Anal. Calcd for $C_8H_{12}N_2O_3S$: C, 44.43; H, 5.59; N, 12.95. Found: C, 44.37; H, 5.58; N, 12.89.

*4.7.8. 5-[3-Methyl-2-(methylimino)-4-oxo-1,3-thiazolidin-5yl]pentanoic acid (**18d**)*

Colourless powder, mp 120–122 °C; IR (Nujol) ν_{max} 1739, 1718, 1638, 1459 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22–1.30 (m, 1H, alk), 1.39–1.55 (m, 3H, alk), 1.66–1.75 (m, 1H, alk), 1.95–2.05 (m, 1H, alk), 2.19 (t, 2H, ^3J=7.2 Hz, alk), 3.00 (s, 3H, NCH_3), 3.03 (s, 3H, NCH_3), 4.33 and 4.36 (2d, 1H, ^3J=4.0 Hz, ^3J=4.4 Hz, cy), 12.02 (br s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.0 (t), 26.3 (t), 29.3 (q), 33.1 (t), 33.5 (t), 38.3 (q), 48.3 (d), 154.8 (s), 174.2 (s), 178.4 (s); MS (EI) *m/z* (%) 244 (35) [M^+], 226 (100), 198 (14), 170 (9), 157 (68). Anal. Calcd for $C_{10}H_{16}N_2O_3S$: C, 49.16; H, 6.60; N, 11.47. Found: C, 49.23; H, 6.56; N, 11.52.

*4.7.9. 5-[3-Ethyl-2-(ethylimino)-4-oxo-1,3-thiazolidin-5yl]-pentanoic acid (**18e**)*

Colourless powder, mp 164–166 °C; IR (Nujol) ν_{max} 3109, 1732, 1667, 1501 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.17 (t, 3H, ^3J=7.2 Hz, NCH_2CH_3), 1.23 (t, 3H, ^3J=7.2 Hz, NCH_2CH_3), 1.36–1.61 (m, 2H, alk), 1.70 (qui, 2H, ^3J=7.6 Hz, alk), 1.75–1.88 (m, 1H, alk), 2.11–2.21 (m, 1H, alk), 2.38 (t, 2H, ^3J=7.2 Hz, alk), 3.33 (q, 2H, ^3J=7.2 Hz, NCH_2CH_3), 3.76 (q, 2H, ^3J=7.2 Hz, NCH_2CH_3), 4.01 and 4.04 (2d, 1H, ^3J=4.0 Hz, ^3J=4.0 Hz, cy), 10.21 (br s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.4 (q), 15.5 (q), 24.0 (t), 26.1 (t), 33.1 (t), 33.6 (t), 37.8 (t), 46.9 (t), 47.9 (d), 150.9 (s), 174.1 (s), 178.8 (s); MS (EI) *m/z* (%) 272 (100) [M^+], 257 (26), 229 (17), 198 (5), 185 (36), 157 (43), 144 (98), 129 (56). Anal. Calcd for $C_{12}H_{20}N_2O_3S$: C, 52.92; H, 7.40; N, 10.29. Found: C, 52.85; H, 7.42; N, 10.34.

*4.7.10. 5-(2-Imino-4-oxo-1,3-thiazolidin-5yl)-3-methyl-pentanoic acid (**18f**)*

Colourless powder, mp 164–166 °C; IR (Nujol) ν_{max} 3247, 3114, 3038, 1705, 1687, 1667 cm^{-1}; ^{1}H NMR (400 MHz,

DMSO-d_6) δ 0.87 (d, 3H, ^3J=6.4 Hz, alk), 1.03–1.47 (m, 2H, alk), 1.57–1.71 (m, 1H, alk), 1.77–1.89 (m, 1H, alk), 1.90–2.07 (m, 2H, alk), 2.14–2.23 (m, 1H, alk), 4.18–4.24 (m, 1H, cy), 8.76 (s, 1H, NH), 8.95 (br s, 1H, NH), 12.01 (br s, 1H, OH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 19.4 (q), 29.3 (t), 30.2 (d), 33.7 (t), 41.1 (t), 56.6 (d), 173.6 (s), 181.3 (s), 189.5 (s); MS (EI) *m/z* (%) 230 (4) [M$^+$], 212 (83), 184 (53), 168 (79), 142 (79), 129 (100), 116 (100). Anal. Calcd for $C_9H_{14}N_2O_3S$: C, 46.94; H, 6.13; N, 12.16. Found: C, 46.98; H, 6.08; N, 12.19.

*4.7.11. 5-[3-Ethyl-2-(ethylimino)-4-oxo-1,3-thiazolidin-5yl]-3-methylpentanoic acid (**18g**)*

Colourless powder, mp 113–116 °C; IR (Nujol) ν_{max} 3118, 1769, 1703, 1556 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.99 (d, 3H, ^3J=7.2 Hz, alk), 1.16 (t, 3H, ^3J=7.2 Hz, NCH_2CH_3), 1.22 (t, 3H, ^3J=7.2 Hz, NCH_2CH_3), 1.36–1.44 (m, 1H, alk), 1.49–1.86 (m, 2H, alk), 1.98 (oc, 1H, ^3J=4.4 Hz, alk), 2.01–2.23 (m, 2H, alk), 2.29–2.38 (m, 1H, alk), 3.30 (q, 2H, ^3J=7.2 Hz, NCH_2CH_3), 3.73 (q, 2H, ^3J=7.2 Hz, NCH_2CH_3), 3.96–4.04 (m, 1H, cy), 9.20 (br s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.4 (q), 15.5 (q), 19.4 (q), 26.8 (t), 30.1 (d), 33.4 (t), 37.8 (t), 41.2 (t), 46.9 (t), 48.2 (d), 151.0 (s), 174.1 (s), 178.2 (s); MS (EI) *m/z* (%) 286 (70) [M$^+$], 271 (21), 243 (18), 185 (32), 157 (48), 144 (100), 129 (54). Anal. Calcd for $C_{13}H_{22}N_2O_3S$: C, 54.52; H, 7.74; N, 9.78. Found: C, 54.64; H, 7.83; N, 9.84.

*4.7.12. 6-(2-Imino-4-oxo-1,3-thiazolidin-5yl)hexanoic acid (**18h**)*

Colourless powder, mp 106–109 °C; IR (Nujol) ν_{max} 3243, 3177, 3092, 1713, 1674, 1611 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.13–1.47 (m, 6H, alk), 1.55–1.68 (m, 1H, alk), 1.91–2.00 (m, 1H, alk), 2.15–2.31 (m, 2H, alk), 4.19 and 4.21 (2d, 1H, ^3J=4.0 Hz, ^3J=4.0 Hz, cy), 8.74 (s, 1H, NH), 8.94 (br s, 1H, NH), 11.98 (br s, 1H, OH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 21.4 (t), 22.5 (t), 24.1 (t), 28.9 (t), 32.8 (t), 53.6 (d), 152.6 (s), 176.8 (s), 180.0 (s); MS (EI) *m/z* (%) 230 (100) [M$^+$], 213 (63), 185 (31), 143 (14), 114 (4). Anal. Calcd for $C_9H_{14}N_2O_3S$: C, 46.94; H, 6.13; N, 12.16. Found: C, 47.02; H, 6.02; N, 12.04.

*4.7.13. 6-[3-Methyl-2-(methylimino)-4-oxo-1,3-thiazolidin-5yl]hexanoic acid (**18i**)*

Colourless powder, mp 93–95 °C; IR (Nujol) ν_{max} 1725, 1712, 1626, 1479 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32–1.51 (m, 4H, alk), 1.57–1.68 (m, 2H, alk), 1.72–1.80 (m, 1H, alk), 2.06–2.18 (m, 1H, alk), 2.32 (t, 2H, ^3J=7.2 Hz, alk), 3.11 (s, 3H, NCH_3), 3.13 (s, 3H, NCH_3), 4.03 and 4.05 (2d, 1H, ^3J=4.0 Hz, ^3J=4.0 Hz, cy), 10.53 (br s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.3 (t), 26.4 (t), 28.3 (t), 29.1 (q), 33.1 (t), 33.7 (t), 38.3 (q), 48.4 (d), 154.5 (s), 174.3 (s), 178.7 (s); MS (EI) *m/z* (%) 258 (100) [M$^+$], 241 (34), 214 (85), 185 (37), 156 (28). Anal. Calcd for $C_{11}H_{18}N_2O_3S$: C, 51.14; H, 7.02; N, 10.84. Found: C, 51.04; H, 7.13; N, 10.72.

*4.7.14. 7-[3-Methyl-2-(methylimino)-4-oxo-1,3-thiazolidin-5yl]heptanoic acid (**18j**)*

Colourless powder, mp 116–118 °C; IR (Nujol) ν_{max} 1743, 1732, 1621, 1504 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.12–1.38 (m, 4H, alk), 1.51–1.72 (m, 3H, alk), 1.83–1.89 (m, 2H, alk), 2.18–2.29 (m, 1H, alk), 2.36 (t, 2H, ^3J=7.2 Hz, alk), 3.11 (s, 3H, NCH_3), 3.13 (s, 3H, NCH_3), 4.19 and 4.21 (2d, 1H, ^3J=4.0 Hz, ^3J=4.0 Hz, cy), 10.72 (br s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.0 (t), 26.1 (t), 27.5 (t), 28.5 (t), 29.7 (q), 33.4 (t), 33.9 (t), 38.8 (q), 48.6 (d), 157.8 (s), 169.0 (s), 176.4 (s); MS (EI) *m/z* (%) 272 (65) [M$^+$], 255 (17), 227 (100), 198 (53), 157 (21), 127 (6). Anal. Calcd for $C_{12}H_{20}N_2O_3S$: C, 52.92; H, 7.40; N, 10.29. Found: C, 52.81; H, 7.53; N, 10.42.

*4.8. General procedure for the syntheses of 2-(1,4,5,6-tetrahydropyrimidin-2-ylthio)cyclohexan-1-one N-phenylsemicarbazone **20a**, 5′,6′-dihydro-2H-spiro[cycloalkane-1,2′-imidazo[2,1-b][1,3]thiazole]-2,3′-dione 2-semicarbazones **21a**,**c**,**f** and 6′,7′-dihydro-2H,5′H-spiro[cycloalkane-1,2′-[1,3]thiazolo[3,2-a]pyrimidine]-2,3′-dione 2-semicarbazones **21b**,**d**,**e**,**g***

Cycloalkenyl-1-diazenes **5a**,**c**,**g**–**i** (1.0 mmol) were added at room temperature to a magnetically stirred solution of imidazolidine-2-thione **19a** or tetrahydropyrimidine-2-thione **19b** (1.0 mmol) in methanol (4 mL) at room temperature. The reaction was allowed to stand under magnetic stirring at room temperature (0.1–1.5 h) until the disappearance of the reagents (monitored by TLC chromatography). Then, the reaction solvent was evaporated under reduced pressure and the final product **20a** was purified by chromatography on silica gel column (elution mixtures: ethyl acetate–cyclohexane) and crystallized from ethyl acetate–cyclohexane. Compounds **21a**–**g** crystallized directly from the reaction medium and were collected as pure products by filtration.

*4.8.1. 2-(1,4,5,6-Tetrahydropyrimidin-2-ylthio)cyclohexan-1-one N-phenylsemicarbazone (**20a**)*

Colourless powder, mp 181–184 °C; IR (Nujol) ν_{max} 3388, 3195, 1691, 1686, 1586 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.29–1.37 (m, 1H, cy), 1.52–1.57 (m, 1H, cy), 1.79–1.94 (m, 7H, cy), 2.99–3.03 (m, 1H, cy), 3.10–3.23 (m, 2H, NCH_2), 3.40–3.45 (m, 2H, NCH_2), 5.96–6.00 (m, 1H, cy), 7.00 (t, 1H, ^3J=7.2 Hz, Ar), 7.31 (t, 2H, ^3J=8.0 Hz, Ar), 7.45 (d, 2H, ^3J=8.0 Hz, Ar), 8.14 (s, 1H, NH), 8.31 (s, 1H, NH), 9.82 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 20.8 (t), 24.1 (t), 24.3 (t), 26.4 (t), 29.3 (t), 40.3 (t), 42.4 (t), 62.1 (d), 118.1 (d), 122.2 (d), 128.9 (d), 138.9 (d), 149.8 (s), 153.3 (s), 177.5 (s); MS (EI) *m/z* (%) 345 (18) [M$^+$], 268 (11), 230 (100), 213 (7), 186 (12), 172 (17). Anal. Calcd for $C_{17}H_{23}N_5OS$: C, 59.10; H, 6.71; N, 20.27. Found: C, 59.01; H, 6.78; N, 20.35.

*4.8.2. 5′,6′-Dihydro-2H-spiro[cyclopentane-1,2′-imidazo[2,1-b][1,3]thiazole]-2,3′-dione 2-semicarbazone (**21a**)*

Colourless powder, mp 182–183 °C; IR (Nujol) ν_{max} 3446, 3254, 3172, 1709, 1645, 1602 cm^{-1}; ^{1}H NMR (400 MHz,

DMSO-d_6) δ 1.60–1.72 (m, 1H, cy), 1.92–2.03 (m, 1H, cy), 2.19–2.30 (m, 2H, cy), 2.36–2.45 (m, 2H, cy), 3.55–3.71 (m, 2H, NCH_2), 4.14 (t, 2H, ^3J=8.0 Hz, NCH_2), 6.20 (br s, 2H, NH_2), 9.28 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 22.4 (t), 27.6 (t), 29.5 (t), 41.6 (t), 60.7 (t), 71.6 (s), 154.9 (s), 156.5 (s), 158.1 (s), 167.2 (s); MS (EI) *m/z* (%) 268 (2) [M^++1], 267 (11) [M^+], 250 (7), 224 (8), 208 (4), 195 (100), 181 (3), 168 (32), 155 (89), 139 (10), 127 (36), 102 (51). Anal. Calcd for $C_{10}H_{13}N_5O_2S$: C, 44.93; H, 4.90; N, 26.20. Found: C, 44.86; H, 4.95; N, 26.12.

*4.8.3. 6′,7′-Dihydro-2H,5′H-spiro[cyclopentane-1,2′-[1,3]thiazolo[3,2-a]pyrimidine]-2,3′-dione 2-semicarbazone (**21b**)*

Colourless powder, mp 218–220 °C; IR (Nujol) ν_{max} 3452, 3283, 3180, 3131, 1717, 1690, 1637 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.67–1.84 (m, 3H, cy), 2.02–2.10 (m, 1H, cy), 2.14–2.19 (m, 1H, cy), 2.30–2.47 (m, 3H, cy), 3.39–3.46 (m, 2H, NCH_2), 3.47–3.65 (m, 2H, NCH_2), 6.18 (br s, 2H, NH_2), 9.29 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 19.0 (t), 22.5 (t), 27.7 (t), 40.5 (t), 45.9 (t), 61.4 (s), 149.3 (s), 155.7 (s), 156.4 (s), 172.5 (s); MS (EI) *m/z* (%) 281 (14) [M^+], 264 (8), 237 (11), 221 (100), 209 (78), 197 (35), 181 (26), 167 (47), 154 (29), 143 (8), 114 (25). Anal. Calcd for $C_{11}H_{15}N_5O_2S$: C, 49.96; H, 5.37; N, 24.89. Found: C, 50.02; H, 5.29; N, 24.97.

*4.8.4. 5′,6′-Dihydro-2H-spiro[cyclohexane-1,2′-imidazo[2,1-b][1,3]thiazole]-2,3′-dione 2-semicarbazone (**21c**)*

Colourless powder, mp 163–166 °C; IR (Nujol) ν_{max} 3416, 3339, 3125, 1716, 1695 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 1.34–1.47 (m, 2H, cy), 1.72–1.82 (m, 1H, cy), 1.85–1.96 (m, 2H, cy), 2.20–2.32 (m, 2H, cy), 3.02 (d, 1H, ^3J=15.2 Hz, cy), 3.64–3.80 (m, 2H, NCH_2), 4.18 (t, 2H, ^3J=9.2 Hz, NCH_2), 5.80 and 6.36 (2br s, 2H, NH_2), 9.60 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ 22.0 (t), 23.5 (t), 23.9 (t), 36.8 (t), 41.5 (t), 60.4 (t), 73.0 (s), 147.7 (s), 156.8 (s), 157.5 (s), 166.3 (s); MS (EI) *m/z* (%) 281 (3) [M^+], 264 (2), 238 (22), 222 (19), 209 (100), 181 (31), 155 (86), 138 (34). Anal. Calcd for $C_{11}H_{15}N_5O_2S$: C, 49.96; H, 5.37; N, 24.89. Found: C, 49.86; H, 5.42; N, 24.92.

*4.8.5. 6′,7′-Dihydro-2H,5′H-spiro[cyclohexane-1,2′-[1,3]thiazolo[3,2-a]pyrimidine]-2,3′-dione 2-semicarbazone (**21d**)*

Colourless powder, mp 212–213 °C; IR (Nujol) ν_{max} 3461, 3184, 3147, 1722, 1699, 1656 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.18–1.31 (m, 2H, cy), 1.77–1.87 (m, 5H, cy), 2.00–2.07 (m, 1H, cy), 2.26–2.32 (m, 1H, cy), 2.96–3.02 (m, 1H, cy), 3.40–3.45 (m, 2H), 3.56–3.65 (m, 2H), 5.16 and 6.35 (2br s, 2H, NH_2), 9.57 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 19.1 (t), 22.4 (t), 23.7 (t), 24.1 (t), 40.3 (t), 46.0 (t), 62.2 (s), 148.6 (s), 149.0 (s), 156.9 (s), 171.7 (s); MS (EI) *m/z* (%) 295 (8) [M^+], 278 (3), 251 (17), 235 (154), 223 (100), 195 (17), 182 (28), 167 (40), 154 (15), 142 (52), 113 (36). Anal. Calcd for $C_{12}H_{17}N_5O_2S$: C, 48.80; H, 5.80; N, 23.71. Found: C, 48.90; H, 5.83; N, 23.72.

*4.8.6. 6′,7′-Dihydro-2H,5′H-spiro[cycloheptane-1,2′-[1,3]thiazolo[3,2-a]pyrimidine]-2,3′-dione 2-semicarbazone (**21e**)*

Colourless powder, mp 198–201 °C; IR (Nujol) ν_{max} 3432, 3179, 3162, 1732, 1705, 1672 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.36–1.80 (m, 8H, cy), 1.97–2.03 (m, 1H, cy), 2.28–2.39 (m, 2H, cy), 2.69–2.74 (m, 1H, cy), 3.36–3.43 (m, 2H, NCH_2), 3.46–3.60 (m, 2H, NCH_2), 5.61 and 6.14 (2br s, 2H, NH_2), 9.55 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 19.1 (t), 25.0 (t), 25.7 (t), 27.2 (t), 29.6 (t), 36.5 (t), 45.9 (t), 62.8 (s), 148.9 (s), 150.9 (s), 156.7 (s), 173.0 (s); MS (EI) *m/z* (%) 309 (4) [M^+], 293 (7), 265 (17), 249 (38), 236 (100), 209 (37), 195 (38), 181 (64), 168 (52), 154 (68), 143 (42), 114 (59). Anal. Calcd for $C_{13}H_{19}N_5O_2S$: C, 50.47; H, 6.19; N, 22.64. Found: C, 50.52; H, 6.14; N, 22.59.

*4.8.7. 5′,6′-Dihydro-2H-spiro[cyclooctane-1,2′-imidazo[2,1-b][1,3]thiazole]-2,3′-dione 2-semicarbazone (**21f**)*

Colourless powder, mp 170–173 °C; IR (Nujol) ν_{max} 3459, 3277, 3193, 3156, 1713, 1633, 1596 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.17–1.55 (m, 8H, cy), 2.26–2.32 (m, 1H, cy), 2.42–2.48 (m, 1H, cy), 2.52–2.58 (m, 1H, cy), 2.70–2.76 (m, 1H, cy), 3.64 (t, 2H, ^3J=8.2 Hz, NCH_2), 4.12 (t, 2H, ^3J=8.2 Hz, NCH_2), 5.87 and 6.40 (2br s, 2H, NH_2), 9.57 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 24.2 (t), 24.6 (t), 24.9 (t), 25.6 (t), 33.7 (t), 40.1 (t), 41.5 (t), 60.3 (t), 74.7 (s), 148.6 (s), 156.8 (s), 157.4 (s), 166.7 (s); MS (EI) *m/z* (%) 309 (2) [M^+], 292 (2), 266 (18), 250 (18), 237 (100), 224 (3), 209 (54), 196 (67), 182 (37), 154 (25), 142 (58), 114 (93). Anal. Calcd for $C_{13}H_{19}N_5O_2S$: C, 50.47; H, 6.19; N, 22.64. Found: C, 50.40; H, 6.11; N, 22.69.

*4.8.8. 6′,7′-Dihydro-2H,5′H-spiro[cyclooctane-1,2′-[1,3]thiazolo[3,2-a]pyrimidine]-2,3′-dione 2-semicarbazone (**21g**)*

Colourless powder, mp 190–193 °C with decomposition; IR (Nujol) ν_{max} 3463, 3307, 3165, 3146, 1732, 1711, 1658 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.23–1.38 (m, 1H, cy), 1.63 (m, 5H, cy), 1.66–1.80 (m, 1H, cy), 1.82–1.90 (m, 1H, cy), 2.19–2.24 (m, 1H, cy), 2.40–2.48 (m, 2H, cy), 2.73–2.79 (m, 1H, cy), 3.16–3.21 (m, 2H, cy), 3.35–3.42 (m, 2H, NCH_2), 3.56 (t, 2H, ^3J=6.0 Hz, NCH_2), 5.78 and 6.47 (2br s, 2H, NH_2), 9.55 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 19.0 (t), 24.3 (t), 24.8 (t), 24.9 (t), 25.0 (t), 25.7 (t), 33.3 (t), 40.2 (t), 45.8 (t), 63.7 (s), 149.0 (s), 149.2 (s), 156.8 (s), 171.8 (s); MS (EI) *m/z* (%) 323 (6) [M^+], 306 (10), 279 (21), 264 (16), 251 (100), 225 (35), 210 (65), 196 (36), 184 (23), 172 (4), 159 (14), 119 (73). Anal. Calcd for $C_{14}H_{21}N_5O_2S$: C, 51.99; H, 6.54; N, 21.65. Found: C, 52.10; H, 6.46; N, 21.57.

*4.9. General procedure for the synthesis of 2-[hexahydro-1,3-benzothiazol-3a(4H)-yl]-N-phenylhydrazinecarboxamides **23a**,**b***

To a magnetically stirred solution of *N*,*N*′-dialkylthioureas **14b**,**c** (1.0 mmol) in methanol (5 mL) at room temperature *N*1-phenyl-2-(1-cyclohexenyl)-1-diazene-1-carboxyamide **5i** (1.0 mmol) was added. The reaction was allowed to stand

under magnetic stirring at room temperature (1.5–3.0 h) until the disappearance of the reagents (monitored by TLC chromatography). Then, the reaction solvent was evaporated under reduced pressure and the final products **23a**,**b** were purified by chromatography on silica gel column (elution mixtures: ethyl acetate–cyclohexane) and crystallized from ethyl acetate–cyclohexane.

*4.9.1. 2-[3-Methyl-2-(methylimino)hexahydro-1,3-benzothiazol-3a(4H)-yl]-N-phenylhydrazinecarboxamide (**23a**)*

Colourless powder, mp 137–139 °C; IR (Nujol) ν_{max} 3491, 3304, 3259, 1716, 1666, 1620, 1580 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.36–1.47 (m, 3H, cy), 1.60–1.69 (m, 2H, cy), 1.78–1.85 (m, 1H, cy), 2.00–2.06 (m, 2H, cy), 2.87 (s, 3H, NCH_3), 3.07 (s, 3H, NCH_3), 3.58–3.65 (m, 1H, cy), 4.29 (br s, 1H, NH), 6.52 (br s, 1H, NH), 7.05 (dt, 1H, ^3J=7.2 Hz, ^4J=0.8 Hz, Ar), 7.29 (t, 2H, ^3J=7.6 Hz, Ar), 7.46 (d, 2H, ^3J=8.4 Hz, Ar), 8.16 (br s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3 (t), 23.0 (t), 28.7 (t), 31.2 (t), 31.3 (q), 40.1 (q), 44.8 (d), 82.0 (s), 118.8 (d), 123.1 (d), 129.0 (d), 138.1 (s), 155.4 (s), 157.2 (s); MS (EI) *m/z* (%) 333 (2) [M^+], 241 (18), 212 (31), 184 (47), 169 (21), 155 (100), 140 (5), 112 (64). Anal. Calcd for $C_{16}H_{23}N_5OS$: C, 57.63; H, 6.95; N, 21.00. Found: C, 57.73; H, 7.01; N, 20.96.

*4.9.2. 2-[3-Ethyl-2-(ethylimino)hexahydro-1,3-benzothiazol-3a(4H)-yl]-N-phenylhydrazinecarboxamide (**23b**)*

Colourless powder, mp 146–150 °C; IR (Nujol) ν_{max} 3356, 3295, 3225, 1673, 1625 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.04–1.12 (m, 6H, $2NCH_2CH_3$), 1.31–1.40 (m, 2H, cy), 1.45–1.58 (m, 3H, cy), 1.71–1.75 (m, 1H, cy), 1.81–1.87 (m, 1H, cy), 2.02–2.07 (m, 1H, cy), 3.06–3.10 (m, 2H, NCH_2CH_3), 3.11–3.20 and 3.22–3.35 (2 m, 2H, NCH_2CH_3), 3.57 (t, 1H, ^3J=5.2 Hz, cy), 5.37 (s, 1H, NH), 6.93 (t, 1H, ^3J=6.8 Hz, Ar), 7.26 (t, 2H, ^3J=6.8 Hz, Ar), 7.36 (br s, 1H, NH), 7.45 (d, 2H, ^3J=7.6 Hz, Ar), 8.54 (br s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 14.2 (q), 16.8 (q), 21.3 (t), 21.9 (t), 29.4 (t), 37.1 (t), 43. 9 (d), 47.9 (t), 81.4 (s), 118.1 (d), 121.7 (d), 128.6 (d), 139.4 (s), 154.5 (s), 156.5 (s); MS (EI) *m/z* (%) 362 (1) [M^++1], 339 (1), 261 (7), 246 (9), 229 (27), 211 (7), 175 (11), 132 (17), 119 (41), 110 (100). Anal. Calcd for $C_{18}H_{27}N_5OS$: C, 59.80; H, 7.53; N, 19.37. Found: C, 59.67; H, 7.82; N, 19.52.

Acknowledgements

The authors thank MIUR (Roma) [PRIN 2005 (2005034305)] and the Università degli Studi di Urbino for the financial support of these investigations. They also thank Dr. Stefano Beretta and Mr. Benoit Caprin for their precious collaboration in the synthetic development of the work.

References and notes

1. (a) Schieberle, P.; Güntert, M.; Sommer, H.; Werkhoff, P. *Food Chem.* **1983**, *56*, 369–372; (b) Mac Leod, G.; Ames, J. *J. Food Sci.* **1987**, *52*, 42–46; (c) Mac Leod, G.; Ames, J. *Flavour Frag. J.* **1986**, *1*, 91–107; (d) Elmore, S.; Mottram, D. J. *J. Agric. Food Chem.* **1997**, *45*, 3603–3607; (e) Ong, P.; Acree, T. *J. Agric. Food Chem.* **1998**, *46*, 2282–2286.
2. (a) Hartman, G.; Jin, Q. Z.; Collins, G.; Lee, K.; Ho, C. T.; Chang, S. J. *J. Agric. Food Chem.* **1983**, *31*, 1030–1033; (b) Bultery, R.; Stean, D.; Ling, L. *J. Agric. Food Chem.* **1994**, *42*, 791–795; (c) Pattenden, G.; Mulqueen, B.; Falck, J. *Tetrahedron Lett.* **1994**, *35*, 5705–5708; (d) Fuganti, C.; Gatti, F. G.; Serra, S. *Tetrahedron* **2007**, *63*, 4762–4767.
3. (a) Hayashi, K.; Sato, C.; Hiki, S.; Kumagai, T.; Tamai, S.; Abe, T.; Nagao, Y. *Tetrahedron Lett.* **1999**, *40*, 3761–3764; (b) Ino, A.; Murabayashi, A. *Tetrahedron* **1999**, *55*, 10271–10282; (c) Higashibayashi, S.; Kohno, M.; Goto, T.; Suzuki, K.; Mori, T.; Hashimoto, K.; Nakata, M. *Tetrahedron Lett.* **2004**, *45*, 3707–3712; (d) Mori, T.; Higashibayashi, S.; Goto, T.; Kohno, M.; Satouchi, Y.; Shinko, K.; Suzuki, K.; Suzuki, S.; Tohmiya, H.; Hashimoto, K.; Nakata, M. *Tetrahedron Lett.* **2007**, *48*, 1331–1335.
4. (a) Caujolee, R.; Baziard-Mouysset, G.; Favrot, J. D.; Payard, M.; Louiseau, P. R.; Amarouch, H.; Linas, M. D.; Seguela, J. P.; Louiseau, P. M.; Bories, C.; Gayral, P. *J. Med. Chem.* **1993**, *28*, 29–35.
5. (a) Chaviara, A. T.; Christidis, P. C.; Papageorgiou, A.; Chrysogelou, E.; Hadjipavlou-Litina, D. J.; Bolos, C. A. *J. Inorg. Biochem.* **2005**, *99*, 2102–2109; (b) Rostom, S. A. F. *Bioorg. Med. Chem.* **2006**, *14*, 6475–6485.
6. (a) Davidson, B. S. *Chem. Rev.* **1993**, *93*, 1771–1791; (b) Michael, J. P.; Pattenden, G. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1–23; (c) Gu, X.-H.; Wan, X.-Z.; Jiang, B. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 569–572.
7. (a) Kearney, P. C.; Fernandez, M.; Flygare, J. A. *J. Org. Chem.* **1988**, *63*, 196–200; (b) Reid, C. W.; Blackburn, N. T.; Legaree, B. A.; Auzanneau, F.; Clarke, A. J. *FEBS Lett.* **2004**, *574*, 73–79; (c) Bonde, C. G.; Gaikwad, N. J. *Bioorg. Med. Chem.* **2004**, *12*, 2151–2161; Ritter, T. K.; Wong, C. H. *Tetrahedron Lett.* **2001**, *42*, 615–618; (d) Kim, S. K.; Son, H.; Nam, G.; Chi, D. Y.; Kim, J. H. *Bioorg. Med. Chem.* **2000**, *10*, 1143–1145.
8. Brown, R. S.; Dowden, J.; Moreau, C.; Potter, V. L. *Tetrahedron Lett.* **2002**, *43*, 6561–6562; (b) Mulqueen, G.; Pattenden, G.; Whiting, D. *Tetrahedron* **1993**, *49*, 5359–5364.
9. Vorbrügen, H.; Krolikiewick, K. *Tetrahedron* **1993**, *49*, 9353–9372.
10. Busacca, C.; Dong, Y.; Spinelli, E. *Tetrahedron Lett.* **1996**, *37*, 2935–2938.
11. Galèotti, N.; Montagne, C.; Pioncet, J.; Join, P. *Tetrahedron Lett.* **1992**, *33*, 2807–2810.
12. (a) Wipf, P.; Fritc, P. *Tetrahedron Lett.* **1994**, *35*, 5397–5400; (b) Muir, J. C.; Pattenden, G.; Ye, T. *Tetrahedron Lett.* **1998**, *39*, 2861–2864; (c) Ino, A.; Murabayashi, A. *Tetrahedron* **2001**, *57*, 1897–1902.
13. Aitken, R. A.; Armstrong, D. P.; Galt, R. H. B.; Mesher, S. T. E. *J. Chem. Soc., Perkin Trans. 1* **1997**, 935–942.
14. (a) Tárraga, A.; Molina, P.; Curiel, D.; Bautista, D. *Tetrahedron: Asymmetry* **2002**, *13*, 1621–1628; Knapp, S.; Yang, C.; Haimowitz, T. *Tetrahedron Lett.* **2002**, *43*, 7101–7104; (b) Bernardi, L.; Bovini, B. F.; Comes-Franchini, M.; Femoni, C.; Fochi, M.; Ricci, A. *Tetrahedron: Asymmetry* **2004**, *15*, 1133–1140; (c) Lu, S.-F.; Du, D.-M.; Zhang, S.-W.; Xu, J. *Tetrahedron: Asymmetry* **2004**, *15*, 3433–3441.
15. Abdel-Jalil, R. J.; Saeed, M.; Voelter, W. *Tetrahedron Lett.* **2001**, *42*, 2435–2437.
16. Tiecco, M.; Testaferri, L.; Santi, C.; Tomassini, C.; Marini, F.; Bagnoli, L.; Temperini, A. *Tetrahedron: Asymmetry* **2002**, *13*, 429–435.
17. (a) Attanasi, O. A.; De Crescentini, L.; Foresti, E.; Galarini, R.; Santeusanio, S.; Serra Zanetti, F. *Synthesis* **1995**, 1397–1400; (b) Attanasi, O. A.; De Crescentini, L.; Favi, G.; Filippone, P.; Lillini, S.; Mantellini, F.; Santeusanio, S. *Org. Lett.* **2005**, *7*, 2469–2471.
18. Attanasi, O. A.; Filippone, P.; Foresti, E.; Guidi, B.; Santeusanio, S. *Tetrahedron* **1999**, *55*, 13423–13444.
19. Attanasi, O. A.; Berretta, S.; De Crescentini, L.; Favi, G.; Filippone, P.; Giorgi, G.; Lillini, S.; Mantellini, F. *Tetrahedron Lett.* **2007**, *48*, 2449–2451.
20. Kolb, H. C.; Finn, M. G.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2001**, *40*, 2004–2021.
21. Attanasi, O. A.; De Crescentini, L.; Favi, G.; Filippone, P.; Golobič, A.; Lillini, S.; Mantellini, F. *Synlett* **2006**, 2735–2738.
22. Crystallographic data for compound **9k** (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 636093. Copies of the data

can be obtained free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(1223)336033 or e-mail: deposit@ccdc.cam.ac.uk].

23. Ballini, R.; Petrini, M. *J. Chem. Soc., Perkin Trans. 1* **1988**, 2563–2565.
24. (a) Eison, M. S.; Taylor, D. P.; Riblet, L. A.; Temple, D. L., Jr. *J. Med. Chem.* **1986**, *29*, 359–369; (b) New, J. S.; Yevich, J. P.; Temple, D. L., Jr.; New, K. B.; Gross, S. M.; Schlemmer, R. F., Jr.; Eison, M. S.; Taylor, D. P.; Riblet, L. A. *J. Med. Chem.* **1988**, *31*, 618–624; (c) New, J. S.; Christopher, W. L.; Yevich, J. P.; Butler, R.; Schlemmer, R. F., Jr.; Vander-Maelen, C. P.; Cipollina, J. A. *J. Med. Chem.* **1996**, *32*, 1147–1156; (d) Hrib, N. J.; Jurcak, J. G.; Bregna, D. E.; Burgher, K. L.; Hartman, H. B.; Kafka, S.; Kerman, L. L.; Konsamut, S.; Roehr, J.; Szewczak, M. R.; Woods-Kettelberger, A. T.; Corbett, R. *J. Med. Chem.* **1996**, *39*, 4044–4057.
25. (a) Solankee, A.; Kapadia, K.; Turel, J. *J. Inst. Chem.* **1993**, *65*, 140; (b) Solankee, A.; Kapadia, K.; Turel, J. *Asian J. Chem.* **1994**, *6*, 169–171; (c) Solankee, A.; Kapadia, K.; Turel, J. *J. Indian Chem. Soc.* **1995**, *72*, 739–740.
26. Crystallographic data for compound **18d** (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 636093. Copies of the data can be obtained free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(1223)336033 or e-mail: deposit@ccdc.cam.ac.uk].