Pergamon

Tetrahedron, Vol. 52, No. 20, pp. 7183-7200, 1996

0040-4020/96 $15.00 + 0.00

PII: S0040-4020(96)00336-5

Isothiazoles. Part VI.[1] Cycloaddition of Azides to Isothiazole Dioxides: Synthesis of Thiadiazabicyclo[3.1.0]hexene Derivatives and their Thermal Rearrangement to Thiazete Dioxides, 1,2,6-Thiadiazine Dioxides and Pyrazoles.

Francesca Clerici,* Franco Galletti, Donato Pocar

Istituto di Chimica Organica, Facoltà di Farmacia, Università di Milano, Via Venezian 21, I-20133 Milano, Italy.

Pietro Roversi

Dipartimento di Chimica Fisica ed Elettrochimica, Facoltà di Chimica, Università di Milano, Via Golgi 19, I-20133 Milano, Italy.

Dedicated to Professor Paolo Grünanger on the occasion of his 70th birthday.

Abstract: 3-Diethylamino-4-(4-methoxyphenyl)-isothiazole 1,1-dioxide (**1**) was made to react with arylalkyl- and arylazides **2**. Cycloadducts **3**, which could be isolated in some cases, afforded N-arylalkyl- or N-aryl-thiadiazabicyclo[3.1.0]hexene derivatives **4** through N_2-elimination. Thermal rearrangements of N-aryl- and N-β-phenylethyl substituted compounds **4b-e**, produced derivatives of 1,2-thiazete 1,1-dioxide **5**, 1,2,6-thiadiazine 1,1-dioxide **6** and pyrazole **7**. The reaction can be optimized to afford compounds **6** in synthetically useful yield. In the case of N-benzyl-thiadiazabicyclo[3.1.0]hexene derivative **4a** the different substitution on the aziridine nitrogen produced a different reaction course, affording the thiadiazine derivative **6a** and the pyrimidine derivative **8**.

Dialkylamino-isothiazole 1,1-dioxides have been demonstrated to be effective reaction partners in 1,3-dipolar cycloaddition reactions with diazoalkanes[2], oxazolones[3], münchnones[3], nitrile oxides[1] all of which occurred highly regioselectively at the C_4-C_5 bond. Through these reactions new heterocyclic syntheses became available based on transformation reactions of the primary bicyclic cycloaddition products which readily afforded functionalized single-ring heterocycles by cleavage of one ring. The thermal ring contraction of *v*-triazolines to aziridines is another well established reaction.[4] On this basis it appeared straightforward to plan a synthetic route to derivatives of the rare heterocycle 2-thia-3,6-diazabicyclo[3.1.0]hexene based on cycloaddition of azides to isothiazole 1,1-dioxides followed by ring contraction.

We now report on the synthesis of derivatives of 2-thia-3,6-diazabicyclo[3.1.0]hexene 2,2-dioxide and on their thermal transformations to S-N-containing heterocycles.

RESULTS

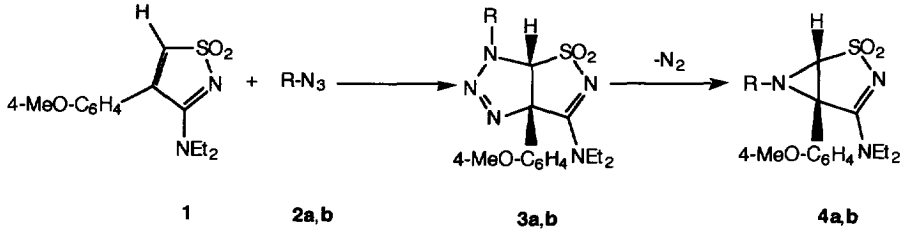
The cycloaddition reactions of 3-diethylamino-4-(4-methoxyphenyl)-isothiazole 1,1-dioxide (**1**) with benzyl azide (**2a**) and 2-phenylethyl azide (**2b**) were performed in refluxing benzene (3-5 h) and both resulted

in the formation of a single product which was identified as the corresponding cycloadduct containing the isothiazolo[4,5-*d*]-*v*-triazole ring (**3a** and **3b**, resp.) (Scheme 1).

At least at the detection limits, a ^{1}H-NMR spectrum of the crude reaction mixtures ruled out the existence of other isomeric cycloadducts.

Refluxing of compounds **3a** and **3b** at higher temperature (anisole, 8-16 h) or short heating neat a few degrees above the melting points, resulted in nitrogen elimination and formation of compounds **4a** and **4b**, respectively, by contraction of the triazoline ring (Scheme 1).

Scheme 1

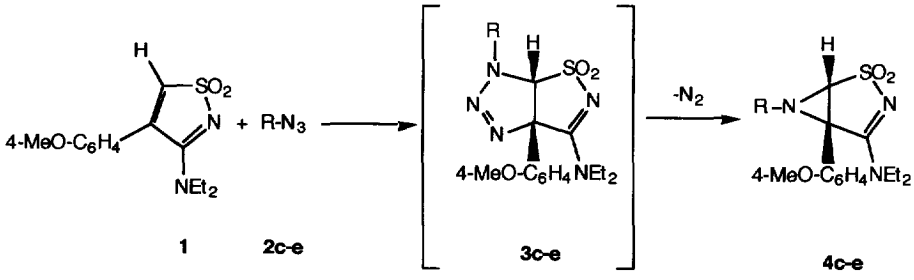


1 **2a,b** **3a,b** **4a,b**

2a, **3a**, **4a**: R=C_6H_5-CH_2
2b, **3b**, **4b**: R=C_6H_5-CH_2-CH_2

In the case of the cycloaddition reaction of substrate **1** with aryl azides **2c-e** the reaction was performed in boiling benzene until substantial disappearance of the starting materials and the aziridine compounds **4c-e** were obtained directly from the reaction mixture as the main reaction products (Scheme 2). A satisfactory yield of the labile condensed *v*-triazoline **3c** could be isolated only after a 75-day reaction at room temperature.

Scheme 2



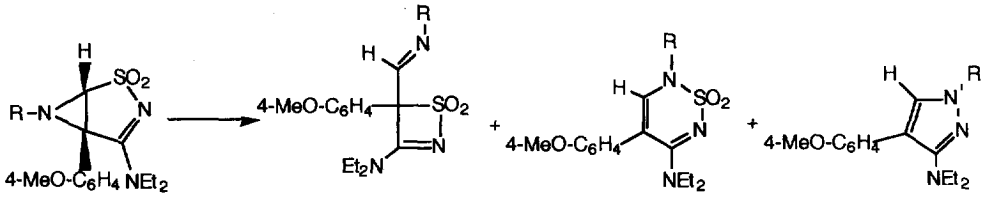
1 **2c-e** **3c-e** **4c-e**

2c,**3c**,**4c**: R= Ph
2d,**3d**,**4d**: R= 4-MeO-C_6H_4
2e,**3e**,**4e**: R= 4-NO_2-C_6H_4

Heating of compounds **4b-e** at their melting points or a few degrees above until complete transformation of the starting materials produced reaction mixtures containing the corresponding thiadiazine dioxides (**6**) as the

main products and thiazete dioxides **5** and pyrazoles **7** (Scheme 3) from which most compounds, i.e. **5c-e**, **6b-e**, **7b,c,e**, could be isolated by chromatography in yields shown in Table 1. Further heating of the above reaction mixtures until no more changes could be observed in the products ratio, resulted in the disappearance of **5**, the thiadiazine **6** and pyrazole **7** derivatives being the sole final and thermally stable reaction products. As a confirmation of this result, heating of pure **6e** and **7e** did not produce any changes, whereas prolonged heating of pure **5e** resulted in a mixture of **6e** and **7e**.

Scheme 3



4,5,6,7	R
b	C_6H_5-CH_2-CH_2
c	C_6H_5
d	4-MeO-C_6H_4
e	4-NO_2-C_6H_4

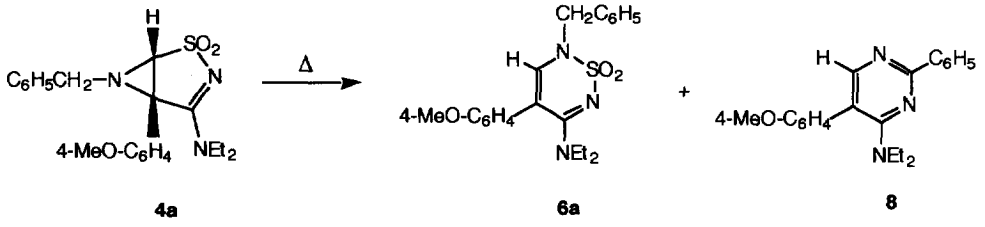
Table 1 *

5b (-)	6b (12%)	7b (1%)
5c (1%)	6c (51%)	7c (2%)
5d (10%)	6d (1 %)	7d (-)
5e (3%)	6e (27 %)	7e (6%)

* In parentheses yield of isolated compounds

The N-benzyl substituted compound **4a** gave on heating at its melting point a partially different outcome with respect to its analogues **4b-e** producing a minor amount of the thiadiazine derivative **6a** and as the main reaction product the pyrimidine compound **8** (Scheme 4).

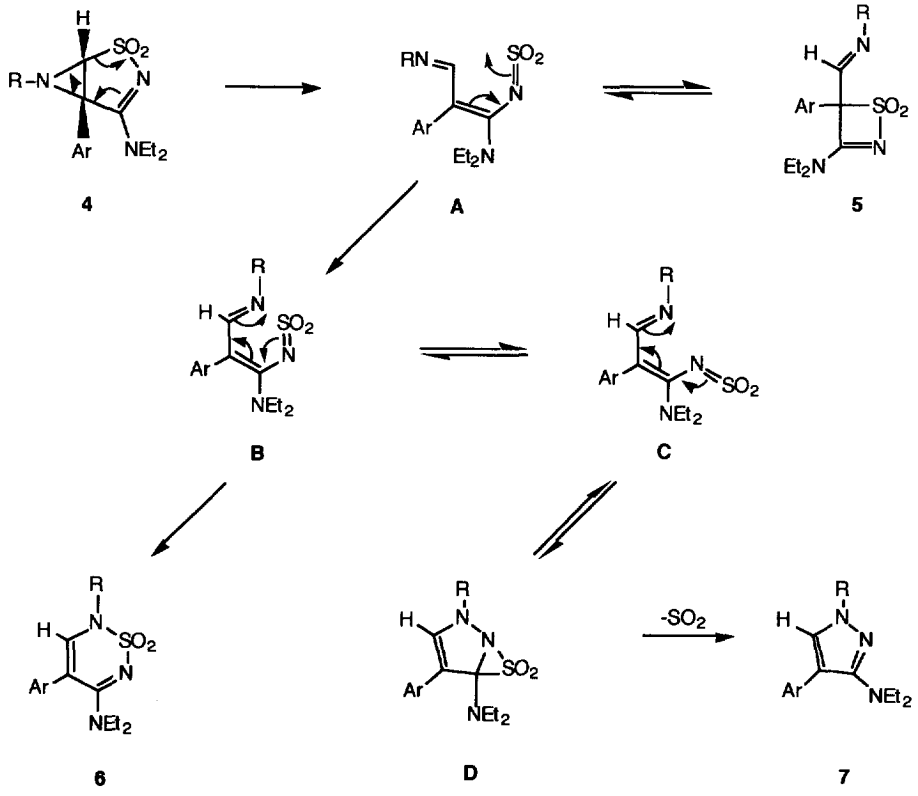
Scheme 4



DISCUSSION

The cycloaddition reaction of both arylalkyl- and arylazides **2** to 3-diethylamino-4-(4-methoxyphenyl)-isothiazole 1,1-dioxide (**1**) was found to be highly regioselective, only one isomer being formed in detectable amounts. This result is in good agreement with the general trend displayed by azides in cycloaddition reactions involving electron-deficient alkenes, being well known that in this case the terminal azido nitrogen attacks the more nucleophilic center of the double bond.[5] In the present case it has been demonstrated through reactions of **1** with nucleophiles that the less electron-poor atom is C-4.[6] The formation of the aziridine ring through nitrogen elimination from the *v*-triazoline structure is another well precedented reaction occurring with the intermediacy of a zwitterionic intermediate.[4] Starting from aryl azides only labile triazolines were formed which were not isolated in fact, except compound **3c** under special conditions. This was not unexpected because it is known that N-aryl-*v*-triazolines, especially when electron-withdrawing substituents are present on the aryl group, are more keen to ring cleavage with respect to their N-alkyl substituted counterparts.[7] The results of the thermal transformation reactions of compounds **4** allow the formulation of a mechanistic model as represented in Scheme 5.

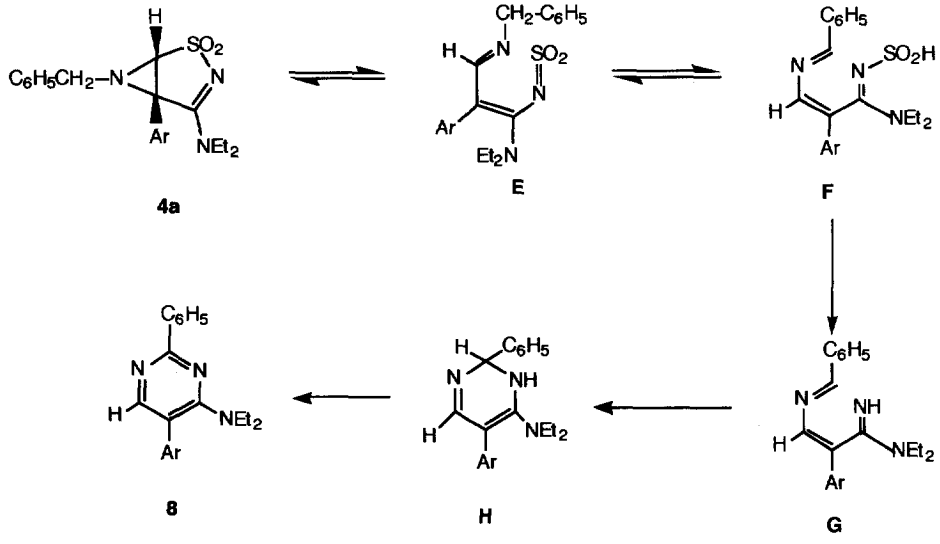
Scheme 5



The valence isomerization process related to the cycloreversion of **4** results in an equilibrium between **4** and the open-chain intermediates **A**, **B**, **C** and the bicyclic intermediate **D**. The s-*trans*-s-*cis* form **A** possesses the same geometry as the parent **4** which is required both to revert to the starting bicyclic system and to cyclize to the four-membered-ring derivative *i. e.* azetine **5**.

Clearly the relatively low stability of the azomethinyl-substituted strained ring in the latter compound with its vinylcyclobutene-like structure makes its formation a reversible, kinetically controlled reaction and accounts for low yields and final transformation into more stable compounds. Conformational equilibrium of **A** with **B** and **C** allows to rationalize products **6** and **7**. The s-*cis*-s-*cis* form **B** is favourable to closure to a six-membered ring leading to **6** which combines both strain absence and electronic stabilization, thus representing the thermodinamically preferred isomer which makes its formation essentially irreversible. Cyclization of the alternative s-*cis*-s-*trans* conformer **C** to the bicyclic intermediate **D** is probably disfavoured by ring strain, accounting for low yields of the final product **7**, but is rendered irreversible by the stabilization determined by the SO_2-extrusion step.[8] It may be well possible that in fact two-step zwitterionic mechanisms rather than concerted processes are to be considered in this picture because of the high electronegativity differences which can stabilize polarized forms. A similar reasoning holds for the thermal transformation of **4a** into **6a**. However, in this case the main reaction path leads to the formation of a pyrimidine compound and a rationalization of this result is as depicted in Scheme 6.

Scheme 6



The relatively high acidity of the benzylic hydrogens favours the existence of a tautomeric equilibrium between the open-chain isomer of **4a** that is **E** and the unstable thionimidic acid **F**. Spontaneous sulfur dioxide elimination and electrocyclization of the resulting diazahexatriene derivative **G** results in the dihydropyrimidine **H** which undergoes aromatization under the reaction conditions. Several examples of spontaneous aromatization of dihydropyrimidines have been reported.[9]

STRUCTURES

The structures of all new compounds were unequivocally established by analytical and spectroscopic evidences. ^{1}H-NMR evidence was used for structural identification of **3a,b** on the basis of a characteristic singlet at δ 4.2-4.3, clearly associated with H-3*a*, and on N.O.E. experiments which demonstrated the spatial proximity of H-3*a* to the methylene or ethylene group in **3a** and **3b**, respectively. In the ^{1}H-NMR spectra of compounds **4a,b** a corresponding singlet signal is present, shifted to higher fields (δ 3.7) and associated with H-6. Structure of compounds **5** was inferred from ^{1}H-NMR spectra which showed a typical singlet associated with the imine hydrogen (δ 8.0-9.0). Performing coupled and decoupled ^{13}C-NMR spectra, besides the signals associated with the diethylamino and 4-methoxy-substituted aryl groups, we could assign beyond doubt a signal in the range of δ 145–155 to the imine carbon and signals in the range of δ 165-170 and δ 95-100 to C-3 and C-4, respectively. Definitive structural proof was obtained by X-ray diffraction (see below). The main feature in the ^{1}H-NMR spectra of compounds **6** was a singlet in the range of δ 6.2–7.0 associated with H-5 and a signal at about δ 140-150 corresponding to C-5. Both in compounds **5** and **6**, a striking feature in the ^{1}H-NMR spectra is the great complexity of the signals associated with the diethylamino group, evidencing the magnetic non equivalence of chemically identical hydrogens. This points to a rotational barrier about the C-N bond which can be explained by an extensive conjugation of the amidine system incorporated in the heterocyclic ring. Final information about the structure of compounds **6** was given by X-ray diffraction (see below). Spectra of compounds **7** showed the signal associated with H-5 at δ 6.80–7.10 and a singlet at δ 110-140 associated with C-5. The ^{1}H-NMR spectrum of compound **8** is characterized by a singlet at δ 8.15 clearly associated with H-6 and ^{13}C-NMR spectrum showed C-6 at δ 157.5.

X-ray diffraction experiments have been performed on crystalline samples of compounds (**5d**) and (**6e**), in order to confirm the spectroscopic findings on these systems and obtain further structural detail. To our knowledge, (**5d**) is the first thiazete S,S dioxide whose geometry has been characterized by X-ray diffraction. Dimensions of the crystals analysed, together with details about data collection, processing and refinement are reported in Table 2.

(5d). Two independent molecules are present in the asymmetric unit. The N-phenyl-imino group has *trans* (E) geometry across the N=C bond. At convergence, a maximum of 0.19 eÅ^{-3} was present in the residual map close to atom C18', one of the methylene carbon atoms in the dimethylamino moiety of molecule B. Moreover, atomic displacement parameters for this atom, and for the methyl carbon C19' bonded to it, are about 1.5 times greater than those of the carbon atoms in the corresponding ethyl chain of molecule A, and show marked anisotropy. These findings suggest the presence of some disorder in this region, but no improvement of the fit could be obtained by splitting the C18'-C19' ethyl group in two conformers with site occupancy factors summing up to unity.

Selected bond distances and angles are gathered in Table 3. Fig. 1 shows *ORTEP*[10] plots of molecule A and B in the asymmetric unit. The orientation of the four membered ring with respect to the viewpoint is the same in the two figures, so that main differences in the geometry of the two molecules can be appreciated visually. In particular, it is seen that the N-phenyl-imino group is nearly planar in molecule A, the torsion angle C5-C4-N2=C3 amounting to -4.4°, while in molecule B planarity is lost: the corresponding torsion angle C5'-C4'-N2'=C3' is 25.9°. A second major difference is apparent at the methoxy groups: in both molecules A and

Table 2. Crystal data and summary of the X-ray diffraction experiments for **5d** and **6e**.

Compound	(5d)	(6e)
crystal dimensions (mm)	0.20x0.125x0.10; 0.25x0.22x0.15	0.20x0.10x0.20; 0.40x0.36x0.26
empirical formula	$C_{21}H_{25}N_3O_4S$	$C_{20}H_{22}N_4O_5S$
formula weight	415.50	430.48
temperature (K)	294(2)	
crystal system	Monoclinic	Orthorhombic
space group	$P2_1/n$ (#14)	Pbca (#61)
a (Å)	17.920(3)	10.894(5)
b (Å)	12.727(2)	12.437(2)
c (Å)	20.227(3)	31.172(4)
β (deg)	111.68(1)	-
V ($Å^3$)	4286.6(13)	4223.4(1.9)
Z	8	8
$F_{(000)}$	1760	1808
density (calcd) (g/cm^3)	1.287	1.355
abs. coeff. μ (Mo Kα) (cm^{-1})	1.8	1.9
diffractometer	Siemens P4	
rad. wavelength (Å)	Mo Kα (0.71073)	
scan technique	ω/2θ	ω
scan speed (deg/min)	variable	
refl.s used for cell determination	24 (18°<2θ<10°)	45(12°<2θ<20°)
reflections collected	20473 (h ±k ±l)	17136 (h -k ± l)
$2\theta_{max}$ (deg)	45	45
no. of independent refls.	5599	2751
refinement method	full-matrix least-squares on F^2	
obs.d data (I>0)	4593	2410
no. of parameters	596	346
final wR(F) (on F>4s(F))	0.062	0.047
final wR(F) (all obs.d data)	0.170	0.112
goodness-of-fit	0.953	0.892
largest ΔF peak ($eÅ^{-3}$)	0.19	0.16

B, the C atoms of these groups lie approximately in the plane of the attached O-phenyl moiety, but the conformations around the PhO-CH_3 bonds in the two molecules are opposite.

S-O distances in molecule A compare fairly well with an average value of 1.430(9) Å for the same bond in several sulfonamides found in the literature.[11] The S-O distances in molecule B are slightly longer, but equivalent within 2esd's to those in A. Bond distances between atoms in the four membered ring in molecule A are equivalent within 1 e.s.d. to the corresponding ones in molecule B, with the only exception of the C-S bond, which is 1.877(6) Å long in A, and 1.866(5) long in B. Both of these values are significantly longer than the average C-S bond length in CSO_2NR_2 moieties reported in the International Tables of Crystallography[11], 1.758(18) Å. Values for the same bond in four thiazetidine S,S dioxides whose structures have been studied by X-ray diffraction[12-15] are in the range 1.761(9)-1.806(2) Å, thus suggesting that the values found for (**5d**) are peculiar of the structure of this thiazete ring. Marked planarity is observed around the nitrogen atoms of the diethylamino group in both molecules A and B; the exocyclic CN bonds are remarkably short: $d_{C3\text{-}N2}$=1.253(7) Å, $d_{C3'\text{-}N2'}$=1.245(10), to be compared with an average value of 1.355(14) Å for this kind of CN bond in the literature[11]; besides, torsion angles close to zero are observed for N1-C1-N3-C18 ,t=3.3(3)°, and N1-C1-N3-C20, t=-2.5(5)°; corresponding values in molecule B are 3.1(4)° and 1.2(7)°. These findings give additional evidence of significant conjugation in the amidine moiety, as already inferred from NMR data.

Four O···H and three N···H intermolecular contacts shorter than the sum of the Van der Waals radii are present in the crystal; all of them involve atoms of symmetry-related molecules (that is, (A-A)- and (B-B)- but not (A-B)-contacts are present). The O···H distances are in the range 2.481 Å-2.628 Å; the N···H distances are in the range 2.585 Å-2.738 Å. Visual inspection of the crystal packing along the crystallographic **b** axis revealed that molecules A are packed close to each other, and span broad regions elongated in the direction of the *n* glide translation, while molecules B are also clustered together, again in regions parallel to the same direction, so that alternating A and B layers are formed, with no hydrogen bond between them.

(6e). Fig 2 shows the *ORTEP*[10] plot of the molecule with the numbering scheme. Table 4 reports selected bond lengths and angles for (**6e**). The geometry of the ring and around the sulfur atom is in keeping with the values of bond distances and bond angles from a number of X-ray diffraction studies of differently substituted 1,2,6-thiadiazine S,S dioxides which have appeared in the literature.[16-26] The majority of these studies has shown the thiadiazine ring adopting an envelope conformation, with the S atom at the flap, at distances from the plane of the remaining atoms in the ring varying between 0.09 and 0.76 Å. The heterocycle in compound (**6e**) is also an envelope, with atom S1 at 0.679(4) Å from the least-squares plane through N1-C1-C2-C3 and N2. A few structures among the published ones has shown the thiadiazine ring in a nearly planar[22,24], or boat-like[17,20,21] arrangement. The presence of relatively bulky substituents in position 2 or 4 on the ring, and the effects of packing forces have been proposed as major reasons for the adoption of the latter conformation.[21] The heterocyclic ring of (**6e**) is in an envelope conformation even in presence of the *p*-methoxyphenyl and *p*-nitrophenyl substituents at C4 and N2, respectively;[27] this seems to rule out the presence of bulky substituents as a main cause for the boat conformation observed in the aforementioned structures.

Also in this compound, like in (**5d**), the geometry around the nitrogen atom of the diethylamino substituent is nearly planar (the sum of bond angles around N4 is 358.4°). When compared with the exocyclic CN bonds of the diethylamino moiety in (**5d**), the C1-N4 bond length is significantly longer: $d_{C1\text{-}N4}$=1.352(5) Å. This observation, and the values of the torsion angles around the exocyclic C1-N4 bond, which are around

Table 3. Selected bond lengths and bond angles in (5d) with esd's in parentheses.

(a) Selected bond lengths (Å)

Mol. A		Mol B	
S1-O1	1.431(3)	S1'-O1'	1.441(4)
S1-O2	1.433(3)	S1'-O2'	1.438(4)
S1-N1	1.652(5)	S1'-N1'	1.647(6)
S1-C2	1.877(6)	S1'-C2'	1.866(5)
C1-C2	1.534(7)	C1'-C2'	1.533(10)
C1-N1	1.331(8)	C1'-N1'	1.328(8)
C2-C3	1.489(6)	C2'-C3'	1.493(7)
C3-N2	1.253(7)	C3'-N2'	1.245(10)

(b) Selected bond angles (degrees)

Mol. A		Mol. B	
O1-S1-O2	117.0(2)	O1'-S1'-O2'	117.4(3)
O1-S1-N1	112.7(2)	O1'-S1'-N1'	113.7(3)
O1-S1-C2	113.7(2)	O1'-S1'-C2'	113.5(2)
O2-S1-C2	115.1(2)	O2'-S1'-C2'	114.2(2)
O2-S1-N1	112.3(2)	O2'-S1'-N1'	111.8(2)
N1-S1-C2	80.7(2)	N1'-S1'-C2'	80.9(2)
N1-C1-C2	106.0(5)	N1'-C1'-C2'	105.8(6)
S1-C2-C1	79.2(3)	S1'-C2'-C1'	79.4(3)
S1-N1-C1	94.0(3)	S1'-N1'-C1'	93.9(4)
N3-C1-C2	127.3(5)	N3'-C1'-C2'	128.0(5)
N1-C1-N3	126.6(4)	N1'-C1'-N3'	126.2(6)
C1-N3-C18	122.7(4)	C1'-N3'-C18'	123.3(6)
C1-N3-C20	119.1(5)	C1'-N3'-C20'	118.0(5)
C18-N3-C20	118.0(5)	C18'-N3'-C20'	118.6(7)
S1-C2-C3	110.0(3)	S1'-C2'-C3'	110.7(4)
S1-C2-C11	115.5(3)	S1'-C2'-C11'	115.0(4)
C1-C2-C3	112.3(3)	C1'-C2'-C3'	112.7(5)
C1-C2-C11	116.2(4)	C1'-C2'-C11'	117.7(5)
C2-C3-N2	121.5(5)	C2'-C3'-N2'	121.8(7)
C3-N2-C4	123.1(4)	C3'-N2'-C4'	121.1(6)

Table 4. Selected bond lengths and bond angles in (6e) with esd's in parentheses.

(a) Selected bond lengths (Å)

Atoms	Bond Length
S1-O1	1.428(3)
S1-O2	1.432(4)
S1-N1	1.585(5)
S1-N2	1.694(3)
N1-C1	1.328(5)
C1-C2	1.468(5)
C2-C3	1.334(6)
C3-N2	1.386(5)
C1-N4	1.352(5)
N4-C10	1.489(7)
N4-C12	1.530(7)
C10-C11	1.494(10)
C12-C13	1.434(8)
C2-C14	1.492(5)
N2-C4	1.422(4)
N3-C7	1.492(6)
N3-O3	1.208(5)
N3-O4	1.221(5)

(b) Selected bond angles (degrees)

Atoms	Bond Angle
O1-S1-O2	117.6(2)
O1-S1-N1	109.0(2)
O1-S1-N2	106.4(2)
O2-S1-N1	115.1(2)
O2-S1-N2	107.3(2)
N1-S1-N2	101.9(2)
S1-N1-C1	121.1(3)
N1-C1-C2	121.5(4)
C1-C2-C3	117.9(4)
C2-C3-N2	124.5(4)
C3-N2-S1	113.6(3)
C1-N4-C10	123.8(5)
C1-N4-C12	117.7(4)
C10-N4-C12	118.4(5)
C1-C2-C14	123.4(4)
C3-C2-C14	118.5(4)
C3-N2-C4	122.3(3)
S1-N2-C4	122.5(3)
O3-N3-O4	124.8(5)
O3-N3-C7	118.2(5)
O4-N3-C7	116.9(5)
C2-C3-N2	121.5(5)

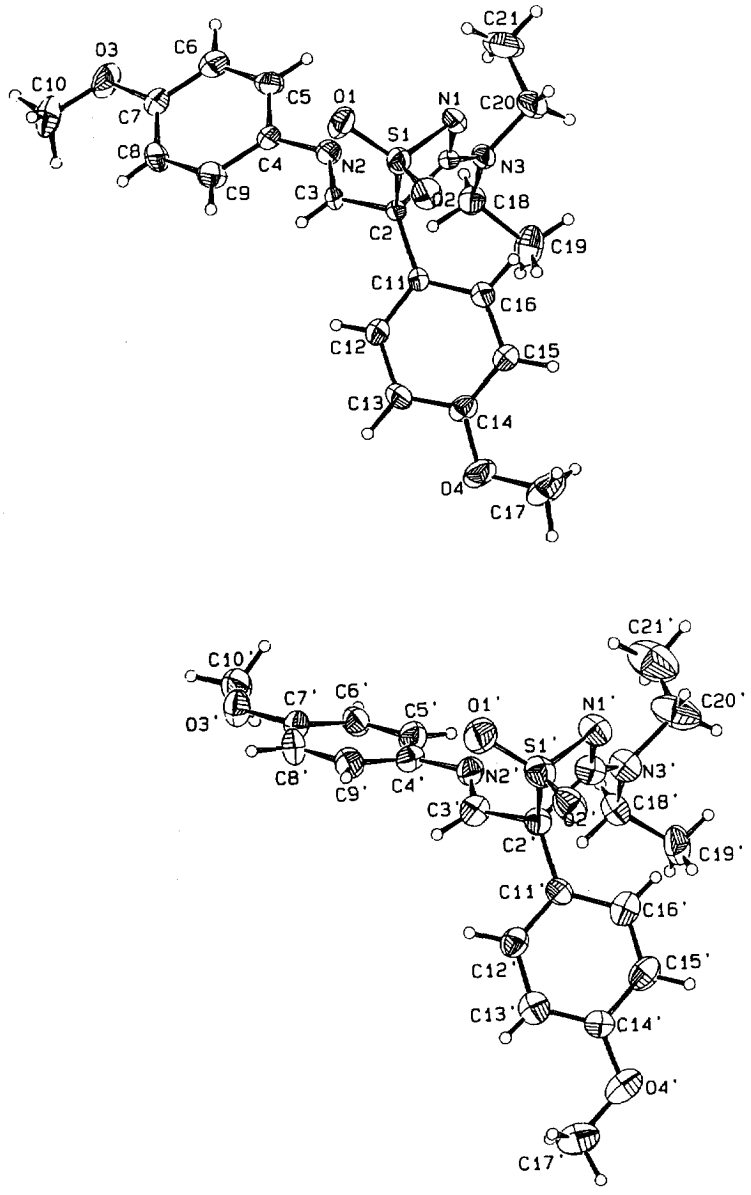


Fig. 1. molecule A (top); molecule B (bottom). ORTEP plot of **5d**. Probability ellipsoids are drawn at 30% probability level. H atoms are represented by circles of arbitrary radius. Atom C1 only has not been labelled.

20° in modulus, suggest that in (**6e**) a lower degree of conjugation with the unsaturated system in the ring is present than that observed in the corresponding amidine fragment of (**5d**).

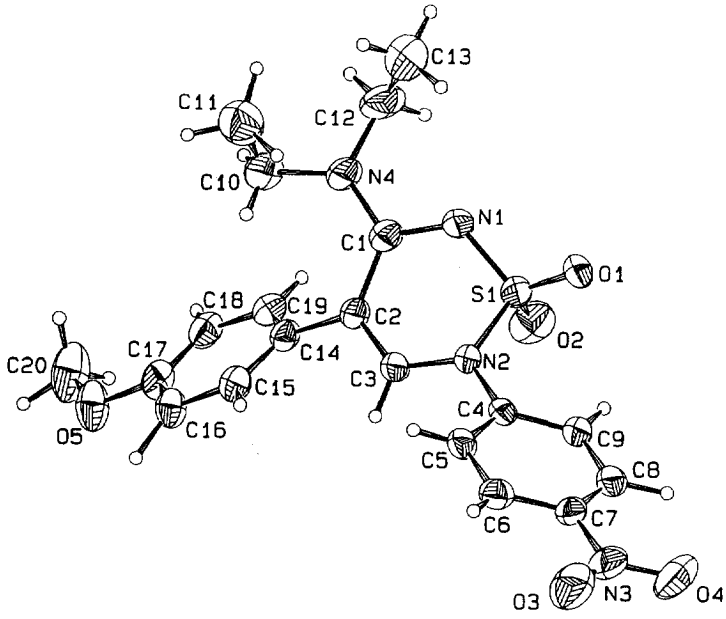


Fig. 2. ORTEP plot of (**6e**). Probability ellipsoids are drawn at 30% probability level. H atoms are represented by circles of arbitrary radius.

CONCLUSIONS

Besides a confirmation of the good reactivity of 3-dialkylamino-isothiazole 1,1-dioxides in the 1,3-dipolar cycloaddition reactions with azides which allow a facile entry to derivatives of the 2-thia-3,6-diazabicyclo[3.1.0]hexene ring, present results offer a new insight in the chemistry of this S,N-containing heterocyclic ring and its rearrangement reactions which result in the formation of uncommon heterocycles as the thiazete **5** or of compounds of potential pharmaceutical interest as the thiadiazines **6**. In this respect synthetic interest is present because on the above experimental basis a direct route for 3-dialkylamino-1,4-diaryl-1,2,6-thiadiazine 1,1-dioxides was developed. Prolonged (16-18 hr) heating at the appropriate temperature (refluxing anisole, ca. 140°C) of compound **1** with azides **2c-e** resulted in the direct formation of the corresponding thiadiazine compounds **6a-c** in up to 60% yield, thus representing a valuable one-pot synthetic method.

Acknowledgments: Thanks are due to the Italian CNR (CSRSRC at Dipartimento di Chimica Fisica of the University of Milano) for the use of the X-ray equipment. We are also grateful with Mr G. Marazzi (Prassis-Sigma Tau, Settimo Milanese, Milano, Italy) for his always kind collaboration. Financial aid of MURST (40%) is aknowledged.

EXPERIMENTAL

Melting points were determined using a Büchi 510 (capillary) or a Electrothermal 9100 apparatus. ^{1}H-NMR spectra (ppm, tetramethylsilane as internal standard, $CDCl_3$ as solvent except when indicated) were obtained with a Bruker AC 200, Bruker AC 300 and a Varian Gemini 200 instruments. Chemical shifts (δ) are given in ppm and the coupling constants (J) are given in Hz. T.L.C. : ready-to-use silica gel plates. Column chromatography: silica gel [Kieselgel 60-70 230 ASTM (Merck)] with the eluant indicated. Flash chromatography (F.C.): silica gel [Kieselgel 230-400 ASTM (Merck)]. Mass spectra were obtained by an electron impact ionization technique at 70 eV from a Finningan INCOS 50 instrument using the direct exposure probe (DEP).

X-Ray data: For both compounds (**5d**) and (**6e**), two specimens were analysed at room temperature. The intensities of three standard reflections were periodically re-measured: they did not show any appreciable decay. Intensities were corrected for Lorentz and polarization, but not for absorption. The structures were solved by direct methods, employing program *SIR92*.[28] Refinements were conducted with program *SHELXL93*.[29] All the data having I>0 were fitted. Positional and anisotropic displacement parameters were varied for non-H atoms. Hydrogen atoms were constrained to idealized valence angles, while the CH distances were allowed to refine, together with isotropic displacement parameters. Coordinates and isotropic displacement parameters for non-H atoms are reported in Tables 5 and 6 for (**5d**) and (**6e**) respectively. Tables of bond lengths, bond angles and torsion angles for both compounds, and tables of anisotropic displacement parameters for non-H atoms have been deposited as supplementary material.

Materials. **1**[30], **2a-e**[31-33] have already been described.

3-Benzyl-4,4-dioxo-6a-(4-methoxyphenyl)-3a,6a-dihydroisothiazolo[4,5-d]-v-triazole (3a). Equimolecular amounts of **1** (2.8 g, 9.4 mmol) and **2a** (8.3 mL of a 1.13 M benzene solution) were refluxed for about 3 hours until disappearance of the reactants (T.L.C. cyclohexane/ethyl acetate 3/2). The solvent was evaporated under reduced pressure and the residue crystallized from dichloromethane/diisopropyl ether.Yield: 91%. M.p.: 107°C. Anal. Calcd. for $C_{21}H_{25}N_5O_3S$ (427) : C 59.02% H 5.85% N 16.38% Found: C 58.68% H 5.76% N 16.19%. ^{1}H-NMR: 0.86 (t, 3H, J=7.1 Hz, CH_3); 1.28 (t, 3H, J=7.1 Hz, CH_3); 3.34-3.70 (m, 4H, CH_2); 3.78 (s, 3H, OCH_3); 4.25 (s, 1H, H-3*a*); 4.90 (d, 1H, J=15.3 Hz, CH_2Ar); 5.52 (d, 1H, J=15.3 Hz, CH_2Ar); 6.87 (AB system, J=8.8 Hz, 2H, Aryl-H); 7.03 (AB system, J=8.8 Hz, 2H, Aryl-H); 7.23-7.36 (m, 5H, Aryl-H).

4,4-Dioxo-6a-(4-methoxyphenyl)-3-(β–phenylethyl)-3a,6a-dihydroisothiazolo[4,5-d]-v-triazole (3b). Equimolecular amounts of **1** (1 g, 3.4 mmol) and **2b** (32 mL of a 0.11 M toluene solution) were refluxed for about 5 hours until disappearance of the reactants (T.L.C. cyclohexane/ethyl acetate 3/2). The solvent was

Table 5. Positional and isotropic displacement parameters for non-H atoms in compounds (**5d**).

Atom	x	y	z	U_{iso}*(Å^2)	Atom	x	y	z	U_{iso}*(Å^2)
S1	-0.31506(9)	-0.7289(1)	0.24456(8)	0.0505(7)	S1'	0.1706(1)	-0.7536(1)	0.3008(1)	0.0715(9)
O1	-0.2869(2)	-0.7152(3)	0.3200(2)	0.068(2)	O1'	0.2057(3)	-0.7639(3)	0.3771(2)	0.095(3)
O2	-0.4003(2)	-0.7270(3)	0.2067(2)	0.064(2)	O2'	0.0931(3)	-0.8006(3)	0.2650(2)	0.086(2)
O3	0.1486(3)	-0.4734(4)	0.4985(2)	0.079(2)	O3'	0.4935(3)	-0.3062(4)	0.5812(2)	0.077(2)
O4	-0.4277(3)	-0.4272(3)	-0.0495(2)	0.076(2)	Q4'	-0.0993(3)	-0.4400(4)	0.0652(2)	0.088(2)
N1	-0.2718(3)	-0.8289(3)	0.2208(2)	0.049(2)	N1'	0.2332(3)	-0.7810(4)	0.2606(3)	0.068(3)
N2	-0.1206(3)	-0.6415(3)	0.2865(2)	0.049(2)	N2'	0.3018(3)	-0.5344(4)	0.3445(3)	0.058(2)
N3	-0.1876(3)	-0.8002(3)	0.1565(2)	0.045(2)	N3'	0.2729(3)	-0.6496(4)	0.1986(3)	0.066(3)
C1	-0.2331(3)	-0.7684(4)	0.1904(3)	0.041(2)	C1'	0.2348(4)	-0.6829(5)	0.2387(4)	0.059(3)
C2	-0.2549(3)	-0.6548(4)	0.2010(3)	0.034(2)	C2'	0.1814(4)	-0.6194(4)	0.2684(3)	0.052(3)
C3	-0.1874(4)	-0.5984(5)	0.2559(3)	0.043(3)	C3'	0.2287(5)	-0.5502(5)	0.3290(3)	0.060(3)
C4	-0.0553(3)	-0.5912(4)	0.3407(3)	0.044(3)	C4'	0.3468(4)	-0.4732(5)	0.4048(3)	0.053(3)
C5	0.0122(4)	-0.6512(5)	0.3725(3)	0.056(3)	C5'	0.4146(4)	-0.4242(5)	0.4024(4)	0.067(4)
C6	0.0791(4)	-0.6113(5)	0.4254(3)	0.063(3)	C6'	0.4643(4)	-0.3650(5)	0.4599(3)	0.062(3)
C7	0.0791(4)	-0.5078(5)	0.4464(3)	0.054(3)	C7'	0.4473(4)	-0.3580(5)	0.5210(3)	0.059(3)
C8	0.0126(4)	-0.4467(5)	0.4136(3)	0.058(3)	C8'	0.3793(4)	-0.4056(5)	0.5231(4)	0.070(4)
C9	-0.0544(4)	-0.4879(5)	0.3613(3)	0.058(3)	C9'	0.3301(5)	-0.4623(5)	0.4662(4)	0.069(4)
C10	0.1518(5)	-0.3685(6)	0.5226(4)	0.085(4)	C10'	0.5643(5)	-0.2540(6)	0.5820(4)	0.081(4)
C11	-0.3029(3)	-0.5955(4)	0.1350(3)	0.041(2)	C11'	0.1050(3)	-0.5727(4)	0.2157(3)	0.050(3)
C12	-0.3034(4)	-0.4873(5)	0.1314(3)	0.054(3)	C12'	0.0601(4)	-0.5016(5)	0.2367(4)	0.060(3)
C13	-0.3466(4)	-0.4332(5)	0.0694(3)	0.061(3)	C13'	-0.0093(4)	-0.4575(5)	0.1883(4)	0.065(4)
C14	-0.3900(3)	-0.4883(6)	0.0093(3)	0.054(3)	C14'	-0.0334(4)	-0.4812(5)	0.1177(4)	0.058(3)
C15	-0.3934(4)	-0.5957(5)	0.0108(3)	0.061(3)	C15'	0.0090(4)	-0.5552(6)	0.0959(4)	0.073(4)
C16	-0.3506(3)	-0.6472(5)	0.0733(3)	0.059(3)	C16'	0.0769(4)	-0.6001(5)	0.1440(3)	0.066(3)
C17	-0.4766(5)	-0.4799(7)	-0.1129(4)	0.092(4)	C17'	-0.1453(5)	-0.3649(7)	0.0860(5)	0.096(4)
C18	-0.1434(4)	-0.7269(5)	0.1277(3)	0.057(3)	C18'	0.2752(5)	-0.5386(5)	0.1791(3)	0.067(4)
C19	-0.1740(5)	-0.7311(7)	0.0472(3)	0.086(4)	C19'	0.2462(7)	-0.5226(8)	0.0993(4)	0.104(5)
C20	-0.1735(4)	-0.9131(5)	0.1523(4)	0.067(4)	C20'	0.3186(6)	-0.7291(9)	0.1731(8)	0.123(7)
C21	-0.0997(6)	-0.9481(6)	0.2122(5)	0.102(5)	C21'	0.4026(8)	-0.7162(9)	0.2130(7)	0.154(9)

Table 6. Positional and isotropic displacement parameters for non-H atoms in compounds (**6e**).

Atom	x	y	z	U_{iso}*(Å^2)
S1	0.90829(9)	0.1009(1)	0.65427(3)	0.0720(5)
O1	1.0107(2)	0.0510(4)	0.66502(8)	0.095(1)
O2	0.9040(3)	0.2275(3)	0.6409(1)	0.102(2)
O3	1.1026(4)	-0.3043(5)	0.4751(1)	0.136(2)
O4	1.2197(3)	-0.1610(4)	0.4854(1)	0.113(2)
O5	0.2629(3)	0.1863(3)	0.5882(1)	0.096(1)
N1	0.8263(3)	0.0694(4)	0.69147(9)	0.076(2)
N2	0.8605(2)	0.0140(3)	0.61337(9)	0.056(1)
N3	1.1327(4)	-0.2094(5)	0.4916(1)	0.087(2)
N4	0.6586(3)	0.0419(4)	0.7180(1)	0.088(2)
C1	0.7226(3)	0.0546(4)	0.6834(1)	0.070(2)
C2	0.6815(3)	0.0498(4)	0.6393(1)	0.056(2)
C3	0.7505(3)	0.0231(4)	0.6080(1)	0.058(2)
C4	0.9281(3)	-0.0387(4)	0.5817(1)	0.050(2)
C5	0.8938(4)	-0.1424(5)	0.5599(1)	0.056(2)
C6	0.9600(4)	-0.1970(5)	0.5301(1)	0.065(2)
C7	1.0598(3)	-0.1470(5)	0.5227(1)	0.061(2)
C8	1.0943(4)	-0.0444(5)	0.5429(1)	0.060(2)
C9	1.0281(3)	0.0121(5)	0.5726(1)	0.057(2)
C10	0.5520(4)	-0.0197(9)	0.7170(2)	0.101(3)
C11	0.5434(7)	-0.1389(7)	0.7409(3)	0.116(3)
C12	0.7010(5)	0.0885(9)	0.7611(2)	0.126(3)
C13	0.7557(7)	-0.0081(9)	0.7837(3)	0.140(4)
C14	0.5699(3)	0.0850(5)	0.6275(1)	0.057(2)
C15	0.5126(4)	0.0202(5)	0.5970(2)	0.063(2)
C16	0.4103(3)	0.0567(5)	0.5839(2)	0.069(2)
C17	0.3644(3)	0.1594(5)	0.6033(2)	0.069(2)
C18	0.4182(4)	0.2252(5)	0.6338(2)	0.071(2)
C19	0.5209(4)	0.1875(5)	0.6450(2)	0.068(2)
C20	0.2057(6)	0.2812(8)	0.6101(4)	0.122(4)

*: Uiso = $1/6\pi^2$ Tr(βG); G=metric tensor; $\beta^{ij}=2\pi^2 U^{ij} a^*_i a^*_j$

evaporated under reduced pressure and the residue crystallized from dichloromethane/diisopropyl ether affording **3b**. Mother liquor was flash chromatographed on silica gel (cyclohexane/ethyl acetate 7/3 as the eluant) yielding a further amount of **3b**. **3b**: Yield: 72%. M.p.: 134°C. Anal. Calcd. for $C_{22}H_{27}N_5SO_3$ (441): C 59.86% H 6.12% N 15.87% Found: C 59.68% H 5.73% N 15.79%. ^{1}H-NMR: 0.82 (t, 3H, J=7.0 Hz, CH_3); 1.23 (t, 3H, J=7.0 Hz, CH_3); 2.92-3.20; 3.28-3.72 (2m, 6H, CH_2); 3.83 (s, 3H, OCH_3); 4.02-4.22 (m, 1H, CH_2); 4.29 (s, 1H, H-3*a*); 4.35-4.52 (m, 1H, CH_2); 6.91 (AB system, J=9.1 Hz, 2H, Aryl-H); 7.00 (AB system, J=9.1 Hz, 2H, Aryl-H); 7.06-7.24 (m, 5H, Aryl-H). *m/z* (413, M^+-N_2).

[2,2-Dioxo-5-(4-methoxyphenyl)-6-phenyl-2-thia-3,6-diaza-bicyclo[3.1.0]-3-hexen-4-yl]-diethylamine (4c). Equimolecular amounts of **1** (0.5 g, 1.7 mmol) and **2c** (0.9 mL of a 3 M benzene solution) were refluxed for about 8 hours until disappearance of the reactants (T.L.C. cyclohexane/ethyl acetate 3/2). The solvent was evaporated under reduced pressure and the residue crystallized from dichloromethane/diisopropyl ether affording **4c**. **4c**: Yield: 74%. M.p.: 166°C. Anal. Calcd. for $C_{20}H_{23}N_3SO_3$ (385): C 62.34% H 5.97% N 10.91% Found: C 62.38% H 5.86% N 10.75%. ^{1}H-NMR: 0.73 (t, 3H, J=7.0 Hz, CH_3); 0.94 (t, 3H, J=7.0 Hz, CH_3); 3.06-3.28; 3.53-3.80 (2m, 4H, CH_2); 3.84 (s, 3H, OCH_3); 4.18 (s, 1H, H-1); 6.95 (AB system, J=8.4 Hz, 2H, Aryl-H); 7.02-7.17 (m, 3H, Aryl-H); 7.22-7.38 (m, 2H, Aryl-H); 7.45 (AB system, J=8.4 Hz, 2H, Aryl-H). *m/z* (385, M^+).

[2,2-Dioxo-5,6-di-(4-methoxyphenyl)-2-thia-3,6-diaza-bicyclo[3.1.0]-3-hexen-4-yl]-diethylamine (4d). Equimolecular amounts of **1** (0.5 g, 1.7 mmol) and **2d** (2 mL of a 0.8 M benzene solution) were refluxed for about 40 hours until disappearance of the reactants (T.L.C. cyclohexane/ethyl acetate 3/2). The solvent was evaporated under reduced pressure and the residue chromatographed on silica gel (cyclohexane/ethyl acetate 7/3 as eluant) affording **4d**, which was crystallized from dichloromethane/diisopropyl ether. **4d**: Yield: 51%. M.p.: 137°C. Anal. Calcd. for $C_{21}H_{25}N_3SO_4$ (415): C 60.72% H 6.02% N 10.12% Found: C 60.68% H 5.76% N 10.00%. ^{1}H-NMR: 0.71 (t, 3H, J=7.0 Hz, CH_3); 0.97 (t, 3H, J=7.0 Hz, CH_3); 3.04-3.29; 3.52-3.73 (2m, 4H, CH_2); 3.77 (s, 3H, OCH_3); 3.83 (s, 3H, OCH_3); 4.14 (s, 1H, H-1); 6.83 (AB system, J=9.0 Hz, 2H, Aryl-H); 6.95 (AB system, J=8.8 Hz, 2H, Aryl-H); 7.04 (AB system, J=9.0 Hz, 2H, Aryl-H); 7.43 (AB system, J=8.8 Hz, 2H, Aryl-H). *m/z* (415, M^+).

[2,2-Dioxo-5-(4-methoxyphenyl)-6-(4-nitrophenyl)-2-thia-3,6-diaza-bicyclo[3.1.0]-3-hexen-4-yl]-diethylamine (4e). Equimolecular amounts of **1** (2.0 g, 6.8 mmol) and **2e** (8 mL of a 0.8 M benzene solution) were refluxed for about 30 hours until disappearance of the reactants (T.L.C. cyclohexane/ethyl acetate 3/2). The solvent was evaporated under reduced pressure and the residue chromatographed on Al_2O_3 (cyclohexane/ethyl acetate 100/0 ---> 0/100 as eluant) affording **4e**, which was crystallized from dichloromethane /diisopropyl ether. **4e**. Yield: 50%. M.p.: 93°C. Anal. Calcd. for $C_{20}H_{22}N_4SO_5$ (430): C 55.81% H 5.12% N 13.02% Found: C 55.34% H 5.14% N 13.03%. ^{1}H-NMR: 0.78 (t, 3H, J=7.0 Hz, CH_3); 1.01 (t, 3H, J=7.0 Hz, CH_3); 3.12-3.34; 3.57-3.70 (2m, 4H, CH_2); 3.87 (s, 3H, OCH_3); 4.27 (s, 1H, H-1); 6.98 (AB system, J=8.8 Hz, 2H, Aryl-H); 7.17 (AB system, J=9.0 Hz, 2H, Aryl-H); 7.44 (AB system, J=8.8 Hz, 2H, Aryl-H); 8.21 (AB system, J=9.0 Hz, 2H, Aryl-H). *m/z* (430, M^+).

General Procedure for Pyrolysis Reactions of Compounds 3 and 4. Compounds **3** and **4** were heated without solvent under nitrogen atmosphere at their melting points and when completely transformed (T. L. C.) were flash chromatographed on silica gel with the eluant indicated. Products obtained were crystallized with CH_2Cl_2/*i*-Pr_2O.

[6-Benzyl-2,2-dioxo-5-(4-methoxyphenyl)-2-thia-3,6-diaza-bicyclo[3.1.0]-3-hexen-4-yl]-diethylamine (4a). From **3a** (200 mg, 0.48 mmol). Eluant for F. C.: cyclohexane/ethyl acetate 3/7. **4a**: Yield: 73%. M.p.: 151°C. Anal. Calcd. for $C_{21}H_{25}N_3SO_3$ (399): C 63.16% H 9.92% N 16.67% Found: C 63.06% H 9.76% N 16.19%. ^{1}H-NMR: 0.35 (t, 3H, J=7.1 Hz, CH_3); 1.30 (t, 3H, J=7.1 Hz, CH_3); 2.31-2.52; 2.56-2.89; 3.26-3.47; 3.49-3.70 (4m, 4H, CH_2); 3.79 (s, 3H, OCH_3); 3.81 (s, 1H, H-1); 3.86 (d, 1H, J=14.0 Hz, CH_2Ar); 4.58 (d, 1H, J=14.0 Hz, CH_2Ar); 6.85 (AB system, J=8.8 Hz, 2H, Aryl-H); 7.27 (AB system, J=8.8 Hz, 2H, Aryl-H); 7.20-7.57 (m, 5H, Aryl-H). *m/z* (399, M^+).

[2,2-Dioxo-5-(4-methoxyphenyl)-6-(β-phenylethyl)-2-thia-3,6-diaza-bicyclo[3.1.0]-3-hexen-4-yl]-diethylamine (4b). From **3b** (330 mg, 0.75 mmol). Eluant for F. C.: petroleum ether/ethyl acetate 7/3. **4b**: Yield: 56%. M.p.: 155°C. Anal. Calcd. for $C_{22}H_{27}N_3SO_3$ (413): C 63.92% H 10.23% N 10.17.% Found: C 63.68% H 10.05% N 10.19%. ^{1}H-NMR: 0.64 (t, 3H, J=7.0 Hz, CH_3); 1.24 (t, 3H, J=7.0 Hz, CH_3); 2.84-3.67 (m, 8H, CH_2); 3.72 (s, 1H, H-1); 3.81 (s, 3H, OCH_3); 6.89 (AB system, J=8.8 Hz, 2H, Aryl-H); 7.18-7.38 (m, 7H, Aryl-H). *m/z* (413, M^+).

6-Benzyl-3-diethylamino-4-(4-methoxyphenyl)-1,2,6-thiadiazine 1,1-dioxide (6a) and 4-Diethylamino-5-(4-methoxyphenyl)-2-phenyl-pyrimidine (8). From **4a** (600 mg, 1.5 mmol). Eluant for F. C.: cyclohexane/ethyl acetate 9/1. **6a**: Yield: 2%. M.p.: 119°C. Anal. Calcd. for $C_{21}H_{25}N_3SO_3$ (399): C 63.16% H 6.26% N 10.53% Found: C 63.34% H 6.14% N 10.03%. ^{1}H-NMR: 0.90-1.15 (m, 6H, CH_3); 3.12-3.42 (m, 4H, CH_2); 3.80 (s, 3H, OCH_3); 4.84 (s, 2H, CH_2Ar); 6.67 (s, 1H, H-5); 6.84 (AB system, J=8.7 Hz, 2H, Aryl-H); 7.06 (AB system, J=8.7 Hz, 2H, Aryl-H); 7.25-7.42 (m, 5H, Aryl-H). **8**: Yield: 16%. M.p.: 114-115°C (CH_2Cl_2/iPr_2O). Anal. Calcd. for $C_{21}H_{23}N_3O$ (333): C 75.67% H 9.13% N 16.67% Found: C 75.18% H 9.16% N 16.89%. ^{1}H-NMR: 1.07 (t, 6H, J=7.0 Hz, CH_3); 3.39 (q, 4H, J=7.0 Hz, CH_2); 3.86 (s, 3H, OCH_3); 6.96 (AB system, J=8.8 Hz, 2H, Aryl-H); 7.31 (AB system, J=8.8 Hz, 2H, Aryl-H); 7.42-7.56 (m, 2H, Aryl-H); 8.13 (s, 1H, H-6); 8.37-8.50 (m, 2H, Aryl-H). *m/z* (333, M^+).

3-Diethylamino-4-(4-methoxyphenyl)-6-(β-phenylethyl)-1,2,6-thiadiazine 1,1-dioxide (6b) and 3-Diethylamino-4-(4-methoxyphenyl)-1-(β-phenylethyl)-pyrazole (7b). From **4b** (340 mg, 0.82 mmol). Eluant for F. C.: cyclohexane/ethyl acetate 9/1. **6b**: Yield: 12%. M.p.: oil. Anal. Calcd. for $C_{22}H_{27}N_3SO_3$ (413): C 63.92% H 10.23% N 10.17% Found: C 63.98% H 10.26% N 10.45%. ^{1}H-NMR: 0.85-1.18 (m, 6H, CH_3); 3.05-3.40 (m, 4H, CH_2); 3.10 (t, J=6.9 Hz, 2H, CH_2Ar); 3.80 (s, 3H, OCH_3); 3.90 (t, J=6.9 Hz, 2H, CH_2); 6.27 (s, 1H, H-5); 6.90 (AB system, J=8.7 Hz, 2H, Aryl-H); 6.82 (AB system, J=8.7 Hz, 2H, Aryl-H); 7.18-7.38 (m, 5H, Aryl-H). *m/z* (413, M^+). **7b**: Yield: trace (ca. 1%). M.p.: oil. ^{1}H-NMR: 1.00 (t, 6H, J=7.1 Hz, CH_3); 3.00-3.80 (m, 6H, CH_2+CH_2Ar); 3.82 (s, 3H, OCH_3); 4.10 (t, J=7.5 Hz, 2H, CH_2); 6.85 (s, 1H, H-5); 6.89 (AB system, J=8.8 Hz, 2H, Aryl-H); 7.08-7.37 (m, 5H, Aryl-H); 7.63 (AB system, J=8.8 Hz, 2H, Aryl-H). *m/z* (349, M^+).

*[1,1-Dioxo-4-(4-methoxyphenyl)-4-(phenyliminomethyl)-1,4-dihydro-[1,2]-thiazet-3-yl]diethylamine (**5c**), 3-Diethylamino-4-(4-methoxyphenyl)-6-phenyl-1,2,6-thiadiazine 1,1-dioxide (**6c**) and 3-Diethylamino-4-(4-methoxyphenyl)-1-phenyl-pyrazole (**7c**).* From **4c** (370 mg, 0.96 mmol). Eluant for F. C.: cyclohexane/ethyl acetate 2/3. **5c**: Yield: 1%. M.p.: oil. Anal. Calcd. for $C_{20}H_{23}N_3SO_3$ (385): C 62.34% H 5.97% N 10.91% Found: C 62.18% H 5.76% N 10.89%. ^{1}H-NMR: 1.00 (t, 3H, J=7.2, 3H, CH_3); 1.33 (t, 3H, J=7.2, 3H, CH_3); 3.07-3.31 (m, 2H, CH_2); 3.52-3.69 (m, 2H, CH_2); 3.85 (s, 3H, OCH_3); 7.01(AB system, J=9.0 Hz, 2H, Aryl-H); 7.18-7.36 (m, 5H, Aryl-H); 7.41 (AB system, J=9.0 Hz, 2H, Aryl-H); 8.55 (s,1H). *m/z* (385, M^+). **6c**: Yield: 51%. M.p.: oil. Anal. Calcd. for $C_{20}H_{23}N_3SO_3$ (385): C 62.34% H 5.97% N 10.91% Found: C 62.00% H 5.96% N 10.51%. ^{1}H-NMR: 0.90-1.21 (m, 6H, CH_3); 3.13-3.52 (m, 4H, CH_2); 3.82 (s, 3H, OCH_3); 6.21 (AB system, J=8.8 Hz, 2H, Aryl-H); 6.96 (s, 1H, H-5); 7.22 (AB system, J=8.8 Hz, 2H, Aryl-H); 7.28-7.56 (m, 5H, Aryl-H). *m/z* (385, M^+). **7c**: Yield: 2%. M.p.: 82°C. Anal. Calcd. for $C_{20}H_{23}N_3O$ (321): C 74.77% H 7.16% N 13.08% Found: C 74.68% H 7.06% N 13.46%. ^{1}H-NMR: 1.02 (m, J=7.1, 6H, CH_3); 3.07 (q, J=7.1, 4H, CH_2); 3.82 (s, 3H, OCH_3); 6.91 (AB system, J=8.7 Hz, 2H, Aryl-H); 7.04 (s, 1H, H-5); 7.28-7.54 (m, 5H, Aryl-H); 7.70 (AB system, J=8.7 Hz, 2H, Aryl-H). *m/z* (321, M^+).

*[1,1-Dioxo-4-(4-methoxyphenyl)-4-(4-methoxyphenyliminomethyl)-1,4-dihydro-[1,2]-thiazet-3-yl]-diethylamine (**5d**), 3-Diethylamino-4,6-di-(4-methoxyphenyl)-1,2,6-thiadiazine 1,1-dioxide (**6d**).* From **4d** (270 mg, 0.61 mmol). Eluant for F. C.: cyclohexane/ethyl acetate 2/3. **5d**: Yield: 10%. M.p.: 121°C. Anal. Calcd. for $C_{21}H_{25}N_3SO_4$ (415): C 60.72% H 6.02% N 10.12% Found: C 60.55% H 5.96% N 10.10%. ^{1}H-NMR: 0.99 (t, 3H, J=7.1 Hz, CH_3); 1.33 (t, 3H, J=7.1 Hz, CH_3); 3.02-3.33; 3.53-3.68 (2m, 4H, CH_2); 3.83 (s, 6H, OCH_3); 6.93 (AB system, J=8.9 Hz, 2H, Aryl-H); 7.00 (AB system, J=8.9 Hz, 2H, Aryl-H); 7.23 (AB system, J=8.9 Hz, 2H, Aryl-H); 7.41 (AB system, J=8.9 Hz, 2H, Aryl-H); 8.55 (s, 1H). *m/z* (415, M^+). **6d**: Yield: < 1%; product was obtained not pure enough for a M. p.. ^{1}H-NMR: 0.87-1.26 (m, 6H, CH_3); 3.14-3.44 (m, 4H, CH_2); 3.81 (s, 6H, OCH_3); 6.84-7.00 (m, 5H, Aryl-H); 7.20 (AB system, J=8.7 Hz, 2H, Aryl-H); 7.40 (AB system, J=9.0 Hz, 2H, Aryl-H). *m/z* (415, M^+).

*[1,1-Dioxo-4-(4-methoxyphenyl)-4-(4-nitrophenyliminomethyl)-1,4-dihydro-[1,2]-thiazet-3-yl]-diethylamine (**5e**), 3-Diethylamino-4-(4-methoxyphenyl)-6-(4-nitrophenyl)-1,2,6-thiadiazine 1,1-dioxide (**6e**) and 3-Diethylamino-4-(4-methoxyphenyl)-1-(4-nitrophenyl)-pyrazole (**7e**).* From **4e** (210 mg, 0.46 mmol). Eluant for F. C.: petroleum ether/ethyl acetate 7/3). **5e**: Yield: 3%. M.p.: 74-76°C. Anal. Calcd. for $C_{20}H_{22}N_4SO_5$ (430): C 55.81% H 5.12% N 13.02% Found: C 55.44% H 5.00% N 12.83%. ^{1}H-NMR: 1.00 (t, 3H, J=7.2 Hz, CH_3); 1.33 (t, 3H, J=7.2 Hz, CH_3); 3.02-3.33; 3.50-3.71 (2m, 4H, CH_2); 3.85 (s, 3H, OCH_3); 7.03 (AB system, J=8.9 Hz, 2H, Aryl-H); 7.07 (AB system, J=8.5 Hz, 2H, Aryl-H); 7.39 (AB system, J=8.5 Hz, 2H, Aryl-H); 8.28 (AB system, J=8.9 Hz, 2H, Aryl-H); 8.53 (s, 1H). *m/z* (430, M^+). **6e**: Yield: 27%. M. p.: 174°C. Anal. Calcd. for $C_{20}H_{22}N_4SO_5$ (430): C 55.81% H 5.12% N 13.02% Found: C 56.14% H 5.24% N 13.33%. ^{1}H-NMR: 0.78-1.44 (m, 6H, CH_3); 2.81-3.75 (m, 4H, CH_2); 3.84 (s, 3H, OCH_3); 6.94 (AB system, J=8.5 Hz, 2H, Aryl-H); 6.98 (s,1H, H-6); 7.25 (AB system, J=8.5 Hz, 2H, Aryl-H); 7.61 (AB system, J=9.1 Hz, 2H, Aryl-H); 8.30 (AB system, J=9.1 Hz, 2H, Aryl-H). *m/z* (430, M^+). **7e**: Yield: 6%. Product was obtained not pure enough for a correct melting point. ^{1}H-NMR: 1.08 (t, J=7.1, 6H, CH_3); 3.11 (q, J=7.1, 4H, CH_2); 3.84 (s, 3H, OCH_3); 6.93 (AB system, J=8.7 Hz, 2H, Aryl-H); 7.11 (s,

1H, H-5); 7.71 (AB system, J=8.7 Hz, 2H, Aryl-H); 7.78 (AB system, J=8.9 Hz, 2H, Aryl-H); 8.34 (AB system, J=8.9 Hz, 2H, Aryl-H). *m/z* (366, M^+).

3-Diethylamino-4-(4-methoxyphenyl)-6-phenyl-1,2,6-thiadiazine 1,1-dioxide (6c) from 1 and 2c. Compound **1** (0.5 g, 1.7 mmol) and **2c** (0.9 mL of a 3M benzene solution) were heated at 140°C for about 16-18 h until transformation of the intermediate **5** was completed affording **6c** (T.L.C. cyclohexane/ethyl acetate 7/3) which was purified by column chromatography (cyclohexane/ethyl acetate 3/1). **6c**: Yield: 60%. Analytical and spectroscopic data have been reported above.

REFERENCES AND NOTES

1. As part V : Clerici, F.; Ferraris, F.; Gelmi, M. L. *Tetrahedron* **1995**, *51*, 12351-12362.
2. Clerici, F.; Ferrario, T.; Gelmi, M. L.; Marelli, R. *J. Chem. Soc. Perkin 1* **1994**, 2533-2536.
3. Baggi, P.; Clerici, F.; Gelmi, M. L.; Mottadelli, S. *Tetrahedron* **1995**, *51*, 2455-2466.
4. Kadaba, P. K., Stanovnik, B., Tisler M., *Advances in Heterocyclic Chemistry* **1984**, 37, 330-349,
5. Huisgen, R. *1,3-Dipolar Cycloaddition Chemistry*, Padwa, A.; Taylor, E. C.; Weissberger, A. Eds., John Wiley and Sons, Inc. New York, 1984; I, pp. 135-137; Houk, K. N.; Yamaguchi, K. ibid., II, pp. 443-444.
6. Carugo, O.; Clerici, F.; Pocar, D. *Tetrahedron* **1993**, *49*, 9117-9126.
7. Kadaba, P. K., Stanovnik, B., Tisler M., *Advances in Heterocyclic Chemistry* **1984**, 37, 329-331,
8. Several examples of related transformations are well represented in: Ghosez, L.; Marchand Brynaert, J. *Comprehensive Organic Synthesis* Trost, B. M.; Fleming, I.; Paquette, L. A. Eds., Pergamon Press, Oxford, 1991, 2.2, pp. 85-123; Durst, T.; Breau, T. ibid., 6.1, pp.675-694; Okamura, W. H.; De Lera, A. ibid., 6.2, pp. 699-745; and ref.s.
9. Brown, D. J. *The Chemistry of Heterocyclic Compounds* , Weissberger, A.; Taylor, E. C. Eds., John Wiley and Sons, Inc. New York, 1985; 16, Suppl. II, pp.406-416 and ref.s.
10. Johnson, C.K. *ORTEPII*, Report ORNL-5138, **1976**, Oak Ridge National Laboratory, Tennessee, USA.
11. *International Tables for X-ray crystallography*, A. J. C. Wilson Ed., Kluwer Academic Publishers, Dordrecht, 1995, vol. C, p. 701.
12. Chiaroni, A.; Riche, C.; Loiseau, P.; Bonnafous, M.; Adam, Y. *Acta Cryst.* **1985**, *C41*, 1265-1267.
13. Meyle, E.; Keller, E.; Otto, H. H. *Liebigs Ann. Chem.* **1985**, 802-812.
14. Müller, M.; Meyle, E.; Paulus, E. F.; Plagge, H.; Otto, H. H. *Liebigs Ann. Chem.* **1989**, 975-983.
15. Belskii, V. K.; Bodrikov, I. V.; Michurin, A. A.; Chumakova, L. I.; Zhivoderov, A. V. *Tetrahedron Letters* **1985**, *26*, 5689-5692.
16. Foces-Foces, C.; Cano, F. H.; García-Blanco, S. *Acta Cryst.* **1975**, *B31*, 2310-2313.

17. Cabezuelo, M. D.; Foces-Foces, C.; Cano, F. H.; García-Blanco, S. *Acta Cryst.* **1978**, *B34*, 3069-3070, and ref.s.
18. Tsann Long, S.; Bennua, B.; Vorbrüggen, H.; Lindner, H. J. *Chem. Ber.* **1981**, *114*, 1269-1278.
19. Desiraju, G. R.; Kamala, R. *Acta Cryst.* **1983**, *C39*, 358-260.
20. Brouant, P. P.; Baldy, A.; Pierrot, M.; Goya, P.; Ochoa, C.; Soyfer, J. C.; Barbe, J. *Acta Cryst.* **1986**, *C42*, 892-894.
21. Goya, P.; Nieves, R.; Ochoa, C.; Rodellas, C.; Martinez-Ripoll, M.; García-Blanco, S. *Can J. Chem.* **1987**, *65*, 298-302, and ref.s.
22. Brouant, P. P.; Barbe, J.; Goya, P.; Ochoa, C. *Can. J. Chem.* **1988**, *66*, 2477-2482, and ref.s.
23. Elguero, J.; Goya, P.; Ochoa, C.; Rodellas, C.; Martinez-Ripoll, M.; García-Blanco, S. *J. Chem. Res.* **1988**, 873-881.
24. Brouant, P. P.; Barbe, J.; Goya, P.; Ochoa, C. *Acta Cryst.* **1989**, *C45*, 495-497.
25. Herrero, A.; Ochoa, C.; Stud, M.; Florencio, F.; Hernández-Fuentes, I.; Abradelo, C.; De Paz, J. L. G. *J. Org. Chem.* **1989**, *54*, 5025-5031.
26. Goya, P.; Paez, J. A.; Alkorta, I.; Carrasco, E.; Grau, M.; Anton, F.; Julia, S.; Martinez-Ripoll, M. *J. Med.Chem.* **1992**, *35*, 3977-3983.
27. We also mention here that the thiadiazine ring of Ref.18 carries a rather bulky ribofuranose moiety on the nitrogen in position 2 and yet the usual envelope conformation is adopted in this case also.
28. Altomare, A.; Cascarano, C.; Giacovazzo, C.; Guagliardi, A. *Journal of Applied Crystallography*, **1993**, *26*, 343-350.
29. Sheldrick, G. M., *SHELXL-93* Program for Crystal Structure Determination, **1993**, Univ. of Cambridge, England.
30. Clerici, F.; Marazzi, G.; Taglietti, M. *Tetrahedron* **1992**, *48*, 3227-3238.
31. Henkel, K.; Weygand, F. *Chem. Ber.* **1943**, *76 B*, 812-818.
32. Smith, P. A.; Beau Brown, B. *J. Am. Chem. Soc.* **1951**, *73*, 2435-2437.
33. Lindsay, R. O.; Allen, C. F. H.*Organic Syntheses* John Wiley and Sons, Inc. New York, 1955, *Collective* 3, p. 710.

(*Received in UK* 23 *February* 1996; *revised* 22 *March* 1996; *accepted* 29 *March* 1996)