5-Aminothiazolium Salts as Potential Cyclic Azomethine Ylides − Base-Induced Intramolecular Cycloaddition Reactions of *N*-(*o*-Allylphenyl)- and *N*-(*o*-(Allyloxy)phenyl)-Substituted Derivatives

Georges Morel*[a], Evelyne Marchand[a], Adile Touimi Benjelloun[a], Sourisak Sinbandhit[b], Olivier Guillou[c], and Philippe Gall[c]

Laboratoire de Synthèse et Electrosynthèse organiques, UMR 6510, Université de Rennes-I,[a]
Campus de Beaulieu, F-35042 Rennes-Cedex, France
Fax: (internat.) + 33-299/286738
E-mail: Georges.Morel@univ-rennes1.fr

Centre Régional de Mesures Physiques de l'Ouest, Université de Rennes-I,[b]
Campus de Beaulieu, F-35042 Rennes-Cedex, France

Laboratoire de Chimie des Matériaux Inorganiques et de Cristallographie, INSA, Rennes,[c]
20 avenue des buttes de Coësmes, F-35043 Rennes-Cedex, France

Received March 27, 1998

Keywords: Isocyanides / Mesoionic compounds / Azomethine ylides / Cycloadditions / Polyheterocycles

A series of 5-aminothiazolium chlorides (**1**) bearing tethered benzene ring on N-3, C-4 or the exocyclic nitrogen atom are prepared by a three-component methodology and subjected to basic treatment. The initially generated mesoionic thiazoles **2** undergo internal 1,3-dipolar cycloaddition across the pendant olefin when the 2-allylphenyl group is connected to the endocyclic N-3. The reaction leads to the formation of original *N*-bridged thiazoloquinolines as a mixture of two regioisomers **3** ,**4** which are readily separated by chromatography. The structural assignments of the cycloadducts are deduced from their spectroscopic NMR properties and unequivocally established by an X-ray diffraction analysis. Intramolecular sequence also occurs using the 2-(allyloxy)phenyl substituent on the same position to give a single regioisomeric 1,4-methanothiazolobenzoxazepine (**7**). On the contrary, hydrolysis and ring-opening or oxidation and rearrangement of the mesoionic intermediates are the exclusive base-promoted conversions of other thiazolium salts **1**.

The synthesis and chemical behaviour of mesoionic ring systems have received much attention in the last twenty years[1][2]. In 1993, we reported the efficient preparation of numerous 5-aminothiazolium salts[3] in the course of a study on the three-component cyclocondensations using isocyanides as cyclization reagents[4][5]. In particular, we showed that the treatment of an aryl chlorodithio or chlorothionoformate with a mixture of *N*-benzylidenealkylamine and *tert*-butyl isocyanide smoothly afforded the 5-(*tert*-butylamino)-4-phenylthiazolium chlorides **1** (R^2 = PhS or *p*-TolO, R^3 = alkyl) which are potential precursors in basic media for cyclic azomethine ylides. Reactivities of the corresponding mesoionic thiazoles **2** were examined by the in situ technique[6] with standard electrophilic alkynes and alkenes[7] and carbon disulfide[8]. The reactions involved an 1,3-dipolar cycloaddition of the "masked" ylides across the carbon−carbon or carbon−sulfur multiple bond, yielding unstable *N*-bridged adducts as the first step, and resulted in practical syntheses of functionalized monocyclic or condensed five-membered heterocycles. For instance, use of CS_2 gave thiazolium-5-thiolates via a subsequent elimination of *tert*-butyl isothiocyanate[8].

We now investigated some examples of the internal olefinic version of these cycloaddition reactions, with the view to construct ring-annulated multicyclic compounds. Intramolecular cycloadditions of mesoionic dipoles represent one of the most powerful methods for the generation of complex systems[2][9]. Such reactions have been studied with a range of mesoionic species i. e. dithiolones[10], sydnones[11], münchnones[12][13], isomünchnones[14] and thioisomünchnones[15]. Internal cycloaddition of suitable münchnones[13] and isomünchnones[16] provided flexible synthetic approaches to several natural products. Another interesting example is the intramolecular cycloaddition of a Reissert salt or open-chain analogue (5-aminooxazolium tetrafluoroborate) on a monosubstituted alkyne to produce a fused pyrrole by HNCO evolution from the primary dipolar adduct[17]. To date, however, the use of mesoionic thiazoles as cyclic azomethine ylides in similar internal reactions was unprecedented. We described here the preparation of eight 5-aminothiazolium chlorides **1** which possess tethered alkenyl moieties and our attempts for their application in heterocyclic chemistry.

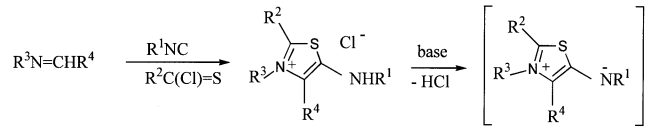
Results and Discussion

Preparation of Thiazolium Salts **1**. As key model we chose to investigate the behaviour of the 5-aminothiazolium system derived from *ortho*-allyl and *ortho*-(allyloxy) anilines or benzaldehyde, such that the benzene backbone containing the unsaturated moiety was attached either to the *endo*cyclic

 © WILEY-VCH Verlag GmbH, D-69451 Weinheim, 1998 1434−193X/98/1111−2631 $ 17.50+.50/0

or *exo*cyclic nitrogen atom (**1a−g**) or to the *endo*cyclic C-4 (**1h**). Formation of the desired salts **1** (and transient mesoionic **2**) involved treating the appropriate benzaldimine and isocyanide R^1NC with an aryl chlorothionoformate, according to the above-mentioned methodology (Scheme 1). All reactions were carried out at room temperature in CH_2Cl_2 solution with an excess of isocyanide. The new salts **1** were obtained as crystalline material or amorphous semisolid in moderate to good yields depending on the substituent groups present (Table 1). The condensation occurred hardly when the starting phenyl chlorodithioformate and electron-poor benzylidene-2-allylaniline were used together for a long period. Extensive decomposition was observed (entry 1). On the contrary, the rate of the one-pot reaction sharply increases with electrophilic *p*-tolyl chlorothionoformate (entry 4) and the aldimines which possess an electron-releasing R^3 or R^4 group, owing to the enhancement of their nucleophilic properties (for instance, compare entry 1 with entries 3 and 7).

Scheme 1



1 **2**

1, **2**	R^1	R^2	R^3	R^4
a	*t*Bu	PhS	2-(CH_2=$CHCH_2$)C_6H_4	Ph
b	*t*Bu	PhS	2-(CH_2=$CHCH_2$)C_6H_4	4-$MeOC_6H_4$
c	*t*Bu	PhS	2-(CH_2=$CHCH_2$)C_6H_4	4-$Me_2NC_6H_4$
d	*t*Bu	*p*-TolO	2-(CH_2=$CHCH_2$)C_6H_4	Ph
e	2-(CH_2=$CHCH_2$)C_6H_4	PhS	Me	Ph
f	2-(CH_2=$CHCH_2O$)C_6H_4	PhS	Me	Ph
g	*t*Bu	PhS	2-(CH_2=$CHCH_2O$)C_6H_4	Ph
h	*t*Bu	PhS	2,6-$Me_2C_6H_3$	2-(CH_2=$CHCH_2O$)C_6H_4

The required benzaldimines were readily generated by condensing the *o*-substituted anilines R^3NH_2 with adequate benzaldehydes R^4CHO under standard conditions[18]. The 2-allyl and 2-(allyloxy)phenyl isocyanides were also available from the corresponding anilines via the well known phase-transfer Hofmann procedure[19].

Structural assignment of salts **1** was based on NMR data and high resolution mass spectra. Selected ^{13}C-NMR-chemical shifts are given in Table 1. The signal of the *endo*-cyclic C-2 bearing the phenylthio or *p*-tolyloxy substituent appears as a singlet (R^3 = aryl) or as a quadruplet (R^3 = Me, $^3J_{CNCH}$ = 3.8 Hz) at rather low field (δ = 164-172) in accordance with earlier observations[3][8][20].

Base-Induced Conversion of Thiazolium Chlorides. Salts **1** have been treated with diverse bases in order to examine the possibilities of obtaining fused pyrrole derivatives. Examples are known in the literature where münchnones (cyclic azomethine ylides) smoothly react with non-activated alkenyl moiety as side-chain dipolarophile on the C-2[12] or nitrogen atom[12][13]. In some cases, the intramolecular reaction was entirely regioselective while in others two regioisomeric products were obtained in various distributions. Most of the compounds isolated correspond to 1:1 primary cycloadducts without subsequent extrusion of carbon dioxide.

Reaction of **1a** with triethylamine or 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) at room temperature afforded rapidly the expected *N*-bridged multicycle system in 60−80% total yield as a 80:20 mixture of two regioisomers (Table 2, entries 1, 2). These complex heterocycles could be separated by silica gel column chromatography. The major product was identified as 3-(*tert*-butylimino)-1,4-methanothiazolo[3,4-*a*]quinoline **3a** whereas the structure of the minor compound was assigned as 2-(*tert*-butylimino)-1,4-methanothiazolo[3,2-*a*]quinoline **4a** as described below. No interconversion of the isolated **3a** and **4a** occurred after several hours at 25°C in CH_2Cl_2 solution, eventually in the presence of NEt_3, thus indicating the observed regiochemistry to result from a kinetic control. In a related fashion, the base treatment of salts **1b**,**c** provided a mixture of the corresponding regioisomeric adducts **3** and **4** in 65% overall yield which were readily separated by chromatography (entries 3−5).

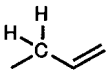
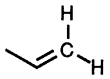
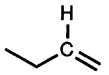
Such intramolecular reactions could be simply performed in water where starting salts **1** were conveniently solubilized. Use of aqueous media as solvent in organic chemistry has been rediscovered in the eighties and often provided evidence of hydrophobic effect induced acceleration[21]. No similar effect was discerned here (entries 2, 5).

The formation of fused-ring compounds **3**, **4** involves the deprotonation of thiazolium chlorides **1** giving unstable mesoionic intermediates **2** as the initial step and a [3+2] cycloaddition of the azomethine ylide functionality across the neighbouring π-bond (Scheme 2).

A more complex and deceiving base-promoted reaction was observed with the analogous 2-(*p*-tolyloxy)thiazolium chloride **1d**. Use of DBN in aqueous solution resulted in obtaining thioamides **5** and **6** contaminated with minor amounts of unidentified compounds (Table 2, entry 6). Cycloaddition occurred only with very poor yield on Al_2O_3/KF mixture as solid support in a biphasic system (entry 7). Al_2O_3-dispersed KF in solid-liquid media has been recognized in the literature to furnish good conditions for anionic activation[22][23][24].

Dominant formation of ring-opened species can be rationalized by assuming the fast hydrolysis of the initially generated mesoionic thiazole **2d** (Scheme 3). The nucleophilic addition of water either on C-2 to give the *p*-tolyl carbamate **5** (way a) or on C-4 to give the α-oxothioamide **6** (way b) has some literature precedent with similar thiazolium-5-aminides[3]. The *p*-tolyl formimidate that would also arise from (b) has not been characterized with certainty in the reaction mixture.

Table 1. Thiazolium chlorides **1**. – Preparation and selected ^{13}C-NMR chemical shifts[a]

Entry	Salt	Reactn Time[b]	Yield, %[c]	C-2	C-4	C-5(s)	 (tm, ^1J)	 (ddt, ^1J, ^3J)	 (ddt, ^1J, ^2J)
1	**1a**	16d	40	168.8 (s)	137 0 (t, ^3J = 3.7 Hz)	144.7	35.2 (128 Hz)	118.2 (154 and 157 Hz, 6 Hz)	133.5 (156 Hz, 2.4 and 7.2 Hz)
2	**1b**	40h	40	168 0 (s)	136.8 (t, ^3J = 3.6 Hz)	144.4	35.4 (126 Hz)	118.3 (155 and 157 Hz, 6.1 Hz)	133.6 (156 Hz, 2.4 and 7.4 Hz)
3	**1c**	40h	55	166.2 (s)	136.6 (br)	143.4	35.5 (123 Hz)	118.1 (154 and 157 Hz, 6.1 Hz)	133.7[d] (156 Hz, 2.4 and 6.9 Hz)
4	**1d**	25h	71	172.3 (s)	135.5 (t, ^3J = 4.3 Hz)	136.0	36.0 (125 Hz)	117.7 (153 and 156 Hz, 5.9 Hz)	134.3 (162 Hz, 2.3 and 6.9 Hz)
5	**1e**	30h	40	163.8 (q, ^3J = 3.7 Hz)	135.8 (m)	142.7	35.8 (127 Hz)	116.1 (154 and 156 Hz, 5.8 Hz)	135.9 (155 Hz, 2.5 and 6.1 Hz)
6	**1f**	30h	62	164.7 (q, ^3J = 3.9 Hz)	137.2 (m)	142.0	69.5 (145 Hz)	117.7 (155 and 157 Hz, 7 Hz)	133.2 (157 Hz, 2.3 and 5.7 Hz)
7	**1g**	30h	46	168.4 (s)	137.7 (br)	144.2	69.2 (146 Hz)	117.8 (155 and 158 Hz, 5 Hz)	131.7 (157 Hz, 3.2 and 4.7 Hz)
8	**1h**	40h	50	164.9 (s)	131.3 (t, ^3J = 4.5 Hz)	145.4	69.5 (145 Hz)	118.7 (155 and 158 Hz, 5.4 Hz)	132.3 (157 Hz, 3.2 and 4.7 Hz)

[a] δ (ppm) and multiplicities in $CDCl_3$ solutions at 75.5 MHz. – [b] The three-component condensations were performed in CH_2Cl_2 solutions at room temp., starting from a 2 M solution of aldimine then adding an excess of isocyanide (2 equiv, except for entries 5 and 6: 1.2 equiv) and aryl chlorothionoformate (1.1 equiv). Specified times were required for the full conversion of starting aldimines, progress of the reaction being monitored by ^{1}H-NMR spectroscopy. – [c] Isolated product yield. – [d] This value was confirmed by a 2-D correlation ^{1}H/^{13}C spectrum.

Table 2. Base-mediated conversion of 5-aminothiazolium chlorides **1**

Entry	Starting Salt	Reaction Conditions[a]			Isolated Products	Distribution of Regio-isomeric Adducts[c]	
		Base	Solvent	Time (h)	Yield (%)[b]	**3**	**4**
1	**1a**	NEt_3	CH_2Cl_2	0.5	**3a** + **4a** (60)	80	20
2	**1a**	DBN	H_2O	1.5	**3a** + **4a** (80)	80	20
3	**1b**	NEt_3	CH_2Cl_2	0.5	**3b** + **4b** (63)	70	30
4	**1c**	NEt_3	CH_2Cl_2	1	**3c** + **4c** (64)	60	40
5	**1c**	NaOH	H_2O	2	**3c** + **4c** (65)	60	40
6	**1d**	DBN	H_2O	2	**5** (25); **6** (20)	–	–
7	**1d**	KF/Al_2O_3	CH_2Cl_2	0.5	**3d** + **4d** (11); **5** (21); **6** (35)	60	40
8	**1g**	DBN	H_2O	1.5	**6** (29); **7** (25); **8g** (7)	–	–
9	**1g**	KF/Al_2O_3	CH_2Cl_2	0.5	**6** (28); **7** (35); **8g** (8)	–	–
10	**1h**	DBN	CH_2Cl_2	2	**8h** (30)	–	–
11	**1f**	DBN	H_2O	1	**9** (25)	–	–

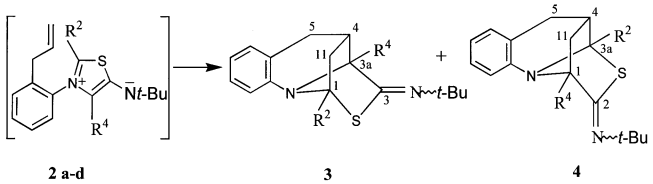
[a] All reactions were conducted at room temp. Specified times were required for the complete transformation of starting salts **1**. – [b] Product yields after crystallization or flash silica-gel chromatography. – [c] These distributions were estimated on the basis on the ^{1}H-NMR spectra of crude mixtures.

The facility of intramolecular cycloadditions depends on the length and nature of the tether connecting the dipole and dipolarophile functionalities[13][14][15]. In order to probe these limits, we have examined the behaviour of some *N*- and *C*-(allyloxy)phenyl-5-aminothiazolium systems.

Salt **1g** was also found to undergo cycloaddition and hydrolysis process under similar homogeneous and heterogeneous conditions, resulting in the formation of products **6**–**8** (entries 8, 9) and other minor compounds which are not isomeric cycloadducts. Thus, in comparison with entries 1–5, the rate of the 1,3-dipolar cycloaddition clearly decreases and alternative pathways become competitive. Moreover, the isolation of a single adduct whose structure was assigned **7** disagrees with the precedent results where the opposite regioselectivity was encountered. It can be presumed that electronic factors play an important role in controling these selectivities which also reflect the strain energy of the ring to be formed.

The mechanism outlined in Scheme 4 could be reasonably postulated for the formation of the *N*-formylamino compound **8**: addition of water on the *exo*cyclic sulfur atom of mesoionic species **2**, elimination of the phenylsulfenate anion and ring-opening hydrolysis of the reduced thiazolium cation. Large quantities of diphenyl disulfide were also

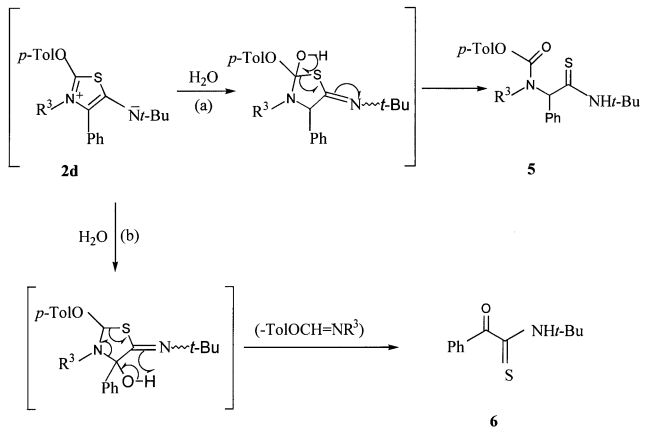
Scheme 2



2 a-d **3** **4**

2–**4**	R^2	R^4
a	PhS	Ph
b	PhS	4-$MeOC_6H_4$
c	PhS	4-$Me_2NC_6H_4$
d	*p*-TolO	Ph

Scheme 3



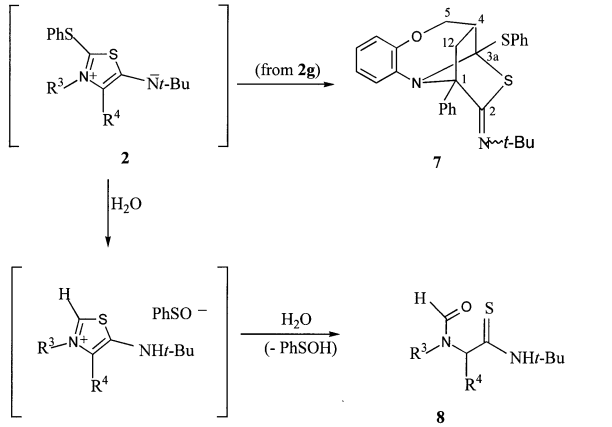
2d **5** **6**

R^3 = 2-(CH_2=$CHCH_2$)C_6H_4

isolated from the reaction mixture. It has been reported that sulfenic acids undergo disproportionation in basic media at room temperature to give the corresponding disulfides and sulfonate[25] or sulfinate[26] anions.

Similar treatment of thiazolium chlorides **1e**,**f**,**h** failed to produce any detectable quantities of condensed heterocycles. The formation of transient reddish mesionic compounds **2** was noted but our efforts to isolate the expected internal cycloadducts were totally unsuccessful. Only the general decomposition and rearrangement of the system were observed, ascribed to hydrolysis and oxidation sidesequences. In the case of salt **1h**, the formamide **8h** was obtained as the major compound in a mixture with other by-products (entry 10). Exposure of **1f** to usual DBN/H_2O conditions afforded the 2-oxothiazolidine **9** in poor isolated yield (entry 11). Although the mechanism of such rearrangement is rather doubtful and has not been thoroughly elucidated, the reaction presumably proceeds through an air-induced oxidation as previously mentioned in related works[4] , inducing a 1,3-migration of the phenylthio group (Scheme 5). Identical complex results were obtained with salt **1e** which also contains an alkenyl chain on the *exo*cyclic nitrogen atom. We have not tried to purify the

Scheme 4

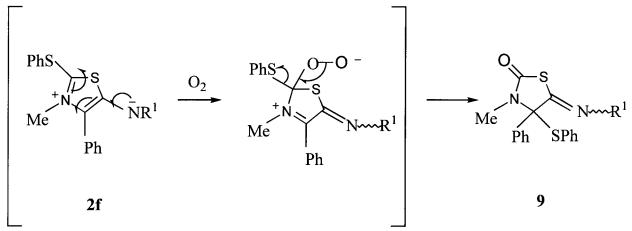


2 **7** **8**

2, **7**, **8**	R^3	R^4
g	2-(CH_2=$CHCH_2O$)C_6H_4	Ph
h	2,6-$Me_2C_6H_3$	2-(CH_2=$CHCH_2O$)C_6H_4

products of this last reaction. The unreactivity of **1e**,**f** in the cycloaddition process can be attributed to the difficulty of the olefinic moiety to attain a parallel plane approach with the transient azomethine ylide. Such steric constraints are evident upon examination of molecular models with six or seven atoms separating the terminal alkene carbon and the reactive center of the dipole.

Scheme 5



2f **9**

R^1 = 2-(CH_2=$CHCH_2O$)C_6H_4

All compounds were characterized by their NMR-spectroscopic properties and elemental analyses or mass spectra. In particular, that products **3**, **4**, **7** are cycloadducts was indicated by the disappearance of the allyl signals. A detailed ^1H- and ^{13}C-NMR examination of fused compounds showed the same pattern of signifiant proton couplings, in good agreement with the assigned structures (cf. Table 3 and Experimental Section). As expected, the stereochemical outcome of the cycloaddition is the consequence of an *endo* approach of the internal olefin with regard to the cyclic dipole. The six-membered ring of the azanorbornane skeleton of cycloadducts **3**, **4**, **7** adopts exclusively a boat conformation in solution (Figure 1). The ^{13}C-NMR spectra of majors isomers **3** exhibited a broad singlet for the C-3 whereas the regioisomers **4** gave rise to long-range coupling constants of about 4.5 and 7.2 Hz between the signals of the imino carbon (C-2) and the protons on C-11. Similar

Table 3. NMR-chemical shifts and multiplicities for main carbon atoms of cycloadducts[a]

No.	C-1 (m)	C-2 (dd, ^3J)	C-3 (s, br)	C-3a (m)	C-4 (dm, ^1J)	C-5 (tm, ^1J)	C-11[b] (tm, ^1J)	C_{arom}[c]
3a	89.6	–	158.8	80.3	37.7 (142 Hz)	35.5 (130 Hz)	49.3 (138 Hz)	136.8 (t, ^3J = 7 Hz)
3b	89.6	–	159.1	79.9	37.8 (142 Hz)	35.5 (131 Hz)	49.4 (136 Hz)	129.0 (t, ^3J = 7.7 Hz)
3c	89.4	–	159.4	79.8	37.9(143 Hz)	35.6 (130 Hz)	49.3 (137 Hz)	124.7 (t, ^3J = 7.5 Hz)
3d	112.1	–	156.6	75.5	36.9 (141 Hz)	35.5 (131 Hz)	47.3 (136 Hz)	136.4 (t, ^3J = 7.1 Hz)
4a	86.6	162.4 (4.4 and 6.9 Hz)	–	86.8	46.6 (145 Hz)	36.7 (134 Hz)	36.9 (134 Hz)	131.1 (m)
4b	86.4	162.5 (4.8 and 7.2 Hz)	–	86.5	46.6 (145 Hz)	36.7 (132 Hz)	37.1 (136 Hz)	129.0 (td, ^3J = 8 and 1.5 Hz)
4c	86.3	163.0 (br)	–	86.7	46.5 (144 Hz)	36.7 (135 Hz)	37.0 (135 Hz)	124.4 (m)
4d	83.6	160.3 (4.2 and 7.5 Hz)	–	108.2	44.8 (146 Hz)	35.5 (133 Hz)	36.0 (135 Hz)	136.8 (m)
7[d]	82.1	162.8 (4.6 and 7.6 Hz)	–	88.7	55.9 (d, 139 Hz)	67.6 (146 Hz)	33.0(td, 135 Hz, ^3J = 5 Hz)	136.3(td, ^3J = 6.7 and 2.2 Hz)

[a] δ (ppm) in $CDCl_3$ solutions at 75.5 MHz. – [b] C-12 for the cycloadduct **7**. – [c] Quaternary carbon atom of the aromatic R^4 on the 1 or 3a position. – [d] All assignments were confirmed by selective heteronuclear decoupling experiments. For instance, in the case of cycloadduct **7**: irradiation on the 12-H_{endo} at δ = 2.51 reduces the C-1 signal to a triplet (^3J = 3 Hz), the C-2 signal to a doublet (^3J = 6.8 Hz), the C-5 signal to a td (^2J = 5.6 Hz) and the C-12 to a dd; irradiation on the 12-H_{exo} at δ = 3.08 causes the C-2 signal to turn into a doublet (^3J = 3.7 Hz), the C-12 signal into a dd and the C_{arom} signal into a triplet (^3J = 7.1 Hz); irradiation on the 5-H′9 at δ = 4.57 reduces the C-5 signal to a dm (^1J = 130 Hz) and the C-12 signal to a triplet (^1J = 133 Hz).

$^3J_{CCCH}$ of 4.6 and 7.6 Hz were found in the case of cycloadduct **7**. Additionally, the relative chemical shifts for C-4 and C-11 compare favourably as indicated in Table 3.

The regiochemistry and stereochemistry of the representative cycloadducts **4a** and **7** were confirmed by NOEDIFF experiments (Figure 1). For **4a**, selective irradiation on the signals of the *ortho* protons of the phenyl group on C-1 (δ = 7.27) causes 8% enhancement of the double doublet at δ = 2.26 which can be easily attributed to the 11-H_{exo} and produces no significant perturbations of other signals. The NOE observed proves unambiguously the regioisomer **4a** and not **3a**. Irradiation on the signal of the 11-H_{endo} (δ = 2.45, ddd) leads to 10% increase of the multiplet at δ = 3.33 (4-H_{endo}). This result shows the *cis*-relative position of corresponding protons in agreement with their coupling constant (J = 7.3 Hz). The NOEDIFF experiments were performed in the same way for the cycloadduct **7**. The 8% NOE observed between the 12-H_{exo} (δ = 3.08, dd) and the *ortho*-protons of the phenyl group on C-1 (δ = 7.37, m) proves the regioisomer **7**. The 10% NOE obtained between the 12-H_{endo} (δ = 2.51, dd) and the 4-H_{endo} (δ = 3.47, m) supports their *cis*-relative position according to the measured coupling constant (J = 8.2 Hz). We have not studied the stereochemistry of the *exo*cyclic C,N double bond for these cycloadducts in solution.

Finally, the structure of another isomeric adduct (**3a**) was firmly established by a single-crystal X-ray diffraction analysis[27]. The ORTEP representation of Figure 2 reveals a *Z*-stereochemistry for the imino double bond in the solid state. Included, as well, are important bond lengths and angles. In particular, the torsion angles values between 4-H

Figure 1. Stereochemical representation of cycloadducts and NOE enhancement data for adducts **4a** (X = H, R^2 = SPh) and **7**

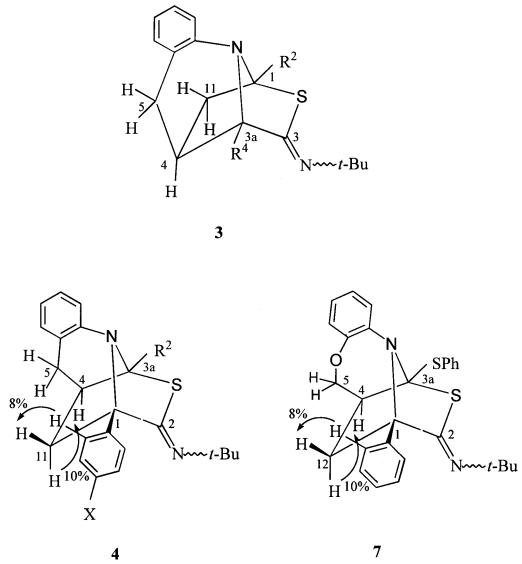
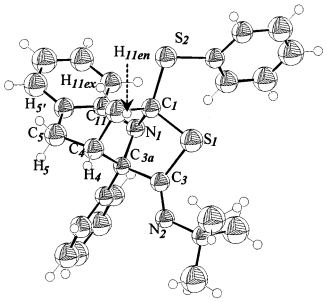


Figure 2. X-ray analysis for cycloadduct **3a**



Atom 1	Atom 2	Distance (Å)
C1	S1	1.8119(1)
C1	C11	1.5393(1)
C1	N1	1.4977(1)
S1	C3	1.7793(1)
C3	C3a	1.5417(1)
C3a	C4	1.5529(1)
C3a	N1	1.4932(1)
C4	C11	1.5506(1)

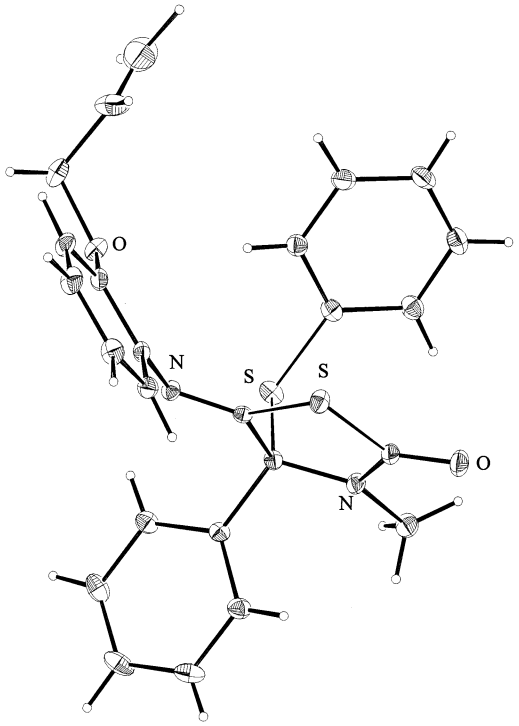
Atom 1	Atom 2	Atom 3	Atom 4	Angle (°)	Torsion Angle (°)
C1	S1	C3		87.922(6)	
S1	C3	C3a		108.050(4)	
C3	C3a	N1		104.151(3)	
C3	C3a	C4		108.595(2)	
C3a	C4	H4		118.068(6)	
C3a	C4	C11		102.025(7)	
C4	C11	H11ex		112.105(6)	
C4	C11	H11en		113.580(4)	
C4	C11	C1		102.835(5)	
C1	C11	H11ex		110.977(3)	
C1	C11	H11en		112.258(4)	
C1	N1	C3a		96.354(5)	
C3	C3a	C4	H4		–51.62(1)
H4	C4	C11	H11en		13.58(1)
H4	C4	C11	H11ex		–105.80(1)
H4a	C4	C5	H5		–59.41(1)
H4a	C4	C5	H5'		58.19(1)

and hydrogen atoms on C-11 (about 14° and 106°) are in excellent agreement with experimental coupling constants $^3J_{endo,endo}$ = 7.2 Hz and $^3J_{endo,exo}$ = 1.5 Hz. The structural assignment of 2-oxothiazolidine **9** was also confirmed by X-ray crystallography (Figure 3)[27].

Conclusion

We have demonstrated the ability of easily accessible 5-aminothiazolium chlorides **1** to undergo smooth intramolecular [3+2] cycloaddition in basic media when the 2-allylphenyl group is the peripheral substituent R^3. The reaction provides novel *N*-bridged thiazoloquinolines with poor to moderate regioselectivity. Attempts to construct larger azapolycycles fail with the exception of salt **1g** which contains also a π-bond in suitable proximity to the dipole center. Main conversion of salts **1d−h** seems to involve competitive hydrolysis or oxidation sequence

Figure 3. ORTEP representation of 2-oxothiazolidine **9**



Experimental Section

General: NMR spectra: Bruker ARX 200 spectrometer (200 MHz for ^{1}H and 50.3 MHz for ^{13}C) or Bruker AM300 WB spectrometer (300 MHz for ^{1}H and 75.5 MHz for ^{13}C) in $CDCl_3$ (internal standard Me_4Si). When necessary, unambiguous ^{13}C-and ^{1}H-NMR assignments were acquired by selective decoupling experiments. − HRMS: Centre Régional de Mesures Physiques de l'Ouest; Varian MAT 311 spectrometer, electron impact mode using a potential of 70 eV, unless otherwise indicated for compound **9**. With the exception of molecular-ion peaks, only mass-spectral fragments with relative intensities of 10% or more are reported. − Infrared spectra: Perkin-Elmer 1420 spectrophotometer; suspensions in nujol. − Elemental analyses: Analytical laboratory CNRS. − Crude products were separated and purified by fractional crystallization, bulb-to-bulb distillation under reduced pressure (Büchi kugelrohr apparatus) or Merck 60 silica-gel column flash-chromatography. Na_2SO_4 was used to dry organic layers after extractions.

Starting Material: The salts **1** that we studied were ultimately derived from 2-allylaniline (→**1a**−**e**), 2-(allyloxy)aniline (→**1f**,**g**) or 2-(allyloxy)benzaldehyde (→**1h**), the preparation of which being variously carried out. 2-Allylaniline was produced as previously described by the amino-Claisen rearrangement[28] of *N*-allylaniline in the presence of a Lewis acid catalyst, i.e. anhydrous $ZnCl_2$[29]. Synthesis of 2-(allyloxy)aniline was performed at room temp. in 72% overall yield according to the following three-steps procedure: condensation of 2-aminophenol with benzaldehyde in CH_2Cl_2 solution on alumina oxide for 24 h; alkylation of the resulting *N*-benzylidene-2-hydroxyaniline with allyl bromide for 36 h using K_2CO_3/acetone as solid-liquid basic medium[10][11][30]; hydrolysis of the obtained *N*-benzylidene-2-(allyloxy)aniline in aqueous HCl solution for 1 h. This third reaction can be considered as the "deprotective" sequence of the amino function[11][30]. 2-(Allyloxy)benzaldehyde was readily available by the similar alkylation of salicylaldehyde under K_2CO_3/acetone conditions[31]. − The condensation of 2-allylaniline with appropriate benzaldehydes R^4CHO on Al_2O_3 without a solvent[18] for 2 d led almost quantitatively to the required aldimines as 85:15 mixtures of two geometric isomers. The *N*-[2-(allyloxy)benzylidene]-2,6-dimethylaniline was similarly prepared in excellent yield from 2-(allyloxy)benzaldehyde and 2,6-dimethylaniline for 5 d. − 2-Allylaniline and 2-(allyloxy)aniline were conveniently converted into the corresponding isocyanides R^1NC according to the usual Hofmann carbylamine reaction: treatment with chloroform in CH_2Cl_2/50% aqueous NaOH system in the presence of benzyltriethylammonium chloride as phase-transfer catalyst[32]. − All other materials were available from commercial sources.

2-(Allyloxy)aniline: B.p. 70−75°C/0.015 Torr. − ^{1}H NMR (200 MHz): δ = 3.74 (br, NH_2), 4.53 (dt, 2 H, *J* = 5.3 and 1.5 Hz), 5.26 (dq, 1 H, *J* = 10.2 and 1.5 Hz), 5.39 (dq, 1 H, *J* = 17.2 and 1.5 Hz), 5.99 (m, 1 H), 6.60−6.90 (m, 4 H).

2-Allyl-N-benzylideneaniline: B.p. 140−145°C/0.02 Torr. − ^{1}H NMR (major isomer, 200 MHz): δ = 3.55 (d, br, 2 H, *J* = 6.6 Hz), 5.00 (m, 2 H), 5.97 (m, 1 H), 6.90−7.90 (m, 9 H), 8.32 (s, 1 H).

2-Allyl-N-(4-methoxybenzylidene)aniline: B.p. 155−160°C/0.015 Torr. − ^{1}H NMR (major isomer, 200 MHz): δ = 3.54 (d, br, 2 H, *J* = 6.6 Hz), 3.87 (s, 3 H), 5.01 (m, 2 H), 5.96 (m, 1 H), 6.95−7.90 (m, 8 H), 8.29 (s, 1 H).

2-Allyl-N-[4-(dimethylamino)benzylidene]aniline: B.p. 160−165°C/0.02 Torr. − ^{1}H NMR (major isomer, 200 MHz): δ = 3.04 (s, 6 H), 3.56 (d, br, 2 H, *J* = 6.6 Hz), 5.00 (m, 2 H), 5.98 (m, 1 H), 6.70−7.80 (m, 8 H), 8.22 (s, 1 H).

2-(Allyloxy)-N-benzylideneaniline: B.p. 165−170°C/0.02 Torr (90% yield based on aminophenol). − ^{1}H NMR (200 MHz): δ = 4.56 (dt, 2 H, *J* = 5 and 1.5 Hz), 5.20 (dq, 1 H, *J* = 10.5 and 1.5 Hz), 5.38 (dq, 1 H, *J* = 17.3 and 1.7 Hz), 6.02 (m, 1 H), 6.90−7.90 (m, 9 H), 8.45 (s, 1 H).

N-[2-(Allyloxy)benzylidene]-2,6-dimethylaniline: ^{1}H NMR (crude product, 200 MHz): δ = 2.15 (s, 6 H), 4.55 (dt, 2 H, *J* = 5.2 and 1.5 Hz), 5.25 (dq, 1 H, *J* = 10.5 and 1.5 Hz), 5.36 (dq, 1 H, *J* = 17.2 and 1.5 Hz), 5.99 (m, 1 H), 6.90−8.25 (m, 7 H), 8.71 (s, 1 H).

2-Allylphenyl Isocyanide: B.p. 60°C/0.015 Torr (56% yield). − IR: $\tilde{\nu}$ = 2120 cm^{-1} (N=C). − ^{1}H NMR (200 MHz): δ = 3.52 (d, br,

2 H, J = 6.5 Hz), 5.13 (m, 2 H), 5.94 (m, 1 H), 7.31 (m, 4 H). − MS: calcd. for $C_{10}H_9N$ *m/z* 143.0735 [M^+], found 143.0734; *m/z* (%): 143 (100), 115 (66), 89 (25).

2-(Allyloxy)phenyl Isocyanide: B.p. 90°C/0.03 Torr (49% yield). − IR: $\tilde{\nu}$ = 2118 cm^{-1} (N≡C). − ^1H NMR (200 MHz): δ = 4.59 (dt, 2 H, J = 5 and 1.5 Hz), 5.30 (dq, 1 H, J = 10.5 and 1.4 Hz), 5.48 (dq, 1 H, J = 17.3 and 1.5 Hz), 6.02 (m, 1 H), 6.90−7.30 (m, 4 H). − ^{13}C NMR (50.3 MHz): δ = 69.3 (tm, ^1J = 145 Hz), 113.1 (dd, ^1J = 164 Hz, ^3J = 8 Hz), 116.3 (br), 117.8 (tm, ^1J = 159 Hz), 120.7 (dm, ^1J = 167 Hz), 127.6 (dd, ^1J = 166 Hz, ^3J = 9 Hz), 130.4 (dm, ^1J = 166 Hz), 132.1 (dm, ^1J = 155 Hz), 153.8 (m), 167.7 (br). − MS: calcd. for $C_{10}H_9NO$ *m/z* 159.0684 [M^+], found 159.0678; calcd. for $C_{10}H_8NO$ *m/z* 158.0606 [M^+ − H], found 158.0605; *m/z* (%): 159 (43), 158 (100), 133 (20).

Preparation of Thiazolium Chlorides **1**: In a general procedure, phenyl chlorodithioformate or *p*-tolyl chlorothionoformate (2 g) was added dropwise to a solution of the suitable aldimine (10 mmol) and isocyanide (20 or 12 mmol) in anhydrous CH_2Cl_2 (5 ml). The mixture was maintained at room temp. for the time indicated in Table 1. The solvent was removed under reduced pressure and the brown residue was triturated with dry Et_2O. The salts **1a**,**d**,**f**,**g** precipitated as colourless solids which were filtered, washed with Et_2O and recrystallized from CH_2Cl_2/Et_2O. Other salts were separated by workup of the crude reaction mixture with Et_2O then H_2O/CH_2Cl_2 according to precedent articles[3][4][20]. They were obtained as crystalline material (**1c**,**e**) or amorphous hemisolids (**1b**,**h**) which were used for next reactions without additional purifications (yields and ^{13}C-NMR data, see Table 1). In the case of salt **1a**, the ethereal filtrate was concentrated to dryness and purified by a flash chromatography with petroleum ether then diethyl ether as eluents to afford a mixture of products **3a** and **4a** (25% yield).Such precocious cycloaddition was probably due to extented contact time (16 d) and basicity of *tert*-butyl isocyanide.

3-(2-Allylphenyl)-5-(tert-butylamino)-4-phenyl-2-(phenylthio)-thiazolium Chloride (**1a**): M.p. 213°C. − ^1H NMR (300 MHz): δ = 1.11 (s, 9 H), 3.04 (ddt, 1 H, J = 16, 6.2 and 1.5 Hz), 3.13 (ddt, 1 H, J = 16, 7.4 and 1.5 Hz), 5.10 (dq, 1 H, J = 17 and 1.5 Hz), 5.17 (dq, 1 H, J = 10 and 1.3 Hz), 5.73 (m, 1 H), 7.25−7.95 (m, 14 H). − $C_{28}H_{29}N_2S_2Cl$ (493.12): calcd. C 68.20, H 5.93, N 5.68, S 13.00; found C 67.84, H 5.92, N 5.72, S 12.67.

3-(2-Allylphenyl)-5-(tert-butylamino)-4-(4-methoxyphenyl)-2-(phenylthio)thiazolium Chloride (**1b**): ^1H NMR (300 MHz): δ = 1.12 (s, 9 H), 3.09 (m, 2 H), 3.66 (s, 3 H), 5.14 (m, 2 H), 5.76 (m, 1 H), 6.60−7.80 (m, 13 H). − MS: calcd. for $C_{29}H_{31}N_2OS_2$ *m/z* 487.1878 [M − Cl]$^+$, found 487.1890.

3-(2-Allylphenyl)-5-(tert-butylamino)-4-[4-(dimethylamino)-phenyl]-2-(phenylthio)thiazolium Chloride (**1c**): M.p. 150°C. − ^1H NMR (300 MHz): δ = 1.15 (s, 9 H), 2.92 (s, 6 H), 3.06 (m, 2 H), 5.10 (dq, 1 H, J = 17 and 1.5 Hz), 5.16 (dq, 1 H, J = 10 and 1.2 Hz), 5.75 (m, 1 H), 6.50−7.75 (m, 13 H). − MS: calcd. for $C_{30}H_{33}N_3S_2$ *m/z* 499.2116 [M − HCl]$^+$, found 499.2137; *m/z* (%): 499 (5), 416 (65), 389 (35), 387 (40), 332 (25), 330 (20), 307 (100), 304 (90).

3-(2-Allylphenyl)-5-(tert-butylamino)-2-[(4-methylphenyl)oxy]-4-phenylthiazolium Chloride (**1d**): M.p. 220°C. − ^1H NMR (200 MHz): δ = 1.10 (s, 9 H), 2.38 (s, 3 H), 3.17 (d, br, 2 H, J = 6 Hz), 5.10 (m, 2 H), 5.79 (m, 1 H), 7.20−8.10 (m, 13 H). − MS: calcd. for $C_{29}H_{31}N_2OS$ *m/z* 455.2157 [M − Cl]$^+$, found 455.2151; *m/z* (%): 455 (3), 397 (10), 339 (20), 291 (10), 236 (10), 232 (100).

5-[(2-Allylphenyl)amino]-3-methyl-4-phenyl-2-(phenylthio)-thiazolium Chloride (**1e**): M.p. 222°C. − ^1H NMR (300 MHz): δ = 3.26 (d, br, 2 H, J = 6.2 Hz), 3.76 (s, 3 H), 4.78 (m, 2 H), 5.67 (m, 1 H), 6.65−7.65 (m, 14 H), 8.32 (br, NH). − $C_{25}H_{23}N_2S_2Cl$ (451.04): calcd. C 66.57, H 5.14, N 6.21, Cl 7.86; found C 66.16, H 5.28, N 6.13, Cl 8.21.

5-{[2-(Allyloxy)phenyl]amino}-3-methyl-4-phenyl-2-(phenylthio)thiazolium Chloride (**1f**): M.p. 172°C. − ^1H NMR (200 MHz): δ = 3.91 (s, 3 H), 4.38 (d, br, 2 H, J = 5 Hz), 5.20 (m, 2 H), 5.90 (m, 1 H), 6.70−7.80 (m, 14 H). − MS: calcd. for $C_{24}H_{20}N_2OS_2$ *m/z* 416.1017 [M^+ − MeCl], found 416.1014; *m/z* (%): 431 (8), 416 (63), 266 (15), 256 (24), 240 (100).

3-[2-(Allyloxy)phenyl]-5-(tert-butylamino)-4-phenyl-2-(phenylthio)thiazolium Chloride (**1g**): M.p. 230°C. − ^1H NMR (300 MHz): δ = 1.10 (s, 9 H), 4.56 and 4.65 (2 ddt, 1 H, J = 13.5, 4.9 and 1.6 Hz), 5.29 (dq, 1 H, J = 17 and 1.6 Hz), 5.32 (dq, 1 H, J = 12 and 1.6 Hz), 5.36 (br, NH), 5.96 (m, 1 H), 7.05−7.70 (m, 14 H). − MS: calcd. for $C_{28}H_{29}N_2OS_2$ *m/z* 473.1721 [M − Cl]$^+$, found 473.1720.

4-[2-(Allyloxy)phenyl]-5-(tert-butylamino)-3-(2,6-dimethylphenyl)-2-(phenylthio)thiazolium Chloride (**1h**): ^1H NMR (300 MHz): δ = 1.02 (s, 9 H), 1.95 (s, 3 H), 2.14 (s, 3 H), 4.52 and 4.62 (2 ddt, 1 H, J = 13.4, 5.3 and 1.5 Hz), 5.27 (dq, 1 H, J = 17 and 1.5 Hz), 5.30 (dq, 1 H, J = 10.7 and 1.5 Hz), 5.94 (m, 1 H), 6.70−7.60 (m, 12 H). − MS: calcd. for $C_{30}H_{33}N_2OS_2$ *m/z* 501.2034 [M − Cl]$^+$, found 501.2030.

Base-Induced Conversion of Thiazolium Chlorides **1**

In CH_2Cl_2 Solution: The salt **1** (3 mmol) was dissolved in dry CH_2Cl_2 (15 ml) and a large excess of NEt_3 or DBN (10 mmol) was added dropwise. A blood-red colour appeared immediately. The mixture was maintained at room temp. for the time indicated in Table 2. The solvent was evaporated in vacuo. The brownish residual syrup was poured into H_2O and extracted with Et_2O. Concentration of the ethereal solution and trituration of the crude oily product with MeOH gave a mixture of cycloadducts **3**, **4** (entries 1, 3, 4) or the formamide **8h** (entry 10) as colourless solids. Cycloadducts were separated by a silica-gel column-chromatography with CH_2Cl_2/hexane (2:1) as eluent, then recrystallized from MeOH.

In a Solid−Liquid System: We prepared a solution of salt **1** (3 mmol) in dry CH_2Cl_2 (15 ml) and we added portionwise a mixture of KF (1.75 g) with Al_2O_3 (1.75 g). The suspension was stirred at room temp. for 30 min. The inorganic part was filtered off and the solvent was removed under reduced pressure.The residue was triturated with MeOH to precipitate the cycloadducts **3d** and **4d** (Table 2, entry 7) or **7** (entry 9) which were collected by filtration and purified by the above-mentioned chromatography or recrystallization. The filtrate was evaporated to dryness and worked up in a similar way to afford the pure thioamides **5**, **6** (eluent: CH_2Cl_2/hexane) or **8g** (eluent: Et_2O). In order to confirm the structure assigned to α-oxothioamide **6**, this compound was also prepared in excellent yield from acetophenone by successive treatment with thionyl chloride and *tert*-butylamine[33].

In Aqueous Solution: DBN (3.7 g) or 5 M aqueous NaOH (6 ml) was added to a solution of salt **1** (3 mmol) in H_2O (150 ml). A red colour appeared immediately and a reddish solid separated quickly. The mixture was stirred at room temp. for about 1.5 h. The regioisomeric cycloadducts **3**, **4** were filtered and separated by chromatography (Table 2, entries 2, 5). In other cases, the reaction products were extracted with Et_2O. Compounds **5**−**7** and **8g** (entries 6, 8) were purified as described above. The oxothiazolidine **9** was isolated by a silica-gel column-chromatography with ether/petroleum ether (1:2) as eluent, then recrystallized from MeOH. − Yields of isolated products: see Table 2; ^{13}C-NMR data of intramolecular cycloadducts: see Table 3.

3(3aH)-(tert-Butylimino)-4,5-dihydro-1,4-methano-3a-phenyl-1-(phenylthio)-1H-thiazolo[3,4-a]quinoline (**3a**): M.p. 168°C. − ^{1}H NMR (300 MHz): δ = 1.09 (s, 9 H), 1.97 (dd, 1 H, *J* = 12.3 and 1.4 Hz, 11-H$_{exo}$), 2.45 (dd, 1 H, *J* = 16.5 and 1.5 Hz, 5-H), 2.89 (ddd, 1 H, *J* = 12.3, 7.2 and 1.2 Hz, 11-H$_{endo}$), 2.89 (m, 1 H, 5-H′), 2.97 (m, 1 H, 4-H$_{endo}$), 6.80−7.30 (m, 14 H). − MS: calcd. for $C_{28}H_{28}N_2S_2$ m/z 456.1694 [M$^+$], found 456.1761. − $C_{28}H_{28}N_2S_2$ (456.66): calcd. C 73.64, H 6.18, N 6.13, S 14.04; found C 73.79, H 6.21, N 6.01, S 13.80.

3(3aH)-(tert-Butylimino)-4,5-dihydro-1,4-methano-3a-(4-methoxyphenyl)-1-(phenylthio)-1H-thiazolo[3,4-a]quinoline (**3b**): M.p. 162°C. − ^{1}H NMR (300 MHz): δ = 1.10 (s, 9 H), 1.95 (d, br, 1 H, *J* = 12.2 Hz, 11-H$_{exo}$), 2.43 (d, br, 1 H, *J* = 15 Hz, 5-H), 2.88 (m, 2 H, 11-H$_{endo}$ and 5-H′), 2.91 (m, 1 H, 4-H$_{endo}$), 3.68 (s, 3 H), 6.65−7.75 (m, 13 H). − MS: calcd. for $C_{28}H_{27}N_2OS_2$ m/z 471.1564 [M$^+$ − CH$_3$], found 471.1600; *m/z* (%): 471 (0.5), 371 (22), 262 (100). − $C_{29}H_{30}N_2OS_2$ (486.69): calcd. C 71.57, H 6.21, N 5.76, S 13.17; found C 71.78, H 6.29, N 6.17, S 13.30.

3(3aH)-(tert-Butylimino)-4,5-dihydro-3a-[4-(dimethylamino)phenyl]-1,4-methano-1-(phenylthio)-1H-thiazolo[3,4a]-quinoline (**3c**): M.p. 208°C. − ^{1}H NMR (300 MHz): δ = 1.11 (s, 9 H), 1.94 (d, br, 1 H, *J* = 12 Hz, 11-H$_{exo}$), 2.40 (dd, 1 H, *J* = 17 and 3 Hz, 5-H), 2.84 (s, 6 H), 2.86 (m, 2 H, 11-H$_{endo}$ and 4-H$_{endo}$), 2.91 (m, 1 H, 5-H′), 6.50−7.72 (m, 13 H). − MS: calcd. for $C_{30}H_{33}N_3S_2$ *m/z* 499.2115 [M$^+$], found 499.2137; calcd. for $C_{25}H_{24}N_2S$ *m/z* 384.1660 [M$^+$ − *t*BuNCS], found 384.1670; *m/z* (%): 499 (10), 384 (25), 275 (100). − $C_{30}H_{33}N_3S_2$ (499.73): calcd. C 72.10, H 6.66, N 8.41, S 12.83; found C 71.97, H 6.69, N 8.38, S 12.84.

3(3aH)-(tert-Butylimino)-4,5-dihydro-1,4-methano-1-[(4-methylphenyl)oxy]-3a-phenyl-1H-thiazolo[3,4-a]quinoline (**3d**): M.p. 190°C. − ^{1}H NMR (300 MHz): δ = 1.12 (s, 9 H), 2.20 (dd, 1 H, *J* = 12.5 and 1.5 Hz, 11-H$_{exo}$), 2.33 (s, 3 H), 2.53 (d, br, 1 H, *J* = 14.5 Hz, 5-H), 2.93 (m, 1 H, 4-H$_{endo}$), 2.96 (d, br, 1 H, *J* = 14.5 Hz, 5-H′), 3.02 (ddd, 1 H, *J* = 12.5, 8.6 and 1.1 Hz, 11-H$_{endo}$), 6.80−7.45 (m, 13 H). − MS (in a mixture with **5d**): calcd. for $C_{29}H_{30}N_2OS$ *m/z* 454.2079 [M$^+$], found 454.2066; calcd. for $C_{28}H_{27}N_2OS$ *m/z* 439.1844 [M$^+$ − CH$_3$], found 439.1871; *m/z* (%) 454 (1), 439 (0.5), 339 (10), 232 (100). − $C_{29}H_{30}N_2OS$ (454.63): calcd. C 76.62, H 6.65, N 6.16; found C 77.02, H 6.47, N 5.99.

2(1H)-(tert-Butylimino)-3a,4-dihydro-1,4-methano-1-phenyl-3a-(phenylthio)-5H-thiazolo[3,2-a]quinoline (**4a**): M.p. 164°C. − ^{1}H NMR (300 MHz): δ = 1.12 (s, 9 H), 2.26 (dd, 1 H, *J* = 13 and 1.5 Hz, 11-H$_{exo}$), 2.45 (ddd, 1 H, *J* = 13, 7.3 and 1.1 Hz, 11-H$_{endo}$), 2.75 (dd, 1 H, *J* = 17 and 1.9 Hz, 5-H), 3.33 (m, 1 H, 4-H$_{endo}$), 3.51 (dd, 1 H, *J* = 17 and 3.7 Hz, 5-H′), 6.55−7.65 (m, 14 H). − $C_{28}H_{28}N_2S_2$ (456.66): calcd. C 73.64, H 6.18, N 6.13, S 14.04; found C 73.79, H 6.27, N 6.16, S 13.82.

2(1H)-(tert-Butylimino)-3a,4-dihydro-1,4-methano-1-(4-methoxyphenyl)-3a-(phenylthio)-5H-thiazolo[3,2-a]quinoline (**4b**): M.p. 206°C. − ^{1}H NMR (300 MHz): δ = 1.11 (s, 9 H), 2.19 (dd, 1 H, *J* = 13 and 1.5 Hz, 11-H$_{exo}$), 2.38 (ddd, 1 H, *J* = 13, 7.3 and 1.1 Hz, 11-H$_{endo}$), 2.72 (dd, 1 H, *J* = 17 and 2 Hz, 5-H), 3.25 (m, 1 H, 4-H$_{endo}$), 3.48 (dd, 1 H, *J* = 17 and 3.7 Hz,5- H′), 3.76 (s, 3 H), 6.48−7.60 (m, 13 H). − MS: calcd. for $C_{29}H_{30}N_2OS_2$ *m/z* 486.1799 [M$^+$], found 486.1777; *m/z* (%): 486 (0.5), 262 (100). − $C_{29}H_{30}N_2OS_2$ (486.69): calcd. C 71.57, H 6.21, N 5.76 ; found C 71.29, H 6.16, N 5.24.

2(1H)-(tert-Butylimino)-3a,4-dihydro-1-[4-(dimethylamino)phenyl]-1,4-methano-3a-(phenylthio)-5H-thiazolo[3,2-a]quinoline (**4c**): M.p. 200°C. − ^{1}H NMR (300 MHz): δ = 1.13 (s, 9 H), 2.20 (dd, 1 H, *J* = 13.2 and 1.5 Hz, 11-H$_{exo}$), 2.34 (ddd, 1 H, *J* = 13.2, 7.3 and 1.2 Hz, 11-H$_{endo}$), 2.71 (dd, 1 H, *J* = 16.9 and 2 Hz, 5-H), 2.89 (s, 6 H), 3.23 (m, 1 H, 4-H$_{endo}$), 3.48 (dd, 1 H, *J* = 16.9 and 3.9 Hz, 5-H′), 6.48−7.60 (m, 13 H). − MS: calcd. for $C_{30}H_{33}N_3S_2$ *m/z* 499.2116 [M$^+$], found 499.2088; *m/z* (%): 499 (8), 334 (25), 307 (90), 275 (100).

2(1H)-(tert-Butylimino)-3a,4-dihydro-1,4-methano-3a-[(4-methylphenyl)oxy]-1-phenyl-5H-thiazolo[3,2-a]quinoline (**4d**): m.p. 188°C. − ^{1}H NMR (300 MHz): δ = 1.14 (s, 9 H), 2.26 (dd, 1 H, *J* = 13 and 1.6 Hz, 11-H$_{exo}$), 2.27 (s, 3 H), 2.40 (ddd, 1 H, *J* = 13, 7.3 and 0.8 Hz, 11-H$_{endo}$), 2.68 (dd, 1 H, *J* = 16.6 and 1.8 Hz, 5-H), 3.39 (m, 1 H, 4-H$_{endo}$), 3.50 (dd, 1 H, *J* = 16.6 and 4 Hz, 5-H′), 6.53−7.32 (m, 13 H).

(4-Methylphenyl) N-(2-allylphenyl)-N-[(tert-butylthiocarbamoyl)phenylmethyl] carbamate (**5**): M.p. 112°C (CH_2Cl_2/petroleum ether). − ^{1}H NMR (200 MHz): δ = 1.55 (s, 9 H), 2.27 (s, 3 H), 3.47 (d, br, 2 H, *J* = 6.5 Hz), 5.15 (m, 2 H), 5.83 (s, 1 H), 5.89 (m, 1 H), 6.85−7.60 (m, 13 H), 9.30 (br, NH). − ^{13}C NMR (50.3 MHz): δ = 20.8 (qt, ^1J = 127 Hz, ^3J = 4.4 Hz), 27.3 (qm, ^1J = 126 Hz), 35.2 (tm, ^1J = 128 Hz), 55.7 (m), 80.5 (dm, ^1J = 145 Hz), 117.0 (tm, ^1J = 156 Hz), 121.1, 127.4, 127.7, 127.9, 128.2, 128.3, 128.5, 128.9, 129.7 (9 non-quat. arom. C), 136.1 (dtd, ^1J = 154 Hz, ^2J = 7 and 2 Hz), 135.2, 138.1, 140.6, 141.4, 148.7 (5 m), 155.3 (d, ^3J = 6.4 Hz), 198.2 (d, ^2J = 6.4 Hz). − $C_{29}H_{32}N_2O_2S$ (472.65): calcd. C 73.70, H 6.82, N 5.93, S 6.78; found C 73.71, H 6.95, N 5.91, S 6.71.

N-tert-Butyl-2-phenyl-2-oxo-thioacetamide (**6**): M.p. 111°C (diethyl ether/petroleum ether). − ^{1}H NMR (300 MHz): δ = 1.58 (s, 9 H), 7.30−7.90 (m, 5 H), 8.03 (br, NH). − ^{13}C NMR (75.5 MHz): δ = 27.3 (qm, ^1J = 127 Hz), 56.9 (m), 128.2 (dd, ^1J = 162 Hz, ^3J = 7.6 Hz), 130.6 (dm, ^1J = 162 Hz), 133.5 (t, ^3J = 7.4 Hz), 133.7 (dm, ^1J = 162 Hz), 187.3 (m), 194.0 (s). − $C_{12}H_{15}NOS$ (221.32): calcd. C 65.12, H 6.83, N 6.33, S 14.49; found C 65.32, H 6.92, N 6.23, S 14.27.

2(1H)-(tert-Butylimino)-3a,4-dihydro-1,4-methano-1-phenyl-3a-(phenylthio)-5H-thiazolo[2,3-d][1,5]benzoxazepine (**7**): M.p. 170°C. − ^{1}H NMR (300 MHz): δ = 1.13 (s, 9 H), 2.51 (dd, 1 H, *J* = 12.8 and 8.2 Hz, 12-H$_{endo}$), 3.08 (dd, 1 H, *J* = 12.8 and 2.5 Hz, 12-H$_{exo}$), 3.47 (m, 1 H, 4-H$_{endo}$), 3.97 (dd, 1 H, *J* = 12.7 and 5 Hz, 5-H), 4.57 (d, 1 H, *J* = 12.7 Hz, 5-H′), 6.65−7.60 (m, 14 H). − $C_{28}H_{28}N_2OS_2$ (472.66): calcd. C 71.15, H 5.97, N 5.93, S 13.57; found C 71.32, H 5.94, N 5.83, S 13.41.

N-[2-(Allyloxy)phenyl]-N-[(tert-butylthiocarbamoyl)phenylmethyl]formamide (**8g**): Oily product − IR: ṽ = 3250 cm^{-1} (NH), 1650 (C=O). − ^{1}H NMR (200 MHz): δ = 1.49 (s, 9 H), 4.45 (d, br, 2 H, *J* = 5.3 Hz), 5.22 (m, 2 H), 5.74 (s, 1 H), 5.88 (m, 1 H), 6.80−7.35 (m, 9 H), 8.15 (s, 1 H), 9.21 (br, NH). − ^{13}C NMR (50.3 MHz): δ = 26.3 (qm, ^1J = 127 Hz), 54.6 (m), 68.3 (tm, ^1J = 145 Hz), 77.6 (dm, ^1J = 149 Hz), 112.1, 120.2, 126.8, 127.1, 128.6, 128.7, 128.9 (7 non-quat. arom. C), 117.3 (tm, ^1J = 157 Hz), 131.3 (dm, ^1J = 156 Hz), 128.9, 134.2, 152.7 (3 m), 163.7 (dd, ^1J = 201 Hz, ^3J = 4.4 Hz), 196.8 (d, ^2J = 5.9 Hz). − MS: calcd. for $C_{22}H_{26}N_2O_2S$ *m/z* 382.1715 [M$^+$], found 382.1720; calcd. for $C_{17}H_{17}NO_2$ *m/z* 267.1259 [M$^+$ − *t*BuNCS], found 267.1265; *m/z* (%): 382 (0.5), 267 (80), 238 (70), 198 (85), 120 (60), 91(50), 57 (90), 41 (100).

N{[2-(Allyloxy)phenyl](tert-butylthiocarbamoyl)methyl}-N-(2,6-dimethylphenyl)formamide (**8h**): M.p. 160°C (MeOH). − IR: ṽ = 3290 cm^{-1} (NH), 1631 (C=O). − ^{1}H NMR (200 MHz): δ = 1.64 (s, 9 H), 1.99 (s, 3 H), 2.33 (s, 3 H), 4.39 (m, 2 H), 5.07 (m, 2 H), 5.68 (m, 1 H), 6.19 (s, 1 H), 6.80−7.70 (m, 7 H), 8.01 (s, 1 H),

10.35 (br, NH). − ^{13}C NMR (50.3 MHz): δ = 19.0, 19.3 (2 qd, ^1J = 127 Hz, ^3J = 4.4 Hz), 27.9 (qm, ^1J = 127 Hz), 56.3 (m), 69.5 (tm, ^1J = 144 Hz), 72.6 (dm, ^1J = 143 Hz), 112.2, 120.7, 128.7, 129.2, 129.4, 130.2, 131.5 (7 non-quat. arom. C), 117.5 (tm, ^1J = 157 Hz), 132.9 (dm, ^1J = 155 Hz), 124.6, 136.6, 137.4, 141.1, 156.2 (5 m), 166.5 (dd, ^1J = 198 Hz, ^3J = 5.9 Hz), 199.0 (d, ^2J = 6.9 Hz). − MS: calcd. for $C_{24}H_{30}N_2O_2S$ *m/z* 410.2028 [M^+], found 410.2020; calcd. for $C_{19}H_{21}NO_2$ *m/z* 295.1572 [M^+ − *t*BuNCS], found 295.1580; *m/z* (%): 410 (7), 295 (85), 294 (50), 266 (95), 254 (70), 226 (60), 149 (78), 147 (58), 146 (57), 132 (100). − $C_{24}H_{30}N_2O_2S$ (410.57): calcd. C 70.21, H 7.36, N 6.82, S 7.81; found C 70.14, H 7.46, N 6.86, S 7.58.

5-[2-(Allyloxy)phenylimino]-3-methyl-4-phenyl-4-(phenylthio)-2-oxothiazolidine (**9**): M.p. 108°C (MeOH). − IR: $\tilde{\nu}$ = 1682 cm^{-1} (C=O), 1622 (C=N). − ^{1}H NMR (300 MHz): δ = 3.15 (s, 3 H), 4.31 (m, 2 H), 5.11 (dq, 1 H, *J* = 10 and 1.5 Hz), 5.12 (dq, 1 H, *J* = 17 and 1.6 Hz), 5.79 (m, 1 H), 6.55−7.70 (m, 14 H). − ^{13}C NMR (50.3 MHz): δ = 28.4 (q, ^1J = 141 Hz), 68.4 (tm, ^1J = 144 Hz), 85.5 (m), 112.9, 118.1, 120.2, 125.4, 126.1, 128.0, 128.1, 128.3, 129.4, 136.2 (10 non-quat. arom. C), 116.3 (tm, ^1J = 155 Hz), 127.4 (t, ^3J = 7.7 Hz), 132.0 (dm, ^1J = 155 Hz), 136.3 (t, ^3J = 7.1 Hz), 139.1 (t, ^3J = 7.9 Hz), 147.5 (m), 164.4 (q, ^3J = 3.1 Hz), 165.6 (s). − MS on a high resolution MS/MS ZabSpec TOF Micromass spectrometer, in the ionization mode positive LSIMS with Cs^+, matrix *m*NBA: calcd. for $C_{25}H_{23}N_2O_2S_{2\ m/z}$ 447.1201 [M+H]$^+$, found 447.1190; calcd. for $C_{19}H_{17}N_2O_2S$ *m/z* 337.1011 [M^+ − PhS], found 337.1023; *m/z* 118.1 [PhC≡NMe$^+$]. − $C_{25}H_{22}N_2O_2S_2$ (446.58): calcd. C 67.24, H 4.97, N 6.27, S 14.36; found C 67.39, H 4.98, N 6.13, S 14.17.

[1] Reviews: C. G. Newton, C. A. Ramsden, *Tetrahedron* **1982**, *38*, 2965−3011; K. T. Potts: *Mesoionic Ring Systems* in *1,3-Dipolar Cycloaddition Chemistry*, (A. Padwa, Ed.), J. Wiley, New York **1984**, vol. 2, chapter 8, pp 1−82; W. D. Ollis, S. P. Stanforth, C. A. Ramsden, *Tetrahedron* **1985**, *41*, 2239−2329.

[2] Review: M. H. Osterhout, W. R. Nadler, A. Padwa, *Synthesis* **1994**, 123−141.

[3] F. Berrée, Y. Malvaut, E. Marchand, G. Morel, *J. Org. Chem.* **1993**, *58*, 6022−6029.

[4] Y. Malvaut, E. Marchand, G. Morel, *J. Org. Chem.* **1992**, *57*, 2121−2127.

[5] E. Marchand, G. Morel, *Tetrahedron Lett.* **1993**, *34*, 2319−2322.

[6] The thiazolium-5-*tert*-butylaminides **2** are not stabilized by an electron-withdrawing substituent on the *exo*cyclic nitrogen atom. They have been trapped by a dipolarophile in the basic medium.

[7] F. Berrée, G. Morel, *Tetrahedron* **1995**, *51*, 7019−7034.

[8] A. Touimi Benjelloun, G. Morel, *Sulfur Lett.* **1996**, *20*, 107−115.

[9] P. A. Wade, *Intramolecular 1,3-Dipolar Cycloadditions* in *Comprehensive Organic Synthesis* (B. M. Trost, I. Fleming, Eds.), Pergamon, Oxford **1991**, vol. 4, pp. 1111−1168.

[10] H. Gotthardt, O.M. Huss, *Liebigs Ann. Chem.* **1981**, 347−353.

[11] H. Meier, H. Heimgartner, *Helv. Chim. Acta* **1986**, *69*, 927−940.

[12] A. Padwa, H. L. Gingrich, R. Lim, *J. Org. Chem.* **1982**, *47*, 2447−2456.

[13] A. Padwa, R. Lim, J. G. MacDonald, H. L. Gingrich, S. M. Kellar, *J. Org. Chem.* **1985**, *50*, 3816−3823.

[14] M. E. Maier, K. Evertz, *Tetrahedron Lett.* **1988**, *29*, 1677−1680; A. Padwa, D. L. Hertzog, W. R. Nadler, M. H. Osterhout, A. T. Price, *J. Org. Chem.* **1994**, *59*, 1418−1427; A. Padwa, D. J. Austin, A. T. Price, *Tetrahedron Lett.* **1994**, *35*, 7159−7162; A. Padwa, D. J. Austin, A. T. Price, M. D. Weingarten, *Tetrahedron* **1996**, *52*, 3247−3260; A. Padwa, M. A. Brodney, J. P. Marino, M. H. Osterhout, A. T. Price, *J. Org. Chem.* **1997**, *62*, 67−77.

[15] K. T. Potts, M. O. Dery, W. A. Juzukonis, *J. Org. Chem.* **1989**, *54*, 1077−1088; D. L. Hertzog, W. R. Nadler, Z. J. Zhang, A. Padwa, *Tetrahedron Lett.* **1992**, *33*, 5877−5880; A. Padwa, S. R. Harring, D. L. Hertzog, W. R. Nadler, *Synthesis* **1994**, 993−1004.

[16] A. Padwa, D. L. Hertzog, W. R. Nadler, *J. Org. Chem.* **1994**, *59*, 7072−7084; J. P. Marino, M. H. Osterhout, A. Padwa, *J. Org. Chem.* **1995**, *60*, 2704−2713; A. Padwa, M. A. Brodney, J. P. Marino, S. M. Sheehan, *J. Org. Chem.* **1997**, *62*, 78−87; J. T. Kuethe, A. Padwa, *J. Org. Chem.* **1997**, *62*, 774−775 and *Tetrahedron Lett.* **1997**, *38*, 1505−1508.

[17] G. Schmitt, Nguyen Dinh An, J. Vebrel, B. Laude, *Bull. Soc. Chim. Belg.* **1986**, *95*, 215−216.

[18] F. Texier-Boullet, *Synthesis* **1985**, 679−681.

[19] H. M. Walborsky, M. P. Periasamy, *Recent Advances in Isocyanide Chemistry*, in *The Chemistry of Triple-Bonded Functional Groups* (S. Pataï, Z. Rappoport, Eds.), J. Wiley, London **1983**, chapter 20, pp. 835−887.

[20] A. Touimi Benjelloun, G. Morel, E. Marchand, *Phosphorus, Sulfur, and Silicon*, in press.

[21] Review: A. Lubineau, J. Augé, Y. Queneau, *Synthesis* **1994**, 741−760.

[22] F. Texier-Boullet, D. Villemin, M. Ricard, H. Moison, A. Foucaud, *Tetrahedron* **1985**, *41*, 1259−1266; F. Texier-Boullet, M. Lequitte, *Tetrahedron Lett.* **1986**, *27*, 3515−3516; J. M. Mélot, F. Texier-Boullet, A. Foucaud, *Synthesis* **1987**, 364−366; R. Latouche, F. Texier-Boullet, J. Hamelin, *Bull. Soc. Chim. Fr.* **1993**, *130*, 535−546 and references therein.

[23] F. Berrée, E. Marchand, G. Morel, *Tetrahedron Lett.* **1992**, 33, 6155−6158.

[24] For recent examples, see: D. Villemin, M. Hachemi, *Synth. Commun.* **1995**, *25*, 2305−2310 and 2311−2318; **1996**, *26*, 1329−1334 and 2449−2459.

[25] T. Yoshimura, E. Tsukurimichi, S. Yamazaki, S. Soga, C. Shimasaki, K. Hasegawa, *J. Chem. Soc., Chem. Commun.* **1992**, 1337−1338.

[26] A. Heckel, W. Pfleiderer, *Helv. Chim. Acta* **1986**, *69*, 1095−1106.

[27] Full details of the X-ray structure determinations have been deposited with the Cambridge Crystallographic Data Centre and can be obtained, on request, with quotation of the registry numbers 101259 for **3a** and 102044 for **9**, the names of the authors and the reference to this article.

[28] Review: R. P. Lutz, *Chem. Rev.* **1984**, *84*, 205−247.

[29] C. D. Hurd, W. W. Jenkins, *J. Org. Chem.* **1957**, *22*, 1418−1423; P. A. S. Smith, S. S. P. Chou, *J. Org. Chem.* **1981**, *46*, 3970−3977; D. Anastasiou, W. R. Jackson, *Aust. J. Chem.* **1992**, *45*, 21−37.

[30] B. D. Tiffany, *J. Am. Chem. Soc.* **1948**, *70*, 592−594.

[31] L. Claisen, O. Eisleb, *Justus Liebigs Ann. Chem.* **1913**, *401*, 95; W. Oppolzer, *Tetahedron Lett.* **1970**, 3091−3094.

[32] W. P. Weber, G. W. Gokel, *Tetrahedron Lett.* **1972**, 1637−1640; W. P. Weber, G. W. Gokel, I. K. Ugi, *Angew. Chem.* **1972**, *84*, 587−588; *Angew. Chem. Int. Ed. Engl.* **1972**, *11*, 530−531.

[33] E. Marchand, G. Morel, *Bull. Soc. Chim. Fr.* **1996**, *133*, 903−912.

[98125]