Three-Component Cyclocondensations. Two Methods for the Efficient Preparation of 5-Aminothiazolium Salts via the Reaction of Isocyanides Either with Dimethylthioformamide and Imino Chloro Sulfides or Benzaldimines and Aryl Chlorothioformates

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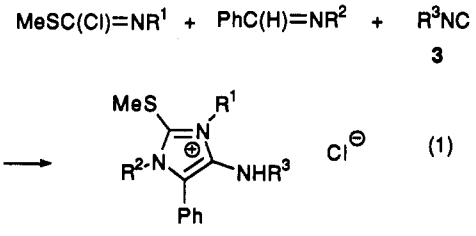
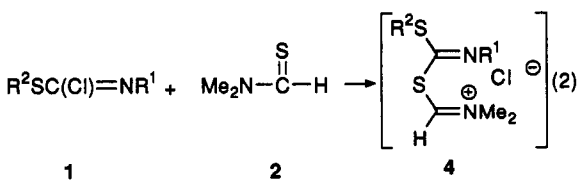
Treatment of imino chloro sulfides with dimethylthioformamide and isocyanides at room temperature provides selectively the 5-amino-4-(dimethylamino)-2-(methylthio)(or phenylthio)thiazolium salts. Similarly, the reactions of *p*-tolyl chlorothionoformate and phenyl chlorodithioformate with a mixture of benzaldimine and isocyanide afford rapidly the 5-amino-4-phenylthiazolium salts. We suggest that these reactions involve the *N*-(thiocarbonyl)formamidinium and benzylideniminium chlorides as transient intermediates, which are trapped by isocyanides according to a [1 + 4] cycloaddition process. The structure of the thiazolium salts and some of their reactivities are discussed.

Introduction

Imino chloro sulfides **1** are easily accessible via the insertion reaction of isocyanides into the S–Cl bond of sulfenyl chlorides, and these very electrophilic compounds have been shown to be excellent starting materials in the field of heterocyclic chemistry.[1,2] In particular, we recently reported the one-pot preparation of a wide variety of useful 4-amino-2-(methylthio)imidazolium salts from a mixture of methyl chlorothioimidate, benzaldimine, and isocyanide **3** (eq 1). *N*-Imidoylbenzylideniminium chlorides were assumed to be intermediates in such cyclocondensations.[3]

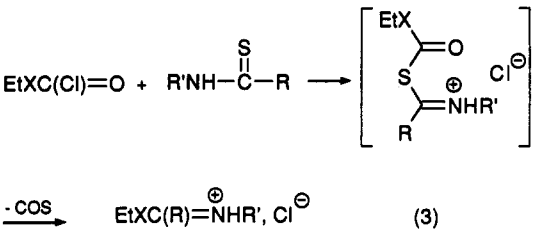


As an extension of this study on the three-compound systems using isocyanides as cyclization reagents, we were intrigued by the possibility that the (*S*-imidoylthio)-methyleniminium salts **4** could be produced from imino chloro sulfides **1** through chlorine substitution by dimethylthioformamide (**2**) (eq 2) and then trapped in situ by



isocyanides to produce thiazolium salts. Thioamides have been recognized for many years as useful and versatile functional groups in heterocyclic synthesis.[4] The high nucleophilicity of the thiocarbonyl group should make it much more reactive with **1** than imino groups.

Variations of the Vilsmeier–Haack reaction[5] have been accomplished with DMF and phenyl chloroformate,[6] alkyl chloroformates,[7] or benzoyl halides[6,8] to give the corresponding dimethyl(acyloxy)formiminium adducts, some of which been isolable at low temperature.[6] These Vilsmeier salts easily react with nucleophiles such as amines, alcohols, and carboxylic acids. The high reactivity of sulfur facilitates the acylation of thioamides[5a,9] and makes dimethylthioformamide (**2**) a more superior reagent than DMF in the Vilsmeier reaction.[10] The ethyl chloroformate[11a,12] and ethyl thiochloroformate[13] effectively add to thioamides giving *S*-(ethoxycarbonyl)(or [(ethylthio)carbonyl])mercaptoiminium salts. But these S-alkylations are followed by spontaneous degradations which lead to carbonyl sulfide and ethyl imidate or ethyl thioimidate hydrochlorides (eq 3, X = O, S).



Therefore, the formation of the "Vilsmeier-like reagents" **4** seems quite reasonable according to eq 2. However, will

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(1) Berrée, F.; Marchand, E.; Morel, G. *Tetrahedron Lett.* **1992**, *33*, 6155.

(2) Bossio, R.; Marcaccini, S.; Pepino, R.; Polo, C.; Torroba, T. *Heterocycles* **1989**, *29*, 1829; **1990**, *31*, 1287. Bossio, R.; Marcaccini, S.; Paoli, P.; Pepino, R.; Polo, C. *Heterocycles* **1990**, *31*, 1855 and references cited therein.

(3) Malvaut, Y.; Marchand, E.; Morel, G. *J. Org. Chem.* **1992**, *57*, 2121.

(4) Takahata, H.; Yamazaki, T. *Heterocycles* **1988**, *27*, 1953.

(5) For reviews, see: Kantlehner, W. In *Iminium Salts in Organic Chemistry*; Böhme, H., Viehe, H. G., Eds.; John Wiley: New York, 1979; Part 2, (a) p 5; (b) p 181.

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(9) (a) Walter, W.; Saha, C. R. *Phosphorus Sulfur* **1985**, *25*, 63. (b) Kobayashi, Y.; Itabashi, K. *Synthesis* **1985**, 671.

(10) Dingwall, J. G.; Reid, D. H.; Wade, K. *J. Chem. Soc. C* **1969**, 913.

(11) (a) Goerdeler, J.; Horstmann, H. *Chem. Ber.* **1960**, *93*, 663. (b) Goerdeler, J.; Stadelbauer, K. *Chem. Ber.* **1965**, *98*, 1556.

(12) Suydam, F. H.; Greth, W. E.; Langerman, N. R. *J. Org. Chem.* **1969**, *34*, 292.

(13) Razniak, S. L.; Flagg, E. M.; Siebenthall, F. *J. Org. Chem.* **1973**, *38*, 2242. Anderson, D.; Zinke, P.; Razniak, S. L. *J. Org. Chem.* **1983**, *48*, 1544.

0022-3263/93/1958-6022$04.00/0

$R^2SC(Cl)=NR^1$ (1)

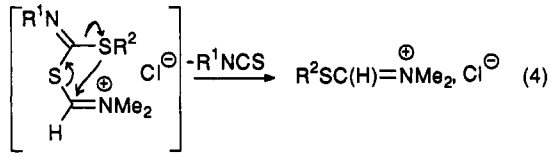
	R^1	R^2
a)	CH_2Ph	Me
b)	CH_2Ph	Ph
c)	CH_2CO_2Et	Me
d)	CH_2CO_2Et	Ph
e)	$CH_2PO(OEt)_2$	Me
f)	i-Pr	Me
g)	$2,6\text{-}Me_2C_6H_3$	Me
h)	t-Bu	Me

R^3NC (3)

a) $R^3 = CH_2Ph$
b) $R^3 = CH_2CO_2Et$
c) R^3 = i-Pr
d) $R^3 = 2,6\text{-}Me_2C_6H_3$
e) R^3 = t-Bu

Figure 1.

the compounds 4 be able to be trapped by isocyanides 3 before their possible decomposition in mercaptomethyleniminium chlorides and the corresponding isothiocyanates (eq 4)? Isocyanides have rarely been reacted with Vilsmeier salts.[14]



4 (4)

The present paper describes the results of this investigation. The scope and limitations of the reaction are discussed in detail, together with some chemical reactivities of the thiazolium salts. In order to test the versatility of this three-component methodology, we have extended the procedure to new preparation of 5-amino-4-phenylthiazolium chlorides via the reaction of *tert*-butyl isocyanide with benzaldimines and aryl chlorothioformates.

Results and Discussion

Preparation of Thiazolium Chlorides 6a–n. We have found that equimolar mixtures of compounds 1 and 2 readily undergo cyclocondensation with a range of isocyanides 3 (Figure 1). The reactions were carried out at room temperature for a few hours in a 0.75 M THF solution containing a large excess of 3. Both 2-(methylthio)- and 2-(phenylthio)thiazolium chlorides may be obtained in satisfying yields under these very mild conditions (Table I). Interestingly, the reaction works well with imidoyl chlorides **1c–e** which possess an electron-withdrawing ester moiety (entries 5–8) and **1g** that carries the bulky 2,6-dimethylphenyl group (entries 13, 14).[15] Most of the cycloadducts were isolated as yellowish solids which were recrystallized without any difficulty.

However, the reaction did not furnish the expected 5-(dimethylamino)thiazolium salts **5** but rather the 4-(dimethylamino) isomers **6** (Scheme I). This regiochemistry was based upon ^{13}C NMR characterizations as well as chemical transformations. Selected ^{13}C NMR chemical shifts are given in Table II. Generally, the multiplicity of the signal attributed to the carbon C-5 which

Table I. Reactions of Imino Chloro Sulfides 1a–h with Dimethylthioformamide (2) and Isocyanides 3. Preparation of Thiazolium Salts 6a–n

entry	educts[a]		reactn time,[b] h	products (% yield)[c]
1	**1a**	**3a**	1	**6a** (75)
2	**1a**	**3b**	1	**6b** (90)
3	**1a**	**3e**	3	**6c** (95)
4	**1b**	**3e**	2	**6d** (88)
5	**1c**	**3d**	12	**6e** (52)
6	**1c**	**3e**	13	**6f** (82)
7	**1d**	**3e**	12	**6g** (82)
8	**1e**	**3a**	13	**6h** (75)
9	**1f**	**3a**	2	**6i** (64)
10	**1f**	**3c**	2	**6j** (55)
11	**1f**	**3d**	12	**6k** (65)
12	**1f**	**3e**	4	**6l** (77)
13	**1g**	**3d**	12	**6m** (53)
14	**1g**	**3e**	12	**6n** (54)
15	**1h**	**3a**	13	**6a** (36); **6c** (31)
16	**1h**	**3d**	15	**6m** (22); **6n** (37)

[a] The reactions were conducted in THF at rt with equimolar quantities of 1, 2 (0.75 M), and a 2-fold excess of isocyanide 3. [b] Time required for the entire conversion of starting compounds 1 and 2. [c] Isolated product yield.

bears the NHR^3 group (δ = 133–146 ppm) proved to be conclusive in establishing structure **6**. For example, the C-5 exhibited a singlet for compounds **6c–g**. The non-decoupled spectra of the corresponding salts **5** would have presented a triplet for the NHR^3-substituted C-4, owing to coupling with the two protons of R^1. The atom C-2 bearing the methylthio or phenylthio function appeared, noteworthy, at high field (δ = 147–166 ppm).

More evidence for the structure of salts **6** was obtained from their reactivity as examplified by the easy conversion of **6a** into pyrrole **8**, in the presence of 1,5-diazabicyclo-[4.3.0]non-5-ene (DBN) and dimethyl acetylenedicarboxylate (Scheme II). The reaction was explained by the deprotonation of **6a** to produce the mesoionic thiazole **7a** which is trapped by the dipolarophile. The reverse cycloaddition proceeds via the loss of benzyl isothiocyanate. This result demonstrates that salts **6** can serve as synthetic equivalents of cyclic azomethine ylides.[16] Further works on the 1,3-dipolar cycloadditions of **7** will be published in the future.

Obtaining the compound **6** can be rationalized by a three-step mechanism as summarized in Scheme I: formation in a small equilibrium concentration[17a] of the (*S*-imidoylthio)methyleniminium salt **4**; fast and reversible rearrangement of the labile 1:1 adduct **4** to the *N*-(thiocarbonyl)formamidinium chloride **9**; [1 + 4] cycloaddition of the unstable cationic species **9** with nucleophilic **3** and subsequent tautomerism. The 1,3 S to N shift of the methyleniminium moiety to produce **9** presumably takes place via the intramolecular attack of the imidoyl nitrogen atom on the highly electrophilic iminium carbon. Similar rearrangements[18] into *N*-benzoylthioamides have been

(14) The reactions of isocyanides and then of H_2O with a series of *N,N*-dialkylamide chlorides afford poor to good yields of the corresponding N-substituted α-keto amides or α-(dialkylamino) malonamides: Ito, Y.; Okano, M.; Oda, R. *Tetrahedron* **1966**, *22*, 447.

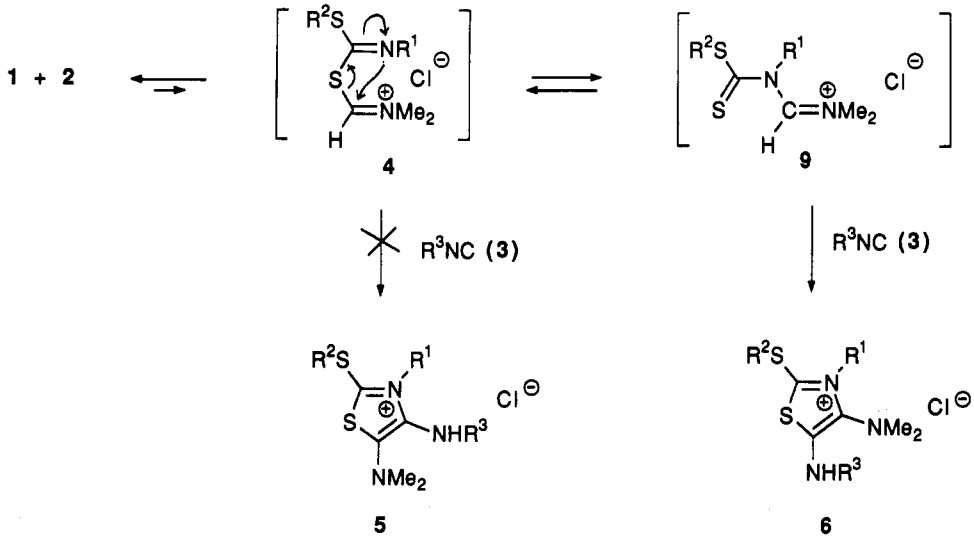
(15) Closely related reactions of methyl thioimidates **1c**, **1g** with benzylidenemethylamine and isocyanide **3e** were very slow under similar conditions and gave corresponding imidazolium chlorides in only poor yields.[3]

(16) Under similar conditions, the 5-(dimethylamino)thiazolium salt **5a**, precursor of a thiocarbonyl ylide, would have probably led to a thiophene via elimination of the dibenzylcarbodiimide: Potts, K. T.; Husain, S.; Husain, S. *J. Chem. Soc., Chem. Commun.* **1970**, 1360.

(17) (a) Without isocyanide, a solution in $CDCl_3$ of **1f** and **2** only involves a slow conversion to isopropyl isothiocyanate and (methylthio)methyleniminium chloride **10**. Starting compounds were still in admixture with these products after 12 h at rt, as shown by successive ^1H NMR analysis (compare with entries 9–12, Table I). (b) R^1NCS and **10** could proceed from the slow decomposition of intermediary **4** or **9**.

(18) See also the related 1,3 S to N thioxotriazine migration which occurs during the ring closure dimerization of imidoyl isothiocyanates: Morel, G.; Marchand, E.; Haquin, C.; Foucaud, A. *J. Org. Chem.* **1986**, *51*, 4043.

Scheme I



	R^1	R^2	R^3		R^1	R^2	R^3
a)	CH_2Ph	Me	CH_2Ph	h)	$CH_2PO(OEt)_2$	Me	CH_2Ph
b)	CH_2Ph	Me	CH_2CO_2Et	i)	i-Pr	Me	CH_2Ph
c)	CH_2Ph	Me	t-Bu	j)	i-Pr	Me	i-Pr
d)	CH_2Ph	Ph	t-Bu	k)	i-Pr	Me	$2,6\text{-}Me_2C_6H_3$
e)	CH_2CO_2Et	Me	$2,6\text{-}Me_2C_6H_3$	l)	i-Pr	Me	t-Bu
f)	CH_2CO_2Et	Me	t-Bu	m)	$2,6\text{-}Me_2C_6H_3$	Me	$2,6\text{-}Me_2C_6H_3$
g)	CH_2CO_2Et	Ph	t-Bu	n)	$2,6\text{-}Me_2C_6H_3$	Me	t-Bu

Table II. Selected ^{13}C NMR Chemical Shifts at 75.469 MHz for Some 5-Aminothiazolium Chlorides 6 and 16,[a] Mult (*J*, Hz)

no.	C-2	C-4 (m)	C-5[b]
6a	149.4 m	136.5	144.5 t (6.0)[c]
6b	152.9 m	136.0	143.9 m (5.6)[c]
6c	163.0 m	146.0	138.2 s
6d	161.2 t (5.2)[c]	144.3	139.2 s
6e	150.7 m	139.5	144.9 s
6f	163.4 m	145.1	137.9 s
6g	160.1 t (4.9)[c]	143.5	139.6 s
6h	146.8 br[d]	134.3	145.8 br
6k	148.7 br	144.6 br	133.5 s
6m	156.1 q (6.4)[e]	139.9	139.8 s
6n	165.8 q (6.3)[e]	146.4	133.2 s
16a	171.1 q (4.6)[c,f]	132.7	135.2 s
16b	171.1 d (6.8)[c]	133.2	136.2 s
16c	171.1 s	133.6 br	137.8 s
16e	162.7 q (4.6)[c]	135.0	144.2 s
16f	161.6 t (5.0)[c]	134.2	144.8 s

[a] δ in $CDCl_3$ solutions. [b] The coupling with the proton on the nitrogen atom was not observed according to a very low coupling constant, except for **6b**: $^2J_{(CNH)} = 3.3$ Hz. [c] $^3J_{(CNCH)}$. [d] Irradiation of all the H atoms caused the broad C-2 signal to turn into a doublet and revealed the coupling constant $^3J_{(CNCP)}$ to be 4.9 Hz. [e] $^3J_{(CSCH)}$. [f] This assignment was confirmed by a heteronuclear decoupling experiment: selective irradiation on the methyl at δ 3.79 (R^1) collapses the C-2 signal to a singlet.

reported for *S*-imidoylthiobenzoates.[9a,11] Thus, the rearrangement of the intermediate salt **4** into formamidinium salt **9** and then trapping with isocyanide **3** would be faster than the decomposition of **4**, as we discussed previously (eq 4).[17b]

A more complex and deceiving reaction occurred when dimethylthioformamide (**2**) and isocyanide **3e** were added to the N-*tert*-butylimidoyl chloride (**1h**) under usual conditions. The ^1H and ^{13}C NMR spectra of the crude product indicated the low formation of the (methylthio)-methyleniminium chloride **10**, along with some unidentified compounds. The salt **10** could not be isolated. Workup of the mixture led to DMF, methyl dithiocarbamate **12**, and methyl thiocarbamate **11** as major product. The overall mechanism is described in Scheme III. The unstable iminium salt **4h** fails to react as described for other species **4** and finally gives **10** and **12** via degradation and hydrolysis.

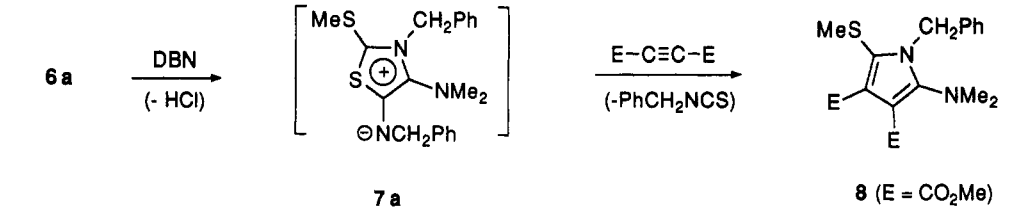
Further evidence for a labile S-adduct like **4h** could be obtained from the following investigation. The *N-tert*-butylimidoyl chloride (**1h**) was added to a 2-fold amount of thioacetamide in CCl_4 at room temperature. MeCN was observed in the ^1H NMR spectra of the solution which was concentrated to give the methyl dithiocarbamate **12** in a high yield.[19] The addition of isocyanide **3e** in excess, at the beginning of the reaction, did not modify this result which is interpreted according to Scheme IV: formation and deprotonation of a (*S*-imidoylthio)ethyleniminium chloride then degradation of the resulting diimidoyl sulfide into **12** and MeCN via a spontaneous cyclic elimination. The decomposition of thiobenzamide into benzonitrile, under the action of an acyl chloride or aryl isocyanate, has been explained via a similar process.[11a,20]

Then, the failure of imidoyl chloride **1h** to incorporate into the thiazolium structure under the combined action of dimethylthioformamide (**2**) and *tert*-butyl isocyanide (**3e**) could be understood by the lack of formamidinium salt **9h** from **4h**, perhaps for steric reasons. The unreactive nature of **1h** has been clearly shown by the use of benzyl isocyanide (**3a**), instead of **3e** (Table I, entry 15). The thiazolium salts **6a** and **6c** were obtained in similar quantities via the reversibility of the formation of **1h** that gives **3e** and methylsulfenyl chloride in small equilibrium

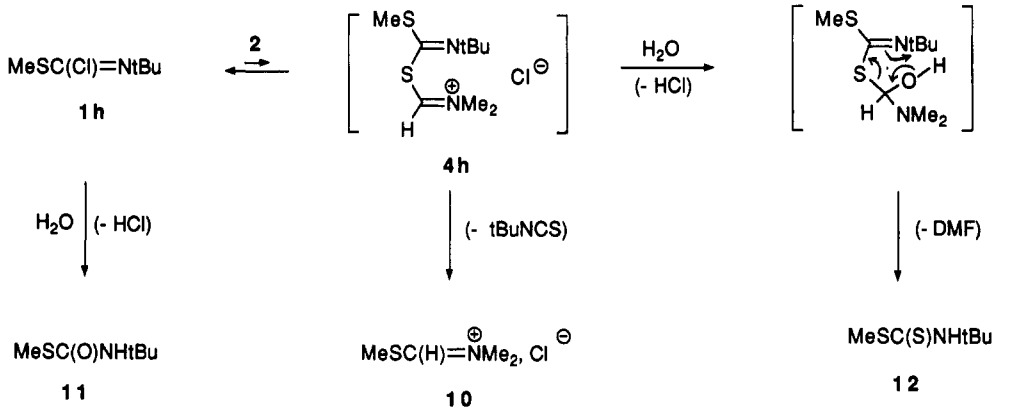
(19) The reaction was also conducted with equimolar quantities of **1h**, thioacetamide, and NEt_3 to give the same result, as described in the Experimental Section. Without NEt_3, the reaction was incomplete and led to a mixture of **11** and **12** (50:50).

(20) Analogously, benzaldehyde oximes are dehydrated to nitriles under the addition of aryl chlorothionoformates: Clive, D. L. J. *J. Chem. Soc., Chem. Commun.* **1970**, 1014.

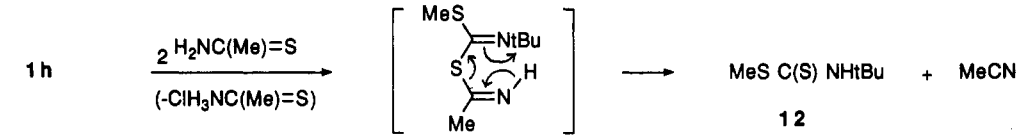
Scheme II



Scheme III



Scheme IV



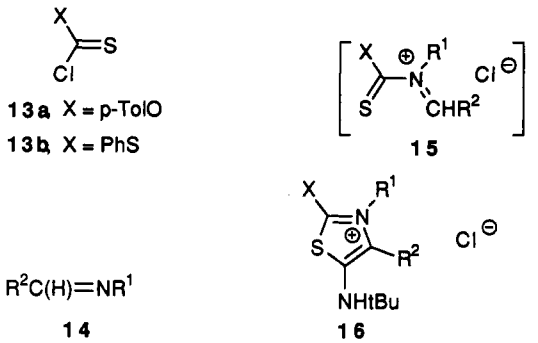
concentration (eq 5). The 2,6-dimethylphenyl isocyanide (**3d**) reacted analogously to produce **6m** and **6n** (entry 16).

$$\underset{\mathbf{1h}}{\text{MeSC(Cl)=NtBu}} \rightleftharpoons \text{MeSCl} + \underset{\mathbf{3e}}{\text{t-BuNC}} \xrightarrow[(3a)]{\text{PhCH}_2\text{NC}}$$

$$\underset{\mathbf{1a}}{\text{MeSC(Cl)=NCH}_2\text{Ph}} \xrightarrow[3a + 3e]{\text{Me}_2\text{NCH=S (2)}} \mathbf{6a + 6c} \qquad (5)$$

Preparation of Thiazolium Chlorides 16a–g. In order to prove the transient formation of formamidinium chloride **9** in the preparation of thiazolium salts **6**, we decided to investigate the reaction of aryl chlorothioformates **13a,b** with a series of aldimines **14** (Figure 2) in the presence of isocyanide **3e**. We expected that **13** and **14** should be able to provide the *N*-(thiocarbonyl)iminium chlorides **15** (similar to **9**) which could be trapped in situ by the isocyanide. Table III shows that fair to good yields of 5-amino-4-phenylthiazolium chlorides **16** were obtained in such a way. However, **14d** was seen to be much less reactive than other benzaldimines. Higher concentration of starting products and longer reaction time are required to generate **16b** in only poor yield (entry 2). When we attempted to use the propylidene-*tert*-butylamine (**14f**) in a similar manner, a fast hydrolysis precluded isolation of cycloadduct **16d** and the reaction led exclusively to the thioamide **21d** (entry 4). Structure **16** was in good agreement with NMR spectral data. Selected ^{13}C chemical shifts are listed in Table II.

These results extend the scope of our three-compound route to 5-aminothiazolium salts which might be difficult to prepare otherwise. Only a few examples of similar heterocycles and corresponding mesoionic thiazoles have



	R^1	R^2
a)	Me	Ph
b)	Et	Ph
c)	CH_2Ph	Ph
d)	i-Pr	Ph
e)	2,6-$Me_2C_6H_3$	Ph
f)	Et	t-Bu

	X	R^1	R^2
a)	p-TolO	Me	Ph
b)	p-TolO	i-Pr	Ph
c)	p-TolO	2,6-$Me_2C_6H_3$	Ph
d)	p-TolO	Et	t-Bu
e)	PhS	Me	Ph
f)	PhS	Et	Ph
g)	PhS	CH_2Ph	Ph

Figure 2.

been reported in the literature.[21-24] Cyclization of cationic species **9** and **15** could be described as thioamidoalkylation[25] of isocyanides **3**. Thioamidoalkylation of nucleo-

(21) Ollis, W. D.; Ramsden, C. A. *Adv. Heterocycl. Chem.* **1976**, *19*, 1. Newton, C. G.; Ramsden, C. A. *Tetrahedron* **1982**, *38*, 2965.

(22) Potts, K. T. Mesoionic Ring Systems. In *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; John Wiley: New York, 1984; Chapter 8, p 1.

(23) Some 5-amino-2-(methylthio)thiazolium iodides have been synthesized from the reaction of *N*-alkyl-2-phenyl(or methyl)glycinonitriles successively with CS_2, acylating agents, and MeI: Shiba, T.; Kato, H. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 964.

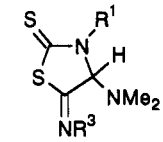
Table III. Reactions of *p*-Tolyl Chlorothionoformate (13a) and Phenyl Chlorodithioformate (13b) with Aldimines 14a–f and *tert*-Butyl Isocyanide (3e). Preparation of Thiazolium Salts 16a–g

entry	educts[a]		reactn time,[b] h	products (% yield)[c]
1	13a	14a	4	16a (81)
2	13a	14d	288[d]	16b (39)
3	13a	14e	2	16c (67)
4	13a	14f	8	21d (43)[e]
5	13b	14a	5	16e (81)
6	13b	14b	10	16f (52)
7	13b	14c	9	16g (61)

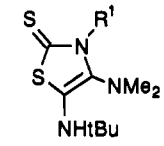
[a] The reactions were performed in $CHCl_3$ at rt with equimolar quantities of 13, 14 (2 M, unless otherwise indicated), and a 2-fold excess of isocyanide 3e. [b] Time required for the entire conversion of starting compounds. [c] Isolated yield. [d] The molarities of 13a and 14d were 4 M. [e] The very hygroscopic salt 16d was converted into 21d during workup of the reactional medium.

philic compounds is well known from *N*-(1-hydroxyalkyl)-thioamides using a strong acid as catalyst.[26–28] For example, a convenient synthesis of 4*H*-1,3,5-thiadiazines proceeds in a such way from aliphatic and aromatic cyanides.[27b] Thioamidoalkylation of isocyanides with a few 3-aza-1-thiabutadienes has afforded good yields of corresponding 5-imino dihydrothiazole derivatives.[29,30a] Some examples could also be found involving the [1 + 4] cyclization process of such heterodienes in the presence of various acetylenic systems,[26,30b] ethyl cyanoformate,[30c] or trimethylsilyl cyanide.[30d] To date, however, the use of isocyanides in a ring-closure reaction with N-unsaturated iminium salts has remained quite limited, as we mentioned in previous articles.[3,31] To our knowledge, there is no literature report related to the participation of *N*-thioacyliminium cations in similar [1 + 4] cycloaddition reactions.

Thermal Degradation and Hydrolysis of Some Thiazolium Chlorides 6 and 16. The 2-(methylthio)-thiazolium salts 6 exhibited good stability except 6l which gave the 5-imino-2-thioxothiazolidine 17l somewhat slowly at room temperature without solvent and much faster with heating. Starting from some other salts 6, this MeCl elimination was also effective in refluxing toluene for 1 h. The products of the reaction were identified as thiazolidines 17 or dihydrothiazoles 18 according to the nature of the substituents R^1 and R^3 (Figure 3). A mixture of tautomeric compounds 17c and 18c could not be isolated and was readily transformed into the 5-imino-4-thiazolidinone 19 on standing under atmospheric oxygen. This autoxidation process[3] takes place via the loss of $HNMe_2$.



17



18c, $R^1 = CH_2Ph$

18n, $R^1 = 2,6\text{-}Me_2C_6H_3$

	R^1	R^3
c)	CH_2Ph	t-Bu
j)	i-Pr	i-Pr
l)	i-Pr	t-Bu
m)	2,6-Me2C6H3	2,6-Me2C6H3

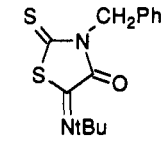


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Figure 3.

Treatment of salts 6 by DBN in THF/H_2O (95:5) gave crystalline compounds to which we assign structure 20. This result can be rationalized by assuming the deprotonation of 6 to produce the mesoionic thiazoles 7 which add to H_2O (Scheme V). Hydrolysis of 2-(tolyloxy)thiazolium salts 16, under atmospheric moisture without solvent, provided the *p*-tolyl carbamates 21. We postulate the intermediate formation of mesoionic compounds 22 which are trapped by H_2O before the ring opening. IR, mass, and NMR spectral data were observed in support of all these assigned structures.

Conclusions

Three-component condensations using isocyanides as cyclization reagents are convenient routes to a variety of 5-aminothiazolium salts 6 and 16 which are reported for the first time. Imino chloro sulfides 1 (except 1h) and aryl chlorothioformates 13 are excellent precursors for these salts and thereby for mesoionic thiazoles 7 and 22 which are well suited for further synthetic manipulations. Studies on the use of other compounds in such methodology are in progress.

Experimental Section

General. Melting points are uncorrected. ^1H NMR (80 Mhz) and ^{13}C NMR (75.5 MHz) spectra were acquired in $CDCl_3$. HRMS were obtained from the Centre Régional de Mesures Physiques de l'Ouest. Infrared spectra were recorded as suspensions in Nujol. Elemental analyses were performed by the analytical laboratory, Centre National de la Recherche Scientifique.

Methyl and phenyl chlorothioimidates 1 were easily available as previously described[32] from the insertion reaction of isocyanides R^1NC into the S–Cl bond of methanesulfenyl chloride and benzenesulfenyl chloride, in dry THF or CCl_4 solutions. Compounds 1 were always used *in situ*. The isopropyl isocyanide 3c[33] and diethyl (isocyanomethyl)phosphonate[34] were obtained according to known procedures. Aldimines 14b,d–f were prepared by condensation of aldehydes with primary amines on Al_2O_3

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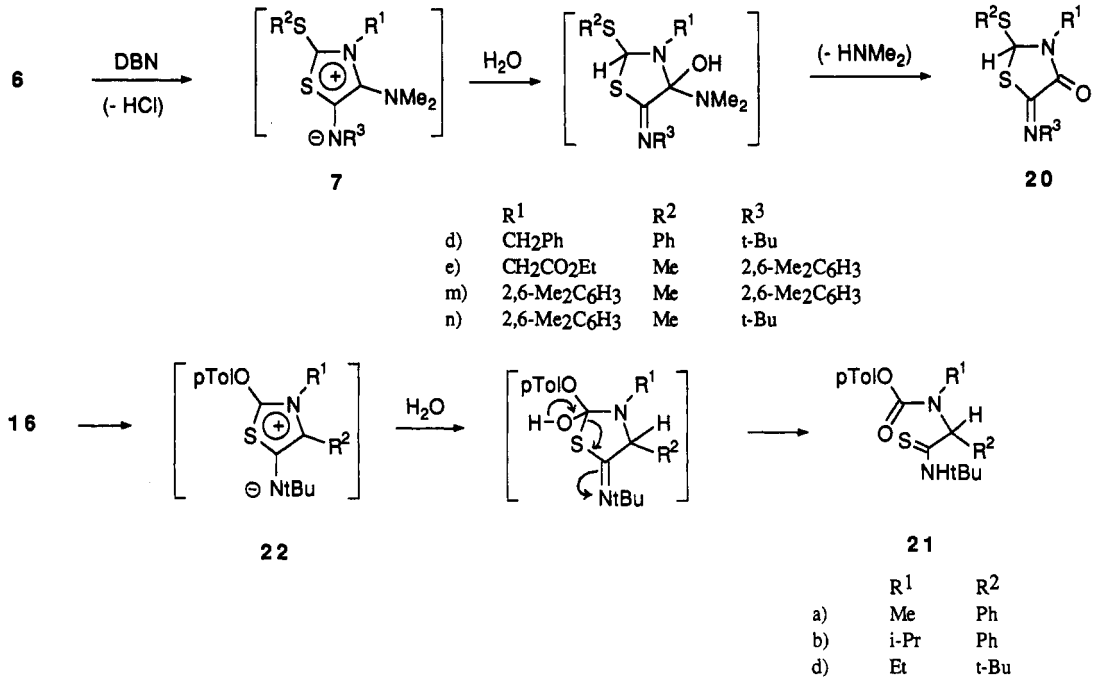
Scheme V



	R^1	R^2	R^3
d)	CH_2Ph	Ph	t-Bu
e)	CH_2CO_2Et	Me	2,6-$Me_2C_6H_3$
m)	2,6-$Me_2C_6H_3$	Me	2,6-$Me_2C_6H_3$
n)	2,6-$Me_2C_6H_3$	Me	t-Bu

	R^1	R^2
a)	Me	Ph
b)	i-Pr	Ph
d)	Et	t-Bu

without a solvent, as reported in the literature.[35] Other materials were available from commercial sources.

The following reactions, except for the hydrolysis of mesoionic thiazoles, were performed under a dry nitrogen atmosphere. Na_2SO_4 was used to dry organic layers after extractions.

Preparation of Thiazolium Chlorides 6a–n. Isocyanide **3** (30 mmol) and dimethylthioformamide (**2**) (15 mmol) were dissolved in anhyd THF (10 mL) and then added to a solution in THF (10 mL) of imidoyl chloride **1a–h** (15 mmol). The mixture was maintained at rt for the time indicated in Table I. A few salts slowly precipitated as yellowish solids from the reactional medium (**6a,g,n**). They were filtered, washed with dry Et_2O, and recrystallized from CH_2Cl_2/Et_2O (1:1). The solvent (filtrate or reactional solution) was removed under reduced pressure. The brownish residual syrup was poured into 50 mL of H_2O/HCl (pH = 1) and washed with Et_2O (2 × 10 mL). The aqueous solution was saturated with NaCl and finally extracted with CH_2Cl_2 (3 × 10 mL). The combined CH_2Cl_2 phases were concentrated to dryness. In some cases, trituration of the residue with THF/Et_2O gave a crystalline material. Salts **6b,i–m** were thus collected by filtration and purified from CH_2Cl_2/Et_2O (1:1) to afford pale yellow crystals. Other salts **6c–f,h** were obtained as viscous oils or amorphous semisolids. ^1H NMR spectrometry confirmed that thiazolium chlorides were greatly preponderant in these final products, along with some unidentified compounds (<5%). Neither bulb-to-bulb distillation nor silica gel column chromatography was effective to purify these crude salts which could be used for further reactions without additional purifications (yields and ^{13}C NMR spectra, see Tables I and II). Salts **6a,c** (50:50) and **6m,n** (35:65) were separated by fractional crystallization from THF/CH_2Cl_2 (Table I, entries 15, 16).

3-Benzyl-5-(benzylamino)-4-(dimethylamino)-2-(methylthio)thiazolium chloride (6a): mp 170 °C dec; ^1H NMR δ 2.58 (s, 3H), 2.80 (s, 6H), 4.47 (s, 2H), 5.32 (s, 2H), 7.20 (m, 10H). Anal. Calcd for $C_{20}H_{24}N_3S_2Cl$: C, 59.19; H, 5.92; N, 10.36. Found: C, 58.84; H, 6.17; N, 10.27.

3-Benzyl-4-(dimethylamino)-5-[[(ethoxycarbonyl)methyl]amino]-2-(methylthio)thiazolium chloride (6b): mp 160 °C dec; ^1H NMR δ 1.25 (t, J = 7 Hz, 3H), 2.75 (s, 3H), 2.85 (s, 6H), 4.10 (d, J = 6 Hz, 2H), 4.17 (q, J = 7 Hz, 2H), 5.37 (s, 2H), 7.20 (m, 5H), 8.17 (br, NH). Anal. Calcd for $C_{17}H_{24}N_3O_2S_2Cl$: C, 50.81; H, 5.98; N, 10.46; S, 15.94; Cl, 8.84. Found: C, 50.62; H, 6.33; N, 10.28; S, 15.50; Cl, 8.88.

3-Benzyl-5-(*tert*-butylamino)-4-(dimethylamino)-2-(methylthio)thiazolium chloride (6c): ^1H NMR δ 1.33 (s, 9H), 2.81 (s, 3H), 2.83 (s, 6H), 5.41 (s, 2H), 5.56 (s, NH), 7.30 (m, 5H); MS calcd for $C_{16}H_{23}N_3S_2$ m/z 321.1333 (MeCl elim), found 321.1333; m/z (rel int) 321 (6), 278 (61), 230 (7), 189 (6), 174 (25), 161 (6), 149 (8), 115 (49), 91 (100).

3-Benzyl-5-(*tert*-butylamino)-4-(dimethylamino)-2-(phenylthio)thiazolium chloride (6d): ^1H NMR δ 1.26 (s, 9H), 2.86 (s, 6H), 5.57 (s, 2H), 5.73 (s, NH), 7.50 (m, 10H); MS calcd for $C_{16}H_{23}N_3S$ m/z 289.1613 m/z 289.1613 (PhSCl elim), found 289.1618; m/z (rel int) 289 (13), 250 (6), 233 (14), 218 (51), 185 (5), 154 (11), 142 (43), 126 (20), 115 (9), 109 (84), 91 (100).

4-(Dimethylamino)-5-[(2,6-dimethylphenyl)amino]-3-[(ethoxycarbonyl)methyl]-2-(methylthio)thiazolium chloride (6e): ^1H NMR δ 1.34 (t, J = 7 Hz, 3H), 2.35 (s, 6H), 2.67 (s, 3H), 2.85 (s, 6H), 4.32 (q, J = 7 Hz, 2H), 4.97 (s, 2H), 7.07 (s, 3H); MS calcd for $C_{17}H_{23}N_3O_2S_2$ m/z 365.1232 (MeCl elim), found 365.1224; m/z (rel int) 365 (1), 322 (100), 205 (36), 187 (15), 164 (11), 145 (13), 132 (30), 130 (27).

5-(*tert*-Butylamino)-4-(dimethylamino)-3-[(ethoxycarbonyl)methyl]-2-(methylthio)thiazolium chloride (6f): ^1H NMR δ 1.30 (t, J = 7 Hz, 3H), 1.32 (s, 9H), 2.86 (s, 6H), 2.92 (s, 3H), 4.30 (q, J = 7 Hz, 2H), 5.02 (s, 2H), 5.50 (br, NH); MS calcd for $C_{13}H_{23}N_3O_2S_2$ m/z 317.1232 (MeCl elim), found 317.1210; m/z (rel int) 317 (32), 274 (64), 260 (23), 231 (7), 218 (33), 115 (28), 89 (100).

5-(*tert*-Butylamino)-4-(dimethylamino)-3-[(ethoxycarbonyl)methyl]-2-(phenylthio)thiazolium chloride (6g): mp 142 °C; ^1H NMR δ 1.31 (s, 9H), 1.32 (t, J = 7 Hz, 3H), 2.91 (s, 6H), 4.31 (q, J = 7 Hz, 2H), 5.18 (s, 2H), 7.60 (m, 5H); MS m/z (rel int) 317 (13), 274 (7), 260 (14), 218 (100), 185 (16), 154 (23), 109 (90). Anal. Calcd for $C_{19}H_{28}N_3O_2S_2Cl$: C, 53.08; H, 6.52; N, 9.78; S, 14.90; Cl, 8.26. Found: C, 53.50; H, 6.53; N, 9.54; S, 14.38; Cl, 8.72.

5-(Benzylamino)-3-[(diethoxyphosphoryl)methyl]-4-(dimethylamino)-2-(methylthio)thiazoliumchloride(6h): ^1H NMR δ 1.31 (t, J = 7 Hz, 6H), 2.66 (s, 3H), 3.01 (s, 6H), 4.17 (m, 4H), 4.49 (d, J = 5 Hz, 2H), 4.71 (d, $^2J_{HCP}$ = 14 Hz, 2H), 7.35 (m, 5H), 7.50 (t, NH); MS calcd for $C_{15}H_{21}N_2O_3PS_2$ m/z 372.0731 [MeCl elim and (M – MeN=CH_2)$^{\cdot+}$], found 372.0729; m/z (rel int) 372 (6), 224 (9), 194 (13), 152 (11), 138 (54), 111 (17), 91 (41), 82 (28), 72 (33), 64 (35), 47 (100).

5-(Benzylamino)-4-(dimethylamino)-2-(methylthio)-3-isopropylthiazolium chloride (6i): mp 158 °C dec; ^1H NMR

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δ 1.57 (d, J = 7 Hz, 6H), 2.63 (s, 3H), 2.96 (s, 6H), 4.50 (d, J = 5 Hz, 2H), 5.07 (m, 1H), 7.30 (m, 5H), 8.90 (br, NH). Anal. Calcd for $C_{16}H_{24}N_3S_2Cl$: C, 53.71; H, 6.71; N, 11.75; S, 17.90; Cl, 9.93. Found: C, 53.50; H, 6.74; N, 12.04; S, 17.58; Cl, 10.07.

4-(Dimethylamino)-2-(methylthio)-3-isopropyl-5-(isopropylamino)thiazolium chloride (6j): mp 120 °C dec; ^{1}H NMR δ 1.37 (d, J = 6.5 Hz, 6H), 1.65 (d, J = 7 Hz, 6H), 2.87 (s, 3H), 2.95 (s, 6H), 3.37 (m, 1H), 5.10 (m, 1H), 6.00 (br, NH); MS calcd for $C_{11}H_{21}N_3S_2$ m/z 259.1177 (MeCl elim), found 259.1178; m/z (rel int) 259 (18), 216 (100), 174 (29), 126 (12), 115 (39), 101 (88). Anal. Calcd for $C_{12}H_{24}N_3S_2Cl$: C, 46.53; H, 7.75; N, 13.57; S, 20.68; Cl, 11.47. Found: C, 46.37; H, 7.98; N, 13.32; S, 20.31; Cl, 11.78.

4-(Dimethylamino)-5-[(2,6-dimethylphenyl)amino]-2-(methylthio)-3-isopropylthiazolium chloride (6k): mp 184 °C dec; ^{1}H NMR δ 1.62 (d, J = 7 Hz, 6H), 2.30 (s, 6H), 2.65 (s, 3H), 2.88 (s, 6H), 5.05 (m, 1H), 7.06 (s, 3H), 9.67 (br, NH); MS calcd for $C_{17}H_{25}N_3S_2$ m/z 335.1490 (HCl elim), found 335.1485; m/z (rel int) 335 (21), 292 (62), 278 (17), 178 (11), 161 (21), 130 (18), 119 (15), 99 (14), 91 (100). Anal. Calcd for $C_{17}H_{26}N_3S_2Cl$: C, 54.91; H, 7.00; N, 11.31; S, 17.23. Found: C, 55.15; H, 7.36; N, 11.53; S, 17.74.

5-(*tert*-Butylamino)-4-(dimethylamino)-2-(methylthio)-3-isopropylthiazolium chloride (6l): mp 50 °C dec (unstable: MeCl elim at rt); ^{1}H NMR δ 1.35 (s, 9H), 1.65 (d, J = 7 Hz, 6H), 2.90 (s, 6H), 3.75 (br, NH), 5.11 (m, 1H); MS calcd for $C_{12}H_{23}N_3S_2$ m/z 273.1333 (MeCl elim), found 273.1326; m/z (rel int) 273 (9), 230 (82), 174 (44), 132 (19), 115 (38), 101 (22), 89 (100).

4-(Dimethylamino)-3-(2,6-dimethylphenyl)-5-[(2,6-dimethylphenyl)amino]-2-(methylthio)thiazolium chloride (6m): mp 202 °C dec; ^{1}H NMR δ 2.12 (s, 6H), 2.37 (s, 6H), 2.46 (s, 6H), 2.66 (s, 3H), 7.02 (s, 3H), 7.30 (m, 3H), 9.72 (br, NH); MS calcd for $C_{21}H_{25}N_3S_2$ m/z 383.1490 (MeCl elim), found 383.1476; m/z (rel int) 383 (55), 340 (32), 252 (15), 220 (11), 205 (80), 187 (29), 176 (26), 163 (39), 161 (39), 132 (65), 130 (100). Anal. Calcd for $C_{22}H_{28}N_3S_2Cl$: C, 60.90; H, 6.46; N, 9.69; Cl, 8.19. Found: C, 60.74; H, 6.35; N, 9.43; Cl, 8.28.

5-(*tert*-Butylamino)-4-(dimethylamino)-3-(2,6-dimethylphenyl)-2-(methylthio)thiazolium chloride (6n): mp 210 °C dec; ^{1}H NMR δ 1.30 (s, 9H), 2.05 (s, 6H), 2.57 (s, 6H), 2.75 (s, 3H), 6.07 (br, NH), 7.30 (m, 3H); MS calcd for $C_{18}H_{27}N_3S_2$ m/z 349.1646 (HCl elim), found 349.1631; m/z (rel int) 349 (3), 335 (45), 278 (71), 219 (17), 178 (25), 175 (96), 119 (54), 44 (100). Anal. Calcd for $C_{18}H_{28}N_3S_2Cl$: C, 56.03; H, 7.26; N, 10.89; S, 16.60; Cl, 9.21. Found: C, 55.89; H, 7.43; N, 10.84; S, 16.50; Cl, 9.55.

Base-Induced Cycloaddition of Thiazolium Salt 6a with Dimethyl Acetylenedicarboxylate. DBN (0.93 g, 7.5 mmol) was added dropwise to a solution of **6a** (2.03 g, 5 mmol) and DMAD (1.06 g, 7.5 mmol) in anhyd CH_2Cl_2 (10 mL). After the solution was stirred at rt for 1 h, the solvent was evaporated and then the residue was poured into 20 mL of Et_2O and washed with H_2O. The ^{1}H NMR analysis of the crude oily product showed the formation of pyrrole **8** and benzyl isothiocyanate in the ratio 50:50. These compounds were separated by a silica gel column chromatography with a mixture of Et_2O/petroleum ether (3:2) as eluent.

1-Benzyl-5-(dimethylamino)-2-(methylthio)-3,4-bis(methoxycarbonyl)pyrrole (8): mp 116 °C (ether/petroleum ether) (1.47 g, 81% yield); ^{1}H NMR δ 2.03 (s, 3H), 2.62 (s, 6H), 3.77 (s, 3H), 3.83 (s, 3H), 5.27 (s, 2H), 7.20 (m, 5H); ^{13}C NMR δ 20.8 (q, ^1J = 141 Hz), 43.2 (qq, ^1J = 136 Hz, ^3J = 4 Hz), 46.5 (tt, ^1J = 140 Hz, ^3J = 5 Hz), 51.5, 52.0 (2q, ^1J = 147 Hz), 108.4 (s, C-4), 121.5 (m, C-2), 122.6 (s, C-3), 126.6, 127.2, 128.6 (dm, dt, dd, ^1J = 161 Hz), 138.1 (m, quat arom C), 147.0 (m, C-5), 164.2, 165.8 (q, ^3J = 4.1 Hz); MS calcd for $C_{18}H_{22}N_2O_4S$ m/z 362.1300 ($M^{\bullet+}$), found 362.1273; m/z (rel int) 362 (23), 271 (100), 239 (24), 207 (12), 91 (28); IR 1718, 1700 cm^{-1}. Anal. Calcd for $C_{18}H_{22}N_2O_4S$: C, 59.67; H, 6.08; N, 7.73; S, 8.84. Found: C, 59.57; H, 6.19; N, 7.47; S, 8.54.

Reaction of the (*tert*-Butylimino)chloromethyl Methyl Sulfide 1h with Dimethylthioformamide (2). By the above-mentioned procedure, an equimolar mixture of **1h** and **2** was treated with 2 equiv of *tert*-butyl isocyanide (**3e**) in THF at rt for 15 h. The crude product was worked in similar conditions. We did not extract any salt from the aqueous solution. On the contrary, concentration of the washing Et_2O gave an oil from which we separated **11** and **12** by a bulb-to-bulb distillation under reduced pressure (bp 50 °C/0.02 Torr).

Methyl *tert*-butylthiocarbamate (11): mp 81 °C (32% yield); ^{1}H NMR δ 1.37 (s, 9H), 2.30 (s, 3H), 5.37 (br, NH); IR 3277, 1650 cm^{-1}. Anal. Calcd for $C_6H_{13}OS$: C, 48.95; H, 8.90; N, 9.51. Found: C, 48.88; H, 9.05; N, 9.29.

Methyl *tert*-butyldithiocarbamate (12): oil (13% yield); ^{1}H NMR δ 1.57 (s, 9H), 2.60 (s, 3H), 7.00 (br, NH); MS calcd for $C_6H_{13}NS_2$ m/z 163.0489 ($M^{\bullet+}$), found 163.0489; m/z (rel int) 163 (25), 116 (16), 91 (13), 60 (11), 57 (100).

The reaction of **1h** (1 mmol) with **2** (1 mmol) was also performed in $CDCl_3$ (0.5 mL) at rt for 15 h. The ^{1}H and ^{13}C NMR analyses of the solution indicated the formation of the (methylthio)methyleniminium chloride **10**, along with starting and some unidentified compounds [**10**: ^{1}H NMR δ 3.10 (s, 3H), 3.52 (s, 3H), 3.92 (s, 3H), 11.27 (s, 1H); ^{13}C NMR δ 17.0 (qd, ^1J = 145 Hz, ^3J = 4 Hz), 42.6, 48.7 (2 qm, ^1J = 143 Hz), 184.8 (dm, ^1J = 198 Hz)]. Salt **10** was still detected in the complex mixture which was obtained when isocyanide **3e** was added to the solution at the beginning of the reaction. Workup of this mixture in the usual way afforded **11** and **12** as described above. The structure of chloride **10** was confirmed by comparison of its NMR spectral properties with those of the corresponding iodide that is easily prepared[36] by treating dimethylthioformamide (**2**) with MeI [MeSC(H)=N$^+$Me$_2$, I$^-$: ^{1}H NMR δ 3.12 (s, 3H), 3.50 (s, 3H), 3.87 (s, 3H), 10.60 (s, 1H)].

Reaction of the *tert*-Butylimino Chloro Sulfide 1h with Thioacetamide. Thioacetamide (0.75 g, 10 mmol) was added to a solution of **1h** (10 mmol) and NEt_3 (1 g, 10 mmol) in dry CCl_4 (20 mL). After the solution was stirred at rt for 5 h, the triethylammonium chloride was filtered off. The ^{1}H NMR analysis of the filtrate showed the formation of MeCN. Evaporation and extraction of the residue with Et_2O gave the methyl dithiocarbamate **12** (1.40 g, 86% yield).

Preparation of Thiazolium Chlorides 16a–g. Isocyanide **3e** (1.66 g, 20 mmol) was added dropwise to a mixture of the appropriate aryl chlorothioformate **13a,b** (10 mmol) and aldimine **14a–f** (10 mmol) dissolved in anhyd $CHCl_3$ (5 mL; 2.5 mL starting from **14d**). The solution was maintained at rt for the time indicated in Table III and then the solvent was evaporated in vacuo (the progress of the reaction was studied by successive ^{1}H NMR analysis of the crude mixture that derived from the concentration of small portions). In most cases, trituration of the residue with Et_2O gave yellowish solid material **16** which was filtrated and recrystallized from CH_2Cl_2/Et_2O (1:1). However, **16b** was purified as described above for salts **6**, and **16d** could not be isolated owing to the fast hydrolysis to **21d** (yields and ^{13}C NMR data are provided in Tables III and II, respectively).

5-(*tert*-Butylamino)-3-methyl-2-[(4-methylphenyl)oxy]-4-phenylthiazolium chloride (16a): mp 208 °C dec; ^{1}H NMR δ 1.05 (s, 9H), 2.40 (s, 3H), 3.79 (s, 3H), 4.27 (br, NH), 7.50 (m, 9H); MS calcd for $C_{21}H_{24}N_2OS$ m/z 352.1609 (HCl elim), found 352.1608; m/z 352 (24), 296 (19), 239 (9), 206 (13), 123 (14), 118 (47), 116 (100). Anal. Calcd for $C_{21}H_{25}N_2OSCl$: C, 64.86; H, 6.43; N, 7.20; S, 8.23; Cl, 9.13. Found: C, 64.64; H, 6.65; N, 7.28; S, 7.88; Cl, 9.23.

5-(*tert*-Butylamino)-2-[(4-methylphenyl)oxy]-4-phenyl-3-isopropylthiazolium chloride (16b): mp 215 °C dec (unstable); ^{1}H NMR δ 1.04 (s, 9H), 1.69 (d, J = 6.8 Hz, 6H), 2.43 (s, 3H), 4.48 (m, 1H), 5.07 (br, NH), 7.35, 7.43 (AB syst, J = 8 Hz, 4H), 7.56 (s, 5H).

5-(*tert*-Butylamino)-3-(2,6-dimethylphenyl)-2-[(4-methylphenyl)oxy]-4-phenylthiazolium chloride (16c): mp 120 °C dec (unstable); ^{1}H NMR δ 1.00 (s, 9H), 2.15 (s, 6H), 2.34 (s, 3H), 5.12 (br, NH), 7.20 (m, 12H).

5-(*tert*-Butylamino)-3-methyl-4-phenyl-2-(phenylthio)thiazolium chloride (16e): mp 198 °C dec; ^{1}H NMR δ 1.05 (s, 9H), 3.87 (s, 3H), 4.08 (br, NH), 7.65 (m, 10H). Anal. Calcd for $C_{20}H_{23}N_2S_2Cl$: C, 61.46; H, 5.89; N, 7.17; Cl, 9.09. Found: C, 61.32; H, 5.87; N, 7.08; Cl, 9.41.

5-(*tert*-Butylamino)-3-ethyl-4-phenyl-2-(phenylthio)thiazolium chloride (16f): mp 135 °C dec; ^{1}H NMR δ 1.07 (s, 9H), 1.27 (t, J = 7 Hz, 3H), 4.00 (br, NH), 4.39 (q, J = 7 Hz, 2H), 7.70 (m, 10H).

(36) Gompper, R.; Elser, W. *Org. Synth.* **1968**, *48*, 97.

3-Benzyl-5-(*tert*-butylamino)-4-phenyl-2-(phenylthio)thiazolium chloride (16g): mp 186 °C dec; ^{1}H NMR δ 1.15 (s, 9H), 4.60 (br, NH), 5.65 (s, 2H), 7.40 (m, 15H). Anal. Calcd for $C_{26}H_{27}N_2S_2Cl$: C, 66.88; H, 5.78; N, 6.00; S, 13.72; Cl, 7.61. Found: C, 66.68; H, 5.97; N, 6.10; S, 13.51; Cl, 7.92.

Thermolysis of Thiazolium Chlorides 6c,j,l–m. A solution of **6** (1 g) in dry toluene (10 mL) was refluxed for 1 h, and then the solvent was removed under reduced pressure. The residue was triturated with MeOH to give a colorless crystalline material (**17j,l,m, 18n, 19**). The mixture **17c, 18c** (2:1) was observed before this treatment by the ^{1}H NMR spectroscopy of the crude oil but rapidly oxidized to **19** under atmospheric O_2 [**17c**: δ 1.26 (s, 9H), 2.36 (s, 6H), 4.76 (s, 1H), 4.37, 5.98 (AB syst, J = 13.6 Hz, 2H), 7.27 (s, 5H); **18c**: δ 1.26 (s, 9H), 2.53 (s, 6H), 5.37 (s, 2H), 7.32 (s, 5H)].

4-(Dimethylamino)-3-isopropyl-5-(isopropylimino)-2-thioxothiazolidine (17j): mp 104 °C (48 % yield); ^{1}H NMR δ 1.18 (d, J = 7 Hz, 6H), 1.41 (d, J = 7 Hz, 6H), 2.36 (s, 6H), 3.08 (m, 1H), 5.03 (m, 1H), 5.16 (s, 1H); ^{13}C NMR δ 18.9, 20.4, 22.7, 23.8 (4 qm, ^1J = 127 Hz), 38.4 (qm, ^1J = 137 Hz), 51.0 (dm, ^1J = 131 Hz), 60.5 (dm, ^1J = 142 Hz), 86.7 (dm, ^1J = 155 Hz, C-4), 155.1 (dd, ^3J = 9.9 Hz, ^2J = 3.8 Hz, C-5), 189.5 (dd, ^3J = 4.3 Hz, C-2); MS calcd for $C_9H_{16}N_2S_2$ m/z 216.0755 [(M − MeN=CH_2)$^{\cdot+}$], found 216.0764; m/z (rel int) 216 (45), 174 (11), 126 (7), 115 (25), 101 (100). Anal. Calcd for $C_{11}H_{21}N_3S_2$: C, 50.96; H, 8.11; N, 16.23; S, 24.71. Found: C, 50.80; H, 8.27; N, 16.05; S, 24.67.

5-(*tert*-Butylimino)-4-(dimethylamino)-3-isopropyl-2-thioxothiazolidine (17l): mp 88 °C (32% yield); ^{1}H NMR δ 1.30 (s, 9H), 1.47 (d, J = 6.5 Hz, 6H), 2.40 (s, 6H), 5.09 (m, 1H), 5.11 (s, 1H); ^{13}C NMR δ 18.9, 20.5 (2 qm, ^1J = 128 Hz), 28.5 (qm, ^1J = 126 Hz), 38.3 (qm, ^1J = 134 Hz), 50.7 (dm, ^1J = 141 Hz), 57.7 (m), 88.6 (dm, ^1J = 155 Hz, C-4), 150.6 (d, ^2J = 4.2 Hz, C-5), 190.6 (dd, ^3J = 4 Hz, C-2); MS calcd for $C_{10}H_{18}N_2S_2$ m/z 230.0911 [(M − MeN=CH_2)$^{\cdot+}$], found 230.0906; m/z (rel int) 230 (89), 174 (19), 132 (18), 115 (35), 89 (100). Anal. Calcd for $C_{12}H_{23}N_3S_2$: C, 52.75; H, 8.43; N, 15.38; S, 23.44. Found: C, 52.87; H, 8.29; N, 15.19; S, 23.84.

4-(Dimethylamino)-3-(2,6-dimethylphenyl)-5-[(2,6-dimethylphenyl)imino]-2-thioxothiazolidine (17m): mp 169 °C (59% yield); ^{1}H NMR 2.13 (s, 6H), 2.17 (s, 3H), 2.36 (s, 3H), 2.60 (s, 6H), 5.44 (s, 1H), 7.01 (s, 3H), 7.14 (s, 3H); ^{13}C NMR δ 17.1, 19.1 (2qd, ^1J = 127 Hz, ^3J = 5 Hz), 40.6 (qm, ^1J = 135 Hz), 91.8 (dm, ^1J = 154 Hz, C-4), 125.0, 128.9, 128.6, 129.0, 129.1 (2d, 3 dm, ^1J = 160 Hz), 125.7, 133.9, 137.7, 138.7, 148.8 (5m, quat arom C), 168.3 (d, ^2J = 4 Hz, C-5), 190.8 (d, ^3J = 4 Hz, C-2); MS calcd for $C_{21}H_{25}N_3S_2$ m/z 383.1490 (M$^{\cdot+}$), found 383.1495; m/z (rel int) 383 (3), 340 (55), 252 (15), 220 (6), 205 (100). Anal. Calcd for $C_{21}H_{25}N_3S_2$: C, 65.80; H, 6.53; N, 10.97; S, 16.71. Found: C, 66.31; N, 6.80; N, 10.91; S, 16.62.

5-(*tert*-Butylamino)-2,3-dihydro-4-(dimethylamino)-3-(2,6-dimethylphenyl)-2-thioxothiazole (18n): mp 216 °C (62% yield); ^{1}H NMR 1.22 (s, 9H), 2.12 (s, 6H), 2.45 (s, 6H), 7.20 (m, 3H); ^{13}C NMR δ 18.1 (qd, ^1J = 127 Hz, ^3J = 4.7 Hz), 29.8 (qm, ^1J = 126 Hz), 42.6 (qq, ^1J = 136 Hz, ^3J = 3.6 Hz), 52.7 (m), 126.2 (s, C-5), 128.4, 129.3 (dm, d, ^1J = 160 Hz), 136.4, 136.5 (2m, quat arom C), 138.5 (m, C-4), 179.9 (s, C-2); MS calcd for $C_{17}H_{25}N_3S_2$ m/z 335.1490 (M$^{\cdot+}$), found 335.1496; m/z (rel int) 335 (91), 278 (100), 219 (14), 175 (79), 119 (71); IR 3250, 1600 cm^{-1}. Anal. Calcd for $C_{17}H_{25}N_3S_2$: C, 60.90; H, 7.46; N, 12.54; S, 19.10. Found: C, 60.74; H, 7.63; N, 12.51; S, 19.19.

3-Benzyl-5-(*tert*-butylimino)-2-thioxo-4-thiazolidinone (19): mp 114 °C (43% yield); ^{1}H NMR δ 1.36 (s, 9H), 5.31 (s, 2H), 7.35 (m, 5H); ^{13}C NMR δ 28.3 (qm, ^1J = 127 Hz), 47.2 (tt, ^1J = 143 Hz, ^3J = 5 Hz), 59.9 (m), 128.3, 128.6, 129.4 (dt, dd, dm, ^1J = 161 Hz), 134.3 (m, quat arom C), 143.8 (s, C-5), 161.8 (t, ^3J = 2.4 Hz, C-4), 192.3 (t, ^3J = 5 Hz, C-2); MS calcd for $C_{14}H_{16}N_2OS_2$ m/z 292.0704 (M$^{\cdot+}$), found 292.0700; m/z (rel int) 292 (17), 236 (7), 149 (6), 91 (41), 57 (100); IR 1730, 1626 cm^{-1}. Anal. Calcd for $C_{14}H_{16}N_2OS_2$: C, 57.53; H, 5.48; N, 9.59; S, 21.92. Found: C, 57.58; H, 5.36; N, 9.48, S 22.20.

Base-Induced Hydrolysis of Thiazolium Chlorides 6d,e,m,n. A mixture of **6** (5 mmol), DBN (0.74 g, 6 mmol), and H_2O (1 mL) was dissolved in THF (15 mL) and maintained at rt for 1 h. After removal of the solvent, the residue was dissolved in Et_2O and washed with H_2O. The etheral solution was concentrated to the colorless crystalline **20** which was purified from EtOH.

3-Benzyl-5-(*tert*-butylimino)-2-(phenylthio)-4-thiazolidinone (20d): mp 113 °C (38% yield); ^{1}H NMR δ 1.10 (s, 9H), 4.55, 5.46 (AB syst, J = 15 Hz, 2H), 5.72 (s, 1H), 7.31 (s, 10H); ^{13}C NMR δ 27.5 (qm, ^1J = 127 Hz), 46.1 (tm, ^1J = 140 Hz), 57.2 (m), 66.0 (ddd, ^1J = 171 Hz, ^3J = 6.4 and 2 Hz, C-2), 126.3, 134.6 (m, quat arom C), 128.4, 128.9, 129.1, 129.2, 130.3, 137.1 (other arom C), 145.4 (s, C-5), 161.5 (m, C-4); MS calcd for $C_{14}H_{17}N_2OS$ m/z 261.1061 [(M − PhS)$^+$], found 261.1074; m/z (rel int) 261 (75), 205 (26), 118 (9), 110 (13), 91 (50), 57 (100); IR 1683, 1610 cm^{-1}. Anal. Calcd for $C_{20}H_{22}N_2OS_2$: C, 64.86; H, 5.94; N, 7.57. Found: C, 64.85; H, 5.99; N, 7.49.

5-[(2,6-Dimethylphenyl)imino]-3-[(ethoxycarbonyl)methyl]-2-(methylthio)-4-thiazolidinone (20e): mp 112 °C (38% yield); ^{1}H NMR δ 1.30 (t, J = 7 Hz, 3H), 1.92 (s, 3H), 2.07 (s, 6H), 4.24 (q, J = 7 Hz, 2H), 4.22, 4.75 (AB syst, J = 17 Hz, 2H), 6.16 (s, 1H), 7.02 (s, 3H); ^{13}C NMR δ 8.6 (qd, ^1J = 140 Hz, ^3J = 4.5 Hz), 14.1 (qt, ^1J = 127 Hz, ^2J = 2 Hz), 17.5 (qd, ^1J = 127 Hz, ^3J = 4.5 Hz), 43.3 (t, ^1J = 142 Hz), 62.1 (tq, ^1J = 148 Hz, ^3J = 4 Hz), 64.1 (dm, ^1J = 171 Hz, C-2), 125.0, 128.5 (d, dm, ^1J = 160 Hz), 125.4, 149.0 (m, quat arom C), 156.0 (s, C-5), 160.7 (br, C-4), 167.4 (m); MS calcd for $C_{16}H_{20}N_2O_3S_2$ m/z 352.0915 (M$^{\cdot+}$), found 352.0922; m/z (rel int) 352 (67), 305 (56), 174 (13), 163 (36), 158 (100), 130 (44); IR 1740, 1690, 1620 cm^{-1}. Anal. Calcd for $C_{16}H_{20}N_2O_3S_2$: C, 54.55; H, 5.68; N, 7.95; S, 18.18. Found: C, 54.94; H, 5.82; N, 8.08; S, 18.17.

3-(2,6-Dimethylphenyl)-5-[(2,6-dimethylphenyl)imino]-2-(methylthio)-4-thiazolidinone (20m): mp 188 °C (34% yield); ^{1}H NMR 1.91 (s, 3H), 2.11 (s, 6H), 2.18 (s, 3H), 2.37 (s, 3H), 6.01 (s, 1H), 7.04 (s, 3H), 7.20 (s, 3H). Anal. Calcd for $C_{20}H_{22}N_2OS_2$: C, 64.86; H, 5.95; N, 7.57; S, 17.30. Found: C, 64.59; H, 6.08; N, 7.88; S, 17.20.

5-(*tert*-Butylimino)-3-(2,6-dimethylphenyl)-2-(methylthio)-4-thiazolidinone (20n): mp 161 °C (59% yield); ^{1}H NMR 1.40 (s, 9H), 1.88 (s, 3H), 2.12 (s, 3H), 2.28 (s, 3H), 5.97 (s, 1H), 7.12 (m, 3H); ^{13}C NMR δ 14.2 (qd, ^1J = 140 Hz, ^3J = 3.7 Hz), 17.8, 19.1 (2 qd, ^1J = 127 Hz, ^3J = 4.6 Hz), 27.6 (qm, ^1J = 126 Hz), 57.7 (m), 65.9 (dq, ^1J = 171 Hz, ^3J = 5.2 Hz, C-2), 129.0, 129.1, 129.3 (2 dm and d, ^1J = 161 Hz), 134.4, 134.8, 138.4 (3m, quat arom C), 145.4 (s, C-5), 160.7 (d, ^3J = 2.2 Hz, C-4). Anal. Calcd for $C_{16}H_{22}N_2OS_2$: C, 59.63; H, 6.83; N, 8.70; S, 19.88. Found: C, 59.46; H, 6.95; N, 8.95; S, 19.75.

Hydrolysis of Thiazolium Chlorides 16a,b,d. A sample of **16** was maintained under atmospheric moisture, without solvent at rt, to afford the corresponding **21** which was suspended in EtOH and filtered. The reaction was quantitative after 6 days for **21a,b** and after a few min for **21d**.

***p*-Tolyl [[(*tert*-butylamino)(thiocarbonyl)]phenylmethyl]-methylcarbamate (21a)**: mp 150 °C; ^{1}H NMR δ 1.40 (s, 9H), 2.22 (s, 3H), 2.92 (s, 3H), 5.97 (s, 1H), 6.83, 7.07 (AB syst, J = 9 Hz, 4H), 7.31 (s, 5H). Anal. Calcd for $C_{21}H_{26}N_2O_2S$: C, 68.10; H, 7.02; N, 7.56; S, 8.64. Found: C, 68.54; H, 7.15; N, 7.60; S, 8.70.

***p*-Tolyl [[(*tert*-butylamino)(thiocarbonyl)]phenylmethyl]-isopropylcarbamate (21b)**: mp 120 °C; ^{1}H NMR δ 1.27 (d, J = 6.5 Hz, 3H), 1.42 (d, J = 6.5 Hz, 3H), 1.45 (s, 9H), 2.20 (s, 3H), 4.51 (m, 1H), 5.50 (s, 1H), 6.71, 7.03 (AB syst, J = 8 Hz, 4H), 7.30 (m, 5H), 9.07 (br, NH). Anal. Calcd for $C_{23}H_{30}N_2O_2S$: C, 69.34; H, 7.53; N, 7.03. Found: C, 69.40; H, 7.48; N, 7.05.

***p*-Tolyl [*tert*-butyl[(*tert*-butylamino)(thiocarbonyl)]-methyl]ethylcarbamate (21d)**: mp 109 °C; ^{1}H NMR δ 1.17 (s, 9H), 1.29 (t, J = 7 Hz, 3H), 1.46 (s, 9H), 2.28 (s, 3H), 3.36, 3.82 (2m, 2H), 4.15 (s, 1H), 6.89, 7.16 (AB syst, J = 8 Hz, 4H); ^{13}C NMR δ 14.6 (qbr, ^1J = 127 Hz), 20.8 (qt, ^1J = 126 Hz, ^3J = 4.2 Hz), 27.3 (qm, ^1J = 127 Hz), 29.5 (qm, ^1J = 126 Hz), 36.3, 55.4 (2m), 87.7 (dm, ^1J = 142 Hz), 121.2 (dd, ^1J = 162.5 Hz, ^3J = 4.6 Hz), 129.9 (dm, ^1J = 160 Hz), 135.2, 148.8, (2m), 157.1 (m), 198.8 (d, ^2J = 6.5 Hz); MS calcd for $C_{20}H_{32}N_2O_2S$ m/z 364.2184 (M$^{\cdot+}$), found 364.2183; m/z (rel int) 364 (7), 248 (100), 192 (5), 177 (5), 145 (5), 140 (14). Anal. Calcd for $C_{20}H_{32}N_2O_2S$: C,65.93;H, 8.79; N, 7.69; S, 8.79. Found: C, 66.18; H, 8.89; N, 7.62; S, 8.60.