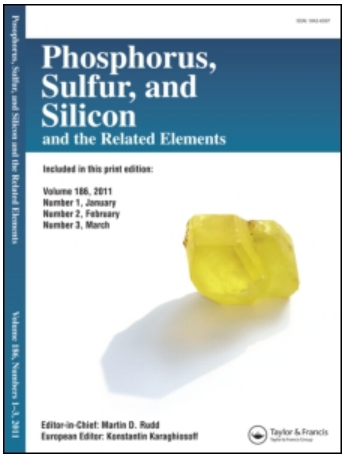

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A MILD AND EFFICIENT TRIPHOSGENE-MEDIATED CYCLODEHYDRATION OF 2-(IMIDOYLTHIO)CARBOXAMIDES. SYNTHESIS AND CHEMISTRY OF 4-AMINO-2-(METHYLTHIO)THIAZOLIUM CHLORIDES

Adile Touimi Benjelloun[a]; Georges Morel[a]; Evel Yne Marchand[a]
[a] Laboratoire de Synthèse et Electrosynthèse organiques, Rennes, France

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A MILD AND EFFICIENT TRIPHOSGENE-MEDIATED CYCLODEHYDRATION OF 2-(IMIDOYLTHIO)CARBOXAMIDES. SYNTHESIS AND CHEMISTRY OF 4-AMINO-2-(METHYLTHIO)THIAZOLIUM CHLORIDES

ADILE TOUIMI BENJELLOUN, GEORGES MOREL* and EVELYNE MARCHAND

Laboratoire de Synthèse et Electrosynthèse organiques, UMR n° 6510, Campus de Beaulieu, 35042 Rennes, France

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4-Aminothiazolium salts **1** are conveniently prepared in a one-step procedure from 2-(imidoylthio)carboxamides **4** and triphosgene in the presence of pyridine. Their chemical reactions are discussed, including addition to dimethyl acetylenedicarboxylate and carbon disulfide in a basic heterogeneous medium.

Keywords: Dehydrative ring closure; ketenimines; thiazolium salts; 2,3-dihydro-2-thioxothiazoles; triphosgene

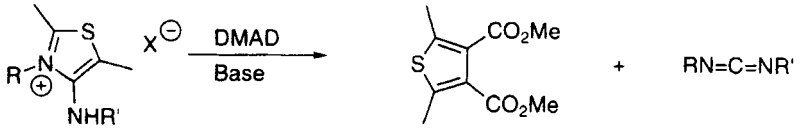
INTRODUCTION

Mesoionic compounds have been known for many years and extensively utilized as substrates in 1,3-dipolar cycloadditions.[1,2] We previously described the generation of 5-(alkylamino)-2-(methylthio) (or phenylthio)thiazolium chlorides[3] which are precursors in basic media for unstabilized mesoionic thiazolium-5-aminides. Their reactivity was studied by the *in situ* technique with several dipolarophiles i.e. electrophilic

* Corresponding author. Fax : (33) 299286738. E.mail : Georges.Morel@univ-rennesl.fr.

alkynes and alkenes[4] or carbon disulfide[5] in the presence of DBN or NEt_3. The reactions involved the cycloaddition of the "masked" azomethine ylides across the considered π-bond, yielding transient N-bridged adducts in the first step, and opened up diverse synthetic possibilities for functionalized heterocycles. In particular, use of dimethyl acetylenedicarboxylate (DMAD) or CS_2 gave 3,4-bis-(methoxycarbonyl)-1H-pyrroles or thiazolium-5-thiolates via a subsequent elimination of an alkyl isothiocyanate. [4,5]

As an extension of this study, we wanted to prepare attractive 4-aminothiazolium halides which are potential precursors for cyclic thiocarbonyl ylides. Base-induced 1,3-dipolar cycloadditions of such species might furnish a variety of sulfur heterocycles, for instance thiophene derivatives from DMAD via the extrusion of a carbodiimide [6,7] (Scheme 1). Only a few examples of similar salts and corresponding mesoionic thiazoles have been reported in the literature. [7–10] Stabilized thiazolium-4-(acylamidines) were usually obtained through the S-alkylation of secondary thioamides [9] or 2-mercaptopyridine [8,10] with α-halonitriles and treatment of the resulting cyanomethylthio compounds with acetyl or benzoyl chloride.



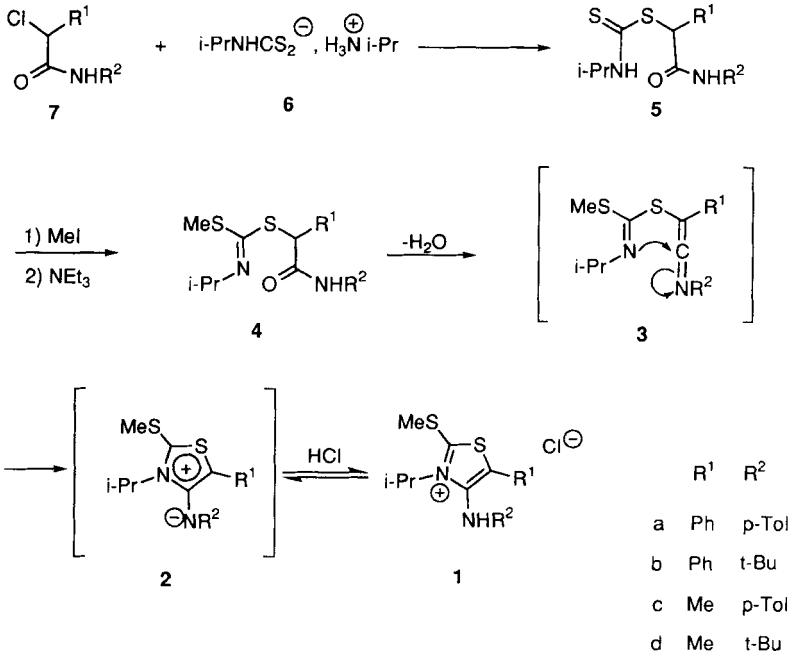
SCHEME 1

The present paper reports the preparation of new 4-amino-2-(methylthio)thiazolium chlorides and some investigation about their chemical behaviour, including attempted cycloaddition reactions with DMAD and CS_2.

RESULTS

Our approach to the synthesis of salts **1** or mesoionic thiazoles **2** was based on the understanding that the valence tautomer **3** could cyclise spontaneously (Scheme 2). Such a preparation was thus reduced to a route for ketenimines **3.** Ghosez and coworkers found that treatment of some tertiary

carboxamides with phosgene/NEt_3 is a good method for obtaining the corresponding keteniminium chlorides. [11] In interesting variations, the bis(trichloromethyl) carbonate (triphosgene) was used instead of $COCl_2$ for dehydrating primary amides to nitriles [12] and secondary formamides to isonitriles. [13] Indeed, as a stable crystalline compound, triphosgene is a safer and easier to handle reagent than either phosgene or diphosgene. This convenient $COCl_2$ substitute has been mentioned in a wide range of synthetic applications, e.g. chloroformylation, carbonylation, chlorination and dehydration. [14] We have therefore examined the reaction between triphosgene and the 2-(imidoylthio)carboxamides **4**. The dehydrations were carried out at room temperature for 30 min in CH_2Cl_2 solution containing one-third equivalent of $(COCl_2)_3$ and a 3-fold excess of pyridine. These very mild conditions allow the isolation of salts **1** in good purity and satisfying yields (Table I).



	R^1	R^2
a	Ph	p-Tol
b	Ph	t-Bu
c	Me	p-Tol
d	Me	t-Bu

SCHEME 2

The suitable starting materials **4** were synthesized according to the route shown in Scheme 2 : alkylation of the ammonium dithiocarbamate **6** with

α-chlorocarboxamides **7** and successive treatment of the resulting amides **5** with iodomethane and NEt_3.

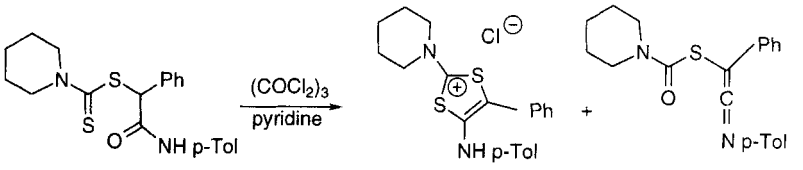
TABLE I Triphosgene-Mediated Preparation of 4-Aminothiazolium and Dithiolium Chlorides **1** and **9**. Selected ^{13}C NMR Chemical Shifts (Endocyclic Carbons)[a]

educt	*salt (%yield)*[b]	*C-2 (m)*	*C-4*	*C-5*
4a	**1a** (70)	168.9	141.6 d (3.5)[c]	130.9 (screened)
4b	**1b** (80)	168.6	145 d (3.2)[c]	130.5 t (3)[d]
4c	**1c** (65)	168.3	143.3 m	127.5 q (6.8)[e]
4d	**1d** (80)	167.2	146.7 m	126.5 qd (4.6)[e] (2,5)[f]
8	**9** (15)	180.8	135 s ζ	140.8 t (9)[d]

[a] δ ppm and multiplicities (J H_z) in $CDCl_3$ solutions at 75.469 MHz. [b] Purified product yield. [c] ^3J (CNCH). [d] ^3J (CCCH). [e] ^2J (CCH). [f] ^3J (CCNH).

Formation of mesoionic systems by dehydrative ring closure has some literature precedent, including the syntheses of thiomünchnones from N-thioacylamino acids[2] and thioisomünchnones from 2-(imidoylthio)acids [2,10] under the action of Ac_2O/NEt_3. To date, however, the use of carboxamides or phosgene source in similar reactions was unprecedented. In order to test the versatility of this methodology, we have extented the procedure to the dithiocarbamate **8**. The required **8** were easily prepared from ammonium piperidinocarbodithioate and α-chloroacetamide **7a**. As summarized in Table I and Scheme 3, only a poor yield of the 2,4-diaminodithiolium chloride **9** was obtained, the ketenimine **10** being strongly dominant in the crude mixture (**9/10** ~ 22 : 78). This relative failure compared with thiazolium cases may be ascribed to competitive addition of phosgene on the C=S bond, inducing the hydrolysis of the dithiocarbamate function through a chloromethyleniminium chloride.[15]

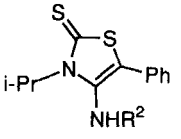
Structural assignments of salts **1, 9** were based on NMR data, high resolution mass spectra or satisfactory elemental analyses. Selected ^{13}C NMR chemical shifts are given in Table I. The endocyclic carbon C-2 bearing the methylthio or piperidino substituent appears as a multiplet at rather low field (δ 167–180 ppm), in good agreement with earlier observations.[3,5]



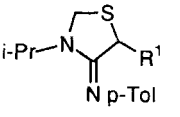
8 9 10

SCHEME 3

More evidence for the structure of thiazolium chlorides **1** was obtained from their reactivity. Degradation of **1a,b** in refluxing toluene for a short time gave the 2-thioxothiazoles *11*, as already observed in similar cases. [3] Compounds **1a, c** were found to undergo rapid reduction with sodium borohydride in EtOH solution. The reaction proceeds via MeSH elimination [5] and N to C tautomerism leading quantitatively to the 2-unsubstituted 4-iminothiazolidines **12.**

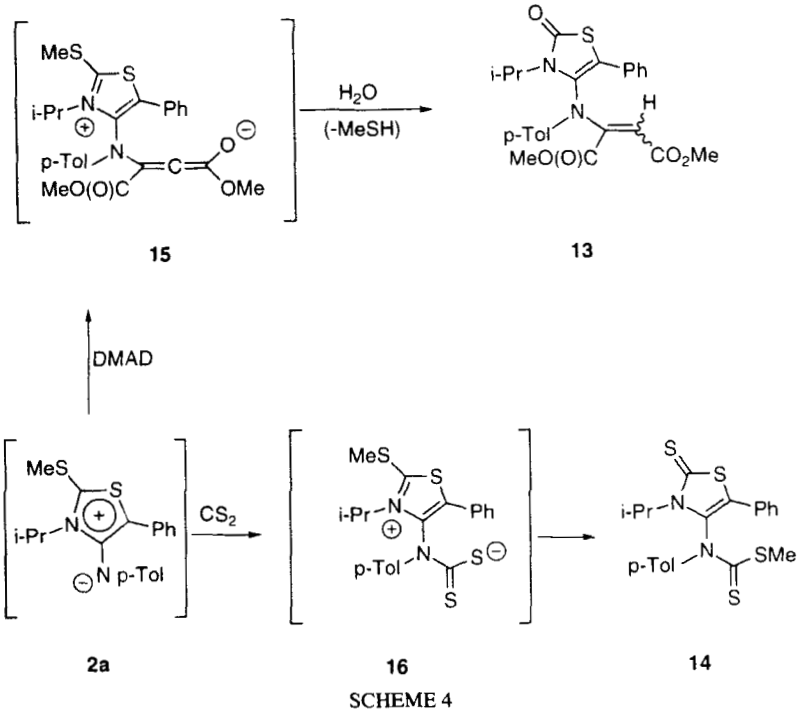


11a : R^2= p-Tol
11b : R^2= t-Bu



12 a : R^1= Ph
12 c : R^1=Me

Reactions of salt **1a** with DMAD and CS_2 were carried out in CH_2Cl_2 at room temperature on alumina-dispersed potassium fluoride as solid support. Such solid-liquid basic medium was found to be more efficient than homogeneous conditions. [16] Addition of the *in situ* generated mesoionic thiazole **2a** takes place exclusively on the exocyclic nitrogen atom to afford the 2,3-dihydro-2-oxo and 2-thioxothiazoles **13** and **14.** Both possible isomers **13** were detected in the crude mixture (**E/Z** ~ 65 : 35). These results can be rationalized by assuming the hydrolysis or rearrangement of transient betaïnes **15** and **16** (Scheme 4). Compound **14** has also been prepared from a CS_2 solution of thioxothiazole *11*a and iodomethane in the presence of KF/Al_2O_3.



SCHEME 4

NMR, mass and IR spectral data were observed in support of assigned structures **10–14**.

In conclusion, this work affords a simple route to the new 4-aminothiazolium chlorides **1**. The kep-step of the synthetic sequence, a cyclodehydration process, is developed here for the first time with triphosgene under fairly mild conditions. The thiazolium-4-aminides **2** react with dipolarophiles as heterocyclic betaïnes [17] instead of cyclic thiocarbonyl ylides.

EXPERIMENTAL

^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 300 MHz and 75.5 MHz, respectively. When necessary, unambigous NMR assignments were acquired by decoupling experiments. HRMS were obtained from the

Centre Regional de Mesures Physiques de l'Ouest, in the electron impact mode, using a potential of 70 eV. Infrared spectra were recorded as suspensions in Nujol. Elemental analyses were performed by the analytical laboratory, CNRS.

The ammonium dithiocarbamate **6** was readily available from i-$PrNH_2$ and carbon disulfide.[18] By a similar procedure, the α-chlorocarboxamides **7** were prepared from the addition of p-toluidine or *tert*-butylamine to 2-chloro-2-phenylacetyl chloride or 2-chloropropionyl chloride. Compounds **7** (50 mmol) were reacted with an equimolar amount of ammonium isopropyldithiocarbamate **6** (or piperidinocarbodithioate) in dry CH_2Cl_2(100 mL). After the mixture was stirred at rt for about 12 h, the ammonium chloride was filtered off and the filtrate was washed with H_2O. Evaporation and trituration of the residue with Et_2O gave the solid materials **5** or **8** (76–80 % yield).

N-(4-Methylphenyl)-2-phenyl-2-[(N-isopropylthiocarbamoyl)thio] acetamide (5a)

mp 148°C (Et_2O) ; ^{1}H NMR δ 1.21 (d, 6H, *J*= 7 Hz), 2.24 (s, 3H), 4.58 (m, 1H), 5.85 (s, 1H), 7–7.5 (m, 9H), 8.67 (br, 1H).

N-tert-Butyl-2-phenyl-2-[(N-isopropylthiocarbamoyl)thio]acetamide (5b)

mp 158°C (MeOH) ; ^{1}H NMR δ 1.11, 1.21 (2d, 6H, *J* = 7 Hz), 1.29 (s, 9H), 4.56 (m, 1H), 5.31 (s, 1H), 6.32 (br, 1H), 7.25–7.45 (m, 5H), 8.85 (br, 1H).

N-(4-Methylphenyl)-2-[(N-isopropylthiocarbamoyl)thio] propionamide (5c)

mp 110°C (Et_2O) ; ^{1}H NMR δ 1.25 (d, 6H, *J*= 7 Hz), 1.55 (d, 3H, *J* = 8 Hz), 2.27 (s, 3H), 4.62 (m, 2H), 7.05, 7.37 (2d, 4H, *J* = 9 Hz), 8 (br, 1H), 9 (br, 1H).

N-tert-Butyl-2-[(N-isopropylthiocarbamoyl)thio]propionamide (5d)

mp 125°C (MeOH) ; ^{1}H NMR 1.26 (d, 6H, *J* = 7 Hz), 1.3 (s, 9H), 1.47 (d, 3H, *J* = 8 Hz), 4.22 (q, 1H, *J* = 8 Hz), 4.66 (m, 1H), 6.6 (br, 1H), 8.5 (br, 1H).

N-(4-Methylphenyl)-2-phenyl-2-[(piperidinothiocarbonyl)thio] acetamide (8)

mp 155°C (Et_2O/petroleum ether) ; IR 3290, 1670, 1630, 1595 cm^{-1} ; ^1H NMR δ 1.62 (br, 6H), 2.25 (s, 3H), 4 (br, 4H), 6.05 (s, 1H), 6.95–7.6 (m, 9H), 8.7 (br, 1H).

MeI (14.2 g) was added dropwise to a solution of carboxamide **5** (50 mmol) in anhyd. CH_2Cl_2 (100 mL). The reactional medium was stirred at rt for 12 h, treated with NEt_3(10 g) and washed with H_2O. The organic phase was dried over Na_2SO_4 and concentrated to dryness. The residue was triturated with petroleum ether to precipitate the starting products **4** (70–75 % yield).

N-(4-Methylphenyl)-2-{[1-(methylthio)-N-isopropylimidoyl]thio} –2-phenylacetamide (4a)

mp 130°C (Et_2O), ^1H NMR δ 1.19, 1.21 (2d, 6H, J = 7 Hz), 2.27 (s, 3H), 2.5 (s, 3H), 3.97 (m, 1H), 5.37 (s, 1H), 7–7.5 (m, 9H), 9.25 (br, 1H).

N-tert-Butyl-2-{[1-(methylthio)-N-isopropylimidoyl]thio}-2-phenylacetamide (4b)

mp 120°C (MeOH) ; IR 3320, 1650, 1565 cm^{-1}; ^1H NMR δ 1.18, 1.19 (2d, 6H, J = 7 Hz), 1.30 (s, 9H), 2.47 (s, 3H), 3.92 (m, 1H), 5.2 (s, 1H), 6.65 (br, 1H), 7.25–7.5 (m, 5H).

N-(4-Methylphenyl)-2-{[1 -(methylthio)-N-isopropylimidoyl]thio} propionamide(4c)

mp 72°C (Et_2O) ; ^1H NMR δ 1.18, 1.21 (2d, 6H, J = 7 Hz), 1.46 (d, 3H, J = 8 Hz), 2.22 (s, 3H), 2.48 (s, 3H), 3.96 (m, 1H), 4.3 (q, 1H, J = 8 Hz), 7.05, 7.37 (2d, 4H, J = 9 Hz), 9.2 (br, 1H).

N-tert-Butyl-2-{[1 -(methylthio)-N-isopropylimidoyl]thio} propionamide (4d)

mp 75°C (MeOH) ; ^1H NMR δ 1.17, 1.18 (2d, 6H, J = 7 Hz), 1.29 (s, 9H), 1.4 (d, 3H, J = 8 Hz), 2.51 (s, 3H), 4.05 (m, 2H), 7.04 (br, 1H).

Dehydrative ring closure

The carboxamide **4** or **8** (50 mmol) was dissolved in dry CH_2Cl_2 (100 mL). We added portionwise the commercially available triphosgene (5.3 g; 10.6 g starting from **8**) then a large excess of pyridine (11.8 g). The mixture was maintained at rt for about 30 min and 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 gave the crystalline ketenimine **10** (70 % yield) in the case of acetamide **8**. The aqueous solution was saturated with NaCl and extracted with CH_2Cl_2 (2 × 15 mL). The combined CH_2Cl_2 phases were dried over Na_2SO_4 and evaporated to dryness. Trituration of the residue with Et_2O gave the salts **1** or **9** as yellowish solids which were recrystallized from CH_2Cl_2/Et_2O (1 : 2) (yields and typical ^{13}C NMR data, see Table I).

4 -[(4 -Methylphenyl)amino]-2-(methylthio)-5-phenyl-3-isopropylthiazolium ε chloride (1a)

mp 205°C dec ; ^1H NMR δ 1.69 (d, 6H, J = 7 Hz), 2.14 (s, 3H), 3.06 (s, 3H), 5.43 (m, 1H), 6.70, 6.86 (2d, 4H, J = 8 Hz), 7.29 (m, 3H), 7.68 (m, 2H) ; MS calcd for $C_{19}H_{20}N_2S_2$ m/z 340.1068 (M^+ -MeCl), found 340.1076 ; m/z (rel int) 340 (89), 298 (77), 264 (17), 207 (100). Anal calcd for $C_{20}H_{23}N_2S_2Cl$: C, 61.46 ; H, 5.89 ; N, 7.17. Found : 61.03 ; 5.90 ; 6.94.

4-(tert-Butylamino)-2-(methylthio)-5-phenyl-3-isopropylthiazolium chloride (1b)

mp 190°C dec ; ^1H NMR δ 0.97 (s, 9H), 1.72 (d, 6H, J= 7 Hz), 3.02 (s, 3H), 5.34 (br, 1H), 5.7 (m, 1H), 7.43 (m, 3H), 7.79 (d, 2H, J = 7 Hz) ; MS calcd for $C_{16}H_{22}N_2S_2$ m/z 306.1224 (M^+ -MeCl), found 306.1231 ; m/z (rel int) 306 (35), 250 (26), 208 (100). Anal calcd for $C_{17}H_{25}N_2S_2Cl$: C, 57.22 ; H, 7.01 ; N, 7.85 ; Cl 9.96. Found : 57.27 ; 6.98 ; 7.62 ; 10.03.

5-Methyl-4-[(4-methylphenyl)amino]-2-(methylthio)-3-isopropylthiazolium chloride (1c) (hygroscopic)

^1H NMR δ 1.65 (d, 6H, J = 7 Hz), 2.24 (s, 3H), 2.36 (s, 3H), 3.06 (s, 3H), 5.28 (m, 1H), 6.73, 6.99 (2d, 4H, J = 8 Hz), 9.43 (br, 1H).

4-(tert-Butylamino)-5-methyl-2 -(methylthio)-3-isopropylthiazolium chloride (1d)

mp 166°C dec ; ^{1}H NMR δ 1.08 (s, 9H), 1.46 (d, 6H, *J*= 7 Hz), 2.45 (s, 3H) ; 2.84 (s, 3H), 5.39 (m, 1H), 5.68 (br, 1H) ; MS calcd for $C_{11}H_{20}N_2S_2$ m/z 244.1068 (M^+ - MeCl), found 244.1082 ; m/z (rel int) 244 (42), 188 (15), 148 (9), 146 (100). Anal calcd for $C_{12}H_{23}N_2S_2Cl$: C, 48.90 ; H, 7.81 ; N, 9.51 ; S, 21.73. Found : 49.17 ; 7.75 ; 9.37 ; 21.43.

4-[(4-Methylphenyl)amino] –5-phenyl-2-piperidinodithiolium chloride (9)

mp 240°C dec ; ^{1}H NMR δ 1.79 (br, 6H), 2.16 (s, 3H), 3.76 (br, 2H), 3.88 (br, 2H), 6.86 (s, 4H), 7.27 (m, 3H), 7.59 (m, 2H), 9.58 (br, 1H) ; MS calcd for $C_{21}H_{22}N_2S_2$ m/z 366.1224 (M^+ - HCl), found 366.1189.

N-(4-Methylphenyl)-phenyl-[(piperidinocarbonyl)thio]ketenimine (10)

mp 129°C (Et_2O) ; IR 1985, 1660 cm-^{1} ; ^{1}H NMR δ 1.19 (br, 6H), 2.33 (s, 3H), 3.53 (br, 4H), 7 (m, 9H) ; ^{13}C NMR δ 21.3 (qt, ^1J = 127 Hz, ^3J = 4.3 Hz), 24.5 (tm, ^1J = 129 Hz), 25.9 (tm, ^1J = 132 Hz), 45.6, 47.1 (2 tm, ^1J = 120 Hz), 63.3 (*C*=C=N, t, ^3J = 4.5 Hz), 124.9, 125.5, 125.6, 128.7, 130.3 (5 CH arom, ^1J =157–163 Hz), 134, 135.9, 138.6 (3 C arom quat), 164.4 (*C*=O, m), 183.8 (C=*C*=N, s). The chemical shifts at 63.3 and 183.8 ppm are in good agreement with values found in the literature for ketenimine carbons.[19] MS calcd for $C_{21}H_{22}N_2OS$ m/z 350.1453 (M^+), found 350.1455 ; m/z (rel int) 350 (40), 121 (100), 112 (87). Anal calcd : C, 72.00 ; H, 6.29 ; N, 8.00 ; S, 9.14. Found : 72.25 ; 6.51 ; 8.06 ; 8.88.

The 4-amino-2,3-dihydro-2-thioxothiazoles **11** were obtained by the thermal degradation of **1a,b** in refluxing toluene for 1 h according to known procedure [3] (80% yield). $NaBH_4$ reductions were performed in EtOH solution for 10 min at rt as previously described.[5]The crude product was worked up in the same way to afford the crystalline 4-iminothiazolidine **12a** (90 % yield) or the colorless oil **12c** (60 % yield).

2,3-Dihydro-4-[(4-methylphenyl)amino]-5-phenyl-3-isopropyl-2-thioxothiazole (11a)

mp 192°C (MeOH) ; ^{1}H NMR δ 1.5 (br, 6H), 2.13 (s, 3H), 4.8 (br, 1H), 5.6 (br, 1H), 6.47, 6.9 (2d, 4H, *J* = 8 Hz), 7.17 (m, 5H) ; ^{13}C NMR δ 18.4 (qm,

^1J = 132 Hz), 19.5 (qt, ^1J = 126 Hz, ^3J = 4.4 Hz), 51.4 (dm, ^1J = 141 Hz), 113.1, 126.3, 127.5, 127.9, 129.2 (5 CH arom, ^1J = 154–160 Hz), 122.5 (C-5, br), 128.3, 128.9 (2 C arom quat), 133 (C-4, br), 141 (C arom quat, t, ^3J = 9 Hz), 182.6 (C-2, d, ^3J = 6.5 Hz).

4-(tert-Butylamino)-2,3-dihydro-5-phenyl-3-isopropyl-2-thioxothiazole (11b)

mp 190°C (MeOH) ; ^{1}H NMR δ 0.93 (s, 9H), 1.82 (d, 6H, J= 7 Hz) , 3.2 (br, 1H), 5.12 (m, 1H), 7.35 (m, 5H) ; ^{13}C NMR δ 18.5 (qm, ^1J = 128 Hz), 30.4 (qm, ^1J = 126 Hz), 52 (dm, ^1J = 140 Hz), 55.6 (m), 122.7 (C-5, t, br),128.5, 129, 129.1 (3 CH arom, ^1J = 162 Hz), 131.5 (C arom quat, t, ^3J = 7 Hz), 138.7 (C-4, d, ^3J = 3.5 Hz), 183.8 (C-2, d, ^3J = 8 Hz) ; MS calcd for $C_{16}H_{22}N_2S_2$ m/z 306.1224 (M^+), found 306.1221 ; m/z (rel int) 306 (32), 250 (25), 208 (100).

4-[(4-Methylphenyl)imino]-5-phenyl-3-isopropylthiazolidine (12a)

mp 80°C (petroleum ether) ; IR 1616 cm^{-1} ; ^{1}H NMR δ 1.29, 1.33 (2d, 6H, J = 7 Hz), 2.19 (s, 3H), 4.38, 4.57 (2d, 2H, J = 7.7 Hz), 4.72 (m, 1H), 5.11 (s, 1H), 6.33, 6.80 (2d, 4H, J = 8 Hz), 6.87 (m, 2H), 7.13 (m, 3H) ; ^{13}C NMR δ 19.1, 19.7, 20.7 (3 qm, ^1J= 126 Hz), 44.6 (C-2, tm, ^1J = 157 Hz), 45.6 (dm, ^1J = 145 Hz), 48.6 (C-5, dm, ^1J = 147 Hz), 121.9, 127, 127.1, 128.4, 128.9 (5 CH arom, ^1J = 157–160 Hz), 131 (C arom quat, q, ^2J = 6.8 Hz), 141.4 (C arom quat, m), 148.1 (C arom quat, t, ^3J = 8.2 Hz), 158.9 (C-4, m) ; MS calcd for $C_{19}H_{22}N_2S$ m/z 310.1503 (M^+), found 310.1492 ; m/z (rel int) 310 (88), 264 (93), 207 (42), 158 (30), 145 (36), 135 (100). Anal calcd : C, 73.55 ; H, 7.10 ; N, 9.03 ; S, 10.32. Found : 73.87 ; 7.24 ; 8.64 ; 9.89.

5-Methyl-4-[(4-methylphenyl)imino]-3-isopropylthiazolidine (12c)

^{1}H NMR δ 1.11 (d, 3H, J = 7.2 Hz) ; 1.14, 1.16 (2d, 6H, J = 7 Hz), 2.21 (s, 3H), 4.16 (q, 1H, J = 7.2 Hz), 4.20, 4.41 (2d, 2H, J = 7.7 Hz), 4.48 (m, 1H), 6.63, 6.96 (2d, 4H, J = 8 Hz) ; ^{13}C NMR δ 18, 18.2, 19.7 (3 qm, ^1J = 126 Hz), 19.8 (screened), 38.6 (dm, ^1J = 147 Hz), 42.4 (C-2, tm, ^1J = 150 Hz), 44 (C-5, dm, ^1J = 150 Hz), 120.7, 128.4 (2 CH arom,

^1J = 158 Hz), 129.8 (C arom quat, screened), 147.6 (C arom quat, t, ^3J = 8.5 Hz), 160.1 (C-4, m).

Attempted cycloaddition reactions were performed from a solution of salt **1a** (2.5 mmol) and DMAD or CS_2 (5 mmol) in dry CH_2Cl_2(10 mL). We added portionwise a mixture of KF (0.3 g) with Al_2O_3 90 (0.52 g) then we stirred the suspension at rt for 1 h. The inorganic part was filtered off and the solvent was removed under reduced pressure. In the case of DMAD, the ^{1}H NMR analysis of the crude oily product showed the formation of **13 E,Z** accompanied by a mixture of dimethyl methylthiofumarate and maleate. Such by-products result from the addition of MeSH to the acetylenic reagent.[20] The 2,3-dihydro-2-thiazolone **13E** and 2-thioxothiazole **14** were purified by alumina column flash chromatography with ether/petroleum ether (1: 4) as eluent, then recrystallized from MeOH. The stereochemical assignment of **13E** was based on the high long range coupling constant for the carbon at 164.6 ppm (^3JCCCH = 9.6 Hz, see below).

2,3-Dihydro-4-{(4-methylphenyl)-[1,2-bis(methoxycarbonyl)vinyl] amino}-5-phenyl-3-isopropyl-2-oxothiazole (13E)

mp 168°C (30 % yield) ; IR 1739, 1690, 1650, 1582 cm^{-1} ; ^{1}H NMR δ 1.08, 1.5 (2d, 6H, J = 6.7 Hz), 2.21 (s, 3H), 3.58 (s, 6H), 4.1 (m, 1H), 5.42 (s, 1H), 6.93, 7.01 (AB syst, 4H, J = 8.7 Hz), 7.2 (m, 5H) ; ^{13}C NMR δ 19.6 (qm, ^1J = 128 Hz), 21.3 (qt, ^1J = 127 Hz, ^3J = 4Hz), 49.9 (dm, ^1J = 139 Hz), 52, 53.3 (2q, ^1J = 148 Hz), 100.1 (=*C*HCO$_2$Me, d, ^1J= 163 Hz), 116.9 (C-5, t, br), 123.4, 127.5, 128.9, 129.2, 130.7 (5 CH arom, ^1J = 160 Hz), 127.2 (=*C*CO$_2$Me, d, ^2J = 2.5 Hz), 130.1, 138.6 (2 C arom quat, t, ^3J = 8.5 Hz), 137 (C arom quat, q, ^2J = 6.5 Hz), 150.2 (C-4, d, ^3J = 3.3 Hz), 164.6 (=C*C*O$_2$Me, dq, ^3J = 9.6 and 4.2 Hz), 167.6 (C-2, d, ^3J = 8 Hz), 166.8 (=CH*C*O$_2$Me, q, ^3J = 4.2 Hz) ; MS calcd for $C_{25}H_{26}N_2O_5S$ m/z 466.1562 (M$^+$), found 466.1563 ; m/z (rel int) 466 (100), 424 (30), 365 (40), 347 (25), 333 (21), 305 (63).

2,3-Dihydro-4-{(4-methylphenyl)-[(methylthio)thiocarbonyl]amino}-5 -phenyl-3-isopropyl-2-thioxothiazole (14)

mp 165°C (43 % yield) ; ^{1}H NMR δ 1.69, 1.98 (2d, 6H, J= 6.9 Hz), 2.31 (s, 3H), 2.64 (s, 3H), 4.54 (m, 1H), 6.85, 7.07 (2d, 4H, J = 8 Hz), 7.42 (m, 5H) ; ^{13}C NMR (at 58°C) δ 18.3, 18.4 (2qm, ^1J = 128 Hz), 20.9 (q,

^1J = 143 Hz), 21 (qt, ^1J = 127 Hz, ^3J = 4.4 Hz), 53.7 (dm, ^1J = 138 Hz), 125.4 (C-5, screned), 126.5, 128.1, 129.3, 129.4, 130.1 (5 CH arom, ^1J = 162 Hz), 129.5 (C arom quat, screened), 135.1 (C-4, d, ^3J = 3.1 Hz), 138.9 (C arom quat, t, ^3J = 10 Hz), 139.4 (C arom quat, q, ^2J = 6.5 Hz), 184.2 (C-2, d, ^3J = 7.9 Hz), 206.5 (S=*C*SMe, q, ^3J = 5.9 Hz) ; MS calcd for $C_{21}H_{22}N_2S_4$ m/z 430.0666 (M^+), found 430.0665 ; m/z (rel int) 430 (4), 164 (100), 149 (8), 121 (48). Anal calcd : C, 58.60 ; H, 5.12 ; N, 6.51 ; S, 29.77. Found : 58.47 ; 5.19 ; 6.38 ; 29.72.

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