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Base-Induced Conversion of 5-Aminothiazolium Salts into Substituted Pyrroles and Pyrrolines via 1,3-Dipolar Cycloadditions with Electron-Deficient Alkynes and Alkenes.

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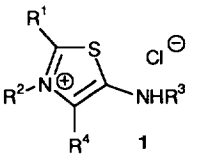
Abstract : A series of mesoionic thiazoles **2** were generated and converted in situ by treating the 5-aminothiazolium chlorides **1** with several electrophilic dipolarophiles in the presence of DBN or NEt_3. The reactions involved an 1,3-dipolar cycloaddition of the "masked" cyclic azomethine ylides across the olefinic or acetylenic π-bond, yielding unstable N-bridged adducts as the first step. Thus, DMAD and methyl propiolate gave functionalized pyrroles via a subsequent extrusion of isothiocyanate. Dimethyl fumarate, maleate and fumaronitrile afforded a variety of polysubstituted pyrrolines, pyrroles and aminobutadienes through base-catalyzed rearrangements of the primary 1 : 1 cycloadducts, with retention of the elements of isothiocyanate. A similar initial cycloadduct **17** was isolated from N-phenylmaleimide which generally led to the condensed imino thiopyrans **20**. Some of the 1,3-dipolar reactional stereoselectivities were deduced from the stereochemistry or distribution of the final products and found to be markedly dependent on the substituent groups present.

Introduction. A few synthetic routes to 5-aminothiazolium salts and corresponding mesoionic thiazolium-5-aminides have been described about twenty years ago but their chemistry has not been extensively explored [1]. In a recent article, we showed that such compounds are now easily accessible via three-component condensations using isocyanides as cyclization reagents.[2] In particular, we described the one-pot and efficient preparation of the 5-*tert*-butylamino-4-phenylthiazolium chlorides **1a, b** from a mixture of aryl chlorothioformate, N-benzylidenemethylamine and *tert*-butyl isocyanide. Similarly, the treatment of imino chlorosulfides with dimethylthioformamide and isocyanides at room temperature provides selectively the 4,5-bis-aminothiazolium salts **1c-l**. [2]



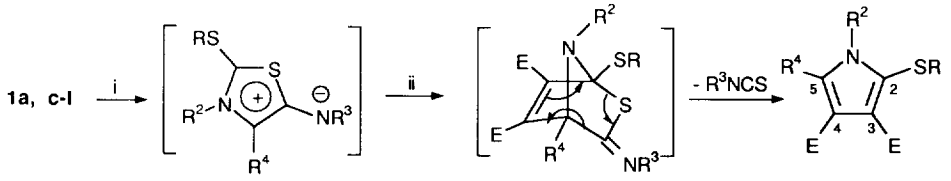
1

	R^1	R^2	R^3	R^4		R^1	R^2	R^3	R^4
a	PhS	Me	t-Bu	Ph	g	MeS	CH_2CO_2Et	t-Bu	Me_2N
b	p-Tol O	Me	t-Bu	Ph	h	PhS	CH_2CO_2Et	t-Bu	Me_2N
c	MeS	CH_2Ph	t-Bu	Me_2N	i	MeS	$CH_2PO(OEt)_2$	CH_2Ph	Me_2N
d	MeS	CH_2Ph	CH_2Ph	Me_2N	j	MeS	i-Pr	t-Bu	Me_2N
e	MeS	CH_2Ph	CH_2CO_2Et	Me_2N	k	MeS	i-Pr	CH_2Ph	Me_2N
f	PhS	CH_2Ph	t-Bu	Me_2N	l	MeS	$2,6\text{-}Me_2C_6H_3$	t-Bu	Me_2N

1,3-Dipolar cycloaddition reactions involving a wide variety of mesoionic ring systems and dipolarophiles have been reported in the literature and used for the synthesis of a large number of five-membered heterocycles.[3] It has been demonstrated that these methods proceed through unstable 1 : 1 primary cycloadducts which decompose to more stable products with the evolution of small molecules such as carbon dioxide or disulfide, carbonyl sulfide, isocyanates or isocyanic acid and also carbodiimides. For instance, the reaction of münchnones and azlactones with acetylenic dipolarophiles was shown to constitute a pyrrole synthesis of very broad scope [4] through the loss of CO_2. In some cases (i.e. intramolecular münchnone [5], isomünchnone and thioisomünchnone [6] cycloadditions) isolated compounds corresponded to the initial cycloadducts, without retro-Diels-Alder process. All these studies have resulted in practical, unique syntheses of numerous functionalized monocyclic and ring annulated heterocycles. However, in comparison with the widespread use of thiazolium-5-thiolates and thiazolium-4 or 5-olates,[3,6,7] similar applications of mesoionic thiazolium-5-aminides are lacking.[8] Moreover, a study of such reactions involving the loss of isothiocyanate has found very little attention.[9]

Salts **1** are potential cyclic azomethine ylides and we decided to examine their dipolar reactivity. We report here their chemical behaviour in a basic medium containing a standard acetylenic or olefinic dipolarophile. Mesoionic thiazoles **2** are not stabilized by an electron-withdrawing substituent group R^3. They can never be isolated and have to be trapped by compounds with a triple or double bond.

Reactions of Salts 1 with Acetylenic Dipolarophiles. In the presence of a slight excess of 1,5-diazabicyclo [4.3.0] non-5-ene (DBN), the 5-aminothiazolium chlorides **1** underwent fast cycloaddition with dimethyl acetylenedicarboxylate (DMAD) at room temperature (Table 1). The reactions afforded the expected pyrroles **4** in good yields and occurred with elimination of *tert*-butyl isothiocyanate as well as benzyl (entries 3, 8, 10) or (ethoxycarbonyl) methyl isothiocyanate (entry 4). These heterocumulenes were easily detected in the reaction medium by ^1H NMR spectroscopy. Starting from **1i** (entry 8), $PhCH_2NCS$ was separated from **4f**, purified by a bulb-to-bulb distillation under reduced pressure and identified by comparison with a commercial product (IR and NMR data). We assume that these reactions proceed through the mesoionic thiazoles **2** and the well recognized 1,3-dipolar cycloaddition-cycloreversion mechanism. The initially-generated adducts **3** involve the spontaneous extrusion of isothiocyanate R^3NCS (Scheme 1).



2 **3** **4**

Scheme 1 i, DBN ; ii, DMAD ; (E = CO_2Me)

	R	R^2	R^4		R	R^2	R^4
4a	Ph	Me	Ph	**4e**	Ph	CH_2CO_2Et	NMe_2
4b	Me	CH_2Ph	NMe_2	**4f**	Me	$CH_2PO(OEt)_2$	NMe_2
4c	Ph	CH_2Ph	NMe_2	**4g**	Me	i-Pr	NMe_2
4d	Me	CH_2CO_2Et	NMe_2	**4h**	Me	$2,6\text{-}Me_2C_6H_3$	NMe_2

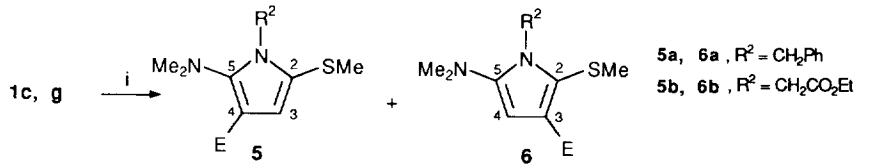
Under the same conditions, cyclization of **1c, g** with methyl propiolate furnished two pyrrole derivatives (Scheme 2). Compound **5** was clearly dominant in these crude mixtures (Table 1, entries 12 and 13). The regioisomers **5** and **6** were separated by a silica gel column chromatography but their structures could

not be fully elucidated in the usual ways, for instance by ^{13}C NMR spectroscopy (Table 5). NOEDIFF experiments were carried out on samples of **5a** and **6a** in order to perform the regioassignments. Selective irradiation of the dimethylamino group in **6a** (δ 2.55) produces a reproducible enhancement (about 15 %) of the singlet at δ 6.31 attributed to the proton on C-4. On the other hand, irradiation of the NMe_2 in **5a** (δ 2.66) causes no significant perturbation of the signal at δ 6.72. These results allow the assignments described in scheme 2. By analogy, structure **5b** was assigned to the major pyrrole which was obtained from the salt **1g**.

Table 1 - Reactions of 5-Aminothiazolium Salts **1** with DMAD and Methyl Propiolate in the Presence of DBN [a].

entry	educts	solvent	Products	
			isothiocyanate, R^3	pyrroles (% yield) [b]
1	**1a**, E-≡-E	CH_2Cl_2	t-Bu	**4a** (78)
2	**1c**, E-≡-E	CH_2Cl_2	t-Bu	**4b** (61)
3	**1d**, E-≡-E	CH_2Cl_2	CH_2Ph	**4b** (81)
4	**1e**, E-≡-E	CH_2Cl_2	CH_2CO_2Et	**4b** (48)
5	**1f**, E-≡-E	CH_2Cl_2	t-Bu	**4c** (74)
6	**1g**, E-≡-E	THF	t-Bu	**4d** (81)
7	**1h**, E-≡-E	CH_2Cl_2	t-Bu	**4e** (60)
8	**1i**, E-≡-E	CH_2Cl_2	CH_2Ph	**4f** (57)
9	**1j**, E-≡-E	CH_2Cl_2	t-Bu	**4g** (50)
10	**1k**, E-≡-E	CH_2Cl_2	CH_2Ph	**4g** (64)
11	**1l**, E-≡-E	MeCN	t-Bu	**4h** (56)
12	**1c**, E-≡	THF	t-Bu	**5a** (30) ; **6a** (16)[c]
13	**1g**, E-≡	THF	t-Bu	**5b** (32) ; **6b** (14)[c]

[a] The reactions were performed at rt for 1 h, starting from a 0.3 M solution of 1 then adding an excess of alkyne (1.5 equiv) and base (1.3 equiv). [b] Purified pyrroles yields after silica gel chromatography and (or) recrystallization. [c] The distributions between the cycloadducts **5**, **6** were estimated on the basis on the ^1H NMR spectra of the crude mixtures (**5a/6a** = 67 : 33 ; **5b/6b** = 70 : 30).



Scheme 2 i, DBN, EC≡CH (- tBuNCS) ; (E = CO_2Me)

Formation of two regioisomeric adducts through 1,3-dipolar cycloaddition reactions with unsymmetrical dipolarophiles has ample precedent in the literature, including cyclic azomethine ylides as münchnones with propiolic esters. The distribution of products depends on the nature and location of the substituents on the starting ylides.[10,11]

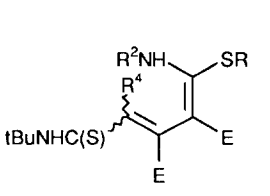
Reactions of Salts 1 with Olefinic Dipolarophiles. In basic media, the reactions of **1c, g** with dimethyl fumarate and maleate proceeded smoothly at room temperature and generally gave a mixture of 1,4-diamino butadiene **7**, pyrrole **8** and tetrahydropyrrolo [3,4-b] pyrrole **9**. The results were strongly dependent on the nature of the starting reagents and base (Table 2). The reaction with dimethyl fumarate

afforded compounds **8** or **9**, according to the presence of NEt_3 or DBN (compare entries 4 and 7 with entries 5 and 8). Under identical conditions, the use of methyl maleate gave mostly products **7** or **8** (entries 6, 9). The butadiene **7l** was only obtained from the thiazolium chloride **1l**. In contrast (as shown in entries 1-3), the reactions of salt **1a** proceeded with the exclusive formation of the 2-pyrrolines **10a** in the presence of NEt_3 but gave only **9a** in the presence of DBN. Both possible diastereoisomers **10a** were detected in the reaction medium and their relative proportions were determined by ^1H NMR spectroscopy (*trans/cis* ~ 62 : 38 and 77 : 23 using fumarate and maleate, respectively). No epimerization of the isolated pure diastereoisomers **10a** occurred under the action of NEt_3 at room temperature for about 15 h, indicating the observed stereochemistry to result from kinetic control. On the other hand, we have verified that both isomers **10a** underwent fast cyclization to **9a** in the presence of DBN [12], consequently to the expected thermodynamic equilibrium (scheme 3). We also observed two isomers for the butadienes **7c** and **7l**, one of them being strongly dominant (~ 85 : 15).

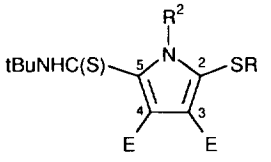
Table 2. Reactions of 5-Aminothiazolium Salts **1** with Dimethyl Fumarate and Maleate in Basic Media.

entry	educts	reactn condns [a]			products distribution [b]				yields [c], %
		solvent	base	time (h)	**7**	**8**	**9**	**10**	
1	**1a**, Fum.	CH_2Cl_2	NEt_3	13	-	-	-	100	**10a** (*trans*) (54) ; **10a** (*cis*) (32)
2	**1a**, Mal.	CH_2Cl_2	NEt_3	14	-	-	-	100	**10a** (*trans*) (64) ; **10a** (*cis*) (12)
3	**1a**, Fum.	CH_2Cl_2	DBN	2	-	-	100	-	**9a** (82)
4	**1c**, Fum.	THF	NEt_3	3	35	65	-	-	**7c** (24) ; **8c** (18)
5	**1c**, Fum.	THF	DBN	0.5	25	-	75	-	**7c** (19) ; **9c** (44)
6	**1c**, Mal.	THF	DBN	0.5	75	5	20	-	**7c** (40)
7	**1g**, Fum.	THF	NEt_3	3	-	77	23	-	**8g** (48)
8	**1g**, Fum.	THF	DBN	0.5	-	10	90	-	**9g** (46)
9	**1g**, Mal.	CH_2Cl_2	DBN	1	-	40	60	-	**9g** (22) ; **8g** (11)
10	**1l**, Fum.	CH_2Cl_2	DBN	1	100	-	-	-	**7l** (71)

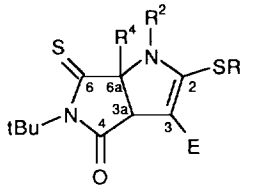
[a] All the reactions were conducted at rt, starting from a 0.3 M solution of 1 then adding the dipolarophile (1.5 - fold excess) and base (1.3 - fold excess). [b] These distributions were calculated on the basis on the ^1H NMR spectra of the crude mixtures. [c] Purified products yields after silica gel chromatography and (or) recrystallization.



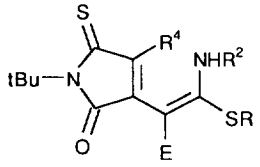
7c, l



8c, g

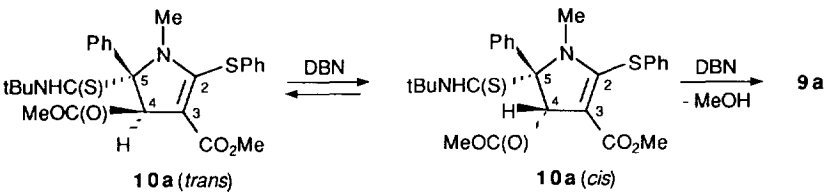


9a, c, g



12c, g

	R	R^2	R^4	
a	Ph	Me	Ph	
c	Me	CH_2Ph	Me_2N	(E = CO_2Me)
g	Me	CH_2CO_2Et	Me_2N	
l	Me	2,6-$Me_2C_6H_3$	Me_2N	

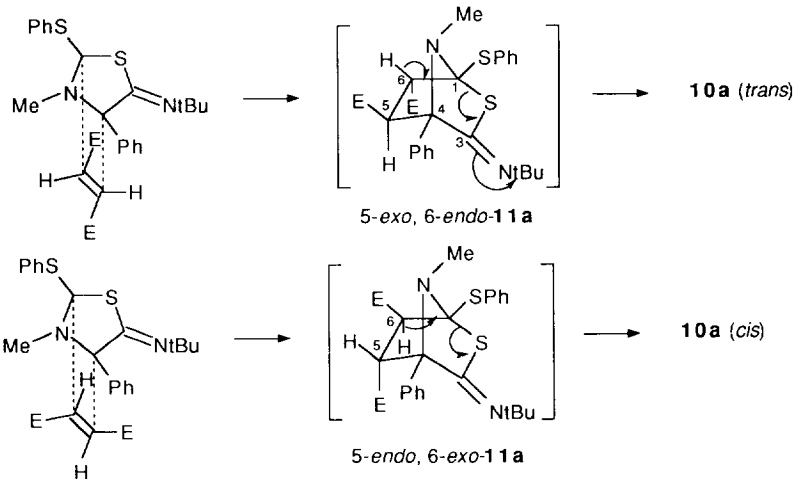


10a (*trans*) **10a** (*cis*)

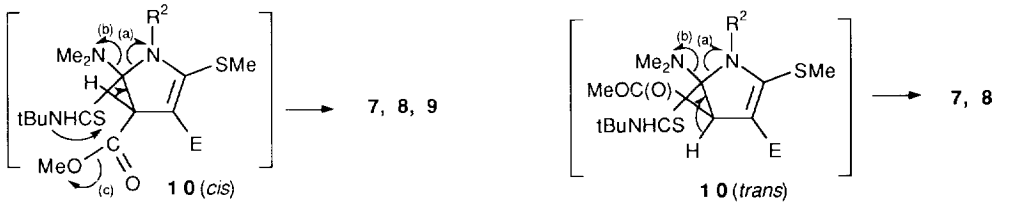
Scheme 3

All these compounds (except isomers **7**) were separated by silica gel column chromatography and were completely characterized by their analytical and spectral data. The shielding of the 4-H and the ester methyl by the *cis*-vic phenyl [13] allowed the stereochemical assignment of the diastereoisomers of **10a** : δ_H 4.82 vs 5.20 for 4-H and 3.69 vs 3.21 for 4-CO_2CH_3. The multiplicity of the ^{13}C NMR signal attributed to the thione carbon confirmed these assignments : the thioxo carbon appears as a doublet for the *trans*-pyrroline ($^3J_{CCCH}$ = 8.5 Hz) and as a singlet for the *cis*-pyrroline, owing to a very low coupling constant (Table 5).

The results in table 2 are rationalized by assuming a typical [3 + 2] cycloaddition of the in situ generated thiazoles **2**. The unstable N-bridged cycloadducts **11** do not extrude the *tert*-butyl isothiocyanate but rather undergo a base-catalyzed rearrangement into the pyrrolines **10** via a 1,5-proton migration from the activated C-6 on the exocyclic nitrogen atom. The formation of pyrroline **10a** (*trans*) from salt **1a** and dimethyl fumarate in the presence of NEt_3 may be interpreted by the predominant formation of the 5-*exo*, 6-*endo*-intermediate **11a** through the transition state described in scheme 4. The minor **10a** (*cis*) arises from the other transition state via the 5-*endo*, 6-*exo*-cycloadduct **11a**. However, it is clear from the small isomer ratio that the two transition states differ little in energy. The major *trans*-pyrroline **10a** obtained from dimethyl maleate and NEt_3 (which preserves the dipolarophile and cycloadduct geometries) requires the predominant formation of the 5-*exo*, 6-*exo*-intermediate **11a** and corresponds to an *endo*-cycloaddition with regard to the dipole. The dihydro pyrroles **10c, g, l** cannot be isolated since they are rapidly transformed in basic media according to three different directions : ring opening route (a) to furnish the diaminodienes **7** ; aromatization step (b) to give the pyrroles **8** via the loss of $HNMe_2$; cyclization process (c) with elimination of MeOH to yield the fused products **9** (Scheme 5). In $CHCl_3$ solution, some of the bicyclic compounds **9** slowly undergo a new rearrangement to afford the thiomaleimides **12** (1,3-C to N proton shift). The process (c) was much slower under the action of NEt_3, as a consequence of which condensed pyrroles **9** were found in lower quantities than in the presence of DBN when we started from **1c, g** and dimethyl fumarate. In the case of entries 5, 8 the formation of compounds **9** could be interpreted by a suitable structure *cis* for the precursors **10** (Scheme 5). This stereochemistry results from the corresponding 5-*endo*, 6-*exo*-intermediates **11**. We presume that the use of maleate leads predominantly to the *trans*-pyrrolines **10**, before isomerisation. This stereochemistry requires an *endo*-transition state with regard to the dipole and the formation of the transient 5-*exo*, 6-*exo*-cycloadducts **11**.



Scheme 4 (E = CO_2Me)



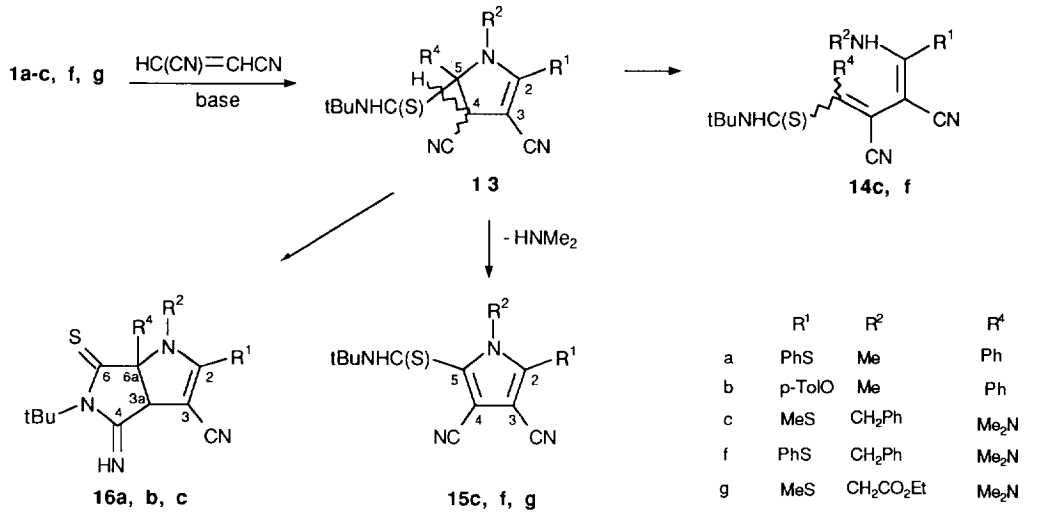
Scheme 5

Treatment of thiazolium chlorides **1** with fumaronitrile afforded similar results. The cycloadditions proceeded rapidly at room temperature to give predominantly one of the following compounds according to the nature of the starting salt and base : diaminobutadiene **14**, pyrrole **15** and fused pyrroline **16** (Table 3). The 2-pyrrolines **13a, b** were obtained in small quantities (together with condensed adducts **16a, b**) from the salts **1a,b** under the action of NEt_3 (a single isomer **13** with an undetermined *cis* or *trans*-structure). The reactions were probably proceeding under thermodynamic control. The results of table 3 can be explained by the 1,3-dipolar trapping of mesoionic thiazoles **2** followed by base-catalyzed rearrangements of the initially-formed cycloadducts (Scheme 6).

Table 3. Reactions of 5-Aminothiazolium Salts **1** with Fumaronitrile in Basic Media (rt, 1 h)[a]

salt	reactn condns		products distribution [b]				yields [c], %
	solvent	base	**13**	**14**	**15**	**16**	
1a	CH_2Cl_2	NEt_3	35	-	-	65	**13a** (32) ; **16a** (61)
1a	CH_2Cl_2	DBN	-	-	-	100	**16a** (89)
1b	CH_2Cl_2	NEt_3	20	-	-	80	**13b** (17) ; **16b** (64)
1b	CH_2Cl_2	DBN	-	-	-	100	**16b** (88)
1c	THF	NEt_3	-	90	2	8	**14c** (55)
1c	THF	DBN	-	17	83	-	**15c** (50)
1f	CH_2Cl_2	DBN	-	22	78	-	**15f** (48)
1g	THF	DBN	-	-	100	-	**15g** (57)

a,b,c : see Table 2.



	R^1	R^2	R^4
a	PhS	Me	Ph
b	p-TolO	Me	Ph
c	MeS	CH_2Ph	Me_2N
f	PhS	CH_2Ph	Me_2N
g	MeS	CH_2CO_2Et	Me_2N

Scheme 6

A few examples of analogous base-induced rearrangements, without any fragmentation, have been reported in the literature, starting from standard electron-deficient olefins and cyclic azomethine ylides as imidazolium-4-olates,[14] munchnones,[15] azlactones [16] and Reissert salts.[17] [3 + 2] Cycloaddition reactions of oxazolium-5-olates generally give 2-pyrrolines via usual CO_2 elimination.[18]

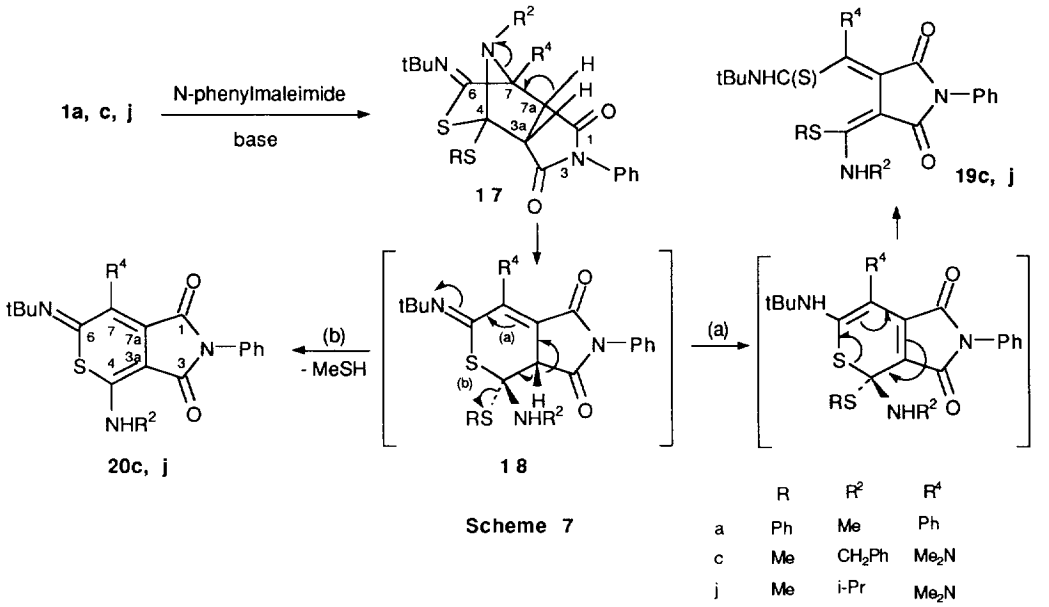
Reactions of Salts 1 with N-phenylmaleimide. The reactivity of mesoionic compounds such as **2a, c, j** as 4π electron-rich system was also demonstrated by their fast 1,3-dipolar cycloaddition with N-phenylmaleimide. Salt **1a** readily underwent addition in the presence of NEt_3 to afford a product which was identified as the 1:1 primary adduct **17a**. The latter was found to be stable in the solid state for several months but was rapidly degraded by DBN to give unidentified compounds. The stereochemical assignment of **17a** was based only on NMR method : the *cis*-protons 3a-H and 7a-H couple with 9.7 Hz, consistent with the experience on structurally related *endo*-adducts (^3J = 8.4-9.6 Hz) while the *exo*-isomers show 6.7-6.8 Hz.[19-21]

Subjected to the same conditions, salts **1c, j** produced two succinimide derivatives **19, 20** in moderate yields (Table 4). Attempts to isolate the primary adducts **17** were fruitless. Compounds **19** and **20** may be the result of a base-induced rearrangement, without the further loss of *tert*-butyl isothiocyanate, as described in scheme 7. In particular, we postulate that the conversion of the unstable species **18** can occur in two ways : ring opening of the six-membered cycle (a) or elimination of MeSH (b).

Table 4. Reactions of Salts **1** with N-Phenylmaleimide in Basic Media (CH_2Cl_2, rt, 1 h)[a]

salt	base	products distribution [b]			yields [c], %
		17	**19**	**20**	
1a	NEt_3	100	-	-	**17a** (83)
1c	NEt_3	-	35	65	**19c** (29) ; **20c** (44)
1c	DBN	-	-	100	**20c** (54)
1j	NEt_3	-	25	75	**20j** (40)
1j	DBN	-	-	100	**20j** (46)

a,b,c : see Table 2.



	R	R^2	R^4
a	Ph	Me	Ph
c	Me	CH_2Ph	Me_2N
j	Me	i-Pr	Me_2N

Scheme 7

In neutral media, stable initial 1 : 1 cycloadducts are frequently isolated from cyclic azomethine ylides and olefinic dipolarophiles.[3] As an example, mesoionic 1,3-thiazol-5-ones readily give such adducts with N-phenylmaleimide [26] and maleic anhydride.[27] Their endo or exo stereochemical features have been discussed.

Conclusion. We have shown that the 5-aminothiazolium salts **1** react easily as cyclic azomethine ylides in basic media. 1,3-Dipolar cycloadditions of the corresponding mesoionic thiazoles **2** occur under fairly mild conditions and open up synthetic possibilities for a variety of functionalized monocyclic or condensed pyrrolines and pyrroles. Numerous examples are given and mechanisms have been suggested to explain the observed rearrangements. Further studies on these systems deserve some attention and other examples using heterocumulenes as dipolarophiles will be published shortly.

Experimental section

General. Melting points are uncorrected. ^1H NMR spectra (80 or 300 MHz) and ^{13}C NMR spectra (75.5 MHz) were recorded in $CDCl_3$. When necessary, unambiguous NMR assignments were acquired by decoupling experiments. HRMS were obtained from the Centre Régional de Mesures Physiques de l'Ouest, in the electron impact mode, using a potential of 70 eV. With the exception of molecular ion peaks, only mass spectral fragments with relative intensities of 15 % or more are reported. Infrared spectra were recorded as suspensions in Nujol. Elemental analyses were performed by the analytical laboratory, CNRS.

The following reactions were conducted under a dry nitrogen atmosphere. Na_2SO_4 was used to dry organic layers after extractions. Crude products were generally fractionated by silica gel column flash

chromatography then purified by recrystallization. Corresponding eluents and solvents will be given below with analytical and spectral data of various compounds.

Reactions of Salts 1 with Acetylenic Dipolarophiles. Preparation of Pyrroles 4, 5, 6. DBN (0.97 g, 7.8 mmol) was added dropwise to a mixture of **1** (6 mmol) and DMAD (1.28 g, 9 mmol) or methyl propiolate (0.76 g, 9 mmol) in anhydrous CH_2Cl_2, THF or MeCN (20 mL, Table 1). The solution was maintained at rt for 1 h then the solvent was removed under reduced pressure. The residue was poured into 30 mL of Et_2O and washed with H_2O. The ^1H NMR analysis of the crude oily product showed the formation of pyrrole and isothiocyanate in the ratio 50 : 50. These compounds were separated by chromatography except for **4d** and **4h** which precipitated by trituration with petroleum ether (yields and ^{13}C NMR spectra, see Tables 1 and 5 ; **4b**, see our preceding article [2]).

Dimethyl 1-Methyl-5-phenyl-2-(phenylthio)-1H-pyrrole-3,4-dicarboxylate (4a) : Et_2O/petroleum ether (1 : 1) as eluent ; mp 103°C (MeOH) ; ^1H NMR δ 3.27 (s, 3H), 3.56 (s, 3H), 3.78 (s, 3H), 7.30 (m, 10H) ; MS calcd for $C_{21}H_{19}NO_4S$ m/z 381.1035 (M^+), found 381.1046 ; m/z (rel int) 381 (100), 318 (30) ; IR 1703 cm^{-1}. Anal. Calcd for $C_{21}H_{19}NO_4S$: C, 66.14 ; H, 4.99 ; N, 3.67 ; S, 8.40. Found : C, 66.44 ; H, 5.00 ; N, 3.65 ; S, 8.06.

Dimethyl 1-Benzyl-5-(dimethylamino)-2-(phenylthio)-1H- pyrrole-3,4-dicarboxylate (4c) : Et_2O/petroleum ether (1 : 1) as eluent ; mp 111°C (MeOH) ; ^1H NMR δ 2.61 (s, 6H), 3.81 (s, 6H), 5.12 (s, 2H), 7.05 (m, 10H) ; MS calcd for $C_{23}H_{24}N_2O_4S$ m/z 424.1457 (M^+), found 424.1462 ; m/z (rel int) 424 (30), 333 (100), 269 (27) ; IR 1700 cm^{-1}. Anal. Calcd for $C_{23}H_{24}N_2O_4S$: C, 65.09 ; H, 5.66 ; N, 6.60 ; S, 7.55. Found : C, 65.44 ; H, 5.95 ; N, 6.73 ; S, 7.63.

Dimethyl 5-(Dimethylamino)-1-[(ethoxycarbonyl)methyl]-2-(methylthio)-1H-pyrrole-3,4-dicarboxylate (4d) : mp 62°C (ether/petroleum ether) ; ^1H NMR δ 1.22 (t, J = 7 Hz, 3H), 2.26 (s, 3H), 2.67 (s, 6H), 3.77 (s, 3H), 3.83 (s, 3H), 4.18 (q, J = 7 Hz, 2H), 4.80 (s, 2H) ; MS calcd for $C_{15}H_{22}N_2O_6S$ m/z 358.1198 (M^+), found 358.1174 ; m/z (rel int) 358 (83), 343 (100), 327 (15), 239 (16), 194 (24) ; IR 1740, 1715, 1700 cm^{-1}. Anal. Calcd for $C_{15}H_{22}N_2O_6S$: C, 50.28 ; H, 6.14 ; N, 7.82 ; S, 8.94. Found : C, 50.34 ; H, 6.21 ; N, 7.72 ; S, 8.80.

Dimethyl 5-(Dimethylamino)-1-[(ethoxycarbonyl)methyl]-2-(phenylthio)-1H- pyrrole-3,4-dicarboxylate (4e) : Et_2O/petroleum ether (1 : 1) as eluent ; bp 180°C (0.02 Torr) (Buchi Kugelrohr apparatus) ; ^1H NMR δ 1.08 (t, J = 7 Hz, 3H), 2.71 (s, 6H), 3.81 (s, 6H), 3.95 (q, J = 7 Hz, 2H), 4.66 (s, 2H), 7.18 (s, 5H) ; MS calcd for $C_{20}H_{24}N_2O_6S$ m/z 420.1355 (M^+), found 420.1375 ; m/z (rel int) 420 (100), 333 (26). Anal. Calcd for $C_{20}H_{24}N_2O_6S$: C, 57.14 ; H, 5.71 ; N, 6.67 ; S, 7.62. Found : C, 56.95 ; H, 5.69 ; N, 6.39 ; S, 7.79.

Dimethyl 1-[(Diethoxyphosphoryl)methyl]-5-(dimethylamino)-2-(methylthio)-1H-pyrrole-3,4-dicarboxylate (4f) : Et_2O as eluent ; crude oil ; ^1H NMR δ 1.31 (t, J = 7 Hz, 6H), 2.40 (s, 3H), 2.77 (s, 6H), 3.80 (s, 3H), 3.85 (s, 3H), 4.11 (m, 4H), 4.56 (d, $^2J_{HCP}$ = 16 Hz, 2H) ; MS calcd for $C_{16}H_{27}N_2O_7PS$ m/z 422.1276 (M^+), found 422.1272 ; m/z (rel int) 422 (100), 407 (74), 375 (27), 271 (15), 149 (26).

Dimethyl 5-(Dimethylamino)-2-(methylthio)-1-isopropyl-1H- pyrrole-3,4-dicarboxylate (4g) : Et_2O/petroleum ether (1 : 2) as eluent ; mp 90°C (MeOH) ; ^1H NMR δ 1.56 (d, J = 7 Hz, 6H), 2.33 (s, 3H), 2.76 (s, 6H), 3.78 (s, 3H), 3.85 (s, 3H), 5.08 (m, 1H) ; MS calcd for $C_{14}H_{22}N_2O_4S$ m/z 314.1300 (M^+), found 314.1322 ; m/z (rel int) 314 (55), 271 (100), 239 (47), 207 (16). Anal. Calcd for $C_{14}H_{22}N_2O_4S$: C, 53.50 ; H, 7.01 ; N, 8.92 ; S, 10.19. Found : C, 53.17 ; H, 7.06 ; N, 8.80 ; S, 10.08.

Dimethyl 5-(Dimethylamino)-1-(2,6-dimethylphenyl)-2-(methylthio)-1H- pyrrole-3,4-dicarboxylate (4h) : mp 97°C (MeOH) ; ^{1}H NMR δ 1.96 (s, 6H), 2.03 (s, 3H), 3.81 (s, 6H), 3.79 (s, 3H), 3.85 (s, 3H), 7.17 (m, 3H) ; MS calcd for $C_{19}H_{24}N_2O_4S$ m/z 376.1457 (M^+), found 376.1445 ; m/z (rel int) 376 (92), 361 (100), 329 (20). Anal. Calcd for $C_{19}H_{24}N_2O_4S$: C, 60.64 ; H, 6.38 ; N, 7.45 ; S, 8.51. Found : C, 60.35 ; H, 6.77 ; N, 7.21 ; S, 8.50.

Methyl 1-Benzyl-5-(dimethylamino)-2-(methylthio)-1H-pyrrole-4-carboxylate (5a) : Et_2O/petroleum ether (1 : 2) as eluent ; bp 160°C (0.02 Torr) (Buchi) ; ^{1}H NMR δ 2.01 (s, 3H), 2.66 (s, 6H), 3.77 (s, 3H), 5.24 (s, 2H), 6.72 (s, 1H), 7.10 (m, 5H) ; MS calcd for $C_{16}H_{20}N_2O_2S$ m/z 304.1245 (M^+), found 304.1257 ; m/z (rel int) 304 (42), 213 (100), 181 (26), 91 (20) ; IR 1700 cm^{-1}. Anal. Calcd for $C_{16}H_{20}N_2O_2S$: C, 63.16 ; H, 6.58 ; N, 9.21. Found : C, 62.78 ; H, 6.73 ; N, 9.01.

Methyl 1-Benzyl-5-(dimethylamino)-2-(methylthio)-1H-pyrrole-3-carboxylate (6a) : mp 68°C (CH_2Cl_2/Et_2O) ; ^{1}H NMR δ 2.12 (s, 3H), 2.55 (s, 6H), 3.80 (s, 3H), 5.31 (s, 2H), 6.31 (s, 1H), 7.10 (m, 5H) ; MS found 304.1248 ; m/z (rel int) 304 (22), 213 (100), 181 (53), 91 (27) ; IR 1720 cm^{-1}. Anal. Found : C, 62.83 ; H, 6.57 ; N, 9.19.

Methyl 5-(Dimethylamino)-1-[(ethoxycarbonyl)methyl]-2-(methylthio)-1H- pyrrole-4-carboxylate (5b) : Et_2O/petroleum ether (1 : 2) as eluent ; mp 49°C (MeOH) ; ^{1}H NMR δ 1.24 (t, J = 7 Hz, 3H), 2.17 (s, 3H), 2.71 (s, 6H), 3.75 (s, 3H), 4.20 (q, J = 7 Hz, 2H), 4.78 (s, 2H), 6.72 (s, 1H) ; MS calcd for $C_{13}H_{20}N_2O_4S$ m/z 300.1144 (M^+), found 300.1146 ; m/z (rel int) 300 (80), 285 (100) ; IR 1745, 1705 cm^{-1}. Anal. Calcd for $C_{13}H_{20}N_2O_4S$: C, 52.00 ; H, 6.67 ; N, 9.33 ; S, 10.67. Found : C, 51.70 ; H, 6.60 ; N, 9.26 ; S, 10.37.

Methyl 5-(Dimethylamino)-1-[(ethoxycarbonyl)methyl]-2-(methylthio)-1H-pyrrole-3-carboxylate (6b) : bp 160°C (0.02 Torr) ; ^{1}H NMR δ 1.26 (t, J = 7 Hz, 3H), 2.31 (s, 3H), 2.57 (s, 6H), 3.80 (s, 3H), 4.21 (q, J = 7 Hz, 2H), 4.81 (s, 2H), 6.24 (s, 1H) ; MS found 300.1136 ; m/z (rel int) 300 (53), 285 (100) ; IR 1740, 1702 cm^{-1}. Anal. Found : C, 51.63 ; H, 6.61 ; N, 9.04.

Reactions of Salts 1 with Olefinic Dipolarophiles. A solution of **1** (6 mmol) in dry CH_2Cl_2 or THF (30 mL) was prepared. Dimethyl fumarate, maleate, fumaronitrile or N-phenylmaleimide (9 mmol) then NEt_3 or DBN (7.8 mmol) were added dropwise and the mixture was stirred at rt for the time indicated in Tables 2, 3 and 4. As precedently described, workup procedure consists of concentration, addition of water, extraction with ether and flash chromatographic separation of the various products (yields and ^{13}C NMR data, see Tables 2-6). Compounds **14f**, **16c** and **19j** were not thoroughly purified and were only characterized by ^{1}H NMR. [**14f** : δ 1.61 (s, 9H), 2.77 (d, 2H), 3.13 (s, 6H), 5.74 (t, br, 1H), 7.25 (m, 10H), 8.42 (br, 1H). **16c** : δ 1.82 (s, 9H), 2.18 (s, 6H), 2.63 (s, 3H), 3.78 (s, 1H), 4.47, 5.35 (AB syst, J = 17.6 Hz, 2H), 7.25 (m, 5H). **19j** : δ 1.25 (d, J = 6 Hz, 6H), 1.38 (s, 9H), 2.26 (s, 3H), 2.77 (s, 3H), 3.01 (s, 3H), 4.07 (m, 1H), 6.86 (br, 1H), 7.30 (s, 5H), 8.55 (d, J = 9 Hz, 1H)].

Dimethyl 1-(Benzylamino)-4-(*tert*-butylthiocarbamoyle)-4-(dimethylamino)-1-(methylthio) butadiene-2,3-dicarboxylate (7c) : Et_2O/petroleum ether (6 : 1) as eluent ; mp 125°C (Et_2O) ; ^{1}H NMR (prevailing isomer) δ 1.38 (s, 9H), 2.23 (s, 3H), 2.95 (s, 6H), 3.62 (s, 6H), 4.67 (m, 2H), 7.27 (s, 5H), 7.62 (br, 1H), 9.31 (t, br, J = 6 Hz, 1H) ; ^{13}C NMR (prevailing isomer) δ 18.5 (q, ^1J = 141 Hz), 27.0 (qm, ^1J = 127 Hz), 43.1 (qq, ^1J = 140 Hz, ^3J = 3.6 Hz), 49.8 (tm, ^1J = 137 Hz), 51.0, 51.1 (2q, ^1J = 145 Hz), 55.6 (m), 96.4, 101.2 (2s), 127.2, 127.3 (2 dm, ^1J = 160 Hz), 128.6 (dd, ^1J = 160 Hz, ^3J = 6 Hz), 138.9, 161.4, 165.9 (3 m), 168.1, 170.2 (2 q, ^3J = 3.7 Hz), 194.4 (s) ; MS calcd for $C_{23}H_{33}N_3O_4S_2$ m/z 479.1912 (M^+), found 479.1918 ; m/z (rel int) 479 (1), 348 (17), 91 (100) ; IR 3322, 1670, 1638 cm^{-1}. Anal.

Calcd for $C_{23}H_{33}N_3O_4S_2$: C, 57.62 ; H, 6.89 ; N, 8.77 ; S, 13.36. Found : C, 57.43 ; H, 6.97 ; N, 8.44 ; S, 13.69.

Dimethyl 4-(*tert*- Butylthiocarbamoyle)-4-(dimethylamino)-1-[(2,6-dimethylphenyl) amino]-1-(methylthio) butadiene-2,3-dicarboxylate (7l) : Et_2O/CH_2Cl_2 (1 : 2) as eluent ; mp 173°C (MeOH) ; ^1H NMR (prevailing isomer) δ 1.46 (s, 9H), 1.71 (s, 3H), 2.20 (s, 3H), 2.30 (s, 3H), 2.93 (s, 6H), 3.62 (s, 3H), 3.66 (s, 3H), 7.02 (s, 3H), 7.75 (br, 1H), 10.33 (br, 1H) ; ^{13}C NMR (prevailing isomer) δ 16.2 (q, ^1J = 142 Hz), 18.6, 19.1 (2 qd, ^1J = 127 Hz, ^3J = 3 Hz), 27.1 (qm, ^1J = 127 Hz), 43.1 (qq, ^1J = 138 Hz, ^3J = 3 Hz), 51.1, 51.2 (2 q, ^1J = 146 Hz), 55.6 (m), 97.5, 101.2 (2s), 126.6 (d, ^1J = 160 Hz), 128.1, 128.5 (2 dm, ^1J = 158 Hz), 135.9, 138.0, 160.7, 165.5 (4 m), 168.3, 170.1 (2 q, ^3J = 3.6 Hz), 194.6 (s) ; MS calcd for $C_{24}H_{35}N_3O_4S_2$ m/z 493.2069 (M^+), found 493.2067 ; m/z (rel int) 493 (61), 446 (20), 377 (17), 362 (17), 350 (15), 345 (21), 315 (54), 314 (48), 295 (49), 283 (21), 178 (84), 91 (100) ; IR 3300, 1660, 1630 cm^{-1}. Anal. Calcd for $C_{24}H_{35}N_3O_4S_2$: C, 58.42 ; H, 7.10 ; N, 8.52 ; S, 12.98. Found : C, 58.29 ; H, 7.00 ; N, 8.47 ; S, 12.91.

Dimethyl 1-Benzyl-5-(*tert*-butylthiocarbamoyl)-2-(methylthio)-1H- pyrrole-3,4-dicarboxylate (8c) : Et_2O/petroleum ether (1 : 1) as eluent ; mp 135°C (MeOH) ; ^1H NMR δ 1.33 (s, 9H), 2.30 (s, 3H), 3.76 (s, 3H), 3.87 (s, 3H), 5.75 (s, 2H), 7.10 (m, 5H) ; MS calcd for $C_{21}H_{26}N_2O_4S_2$ m/z 434.1334 (M^+), found 434.1339 ; m/z (rel int) 434 (10), 377 (33), 223 (16), 91 (100) ; IR 3260, 1700 cm^{-1}. Anal. Calcd for $C_{21}H_{26}N_2O_4S_2$: C, 58.06 ; H, 5.99 ; N, 6.45 ; S, 14.75. Found : C, 58.30 ; H, 5.84 ; N, 6.29 ; S, 14.63.

Dimethyl 5-(*tert*-Butylthiocarbamoyl)-1-[(ethoxycarbonyl)methyl]-2-(methylthio)-1H-pyrrole-3,4-dicarboxylate (8g) : Et_2O/petroleum ether (1 : 1) as eluent ; mp 138°C (MeOH) ; ^1H NMR δ 1.27 (t, J = 7 Hz, 3H) ; 1.56 (s, 9H), 2.31 (s, 3H), 3.77 (s, 3H), 3.84 (s, 3H), 4.20 (q, J = 7 Hz, 2H), 5.31 (s, 2H), 7.86 (br, 1H) ; MS calcd for $C_{18}H_{26}N_2O_6S_2$ m/z 430.1232 (M^+), found 430.1250 ; m/z (rel int) 430 (69), 401 (27), 341 (37), 313 (24), 309 (100) ; IR 3280, 1745, 1705 cm^{-1}. Anal. Calcd for $C_{18}H_{26}N_2O_6S_2$: C, 50.23 ; H, 6.05 ; N, 6.51 ; S, 14.88. Found : C, 50.11 ; H, 6.01 ; N, 6.47 ; S, 14.83.

Methyl 5-*tert*-Butyl-1-methyl-4-oxo-6a-phenyl-2-(phenylthio)-6-thioxo-3a,4,5,6a-tetrahydro-1H, 6H-pyrrolo [3,4-b] pyrrole-3-carboxylate (9a) : Et_2O/petroleum ether (1 : 1) as eluent ; mp 131°C (MeOH) ; ^1H NMR δ 1.78 (s, 9H), 2.80 (s, 3H), 3.65 (s, 3H), 3.98 (s, 1H), 7.20 (m, 10H) ; MS calcd for $C_{25}H_{26}N_2O_3S_2$ m/z 466.1385 (M^+), found 466.1372 ; m/z (rel int) 466 (100), 410 (27), 377 (15), 350 (21), 323 (89) ; IR 1745, 1680 cm^{-1}. Anal. Calcd for $C_{25}H_{26}N_2O_3S_2$: C, 64.38 ; H, 5.58 ; N, 6.01. Found : C, 64.30 ; H, 5.57 ; N, 6.07.

Methyl 1-Benzyl-5-*tert*-butyl-6a-(dimethylamino)-2-(methylthio)-4-oxo-6-thioxo-3a,4,5,6a-tetrahydro-1H, 6H-pyrrolo [3,4-b] pyrrole-3-carboxylate (9c) : Et_2O/petroleum ether (2 : 1) as eluent ; mp 128°C (MeOH) ; ^1H NMR δ 1.66 (s, 9H), 2.16 (s, 6H), 2.41 (s, 3H), 3.81 (s, 3H), 4.06 (s, 1H), 4.70, 5.31 (AB syst, J = 17.4 Hz, 2H), 7.08 (m, 5H) ; MS calcd for $C_{22}H_{29}N_3O_3S_2$ m/z 447.1650 (M^+), found 447.1653 ; m/z (rel int) 447 (11), 300 (17), 91 (100) ; IR 1750, 1670 cm^{-1}. Anal. Calcd for $C_{22}H_{29}N_3O_3S_2$: C, 59.06 ; H, 6.49 ; N, 9.40 ; S, 14.32. Found : C, 59.13 ; H, 6.65 ; N, 9.27 ; S, 14.73.

Methyl 5-*tert*-Butyl-6a-(dimethylamino)-1-[(ethoxycarbonyl) methyl]-2-(methylthio)-4-oxo-6-thioxo-3a,4,5,6a-tetrahydro-1H, 6H- pyrrolo [3,4-b] pyrrole-3-carboxylate (9g) : Et_2O/petroleum ether (2 : 1) as eluent ; mp 100°C (CH_2Cl_2/Et_2O) ; ^1H NMR δ 1.20 (t, J = 7 Hz, 3H), 1.70 (s, 9H), 2.11 (s, 6H), 2.45 (s, 3H), 3.77 (s, 3H), 3.98 (s, 1H), 4.10 (m, 2H), 4.63, 4.25 (AB syst, J = 18 Hz, 2H) ; MS calcd for $C_{19}H_{29}N_3O_5S_2$ m/z 443.1549 (M^+), found 443.1582 ; m/z (rel int) 443 (26), 428

(77), 372 (100), 340 (50), 327 (23), 300 (32), 285 (29) ; IR 1735, 1665 cm^{-1}. Anal. Calcd for $C_{19}H_{29}N_3O_5S_2$: C, 51.47 ; H, 6.55 ; N, 9.48 ; S, 14.45. Found : C, 51.44 ; H, 6.80 ; N, 9.32 ; S, 14.29.

Dimethyl 5-(tert-Butylthiocarbamoyle)-1-methyl-5-phenyl-2-(phenylthio)-4,5-dihydro-1H-pyrrole-3,4-dicarboxylate (10a) : Et_2O/petroleum ether (1 : 1) as eluent ; *trans*-isomer : mp 179°C (MeOH) ; ^1H NMR δ 1.50 (s, 9H), 2.46 (s, 3H), 3.21 (s, 3H), 3.63 (s, 3H), 5.20 (s, 1H), 7.30 (m, 10H), 8.01 (br, 1H) ; MS calcd for $C_{26}H_{30}N_2O_4S_2$ m/z 498.1647 (M^+), found 498.1647 ; m/z (rel int) 498 (1), 382 (94), 381 (82), 350 (100), 318 (39), 292 (24), 273 (52) ; IR 3325, 1741, 1698 cm^{-1}. Anal. Calcd for $C_{26}H_{30}N_2O_4S_2$: C, 62.65 ; H, 6.02 ; N, 5.62 ; S, 12.85. Found : C, 62.64 ; H, 6.11 ; N, 5.62 ; S, 12.47 ; *cis*-isomer : mp 133°C (MeOH) ; ^1H NMR δ 1.44 (s, 9H), 2.13 (s, 3H), 3.65 (s, 3H), 3.69 (s, 3H), 4.82 (s, 1H), 7.30 (m, 10H), 8.10 (br, 1H) ; MS calcd for $C_{25}H_{26}N_2O_3S_2$ m/z 466.1385 $(M\text{-}MeOH)^+$, found 466.1379 ; m/z (rel int) 466 (89), 410 (33), 389 (16), 350 (22), 323 (100) ; IR 3275, 3250, 1720, 1687 cm^{-1}. Anal. Found : C, 62.58 ; H, 6.01 ; N, 5.65 ; S, 12.94.

4-[β-(Benzylamino)-α-(methoxycarbonyl)-β-(methylthio) vinyl]-1-*tert*-butyl-3-(dimethylamino)-2-thiomaleimide (12c) : mp 98°C (MeOH) ; ^1H NMR δ 1.73 (s, 9H), 2.25 (s, 3H), 2.93 (s, 6H), 3.62 (s, 3H), 4.70 (d, J = 6 Hz, 2H), 7.30 (s, 5H), 9.66 (br, 1H) ; ^{13}C NMR δ 17.8 (q, ^1J = 141 Hz), 24.4 (qm, ^1J = 128 Hz), 42.7 (qq, ^1J = 137 Hz, ^3J = 3.9 Hz), 49.7 (tm, ^1J = 138 Hz), 51.2 (q, ^1J = 146 Hz), 60.4 (m), 91.8 (d, ^3J = 2 Hz), 106.6 (s), 127.0 (dm, ^1J = 158 Hz), 127.4 (dt, ^1J = 161 Hz, ^3J = 6.8 Hz), 128.7 (dd, ^1J = 160 Hz, ^3J = 6.8 Hz), 138.6, 152.7, 164.0 (3 m), 169.2 (q, ^3J = 3.8 Hz), 174.9, 199.3 (3s) ; MS calcd for $C_{22}H_{29}N_3O_3S_2$ m/z 447.1650 (M^+), found 447.1678 ; m/z (rel int) 447 (29), 91 (100) ; IR 3180, 1717, 1640 cm^{-1}. Anal. Calcd for $C_{22}H_{29}N_3O_3S_2$: C, 59.06 ; H, 6.49 ; N, 9.40. Found : 58.66 ; H, 6.69 ; N, 9.12.

1-*tert*-Butyl-3-(dimethylamino)-4-[β-[[(ethoxycarbonyl)methyl] amino]-α-(methoxycarbonyl)-β-(methylthio) vinyl]-2-thiomaleimide (12g) : mp 209°C (MeOH) ; ^1H NMR δ 1.24 (t, J = 7 Hz, 3H), 1.49 (s, 9H), 2.36 (s, 3H), 3.27 (s, 6H), 3.68 (s, 3H), 4.17 (q, J = 7 Hz, 2H), 4.57 (s, 2H), 7.70 (br, 1H) ; ^{13}C NMR δ 14.2 (qt, ^1J = 127 Hz, ^2J = 3.0 Hz), 20.6 (q, ^1J = 142 Hz), 27.0 (qm, ^1J = 127 Hz), 42.6 (t, ^1J = 141 Hz), 45.1 (qbr, ^1J = 137 Hz), 50.8 (q, ^1J = 147 Hz), 56.7 (m), 61.4 (tq, ^1J = 148 Hz, ^2J = 4.5 Hz), 97.8, 114.9 (2s), 133.3, 161.6 (2m), 162.7 (s), 164.3 (q, ^3J = 4.0 Hz), 169.3 (m), 190.0 (s) ; MS calcd for $C_{19}H_{29}N_3O_5S_2$ m/z 443.1549 (M^+), found 443.1539 ; m/z (rel int) 443 (100), 428 (22), 386 (15), 354 (22), 340 (20), 338 (16), 315 (17), 313 (19) ; IR 3240, 1740, 1705 cm^{-1}. Anal. Calcd for $C_{19}H_{29}N_3O_5S_2$: C, 51.47 ; H, 6.55 ; N, 9.48. Found : C, 51.07 ; H, 6.65 ; N, 9.09.

5-(*tert*-Butylthiocarbamoyle)-1-methyl-5-phenyl-2-(phenylthio)-4,5-dihydro-1H-pyrrole-3,4-dicarbonitrile (13a) : Et_2O/petroleum ether (4 : 1) as eluent ; mp 130°C (MeOH) ; ^1H NMR δ 1.36 (s, 9H), 2.70 (s, 3H), 6.36 (s, 1H), 7.30 (m, 10H) ; MS calcd for $C_{24}H_{24}N_4S_2$ m/z 432.1442 (M^+), found 432.1433 ; m/z (rel int) 432 (8), 315 (100) ; IR 3280, 2240, 2185 cm^{-1}. Anal. Calcd for $C_{24}H_{24}N_4S_2$: C, 66.67 ; H, 5.56 ; N, 12.96 ; S, 14.81. Found : C, 66.50 ; H, 5.53 ; N, 12.80 ; S, 14.50.

5-(*tert*-Butylthiocarbamoyle)-1-methyl-2-[(4-methylphenyl)oxy]-5-phenyl-4,5-dihydro-1H-pyrrole-3,4-dicarbonitrile (13b) : Et_2O/petroleum ether (3 : 2) as eluent ; mp 210°C (MeOH) ; ^1H NMR δ 1.38 (s, 9H), 2.26 (s, 3H), 2.76 (s, 3H), 6.01 (s, 1H), 7.25 (m, 9H) ; MS calcd for $C_{25}H_{26}N_4OS$ m/z 430.1827 (M^+), found 430.1856 ; m/z (rel int) 430 (1), 313 (100) ; IR 3270, 2238, 2181 cm^{-1}. Anal. Calcd for $C_{25}H_{26}N_4OS$: C, 69.77 ; H, 6.05 ; N, 13.02 ; S, 7.44. Found : C, 69.61 ; H, 6.08 ; N, 12.73 ; S, 7.14.

Table 5. Selected ^{13}C NMR Chemical Shifts at 75.469 MHz for the Substituted Pyrroles **4, 5, 6, 8, 15** and Dihydro Pyrroles **10, 13** (endocyclic and possible thione carbons)[a], Mult (*J*, Hz).

n°	C-2	C-3	C-4	C-5 (m)	C=S
4a	121.4 q (3.7)[b]	125.0 s	113.5 s	140.5	-
4c	115.9 t (4.3) [b]	125.3 s	108.2 s	148.3	-
4d	121.6 m	122.5 s	108.4 s	146.9	-
4e	116.0 t (4.0) [b]	125.2 s	108.2 s	148.3	-
4f	122.2 m	122.4 s	109.1 s	146.7	-
4g	119.6 m	123.5 s	108.5 s	147.3	-
4h	121.4 q (4.6) [c]	122.1 s	106.1 s	147.2	-
5a	119.8 m	116.8 d (177.0) [d]	108.3 d (2.2) [e]	148.6	-
6a	125.2 m	117.9 d (2.2) [e]	99.1 d (174.5)[d]	146.2	-
5b	119.5 m	117.5 d (177.7) [d]	108.5 d (2.2) [e]	148.6	-
6b	125.1 m	118.2 d (2.1) [e]	98.9 d (175.0) [d]	145.9	-
8c	129.1 q (4.8) [c]	112.7 s	121.6 s	138.5	186.4 s
8g	129.5 q (4.4) [c]	112.9 s	121.6 s	138.4	185.9 s
15c	137.8 q (4.8) [c]	94.6 s	100.9 s	142.9	182.4 s
15f	133.8 t (4.2) [b]	94.8 s	103.8 s	143.5	182.2 s
15g	138.3 q (5.0) [c]	94.5 s	101.9 s	142.8	181.8 s
10a (*trans*)	152.9 m	101.9 d (5.9) [e]	60.4 d (140.0) [d]	84.5	199.0 d (8.5) [f]
10a (*cis*)	155.2 m	109.7 d (4.9) [e]	60.7 d (146.5) [d]	85.7	195.8 s
13a	156.2 m	80.6 d (7.5) [e]	46.6 d (145.5) [d]	85.0	194.2 d (8.5) [f]
13b	164.3 m	54.4 d (7.0) [e]	44.9 d (146.7) [d]	81.0	195.1 d (7.5) [f]

[a] The ring carbons are numbered in the way to have the methylthio, phenylthio or aryloxy group on the C-2. [b] $^3J_{(CNCH)}$. [c] $^3J_{(CSCH)}$. [d] ^1J. [e] $^2J_{(CCH)}$. [f] $^3J_{(CCCH)}$.

Table 6. Selected ^{13}C NMR Chemical Shifts at 75.469 MHz for the Fused Pyrroles **9, 16** and Thiopyrans **17, 20**, Mult (*J*, Hz).

n°	C-1	C-2 (m)	C-3	C-3a	C-4	C-6	C-6a (m)	C-7 (m)	C-7a
9a	-	154.2	99.3 d (6.0) [a]	58.4 d (148.6) [b]	176.4 d (3.7) [a]	206.9 d (3.8) [c]	80.2	-	-
9c	-	160.8	96.7 d (6.0) [a]	43.3 d (142.6) [b]	177.3 d (5.5) [a]	204.7 d (1.5) [c]	90.4	-	-
9g	-	159.4	97.9 d (6.2) [a]	42.9 d (143.3) [b]	176.7 d (5.3) [a]	204.7 d (1.9) [c]	89.3	-	-
16a	-	158.0	78.2 d (4.9) [a]	58.5 d (148.0) [b]	168.9 br	204.0 d (6.0) [c]	82.3	-	-
16b	-	165.3	52.5 d (4.6) [a]	55.9 d (147.9) [b]	169.9 br	204.6 d (4.9) [c]	78.2	-	-
17a	172.0 t (3.4) [a,c]	-	172.3 t (4.7) [a,c]	51.9 dd (146.6[b], 3.3[a])	92.0 m	155.5 d (5.9) [c]	-	81.5	53.9 dd (147.0[b], 3.3[a])
20c	164.3 s	-	166.0 s	91.4 s	152.1 t (4.3) [d]	140.1 s	-	138.4	113.5 s
20j	164.3 s	-	166.0 s	89.9 s	151.8 d (2.6) [d]	140.3 s	-	137.8	114.5 s

[a] $^2J_{(CCH)}$. [b] ^1J. [c] $^3J_{(CCCH)}$. [d] $^3J_{(CNCH)}$.

1-(Benzylamino)-4-(*tert*-butylthiocarbamoyle)-4-(dimethylamino)-1-(methylthio) butadiene-2,3-dicarbonitrile (14c, one isomer) : Et_2O/CH_2Cl_2 (3 : 1) as eluent ; mp 162°C (Et_2O/CH_2Cl_2) ; ^1H NMR δ 1.61 (s, 9H), 2.32 (s, 3H), 3.16 (s, 6H), 4.66 (d, J = 6 Hz, 2H), 5.87 (t, J = 6 Hz, 1H), 7.35 (s, 5H), 8.43 (br, 1H) ; ^{13}C NMR δ 17.3 (q, ^1J = 142 Hz), 26.9 (qm, ^1J = 127 Hz), 42.0 (qq, ^1J = 139 Hz, ^3J = 3.4 Hz), 49.2 (tm, ^1J = 139 Hz), 57.3 (m), 63.5 (s), 78.6 (d, ^3J = 1.5 Hz), 121.0, 122.6 (2s), 127.2 (dd, ^1J = 161 Hz, ^3J = 5.5 Hz), 127.5 (dt, ^1J = 161 Hz, ^3J = 4 Hz), 128.7 (dm, ^1J = 158 Hz), 138.2, 161.5, 164.0 (3m), 189.9 (s) (Selective irradiation on the dimethylamino group at δ 3.18 causes the C-4 signal at δ 164.0 to turn into a doublet, or into a singlet in the presence of D_2O, and reveals the coupling constant $^3J_{(CCNH)}$ to be 2.4 Hz) ; MS calcd for $C_{21}H_{27}N_5S_2$ m/z 413.1708 (M^+), found 413.1728 ; m/z (rel int) 413 (3), 91 (100) ; IR 3340, 3275, 2160 cm^{-1}. Anal. Calcd for $C_{21}H_{27}N_5S_2$: C, 61.02 ; H, 6.54 ; N, 16.95 ; S, 15.50. Found : C, 61.04 ; H, 6.59 ; N, 16.80 ; S, 15.31.

1-Benzyl-5-(*tert*-butylthiocarbamoyle)-2-(methylthio)-1H-pyrrole-3,4 dicarbonitrile (15c) : Et_2O/petroleum ether (2 : 1) as eluent ; mp 181°C (MeOH) ; ^1H NMR δ 1.37 (s, 9H), 2.40 (s, 3H), 5.72 (s, 2H), 7.15 (m, 5H), 7.66 (br, 1H) ; MS calcd for $C_{19}H_{20}N_4S_2$ m/z 368.1129 (M^+), found 368.1141 ; m/z (rel int) 368 (23), 91 (100) ; IR 3278, 2220 cm^{-1}. Anal. Calcd for $C_{19}H_{20}N_4S_2$: C, 61.96 ; H, 5.43 ; N, 15.22 ; S, 17.39. Found : C, 62.18 ; H, 5.49 ; N, 15.07 ; S, 17.48.

1-Benzyl-5-(*tert*-butylthiocarbamoyle)-2-(phenylthio)-1H-pyrrole-3,4 dicarbonitrile (15f) : Et_2O/petroleum ether (2 : 1) as eluent ; mp 149°C (MeOH) ; ^1H NMR δ 1.35 (s, 9H), 5.66 (s, 2H), 7.05 (m, 10H), 7.57 (br, 1H) ; MS calcd for $C_{24}H_{22}N_4S_2$ m/z 430.1286 (M^+), found 430.1298 ; m/z (rel int) 430 (27), 167 (72), 91 (100) ; IR 3290, 2223 cm^{-1}. Anal. Calcd for $C_{24}H_{22}N_4S_2$: C, 66.98 ; H, 5.12 ; N, 13.02 ; S, 14.88. Found : C, 66.73 ; H, 5.46 ; N, 12.79 ; S, 14.78.

5-(*tert*-Butylthiocarbamoyle)-1-[(ethoxycarbonyl)methyl]-2-(methylthio)-1H-pyrrole-3,4-dicarbonitrile (15g) : Et_2O as eluent ; mp 102°C (MeOH) ; ^1H NMR δ 1.27 (t, J = 7 Hz, 3H), 1.59 (s, 9H), 2.43 (s, 3H), 4.23 (q, J = 7 Hz, 2H), 5.30 (s, 2H), 7.89 (br, 1H) ; MS calcd for $C_{16}H_{20}N_4O_2S_2$ m/z 364.1028 (M^+), found 364.1035 ; m/z (rel int) 364 (100), 308 (30), 279 (19), 276 (21), 261 (30), 247 (18), 236 (30), 235 (39), 201 (34) ; IR 3280, 2223, 1750 cm^{-1}. Anal. Calcd for $C_{16}H_{20}N_4O_2S_2$: C, 52.75 ; H, 5.49 ; N, 15.38 ; S, 17.58. Found : C, 52.65 ; H, 5.67 ; N, 15.33 ; S, 17.61.

5-*tert*-Butyl-4-imino-1-methyl-6a-phenyl-2-(phenylthio)-6-thioxo-3a,4,5,6a-tetrahydro-1H, 6H-pyrrolo [3,4-b] pyrrole-3-carbonitrile (16a) : Et_2O/petroleum ether (3 : 2) as eluent ; mp 175°C (MeOH) ; ^1H NMR δ 1.86 (s, 9H), 2.83 (s, 3H), 3.70 (s, 1H), 7.30 (m, 10H) ; MS calcd for $C_{24}H_{24}N_4S_2$ m/z 432.1442 (M^+), found 432.1433 ; m/z (rel int) 432 (48), 376 (38), 318 (15), 315 (18), 291 (100), 290 (77), 267 (34) ; IR 3260, 2187, 1670 cm^{-1}. Anal. Calcd for $C_{24}H_{24}N_4S_2$: C, 66.67 ; H, 5.56 ; N, 12.96 ; S, 14.81. Found : C, 66.50 ; H, 5.53 ; N, 12.80 ; S, 14.58.

5-tert-Butyl-4-imino-1-methyl-2-[(4-methylphenyl)oxy]-6a-phenyl-6-thioxo-3a,4,5,6a-tetrahydro-1H, 6H-pyrrolo [3,4-b] pyrrole-3-carbonitrile (16b) : Et_2O/petroleum ether (3 : 2) as eluent ; mp 151°C (MeOH) ; ^1H NMR δ 1.86 (s, 9H), 2.28 (s, 3H), 2.98 (s, 3H), 3.56 (s, 1H), 7.15 (m, 9H), 8.40 (br, 1H) ; MS calcd for $C_{25}H_{26}N_4OS$ m/z 430.1827 (M^+), found 430.1813 ; m/z (rel int) 430 (75), 374 (37), 373 (25), 341 (16), 316 (44), 314 (16), 289 (100), 267 (27), 197 (65) ; IR 3230, 2180, 1670 cm^{-1}. Anal. Calcd for $C_{25}H_{26}N_4OS$: C, 69.77 ; H, 6.05 ; N, 13.02 ; S, 7.44. Found : C, 69.95 ; H, 6.11 ; N, 12.95 ; S, 7.15.

***endo*-6-(tert-Butylimino)-2,7-diphenyl-2,3,3a,4,7,7a-hexahydro-4,7-*epi*-(N-methylimino)-4-(phenylthio)-1H, 6H-pyrrolo [3,4-c] thiopyran-1,3-dione (17a)** : Et_2O/petroleum ether (1 : 1) as eluent ; mp 185°C (MeOH) ; ^1H NMR δ 1.15 (s, 9H), 2.52 (s, 3H), 3.28, 3.39

(AB syst, J = 9.7 Hz, 2H), 7.65 (m, 15H) ; MS calcd for $C_{30}H_{29}N_3O_2S_2$ m/z 527.1701 (M^+), found 527.1709 ; calcd for $C_{25}H_{20}N_2O_2S$ m/z 412.1245 (M-*t*-BuNCS)$^+$, found 412.1263 ; m/z (rel int) 527 (0.1), 412 (56), 335 (16), 302 (25), 188 (28), 184 (100) ; IR 1770, 1712, 1642 cm^{-1}. Anal. Calcd for $C_{30}H_{29}N_3O_2S_2$: C, 68.31 ; H, 5.50 ; N, 7.97. Found : C, 68.46 ; H, 5.46 ; N, 7.90.

3-[(Benzylamino)-(methylthio)methylene]-4-[(*tert*-butylthiocarbamoyle)-(dimethylamino)methylene]-1-phenylsuccinimide (19c) : Ethyl acetate as eluent ; mp 190°C (MeOH) ; ^1H NMR δ 1.40 (s, 9H), 2.13 (s, 3H), 2.77 (s, 3H), 3.01 (s, 3H), 4.73 (d, J = 6 Hz, 2H), 6.88 (br, 1H), 7.30 (m, 10H), 9.31 (t, br, 1H) ; ^{13}C NMR δ 17.1 (q, ^1J = 142 Hz), 29.7 (qm, ^1J = 126 Hz), 38.1 (qq, ^1J = 138 Hz), 42.6 (qq, ^1J = 138 Hz, ^3J = 3.3 Hz), 49.2 (tm, ^1J = 138 Hz), 57.8 (m), 98.0, 105.5 (2s), 126.6, 127.1 (2 dm, ^1J = 160 Hz), 127.3, 127.4 (2 dt, ^1J = 159 Hz, ^3J = 7.1 Hz), 128.6, 128.7 (2 dd, ^1J = 161 Hz, ^3J = 7.1 Hz), 132.7 (t, ^3J = 7.2 Hz), 137.4, 138.3, 158.6 (3m), 167.3, 168.0, 187.2 (3s) ; MS calcd for $C_{22}H_{21}N_3O_2S$ m/z 391.1354 [M-BuNHC(S)H]$^+$, found 391.1367 ; m/z (rel int) 391 (27), 384 (29), 327 (38), 300 (100) ; IR 3202, 1692, 1644 cm^{-1}. Anal. Calcd for $C_{27}H_{32}N_4O_2S_2$: C, 63.78 ; H, 6.30 ; N, 11.02. Found : C, 63.39 ; H, 6.48 ; N, 10.75.

4-(Benzylamino)-6-(*tert*-butylimino)-7-(dimethylamino)-2-phenyl-1H, 6H-pyrrolo [3,4-c] thiopyran-1,3 (2H)-dione (20c) : Ethyl acetate/pentane (1 : 1) as eluent ; mp 200°C (EtOH) ; ^1H NMR δ 1.40 (s, 9H), 2.96 (s, 6H), 4.46 (br, 2H), 7.30 (m, 10H), 8.56 (br, 1H) ; MS calcd for $C_{26}H_{28}N_4O_2S$ m/z 460.1933 (M^+), found 460.1919 ; m/z (rel int) 460 (14), 403 (69), 313 (21), 91 (100) ; IR 3286, 1720, 1657 cm^{-1}. Anal. Calcd for $C_{26}H_{28}N_4O_2S$: C, 67.83 ; H, 6.09 ; N, 12.17 ; S, 6.96. Found : C, 67.99 ; H, 6.14 ; N, 12.10 ; S, 6.66.

6-(*tert*-Butylimino)-7-(dimethylamino)-2-phenyl-4-(isopropylamino)-1H, 6H-pyrrolo [3,4-c] thiopyran-1,3 (2H)-dione (20j) : Et_2O/petroleum ether (2 : 1) as eluent ; mp 136°C (MeOH) ; ^1H NMR δ 1.27 (d, J = 6 Hz, 6H), 1.46 (s, 9H), 2.95 (s, 6H), 3.77 (m, 1H), 7.40 (s, 5H), 8.13 (br, 1H) ; MS calcd for $C_{22}H_{28}N_4O_2S$ m/z 412.1933 (M^+), found 412.1933 ; m/z (rel int) 412 (21), 355 (100), 329 (18), 311 (23), 296 (15) ; IR 3250, 1720, 1660 cm^{-1}. Anal. Calcd for $C_{22}H_{28}N_4O_2S$: C, 64.08 ; H, 6.80 ; N, 13.59 ; S, 7.77. Found : C, 64.17 ; H, 6.77 ; N, 13.49 ; S, 7.97.

References and Notes

1 Shiba, T. ; Kato, H. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 1864-1868 ; **1973**, *46*, 964-967. Grashey, R. ; Jaenchen, E. ; Litzke, *J. Chem. Ztg.* **1973**, *97*, 657-658.

2 Berrée, F. ; Malvaut, Y. ; Marchand, E. ; Morel, G. *J. Org. Chem.* **1993**, *58*, 6022-6029.

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

4 Pioneering papers : Bayer, H.O. ; Gotthardt, H. ; Huisgen, R. *Chem. Ber.* **1970**, *103*, 2356-2367. Huisgen, R. ; Gotthardt, H. ; Bayer, H.O. ; Schaefer, F.C. *Chem. Ber.* **1970**, *103*, 2611-2624. For recent review, see : Bean, G.P. The Synthesis of 1H-Pyrroles. In *Pyrroles* ; Jones, R.A., Ed. ; Wiley, J. : New York, **1990**, vol. 48, part one, pp. 165-168.

5 Padwa, A. ; Lim, R. ; Mac Donald, J.G. ; Gingrich, H.L. ; Kellar, S.M. *J. Org. Chem.* **1985**, *50*, 3816-3823.

6 Review : Osterhout, M.H. ; Nadler, W.R. ; Padwa, A. *Synthesis* **1994**, 123-141.

7 Barrett, G.C. *Tetrahedron* **1980**, *36*, 2023-2058.

8 The potentiality of 5-aminothiazolium salts **1** to serve as synthetic equivalents of cyclic azomethine ylides **2** in basic media has only been mentioned in our earlier report [2] where we described the easy preparation of one pyrrole (**4b**) through the use of DMAD.

9 To our knowledge and except the above example, [8] extrusion of isothiocyanate from mesoionic compounds was only related for the rearrangement of the 4-methyl-5-phenyl-1,3,4-thiadiazolium-2-anilide into the corresponding 1,3,4-triazolium-2-thiolate. This isomerisation proceeds via a cycloaddition with phenyl isothiocyanate : Ollis, W.D. ; Ramsden, C.A. *J. Chem. Soc., Perkin Trans. I* **1974**, 633-638.

10 Padwa, A. ; Burgess, E.M. ; Gingrich, H.L. ; Roush, D.M. *J. Org. Chem.* **1982**, *47*, 786-791. Dalla Croce, P. ; La Rosa, C. *Heterocycles* **1988**, *27*, 2825-2832 and references cited therein for the works by R. Huisgen, H. Gotthardt et al..

11 Texier, F. ; Mazari, M. ; Yebdri, O. ; Tonnard, F. ; Carrié, R. *Bull. Soc. Chim. Fr.* **1991**, *128*, 962-967.

12 Similarly, dimethyl maleate rapidly gives isomeric fumarate in the presence of DBN but is quite stable in the presence of NEt3.

13 Sustmann, R. ; Huisgen, R. ; Huber, H. *Chem. Ber.* **1967**, *100*, 1802-1813.

14 For instance, the mesoionic tetraphenylimidazolium-4-olate was found to be sluggishly reactive towards dimethyl fumarate and maleate giving succinimidopyrrolines via a process like (c), Scheme 5 : Singh, G. ; Pande, P.S. *Tetrahedron Lett.* **1974**, 2169-2170.

15 Friedrichsen, W. ; Schröer, W.D. *Tetrahedron Lett.* **1977**, 1603-1604.

16 Texier, F. ; Yebdri, O. ; Laidoudi, A. ; Talbi, B. ; Balegroune, F. ; Germain, G. *Tetrahedron Lett.* **1983**, *24*, 189-192.

17 Schmitt, G. ; Laude, B. ; Vebrel, J. ; Rodier, N. ; Theobald, F. *Bull. Soc. Chim. Belg.* **1989**, *98*, 113-123.

18 Benages, I.A. ; Albonico, S.M. *J. Org. Chem.* **1978**, *43*, 4273-4276. Texier, F. ; Mazari, M. ; Yebdri, O. ; Tonnard, F. ; Carrié, R. *Tetrahedron* **1990**, *46*, 3515-3526 and references therein.

19 Gotthardt, H. ; Christl, B. *Chem. Ber.* **1978** , *111*, 3029-3036.

20 Padwa, A. ; Hertzog, D.L. *Tetrahedron* **1993**, *49*, 2589-2600.

21 Similar observations have been made for the vicinal *cis*-coupling constants of 2,3-disubstituted-*endo*-bornane derivatives (^3J = 8.8 - 9.9 Hz for *exo* -H-2 and H-3) [22] which are uniformly larger than those of *exo*-compounds (^3J = 7-8.1 Hz for *endo*-H-2 and H-3), [23] probably for steric reasons.[24] Likewise, the H-2/H-3 vicinal *cis*-coupling constants observed in 7-azanorbornanes and 7-azanorbornene complexes are smaller in *exo*-isomers (*endo*-ring protons, $^3J \leq 9.6$ Hz) than in *endo*-isomers (*exo*-ring protons, $^3J > 9.6$ Hz).[25]

22 Banks, M.R. ; Blake, A.J. ; Cadogan, J.I.G. ; Dawson, I.M. ; Gosney, I. ; Grant, K.J. ; Gaur, S. ; Hodgson, P.K.G. ; Knight, K.S. ; Smith, G.W. ; Stevenson, D.E. *Tetrahedron* **1992**, *48*, 7979-8006.

23 Bonner, M.P. ; Thornton, E.R. *J. Am. Chem. Soc.* **1991**, *113*, 1299-1308.

24 Daniel, A. ; Pavia, A.A. *Bull. Soc. Chim. Fr.***1971**, 1060-1074.

25 Gonzalez, J. ; Koontz, J.I. ; Hodges, L.M. ; Nilsson, K.R. ; Neely, L.K. ; Myers, W.H. ; Sabat, M. ; Harman, W.D. *J. Am. Chem. Soc.* **1995**, *117*, 3405-3421.

26 Potts, K.T. ; Baum, J. ; Houghton, E. ; Roy, D.N. ; Singh, U.P. *J. Org. Chem.* **1974**, *39*, 3619-3627.

27 Barrett, G.C. ; Walker, R. *Tetrahedron* **1976**, *32*, 571-577 and 579-581.

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