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2-Aza-1,3-Dienes with Electron-Releasing Substituents at the 1,3 positions . Reagents for the Construction of Pyridine and Pyrimidine Derivatives.

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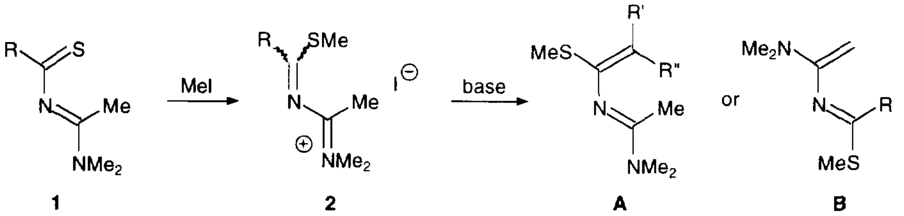
Abstract : New 2-aza-1,3-dienes bearing 1 and 3-donor substituents are prepared from N-thioacylacetamidines through deprotonation of N-ylidene acetamidinium iodides. The 2-aza-3-(dimethylamino)-1-(methylthio)-1-phenylbutadiene (**3**) is trapped *in situ* by the residual precursor salt acting as a heterodienophile to give the pyrimidine **5**. Substituted 2-aza-1-(dimethylamino)-3-(methylthio) analogues react readily with a variety of electron-deficient dienophiles to yield pyridine or pyrimidine derivatives. The stereochemistry of the hetero Diels-Alder reaction in the cases of dimethyl fumarate and acrylonitrile has been assigned by X-ray diffraction analyses of the resulting tetrahydropyridines and corresponds to an exo selectivity. The number and nature of cycloadducts in the cases of dimethyl acetylenedicarboxylate and phenyl isothiocyanate depend on C-4 substitution. The results obtained from the C-4 unsubstituted azabutadiene **8** are explained by an allylic rearrangement involving the 1,3-migration of dimethylamino group in the primary [4 + 2] adduct. Copyright © 1996 Elsevier Science Ltd

INTRODUCTION

During the last fifteen years, the synthetic value of the Diels-Alder methodology for the construction of six-membered heterocyclic systems has been demonstrated by the use of conjugated heterodienes which exhibit high regioselectivity in their cycloadditions with unsymmetrical dienophiles.[1,2] In this context, the ability of various 2-aza-1,3-dienes to participate in Diels-Alder reactions has received much attention. Thus, the preparation [3] and [4 + 2] cycloaddition reactions of acyclic 2-azadienes bearing electron-releasing [1,2] or electron-withdrawing [2,4,5] substituents, as well as electronically neutral [2,4,6] or mixed 2-azadienes with both donor and attracting groups[5a,7] have been recently studied. In this series, the derivatives that carry an electron-releasing substituent at C-1 [8] or C-3 [9] or two such substituents in positions 1 and 3 [10-12] are a class of heterodienes of great interest, owing to their remarkable aza Diels-Alder reactivity with a variety of electron-poor dienophiles (normal electronic demand, HOMO diene - controlled cycloadditions). Moreover, the electron-donating groups are amenable to elimination from the primary cycloadducts, inducing aromatization to afford functionalized pyridine or pyrimidine rings. [8,10,11]

Further access to 2-azadienes with different 1 and 3-donor substituents would be desirable as these systems are potential precursors to numerous cycloadducts. The deprotonation of 1-alkyl-2-azavinamidinium perchlorates to 1,3-diamino-2-aza-1,3-dienes, already described,[11] focused our attention on the base-induced conversion of N-ylidene amidinium salts as a potentially useful route to such dienes. We report here the ready preparation of new 1,3-electron-releasing substituted 2-aza-1,3-dienes and describe our investigations on their use in the synthesis of pyridine and pyrimidine derivatives. The substrates employed in this study were selected on the basis of their ability to reveal information about reaction mechanisms and other features, including the stereochemical and regiochemical preferences governed by electronic and steric factors. In particular, we have developed a short and efficient approach to 1-amino-3-(methylthio)-2-azadienes (**A**) or 3-amino-1-(methylthio) analogues (**B**) from the readily available 3-aza-1-thiabutadienes **1** (N-thioacylacetamidines) and corresponding amidinium salts **2**, depending on the nature of the substituent R (Scheme 1).

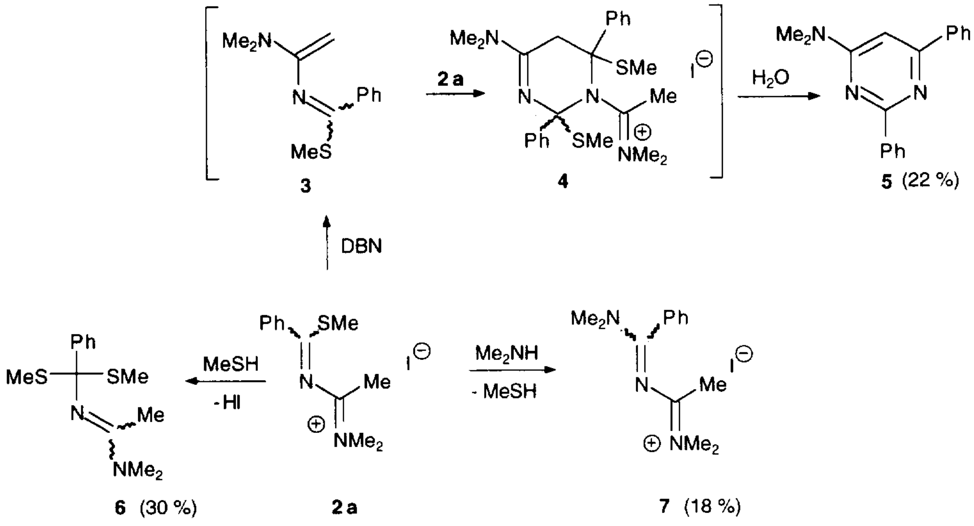


a, R = Ph c, R = Et
b, R = Me d, R = i-Pr

(from **2b-d**, R = CHR'R")

Scheme 1

2-Aza-3-(dimethylamino)-1-(methylthio)-1-phenylbutadiene (**3**). This type **B** compound was found to be easily accessible through the methylation of the N,N-dimethyl-N'-(thiobenzoyl) acetamidine (**1a**) and the deprotonation of the resulting N-benzylidene amidinium iodide **2a**. The second step takes place by simply mixing **2a** with a slight excess of DBN in CH_2Cl_2 at room temperature. The diene **3** could not however be isolated but was trapped *in situ* by the remaining precursor **2a** which reacts as a heterodienophile in a cycloaddition process (Scheme 2). N-Activated imines have recently been shown to be excellent partners in Diels-Alder reactions with electron-rich dienes.[13,14] Therefore, the formation of pyrimidine **5** can be rationalized by hydrolysis and aromatization of the [4 + 2] cycloadduct **4**. Such processes also give methanethiol and dimethylamine as by-products .The yield of purified adduct **5** was lowered by the formation of acetamidine **6** and 2-azavinamidinium iodide **7**. The ambident electrophilic nature of N-benzylidene amidinium salts[15,16] explains the rapid addition of MeSH and Me_2 NH to starting compound **2a** (Scheme 2).

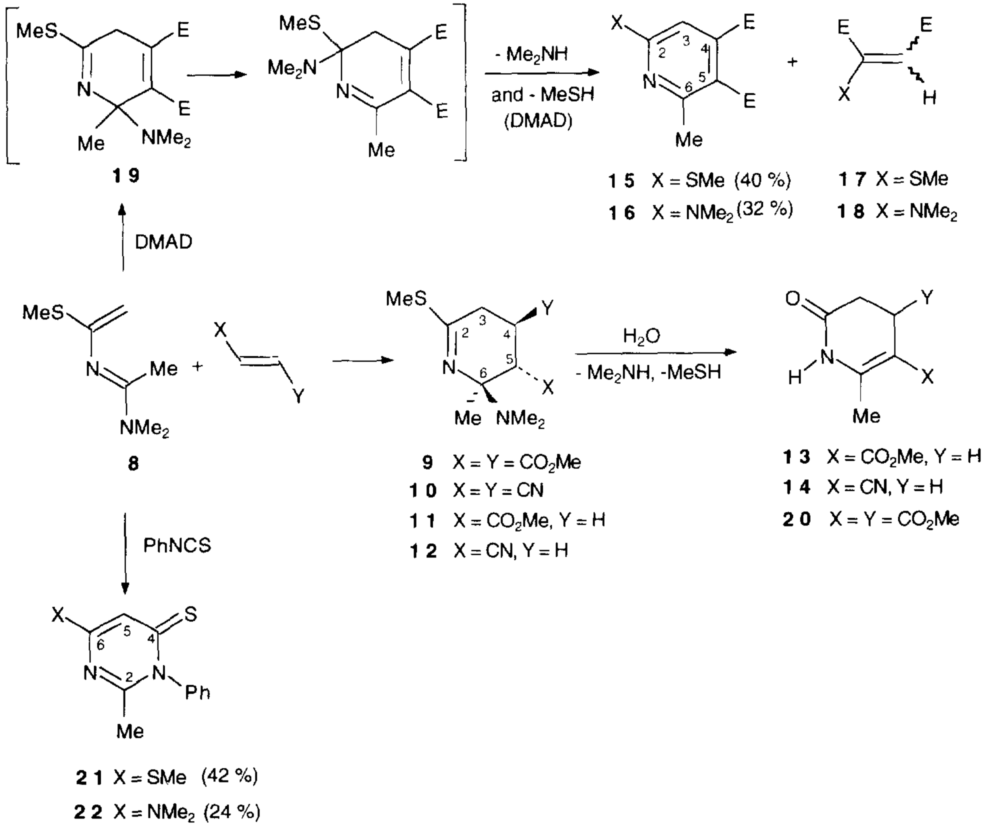


Scheme 2

3-Aza-4-(dimethylamino)-2-(methylthio)-1,3-pentadiene (8). This 1,1,3-trisubstituted 2-azabutadiene of type A (see Scheme 3) was generated from the ethylidene acetamidinium iodide **2b** by treatment with DBN. The reaction was highly regioselective, a single isomer being detected in the crude product. Structural assignment of **8**, based upon ^{1} H and ^{13}C NMR spectral data, was confirmed by heteronuclear decoupling and NOEDIFF experiments (cf Experimental Section).[17] In particular, a NOE enhancement was observed between the C-methyl resonance and one of the methylene protons, indicating a corresponding syn relationship (Figure 1). This interaction was in good agreement with the postulated *E*-s-cis structure .[18]

We have succeeded in using **8** in [4 + 2] cycloaddition reactions with representative electron-deficient dienophiles at room temperature (Table 1). Dimethyl fumarate, fumaronitrile, methyl acrylate and acrylonitrile exhibited excellent reactivity toward **8**, cleanly providing the corresponding tetrahydropyridines **9-12**, each as a single isomer (entries 1-4). Compounds **11**, **12** were rapidly hydrolyzed to the dihydropyridinones **13**, **14** on storage (Scheme 3). The stereochemical assignments of **9** were deduced from ^{1}H NMR spectral data (cf Experimental Section) and firmly established by X-ray single-crystal diffraction analysis. The ORTEP representation of the structure **9** illustrates, in particular, the pseudo equatorial orientation of the dimetylamino and two methoxycarbonyl groups in a twisted conformation (Figure 2)[19]. This stereochemistry (where H_5 and Me on C-6 are in a trans relative position) could reasonably be extrapolated for cycloadducts **11**,**12**. The exclusive formation of tetrahydropyridines **9-12** can be understood in terms of a Diels-Alder process with an exo selectivity referring to the C-1 of 2-azabutadiene **8**. Similar stereoselectivities have been reported for the [4 + 2] cycloadditions of 2-aza-1-phenyl-3-siloxybutadienes, [9a,9b] N-thioacylamidines [20] or N-selenoacylamidines [21] to α,β-unsaturated carbonyl derivatives.

A more complex and rapid reaction occurred when **8** was added to an excess of dimethyl acetylenedicarboxylate (entry 5). ^{1}H NMR analysis of the crude product indicated the formation of two cycloadducts, the 2-(methylthio)-pyridine **15** and the 2- (dimethylamino) analogue **16**. These compounds have been fully characterised by their ^{13}C NMR spectral data , in particular by the long-range coupling constants ^2J and ^3J (see the multiplicities of endocyclic and ring-connected carbons, Table 2). Large quantities of vinyl sulfides **17** and enamines **18** (both two isomers) were also obtained. Such by -products result from the addition of methanethiol [22] and dimethylamine [23] to DMAD (32 : 25 : 18 : 25 was the ratio of **15**, **16**, **17** and **18**). The unexpected formation of **16** (and **17**) was not due to isomerisation of **8** into the type **B** azadiene, through a 1,5-hydrogen shift [8a, 24], followed by [4+2] cycloaddition reaction of heterodiene **B** with DMAD. Thus, only starting isomer was detected by ^{1}H NMR in CD_2Cl_2 solution of **8** left for several days without dienophile and the reactions summarized in Table 1 (e.g. entries 1-4) never involved the type **B** heterodiene. Under similar conditions (20°C), control experiments have established that **8** and **15** were recovered unchanged after prolonged contact with $HNMe_2$ (i.e. substitution of the methylthio group by a dimethylamino group did not take place). Morever, the dimethylamine resulting from the formation of **15** was promptly trapped by DMAD to give the enamine **18** with a quantitative yield. [23] The simultaneous formation of pyridines **15**, **16** could be rationalized by an allylic rearrangement of the initial [4 + 2] adduct **19**, followed by 1,2-elimination of Me_2NH or MeSH (Scheme 3). Such a 1,3-migration of an amino group has previously been reported for 4-(dialkylamino)-4H-thiopyrans [25,26] and 4-(dialkylamino)-4H-1,4-thiazines. [27]

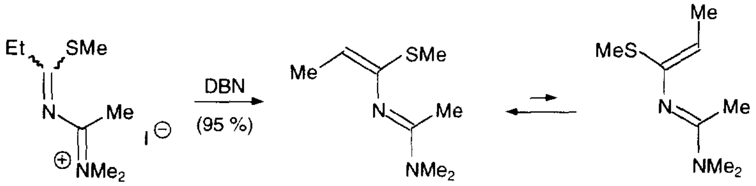


Scheme 3 (E = CO_2Me)

The tetrahydropyridine **9** was gradually converted by oxidation and hydrolysis processes into a mixture of pyridine **15** and dihydropyridinone **20** on standing at room temperature under atmospheric oxygen. Similar oxidation of tetrahydropyridines has previously been reported.[8c]

Effective Diels-Alder reactions between unactivated 2-azabutadienes and heterocumulenes[28] have been demonstrated by Barluenga et al. We have found that phenyl isothiocyanate reacts in a regioselective manner with the diene **8** to produce a mixture of two pyrimidinethiones (**21**, **22**), probably through an analogous 1,3-migration of the dimethylamino group (Table 1, entry 6). Thiourea and methyl dithiocarbamate resulting from the additions of Me_2NH and MeSH to phenyl isothiocyanate were also obtained and characterized.

3-Aza-2-(dimethylamino)-4-(methylthio)-2,4-hexadiene (23) This 2-azabutadiene of type **A** was obtained in good yield by the usual two step approach from the N-(thiopropionyl) acetamidine **1c** and the corresponding amidinium salt **2c**. Two isomeric forms **23a** (60 %) and **23b** (40 %) were detected in the crude reaction medium. The **23a** : **23b** ratio increased to 83 : 17 by equilibration in CH_2Cl_2 or $CDCl_3$ solution at room temperature for about two days. No further change was observed by ^1H NMR spectroscopy over a range of temperature from - 90°C to 100°C in either CD_2Cl_2 or toluene-d_8 solution, indicating the 83 : 17 ratio to be a thermodynamic equilibrium mixture (Scheme 4). These stereoisomers could not be separated by fractional distillation or by column chromatography.



2c **23a** **23b**

Scheme 4

The structural and stereochemical assignments of azadienes **23** were based on ^1H NMR spectroscopic data. Interestingly, large NOE enhancements were observed between the proton on C-5 and the S-methyl resonance (**23a**) or C-methyl resonance (**23b**) as described in Figure 1. The latter effect clearly supports the 2,4 (*E*,*Z*) configuration and preferential s-cis conformation for **23b** in solution. In the case of **23a**, the stereochemistry about the C=N π-bond is also assumed to be *E* and the conformation of the azadiene grouping is probably (and predominately) trans as shown. Such a trans conformation seems reasonable in light of Worley's earlier findings.[29] More recently, Ghosez and coworkers have also assigned a s-trans conformation to some 2-azadiene backbones on the basis on long range $^4J_{CH}$ and $^5J_{CH}$ coupling constants (W arrangements).[30]

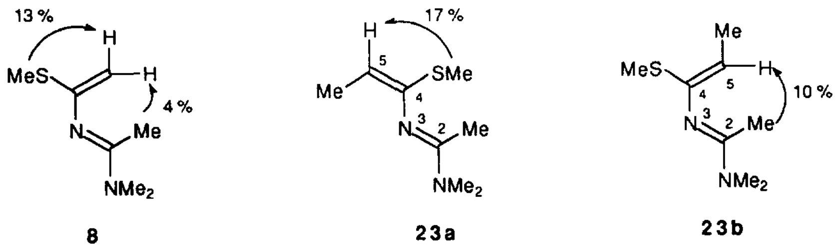


Figure 1 NOE enhancement data for azadienes **8** and **2 3**.

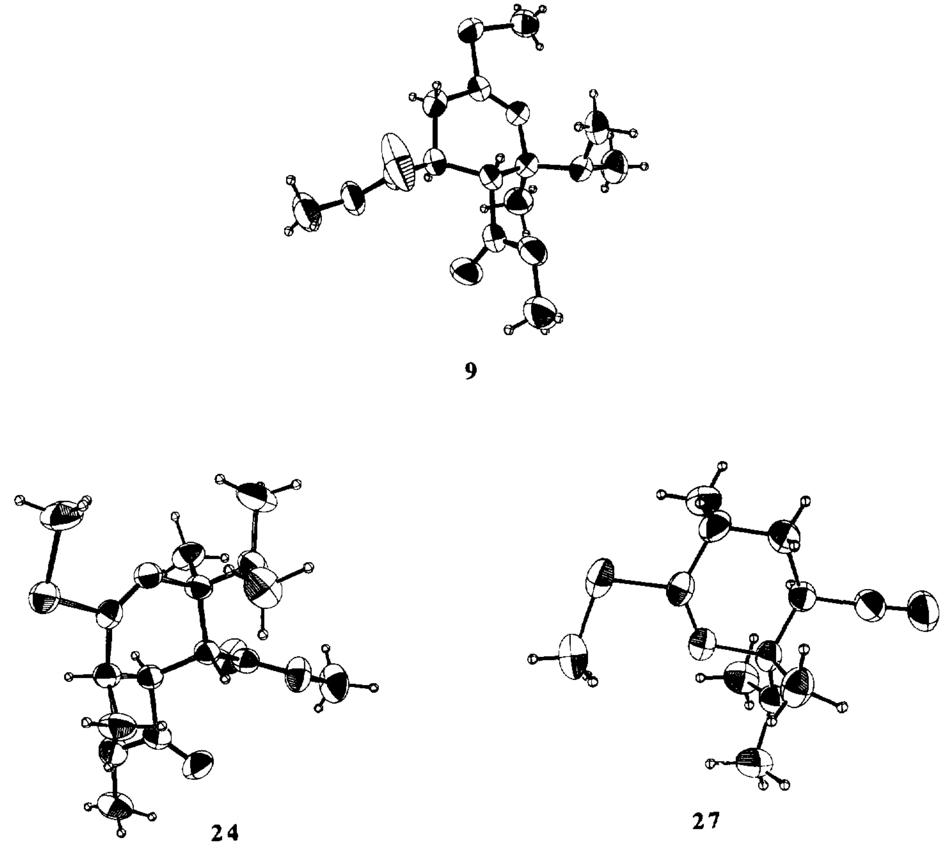
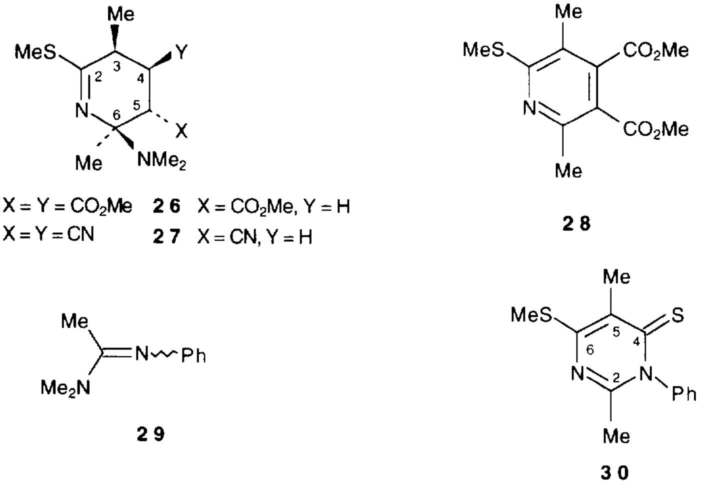


Figure 2 ORTEP Representations of Tetrahydropyridines **9**, **24** and **27**.

Cycloaddition reactions of the 83 : 17 mixture of **23a** and **23b** have been explored with standard electron-poor dienophiles. Reactions were generally carried out at room temperature in CH_2Cl_2 solution (Table 1). Only the 2,4 (*E,Z*) azadiene **23b** appears to be reactive under these conditions.[31] Thus, dimethyl fumarate gave a single tetrahydropyridine **24** which was characterized by spectroscopic (see the Experimental Section) and X-ray crystallographic methods (Figure 2).[19] The tetrahydropyridine **24** was found to possess the H_4/Me on C-3 and H_5/Me on C-6 trans relative stereochemistry with full preservation of the dienophile geometry, in agreement with an exo selectivity referring to the C-1 of 2-azabutadiene **23b.** Reactions of **23** with fumaronitrile, methyl acrylate and acrylonitrile produced the corresponding tetrahydropyridines **25**, **26** and **27** (Figure 3) in satisfactory yields (formation of one stereoisomer). The stereochemistry demonstrated for **24** could be extrapolated for cycloadducts **25**,**26** on the basis on ^1H NMR results and was clearly established for **27** by an X-ray diffraction analysis (Figure 2).[19] Use of DMAD led to the pyridine **28** after the spontaneous elimination of dimethylamine. Use of phenyl isothiocyanate resulted in a mixture of N-phenyl acetamidine **29** and pyrimidinethione **30** (entry 12).[32] Enamines and thiourea resulting from the additions of Me_2 NH to DMAD and PhNCS were also obtained but we did not observe the loss of MeSH.[33]



24 X = Y = CO_2Me **26** X = CO_2Me, Y = H
25 X = Y = CN **27** X = CN, Y = H

28

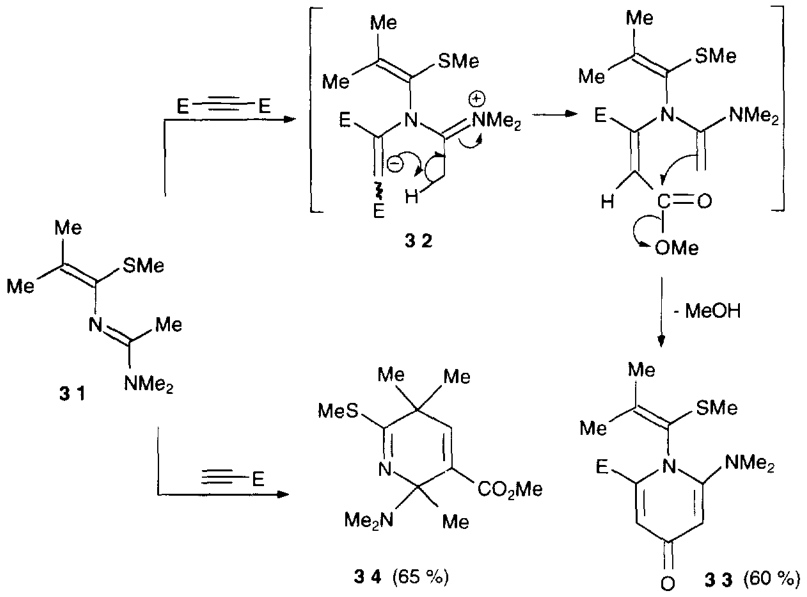
29

30

Figure 3

3-Aza-2-(dimethylamino)-5-methyl-4-(methylthio)-2,4-hexadiene (31). The versatility of our methodology for 2-azadienes synthesis was further demonstrated by the ready preparation of the type **A** heterodiene **31** through a pathway involving methylation of acetamidine **1d** and regioselective deprotonation of the amidinium salt **2d** by DBN . No experiment was effected to prove the stereochemical course of the reaction by NOEDIFF.

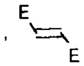
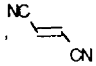
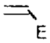
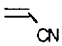
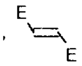
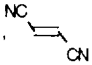
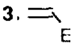
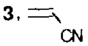
The behaviour of **31** has been investigated toward three electrophilic dienophiles. Methyl fumarate failed to react with **31**, which was quantitatively recovered, even refluxing in CH_2Cl_2 for 44 h. DMAD involved a Michael N-addition [8b] and afforded the dihydropyridinone **33** (Table 1, entry 13). This ring closure can be rationalized by the rearrangement of an initial zwitterionic form **32**, followed by the nucleophilic substitution of MeOH (Scheme 5). Such results support the assumed s-trans conformation for the starting azadiene **31**. On the contrary, methyl propiolate underwent a slow cycloaddition reaction with **31** to produce **34** exclusively. This process could occur by a nonconcerted pathway [34] through a zwitterion generated from the s-trans conformation of azadiene. But a concerted asynchronous pathway from a non planar s-cis conformation could also be postulated. Cycloaddition by a concerted or a non-concerted mechanism should follow the same regiochemistry.



Scheme 5 (E = CO_2Me)

In summary, we have demonstrated the ability of electron-rich heterodienes **3**, **8** and **23b** to undergo [4 + 2] cycloaddition reactions, according to their assigned (preferential) s-cis conformation. The ease with which such compounds are prepared from readily available N-thioacylamidines **1** is noteworthy. Deprotonation of salts **2b**-**d** appears to occur exclusively at the α-imidoyl position to give type **A** compounds (Scheme 1) rather at the acetamidinium position, perhaps due to the fact that this regiocontrol leads to generation of more conjugated dienes. Hetero Diels-Alder reactions are conducted under rather mild conditions and provide efficient synthetic method for substituted pyridine and pyrimidine derivatives. Tetrahydropyridines were formed with direct diastereoselective control on four asymmetric carbons. Starting from DMAD or PhNCS and C-4 unsubstituted azadiene **8**, the course of the sequence for the aromatization process of primary cycloadduct reveals an unexpected rearrangement, with the 1,3-migration of the dimethylamino group. Such a rearrangement could not be demonstrated with 2-azadienes bearing identical 1 and 3-leaving groups.[11] We believe that studies on similar heterodienic systems deserve further attention.

Table 1 - Reactions of Azadienes with some Electrophilic Dienophiles (E = CO_2Me)

Entry	Educts	Reactn condns[a] dienophile molar eq.	time (h), Temp.	Products distribution[b]	Isolated yields[c],%
1	**8**, 	1.1	38,rt	**9** (100)	**9** (77)
2	**8**, 	1.5	1,rt	**10** (100)	**10** (64)
3	**8**, 	1.5	30,reflux	**11** (100)	**11** (65)
4	**8**, 	1.5	24,reflux	**12** (100)	**12** (75)
5	**8**, E—≡—E	2.2	1,rt	**15** (55) ; **16** (45)	**15** (40) ; **16** (32)
6	**8**, PhNCS	3	48,rt	**21** (60) ; **22**(40)	**21** (42) ; **22** (24)
7	**23**, 	1.2	30,reflux	**24** (100)	**24** (67)
8	**23**, 	1.5	3,rt	**25** (100)	**25** (60)
9	**23**, 	1.5	48,reflux	**26** (100)	**26** (56)
10	**23**, 	1.5	40,reflux	**27** (100)	**27** (70)
11	**23**, E—≡—E	2.2	15,rt	**28** (100)	**28** (62)
12	**23**, PhNCS	3	120,rt	**29** (30) ; **30** (70)	**29** (10) ; **30** (58)
13	**32**, E—≡—E	1.5	4,rt	**33** (100)	**33**(60)
14	**32**, ≡—E	1.5	40,rt	**34** (100)	**34** (65)

[a] The reactions were performed in CH_2Cl_2, starting from a 1M solution of diene then adding an excess of dienophile. Specified times are required for the full conversion of starting dienes.[b] These distributions were estimated on the basis on the ^1H NMR spectra of crude mixtures. [c] Purified products yields after flash silica gel chromatography.

Table 2. Selected ^{13}C NMR Chemical Shifts at 75.469 MHz for some Pyridine and Pyrimidine Derivatives (endocyclic carbons and ring-connected exocyclic carbons)[a,b], Mult (*J*, Hz).

N°	C-2	C-3	C-4	C-5	C-6	C-CH_3	*C*N or *C*(O)OMe
9	161.5m	32.9dddd (130, 134[c]; 2, 4[d,e])	39.2dm (136[c])	46.3dm (134[c])	77.8m	23.3qd (128[c]; 4[e])	173.0m, 173.4m
10	160.7m	32.3ddd (133,136[c]; 2[d])	26.5dm (141[c])	35.4dm (140[c])	76.5m	23.7qd (129[c];1[e])	117.5d, 117.7t (6[e])
15	162.2qd (4[f];1.5[d])	118.1d (170[c])	136.7s	123.4m	156.9q (6.5[d])	23.0q (128[c])	165.7m, 168.8q (4[g])
16	158.6m	101.9d (166[c])	140.9s	112.9qd (3[e])	157.4q (6.5[d])	23.7q (128[c])	167.8m, 168.6q (4[g])
21	158.4q (7[d])	-	184.0d (3[d])	120.6d (175[c])	164.2q (4.5[f])	25.0q (131[c])	-
22	158.6q (7[d])	-	181.1d (1.5[d])	102.6d (170[c])	156.3m	25.2q (130[c])	-
24	166.0m	36.7dm (134[c])	41.4dm (134[c])	43.7dm (134[c])	78.1m	16.0qt (128 [c]; 5.5[de]) 24.5qd (128[c]; 3.5[e])	172.5m, 173.4m
25	165.7m	32.1dm (140[c])	31.3dm (139[c])	35.1dm (135[c])	76.9m	16.4qm; 24.2qd (129[c]; 3[e])	116.7d, 117.7d(7.5)
26	167.4m	34.1dm (132[c])	29.5tm (131[c])	40.0dm (131[c])	77.3m	20.3qm; 22.5qd (128[c]; 4[e])	177.9m
27	168.2m	28.0dm (133[c])	30.0tm (131[c])	33.5dm (132[c])	76.0m	19.8qm,22.9qd (128[c]; 4[e])	120.9dt (10[d];3[e])
28	162.5m	118.7q (3[d])	140.4q (5[e])	124.5q (6[e])	155.3q (6.5[d])	14.8q, 24.1q (129 [c])	167.3q, 167.9q (4[g])
30	156.0q (7[d])	-	182.4q (5[e])	128.9q (6[d])	160.6m	17.7q, 25.3q (130[c])	-
34	168.0m	38.3m	142.3dm (162[c])	133.9m	75.9m	27.4qm, 28.1q, 28.6qm (129[c])	166.8m

[a] The ring carbons are numbered in the way to have the methylthio or dimethylamino group on the C-2 for pyridine derivatives **9**, **10**, **15**, **16**, **24-28**, **34** and on the C-6 for pyrimidine derivatives **21**, **22**, **30**.

[b] The multiplicity of signals attributed to exo-cyclic carbons can be conclusive in establishing the regiochemistry for **21**, **22**, **26**, **27**, **34**. That of quat arom C about 141 ppm (3-phenyl group for pyrimidines) is always a triplet, $^{3}J_{(CCCH)} = 9$ Hz. [c] ^{1}J. [d] $^{2}J_{(CCH)}$. [e] $^{3}J_{(CCCH)}$. [f] $^{3}J_{(CSCH)}$. [g] $^{3}J_{(COCH)}$.

EXPERIMENTAL SECTION

General. Melting points are uncorrected. ^{13}C and ^{1}H NMR spectra were recorded in $CDCl_3$ at 50.3 or 75.5 MHz and 200 or 300 MHz, respectively. 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 peaks with relative intensities of 12 % or more are reported. Elemental analyses were performed by the analytical laboratory, CNRS.

Thioacylacetamidines **1** and acetamidinium salts **2** were easily prepared at rt according to the following known procedures : condensation of primary thioamides with the dimethylacetamide dimethyl acetal in CH_2Cl_2 solution [35] ; alkylation of acetamidines with methyl iodide [15] in THF solution. The compounds **1a** [26,35] and **2a** [15] have previously been reported. The crude thioacetylacetamidine **1b** (94 % yield) was washed three times with petroleum ether and treated with MeI without additional purification. However, a small quantity of **1b** was purified, just before the spectrum-analysis, by a bulb-to-bulb distillation under vacuum or a silica gel short-column chromatography with $AcOEt/NEt_3$ (99 : 1) as eluent. Yields of **1c** (60 %) and **1d** (51 %) refer to crude oily products after flash chromatography on silica gel 60 with AcOEt as eluent. Elemental analyses could not be obtained for the thioacylacetamidines due to hydrolysis of the samples on storage. The salts **2b** and **2d** (92 % and 85 % yields) precipitated as yellowish crystalline materials from the reaction media. They were filtered, washed with dry ether and recrystallized from CH_2Cl_2/Et_2O (1 : 1). Crude salt **2c** (87 % yield) was used without further purification.

3-Aza-4-(dimethylamino)-2-methyl-1-thia-1,3-pentadiene (1b) : bp 115-120°C/0.01 mm Hg ; mp 40-43°C (ether/petroleum ether) ; ^{1}H NMR δ 2.46 (s, 3H), 2.58 (s, 3H), 3.15 (s, 3H), 3.20 (s, 3H) ; ^{13}C NMR δ 18.2 (q, ^{1}J = 131 Hz), 36.9 (q, ^{1}J = 128 Hz), 39.1, 39.4 (2 qm, ^{1}J = 136 Hz), 168.2 (m), 206.7 (q, ^{2}J = 5 Hz) ; MS calcd for $C_6H_{12}N_2S$ *m/z* 144.0721 (M^{+}), found 144.0716 ; *m/z* (rel int) 144 (77), 129 (64), 111 (70), 103 (17), 70 (25), 68 (14), 60 (42), 59 (45), 58 (36), 56 (100).

3-Aza-2-(methylthio)-2-pentene-4-dimethyliminium iodide (2b) : mp 148-150°C dec. ; ^{1}H NMR 2.46 (s, 3H), 2.60 (s, 3H), 2.74 (s, 3H), 3.37 (s, 3H), 3.72 (s, 3H). Anal. Calcd for $C_7H_{15}IN_2S$: C, 29.37 ; H, 5.24 ; N, 9.79 ; S, 11.19. Found : C, 29.25 ; H, 5.10 ; N, 9.77 ; S, 11.22.

3-Aza-4-(dimethylamino)-2-ethyl-1-thia-1,3-pentadiene (1c) : ^{1}H NMR δ 1.20 (t, 3H, J = 7 Hz), 2.44 (s, 3H), 2.72 (q, 2H, J = 7 Hz), 3.14 (s, 3H), 3.24 (s, 3H) ; ^{13}C NMR δ 13.6 (qt, ^{1}J = 127 Hz, ^{2}J = 4.5 Hz), 18.2 (q, ^{1}J = 131 Hz), 39.0, 39.5 (2 qq, ^{1}J = 140 Hz, ^{3}J = 3 Hz), 42.4 (t q, ^{1}J = 128 Hz, ^{2}J = 4.5 Hz), 168.4, 210.9 (2m).

3-Aza-4-(methylthio)-3-hexene-2-dimethyliminium iodide (2c) : mp 63°C dec. ; ^{1}H NMR δ 1.32 (t, 3H, J = 7 Hz), 2.52 (s, 3H), 2.78 (s, 3H), 2.86 (q, 2H, J = 7 Hz), 3.38 (s, 3H), 3.76 (s, 3H).

3-Aza-4-(dimethylamino)-2-isopropyl-1-thia-1,3-pentadiene (1d) : ^{1}H NMR 1.18 (d, 6H, J = 7 Hz), 2.42 (s, 3H), 2.98 (m, 1H), 3.14 (s, 3H), 3.24 (s, 3H) ; ^{13}C NMR δ 17.9 (q, ^{1}J = 131 Hz), 22.4 (qm, ^{1}J = 128 Hz), 38.8, 39.4 (2 qq, ^{1}J = 140 Hz, ^{3}J = 3 Hz), 46.7 (dm, ^{1}J = 131 Hz), 167.7, 215.8 (2m).

3-Aza-5-methyl-4-(methylthio)-3-hexene-2-dimethyliminium iodide (2d) : mp 151°C dec ; ^{1}H NMR δ 1.26 (d, 6H, J = 7 Hz), 2.44 (s, 3H), 2.74 (s, 3H), 3.16 (m, 1H), 3.30 (s, 3H), 3.72 (s, 3H). Anal. Calcd for $C_9H_{19}IN_2S$: C, 34.39 ; H, 6.05 ; I, 40.44 ; N, 8.91 ; S, 10.19. Found : C, 34.59 ; H, 6.31 ; I, 40.11 ; N, 8.87 ; S, 9.99.

DBN-Induced Reaction of Acetamidinium Iodide 2a. DBN (0.87 g, 7 mmol) was added to a solution of **2a** (1.75 g, 5 mmol) in anhyd CH_2Cl_2 (20 mL). The mixture was stirred for 15 min at rt. After removal of the solvent, the residue was treated with Et_2O (70 mL) and washed twice with H_2O. The etheral solution was dried over Na_2SO_4 and concentrated to a syrup. Pyrimidine **5** was isolated by crystallization from petroleum ether (0.3 g, 22 % yield) while acetamidine **6** remained in the filtrate as oily material (0.4 g, 30 % yield). 2-Azavinamidinium iodide **7** (0.31 g, 18 % yield) was extracted with CH_2Cl_2 from the aqueous solution and identified by comparison with an authenticated sample [15]. Elemental analysis could not be obtained for **6** due to decomposition of the sample during the bulb-to-bulb distillation (160°C/0.03 mm Hg).

4-(Dimethylamino)-2,6-diphenylpyrimidine (5) : mp 180°C (MeOH/MeCN) ; ^1H NMR δ 3.16 (s, 6H), 6.67 (s, 1H), 7.35 - 8.65 (m, 10H) ; ^{13}C NMR δ 37.2 (qq, ^1J = 137 Hz, ^3J = 3 Hz), 96.0 (d, ^1J = 163 Hz), 127.1 (dt, ^1J = 159 Hz, ^3J = 7 Hz), 128.1, 128.3, 128.6 (3 dm, ^1J = 160 Hz), 129.8, 130.0 (2 dt, ^1J = 160 Hz, ^3J = 7.5 Hz), 138.8 (m), 138.9 (t, ^3J = 7 Hz), 162.9 (t, ^3J = 3.5 Hz), 163.2, 163.3 (2m) ; MS calcd for $C_{18}H_{17}N_3$ *m/z* 275.1422 ($M^{+\cdot}$), found 275.1425 ; *m/z* (rel int) 275 (84), 260 (91), 246 (100), 232 (27), 129 (19), 128 (48), 104 (40), 102 (65). Anal. Calcd for $C_{18}H_{17}N_3$: C, 78.51 ; H, 6.22 ; N, 15.26. Found : C, 78.54 ; H, 6.60 ; N, 15.17.

N,N-Dimethyl-N'-[bis (methylthio) phenylmethyl] acetamidine (6) : yellowish oil ; ^1H NMR δ 1.79 (s, 3H), 1.85 (s, 6H), 2.90 (s, 6H), 7.10-7.60 (m, 5H) ; ^{13}C NMR δ 13.6 (q, ^1J = 139 Hz), 17.2 (q, ^1J = 128 Hz), 38.2 (qq, ^1J = 137 Hz, ^3J = 3 Hz), 81.9 (m), 126.6 (dt, ^1J = 160 Hz, ^3J = 7.5 Hz), 126.8 (dm, ^1J = 158 Hz), 127.7 (dd, ^1J= 159 Hz, ^3J = 7.5 Hz), 146.2 (t, ^3J = 7.5 Hz), 160.4 (m) ; MS calcd for $C_{12}H_{17}N_2S$ m/z 221.1112 (M^+-MeS), found 221.1108 ; calcd for $C_{11}H_{13}N_2S$ *m/z* 205.0799 (M^+-MeSH-Me), found 205.0811 ; *m/z* (rel int) 221 (21), 205 (100), 173 (13), 121 (35), 103 (27), 102 (14).

3-Aza-4-(dimethylamino)-2-(methylthio)-1,3-pentadiene (8). Salt **2b** (5.72 g, 20 mmol) was treated with DBN (3.70 g, 30 mmol) in 50 mL of anhyd CH_2Cl_2 for 30 min at rt. The solvent was removed under reduced pressure. H_2O (40 mL) was added to the viscous residue then we extracted twice with ether. The etheral phases were combined, dried over Na_2SO_4 and evaporated to give **8** as a colourless oil (2.84 g, 90 % yield). This crude product (purity ≥ 99 %) could be used for cycloaddition reactions without further purification. A sample for analysis was obtained by distillation under vacuum : bp 35-38°C/0.09 mm Hg ; ^1H NMR δ 2.00 (s, 3H), 2.17 (s, 3H), 2.94 (s, 6H), 4.22 (d, 1H, J = 0.4 Hz), 4.25 (d, 1H, J = 0.4 Hz) ; *NOEDIFF experiments* : Selective irradiation on the methylthio group (δ 2.17) produces the enhancement (about 13 %) of the doublet at δ 4.22 (which was attributed to the cis-proton $H_1{}^a$) and causes no significant perturbation of the doublet at δ 4.25 ($H_1{}^b$) ; on the contrary, irradiation on the C-methyl (δ 2.00) causes the enhancement (about 4 %) of the signal at δ 4.25 ; ^{13}C NMR δ 13.9 (q, ^1J = 128 Hz), 15.5 (q, ^1J = 139 Hz), 37.9 (qbr, ^1J = 137 Hz), 91.6 (t, ^1J = 159 Hz), 153.6 (q, ^3J = 4 Hz), 158.7 (m) ; *Heteronuclear decoupling experiments* : irradiation on the methylthio at δ 2.17 collapses the C-2 signal (δ 153.6) to a singlet and irradiation on the dimethylamino at δ 2.94 causes the C-4 signal (δ 158.7) to turn into a quadruplet, revealing the coupling constant ^2J (CCH) to be 5.5 Hz ; MS calcd for $C_7H_{14}N_2S$ *m/z* 158.0878 ($M^{+\cdot}$), found 158.0888 ; *m/z* (rel int) 158 (10), 143 (41), 111 (49), 73 (13), 70 (22), 68 (100), 56 (71). Anal. Calcd for $C_7H_{14}N_2S$: C, 53.16 ; H, 8.86 ; N, 17.72 ; S, 20.25. Found : C, 53.19 ; H, 9.20 ; N, 17.94 ; S, 19.89.

Cycloaddition Reactions of 2-Azadiene 8. General Procedure. A solution of compound **8** (1.58 g, 10 mmol) in CH_2Cl_2 (10 mL) was cooled to 0°C under a dry nitrogen atmosphere. The dienophile (22 mmol for DMAD and PhNCS ; 11 mmol for the others) was added dropwise and the mixture was allowed to warm up to rt until no starting material was detected in the ^1H NMR spectrum (times are indicated in Table 1). The reactional medium was concentrated to dryness in vacuo and the residue was purified by a flash chromatography on silica gel (eluent : Et$_2$O). In the cases of tetrahydropyridines, trituration of the eluate with MeOH (**9**) or Et$_2$O (**10**) gave a solid material which was collected by filtration, whereas **11** and **12** have to be distilled under vacuum. Elemental analyses could not be obtained for **11**, **12** owing to their fast hydrolysis to dihydropyridinones **13**, **14**. Starting from DMAD, the various cycloadducts (pyridines **15**, **16**) and by-products (identified as dimethyl methylthiofumarate and maleate **17** [36] and corresponding enamines **18** [37]) were separated by a second silica gel column chromatography with mixtures of Et$_2$O/petroleum ether (30 : 70 and 70 : 30) as eluents. The pyrimidinethiones **21**, **22** were isolated (and separated from by-products, Me$_2$NC(S)NHPh [38] and MeSC(S)NHPh [39]) by a fractional crystallization from Et$_2$O (yields and ^{13}C NMR spectral data, see Tables 1 and 2).

Dimethyl 6-(Dimethylamino)-6-methyl-2-(methylthio)-3,4,5,6-tetrahydropyridine-4,5-dicarboxylate (9) : mp 97-98°C (MeOH) ; ^{1}H NMR δ 1.29 (s, 3H), 2.31 (s, 3H), 2.37 (s, 6H), 2.39 (dd, 1H, $J\ H_3{}^aH_3{}^b$ = 17.7 Hz, $J\ H_3{}^aH_4$ = 10.4 Hz), 2.67 (dd, 1H, $J\ H_3{}^aH_3{}^b$ = 17.7 Hz, $J\ H_3{}^bH_4$ = 6.5 Hz), 3.12 (d, 1H, $J\ H_4H_5$ = 12.1 Hz), 3.22 (m, 1H, $J\ H_3{}^aH_4$ = 10.4 Hz, $J\ H_3{}^bH_4$ = 6.5 Hz, $J\ H_4H_5$ = 12.1 Hz), 3.69 (s, 3H), 3.72 (s, 3H) ; MS calcd for $C_{13}H_{22}N_2O_4S$ *m/z* 302.1300 (M$^+$), found 302.1303 ; *m/z* (rel int) 302 (16), 287 (39), 271 (13), 255 (100), 198 (19), 195 (36), 158 (23), 143 (53). Anal. Calcd for $C_{13}H_{22}N_2O_4S$: C, 51.66 ; H, 7.28 ; N, 9.27 ; S, 10.60. Found : C, 51.39 ; H, 7.36 ; N, 9.57 ; S, 10.85.

6-(Dimethylamino)-6-methyl-2-(methylthio)-3,4,5,6-tetrahydropyridine-4,5-dicarbonitrile (10) : mp 136°C (CH$_2$Cl$_2$/petroleum ether) ; ^{1}H NMR δ 1.49 (s, 3H), 2.31 (s, 3H), 2.36 (s, 6H), 2.60 (ddd, 1H, $JH_3{}^aH_3{}^b$ = 17.6 Hz, $JH_3{}^aH_4$ = 6.7 Hz, $JH_3{}^aH_5$ = 4.3 Hz), 2.80 (ddd, 1H, $JH_3{}^aH_3{}^b$ = 17.6 Hz, $JH_3{}^bH_4$ = 4.2 Hz, $JH_3{}^bH_5$ = 1.6 Hz), 3.25 (m, 2H) ; MS calcd for $C_{11}H_{16}N_4S$ m/z 236.1096 (M$^+$), found 236.1101 ; m/z (rel int) 236 (28), 221 (16), 192 (15), 189 (48), 158 (57), 143 (79), 111 (100), 110 (73). Anal. Calcd for $C_{11}H_{16}N_4S$: C, 55.93 ; H, 6.78 ; N, 23.72 ; S, 13.56. Found : C, 55.69 ; H, 6.85 ; N, 23.45 ; S, 13.70.

Methyl 6-(Dimethylamino)-6-methyl-2-(methylthio)-3,4,5,6-tetrahydro-pyridine-5-carboxylate (11) : bp 110°C/0.02 mm Hg ; ^{1}H NMR δ 1.28 (s, 3H), 2.00 (m, 2H), 2.28 (s, 3H), 2.30 (m, 2H), 2.32 (s, 6H), 2.92 (dd, 1H, $JH_4{}^aH_5$ = 12 Hz, $JH_4{}^bH_5$ = 4 Hz), 3.68 (s, 3H).

6-(Dimethylamino)-6-methyl-2-(methylthio)-3,4,5,6-tetrahydropyridine-5-carbonitrile (12) : bp 120°C/0.02 mm Hg ; mp 67°C (petroleum ether) ; ^{1}H NMR δ 1.47 (s, 3H), 2.20 (m, 4H), 2.29 (s, 3H), 2.37 (s, 6H),3.02 (dd, 1H, $JH_4{}^aH_5$ = 12 Hz, $JH_4{}^bH_5$ = 4.3 Hz).

Methyl 6-Methyl-1,2,3,4-tetrahydro-2-pyridinone-5-carboxylate (13) : mp 152°C (MeOH) ; ^{1}H NMR δ 2.32 (s, 3H), 2.48 (m, 2H), 2.66 (m, 2H), 3.74 (s, 3H), 9.16 (br, NH) ; ^{13}C NMR δ 18.5 (qd, ^1J = 130 Hz, ^3J = 2.3 Hz), 21.4, 30.2 (2 t m, ^1J = 132 Hz), 51.3 (q, ^1J = 147 Hz), 103.9, 146.3, 167.7, 173.0 (4 m). Anal. Calcd for $C_8H_{11}NO_3$: C, 56.80 ; H, 6.50 ; N, 8.28. Found : C, 56.94 ; H, 6.56 ; N, 8.56.

6-Methyl-1,2,3,4-tetrahydro-2-pyridinone-5-carbonitrile (14) : mp 218°C (MeOH) ; ^{1}H NMR δ 2.20 (s, 3H), 2.65 (m, 4H), 9.12 (br, NH) ; ^{13}C NMR δ 18.7 (qd, ^1J = 130 Hz, ^3J = 2 Hz), 21.6 (tm, ^1J = 135 Hz), 29.1 (tm, ^1J = 131 Hz), 86.3 (m), 117.8 (s), 149.2, 174.4 (2m).

Dimethyl 6-Methyl-2-(methylthio) pyridine-4,5-dicarboxylate (15) : mp 59°C (MeOH) ; ^{1}H NMR δ 2.57 (s, 3H), 2.58 (s, 3H), 3.90 (s, 3H), 3.92 (s, 3H), 7.43 (s, 1H) ; MS calcd for $C_{11}H_{13}NO_4S$ *m/z* 255.0565 (M$^+$), found 255.0563 ; *m/z* (rel int) 255 (100), 254 (32), 224 (20), 209

(19), 119 (46), 116 (27), 113 (16). Anal. Calcd for $C_{11}H_{13}NO_4S$: C, 51.76 ; H, 5.10 ; N, 5.49 ; S, 12.55. Found : C, 51.67 ; H, 5.06 ; N, 5.46 ; S 12.97.

Dimethyl 2-(Dimethylamino)-6-methyl pyridine-4,5-dicarboxylate (16) : mp 64°C (petroleum ether) ; ^{1}H NMR δ 2.53 (s, 3H), 3.12 (s, 6H), 3.83 (s, 3H), 3.87 (s, 3H), 6.58 (s, 1H) ; MS calcd for $C_{12}H_{16}N_2O_4$ *m/z* 252.1110 ($M^{+\cdot}$), found 252.1111 ; *m/z* (rel int) 252 (50), 237 (61), 223 (100), 221 (61), 191 (16), 177 (13). Anal. Calcd for $C_{12}H_{16}N_2O_4$: C, 57.14 ; H, 6.35 ; N, 11.11. Found : C, 57.26 ; H, 6.20 ; N, 11.10.

2-Methyl-6-(methylthio)-3-phenyl-4 (3H)-pyrimidinethione (21) : mp 168°C (MeOH) ; ^{1}H NMR δ 2.20 (s, 3H), 2.48 (s, 3H), 7.22 (m, 2H), 7.28 (s, 1H), 7.53 (m, 3H). Anal. Calcd for $C_{12}H_{12}N_2S_2$: C, 58.06 ; H, 4.83 ; N, 11.29 ; S, 25.80. Found : C, 57.78 ; H, 4.78 ; N, 11.56 ; S, 25.69.

6-(Dimethylamino)-2-methyl-3-phenyl-4 (3H)-pyrimidinethione (22) : mp 225°C (CH_2Cl_2/petroleum ether) ; ^{1}H NMR δ 2.15 (s, 3H), 3.12 (br, 6H), 6.75 (s, 1H), 7.21 (m, 2H), 7.50 (m, 3H). Anal. Calcd for $C_{13}H_{15}N_3S$: C, 63.67 ; H, 6.12 ; N, 17.14 ; S, 13.06. Found : C, 63.32 ; H, 6.01 ; N, 17.16 ; S, 13.34.

Oxidation and Hydrolysis of Tetrahydropyridine 9. The solid **9** (0.9 g, 3 mmol) was maintained without solvent under atmospheric O_2 for about one month to afford a white powder which was analyzed by ^{1}H NMR (**15**/**20**, 50 : 50). Recrystallization of this material from MeOH gave a pure sample of hydrolyzed product **20** (0.24 g, 35 % yield).

Dimethyl 6-Methyl-1,2,3,4-tetrahydro-2-pyridinone-4,5-dicarboxylate (20) : mp 165°C ; ^{1}H NMR δ 2.37 (s, 3H), 2.68 (dd, 1H, $J_{H_{3}^{a}H_{3}^{b}}$ = 16.8 Hz, $J_{H_{3}^{a}H_4}$ = 7.8 Hz), 2.87 (dd, 1H, $J_{H_{3}^{a}H_{3}^{b}}$ = 16.8 Hz, $J_{H_{3}^{b}H_4}$ = 2.4 Hz), 3.70 (s, 3H), 3.76 (s, 3H), 3.95 (dd, 1H, $J_{H_{3}^{a}H_4}$ = 7.8 Hz, $J_{H_{3}^{b}H_4}$ = 2.4 Hz), 9.06 (br, NH) ; ^{13}C NMR δ 19.0 (qd, ^1J = 130 Hz, ^3J = 2 Hz), 32.7 (ddt, ^1J = 128 and 138 Hz, ^3J =4 Hz), 38.3 (dt, ^1J = 137 Hz, ^2J = 3.5 Hz), 51.6, 52.6 (2q, ^1J = 147 Hz), 102.0, 148.2, 166.8, 170.8, 172.7 (5m) ; MS calcd for $C_{10}H_{13}NO_5$ *m/z* 227.0794 ($M^{+\cdot}$), found 227.0798 ; *m/z* (rel int) 227 (13), 168 (100), 136 (46). Anal. Calcd for $C_{10}H_{13}NO_5$: C, 52.86 ; H, 5.73 ; N, 6.17. Found : C, 52.82 ; H, 5.88 ; N, 6.32.

3-Aza-2-(dimethylamino)-4-(methylthio)-2,4-hexadiene (23). The procedure was identical with that described for the preparation of **8**. Salt **2c** (6 g, 20 mmol) was deprotonated by DBN (3.70 g, 30 mmol) in 50 mL of CH_2Cl_2 at rt for 30 min. ^{1}H NMR analysis of the crude oily product (3.27 g, 95 % yield) showed the formation of **23a**, **23b** in the ratio 60 : 40. After the mixture was maintained at rt for 48 h in CH_2Cl_2 solution or without any solvent, a second NMR analysis revealed the ratio to get 83 : 17. These isomers were hydrolyzed by a silica gel column chromatography and could not be separated by a bulb-to-bulb distillation under reduced pressure : bp 80°C//0.03 mm Hg. Anal. Calcd for $C_8H_{16}N_2S$: C, 55.81 ; H, 9.30 ; N, 16.28 ; S, 18.60. Found : C, 56.01 ; H, 9.30 ; N, 16.26 ; S, 18.35. *Major isomer* (**23a**) : ^{1}H NMR δ 1.44 (d, 3H, J = 6.7 Hz), 1.88 (s, 3H), 2.14 (s, 3H), 2.97 (s, 6H), 4.77 (q, 1H, J = 6.7 Hz) ; *NOE experiment* : Selective irradiation on the methylthio group (δ 2.14) produces the enhancement (17 %) of the quadruplet at δ 4.77 (cis-proton H_5) ; on the contrary, irradiation on the methyl at δ 1.88 and irradiation on the NMe_2 (δ 2.97) cause no significant perturbation of the signals at δ 1.44, 4.77 ; ^{13}C NMR δ 12.8 (qd, ^1J = 126 Hz, ^2J = 3.5 Hz), 14.3 (q, ^1J = 128 Hz), 14.8 (q, ^1J = 139 Hz), 38.0 (qq, ^1J = 137 Hz, ^3J = 3 Hz), 103.6 (dq, ^1J = 158 Hz, ^2J = 7 Hz), 143.2, 158.6 (2m) ; *Selective decoupling experiments* : irradiation on the methylthio protons (δ 2.14) reduces the corresponding carbon signal (δ 14.8) to a singlet and the C-4 signal (δ 143.2) to a quadruplet (J_{CCCH} = 4 Hz) ; irradiation on the methyl at δ 1.88 collapses the C-1 signal (δ 14.3) to a singlet. *Minor isomer* (**23b**) : ^{1}H NMR δ 1.70 (d, 3H, J = 6.9 Hz), 1.95 (s, 3H), 2.05 (s, 3H), 2.95 (s, 6H), 4.69 (q, 1H, J = 6.9 Hz) ; *NOE experiment* : Selective irradiation on the methyl on C-2 (δ 1.95) produces the enhancement (10 %) of the quadruplet at δ 4.69 (trans-proton H_5) ; irradiations on the methylthio (δ 2.05) and NMe_2 groups (δ 2.95) cause no perturbation of this quadruplet (as precedently, NMR signals were assigned by heteronuclear decoupling experiments) ; ^{13}C NMR δ 13.2 (q, ^{1}J = 140 Hz), 13.6 (qd, ^{1}J = 126 Hz, ^{2}J = 3.5Hz), 14.4 (q, ^{1}J = 128 Hz),38.0 (qq, ^{1}J = 137 Hz, ^{3}J = 3 Hz), 106.2 (dq, ^{1}J = 155 Hz, ^{2}J = 7 Hz), 142.6, 158.9 (2m).

Cycloaddition reactions of 2-azadienes mixture 23a and 23b. The procedure was identical with that described for the reactions of **8** (conditions are indicated in Table 1). After evaporation of the solvent the residue was treated in the same way. Yields of Table 1 refer to isolated compounds, purified either by crystallization from Me OH (**24, 28, 30**), from Et_2O (**25, 27**) or by a bulb-to-bulb distillation (**26**) (^{13}C NMR spectra, see Table 2). The acetamidine **29** was identified by comparison with an authenticated sample prepared by condensation of aniline with the dimethylacetamide dimethyl acetal.

Dimethyl 3,6-Dimethyl-6-(dimethylamino)-2-(methylthio)-3,4,5,6-tetrahydropyridine-4,5-dicarboxylate (24): mp 113°C (MeOH) ; ^{1}H NMR δ 1.10 (d, 3H, J = 7.3 Hz), 1.27 (s, 3H), 2.29 (s, 3H), 2.37 (s, 6H), 2.76 (qd, 1H, J = 7.3 Hz, JH_3H_4 = 4.9 Hz), 3.25 (dd, 1H, JH_4H_5 = 12.6 Hz, JH_3H_4 = 4.9 Hz), 3.29 (d, 1H, JH_4H_5 = 12.6 Hz), 3.70 (s, 3H), 3.72 (s, 3H) ; MS calcd for $C_{14}H_{24}N_2O_4S$ m/z 316.1457 (M^{+}), found 316.1466 ; m/z (rel int) 316 (14), 301 (18), 285 (14), 270 (12), 269 (100), 209 (36), 172 (61), 157 (33), 143 (33). Anal. Calcd for $C_{14}H_{24}N_2O_4S$: C, 53.16 ; H, 7.59 ; N, 8.86 ; S, 10.13. Found : C, 53.39 ; H, 7.70 ; N, 8.73 ; S, 10.09.

3,6-Dimethyl-6-(dimethylamino)-2-(methylthio)-3,4,5,6-tetrahydro-pyridine-4,5-dicarbonitrile (25) : mp 150°C (CH_2Cl_2/petroleum ether) ; ^{1}H NMR δ 1.46 (d, 3H, J = 7.4 Hz), 1.52 (s, 3H), 2.28 (s, 3H), 2.35 (s, 6H), 2.75 (qdd, 1H, J = 7.4 Hz, JH_3H_4 = 3.9 Hz, JH_3H_5 = 0.7 Hz), 3.35 (dbr, 1H, JH_4H_5 = 12.6 Hz), 3.39 (dd, 1H, JH_4H_5 = 12.6 Hz, JH_3H_4 = 3.9 Hz) ; MS calcd for $C_{12}H_{18}N_4S$ m/z 250.1252 (M^{+}), found 250.1245 ; m/z (rel int) 250 (5), 235 (19), 207 (13), 203 (44), 172 (88), 157 (55), 148 (13), 129 (14), 126 (65), 125 (80), 110 (100). Anal. Calcd for $C_{12}H_{18}N_4S$: C, 57.60 ; H, 7.20 ; N, 22.40 ; S, 12.80. Found : C, 57.35 ; H, 7.19 ; N, 22.29 ; S, 12.50.

Methyl 3,6-Dimethyl-6-(dimethylamino)-2-(methylthio)-3,4,5,6-tetrahydropyridine-5-carboxylate (26) : bp 115°C/0.025 mm Hg ; ^{1}H NMR δ 1.25 (d, 3H, J = 7.4 Hz), 1.30 (s, 3H), 1.59 (ddd, 1H, $JH_4{}^aH_4{}^b$ = 13.8 Hz, $JH_4{}^aH_5$ = 3.5 Hz, $JH_3H_4{}^a$ = 1.6 Hz), 2.24 (ddd, 1H, $JH_4{}^aH_4{}^b$ = 13.8 Hz, $JH_4{}^bH_5$ = 13.1 Hz, $JH_3H_4{}^b$ = 6.5 Hz), 2.27 (s, 3H), 2.36 (s, 6H), 2.45 (m, 1H), 3.05 (dd, 1H, $JH_4{}^bH_5$ = 13.1 Hz, $JH_4{}^aH_5$ = 3.5 Hz), 3.69 (s, 3H). Anal. Calcd for $C_{12}H_{22}N_2O_2S$: C, 55.81 ; H, 8.52 ; N, 10.85 ; S, 12.40. Found : C, 55.75 ; H, 8.68 ; N, 10.81 ; S, 12.63.

3,6-Dimethyl-6-(dimethylamino)-2-(methylthio)-3,4,5,6-tetrahydro-pyridine-5-carbonitrile (27) : mp 80°C (petroleum ether) ; ^{1}H NMR δ 1.26 (d, 3H, J = 7.4 Hz), 1.47 (s, 3H), 1.92 (ddd, 1H, $JH_4{}^aH_4{}^b$ = 13.6 Hz, $JH_4{}^aH_5$ = 3.8 Hz, $JH_3H_4{}^a$ = 2.1Hz), 2.21 (ddd, 1H, $JH_4{}^aH_4{}^b$ = 13.6 Hz, $JH_4{}^bH_5$ = 12.5 Hz, $JH_3H_4{}^b$ = 6.5 Hz), 2.26 (s, 3H), 2.35 (s, 6H), 2.47 (qdd, 1H, J = 7.4 Hz, $JH_3H_4{}^b$ = 6.5 Hz, $JH_3H_4{}^a$ = 2.1 Hz), 3.14 (dd, 1H, $JH_4{}^bH_5$ = 12.5 Hz, $JH_4{}^aH_5$ = 3.8 Hz). Anal. Calcd for $C_{11}H_{19}N_3S$: C, 58.66 ; H, 8.44 ; S, 14.22. Found : C, 58.23 ; H, 8.53 ; S, 14.11.

Dimethyl 3,6-Dimethyl-2-(methylthio) pyridine-4,5-dicarboxylate (28) : mp 56°C (MeOH) ; ^{1}H NMR δ 2.20 (s, 3H) ; 2.57 (s, 3H) ; 2.67 (s, 3H) ; 3.85 (s, 3H) ; 3.90 (s, 3H). MS calcd for $C_{12}H_{15}NO_4S$ m/z 269.0722 (M^{+}), found 269.0707 ; m/z (rel int) 269 (100), 254 (16), 238 (25), 236 (62), 210 (15), 204 (23). Anal. Calcd for $C_{12}H_{15}NO_4S$: C, 53.53 ; H, 5.58 ; N, 5.20 ; S, 11.90. Found : C, 53.26 ; H, 5.69 ; N, 5.19 ; S, 12.06.

N,N-Dimethyl-N'-phenyl acetamidine (29) : bp 85°C/0.02 mm Hg ; ^1H NMR δ 1.83 (s, 3H), 2.96 (s, 6H), 6.68 (d, 2H, *J* = 8 Hz), 6.90 (t, 1H, *J* = 8 Hz), 7.20 (t, 1H, *J* = 8 Hz) ; ^{13}C NMR δ 14.8 (q, ^1J = 128 Hz), 37.8 (qq, ^1J = 137 Hz, ^3J = 3.5 Hz), 121.2 (dt, ^1J = 161 Hz, ^3J = 7.5 Hz), 122.4 (dm, ^1J = 156 Hz), 128.6 (dd, ^1J = 158 Hz, ^3J = 8 Hz), 152.3 (tm, ^3J = 8.5 Hz), 157.1 (m).

2,5-Dimethyl-6-(methylthio)-3-phenyl-4 (3H)-pyrimidinethione (30) : mp 162°C (MeOH) ; ^1H NMR δ 2.22 (s, 3H), 2.40 (s, 3H), 2.56 (s, 3H), 7.16 (m, 2H), 7.53 (m, 3H). MS calcd for $C_{13}H_{14}N_2S_2$ *m/z* 262.0598 ($M^{+\cdot}$), found 262.0588 ; *m/z* (rel int) 262 (100), 261 (27), 247 (13), 229 (41), 173 (14), 171 (26). Anal. Calcd for $C_{13}H_{14}N_2S_2$: C, 59.54 ; H, 5.34 ; N, 10.69 ; S, 24.43. Found : C, 59.86 ; H, 5.30 ; N, 10.52 ; S, 24.14.

3-Aza-2-(dimethylamino)-5-methyl-4-(methylthio)-2,4-hexadiene (31). By the above-mentioned procedure, salt **2d** (6.28 g, 20 mmol) was treated with an excess of DBN at rt for 30 min. After removal of the solvent, the residue was worked in similar conditions to give **31** as a crude oil of good purity (3.53 g, 95 % yield) : bp 80°C/0.03 mm Hg (bulb-to-bulb distillation) ; ^1H NMR δ 1 .48 (s, 3H), 1.82 (s, 3H), 1.85 (s, 3H), 2.04 (s, 3H), 3.00 (s, 6H). Anal. Calcd for $C_9H_{18}N_2S$: C, 58.06 ; H, 9.67 ; N, 15.05 ; S, 17.20. Found : C, 57.97 ; H, 9.69 ; N, 15.03 ; S, 17.28.

Reactions of 2-azadiene 31.DMAD or methyl propiolate (15 mmol) was added to a solution of **31** (1.86 g, 10 mmol) in dry CH_2Cl_2 (10 mL). The mixture was maintained at rt for 4 h or 40 h, respectively. The dihydropyridines were isolated according to usual conditions, by crystallization from Et_2O (**33**) or by a bulb-to-bulb distillation under reduced pressure (**34**) (yields are indicated in Table 1).

Methyl 2-(Dimethylamino)-1-[2-methyl-1-(methylthio)-1-propenyl]-4-oxo-1,4-dihydropyridine-6-carboxylate (33) : mp 128°C (CH_2Cl_2/petroleum ether) ; ^1H NMR δ 1.80 (s, 3H) ; 1.88 (s, 3H), 2.12 (s, 3H), 3.12 (s, 6H), 3.70 (s, 3H), 4.80 (s, 1H), 5.96 (s, 1H) ; ^{13}C NMR δ 13.8 (q, ^1J = 140 Hz), 21.2, 21.6 (2 qq, ^1J = 127 Hz, ^3J = 4 Hz), 40.9 (qq, ^1J = 139 Hz, ^3J = 2.5 Hz), 51.9 (q, ^1J = 147 Hz), 84.6 (d, ^1J = 175 Hz), 98.9 (d, ^1J = 164 Hz), 125.5, 139.2 (2m), 142.7 (d, ^2J = 7 Hz), 166.1 (q, ^3J =4 Hz), 169.1 (m), 179.5 (dd, ^2J = 4.5 and 1.5 Hz). Anal. Calcd for $C_{14}H_{20}N_2O_3S$: C, 56.75 ; H, 6.75 ; N, 9.46 ; S, 10.81 Found : C, 56.77 ; H, 6.78 ; N, 9.64 ; S, 10.82.

Methyl 6-(Dimethylamino)-2-(methylthio)-3,3,6-trimethyl-3,6-dihydro-pyridine-5-carboxylate (34) : bp 100°C/0.02 mm Hg ; mp 45°C ; ^1H NMR δ 1.28 (s, 3H), 1.33 (s, 3H), 1.52 (s, 3H), 2.26 (s, 6H), 2.30 (s, 3H), 3.76 (s, 3H), 6.46 (s, 1H) ; ^{13}C NMR, Table 2. Anal. Calcd for $C_{13}H_{22}N_2O_2S$: C, 55.77 ; H, 8.14 ; N, 10.37 ; S, 11.85. Found : C, 55.84 ; H, 8.25 ; N, 10.44 ; S, 11.73.

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(17) All these experimental results clearly disagree with the spectra that would be expected for the isomeric 3-aza-2-(dimethylamino)-4-(methylthio)-1,3-pentadiene (type **B** compound). The exclusive formation of heterodiene **8** was perhaps under a thermodynamic control [8a]. We remark effectively that introduction of a dimethylamino group on C-1 stabilizes the conjugated 2-azabutadiene **8** which can be readily isolated contrary to heterodiene **3**.

(18) Although the exact structure of **8** cannot be asserted with certainty, the suggested *E* configuration and relative increased population of the s-cisoid versus s-transoid conformation for this azadiene system in solution have some literature precedent in closely related α,β-unsaturated amidines [10a]. See also ref. (29).

(19) Full details of the X-ray structure determination have been deposited with the Cambridge Crystallographic Data Centre and can be obtained, on request, from the Director, 12 Union Road, Cambridge, CB2 1EZ, U.K..

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(31) For example, addition of fumaronitrile to a 75:25 mixture of **23a/23b** (CH_2Cl_2, rt, 1 h) produced the single cycloadduct **25** in 70 % yield. **23b** was entirely consumed and we detected only **23a** as residual diene. Use of dimethyl fumarate with a 60:40 mixture of stereoisomers allowed similar observations at rt. These results demonstrate that the equilibration between **23a**, **23b** was slower than the cycloaddition of isomer **23b**.

(32) One of the referees has suggested that the undesirable formation of acetamidine **29** presumably took place by a [2+2] cycloaddition reaction between the carbon-nitrogen double bonds of azadiene and isothiocyanate, followed by a retroaddition process.

(33) It is possible that the primary cycloadducts in the cases of DMAD and PhNCS suffer rapid dimethylamino elimination so as to relieve steric hindrance thus precluding allylic migration to occur.

(34) C-Michael addition has been mentioned in the case of DMAD and s-trans 2-aza-1-(dimethylamino)-1-phenyl-1,3-pentadiene (*E,E* and *E,Z* mixture) [31].

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