

Cyrille Landreau, David Deniaud, Alain Reliquet,
Françoise Reliquet and Jean Claude Meslin*Laboratoire de Synthèse Organique, UMR CNRS 6513, Faculté des Sciences et des Techniques,
BP 92208, 2, rue de la Houssinière, F44322 Nantes Cedex 03 France.

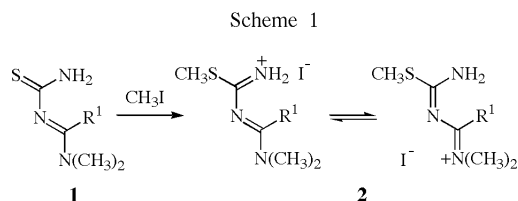
Received May 11, 2000

Triazapentadienium iodides **2** prepared from *N'*-thiocarbamoylformamidines **1** are efficient intermediates in heterocyclic synthesis. They react with ketenes, sulfenes, phenyl isocyanate or isothiocyanate and dimethyl acetylenedicarboxylate affording the corresponding dihydropyrimidinones **3**, thiadiazinedioxides **5**, triazinones **6**, triazinethiones **7** and pyrimidines **9**.

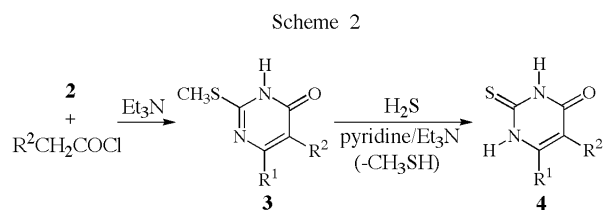
J. Heterocyclic Chem., **38**, 93 (2001).

The synthetic value of 1,3-diazadienes in heterocyclic chemistry has been widely demonstrated [1]. During the last fifteen years [4 + 2] cycloaddition reactions of acyclic 1,3-diazadienes, especially with ketenes, have been studied giving rise to various dihydropyrimidines [2-9].

The problems encountered in the preparation of stable 1-substituted-1,3-diazadienes were recently solved by the use of cationic precursors [10].



We report here the reactivity of triazadienium iodides **2** in [4 + 2] cycloaddition reactions affording methylsulfanyldihydropyrimidinones **3** and thioxotetrahydropyrimidinones **4**, thiadiazinedioxides **5**, triazinones **6**, triazinethiones **7** and pyrimidines **9**.



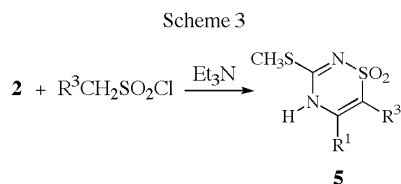
Compound	R ¹	R ²	Yield (%)	Mp (°C)
3a	H	CO ₂ CH ₃	82	205
3b [18]	H	CO ₂ C ₂ H ₅	63	133
3c	CH ₃	CO ₂ CH ₃	84	179
3d	CH ₃	CO ₂ C ₂ H ₅	84	149
3e	CH ₃	C ₆ H ₅	97	196
4a	H	CO ₂ CH ₃	72	181
4b [19]	H	CO ₂ C ₂ H ₅	77	244
4c	CH ₃	CO ₂ CH ₃	90	232
4d	CH ₃	CO ₂ C ₂ H ₅	97	211
4e [20]	CH ₃	C ₆ H ₅	98	289

These types of compounds exhibit important pharmacological potential. Recently *S*-alkylsulfanylpurimidine and *S*-alkylsulfanylpurimidinone derivatives have been identified as highly specific reverse transcriptase inhibitors of human immunodeficiency virus type 1 [11,12]. Thioxo derivatives showed a diverse range of biological properties such as hyperthyroidism treatment, anticarcinogenic, cardiovascular and antihypertensive activities [13-14]. To our knowledge, only few monocyclic thiadiazinedioxides were previously reported [10,15] even though fused pyrido derivatives were found to be important in several pharmacological fields [16].

We have prepared *N'*-thiocarbamoylformamidines **1** following Brederick procedure [17]. Subsequent alkylation using methyl iodide led to *S*-methyl salts **2** in high yields (Scheme 1).

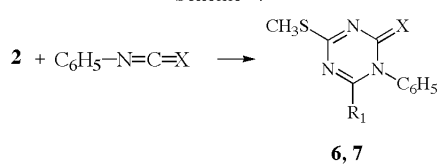
Ketenes were prepared *in situ* from acid chlorides (methyl or ethyl malonyl chloride, phenylacetyl chloride) and reacted with *S*-methyl iodides **2** to give the corresponding dihydropyrimidinones **3**. The [4 + 2] cycloaddition proceeded smoothly and was followed by loss of dimethylamine. Addition of triethylamine was necessary to neutralize the two equivalents of the hydracids generated in these reactions.

Then the methylsulfanylimine group of compounds **3** was eliminated by treatment with hydrogen sulfide to yield thioxotetrahydropyrimidinones **4** (Scheme 2).



Compound	R ¹	R ³	Yield %	Mp (°C)
5a	H	H	46	144
5b	H	CH ₃	86	221
5c	H	C ₆ H ₅	77	149
5d	CH ₃	H	69	223-225
5e	CH ₃	CH ₃	39	206
5f	CH ₃	C ₆ H ₅	66	>300

Scheme 4

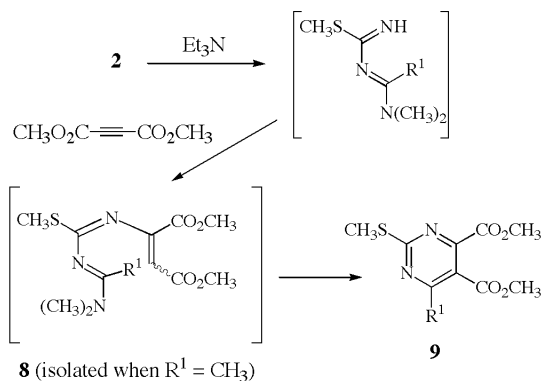


Compound	R^1	X	Yield (%)	Mp ($^\circ\text{C}$)
6a	H	O	55	160
6b	CH_3	O	92	143
7a	H	S	80	228
7b	CH_3	S	83	136-137

Sulfenes prepared from the corresponding sulfonic acid chlorides (mesyl chloride, ethanesulfonyl chloride, α -toluenesulfonyl chloride) reacted readily with salts **2**, using the same conditions (*vide supra*), to afford 2H-1,2,4-thiadiazine-1,1-dioxides **5** (Scheme 3).

A cyclization reaction took place with compounds **2** in the presence of phenyl isocyanate or phenyl isothiocyanate resulting in the formation of triazin-2(1H)-ones **6** and triazin-2(1H)-thiones **7** respectively in good yields (Scheme 4).

Scheme 5



Compound	R^1	Yield (%)	Mp ($^\circ\text{C}$)
9a [21]	H	48	133
9b	CH_3	63	oil

The reaction of salts **2** with dimethyl acetylenedicarboxylate afforded 2-methylsulfanylpurimidines **9**. Starting from **2b**, we have isolated a rather unstable intermediate compound **8** identified as a linear adduct between the unsubstituted imine group of the diazadiene and the triple bond of the acetylenic reagent. A ring closure of intermediate **8** followed by the loss of dimethylamine provided pyrimidine **9b** on heating at 110° for 18 hours (Scheme 5).

Although most of our compounds were expected to be generated by a classical Diels-Alder cycloaddition, the later result indicated obviously that in this case the

operative pathway to afford the heterocyclic products is an addition reaction followed by an intramolecular Diels-Alder cyclization.

In summary, we have demonstrated the ability of triazapentadienium salts **2** to undergo annulation reactions under rather mild conditions providing an efficient synthetic method for the preparation of various pyrimidine derivatives. Moreover reactions with sulfenes afforded novel 4H-1,2,4-thiazine-1,1-dioxides in satisfactory yields.

EXPERIMENTAL

All reagents were purchased from Acros Organics and Aldrich. Elemental analyses were performed by the C.N.R.S. Analysis Laboratory (Vernaison). Column chromatography was conducted on silica gel 60 (40-63 μm), available from E. Merck. Thin layer chromatography was performed on 0.5 mm x 20 cm x 20 cm E. Merck silica gel plate (60 F-254). Melting points measured using a Reichert microscope are uncorrected. The ^{13}C and ^1H -nmr spectra were recorded at room temperature using a BRUKER AC200 at 50 and 200 MHz respectively. Chemical shifts (δ) are given in ppm downfield from tetramethylsilane as internal standard. Mass spectra were determined with a Hewlett Packard 5989 spectrometer. The ir spectra were obtained using a BRUKER Vector22 spectrometer.

General Procedure for the Reaction of Thiourea with Amide Dimethyl Acetals.

N,N-Dimethyl formamide dimethyl acetal (for **1a**, 13 mmoles) or *N,N*-dimethyl acetamide dimethyl acetal (for **1b**, 13 mmoles) was added to a suspension of thiourea (10 mmoles) in methanol (for **1a**, 10 ml) or methylene chloride (for **1b**, 10 ml). The mixture was heated under reflux for 4 hours. The solvent was removed and the residue was crystallized from methanol (for **1a**) or diethyl ether (for **1b**).

2-Amino-4-dimethylamino-1,3-thiazabuta-1,3-diene (**1a**).

This compound was obtained in 70% yield, mp 165° [17].

2-Amino-4-dimethylamino-1,3-thiazapenta-1,3-diene (**1b**).

This compound was obtained in 76% yield, mp $128\text{-}130^\circ$; ir (potassium bromide): ν_{max} 3278, 3123, 1583, 1366 cm^{-1} ; ^1H nmr (hexadeuteriodimethylsulfoxide): δ 2.17 (s, 3H, CH_3), 2.93 (s, 6H, $\text{N(CH}_3)_2$), 7.66 and 8.05 (2s, 2H, 2NH); ^{13}C nmr (hexadeuteriodimethylsulfoxide): δ 16.5 (CH_3), 37.9 ($\text{N(CH}_3)_2$), 159.0 (CCH_3), 194.0 (CS); ms: m/z 145 (M^+), 129 ($\text{M}^+ - \text{NH}_2$), 112 ($\text{M}^+ - \text{SH}$).

Anal. Calcd. for $\text{C}_5\text{H}_{11}\text{N}_3\text{S}$: C, 41.35; H, 7.63; N, 28.94. Found: C, 41.05; H, 7.72; N, 29.16.

General Procedure for Addition of Methyl Iodide on Thiazadienes **1**.

A suspension of thiazadiene **1** (5 mmoles) in methyl iodide (4 ml) and tetrahydrofuran (4 ml) was stirred for 18 hours at room temperature. The mixture was evaporated under reduced pressure. After addition of diethyl ether (40 ml), compounds **2** were precipitated and collected by filtration.

1,1-Dimethyl-4-methylsulfanyl-1,3,5-triazapentadienium Iodide (2a).

This compound was prepared from **1a** in 98% yield, mp 148°; ir (potassium bromide): ν max 3232, 3070, 1624, 1521 cm^{-1} ; ^1H nmr (hexadeuteriodimethylsulfoxide): δ 2.55 (s, 3H, SCH_3), 3.11 and 3.27 (2s, 6H, $\text{N}(\text{CH}_3)_2$), 8.39 (s, 1H, CH), 9.53 (s, 2H, NH_2); ^{13}C nmr (hexadeuteriodimethylsulfoxide): δ 14.4 (SCH_3), 35.9 and 41.9 ($\text{N}(\text{CH}_3)_2$), 158.7 (CH), 178.2 (CS).

Anal. Calcd. for $\text{C}_5\text{H}_{12}\text{IN}_3\text{S}$: C, 21.99; H, 4.43; N, 15.38. Found: C, 21.71; H, 4.60; N, 15.55.

1,1,2-Trimethyl-4-methylsulfanyl-1,3,5-triazapentadienium Iodide (2b).

This compound was prepared from **1b** in 95% yield, mp 180°; ir (potassium bromide): ν max 3258, 3108, 1629, 1569 cm^{-1} ; ^1H nmr (hexadeuteriodimethylsulfoxide): δ 2.29 (s, 3H, CH_3), 2.41 (s, 3H, SCH_3), 3.13 and 3.23 (2s, 6H, $\text{N}(\text{CH}_3)_2$), 9.01 (s, 2H, NH_2); ^{13}C nmr (hexadeuteriodimethylsulfoxide): δ 14.3 (SCH_3), 18.5 (CH_3), 39.2 and 39.8 ($\text{N}(\text{CH}_3)_2$), 166.4 (CCH_3), 172.0 (CS).

Anal. Calcd. for $\text{C}_6\text{H}_{14}\text{IN}_3\text{S}$: C, 25.10; H, 4.91; N, 14.63. Found: C, 24.88; H, 5.04; N, 14.61.

General Procedure for the Reaction Between Triazapentadienium Iodides **2** and Acyl Chlorides or Sulfonyl Chlorides.

To a solution of iodide **2** (2 mmoles) in dry methylene chloride (10 ml), acyl chloride (for **3**, 2.4 mmoles) or sulfonyl chloride (for **5**, 2.4 mmoles) was added under a nitrogen atmosphere. The mixture was stirred for 4 hours at room temperature, cooled to 0° then triethylamine (4.8 mmoles) was added. The reaction mixture was stirred overnight. The solvent was removed and the residue was purified by flash chromatography (silica gel, methylene chloride/ethyl acetate 9/1). Products **3** and **5** were crystallized from appropriate solvents.

5-Methoxycarbonyl-2-methylsulfanylpurimidin-4(3H)-one (3a).

This compound was prepared from **2a** and methyl malonyl chloride in 82% yield, mp 205° (from diethyl ether); ir (potassium bromide): ν max 1741, 1651 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 2.60 (s, 3H, SCH_3), 3.97 (s, 3H, OCH_3), 8.75 (s, 1H, CH), (NH, exchange); ^{13}C nmr (deuteriochloroform): δ 13.0 (SCH_3), 51.6 (OCH_3), 111.5 (CCO), 158.0 (NCH), 159.0, 164.1 and 168.1 (SCN and 2CO); ms: m/z 200 (M^+), 168 ($\text{M}^+ - \text{CH}_3\text{OH}$), 112.

Anal. Calcd. for $\text{C}_7\text{H}_8\text{N}_2\text{O}_3\text{S}$: C, 41.99; H, 4.03; N, 13.99. Found: C, 42.23; H, 3.97; N, 14.27.

5-Ethoxycarbonyl-2-methylsulfanylpurimidin-4(3H)-one (3b).

This compound was prepared from **2a** and ethyl malonyl chloride in 63% yield, mp 133° (from diethyl ether) [18].

5-Methoxycarbonyl-6-methyl-2-methylsulfanylpurimidin-4(3H)-one (3c).

This compound was prepared from **2b** and methyl malonyl chloride in 84% yield, mp 179° (from diethyl ether); ir (potassium bromide): ν max 1734, 1635 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 2.57 and 2.58 (2s, 6H, CH_3 and SCH_3), 3.97 (s, 3H, OCH_3), 12.34 (broad s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ 13.6 (SCH_3), 24.2 (CH_3), 52.6 (OCH_3), 110.2 (CCO), 164.6, 166.8, 167.2 and 167.4 (CCH_3 , SCN and 2CO); ms: m/z 214 (M^+), 182 ($\text{M}^+ - \text{CH}_3\text{OH}$), 126.

Anal. Calcd. for $\text{C}_8\text{H}_{10}\text{N}_2\text{O}_3\text{S}$: C, 44.85; H, 4.70; N, 13.08. Found: C, 45.17; H, 4.50; N, 13.35.

5-Ethoxycarbonyl-6-methyl-2-methylsulfanylpurimidin-4(3H)-one (3d).

This compound was prepared from **2b** and ethyl malonyl chloride in 84% yield, mp 149° (from diethyl ether); ir (potassium bromide): ν max 1734, 1635 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 1.42 (t, 3H, $J = 7.2$ Hz, CH_2CH_3), 2.57 and 2.58 (2s, 6H, SCH_3 and CH_3), 4.43 (q, 2H, $J = 7.2$ Hz, CH_2CH_3), (NH, exchange); ^{13}C nmr (deuteriochloroform): δ 13.6 (SCH_3), 14.2 (CH_2CH_3), 24.2 (CCH_3), 61.9 (CH_2CH_3), 110.0 (CCO), 165.1 and 167.1 (CCH_3 , SCN and 2CO); ms: m/z 228 (M^+), 182 ($\text{M}^+ - \text{C}_2\text{H}_5\text{OH}$), 126.

Anal. Calcd. for $\text{C}_9\text{H}_{12}\text{N}_2\text{O}_3\text{S}$: C, 47.36; H, 5.30; N, 12.27. Found: C, 47.51; H, 5.03; N, 12.42.

6-Methyl-2-methylsulfanyl-5-phenylpyrimidin-4(3H)-one (3e).

This compound was prepared from **2b** and phenylacetyl chloride in 97% yield, mp 196° (from diethyl ether); ir (potassium bromide): ν max 1646 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 2.20 (s, 3H, CH_3), 2.55 (s, 3H, SCH_3), 7.25-7.47 (m, 5H, C_6H_5), 10.27 (broad s, 1H, NH); ^{13}C nmr (hexadeuteriodimethylsulfoxide): δ 12.7 (SCH_3), 22.4 (CCH_3), 120.2 (CC_6H_5), 127.2, 128.0 and 130.3 (SCHAR), 134.3 (Car), 148.0 (CCH_3), 159.6 and 162.2 (SCN and CO); ms: m/z 232 (M^+).

Anal. Calcd. for $\text{C}_{12}\text{H}_{12}\text{N}_2\text{OS}$: C, 62.05; H, 5.21; N, 12.06. Found: C, 61.96; H, 5.18; N, 12.01.

3-Methylsulfanyl-4H-1,2,4-thiadiazine-1,1-dioxide (5a).

This compound was prepared from **2a** and methanesulfonyl chloride in 46% yield, mp 144° (from methylene chloride); ir (potassium bromide): ν max 1646, 1570, 1258, 1119 cm^{-1} ; ^1H nmr (hexadeuteriodimethylsulfoxide): δ 2.42 (s, 3H, SCH_3), 6.26 (d, 1H, $J = 8.6$ Hz, SO_2CH), 7.01 (d, 1H, $J = 8.6$ Hz, NCH), 11.71 (broad s, 1H, NH); ^{13}C nmr (hexadeuteriodimethylsulfoxide): δ 13.8 (SCH_3), 103.5 (SO_2CH), 132.6 (NCH), 160.9 (SCN); ms: m/z 178 (M^+), 114 ($\text{M}^+ - \text{SO}_2$), 81, 74.

Anal. Calcd. for $\text{C}_4\text{H}_6\text{N}_2\text{O}_2\text{S}_2$: C, 26.96; H, 3.39; N, 15.72. Found: C, 30.21; H, 3.51; N, 15.55.

6-Methyl-3-methylsulfanyl-4H-1,2,4-thiadiazine-1,1-dioxide (5b).

This compound was prepared from **2a** and ethanesulfonyl chloride in 86% yield, mp 221° (from diethyl ether); ir (potassium bromide): ν max 1660, 1574, 1515, 1279, 1132 cm^{-1} ; ^1H nmr (hexadeuteriodimethylsulfoxide): δ 1.96 (d, 3H, $J = 1.2$ Hz, CH_3), 2.41 (s, 3H, SCH_3), 6.84 (q, 1H, $J = 1.2$ Hz, CH), 11.69 (broad s, 1H, NH); ^{13}C nmr (hexadeuteriodimethylsulfoxide): δ 10.9 (CH_3), 13.0 (SCH_3), 112.6 (CCH_3), 128.5 (NCH), 159.5 (SCN); ms: m/z 192 (M^+), 128 ($\text{M}^+ - \text{SO}_2$), 95, 54.

Anal. Calcd. for $\text{C}_5\text{H}_8\text{N}_2\text{O}_2\text{S}_2$: C, 31.24; H, 4.19; N, 14.57. Found: C, 31.27; H, 4.40; N, 14.68.

3-Methylsulfanyl-6-phenyl-4H-1,2,4-thiadiazine-1,1-dioxide (5c).

This compound was prepared from **2a** and α -toluenesulfonyl chloride in 77% yield, mp 149° (from diethyl ether); ir (potassium bromide): ν max 1639, 1569, 1506, 1258, 1143, 1118

cm⁻¹; ¹H nmr (deuteriochloroform): δ 2.50 (s, 3H, SCH₃), 6.66 (d, 1H, J = 5.8 Hz, CH), 7.33-7.54 (m, 5H, C₆H₅), 9.43 (d, 1H, J = 5.8 Hz, NH); ¹³C nmr (hexadeuteriodimethylsulfoxide): δ 13.1 (SCH₃), 117.6 (CC₆H₅), 127.6, 128.4, 128.6, 129.3 and 130.1 (5CHar, Car and NCH), 159.4 (SCN); ms: m/z 254 (M⁺), 190 (M⁺ - SO₂), 157, 117, 90.

Anal. Calcd. for C₁₀H₁₀N₂O₂S₂: C, 47.23; H, 3.96; N, 11.01. Found: C, 47.02; H, 4.13; N, 11.27.

5-Methyl-3-methylsulfanyl-4H-1,2,4-thiadiazine-1,1-dioxide (5d).

This compound was prepared from **2b** and methanesulfonyl chloride in 69% yield, mp 223-225° (from diethyl ether/methylene chloride 1/1); ir (potassium bromide): ν max 1653, 1581, 1120 cm⁻¹; ¹H nmr (hexadeuteriodimethylsulfoxide): δ 1.98 (s, 3H, CH₃), 2.43 (s, 3H, SCH₃), 6.18 (s, 1H, CH), 11.77 (broad s, 1H, NH); ¹³C nmr (hexadeuteriodimethylsulfoxide): δ 13.0 (SCH₃), 18.5 (CH₃), 100.9 (CH), 142.7 (CCH₃), 159.2 (SCN); ms: m/z 192 (M⁺), 128 (M⁺ - SO₂), 95, 54.

Anal. Calcd. for C₅H₈N₂O₂S₂: C, 31.24; H, 4.19; N, 14.57. Found: C, 31.18; H, 4.32; N, 14.46.

5,6-Dimethyl-3-methylsulfanyl-4H-1,2,4-thiadiazine-1,1-dioxide (5e).

This compound was prepared from **2b** and ethanesulfonyl chloride in 39% yield, mp 206° (from diethyl ether); ir (potassium bromide): ν max 1661, 1579, 1509, 1142 cm⁻¹; ¹H nmr (deuteriochloroform): δ 2.06 and 2.11 (2s, 6H, NCCH₃ and SCCH₃), 2.49 (s, 3H, SCH₃), 9.14 (broad s, 1H, NH); ¹³C nmr (hexadeuteriodimethylsulfoxide): δ 8.6 (SCCH₃), 13.0 (SCH₃), 15.5 (NCCH₃), 108.2 (SCCH₃), 137.2 (NCCH₃), 158.9 (SCN); ms: m/z 206 (M⁺), 142 (M⁺ - SO₂), 109, 68.

Anal. Calcd. for C₆H₁₀N₂O₂S₂: C, 34.94; H, 4.89; N, 13.58. Found: C, 34.65; H, 4.71; N, 13.24.

5-Methyl-3-methylsulfanyl-6-phenyl-4H-1,2,4-thiadiazine-1,1-dioxide (5f).

This compound was prepared from **2b** and α-toluenesulfonyl chloride in 66% yield, mp >300° (from methylene chloride); ir (potassium bromide): ν max 1653, 1582, 1509, 1274, 1131 cm⁻¹; ¹H nmr (hexadeuteriodimethylsulfoxide): δ 1.88 (s, 3H, CH₃), 2.47 (s, 3H, SCH₃), 7.37-7.42 (m, 5H, C₆H₅), 11.82 (broad s, 1H, NH); ¹³C nmr (hexadeuteriodimethylsulfoxide): δ 13.1 (SCH₃), 16.8 (CH₃), 114.6 (CC₆H₅), 128.4, 128.6, 129.0 and 131.2 (5CHar and Car), 138.9 (CCH₃), 159.2 (SCN); ms: m/z 268 (M⁺), 204 (M⁺ - SO₂), 171, 131, 104.

Anal. Calcd. for C₁₁H₁₂N₂O₂S₂: C, 49.23; H, 4.51; N, 10.44. Found: C, 49.51; H, 4.33; N, 10.70.

General Procedure for the Reaction Between Methylsulfanylpyrimidinones **3 and Hydrogen Sulfide.**

Hydrogen sulfide was passed for 4 hours through a solution of methylsulfanyl-pyrimidinone **3** (2 mmoles) in triethylamine (7 ml) and pyridine (7 ml). The solvents were removed and the residue was purified by flash chromatography (silica gel, methylene chloride/ethyl acetate 1/1). The product was crystallized from an appropriate solvent.

5-Methoxycarbonyl-2-thioxo-1,2,3,4-tetrahydropyrimidin-4-one (4a).

This compound was obtained from **3a** in 72% yield, mp 181° (from ethyl acetate); ir (potassium bromide): ν max 1717, 1616, 1549, 1458, 1216, 1165 cm⁻¹; ¹H nmr (hexadeuteriodimethylsulfoxide): δ 3.70 (s, 3H, OCH₃), 7.96 (s, 1H, CH); 10.77 (broad s, 2H, 2NH); ¹³C nmr (hexadeuteriodimethylsulfoxide): δ 51.7 (OCH₃), 106.8 (CCO), 147.6 (CH), 157.1 (CCO), 162.8 (NCO), 176.5 (CS); ms: m/z 186 (M⁺), 170, 139, 69.

Anal. Calcd. for C₆H₆N₂O₃S: C, 38.71; H, 3.25; N, 15.05. Found: C, 39.98; H, 3.35; N, 15.28.

5-Ethoxycarbonyl-2-thioxo-1,2,3,4-tetrahydropyrimidin-4-one (4b).

This compound was obtained from **3b** in 77% yield, mp 244° (from ethyl acetate) [19].

5-Methoxycarbonyl-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidin-4-one (4c).

This compound was obtained from **3c** in 90% yield, mp 232° (from diethyl ether/methylene chloride 1/1); ir (potassium bromide): ν max 1726, 1628, 1559, 1164 cm⁻¹; ¹H nmr (hexadeuteriodimethylsulfoxide): δ 2.50 (s, 3H, CH₃), 3.73 (s, 3H, OCH₃), 12.61 (broad s, 2H, 2NH); ¹³C nmr (hexadeuteriodimethylsulfoxide): δ 17.2 (CH₃), 52.1 (OCH₃), 108.9 (CCO), 154.9 (CCH₃), 157.9 (CCO), 164.4 (NCO), 175.4 (CS); ms: m/z 200 (M⁺), 169 (M⁺ - CH₃O), 168.

Anal. Calcd. for C₇H₈N₂O₃S: C, 41.99; H, 4.03; N, 13.99. Found: C, 42.37; H, 4.27; N, 14.11.

5-Ethoxycarbonyl-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidin-4-one (4d).

This compound was obtained from **3d** in 97% yield, mp 211° (from 50/50 diethyl ether/methylene chloride); ir (potassium bromide): ν max 1717, 1653, 1558, 1165 cm⁻¹; ¹H nmr (hexadeuteriodimethylsulfoxide): δ 1.23 (t, 3H, J = 7.2 Hz, CH₂CH₃), 2.20 (s, 3H, CH₃), 4.20 (q, 2H, J = 7.2 Hz, CH₂CH₃), 12.56 (broad s, 2H, 2NH); ¹³C nmr (deuteriochloroform): δ 14.0 (CH₂CH₃), 17.1 (CH₃), 60.9 (CH₂CH₃), 109.3 (CCO), 154.3 (CCH₃), 157.9 (CCO), 163.8 (NCO), 175.5 (CS); ms: m/z 214 (M⁺), 169 (M⁺ - C₂H₅O), 142.

Anal. Calcd. for C₈H₁₀N₂O₃S: C, 44.85; H, 4.70; N, 13.08. Found: C, 45.12; H, 4.88; N, 13.33.

6-Methyl-5-phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidin-4-one (4e).

This compound was obtained from **3e** in 98% yield, mp 289° (from diethyl ether/methylene chloride 1/1) [20].

General Procedure for the Reaction Between Triazapentadienium Iodides **2 and Phenyl Isocyanate or Phenyl Isothiocyanate.**

A solution of iodide **2** (2 mmoles) and phenyl isocyanate or phenyl isothiocyanate (2.2 mmoles) in dry tetrahydrofuran (10 ml) was stirred at room temperature (for compounds **6**) or heated under reflux (for compounds **7**) for 6 hours under a nitrogen atmosphere. The reaction mixture was cooled to 0° and triethylamine (4.4 mmoles) was added. The mixture was stirred for 18 hours at room temperature. The solvent was removed and

the residue was purified by flash chromatography (silica gel, methylene chloride/ethyl acetate 9:1). The product was crystallized from an appropriate solvent.

4-Methylsulfanyl-1-phenyl-1,3,5-triazin-2(1H)-one (**6a**).

This compound was prepared from **2a** and phenyl isocyanate in 55% yield, mp 160° (from diethyl ether); ir (potassium bromide): ν max 1730, 1612, 1457, 1233 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 2.58 (s, 3H, SCH_3), 7.35-7.55 (m, 5H, C_6H_5), 8.07 (s, 1H, CH); ^{13}C nmr (deuteriochloroform): δ 14.4 (SCH_3), 126.2, 129.7 and 129.8 (5CHar), 136.4 (Car), 151.2 (CO), 155.9 (CH), 184.4 (SCN); ms: m/z 219 (M^+), 204 ($\text{M}^+ - \text{CH}_3$), 104, 77.

Anal. Calcd. for $\text{C}_{10}\text{H}_9\text{N}_3\text{OS}$: C, 54.78; H, 4.14; N, 19.16. Found: C, 54.58; H, 4.32; N, 18.87.

6-Methyl-4-methylsulfanyl-1-phenyl-1,3,5-triazin-2(1H)-one (**6b**).

This compound was prepared from **2b** and phenyl isocyanate in 92% yield, mp 143° (from diethyl ether); ir (potassium bromide): ν max 1705, 1684, 1571, 1479, 1286 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 2.14 (s, 3H, CH_3), 2.56 (s, 3H, SCH_3), 7.21-7.56 (m, 5H, C_6H_5); ^{13}C nmr (deuteriochloroform): δ 14.2 (SCH_3), 23.0 (CH_3), 127.1, 129.7 and 130.1 (5CHar), 136.3 (Car), 152.8 (CCH_3), 166.3 (CO), 183.3 (SCN); ms: m/z 233 (M^+), 218 ($\text{M}^+ - \text{CH}_3$), 118, 77.

Anal. Calcd. for $\text{C}_{11}\text{H}_{11}\text{N}_3\text{OS}$: C, 56.63; H, 4.75; N, 18.01. Found: C, 56.49; H, 4.78; N, 17.72.

4-Methylsulfanyl-1-phenyl-1,3,5-triazin-2(1H)-thione (**7a**).

This compound was prepared from **2a** and phenyl isothiocyanate in 80% yield, mp 228° (from diethyl ether); ir (potassium bromide): ν max 1583, 1442, 1237 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 2.63 (s, 3H, SCH_3), 7.28-7.55 (m, 5H, C_6H_5), 8.02 (s, 1H, NCH); ^{13}C nmr (hexadeuteriodimethylsulfoxide): δ 13.8 (SCH_3), 127.4, 129.3 and 129.4 (5CHar), 140.3 (Car), 156.2 (NCH), 177.6 (CS), 181.7 (SCN); ms: m/z 235 (M^+), 220 ($\text{M}^+ - \text{CH}_3$), 104, 77.

Anal. Calcd. for $\text{C}_{10}\text{H}_9\text{N}_3\text{S}_2$: C, 51.04; H, 3.85; N, 17.86. Found: C, 51.12; H, 4.03; N, 18.04.

6-Methyl-4-methylsulfanyl-1-phenyl-1,3,5-triazin-2(1H)-thione (**7b**).

This compound was prepared from **2b** and phenyl isothiocyanate in 83% yield, mp 136-137° (from diethyl ether); ir (potassium bromide): ν max 1569, 1558, 1469, 1450, 1260 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 2.15 (s, 3H, CCH_3), 2.61 (s, 3H, SCH_3), 7.19-7.58 (m, 5H, C_6H_5); ^{13}C nmr (deuteriochloroform): δ 14.3 (SCH_3), 24.3 (CH_3), 126.9, 129.8 and 130.5 (5CHar), 139.9 (Car), 164.7 (CCH_3), 177.5 (CS), 184.0 (SCN); ms: m/z 249 (M^+), 234 ($\text{M}^+ - \text{CH}_3$), 202, 118, 77.

Anal. Calcd. for $\text{C}_{11}\text{H}_{11}\text{N}_3\text{S}_2$: C, 52.99; H, 4.45; N, 16.85. Found: C, 52.77; H, 4.16; N, 16.63.

General Procedure for the Reaction Between Triazapentadienium Iodides **2** and Dimethyl Acetylenedicarboxylate.

Dimethyl acetylenedicarboxylate (2 mmol) was added to a solution of iodide **2** (2 mmol) in dry methylene chloride (10 ml) under a nitrogen atmosphere. The mixture was stirred

for 15 minutes at room temperature, cooled to 0° then triethylamine (4 mmol) was added. The reaction mixture was stirred for 18 hours at room temperature. The solvent was removed and the residue was purified by flash chromatography (silica gel, methylene chloride/ethyl acetate 4:1). Products **8** and **9** were obtained.

Methyl 3-Methoxycarbonyl-7-dimethylamino-5-methylsulfanyl-4,6-diazaocta-2,4,6-trienoate (**8**).

This compound was prepared from **2b** and dimethyl acetylenedicarboxylate in 79% yield (yellow oil, Rf methylene chloride = 0.2); ^1H nmr (deuteriochloroform): δ 2.17 (s, 3H, CH_3), 2.40 (s, 3H, SCH_3), 2.96 (s, 6H, $\text{N}(\text{CH}_3)_2$), 3.70 and 3.79 (2s, 6H, 2OCH_3).

4,5-Dimethoxycarbonyl-2-methylsulfanylpuridine (**9a**).

This compound was prepared from **2a** and dimethyl acetylenedicarboxylate in 48% yield, mp 133° (from diethyl ether) [21].

4,5-Dimethoxycarbonyl-6-methyl-2-methylsulfanylpuridine (**9b**).

A solution of **8** (1.2 mmol) in dry toluene (40 ml) was heated for 18 hours at 110°. The solvent was removed and the residue was purified by flash chromatography (silica gel, methylene chloride/ethyl acetate 4:1) to give a yellow oil in 80% yield (Rf methylene chloride = 0.7); ir (potassium bromide): ν max 1739, 1695, 1549, 1234 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 2.61 and 2.62 (2s, 6H, CH_3 and SCH_3), 3.92 and 3.96 (2s, 6H, 2OCH_3); ^{13}C nmr (deuteriochloroform): δ 14.3 (SCH_3), 23.3 (CH_3), 53.0 and 53.4 (2OCH_3), 119.7 (CCO), 155.4, 165.0, 166.2 and 167.7 (CCH_3 , NCCO and 2CO), 174.3 (SCN); ms: m/z 256 (M^+), 224 ($\text{M}^+ - \text{CH}_3\text{OH}$), 196, 166, 138.

Acknowledgement.

The authors wish to express their gratitude to the French Ministry of Education and CNRS for financial support.

REFERENCES AND NOTES

- [1] D. L. Boger and S. M. Weinreb, *Hetero Diels-Alder Methodology in Organic Synthesis*, Academic Press, New York 1987, p 272.
- [2] S. N. Mazumdar, I. Ibnusaud and M. P. Mahajan, *Tetrahedron Lett.*, **27**, 5875 (1986).
- [3] P. Luthardt and E. U. Wurthwein, *Tetrahedron Lett.*, **29**, 921 (1988).
- [4] J. Barluenga, M. Tomas, A. Ballesteros and A. L. Lopez, *Tetrahedron Lett.*, **30**, 4573 (1989).
- [5] S. N. Mazumdar and M. P. Mahajan, *Tetrahedron*, **47**, 1473 (1991).
- [6] S. N. Mazumdar, S. Mukherjee, A. K. Sharma, D. Sengupta and M. P. Mahajan, *Tetrahedron*, **50**, 7579 (1994).
- [7] A. K. Sharma and M. P. Mahajan, *Heterocycles*, **40**, 787 (1995).
- [8] P. D. Dey, A. K. Sharma, S. N. Rai and M. P. Mahajan, *Tetrahedron*, **51**, 7459 (1995).
- [9] A. K. Sharma and M. P. Mahajan, *Tetrahedron*, **53**, 13841 (1997).
- [10] C. Friot, A. Reliquet, F. Reliquet and J. C. Meslin, *Synthesis*, **5**, 695 (2000).

- [11] A. Mai, M. Artico, G. Sbardella, S. Massa, A. G. Loi, E. Tramontano, P. Scano and P. La Colla, *J. Med. Chem.*, **38**, 3258 (1995).
- [12] R. A. Nugent, S. T. Schlachter, M. J. Murphy, G. J. Cleek, T. J. Poel, D. G. Wishka, D. R. Graber, Y. Yagi, B. J. Keiser, R. A. Olmsted, L. A. Kopta, S. M. Swaney, S. M. Poppe, J. Morris, W. G. Tarpley and R. C. Thomas, *J. Med. Chem.*, **41**, 3793 (1998).
- [13] C. O. Kappe and P. J. Roschger, *J. Heterocyclic Chem.*, **26**, 55 (1989) and references therein.
- [14] C. O. Kappe, *Tetrahedron*, **49**, 6937 (1993).
- [15] S. N. Mazumdar, M. Sharma and M. P. Mahajan, *Tetrahedron Lett.*, **28**, 2641 (1987).
- [16] P. de Tullio, B. Pirotte, F. Somers, S. Boverie, F. Lacan and J. Delarge, *Tetrahedron*, **54**, 4935 (1998) and references therein.
- [17] H. Brederick, F. Effenberger and A. Hoffmann, *Chem. Ber.*, **97**, 61 (1964).
- [18] C. W. Todd, J. H. Fletcher and D. S. Tarbell, *J. Am. Chem. Soc.*, **65**, 350 (1943).
- [19] E. R. Garrett and D. J. Weber, *J. Pharm. Sci.*, **59**, 1383 (1970).
- [20] Y. Watanabe, H. Usui, T. Shibano, T. Tanaka and M. Kanao, *Chem. Pharm. Bull.*, **38**, 2726 (1990).
- [21] I. Ibnsaud, E. J. P. Malar and N. Sundaram, *Tetrahedron Lett.*, **31**, 7357 (1990).