Cationic 1,3-Diazadienes in Annulation Reactions. Synthesis of Pyrimidine, Thiadiazinedioxide and Triazine Derivatives

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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**.

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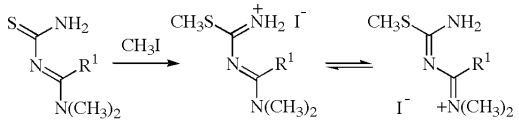
The synthetic value of 1,3-diazadienes in heterocyclic chemistry has been widely demonstrated [1]. During the last fifteen years [4 + 2] cycloaddition reactions of acyclic 1,3-diazadienes, especially with ketenes, have been studied giving rise to various dihydropyrimidines [2-9].

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

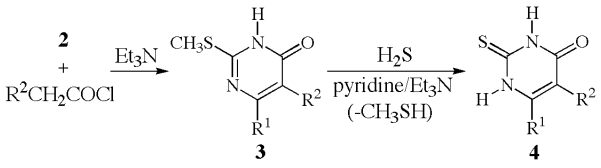
Scheme 1



1 **2**

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**.

Scheme 2



3 **4**

Compound	R^1	R^2	Yield (%)	Mp (°C)
3a	H	CO_2CH_3	82	205
3b [18]	H	$CO_2C_2H_5$	63	133
3c	CH_3	CO_2CH_3	84	179
3d	CH_3	$CO_2C_2H_5$	84	149
3e	CH_3	C_6H_5	97	196
4a	H	CO_2CH_3	72	181
4b [19]	H	$CO_2C_2H_5$	77	244
4c	CH_3	CO_2CH_3	90	232
4d	CH_3	$CO_2C_2H_5$	97	211
4e [20]	CH_3	C_6H_5	98	289

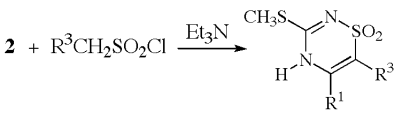
These types of compounds exhibit important pharmacological potential. Recently *S*-alkylsufanylpyrimidine and *S*-alkylsulfanylpyrimidinone derivatives have been identified as highly specific reverse transcriptase inhibitors of human immunodeficiency virus type 1 [11,12]. Thioxo derivatives showed a 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 Bredereck procedure [17]. Subsequent alkylation using methyliodide 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*-methyliodides **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).

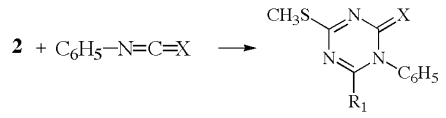
Scheme 3



5

Compound	R^1	R^3	Yield %	Mp (°C)
5a	H	H	46	144
5b	H	CH_3	86	221
5c	H	C_6H_5	77	149
5d	CH_3	H	69	223-225
5e	CH_3	CH_3	39	206
5f	CH_3	C_6H_5	66	>300

Scheme 4



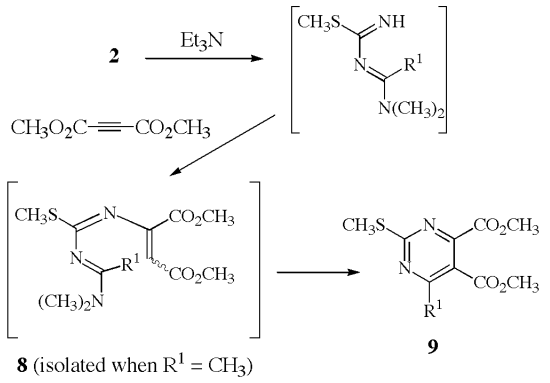
6, 7

Compound	R^1	X	Yield (%)	Mp (°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 2*H*-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(1*H*)-ones **6** and triazine-2(1*H*)-thiones **7** respectively in good yields (Scheme 4).

Scheme 5



8 (isolated when $R^1 = CH_3$)

9

Compound	R^1	Yield (%)	Mp (°C)
9a [21]	H	48	133
9b	CH_3	63	oil

The reaction of salts **2** with dimethyl acetylenedicarboxylate afforded 2-methylsulfanylpyrimidines **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 4*H*-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 ^{1}H-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 128-130°; ir (potassium bromide): *ν* max 3278, 3123, 1583, 1366 cm^{-1}; ^{1}H nmr (hexadeuteriodimethylsulfoxide): δ 2.17 (s, 3H, CH_3), 2.93 (s, 6H, $N(CH_3)_2$), 7.66 and 8.05 (2s, 2H, 2NH); ^{13}C nmr (hexadeuteriodimethylsulfoxide): δ 16.5 (CH_3), 37.9 ($N(CH_3)_2$), 159.0 (CCH_3), 194.0 (CS); ms: m/z 145 (M^+), 129 (M^+ - NH_2), 112 (M^+ - SH).

Anal. Calcd. for $C_5H_{11}N_3S$: 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): *v* max 3232, 3070, 1624, 1521 cm^{-1}; ^1H nmr (hexadeuteriodimethylsulfoxide): δ 2.55 (s, 3H, SCH_3), 3.11 and 3.27 (2s, 6H, $N(CH_3)_2$), 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 ($N(CH_3)_2$), 158.7 (CH), 178.2 (CS).

Anal. Calcd. for $C_5H_{12}IN_3S$: 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): *v* 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, $N(CH_3)_2$), 9.01 (s, 2H, NH_2); ^{13}C nmr (hexadeuteriodimethylsulfoxide): δ 14.3 (SCH_3), 18.5 (CH_3), 39.2 and 39.8 ($N(CH_3)_2$), 166.4 (*C*CH_3), 172.0 (CS).

Anal. Calcd. for $C_6H_{14}IN_3S$: 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 Triazapentadienum 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-methylsulfanylpyrimidin-4(3*H*)-one (**3a**).

This compound was prepared from **2a** and methyl malonyl chloride in 82% yield, mp 205° (from diethyl ether); ir (potassium bromide): *v* 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 (*C*CO), 158.0 (NCH), 159.0, 164.1 and 168.1 (SCN and 2CO); ms: m/z 200 (M^+), 168 (M^+ -CH_3OH), 112.

Anal. Calcd. for $C_7H_8N_2O_3S$: C, 41.99; H, 4.03; N, 13.99. Found: C, 42.23; H, 3.97; N, 14.27.

5-Ethoxycarbonyl-2-methylsulfanylpyrimidin-4(3*H*)-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-methylsulfanylpyrimidin-4(3*H*)-one (**3c**).

This compound was prepared from **2b** and methyl malonyl chloride in 84% yield, mp 179° (from diethyl ether); ir (potassium bromide): *v* 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 (*C*CO), 164.6, 166.8, 167.2 and 167.4 (*C*CH_3, SCN and 2CO); ms: m/z 214 (M^+), 182 (M^+ - CH_3OH), 126.

Anal. Calcd. for $C_8H_{10}N_2O_3S$: C, 44.85; H, 4.70; N, 13.08. Found: C, 45.17; H, 4.50; N, 13.35.

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

This compound was prepared from **2b** and ethyl malonyl chloride in 84% yield, mp 149° (from diethyl ether); ir (potassium bromide): *v* 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 (*C*CH_3), 61.9 (CH_2CH_3), 110.0 (*C*CO), 165.1 and 167.1 (*C*CH_3, SCN and 2CO); ms: m/z 228 (M^+), 182 (M^+ - C_2H_5OH), 126.

Anal. Calcd. for $C_9H_{12}N_2O_3S$: 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(3*H*)-one (**3e**).

This compound was prepared from **2b** and phenylacetyl chloride in 97% yield, mp 196° (from diethyl ether); ir (potassium bromide): *v* 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 (*C*CH_3), 120.2 (*C*C_6H_5), 127.2, 128.0 and 130.3 (5CHar), 134.3 (Car), 148.0 (*C*CH_3), 159.6 and 162.2 (SCN and CO); ms: m/z 232 (M^+).

Anal. Calcd. for $C_{12}H_{12}N_2OS$: C, 62.05; H, 5.21; N, 12.06. Found: C, 61.96; H, 5.18; N, 12.01.

3-Methylsulfanyl-4*H*-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): *v* 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 (M^+ - SO_2), 81, 74.

Anal. Calcd. for $C_4H_6N_2O_2S_2$: C, 26.96; H, 3.39; N, 15.72. Found: C, 30.21; H, 3.51; N, 15.55.

6-Methyl-3-methylsulfanyl-4*H*-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): *v* 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 (*C*CH_3), 128.5 (NCH), 159.5 (SCN); ms: m/z 192 (M^+), 128 (M^+ - SO_2), 95, 54.

Anal. Calcd. for $C_5H_8N_2O_2S_2$: C, 31.24; H, 4.19; N, 14.57. Found: C, 31.27; H, 4.40; N, 14.68.

3-Methylsulfanyl-6-phenyl-4*H*-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): *v* max 1639, 1569, 1506, 1258, 1143, 1118

cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 2.50 (s, 3H, SCH_3), 6.66 (d, 1H, J = 5.8 Hz, CH), 7.33-7.54 (m, 5H, C_6H_5), 9.43 (d, 1H, J = 5.8 Hz, NH); ^{13}C nmr (hexadeuteriodimethylsulfoxide): δ 13.1 (SCH_3), 117.6 (CC_6H_5), 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^+ - SO_2), 157, 117, 90.

Anal. Calcd. for $C_{10}H_{10}N_2O_2S_2$: C, 47.23; H, 3.96; N, 11.01. Found: C, 47.02; H, 4.13; N, 11.27.

5-Methyl-3-methylsulfanyl-4*H*-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}; ^{1}H nmr (hexadeuteriodimethylsulfoxide): δ 1.98 (s, 3H, CH_3), 2.43 (s, 3H, SCH_3), 6.18 (s, 1H, CH), 11.77 (broad s, 1H, NH); ^{13}C nmr (hexadeuteriodimethylsulfoxide): δ 13.0 (SCH_3), 18.5 (CH_3), 100.9 (CH), 142.7 (CCH_3), 159.2 (SCN); ms: m/z 192 (M^+), 128 (M^+ - SO_2), 95, 54.

Anal. Calcd. for $C_5H_8N_2O_2S_2$: C, 31.24; H, 4.19; N, 14.57. Found: C, 31.18; H, 4.32; N, 14.46.

5,6-Dimethyl-3-methylsulfanyl-4*H*-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}; ^{1}H nmr (deuteriochloroform): δ 2.06 and 2.11 (2s, 6H, $NCCH_3$ and $SCCH_3$), 2.49 (s, 3H, SCH_3), 9.14 (broad s, 1H, NH); ^{13}C nmr (hexadeuteriodimethylsulfoxide): δ 8.6 ($SCCH_3$), 13.0 (SCH_3), 15.5 ($NCCH_3$), 108.2 ($SCCH_3$), 137.2 ($NCCH_3$), 158.9 (SCN); ms: m/z 206 (M^+), 142 (M^+ - SO_2), 109, 68.

Anal. Calcd. for $C_6H_{10}N_2O_2S_2$: 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-4*H*-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}; ^{1}H nmr (hexadeuteriodimethylsulfoxide): δ 1.88 (s, 3H, CH_3), 2.47 (s, 3H, SCH_3), 7.37-7.42 (m, 5H, C_6H_5), 11.82 (broad s, 1H, NH); ^{13}C nmr (hexadeuteriodimethylsulfoxide): δ 13.1 (SCH_3), 16.8 (CH_3), 114.6 (CC_6H_5), 128.4, 128.6, 129.0 and 131.2 (5CHar and Car), 138.9 (CCH_3), 159.2 (SCN); ms: m/z 268 (M+), 204 (M^+ - SO_2), 171, 131, 104.

Anal. Calcd. for $C_{11}H_{12}N_2O_2S_2$: 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 Methylsulfanyl-pyrimidinones **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}; ^{1}H nmr (hexadeuteriodimethylsulfoxide): δ 3.70 (s, 3H, OCH_3), 7.96 (s, 1H, CH); 10.77 (broad s, 2H, 2NH); ^{13}C nmr (hexadeuteriodimethylsulfoxide): δ 51.7 (OCH_3), 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 $C_6H_6N_2O_3S$: 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-tetrahydro-pyrimidin-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}; ^{1}H nmr (hexadeuteriodimethylsulfoxide): δ 2.50 (s, 3H, CH_3), 3.73 (s, 3H, OCH_3), 12.61 (broad s, 2H, 2NH); ^{13}C nmr (hexadeuteriodimethylsulfoxide): δ 17.2 (CH_3), 52.1 (OCH_3), 108.9 (CCO), 154.9 (CCH_3), 157.9 (CCO), 164.4 (NCO), 175.4 (CS); ms: m/z 200 (M^+), 169 (M^+ - CH_3O), 168.

Anal. Calcd. for $C_7H_8N_2O_3S$: 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}; ^{1}H nmr (hexadeuteriodimethylsulfoxide): δ 1.23 (t, 3H, J = 7.2 Hz, CH_2CH_3), 2.20 (s, 3H, CH_3), 4.20 (q, 2H, J = 7.2 Hz, CH_2CH_3), 12.56 (broad s, 2H, 2NH); ^{13}C nmr (deuteriochloroform): δ 14.0 (CH_2CH_3), 17.1 (CH_3), 60.9 (CH_2CH_3), 109.3 (CCO), 154.3 (CCH_3), 157.9 (CCO), 163.8 (NCO), 175.5 (CS); ms: m/z 214 (M^+), 169 (M^+ - C_2H_5O), 142.

Anal. Calcd. for $C_8H_{10}N_2O_3S$: 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(1*H*)-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 (M^+ - CH_3), 104, 77.

Anal. Calcd. for $C_{10}H_9N_3OS$: 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(1*H*)-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 (*C*CH_3), 166.3 (CO), 183.3 (SCN); ms: m/z 233 (M^+), 218 (M^+ - CH_3), 118, 77.

Anal. Calcd. for $C_{11}H_{11}N_3OS$: 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(1*H*)-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 (M^+ - CH_3), 104, 77.

Anal. Calcd. for $C_{10}H_9N_3S_2$: 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(1*H*)-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 (*C*CH_3), 177.5 (CS), 184.0 (SCN); ms: m/z 249 (M^+), 234 (M^+ - CH_3), 202, 118, 77.

Anal. Calcd. for $C_{11}H_{11}N_3S_2$: 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 Triazapentadienum Iodides **2** and Dimethyl Acetylenedicarboxylate.

Dimethyl acetylenedicarboxylate (2 mmoles) was added to a solution of iodide **2** (2 mmoles) 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 mmoles) 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, $N(CH_3)_2$), 3.70 and 3.79 (2s, 6H, $2OCH_3$).

4,5-Dimethoxycarbonyl-2-methylsulfanylpyrimidine (**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-methylsulfanyl-pyrimidine (**9b**).

A solution of **8** (1.2 mmoles) 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 (*C*CO), 155.4, 165.0, 166.2 and 167.7 (*C*CH_3, N*C*CO and 2CO), 174.3 (SCN); ms: m/z 256 (M^+), 224 (M^+ - CH_3OH), 196, 166, 138.

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