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Regioselective Iminophosphorane-Mediated Annelation of a 1,3,4-Thiadiazole Ring into a 1,2,4-Triazine Ring: Preparation of Novel Mesoionic Compounds Derived from [1,3,4]Thiadiazolo[2,3-c]- and [1,3,4]Thiadiazolo[3,2-d][1,2,4]triazines.

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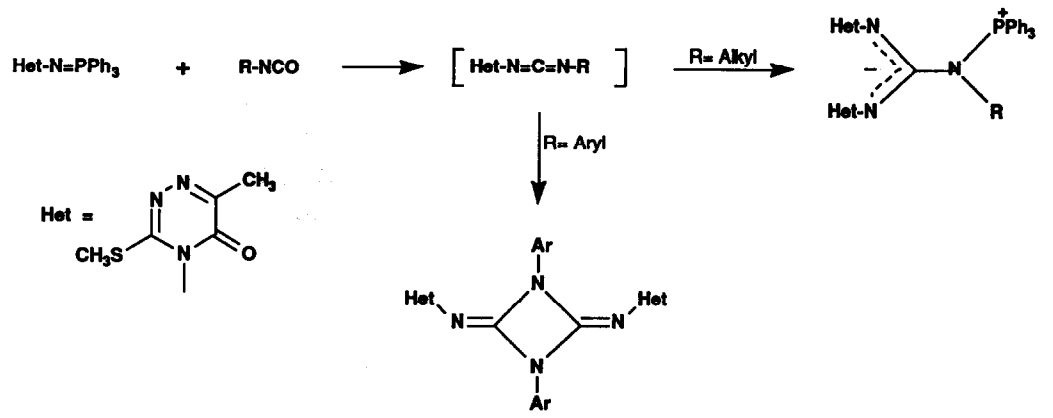
Abstract. *Aza Wittig-type reaction of iminophosphorane* ***1*** *derived from 4-amino-2,6-dimethyl-5-oxo-3-thioxo-2,3,4,5-tetrahydro-1,2,4-triazine with several types of iso(thio)cyanates leads to [1,3,4]thiadiazolo[2,3-c][1,2,4]triazines* ***2, 3*** *and* ***6*** *which display mesoionic or zwitterionic character. The thioanalog iminophosphorane* ***8*** *reacts with iso(thio)cyanates to give in regioselective fashion the [1,3,4]thiadiazolo[3,2-d][1,2,4]triazines* ***9, 12*** *and* ***16.***

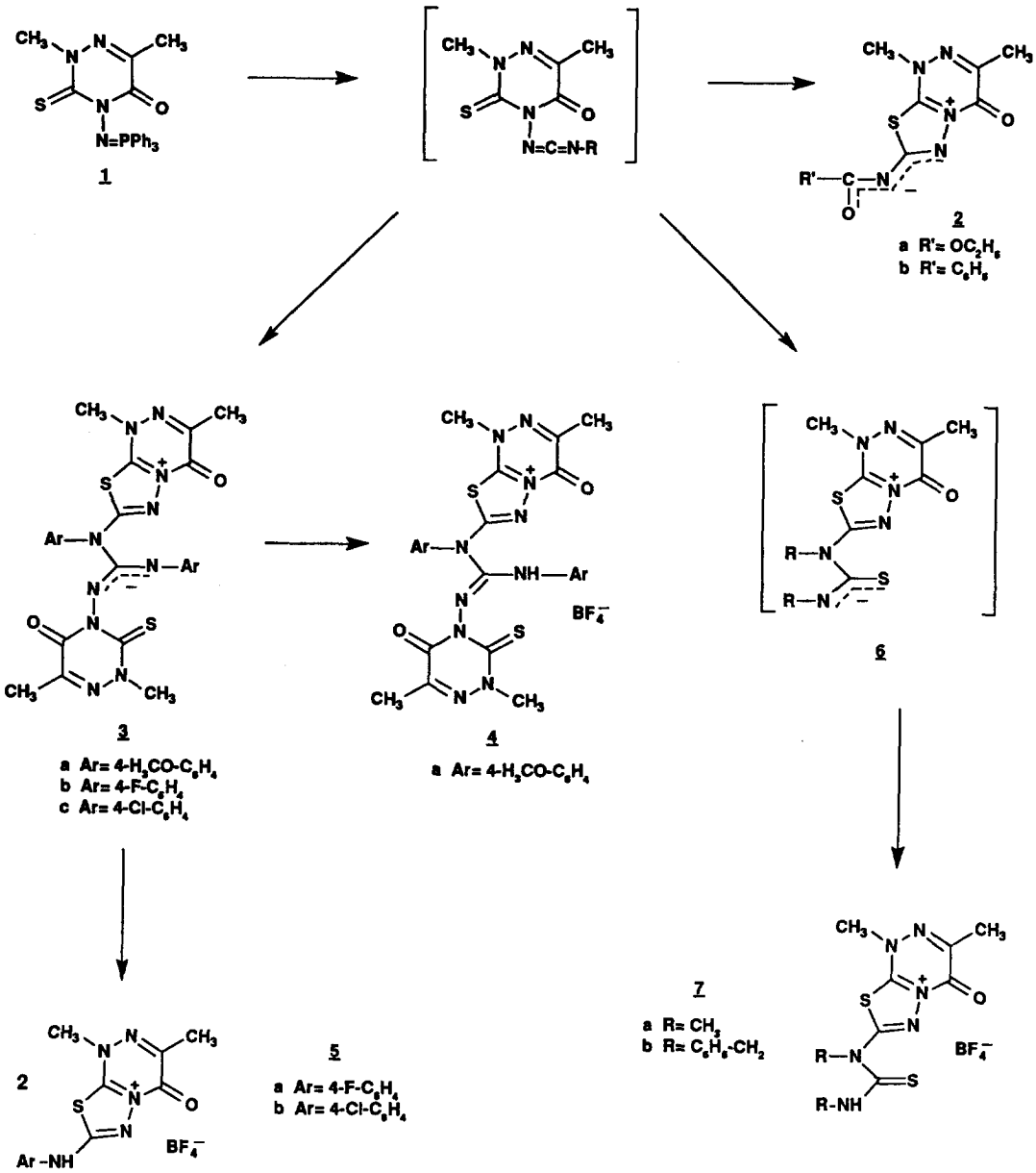
Iminophosphoranes derived from N-aminoheterocycles are valuable precursors for the preparation of fused heterocycles[1]. In two previous papers we have reported the reaction of the iminophosphorane derived from 4-amino-6-methyl-3-methylthio-5-oxo-4,5-dihydro-1,2,4-triazine with isocyanates and the reaction products were strongly dependent on the nature of the isocyanate. Thus, with aromatic isocyanates the reaction products were found to be (Z,Z)-1,3-diaryl-2,4-bis(heteroaryl)-1,3-diazetidines[2], whereas with aliphatic isocyanates the reaction led to betaines derived from λ^5-phosphiniminium salts[3]. In both cases a carbodiimide (aza-Wittig product) was postulated as intermediate. In the first case, the carbodiimide undergoes [2+2] cycloaddition to give the 1,3-diazetidines, whereas in the reaction with aliphatic isocyanates the initial carbodiimide reacts with the starting iminophosphorane through a [2+2] cycloaddition to give a 1,3,2-diazaphosphetidine and subsequent ring-chain isomerism leads to the betaines.

We now study the reaction of iminophosphoranes derived from related 4-amino-1,2,4-triazines with different isocyanates or isothiocyanates in order to see the influence of the heterocyclic ring on the nature of the reaction products. In others words, whether conveniently functionalized 1,2,4-triazine rings could be able to trap the intermediate carbodiimide affording fused mesoionic compounds.



Results. Iminophosphorane **1**, available from 4-amino-2,6-dimethyl-5-oxo-3-thioxo-2,3,4,5-tetrahydro-1,2,4-triazine and triphenylphosphine dibromide[4] reacts with benzoyl- and ethoxycarbonyl isothiocyanate in dry benzene at room temperature to give the previously unreported mesoionic compounds [1,3,4]thiadiazolo[2,3-c][1,2,4]triazinium-7-aminides **2** in excellent yields. In the ^{13}C n.m.r. spectrum of **2a** the C- and N-methyl groups appear at δ 16.84 and 46.43 ppm respectively; the assignments of the quaternary carbon atoms have been made through gate-decoupled and COLOC experiments: C_{8a}=159.43 ppm (^3J=3.4 Hz), C_4=146.28 ppm (^3J=3.3 Hz), C_3=149.81 ppm (^2J=7.2 Hz), C_7=162.03 ppm. Mass spectra show the expected molecular ion peaks in low intensity. Iminophosphorane **1** also reacts with aromatic isocyanates or isothiocyanates in dry benzene at room temperature to give the zwitterionic compounds **3**, isolated as orange crystals in fair yields. The first indication of a structure type **3** is obtained from ^1H and ^{13}C n.m.r. spectra which clearly show that there are two set of signals for the aryl groups and for the triazine rings. The ^{13}C n.m.r. spectroscopic data are valuable in order to distinguish between the two triazine rings, especially the chemical shift of the C_3 carbon atom. In 4-amino-2,6-dimethyl-5-oxo-3-thioxo-2,3,4,5-tetrahydro-1,2,4-triazine the C_3 carbon atom appears at δ 167.58 ppm, in compounds **2** the carbon atom C_{8a} appears at δ 159.43 ppm whereas in compounds **3** appear two signals at δ 160.25 and 171.06 ppm due to the C_{8a} of the fused triazine and to the C_3 of the triazine portion respectively, which seems to indicate that one of the triazine rings displays cationic character. When ethanolic solutions of compounds **3** are treated with tetrafluoroboric acid at room temperature either the salts **4** or **5** are obtained. The n.m.r. data of compounds **4** are very similar to those of compounds **3** whereas in compounds **5** only one aryl group and one cationic triazine ring is disclosed. The formation of the salts **4** and **5** can be understood by initial protonation of the central anionic guanidino moiety to give **4**, further protonation on the guanidinio group followed by cyclization by nucleophilic attack of the thiocarbonyl group of the neutral triazine ring on the carbon of the guanidinio portion leads to two molecules of **5**.

Finally, iminophosphorane **1** reacts with methyl and benzylisothiocyanate in dry benzene at room temperature to give the corresponding zwitterionic compounds **6** as highly insoluble orange solids which are converted into the salts **7** by treatment with tetrafluoroboric acid at room temperature (Scheme 1). The

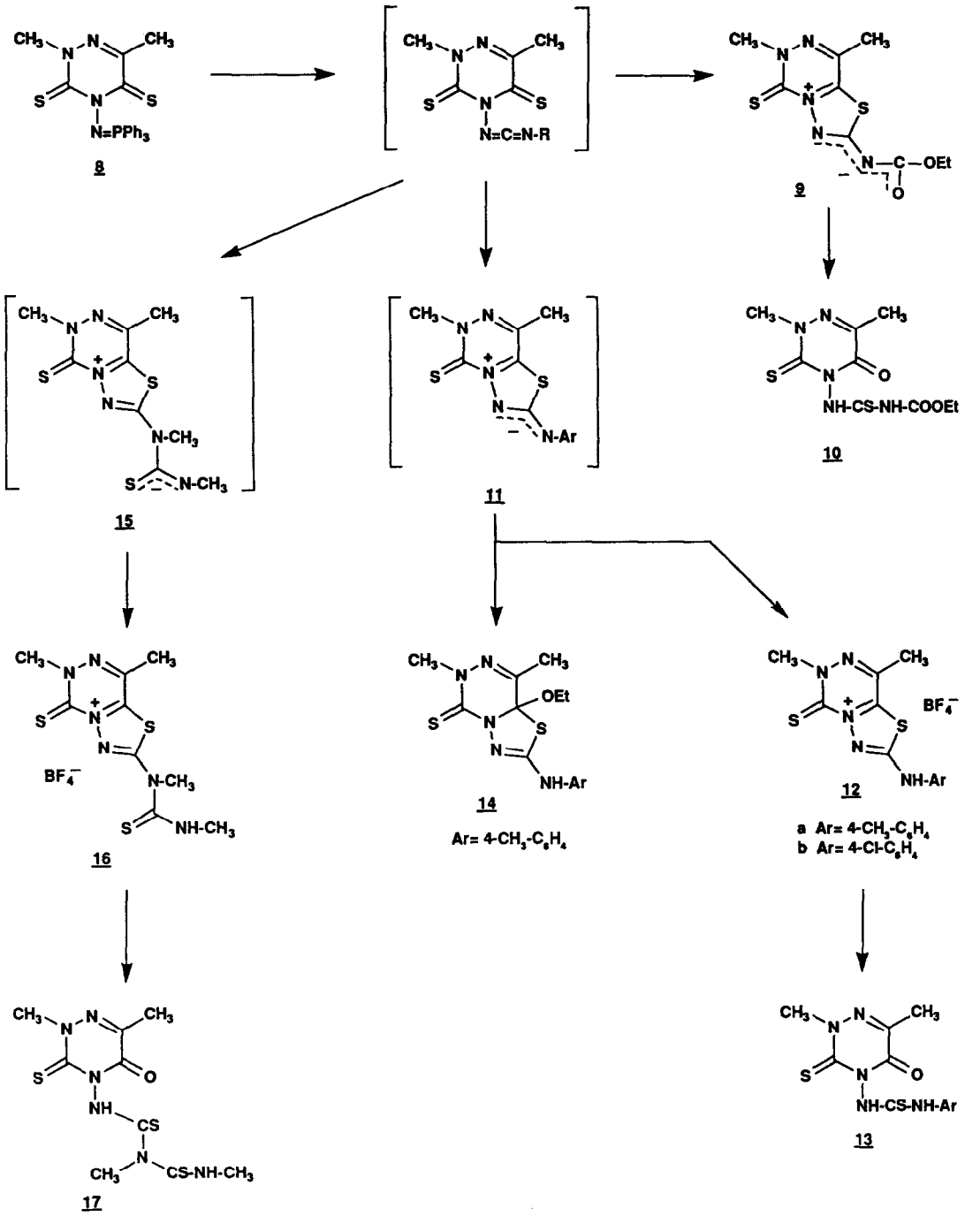

1
N=C=N-R
2
a R'= OC2H5
b R'= C6H5
3
a Ar= 4-H3CO-C6H4
b Ar= 4-F-C6H4
c Ar= 4-Cl-C6H4
4
a Ar= 4-H3CO-C6H4
6
7
a R= CH3
b R= C6H5-CH2
2
Ar-NH
5
a Ar= 4-F-C6H4
b Ar= 4-Cl-C6H4

Scheme 1

^{1}H n.m.r. spectrum of **7a** shows characteristically the two methyl groups on the triazine ring at δ 2.47 and 4.15 ppm respectively, whereas the two methyl groups on the side chain at position 7 appear as a doublet at δ 3.07 ppm and a singlet at δ 3.84 ppm. In the ^{13}C n.m.r. spectrum the chemical shifts of the ring carbon atoms clearly show the cationic character of this ring, in addition a new signal due to the thiocarbonyl group of the thiourea substituent appears at δ 179 ppm.

The formation of fused 1,2,4-triazines **2**, **3** and **6** can be understood keeping in mind that the stability of mesoionic aminides strongly depends on the nature of the substituent linked to the exocyclic nitrogen atom. Thus, it is well-known that mesoionic aminides bearing aryl or electron-withdrawing groups linked to the exocyclic nitrogen atom are stable[5], whereas mesoionic aminides in which the exocyclic nitrogen atom is attached to an alkyl group are rare[6]. This fact could be due to the instability of these compounds associated with the high negative charge density on the exocyclic nitrogen atom. In all cases it is assumed that the reaction of iminophosphorane **1** with isocyanates leads to a carbodiimide as intermediate through an aza Wittig-type reaction followed by cyclization to give a mesoionic aminide; further evolution of this fused mesoionic compound depends on the nature of the R group. Thus, the formation of **2** is a representative example of highly stabilized aminides where the exocyclic negative charge is delocalized on the adjacent carbonyl group. In the conversion **1**→**3** the initial mesoionic aminide reacts with a second molecule by nucleophilic attack of the exocyclic negatively charged nitrogen atom on the C-2 carbon atom of the [1,3,4]thiadiazolium ring of the second molecule with concomitant ring-opening of the five-membered ring to give **3**. A similar reaction pathway for the conversion **1**→**6** could take place, in this case the highly reactive mesoionic aminide reacts with a second molecule of the isothiocyanate to give **6**.

On the other hand, iminophosphorane **8**, available from 4-amino-2,6-dimethyl-3,5-dithioxo-2,3,4,5-tetrahydro-1,2,4-triazine[7] and triphenylphosphine dibromide, reacts in regioselective fashion with ethoxycarbonyl isothiocyanate in dry benzene at room temperature to give the mesoionic compound [1,3,4]thiadiazolo[3,2-d][1,2,4]triazinium-6-aminide **9** in excellent yield. ^{1}H and ^{13}C n.m.r. data confirmed the proposed structure **9**. In addition when compound **9** was treated with aqueous ethanol at room temperature the thiourea derivative **10** was isolated. Compound **10** can be also prepared from 4-amino-2,6-dimethyl-5-oxo-3-thioxo-2,3,4,5-tetrahydro-1,2,4-triazine and ethoxycarbonyl isothiocyanate. Iminophosphorane **8** also reacts with aromatic isocyanates to give the mesoionic compounds **11** as deep purple solids; due to the low solubility showed in the most common solvents n.m.r. data are not available, however chemical evidence of structure **11** has been firmly stablished by the two following facts: a) when ethanolic suspensions of **11** are treated with tetrafluoroboric acid the fused [1,2,4]triazinium salts **12** are obtained in good yields, which by treatment with aqueous ethanol undergo ring-opening to give the thioureas **13**. Compounds **13** can also be prepared from 4-amino-2,6-dimethyl-5-oxo-3-thioxo-2,3,4,5-tetrahydro-1,2,4-triazine and the appropriate isothiocyanate; b) when compounds **11** are treated with ethanol at room temperature the neutral fused 1,2,4-triazines **14** are isolated in good yields. In the ^{13}C n.m.r. spectrum of **12a** the C- and N-methyl groups appear at δ 19.70 and 49.35 ppm respectively, the assignments of the quaternary carbon atoms of the 1,2,4-triazine ring have been made through gate-decoupled and COLOC


8
N=PPh3
N=C=N-R
9
OEt
10
NH-CS-NH-COOEt
15
N-CH3
N-CH3
11
N-Ar
16
BF4−
NH-CH3
14
OEt
NH-Ar
Ar= 4-CH3-C6H4
12
BF4−
NH-Ar
a Ar= 4-CH3-C6H4
b Ar= 4-Cl-C6H4
13
NH-CS-NH-Ar
17
NH
CS
CS-NH-CH3

Scheme 2

experiments: C_3=161.0 ppm (^3J=3.6 Hz), C_{7a}=150.52 ppm (^3J=3.5 Hz), C_6=139.72 ppm (^2J=7.3 Hz), C_6=161.17 ppm. In the ^{13}C n.m.r. spectrum of **14** the quaternary carbon atom C_{7a} appears at δ 98.68 ppm, in addition to the characteristic signals due to the ethoxy group.

Compounds type **14** have been postulated as intermediates in the isomerization of monocyclic 1,3,4-thiadiazolium-2-aminides into [1,3,4]triazolium-2-thiolates, however they had never been isolated[8].

Finally, iminophosphorane **8** reacts with methyl isothiocyanate at room temperature to give the mesoionic compound **15** as an orange solid which by treatment with tetrafluoroboric acid is converted into the 1,2,4-triazinium salt **16**. Further treatment with aqueous ethanol leads to the thiourea derivative **17** (Scheme 2). Structural elucidation of compounds **16** and **17** has been accomplished by spectroscopic and analytical data.

The formation of the thiourea derivatives **14** and **17** clearly shows the abilability of the [1,3,4]thiadiazolo[3,2-d][1,2,4]triazinium salts to undergo ring-opening of the thiadiazole ring.

In conclusion, carbodiimides derived from aza Wittig-type reaction between iso(thio)cyanates and iminophosphoranes derived from 4-amino-3-thioxo-5-oxo(thioxo)-2,3,4,5-tetrahydro-1,2,4-triazine undergo cyclization to give fused thiadiazolo-triazines. It is worth noting that the mode of achieving the cyclization depends on the nature of the exocyclic heteroatom in position 5. Thus, for the 5-oxo derivative **1** the cyclization is through the thiocarbonyl group at position 3 to give [1,3,4]thiadiazolo[2,3-c][1,2,4]triazine derivatives, whereas for the 5-thioxo derivative **8** cyclization occurs by nucleophilic attack of the sulfur atom at position 5 to give the previously unreported [1,3,4]thiadiazolo[3,2-d][1,2,4]triazine derivatives.

Experimental:

All melting points were determined on a Kofler hot-plate melting point apparatus and are uncorrected. IR spectra were obtained as Nujol emulsions on a Nicolet FT-5DX spectrophotometer. ^1H and ^{13}C NMR spectra were recorded on a Bruker AC-200, and chemical shifts are expressed in parts per million (δ) relative to internal Me_4Si. Two-dimensional spectra,gate-decoupled and DEPT experiments were recorded using standard conditions. Electron-impact mass spectra were carried out on a Hewlett-Packard 5993C spectrometer at an ionization potential of 70 eV. Microanalyses were performed on a Perkin-Elmer 240C instrument.

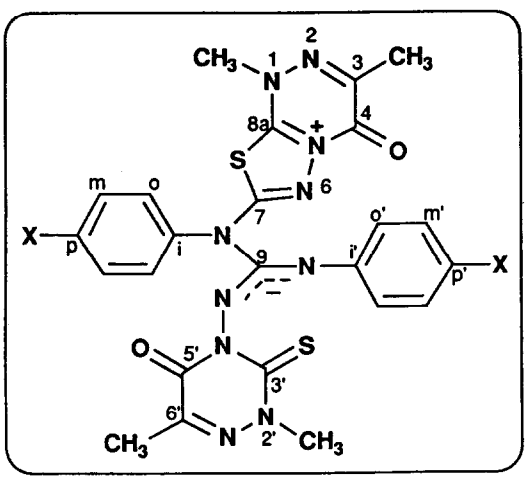
Materials. 4-Amino-2,6-dimethyl-5-oxo-3-thioxo-2,3,4,5-tetrahydro[1,2,4]triazine[9], 4-amino-2,6-dimethyl-3,5-ditioxo-2,3,4,5-tetrahydro[1,2,4]triazine[7] and 2,6-dimethyl-4-triphenylphosphoranylideneamino-5-oxo-3-thioxo-2,3,4,5-tetrahydro[1,2,4]triazine **1**[4] were prepared as described in the literature.

General Procedure for the Reaction of Iminophosphorane (1) with Iso(thio)cyanates.

A solution of the appropriate isocyanate or isothiocyanate (2.5 mmol) in dry benzene (5 ml) was added dropwise at 0°C to a well-stirred solution of iminophosphorane **1** (1.08 g, 2.5 mmol) in the same solvent (20 ml).The reaction mixture was stirred at room temperature for 5 h and the separated solid was collected by filtration, air-dried and recrystallized from the adequate solvent.

1,3-Dimethyl-4-oxo-[1,3,4]thiadiazolo[2,3-c][1,2,4]triazylium-7-ethoxycarbonyl aminide (2a) (95 %), m.p. 208-210°C (colourless prisms from chloroform). (Found: C, 39.90; H, 4.23; N,25.82. $C_9H_{11}N_5O_3S$ requires: C, 40.14; H, 4.11; N, 26.00); i.r. (Nujol) 1727, 1636, 1261, 1229, and 1086 cm^{-1}; ^1H n.m.r. δ (DMSO-d_6): 1.22 (t, 3H, J=7.1 Hz, CH_3-CH_2O), 2.40 (s, 3H, CH_3-C_3), 4.07 (s, 3H, CH_3-N_1), 4.08 (q, 2H, J=7.1 Hz, CH_3-CH_2O); ^{13}C n.m.r. δ (DMSO-d_6): 14.54 (CH_3-CH_2O), 16.84 (CH_3-C_3), 46.43 (CH_3-N_1), 60.80 (CH_3-CH_2O), 146.28 (C_4), 149.81 (C_3), 159.43 (C_{8a}), 162.03 (C_7), 164.59 ($COOCH_2$); m/z (%) 269 (M^+, 5), 197 (20), 128 (25), 87 (70), 45 (100).

1,3-Dimethyl-4-oxo-[1,3,4]thiadiazolo[2,3-c][1,2,4]triazylium-7-benzoylaminide (2b) (98 %), m.p. 318-320°C (yellow prisms from dimethylformamide) (Found: C, 51.65; H, 3.52; N, 23.20. $C_{13}H_{11}N_5O_2S$ requires C, 51.81; H, 3.67; N, 23.24); i.r. (Nujol) 1716,1557,1512,1055, 905 and 723 cm^{-1}; ^1H n.m.r. δ (DMSO-d_6): 2.45 (s, 3H, CH_3-C_3), 4.15 (s, 3H, CH_3-N_1), 7.55-8.30 (m, 5H, Ar); m/z (%) 301(M^+,5), 224 (7), 105 (100), 86 (6), 77 (56), 51 (19).



Betaine 3a (Ar=4-$CH_3OC_6H_4$) (59 %), m.p. 140-142°C (orange prisms from benzene) (Found: C, 51.31; H, 4.23; N, 22.95. $C_{26}H_{26}N_{10}O_4S_2$ requires: C, 51.47; H, 4.32; N, 23.08); i.r. (Nujol) 1692, 1683, 1627, 1613, 1506 and 1248 cm^{-1}; ^1H n.m.r. δ($CDCl_3$): 1.92 (s, 3H, CH_3-$C_{6'}$), 2.39 (s, 3H, CH_3-C_3), 3.69 (s, 6H, CH_3-$N_{2'}$ + CH_3O-Ar), 3.70 (s, 3H, CH_3O-Ar), 3.74 (s, 3H, CH_3-N_1), 6.54 (d, 2H, J=8.7 Hz, Ar), 6.82 (d, 4H, J=8.7 Hz, Ar), 7.57 (d, 2H, J=8.7 Hz, Ar); ^{13}C n.m.r. δ ($CDCl_3$): 16.66 (CH_3-$C_{6'}$), 17.07 (CH_3-C_3), 44.68 (CH_3-$N_{2'}$), 46.76 (CH_3-N_1), 55.35 (CH_3O-Ar), 55.62 (CH_3O-Ar), 112.72 ($C_{m'}$), 114.18 (C_m), 124.93 ($C_{o'}$), 129.94 ($C_{i'}$), 130.15 (C_o), 134.98 (C_i), 144.08 ($C_{6'}$), 145.84 (C_4), 147.69 (C_9), 150.58 ($C_{5'}$), 151.06 (C_3), 155.85 ($C_{p'}$), 157.60 (C_7), 159.02 (C_p), 160.28 (C_{8a}), 172.40 ($C_{3'}$); m/z (%) 294 (6), 165 (100), 150 (73), 122 (75), 70 (38), 63 (13).

Betaine 3b (Ar=4-F-C_6H_4) (99 %) m.p. 147-149°C (orange prisms from benzene) (Found: C, 49.38;

H, 3.31; N, 23.92. $C_{24}H_{20}F_2N_{10}O_2S_2$ requires C, 49.48; H, 3.46; N, 24.04); i.r. (Nujol) 1699, 1608, 1582, 1499, 1209, 848 and 699 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 1.92 (s, 3H, CH_3-$C_{6'}$), 2.39 (s, 3H, CH_3-C_3), 3.69 (s, 3H, CH_3-N_2), 3.77 (s, 3H, CH_3-N_1), 6.70-7.01 (m, 6H, Ar), 7.59-7.65 (m, 2H, Ar); ^{13}C n.m.r. δ ($CDCl_3$): 16.64 (*C*H_3-$C_{6'}$), 17.09 (*C*H_3-C_3), 44.73 (CH_3-N_2), 46.87 (CH_3-N_1), 114.01 (d, ^2J=22.1 Hz, $C_{m'}$), 115.92 (d, ^2J=22.8 Hz, C_m), 125.03 (d, ^3J=7.8 Hz, $C_{o'}$), 130.90 (d, ^3J=8.7 Hz, C_o), 132.94 (d, ^4J=3.1 Hz, $C_{i'}$), 138.00 (d, ^4J=2.0 Hz, C_i), 144.21 ($C_{6'}$), 145.64 (C_4), 147.45 (C_9), 150.67 ($C_{5'}$), 151.63 (C_3), 157.32 (C_7), 159.36 (d, ^1J=242.3 Hz, $C_{p'}$), 160.23 (C_{8a}), 162.16 (d, ^1J=247.7 Hz, C_p), 172.34 ($C_{3'}$); m/z (%) 274 (9), 230 (21), 157 (20), 153 (100), 136 (25), 95 (55), 83 (32).

Betaine 3c (Ar=4-Cl-C_6H_4) (56 %) m.p. 167-169°C (orange prisms from benzene) (Found: C, 46.72; H, 3.16; N, 22.59. $C_{24}H_{20}Cl_2N_{10}O_2S_2$ requires C, 46.83; H, 3.27; N, 22.75); i.r. (Nujol) 1693, 1597, 1568, 1551, 1529, 1166 and 843 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 1.93 (s, 3H, CH_3-$C_{6'}$), 2.44 (s, 3H, CH_3-C_3), 3.72 (s, 3H, CH_3-N_2), 3.86 (s, 3H, CH_3-N_1), 6.79 (d, 2H, J=8.5 Hz, Ar), 6.98 (d, 2H, J=8.5 Hz, Ar), 7.36 (d, 2H, J=8.6 Hz, Ar), 7.63 (d, 2H, J=8.6 Hz, Ar); ^{13}C n.m.r. δ ($CDCl_3$): 16.61 (*C*H_3-$C_{6'}$), 17.20 (*C*H_3-C_3), 45.04 (CH_3-N_2), 46.95 (CH_3-N_1), 125.11 ($C_{o'}$), 127.35 ($C_{m'}$), 129.31 (C_o), 130.59 (C_m), 128.33 ($C_{p'}$), 134.24 (C_p), 135.69 ($C_{i'}$), 141.24 (C_i), 144.23 ($C_{6'}$), 145.59 (C_4), 147.45 (C_9), 150.79 ($C_{5'}$), 151.81 (C_3), 157.29 (C_7), 160.11 (C_{8a}), 172.36 ($C_{3'}$); m/z (%) 290 (5), 171 (41), 169 (97), 157 (36), 134 (100), 125 (35), 111 (90), 75 (65).

Treatment of Compounds (3) with Tetrafluoroboric Acid.

To a solution of the appropriate compound **3** (2.5 mmol) in ethanol (20 ml) was added tetrafluoroboric acid (0.44 g, 5 mmol). The mixture was stirred at room temperature for 7 h. Then, the solid was separated by filtration and recrystallized from the adequate solvent to give **4** or **5**.

(4a) (Ar=4-CH_3O-C_6H_4) (51 %) m.p. 207-209°C (colourless prisms from dimethylsulfoxide) (Found: C,44.83; H, 3.79; N, 20.03. $C_{26}H_{27}BF_4N_{10}O_4S_2$ requires C, 44.96; H, 3.92; N, 20.16); i.r. (Nujol) 3296, 1733, 1602, 1512, 1499, 1248, 1080 and 828 cm^{-1}; ^1H n.m.r. δ (DMSO-d_6): 2.16 (s, 3H, CH_3-$C_{6'}$), 2.41 (s, 3H, CH_3-C_3), 3.67 (s, 3H, C*H*$_3$O-Ar), 3.77 (s, 3H, C*H*$_3$O-Ar), 3.86 (s, 3H, CH_3-N_2), 4.08 (s, 3H, CH_3-N_1), 6.74 (br s, 4H, Ar), 6.98 (d, 2H, J=8.6 Hz, Ar), 7.14 (d, 2H, J=8.6 Hz, Ar), 9.50 (br s, 1H, NH); ^{13}C n.m.r. δ (DMSO-d_6): 16.65 (*C*H_3-$C_{6'}$), 16.89 (*C*H_3-C_3), 46.44 (CH_3-N_1), 46.63 (CH_3-N_2), 55.45 (*C*H_3O-Ar), 55.55 (*C*H_3O-Ar), 113.91 ($C_{m'}$), 114.77 (C_m), 126.17 ($C_{o'}$), 128.43 ($C_{i'}$), 128.61 (C_i), 128.96 (C_o), 145.79 ($C_{6'}$), 145.80 (C_4), 149.35 ($C_{5'}$), 152 75 (C_3), 155.12 (C_9), 157.12 (C_7), 158.00 ($C_{p'}$), 159.56 (C_p), 160.25 (C_{8a}), 171.06 ($C_{3'}$); m/z (%) 254 (8), 239 (10), 165 (100), 150 (42), 122 (44), 64 (11).

1,3-Dimethyl-7-[(4-fluorophenyl)amino]-4-oxo-[1,3,4]thiadiazolo[2,3-c][1,2,4]triazinium Tetrafluoroborate (5a) (77 %), m.p. 218-220°C (colourless prisms from ethanol) (Found: C, 37.89; H, 2.81; N, 18.33. $C_{12}H_{11}BF_5N_5OS$ requires C, 38.02; H, 2.92; N, 18.47); i.r. (Nujol) 3336, 1744, 1580, 1530, 1386, 1234, 1108, 1080 and 836 cm^{-1}; ^1H n.m.r. δ (DMSO-d_6): 2.49 (s, 3H, CH_3-C_3), 4.19 (s, 3H, CH_3-N_1), 7.34 (t, 2H, J=8.6 Hz, H_m), 7.65 (dd, 2H, J=4.5, 8.6 Hz, H_o), 11.47 (s, 1H, NH); ^{13}C n.m.r. δ (DMSO-d_6):

17.00 (CH_3-C_3), 47.82 (CH_3-N_1), 116.43 (d, ^2J=22.9 Hz, C_m), 121.10 (d, ^3J=8.2 Hz, C_o), 134.42 (d, ^4J=2.3 Hz, C_i), 145.69 (C_4), 153.21 (C_3), 154.34 (C_7), 158.90 (d, ^1J=242.2 Hz, C_p), 160.38 (C_{8a}); m/z (%) 274 (10), 230 (11), 153 (100), 136 (51), 103 (34), 95 (56), 75 (24), 49 (42).

7-[(4-Chlorophenyl)amino]-1,3-dimethyl-4-oxo-[1,3,4]thiadiazolo[2,3-c][1,2,4]triazinium Tetrafluoroborate (5b) (85 %), m.p. 216-218°C (colourless prisms from ethanol) (Found: C, 36.30; H, 2.62; N, 17.61. $C_{12}H_{11}BClF_4N_5OS$ requires C, 36.43; H, 2.80; N, 17.70); i.r. (Nujol) 3330, 1733, 1619, 1580, 1534, 1495, 1080 and 838 cm^{-1}; ^1H n.m.r. δ (DMSO-d_6): 2.49 (s, 3H, CH_3-C_3), 4.19 (s, 3H, CH_3-N_1), 7.55 (d, 2H, J=8.8 Hz, H_m), 7.64 (d, 2H, J=8.8 Hz, H_o), 11.55 (s, 1H, NH); ^{13}C n.m.r. δ (DMSO-d_6): 16.96 (CH_3-C_3), 47.78 (CH_3-N_1), 120.47 (C_o), 128.50 (C_i), 129.51 (C_m), 136.77 (C_p), 145.60 (C_4), 153.18 (C_3), 153.93 (C_7), 160.30 (C_{8a}); m/z (%) 290 (7), 192 (6), 171 (30), 169 (100), 152 (39), 111 (46), 75 (34), 49 (49).

7-Substituted 1,3-Dimethyl-4-oxo-[1,3,4]thiadiazolo[2,3-c][1,2,4]triazinium Tetrafluoroborates (7).

A solution of methyl or benzylisothiocyanate (2.5 mmol) in dry benzene (10 ml) was added dropwise at 0°C to a well-stirred solution of iminophosphorane **1** (1.08 g, 2.5 mmol) in the same solvent (20 ml). The reaction mixture was stirred at room temperature for 24 h. The orange precipitated solid **6** was filtered and air-dried. To a suspension of compound **6** (2.5 mmol) in ethanol (20 ml) was added tetrafluoroboric acid (5 mmol) and the resultant mixture was stirred at room temperature for 8 h. The white solid was collected by filtration and recrystallized from the same solvent to give **7**.

(7a) (R=CH_3) (66 %), m.p. 179-181°C (colourless prisms from ethanol) (Found: C, 28.89; H, 3.41; N, 22.43. $C_9H_{13}BF_4N_6OS_2$ *requires* C, 29.04; H, 3.52; N, 22.58); *i.r.* (Nujol) 3358, 1738, 1557, 1517, 1387, 1080 and 707 cm^{-1}; ^1H n.m.r. δ (DMSO-d_6): 2.47 (s, 3H, CH_3-C_3), 3.07 (d, 3H, J=3.5 Hz, CH_3NH), 3.84 (s, 3H, CH_3N-C=S), 4.15 (s, 3H, CH_3-N_1), 9.72 (q, 1H, J=3.5 Hz, NH); ^{13}C n.m.r. δ (DMSO-d_6): 16.94 (CH_3-C_3), 33.55 (CH_3NH), 37.65 (CH_3-N-C=S), 45.90 (CH_3-N_1), 146.13 (C_4), 152.73 (C_3), 155.52 (C_{8a}), 157.46 (C_7), 178.97 (C=S); m/z (%) 283 (9), 211 (56), 73 (100), 72 (52), 45 (39).

(7b) (R=C_6H_5-CH_2) (41 %), m.p. 154-156°C (colourless prisms from ethanol) (Found: C, 47.93; H, 3.88; N, 15.90. $C_{21}H_{21}BF_4N_6OS_2$ requires C, 48.10; H, 4.03; N, 16.02); i.r. (Nujol) 3330, 1727, 1533, 1505, 1294, 1080 and 714 cm^{-1}; ^1H n.m.r. δ (DMSO-d_6): 2.43 (s, 3H,CH_3-C_3), 4.15 (s, 3H, CH_3-N_1), 4.81 (d, 2H, J=4.5 Hz, CH_2NH), 5.85 (s, 2H, CH_2-N), 7.02-7.43 (m, 10H, Ar), 10.33 (t, 1H, J=4.5 Hz, NH); ^{13}C n.m.r. δ (DMSO-d_6): 16.90 (CH_3-C_3), 45.88 (CH_3-N_1), 49.65 (CH_2-NH), 52.05 (CH_2N), 126.38, 127.25, 127.31, 127.96, 128.31, 128.81, 133.75 (q), 136.21 (q), 146.03 (C_4), 152.79 (C_3), 155.65 (C_{8a}), 157.56 (C_7), 178.65 (C=S); m/z (%) 150 (5), 149 (29), 91 (100), 89 (10), 65 (12).

2,6-Dimethyl-3,5-dithioxo-4-triphenylphosphoranylideneamino-2,3,4,5-tetrahydro[1,2,4]triazine (8).

Carbon tetrachloride (2.7 ml) was added dropwise at room temperature to a well stirred solution of 4-amino-2,6-dimethyl-3,5-dithioxo-2,3,4,5-tetrahydro[1,2,4]triazine (0.47 g, 2.5 mmol), triphenylphosphine

(1.31 g, 5 mmol) and triethylamine (4 ml) in dry acetonitrile (14 ml). The reaction mixture was stirred at room temperature for 24 h. Then, the red precipitated solid was collected by filtration and washed with cold ethanol (3 x 10 ml), dried and recrystallized from ethyl acetate to give **8** (90 %) m.p. 182°C as orange crystals. (Found: C, 61.51; H, 4.68; N, 12.38. $C_{23}H_{21}N_4PS_2$ requires C, 61.59; H, 4.72; N, 12.49); i.r. (Nujol) 1562, 1440, 1314, 1230, 1161, 1113, 844, 725 and 689 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 2.28 (s, 3H, CH_3-C_6), 3.80 (s, 3H, CH_3-N_2), 7.32-7.51 (m, 9H, Ar), 7.81-7.91 (m, 6H, Ar); ^{13}C n.m.r. δ ($CDCl_3$): 22.58 (CH_3-C_6), 48.65 (CH_3-N_2), 127.93 (d, ^3J=12.3 Hz, C_m), 128.98 (d, ^1J=98.7 Hz, C_i), 131.58 (d, ^4J=2.8 Hz, C_p), 133.30 (d, ^2J=9.6 Hz, C_o), 148.97 (C_6), 172.64 (d, ^3J=4.2 Hz, C_3), 176.69 (d, ^3J=3.7 Hz, C_5); m/z (%) 448 (M+, 19), 276 (44), 262 (52), 183 (100), 108 (82), 77 (25).

2,8-Dimethyl-3-thioxo-[1,3,4]thiadiazolo[3,2-d][1,2,4]triazylium-6-ethoxycarbonylaminide (9). This compound was prepared by the same procedure as described for **2a**. Yield 97 %, m.p. 212-214°C (colourless prisms from dimethylsulfoxide) (Found: C, 37.77; H, 3.34; N, 24.46. $C_9H_{11}N_5O_2S_2$ requires C, 37.88; H, 3.88; N, 24.54); i.r. (Nujol) 1614, 1540, 1470, 1353, 1256, 1205, 1149 and 788 cm^{-1}; ^1H n.m.r. δ (DMSO-d_6): 1.25 (t, 3H, J=7.0 Hz, CH_3CH_2), 2.62 (s, 3H, CH_3-C_8), 4.13 (q, 2H, J=7.0 Hz, CH_3CH_2), 4.17 (s, 3H, CH_3-N_2); ^{13}C n.m.r. δ (DMSO-d_6): 14.39 (CH_3CH_2), 19.24 (CH_3-C_8), 48.93 (CH_3-N_2), 61.17 (CH_3CH_2), 140.01 (C_8), 147.13 (C_{7a}), 161.65 (C_3), 164.41 (CO), 168.64 (C_6); m/z (%) 285 (M^+, 19), 240 (15), 213 (100), 173 (80), 158 (28), 102 (31), 72 (50).

General Procedure for the Preparation of 6-Substituted 2,8-Dimethyl-3-thioxo-[1,3,4]thiadiazolo[3,2-d][1,2,4]triazinium Tetrafluoroborates (12) and (16).

To a solution of iminophosphorane **8** (1.12 g, 2.5 mmol) in dry benzene (20 ml) was added dropwise at 0°C a solution of the appropriate isocyanate (3 mmol) in the same solvent (20 ml). The mixture was allowed to warm at room temperature and stirred for 8 h. The deep violet precipitated solid was collected by filtration, washed with ether (2x20 ml) and air-dried to give **11** (69-80 %) or **15** (63 %).

To a suspension of compound **11** or **15** (2.5 mmol) in ethanol (20 ml) was added tetrafluoroboric acid (0.44 g, 5 mmol) and the resultant mixture was stirred at room temperature for 3 h. The white solid was separated by filtration, washed with ether (2x20 ml) and recrystallized from dimethylsulfoxide to give **12** or **16**.

(12a) (Ar=4-H_3C-C_6H_4) (85 %) m.p. 214-216°C as white crystals. (Found: C, 39.79; H, 3.49; N, 17.74. $C_{13}H_{14}BF_4N_5S_2$ requires C, 39.91; H, 3.60; N, 17.90); i.r. (Nujol) 3296, 1609, 1557, 1365, 1117, 1077, 998 and 813 cm^{-1}; ^1H n.m.r. δ (DMSO-d_6): 2.33 (s, 3H, CH_3-Ar), 2.69 (s, 3H, CH_3-C_8), 4.21 (s, 3H, CH_3-N_2), 7.30 (d, 2H, J=8.3 Hz, C_m), 7.57 (d, 2H, J=8.3 Hz, C_o), 12.00 (br s, 1H, NH); ^{13}C n.m.r. δ (DMSO-d_6): 19.70 (CH_3-C_8), 20.57 (CH_3-Ar), 49.35 (CH_3-N_2), 119.18 (C_o), 130.13 (C_m), 135.09 (C_p), 135.24 (C_i), 139.72 (C_8), 150.52 (C_{7a}), 161.06 (C_3), 161.17 (C_6); m/z (%) 303 (47), 173 (24), 158 (58), 149 (88), 117 (99), 91 (94), 49 (100).

(12b) (Ar=4-Cl-C_6H_4) (73 %), m.p. 208-210°C, as colourless prisms. (Found: C, 34.89;H, 2.66; N,

16.93. $C_{12}H_{11}BClF_4N_5S_2$ requires C, 35.01; H, 2.69; N, 17.01); i.r. (Nujol) 3296, 1605, 1557, 1464, 1366, 1117, 1090, 971 and 823 cm^{-1}; ^1H n.m.r. δ (DMSO-d_6): 2.73 (s, 3H, CH_3-C_8), 4.23 (s, 3H, CH_3-N_2), 7.57 (d, 2H, J=8.8 Hz, C_o), 7.73 (d, 2H, J=8.8 Hz, C_m), 12.29 (br s, 1H, NH); ^{13}C n.m.r. δ (DMSO-d_6): 19.81 (CH_3-C_8), 49.47 (CH_3-N_2), 120.83 (C_o), 129.38 (C_p), 129.74 (C_m), 136.59 (C_i), 140.02 (C_8), 151.19 (C_{7a}), 161.09 (C_6), 161.22 (C_3); m/z (%) 323 (8), 171 (36), 169 (100), 158 (15), 111(50), 75 (35), 49 (61).

(16) (80 %), m.p. 170-172°C, as colourless prisms. (Found: C, 27.74; H, 3.29; N, 21.52. $C_9H_{13}BF_4N_6S_3$ requires C, 27.84; H, 3.37; N, 21.65); i.r. (Nujol) 3347, 1550, 1519, 1464, 1378, 1287 and 1070 cm^{-1}; ^1H n.m.r. δ (DMSO-d_6): 2.75 (s, 3H, CH_3-C_8), 3.10 (d, 3H, J=4.1 Hz, CH_3NH), 4.00 (s, 3H, CH_3NCS), 4.24 (s, 3H, CH_3-N_2), 9.86 (q, 1H, J=4.1 Hz, NH); ^{13}C n.m.r. δ (DMSO-d_6): 18.88 (*C*H_3-C_8), 33.47 (CH_3NH), 38.34 (*C*H_3NCS), 49.03 (CH_3-N_2), 140.38 (C_8), 144.47 (C_{7a}), 161.80 (C_3), 163.74 (C_6), 179.05 (C=S); m/z (%) 227 (97), 210 (7), 173 (41), 158 (29), 102 (29), 73 (100), 49 (96).

Preparation of Compound (14).

A suspension of compound **11** (Ar=4-H_3C-C_6H_4) (0.76 g, 2.5 mmol) in ethanol (20 ml) was stirred at room temperature for 15 h, during which time it slowly turned from violet to pale yellow. The solid was separated by filtration washed with ether (2x10 ml) and recrystallized fron dimethylsulfoxide to give **14** (81 %), m.p. 310-312°C as white crystals. (Found: C, 51.43; H, 5.37; N, 19.89. $C_{15}H_{19}N_5OS_2$ requires C, 51.55; H, 5.48; N, 20.04); i.r. (Nujol) 3251, 1580, 1408, 1294, 1054, 974 and 822 cm^{-1}; ^1H n.m.r. δ (DMSO-d_6): 1.10 (t, 3H, J=6.9 Hz, C$H_3$$CH_2$), 2.26 (s, 3H, C$H_3$-Ar), 2.32 (s, 3H, CH_3-C_8), 3.20-3.60 (m, 2H, CH_2), 3.73 (s, 3H, CH_3-N_2), 7.14 (d, 2H, J=8.1 Hz, H_m), 7.53 (d, 2H, J=8.1 Hz, H_o), 10.07 (s, 1H, NH); ^{13}C n.m.r. δ (DMSO-d_6): 14.36 (*C*$H_3$$CH_2$), 19.92 (*C*$H_3$-$C_8$), 20.29 (*C*$H_3$-Ar), 43.15 ($CH_3$-$N_2$), 59.08 ($CH_2$), 98.68 ($C_{7a}$), 117.96 ($C_o$), 129.30 ($C_m$), 131.37 ($C_p$), 137.47 ($C_i$), 140.87 ($C_8$), 146.20 ($C_6$), 166.48 ($C_3$); m/z (%) 303 (32), 158 (53), 131 (51), 117 (100), 85 (66), 58 (66).

General Procedure for the Preparation of Thiourea Derivatives (10), (13) and (17).

To a suspension of compound **9**, **12** or **16** (2.5 mmol) in ethanol (20 ml) was added water (2 ml) and the mixture was stirred at room temperature for 24 h. The solid was collected by filtration, air-dried and recrystallized from ethanol or dimethylsulfoxide to give the corresponding thiourea derivatives **10**, **13** or **17**.

(10) (89 %), m.p. 198-200°C (colourless prisms from ethanol). (Found: C, 35.51; H, 4.22; N, 22.91. $C_9H_{13}N_5O_3S_2$ requires C, 35.63; H, 4.32; N, 23.08); i.r. (Nujol) 3251, 1736, 1717, 1516, 1330, 1999, 1048 and 763 cm^{-1}; ^1H n.m.r. δ (DMSO-d_6): 1.28 (t, 3H,J=7.1 Hz, C$H_3$$CH_2$), 2.24 (s, 3H,$CH_3$-$C_6$), 3.88 (s, 3H, CH_3-N_2), 4.24 (q, 2H, J=7.1 Hz, CH_2), 11.66 (s, 1H, NH), 11.77 (s, 1H, NH); ^{13}C n.m.r. δ (DMSO-d_6): 14.08 (*C*$H_3$$CH_2$), 16.64 (*C*$H_3$-$C_6$), 46.66 ($CH_3$-$N_2$), 62.49 ($CH_2$), 146.46 ($C_6$), 149.90 ($C_5$), 159.99 (CO), 173.05 ($C_3$), 180.12 (C=S); m/z (%) 303 (M^+, 5), 287 (8), 189 (13), 156 (100), 142 (87), 128 (94), 70 (54).

(13a) (84 %), mp. 125-127°C (colourless needles from ethanol). (Found: C, 48.44; H, 4.61; N, 21.69. $C_{13}H_{15}N_5OS_2$ requires C, 48.57; H, 4.70; N, 21.78); i.r. (Nujol) 3251, 3183, 1704, 1537, 1442, 1318 and

751 cm^{-1}; ^1H n.m.r. δ (DMSO-d_6): 2.24 (s, 3H, CH_3-C_6), 2.28 (s, 3H, CH_3-Ar), 3.88 (s, 3H, CH_3-N_2), 7.12-7.20 (m, 4H, Ar), 9.68 (s, 1H, NH), 10.41 (s, 1H, NH); ^{13}C n.m.r. δ (DMSO-d_6): 16.70 (*C*H_3-C_6), 20.53 (*C*H_3-Ar), 46.81 (CH_3-N_2), 128.25 (C_p), 128.71 (C_o), 134.76 (C_i), 135.94 (C_m), 147.00 (C_6), 151.44 (C_5), 174.12 (C_3), 179.60 (C=S); m/z (%) 303 (10), 172 (88), 157 (11), 149 (100), 148 (36), 91 (83), 74 (47).

(13b) (96 %), m.p. 278-280°C (colourless needles fron dimethylsulfoxide). (Found: C, 42.06; H, 3.51; N, 20.36. $C_{12}H_{12}ClN_5OS_2$ requires C, 42.16; H, 3.54; N,20.48); i.r. (Nujol) 3262, 3200, 1699, 1534, 1485, 1302 and 849 cm^{-1}; ^1H n.m.r. δ (DMSO-d_6): 2.25 (s, 3H, CH_3-C_6), 3.90 (s, 3H, CH_3-N_2), 7.33-7.37 (m, 4H, Ar), 7.40 (s, 1H, NH), 10.54 (s, 1H, NH); ^{13}C n.m.r. δ (DMSO-d_6): 16.71 (*C*H_3-C_6), 46.78 (CH_3-N_2), 127.40 (C_p), 128.05 (C_o), 129.70 (C_i), 137.39 (C_m), 146.78 (C_6), 151.38 (C_5), 173.94 (C_3), 179.75 (C=S); m/z (%) 323 (41), 195 (51), 180 (46), 137 (100), 111 (83), 75 (65).

(17) (44 %), m.p. 128-130°C (white prisms from dimethylsulfoxide). (Found: C, 33.82; H, 4.36; N, 26.21. $C_9H_{14}N_6OS_3$ requires C, 33.94; H, 4.43; N, 26.39); i.r. (Nujol) 3330, 1699, 1534, 1432, 1319, 1070 and 719 cm^{-1}; ^1H n.m.r. δ (DMSO-d_6): 2.27 (s, 3H, CH_3-C_6), 3.03 (d, 3H, J=4.3 Hz, CH_3NH), 3.59 (s, 3H, CH_3NCS), 3.92 (s, 3H, CH_3-N_2), 7.50 (s, 1H, NH), 9.58 (q, 1H, J=4.3 Hz, NH); ^{13}C n.m.r. δ (DMSO-d_6): 16.53 (*C*H_3-C_6), 32.60 (CH_3NH), 41.97 (CH_3NCS), 46.63 (CH_3-N_2), 146.43 (C_6), 150.22 (C_5), 173.11 (C_3), 182.36 (C=S), 183.26 (C=S); m/z (%) 156 (10), 104 (100), 76 (23), 74 (39), 60 (14).

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