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Synthesis of Fused 1,2,4-Thiadiazoles from 5-Chloro-1,2,4-thiadiazol-3(2H)-ones

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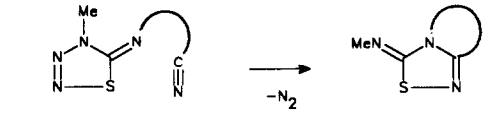
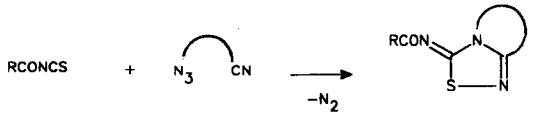
Dedicated to Prof. L. Ghosez on the occasion of his 60th birthday.

Abstract. Fused 1,2,4-thiadiazoles (**14-18** and **26-31**) are conveniently prepared by reacting the chlorothiadiazolone **12** with ω-aminonitriles and aminoazoles. During these reactions the original thiadiazole ring is opened and a new, fused thiadiazole ring is formed, probably via a hypervalent sulfur intermediate. The products derived from the aminoazoles were analyzed by X-ray crystallography and found to have structures different from those published earlier.[7]

In previous articles[1,2] we have reported that fused 1,2,4-thiadiazoles are obtained by thermolysis of 5-(cyano tethered)imino-1,2,3,4-thiatriazolines (**1**→**2**) or by reacting acyl isothiocyanates with ω-azidonitriles (**3** + **4** → **5**). We have now investigated the reactions of 5-chloro-1,2,4-thiadiazol-3(2*H*)-ones with ω-aminonitriles and aminoazoles, leading also to fused thiadiazoles.



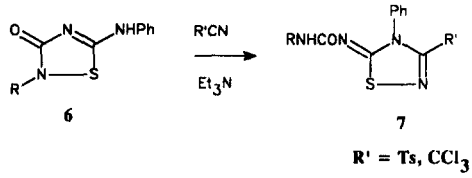
1 **2**



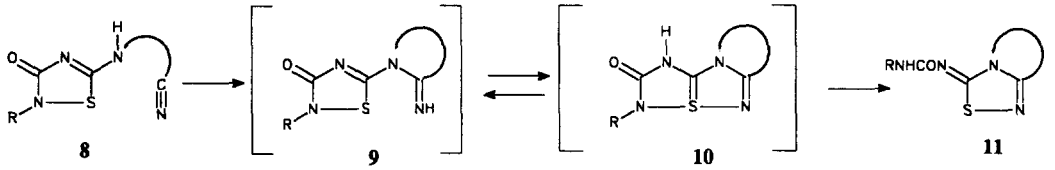
3 **4** **5**

Our first approach is based on the knowledge that 5-amino-substituted 1,2,4-thiadiazol-3(2*H*)-ones **6** react with electrophilic nitriles to give rearranged thiadiazoles **7**.[3] When these reactions are carried out intramoleculary, fused 1,2,4-thiadiazoles should result, and we surmised that the favourable entropy effect

might allow unactivated nitrile functions to react. According to our proposed Scheme 1, **9** and possibly also the hypervalent sulfur heterocycle **10**,[4] are intermediates in the conversion of **8** to **11**. The results are discussed below.

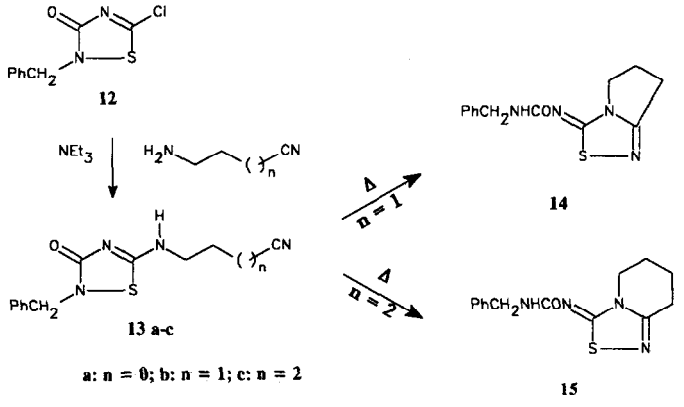


Scheme 1



The starting material **12**, used in this work, was prepared by chlorination of methoxymethyl isothiocyanate in the presence of benzyl isocyanate following the procedure of Keilen and Undheim.[5] This compound reacted with 3-aminopropionitrile, 4-aminobutyronitrile and 5-aminovaleronitrile at room temperature to give the substitution products **13a-c**. Whereas **13a** remained unchanged when heated at 140°C, **13b** and **13c** rearranged at 60 °C in chloroform solution to give the fused heterocycles **14** and **15** respectively. They were characterized by IR, ^{1}H NMR, ^{13}C NMR, mass spectra and microanalyses (see Experimental). In particular, the IR spectra were devoid of nitrile absorptions at about 2250 cm^{-1} and the ^{1}H NMR spectra showed the presence of two doublets for the benzyl methylene protons due to restricted rotation around the amide side-chain.

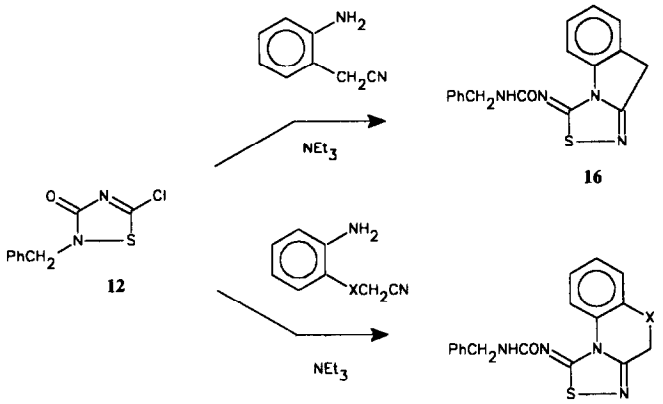
Scheme 2



The isomerizations of **13b,c** in DMSO-d_6 at 60 °C were followed kinetically by ^{1}H NMR spectroscopy and gave the following first-order rate constants: $k_1 = 3.25 \times 10^{-6}$ s^{-1} for **13b**, and $k_1 = 2.14 \times 10^{-6}$ s^{-1} for **13c**. Thus, the formation of a 5:5 fused heterocycle **14** is favoured over a 5/6 fused system **15**; and a 5/4 fused thiadiazole is not formed at all from **13a**. The same conclusion was reached for intramolecular cycloaddition-elimination reactions.[1]

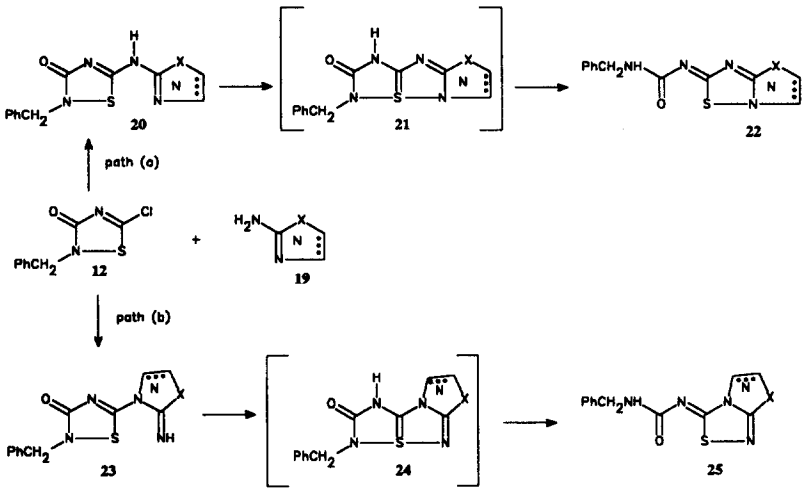
We also investigated the reactions of **12** with *o*-aminobenzyl cyanide, *o*-aminophenoxyacetonitrile and *o*-aminophenylthioacetonitrile, and obtained the rearranged products **16-18** directly at room temperature (Scheme 3). Here, the facility of the cycloaddition-ring opening reactions is caused by the mutual *ortho* disposition of the two interacting groups.

Scheme 3

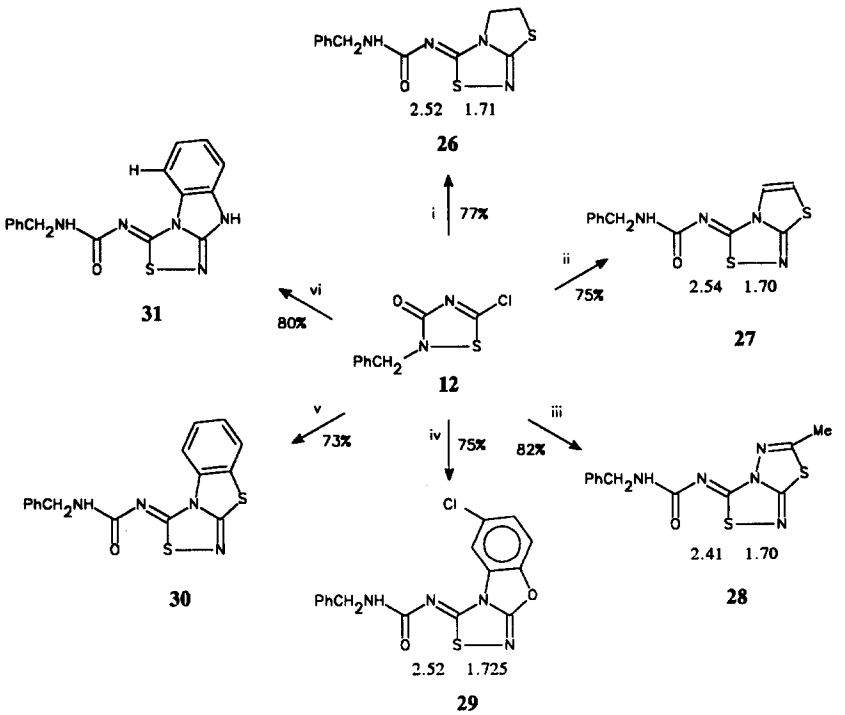


A second approach towards the synthesis of fused 1,2,4-thiadiazoles involves the reactions of **12** with aminoazoles **19** (Scheme 4). The latter may displace the chlorine atom of **12** either by the amine or the ring nitrogen atom, and evidence for both the possibilities is present in the literature.[6] The two substitution products **20** and **23** are potential candidates for rearranging to fused thiadiazoles through the thiapentalenic intermediates **21** and **24**. In fact, **12** reacted with 2-amino-4,5-dihydrothiazole, 2-aminothiazole, 2-amino-5-methyl-1,3,4-thiadiazole, 2-amino-5-chlorobenzoxazole, 2-aminobenzothiazole and 2-aminobenzimidazole to give single products, whose spectral data were interpretable in terms of either structure **22** or **25**. Since no unequivocal ^{13}C NMR criterion could be found to distinguish between the two isomeric structures, we have subjected the products to a single crystal X-ray analysis. They all correspond to structure **25** (Scheme 5). In our preliminary communication on the subject,[7] we had overlooked path (b) and attributed structure **22** to the products.

Scheme 4



Scheme 5



Reagents : i, 2-amino-4,5-dihydrothiazole; ii, 2-aminothiazole; iii, 2-amino-5-methyl-1,3,4-thiadiazole; iv,2-amino-5-chlorobenzoxazole; v, 2-aminobenzothiazole; vi, 2-aminobenzimidazole

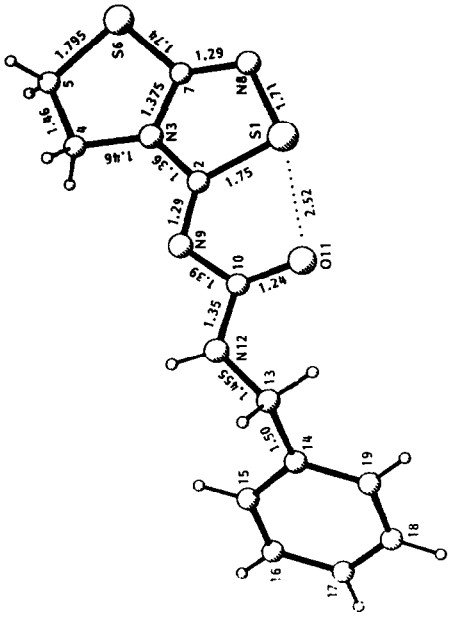


Fig. 1. Molecular structure of **26**

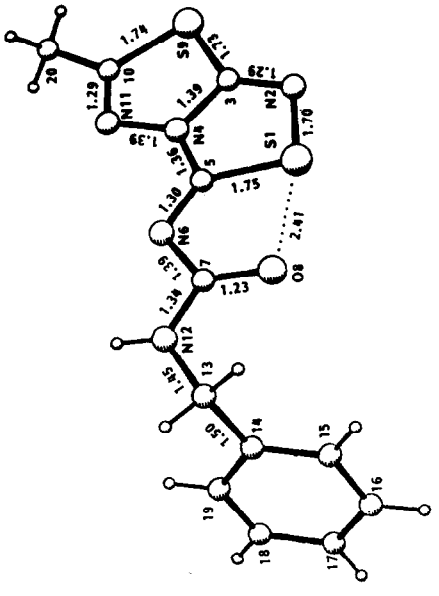


Fig. 3. Molecular structure of **28**

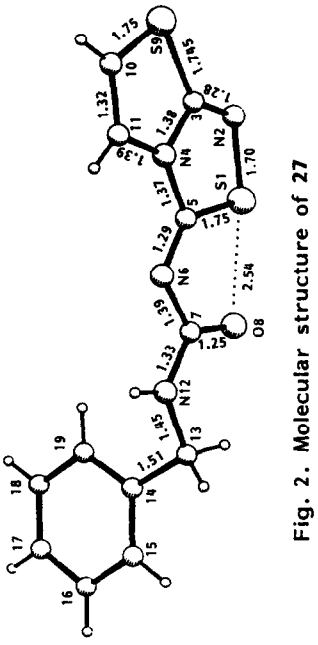


Fig. 2. Molecular structure of **27**

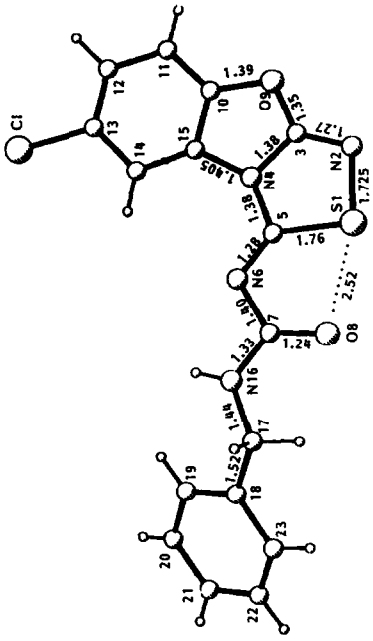
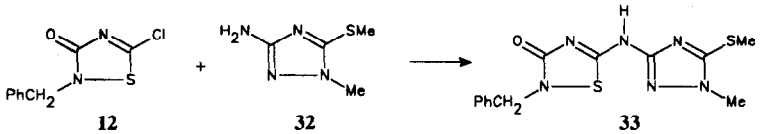


Fig. 4. Molecular structure of **29**

The X-ray structure analyses revealed that the carbamoylimine substituent is nearly coplanar with the thiadiazole ring with a carbonyl-oxygen...sulfur distance ranging between 2.41 and 2.54 Å (Figs 1-4). This is significantly less than the sum of the corresponding van der Waals radii (3.2 Å) and slightly shorter than the Huggins constant energy distance of 2.58 Å,[8] indicating little or no covalent bonding but rather a close interacting contact. The molecular structure of **30** is not included in this paper since the crystallographic data could not be refined due to much disorder in the crystal lattice; the available results, however, confirm the [1,2,4]thiadiazolo[3,4,b]benzothiazole skeleton of **30**.

No suitable crystals could be obtained from **31**, but its structure is suggested on the similarity of the NMR spectra with those of **29** and **30**. In particular, the benzo H-5 atom (indicated on the drawing) absorbs as two doublets, at δ 8.1 (major) and 7.95 (minor), separated by 0.15 ppm. This splitting is also found for the H-5 atoms of **29** and **30**, and is explained by the presence of two conformations of the side-chain amide function.

The only exception found to path (b) of Scheme 4 is the behaviour of **12** towards the aminotriazole **32** which yielded the substitution product **33**. This compound proved to be thermostable when heated in DMSO solution at 100 °C.



12 **32** **33**

EXPERIMENTAL

Melting points were determined using a Reichert Thermovar apparatus. IR spectra were recorded on a Perkin Elmer 1720 FT spectrometer, NMR spectra on a Bruker WM-250 or AMX 400 spectrometer, and mass spectra (EI) on a Hewlett Packard 5989A or Kratos MS50 TC (for high resolution) instrument, both operating at 70 eV. X-Ray studies were carried out on a Huber 4-circle diffractometer with graphite-monochromatized MoKα (λ = 0.71069 Å) or CuKα radiation (λ = 1.54178 Å), and the structures were solved by direct methods[12] and refined by least-squares methods.

Synthesis of 13a-c: General procedure.

A solution of **12** (0.5 g, 2.2 mmol)[5], ω-aminonitrile (1 equiv) and triethylamine (242 mg, 1.1 equiv) in dry chloroform (20 ml) was stirred at room temperature for 30 min. The reaction mixture was washed with water (3 x 10 ml), dried ($MgSO_4$) and evaporated, and the residue crystallized from ethanol.

2-Benzyl-5-(2-cyanoethylamino)1,2,4-thiadiazol-3(2*H*)-one (13a) was obtained in 57 % yield, mp 155-156 °C (from EtOH); IR (KBr) 3250 (m, NH), 2250 (w, CN), 1642 cm^{-1} (s, CO); ^1H NMR (250 MHz, DMSO-d_6) δ 2.8 (t, 2H, CH_2CN), 3.6 (br t, 2H, CH_2N), 4.7 (s, 2H, benzyl CH_2), 7.2-7.4 (m, 5H, Ph), 8.75 (br, 1H, NH); ^{13}C NMR (DMSO-d_6) δ 17.2 and 38.9 (CH_2CH_2N), 46.3 (benzyl CH_2), 118.9 (CN), 127.7 (x 2), 128.6 and 137.3 (Ph C-atoms), 164.9 (C-3), 170.2 (C-5); mass spectrum, m/z (%) 260 (6, $M^{\cdot+}$), 122 (30, $CN(CH_2)_2N{=}C{=}NCO^+$), 106 (23), 91 (100, $C_7H_7^+$). Anal. Calcd for $C_{12}H_{12}N_4OS$ (mol wt 260.3): C, 55.37; H, 4.65. Found: C, 55.28; H, 4.61.

2-Benzyl-5-(3-cyanopropylamino)-1,2,4-thiadiazol-3(2*H*)-one (13b) was obtained in 55 % yield, mp 152-153 °C (from EtOH); IR (KBr) 3205 (m, NH), 2245 (m, CN), 1646 cm^{-1} (s, CO); ^1H NMR (400 MHz, DMSO-d_6) δ 1.85 (quintet, 2H, C-CH_2-C),

2.55 (t, 2H, CH_2CN), 3.4 (br t, 2H, CH_2N), 4.7 (s, 2H, benzyl CH_2), 7.2-7.4 (m, 5H, Ph), 8.6 (br, 1H, NH); ^{13}C NMR (DMSO-d_6) δ 13.8, 24.3 and 42.1 ($CH_2CH_2CH_2N$), 46.2 (benzyl CH_2), 120.0 (CN), 127.6 (x 2), 128.5 and 137.3 (Ph C-atoms), 165.2 (C-3), 169.6 (C-5); mass spectrum, m/z (%) 274 (60, $M^{\cdot+}$), 168 (100, $M^{\cdot+}$ - $PhCH_2NH$), 142 (17), 141 (12), 100 (19), 91 (29, $C_7H_7^+$). Anal. Calcd for $C_{13}H_{14}N_4OS$ (mol wt 274): C, 56.92; H, 5.14. Found: C, 56.88; H, 5.25.

2-Benzyl-5-(4-cyanobutylamino)-1,2,4-thiadiazol-3(2*H*)-one (13c) was obtained in 67 % yield, mp 134-134.5 °C (from EtOH); IR (KBr) 3232 (m, NH), 2247 (w, CN), 1644 cm^{-1} (s, CO); ^1H NMR (400 MHz, DMSO-d_6) δ 1.5-1.65 (m, 4H, C-CH_2-CH_2-C), 2.5 (t, 2H, CH_2CN), 3.35 (br t, 2H, CH_2N), 4.7 (s, 2H, benzyl CH_2), 7.2-7.4 (m, 5H, Ph), 8.45 (br, 1H, NH); ^{13}C NMR (DMSO-d_6) δ 15.7, 22.1, 27.6 and 42.5 ($CH_2CH_2CH_2CH_2N$), 46.3 (benzyl CH_2), 120.4 (CN), 127.6 (x 2), 128.5 and 137.3 (Ph C-atoms), 165.3 (C-3), 169.8 (C-5); mass spectrum, m/z 288 (30, $M^{\cdot+}$), 182 (100, $M^{\cdot+}$ - $PhCH_2NH$), 156 (19), 114 (20), 91 (48, $C_7H_7^+$); $M^{\cdot+}$ calcd: 288.1045; Found: 288.1037. Anal. Calcd for $C_{14}H_{16}N_4OS$ (mol wt 288): C, 58.31; H, 5.59. Found: C, 58.24; H, 5.45.

3-(Benzylcarbamoylimino)-6,7-dihydro-3*H*,5*H*-pyrrolo[2,1-c][1,2,4]thiadiazole (14).

A solution of **13b** (0.5 g, 2.2 mmol) in dry chloroform (20 ml) was heated at 60 °C for 60 h. After removal of the solvent, the residue was crystallized from chloroform/diethyl ether to give **14** in 72 % yield (0.36 g), mp 169.5-171 °C (from EtOH); IR (KBr) 3400 (br, NH), 1606 cm^{-1} (s); ^1H NMR (400 MHz, DMSO-d_6) δ 2.5 (quintet, 2H, H-6), 2.76 (t, 2H, H-7), 3.87 (t, 2H, H-5), 4.28 and 4.45 (two d in ratio 90:10, 2H, benzyl CH_2), 7.2-7.3 (m, 5H, Ph), 8.12 and 7.5 (two t in ratio 90:10, 1H, NH); ^{13}C NMR (DMSO-d_6) δ 24.6 (C-6 and C-7) 43.5 (benzyl CH_2, $^1J_{CH}$ = 137 Hz), 44.3 (C-5), 126.6, 127.0, 128.2 and 140.2 (Ph C-atoms), 161.8 (C-7a), 163.3 (CO), 170.6 (C-3); mass spectrum, m/z (%) 274 (60, $M^{\cdot+}$), 168 (100, $M^{\cdot+}$ - $PhCH_2NH$), 142 (17, $M^{\cdot+}$ - $PhCH_2NCO$), 100 (17), 91 (24, $C_7H_7^+$); $M^{\cdot+}$ calcd: 274.0888; Found: 274.0892. Anal. Calcd for $C_{13}H_{14}N_4OS$ (mol wt 274): C, 56.92; H, 5.14. Found: C, 56.76; H, 5.09.

3-(Benzylcarbamoylimino)-5,6,7,8-tetrahydro-3*H*-[1,2,4]thiadiazolo[4,3-a]pyridine (15).

A solution of **13c** (0.5 g, 2.2 mmol) in dry chloroform (20 ml) was heated at 60 °C for 70 h. After removal of the solvent, the residue was crystallized from ethanol to give **15** in 55 % yield (0.35 g), mp 168-169.5 °C; IR (KBr) 3312 (m, NH) 1625 cm^{-1} (s); ^1H NMR (400 MHz, DMSO-d_6) δ 1.83 (m, 2H, H-7), 1.93 (m, 2H, H-6), 2.75 (t, 2H, H-8), 3.85 (t, 2H, H-5), 4.30 and 4.48 (two d in ratio 90:10, $^3J_{CH}$ = 6 Hz, 2H, benzyl CH_2), 7.2 - 7.35 (m, 5H, Ph), 8.05 and 7.5 (two t in ratio 90:10, 1H, NH); ^{13}C NMR (DMSO-d_6) δ 19.3 and 21.4 (C-6 and C-7), 26.9 (C-8), 43.5 (benzyl CH_2), 45.7 (C-5), 126.5, 127.0, 128.1 and 140.2 (Ph C-atoms), 153.5 (C-8a), 163.1 (CO), 173.9 (C-3); mass spectrum, m/z (%) 288 (23, $M^{\cdot+}$), 182 (100, $M^{\cdot+}$ - $PhCH_2NH$), 156 (14), 114 (16), 91 (33, $C_7H_7^+$). Anal. Calcd for $C_{14}H_{16}N_4OS$ (mol wt 288): C, 58.31; H, 5.59. Found: C, 58.22; H, 5.53.

3-(Benzylcarbamoylimino)-3*H*,9*H*-[1,2,4]thiadiazolo[4,3-a]indole (16).

A solution of **12** (1.0 g, 4.4 mmol), o-aminobenzyl cyanide[9] (581 mg, 4.4 mmol) and triethylamine (485 mg, 4.8 mmol) in dry ethanol (50 ml) was stirred at room temperature for 6 h. After removal of the solvent, the residue was washed successively with water (5 x 50 ml), ethanol (2 x 10 ml) and diethyl ether (2 x 10 ml), and dried in vacuo to give **16** in 48 % yield (660 mg), mp 203-204 °C (from EtOH); IR (KBr) 3309 (m, NH), 1621 cm^{-1} (s); ^1H NMR (250 MHz, DMSO-d_6) δ 4.05 (s, 2H, H-9), 4.35 and 4.58 (two d in ratio 90:10, $^3J_{CH}$ = 6 Hz, 2H, benzyl CH_2), 7.1-7.6 (m, 8 aromatic H), 8.20 and 8.0 (two d in ratio 90:10, 1H, H-5), 8.35 and 7.83 (two t in ratio 90:10, 1H, NH); ^{13}C NMR (DMSO-d_6) δ 29.8 (C-9), 43.7 (benzyl CH_2), 113.6 (C-5), 126.0-128.2 (6 aromatic C-atoms), 132.0 (C-8a), 137.4 (C-4a), 139.8 (Ph Ci), 158.6 (C-9a), 163.0 (CO), 167.2 (C-3); mass spectrum, m/z (%) 322 (20, $M^{\cdot+}$), 216 (79, $M^{\cdot+}$ - $PhCH_2NH$), 190 (14, $M^{\cdot+}$ - $PhCH_2NCO$), 162 (16), 132 (100, $M^{\cdot+}$-

$PhCH_2NCO$ - NCS), 91 (57, $C_7H_7^+$). Anal. Calcd for $C_{17}H_{14}N_4OS$ (mol wt 322): C, 63.34; H, 4.38. Found: C, 63.09; H, 4.42.

3-(Benzylcarbamoylimino)-3*H*,10*H*-[1,2,4]thiadiazolo[3,4-c][1,4]benzoxazine (17).

A solution of **12** (1.0 g, 4.4 mmol), o-aminophenoxyacetonitrile[10] (650 mg, 4.4 mmol) and triethylamine (485 mg, 4.8 mmol) in dry ethanol (50 ml) was stirred at room temperature for 3 h. The solvent was removed and the resulting brown oil was triturated with diethyl ether to give a solid residue. After washing successively with water (5 x 50 ml), ethanol (2 x 10 ml) and diethyl ether (2 x 10 ml), and drying in vacuo, **17** was obtained in 48 % yield (703 mg), mp 145.5-146.5 °C (from EtOH); IR (KBr) 3235 (m, NH), 1641 cm^{-1} (s); ^1H NMR (250 MHz, DMSO-d_6) δ 4.35 and 4.50 (two d in ratio 90:10, $^3J_{CH}$ = 6 Hz, 2H, benzyl CH_2), 5.15 and 5.25 (two s in ratio 90:10, 2H, H-10), 7.1-7.45 (m, 8 aromatic H), 8.55 and 8.0 (two t in ratio 90:10, 1H, NH), 9.1 and 8.6 (two d in ratio 90:10, 1H, H-5); ^{13}C NMR (DMSO-d_6) δ 43.7 (benzyl CH_2), 64.7 (C-10), 117.3 (C-8), 120.3 (C-6), 122.7 (C-5), 125.6 (C-4a), 126.7, 126.8, 127.3 and 128.3 (aromatic C-atoms), 139.6 (Ph Ci), 146.2 (C-8a), 147.2 (C-10a), 162.7 (CO), 169.9 (C-3); mass spectrum, m/z (%) 338 (48, $M^{\cdot+}$), 232 (100, $M^{\cdot+}$ - $PhCH_2NH$), 206 (28), 178 (19), 148 (80, $PhCH_2NHCON^{\cdot+}$), 106 (16, $PhCH_2NH^+$), 91 (89, $C_7H_7^+$). Anal. Calcd for $C_{17}H_{14}N_4O_2S$ (mol wt 338): C, 60.34; H, 4.17. Found: C, 60.17; H, 4.11.

3-(Benzylcarbamoylimino)-3*H*,10*H*-[1,2,4]thiadiazolo[3,4-c][1,4]benzothiazine (18).

A solution of **12** (1.0 g, 4.4 mmol), o-aminophenylthioacetonitrile[11] (725 mg, 4.4 mmol) and triethylamine (485 mg, 4.8 mmol) in dry ethanol (50 ml) was stirred at room temperature for 3 h. The solvent was removed and the resulting brown oil was triturated with diethyl ether to give a solid residue. After washing successively with water (5 x 50 ml), ethanol (2 x 10 ml) and diethyl ether (2 x 10 ml), and drying in vacuo, **18** was obtained in 44 % yield (693 mg), mp 151-152 °C (from EtOH); IR (KBr) 3279 (m, NH), 1615 cm^{-1} (s); ^1H NMR (250 MHz, DMSO-d_6) δ 4.07 (s, 2H, H-10), 4.3 and 4.4 (two d in ratio 83:17, $^3J_{CH}$ = 6 Hz, 2H, benzyl CH_2), 7.2-7.5 (m, 7 aromatic H), 7.6 (d, 1H, H-8), 8.35 and 7.95 (two t in ratio 83:17, 1H, NH), 8.65 and 8.25 (two d in ratio 83:17, 1H, H-5); ^{13}C NMR (DMSO-d_6) δ 28.3 (C-10), 43.6 (benzyl CH_2), 123.8 (C-5), 126.3-128.9 and 134.3 (8 aromatic C-atoms), 139.6 (Ph Ci), 150.5 (C-10a), 162.7 (CO), 171.2 (C-3); mass spectrum, m/z (%) 354 (35, $M^{\cdot+}$), 321 (11), 248 (96, $M^{\cdot+}$ - $PhCH_2NH$), 222 (26, $M^{\cdot+}$ - $PhCH_2NCO$), 164 (62, $M^{\cdot+}$ - $PhCH_2NCO$ - NCS), 106 (14), 91 (100, $C_7H_7^+$). Anal. Calcd for $C_{17}H_{14}N_4OS_2$ (mol wt 354): C, 57.61; H, 3.98. Found: C, 57.61; H, 4.04.

Synthesis of 26-31 and 33: General procedure.

A suspension of **12** (1.0 g, 4.4 mmol), aminoazole (1 equiv) and triethylamine (535 mg, 5.3 mmol) in dry ethanol (50 ml) was stirred at room temperature (1h for **26**, 12 h for **28**, 1 day for **31**) or heated at 60 °C (2 h for **33**, 12 h for **29** and 30 h for **27** and **30**). After removal of the solvent, the residue was washed successively with water (5 x 50 ml), ethanol (2 x 10 ml) and diethyl ether (2 x 20 ml), and dried in vacuo.

3-(Benzylcarbamoylimino)-5,6-dihydro-3*H*-thiazolo[2,3-c][1,2,4]thiadiazole (26) was obtained from 2-amino-4,5-dihydrothiazole in 77 % yield, mp 163 °C (from EtOH); IR (KBr) 3310 (m, NH), 1635 cm^{-1} (s); ^1H NMR (250 MHz, DMSO-d_6) δ 3.95 (t, 2H, H-6), 4.2 (t, 2H, H-5), 4.3 and 4.45 (two d in ratio 86:14, $^3J_{CH}$ = 6 Hz, 2H, benzyl CH_2), 7.1-7.35 (m, 5H, Ph), 8.3 (t, 1H, NH); ^{13}C NMR (DMSO-d_6) δ 33.5 (C-6), 43.5 (benzyl CH_2), 45.1 (C-5), 126.5, 127.0, 128.1 and 139.9 (Ph C-atoms), 156.8 (C-7a), 163.0 (CO), 170.2 (C-3); mass spectrum, m/z (%) 292 (54, $M^{\cdot+}$), 186 (100, $M^{\cdot+}$ - $PhCH_2NH$), 160 (25, $PhCH_2NHCONC^{\cdot+}$), 159 (14, $M^{\cdot+}$ - $PhCH_2NCO$), 106 (12, $PhCH_2NH^+$), 91 (86, $C_7H_7^+$). Anal. Calcd for $C_{12}H_{12}N_4OS_2$ (mol wt 292): C, 49.30; H, 4.14. Found: C, 49.14; H, 4.07. Crystal data: size 0.002 x 0.03 x 0.07 mm, orthorombic space group Pbca with a = 7.789(4), b = 28.757(6) and c = 11.636(2) Å, Z= 8, V = 2606(2) $Å^3$, D_x = 1.49

gcm^{-3}, R = 0.054 for 1723 observed reflections (I > 2σ(I)). Fig 1 shows a view of the molecule with an arbitrary non-systematic numbering scheme and selected bond lengths. The NCO group and thiadiazole ring are nearly coplanar, with a maximum deviation from the best plane through the eight atoms of 0.021 Å.

3-(Benzylcarbamoylimino)-3*H*-thiazolo[2,3-c][1,2,4]thiadiazole (27) was obtained from 2-aminothiazole in 75 % yield, mp 170-171 °C (from EtOH); IR (KBr) 3309 (m, NH); 1616 cm^{-1} (s); ^1H NMR (250 MHz, DMSO-d_6) δ 4.35 and 4.55 (two d in ratio 88:12, $^3J_{CH}$ = 6 Hz, 2H, CH_2), 7.28 and 7.52 (two d, $^3J_{CH}$ = 5 Hz, 2H, H-5 and H-6), 7.15-7.3 (m, 5H, Ph), 8.2 and 7.7 (two t in ratio 88:12, 1H, NH); ^{13}C NMR (DMSO-d_6) δ 43.7 (CH_2), 115.4 and 117.3 (C-5 and C-6), 126.6, 127.1, 128.1 and 139.7 (Ph C-atoms), 154.8 (C-7a, $^3J_{CH}$ = 6.5 and 7 Hz), 162.8 (CO), 168.3 (C-3); mass spectrum, m/z (%) 290 (25, $M^{\cdot+}$), 191 (17), 184 (32, $M^{\cdot+}$- $PhCH_2NH$), 157 (19, $M^{\cdot+}$- $PhCH_2NCO$), 130 (20, $M^{\cdot+}$- $PhCH_2NHCONC$), 100 (76), 91 (100, $C_7H_7^+$). Anal. Calcd for $C_{12}H_{10}N_4OS_2$ (mol wt 290): C, 49.64; H, 3.47. Found: C, 49.45; H, 3.53. Crystal data: size 0.05 x 0.25 x 0.30 mm, orthorhombic space group $p2_12_12_1$ with a = 8.049(2), b = 11.731(3) and c = 13.682(2) Å, Z = 4, V = 1291.9(4) $Å^3$, D_x = 1.493 gcm^{-3}, R = 0.051 for 2249 observed reflections (I > 2σ(I)). Fig 2 shows a view of the molecule with an arbitrary non-systematic numbering scheme and selected bond lengths. The NCO group and the thiadiazole ring are nearly coplanar, with a maximum deviation from the best plane through the eight atoms of 0.032 Å.

3-(Benzylcarbamoylimino)-6-methyl-3*H*-[1,3,4]thiadiazolo[2,3-c][1,2,4]thiadiazole (28) was obtained from 2-amino-5-methyl-1,3,4-thiadiazole in 82 % yield, mp 239-240 °C (from EtOH); IR (KBr) 3295 (m, NH), 1613 cm^{-1} (s); ^1H NMR (400 MHz, DMSO-d_6) δ 2.65 and 2.42 (two s in ratio 90:10, 3H, CH_3), 4.32 and 4.52 (two d in ratio 90:10, $^3J_{CH}$ = 6 Hz, 2H, CH_2), 7.2-7.4 (m, 5H, Ph), 8.52 and 7.85 (two t in ratio 90:10, 1H, NH); ^{13}C NMR (DMSO-d_6) δ 18.2 (CH_3), 43.7 (CH_2, $^1J_{CH}$ = 140 Hz), 126.7, 127.1, 128.3 and 139.8 (Ph C-atoms), 153.7 (C-7a), 162.5 (C-6), 162.9 (CO), 165.7 (C-3): mass spectrum, m/z (%) 305 (7, $M^{\cdot+}$), 199 (30, $M^{\cdot+}$- $PhCH_2NH$), 191 (27), 173 (16, $M^{\cdot+}$- $PhCH_2NCO$), 132 (13, $PhCHNCO^+$), 116 (18), 115 (21), 106 (17, $PhCH_2NH^+$), 91 (100, $C_7H_7^+$). Anal. Calcd for $C_{12}H_{11}N_5OS_2$ (mol wt 305): C, 47.20; H, 3.63. Found: C, 47.08, H, 3.53. Crystal data: size 0.20 x 0.18 x 0.03 mm, monoclinic space group C2/c with a = 25.518(7), b = 7.338(2), c = 14.781(9) Å and β = 105.67(7)°, Z = 8, V = 2665(2) $Å^3$, D_x = 1.522 gcm^{-3}, R = 0.063 for 1342 observed reflections (I > 2σ(I)). Fig 3 shows a view of the molecule with arbitrary non-systematic numbering scheme and selected bond lengths. The NCO group and the 1,2,4-thiadiazole ring are coplanar, with a maximum deviation from the best plane through the eight atoms of 0.013 Å.

3-(Benzylcarbamoylimino)-6-chloro-3*H*-[1,2,4]thiadiazolo[3,4-b]benzoxazole (29) was obtained from 2-amino-5-chlorobenzoxazole in 75 % yield, mp 181-183 °C; IR (KBr) 3248 (m, NH), 1667 and 1635 cm^{-1} (s); ^1H NMR (250 MHz, DMSO-d_6) δ 4.35 and 4.55 (two d in ratio 90:10, 2H, CH_2), 7.15-7.4 (m, 5H, Ph), 7.5 (dd, 1H, H-7), 7.65 (d, 1H, H-8), 7.85 and 7.70 (two d in ratio 90:10, 1H, H-5), 8.55 and 8.05 (two t in ratio 90:10, 1H, NH); ^{13}C NMR (DMSO-d_6) δ 43.7 (CH_2), 112.7 (C-5), 113.3 (C-8), 126.0-128.3 (6 aromatic C-atoms), 139.4 (Ph Ci), 149.2 (C-8a), 152.2 (C-9a), 162.8 (CO), 166.0 (C-3). mass spectrum, m/z (%) 358 (4, $M^{\cdot+}$), 252 (12, $M^{\cdot+}$- $PhCH_2NH$), 168 (28), 148 (19), 91 (100, $C_7H_7^+$). Anal. Calcd for $C_{16}H_{11}ClN_4O_2S$ (mol wt 358):C, 53.56; H, 3.09. Found: C, 53.40; H, 3.10. Crystal data: size 0.12 x 0.12 x 0.35 mm, monoclinic space group $P2_1/a$ with a = 8.294(2), b = 12.2660(14), c = 15.419(2) Å and β = 101.61(2)°, Z = 4, V = 1536.5(4) $Å^3$, D_x = 1.551 gcm^{-3}, R = 0.045 for 1732 observed reflections (I > 2σ(I)). Fig 4 shows a view of the molecule with arbitrary non-systematic numbering scheme and selected bond lengths. The NCO group and the thiadiazole ring are almost coplanar, with a maximum deviation from the best plane through the eight atoms of 0.049 Å.

3-(Benzylcarbamoylimino)-3*H*-[1,2,4]thiadiazolo[3,4-b]benzothiazole (30) was obtained from 2-aminobenzothiazole in 73 % yield, mp 206-207 °C (from EtOH); IR (KBr) 3325 (m, NH), 1627 cm^{-1} (s); ^1H NMR (250 MHz, DMSO-d_6) δ 4.4 and 4.6 (two d in ratio 8:1, $^3J_{CH}$ = 6 Hz, 2H, CH_2), 7.1-7.6 (m, 7 aromatic H), 7.9 and 7.75 (two d in ratio 8:1, 1H, H-5), 8.55 and 8.0 (two t in ratio 8:1, 1H, NH), 8.73 and 8.50 (two d in ratio 8:1, 1H, H-8); ^{13}C NMR (DMSO-d_6) δ 43.7 (CH_2), 115.5,

124.0, 126.5-128.0, 131.5 and 139.4 (aromatic C-atoms), 152.9 (C-9a), 162.5 (CO), 168.4 (C-3); mass spectrum, m/z (%) 340 (43, $M^{\cdot+}$), 234 (50, $M^{\cdot+}$- $PhCH_2NH$), 207 (11, $M^{\cdot+}$- $PhCH_2NCO$), 180 (27, $M^{\cdot+}$- $PhCH_2NHCONC$), 150 (86), 148 (11), 91 (100, $C_7H_7^+$). Anal. Calcd for $C_{16}H_{12}N_4OS_2$ (mol wt 340): C, 56.45; H, 3.55. Found: C, 56.23; H, 3.56

3-(Benzylcarbamoylimino)-3*H*,9*H*-[1,2,4]thiadiazolo[4,3-a]benzimidazole (31) was obtained from 2-aminobenzimidazole in 80 % yield, mp 230-231 °C (from EtOH); IR (KBr) 3429 (m, NH), 3100 (br, NH), 1645 cm^{-1} (s); ^1H NMR (250 MHz, DMSO-d_6) δ 4.35 and 4.6 (two d in ratio 90:10, $^3J_{CH}$ = 6 Hz, 2H, CH_2), 7.1-7.4 (m, 8 aromatic H), 8.1 and 7.95 (two d in ratio 90:10, 1H, H-5), 8.25 and 7.75 (two t in ratio 90:10, 1H, NH), 11.9 (br, 1H, NH); ^{13}C NMR (DMSO-d_6) δ 43.6 (CH_2), 110.8, 112.9, 120.7, 123.8, 125.9, 126.8, 127.2, 128.1, 136.5 and 139.9 (aromatic C-atoms), 148.1 (C-9a), 163.0 (CO), 167.2 (C-3); mass spectrum, m/z (%) 323 (7, $M^{\cdot+}$), 217 (23, $M^{\cdot+}$- $PhCH_2NH$), 190 (10, $M^{\cdot+}$- $PhCH_2NCO$), 163 (34, $M^{\cdot+}$- $PhCH_2NHCONC$), 133 (92, $PhCH_2NCO^{\cdot+}$), 105 (16, $PhCH_2N^{\cdot+}$), 104 (21), 91 (100, $C_7H_7^+$). Anal. Calcd for $C_{16}H_{13}N_5OS$ (mol wt 323):C, 59.43; H, 4.05. Found: C, 59.21; H, 4.17.

2-Benzyl-5-(1-methyl-5-methylthio-1,2,4-triazol-3-yl)amino-1,2,4-thiadiazol-3(2*H*)-one (33) was obtained from 3-amino-1-methyl-5-methylthio-1,2,4-triazole in 66 % yield, mp 203-204 °C; IR (KBr) 3200-2600 (br, NH), 1691 (s, CO), 1616 cm^{-1} (s); ^1H NMR (400 MHz, DMSO-d_6) δ 2.6 (s, 3H, MeS), 3.6 (s, 3H, CH_3), 4.7 (s, 2 H, CH_2), 7.3-7.4 (m, 5H, Ph), 12.2 (br, 1H, NH); ^{13}C NMR (C_5D_5N at 90 °C) δ 15.8 (MeS), 32.3 (Me), 47.3 (CH_2), 128.2, 128.4, 129.2 and 137.9 (Ph C-atoms), 152.4 (triazole C-5), 159.8 (thiadiazole C-3), 161.2 (triazole C-3), 163.7 (thiadiazole C-5): mass spectrum, m/z (%) 334 (16, $M^{\cdot+}$), 196 (28), 106 (21, $PhCH_2NH^+$), 91 (100, $C_7H_7^+$). Anal. Calcd for $C_{13}H_{14}N_6OS_2$ (mol wt 334): C, 46.69; H, 4.22. Found: C, 46.44, H, 4.11.

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   Note: The ring carbon absorptions of compound **12** in the ^{13}C NMR spectrum ($CDCl_3$) were erroneously assigned by these authors; they should read C-3 at δ 162.8 ($^3J_{CH}$ = 2.5 Hz) and C-5 at δ 166.8
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