On Triazoles XXXVIII [1]. The Reaction of Isomeric 5-Amino-3-morpholino-1*H*-1,2,4-triazolylcarbothiohydrazides with Ortho Esters

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The reaction of isomeric differently methylated 5-amino-3-morpholino-1*H*-1,2,4-triazolylcarbothiohydrazides with ortho esters were studied. Except of the case of triethyl orthoacetate instead of the expected [1,2,4]triazolo[1,5-*d*][1,2,4,6]tetrazepin-5(7*H*)-thione (**6**) derivatives different rearranged products such as **7**, **8**, **21**, **23**, **25**, and **27** were obtained, derivatives **23** and **27** representing a novel ring system. Possible explanations were given for the formation of the rearranged products.

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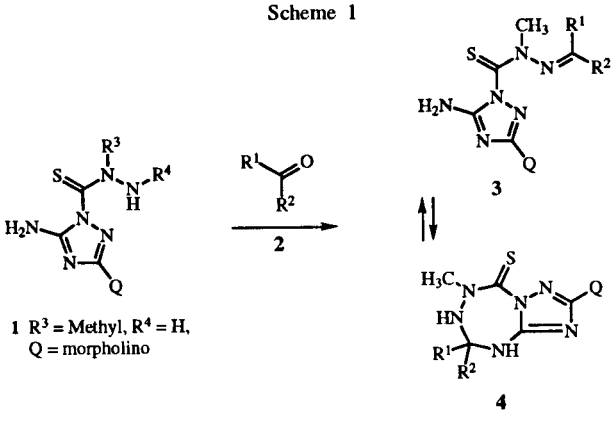
In previous papers of this series [2-4] we have described the reaction of different 1-(5-amino-3-Q-1*H*-1,2,4-triazol-1-yl)-*N*-methylcarbothiohydrazides (**1**, R^3 = methyl, R^4 = H). with aldehydes (**2**, R^1 = alkyl, aryl, R^2 = H) [2], and linear (**2**, R^1 = methyl, R^2 = ethyl) [2], cyclic [**2**, $R^1 + R^2 = (CH_2)_{4-11}$] [3-4] and heterocyclic [**2**, $R^1 + R^2 = (CH_2)_2$-N(Ph)$(CH_2)_2$ and $CH_2S(CH_2)_3$] [4] ketones to yield the corresponding **4** type 5,6,7,8-tetrahydro-9*H*-[1,2,4]triazolo-[1,5-*d*][1,2,4,6]tetrazepin-5-thiones (Scheme 1).

Scheme 1



1 R^3 = Methyl, R^4 = H, Q = morpholino

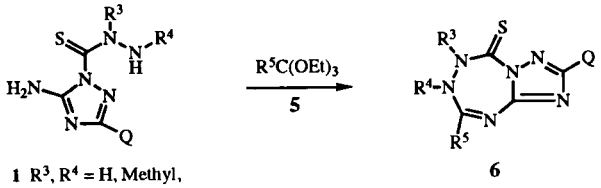
2

3

4

However, derivatives **4** formed from aromatic aldehydes (**2**, R^1 = aryl, R^2 = H) appeared in crystalline form depending on the conditions of crystallisation and the solvent used either in chain **3** or ring **4** tautomeric forms. In solution a tautomeric equilibrium between the two formes **3** and **4** developed [2] making uncertain their possible further biological development as they would hardly meet the stability requirements of a potential drug. To get rid of the above problems we decided to synthesise **6** type 8,9-dehydrogenated analogues of **4** (Scheme 2) that could not exist in type **3** chain tautomeric form. Derivatives **6** were expected to be formed in the reaction of the corresponding derivatives **1** with different orthoesters **5** (Scheme 2).

Scheme 2



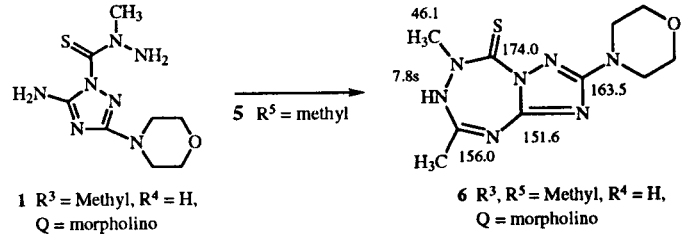
1 R^3, R^4 = H, Methyl, Q = morpholino

5

6

First the reaction of **1** (R^3 = methyl, R^4 = H, Q = morpholino) with triethyl orthoacetate (**5**, R^5 = methyl) was performed to yield the expected derivative **6** (R^3 = R^5 = methyl, R^4 = H, Q = morpholino) as proved by its very analogues cmr spectra with that of the tetrahydro analogue **4** (R^1 = methyl, R^2 = H, Q = morpholino) synthesised previously [2] (Scheme 3). Moreover the NH signal of **6**

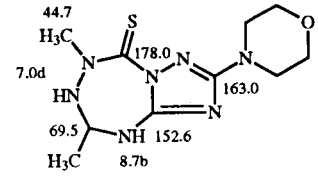
Scheme 3



1 R^3 = Methyl, R^4 = H, Q = morpholino

5 R^5 = methyl

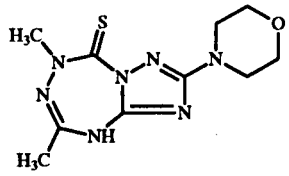
6 R^3, R^5 = Methyl, R^4 = H, Q = morpholino



4 R^1 = Methyl, R^2 = H, Q = morpholino

(R^3 = R^5 =methyl, R^4 = H, Q = morpholino) appearing shifted downfield as compared with that of **4** (R^1 = methyl, R^2 = H, Q = morpholino) as well as the practically unchanged N-CH_3 signal of **6** (R^3 = R^5 = methyl, R^4 = H, Q = morpholino) as compared with that of **4** (R^1 = methyl, R^2 = H, Q = morpholino) proved also the dominant tautomeric structure of **6** (R^3 = R^5 = methyl, R^4 = H, Q = morpholino) in DMSO-d_6 solution. In case of the

Scheme 4

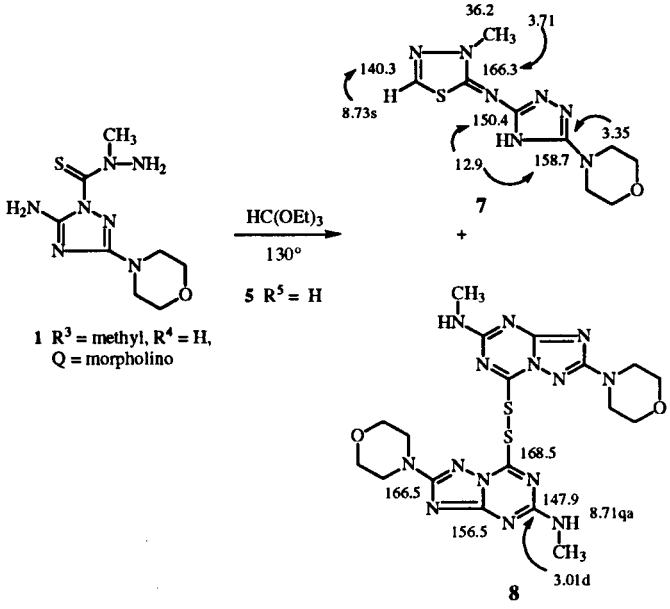


6a R^3, R^5 = methyl, R^4 = H

tautomeric form **6a** (R^3 = R^5 = methyl, R^4 = H, Q = morpholino) (Scheme 4) as a consequence of the double bond in position 7 both, the NH and NCH_3 signals were be expected shifted strongly downfield compared to those in derivative **4** (R^1 = methyl, R^2 = H, Q = morpholino).

Next the reaction of **1** (Q = morpholino, R^3 = methyl, R^4 = H) with triethyl orthoformate (**5**, R^5 = H) was studied to yield two quite unexpected products **7** and **8** (Scheme 5).

Scheme 5



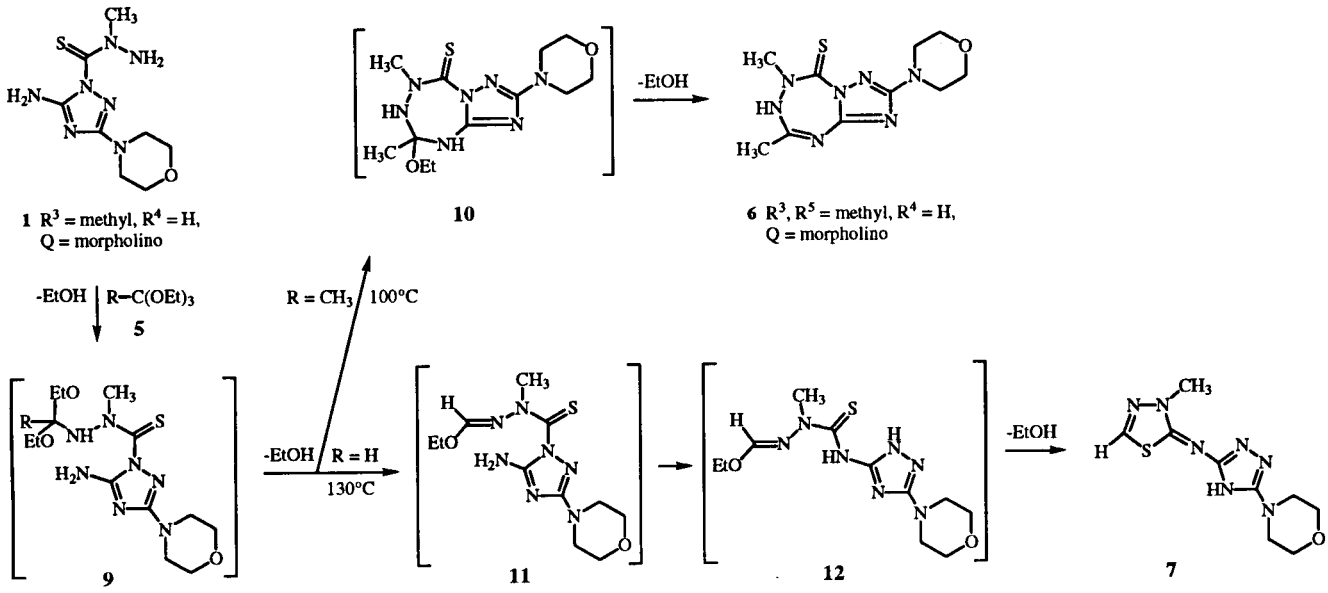
The structure of derivative **7** was corroborated by its pmr and cmr spectra. In the pmr besides the morpholino triplets two singlets corresponding to the NCH_3 and the thiadiazolo CH protons and a broad NH signal were observed while in the cmr besides the morpholino and NCH_3 carbons four quaternary carbon atoms were visible corresponding - as proved by INEPT experiments (Scheme 5) - to the thiadiazole C-2 and C-5 (166.3 and 140.3 ppm, respectively) and the triazole C-3 and C-5 (158.7 and 150.4 ppm, respectively) carbon atoms. Taking into account our previous results obtained with different mono and bicyclic *N*-substituted 5-amino-1,2,4-triazole derivatives [5,7-17] the chemical shifts of the triazole carbon atoms proved also the 4*H* tautomeric structure of the triazole ring of **7**.

The formation of derivative **7** instead of the expected derivative **6** (R^3 = methyl, R^4 = R^5 = H, Scheme 2) as it happened in case of triethyl orthoacetate (**5**, R = methyl, Scheme 3) may be explained as follows (Scheme 6): In both cases, *i.e.* in the reaction of triethyl orthoacetate (**5**, R = CH_3) and triethyl orthoformate (**5**, R = H) the initial step of the reactions is the formation of the corresponding intermediate **9** (R = CH_3 and H, respectively). However, in case of **9** (R = CH_3) the +I effect of the methyl group activates the ethoxy groups thus the reaction proceeds just at 100° making possible the formation of the intermediate **10** that is stabilised through the splitting a molecule of ethanol to yield **6** (R^3 = R^5 = methyl, R^4 = H, Q = morpholino). To the contrary in case of triethyl orthoformate (**5**, R = H) the R group of **9** corresponds to a hydrogen atom that does not activate the ethoxy groups. Consequently the reaction proceeds only at 130° at which temperature the intermediate **11** is formed in which the C=N double bond increases the positive charge of the thiocarbonyl carbon atom enhancing the possibility of the rearrangement to intermediate **12** which may also exist in its enolic form characterised by conjugated double bonds and is stabilised through the splitting of a molecule of ethanol to yield **7**.

The structure of derivative **8** was deduced from its pmr, cmr and ms data. The ms spectrum taken in FAB conditions pointed out that the molecular weight of **8** is 532 and should consist from two equivalent parts that could easily split to form the base peak of the spectra corresponding to the half of the molecular weight (266). In the pmr spectra besides the morpholino protons an $NHCH_3$ moiety was only visible (Scheme 5). In the cmr apart from the morpholino and $NHCH_3$ carbons four quaternary carbon atoms were visible from which the one appearing at 147.9 ppm should be in the neighbourhood of the $NHCH_3$ moiety (see its long range coupling in Experimental). Taking in acoount the chemical shifts of the other three quaternary carbon atoms being in good agreement with the chemical shifts of the "aromatised" [1,2,4]triazolo[1,5-*a*]pyrimidines [1] the [1,2,4]triazolo[1,5-*a*][1,3,5]triazine structure could be proposed for the heterocyclic skeleton of **8**.

A possible explanation of the formation of derivative **8** can be the reaction sequence shown on Scheme 7. Thus the first step of the reaction is the formation of the expected **6** type derivative **13** in which the nitrogen atom 7 makes an intramolecular nucleophilic attack against the positively charged carbon atom 5 of the thiocarbonyl moiety to yield a highly unstable diaziridine **14**. This is easily rearranged to derivative **15** in which the methylamino nitrogen atom can make a further nucleophilic attack against the pyrimidine carbon atom 7 activated by the electron withdrawing effect of the nitrogen atom 8 to yield the diaziridine **16**. This is stabilised though the

Scheme 6



1 R^3 = methyl, R^4 = H, Q = morpholino

10

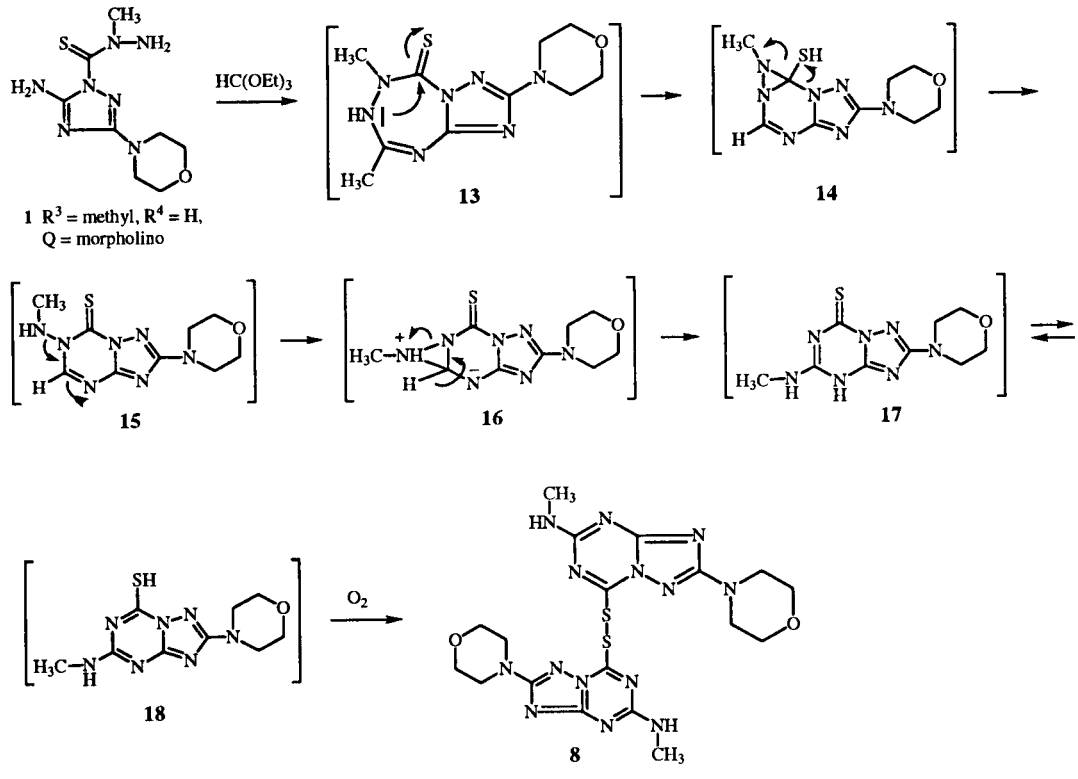
6 R^3, R^5 = methyl, R^4 = H, Q = morpholino

9 11 12 7

formation of **17** which is in tautomeric equilibrium with its enolic form **18** that can be easily oxidised with the atmospheric oxygen to yield **8**. The above explanation is in agreement with the experimental data, namely that the more vigorous stirring of the reaction mixture increased the rate and the yield of the formation of **8**.

As a continuation of the above studies the reaction was repeated with the isomeric **1** (R^3 = H, R^4 = methyl, Q = morpholino) (Scheme 8). In this case - as expected - the most nucleophilic center of **1** appeared to be the sulphur atom of the unsubstituted thioamide moiety, thus through intermediates **19** and **20** a 1,2,4-triazolo[1,5-*c*][1,3,5]thiadiazine

Scheme 7

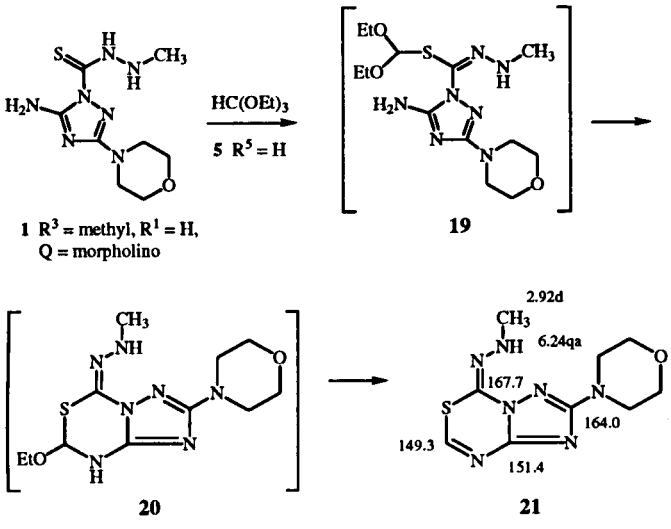


1 R^3 = methyl, R^4 = H, Q = morpholino

13 14 15 16 17 18 8

derivative **21** was obtained as proved by the primary coupling between the methyl and NH protons in the pmr spectra appearing as a doublet and quartet, respectively, as well as its cmr data (Scheme 8).

Scheme 8



To get rid of the above ring closure leading to the six membered thiadiazine ring the reactions were repeated with the *N,N'*-dimethylcarbothiohydrazide derivative **1** (R^3 = R^4 = methyl, Q = morpholino) (Scheme 9). In these cases the expected type **6** derivatives **22** were most probably formed as intermediates, but they again underwent different rearrangements.

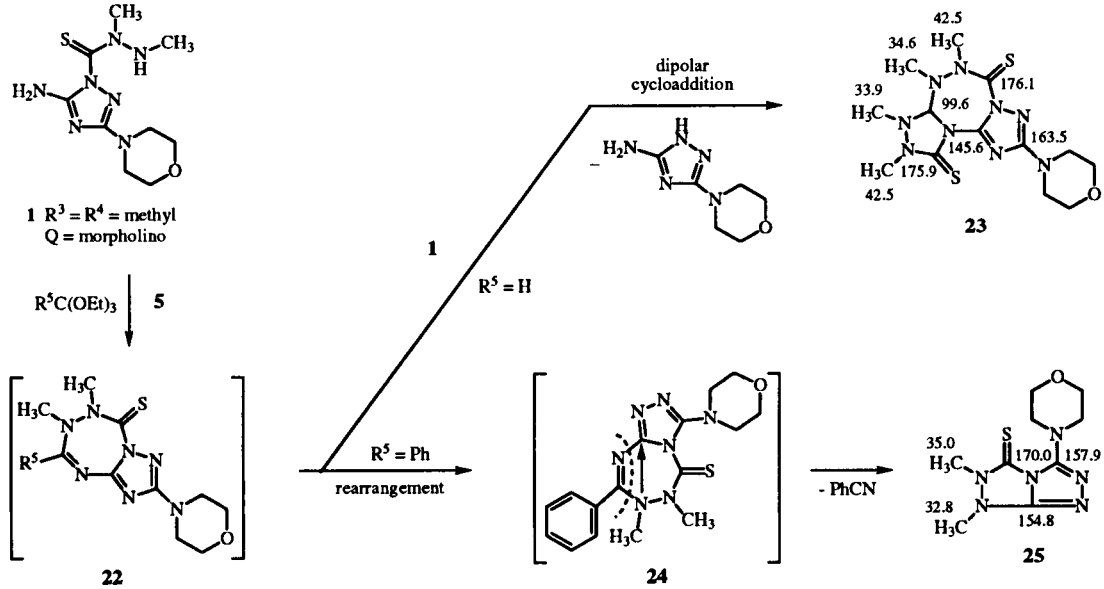
Thus in case of triethyl orthoformate (**5**, R^5 = H) a dipolar cycloaddition reaction occurred with a thiohydrazide moiety splitted from a further molecule of the starting material to yield derivative **23** as proved by its ms molecular ion and cmr spectra (Scheme 9) characterised by two C=S and four NCH_3 bands.

On the other hand repeating the above reaction with triethyl orthobenzoate (**5**, R^5 = phenyl) a [1,2,4]triazolo-[3,4-*c*][1,2,4]triazole derivative **25** was isolated the structure of which was proved again by ms and nmr measurements (Scheme 9). The formation of **25** could be explained through a sigmatropic rearrangement of the intermediate **22** (R^5 = phenyl) to yield **24** in which an intramolecular nucleophilic attack of the tetrazepine nitrogen atom against the triazole carbon atom occurred followed by splitting of a molecule of benzonitrile that could be detected in the reaction mixture by gc.

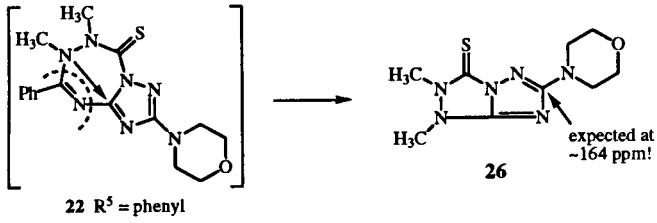
However, the splitting of the benzonitrile moiety might also have occurred directly from the intermediate **22** to yield **26** (Scheme 10). The formation of **26** could be easily excluded on the basis of the chemical shifts of the triazole carbon atoms. It was known [5-17] that the triazole carbon atoms 3 of the 1-substitued-5-amino-3-morpholino-1*H*-1,2,4-triazoles appeared independently of the quality of substituents at position 1 at about 164 ppm (see also their chemical shifts on Schemes 3, 8 and 9), while in case of 4-substitued-3-morpholino-4*H*-1,2,4-triazoles they were expected at about 156-158 ppm (see *e.g.* on Scheme 5). The chemical shift of 157.9 ppm obtained for the corresponding carbon atom 3 of **25** (Scheme 9) excludes unambiguously the possibility of structure **26**.

At last **1** (R^3 =R^4 =methyl, Q = morpholino) was reacted with triethyl orthoacetate (**5**, R^5 = methyl) to yield **27** (Scheme 11) in which the steric hindrance among the methyl groups at 7, 7a and 8 positions made impossible

Scheme 9



Scheme 10

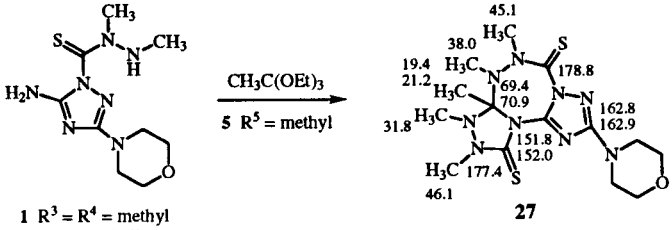


22 R^5 = phenyl

26

the free rotation around the carbon atom 7a thus the two conformers turned to be isomers causing doubling of the

Scheme 11



1 $R^3 = R^4$ = methyl
Q = morpholino

27

7a methyl, 7a and 11a carbon atoms, respectively, and through the conjugated double bond of that of the carbon atom 2 in the cmr (Scheme 11).

Derivatives **23** and **27** represent a novel ring system.

EXPERIMENTAL

Melting points were determined on a Koffler-Boëtius micro apparatus and are uncorrected. The infrared spectra were obtained as potassium bromide pellets using Perkin-Elmer 577 spectrophotometer. The ^{1}H-nmr and the ^{13}C-nmr measurements were performed using Bruker DRX-500, Bruker WM-250 and Bruker WP-80 SY instruments. The ms spectra were recorded on a Kratos MS25RFA instrument using direct inlet probe.

6,8-Dimethyl-2-morpholino-5,6-dihydro[1,2,4]triazolo[1,5-*d*]-[1,2,4,6]tetrazepine-5(7*H*)-thione **6** ($R^3 = R^5$ = methyl, R^4 = H, Q = morpholino).

The mixture of 2.57 g (0.01 mole) of 1-(5-amino-3-morpholino-1*H*-1,2,4-triazol-1-yl)-*N*-methylcarbothiohydrazide (**1**, R^3 = methyl, R^4 = H, Q = morpholino) [7] and 7 ml of triethyl orthoacetate (**5**, R^5= methyl) was refluxed with stirring for 6 hours. The solution obtained was evaporated *in vacuo* to dryness and the residual oily product was chromatographed on a silica gel column (eluent a 19:1 mixture of chloroform and methanol) to yield 0.61 g (22%) of 6,8-dimethyl-2-morpholino-5,6-dihydro[1,2,4]triazolo[1,5-*d*][1,2,4,6]tetrazepine-5(7*H*)-thione **6** ($R^3 = R^5$ = methyl, R^4 = H, Q = morpholino), that after recrystallisation from acetonitrile melted at 203-205°; ir: ν NH = 3200 and 3150 cm^{-1}, ν C=S = 1290 cm^{-1}; pmr (deuteriochloroform): δ ppm 2.16 (s, 3H, CCH_3), 3.41 [t (J = 4 Hz), 4H, NCH_2], 3.64 (s, 3H, NCH_3), 3.74 [t (J = 4 Hz), 4H, OCH_2], 7.8 (s, 1H, NH); cmr (deuteriochloroform): δ ppm 20.6 (CCH_3), 46.1 (NCH_3 and NCH_2), 66.3 (OCH_2), 151.6 (C-9a), 156.0 (C-8), 163.5 (C-2), 174.0 (C=S);

Anal. Calcd. for $C_{10}H_{15}N_7OS$ (MW 281.34): C, 42.69; H, 5.37; N, 34.85; S, 11.40. Found: C, 42.77; H, 5.60; N, 34.73; S, 11.50.

2,3-Dihydro-2-[(3-morpholino-4*H*-1,2,4-triazol-5-yl)imino]-3-methyl[1,3,4]thiadiazole (**7**) and Di{2-morpholino-7-methylamino-[1,2,4]triazolo[1,5-*a*][1,3,5]triazin-5-yl} Disulphide (**8**).

The mixture of 1.23 g (0.005 mole) of 1-(5-amino-3-morpholino-1*H*-1,2,4-triazol-1-yl)-*N*-methylcarbothiohydrazide (**1**, R^3 = methyl, R^4 = H, Q = morpholino) [7] and 4 ml of triethyl orthoformate (**5**, R^5= H) was refluxed with stirring for 10 hours. The solution crystallised while hot. After cooling the crystals that precipitated were filtered and washed with 2-propanol to yield 0.20 g (15%) of di{2-morpholino-7-methylamino-[1,2,4]triazolo[1,5-*a*][1,3,5]triazin-5-yl} disulphide (**8**), that after recrystallisation from dimethylformamide melted at 320-322°; ir: ν S-S = 1276 cm^{-1}, ν COC = 1116 cm^{-1}; pmr (DMSO-d_6, 297°K): δ ppm 3.01 [d (J = 4.2 Hz), 3H, $NHCH_3$], 3.51 [t (J = 4.5 Hz), 4H, NCH_2], 3.72 [t (J = 4.5 Hz), 4H, OCH_2], 8.71 [qa (J = 4.2 Hz), 1H, NH]; taken at 330° this peak was shifted to 8.5 ppm; cmr (DMSO-d_6, 297°K): δ ppm 27.4 (CH_3), 45.6 (NCH_2), 65.6 (OCH_2), 147.9 (C-7), 156.5 (C-8a), 166.5 (C-2), 168.5 (C-5); ^{1}H-^{13}C long range correlation between 3.01 ppm and 147.9 ppm; ms: (FAB$^+$) $(M+1)^+$ = 533 (50%), $(M/2)^+$ = 266 (100%).

Anal. Calcd. for $C_{18}H_{24}N_{14}O_2S_2$ (MW 532.61): C, 40.59; H, 4.54; N, 36.82; S, 12.04. Found: C, 40.44; H, 4.60; N, 36.94; S, 11.89.

The mother liquor was evaporated to dryness, the residue was dissolved in 30 ml of hot water, treated with charcoal, filtered and allowed to crystallise. After cooling the crystals that precipitated were filtered and recrystallised from water to yield 0.15 g (11%) of 2,3-dihydro-2-[(3-morpholino-4*H*-1,2,4-triazol-5-yl)imino]-3-methyl[1,3,4]thiadiazole (**7**) mp 298-300°; ir: ν NH = 3190 and 3130 cm^{-1}, ν COC = 1108 cm^{-1}; pmr (DMSO-d_6, 297°K): δ ppm 3.35 (bs, xH, NCH_2 + HDO), 3.71 [bs, 7H, OCH_2 + NCH_3), 8.73 (s, 1H, CH), 12.9 (s, 1H, NH); pmr (DMSO-d_6, 373°K): δ ppm 3.40 [t (J = 4.5 Hz), 4H, NCH_2), 3.73 (s, 3H, NCH_3), 3.74 [t (J = 4.5 Hz), 4H, OCH_2)], 8.67 (s, 1H, CH); cmr (DMSO-d_6, 293°K): δ ppm 36.2 (NCH_3), 46.0 (NCH_2), 65.4 (OCH_2), 140.3 (C-5), 150.4 (C-5'), 158.7 (C-3'), 166.3 (C-2); INEPT (7 Hz); irradiated at 3.35 ppm, INEPT at 158.7 ppm; irradiated at 3.71 ppm, INEPT at 166.3 ppm, irradiated at 8.73 ppm, INEPT at 140.3 ppm, irradiated at 12.9 ppm INEPT at 150.4 and 158.7 ppm; ms: (EI) M^+ = 267.

Anal. Calcd. for $C_9H_{13}N_7OS$ (MW 267.31): C, 40.44; H, 4.90; N, 36.68; S, 11.99. Found: C, 40.36; H, 5.05; N, 36.70; S, 12.08.

N-Methyl-*N'*{2-morpholino[1,2,4]triazolo[1,5-*c*][1,3,5]thiadiazin-5-ylidene}hydrazine (**21**)

The mixture of 1.28 g (0.005 mole) of 1-(5-amino-3-morpholino-1*H*-1,2,4-triazol-1-yl)-*N'*-methylcarbothiohydrazide (**1**, R^3 = H, R^4 = methyl, Q = morpholino) [7], 100 ml of methanol and 3 ml (0.0023 mole) of triethyl orthoformate (**5**, R^5 = H) was refluxed with stirring for 40 hours. The solution obtained was evaporated *in vacuo* to dryness and the residue recrystallised from 2-propanol to yield 0.62 (46%) of *N*-methyl-*N'*{2-morpholino[1,2,4]triazolo[1,5-*c*][1,3,5]thiadiazin-5-ylidene}-hydrazine (**21**), mp 184-186°; ir: ν NH = 3250 cm^{-1}; pmr (deuteriochloroform): δ ppm 2.92 [d (J = 5.8 Hz), 3H, CH_3], 3.69 [t (J = 4.5 Hz), 4H, NCH_2], 3.79 [t (J = 4.5 Hz), 4H, OCH_2], 6.24 [q (J = 5.8 Hz), 1H, NH], 8.4 (s, 1H, CH); cmr

(deuteriochloroform): δ ppm 38.9 (CH_3), 45.7 (NCH_2), 66.3 (OCH_2), 149.3 (C-7), 151.4 (C-8a), 164.7 (C-2), 167.7 (C-5);

Anal. Calcd. for $C_9H_{13}N_7OS$ (MW 267.31): C, 40.44 ; H, 4.90; N, 36.68; S, 11.99. Found: C, 40.30; H, 4.99; N, 36.52; S, 12.06.

5,6,7,7a,8,9-Hexahydro-2-morpholino-6,7,8,9-tetramethyl-10*H*-[1,2,4]triazolo[4,3-*f*][1,2,4]triazolo[1,5-*d*]tetrazepine-5,10-dithione (**23**)

The mixture of 1.36 g (0.005 mole) of 1-(5-amino-3-morpholino-1*H*-1,2,4-triazol-1-yl)-*N,N'*-dimethylcarbothiohydrazide (**1**, $R^3 = R^4$ = methyl, Q = morpholino) [7] and 4.0 ml of triethyl orthoformate (**5**, R^5 = H) was refluxed with stirring for 16 hours. After cooling the crystals that precipitated were filtered and recrystallised from acetonitrile to yield 0.62 g (32%) of 5,6,7,7a,8,9-hexahydro-2-morpholino-6,7,8,9-tetramethyl-10*H*-[1,2,4]triazolo[4,3-*f*][1,2,4]triazolo[1,5-*d*]tetrazepine-5,10-dithione (**23**), mp 262-265°; ir: ν C=S = 1270 and 1256 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.70 (s, 3H, CH_3-7), 2.80 (s, 3H, CH_3-8), 3.32 (m, 7H, NCH_2 + CH_3-6), 3.37 (s, 3H, CH_3-9), 3.70 (t, 4H, OCH_2), 6.1 (s, 1H, CH-7a); cmr (DMSO-d_6): δ ppm 33.9 (CH_3-8), 34.6 (CH_3-7), 42.5 (CH_3-6 and 9), 45.6 (NCH_2), 65.6 (OCH_2), 99.6 (C-7a), 145.6 (C-11a), 163.5 (C-2), 175.9 (C-10), 176.1 (C-5); ms: (El) M^+ = 383, (Cl) $(M+1)^+$ = 384.

Anal. Calcd. for $C_{13}H_{21}N_9OS_2$ (MW 383.50): C, 40.72; H, 5.52; N, 32.87; S, 16.72. Found: C, 40.62; H, 5.68; N, 33.01; S, 16.70.

6,7-Dihydro-6,7-dimethyl-3-morpholino[1,2,4]triazolo[3,4-*c*]-[1,2,4]triazole-5(5*H*)-thione (**25**).

The mixture of 1.36 g (0.005 mole) of 1-(5-amino-3-morpholino-1*H*-1,2,4-triazol-1-yl)-*N,N'*-dimethylcarbothiohydrazide (**1**, $R^3 = R^4$ = methyl, Q = morpholino) [7] and 4.0 ml of triethyl orthobenzoate (**5**, R^5 = phenyl) was refluxed with stirring for 24 hours. After cooling the crystals that precipitated were filtered and washed with acetonitrile to yield 0.14 g (11%) of 6,7-dihydro-6,7-dimethyl-3-morpholino[1,2,4]triazolo[3,4-*c*][1,2,4]triazole-5(5*H*)-thione (**25**), mp 245-248°; ir: ν C=S = 1267 cm^{-1}, ν C=N = 1645 and 1579 cm^{-1}; pmr (DMSO-d_6): δ ppm 3.39 [t (J = 4.9 Hz), 4H, NCH_2], 3.59 (s, 3H, NCH_3-7), 3.66 [t (J = 4.9 Hz), 4H, OCH_2], 3.68 (s, 3H, NCH_3-6); cmr (DMSO-d_6): δ ppm 32.8 (CH_3-7), 35.0 (CH_3-6), 45.8 (NCH_2), 65.6 (OCH_2), 154.8 (C-7a), 157.9 (C-3), 170.0 (C-5); ms: (El) M^+ = 254, (Cl) $(M+1)^+$ = 255.

Anal. Calcd. for $C_9H_{14}N_6OS$ (MW 254.32): C, 42.51; H, 5.55; N, 33.05; S, 12.61. Found: C, 42.55; H, 5.73; N, 33.12; S, 12.55.

5,6,7,7a,8,9-Hexahydro-2-morpholino-6,7,7a,8,9-pentamethyl-10*H*-[1,2,4]triazolo[4,3-*f*][1,2,4]triazolo[1,5-*d*]tetrazepine-5,10-dithione (**27**)

The mixture of 1.36 g (0.005 mole) of 1-(5-amino-3-morpholino-1*H*-1,2,4-triazol-1-yl)-*N,N'*-dimethylcarbothiohydrazide (**1**, $R^3 = R^4$ = methyl, Q = morpholino) [7] and 4.0 ml of triethyl orthoacetate (**5**, $R^5 = CH_3$) was refluxed with stirring for 16 hours. After cooling the crystals that precipitated were filtered off and recrystallised from acetonitrile to yield 0.25 g (25%) of 5,6,7,7a,8,9-hexahydro-2-morpholino-6,7,7a,8,9-pentamethyl-10*H*-[1,2,4]triazolo[4,3-*f*][1,2,4]triazolo[1,5-*d*]tetrazepine-5,10-dithione (**27**), mp 216-218°; ir: ν C=S = 1293 and 1269 cm^{-1}; pmr (DMSO-d_6): δ ppm 1.23 (s, 1.5 H, CH_3-7a "in"), 1.24 (s, 1.5 H, CH_3-7a "out"), 2.49 (s, 3H, CH_3-8), 2.61 (s, 3H, CH_3-7), 3.23 [t (J = 4.6 Hz), 4H, NCH_2)], 3.53 (s, 3H, CH_3-9), 3.54 (s, 3H, CH_3-9), 3.64 [t (J = 4.6 Hz), 4H, OCH_2]; cmr (DMSO-d_6): δ ppm 19.4 and 21.2 (C-7a "in" and "out"), 31.8 (CH_3-8), 38.0 (CH_3-7), 45.1 (CH_3-6), 45.7 (NCH_2), 46.1 (CH_3-9), 65.7 (OCH_2), 69.4 and 70.9 (C-7a), 151.8 and 152.0 (C-11a), 162.8 and 162.9 (C-2), 177.4 (C-10), 178.8 (C-5); ms: (El) M^+ = 397, (Cl) $(M+1)^+$ = 398.

Anal. Calcd. for $C_{14}H_{23}N_9OS_2$ (MW 397.53): C, 42.30; H, 5.83; N, 31.71; S, 16.13. Found: C, 42.42; H, 5.88; N, 31.68; S, 16.20.

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