Study on the Preparation of Heteroaryl Substituted Enamines. A Simple Synthesis of Heteroaryl Substituted Acetaldoximes from Enamines

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A comparative study of the reactivity of methyl groups towards *N,N*-dimethylformamide dimethyl acetal and *tert*-butoxybis(dimethylamino)methane was carried out on methyl substituted six-membered nitrogen containing heterocycles **1** to give enamines **2**, which were easily transformed to oximes by treating with hydroxylamine hydrochloride in methanol. Most of them were isolated as *(E,Z)*-oximes of heteroarylacetaldehyde (**11**), but 5-(1,2,4-triazinyl) substituted derivatives as *(E,Z)*-oximes of 2,5-dihydro-1,2,4-triazin-*(Z)*-5-ylideneacetaldehyde (**11t**, **11u**, and **12**). Oximes were finally transformed to the corresponding acetonitriles **16** and 3-(dimethylamino)acrylonitriles **17**.

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Unsubstituted derivatives of heteroareneacetaldoximes were in spite of their simplicity represented until several years ago only by few examples. Quinoline-2-acetaldoxime was prepared from quinoline-2-acetaldehyde and hydroxylamine [1]. Pyridine-3-acetaldoxime, an intermediate in the synthesis of central dopamine agonists [2], was obtained by hydrogenation of 3-(2-nitrovinyl)pyridine [3].

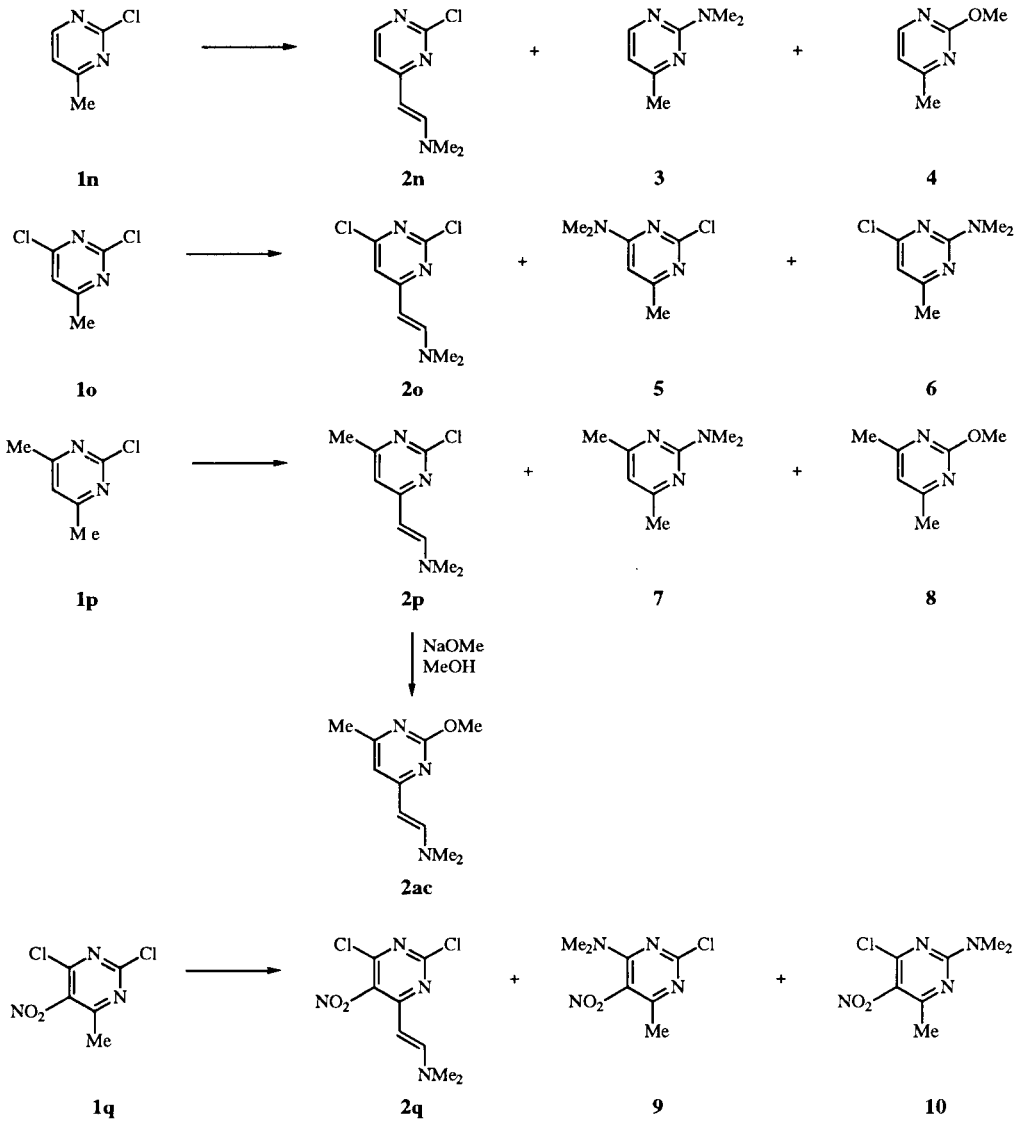
Several years ago we have intensively studied the preparation and the reactions of heteroaryl substituted formamidoximes [4,5] and also in one case the formation of 1,2,4-triazinyl substituted acetaldoxime (**11ad**, Scheme 2) was observed [6]. According to this investigation and later studies on heterocyclic enamines [7,8] a new short synthesis of these simple heterocyclic compounds has been developed.

Dimethylaminovinyl substituted heterocycles **2** have become common starting compounds for many transformations. It was found that some of them stimulated the growth of wheat roots and inhibited the growth of the aerial parts [9]. Recently, they were synthesized from methyl substituted heterocycles mainly by two types of reagents, such as dimethylformamide acetals and aminal esters. The reaction with *tert*-butoxybis(dimethylamino)methane (Bredereck reagent), the most reactive aminal ester, was more systematically studied and it was approved that most of basic methyl substituted six-membered heterocycles give enamines [7,10]. In the other case the reactions with *N,N*-dimethylformamide dimethyl acetal (DMFDMA), as the most often used acetal, appears in literature mainly as applicative examples and only the reactivity of picolines was systematically studied [11]. It is evident that for the reaction with DMFDMA much more reactive methyl groups are required than with Bredereck reagent; systems must be therefore activated by electron-donating groups, *N*-oxidation and *N*-quaternization. Among the systems without activating elements it has been known that 5-methyl substituted 1,2,4-triazines [8] and 2-methyl substituted 1,2,5-triazines [12] smoothly, 4-methylpyrimidine partially [10] and 4,6-methylpyrimidine very purely [12] reacted with DMFDMA.

In this study we extended the systematic approach to the reactivity of DMFDMA from picolines to some other methyl substituted heterocycles which include a six-membered nitrogen ring. The comparative results are shown in Table 1, including also the above-mentioned examples from literature.

Thus, methyl derivatives of unsubstituted six-membered systems containing one or two nitrogen atoms (**1a,b,h,i,j**) did not react with DMFDMA. The exception was 4-methylpyrimidine (**1k**), which is a borderline system between them and the more reactive triazines, so it was more intensively studied. One electron withdrawing group, such as a methyl group at the 5 position, an alkoxy, or a mercapto group, diminishes the reactivity of the methyl group towards DMFDMA, while a nitro, halo, cyano or other electron donating groups on 4-methylpyrimidine enhances the reactivity, so the enamines **2n-r** could be obtained. In the reaction of chloro substituted pyrimidines **1n-1q** chloro groups could be substituted with degradation products of DMFDMA forming various dimethylamino and methoxy substituted pyrimidines as by-products **3-10** (Scheme 1). The quaternization of the nitrogen atom enhances the reactivity of unreactive picolines and a smooth formation of enamines **2c-2g** was observed. Among bicyclic systems only methyl substituted nitrogen-rich systems **1z,1aa,1ab** reacted, while the reaction with 2-methyl substituted quinolines **1w,x** and quinoxalines **1y** gave no results. Some so far unknown enamines **2l,s,x,y** from less reactive species were finally prepared by the Bredereck reagent, but for 4-((*E*)-2-(*N,N*-dimethylamino)ethenyl)-2-methoxy-6-

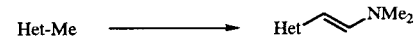
Scheme 1



methylpyrimidine (**2ac**) it was more convenient to prepare it from 2-chloro-4-((*E*)-2-(*N,N*-dimethylamino)ethenyl)-6-methylpyrimidine (**2p**) and sodium methoxide in methanol.

Most of the heteroaryl substituted enamines **2** easily reacted with hydroxylamine hydrochloride by stirring the reaction mixture in methanol at room temperature to give the corresponding acetaldoximes **11** (Scheme 2). Chloropyrimidinyl substituted enamines **2n-2q** gave very unstable products, which could not be isolated, while enamines **2c-2g**, derived from quaternized pyridines, were completely inert towards hydroxylamine hydrochloride. In all other cases, mixtures of two inseparable isomers were isolated. Theoretically four structures such as the (*E*) and (*Z*)-enamine forms or the (*E*) and (*Z*)-oxime forms could be formed (Scheme 2). Although the only known example **11ad** indicated as the (*Z*)-enamine form [6], this form was found in none of our isolated mixtures of isomers. The ^{1}H nmr spectra show triplet-doublet pairs for the ethylene structural moiety of both isomers, what is characteristic of the oxime form. The shielding effect of the nitrogen electron pair in many aliphatic and aromatic oximes was studied and it was found that the proton which is in the *cis* position with respect to the hydroxy group appears at lower field [13]. This observation was applied to the heteroaromatic aldoximes and confirmed by means of the NOESY nmr method. Thus, the NOESY spectrum of pyrimidine-4-acetaldoxime (**11k**) exhibited correlation between protons of the methylene and the hydroxy group only for the major isomer, identified therefore as (*Z*). The triplet of the major (*Z*) isomer for the proton at the oxime double bond was found at lower field in

Table 1



1 2

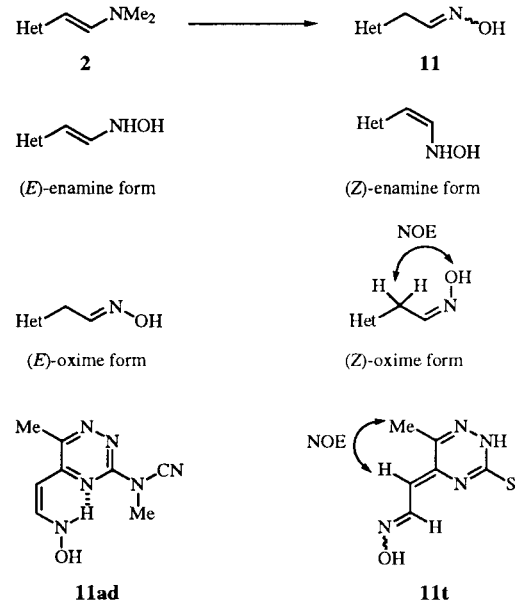
Starting compound	basic system	Heterocyclic site	other substituents	Product with DMFDMA	Bredereck reagent
1a	pyridine	2		no	**2a** [10]
1b	pyridine	4		no	**2b** [10]
1c	pyridinium	2	1-Me, iodide	**2c**	
1d	pyridinium	2	1-Et, iodide	**2d**	
1e	pyridinium	4	1-Me, iodide	**2e**	
1f	pyridinium	4	1-Et, iodide	**2f**	
1g	pyridinium	4	1-Bn, chloride	**2g**	
1h	pyridazine	3		no	**2h** [7]
1i	pyrazine	2		no	**2i** [7]
1j	pyrimidine	2		no	**2j** [7]
1k	pyrimidine	4		**2k** [a] [10]	**2k** [10]
1l	pyrimidine	4	5-Me	no	**2l** [b]
1m	pyrimidine	4	6-Me	**2m** [b] [12]	**2m** [b]
1n	pyrimidine	4	2-Cl	**2n,3,4** [c]	
1o	pyrimidine	4	2-Cl, 6-Cl	**2o,5,6** [a],[c]	
1p	pyrimidine	4	2-Cl, 6-Me	**2p,7,8** [a],[b],[c]	
1q	pyrimidine	4	2-Cl, 6-Cl, 5-NO_2	**2q,9,10** [c]	
1r	pyrimidine	4	2-OMe, 6-OMe, 5-NO_2	**2r** [a][12]	**2r** [15]
1s	pyrimidine	4	2-SH	no	**2s**
1t	1,2,4-triazine	5	3-SEt, 6-Me	**2t** [8]	
1u	1,2,4-triazine	5	3-SEt, α,6-$CH_2CH_2CH_2$	**2u** [8]	
1v	1,2,5-triazine	2	4-Ph, 6-Ph	**2v** [12]	
1w	quinoline	2		no	**2w** [10]
1x	quinoline	2	6-Me	no	**2x**
1y	quinoxaline	2		no	**2y** [b]
1z	*s*-triazolo[4,3-*b*]pyridazine	8	6-Cl, 7-Me	**2z** [b]	
1aa	*s*-triazolo[4,3-*a*]pyrimidine	5	7-Me	**2aa** [b]	
1ab	*s*-triazolo[1,5-*a*]pyrimidine	7	5-Me	**2ab** [b]	

[a] Some starting material was recovered. [b] Only more reactive group reacted. [c] For structures see Scheme 1.

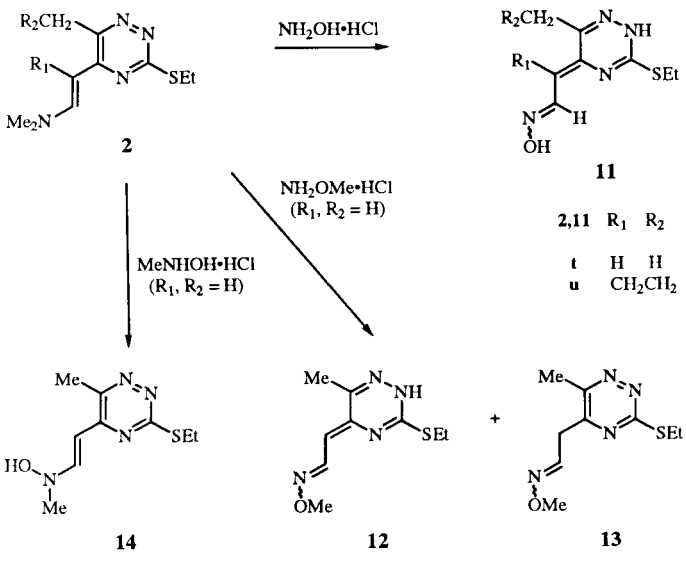
comparison to the corresponding triplet of the minor component, what is in accordance to the previous observations on aliphatic and aromatic oximes.

A different structure was identified for 5-(1,2,4-triazinyl) substituted derivatives **11t** and **11u** (Scheme 3). The ^1H nmr spectra showed two doublets for ethylene protons with the coupling constants of about $J_{CHCH} = 10$ Hz, essentially equal for both isomers. The (*E,Z*)-enamine mixture is not possible, because the coupling constants of the isomers should be different, therefore the oxime structure with an *exo* double bond on the 5 position of the triazine ring was proposed. The 5-*exo* double bonds with the protonation of the nitrogen atom at the 2 position are common in similar systems [8,14] and a non-coupled signal $\delta_{NH} = 11\text{-}12$ ppm for this proton is in accord with published data [8]. The configuration around the *exo* doubled bond is (*Z*) according to our earlier investigation [8] and is now supported by the NOESY correlation between the proton at the *exo* bond and the protons of the 6-methyl group of the triazine ring. Compound **11t** was therefore found to be a mixture of (*E*) and (*Z*) oximes of (*Z*)-(2,5-

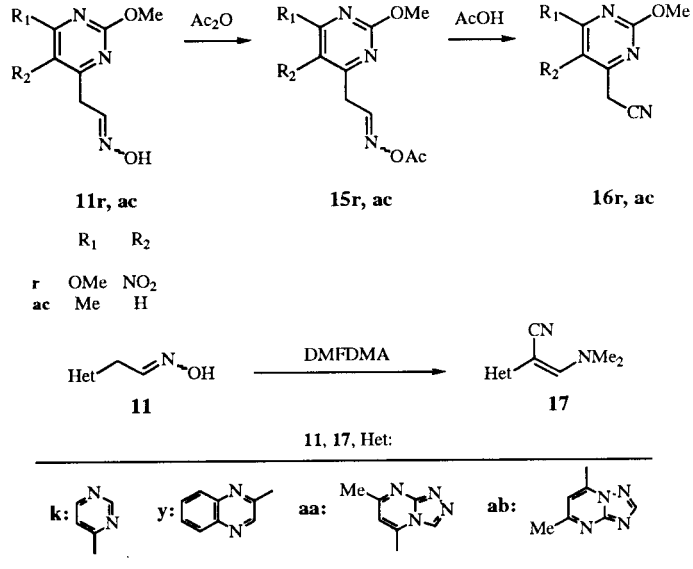
Scheme 2

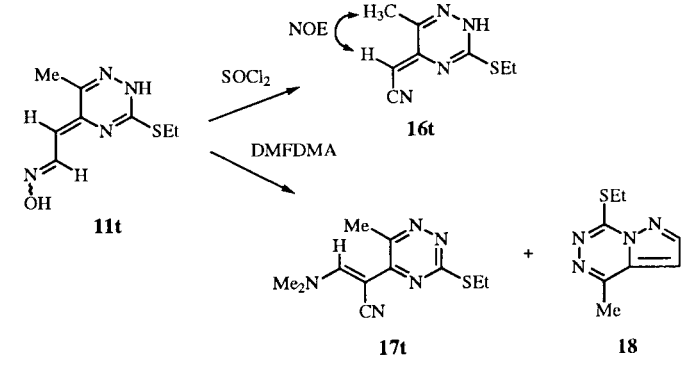


Scheme 3



Scheme 4





dihydro-3-ethylmercapto-6-methyl[1,2,4]triazin-5-yl-idene)acetaldehyde and compound **11u** as the 3-ethylmercapto-2,6,7,8-tetrahydrobenzo[1,2,4]triazine-5-carboxaldoxime. The differentiation between the *exo*-oxime forms and the enamine form was further accomplished by comparation of the two methyl derivatives, prepared in a similar manner from the same starting compound **2t**. Both products such as compound **12**, prepared with *O*-methylhydroxylamine hydrochloride, and the compound **14** prepared with *N*-methylhydroxylamine hydrochloride have coupling constants of about J_{CHCH} = 10 Hz, but the *O*-methyl derivative exhibits a double set of signals in the ^{1}H nmr spectrum and similar physical properties as the unsubstituted oxime **11t**, while the *N*-methyl derivative, which exists only in the hydroxyamino form, shows a single set of signals and physical and chromatographic properties (R_f value, yellow spot) which are closely related to the starting enamine **2t**. Furthermore, the ^{1}H nmr spectrum of the *O*-methyl derivative shows also the presence of small quantities of both isomers of *O*-methyl-3-ethyl-

Table 2

Reaction of Methyl Substituted Heterocycles with *N,N*-Dimethylformamide Dimethyl Acetal

Compound [a]	Reaction time	Solvent	Yield [d] (%)	Solvent for purification on silica gel	Melting point (°C)	Solvent of crystallization
2c [b]	10 min	DMF	82	chloroform/methanol 4:1	205-208	ethanol
2d	2 min	DMF	63	chloroform/methanol 9:1	189-190	ethanol
2e [c]	10 min	toluene	34	chloroform/methanol 9:1	149-150	ethanol
2f	2 min	DMF	78	chloroform/methanol 9:1	144-145	1-propanol
2g	5 min	DMF	94	ethyl acetate/chloroform/methanol 8:2:5	250-255	ethanol/acetone/ether
2r	5 h	DMF	59 [e]	ether/petroleum ether 3:1	161-162 [f]	tetrachloromethane
2z	5 min	DMF	92	purification not necessary	195-196	toluene
2aa	5 min	DMF	86	chloroform/methanol 4:1	256-259 dec	acetonitrile
2ab	10 min	DMF	94	chloroform/methanol 4:1	162-164 dec	toluene

[a] For compounds **2n-2q** see Experimental. [b] In the literature. [11] Reaction time 10 hours, yield 73%, mp 196-198° dec. [c] In the literature. [11] Reaction time 10 hours in DMF, yield 71%, mp 151-154° dec. [d] For non-crystallized product. [e] The quantitative yield after adding water to the reaction mixture was reported [12], but according to our duplication of the experiment, this product contained essential amounts of starting material (about 35%), while the product, obtained by the Bredereck reagent in 77%, contained no starting material [15]. [f] Lit [12], 160-162°, [15], 157-159°.

Table 3

Reaction of Methyl Substituted Heterocycles with *tert*-Butoxybis(dimethylamino)methane

Compound	Reaction time	Yield [b] (%)	Melting point (°C)	Solvent of crystallization
2l	60 min	53	109-110	cyclohexane
2m [a]	60 min	62	144-147 [d]	cyclohexane
2s	15 min	44	233-236	DMF
2x	3 h	98 [c]	oil	—
2y	15 min	98	102-103	heptane

[a] With DMFDMA in 6% yield [12]. [b] After recrystallization. [c] For the product after evaporation of the reaction mixture. [d] In the literature [12] mp 92-95°.

mercapto-6-methyl[1,2,4]triazine-5-acetaldoxime (**13**), the aryl analogue of compound **12**.

Heteroaryl substituted derivatives of acetaldoxime could be transformed into the corresponding acetonitriles **16** by two procedures; firstly by thionyl chloride and secondly by reaction with acetic anhydride and further transformation of the so obtained *O*-acetyloxime **15** into a nitrile by heating in acetic acid. Again the corresponding 1,2,4-triazine derivative **16t** exhibited the (*Z*)-5-*exo* form which was confirmed by the NOESY spectrum. The aldoximes **11** were transformed by heating with DMFDMA into 2-heteroaryl substituted 3-dimethylaminoacrylonitrile **17**. In one case, besides 2-(3-ethylmercapto-6-methyl-5-(1,2,4-triazinyl))-3-dimethylaminoacrylonitrile (**17t**), also 7-methylmercapto-4-methylpyrrazolo[1,5-*d*][1,2,4]triazine (**18**) was isolated as a minor compound (Scheme 4).

EXPERIMENTAL

Melting points were taken on a Kofler micro hot stage. The ^{1}H nmr spectra were obtained on a Varian EM-360 or Varian VXR-300 instruments with TMS as the internal standard and elemental analyses for C, H, and N were obtained on a Perkin-Elmer Analyser 2400. All chromatographic purifications were carried out on silica gel E. Merck 0.063-0.200 mm.

Reaction of Methyl Substituted Heterocycles **1** with *N,N*-Dimethylformamide Dimethyl Acetal. General procedure.

A mixture of **1** (10 mmoles), DMFDMA (15 mmoles) and a solvent (15 ml) was heated under reflux for 5 minutes to 14 hours. After evaporation of the solvent *in vacuo*, the residue was purified by column chromatography on silica gel to yield compounds **2**, which were used in further transformations. For analytical purposes products were additionally purified by crystallization. Reaction conditions and other experimental details are summarized in Table 2.

According to this procedure the following compounds were prepared:

2-((*E*)-2-(*N,N*-Dimethylamino)ethenyl)-1-methylpyridinium Iodide (**2c**).

This compound was prepared from 1,2-dimethylpyridinium iodide (**1c**); ^{1}H nmr (deuteriochloroform): δ 3.10, 3.39 (s, s, 6H, NMe_2), 4.00 (s, 3H, 1-Me), 5.00 (d, C*H*=CHN), 6.83 (m, 5-H), 7.61 (m, 4-H), 8.00-8.30 (m, 3H, 3-H, 6-H , CH=C*H*N). $J_{CH=CH}$ = 12.2 Hz, $J_{4\text{-}H,5\text{-}H}$ = 7 Hz.

Anal. Calcd. for $C_{10}H_{15}IN_2$: C, 41.43; H, 5.21; N, 9.65. Found: C, 41.35; H, 5.20; N, 9.65.

2-((*E*)-2-(*N,N*-Dimethylamino)ethenyl)-1-ethylpyridinium Iodide (**2d**).

This compound was prepared from 1-ethyl-2-methylpyridinium iodide (**1d**); ^{1}H nmr (DMSO-d_6): δ 1.37 (t, 3H, CH_2CH_3), 2.1, 2.2 (s, s, broad, 6H, NMe_2), 4.35 (q, 2H, CH_2CH_3), 5.21 (d, C*H*=CHN), 7.02 (m, 5-H), 7.6-8.3 (m, 4H, 3-H, 4-H, 6-H, CH=C*H*N); $J_{CH=CH}$ = 12.6 Hz, $J_{CH_2CH_3}$ = 7.0 Hz.

Anal. Calcd. for $C_{11}H_{17}IN_2$: C, 43.44; H, 5.63; N, 9.21. Found: C, 43.34; H, 5.73; N, 9.00.

4-((*E*)-2-(*N,N*-Dimethylamino)ethenyl)-1-methylpyridinium Iodide (**2e**).

This compound was prepared from 1,4-dimethylpyridinium iodide (**1e**); ^{1}H nmr (deuteriochloroform): δ 2.9, 3.4 (s, s, broad, 6H, NMe_2), 4.03 (s, 3H, 1-Me), 5.13 (d, C*H*=CHN), 7.28 (d, 2H, 3-H, 5-H), 7.92 (d, 2H, 2-H, 6-H), 7.95 (d, CH=C*H*N), $J_{CH=CH}$ = 12.6 Hz, $J_{2\text{-}H,3\text{-}H}$ = 7.5 Hz.

Anal. Calcd. for $C_{10}H_{15}IN_2$: C, 41.43; H, 5.21; N, 9.65. Found: C, 41.66; H, 5.39; N, 9.85.

4-((*E*)-2-(*N,N*-Dimethylamino)ethenyl)-1-ethylpyridinium Iodide (**2f**).

This compound was prepared from 1-ethyl-4-methylpyridinium iodide (**1f**); ^{1}H nmr (DMSO-d_6): δ 1.39 (t, 3H, CH_2CH_3), 2.8 , 3.2 (s, s, broad, 6H, NMe_2), 4.14 (q, 2H, CH_2CH_3), 5.28 (d, C*H*=CHN), 7.30 (d, 2H, 3-H, 5-H), 8.05 (d, CH=C*H*N), 8.12 (d, 2H, 2-H, 6-H), $J_{CH_2CH_3}$ = 7.2 Hz, $J_{CH=CH}$ = 12.7 Hz, $J_{2\text{-}H,3\text{-}H}$ = 7.6 Hz.

Anal. Calcd. for $C_{11}H_{17}IN_2$: C, 43.44; H; 5.63; N, 9.21. Found: C, 43.19; H, 5.76; N, 8.94.

1-Benzyl-4-((*E*)-2-(*N,N*-dimethylamino)ethenyl)pyridinium Chloride (**2g**).

This compound was prepared from 1-benzyl-4-methylpyridinium chloride (**1g**); ^{1}H nmr (DMSO-d_6): δ 3.05, 3.20 (s, s, broad, 6H, NMe_2), 5.34 (d, C*H*=CHN), 5.41 (s, 2H, CH_2Ph), 7.44 (d, 2H, 3-H, 5-H), 7.46 (s, 5H, Ph), 8.21 (d, CH=C*H*N), 8.32 (d, 2H, 2-H, 4-H), $J_{CH=CH}$ = 11 Hz, $J_{2\text{-}H,3\text{-}H}$ = 7 Hz.

Anal. Calcd. for $C_{16}H_{19}ClN_2$: C, 69.94; H, 6.97; N, 10.19. Found: C, 69.69; H, 7.09; N, 10.17.

8-((*E*)-2-(*N,N*-Dimethylamino)ethenyl)-6-chloro-7-methyl-*s*-triazolo[4,3-*b*]pyridazine (**2z**).

This compound was prepared from 6-chloro-7,8-dimethyl-*s*-triazolo[4,3-*b*]pyridazine (**1z**); ^{1}H nmr (deuteriochloroform): δ 2.31 (s, 3H, 7-Me), 3.06 (s, 6H, NMe_2), 5.12 (d, C*H*=CHN), 8.73 (s, 3-H), 9.20 (d, CH=C*H*N), $J_{CH=CH}$ = 12.6 Hz.

Anal. Calcd. for $C_{10}H_{12}ClN_5$: C, 50.53; H, 5.09; N, 29.46. Found: C, 50.90; H, 5.16; N, 29.57.

5-((*E*)-2-(*N,N*-Dimethylamino)ethenyl)-7-methyl-*s*-triazolo-[4,3-*a*]pyrimidine (**2aa**).

This compound was prepared from 5,7-dimethyl-*s*-triazolo[4,3-*a*]pyrimidine (**1aa**); ^{1}H nmr (DMSO-d_6): δ 2.41 (s,

3H, 7-Me), 3.09 (s, 6H, NMe_2), 5.35 (d, C*H*=CHN), 6.76 (s, 6-H), 7.97 (d, CH=C*H*N), 9.28 (s, 3-H), $J_{CH=CH}$ = 12.5 Hz.

Anal. Calcd. for $C_{10}H_{13}N_5$: C, 59.10; H, 6.44; N, 34.46. Found: C, 58.98; H, 6.55; N, 34.25.

7-((*E*)-2-(*N,N*-Dimethylamino)ethenyl)-5-methyl-*s*-triazolo-[1,5-*a*]pyrimidine (**2ab**).

This compound was prepared from 5,7-methyl-*s*-triazolo-[1,5-*a*]pyrimidine (**1ab**); ^1H nmr (deuteriochloroform): δ 2.50 (s, 3H, 5-Me), 3.04 (s, 6H, NMe_2), 5.38 (d, C*H*=CHN), 6.46 (s, 6-H), 8.12 (d, CH=C*H*N), 8.26 (s, 2-H), $J_{CH=CH}$ = 13 Hz.

Anal. Calcd. for $C_{10}H_{13}N_5$: C, 59.10; H, 6.44; N, 34.46. Found: C, 58.78; H, 6.54; N, 34.10.

Reaction of 4-Chloro-2-methylpyrimidine (**1n**) with DMFDMA.

A mixture of 4-chloro-2-methylpyrimidine (**1n**) (730 mg, 5 mmoles), DMFDMA (1.02 g, 8.5 mmoles) and DMF (4 mmoles) was heated under reflux for 90 minutes. The solvent was then evaporated *in vacuo* and the residue was separated by column chromatography (silica gel with ether-petroleum ether 3:1, (v/v), as the solvent) to give the following compounds:

2-Dimethylamino-4-methylpyrimidine (**3**).

This compound, isolated as the first fraction in 4% yield as an oil, was identical with the compound, prepared by an independent method [16]; ^1H nmr (deuteriochloroform): δ 2.29 (s, 3H, 4-Me), 3.13 (s, 6H, NMe_2), 6.48 (d, 5-H), 8.05 (d, 5-H), $J_{5\text{-}H,6\text{-}H}$ = 4.9 Hz.

2-Methoxy-4-methylpyrimidine (**4**).

This compound, isolated as the second fraction in 6% yield as an oil, was identical with the compound, prepared by an independent method [17]; ^1H nmr (deuteriochloroform): δ 2.41 (s, 3H, 4-Me), 3.92 (s, 3H, OMe), 6.68 (d, 5-H), 8.22 (d, 6-H), $J_{5\text{-}H,6\text{-}H}$ = 4.9 Hz.

4-((*E*)-2-(*N,N*-Dimethylamino)ethenyl)-2-chloropyrimidine (**2n**).

This compound was isolated as the third fraction in 41% yield, mp 102-103° (from cyclohexane); ^1H nmr (deuteriochloroform): δ 2.93 (s, 6H, NMe_2), 4.88 (d, C*H*=CHN), 6.45 (d, 5-H), 7.70 (d, CH=C*H*N), 7.89 (d, 6-H), $J_{CH=CH}$ = 12.6 Hz, $J_{5\text{-}H,6\text{-}H}$ = 5.4 Hz.

Anal. Calcd. for $C_8H_{10}ClN_3$: C, 52.32; H, 5.49; N, 22.77. Found: C, 52.57; H, 5.61; N, 22.97.

Reaction of 2,4-Dichloro-6-methylpyrimidine (**1o**) with DMFDMA.

A mixture of 2,4-dichloro-6-methylpyrimidine (**1o**) (650 mg, 4 mmoles), DMFDMA (1.27 g, 10 mmoles) and toluene (5 ml) was heated under reflux for 14 hours. The solvent was then evaporated *in vacuo* and the residue was separated by column chromatography (silica gel with ether-petroleum ether 3:1, (v/v), as solvent) to give the following compounds:

2-Dimethylamino-4-chloro-6-methylpyrimidine (**5**).

This compound was isolated as the first fraction together with the starting compound. The mixture was separated on a new column of silica gel by elution with ether-petroleum ether 1:3, (v/v), to give the compound **5** in 27% yield, mp 32-35°, lit [16] 35-36°; ^1H nmr (deuteriochloroform): δ 2.29 (s, 3H, 6-Me), 3.15 (s, 6H, NMe_2), 6.31 (s, 5-H). The product was identical with the compound, prepared by an independent method [16].

As a later fraction the starting compound was recovered in 14% yield.

2,6-Dichloro-4-((*E*)-2-(*N,N*-dimethylamino)ethenyl)pyrimidine (**2o**).

This compound was isolated as the second fraction in 7% yield, mp 121-123° (from ether-petroleum ether); ^1H nmr (deuteriochloroform): δ 2.93 (s, 6H, NMe_2), 4.84 (d, C*H*=CHN), 6.47 (s, 5-H), 7.18 (d, CH=C*H*N), $J_{CH=CH}$ = 12.7 Hz.

Anal. Calcd. for $C_8H_9Cl_2N_3$: C, 44.06; H, 4.17; N, 19.27. Found: C, 44.15; H, 4.17; N, 19.38.

4-Dimethylamino-2-chloro-6-methylpyrimidine (**6**).

This compound, isolated as the third fraction in 31% yield, was identical with the compound, prepared by an independent method [18], mp 76-81°, lit [18] 87°; ^1H nmr (deuterichloroform): δ 2.30 (s, 3H, 6-Me), 3.04 (s, 6H, NMe_2), 6.10 (s, 5-H).

Reaction of 2-Chloro-4,6-dimethylpyrimidine (**1p**) with DMFDMA.

A mixture of 2-chloro-4,6-dimethylpyrimidine (**1p**) (10 g, 70 mmoles), DMFDMA (12.6 g, 105 mmoles) and DMF (40 ml) was heated under reflux for 5 hours. During the reaction DMFDMA was added after two and four hours (2 g each time). Finally, the solvent was evaporated *in vacuo* and the residue was separated by column chromatography (silica gel with ether-petroleum ether 3:1, (v/v), as the solvent) to give the following compounds:

2-Dimethylamino-4,6-dimethylpyrimidine (**7**).

This compound, isolated as the first fraction in 1% yield, was identical with the compound, prepared by an independent method [19]; ^1H nmr (deuteriochloroform): δ 2.21 (s, 6H, 4-Me, 6-Me), 3.08 (s, 6H, NMe_2), 6.11 (s, 5-H).

The starting compound was recovered (12%) as the second fraction.

4,6-Dimethyl-2-methoxypyrimidine (**8**).

This compound, isolated as the third fraction in 5% yield as an oil, was identical with the compound, prepared by an independent method [20]; ^1H nmr (deuteriochloroform): δ 2.34 (s, 6H, 4-Me, 6-Me), 3.89 (s, 3H, OMe), 6.53 (s, 5-H).

4-((*E*)-2-(*N,N*-Dimethylamino)ethenyl)-2-chloro-6-methylpyrimidine (**2p**).

This compound, which was eluted from the column as the fourth fraction in 38% yield, slowly decomposed changing in color from yellow *via* red to black. Repeated chromatographic purification followed by precipitation from ether solution with petroleum ether and final crystallization from cyclohexane gave a stable, analytically pure yellow compound, mp 83-84°; ^1H nmr (deuteriochloroform): δ 2.27 (s, 3H, 6-Me), 2.90 (s, 6H, NMe_2), 4.86 (d, C*H*=CHN), 6.36 (s, 5-H), 7.71 (d, CH=C*H*N), $J_{CH=CH}$ = 12.6 Hz.

Anal. Calcd. for $C_9H_{12}ClN_3$: C, 54.69; H, 6.12; N, 21.26. Found: C, 54.63; H, 6.13; N, 21.13.

Reaction of 2-Chloro-4,6-dimethyl-5-nitropyrimidine (**1q**) with DMFDMA.

A mixture of 2-chloro-4,6-dimethyl-5-nitropyrimidine (**1q**) (1.4 g, 5 mmoles), DMFDMA (1.27 g, 10 mmoles) and toluene (15 ml) was stirred at room temperature for 10 minutes. The sol-

vent was evaporated *in vacuo* and the residue was separated by column chromatography on silica gel. By elution with ether-petroleum ether 1:3, (v/v), as the solvent, the following compounds were isolated:

2-Dimethylamino-4-chloro-6-methyl-5-nitropyrimidine (**9**).

This compound was isolated as the first fraction in 3% yield, mp 107-108° (from petroleum ether); ^{1}H nmr (deuteriochloroform): δ 2.42 (s, 3H, 6-Me), 3.18 (s, 6H, NMe_2).

Anal. Calcd. for $C_7H_9ClN_4O$: C, 38.81; H, 4.17; N, 25.86. Found: C, 39.08; H, 4.19; N, 25.64.

4-Dimethylamino-2-chloro-6-methyl-5-nitropyrimidine (**10**).

This compound, isolated as the second fraction in 4% yield, was identical with the title compound, prepared by an independent method [20], mp 88-94°, lit [20] 97-98°; ^{1}H nmr (deuteriochloroform): δ 2.42 (s, 3H, 6-Me), 3.06 (s, 6H, NMe_2).

By further elution with ether-petroleum ether 3.1, (v/v), as the solvent, the following compound was isolated as the third fraction:

2,6-Dichloro-4-((*E*)-2-(*N,N*-dimethylamino)ethenyl)-5-nitropyrimidine (**2q**).

The yield was 4.5%, mp 161-164° (from cyclohexane); ^{1}H nmr (deuteriochloroform): δ 2.78, 3.20 (s, s, 6H, NMe_2), 4.87 (d, C*H*=CHN), 8.05 (d, CH=C*H*N), $J_{CH=CH}$ = 11.8 Hz.

Anal. Calcd. for $C_8H_8Cl_2N_4O_2$: C, 36.52; H, 3.07; N, 21.30. Found: C, 36.66; H, 3.16; N, 21.13.

Reaction of Methyl Substituted Heterocycles **1** with *tert*-Butoxybis(dimethylamino)methane. General Procedure.

A mixture of **1** (10 mmoles), *tert*-butoxybis(dimethylamino)methane (15 mmoles) and DMF (15 ml) was heated under reflux for 15 minutes to 3 hours. The solvent was evaporated *in vacuo*. The residue was purified by crystallization or used as crude oils. The purification on silica gel was only partially effective due to a decomposition into other, still more labile compounds, which could not be isolated in pure form.

Reaction conditions are summarized in Table 3.

According to this procedure the following compounds were prepared:

4-((*E*)-2-(*N,N*-Dimethylamino)ethenyl)-5-methylpyrimidine (**2l**).

This compound was prepared from 4,5-dimethylpyrimidine (**1l**); ^{1}H nmr (deuteriochloroform): δ 2.08 (s, 3H, 5-Me), 2.94 (s, 6H, NMe_2), 5.06 (d, C*H*=CHN), 8.06 (d,CH=C*H*N), 8.18 (s, 6-H), 8.74 (s, 2-H), $J_{CH=CH}$ = 12 Hz.

Anal. Calcd. for $C_8H_{11}N_3$: C, 66.23; H, 8.02; N, 25.74. Found: C, 65.94; H, 8.06; N, 25.91.

4-((*E*)-2-(*N,N*-Dimethylamino)ethenyl)-6-methylpyrimidine (**2m**).

This compound was prepared from 4,6-dimethylpyrimidine (**1m**) and was identical to the compound prepared according to the procedure from literature [12]; ^{1}H nmr (deuteriochloroform): δ 2.33 (s, 3H, 6-Me), 2.90 (s, 6-H, NMe_2), 4.95 (d, C*H*=CHN), 6.60 (s, 5-H), 7.73 (d, CH=C*H*N), 8.64 (s, 2-H), $J_{CH=CH}$ = 13 Hz.

4-((*E*)-2-(*N,N*-Dimethylamino)ethenyl)-2-mercaptopyrimidine (**2s**).

This compound was prepared from 4-methyl-2-mercaptopyrimidine (**1s**); ^{1}H nmr (deuteriochloroform): δ 3.05 (s, broad, 6H, NMe_2), 5.07 (d, C*H*=CHN), 6.48 (d, 5-H), 7.54 (d, 6-H), 7.98 (d, CH=C*H*N), S*H* exchanged, $J_{CH=CH}$ = 13 Hz, $J_{5\text{-}H,6\text{-}H}$ = 7 Hz.

Anal. Calcd. for $C_8H_{11}N_3S$: C, 53.01; H, 6.11; N, 23.18. Found: C, 53.46; H, 6.40; N, 23.50.

2-((*E*)-2-(*N,N*-Dimethylamino)ethenyl)-6-methylquinoline (**2x**).

This compound was prepared from 2,6-dimethylquinoline (**1x**); ^{1}H nmr (deuteriochloroform): δ 2.42 (s, 3H, 6-Me), 2.92, 2.96 (s, s, 6H, NMe_2), 5.31 (d, C*H*=CHN), 7.0-7.9 (m, m, 7H, CH=C*H*N, Ar), $J_{CH=CH}$ = 13.5 Hz.

2-((*E*)-2-(*N,N*-Dimethylamino)ethenyl)quinoxaline (**2y**).

This compound was synthesized from 2-methylquinoxaline (**1y**); ^{1}H nmr (deuteriochloroform): δ 3.03 (s, 6H, NMe_2), 5.39 (d, C*H*=CHN), 7.4-8.2 (m, 4H, 5-H, 6-H, 7-H, 8-H), 7.91 (d, CH=C*H*N), 8.74 (s, 3-H), $J_{CH=CH}$ = 14 Hz.

Anal. Calcd. for $C_{12}H_{13}N_3$: C, 72.34; H, 6.58; N, 21.09. Found: C, 71.53; H, 6.79; N, 20.44.

Elemental analysis could not be improved by repeated crystallizations because of the presence of a decomposition product. We succeeded in isolating it from crude mixture by column chromatography on silica gel, eluting with ether, as a fast darkening yellow semisolid. According to the nmr data, [^{1}H nmr (deuteriochloroform): δ 5.69 (d, 1H, J = 3.8 Hz), 7.5-8.4 (m, 5-H), 8.59 (s, 1H), 8.63 (d, 1H, J = 3.6 Hz)] it seemed to be (*Z*)-2-(2-hydroxyethenyl)quinoxaline, but because of its short life the structure could not be confirmed by other methods.

4-((*E*)-2-(*N,N*-Dimethylamino)ethenyl)-2-methoxy-6-methylpyrimidine (**2ac**).

Freshly isolated 2-chloro-4-((*E*)-2-(*N,N*-dimethylamino)-ethenyl)-6-methylpyrimidine (**2p**) (5.08 g, 25 mmoles) was heated under reflux in sodium methoxide solution (prepared from 7 g of sodium and 100 ml methanol) for 1 hour. The reaction mixture was then concentrated to about 30 ml, diluted with 60 ml of water and the product was extracted by chloroform (three times, 60 ml each time). After drying of the organic layers with magnesium sulphate chloroform was evaporated to give a brown oil (4.9 g, assay 75% (area, gc), yield 71%), suitable for further transformations, bp 164-165° (7 mbar); ^{1}H nmr (deuteriochloroform): δ 2.23 (s, 3H, 6-Me), 2.87 (s, 6H, NMe_2), 3.87 (s, 3H, OMe), 4.86 (d, C*H*=CHN), 6.17 (s, 5-H), 7.66 (d, CH=C*H*N), $J_{CH=CH}$ = 12.7 Hz.

Synthesis of Acetaldoximes **11**. General Procedures.

Method A. Pyrimidine-4-acetaldoxime (**11k**).

A mixture of 4-((*E*)-2-(*N,N*-dimethylamino)ethenyl)pyrimidine (**2k**) (447 mg, 3 mmoles), hydroxylamine hydrochloride (230 mg, 3.3 mmoles) and methanol (4 ml) was stirred at room temperature for 15 minutes. The solvent was evaporated *in vacuo*, the residue was purified by a column chromatography (silica gel, chloroform-methanol 20:1, (v/v)) to give the product, yield 79%, mp 99-106° (from benzene); ^{1}H nmr (deuteriochloroform): δ (*Z*)-**11k**: 3.86 (d, 2H, CH_2), 6.99 (t, C*H*CH_2), 7.19 (dd, 5'-H), 8.54 (d, 4'-H), 9.06 (d, 2'-H), J_{CH_2CH} = 5.3 Hz, $J_{4\text{-}H,5\text{-}H}$ = 4.9 Hz, $J_{2\text{-}H,5\text{-}H}$ = 1.5 Hz; δ (*E*)-**11k**: 3.69 (d, 2H, CH_2), 7.56 (t, C*H*CH_2), J_{CH_2CH} = 6 Hz. Other signals are identical or overlapped, ratio (*Z*)-**11k**:(*E*)-**11k** = 1:5.

Anal. Calcd. for $C_6H_7N_3O$: C, 52.55; H, 5.14; N, 30.64. Found: C, 52.30; H, 4.93; N, 30.55.

According to the same procedure the following compounds were prepared:

Pyrazine-2-acetaldoxime (**11i**).

This compound was prepared from 2-((*E*)-2-(*N,N*-dimethylamino)ethenyl)pyrazine (**2i**) and isolated from a column by ether-petroleum ether 1.1 (v/v), yield 78%, mp 60-79° (from diisopropyl ether); ^{1}H nmr (deuteriochloroform): (*Z*)-**11i**: δ 4.01 (d, 2H, C*H*$_2$), 7.13 (t, C*H*CH$_2$), 8.5-8.63 (m, 3H, 3'-H, 5'-H, 6'-H), 10.55 (s, broad, O*H*), $J_{CH_2\text{-}CH}$ = 5.5 Hz; (*E*)-**11i**: δ 3.78 (d, 2H, C*H*$_2$), 7.72 (t, C*H*CH$_2$), 10.11 (s, broad, O*H*), J_{CH_2CH} = 6 Hz. Other signals are identical or overlapped, ratio (*Z*)-**11i**:(*E*)-**11i** = 56:44.

Anal. Calcd. for $C_6H_7N_3O$: C, 52.55; H, 5.15; N, 30.64. Found: C, 52.81; H, 5.17; N, 30.31.

2,6-Dimethoxy-5-nitropyrimidine-4-acetaldoxime (**11r**).

This compound was prepared from 2,6-dimethoxy-4-((*E*)-2-(*N,N*-dimethylamino)ethenyl)-5-nitropyrimidine (**2r**) and isolated from a column by ether-petroleum ether 1:1, (v/v), yield 65%, mp 90-95° (ether/petroleum ether); ^{1}H nmr (deuteriochloroform): δ (*Z*)-**11r**: 3.86 (d, 2H, CH$_2$), 4.03 and 4.07 (s, s, 3H, OMe), 7.06 (t, C*H*CH$_2$), 9.1 (s, broad, OH), J_{CH_2CH} = 5 Hz; δ (*E*)-**11r**: 3.70 (d, 2H, CH$_2$), 7.59 (t, C*H*CH$_2$). Other signals are identical or overlapped, ratio (*Z*)-**11r**:(*E*)-**11r** = 62:38.

Anal. Calcd. for $C_8H_{10}N_4O_5$: C, 39.67; H, 4.16; N, 23.55. Found: C, 39.51; H, 4.20; N, 23.26.

Quinoxaline-2-acetaldoxime (**11y**).

This compound was synthesized from 2-((*E*)-2-(*N,N*-dimethylamino)ethenyl)quinoxaline (**2y**) and isolated from a column with ether-petroleum ether 1:1, (v/v), yield 76%, mp 110-113° (from tetrachloromethane); ^{1}H nmr (deuteriochloroform): δ (*Z*)-**11y**: 4.25 (d, 2H, CH$_2$), 7.36 (t, C*H*CH$_2$), 7.7-8.4 (m, 4H, 5'-H, 6'-H, 7'-H, 8'-H), 8.98 (s, 3'-H), J_{CH_2CH} = 5.5 Hz, δ (*E*)-**11y**: 4.03 (d, 2H, CH$_2$), 8.93 (s, 3'-H), J_{CH_2CH} = 6 Hz. Other signals are identical or overlapped, ratio (*Z*)-**11y**:(*E*)-**11y** = 62:38.

Anal. Calcd. for $C_{10}H_9N_3O$: C, 64.16; H, 4.85; N, 22.45. Found: C, 64.47; H, 4.98; N, 22.32.

2-Methoxy-6-methylpyrimidine-4-acetaldoxime (**11ac**).

This compound was synthesized from 4-((*E*)-2-(*N,N*-dimethylamino)ethenyl)-2-methoxy-6-methylpyrimidine (**2ac**) and isolated from a column by ether, yield 74%, mp 75-95° (from benzene-petroleum ether); ^{1}H nmr (deuteriochloroform): δ (*Z*)-**11ac**: 2.40 (s, 3H, 6-Me), 3.74 (d, 2H, CH$_2$), 3.95 (s, 3H, OMe), 6.63 (s, 5'-H), 7.00 (t, C*H*CH$_2$), 9.5 (s, broad, OH), J_{CH_2CH} = 5.4 Hz; δ (*E*)-**11ac**: 3.54 (d, 2H, CH$_2$), 7.57 (t, C*H*CH$_2$), 9.1 (s, broad, OH), J_{CH_2CH} = 6.3 Hz. Other signals are identical or overlapped, ratio (*Z*)-**11ac**:(*E*)-**11ac** = 3:4.

Anal. Calcd. for $C_8H_{11}N_3O_2$: C, 53.03; H, 6.12; N, 23.19. Found: C, 53.05; H, 6.20; N, 23.25.

Method B. 7-Methyl-*s*-triazolo[4,3-*a*]pyrimidine-5-acetaldoxime (**11aa**).

A mixture of 5-((*E*)-2-(*N,N*-dimethylamino)ethenyl)-7-methyl-*s*-triazolo[4,3-*a*]pyrimidine (**2aa**) (406 mg, 2 mmoles), hydroxylamine hydrochloride (154 mg, 2.2 mmoles) and methanol (5 ml) was stirred at room temperature for 2 hours. The precipitated product was filtered and washed with methanol, yield 63%, mp 189-190° dec (from ethanol); ^{1}H nmr (DMSO-d$_6$): δ (*Z*)-**11aa**: 2.45 (s, 3H, 7-Me), 4.01 (d, 2H, CH$_2$), 6.80 (s, 6-H), 6.91 (t, C*H*CH$_2$), 8.86 (s, 3-H), 11.36 (s, OH), J_{CH_2CH} = 5.1 Hz; δ (*E*)-**11aa**: 3.89 (d, 2H, CH$_2$), 7.45 (t, C*H*CH$_2$), 10.77 (s, OH). Other signals are identical or overlapped, ratio (*Z*)-**11aa** = (*E*)-**11aa** 55:45.

Anal. Calcd. for $C_8H_9N_5O$: C, 50.26; H, 4.75; N, 36.63. Found: C, 50.48; H, 4.83; N, 36.81.

According to the same procedure the following compounds were prepared:

2-(2,5-Dihydro-3-ethylmercapto-6-methyl[1,2,4]triazin-(*Z*)-5-ylidene)acetaldoxime (**11t**).

This compound was synthesized from 2,5-dihydro-5-((*E*)-2-(*N,N*-dimethylamino)ethenyl)-3-ethylmercapto-6-methyl[1,2,4]-triazine (**2t**) [8] and purified by column chromatography (silica gel, ether), yield 98%, mp 175-177° dec (from acetonitrile); ^{1}H nmr (DMSO-d$_6$): δ (*Z*)-**11t**: 1.33 (t, 3H, CH$_2$*Me*), 1.96 (s, 3H, 6'-Me), 3.09 (q, 2H, C*H*$_2$Me), 5.80 (d, 2-H), 7.86 (d, 1-H), 10.64 (s, OH), 11.9 (s, 2'-H), $J_{CH_2CH_3}$ = 7 Hz, $J_{1\text{-}H,2\text{-}H}$ = 10 Hz; δ (*E*)-**11t**: 1.3 (t, 3H, CH$_2$*Me*), 3.04 (q, 2H, C*H*$_2$Me), 5.44 (d, 2-H), 8.31 (d, 1-H), 10.53 (s, OH), 11.65 (s, 2'-H). Other signals are identical or overlapped, (*Z*)-**11t**:(*E*)-**11t** = 1:1.

Anal. Calcd. for $C_8H_{12}N_4OS$: C, 45.27; H, 5.70; N, 26.39. Found: C, 45.43; H, 5.95; N, 26.51.

3-Ethylmercapto-2,6,7,8-tetrahydrobenzo[1,2,4]triazine-5-carboxaldoxime (**11u**).

This compound was synthesized from 5-((*E*)-2-(*N,N*-dimethylamino)methylene-3-ethylmercapto-2,6,7,8-tetrahydrobenzo[1,2,4]triazine (**2u**) [8], purified by column chromatography (silica gel, ether-petroleum ether (v/v)) with final addition of the mixture chloroform-ether 1:1 (v/v) to evaporated fraction to give crystals, yield 29%, mp 184-187° (from acetonitrile); ^{1}H nmr (DMSO-d$_6$): δ 1.27 (t, 3H, CH$_2$*Me*), 1.4-2.0 (s, broad, 2H, 7-CH$_2$), 2.1-2.5 (s, broad, 6-CH$_2$, 8-CH$_2$), 2.98 (q, 2H, C*H*$_2$Me), 8.36 (s, CH=NOH), 10.66 (s, OH), 11.38 (s, 2-H), $J_{CH_2CH_3}$ = 7 Hz.

Anal. Calcd. for $C_{10}H_{14}N_4OS$: C, 50.40; H, 5.92; N, 23.51. Found: C, 50.64; H, 6.15; N, 23.26.

6-Chloro-7-methyl-*s*-triazolo[4,3-*b*]pyridazine-8-acetaldoxime (**11z**).

This compound was synthesized from 8-((*E*)-2-(*N,N*-dimethylamino)ethenyl)-6-chloro-7-methyl-*s*-triazolo[4,3-*b*]pyridazine (**2z**). The general procedure was slightly changed by adding water to the reaction mixture to precipitate the product, yield 78%, mp 211-216° (from ethanol); ^{1}H nmr (DMSO-d$_6$): δ 2.35 (s, 3H, 7-Me), 4.07 (d, 2H, CH$_2$), 6.95 (t, C*H*CH$_2$), 9.47 (s, 3'-H), 11.25 (s, OH), J_{CH_2CH} = 5.1 Hz, predominantly one isomer.

Anal. Calcd. for $C_8H_8ClN_5O$: C, 42.59; H, 3.57; N, 31.04. Found: C, 43.04; H, 3.72; N, 30.91.

5-Methyl-*s*-triazolo[1,5-*a*]pyrimidine-7-acetaldoxime (**11ab**).

This compound was synthesized from 7-((*E*)-2-(*N,N*-dimethylamino)ethenyl)-5-methyl-*s*-triazolo[1,5-*a*]pyrimidine (**2ab**), yield 73%, mp 159-161° dec (from ethanol); ^{1}H nmr (DMSO-d$_6$): δ (*Z*)-**11ab**: 2.56 (s, 3H, Me), 4.07 (d, 2H, CH$_2$), 6.94 (t, C*H*CH$_2$), 7.10 (d, 6'-H), 7.94 (s, 2-H), 11.20 (s, OH), J_{CH_2CH} = 6.0 Hz, $J_{6\text{-}H,CH_2}$ = 1.6 Hz; δ (*E*)-**11ab**: 3.99 (d, 2H, CH$_2$), 7.52 (t, C*H*CH$_2$), 10.72 (s, OH). Other signals are identical or overlapped, ratio (*Z*)-**11ab**:(*E*)-**11ab** = 55:45.

Anal. Calcd. for $C_8H_9N_5O$: C, 50.26; H, 4.75; N, 36.63. Found: C, 50.30; H, 4.84; N, 36.70.

2-(2,5-Dihydro-3-ethylmercapto-6-methyl-1,2,4-triazin-5-ylidene)-*O*-methylacetaldoxime (**12**).

This compound was synthesized from 2,5-dihydro-5-((*E*)-2-(*N,N*-dimethylamino)ethenyl)-3-ethylmercapto-6-methyl[1,2,4]–triazine (**2t**) and *O*-methylhydroxylamine hydrochloride according to the procedure B, yield 51%, mp 120-123° (from toluene); ^{1}H nmr (deuteriochloroform): δ (*Z*)-**12**: 1.35 (t, 3H, CH_2*Me*), 2.02 (s, 3H, 6'-Me), 3.08 (q, 2H, CH_2Me), 3.91 (s, 3H, OMe), 5.80 (d, 2-H), 7.91 (d, 1-H), 9.2 (s, 2'-H), $J_{1\text{-}H,2\text{-}H}$ = 9.5 Hz; δ (*E*)-**12**: 1.97 (s, 3H, 6'-Me), 3.87 (s, 3H, OMe), 5.42 (d, 2-H), 8.43 (d, 1-H), 8.9 (s, 2'-H), $J_{1\text{-}H,2\text{-}H}$ = 9.5 Hz. Other signals are identical or overlapped, ratio (*Z*)-**12**:(*E*)-**12** = 1:1.

Anal. Calcd. for $C_9H_{14}N_4OS$: C, 47.77; H, 6.24; N, 24.76. Found: C, 47.89; H, 6.44; N, 24.77.

The non-crystallized product contained up to 15% of *O*-methyl-(*Z*)-2,5-dihydro-3-ethylmercapto-6-methyl[1,2,4]triazine-5-acetaldoxime (**13**) as observed in ^{1}H nmr spectrum, δ (*Z*)-**13**: 1.43 (t, 3H, CH_2CH_3), 2.63 (s, 6'-Me), 3.78 (d, 2H, $CHCH_2$), 7.13 (t, $CHCH_2$), J_{CH_2CH} = 5.0 Hz; (*E*)-**13**: 2.64 (s, 6'-Me), 3.85 (s, 3H, OMe), 3.62 (d, 2H, $CHCH_2$), 7.62 (t, $CHCH_2$), J_{CH_2CH} = 5 Hz, other peaks were overlapped with signals of **12**, ratio (*Z*)-**13**:(*E*)-**13** = 3:1.

3-Ethylmercapto-(*E*)-5-(2-(*N*-hydroxy-*N*-methylamino)ethenyl)-6-methyl-1,2,4-triazine (**14**).

This compound was synthesized from 2,5-dihydro-5-((*E*)-2-(*N,N*-dimethylamino)ethenyl)-3-ethylmercapto-6-methyl[1,2,4]–triazine (**2t**) and *N*-methylhydroxylamine hydrochloride according to the procedure A for aldoximes, yield 57%, mp 176-178° (from acetonitrile); ^{1}H nmr (deuteriochloroform): δ 1.34 (t, 3H, CH_2*Me*), 2.04 (s, 3H, 6-Me), 3.06 (q, 2H, CH_2Me), 3.70 (s, 3H, NMe), 5.90 (d, C*H*=CHN), 7.80 (d, CH=C*H*N), $J_{CH_2CH_3}$ = 7.5 Hz, $J_{CH=CH}$ = 10 Hz.

Anal. Calcd. for $C_9H_{14}N_4OS$: C, 47.77; H, 6.24; N, 24.76. Found: C, 47.71; H, 6.43; N, 24.51.

(*Z*)-5-Cyanomethylene-2,5-dihydro-3-ethylmercapto-6-methyl-1,2,4-triazine (**15t**).

A solution of thionyl chloride (0.36 g, 3 mmoles) in chloroform (4 ml) was added dropwise at 0° to the mixture of 2-(2,5-dihydro-3-ethylmercapto-6-methyl-1,2,4-triazin-5-(*Z*)-ylidene)acetaldoxime (**11t**) (0.31 g, 1.5 mmoles) in chloroform (8 ml) for 15 minutes, then the mixture was stirred at room temperature for 3 hours. The precipitated product was filtered and washed with chloroform, yield 71%, mp 123-125° (from toluene-heptane); ^{1}H nmr (deuteriochloroform): δ 1.36 (t, 3H, CH_2*Me*), 2.03 (s, 3H, 6-Me), 3.16 (q, 2H, CH_2Me), 4.34 (s, C*H*CN), 9.8 (s, broad, 2-H), $J_{CH_2CH_3}$ = 7 Hz.

Anal. Calcd. for $C_8H_{10}N_4S$: C, 49.46; H, 5.17; N, 28.84. Found: C, 49.57; H, 5.42; N, 28.57.

6-Cyanomethyl-2,4-dimethoxy-5-nitropyrimidine (**16r**).

2,6-Dimethoxy-5-nitropyrimidine-4-acetaldoxime (**11r**) (80 mg, 0.3 mmole) was stirred in acetic acid at room temperature for 5 minutes. After the addition of water to the mixture, neutralization with sodium hydrogen carbonate, extraction with ether, drying of the extract with anhydrous magnesium sulphate and evaporation of the ether provided 105 mg of an oil which was purified for spectral analyses by column chromatography (silica gel, ether) to give 2-(2,6-dimethoxy-5-nitropyrimidin-4-yl)-*O*-acetylacetaldoxime (**15r**), yield 33%; ^{1}H nmr (deuteriochloroform): δ 2.16, 2.20 (s, s, 3H, $COCH_3$, (*Z*), (*E*)), 3.91 and 4.00 (d, d, 2H, CH_2, (*Z*), (*E*)), 4.04, 4.10 (s, s, 3H, OMe), 7.49, 7.94 (t, t, $CHCH_2$, (*Z*), (*E*)), $J_{CH=CH}$ = 5.9 Hz and 7.7 Hz, ratio = 1:3.

Crude **15r** was heated under reflux in acetic acid for 1 hour, the reaction mixture was cooled, diluted with water, neutralized with sodium carbonate and extracted with ether (three times). The organic layer was dried over magnesium sulphate and evaporated to give **16r**, yield 63%, mp 86-88° (from tetrachloromethane), lit [58] 75-77°; ^{1}H nmr (deuteriochloroform): δ 4.02 (s, 2H, CH_2), 4.10 (s, 3H, OMe).

Anal. Calcd. for $C_8H_8N_4O_4$: C, 42.86; H, 3.60; N, 24.99. Found: C, 42.91; H, 3.59; N, 25.07.

4-Cyanomethyl-6-methyl-2-methoxypyrimidine (**16ac**).

2-Methoxy-6-methylpyrimidine-4-acetaldoxime (**11ac**) (905 mg, 5 mmoles) was stirred in acetic anhydride (10 ml) at room temperature for 30 minutes. After isolation as described for **15r**, 1.3 g of a yellow oil was obtained containing mainly *O*-acetyl-2-(2-methoxy-6-methylpyrimidin-4-yl)acetaldoxime (**15ac**). For spectral analyses the compound was purified by column chromatography [silica gel, ether-petroleum ether 3:1, (v/v)]; ^{1}H nmr (deuteriochloroform): δ 2.04 (s, 3H, COMe), 2.45 (s, 3H, 6'-Me), 3.94 (s, 3H, OMe), 3.8-4.0 (s, 2H, CH_2), 6.65 (s, 5'-H), 7.44 and 7.90 (t, t, $CHCH_2$, (*Z*), (*E*)).

Crude **15ac** was heated under reflux in acetic acid (30 ml) for 3 hours. The solvent was then evaporated and water was added to the residue. After neutralization by sodium hydrogencarbonate the product was extracted with ether (three times), the organic fractions were combined, dried with magnesium sulphate and evaporated to give an oil which was further purified by column chromatography (silica gel, ether as solvent) to afford the product **16ac** in yield 51%, mp 76-77° (from cyclohexane); ^{1}H nmr (deuteriochloroform): δ 2.44 (s, 3H, 6'-Me), 3.73 (s, 2H, CH_2), 3.94 (s, 3H, OMe), 6.85 (s, 5'-H).

Anal. Calcd. for $C_8H_9N_3O$: C, 58.89; H, 5.56; N, 25.75. Found: C, 58.94; H, 5.56; N, 25.76.

3-Dimethylamino-2-(2-pyrazinyl)acrylonitrile (**17k**).

Mixture of pyrimidine-4-acetaldoxime (**11k**) (1.37 g, 10 mmoles), *N,N*-dimethylformamide dimethyl acetal (3.6 g, 30 mmoles) and toluene (25 ml) was heated under reflux for 5 minutes, then the toluene was evaporated. The residue was purified by column chromatography on silica gel, first eluting with ether to eliminate non-polar impurities, then with ether-methanol 20:1, (v/v)) to give the main compound, yield 23%, mp 137-139° (from toluene); ^{1}H nmr (deuteriochloroform): δ 3.34 (s, 6H, NMe_2), 7.20 (dd, 5'-H), 8.22 (s, 3-H), 8.39 (d, 4'-H), 8.74 (d, 2'-H), $J_{4\text{-}H,5\text{-}H}$ = 4.7 Hz, $J_{2\text{-}H,5\text{-}H}$ = 1.2 Hz.

Anal. Calcd. for $C_9H_{10}N_4$: C, 62.05; H, 5.79; N, 32.16, calcd. for $C_9H_{10}N_4 \cdot 1/2H_2O$: C, 59.00; H, 6.09; N, 30.57. Found: C, 59.25; H, 5.77; N, 30.59.

Using the same procedure, but different reaction times, compounds **17y-17ab** were prepared.

3-Dimethylamino-2-(2-quinoxalinyl)acrylonitrile (**17y**).

This compound was synthesized from quinoxaline-2-acetaldoxime (**11y**) by heating under reflux for 10 minutes, yield 19%, mp 142-143° (from cyclohexane); ^{1}H nmr (deuteriochloroform): δ 3.44 (s, 6H, NMe_2), 7.5-8.2 (m, 4H, 5'-H, 6'-H, 7'-H, 8'-H), 8.32 (s, 3-H), 9.14 (s, 3'-H).

Anal. Calcd. for $C_{13}H_{12}N_4$: C, 69.62; H, 5.39; N, 24.98. Found: C, 69.42; H, 5.66; N, 24.69.

5-(1-Cyano-2-(*N,N*-dimethylamino)ethen-1-yl)-7-methyl-*s*-triazolo[4,3-*a*]pyrimidine (**17aa**).

This compound was obtained from 7-methyl-*s*-triazolo-[4,3-*a*]pyrimidine-5-acetaldoxime (**11aa**) by heating under reflux for 5 minutes, yield 46%, mp 266-267 dec (from ethanol); ^{1}H nmr (DMSO-d_6, 134°): δ 2.46 (s, 3H, 7-Me), 3.24 (s, 6H, NMe_2), 6.60 (s, 6-H), 7.65 (s, C*H*NMe_2), 8.98 (s, 3-H).

Anal. Calcd. for $C_{11}H_{12}N_6$: C, 57.88; H, 5.30; N, 36.82. Found: C, 58.27; H, 5.42; N, 37.16.

7-(1-Cyano-2-(*N,N*-dimethylamino)ethen-1-yl)-5-methyl-*s*-triazolo[1,5-*a*]pyrimidine (**17ab**).

This compound was synthesized from 5-methyl-*s*-triazolo[1,5-*a*]pyrimidine-7-acetaldoxime (**11ab**) by heating under reflux for 10 minutes, yield 71%, mp 235-236° dec (from toluene); ^{1}H nmr (DMSO-d_6, 110°): δ 2.51 (s, 3H, 5-Me), 3.32 (s, 6H, NMe_2), 6.80 (s, 6-H), 8.34 (s, C*H*NMe_2), 9.09 (s, 2-H).

Anal. Calcd. for $C_{11}H_{12}N_6$: C, 57.88; H, 5.30; N, 36.82. Found: C, 57.82; H, 5.38; N, 36.85.

Reaction of 2-(2,5-Dihydro-3-ethylmercapto-6-methyl-1,2,4-triazin-5-ylidene)acetaldoxime with DMFDMA (**11t**).

The reaction was accomplished *via* the above-mentioned procedure by heating under reflux for 1 minute to give two products after isolation.

7-Ethylmercapto-4-methylpyrazolo[1,5-*d*][1,2,4]triazine (**18**).

This compound was obtained by elution with ether, yield 7%, mp 75-76° (from heptane); ^{1}H nmr (deuteriochloroform): δ 1.51 (t, 3H, CH_2*Me*), 2.74 (s, 3H, 4-Me), 3.44 (t, 2H, CH_2*Me*), 6.74 (s, 3-H), 8.07 (s, 2-H), $J_{CH_2CH_3}$ = 7 Hz, $J_{2\text{-}H,3\text{-}H}$ = 2 Hz.

Anal. Calcd. for $C_8H_{10}N_4S$: C, 49.46; H, 5.19; N, 28.84. Found: C, 49.13; H, 5.26; N, 28.76.

3-Dimethylamino-2-(3-ethylmercapto-6-methyl-1,2,4-triazin-5-yl)acrylonitrile (**17t**).

This compound was obtained by elution with ether-methanol 20:1 (v/v), yield 57%, mp 124° (from diisopropyl ether); ^{1}H nmr (deuteriochloroform): δ 1.43 (t, 3H, CH_2*Me*), 2.85 (s, 3H, 6'-Me), 3.23 (q, 2H, C*H*$_2$Me), 3.4 (s, broad, 6H, NMe_2), 8.16 (s, 3-H), $J_{CH_2CH_3}$ = 7 Hz.

Anal. Calcd. for $C_{11}H_{15}N_5S$: C, 52.99; H, 6.06; N, 28.09. Found: C, 53.38; H, 6.06; N, 28.37.

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