Tetrahedron, Vol. 37, pp. 1787 to 1793, 1981
Printed in Great Britain

0040-4020/81/091787-07$02.00/0
Pergamon Press Ltd.

SYNTHESES AND TRANSFORMATIONS OF SOME HETEROCYCLIC HYDROXYLAMINES

ALENKA TOMAŽIČ, MIHA TIŠLER and BRANKO STANOVNIK
Department of Chemistry, E. Kardelj University, 61000 Ljubljana, Yugoslavia

(*Received in UK* 21 *October* 1980)

Abstract—Syntheses of some hydroxylaminoazines, their quaternized derivatives or N-oxides and N-amino compounds are described. Several transformations of these compounds and cyclization reactions are presented.

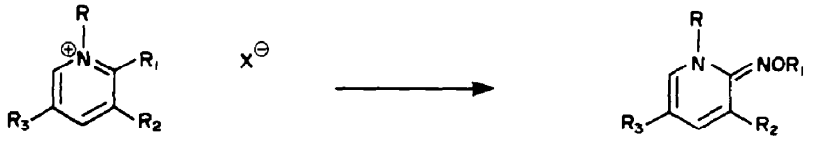
The mutagenic activity of hydroxylamine and some substituted hydroxylamines is well documented.[1] The chemistry of hydroxylamines, substituted with heterocyclic residues has been less well investigated and recently we have described syntheses of some azinylhydroxylamines.[2] We now report on some new results concerning the syntheses and transformations of particular model compounds.

An introduction of a hydroxylamino function into an azine system by direct nucleophilic displacement proved to be limited to those azines which possess electron attracting groups.[2] In view of these findings the corresponding halo substituted quaternized pyridines, pyridine N-oxides and N-amino compounds were investigated. Quaternized pyridines (**1**) reacted with free hydroxylamine or O-benzylhydroxylamine to give the hydroxyimino derivatives or their O-benzyl analogs (**2**). No ring opening products could be detected as has been observed with amines[3] or when strong electron attracting groups are bound to the ring N atom.[4] However, compound **1d** reacted in a different way yielding besides the anticipated product **2g** another compound in almost the same amount which by NMR examination and colour test[5] was not an oxime nor a N-oxide. The structure of this product was **3a** and is most probably formed by Et group transfer from the quaternized compound. A tlc examination of the progress of the reaction revealed that both compounds are formed simultaneously.

The following order of reactivity for nucleophilic displacement has been established for pyridine N-oxides: 4, 2 ≫ 3 (in some cases 2 > 4 > 3).[6] Substituted pyridine N-oxides **4a**, **4c**, **4e** and **4g** reacted with hydroxylamine or O-benzylhydroxylamine to give the anticipated compounds **4b**, **4d**, **4f** and **4h**. In the case of **4c** the F atom at position 3 was displaced in preference to the nitro group at position 4 in spite of the greater reactivity of a *para* bound leaving group towards nucleophiles in pyridine N-oxides.[6]

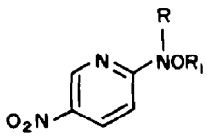
N-Amino heterocycles have become readily available by the introduction of the versatile N-amination reagent, O-mesitylenesulfonylhydroxylamine.[7] By this method we have prepared several N-amino pyridinium (**5a–5d**) and pyridazinium mesitylenesulfonates (**6**). When **5a** reacted with hydroxylamine or O-benzylhydroxylamine the neutral 2-hydroxyimino (**7a**) or 2-O-benzyloxyimino (**7b**) derivatives were obtained. On the other hand, **5b** was transformed with hydroxylamine into the corresponding mesitylenesulfonate salt (**5e**), whereas the reaction with O-benzylhydroxylamine failed. An alternative dipolar structure (**7d**) is conceivable for compounds **7a** and **7b**, but correlation of NMR spectra of these two compounds with spectra of 2-substituted pyridines and 2-substituted N-alkyl or N-benzylpyridinium salts favours the proposed structure. Also in the case of **5e** the tautomeric counterpart of the carboxamido function could be an iminohydroxamate group, but this seems to be unlikely in accordance with previous studies on amidoximes.[8,9]

Different results were observed when reacting halopyrimidines with hydroxylamines. Although few halopyrimidines are known to react in a normal manner,[10–12] we found that 2-chloropyrimidine was transformed with hydroxylamine into 2-aminopyrimidine N-oxide (**8**). The reaction involves ring opening and recyclization, a

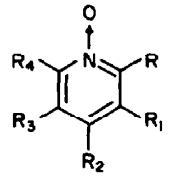


	R	R_1	R_2	R_3	X
1a	Et	Br	H	H	Br
1b	$PhCH_2$	Br	H	H	Br
1c	Et	Cl	NO_2	H	BF_4
1d	Et	Cl	H	NO_2	BF_4

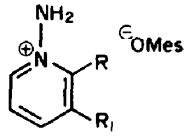
	R	R_1	R_2	R_3
2a	Et	H	H	H
2b	$PhCH_2$	H	H	H
2c	Et	$PhCH_2$	H	H
2d	$PhCH_2$	$PhCH_2$	H	H
2e	Et	$PhCH_2$	NO_2	H
2f	Et	$PhCH_2$	H	NO_2
2g	Et	H	H	NO_2



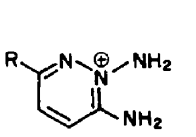
	R	R_1
3a	H	Et
3b	H	Me
3c	Me	Me
3d	Me	H



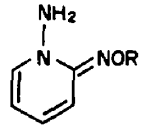
	R	R_1	R_2	R_3	R_4
4a	Cl	H	H	H	Cl
4b	NHOH	H	H	H	Cl
4c	H	F	NO_2	H	H
4d	H	$NHOCH_2Ph$	NO_2	H	H
4e	Cl	NO_2	H	H	H
4f	$PhCH_2ONH$	NO_2	H	H	H
4g	Cl	H	H	NO_2	H
4h	$PhCH_2ONH$	H	H	NO_2	H



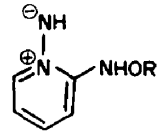
	R	R_1
5a	Cl	H
5b	CN	H
5c	PhCO	H
5d	H	Br
5e	$-C(=NOH)-NH_2$	H



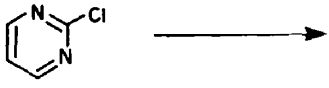
	R
6a	H
6b	Cl



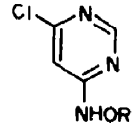
	R
7a	H
7b	$PhCH_2$
7c	CF_3CO



7d



8



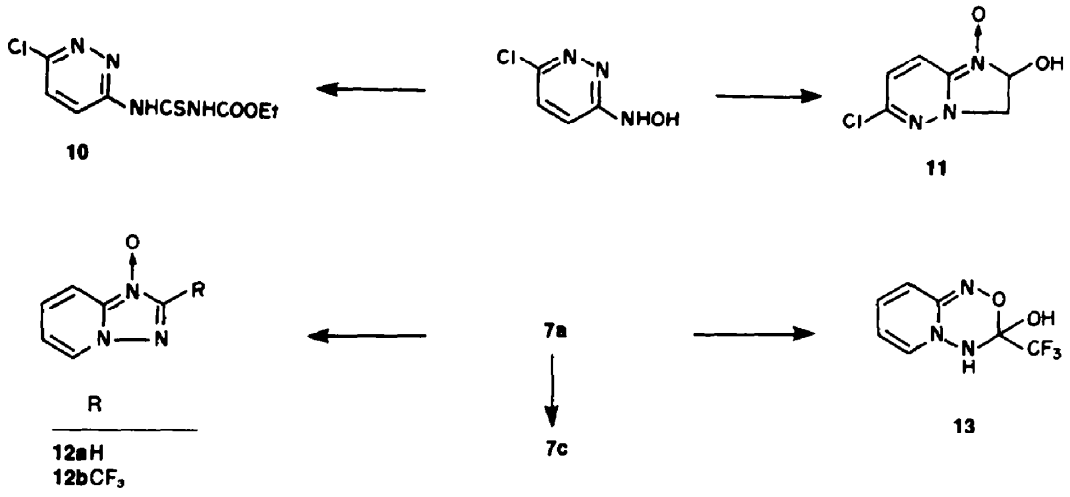
	R
9a	H
9b	$PhCH_2$

phenomenon which was observed recently in many reactions of pyrimidines with nucleophiles.[13] 4,6-Dichloropyrimidine, however, reacted in a normal manner to give a monosubstituted derivative (**9**).

The reactivity of hydroxylamines has been described in detail.[14] Our interest was concentrated on reactions which would lead to new heterocycles. When 6-chloro-3-hydroxylaminopyridazine reacted with carbethoxy isothiocyanate, a compound was formed for which, supported by analytical and spectroscopic data, structure **10** could be assigned. Since as by-product sulfur was formed, a redox process must be involved during which the hydroxylamino function was transformed in an amino function. Similar sulfur formation was observed when benzamidoxime reacted with phenyl isothiocyanate.[15] 6-Chloro-3-hydroxylaminopyridazine reacted with bromoacetaldehyde to give an imidazo(1,2-b)pyridazine 1-oxide derivative (**11**). This compound and the later described s-triazolo(1,5-a)pyridine 1-oxides represent additional examples to the few recently prepared azoloazine 1-oxides.[16,17]

Alkylations of hydroxylamines take place almost exclusively to give N-substituted products.[18] Although 2-hydroxylamino-5-nitropyridine did not react with diethyl sulfate in alkaline solution, it could be methylated with diazomethane to give a monomethylated (**3b**) and dimethylated product (**3c**). The structure of the O-monomethylated product was self evident, since the isomeric N-Me derivative (**3d**) was obtained from the reaction between 2-chloro-5-nitropyridine and N-methylhydroxylamine. For the last reaction one could consider also the possibility of O-alkylation, but it was shown[19] that such compounds are rather unstable.

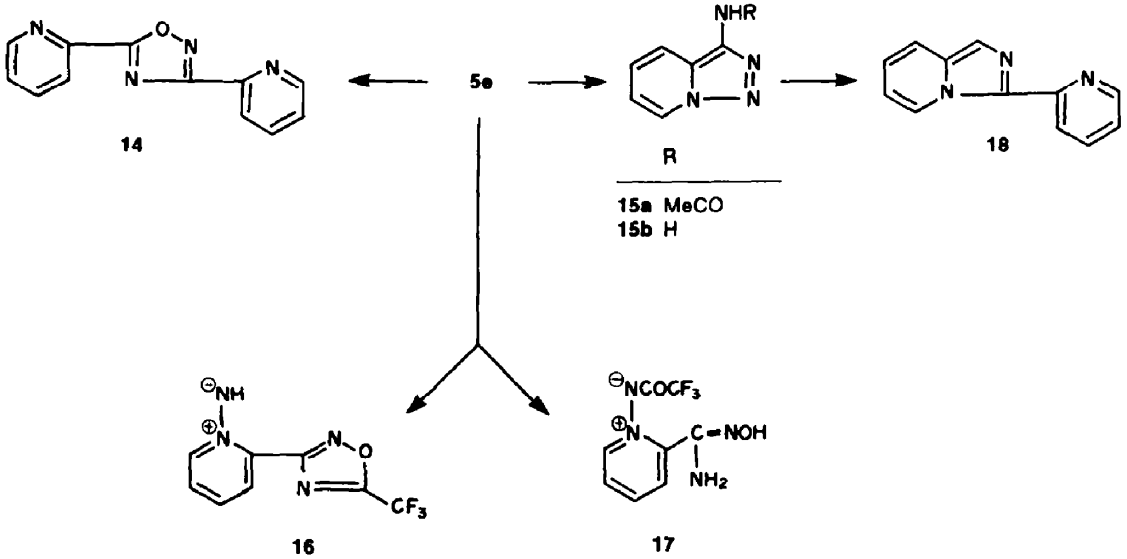
Since compounds of the type **7** appeared to be useful for the preparation of bicyclic systems, some experiments were focussed in this direction. Compound **7a** reacted with formic acid to give s-triazolo(1,5-a)pyridine 1-oxide (**12a**) and the deoxygenated parent system as by-product. At still higher temperature the latter was the sole product. In a better synthetic procedure the 1-oxide could be prepared in the presence of N,N-dimethylformamide dimethyl acetal, a one carbon unit precursor. This reagent was used with success previously for the synthesis of the parent system.[20] With trifluoroacetic anhydride the trifluoromethyl analog (**12b**) could be prepared, whereas under different reaction or isolation conditions two other compounds were isolated and identified. One was the O-acylated derivative (**7c**) and the other the bicyclic compound **13**. The NMR spectra of both components are very similar, but the IR spectra are



very different (no CO absorption band for **13**). The structure of **13** represents a covalent hydrate and its IR spectrum in the 2800–3700 cm^{-1} region is very similar to a related covalent hydrate of the hydroxythiazoloazinium type.[21] Probably **13** which was formed at room temperature, is an intermediate in the formation of both **7c** and **12b**. Compound **7a** reacted also with phenyl isocyanate to afford a mixture of N,N'-diphenylurea and N-phenyl-N'-(pyridyl-2-)urea. Although several mechanistic interpretations could account for this unusual transformation, a firm proof is lacking.

Compound **5e** showed a different reactivity when compared with other compounds of type **5**. When heated *in vacuo* it was transformed into a disubstituted 1,2,4-oxadiazole (**14**). A possible explanation is thermal decomposition of **5e** into the corresponding nitrile oxide which undergoes in the first step a 1,3-dipolar cycloaddition with the starting amidoxime to give **14**. It should be mentioned that a similar oxadiazole derivative was formed thermally from benzamidoxime.[22]

Compound **5e**, when treated with trifluoroacetic anhydride was transformed into almost equal amounts of the acylated derivative (**17**) and oxadiazolyl compound (**16**). Usually acylation of an amidoxime function proceeds at the O atom,[23] but with the investigated multidentate compound besides O-acylation and ring closure to **16** also the N-amino function was acylated to give **17**. The proposed structure for **17** seems to be more likely than that of the isomeric O-trifluoroacetyl derivative because of the IR spectrum and MS fragmentation pattern. Compound **16** and related N-amino compounds reveal strong M-15 fragmentation which is absent for **17** and should be observable in the case of the O-acyl derivative. On the other hand, acetylation gave different results. Compound **5e** afforded upon acetylation a product, for which analytical and spectroscopic data suggested the structure of a substituted v-triazolo(1,5-a)pyridine (**15a**). The formation of this bicycle is an alternative synthetic route to that described recently[24] in which oximes of pyridyl aldehydes and ketones were treated with O-mesitylenesulfonylhydroxylamine and subsequently cyclized with polyphosphoric acid. The bicyclic compound **15a** or its desacetylated derivative **15b** was easily transformed under the influence of $NaHCO_3$ or HCl into another bicyclic system (**18**). The structure of the latter was confirmed by X-ray analysis[25] and by independent synthesis from pyridyl-2-aldehyde in the presence of ammonium sulfate. On hand of all above observations



one may conclude that the hydroxylamino function in 6-membered heterocycles can be successfully involved in the preparation of various bicyclic compounds.

EXPERIMENTAL

M.ps were determined on a Kofler hot plate m.p. apparatus. The NMR spectral measurements were performed on a JEOL JNM C-60 HL spectrometer with TMS as internal standard. Mass spectra were recorded on a Hitachi-Perkin-Elmer RMU-6L spectrometer.

1-Ethyl-2-hydroxyimino-1,2-dihydropyridine (**2a**). A soln of **1a** (1.0 g) in EtOH (10 ml) was treated with an alcoholic soln of free hydroxylamine (0.2 mole in 330 ml EtOH)[26] and the mixture was heated under reflux for 15 min. Upon evaporation to dryness, the residue was dissolved in H_2O (5 ml), solid Na_2CO_3 was added until pH 8–8.5 and the mixture was extracted with $CHCl_3$ (5 times with 5 ml). The combined extracts were dried over Na_2SO_4 and after evaporation of the solvent the product was crystallized from n-hexane (0.3 g, 52%), m.p. 119–121°. ^1H NMR $\delta(CDCl_3)$ 6.85 (m, H_3, H_4 and H_6), 5.6 (dxdxd, H_5), 3.65 (q, CH_2), 1.30 (t, Me), $J_{5,6} = 5.0$, $J_{4,5} = 6.0$, $J_{3,5} = J_{4,6} = 2.5$, $J_{Et} = 6.75$ Hz. MS: 138 (M^+, 42%). (Found: C, 60.96; H, 7.43; N, 20.18. Calc. for $C_7H_{10}N_2O$: C, 60.85; H, 7.30; N, 20.28%).

In a similar manner *1-benzyl-2-hydroxyimino-1,2-dihydropyridine* (**2b**) was prepared in 62% yield from **1b** at r.t. after 20 min. The crude product was crystallized from a mixture of EtOH and n-hexane (6:1), m.p. 148–150°. ^1H NMR $\delta(CDCl_3)$ 6.9 (m, Ph), 4.48 (s, CH_2), 6.30 (m, H_3 and H_4), 5.20 (dxdxd, H_5), $J_{5,6} = 5.5$, $J_{4,5} = J_{3,4} = 8.0$, $J_{4,6} = 3.0$ Hz. MS: 200 (M^+, 20%). (Found: C, 71.75; H, 6.27; N, 13.79. Calc. for $C_{12}H_{12}N_2O$: C, 71.98; H, 6.04; N, 13.99%).

1 - Ethyl - 2 - (O - benzylhydroxyimino) - 1,2 - dihydropyridine(**2c**). A soln of **1a** (0.38 g) in CH_2Cl_2 (25 ml) and O-benzylhydroxylamine[27] (0.35 g) was stirred at r.t. for 18 hr and then evaporated to dryness. The residue was dissolved in H_2O (5 ml) and extracted with $CHCl_3$ (5 times with 10 ml). The combined extracts were evaporated to 20 ml, HCl gas was introduced and the separated O-benzylhydroxylamine hydrochloride was extracted from the $CHCl_3$ soln with H_2O. The $CHCl_3$ extract was dried over Na_2SO_4, the solvent evaporated and the residue sublimed at 140–150°/10 mm (0.18 g, 55%). ^1H NMR δ(DMSO-d_6) 7.22 (m, Ph), 7.05 (d×d×d, H_6), 6.75 (d×d×d, H_4), 6.50 (d×d, H_3), 5.50 (d×d×d, H_5), 4.75 (s, CH_2), 3.58 (q, CH_2), 1.12 (t, CH_3), $J_{5,6} = 6.7$, $J_{4,5} = J_{3,4} = 6.0$, $J_{3,5} = 2.1$, $J_{4,6} = 1.0$, $J_{Et} = 6.75$ Hz. (Found: C, 73.42; H, 6.97; N, 12.01. Calc. for $C_{14}H_{16}N_2O$: C, 73.65; H, 7.06; N, 12.27%).

1 - Benzyl - 2 - (O - benzylhydroxyimino) - 1,2 - dihydropyridine (**2d**). This was prepared as described for the above analog from **1b** in 42% yield (sublimed at 180°/10 mm), ^1H NMR δ(DMSO-d_6) 7.25 m, 2 Ph), 6.70 (m, H_3 and H_4), 5.60 (d×d×d, H_5), 4.80 (s, 2 CH_2), $J_{5,6} = 5.0$, $J_{3,4} = J_{4,5} = 7.0$, $J_{3,5} = J_{4,6} = 2.0$ Hz. MS: 290 (M^+, 12%). (Found: C, 78.16; H, 6.33; N, 9.98. Calc. for $C_{19}H_{18}N_2O$: C, 78.59; H, 6.25; N, 9.98%).

1 - Ethyl - 2 - (O - benzylhydroxyimino) - 3 - nitro - 1,2 - dihydropyridine (**2e**). This was prepared from **1c** in 56% yield (sublimed at 160–170°/10 mm), ^1H NMR δ(DMSO-d_6) 7.38 (m, Ph), 7.70 (d, H_4 and H_6), 5.75 (d×d, H_5), 4.93 (s, CH_2), 4.93 (s, CH_2), 3.90 (q, CH_2), 1.25 (t, Me), $J_{4,5} = J_{5,6} = 7.0$, $J_{Et} = 6.75$ Hz. (Found: C, 61.25; H, 5.70; N, 15.51. Calc. for $C_{14}H_{15}N_3O_3$: C, 61.53; H, 5.53; N, 15.38%). MS: 273 (M^+, 52%).

1 - Ethyl - 2 - (O - benzylhydroxyimino) - 5 - nitro - 1,2 - dihydropyridine (**2f**) was obtained from **1d** in 90% yield (sublimed at 180–190°/10 mm). ^1H NMR δ ($CDCl_3$) 8.30 (d, H_6), 7.45 (m, H_4 and Ph), 6.80 (d, H_3), 5.05 (s, CH_2), 3.85 (q, CH_2), 1.35 (t, Me), $J_{4,6} = 2.5$, $J_{3,4} = 11.0$, $J_{Et} = 6.75$ Hz. MS: 273 (M^+, 26%). (Found: C, 61.34; H, 5.60; N, 15.32, Calc. for $C_{14}H_{15}N_3O_3$: C, 61.53; H, 5.53: N, 15.38%).

1 - Ethyl - 2 - hydroxyimino - 5 - nitro - 1,2 - dihydropyridine (**2g**) *and* *2 - (O - ethylhydroxylamino) - 5 - nitropyridine* (**3a**). A mixture of **1d** (0.79 g) in EtOH (15 ml) and ethanolic NH_2OH (23 ml)[26] was heated at 60° for 15 min. Upon evaporation to dryness the residue was dissolved in H_2O (10 ml) and extracted with $CHCl_3$ (5 times of 20 ml). The extracts were dried over Na_2SO_4, filtered, the solvent was evaporated to dryness and the residue dissolved in 1,2-dimethoxyethane (2 ml). Tlc separation (PSC-Fertigplatten, Kieselgel 60 F_{254}, 2 mm, Merck, mobile phase $CHCl_3$:EtOH, 10:1) afforded two products. Compound with R_f 0.80 was eluted with EtOH and identified as **2g**, m.p. 170–171° (from water) (yield 0.22 g, 41%). ^1H NMR $\delta(CDCl_3)$ 8.20 (d, H_6), 7.38 (d×d, H_4), 6.73 (d, H_3), 3.75 (q, CH_2), 1.35 (t, Me), $J_{3,4} = 10.5$, $J_{4,6} = 2.4$, $J_{Et} = 6.75$ Hz. MS: 183 (M^+, 72%). (Found: C, 45.76; H, 5.12; N, 23.05. Calc. for $C_7H_9N_3O_3$: C, 45.90; H, 4.95; N, 22.94%).

Compound **3a** with $R_f = 0.67$ was eluted with EtOH, the solvent evaporated to dryness and the residue crystallized from $CHCl_3$ and CCl_4 (4:1) (Yield 0.2 g, 37%), m.p. 155–158°. ^1H NMR $\delta(CDCl_3)$ 10.05 (d, H_6), 8.0 (d×d, H_4), 7.58 (broad s, NH), 6.58 (d, H_3), 3.43 (q, CH_2), 1.38 (t, Me), $J_{3,4} = 9.45$, $J_{4,6} = 2.55$, $J_{Et} = 6.75$ Hz. MS: 183 (M^+, 87%). (Found: C, 45.88; H, 5.13; N, 23.09. Calc. for $C_7H_9N_3O_3$: C, 45.90; H, 4.95; H, 22.94%).

2 - Hydroxylamino - 6 - chloropyridine 1 - oxide (**4b**). A soln of **4a** (0.7 g) in EtOH (10 ml) was treated with ethanolic NH_2OH (35 ml) and the mixture was left at r.t. for 6 days. Upon evaporation to dryness the residue was dissolved in H_2O (8 ml) and the soln extracted with $CHCl_3$ (5 times with 5 ml). The dried extracts (Na_2SO_4) were evaporated to dryness and the residue was crystallized from EtOH and n-hexane (3:1) (yield 0.7 g, 24%), m.p. 130–132°. ^1H NMR δ(DMSO-d_6) 6.75 (m, H_3, H_4 and H_5), MS: 160 (M^+, 14%). (Found: C, 37.16; H, 3.23; N, 17.32. Calc. for $C_5H_5N_2O_2$: C, 37.41; H, 3.14; N, 17.45%).

3-(O-Benzylhydroxylamino)-4-nitropyridine 1-oxide (**4d**). Compound **4c** (0.12 g) was dissolved in CH_2Cl_2 (10 ml) and O-benzylhydroxylamine (0.18 g) was added. The mixture was stirred at r.t. for 23 hr, the solvent was evaporated and the residue treated with diethyl ether (3 ml). The residue was filtered off, dissolved in H_2O (5 ml) and the separated product filtered after 30 min. The obtained product was crystallized from 1,2-dimethoxyethane and diethyl ether (2:1) (yield 0.05 g, 25%), m.p. 144–145°. ^1H NMR δ(DMSO-d_6) 7.45 (m, Ph), 8.15 (d, H_2), 8.08 (d, H_6), 7.70 (d×d, H_5), 5.03 (s, CH_2), $J_{5,6} = 7.0$, $J_{2,6} = 2.5$, $J_{2,5} = 2.0$ Hz. MS: 261 (M^+, 26%). (Found: C, 55.11; H, 4.09; 16.26. Calc. for $C_{12}H_{11}N_3O_4$: C, 55.17; H, 4.24; N, 16.09%).

In a similar manner, *2-(O-Benzylhydroxylamino)-3-nitropyridine 1-oxide* (**4f**) was prepared from **4e** in 66% yield, m.p. 120–123° (from CCl_4). ^1H NMR $\delta(CDCl_3)$ 8.40 (d×d, H_6), 7.70 (d×d, H_4), 7.50 (m, Ph), $J_{5,6} = 7.0$, $J_{4,5} = 9.0$, $J_{4,6} = 2.0$ Hz. MS: 261 (M^+, 2%). (Found: C, 54.82; H, 4.38; N, 15.92. Calc. for $C_{12}H_{11}N_3O_4$: C, 55.17; H, 4.24; N, 16.09%).

2 - (O - Benzylhydroxylamino) - 5 - nitropyridine 1 - oxide (**4h**) was prepared from **4g** in 8% yield, m.p. 155° (from CCl_4). ^1H NMR δ(DMSO-d_6) 8.57 (d, H_6), 7.60 (d×d, H_4), 7.12 (m, Ph), 6.67 (d, H_3), 4.80 (s, CH_2), $J_{4,6} = 2.5$, $J_{3,4} = 9.5$ Hz. MS: 261 (M^+, 11%). (Found: C, 55.06; H, 4.45; N, 16.28. Calc. for $C_{12}H_{11}N_3O_4$: C, 55.17; H, 4.24; N, 16.09%).

General method for the preparation of 1-aminopyridinium mesitylenesulfonates (**5**). A soln of the corresponding pyridine in CH_2Cl_2 was cooled to −5° and under stirring a soln of O-mesitylenesulfonyl hydroxylamine in CH_2Cl_2 was added. After the mixture warmed up to r.t., stirring was continued for 15 min and the mixture was evaporated to dryness at r.t. The residual oil crystallized after addition of diethyl ether and cooling in a dry ice and acetone mixture. The products were crystallized from a mixture of MeOH and EtOAc (1:20). For analytical purposes the compounds were again crystallized as indicated.

In this manner *1-amino-2-chloropyridinium mesitylenesulfonate* (**5a**) was prepared in 59% yield, m.p. 117° (from MeOH and EtOAc, 1:20) (Lit.[28] gives m.p. 116–117°). ^1H NMR $\delta(D_2O)$ 8.09 (d×d×d, H_6), 7.58 (d×d×d, H_4), 7.42 (d×d×d, H_3), 7.20 (d×d×d, H_5), 6.38 (s, H_3 and H_5), 2.34 (s, 2'-Me and 6'-Me), 2.03 (s, 4'-Me), $J_{5,6} = 6.0$, $J_{4,6} = J_{3,6} = 0.75$, $J_{3,4} = J_{4,5}$, $J_{3,5} = 2.5$ Hz. (Found: C, 51.18; H, 4.96; N, 8.46. Calc. for $C_{14}H_{17}ClN_2O_3S$: C, 51.14; H, 5.21; N, 8.52%).

1-Amino-2-cyanopyridinium mesitylenesulfonate (**5b**) was prepared in 47% yield, m.p. 235–239° (from EtOH and thereafter from n-PrOH and diethyl ether, 20:1) (Lit.[28] gives m.p. 236–237°). ^1H NMR δ(DMSO-d_6) 8.48 (d×d×d, H_6), 8.10 (m, H_3 and H_4), 7.75 (d×d×d, H_5), 6.23 (s, H_3 and H_5), 2.30 (s, 2'- and 6'-Me), 2.00 (s, 4'-Me), $J_{4,5} = J_{5,6} = 6.0$, $J_{4,6} = 1.5$, $J_{3,5} = 2.5$ Hz.

(Found: C, 56.64; H, 5.26; N, 13.21. Calc. for $C_{15}H_{17}N_3S$: C, 56.41; H, 5.37; N, 13.16%).

1-*Amino-2-benzoylpyridinium mesitylenesulfonate* (**5c**) was prepared in 75% yield, m.p. 181–185° (from MeOH and EtOAc, 1:20, and then from n-PrOH and finally from EtOH) (lit.[28] gives m.p. 178–179°). ^{1}H NMR δ(CD_3OD) 8.30 (m, H_6), 7.82 (d × d × d, H_4), 7.22 (m, Ph and H_3 and H_5), 6.30 (s, H_3 and H_5), 2.38 (s, 2'- and 6'-Me), 2.03 (s, 4'-Me), $J_{5,6}$ = 5.0, $J_{3,4}$ = $J_{4,5}$ = 7.5, $J_{3,5}$ = 1.5 Hz. (Found: C, 63.01; H, 5.70; N, 7.07. Calc. for $C_{21}H_{22}N_2O_4S$: C, 63.30; H, 5.56; N, 7.03%).

1-*Amino-3-bromopyridinium mesitylenesulfonate* (**5d**) was prepared in 68% yield, m.p. 160–162° (from EtOH and diethyl ether, 1:1). (Found: C, 45.11; H, 4.76; N, 7.43. Calc. for $C_{14}H_{17}BrN_2O_3S$: C, 45.05; H, 4.59; N, 7.15%).

2,3-*Diaminopyridazinium mesitylenesulfonate* (**6a**). A soln of 3-aminopyridazine in MeOH (1.6 g in 20 ml) was cooled to 0° and a soln of O-mesitylenesulfonyl hydroxylamine in MeOH (3.62 g in 20 ml) was added dropwise. The mixture was stirred at room temp for 15 min and then evaporated to dryness. The residue was treated with diethyl ether (8 ml) and after cooling in a mixture of dry ice and acetone crystals separated from the soln. The product was crystallized from MeOH and diethyl ether, 1:10 (3.1 g, 60%). M.p. 138–140° (Lit.[29] gives m.p. 139–140°). ^{1}H NMR δ(CD_3OD) 7.55 (d × d, H_6), 7.05 (m, H_4 and H_5), 6.25 (s, H_3 and H_5), 2.24 (s, 2'- and 6'-Me), 2.03 (s, 4'-Me), $J_{5,6}$ = 6.0, $J_{4,6}$ = 3.0 Hz. (Found: C, 50.69; H, 6.03. Calc. for $C_{13}H_{18}N_4O_3S$: C, 50.31; H, 5.85%).

2,3 - *Diamino* - 6 - *chloropyridiazinium mesitylenesulfonate* (**6b**) was prepared similarly in 63% yield, m.p. 249–253° (from MeOH and diethyl ether, 1:5) (Lit.[29] gives m.p. 244–245°). ^{1}H NMR δ(CD_3OD) 7.10 and 6.95 (d, H_4 and H_5), 6.30 (s, H_3 and H_5) 2.38 (s, 2'- and 6'-Me), 2.03 (s, 4'-Me), $J_{4,5}$ = 9.0 Hz. (Found: C, 45.39; H, 5.01; N, 16.16. Calc. for $C_{13}H_{17}ClN_4O_3S$: C, 45.28; 4.97; N, 16.25%).

1-*Amino-2-hydroxyimino*-1,2-*dihydropyridine* (**7a**). A soln of **5a** (1.5 g) in EtOH (8 ml) was treated with an ethanolic soln of hydroxylamine (38 ml) and the mixture was left at r.t. for 71 hr. Upon evaporation to dryness, the residue was dissolved in water (20 ml), Na_2CO_3 aq was added until pH = 8 and the soln evaporated to about 30 ml. Upon extraction with $CHCl_3$ (5 times with 50 ml) the dried extracts (over Na_2SO_4) were evaporated and the residue crystallized from $CHCl_3$ and CCl_4, 1:4. (0.36 g, 61%), m.p. 118–121°. ^{1}H NMR δ($CDCl_3$) 6.75 (d × d × d, H_6), 6.35 (d × d × d, H_4), 6.28 (d × d, H_3), 5.10 (d × d × d, H_5) $J_{5,6}$ = 6.0, $J_{4,5}$ = 9.0, $J_{3,6}$ = 1.0, $J_{3,5}$ = 2.0, $J_{4,6}$ = 1.5 Hz. MS: 125 (M^+, 38%). (Found: C, 47.85; H, 5.60; N, 33.53. Calc. for $C_5H_7N_3O$: C, 47.99; H, 5.64; N, 33.58%).

1 - *Amino* - 2 - (O - *benzylhydroxyimino*) - 1,2 - *dihydropyridine* (**7b**). This was prepared from **5a** (0.2 g) and O-benzylhydroxylamine (0.15 g) in CH_2Cl_2 (25 ml) at r.t. after 18 hr. After the workup as described above the product was sublimed at 160–170°/14 mm (yield 0.04 g, 30%). ^{1}H NMR δ(DMSO-d_6) 6.95 (m, H_6 and Ph), 6.55 (d × d × d, H_4), 6.25 (d × d, H_3), 5.25 (d × d × d, H_5), 4.65 (s, CH_2), $J_{3,4}$ = $J_{4,5}$ = 8.0, $J_{5,6}$ = 6.0, $J_{3,5}$ = $J_{4,6}$ = 2.0 Hz. MS: 215 (M^+, 28%). (Found: C, 67.02; H, 6.19; N, 19.64. Calc. for $C_{12}H_{13}N_3O$: C, 66.95; H, 6.09; N, 19.52%).

1 - *Amino* - 2 - *carboxamidoximopyridinium mesitylenesulfonate* (**5e**). Compound **5b** (0.2 g) in EtOH (3 ml) was treated with ethanolic NH_2OH (5.2 ml)[26] and the mixture was stirred at r.t. for 2.5 hr. Upon evaporation to dryness, the residue was dissolved in diethyl ether (10 ml), the product filtered and crystallized from n-PrOH and diethyl ether, 1:1 (yield 0.07 g, 31%), m.p. 185–188°. ^{1}H NMR δ(CD_3OD) 8.10 (d × d × d, H_6), 7.55 (m, H_3 and H_4), 7.32 (d × d × d, H_5), 6.30 (s, H_3 and H_5), 2.38 (s, 2'- and 6'-Me). 2.05 (s, 4'-Me), $J_{5,6}$ = 6.0, $J_{3,6}$ = $J_{4,6}$ = 0.75, $J_{3,5}$ = 3.0 Hz. (Found: C, 51.52; H, 5.50; N, 16.10. Calc. for $C_{15}H_{20}N_4O_4S$: C, 51.12; H, 5.72; N, 15.90%).

2-*Aminopyrimidine* 1-*oxide* (**8**). A soln of 2-chloropyrimidine (0.15 g) in EtOH (5 ml) was treated with an ethanolic soln of free hydroxylamine (12 ml)[26] and the mixture was heated under reflux for 3.5 hr. Upon evaporation to dryness, the residue was dissolved in H_2O (3 ml), a soln of Na_2CO_3 was added until pH = 8 and the mixture was again evaporated to dryness. The oily residue solidified at −10° and the product was crystallized from EtOH an diethyl ether, 2:1 (yield 0.42 g, 29%), m.p. 193°. (Lit.[30] gives m.p. 185–187°). ^{1}H NMR δ(DMSO-d_6) 7.93 (d × d, H_6), 7.43 (d × d, H_4), 6.34 (d × d, H_5), $J_{5,6}$ = 6.5, $J_{4,5}$ = 4.5, $J_{4,6}$ = 1.5 Hz. MS: 111 (M^+, 100%). (Found: C, 43.50; H, 4.61; N, 37.78. Calc. for $C_4H_5N_3O$: C, 43.25; H, 4.54; N, 37.82%).

4-*Hydroxylamino-6-chloropyrimidine* (**9a**). a mixture of 4,6-dichloropyrimidine (0.2 g) in EtOH (6 ml) and ethanolic NH_2OH (10 ml)[26] was left in a closed flask at r.t. for 48 hr. Upon evaporation to dryness, the residue was dissolved in H_2O (10 ml), Na_2CO_3 aq was added until pH = 8 and the mixture was evaporated to dryness. The residue was extracted with $CHCl_3$ (5 times of 10 ml) and from the extracts the product obtained was crystallized from 1,2-dimethoxyethane (yield 0.05 g, 25%), m.p. 172–174°. ^{1}H NMR δ(DMSO-d_6) 7.65 (d, H_2), 6.12 (d, H_5), $J_{2,5}$ = 0.9 Hz. MS: 145 (M^+, 100%). (Found: C, 33.88; H, 3.17. Calc. for $C_4H_4ClN_3O$: C, 33.91; H, 2.77%).

4-(O-*Benzylhydroxyamino*)-6-*chloropyrimidine* (**9b**). This was obtained in a similar manner from 4,6-dichloropyrimidine and O-benzylhydroxylamine (after 2.5 hr at 90°) in 27% yield. The product was extracted from the mixture with diethyl ether and crystallized from CCl_4, m.p. 128–130°. ^{1}H NMR δ($CDCl_3$) 7.67 (s, H_2), 6.90 (broad s, Ph), 6.35 (s, H_5), 4.55 (s, CH_2). MS: 235 (M^+, 63%) (Found: C, 56.31; H, 4.29; N, 17.81. Calc. for $C_{11}H_{10}ClN_3O$: C, 56.06; H, 4.28; N, 17.38%).

N - (6 - *Chloropyridazinyl* - 3) - *N'* - (*carbethoxy*)*thiourea* (**10**). 3-Hydroxylamino-6-chloropyridazine (0.4 g)[31] was dissolved in CH_2Cl_2 (10 ml) and treated with carbethoxy isothiocyanate (0.361 g). The mixture was stirred at r.t. for 30 min and then evaporated to dryness. The residue was dissolved in 1,2-dimethoxyethane (12 ml), the soln warmed and filtered. Upon evaporation to dryness the product was recrystallized from 1,2-dimethoxyethane (4 ml) yield 0.03 g, 4%, m.p. 170° (Lit.[32] gives m.p. 170°). ^{1}H NMR δ (DMSO-d_6) 8.10 and 7.85 (d, H_4 and H_5), 4.28 (q, CH_2), 2.30 (t, Me), $J_{4,5}$ = 10.0, J_{Et} = 6.75 Hz. MS: 260 (M^+, 22%). (Found: C, 36.84; H, 3.17; N, 21.35. Calc. for $C_8H_9ClN_4O_2S$: C, 36.86; H, 3.48; N, 21.49%).

Reaction between 2-*hydroxylamino-5-nitropyridine and diazomethane.* A soln of 2-hydroxylamino-5-nitropyridine (0.15 g) in EtOH (7 ml) was treated with an ethereal soln of diazomethane (excess) and the mixture was stirred at r.t. for 12 hr. The solvent was evaporated and the residue separated by tlc (PSC-Fertigplatten Kieselgel 60 F_{254}, 2 mm, Merck, solvent mixture $CHCl_3$ and EtOH, 10:1). The compound with R_f = 0.81 was identified as **3c** and compound with R_f = 0.61 as **3b**. Both were eluted with EtOH.

Compound **3c** was crystallized from H_2O (yield, 0.012 g, 7%). M.p. 75°. ^{1}H NMR δ($CDCl_3$) 8.23 (d, H_6), 7.38 (d × d, H_4), 6.65 (d, H_3), 3.80 (s, OMe), 3.38 (s, NME), $J_{3,4}$ = 10.5, $J_{4,6}$ = 2.3 Hz. MS: 183 (M^+, 100%). (Found: C, 45.95; H, 5.21; N, 22.62. Calc. for $C_7H_9N_3O_3$: C, 45.90; H, 4.95; N, 22.94%).

Compound **3b** was crystallized from EtOAc (yield 8 mg, 5%), m.p. 225–229°. ^{1}H NMR δ(DMSO-d_6), 8.85 (d, H_6), 7.37 (d × d, H_4), 6.60 (d, H_3), 3.31 (s, OMe), $J_{3,4}$ = 10.5, $J_{4,6}$ = 3.0 Hz. MS: 169 (M^+, 100%). (Found: C, 42.45; H, 4.40; N, 25.13. Calc. for $C_6H_7N_3O_3$: C, 42.60; H, 4.17; N, 24.85%).

2-(N-*Methylhydroxylamino*)-5-*nitropyridine* (**3d**). A soln of 2-chloro-5-nitropyridine (0.3 g) in EtOH (10 ml) was treated with an ethanolic soln of N-methylhydroxylamine (prepared from 0.8 g of its hydrochloride and 10 ml of ethanolic NaOEt and filtered from NaCl). The mixture was stirred at r.t. for 17 hr and evaporated to dryness. The residue was suspended in H_2O (5 ml), neutralized with $NaHCO_3$, filtered and evaporated to dryness. The residue was extracted with $CHCl_3$ (3 times of 10 ml), the solvent evaporated and the residue crystallized from $CHCl_3$ (5 ml) (yield 0.21 g, 65%), m.p. 151°. ^{1}H NMR δ(DMSO-d_6) 8.85 (d × d, H_6), 8.15 (d × d, H_4), 6.88 (d, H_3), 3.40 (s, NMe), $J_{3,4}$ = 9.6, $J_{4,6}$ = 2.85, $J_{3,6}$ = 0.75 Hz. MS: 169 (M^+, 100%). (Found: C, 42.81; H, 4.28; N, 24.75. Calc. for $C_6H_7N_3O_3$: C, 42.60; H, 4.17; N, 24.85%).

2 - *Hydroxy* - 6 - *chloro* - 2,3 - *dihydroimidazo* (1,2-b)*pyridazine* (**11**). A soln of 3-hydroxylamino-6-chloropyridazine (1.0 g)[31] in 1,2-dimethoxyethane was treated with soln containing bromoacetaldehyde dimethyl acetal (4 g), conc HBr (1.2 ml) and H_2O (1.2 ml). The mixture was stirred at r.t. for 14 hr, evaporated to dryness and the residue was dissolved in H_2O. The product was

filtered off and the filtrate extracted with $CHCl_3$ (5 times of 10 ml). Upon evaporation of the solvent the residue was combined with the product and crystallized from EtOH (yield 0.26 g, 20%), m.p. 165–166°. ^1H NMR $\delta(CD_3OD$ 6.75 (s, H_7 and H_8), 5.5 (m, H_2), 3.93 (m, 3-CH_2), $J_{gem} = 2$ Hz. MS: 187 (M^+, 100%). (Found: C, 38.66; H, 3.23; N, 22.20. Calc. for $C_6H_6ClN_3O_2$: C, 38.42; H, 3.23; N, 22.40%).

s-Triazolo(1,5-a)*pyridine* 1-*oxide* (**12a**). (a) A mixture of **7a** (0.27 g), benzene (13 ml) and N,N-dimethylformamide dimethyl acetal (0.32 ml) was heated under reflux for 13 hr cooled and the product filtered off. It was crystallized from $CHCl_3$ (6 ml) (yield 0.16 g, 54%), m.p. 105° and after solidification at 165–169°. ^1H NMR δ ($CDCl_3$) 8.20 (s, H_2), 8.05 (d × d × d, H_5), 7.63 (d × d, H_8), 7.28 (d × d × d, H_7), 6.80 (d × d × d, H_6), $J_{5,6} = 7.0$, $J_{6,7} = J_{7,8} = 8.0$, $J_{6,8} = J_{5,7} = 2.0$ Hz. MS: 135 (M^+, 100%). (Found: C, 47.08; H, 4.83; N, 27.22. Calc. for $C_6H_5N_3O \cdot H_2O$: C, 47.05; H, 4.61; N, 27.44%).

(b) Compound **7a** (0.47 g) and formic acid (4.3 ml of 88%) were heated at 170° for 3 hr. Upon evaporation to dryness, the residue was dissolved in H_2O (3 ml) and extracted with diethyl ether. Upon evaporation s-triazolo (1,5-a)pyridine was obtained as by-product (0.02 g). The aqueous layer was evaporated to dryness and the residue crystallized from benzene and thereafter from a mixture of benzene and $CHCl_3$, 5:1 (yield 0.15 g, 29%). The compound was in all respects identical with that obtained as described under (a). If this reaction was performed in an autoclave at 196° only s-triazolo(1,5-a)pyridine was obtained in 48% yield.

2 - *Trifluoromethyl* - *s* - *triazolo*(1,5-a)*pyridine* 1 - *oxide* (**12b**). A mixture of **7a** (0.215 g), benzene (13 ml) and trifluoroacetic anhydride (1 ml) was heated under reflux for 14 hr. Upon evaporation to dryness the residue was treated with petroleum ether (2 ml) and the mixture left at −7° overnight. The solvent was evaporated, water (5 ml) was added and the product filtered and crystallized from a mixture of $CHCl_3$ and diethyl ether, 1:1 (yield 60 mg, 17%), m.p. 189–191°. MS: 203 (M^+, 100%). (Found: C, 41.45; H, 1.98; N, 20.70. Calc. for $C_7H_4F_3N_3O$: C, 41.39; H, 1.98; N, 20.69%).

1 - *Amino* - 2 - |0 - (*trifluoroacetyl*)*hydroxyimino*| - 1,2 - *dihydropyridine* (**7c**). A mixture of **7a** (0.215 g), benzene (7 ml) and trifluoroacetic anhydride (1 ml) was heated under reflux for 14 hr, evaporated to dryness and the residue treated with petroleum ether, chilled on dry ice, the solvent decanted and to the residue H_2O (2 ml) was added. The product was filtered off and crystallized from CCl_4 (yield 75 mg, 41%), m.p. 81–82°. ^1H NMR $\delta(CDCl_3)$ 8.03 (d × d × d, H_6), 7.58 (d × d × d, H_3), 7.40 (d × d × d, H_4), 6.96 (d × d × d, H_5), $J_{5,6} = J_{4,5} = 6.3$, $J_{3,6} = J_{4,6} = 1.0$, $J_{3,5} = 2.3$; $J_{3,4} = 8.2$ Hz. MS: 221 ($M^+ - 18$; 10%). (Found: C, 38.27; H, 3.0; N, 18.99. Calc. for $C_7H_6F_3N_3O_2$: C, 38.02; H, 2.73; N, 19.00%).

3 - *Hydroxy* - 3 - *trifluoromethyl* - 3,4 - *dihydropyrido*(2,1-c) - 1,2,4,5 - *oxatriazine* (**13**). A mixture of **7a** (0.1 g), benzene (5 ml) and trifluoroacetic anhydride (1 ml) was left to stand at r.t. for 15 min and then evaporated to dryness. The residue was dissolved in H_2O, neutralized with $NaHCO_3$, the soln evaporated to dryness and the residue extracted with $CHCl_3$. The product, obtained from the extracts was crystallized from CCl_4 (yield 82 mg, 45%), m.p. 143–144°. ^1H NMR $\delta(CDCl_3)$ 7.92 (d × d × d, H_5), 7.50 (d × d × d, H_8), 7.15 (d × d × d, H_7), 6.78 (d × d × d, H_6), $J_{5,6} = 6.4$, $J_{5,7} = 1.0$, $J_{5,8} = 0.9$, $J_{7,8} = 8.4$, $J_{6,8} = 1.3$, $J_{6,7} = 6.3$ Hz. MS: 221 ($M^+ - 18$, 50%). (IR: no CO). (Found: C, 38.20; H, 2.95; N, 19.03. Calc. for $C_7H_6F_3N_3O_2$: C, 38.02; H, 2.73; N, 19.00%).

Reaction between **7a** *and phenyl isocyanate.* A mixture of **7a** (0.14 g), benzene (12 ml) and phenyl isocyanate (0.13 ml) was heated under reflux for 1 hr and then evaporated to dryness. The residue was dissolved in hot CCl_4 and the solid was identified as N,N'-diphenylurea. The filtrate was evaporated to dryness and N-phenyl-N'-(pyridyl-2) urea crystallized from n-PrOH and then from aqueous EtOH (50%) (yield 60 mg, 25%), m.p. 190–193°. ^1H NMR δ(DMSO-d_6) 7.85 (d × d × d, H_6), 6.95 (m, H_3, H_4, H_5 and Ph), $J_{5,6} = 6.0$ Hz. MS: 213 (M^+, 18%). (Found: C, 67.44; H, 5.40; N, 19.81. Calc. for $C_{12}H_{11}N_3O$: C, 67.59; H, 5.20; N, 19.71%).

3,5-*Bis*-(*pyridyl*-2')-1,2,4-*oxadiazole* (**14**). Compound **5e** (0.3 g) was heated at 165°/25 mm for 1 hr in a sublimation tube. The sublimate was recrystallized from H_2O (yield 74 mg, 38%), m.p. 173–175°. ^1H NMR δ(DMSO-d_6) 8.52 (m, 2 $H_{6'}$), 7.70 (m, 2 $H_{3'}$, 2 $H_{4'}$, 2 $H_{5'}$). MS: 224 (M^+, 100%). High resolution MS: 224.0705, calc. 224.0698. (Found: C, 64.39; H, 3.72; N, 24.94. Calc. for $C_{12}H_8N_4O$: C, 64.29; H, 3.60; N, 24.99%).

1-*Acetylamino*-*v*-*triazolo*(1,5-a)*pyridine* (**15a**). A mixture of **5e** (0.15 g) and Ac_2O (0.4 ml) was left at r.t. for 26 hr. Upon evaporation to dryness, the residue was dissolved in H_2O (4 ml), Na_2CO_3 was added until pH = 8, and the mixture again evaporated to dryness. The residue was extracted with $CHCl_3$ and the crude product, obtained from the extracts, was mixed with H_2O (50 ml) and the product filtered. It was crystallized from EtOH (yield 20 mg, 26%), m.p. 163–165°. ^1H NMR δ(DMSO-d_6) 8.53 (d × d × d, H_5), 7.53 (d × d × d, H_8), 6.95 (d × d × d, H_7), 6.75 (d × d × d, H_6), 2.04 (s, Me), $J_{5,6} = 5.5$, $J_{5,7} = 2.5$, $J_{5,8} = 1.5$, $J_{7,8} = 8.0$, $J_{6,8} = 3.0$, $J_{6,7} = 7.5$ Hz. MS: 176 (M^+, 9%). (Found: C, 54.18; H, 4.78; N, 31.93. Calc. for $C_8H_8N_4O$: C, 54.54; H, 4.58; N, 31.80%).

1 - *Imino* - 2 - (5 - *trifluoromethyl* - 1,2,4 - *oxadiazol* - 3 - *yl*)*pyridine* (**16**). A mixture of **5e** (0.6 g) and trifluoroacetic anhydride (3 ml) was left at r.t. for 21 hr. Upon evaporation *in vacuo*, the residue was treated with H_2O (10 ml) and the separated product filtered off. It consisted of **17**. The filtrate was neutralized with $NaHCO_3$ and evaporated to dryness. The residue was extracted with EtOH, the solvent evaporated and the residue trated with H_2O (5 ml). After several hr the separated product (**16**) was filtered off and crystallized from a mixture of $CHCl_3$ and CCl_4 (1:4) and then from H_2O (yield 0.13 g, 33%), m.p. 218–220°. ^1H NMR δ(DMSO-d_6) 8.05 (d × d × d, H_6) 7.53 (m, H_3 and H_4), 7.25 (d × d × d, H_5), $J_{5,6} = 6.0$, $J_{4,6} = J_{3,6} = 1.0$, $J_{4,5} = 7.5$, $J_{3,5} = 3.0$ Hz. MS: 230 (M^+, 5%). IR: no CO absorption. (Found: C, 41.88; H, 2.46; N, 24.19. Calc. for $C_8H_5F_3N_4O$: C, 41.75; H, 2.19; N, 24.34%).

Compound **17** was crystallized from H_2O and then from EtOH (yield 0.175 g, 41%), m.p. 200–202°. ^1H NMR δ(DMSO-d_6) 8.15 (d × d × d, H_6), 7.55 (m, H_3, H_4 and H_5), $J_{5,6} = 5.2$, $J_{3,6} = J_{4,6} = 0.9$ Hz. MS: 248 (M^+, 34%). (Found: C, 38.81; H, 3.07; N, 22.62. Calc. for $C_8H_7F_3N_4O_2$: C, 38.72; H, 2.84; N, 22.58%).

1-*Amino*-*v*-*triazolo*(1,5-a)*pyridine* (**15b**). Compound **15a** (0.11 g) was dissolved in HCl aq (1:1, 10 ml) and left for 21 hr at r.t. Na_2CO_3 aq was added until pH = 8 and the mixture was evaporated to dryness. Upon extraction with $CHCl_3$ the product obtained from the extracts was crystallized from a mixture of $CHCl_3$ and CCl_4 (1:3) (yield 56 mg, 66%), m.p. 113–116°. ^1H NMR $\delta(CDCl_3)$ 7.85 (d × d × d, H_5), 6.95 (d × d × d, H_8), 6.35 (m, H_6 and H_7), $J_{5,6} = 5.6$, $J_{5,7} = 2.1$, $J_{5,8} = 1.0$, $J_{6,8} = 2.6$, $J_{7,8} = 7.5$ Hz. MS: 134 (M^+, 6%). (Found: C, 53.79; H, 4.77; N, 41.54. Calc. for $C_6H_6N_4$: C, 53.73; H, 4.51; N, 41.76%).

3-(*Pyridyl*-2')-*imidazo*(1,5-a)*pyridine* (**18**). (a) A mixture of **15a** (54 mg), EtOH aq (20 ml of 50%) and conc HCl (0.3 ml) was heated under reflux for 1 hr. EtOH was evaporated and the soln treated with Na_2CO_3 until pH = 8. The separated product was filtered off and crystallized from aqueous EtOH (10%) (yield 0.18 g, 30%), m.p. 120–121°. ^1H NMR $\delta(CDCl_3)$ 9.20 (d × d × d, $H_{6'}$), 7.95 (d × d × d, H_5), 7.70 (d × d × d, H_8), 7.18 (d × d × d, $H_{4'}$), 6.98 (s, H_1), 6.95 (d × d, $H_{3'}$), 6.55 (d × d × d, $H_{5'}$), 6.22 (m, H_6 and H_7), $J_{5,6} = 4.4$, $J_{5,7} = 1.8$, $J_{5,8} = 0.8$, $J_{6,8} = J_{5,8} = 1.0$, $J_{7,8} = 7.4$, $J_{5',6'} = 5.3$, $J_{4',6'} = 1.7$, $J_{3',4'} = 6.6$, $J_{3',6'} = 1.4$, $J_{3',5'} = 1.2$, $J_{4',5'} = 4.5$ Hz. MS: 195 (M^+, 100%). (Found: C, 74.06; H, 4.61; N, 21.44. Calc. for $C_{12}H_9N_3$: C, 73.83; H, 4.65; N, 21.52%).

(b) If **15a** was heated in $NaHCO_3$ aq for 3 hr, **18** was obtained in 16% yield.

(c) Compound **15b** (70 mg), 50% EtOH (2.6 ml) and conc HCl (0.4 ml) were heated under reflux for 1 hr, EtOH was evaporated and the residue neutralized with Na_2CO_3. Compound **18** was obtained in 35% yield and was identical in all respects with the product obtained under (a).

(d) A mixture of pyridine-2-carboxaldehyde (1 g), H_2O (5 ml) and ammonium sulfate (0.5 g) was left at r.t. for 24 hr. The product was sublimed at 100°/15 mm (yield 37%), m.p. 120–122° (Lit.[33,34] give m.p. 115–117° and 109°, respectively).

Acknowledgement—We are indebted to the Slovene Research

Community for financial support and for a postgraduate grant to A.T.

REFERENCES

[1]E. I. Badowsky, *Progr. Nucleic Acid Res.* **16**, 125 (1976).
[2]A. Tomažič, M. Tišler and B. Stanovnik, *J. Heterocyclic Chem.* **16**, 861 (1979).
[3]R. S. Sagitullin, S. P. Gromov and A. N. Kost, *Tetrahedron* **34**, 2213 (1978).
[4]Y. Tamura, N. Tsujimoto and M. Mano, *Chem. Pharm. Bull.* **19**, 130 (1971).
[5]N. A. Coats and A. R. Katritzky, *J. Org. Chem.* **24**, 1836 (1959).
[6]A. R. Katritzky and J. M. Lagowski, *Chemistry of the Heterocyclic N-oxides*. Academic Press, New York (1971).
[7]Y. Tamura, J. Minamikawa and M. Ikeda, *Synthesis* 1 (1977).
[8]O. Exner and V. Jehlička, *J. Chem. Soc.* Perkin II, 567 (1974).
[9]O. Exner and N. Motekov, *Coll. Czech. Chem. Commun.* **43**, 2740 (1978).
[10]W. Klötzer and M. Herberz, *Monatsh. Chem.* **99**, 847 (1968).
[11]P. K. Chang, *J. Med. Chem.* **8**, 884 (1965).
[12]W. Pfleiderer and H. Ferch, *Liebigs Ann.* **615**, 52 (1958).
[13]H. C. Van der Plas, *Ring Transformations of Heterocycles*, Vols. 1 and 2. Academic Press, London (1973).
[14]B. Zeeh and H. Metzger, *Houben-Weyl, Methoden der organischen Chemie* X/1, p. 1239. Thieme Verlag, Stuttgart (1971).
[15]C. Gheorghiu and A. Barbos, *Ann. Sci. Univ. Jassy* **26**, I, 271 (1940); *Chem. Abstr.* **34**, 4388 (1940).
[16]K. Satoh, T. Miyasaka and K. Arakawa, *Chem. Letters* 1501 (1977).
[17]E. S. Hand and W. W. Paudler, *J. Org. Chem.* **43**, 658 (1978).
[18]J. Keck, *Methodicum Chimicum* (Edited by F. Korte), Bd. 6, p. 53. Thieme Verlag, Stuttgart (1974).
[19]T. Sheradsky, G. Salemnick and Z. Nir, *Tetrahedron* **28**, 3833 (1972).
[20]S. Polanc, B. Verček, B. Šek, B. Stanovnik and M. Tišler, *J. Org. Chem.* **39**, 2143 (1974).
[21]B. Stanovnik, M. Tišler and A. Vrbanič, *Ibid.* **34**, 996 (1969).
[22]G. Leandri and P. Rebora, *Ann. Chim. Rome* **46**, 953 (1956).
[23]F. Eloy and R. Lenaers, *Chem. Revs* **62**, 155 (1962).
[24]Y. Tamura, J. H. Kim, Y. Miki, H. Hayashi and M. Ikeda, *J. Heterocyclic Chem.* **12**, 481 (1975).
[25]We are indebted for the X-ray analysis to Dr. I. Leban, Laboratory of inorganic chemistry. Full details will be published elsewhere.
[26]G. Brauer, *Handbuch der präparativen Anorganischen Chemie*, Bd. I, p. 450. Enke Verlag, Stuttgart (1962).
[27]B. J. R. Nicolaus, G. Pagani and E. Tests, *Helv. Chim. Acta* **45**, 1381 (1962).
[28]Y. Tamura, J. Minamikawa, Y. Miki, S. Matsugashita and M. Ikeda, *Tetrahedron Letters* 4133 (1972).
[29]Y. Tamura, J. H. Kim and M. Ikeda, *J. Heterocyclic Chem.* **12**, 107 (1975).
[30]L. W. Deady, *Synthet. Commun.* 509 (1977).
[31]A. Tomažič, M. Tišler and B. Stanovnik, *J. Heterocyclic Chem.* **16**, 861 (1979).
[32]M. Zupan, B. Stanovnik and M. Tišler, *J. Org. Chem.* **37**, 2960 (1972).
[33]E. Abushanab, *Tetrahedron Letters* 1441 (1971).
[34]J. D. Bower and G. R. Ramage, *J. Chem. Soc.* 2834 (1955).