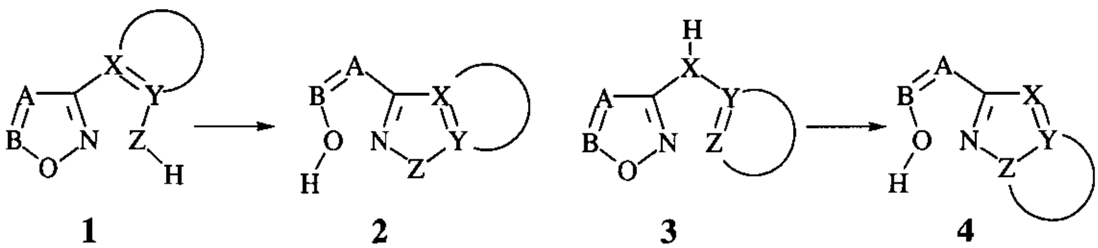
REARRANGEMENT OF 3-(*N*-HETEROARYLAMINO)-1,2,5-OXADIAZOLES: TRIAZOLO[1,5-*a*]QUINOLINES AND TRIAZOLO[1,5-*a*]PYRIDINES[1]

Giuseppe Cusmano*, Gabriella Macaluso, and Michelangelo Gruttadauria

Dipartimento di Chimica Organica dell'Università di Palermo
Via Archirafi 20, 90123 Palermo, Italy

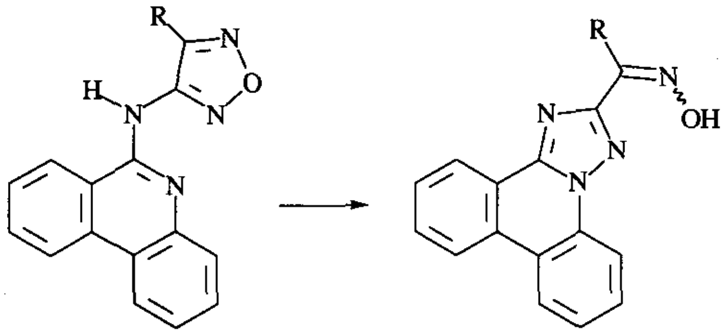
Abstract --- The rearrangement reaction of 1,2,5-oxadiazole derivatives bearing quinoline and pyridine heterocycles in a **N-C-N** side chain sequence was investigated. Triazolo[1,5-*a*]quinoline and triazolo[1,5-*a*]pyridine oximes were obtained in good yield.

The "mononuclear heterocyclic rearrangements" (mhr) have been a useful method to synthesize heterocyclic systems.[2-4] The rearrangements of systems bearing a side chain incorporated in an aromatic or heteroaromatic ring give rise to fused heterocyclic systems.[5-12]



An example of the rearrangement of type **3** ⟶ **4** is represented by the transformation of 3-(6-phenanthridinamino)-1,2,5-oxadiazole derivatives (**5**) into the 1,2,4-triazolo[1,5-*f*]-phenanthridine ring system (**6**).[5]

The peculiarity of this transformation consists in the fact that the **N-C-N** side chain sequence is a part of a phenanthridine moiety bound to a 1,2,5-oxadiazole ring.



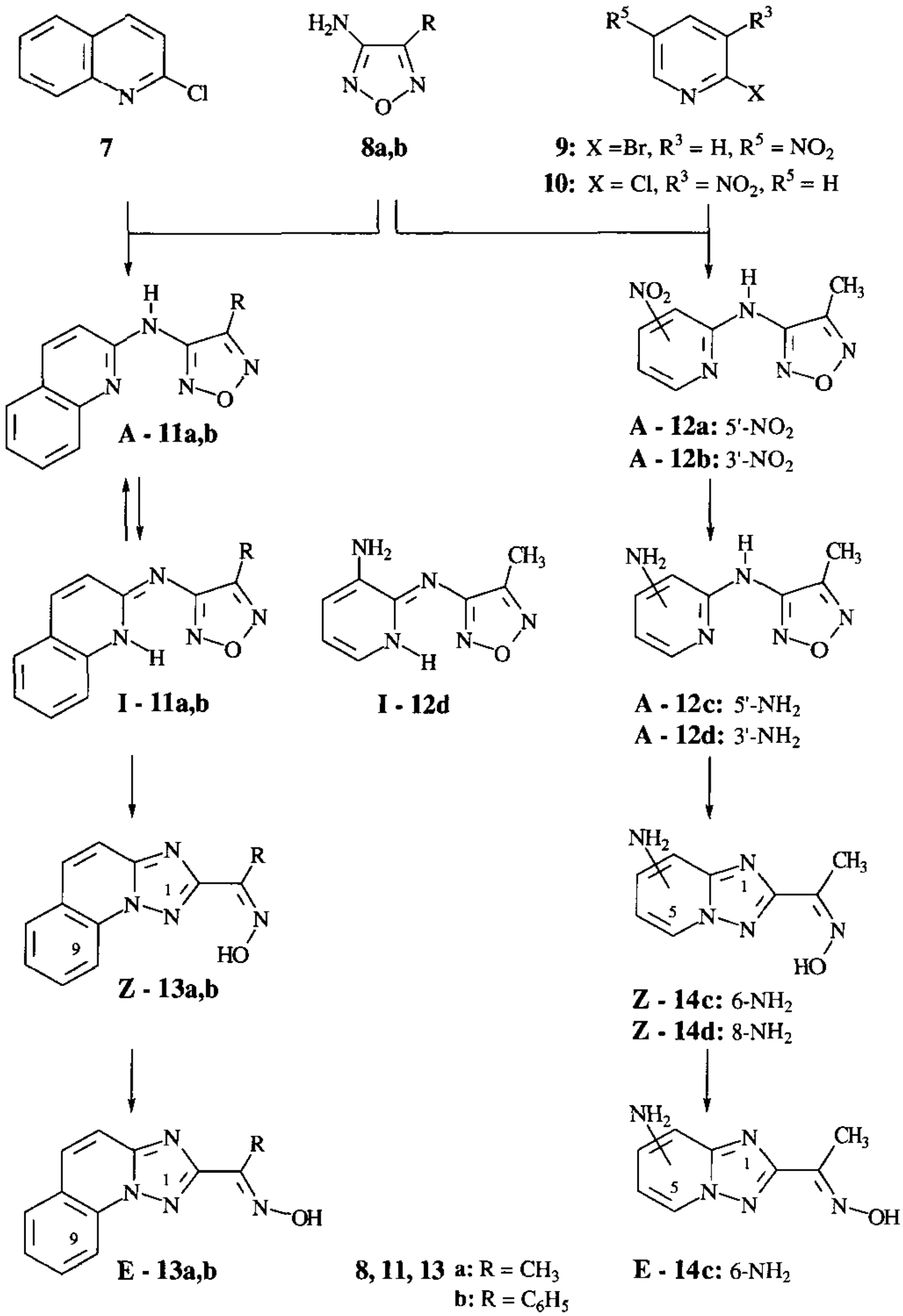
5 **6**

In this paper we describe the behaviour of 1,2,5-oxadiazoles bearing different heterocycles in the **N-C-N** side chain sequence.

We synthesized the 3-(2-quinolinamino)- and 3-(2-pyridinamino)-1,2,5-oxadiazole derivatives (**11** and **12**) as compounds to be rearranged. The reaction of the 4-substituted 3-amino-1,2,5-oxadiazoles (**8a,b**) with 2-chloroquinoline without solvent at 170°C afforded the expected derivatives (**11a,b**); similarly, the reaction of 4-methyl-3-amino-1,2,5-oxadiazole (**8a**) with 2-bromo-5-nitropyridine or 2-chloro-3-nitropyridine yielded compounds (**12a,b**). In turn, the amino compounds (**12c,d**) were obtained in excellent yields by catalytic reduction of the corresponding nitro derivatives (**12a,b**).

The structure of the compounds (**11** and **12**) was confirmed by analytical as well as spectroscopic data. The nmr spectra of **11** and **12** in $CDCl_3$, DMSO-d_6 and $CDCl_3$/DMSO-d_6 evidenced a tautomeric equilibrium between the amino form **A** and the imino form **I**. Such an equilibrium strongly depends on the nature of the solvent, on the heterocycles themselves and on the substituents bound to them.[13]

Compound (**11a**) exists in chloroform both under the imino form (**I**, 50%) and the amino form (**A**, 50%). Similarly **11b** exists in both forms (**I**, 67% and **A**, 33%). The NH singlet at δ 11.74-11.89 was assigned to the imino form because of intramolecular hydrogen bonding with the oxadiazole ring. The NH signal in the amino form of **11a** overlaps with the aromatic proton signals, while that of **11b** appears at δ 9.76. Furthermore the *ortho* protons


7
8a,b
9: X =Br, R^3 = H, R^5 = NO_2
10: X = Cl, R^3 = NO_2, R^5 = H
A - 11a,b
A - 12a: 5'-NO_2
A - 12b: 3'-NO_2
I - 11a,b
I - 12d
A - 12c: 5'-NH_2
A - 12d: 3'-NH_2
Z - 13a,b
Z - 14c: 6-NH_2
Z - 14d: 8-NH_2
E - 13a,b
8, 11, 13 a: R = CH_3
b: R = C_6H_5
E - 14c: 6-NH_2

of the phenyl substituent on the oxadiazole ring of the imino form of **11b**, deshielded by anisotropic effect of the imino nitrogen, appear at δ 8.35-8.45. In the more polar solvent DMSO-d_6, the tautomeric equilibrium is mainly shifted towards the amino form. In fact **11a** shows only signals due to the amino form and **11b** shows a 30/70 imino-amino ratio. The stability of the imino form in $CDCl_3$ is mainly due to intramolecular hydrogen bonding.[13,14] This imino form is particularly favoured in the conformatin of **11b** that bears the phenyl ring and the chelate form coplanar. Intermolecular hydrogen bonding with the solvent DMSO-d_6 makes the imino form relatively less stable with consequent shift of the equilibrium towards the amino form.

In the case of pyridine derivatives (**12a,d**) the amino-imino equilibrium is detectable only for the 3'-amino-(2-pyridinamino) derivative (**12d**). In fact **12d** in DMSO-d_6 shows signals corresponding to 7% of the imino form (**I-12d**), which in $CDCl_3$/DMSO-d_6 1:1 and in $CDCl_3$ increases up to 20% and 100%, respectively. Probably this is due to an additional hydrogen bond between the 3'-amino group and the imino nitrogen. On the contrary nmr spectra of **12a-c** show only signals attributable to the amino form both in DMSO-d_6 and $CDCl_3$ as a consequence of a higher relative stabilization by aromaticity of the amino form in the pyridine system.

The transformation of the quinolinamino derivatives (**11a,b**) was carried out in anhydrous dimethylformamide and potassium *t*-butoxide at 120-130°C. The rearrangement products 1,2,4-triazolo[1,5-*a*]quinoline derivatives (**13a,b**) were obtained in good yield (66-70%).

Differently, the pyridinamino derivatives (**12c,d**) could be rearranged into the corresponding 1,2,4-triazolo[1,5-*a*]pyridines (**14c,d**) in 68-85% yield by refluxing in ethanol and potassium hydroxide as a base.

In the case of the nitro compounds (**12a,b**) the transformation reaction did not occur. In DMF/potassium *t*-butoxide, only intractable tars were obtained, whereas in ethanol/potassium hydroxide, only starting material was recovered. This lack of reactivity can be ascribed to the decreased nucleophilic character of the pyridine nitrogen.

The structures of the compounds (**13** and **14**) were assigned on the basis of spectroscopic data. In particular the triazoloquinoline structure was supported by the value of the chemical shift of the H-9 proton signal at δ 8.37-8.60, which is deshielded by the nitrogen of the triazole ring and is in agreement with the reported chemical shift of the corresponding proton (H-5) of the triazolophenanthridine derivatives.[15] The triazolopyridine structure (**14**) was assigned on the basis of the nmr data which are in agreement with those reported for the same ring system.[16]

The configuration of oximes (**13** and **14**) was based on the comparison of the OH proton chemical shift in different solvents ($CDCl_3$, DMSO-d_6 or $CDCl_3$/DMSO-d_6). The expected **Z**-oximes deriving from the rearrangement process, under the reaction condition or as an effect of the separation procedure, completely or in part can isomerize to the corresponding **E**-stereoisomers. In fact rearrangement of **11a** afforded only the oxime (**E-13a**), the rearrangement of **11b** and **12c** gave both the **E**- and the **Z**-oximes, whereas in the case of the rearrangement of **12d** only **Z-14d** was isolated.

In conclusion the above results confirm the ductility of mhr in the synthesis of fused heterocycles due to the possibilities of a wide choice of side chains incorporated in heterocyclic ring systems.

EXPERIMENTAL

Melting points were determined with a Kofler hot-stage apparatus; ir spectra (nujol mull) were recorded on a Perkin-Elmer infrared spectrophotometer (model 297); uv spectra (ethanol) were determined with a JASCO 7800 spectrophotometer; ^{1}H nmr spectra were recorded on a Bruker AC-E Series 250 MHz spectrometer. Chemical shifts are reported as δ values (ppm) relative to TMS as an internal standard. Flash chromatography was performed on Merck silica gel (0.040-0.063 mm). The 3-amino-4-methyl- and the 3-amino-4-phenyl-1,2,5-oxadiazoles (**8a,b**) were prepared by the methods described in the literature.[17,18]

General Method for the Preparation of 3-(*N*-Heteroarylamino)-1,2,5-oxadiazoles.

A mixture of 3-amino-4-methyl-1,2,5-oxadiazole (**8a**) or 3-amino-4-phenyl-1,2,5-

oxadiazole (**8b**) (30 mmol) and appropriate halo derivative (6 mmol) was heated in an oil bath at 170°C for 18 h in the case of the 3-(2-quinolinamino)-1,2,5-oxadiazoles (**11a,b**). In the case of the 3-(2-pyridinamino)-1,2,5-oxadiazoles (**12a,b**) the oil bath was heated at 170-190°C for 0.5-2 h. After cooling this mixture was treated with 10 ml of THF. Compounds (**11a,b**) resulted insoluble in THF and could be filtered off, whereas in the case of compounds (**12a,b**) the resulting solution was chromatographed.

Compound (11a) (R = CH_3): yield 70%, mp 136-138°C (methanol); uv λ_{max} nm (log ε): 253 (3.96), 306 (3.19), 319 (3.16); ir: 3240, 3210, 3180 cm^{-1} (NH), 1635, 1605 cm^{-1} (CN); ^1H nmr (DMSO-d_6) δ: 2.43 (s, 3H, CH_3), 7.43 (m, 1H, 7'-H), 7.60 (d, 1H, 3'-H, J = 8.9 Hz), 7.67 (m, 1H, 6'-H), 7.74 (d, 1H, 5'-H, J = 8.1 Hz), 7.87 (d, 1H, 8'-H, J = 7.9 Hz), 8.30 (d, 1H, 4'-H, J = 8.9 Hz), 10.18 (s, 1H, NH); ^1H nmr ($CDCl_3$) δ: two tautomers 50% imino form **I** and 50% amino form **A**, 2.41 (s, CH_3 **A** and **I**), 6.96 (dd, 8'-H **I**, J = 9.4, 1.4 Hz), 7.2-7.8 (m, 5H, 3',5',6',7'-H, 4'-H **I** and NH **A**), 8.00 (d, 3'-H **A**, J = 8.9 Hz), 8.17 (d, 4'-H **A**, J = 8.9 Hz), 11.74 (br s, NH **I**). *Anal.* Calcd for $C_{12}H_{10}N_4O$: C, 63.71; H, 4.46; N, 24.76. Found: C, 63.44; H, 4.50; N, 24.65.

Compound (11b) (R = C_6H_5): yield 87%, mp 142-144°C (methanol); uv λ_{max} nm (log ε): 251 (4.43), 270sh (4.22), 325sh (3.80), 340 (3.90), 370 (3.70), 387 (3.58); ir: 3250, 3160 cm^{-1} (NH), 1630, 1600 cm^{-1} (CN); ^1H nmr (DMSO-d_6) δ: two tautomers 30% imino form **I** and 70% amino form **A**, 7.27 (d, 3'-H **I**, J = 8.9 Hz), 7.3-7.6 (m, 3',6', 7'-H **A**, Ar-H of C_6H_5 **A**, 5',6',7',8'-H **I** and *meta* - and *para*-H of C_6H_5 **I**), 7.75 (d, 5',8'-H **A**, J = 7.9 Hz), 7.83 (br m, *ortho*-H of C_6H_5 **I**), 8.14 (br d, 4'-H **A** and **I**, J = 8.9 Hz), 10.16 (br s, NH **A**), 12.10 (br s, NH **I**); ^1H nmr ($CDCl_3$) δ: two tautomers 67% imino form **I** and 33% amino form **A**, 7.06 (dd, 8'-H **I**, J = 9.3, 1.8 Hz), 7.28-7.7 (m, 6',7'-H **A**, 3',6',7'-H **I**, Ar-H of C_6H_5 **A** and *meta*-H, *para*-H of C_6H_5 **I**), 7.75 and 7.77 (d merged with a m, 5'-H **I** and 5',8'-H **A**), 8.23 (m, 3',4'-H **A**), 8.35-8.45 (2 d, 4'-H **I** and *ortho*-H of C_6H_5 **I**), 9.76 (s, NH **A**), 11.89 (br s, NH **I**). *Anal.* Calcd for $C_{17}H_{12}N_4O$: C, 70.82; H, 4.20; N, 19.43. Found: C, 70.64; H, 4.16; N, 19.37.

Compound (12a) (5'-NO_2): elution performed with cyclohexane-ethyl acetate 2:1; yield 53%, mp 161-162°C (methanol); uv λ_{max} nm (log ε): 245sh (4.07), 332 (4.66); ir: 3320 cm^{-1} (NH), 1600, 1570 cm^{-1} (CN); ^1H nmr (DMSO-d_6) δ: 2.41 (s, 3H, CH_3), 7.63 (d, 1H, 3'-H, *J* = 9.4 Hz), 8.58 (dd, 1H, 4'-H, *J* = 9.4, 2.5 Hz), 9.15 (d, 1H, 6'-H, *J* = 2.5 Hz), 10.85 (s, 1H, NH); ^1H nmr ($CDCl_3$) δ: 2.48 (s, 3H, CH_3), 7.46 (s, 1H, NH), 8.06 (d, 1H, 3'-H, *J* = 9.2 Hz), 8.56 (dd, 1H, 4'-H, *J* = 9.2, 2.6 Hz), 9.16 (d, 1H, 6'-H, *J* = 2.6 Hz). *Anal.* Calcd for $C_8H_7N_5O_3$: C, 43.44; H, 3.19; N, 31.66. Found: C, 43.38; H, 3.21; N, 31.68.

Further elution with cyclohexane-ethyl acetate 1:1 gave 1.29 g (13 mmol) of the starting 3-amino-4-methyl-1,2,5-oxadiazole (**8a**).

Compound (12b) (3'-NO_2): elution performed with cyclohexane-ethyl acetate 2:1; yield 58%, mp 125-126°C (methanol); uv λ_{max} nm (log ε): 235sh (4.32), 270 (3.94), 364 (3.79); ir: 3340 cm^{-1} (NH), 1605, 1590 cm^1 (CN); ^1H nmr (DMSO-d_6) δ: 2.24 (s, 3H, CH_3), 7.16 (dd, 1H, 5'-H, *J* = 8.2, 4.2 Hz), 8.51 (dd, 1H, 6'-H, *J* = 4.2, 1.6 Hz), 8.59 (dd, 1H, 4'-H, *J* = 8.2, 1.6 Hz), 10.08 (s, 1H, NH); ^1H nmr ($CDCl_3$) δ: 2.39 (s, 3H, CH_3), 7.09 (dd, 1H, 5'-H, *J* = 8.1, 4.2 Hz), 8.56 (d, 1H, 6'-H, *J* = 4.2 Hz), 8.58 (d, 1H, 4'-H, *J* = 8.1 Hz), 9.84 (s, 1H, NH). *Anal.* Calcd for $C_8H_7N_5O_3$: C, 43.44; H, 3.19; N, 31.66. Found: C, 43.61; H, 3.18; N, 32.01.

Further elution with cyclohexane-ethyl acetate 1:1 gave 1.68 g (17 mmol) of the starting 3-amino-4-methyl-1,2,5-oxadiazole (**8a**).

Reduction of 3-(Nitro-2-pyridinamino)-4-methyl-1,2,5-oxadiazoles (12a,b): 3-(Amino-2-pyridinamino)-4-methyl-1,2,5-oxadiazoles (12c,d).

A mixture of compounds (**12a,b**) (880 mg, 4 mmol), 10% palladium on charcoal (90 mg) and ethanol (150 ml) was shaken under hydrogen in a Parr apparatus at room temperature at 30 psi for 90 min. The catalyst was filtered off and the solvent was evaporated *in vacuo*. The residue was purified by chromatography (cyclohexane-ethyl acetate 1:1).

Compound (12c) (5'-NH_2): yield 90%, mp 162-163°C (light petroleum, bp 40-70°C); uv λ_{max} nm (log ε): 245 (4.10), 285 (3.73), 322 (3.71); ir: 3400, 3300, 3250, 3190 weak, 3150 weak cm^{-1} (NH_2, NH), 1600, 1570 cm^{-1} (CN); ^1H nmr (DMSO-d_6) δ: 2.36 (s, 3H, CH_3), 4.98 (s, 2H, NH_2), 7.05 (dd, 1H, 4'-H, J = 8.8, 2.4 Hz), 7.43 (d, 1H, 3'-H, J = 8.8 Hz), 7.70 (d, 1H, 6'-H, J = 2.4 Hz), 9.24 (s, 1H, NH); ^1H nmr ($CDCl_3$) δ: 2.38 (s, 3H, CH_3), 3.59 (s, 2H, NH_2), 6.90 (br s, 1H, NH), 7.14 (dd, 1H, 4'-H, J = 8.8, 3.0 Hz), 7.75 (dd, 1H, 3'-H, J = 8.8, 0.6 Hz), 7.79 (dd, 1H, 6'-H, J = 3.0, 0.6 Hz). *Anal.* Calcd for $C_8H_9N_5O$: C, 50.26; H, 4.74; N, 36.63. Found: C, 50.28; H, 4.71; N, 36.72.

Compound (12d) (3'-NH_2): yield 92%, mp 126-127°C (light petroleum, bp 40-70°C); uv λ_{max} nm (log ε): 235sh (3.82), 268sh (3.63), 310 (3.87), 362 (3.55), 375sh (3.47); ir: 3400, 3310, 3140, 3100 cm^{-1} (NH_2, NH), 1630, 1590 cm^{-1} (CN); ^1H nmr (DMSO-d_6) δ: two tautomers 7% imino form **I** and 93% amino form **A**, 2.16 (s, CH_3 **A**), 2.30 (s, CH_3 **I**), 5.15 (s, NH_2 **A**), 5.65 (s, NH_2 **I**), 6.50 (br m, 4'-H **I**), 6.79 (dd, 5'-H **A**, J = 7.5, 4.8 Hz), 6.99 (d, 4'-H **A**, J = 7.5 Hz), 7.24 (dd, 5'-H **I**, J = 8.5, 5.0 Hz), 7.48 (d, 6'-H **A**, J = 4.8 Hz), 8.36 (d, 6'-H **I**, J = 5.0 Hz), 8.75 (s, NH **A**); ^1H nmr ($CDCl_3$/DMSO-d_6 1/1) δ: two tautomers 20% imino form **I** and 80% amino form **A**, 2.19 (s, CH_3 **A**), 2.35 (s, CH_3 **I**), 4.93 (s, NH_2 **A**), 5.45 (s, NH_2 **I**), 6.38 (br t, 5'-H **I**, J = 7.0 Hz), 6.74 (dd, 5'-H **A**, 4'-H **I**, J = 7.7, 4.8 Hz), 6.99 (dd, 4'-H **A**, J = 7.7, 1.5 Hz), 7.17 (br d, 6'-H **I**, J = 7.0 Hz), 7.50 (dd, 6'-H **A**, J = 4.8, 1.5 Hz), 8.65 (s, NH **A**), 11.70 (br s, NH **I**); ^1H nmr ($CDCl_3$) δ: 100% imino form **I**, 2.41 (s, 3H, CH_3), 4.58 (br s, 2H, NH_2), 6.47 (br t, 1H, 5'-H, J = 6.7 Hz), 6.74 (br d, 1H, 4'-H, J = 6.8 Hz), 7.10 (br d, 1H, 6'-H, J = 5.3 Hz), 11.75 (br s, NH). *Anal.* Calcd for $C_8H_9N_5O$: C, 50.26; H, 4.74; N, 36.63. Found: C, 50.18; H, 4.76; N, 37.06.

Rearrangement of 3-(2-Quinolinamino)-1,2,5-oxadiazoles (11a,b) into the E-Oxime of 2-Acetyl-1,2,4-triazolo[1,5-*a*]quinoline (E-13a) and E/Z - Oximes of 2-Benzoyl-1,2,4-triazolo[1,5-*a*]quinoline (E/Z-13b)

A mixture of **11a,b** (2 mmol) and potassium *t*-butoxide (250 mg, 2.2 mmol) in anhydrous DMF (20 ml) was heated at 120-130°C for 2 h. After cooling, the reaction mixture was diluted with water and neutralized with acetic acid, then the solid was filtered off.

E-Oxime of 2-Acetyl-1,2,4-triazolo[1,5-*a*]quinoline (E-13a): yield 66%, mp 254°C (ethanol); uv λ_{max} nm (log ε): 247 (4.66), 282sh (3.98), 292sh (3.92), 313 (3.48), 326 (3.29); ir: 3180 weak cm^{-1} (NH), 1610, 1560 cm^{-1} (CN); ^1H nmr (DMSO-d_6) δ: 2.43 (s, 3H, CH_3), 7.67 (m, 1H, 7-H), 7.80 (d, 1H, 4-H, *J*= 9.1 Hz), 7.88 (m, 1H, 8-H), 8.15 (d, 2H, 5,6-H, *J* = 8.8 Hz), 8.45 (d, 1H, 9-H, *J* = 8.2 Hz), 11.73 (s, 1H, OH); ^1H nmr ($CDCl_3$) δ: 2.54 (s, 3H, CH_3), 7.59 (m, 1H, 7-H), 7.68 (d, 1H, 4-H, *J* = 9.5 Hz), 7.79 (m, 1H, 8-H), 7.84 (d, 1H, 6-H, *J* = 8.3 Hz), 7.91 (d, 1H, 5-H, *J* = 9.5 Hz), 8.60 (d, 1H, 9-H, *J* = 8.4 Hz), 10.34 (br s, 1H, OH). *Anal.* Calcd for $C_{12}H_{10}N_4O$: C, 63.71; H, 4.46; N, 24.76. Found: C, 63.78; H, 4.46; N, 24.57.

E/Z-Oximes of 2-Benzoyl-1,2,4-triazolo[1,5-*a*]quinoline (E/Z-13b): yield 70%, mp 198-202°C (ethanol); uv λ_{max} nm (log ε): 241 (4.57), 280sh (4.10), 290sh (3.94), 321 (3.42); ir: 3160 weak cm^{-1} (OH), 1610 cm^{-1} (CN); ^1H nmr (DMSO-d_6) δ: **E/Z** ratio 74:26, 7.3-7.6 (m, 5H, C_6H_5 **E** and **Z**), 7.6-7.78 (m, 7-H **E** and 7,4-H **Z**), 7.79 (d, 4-H **E**, *J* = 9.4 Hz), 7.82-7.95 (m, 1H, 8-H **E** and **Z**), 8.15 (d, 1H, 6-H **E** and **Z**, *J* = 9.3 Hz), 8.19 and 8.21 (2d, 1H, 5-H **Z**, *J* = 9.1 and 5-H **E**, *J* = 9.4 Hz), 8.37 (d, 9-H **E**, *J* = 8.2 Hz), 8.47 (d, 9-H **Z**, *J* = 8.2 Hz), 11.96 (s, OH **Z**), 11.98 (s, OH **E**); ^1H nmr ($CDCl_3$) δ: **E/Z** ratio 74:26, 7.4-8.1 (m, 10H, Ar-H **E** and **Z**), 8.50 and 8.54 (2 d, 1H, 9-H **E**, *J* = 8.6 Hz and 9-H **Z**, *J* = 8.7 Hz), 9.29 (br s, OH **E**), 13.03 (s, OH **Z**). *Anal.* Calcd for $C_{17}H_{12}N_4O$: C, 70.82; H, 4.20; N, 19.43. Found: C, 70.66; H, 4.25; N, 19.33.

Rearrangement of 3-(2-Pyridinamino)-4-methyl-1,2,5-oxadiazoles (12c) and (12d): E- and Z-Oximes of 2-Acetyl-6-amino-1,2,4-triazolo[1,5-*a*]pyridine (E-14c) and (Z-14c), Z-Oxime of 2-Acetyl-8-amino-1,2,4-triazolo-[1,5-*a*]pyridine (Z-14d).

Compounds (**12c,d**) (380 mg, 2 mmol) were dissolved in ethanol (20 ml), then solid KOH (270 mg, 4.8 mmol) was added. The solution was refluxed for 60 min. After cooling the reaction mixture was neutralized with acetic acid and concentrated *in vacuo*. The residue was purified by chromatography (cyclohexane-ethyl acetate 2:1, 1:1).

E-Oxime of 2-Acetyl-6-amino-1,2,4-triazolo[1,5-*a*]pyridine (E-14c): yield 53%, mp 265°C (light petroleum, bp 40-70°C); uv λ_{max} nm (log ε): 238 (3.72), 250sh (3.68), 290sh (3.07); ir: 3440, 3400, 3340, 3240, 3180 weak cm^{-1} (NH_2, OH), 1650, 1600, 1550 cm^{-1} (CN); ^1H nmr (DMSO-d_6) δ: 2.25 (s, 3H, CH_3), 5.46 (s, 2H, NH_2), 7.28 (dd, 1H, 7-H, J = 9.4, 1.8 Hz), 7.65 (d, 1H, 8-H, J = 9.4 Hz), 8.06 (d, 1H, 5-H, J = 1.8 Hz), 12.03 (s, 1H, OH); ^1H nmr (DMSO-d_6/$CDCl_3$ 1/3) δ: 2.29 (s, 3H, CH_3), 3.50 (br s, NH_2 + H_2O), 7.37 (d, 1H, 7-H, J = 9.5 Hz), 7.55 (d, 1H, 8-H, J = 9.5 Hz), 8.09 (s, 1H, 5-H), 9.20 (br s, 1H, OH). *Anal.* Calcd for $C_8H_9N_5O$: C, 50.26; H, 4.74; N, 36.63. Found: C, 50.43; H, 4.75; N, 36.60.

Z-Oxime of 2-Acetyl-6-amino-1,2,4-triazolo[1,5-*a*]pyridine (Z-14c): yield 32%, mp 235°C (light petroleum, bp 40-70°C); uv λ_{max} nm (log ε): 240 (4.25), 288sh (3.55); ir: 3450, 3350, 3240, 3190 weak cm^{-1} (NH_2, OH), 1635, 1600, 1550 cm^{-1} (CN); ^1H nmr (DMSO-d_6) δ: 2.23 (s, 3H, CH_3), 5.33 (s, 2H, NH_2), 7.21 (dd, 1H, 7-H, J = 9.5, 1.7 Hz), 7.56 (d, 1H, 8-H, J = 9.5 Hz), 8.01 (s, 1H, 5-H), 11.48 (s, 1H, OH). *Anal.* Calcd for $C_8H_9N_5O$: C, 50.26; H, 4.74; N, 36.63. Found: C, 50.34; H, 4.79; N, 36.48.

Z-Oxime of 2-Acetyl-8-amino-1,2,4-triazolo[1,5-*a*]pyridine (Z-14d): yield 68%, mp 166-169°C (methanol); uv λ_{max} nm (log ε): 239 (4.26), 294 (3.92); ir: 3460, 3340, 3220, 3190 cm^{-1} (NH_2, OH), 1615, 1565 cm^{-1} (CN); ^1H nmr (DMSO-d_6) δ: 2.28 (s, 3H, CH_3), 6.14 (s, 2H, NH_2), 6.64 (d, 1H, 7-H, J = 7.7 Hz), 6.99 (t, 1H, 6-H, J = 7.4 Hz), 8.18 (d, 1H, 5-H, J = 6.5 Hz), 12.03 (s, 1H, OH); ^1H nmr ($CDCl_3$) δ: 2.40 (s, 3H, CH_3), 4.52 (s, 2H, NH_2), 6.66 (d, 1H, 7-H, J = 7.7 Hz), 6.91 (t, 1H, 6-H, J = 7.1 Hz), 8.01 (d, 1H, 5-H, J = 6.6 Hz), 13.16 (br s, 1H, OH). *Anal.* Calcd for $C_8H_9N_5O$: C, 50.26; H, 4.74; N, 36.63. Found: C, 50.41; H, 4.72; N, 36.69.

ACKNOWLEDGEMENTS

We thank the Italian MURST for financial support.

REFERENCES AND NOTES

1. Presented at the "III RSC-SCI Joint Meeting on Heterocyclic Chemistry", Sciacca (Italy) 6-9 May 1992.
2. A. J. Boulton, A. R. Katritzky, and A. M. Hamid, *J. Chem. Soc. C*, 1967, 2005.
3. M. Ruccia, N. Vivona, and D. Spinelli, '*Advances in Heterocyclic Chemistry* : Mononuclear Heterocyclic Rearrangements', Vol. 29, ed. by A. R. Katritzky, Academic Press, Inc., London, 1981, pp. 141-169.
4. N. Vivona, S. Buscemi, V. Frenna, and G. Cusmano, '*Advances in Heterocyclic Chemistry* : Ring Transformations of Five-Membered Heterocycles', Vol. 56, ed. by A. R. Katritzky, Academic Press, Inc., London, 1993, p. 000.
5. G. Cusmano, G. Macaluso, M. Gruttadauria, and S. Buscemi, *Heterocycles*, 1990, **31**, 869.
6. I. Bata, G. Heja, P. Kiss, and D. Korbonitz, *J. Chem. Soc., Perkin Trans. 1,* 1986, 9.
7. N. Vivona, G. Cusmano, G. Macaluso, V. Frenna, and M. Ruccia, *J. Heterocycl. Chem.*, 1979, **16**, 783.
8. D. Korbonitz, I. Kanzel-Szvoboda, and K. Horvath, *J. Chem. Soc., Perkin Trans. 1,* 1982, 759.
9. D. Korbonitz and P. Kolonits, *Acta Chem. Hung.*, 1990, **127**, 795.
10. M. Kocevar, M. Tisler, and B. Stanovnik, *Heterocycles*, 1982, **19**, 339.
11. M. Kocevar, M. Tisler, and B. Stanovnik, *Monatsh. Chem.*,1982, **113**, 731.
12. G. Macaluso, G. Cusmano, G. Cirrincione, A. M. Almerico, and P. Diana, *Heterocycles*, 1991, **32**, 1973.

13. C. D. Johnson, '*Comprehensive Heterocyclic Chemistry* : Pyridines and Their Benzo Derivatives: (i) Structure', Vol. 2, eds. by A. J. Boulton and A. McKillop, Pergamon Press, Oxford, 1984, pp. 99-164.

14. R. Mondelli and L. Merlini, *Tetrahedron*, 1966, **22**, 3253.

15. G. Cirrincione, G. Dattolo, A. M. Almerico, E. Aiello, G. Cusmano, G. Macaluso, M. Ruccia, and W. Hinz, *J. Heterocycl. Chem.*, 1986, **23**, 1273.

16. T. Huynh-Dinh, J. Igolen, J. P. Marquet, E. Bisagni, and J. M. Lhoste, *J. Org. Chem.*, 1976, **41**, 3124.

17. S. Cusmano and T. Tiberio, *Gazz. Chim. Ital.*, 1951, **81**, 106.

18. F. Angelico and S. Cusmano, *Gazz. Chim. Ital.*, 1936, **66**, 3.

Received, 18th January, 1993