SYNTHESIS OF TRIAZOLO[4,5-*f*]QUINOLINES. AN UNUSUAL CASE OF DISPLACEMENT OF NITRO GROUP IN THE REACTION OF 8-ACETYLAMINO-6-CHLORO-5-NITROQUINOLINE WITH HYDRAZINE AND METHYLHYDRAZINE

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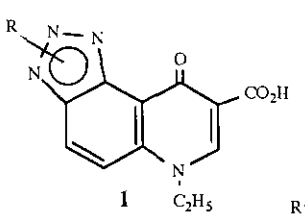
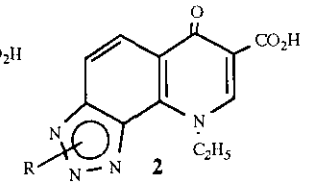
Abstract - Nitration of 1H-, 3-methyl- and 2-methyltriazolo[4,5-*f*]quinolines (**6a-c**) as a way to obtain the desired 4-aminotriazolo[4,5-*f*]quinolines (**4**) for a medicinal chemistry project was successful only in the case of **6c**. Attempted building up of the triazole ring starting from 8-acetylamino-6-chloro-5-nitroquinoline (**8**) with ammonia, hydrazine and methylhydrazine at 150 °C in ethanol failed. However, the results obtained from these reactions allowed us to observe that, during nucleophilic aromatic substitution of chlorine by these bases an unusual displacement of the nitro group by hydrogen occurred. Comparison of these results with those obtained using different substrates allowed us to evaluate the influence of both *para*-acetylamino group and pyridine ring in this type of nucleophilic aromatic substitution.

In preceding papers we have reported the preparation of new triazolo[4,5-*f*]-[1,2] and [4,5-*h*]quinolines[3] referring to the structures (**1**, **2**, **3**) designed for possible antibacterial, antimalarial and anticancer activities.



1

R= H, 1-CH_3, 2-CH_3, 3-CH_3;



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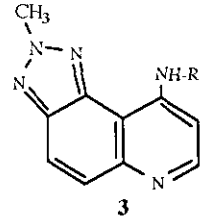
R= H, 1-CH_3, 2-CH_3, 3-CH_3;

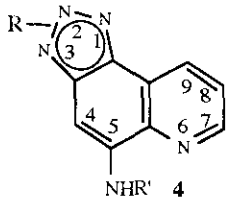


3

R= alkylamino, alkylaminodialkyl (as in compouds **4**)

Compounds (**1**) and (**2**) have shown to be endowed with a moderate antibacterial activity towards *Escherichia coli* [2,3] whereas compounds (**3**) exhibited an interesting *in vitro* cell growth inhibition activity in a large range of human tumor cell-lines at the National Cancer Institute (Bethesda).[4] In this context we had also designed compounds of structure (**4**) in order to investigate the influence of the different position

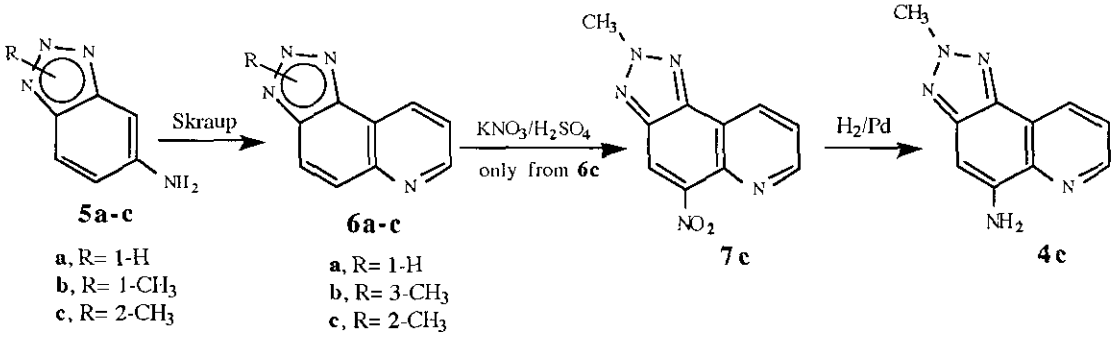
of the aminoalkyl side chain in comparison with compounds of structure (**3**) in either anticancer or antimalarial screening as possible intercalating agents.



4

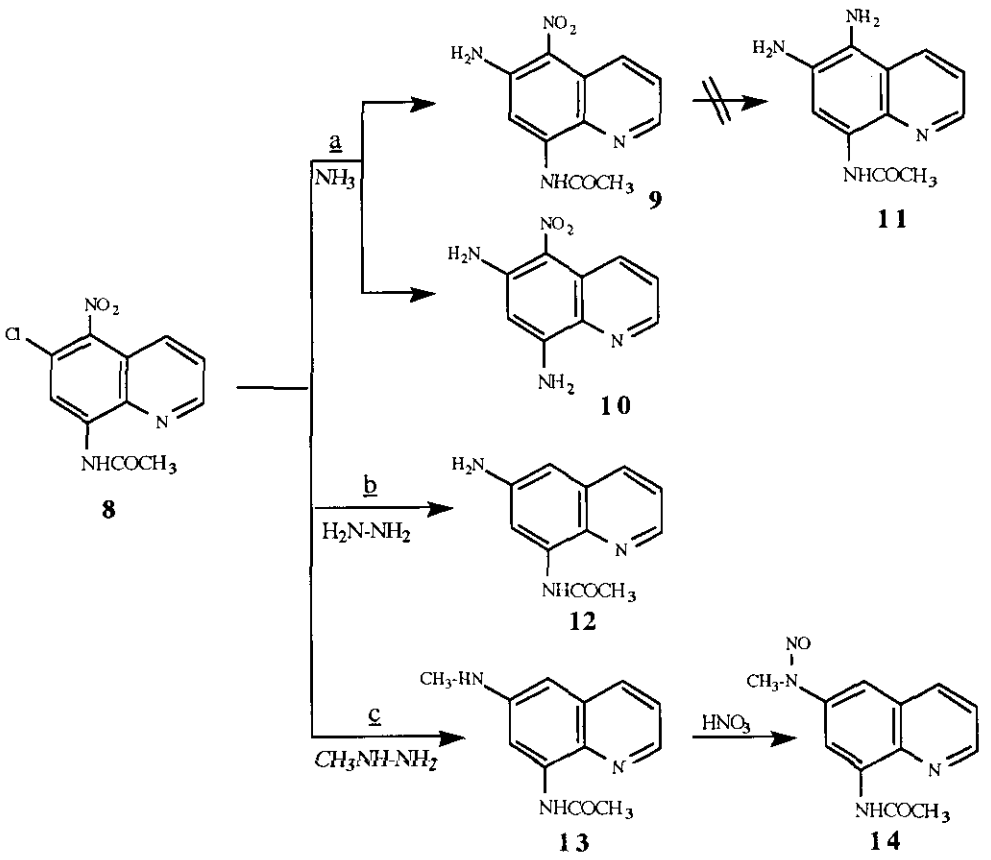
All these projects considered formation of the triazoloquinolines by quinoline ring closure starting from unsubstituted or 1(2)-methyl-substituted 5-aminobenzotriazoles (**5a-c**) and the appropriate reagents. In particular when 5-aminobenzotriazoles and acetylenic esters (dimethyl acetylenedicarboxylate and methyl propiolate) were used, along with the expected triazoloquinoline formation a variety of compounds and interesting rearrangements were observed.[5,6]

Now, we describe the attempted preparations of compounds (**4a-c**) as necessary intermediates to the desired **4**. A linear synthetic approach to obtain the triazolo[4,5-*f*]quinolines (**4**) is outlined in Scheme 1.



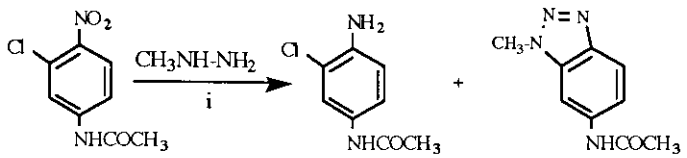
Scheme 1

Skraup synthesis on the known 5-aminobenzotriazoles (**5a-c**) gave the expected triazoloquinolines (**6a-c**) in fair yields. Only compound (**6a**) was previously described[7] without any spectroscopic data (UV, IR and ^{1}H-NMR) which were consistent with those of the new **6b,c**. From various attempts at nitration of **6a-c** we successfully obtained only compound (**7c**), while in other cases (**6a,b**) the reaction failed despite the various conditions used, where we modulated either the nitrating agent (KNO_3/H_2SO_4, fuming nitric acid etc) or the temperature (0-100 °C). This result was disappointing and apparently an explanation for this could be ascribed to the strong deactivating effects of both triazole and pyridine rings to the electrophilic substitution. On the other hand, the formation of **7c** may be due to the *ortho*-quinonoid structure of the compound (**6c**) which makes the C-5 position more susceptible to an electrophilic attack possibly because of vinylogous enamine character. Hydrogenation of **7c** gave the desired **4c** in good yield. An alternative route to obtain **7a,b** was explored according to the reactions outlined in Scheme 2 starting from the known 8-acetylamino-6-chloro-5-nitroquinoline (**8**), purposely prepared adapting a method previously described by Gilman *et al.*[8]



Scheme 2

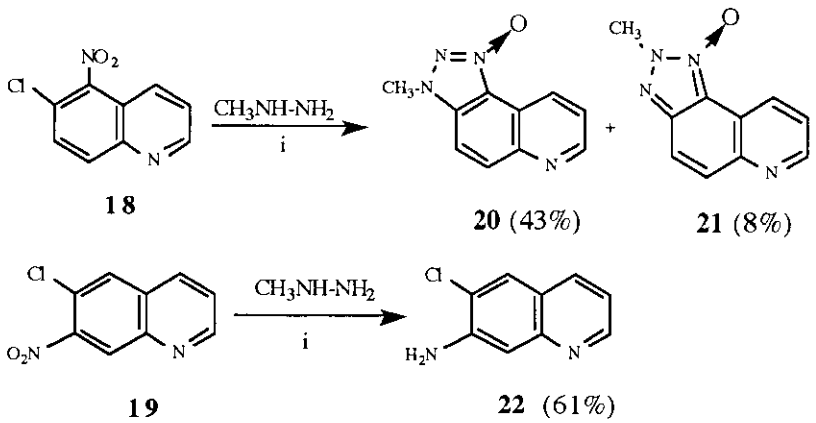
The hypothesis we worked on was based upon the expected activated replacement of the chlorine by the nucleophilic ammonia (route a) to give compound (**9**), to be converted into the diamine (**11**) and eventually into the triazoloquinoline (**4a-c**). Route a showed to be impracticable since compound (**9**), formed in 59% yield along with its deacetylated product (**10**) (20% yield), could in no way be reduced to the diamine (**11**). Nor was route b more satisfactory. Reaction of **8** with 98% hydrazine hydrate at 150-160 °C in ethanol gave compound (**12**). Its formation clearly indicated that the displacement of chlorine was also accompanied by replacement of the nitro group by hydrogen coming from disproportion of hydrazine. An identical behavior was observed when the reaction was carried out with methylhydrazine (route c), which gave compound (**13**). The attempted nitrations of **13** to restore the nitro group in position 5 were unsuccessful and the only product isolated was the *N*-nitroso compound (**14**). The observed cases of displacement of the nitro group in quinoline derivatives are very unusual since in other analogous cases the nucleophilic displacement takes place at the activated carbon bearing chlorine,[9] while the reducing effect of the hydrazine on nitro group is often observed.[10] Apparently, there was no reason why the triazole could not be formed in this way, unless to think about a possible *para*-effect attributable to acetylamino group in C-8 position and to partecipation of the heteroring. To prove that this was the case, we have repeated the reaction with methylhydrazine on 3-chloro-4-nitroacetanilide (**15**), 6-chloro-5-nitroquinoline (**18**), 6-chloro-7-nitroquinoline (**19**) and 2-chloronitrobenzene (**23**) and compared these results.



15 **16** (35%) **17** (24%)

Scheme 3. i, ethanol at 150 °C for 5 h

The reaction of **15** with methylhydrazine (Scheme 3) carried out under the same conditions reported for compound (**8**) showed that the base displaced chlorine to some extent, to give the known 6-acetylamino-1-methyl-1*H*-benzotriazole (**17**) (24%), identical to an authentic specimen described by Kamel *et al.*,[11] along with the known amine (**16**) (35%)[12] thus indicating that a competitive reduction took place together with the nucleophilic substitution followed by ring closure. It is likely that owing to these conditions formation of the corresponding benzotriazole-*N*-oxide of **17** is hard to isolate. When we submitted the compound (**18**) to reaction with methylhydrazine, ring closure occurred and the triazoloquinoline-*N*-oxides (**20**) (43%) and (**21**) (8%) were isolated in 5:1 ratio, according to an often observed cyclization.[13] In the case of compound (**19**), the reduction of the nitro group to the amine (**22**) (61%) was observed (Scheme 4).

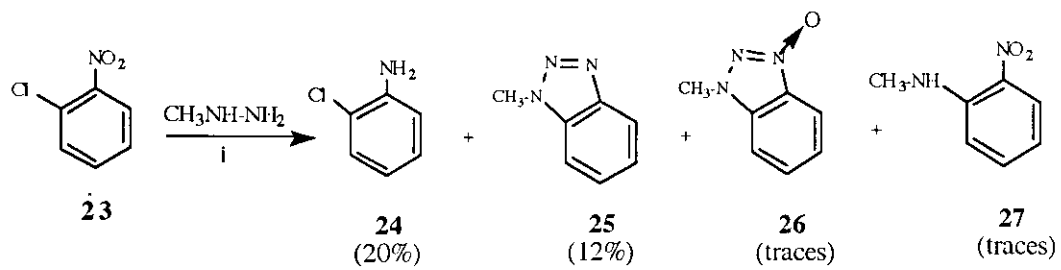


18 **20** (43%) **21** (8%)

19 **22** (61%)

Scheme 4. i, ethanol at 150 °C for 5 h

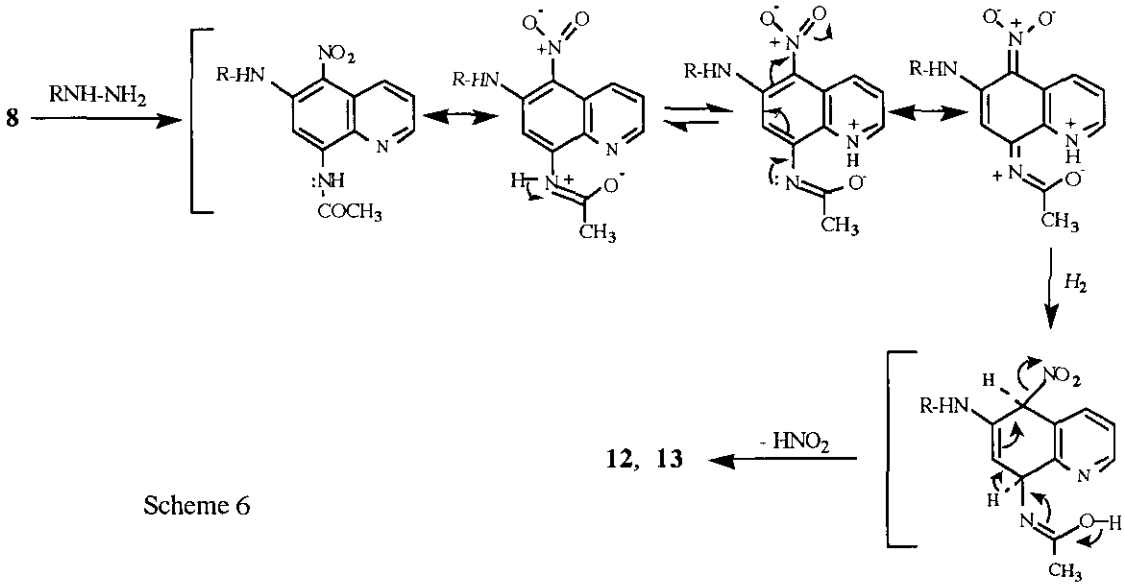
In the end, the reaction of 2-chloronitrobenzene (**23**) with methylhydrazine gave a reaction mixture of 2-chloroaniline (**24**) (20% yield), the known 1-methyl-1*H*-benzotriazole (**25**) (12%)[14] and 1-methyl-1*H*-benzotriazole-*N*-oxide (**26**) (traces)[15] and *N*-methylamino-2-nitrobenzene (**27**) (traces)[16] (Scheme 5).



23 **24** (20%) **25** (12%) **26** (traces) **27** (traces)

Scheme 5. i, ethanol at 150 °C for 5 h

The compounds isolated in our experiments allowed us to establish that the routes designed for to construct the triazole ring starting from **8** are impracticable at the present stage. To our knowledge intermolecular displacement of a nitro group adjacent to chlorine is not very common, although various cases have been reported.[16] In the cases examined when a *para*-acetylamino group is present (compounds **8** and **15**) we observed a striking difference of reactivity of the chloro and nitro groups compared with other cases (**18**, **19** and **23**) which showed both expected reductions and cyclizations. It is our opinion that in this different behavior a certain role is played by the heteroring that, owing to a certain fixity of the double bonds in the quinoline ring, stabilizes the *para*-nitroacetanilide moiety to exist in quinonoid anion form due to the alkaline medium. This intermediate would suffer a Michael addition of hydrogen on quinone system causing elimination of the nitro group due to a rearomatisation process induced by the high temperature (*Scheme 6*).



Scheme 6

EXPERIMENTAL

Melting points are uncorrected and were taken in open capillaries on a 510 Buchi melting point apparatus. IR spectra, unless otherwise specified, were recorded as nujol mulls on a Perkin Elmer 781 spectrophotometer and are expressed in cm^{-1}. UV spectra are qualitative and were recorded in nm for ethanol solutions with a Perkin Elmer Lambda 5 instrument. ^{1}H-NMR spectra were recorded at 200 MHz on a Varian XL-200 instrument, ^{13}C-NMR spectra were recorded on the same instrument at 50 MHz. Chemical shifts are reported in ppm (δ) relative to tetramethylsilane as internal standard. MS spectra were determined by a Finningan Mat-TSQ 700 spectrometer and a combined HP 5790 (GC) - HP 5970 A (MS) apparatus. Column chromatographies were performed using 70-230 mesh (Merck silica gel 60) and 230-400 mesh (Merck silica gel 60) silica gel. Light petroleum refers to the fraction with bp 40-60°C. Elemental analyses were performed at the Laboratorio di Microanalisi, Dipartimento di Scienze Farmaceutiche, University of Padova.

Intermediates

5-Aminobenzotriazoles (**5a-c**) were prepared as described.[2] Compound (**15**) was prepared according to the indications of the literature.[18] Compounds (**18**) and (**19**) were obtained as described by Fourneau *et al.*[19] but their purification was accomplished by chromatography (silica gel column and ether as eluent) and the physical properties are reported below.

6-Chloro-5-nitroquinoline (**18**). yield 30%; mp 128-130 °C (lit.,[19] 129 °C).

6-Chloro-7-nitroquinoline (**19**). yield: 16%; mp 159-161 °C (lit.,[9] 160 °C).

General procedure for preparation of triazolo[4,5-*f*]quinolines (6a-c). In a three necked round flask containing the 5-aminobenzotriazole (**5a-c**) (3 g, 20.2-22.4 mmol), dry glycerol (12 g, 130.30 mmol) and arsenic pentoxide hydrate (20 g, 87 mmol), externally cooled at 0°C with an ice bath, concd sulfuric acid (5 mL) was added slowly under stirring. Once the temperature raised to ambient, the mixture was heated at 150-160 °C for 6 h. After cooling, the mixture was poured onto ice (100 g) and made neutral with concentrated ammonia solution. The precipitate was filtered off, thoroughly washed with water and dried to give:

1*H*-Triazolo[4,5-*f*]quinoline (**6a**). yield: 70%; mp 258-260 °C (lit.,[7] 260 °C).

3-Methyl-3*H*-triazolo[4,5-*f*]quinoline (**6b**). yield: 55%; mp 163-165 °C (from acetone); IR 1590, 1540 cm^{-1}; UV: λ_{max} 316, 303, 284, 274, 245, 214 nm; ^{1}H-NMR ($CDCl_3$): δ 9.06 (1H, d, J = 6.4 Hz, H-7), 9.00 (1H, dd, J = 1.6 and 4.4 Hz, H-9), 8.11 (1H, d, J = 9.2 Hz, H-4), 7.77 (1H, d, J = 9.2 Hz, H-5), 7.65 (1H, dd, J = 8.2 and 4.4 Hz, H-8), 4.41 (3H, s, Me-N). Anal. Calcd for $C_{10}H_8N_4$: C, 65.20; H, 4.38; N, 30.42. Found: C, 64.93; H, 4.30; N, 30.62.

2-Methyl-2*H*-triazolo[4,5-*f*]quinoline (**6c**). yield 51%; mp 76-77 °C (from ether); IR: 1660, 1590, 1530 cm^{-1}; UV: λ_{max} 318, 304, 288 infl, 255, 214 nm; ^{1}H-NMR ($CDCl_3$): δ 8.97 (1H, dd, J = 4.4 and 1.6 Hz, H-7), 8.79 (1H, dd, J = 8.2 and 1.6 Hz, H-9), 7.99 (1H, d, J = 9.4 Hz, H-4), 7.93 (1H, d, J = 9.4 Hz, H-5), 7.50 (1H, dd, J = 8.2 and 4.4 Hz, H-8), 4.56 (3H, s, Me-N). Anal. Calcd for $C_{10}H_8N_4$: C, 65.20 ; H, 4.38; N, 30.42. Found: C, 65.01; H, 4.47; N, 30.32.

2-Methyl-5-nitro-2*H*-triazolo[4,5-*f*]quinoline (**7c**). A solution of **6c** (0.93 g, 5.05 mmol) in concd sulfuric acid (5 mL) was added dropwise to a mixture, previously cooled at 0 °C, constituted by KNO_3 (0.9 g, 89 mmol) and concd sulfuric acid (3.5 mL, d = 1.84). The mixture was stirred at rt for 12 h, poured onto ice (100 g) and extracted with chloroform. The combined extracts were dried on anhydrous sodium sulfate and evaporated *in vacuo* to give a crude product (0.93 g) which after silica gel column chromatography, using ether as eluent, and recrystallization from ether yielded **7c** (0.43 g, 37%); mp 217-218 °C; IR: 1620, 1530, 1510 cm^{-1}; UV: λ_{max} 320, 305, 286 infl, 250, 214 nm; ^{1}H-NMR ($CDCl_3$+ DMSO-d_6): δ 9.04 (1H, dd, J = 4.4 and 1.8 Hz, H-7), 8.90 (1H, dd, J = 8.4 and 1.8 Hz, H-9), 8.50 (1H, s, H-4), 7.82 (1H, dd, J = 8.4 and 4.4 Hz, H-8), 4.63 (3H, s, Me-N). Anal. Calcd for

$C_{10}H_7N_5O_2$: C, 52.40; H, 3.08; N, 30.56. Found: C, 52.35; H, 3.05; N, 30.71; and 0.49 g (53%) of unreacted **6c**.

5-Amino-2-methyl-2*H*-triazolo[4,5-*f*]quinoline (4c). To a solution of **7c** (1.18 g, 5.15 mmol) in dry THF (200 mL) 10% palladised charcoal (0.12 g) was added and the mixture hydrogenated under stirring and moderate pressure (3 atm). After filtration of the catalyst and evaporation of the solvent *in vacuo* a crude product (1.2 g) was obtained and recrystallized from ether to give **4c** (0.33 g, 32%); mp 174-176 °C; IR: 3430, 3320, 1630, 1600, 1590 cm^{-1}; UV: λ_{max} 338, 288 sh, 280, 264 infl, 254, 215 nm; ^{1}H-NMR ($CDCl_3$): δ 8.87 (1H, dd, J = 4.4 and 1.8 Hz, H-7), 8.74 (2H, dd, J = 8.2 and 1.8 Hz, H-9), 7.57 (1H, dd, J = 8.2 and 4.4 Hz, H-8), 7.02 (1H, s, H-4), 5.17 (2H, br s, NH_2), 4.44 (3H, s, Me-N). Anal. Calcd for $C_{10}H_9N_5$: C, 60.29; H, 4.55; N, 35.16. Found: C, 60.18; H, 4.67; N, 34.95. From the recrystallization mother liquors compound (**7c**) (0.53 g, 45%) was recovered unchanged.

Reaction of the 8-acetylamino-6-chloro-5-nitroquinoline (8) with ammonia to give 8-acetylamino-6-amino-5-nitroquinoline (9) and 6,8-diamino-5-nitroquinoline (10) - (route a). A solution of **8** (1 g, 3.76 mmol), prepared as described,[8] in dry ethanol (65 mL) saturated with dry gaseous ammonia was heated in a sealed steel vessel at 160 °C under stirring for 3 h. On cooling, a solid was collected to give **9** (0.55 g, 59%); mp 307-310 °C; IR: 3420, 3315, 3250, 2570, 2480, 2370, 1690, 1655, 1580 cm^{-1}; UV: λ_{max} 410, 320, 245 infl, 236 nm; ^{1}H-NMR (DMSO-d_6): δ 10.29 (1H, s, NH-CO), 9.16 (1H, d, J = 8.4 Hz, H-4), 8.60 (1H, d, J = 4 Hz, H-2), 8.55 (2H, s, NH_2), 8.39 (1H, s, H-7), 7.36 (1H, dd, J = 8.4 and 4 Hz, H-3), 2.32 (3H, s, Me); ^{13}C-NMR (DMSO-d_6): δ 170.0 (CO), 149.9 (s), 144.6 (d), 139.9 (s), 133.7 (s), 131.5 (d), 124.8 (d), 124.4 (s), 117.7 (s), 107.3 (d), 24.8 (q). Anal. Calcd for $C_{11}H_{10}N_4O_3$: C, 53.66; H, 4.09; N, 22.76. Found: C, 53.28; H, 3.97; N, 22.47. The mother liquors were evaporated *in vacuo* to give a residue which after chromatography on silica gel column, eluting with a mixture of ether-light petroleum in a 8:2 ratio, gave compound (**10**) (0.15 g, 20%) with mp 203-206 °C (crystallized from acetone); IR: 3440, 3400, 3320, 3275, 1635, 1590 cm^{-1}; UV: λ_{max} 407, 320, 247, 208 nm; ^{1}H-NMR ($CDCl_3$+DMSO-d_6): δ 9.37 (1H, d, J = 8.4 Hz, H-4), 8.50 (1H, d, J = 4.2 Hz, H-2), 8.33 (2H, br s, NH_2), 7.52 (1H, dd, J = 8.4 and 4.2 Hz, H-3), 7.04 (2H, br s, NH_2), 6.33 (1H, s, H-7). Anal. Calcd for $C_9H_8N_4O_2$: C, 52.94; H, 3.95; N, 27.44. Found: C, 53.15; H, 3.84; N, 27.28.

Reaction of the 8-acetylamino-6-chloro-5-nitroquinoline (8) with 98% hydrazine hydrate to give 8-acetylamino-6-aminoquinoline (12) - (route b). This compound was obtained in a similar manner to the above preparation from **8** (1.70 g, 6.4 mmol) and 98% hydrazine hydrate (1.28 g, 39.2 mmol) in dry ethanol (50 mL). Purification of the crude product by flash chromatography on silica gel column using a mixture of ether-acetone (9:1) as eluent, afforded **12** (0.24 g, 19%), mp 153-155 °C; IR: 3420, 3338, 1685, 1640 cm^{-1}; UV: λ_{max} 363, 304, 256, 227, 199 nm; ^{1}H-NMR ($CDCl_3$+DMSO-d_6): δ 9.75 (1H, s, NH-CO), 8.45 (1H, d, J = 4.2 Hz, H-2), 8.28 (1H, d, J = 2 Hz, H-7), 7.84 (1H, d, J = 8.2 Hz, H-4), 7.29 (1H, dd, J = 8.2 and 4.2 Hz, H-3), 6.56 (1H, d, J = 2 Hz, H-5), 4.70 (2H, br s, NH_2), 2.32 (3H, s, Me). Anal. Calcd for $C_{11}H_{11}N_3O$: C, 65.67; H, 5.51; N, 20.88. Found: C, 65.38; H, 5.45; N, 21.07.

Reaction of the 8-acetylamino-6-chloro-5-nitroquinoline (8) with methylhydrazine to give 8-acetylamino-6-methylaminoquinoline (13) - (route c). From **8** (0.88 g, 3.3 mmol) and methylhydrazine (0.46 g, 10 mmol) in dry ethanol (50 mL) in a similar manner to the above preparation, using a mixture of ether-acetone in a 7:3 ratio as eluent, we obtained the compound (**13**) (0.33 g, 46%); mp 188-190 °C; IR: 3340, 1685, 1635 cm^{-1}; UV: λ_{max} 376, 304, 265, 229 nm; ^{1}H-NMR ($CDCl_3$): δ 9.71 (1H, s, NH-CO), 8.45 (1H, d, J = 4.8 Hz, H-2), 8.26 (1H, d, J = 2.4 Hz, H-7), 7.89 (1H, d, J = 7.6 Hz, H-4), 7.28 (1H, dd, J = 7.6 and 4.8 Hz, H-3), 6.35 (1H, d, J = 2.4 Hz, H-5), 4.20 (1H, br s, NH-Me), 2.91 (3H, s, Me-N), 2.32 (3H, s, Me-CO); ^{13}C-NMR ($CDCl_3$): δ 168.8 (C=O), 147.8 (s), 143.3 (d), 134.6 (s), 133.8 (d), 133.7 (s), 129.9 (d), 121.9 (d), 108.2 (d), 96.1 (d), 30.5 (q), 25.1 (q); MS *m/z* 215 (M^+). Anal. Calcd for $C_{12}H_{13}N_3O$: C, 66.95; H, 6.09; N, 19.52. Found: C, 67.07; H, 5.94; N, 19.55.

8-Acetylamino-*N*-nitroso-6-methylaminoquinoline (14). A solution of KNO_3 (0.25 g, 2.47 mmol) in concd sulfuric acid (2 mL) was added dropwise under stirring to a solution of **13** (0.35 g, 1.63 mmol) in concd sulfuric acid (1 mL) externally cooled with an ice bath. Stirring was continued at rt for 1 h. The mixture was made alkaline with concd ammonia solution and the resulting precipitate was collected by filtration (0.32 g). The alkaline mother liquors were then extracted with chlorofom from evaporation of which further solid (0.09 g) was obtained. The combined fractions were submitted to flash chromatography on silica gel column, eluting with ether to give compound (**14**) (0.12 g, 32%); mp 189-191 °C; IR: 3340, 1680, 1630 cm^{-1}; UV: λ_{max} 320 infl, 280, 243, 220 sh nm; ^{1}H-NMR ($CDCl_3$): δ 9.84 (1H, s, NH-CO), 9.07 (1H, d, J = 2 Hz, H-5), 8.81 (1H, d, J = 2.8 Hz, H-2), 8.20 (1H, d, J = 7.8 Hz, H-4), 7.65 (1H, d, J = 2 Hz, H-5), 7.52 (1H, dd, J = 8.2 and 4.2 Hz, H-3), 3.55 (3H, s, Me-N), 2.38 (3H, s, Me-CO); ^{13}C-NMR ($CDCl_3$): δ 169.4 (C=O), 148.8 (d), 139.8 (s), 137.0 (s), 136.9 (d), 135.8 (s), 127.9 (s), 123.1 (d), 109.7 (d), 108.2 (d), 31.1 (q), 24.6 (q); MS *m/z* 244 (M^+). Anal. Calcd for $C_{12}H_{12}N_4O_2$: C, 59.01; H, 4.95; N, 22.94. Found: C, 58.88; H, 5.02; N, 23.10.

Reaction of the 6-chloro-5-nitroquinoline (18) with methylhydrazine to give 3-methyl-3*H*-triazolo[4,5-*f*]quinoline-1-oxide (20) and 2-methyl-2*H*-triazolo[4,5-*f*]quinoline-1-oxide (21). In a sealed steel vessel a mixture of compound (**18**) (2 g, 9.59 mmol) in dry ethanol (35 mL) and methylhydrazine (2.2 g, 47.8 mmol) was heated under stirring at 160 °C for 4 h. On cooling, after removal of the solvent the solid residue was purified by chromatography on silica gel column, eluting with a mixture ether-acetone 9:1, to give compound (**20**) (0.82 g, 42.7%), mp 182-183 °C; IR: 1650, 1630, 1580 cm^{-1}; UV: λ_{max} 306, 265, 221, 203 nm; ^{1}H-NMR ($CDCl_3$): δ 9.34 (1H, dd, J = 8 and 1.8 Hz, H-9), 8.97 (1H, dd, J = 4.6 and 1.8 Hz, H-7), 7.93 (1H, d, J = 9.4 Hz, H-4), 7.80 (1H, d, J = 9.4 Hz, H-5), 7.62 (1H, dd, J = 8 and 4.6 Hz, H-8), 4.33 (3H, s, Me); MS *m/z* 200 (M^+). Anal. Calcd for $C_{10}H_8N_4O$: C, 59.99; H, 4.03; N, 27.99. Found: C, 59.84; H, 3.88; N, 27.92. Further elution of the column with mixtures containing increasing percentage of acetone gave at first an inseparable 1:1 mixture of the compounds (**20**) and (**21**) (0.64 g, 33%) and then compound (**21**) (0.15 g, 8%) was obtained, mp 310-312 °C; IR: 1640, 1630, 1580 cm^{-1}; UV: λ_{max} 332, 254, 242 infl, 208 nm; ^{1}H-NMR ($CDCl_3$): δ 9.65 (1H, dd, J = 8.4 and 1.8 Hz, H-9), 9.03 (1H, dd, J = 4.6 and 1.8 Hz, H-7), 8.19 (1H, d, J = 9.4 Hz, H-

4), 7.72 (1H, dd, J = 8 and 4.6 Hz, H-8), 7.71 (1H, d, J = 9.4 Hz, H-5), 4.22 (3H, s, Me); MS *m/z* 200 (M^+). Anal. Calcd for $C_{10}H_8N_4O$: C, 59.99; H, 4.03; N, 27.99. Found: C, 59.70; H, 3.94; N, 27.71.

Reaction of the 6-chloro-7-nitroquinoline (19) with methylhydrazine to give 6-chloro-7-aminoquinoline (22). *In a similar manner as for compound* (**18**), *from* **19** *(1.46 g, 7 mmol) and* methylhydrazine (2.2 g, 47.8 mmol) by the work-up of the reaction mixture (chromatography on silica gel column, ether-acetone 9:1 mixture as eluent) we obtained compound (**22**) (0.76 g, 60.8%), mp 147-149 °C; IR: 3460, 3300, 3140, 1640, 1610, 1590 cm^{-1}; UV: λ_{max} 358, 276, 245, 213 nm; ^{1}H-NMR ($CDCl_3$): δ 8.75 (1H, dd, J = 4.2 and 1 Hz, H-2), 7.92 (1H, dd, J = 8.2 and 1 Hz, H-4), 7.74 (1H, s, H-8), 7.33 (1H, s, H-5), 7.15 (1H, dd, J = 8.2 and 4.2 Hz, H-3), 4.50 (1H, br s, NH_2); MS *m/z* 178 (M^+). Anal. Calcd for $C_9H_7N_2Cl$: C, 60.52; H, 3.95; N, 15.68; Cl, 19.85. Found: C, 60.22; H, 3.89; N, 15.37; Cl, 19.58.

Reaction of the 3-chloro-4-nitroacetanilide (15) with methylhydrazine to give 4-amino-3-chloroacetanilide (16) and 5-acetylamino-1-methyl-1*H*-benzotriazole (17). Compound (**15**) (1 g, 4.66 mmol) was reacted with methylhydrazine (0.7 g, 15.2 mmol) in ethanol (20 mL) as above. The work-up of the reaction mixture (chromatography on silica gel column, ether-light petroleum 7:3 mixture as eluent) gave in the order: compound (**16**) (0.30 g, 35%), mp 105-107 °C identical to that described in the literature;[12] MS *m/z* 186 (M^+); compound (**17**) (0.21 g, 24%), mp 176-177 °C (from ether) identical to that previously described;[11] MS *m/z* 190 (M^+).

Reaction of the 2-chloronitrobenzene (23) with methylhydrazine to give 2-cloroaniline (24), 1-methyl-1*H*-benzotriazole (25), 1-methyl-1*H*-benzotriazole-*N*-oxide (26) and 2-methylaminonitrobenzene (27). Compound (**23**) (2 g, 12.7 mmol) dissolved in dry ethanol (40 mL) reacted with methylhydrazine (1.40 g, 30.4 mmol) in an identical manner as for the preceding cases. The work-up of the reaction mixture oily residue (flash chromatography on silica gel column, ether-light petroleum 7:3 as eluent) gave in the order: starting **23** (0.44 g, 22%); compound (**24**) (0.32 g, 20%) identical to that commercially available; compound (**25**) (0.22 g, 12%), MS *m/z* 133 (M^+), identical to that previously described;[14] and finally traces of compounds (**26**),[15] MS *m/z* 149 (M^+), and (**27**),[16] MS *m/s* 152 (M^+).

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Received, 29th June, 1998