Polycondensed Nitrogen Heterocycles. Part 25. Aminopyrrolo[1,2-*f*]phenanthridines by Decomposition of 2-(3-Azidophenyl)-1-arylpyrroles [1]

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Acid catalyzed decomposition of the azido derivatives **4a-c** gave rise to amino-hydroxy-phenylpyrroles of type **7** and **8** upon hydrolysis of the intermediate aryl nitrenium ions, together with the hydrogen abstraction compounds of type **3**. The aminopyrrolo[1,2-*f*]phenanthridines **10**, **11**, and **12** were obtained by treatment with TFMSA of the azide **4d** in which the ring being attacked was made more nucleophilic by the introduction of the methoxy group.

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Pyrrolo[1,2-*f*]phenanthridine derivatives, structurally related to the anticancer drug ethidium bromide, have been one of the targets of our research projects on polycondensed nitrogen heterocycles either for their synthetic and structural interest and for their potential biological activity. In particular this aspect is assuming increasing interest also in the light of the importance of the phenanthridine moiety as an effective pharmacophore in classes of DNA-intercalating antitumor agents [2].

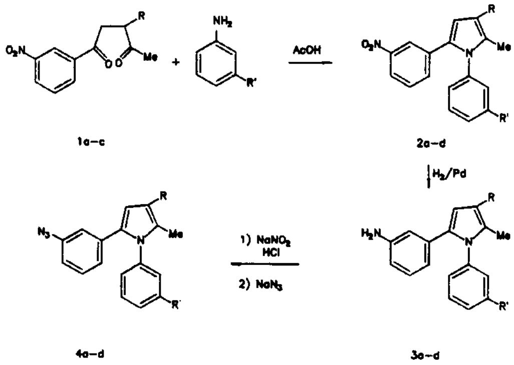
We have already reported the synthesis of pyrrolo[1,2-*f*]phenanthridines by a Pschorr-type cyclization of 1-(2-aminophenyl)-2-aryl- or 2-(2-aminophenyl)-1-arylpyrroles and some preliminary results on their activity against leukemia P 388 cells [3,4]. However the synthetic approach that implied the use of 2-aryl-1-(2-aminophenyl)pyrroles as starting material did not allow the isolation of pyrrolophenanthridine derivatives in preparative yield, since several undesired by-products were always obtained.

Recently a new method to prepare pyrrolo[1,2-*f*]phenanthridine, by electrochemical and/or photochemical cyclization of 1-phenyl-2-(2-chlorophenyl)pyrrole, was reported, but limited to the parent compound [5].

Considering that all these synthetic methods mainly involve radical pathways and that only in the Pschorr-type cyclization ionic intermediates are seldom involved, now we oriented our proposed synthesis towards a cyclocondensation reaction that could proceed with a definitely ionic mechanism. In fact it is well acknowledged that the intramolecular cyclization of arylnitrenium ions, generated from the acid catalyzed decomposition of azide or hydroxylamine derivatives, proceed *via* the intermediacy of a π-carbocation [6,7]. This remote functionalization of arylnitrenium ions has been already successful for the formation of phenanthrene [8] and phenanthridine derivatives [9]. Therefore azidophenyl compounds of type **4** could be suitable starting materials for the synthesis of pyrrolo[1,2-*f*]phenanthridines.

To this purpose 2-(3-azidophenyl)-1-arylpyrroles **4a-c** were prepared according to the Scheme 1. The reaction of 1,4-diketones **1a-c** with aniline in acetic acid gave good yields of the 2-(3-nitrophenyl)pyrroles **2a-c**. Catalytic reduction of the nitro group over palladium on charcoal led to the corresponding aminophenyl derivatives **3a-c** in 77-88% yields. These compounds were diazotized in hydrochloric acid and the diazonium salts were directly reacted with an excess of sodium azide to give the 2-(3-azidophenyl)pyrroles **4a-c** in good to excellent yields. Derivatives **4** were easily identified by the ir spectra which showed strong absorption bands at 2110-2103 cm^{-1}, and by mass spectrometry. In fact all the azides gave the expected molecular ions although, in the case of compound **4a**, only if the spectrum was measured at low voltage (7 eV). The loss of nitrogen, peculiar of aromatic azides, was observed only in the case of derivatives **4a** and **4c**.

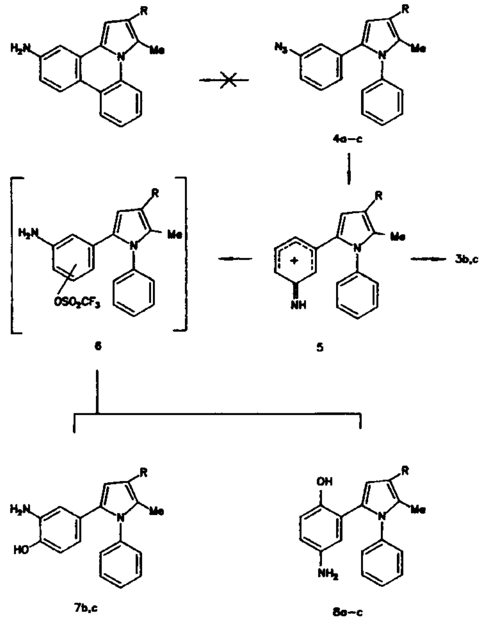
Scheme 1



a R = R' = H; **b** R = COMe, R' = H; **c** R = COOEt, R' = H; **d** R = COOEt, R' = OMe

2-(3-Azidophenyl)-1-phenylpyrroles **4a-c** in dichloromethane solution were decomposed by treatment with 2 equivalents of trifluoromethanesulfonic acid (TFMSA) from 0° to room temperature. Isolation of the products was difficult because of extensive formation of tars especially in the case of azide **4a**. From the reaction mixture it was impossible to isolate the expected aminopyrrolo[1,2-*f*]phenanthridines but together with the 2-(3-aminophenyl)-1-phenylpyrroles **3b,c** (20-11% yield), 2-(3-amino-4-hydroxyphenyl)-1-phenylpyrroles **7b,c** (7-15% yield) and 2-(5-amino-2-hydroxyphenyl)-1-phenylpyrroles **8a-c** (10-36% yield) were obtained.

Scheme 2

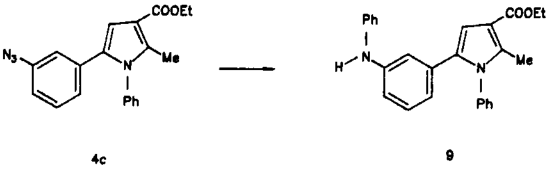


a R = H; b R = COMe; c R = COOEt

It is likely that protonation of the pyrrole moiety by the strong acid deactivates the aromatic nucleus in the 1 position so that triflate competes with the phenyl for the arylnitrenium ion to give intermediates of type **6** and therefore the intramolecular cyclization to pyrrolo[1,2-*f*]phenanthridine is not observed. The hydroxyphenyl compounds **7** and **8** could be originated from hydrolysis of the intermediate triflate **6** during the workup even if reaction with water can not be excluded, whereas the amino compounds **3** arise from hydrogen-abstraction.

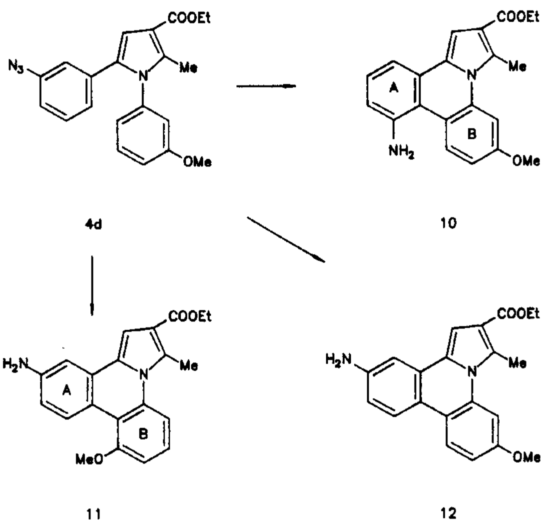
The poor nucleophilic character of the phenyl in the 1 position of the pyrrole ring shown in the decomposition in TFMSA/dichloromethane, results more evident in benzene, in which compound **9** was the only isolated product (34% yield) upon treatment with TFMSA. In fact in this case intermolecular *N*-substitution by the nitrenium ion is the preferred reaction pathway.

Scheme 3



In the light of these experimental results the introduction of suitable substituents, such as a methoxy group, in the 1-phenyl ring could favour the intramolecular cyclization reaction. Therefore the azide **4d** was prepared and decomposed in dichloromethane with 2 equivalents of TFMSA, from 0° to room temperature. The reaction was complete in 8 hours and the overall yield in pyrrolo[1,2-*f*]phenanthridine derivatives was 90%.

Scheme 4



As expected in this acid catalyzed decomposition in which the ring being attacked was made more nucleophilic, intermolecular side-reactions were not observed and the intermediate arylnitrenium ion analogous of **5** exclusively reacts to give the title compounds **10, 11** and **12**. Actually derivative **11** was always obtained in mixture with isomer **12** and attempts to obtain **11** as pure sample failed. A gc/ms analysis showed that compound **11** had a retention time of 16.386 minutes and compound **12** had a retention time of 16.708 minutes. The ^{1}H and ^{13}C nmr data for compound **11** were obtained by subtracting the signals due to compound **12** from the spectra of the mixture.

Steric effects by the substituents *ortho* to the positions of attack do not appear to be relevant with this aryl π-carbocation since all the possible isomeric pyrrolo[1,2-*f*]phenanthridines were identified with the sole exception of the 8,9-disubstituted derivative in which steric hindrance to planarity in the intermediate could be expected. The correct structure of the three isomers was assigned on the basis of the spectral data. By comparison of the ^{1}H nmr spectra the structure of derivative **12** was easily recognized from the chemical shift and the multiplicity of the signals due to the protons in positions 5, 7, 8, 9, 10, and 12, whereas the difference between compounds **10** and **11** is not straightforward. In fact the pattern of signals observed in both ^{1}H nmr spectra could fit either derivative

10 or **11** since the electronic effects that the amino and methoxy substituents exert on the neighbouring protons are quite similar and therefore the signals due to the protons of the ring A and B in compound **11** could be misleadingly attributed to the protons of ring B and A respectively in derivative **10**. However the correct assignment was achieved by comparison of these spectra with ^{1}H nmr data of other pyrrolo[1,2-*f*]phenanthridines for which the unambiguous attribution of all the resonances has already been made by us [4,10]. In fact by using additivity rules for the effect of substituents, a good agreement between the expected and the observed chemical shifts for all the protons was found.

In conclusion this synthetic method involving the acid decomposition of 2-(3-azidophenyl)-1-arylpyrroles is suitable to prepare aminopyrrolo[1,2-*f*]phenanthridine even if only when there is an activating group, which is finally found in 6 or 8 position of the cyclized products. But it is out of doubt that this synthetic approach has the advantage of functionalizing the phenanthridine moiety with amino groups (and also methoxy groups) in positions suitable for a better intercalation with DNA [11].

The results of DNA-binding studies and of the screening tests for the antitumor activity will be reported elsewhere.

EXPERIMENTAL

All melting points were taken on a Buchi-Tottoli capillary apparatus and are uncorrected; ir spectra were determined in bromoform with a Jasco FT/IR 5300 spectrophotometer; ^{1}H and ^{13}C nmr spectra were measured at 250 and 62.8 MHz respectively in DMSO solution, unless otherwise specified, using a Bruker AC-E series 250 MHz spectrometer (TMS as internal reference); mass spectra were obtained with a JEOL JMS-01 SG-2 double focusing mass spectrometer operating with an electron beam energy of 75 eV and 10 Kv accelerating voltage and with a HP 5890 Series II and HP 5989A-GC/MS apparatus. Column chromatography was performed with Merck silica gel 230-400 Mesh ASTM.

Preparation of 1-(3-Nitrophenacyl)-3-R-1,4-pentandiones **1a-c**.

To a solution of sodium ethylate (80 mmoles) in absolute ethanol, acetylacetone or ethyl acetoacetate (80 mmoles) was added. After 20 minutes, 3-nitrophenacyl bromide (80 mmoles) was added in small portions with stirring and cooling (ice bath). The reaction mixture was allowed to room temperature and stirred for 2 days. Evaporation of the solvent under reduced pressure gave a residue which was shaken with water and extracted with dichloromethane. The organic layer was dried over anhydrous sodium sulphate and evaporated *in vacuo*. The so obtained viscous oil was chromatographed using dichloromethane as eluant. In the case of acetylacetone, the first product eluted was compound **1a** (R = H) which was recrystallized from ethanol (24%) mp 58°; ir: 1720 and 1700 (CO) cm^{-1}; ^{1}H nmr: δ 2.26 (s, 3H, CH_3), 2.89 (t, J = 4.8 Hz, 2H, CH_2), 3.33 (t, J = 4.8 Hz, 2H, CH_2), 7.64-8.72 (m, 4H, C_6H_4).

Anal. Calcd. for $C_{11}H_{11}NO_4$: C, 59.72; H, 5.01; N, 6.33. Found: C, 59.78; H, 5.04; N, 6.20.

Further elution gave compound **1b** (R = $COCH_3$) which was recrystallized from ethanol (43%) mp 76-77°; ir: 1725, 1700 and 1690 (CO) cm^{-1}, the ^{1}H nmr spectrum was in agreement with the two tautomeric structures: $-CH_2-(COCH_3)CH-COCH_3$ (A) $\leftrightharpoons$ $-CH_2-(COCH_3)C=C(OH)CH_3$ (B) in equilibrium in DMSO: δ 2.03 (s, 3H, $COCH_3$ B), 2.29 (s, 6H, 2 x CH_3 A), 3.24 (s, 3H, $C(OH)CH_3$ B), 3.65 (s, 2H, CH_2 B), 3.68 (d, J = 6.3 Hz, 2H, CH_2 A), 4.30 (s, 1H, exchangeable OH B), 4.45 (t, J = 6.3 Hz, 1H, CH A), 7.76-8.70 (m, 4H, C_6H_4 A and C_6H_4 B).

Anal. Calcd. for $C_{13}H_{13}NO_5$: C, 59.31; H, 4.98; N, 5.32. Found: C, 59.36; H, 5.03; N, 5.30.

If the reaction is carried out in refluxing ethanol the yields of compounds **1a** and **1b** are 12% and 58% respectively.

Compound **1c** (R = COOEt) was recrystallized from ethanol (73%) mp 66-67°; ir: 1735, 1715 and 1695 (CO) cm^{-1}; ^{1}H nmr: δ 1.32 (t, J = 7.5 Hz, 3H, CH_3), 2.48 (s, 3H, CH_3), 3.62 (d, J = 7.2 Hz, 2H, CH_2), 4.18 (q, J = 7.5 Hz, 2H, CH_2), 4.28 (t, J = 7.2 Hz, 1H, CH), 7.72-8.84 (4H, m, C_6H_4).

Anal. Calcd. for $C_{14}H_{15}NO_6$: C, 57.33; H, 5.16; N, 4.78. Found: C, 57.52; H, 5.09; N, 4.72.

Preparation of 5-Methyl-2-(3-nitrophenyl)-4-R-1-(3-R′-phenyl)pyrroles **2a-d**.

A solution of diketones **1a-c** (60 mmoles) and aniline or 3-methoxyaniline (60 mmoles) in acetic acid was refluxed for 3 hours. After cooling, the resultant brown solution was poured onto crushed ice. The precipitate was collected, air dried and chromatographed (eluant dichloromethane).

Compound **2a** (R = R′ = H) was recrystallized from ethanol (48%) mp 114-115°; ir: 1530 (NO_2) cm^{-1}; ^{1}H nmr: δ 2.09 (s, 3H, CH_3), 6.14 (d, J = 3.6 Hz, 1H, CH), 6.58 (d, J = 3.6 Hz, 1H, CH), 7.20-7.96 (m, 9H, C_6H_4 and C_6H_5); ms: m/z 278.

Anal. Calcd. for $C_{17}H_{14}N_2O_2$: C, 73.36; H, 5.07; N, 10.07. Found: C, 72.95; H, 4.84; N, 9.98.

Compound **2b** (R = $COCH_3$, R′ = H) was recrystallized from ethanol (60%) mp 143°; ir: 1660 (CO) cm^{-1}; ^{1}H nmr: δ 2.44 (s, 3H, CH_3), 2.52 (s, 3H, CH_3), 6.82 (s, 1H, CH), 7.04-8.04 (m, 9H, C_6H_4 and C_6H_5); ms: m/z 320.

Anal. Calcd. for $C_{19}H_{16}N_2O_3$: C, 71.24; H, 5.03; N, 8.75. Found: C, 70.75; H, 4.95; N, 8.61.

Compound **2c** (R = COOEt, R′ = H) was recrystallized from ethanol (75%) mp 99-100°; ir: 1695 (CO) cm^{-1}; ^{1}H nmr: δ 1.40 (t, J = 7.2 Hz, 3H, CH_3), 2.42 (s, 3H, CH_3), 4.36 (q, J = 7.2 Hz, 2H, CH_2), 6.98 (s, 1H, CH), 7.10-8.10 (m, 9H, C_6H_4 and C_6H_5); ms: m/z 350.

Anal. Calcd. for $C_{20}H_{18}N_2O_4$: C, 68.56; H, 5.18; N, 8.00. Found: C, 68.42; H, 5.35; N, 7.97.

Compound **2d** (R = COOEt, R′ = OCH_3) was recrystallized from ethanol (77%) mp 88-90°; 1695 (CO) cm^{-1}; ^{1}H nmr: δ 1.38 (t, J = 7.2 Hz, 3H, CH_3), 2.44 (s, 3H, CH_3), 3.76 (s, 3H, CH_3), 4.33 (q, J = 7.2 Hz, 2H, CH_2), 6.73 (s, 1H, CH), 6.81-7.94 (m, 8H, 2 x C_6H_4); ms: m/z 380.

Anal. Calcd. for $C_{21}H_{20}N_2O_5$: C, 66.30; H, 5.30; N, 7.37. Found: C, 66.46; H, 5.25; N, 7.50.

Preparation of 2-(3-Aminophenyl)-5-methyl-4-R-1-(3-R′-phenyl)pyrroles **3a-d**.

A solution of nitro derivatives **2a-d** (10 mmoles) in ethanol was reduced overnight over 10% Pd on charcoal in a Parr apparatus at 50 psi at room temperature. Removal of the catalyst and evaporation of the solvent under reduced pressure gave the amino derivatives **3a-d**.

Compound **3a** (R = R′ = H) was recrystallized from ethanol

(88%) mp 92-93°; ir: 3440 and 3360 (NH_2) cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.11 (s, 3H, CH_3), 3.42 (broad s, 2H, NH_2), 6.06 (d, J = 3.5 Hz, 1H, CH), 6.32 (d, J = 3.5 Hz, 1H, CH), 6.42-7.35 (m, 9H, C_6H_4 and C_6H_5); ms: m/z 248.

Anal. Calcd. for $C_{17}H_{16}N_2$: C, 82.22; H, 6.50; N, 11.28. Found: C, 82.00; H, 6.47; N, 11.04.

Compound **3b** (R = $COCH_3$, R' = H) was recrystallized from ethanol (77%) mp 139-140°; ir: 3455 and 3350 (NH_2), 1640 (CO) cm^{-1}; ^1H nmr: δ 2.40 (s, 3H, CH_3), 2.48 (s, 3H, CH_3), 3.52 (broad s, 2H, NH_2), 6.68 (s, 1H, CH), 6.28-7.44 (m, 9H, C_6H_4 and C_6H_5); ms: m/z 290.

Anal. Calcd. for $C_{19}H_{18}N_2O$: C, 78.59; H, 6.25; N, 9.65. Found: C, 78.22; H, 6.45; N, 9.51.

Compound **3c** (R = COOEt, R' = H) was recrystallized from ethanol (70%) mp 148-149°; ir: 3465 and 3365 (NH_2), 1685 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.40 (t, J = 7.2 Hz, 3H, CH_3), 2.40 (s, 3H, CH_3), 3.48 (broad s, 2H, NH_2), 4.36 (q, J = 7.2 Hz, 2H, CH_2), 6.76 (s, 1H, CH), 6.28-7.44 (m, 9H, C_6H_4 and C_6H_5); ms: m/z 320.

Anal. Calcd. for $C_{20}H_{20}N_2O_2$: C, 74.97; H, 6.29; N, 8.74. Found: C, 74.88; H, 6.46; N, 8.70.

Compound **3d** (R = COOEt, R' = OCH_3) was recrystallized from ethanol (85%) mp 129-131°; ir: 3435 and 3353 (NH_2), 1692 (CO) cm^{-1}; ^1H nmr: δ 1.35 (t, J = 7.1 Hz, 3H, CH_3), 2.39 (s, 3H, CH_3), 3.23 (broad s, 2H, NH_2), 3.70 (s, 3H, CH_3), 4.29 (q, J = 7.1 Hz, 2H, CH_2), 6.74 (s, 1H, CH), 6.41-7.29 (m, 8H, 2 x C_6H_4); ms: m/z 350.

Anal. Calcd. for $C_{21}H_{22}N_2O_3$: C, 71.98; H, 6.33; N, 8.00. Found: C, 72.09; H, 6.55; N, 7.85.

Preparation of 2-(3-Azidophenyl)-5-methyl-4-R-1-(3-R'-phenyl)pyrroles **4a-d**.

To a suspension of the amines **3a-d** (5 mmoles) in water (30 ml) hydrochloric acid (36%, 1.4 ml) was added and the mixture was diazotized with sodium nitrite (5 mmoles) in water (2 ml) at 0-5° (in the case of compound **4d** the reaction was carried out at 30°). After 15 minutes sodium azide (10 mmoles) in water (5 ml) was added dropwise at 0-5° and the mixture was stirred for further 24 hours at room temperature. The orange precipitate was filtered off, air dried and recrystallized from ethanol.

Compound **4a** (R = R' = H) (53%) had mp 67°; ir: 2104 (N_3) cm^{-1}; ^1H nmr: δ 2.10 (s, 3H, CH_3), 6.07 (d, J = 3.5 Hz, 1H, CH), 6.38 (d, J = 3.5 Hz, 1H, CH), 6.64-7.37 (m, 9H, C_6H_5 and C_6H_4); ms: m/z 274 (M^+), 246 (M^+-N_2).

Anal. Calcd. for $C_{17}H_{14}N_4$: C, 74.43; H, 5.14; N, 20.43. Found: C, 74.80; H, 5.19; N, 19.95.

Compound **4b** (R = $COCH_3$, R' = H) (45%) had mp 88-89°; ir: 2110 (N_3), 1653 (CO) cm^{-1}; ^1H nmr: δ 2.44 (s, 3H, CH_3), 2.52 (s, 3H, CH_3), 6.76 (s, 1H, CH), 6.60-7.48 (m, 9H, C_6H_4 and C_6H_5); ms: m/z 316.

Anal. Calcd. for $C_{19}H_{16}N_4O$: C, 72.13; H, 5.10; N, 17.71. Found: C, 71.94; H, 5.15; N, 17.64.

Compound **4c** (R = COOEt, R' = H) (87%) had mp 105-106°; ir: 2103 (N_3), 1694 (CO) cm^{-1}; ^1H nmr: δ 1.40 (t, J = 7.2 Hz, 3H, CH_3), 2.42 (s, 3H, CH_3), 4.36 (q, J = 7.2 Hz, 2H, CH_2), 6.88 (s, 1H, CH), 6.70-7.52 (m, 9H, C_6H_4 and C_6H_5); ms: m/z 346 (M^+), 318 (M^+-N_2).

Anal. Calcd. for $C_{20}H_{18}N_4O_2$: C, 69.35; H, 5.24; N, 16.18. Found: C, 69.42; H, 5.28; N, 16.01.

Compound **4d** (R = COOEt, R' = OCH_3) (72%) mp 50°; ir: 2105 (N_3), 1701 (CO), cm^{-1}; ^1H nmr: δ 1.39 (t, J = 7.2 Hz, 3H, CH_3), 2.43 (s, 3H, CH_3), 3.76 (s, 3H, CH_3), 4.34 (q, J = 7.2 Hz, 2H, CH_2), 6.85 (s, 1H, CH), 6.68-7.36 (m, 8H, 2 x C_6H_4); ms: m/z 376.

Anal. Calcd. for $C_{21}H_{20}N_4O_3$: C, 67.01; H, 5.36; N, 14.89. Found: C, 67.19; H, 5.41; N, 14.68.

Decomposition of Azido Compounds **4a-c** in TFMSA.

To a solution of azido derivatives **4a-c** (3 mmoles) in absolute dichloromethane (20 ml) was added dropwise TFMSA (6 mmoles) at 0°. The reactants were allowed to room temperature and stirred for further 24 hours. The reaction mixture was evaporated under reduced pressure and the residue was shaken with water. It was then extracted with dichloromethane and the organic layer was dried over sodium sulphate and evaporated under reduced pressure to give a brown residue which was chromatographed (eluant dichloromethane).

The only isolable product obtained from the decomposition of the azide **4a** was compound **8a** (R = H) (10%), mp 145°; ir: 3464 and 3371 (NH_2), 2900 (broad OH) cm^{-1}; ^1H nmr: δ 2.07 (s, 3H, CH_3), 3.37 (broad s, 1H, OH), 5.36 (broad s, 2H, NH_2), 6.06 (d, J = 3.35 Hz, 1H, pyrrole H-4), 6.21 (d, J = 3.35 Hz, 1H, pyrrole H-3), 6.31 (d, J = 2.8 Hz, 1H, C_6H_3, H-3), 6.40 (dd, J = 8.8 Hz, J = 2.8 Hz, 1H, C_6H_3, H-4), 6.86 (d, J = 8.8 Hz, 1H, C_6H_3, H-5), 7.12 (dd, J = 6.9 Hz, J = 1.6 Hz, 2H, C_6H_5, H-2 and H-6), 7.28-7.42 (m, 3H, C_6H_5, H-3, H-4 and H-5); ^{13}C nmr: ppm 13.4 (q), 107.9 (d), 111.1 (d), 113.0 (d), 116.2 (d), 120.8 (s), 122.1 (d), 127.1 (s), 127.5 (d), 127.8 (d), 129.1 (d), 131.1 (s), 137.1 (s), 138.5 (s), 148.7 (s); ms: m/z 264.

Anal. Calcd. for $C_{17}H_{16}N_2O$: C, 77.25; H, 6.10; N, 10.60. Found: C, 77.10; H, 5.91; N, 10.78.

In the case of the decomposition of the azides **4b-c**, the first products eluted were derivatives of type **7**.

Compound **7b** (R = $COCH_3$) had mp 158° (7%); ir: 3424 and 3356 (NH_2), 3260 (broad OH), 1640 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.41 (s, 3H, CH_3), 2.49 (s, 3H, CH_3), 4.78 (very broad, 3H, NH_2 and OH), 6.51 (dd, J = 8.1 Hz, J = 1.7 Hz, 1H, C_6H_3, H-6), 6.77 (s, 1H, pyrrole H-3), 6.99 (d, J = 8.1 Hz, 1H, C_6H_3, H-5), 7.01 (d, J = 1.7 Hz, 1H, C_6H_3, H-2), 7.13 (dd, J = 6.3 Hz, J = 1.7 Hz, 2H, C_6H_5, H-2 and H-6), 7.39-7.48 (m, 3H, C_6H_5, H-3, H-4 and H-5); ^{13}C nmr (deuteriochloroform): ppm 13.0 (q), 28.6 (q), 111.6 (d), 111.9 (s), 121.5 (d), 121.7 (s), 125.7 (s), 128.3 (d), 128.8 (d), 129.1 (d), 129.5 (d), 129.7 (d), 133.5 (s), 137.3 (s), 138.5 (s), 148.0 (s), 195.1 (s), ms: m/z 306.

Anal. Calcd. for $C_{19}H_{18}N_2O_2$: C, 74.49; H, 5.92; N, 9.15. Found: C, 74.28; H, 5.85; N, 9.34.

Compound **7c** (R = COOEt) was recrystallized from ethanol (15%) mp 144°; ir: 3430 and 3360 (NH_2), 3264 (broad OH), 1686 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.37 (t, J = 7.1 Hz, 3H, CH_3), 2.39 (s, 3H, CH_3), 4.01 (very broad, 3H, NH_2 and OH), 4.32 (q, J = 7.1 Hz, 2H, CH_2), 6.38 (dd, J = 8.6 Hz, J = 2.2 Hz, 1H, C_6H_3, H-6), 6.64 (d, J = 2.2 Hz, 1H, C_6H_3, H-2), 6.80 (s, 1H, pyrrole H-3), 6.92 (d, J = 8.6 Hz, 1H, C_6H_3, H-5), 7.13 (dd, J = 7.6 Hz, J = 2.2 Hz, 2H, C_6H_5, H-2 and H-6), 7.37-7.44 (m, 3H, C_6H_5, H-3, H-4 and H-5); ^{13}C nmr (deuteriochloroform): ppm 12.5 (q), 14.6 (q), 59.7 (t), 111.1 (d), 113.1 (s), 118.3 (d), 120.3 (s), 121.1 (s), 121.5 (d), 128.4 (d), 128.6 (d), 129.5 (d), 129.7 (d), 131.9 (s), 133.5 (s), 137.7 (s), 138.8 (s), 165.4 (s); ms: m/z 336.

Anal. Calcd. for $C_{20}H_{20}N_2O_3$: C, 71.41; H, 5.99; N, 8.33. Found: C, 71.60; H, 6.07; N, 8.53.

Further elution gave derivatives of type **8**.

Compound **8b** (R = $COCH_3$) was recrystallized from ethanol (30%), mp 140° dec; ir: 3468 and 3370 (NH_2), 3252 (broad OH), 1645 (CO) cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 2.45 (s, 3H, CH_3), 2.51 (s, 3H, CH_3), 3.65 (very broad s, 3H, NH_2 and OH), 6.32 (d, J = 2.9 Hz, 1H, C_6H_3, H-6), 6.50 (dd, J = 8.9 Hz, J = 2.9 Hz, 1H, C_6H_3, H-4), 6.82 (s, 1H, pyrrole H-3), 6.94 (d, J = 8.9 Hz, 1H, C_6H_3, H-3), 7.16 (dd, J = 5.1 Hz, J = 1.8 Hz, 2H, C_6H_5, H-2 and H-6), 7.37-7.42 (m, 3H, C_6H_5, H-3, H-4 and H-5); ^{13}C nmr (deuteriochloroform): ppm 13.1 (q), 28.7 (q), 113.5 (d), 114.6 (d), 117.7 (d), 121.6 (s), 122.5 (d), 126.4 (s), 127.3 (s), 128.1 (d), 128.3 (d), 129.0 (d), 137.1 (s), 137.8 (s), 139.3 (s), 145.8 (s), 195.2 (s); ms: m/z 306.

Anal. Calcd. for $C_{19}H_{18}N_2O_2$: C, 74.49; H, 5.92; N, 9.15. Found: C, 74.35; H, 5.98; N, 9.30.

Compound **8c** (R = COOEt) was recrystallized from ethanol (36%), mp 152°; ir: 3476 and 3380 (NH_2), 3200 (broad OH), 1676 (CO) cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.36 (t, J = 7.1 Hz, 3H, CH_3), 2.41 (s, 3H, CH_3), 4.15 (broad s, 3H, NH_2 and OH), 4.30 (q, J = 7.1 Hz, 2H, CH_2), 6.44 (d, J = 2.8 Hz, 1H, C_6H_3, H-6), 6.52 (dd, J = 8.6 Hz, J = 2.8 Hz, 1H, C_6H_3, H-4), 6.84 (s, 1H, pyrrole H-3), 6.88 (d, J = 8.6 Hz, 1H, C_6H_3, H-3), 7.12 (dd, J = 7.7 Hz, J = 2.0 Hz, 2H, C_6H_5, H-2 and H-6), 7.31-7.36 (m, 3H, C_6H_5, H-3, H-4 and H-5); ^{13}C nmr (deuteriochloroform): ppm 12.7 (q), 14.5 (q), 59.6 (t), 113.1 (s), 113.2 (d), 115.2 (d), 115.9 (s), 118.4 (d), 122.5 (d), 126.8 (s), 127.6 (s), 128.2 (d), 128.2 (d), 128.9 (d), 137.4 (s), 138.4 (s), 139.6 (s), 165.0 (s); ms: m/z 336.

Anal. Calcd. for $C_{20}H_{20}N_2O_3$: C, 71.41; H, 5.99; N, 8.33. Found: C, 71.55; H, 6.12; N, 8.15.

Further elution gave the amino compounds **3b** (20%) and **3c** (11%), identical (mp and ir) with pure samples.

Decomposition of Azido Compound **4c** in TFMSA/Benzene.

To a solution of azido derivative **4c** (2 mmoles) in absolute benzene (50 ml) was added dropwise TFMSA (4 mmoles) at 0°. The reactants were allowed to room temperature and stirred for further 24 hours. The reaction mixture was evaporated under reduced pressure and the residue was chromatographed (eluant dichloromethane) to give 2-(3-anilinophenyl)-4-carbethoxy-5-methyl-1-phenylpyrrole (**9**) which was recrystallized from ethanol (34%), mp 124°; ir: 3416 (NH), 1690 (CO) cm^{-1}; ^{1}H nmr: δ 1.28 (t, J = 7.0 Hz, 3H, CH_3), 2.30 (s, 3H, CH_3), 4.22 (q, J = 7.0 Hz, 2H, CH_2), 6.63 (s, 1H, pyrrole H-3), 6.57-6.82 (m, 6H, ArH), 7.04-7.27 (m, 5H, ArH), 7.50-7.52 (m, 3H, ArH), 8.09 (s, 1H, NH); ms: m/z 396.

Anal. Calcd. for $C_{26}H_{24}N_2O_2$: C, 78.76; H, 6.10; N, 7.07. Found: C, 78.65; H, 5.98; N, 7.10.

Decomposition of Azido Compound **4d** in TFMSA.

To a solution of azido derivative **4d** (3 mmoles) in absolute dichloromethane (20 ml) was added dropwise with stirring TFMSA (6 mmoles) at 0°. The reactants were allowed to reach room temperature and stirred for further 8 hours. The reaction mixture was evaporated under reduced pressure and the residue was shaken with water. It was then extracted with dichloromethane and the organic layer was dried over sodium sulphate and evaporated under reduced pressure to give a brown residue which was chromatographed (eluant dichloromethane). The first compound eluted was 9-amino-2-carbethoxy-6-methoxy-3-methylpyrrolo[1,2-*f*]phenantridine (**10**), which was recrystallized from ethanol (15%), mp 171°; ir: 3416 and 3335 (NH_2), 1694 (CO) cm^{-1}; ^{1}H nmr: [12] δ 1.33 (t, J = 7.1 Hz, 3H, CH_3), 3.15 (s, 3H, CH_3), 3.91 (s, 3H, CH_3), 4.29 (q, J = 7.1 Hz, 2H, CH_2), 5.49 (s, 2H, NH_2), 6.83 (d, J = 7.8 Hz, 1H, H-10), 7.06 (dd, J = 9.1 Hz, J = 2.4 Hz, 1H, H-7), 7.14 (t, J = 7.8 Hz, 1H, H-11), 7.22 (s, 1H, H-1), 7.40 (d, J = 7.8 Hz, 1H, H-12), 7.71 (d, J = 2.4 Hz, 1H, H-5), 9.06 (d, J = 9.1 Hz, 1H, H-8); ^{13}C nmr: ppm 14.3 (q), 15.6 (q), 55.3 (q), 60.1 (t), 102.8 (d), 103.4 (d), 110.8 (d), 111.4 (d), 112.5 (s), 115.2 (d), 115.9 (s), 117.8 (s), 126.4 (s), 127.1 (s), 127.8 (d), 129.6 (d), 132.0 (s), 133.8 (s), 145.5 (s), 157.5 (s), 164.6 (s); ms: m/z 348.

Anal. Calcd. for $C_{21}H_{20}N_2O_3$: C, 72.39; H, 5.79; N, 8.04. Found: C, 72.50; H, 5.89; N, 8.10.

The second fraction eluted (25%) was a 1.5:1 mixture of 11-amino-2-carbethoxy-8-methoxy-3-methylpyrrolo[1,2-*f*]phenantridine (**11**), and compound **12**; ir: 3466 and 3353 (NH_2), 1692 (CO) cm^{-1}; ^{1}H nmr: [12] δ 1.35 (t, J = 7.1 Hz, 3H, CH_3), 3.10 (s, 3H, CH_3), 4.01 (s, 3H, CH_3), 4.28 (q, J = 7.1 Hz, 2H, CH_2), 5.52 (s, 2H, NH_2), 6.71 (dd, J = 9.0 Hz, J = 2.3 Hz, 1H, H-10), 7.11 (d, J = 6.8 Hz, 1H, H-7), 7.13 (s, 1H, H-1), 7.25 (d, J = 2.2 Hz, 1H, H-12), 7.36 (t, J = 8.4 Hz, 1H, H-6), 7.89 (d, J = 8.4 Hz, 1H, H-5), 8.86 (d, J = 9.0 Hz, 1H, H-9); ^{13}C nmr: ppm 14.3 (q), 16.3 (q), 55.9 (q), 60.2 (t), 101.6 (d), 104.4 (d), 108.3 (d), 111.0 (d), 113.6 (s), 114.1 (d), 115.8 (s), 125.3 (s), 125.5 (d), 126.8 (s), 129.1 (s), 129.4 (d), 132.4 (s), 133.3 (s), 148.4 (s), 157.4 (s), 164.6 (s); ms: [13] m/z 348.

The last compound eluted was 11-amino-2-carbethoxy-6-methoxy-3-methylpyrrolo[1,2-*f*]phenantridine (**12**), which was recrystallized from ethanol (50%), mp 206°; ir: 3466 and 3356 (NH_2), 1694 (CO) cm^{-1}; ^{1}H nmr: δ 1.34 (t, J = 6.9 Hz, 3H, CH_3), 3.18 (s, 3H, CH_3), 3.87 (s, 3H, CH_3), 4.27 (q, J = 6.9 Hz, 2H, CH_2), 5.43 (s, 2H, NH_2), 6.76 (dd, J = 8.8 Hz, J = 2.1 Hz, 1H, H-10), 7.01 (dd, J = 9.0 Hz, J = 2.1 Hz, 1H, H-7), 7.12 (s, 1H, H-1), 7.17 (d, J = 2.1 Hz, 1H, H-12), 7.79 (d, J = 2.1 Hz, 1H, H-5), 7.97 (d, J = 8.8 Hz, 1H, H-9), 8.21 (d, J = 9.0 Hz, 1H, H-8); ^{13}C nmr: ppm 14.3 (q), 15.8 (q), 55.2 (q), 59.4 (t), 101.9 (d), 102.9 (d), 104.4 (d), 111.5 (d), 114.2 (s), 115.2 (d), 115.3 (s), 117.5 (s), 123.2 (d), 123.9 (d), 125.2 (s), 129.0 (s), 132.4 (s), 133.0 (s), 148.4 (s), 157.0 (s), 164.6 (s); ms: m/z 348.

Anal. Calcd. for $C_{21}H_{20}N_2O_3$: C, 72.39; H, 5.79; N, 8.04. Found: C, 72.49; H, 5.70; N, 7.98.

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[12] Coupling constants (J_m < 1.5 Hz) were not observed.

[13] Analysis (gc/ms) of this mixture was achieved by using a Fused-Silica capillary column cross linked methylsilicone (film thickness 0.33 μ, length 12.5 m); He carrier (10 psi); oven program = 2 minutes 70°, 20°/minutes to 350°, 10 minutes 350°; inlet 250°, detector 300°, quad 125°. Under these conditions the retention time of compound **11** was 16.386 minutes, that of compound **12** was 16.708 minutes.