POLYCONDENSED NITROGEN HETEROCYCLES. PART 26. AMINOPYRROLO[1,2-*f*]PHENANTHRIDINES BY DECOMPOSITION AND CYCLIZATION OF 2-ARYL-1-(3-AZIDOPHENYL)PYRROLES§

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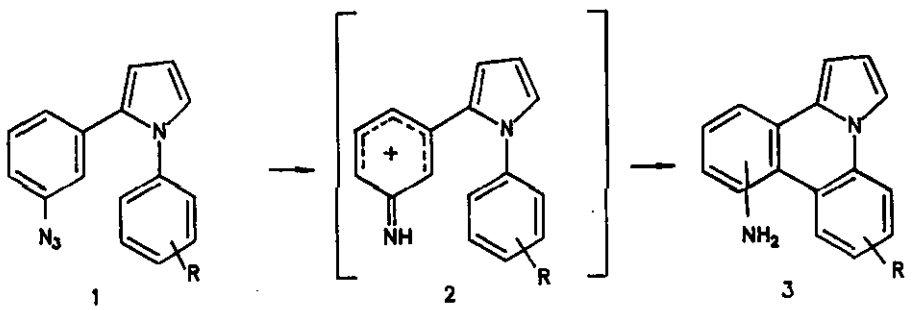
Abstract - Acid catalyzed decomposition of 1-(3-azidophenyl)pyrroles (**8a-d**) afforded the 6-amino- and 8-aminopyrrolo[1,2-*f*]phenanthridines of type (**11**) and (**12**) through cyclization of the intermediate protosolvated arylnitrenium ions (**9**). In the case of azide (**8a,b**) intermolecular side-reactions led also to the hydroxyphenyl derivatives (**10**).

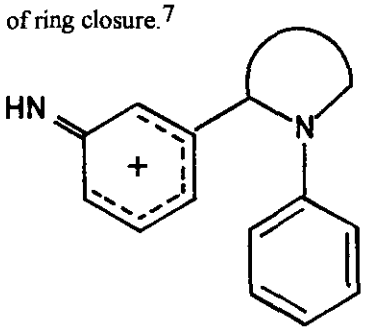
In connection with our studies[1] on polycondensed nitrogen heterocycles we became interested in the synthesis of pyrrolo[1,2-*f*]phenanthridine derivatives as potential antineoplastic agents, being structurally related to the anticancer drug ethidium bromide. In fact these compounds are assuming increasing importance in medicinal chemistry because of the proposal of the phenanthridine moiety as effective pharmacophore in classes of DNA-intercalating antitumor agents.[2] We have already studied some of the synthetic features connected with the possibility of obtaining derivatives variously functionalized also in the phenanthridine ring,[3,4] and, more recently, we have described the synthesis of 9-amino- and 11-amino-pyrrolo[1,2-*f*]phenanthridines by decomposition of 1-aryl-2-(3-azidophenyl)pyrroles of type (**1**) in trifluoromethanesulfonic acid (TFMSA).[5]



Scheme 1

This method has the advantage of introducing in the phenanthridine moiety an amino group in positions crucial for a better DNA-intercalation.[6] But although it represented an improvement with respect to the Pschorr-type cyclization achieved previously on 1-(2-aminophenyl)pyrroles,[4] it was suitable for the preparation of pyrrolo[1,2-*f*]phenanthridines only when an activating methoxy group was present in the substituent in the 1 position of the pyrrole ring. In fact in all the other cases the electronic effects of the pyrrole nitrogen in the intermediate protosolvated arylnitrenium ion (**2**) (R=H) are unfavourable for the intramolecular cyclization: the phenyl in the 1 position resulted not enough nucleophilic to achieve the expected ring closure to derivatives (**3**).

It is reasonable to suppose, however, that quite different results could be obtained if the relative positions of the substituents in 1 and 2 of the pyrrole ring in derivatives of type (**1**) are inverted. Therefore azidophenylpyrroles of type (**8**) could be suitable starting compounds for the synthesis of aminopyrrolo[1,2-*f*]phenanthridines. In this case the same electronic effects exerted by the pyrrole nitrogen could enhance the electrophilic character of the phenyl in the 1 position in the intermediate nitrenium ion. This hypothesis is supported by the results obtained in the remote intramolecular functionalization of 3-azidophenyl derivatives *via* the intermediate aryl nitrenium ions of type (**4**) and (**5**), the latter being the only capable of ring closure.[7]



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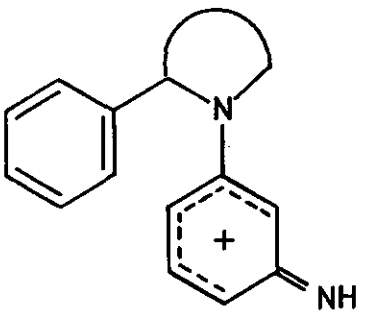

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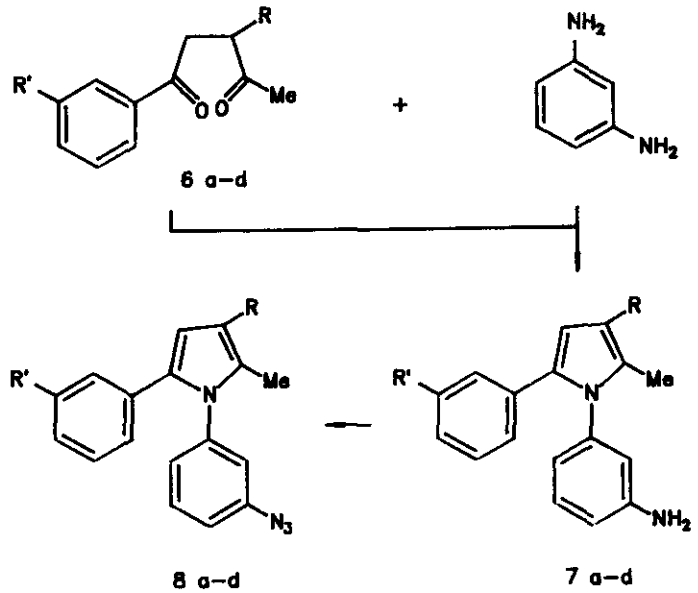
Scheme 2

To this purpose the 2-aryl-1-(3-azidophenyl)pyrroles (**8a-d**) were prepared according to the Scheme 3. The reaction of 1,4-diketones (**6a-d**) with 1,3-phenylenediamine gave 73-80% yields of the 1-(3-aminophenyl)-pyrroles (**7a-d**). These compounds were diazotized with sodium nitrite in acid solution and the diazonium salts directly reacted with an excess of sodium azide to give the 1-(3-azidophenyl)pyrroles (**8a-d**) in good yields. Derivatives (**8**) were easily identified by the ir spectra which showed strong absorption bands at *ca* 2110 cm^{-1}.

The azido compounds (**8a-d**) were decomposed in dichloromethane solution by treatment with a three fold excess of TFMSA from 0°C to room temperature. From the reaction mixture it was possible to isolate all the isomeric aminopyrrolo[1,2-*f*]phenanthridine derivatives of type (**11**) and (**12**), in good overall yields (Scheme 4).



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

Scheme 3

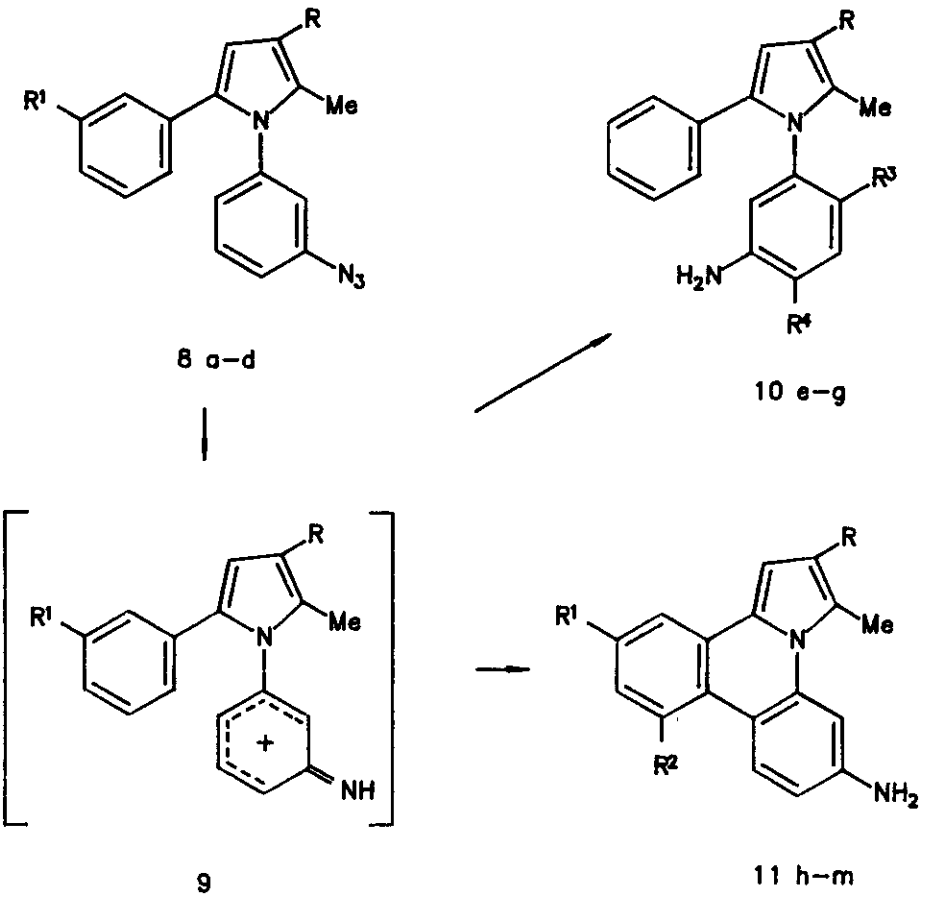
As expected, in fact, the electronic effect that the pyrrole nucleus exerts in the intermediate protosolvated arylnitrenium ions of type (**9**) favoured the ring closure, and steric effects do not appear to be relevant with this aryl π-carbocation since it was possible to isolate even the derivatives (**12k,m**) originated from ortho-ortho cyclization. Only in the case of the azides (**8a,b**) intermolecular side-reactions leading to the hydroxyphenyl derivatives of type (**10**) were observed. Probably in these intermediate nitrenium ions the phenyl in the 2 position of the pyrrole ring is nucleophilic enough to allow the formation of pyrrolo[1,2-*f*]phenanthridine, but not so strong to avoid the competing intermolecular nucleophilic reactions with triflate or water.

The correct structure to all the isomers was assigned on the basis of the spectral data. In particular by comparison of the ^{1}H nmr data with those of the other pyrrolo[1,2-*f*]phenanthridines already described by us,[3-5,8] and by using additivity rules for the effect of the substituents, it was possible to assign the resonances of all the protons in the twelve isomeric aminopyrrolo[1,2-*f*]phenanthridines (**11h-m** and **12h-m**).

In conclusion this synthetic method involving the acid decomposition of 2-aryl-1-(3-azidophenyl)pyrroles is suitable to prepare in good yields 6-amino- and/or 8-aminopyrrolo[1,2-*f*]phenanthridines.

EXPERIMENTAL

All melting points were taken on a Büchi-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-d_6 solution, unless otherwise specified, using a Bruker AC-E series 250 MHz spectrometer (TMS as internal reference); mass spectra were obtained with a HP 5890



a R = COMe, R^1 = H;
b R = COOEt, R^1 = H;
c R = COMe, R^1 = OMe;
d R = COOEt, R^1 = OMe;
e R = COMe, R^3 = OH, R^4 = H;
f R = COOEt, R^3 = OH, R^4 = H;
g R = COOEt, R^3 = H, R^4 = OH;
h R = COMe, R^1 = R^2 = H;
i R = COOEt, R^1 = R^2 = H;
j R = COMe, R^1 = OMe; R^2 = H;
k R = COMe, R^1 = H; R^2 = OMe;
l R = COOEt, R^1 = OMe; R^2 = H;
m R = COOEt, R^1 = H; R^2 = OMe.

Scheme 4

Series II and HP 5989A GC/MS apparatus. Column chromatography was performed with Merck silica gel 230-400 Mesh ASTM.

Preparation of 1-(3-Aminophenyl)-5-methyl-2-phenylpyrroles (7a-d).

A solution of 1,3-phenylenediamine (216 mg, 20 mmol), the suitable diketone **(6a)**,[9] **(b)**[10],**(c)**[11],**(d)**[11] (20 mmol) and *p*-toluenesulfonic acid (50 mg, 0.26 mmol) in absolute ethanol (60 ml) was refluxed for 5 h. After cooling, the resultant brown solution was evaporated under reduced pressure and the residue was purified by column chromatography (eluant dichloromethane).

3-Acetyl-1-(3-aminophenyl)-2-methyl-5-phenylpyrrole (**7a**) was recrystallized from ethanol (73%), mp 142°C; ir: 3449 and 3356 (NH_2), 1647 (CO) cm^{-1}; ^1H nmr: δ 2.31 (s, 3H, CH_3), 2.41 (s, 3H, CH_3), 5.36 (s, 2H, NH_2), 6.34 (d, J = 2.1 Hz, 1H, 1-C_6H_4 H-2), 6.36 (dd, J = 8.7, 1.4 Hz, 1H, 1-C_6H_4 H-4), 6.62 (dd, J = 8.5, 2.1 Hz, 1H, 1-C_6H_4 H-6), 6.87 (s, 1H, pyrrole CH), 7.10 (t, J = 7.9 Hz, 1H, 1-C_6H_4 H-5), 7.14-7.24 (m, 5H, 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.

1-(3-Aminophenyl)-3-ethoxycarbonyl-2-methyl-5-phenylpyrrole (**7b**) was recrystallized from ethanol (75%), mp 136°C; ir: 3472 and 3374 (NH_2), 1688 (CO) cm^{-1}; ^1H nmr: δ 1.29 (t, J = 7.1 Hz, 3H, CH_3), 2.34 (s, 3H, CH_3), 4.23 (q, J = 7.1 Hz, 2H, CH_2), 5.37 (s, 2H, NH_2), 6.37 (d, J = 2.0 Hz, 1H, 1-C_6H_4 H-2), 6.39 (dd, J = 8.4, 1.6 Hz, 1H, 1-C_6H_4 H-4), 6.65 (dd, J = 7.9, 1.2 Hz, 1H, 1-C_6H_4 H-6), 6.71 (s, 1H, pyrrole CH), 7.11 (t, J = 7.9 Hz, 1H, 1-C_6H_4 H-5), 7.14-7.23 (m, 5H, 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.

3-Acetyl-1-(3-aminophenyl)-5-(3-methoxyphenyl)-2-methylpyrrole (**7c**) was recrystallized from ethanol (80%), mp 134°C; ir: 3464 and 3368 (NH_2), 1647 (CO) cm^{-1}, ^1H nmr: δ 2.32 (s, 3H, CH_3), 2.41 (s, 3H, CH_3), 3.59 (s, 3H, CH_3), 5.38 (s, 2H, NH_2), 6.36 (d, J = 1.0 Hz, 1H, 1-C_6H_4 H-2), 6.39 (dd, J = 8.0, 1.0 Hz, 1H, 1-C_6H_4 H-4), 6.63 (dd, J = 8.2, 2.4 Hz, 1H, 2-C_6H_4 H-4), 6.67 (d, J = 2.4 Hz, 1H, 2-C_6H_4 H-2), 6.71 (dd, J = 8.1, 2.4 Hz, 1H, 2-C_6H_4 H-6), 6.81 (dd, J = 8.0, 1.0 Hz, 1H, 1-C_6H_4 H-6), 6.91 (s, 1H, pyrrole CH), 7.13 (t, J = 8.0 Hz, 2H, 1-C_6H_4 H-5, and 2-C_6H_4 H-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, 74.87; H, 6.22; N, 8.69.

1-(3-Aminophenyl)-3-ethoxycarbonyl-5-(3-methoxyphenyl)-2-methylpyrrole (**7d**) was isolated as an oil which solidified on standing (80%), mp 97°C; ir: 3466 and 3372 (NH_2), 1696 (CO) cm^{-1}, ^1H nmr: δ 1.35 (t, J = 7.0 Hz, 3H, CH_3), 2.37 (s, 3H, CH_3), 3.64 (s, 3H, CH_3), 4.28 (q, J = 7.0 Hz, 2H, CH_2), 5.42 (s, 2H, NH_2), 6.39 (d, J = 2.0 Hz, 1H, 1-C_6H_4 H-2), 6.46 (dd, J = 7.9, 1.2 Hz, 1H, 1-C_6H_4 H-4), 6.68 (dd, J = 8.0, 1.2 Hz, 1H, 2-C_6H_4 H-4), 6.70 (d, J = 2.1 Hz, 1H, 2-C_6H_4 H-2), 6.72 (dd, J = 7.9, 1.4 Hz, 1H, 1-C_6H_4 H-6), 6.74 (s, 1H, pyrrole CH), 6.84 (dd, J = 7.9, 1.4 Hz, 1H, 2-C_6H_4 H-6), 7.18 (t, J = 8.0 Hz, 2H, 1-C_6H_4 H-5, and 2-C_6H_4 H-5); 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 1-(3-Azidophenyl)-5-methyl-2-phenylpyrroles (8a-d).

METHOD A

To a suspension of the amines (**7a,b**) (10 mmol) in water (20 ml) hydrochloric acid (36%, 2.8 ml) was added and the mixture was diazotized with sodium nitrite (69 mg, 10 mmol) in water (20 ml) at room temperature.

After 30 min sodium azide (130 mg, 20 mmol) was added in small portions and the mixture was stirred for further 24 h at room temperature. The orange precipitate was filtered off, air dried and recrystallized from ethanol.

METHOD B

To a solution of the amines (**7c,d**) (10 mmol) in acetic acid (20 ml) sodium nitrite (69 mg, 10 mmol) in water (20 ml) was added at room temperature. The reactants were stirred for 4 h before the addition of sodium azide (130 mg, 20 mmol), in small portions at room temperature. The reaction mixture was stirred for further 24 h, poured onto crushed ice/water. The solid was filtered off, air dried and recrystallized from ethanol.

3-Acetyl-1-(3-azidophenyl)-2-methyl-5-phenylpyrrole (**8a**) (68%) had mp 112°C; ir: 2110 (N_3), 1653 (CO) cm^{-1}; ^1H nmr: δ 2.33 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 6.89 (s, 1H, pyrrole CH), 7.03-7.10 (m, 2H, 2-C_6H_5 H-2 and H-6), 7.05 (d, J = 1.8 Hz, 1H, 1-C_6H_4 H-2), 7.10 (dd, J = 8.3, 1.8 Hz, 1H, 1-C_6H_4 H-6), 7.16-7.24 (m, 3H, 2-C_6H_5 H-3, H-4, and H-5), 7.23 (dd, J = 8.3, 1.8 Hz, 1H, 1-C_6H_4 H-4), 7.48 (t, J = 8.3 Hz, 1H, 1-C_6H_4 H-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.

1-(3-Azidophenyl)-3-ethoxycarbonyl-2-methyl-5-phenylpyrrole (**8b**) (85%) had mp 95°C; ir: 2110 (N_3), 1694 (CO) cm-1; 1H nmr: δ 1.28 (t, J=7.0 Hz, 3H, CH_3), 2.33 (s, 3H, CH_3), 4.23 (q, J=7.0 Hz, 2H, CH_2), 6.68 (s, 1H, pyrrole CH), 7.02-7.08 (m, 2H, 2-C_6H_5 H-2 and H-6), 7.05 (d, J = 1.5 Hz, 1H, 1-C_6H_4 H-2), 7.06 (dd, J = 8.4, 2.2 Hz, 1H, 1-C_6H_4 H-6), 7.14-7.18 (m, 3H, 2-C_6H_5 H-3, H-4, and H-5), 7.22 (dd, J = 8.4, 1.5 Hz, 1H, 1-C_6H_4 H-4), 7.47 (t, J = 8.4 Hz, 1H, 1-C_6H_4 H-5); ms: m/z 346. 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.

3-Acetyl-1-(3-azidophenyl)-5-(3-methoxyphenyl)-2-methylpyrrole (**8c**) (67%) had mp 104°C; ir: 2108 (N_3), 1653 (CO) cm^{-1}; ^1H nmr: δ 2.33 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 3.60 (s, 3H, CH_3), 6.64 (d, J = 1.8 Hz, 2-C_6H_4 H-2), 6.69 (dd, J = 7.9, 1.8 Hz, 2-C_6H_4 H-6), 6.74 (dd, J = 7.9, 1.8 Hz, 2-C_6H_4 H-4), 6.93 (s, 1H, pyrrole CH), 7.07 (dd, J = 7.7, 1.9 Hz, 1-C_6H_4 H-6), 7.08 (d, J = 1.9 Hz, 1-C_6H_4 H-2), 7.12 (t, J = 7.9 Hz, 2-C_6H_4 H-5), 7.24 (dd, J = 7.9, 1.9 Hz, 1-C_6H_4 H-4), 7.50 (t, J = 7.9 Hz, 1-C_6H_4 H-5); ms: m/z 346. Anal. Calcd for $C_{20}H_{18}N_4O_2$: C 69.35; H, 5.24; N, 16.18. Found: C, 69.38; H, 5.19; N, 16.22.

1-(3-Azidophenyl)-3-ethoxycarbonyl-5-(3-methoxyphenyl)-2-methylpyrrole (**8d**) (75%) had mp 70°C; ir: 2108 (N_3), 1699 (CO), cm^{-1}; ^1H nmr: δ 1.29 (t, J=7.0 Hz, 3H, CH_3), 2.32 (s, 3H, CH_3), 3.59 (s, 3H, CH_3), 4.23 (q, J=7.0 Hz, 2H, CH_2), 6.60 (d, J = 1.3 Hz, 1H, 2-C_6H_4 H-2), 6.66 (dd, J = 8.0, 1.3 Hz, 2-C_6H_4 H-6), 6.71 (s, 1H, pyrrole CH), 6.72 (dd, J = 8.0, 1.3 Hz, 2-C_6H_4 H-4), 7.05-7.08 (m, 2H, 1-C_6H_4 H-2 and H-6), 7.11 (t, J = 8.0 Hz, 2-C_6H_4 H-5), 7.24 (dd, J = 8.1, 1.8 Hz, 1-C_6H_4 H-4), 7.50 (t, J = 8.1 Hz, 1-C_6H_4 H-5); 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 (8a-d) in TFMSA.

To a solution of azido derivatives (**8a-d**) (6 mmol) in absolute dichloromethane (50 ml) trifluoromethanesulfonic acid (2.7 g, 18 mmol) was added dropwise at 0°C. The reactants were allowed to room temperature and stirred for further 24 h. The reaction mixture was evaporated under reduced pressure, treated with a saturated solution of sodium bicarbonate (150 ml), and extracted with dichloromethane (4 x 100 ml). The

organic layer was dried over sodium sulphate and evaporated under reduced pressure to give a brown residue which was chromatographed.

In the case of the decomposition of derivative (**8a**) elution with dichloromethane gave the 2-acetyl-8-amino-3-methylpyrrolo[1,2-*f*]phenanthridine (**12h**) (8%), which was recrystallized from ethanol, mp 215°C; ir: 3385 and 3344 (NH_2), 1647 (CO) cm^{-1}; ^1H nmr: δ 1.28 (s, 3H, CH_3), 2.59 (s, 3H, CH_3), 5.78 (s, 2H, NH_2), 6.99 (d, J = 8.0 Hz, 1H, H-7), 7.30 (t, J = 8.0 Hz, 1H, H-6), 7.42-7.53 (m, 2H, H-10 and H-11), 7.62 (d, J = 8.0 Hz, 1H, H-5), 7.65 (s, 1H, H-1), 8.21 (dd, J = 7.6, 1.2 Hz, 1H, H-12), 8.98 (dd, J = 7.7, 1.3 Hz, 1H, H-9); ^{13}C nmr: ppm 16.84 (q), 29.57 (q), 103.73 (d), 110.72 (d), 114.94 (d), 121.26 (s), 124.24 (s), 125.61 (s), 125.83 (s), 127.90 (d), 128.32 (d), 128.60 (d), 128.85 (d), 129.59 (d), 131.77 (s), 135.29 (s), 136.69 (s), 148.19 (s), 195.65 (s); ms: m/z 288. Anal. Calcd for $C_{19}H_{16}N_2O$: C, 79.14; H, 5.59; N, 9.72. Found: C, 77.19; H, 5.46; N, 9.50.

Further elution with dichloromethane:ethyl acetate 9:1 gave the 3-acetyl-1-(3-amino-6-hydroxyphenyl)-2-methyl-5-phenylpyrrole (**10e**) (10%), which was recrystallized from ethanol, mp 157°C, ir: 3453 and 3349 (NH_2), 2926 (broad OH), 1655 (CO) cm^{-1}; ^1H nmr: δ 2.34 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 5.85 (s, 3H, NH_2 and OH), 6.68-6.72 (m, 2H, C_6H_5 H-2 and H-6), 6.90 (s, 1H, pyrrole CH), 7.10 (d, J = 8.0 Hz, 1H, C_6H_3 H-5), 7.11 (dd, J = 8.4, 2.0 Hz, 1H, C_6H_3 H-4), 7.12 (d, J = 2.0 Hz, 1H, C_6H_3 H-2), 7.18-7.28 (m, 3H, C_6H_5 H-3, H-4, and H-5); ^{13}C nmr: ppm 12.26 (q), 28.61 (q), 110.57 (d), 114.07 (d), 114.67 (d), 120.23 (s), 121.58 (s), 123.15 (d), 126.84 (d), 126.91 (d), 128.10 (d), 130.18 (s), 131.63 (s), 132.89 (s), 133.30 (s), 136.56 (s), 149.79 (s), 194.00 (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, 75.19; H, 5.66; N, 9.45.

The last compound eluted was the 2-acetyl-6-amino-3-methylpyrrolo[1,2-*f*]phenanthridine (**11h**) (60%), which was recrystallized from ethanol, mp 216°C; ir: 3449 and 3360 (NH_2), 1653 (CO) cm^{-1}; ^1H nmr: δ 2.54 (s, 3H, CH_3), 3.15 (s, 3H, CH_3), 5.78 (s, 2H, NH_2), 6.75 (dd, J = 8.8, 1.7 Hz, 1H, H-7), 7.32-7.36 (m, 2H, H-10 and H-11), 7.59 (s, 1H, H-1) 7.61 (d, J = 1.7 Hz, 1H, H-5), 8.08 (d, J = 8.8 Hz, 1H, H-8), 8.14 (dd, J = 8.8, 2.0 Hz, 1H, H-12), 8.18 (dd, J = 8.8, 2.0 Hz, 1H, H-9); ^{13}C nmr: ppm 17.94 (q), 30.91 (q), 103.26 (d), 105.04 (s), 105.23 (d), 113.29 (s), 113.65 (d), 122.58 (d), 123.82 (d), 124.99 (s), 126.81 (d), 127.18 (s), 127.51 (d), 127.95 (d), 130.22 (s), 132.48 (s), 136.70 (s), 150.81 (s), 197.14 (s); ms: m/z 288. Anal. Calcd for $C_{19}H_{16}N_2O$: C, 79.14; H, 5.59; N, 9.72. Found: C, 78.00; H, 5.56; N, 9.90.

In the case of the decomposition of derivative (**8b**) elution with dichloromethane gave the the 1-(3-amino-4-hydroxyphenyl)-3-ethoxycarbonyl-2-methyl-5-phenylpyrrole (**10g**) (7%), which was recrystallized from ethanol, mp 118°C, ir: 3501 and 3362 (NH_2), 3225 (broad OH), 1688 (CO) cm^{-1}; ^1H nmr: δ 1.34 (t, J = 7.1 Hz, 3H, CH_3), 2.38 (s, 3H, CH_3), 4.28 (q, J = 7.1 Hz, 2H, CH_2), 5.80 (s, 3H, NH_2 and OH), 6.62 (dd, J = 8.7, 2.6 Hz, 1H, 1-C_6H_3 H-6), 6.72 (d, J = 2.6 Hz, 1H, 1-C_6H_3 H-2), 6.74 (s, 1H, pyrrole CH), 7.12-7.16 (m, 2H, 2-C_6H_5 H-2 and H-6), 7.22-7.27 (m, 3H, 2-C_6H_5 H-3, H-4 and H-5), 7.36 (d, J = 8.7 Hz, 1H, 1-C_6H_3 H-5); ^{13}C nmr: ppm 11.97 (q), 14.34 (q), 58.98 (t), 109.36 (d), 112.09 (s), 115.83 (d), 116.62 (d), 122.36 (d), 126.69 (d), 127.26 (d), 128.12 (d), 131.55 (s), 133.05 (s), 135.68 (s), 137.34 (s), 137.80 (s), 141.50 (s), 164.23 (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, 71.19; H, 5.66; N, 8.45.

The second compound eluted was 1-(3-amino-6-hydroxyphenyl)-3-ethoxycarbonyl-2-methyl-5-phenylpyrrole (**10f**) (10%), which was recrystallized from ethanol, mp 141°C, ir: 3466 and 3370 (NH_2), 2960 (broad OH), 1717 (CO) cm^{-1}; ^1H nmr: δ 1.35 (t, J = 7.1 Hz, 3H, CH_3), 2.40 (s, 3H, CH_3), 4.28 (q, J = 7.1 Hz, 2H, CH_2), 5.92 (s, 3H, NH_2 and OH), 6.73 (dd, J = 7.9, 2.8 Hz, 1H, 1-C_6H_3 H-4), 6.74 (s, 1H, pyrrole CH), 6.80 (d, J = 2.8 Hz, 1H, 1-C_6H_3 H-2), 7.11-7.27 (m, 3H, 2-C_6H_5 H-3, H-4 and H-5), 7.27 (d, J = 7.9 Hz, 1H, 1-C_6H_3 H-5), 7.72-7.77 (m, 2H, 2-C_6H_5 H-2 and H-6); ^{13}C nmr: ppm 12.14 (q), 14.09 (q), 59.38 (t), 109.93 (d), 113.00 (d), 114.92 (d), 123.44 (d), 127.18 (d), 128.30 (s), 128.42 (d), 130.66 (s), 131.81 (d), 131.91 (s), 133.47 (s), 133.60 (s), 137.87 (s), 150.12 (s), 164.47 (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, 71.58; H, 5.76; N, 8.53.

Further elution with dichloromethane: ethyl acetate 9:1 gave the 8-amino-2-ethoxycarbonyl-3-methylpyrrolo[1,2-*f*]phenanthridine (**12i**) (10%), which was recrystallized from ethanol, mp 181°C; ir: 3400 and 3362 (NH_2), 1698 (CO) cm^{-1}; ^1H nmr: δ 1.33 (t, J = 7.0 Hz, 3H, CH_3), 3.08 (s, 3H, CH_3), 4.28 (q, J = 7.0 Hz, 2H, CH_2), 5.73 (s, 2H, NH_2), 6.93 (d, J = 8.0 Hz, 1H, H-7), 7.25 (t, J = 8.0 Hz, 1H, H-6), 7.33-7.44 (m, 1H, H-10), 7.35 (s, 1H, H-1), 7.58 (d, J = 8.0 Hz, 1H, H-5), 7.65-7.73 (m, 1H, H-11), 8.12 (dd, J = 8.2, 2.0 Hz, 1H, H-12), 8.92 (dd, J =8.2, 1.6 Hz, 1H, H-9); ^{13}C nmr: ppm 10.70 (q), 28.26 (q), 59.34 (t), 102.42 (d), 107.39 (d), 114.53 (d), 115.78 (s), 122.49 (d), 124.96 (s), 125.14 (s), 125.57 (s), 126.87 (d), 127.67 (d), 128.59 (d), 128.76 (s), 131.61 (d), 132.77 (s), 135.14 (s), 147.90 (s), 166.89 (s); ms: m/z 318. Anal. Calcd for $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.30; H, 5.56; N, 8.90.

The last compound eluted was the 6-amino-2-ethoxycarbonyl-3-methylpyrrolo[1,2-*f*]phenanthridine (**11i**) (60%), which was recrystallized from ethanol, mp 178°C; ir: 3526 and 3350 (NH_2), 1672 (CO) cm^{-1}; ^1H nmr: δ 1.34 (t, J = 7.2 Hz, 3H, CH_3), 3.20 (s, 3H, CH_3), 4.30 (q, J = 7.2 Hz, 2H, CH_2), 5.79 (s, 2H, NH_2), 6.77 (dd, J = 8.7, 1.9 Hz, 1H, H-7), 7.31-7.37 (m, 2H, H-10 and H-11), 7.36 (s, 1H, H-1), 7.65 (d, J = 1.9 Hz, 1H, H-5), 8.06 (d, J = 8.7 Hz, 1H, H-8), 8.15 (dd, J = 8.9, 2.3 Hz, 1H, H-12), 8.19 (dd, J = 8.9, 2.4 Hz, 1H, H-9); ^1H nmr (salt): δ 1.37 (t, J = 7.1 Hz, 3H, CH_3), 3.18 (s, 3H, CH_3), 4.32 (q, J = 7.1 Hz, 2H, CH_2), 7.31 (dd, J = 8.8, 1.2 Hz, 1H, H-7), 7.41 (s, 1H, H-1), 7.45-7.51 (m, 2H, H-10 and H-11), 8.11 (dd, J = 7.9, 1.5 Hz, 1H, H-12), 8.24 (d, J = 1.2 Hz, 1H, H-5), 8.32 (dd, J = 7.9, 1.5 Hz, 1H, H-9), 8.54 (d, J = 8.8 Hz, 1H, H-8), 8.68 (broad s, 3H, $^+NH_3$); ^{13}C nmr: ppm 14.32 (q), 16.01 (q), 59.53 (t), 103.07 (d), 103.21 (s), 110.05 (d), 115.87 (s), 117.81 (d), 120.06 (s), 122.37 (d), 122.62 (d), 124.00 (s), 124.83 (s), 125.74 (d), 126.80 (d), 128.52 (d), 132.80 (s), 134.40 (s), 135.79 (s), 164.54 (s); ms: m/z 318. Anal. Calcd for $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.54; H, 5.47; N, 8.75.

In the case of the decomposition of derivative (**8c**) elution with dichloromethane gave the 2-acetyl-8-amino-11-methoxy-3-methylpyrrolo[1,2-*f*]phenanthridine (**12j**) (15%), which was recrystallized from ethanol, mp 158°C; ir: 3445 and 3407 (NH_2), 1647 (CO) cm^{-1}; ^1H nmr: δ 2.55 (s, 3H, CH_3), 3.05 (s, 3H, CH_3), 3.92 (s, 3H, CH_3), 5.58 (s, 2H, NH_2), 6.93 (d, J = 7.9 Hz, 1H, H-7), 6.98 (dd, J = 9.2, 2.6 Hz, 1H, H-10), 7.20 (t, J = 8.2 Hz, 1H, H-6), 7.56 (d, J = 8.2 Hz, 1H, H-5), 7.66 (d, J = 2.6 Hz,1H, H-12), 7.68 (s, 1H, H-1), 8.88 (d, J = 9.2 Hz, 1H, H-9); ^{13}C nmr: ppm 16.87 (q), 29.56 (q), 55.59 (q), 104.40 (d), 105.41 (d), 108.12 (d), 11.23 (s), 113.90 (d), 114.92 (d), 119.27 (s), 124.18 (s), 126.77 (d), 127.22 (d), 127.29 (s), 128.76 (s), 131.83 (s), 134.42 (s), 147.34 (s), 158.25 (s), 195.65 (s); ms: m/z 318. Anal. Calcd for $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.54; H, 5.47; N, 8.75.

The second fraction eluted (10%) was an unseparable 3:1 mixture of (**12j**) and of the 2-acetyl-8-amino-9-methoxy-3-methylpyrrolo[1,2-*f*]phenanthridine (**12k**), ir: 3445 and 3407 (NH_2), 1647 (CO) cm^{-1}; ^1H nmr: δ 2.51 (s, 3H, CH_3), 3.01 (s, 3H, CH_3), 3.94 (s, 3H, CH_3), 5.59 (s, 2H, NH_2), 6.86 (d, J = 7.8 Hz, 1H, H-7), 7.08 (d, J = 8.3 Hz, 1H, H-10), 7.28 (d, J = 7.8 Hz, 1H, H-5), 7.33 (t, J = 7.8 Hz, 1H, H-6), 7.46 (t, J = 8.3 Hz, 1H, H-11), 7.69 (s, 1H, H-1), 7.73 (d, J = 8.3 Hz, 1H, H-12); ^{13}C nmr: ppm 16.63 (q), 29.56 (q), 56.27 (q), 104.95 (d), 106.39 (d), 108.59 (s), 110.06 (d), 113.79 (d), 114.75 (d), 124.71 (s), 126.77 (s), 128.20 (d), 128.41 (d), 129.18 (s), 129.21 (s), 132.41 (s), 135.03 (s), 147.57 (s), 155.04 (s), 195.64 (s); ms: m/z 318.

Further elution with dichloromethane: ethyl acetate 9:1 gave the 2-acetyl-6-amino-9-methoxy-3-methyl-pyrrolo[1,2-*f*]phenanthridine (**11k**) (25%), which was recrystallized from ethanol, mp 182°C; ir: 3457 and 3360 (NH_2), 1647 (CO) cm^{-1}; ^1H nmr: δ 2.55 (s, 3H, CH_3), 3.13 (s, 3H, CH_3), 3.99 (s, 3H, CH_3), 5.73 (s, 2H, NH_2), 6.71 (dd, J = 8.9, 1.9 Hz, 1H, H-7), 7.02 (d, J = 7.9 Hz, 1H, H-10), 7.31 (t, J = 7.9 Hz, 1H, H-11), 7.55 (s, 1H, H-1), 7.57 (d, J = 1.9 Hz, 1H, H-5), 7.75 (d, J = 7.9 Hz, 1H, H-12), 9.01 (d, J = 8.9 Hz, 1H, H-8); ^{13}C nmr: ppm 16.59 (q), 29.32 (q), 55.62 (q), 102.05 (d), 104.09 (d), 109.14 (d), 111.38 (d), 111.82 (s), 114.92 (d), 115.24 (s), 123.93 (s), 125.68 (s), 126.50 (d), 128.71 (s), 129.89 (d), 130.61 (s), 134.79 (s), 148.32 (s), 156.33 (s), 195.52 (s); ms: m/z 318. Anal. Calcd for $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.28; H, 5.65; N, 8.97.

The last compound eluted was the the 2-acetyl-6-amino-11-methoxy-3-methylpyrrolo[1,2-*f*]phenanthridine (**11j**) (40%), which was recrystallized from dichloromethane, mp 223°C; ir: 3345 and 3225 (NH_2), 1653 (CO) cm^{-1}; ^1H nmr: δ 2.56 (s, 3H, CH_3), 3.17 (s, 3H, CH_3), 3.90 (s, 3H, CH_3), 5.77 (s, 2H, NH_2), 6.76 (dd, J = 8.4, 1.4 Hz, 1H, H-7), 6.97 (dd, J = 8.6, 1.5 Hz, 1H, H-10), 7.60 (d, J = 1.4 Hz, 1H, H-12), 7.63 (d, J = 1.5 Hz, 1H, H-5), 7.68 (s, 1H, H-1), 8.06 (d, J = 8.4 Hz, 1H, H-8), 8.10 (d, J = 8.6 Hz, 1H, H-9); ^{13}C nmr: ppm 16.44 (q), 29.38 (q), 55.29 (q), 101.88 (d), 104.17 (d), 104.63 (d), 112.30 (s), 112.31 (d), 115.07 (d), 119.19 (s), 122.85 (d), 123.41 (s), 124.60 (d), 124.72 (s), 128.64 (s), 131.05 (s), 134.21 (s), 148.14 (s), 157.82 (s), 195.62 (s); ms: m/z 318. Anal. Calcd for $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.58; H, 5.65; N, 8.77.

In the case of the decomposition of derivative (**8d**) elution with dichloromethane gave the 8-amino-2-ethoxycarbonyl-11-methoxy-3-methylpyrrolo[1,2-*f*]phenanthridine (**12l**) (11%), which was recrystallized from ethanol, mp 146°C; ir: 3401 and 3310 (NH_2), 1701 (CO) cm^{-1}; ^1H nmr: δ 1.35 (t, J = 7.0 Hz, 3H,CH_3), 3.09 (s, 1H, CH_3), 3.91 (s, 3H, CH_3), 4.29 (q, J = 7.0 Hz, 2H, CH_2), 5.59 (s, 2H, NH_2), 6.93 (d, J = 7.8 Hz, 1H, H-7), 6.97 (dd, J = 9.2, 2.6 Hz, 1H, H-10), 7.21 (t, J = 8.1 Hz, 1H, H-6), 7.45 (s, 1H, H-1), 7.58 (d, J = 8.3 Hz, 1H, H-5), 7.61 (d, J = 2.4 Hz, 1H, H-12), 8.89 (d, J = 9.2 Hz, 1H, H-9); ^{13}C nmr: ppm 14.36 (q), 16.27 (q), 55.33 (q), 59.33 (t), 102.87 (d), 104.85 (d), 105.03 (s), 107.67 (d), 110.76 (s), 113.97 (d), 114.51 (d), 115.72 (s), 118.99 (s), 126.54 (d), 126.83 (d), 126.68 (s), 132.84 (s), 134.26 (s), 147.06 (s), 157.98 (s), 164.68 (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, 72.51; H, 5.86; N, 8.16.

Further elution with dichloromethane:ethyl acetate 9:1 gave the 8-amino-2-ethoxycarbonyl-9-methoxy-3-methylpyrrolo[1,2-*f*]phenanthridine (**12m**) (9%), which was recrystallized from ethanol, mp 208°C; ir: 3410 and 3356 (NH_2), 1698 (CO) cm^{-1}; ^1H nmr: δ 1.38 (t, J = 7.1 Hz, 3H, CH_3), 3.09 (s, 1H, CH_3), 4.00 (s, 3H,

CH_3), 4.33 (q, J = 7.1 Hz, 2H, CH_2), 5.61 (s, 2H, NH_2), 6.91 (d, J = 8.1 Hz, 1H, H-7), 7.12 (d, J = 7.8 Hz, 1H, H-10), 7.29 (s, 1H, H-1), 7.33 (d, J = 8.1 Hz, 1H, H-5), 7.39 (t, J = 8.1 Hz, 1H, H-6), 7.48 (t, J = 7.8 Hz, 1H, H-11), 7.75 (d, J = 7.8 Hz, 1H, H-12); ^{13}C nmr: ppm 14.60 (q), 16.22 (q), 50.28 (q), 59.60 (t), 103.85 (d), 103.95 (s), 106.23 (d), 108.38 (s), 110.05 (d), 113.68 (d), 114.76 (d), 116.47 (s), 128.26 (d), 128.45 (d), 129.02 (s), 129.42 (s), 133.65 (s), 135.20 (s), 147.60 (s), 155.01 (s), 164.70 (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, 72.53; H, 5.95; N, 8.28.

The third compound eluted was the 6-amino-2-ethoxycarbonyl-9-methoxy-3-methyl-pyrrolo[1,2-*f*]phenanthridine (**11m**) (35%), which was recrystallized from ethanol, mp 194°C; ir: 3463 and 3355 (NH_2), 1692 (CO) cm^{-1}; ^1H nmr: δ 1.34 (t, J = 7.1 Hz, 3H, CH_3), 3.15 (s, 1H, CH_3), 3.98 (s, 3H, CH_3), 4.29 (q, J = 7.1 Hz, 2H, CH_2), 5.73 (s, 2H, NH_2), 6.70 (dd, J = 9.1, 2.2 Hz, 1H, H-7), 7.02 (d, J = 8.2 Hz, 1H, H-10), 7.29 (t, J = 7.8 Hz, 1H, H-11), 7.32 (s, 1H, H-1), 7.58 (d, J = 2.1 Hz, 1H, H-5), 7.71 (d, J = 7.7 Hz, 1H, H-12), 9.02 (d, J = 9.1 Hz, 1H, H-8); ^{13}C nmr: ppm 14.58 (q), 16.54 (q), 55.89 (q), 59.59 (t), 101.93 (d), 103.10 (d), 109.48 (d), 111.54 (d), 111.85 (s), 115.32 (d), 115.52 (s), 116.01 (s), 125.74 (s), 126.81 (d), 129.14 (s), 130.14 (d), 132.21 (s), 135.17 (s), 148.63 (s), 156.55 (s), 164.99 (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, 72.29; H, 5.73; N, 7.94.

Elution with methanol gave the 6-amino-2-ethoxycarbonyl-11-methoxy-3-methylpyrrolo[1,2-*f*]phenanthridine (**11l**) (40%), which was recrystallized form ethanol, mp 210°C; ir: 3459 and 3364 (NH_2), 1688 (CO) cm^{-1}; ^1H nmr: δ 1.35 (t, J = 7.1 Hz, 3H, CH_3), 3.19 (s, 1H, CH_3), 3.88 (s, 3H, CH_3), 4.29 (q, J = 7.1 Hz, 2H, CH_2), 5.65 (s, 2H, NH_2), 6.74 (dd, J = 8.7, 1.5 Hz, 1H, H-7), 6.94 (dd, J = 8.9, 2.5 Hz, 1H, H-10), 7.44 (s, 1H, H-1), 7.53 (d, J = 2.5 Hz, 1H, H-12), 7.64 (d, J = 1.5 Hz, 1H, H-5), 8.05 (d, J = 8.7 Hz, 1H, H-8), 8.08 (d, J = 8.9 Hz, 1H, H-9); ^{13}C nmr: ppm 14.64 (q), 16.49 (q), 55.58 (q), 59.59 (t), 101.79 (d), 103.28 (d), 104.81 (d), 112.28 (s), 112.36 (s), 112.46 (d), 115.52 (s), 115.67 (d), 119.49 (s), 123.01 (d), 124.80 (d), 129.11 (s), 132.71 (s), 134.59 (s), 148.63 (s), 158.09 (s), 165.07 (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, 72.18; H, 5.60; N, 7.99.

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