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FUSED CARBAZOLES BY TANDEM AZA WITTIG/ELECTROCYCLIC RING CLOSURE. PREPARATION OF 6H-PYRIDO[4,3-b] CARBAZOLE, 11H-PYRIDO[4,3-a]CARBAZOLE AND 11H-PYRIDO[3,4-a]CARBAZOLE DERIVATIVES.

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Abstract.- Aza Wittig type reaction of iminophosphoranes **3**, **12** and **16**, prepared from the appropriate formylcarbazole by sequential treatment with ethyl azidoacetate and triphenylphosphine, with isocyanates leads to the linear 6*H*-pyrido[4,3-b] carbazole **5**, the angular 11*H*-pyrido[4,3-a]carbazole **13** and the isomeric 11*H*-pyrido[3,4-a]carbazole **19** respectively.

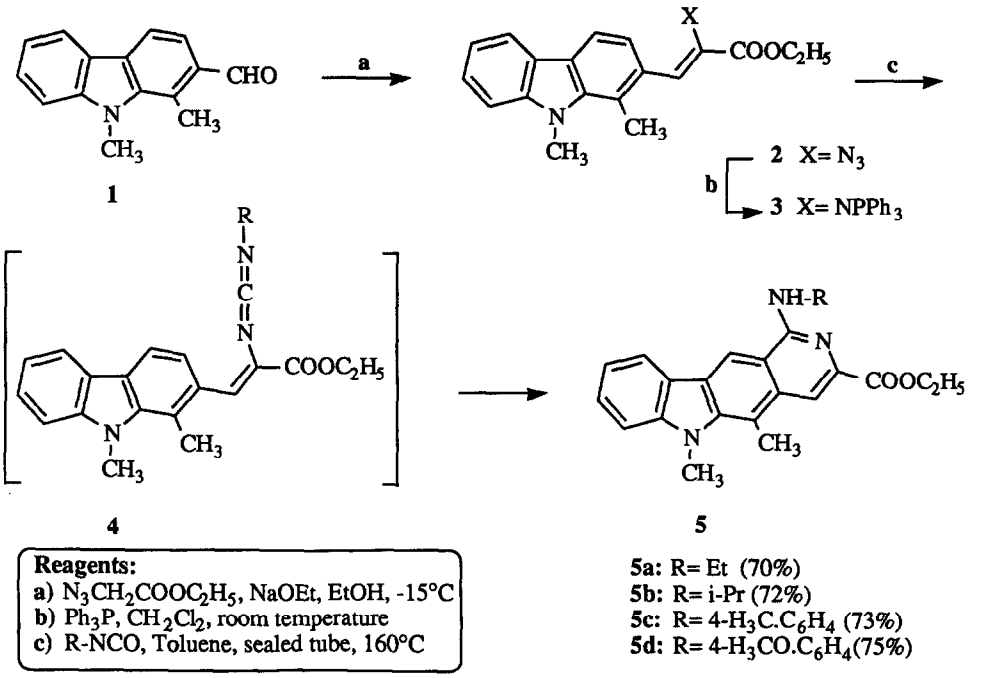
Pyridocarbazoles of both natural and unnatural origin have attracted considerable interest because of their remarkable multimodality of biological action[1]. As a consequence a great number of syntheses of ellipticine (*6H*-pyrido[4,3-b]carbazole) and related pyridocarbazole alkaloids have been reported and comprehensively reviewed[2].

We recently reported[3] a procedure for pyrido annelation into a preformed aromatic or heteroaromatic ring, based on the thermally induced 6π-electrocyclization of β-aryl(heteroaryl)vinyl carbodiimides. The reaction constitutes an efficient aproach for the synthesis of 7*H*-pyrido[4,3-c]carbazole and 10*H*-pyrido[4,3-b]carbazole derivatives[4]. As a further extension of the above methodology we would now like to report an expedient synthesis of linear 6*H*-pyrido[4,3-b]carbazole ring system and the angular isomers 11*H*-pyrido[3,4-a] and 11*H*-pyrido[4,3-a]carbazole ring systems.

Results. The plant alkaloids ellipticine and olivacine display significant antitumor activity in a variety of experimental models both *in vivo* and *in vitro*[5]. Recently, it has been reported[6] that substitution at the 1-position of ellipticine derivatives by an amino functionality markedly increased the biological properties in these compounds. This observation prompted us to prepare the hitherto unknown series 1-amino-substituted-6*H*-pyrido[4,3-b]carbazole derivatives (1-amino-substituted olivacines) **5**.

The 1,9-dimethyl-2-formylcarbazole[7] **1** was condensed with ethyl azidoacetate in the presence of sodium ethoxide at -15°C to give the ethyl α-azido-β-[2-(1,9-dimethyl)carbazolyl]acrylate **2** in 67% yield, the stereochemistry about the double bond is not known but is assumed to be Z, the more thermodynamically stable isomer[8]. The iminophosphorane **3** was prepared in 95% yield by Staudinger reaction of **2** with triphenylphosphine in dichloromethane at room temperature. The IR spectrum of **3** shows a carbonyl absorption band at 1698 cm^{-1}, and the ^{1}H-NMR-spectrum displays among others signals a doublet at δ= 7.19 ppm ($^4J_{P-H}$= 6.4Hz) due to the β-proton, in addition the

two methyl groups appear at δ=2.79 ppm (C_1-methyl) and 4.05 ppm (N-methyl) as singlets. Mass spectrum shows the expected molecular ion peak as the base peak.

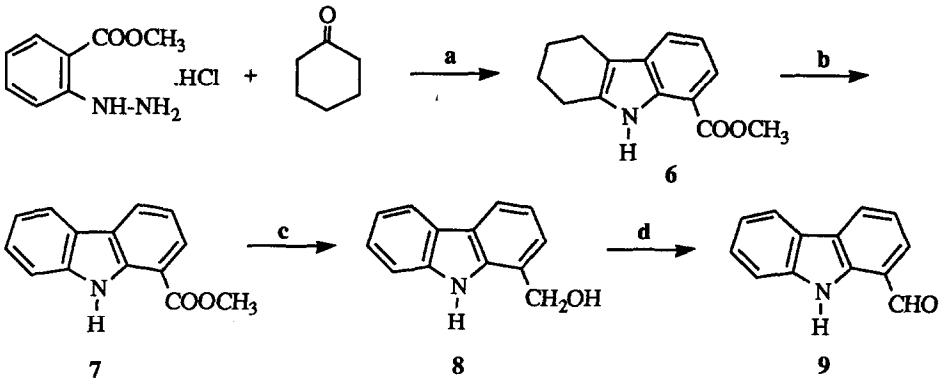


Scheme 1

Aza-Wittig type reaction of the iminophosphorane **3** with aromatic or aliphatic isocyanates in dry toluene at 160°C in a sealed tube for 22h yielded pyridocarbazoles **5** in 70-75% yields. (Scheme 1). The IR spectra of the 6*H*-pyrido[4,3-b]carbazoles **5** show absorption bands due to the NH group at 3397-3330 cm^{-1} and to the ester group in the region 1711-1708 cm^{-1}. In the ^{1}H-NMR spectra the H-4 and H-11 protons appear as singlets at δ= 8.10-8.21 ppm and δ= 7.30-8.12 ppm respectively, whereas the two methyl groups appear at δ= 2.78-2.93 ppm (C-methyl) and δ= 3.78-3.91 ppm (N-methyl) respectively. The ^{1}H-NMR spectra of **5a** (R=Et) and **5b** (R=i-Pr) suggest an exocyclic amino group, e.g. in **5b** the methine proton appears as a multiplet and the exocyclic amino proton as a doublet. Salient features of the ^{13}C-NMR spectra are given in Table1.

This approach has also been shown to be useful for the preparation of the otherwise not readily available 11H-pyrido[4,3-a]carbazoles **13**, under neutral conditions. So far the only reported syntheses of this ring system is based on the photocyclodehydrogenation of 1-(2-indolyl)-2-(3-pyridyl)acrylonitriles[9]. The 1-formylcarbazole **9**, required as starting material, has been prepared in low yield, by condensation of diethyl monoalkylmalonates with carbazole followed by bromination, displacement of bromine by secondary amines and further reduction with lithium aluminum hydride[10]. In our hands, this procedure did not give satisfactory results, so compound **9** was prepared by

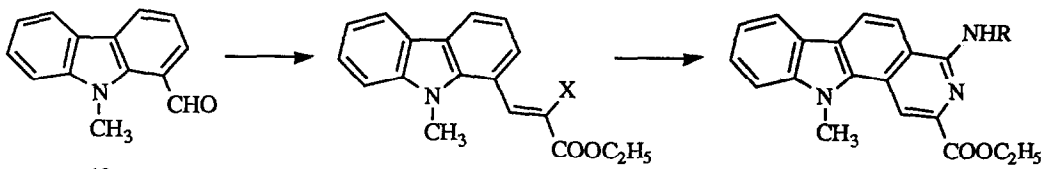
an alternative method involving: a) indolization between cyclohexanone and methyl 2-hydrazinobenzoate (75%); b) catalytic dehydrogenation (80%); c) reduction with lithium aluminium hydride (90%) and d) oxidation with chromic anhydride (70%)(Scheme 2).



Reagents:
a) AcOH, Δ, (75%)
b) Pd-C, 260°C, (80%)
c) $LiAlH_4$, Et_2O, (90%)
d) Jones reagent, (70%)

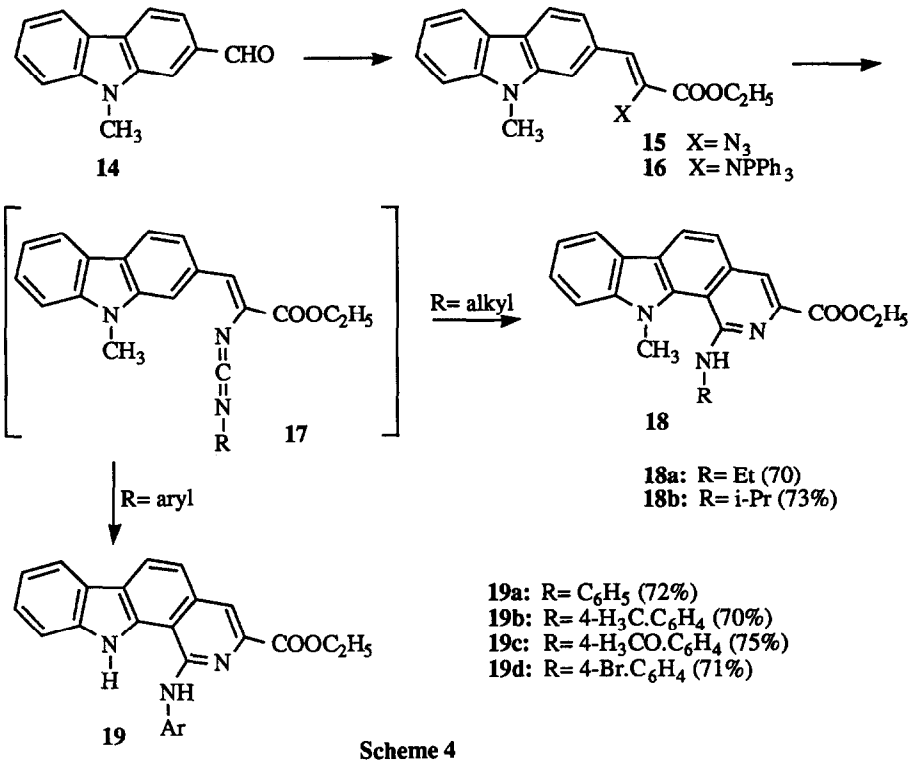
Scheme 2

The key intermediate iminophosphorane **12** was easily prepared from 1-formyl-9-methylcarbazole **10**, available from **9** by alkylation with methyl iodide in the presence of sodium hydride, by standard chemistry: condensation with ethyl azidoacetate afforded **11** in 60% yield, and further treatment with triphenylphosphine yielded **12** in 80% yield. Iminophosphorane **12** reacted with aliphatic or aromatic isocyanates in dry toluene at 160°C for 24h to give the corresponding 11*H*-pyrido[4,3-a]carbazoles **13** in 74-85% yields (Scheme 3). In the ^{1}H-NMR spectra of compounds **13** the H-5 and H-6 protons appear as doublets (J=8.6Hz) at δ= 8.03-8.37 ppm and δ= 8.35-8.60 ppm respectively. Salient features of the ^{13}C-NMR spectra are given in Table 1.



Scheme 3

The aforementioned pyrido annelation methodology is also applicable to the preparation of the isomeric 11*H*-pyrido[3,4-a]carbazole. This ring system constitutes the ABCD framework of the alkaloid subincanine isolated from Aspidosperma subincanum[11], and the only method reported for its preparation involves photocyclodehydrogenation of 1-(2-indolyl)-2-(4-pyridyl)acrylonitriles[9,12]. The 2-formyl-9-methylcarbazole **14**, available from 9-benzenesulfonyl-2-formylcarbazole[13] by sequential treatment with sodium hydroxide, methyl iodide/sodium hydride, was converted into the iminophosphorane **16** in 60% overall yield by the same protocol used for the preparation of iminophosphoranes **3** and **12**. An aza-Wittig type reaction of the iminophosphorane **16** with aliphatic or aromatic isocyanates in dry refluxing toluene for 8h gave the corresponding carbodiimides **17** which either could



Scheme 4

be isolated as viscous oils or used without purification for the next step. Heating of a toluene solution of carbodiimide **17** (R=alkyl) at 165°C for 24h in a glass sealed tube afforded **18** in 70-73% yields in a completely regioselective fashion. The isomeric linear pyridocarbazoles could not be detected by thin layer chromatography or ^{13}C-NMR analyses of the crude product. However, heating of carbodimide **17** (R=aryl) under the same conditions led to the unexpected demethylated pyridocarbazoles **19** in 70-75% yields as the sole reaction product (Scheme 4). Similar results were obtained when aliphatic or aromatic isothiocyanates were used instead of isocyanates. When carbodiimides **17** (R=aryl) were heated in nitrobenzene under the same conditions, an mixture of **18** and **19** was obtained, which were separated by column chromatography.

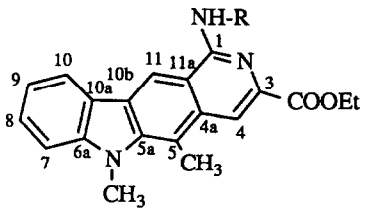
Thermal behaviour of carbodiimides **17** (R=aryl) came as a surprise because dealkylation of N-alkylcarba-

zoles and N-alkylindoles requires stronger conditions (temperature up to 300°C) and in some cases is promoted by sulfur[14]. Molecular models of compounds **19** reveals that the aromatic ring at 1-position and the N-methyl group are very close, and probably as a consequence of steric interaction the dealkylation process takes place.

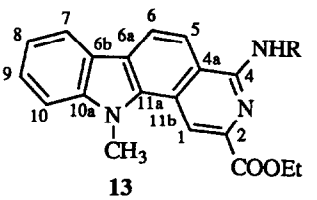
The identity of compounds **18** and **19** was accomplished by 2D-NMR, HCCR, and DEPT experiments. In the ^{1}H-NMR spectra of compounds **18** the H-4 proton appears as a singlet at δ= 7.88-7.93 ppm, and the H-5 and H-6 protons appear as doublets at δ= 7.56-7.59 ppm and δ= 8.19-8.22 ppm respectively, whereas in compounds **19** the H-4 proton appears at δ= 7.27-7.36 ppm and the H-5 and H-6 protons show signals at δ= 7.22-7.24 ppm and δ= 8.06-8.28 ppm respectively. Salient features of the ^{13}C-NMR spectra are given in Table 1.

The present study demonstrated that the tandem aza Wittig/electrocyclic ring closure is a viable alternative to the methods previously reported for the preparation of either linear or angular pyridocarbazoles. Our approach is simple, direct and leads from formylcarbazoles to the key intermediates iminophosphoranes, which undergo cyclization in good yields. Further, this methodology offers an entry to variety of substituted olivacines with a high degree of functionality.

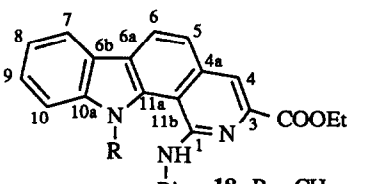
Table 1. ^{13}C Chemical Shifts (ppm) for Carbon Atoms in the Heteroaromatic Ring of Several 7*H*-Pyrido[4,3-b] carbazoles (**5**), 11*H*-Pyrido[4,3-a]carbazoles (**13**) and 11*H*-Pyrido[3,4-a]carbazoles (**18**) and (**19**).



5



13



18 R = CH_3
19 R = H

Carbon Atoms	Compound 5a	5c	13b	13d	18b	19b
C-1	155.88 (d) J=3.5	152.19 (s)	107.19 (d) J=166.2	109.25 (d) J=166.3	153.36 (s)	148.59 (s)
C-2	____	____	134.60 (m)	134.41 (m)	____	____
C-3	138.71 (s)	137.70 (m)	____	____	139.65 (s)	139.65 (m)
C-4	110.78 (d) J=164.7	112.44 (d) J=165.5	155.03 (d) J=3.5	152.37 (d) J=3.6	114.14 (dd) J=167.2 J=4.5	110.87 (dm) J=166.4
C-4a	134.04 (m)	134.32 (m)	117.3 (m)	117.67 (m)	137.46 (d) J=8.1	132.92 (m)
C-5	113.95 (d) J=4.9	114.28 (m)	114.23 (d) J=162.1	113.81 (d) J=162.2	120.87 (dd) J=162.4 J=4.4	118.17 (dd) J=161.8 J=5.7

C-5a	141.02 (m)	141.0 (m)	____	____	____	____
C-6	____	____	120.43 (d)	120.55 (d)	122.76 (d)	123.86 (d)
			J=161.8	J=162.5	J=160.3	J=159.5
C-6a	144.17 (m)	144.28 (m)	121.68 (m)	121.65 (m)	124.55 (m)[a]	122.31 (m)
C-6b	____	____	121.38 (m)	121.14 (m)	124.77 (m)[a]	123.35 (m)
C-7	108.59 (dd)	108.74 (dd)	120.26 (dd)	119.75 (d)	119.68 (dd)	120.25 (dd)
	J=160.3	J=161.0	J=160.1	J=159.5	J=159.1	J=158.2
	J=8.0	J=7.6	J=7.4		J=7.4	J=7.3
C-8	127.44 (dd)	127.73 (dd)	119.67 (dd)	119.41 (dd)	121.36 (dd)	119.80 (dd)
	J=160.2	J=162.0	J=161.0	J=161.2	J=161.1	J=160.5
	J=8.3	J=7.6	J=7.5	J=7.4	J=7.5	J=7.5
C-9	119.38 (dd)	119.54 (dd)	125.97 (dd)	125.77 (dd)	126.17 (dd)	126.28 (dd)
	J=160.9	J=159.5	J=160.1	J=160.2	J=161.1	J=159.7
	J=7.0	J=7.7	J=7.5	J=8.5	J=7.6	J=7.7
C-10	120.27 (dd)	120.49 (dd)	109.86 (dd)	109.42 (dd)	111.43 (dd)	111.72 (dd)
	J=158.7	J=160.3	J=161.7	J=161.8	J=160.5	J=161.0
	J=8.5	J=8.1	J=8.0	J=8.3	J=7.9	J=7.3
C-10a	122.41 (m)	122.27 (m)	141.0 (m)	140.96 (m)	145.48 (m)	145.68 (m)
C-10b	125.56 (d)	126.0 (m)	____	____	____	____
	J=2.4					
C-11	110.33 (d)	110.28 (dm)	____	____	____	____
C-11a	114.31 (m)	114.53 (m)	139.62 (tm)	138.59 (m)	138.65 (m)	137.74 (m)
			J=4.7			
C-11b	____	____	124.33 (m)	124.43 (m)	108.37 (t)	112.55 (m)
					J=5.9	

[a] Interchangeables.

EXPERIMENTAL

All melting points were determined on a Kofler hot-plate melting point apparatus and are uncorrected. IR spectra were obtained as Nujol emulsion on a Nicolet-5DX spectrophotometer. NMR spectra were recorded on a Bruker AC-200 (200 MHz) and on a Varian Unity-300 (300 MHz). Mass spectra were recorded on a Hewlett-Packard 5993C spectrometer. Microanalyses were performed on a Perkin-Elmer 240C instrument.

Materials. 1,9-Dimethyl-2-formylcarbazole[7] **1** and 9-Benzenesulfonyl-2-formylcarbazole[13] were prepared as described in the literature.

Methyl 5,6,7,8-tetrahydrocarbazole-1-carboxylate (6).

A mixture of methyl 2-hydrazinobenzoate hydrochloride (10g, 49 mmol) and cyclohexanone (5.1g, 51.8 mmol) in acetic acid (500 ml) was refluxed under nitrogen for 3h. After cooling, the mixture was extracted with benzene (3x150 ml) and washed with 5% sodium bicarbonate solution and then with water. The benzene solution

was dried over anhydrous sodium sulfate and filtered. Concentration to dryness yielded a solid which was recrystallized from methanol to give **6** (8.5 g, 75%), m.p. 126-128°C (lit[15] :123-124°C), (yellow prisms). (Found: C, 73.25; H, 6.65; N, 6.05. $C_{14}H_{15}NO_2$ requires: C, 73.34; H, 6.59; N, 6.11); i.r. (Nujol) 3303, 1683, and 1579 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 1.86-1.94 (m, 4H, 2H-6+2H-7), 2.69-2.78 (m, 4H, 2H-5+2H-8), 3.97 (s, 3H, $COOCH_3$), 7.09 (t, 1H, J=7.7Hz, H-3), 7.65 (d, 1H, J=7.7Hz, H-2), 7.80 (d, 1H, J=7.7Hz, H-4), 9.40 (s, 1H, NH); ^{13}C n.m.r. δ ($CDCl_3$): 20.8 (C-6+C-7), 23.1 (C-8), 23.2 (C-5), 51.6 (CH_3), 110.0 (C-4b), 111.5 (C-4a), 118.2 (C-3), 123.0 (C-4), 123.2 (C-2), 129.0 (C-1), 135.4 (C-9a), 135.7 (C-8a), 168.2 (CO); m/z (%): 229 (M^+, 35), 169 (100).

Methyl carbazole-1-carboxylate (7).

Methyl 5,6,7,8-tetrahydrocarbazole-1-carboxylate **6** (6g, 26.2 mmol) and 10% Pd-C (0.96g) was heated at 260°C for 2.5h. After cooling, the mixture was extracted with boiling ethanol (300 ml) and the catalyst was removed by filtration. The filtrate was cooled to room temperature to give **7** (4.72g, 80%), m.p. 142-143°C (lit[16]:135-137°C), (colorless plates). (Found: C, 74.54; H, 5.03; N, 6.10. $C_{14}H_{11}NO_2$ requires: C, 74.65; H, 4.92; N, 6.22); i.r. (Nujol) 3410, 1682 and 1604 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 3.98 (s, 3H, CH_3), 7.21 (td, 1H, J=7.8, 0.9Hz, H-6), 7.25 (t, 1H, J=7.5Hz, H-7), 7.45 (dd, 1H, J=7.8, 0.9Hz, H-8), 7.47 (t, 1H, J=7.8, H-3), 8.04 (dd, 1H, J=7.5, 0.9Hz, H-2), 8.05 (d, 1H, J=8.1Hz, H-5), 8.22 (dd, 1H, J=8.0, 0.9Hz, H-4), 9.90 (s, 1H, NH); ^{13}C n.m.r. δ ($CDCl_3$): 52.0 (CH_3), 111.2 (C-8), 111.6 (C-4b), 118.5 (C-6), 120.0 (C-3), 120.4 (C-5), 122.5 (C-4a), 124.7 (C-1), 125.5 (C-4), 126.6 (C-7), 127.4 (C-2), 139.7 (C-9a), 141.0 (C-8a), 167.9 (CO); m/z (%): 225 (M^+, 40), 193 (100).

1-Hydroxymethylcarbazole (8).

To a suspension of lithium aluminum hydride (0.76 g, 20 mmol) in dry diethyl ether (75 ml) was added a solution of **7** (3 g, 13.3 mmol) in dry diethyl ether (100 ml). After 1h stirring at room temperature, the mixture was hydrolyzed with ammonium chloride saturated solution (30 ml). The organic layer was washed with water (3x25 ml), dried over anhydrous sodium sulfate and evaporated to give **8** which was recrystallized from ethanol (2.36g, 90%), m.p. 136-137°C (colorless plates). (Found: C, 79.02; H, 5.71; N, 7.00. $C_{13}H_{11}NO$ requires: C, 79.17; H, 5.62; N, 7.1); i.r. (Nujol) 3405, 1455 and 998 cm^{-1}; ^1H n.m.r. δ (DMSO-d_6): 4.89 (d, 2H, J=5.5Hz, CH_2OH), 5.31 (t, 1H, J=5.5Hz, CH_2OH), 7.14 (t, 2H, J=7.6Hz, H-6+H-7), 7.37 (t, 1H, J=7.8Hz, H-3), 7.39 (d, 1H, J=7.6Hz, H-8), 7.55 (d, 1H, J=7.8Hz, H-2), 8.00 (d, 1H, J=7.7Hz, H-4), 8.09 (d, 1H, J=7.7Hz, H-5), 11.09 (s, 1H, NH); ^{13}C n.m.r. δ (DMSO-d_6): 60.5 (CH_2), 111.3 (C-8), 118.4 (C-6), 118.6 (C-3), 118.9 (C-5), 120.2 (C-4), 122.5 (C-4b), 122.6 (C-4a), 125.1 (C-1+ C-7), 125.5 (C-2), 137.6 (C-9a), 140.0 (C-8a); m/z (%): 197 (M^+, 41), 179 (100).

1-Formylcarbazole (9).

To a solution of 1-hydroxymethylcarbazole **8** (5g, 25 mmol) in acetone (200 ml) at 0°C was added Jones reagent (40 mmol). After 2h stirring at room temperature, the mixture was filtered over celite. The filtrate was extracted with dichloromethane, washed with water (3x40 ml), dried over anhydrous sodium sulfate, filtered and evaporated to dryness. The crude product was chromatographed on a silica gel column, eluting with dichloromethane/n-hexane (1:1) to give **9** (3.5g, 70%), m.p. 146-147°C (lit[10]: 146°C), (yellow prisms). (Found: C, 79.88; H, 4.77; N, 7.05. $C_{13}H_9NO$ requires: C, 79.98; H, 4.65; N, 7.17); i.r. (Nujol) 3393, 1674, 1601 and 1352 cm-1; ^1H n.m.r. δ ($CDCl_3$): 7.27 (td, 1H, J=7.8, 1.0Hz, H-7), 7.31 (t, 1H, J=7.6Hz, H-6), 7.47 (td, 1H, J=8.0, 1.0Hz, H-3), 7.51 (dd, 1H, J=7.8, 0.9Hz, H-8), 7.78 (dd, 1H, J=7.6, 1.0Hz, H-2), 8.07 (dd, 1H, J=7.8, 0.6Hz, H-4), 8.27 (dd, 1H, J=7.6, 0.6Hz, H-5), 10.15 (s, 1H, CHO), 10.20 (br, 1H, NH); ^{13}C n.m.r. δ ($CDCl_3$): 111.5 (C-8), 118.8 (C-6), 120.5 (C-3+C-5), 119.6 (C-4b), 122.0 (C-4a), 124.7 (C-1), 126.3 (C-4), 127.0 (C-7), 131.3 (C-2), 138.1 (C-9a), 140.1 (C-8a), 193.5 (CO); 196 (M^++1,13), 195 (M^+,100), 167 (56), 139 (71).

1-Formyl-9-methylcarbazole (10).

To a suspension of sodium hydride (0.16g, 6.8 mmol) in dry DMF (30 ml) a solution of 1-formylcarbazole **9** (1.12g, 5.75 mmol) in the same solvent (20 ml) was added under nitrogen at 0°C. After 1h stirring at room temperature the solution was cooled at 0°C and methyl iodide (1.92g, 14 mmol) was added. The reaction mixture was stirred at room temperature for 1h, and then poured into cold water (75 ml). The precipitated was filtered and recrystallized from ethanol to give **10** (1.08g, 90%), m.p. 119-120°C (colorless prisms). (Found: C, 80.25; H, 5.41; N, 6.58. $C_{14}H_{11}NO$ requires : C, 80.36; H, 5.30; N, 6.69); i.r. (Nujol) 1679, 1665 and 1132 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 4.04 (s, 3H, CH_3N), 7.25 (t, 1H, J=7.7Hz, H-6), 7.26 (td, 1H, J=7.8, 1.0Hz, H-7), 7.37 (d, 1H, J=8.0Hz, H-8), 7.49 (td, 1H, J=8.0, 1.1Hz, H-3), 7.86 (dd, 1H, J=7.7, 1.1Hz, H-2), 8.00 (d, 1H, J=7.8Hz, H-4), 8.21 (dd, 1H, J=7.8, 0.9Hz, H-5), 10.29 (s, 1H, CHO); ^{13}C n.m.r. δ ($CDCl_3$): 34.6 (CH_3N), 109.4 (C-8), 118.3 (C-6), 119.9 (C-3), 120.1 (C-5), 121.7 (C-4b), 122.2 (C-4a), 125.50 (C-1), 126.3 (C-4), 126.6 (C-7), 132.1 (C-2), 139.2 (C-9a), 142.1 (C-8a), 190.47 (CO); m/z (%): 209 (M^+,10), 195 (100).

2-Formyl-9-methylcarbazole (14).

A mixture of 9- benzenesulfonyl-2-formylcarbazole (4.56g, 13.6 mmol), 10% sodium hydroxide (30 ml) and ethanol (150 ml) was refluxed for 4h. The solution was concentrated until 40 ml to give a solid, which was filtered, washed with water (3x20 ml) and recrystallized from ethyl acetate/n-hexane (1:1) to give 2-formylcarbazole (2.0g, 75%) m.p. 158-160°C (yellow prisms); Found: C, 79.85; H, 4.77; N, 7.03. $C_{13}H_9NO$ requires: C, 79.98; H, 4.65; N, 7.17; i.r. (Nujol) 3395, 1678 and 1603 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 7.25 (t, 1H, J=8.0Hz, H-7), 7.44 (t, 1H, J=8.0Hz, H-6), 7.46 (d, 1H, J=8.1Hz, H-8), 7.72 (d, 1H, J=7.8Hz, H-3), 7.90 (s, 1H, H-1), 8.09 (d, 1H, J=7.8Hz, H-4), 8.13 (d, 1H, J=8.1Hz, H-5), 8.59 (br, 1H, NH), 10.08 (s, 1H, CHO); m/z (%): 196 (M^++1, 10) 195 (M^+, 100), 167 (51).

To a suspension of sodium hydride (0.16g, 6.8 mmol) in dry DMF (30ml) a solution of 2-formylcarbazole (1.12g, 5.75 mmol) in the same solvent (20 ml) was added under nitrogen at 0°C. After 1h stirring at room temperature the solution was cooled at 0°C and methyl iodide (1.92g, 14 mmol) was added. The reaction mixture was stirred at room temperature for 1h, and then poured into cold water (75 ml). The separated solid was filtered and recrystallyzed from ethyl acetate/n-hexane (1:1) to give **14** (1.08g, 90%), m.p. 82-83°C (yellow prisms). (Found: C, 80.25; H, 5.4; N, 6.57. $C_{14}H_{11}NO$ requires: C, 80.36; H, 5.30; N, 6.69); i.r. (Nujol) 1678, 1660, 1210 and 1130 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 3.66 (s, 3H, CH_3N), 7.21 (t, 1H, J=7.8Hz, H-7), 7.26 (d, 1H, J=8.0Hz, H-8), 7.47 (t, 1H, J=7.8Hz, H-6),7.60 (d, 1H, J=8.0Hz, H-3), 7.72 (s, 1H, H-1), 8.00 (d, 2H, J=8.0Hz, H-4+H-5), 10.02 (s, 1H, CHO); ^{13}C n.m.r. δ ($CDCl_3$): 28.8 (CH_3N), 108.7 (C-8), 109.3 (C-1), 119.4 (C-7), 120.1 (C-5),120.8 (C-3), 121.1 (C-4), 121.6 (C-4b), 127.4 (C-6), 127.6 (C-4a), 133.6 (C-2), 140.3 (C-9a), 142.4 (C-8a), 192.3 (CO); m/z (%): 209 (M^+, 100), 180 (57).

Preparation of Ethyl α-Azido-β-(carbazolyl)acrylates (2, 11 and 15).

Ethyl azidoacetate (5.16 g, 40 mmol) and a solution of the appropriate formylcarbazole **2**, **11** or **15** (10 mmol) in dry tetrahydrofuran were added dropwise under nitrogen at -15°C to a well-stirred solution containing sodium (0.92 g) in dry ethanol (50 ml). The reaction mixture was stirred at -15°C for 7h, poured into aqueous 30% ammomium chloride (100 ml) and then extracted with dichloromethane (3x30 ml). The combined organic layers were washed with water (3x10 ml), dried over anhydrous sodium sulfate, and filtered. Concentration to dryness yielded a crude material which was recrystallized from the appropriate solvent.

Ethyl α-Azido-β-[2-(1,9-dimethyl)carbazolyl]acrylate (2). (67%), m.p. 116-118°C (yellow prisms from dichloromethane/diethyl ether 1:1).(Found : C, 68.15; H, 5.45; N, 16.68.$C_{19}H_{18}N_4O_2$ requires: C, 68.26; H, 5.39; N, 16.77); i.r. (Nujol) 2116 (azide) and 1696 (COOEt) cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 1.42 (t, 3H, J=6.96Hz), 2.69 (s,

3H, CH_3-C-1), 3.96 (s, 3H, CH_3-N), 4.39 (q, 2H, J=6.96Hz), 7.20 (td, 1H, J=7.69, 0.73Hz, H-6), 7.28 (d, 1H, J=8.42Hz, H-8), 7.34 (s, 1H, H-β), 7.44 (td, 1H, J=8.42, 1.47Hz, H-7), 7.59 (d, 1H, J=8.05Hz, H-3), 7.89 (d, 1H, J=8.06Hz, H-4), 8.00 (d, 1H, J=7.69Hz, H-5); ^{13}C n.m.r. δ ($CDCl_3$): 14.2 (*CH_3*-CH_2O), 16.0 (CH_3-C-1), 33.2 (*CH_3*N), 62.2 (CH_3-*CH_2*O), 108.8 (C-8), 117.4 (C-4), 119.2 (C-6), 120.1 (C-5), 120.2 (C-1), 121.1 (C-3), 122.6 (C-α), 124.3 (C_{4a}), 125.8 (C-β), 126.2 (C-7), 126.4 (C-4b), 130.4 (C-2), 140.1 (C-9a), 142.7 (C-8a), 163.5 (CO); m/z (%); 334 (M^+, 4), 306 (70), 260 (100).

Ethyl α-Azido-β-[1-(9-methyl)carbazolyl]acrylate (11). (60%), m.p. 68-70°C (yellow prisms from dichloromethane/n-hexane 1:1). (Found: C, 67.60; H , 5.18; N, 17.40.$C_{18}H_{16}N_4O_2$ requires: C, 67.49; H, 5.03; N, 17.49); i.r. (Nujol) 2120 (azide) and 1697 (COOEt) cm^{-1}; ^{1}H n.m.r. δ ($CDCl_3$): 1.40 (t, 3H, J=7.1Hz), 3.87(s, 3H, CH_3-N), 4.38 (q, 2H, J=7.1Hz), 7.18 (t, 2H, J=7.6Hz, H-6+H-7), 7.27 (d, 1H, J=8.0Hz, H-8), 7.43 (t, 1H, J=7.7Hz, H-3), 7.63 (s, 1H, H-β), 7.81 (d, 1H, J=7.6Hz, H-2), 7.98 (d, 1H, J=7.7Hz, H-4), 7.99 (d, 1H, J=7.7Hz, H-5); ^{13}C n.m.r. δ ($CDCl_3$): 14.2 (*CH_3*-CH_2O), 32.9 (*CH_3*-N), 62.2 (CH_3-*CH_2*O), 108.7 (C-8), 116.6 (C-α), 118.6 (C-6), 119.4 (C-3), 119.9 (C-5), 121.3 (C-4), 122.4 (C-4b), 123.1 (C-7), 124.1 (C-4a), 125.8 (C-1), 126.0 (C-β), 127.7 (C-2), 138.8 (C-9a), 141.7 (C-8a), 163.27 (CO); m/z (%): 320 (M^+, 2), 192 (100).

Ethyl α-Azido-β- [2-(9-methyl)carbazolyl]acrylate (15). (75%), m.p. 117-119°C (yellow prisms from dichloromethane/ diethyl ether 1:1). (Found: C, 67.40; H, 5.15; N, 17.39. $C_{18}H_{16}N_4O_2$ requires: C, 67.50; H, 5.00; N, 17.50); i.r. (Nujol) 2118 (azide) and 1698 (COOEt) cm^{-1}; ^{1}H n.m.r. δ ($CDCl_3$):1.40 (t, 3H, J=7.0Hz), 3.77 (s, 3H, CH_3N), 4.36 (q, 2H, J=7.0Hz), 7.07 (s, 1H, H-β), 7.20 (td, 1H, J=8.1, 1.1Hz, H-6), 7.33 (d, 1H, J=8.1Hz, H-8), 7.46 (td, 1H, J=8.1, 1.1Hz, H-7), 7.54 (dd, 1H, J=8.1, 1.5Hz, H-3), 9.94 (s, 1H, H-1), 8.00 (d, 1H, J=8.1Hz, H-4), 8.04 (d, 1H, J=7.7Hz, H-5); ^{13}C n.m.r. δ ($CDCl_3$): 14.2 (*CH_3*-CH_2O), 29.0 (CH_3N), 62.1 (CH_3-*CH_2*O), 108.6 (C-8), 110.3 (C-1), 119.2 (C-6), 120.0 (C-5), 120.6 (C-4), 122.3 (C-α), 122.3 (C-3), 123.8 (C-4a), 124.3 (C-4b), 126.5 (C-7), 126.7 (C-β), 130.5 (C-2), 140.8 (C-9a), 142.0 (C-8a), 163.7 (CO); m/z (%): 320 (M^+, 2) 219 (100).

General Procedure for the Preparation of Ethyl α-[(Triphenylphosphoranylidene)amino]-β-(carbazolyl) acrylates (3), (12) and (16).

To a solution of triphenylphosphine (1.05g, 4 mmol) in dry dichloromethane (10 ml) was added dropwise under nitrogen at 0°C a solution of the appropriate ethyl α-azido-β-(carbazolyl)propanoate **3**, **12** or **16** (4 mmol) in the same solvent (10 ml). The reaction mixture was stirred at room temperature for 12 h, and the solvent was removed under reduced pressure at 25°C, the residual material was recrystallized from benzene/n-hexane (1:1).

Ethyl α-[(Triphenylphosphoranylidene)amino]-β-[2-(1,9-dimethyl)carbazolyl]acrylate (3). (95%), m.p. 185-187°C (yellow prisms). (Found: C, 78.00; H, 5.92; N, 5.00. $C_{37}H_{33}N_2O_2P$ requires: C, 78.17; H, 5.81; N, 4.93): i.r. (Nujol) 1698, 1589, 1111 and 1045 cm^{-1}; ^{1}H n.m.r. δ ($CDCl_3$): 1.03 (t, 3H, J=7.0Hz), 2.79 (s, 3H, CH_3-C-1), 3.91 (q, 2H, J=7.1Hz), 4.05 (s, 3H, CH_3N), 7.19 (d, 1H, J_{H-P}=6.4Hz, H-β), 7.3-7.5 (m, 12H, H-6+H-3+H-7+6H_m+3H_p), 7.7-7.8 (m, 6H, J_{H-P}=12.0Hz, H_o), 7.80 (d, 1H, J=8.3Hz, H-8), 8.02 (d,1H, J=7.6 Hz, H-4), 8.37 (d, 1H, J=8.2Hz, H-5); ^{13}C n.m.r. δ ($CDCl_3$): 14.1 (*CH_3*-CH_2O), 16.0 (CH_3-C-1), 33.4 (CH_3N), 60.6 (CH_3-*CH_2*O), 108.5 (C-3), 116.2 (d, $^3J_{P-C}$=18.9Hz, C-β), 118.6 (C-8), 118.9 (C-1), 119.6 (C-4), 122.0 (C-4b), 122.4 (C-5), 123.4 (C-4a), 125.0 (C-6), 128.0 (d, $^3J_{P-C}$=12.1Hz, C_m), 128.3 (C-7), 130.8 (d, $^4J_{P-C}$= 2.1Hz, C_p), 132.0 (C-2), 132.5 (d, $^2J_{P-C}$=9.7Hz, C_o), 134.9 (d, $^1J_{P-C}$=85.7Hz, C_i), 136.1 (d, $^2J_{P-C}$=5.3Hz, C-α), 140.8 (C-9a), 142.6 (C-8a), 168.36 (d, $^3J_{P-C}$=7.0Hz, CO); m/z (%): 568 (M^+, 100), 284 (70).

Ethyl α-[(Triphenylphosphoranylidene)amino]-β-[1-(9-methyl)carbazolyl]acrylate (12). (80%), m.p. 142-143°C (yellow prisms). (Found: C, 77.85; H, 5.73; N, 4.92. $C_{36}H_{31}N_2O_2P$ requires: C, 77.96; H, 5.63; N, 5.05); i.r. (Nujol) 1702 , 1593 and 1104 cm^{-1}; ^{1}H n.m.r. δ ($CDCl_3$): 1.06 (t, 3H, J=7.2Hz), 3.96 (q, 2H, J=7.2Hz), 4.04 (s,

3H, CH_3N), 7.11 (t, 1H, J=7.6Hz, H-6), 7.21 (td, 1H, J=7.6, 1.0Hz, H-7), 7.28-7.34 (m, 8H, $6H_m$+H-3+H-8), 7.40 (td, 3H, J=7.6, 1.5Hz, H_p), 7.50 (d, 1H, J_{H-P}=6.0Hz, H-β), 7.61-7.68 (m, 6H, J_{H-P}=11.9Hz, H_o), 7.93 (dd, 1H, J=7.6, 1.0Hz, H-2), 8.06 (d, 1H, J=7.9Hz, H-4), 8.35 (d, 1H, J=7.6Hz, H-5); ^{13}C n.m.r. δ ($CDCl_3$): 14.1 (*CH_3*-CH_2O), 32.7 (CH_3N), 60.7 (CH_3-*CH_2*O), 108.6 (C-8), 118.4 (C-6), 118.5 (C-4), 118.5 (d, $^3J_{P-C}$=19Hz, C-β), 118.7 (C-5), 119.7 (C-3), 122.0 (C-1), 123.1 (C-4b), 123.6 (C-4a), 125.3 (C-7), 128.1 (d, $^3J_{P-C}$=12.2Hz, C_m), 128.2 (C-2), 129.7 (d, $^1J_{P-C}$=103Hz, C_i), 131.0 (d, $^4J_{P-C}$=2.5Hz, C_p),132.5 (d, $^2J_{P-C}$=9.8Hz, C_o), 136.0 (d, $^2J_{P-C}$=6.0Hz, C-α), 139.0 (C-9a), 141.8 (C_{8a}), 167.9 (d, $3J_{P-C}$=6.5Hz, CO); m/z (%): 554 (M^+, 40), 183 (100).

Ethyl α-[(Triphenylphosphoranylidene)amino]-β-[2-(9-methyl)carbazolyl]acrylate (16). (80%), m.p. 192-193°C (yellow prisms). (Found: C, 77.82; H, 5.73; N, 4.95. $C_{36}H_{31}N_2O_2P$ requires: C,77.98; H,5.60; N, 5.05); i.r. (Nujol) 1692, 1573 and 1042 cm^{-1}; ^{1}H n.m.r. δ ($CDCl_3$): 0.99 (t, 3H, J=7.0Hz), 6.99 (d, 1H, J_{H-P}=7.0Hz, H-β), 7.15 (td, 1H, J=8.1, 1.2Hz, H-6), 7.27 (d, 1H, J=8.2Hz, H-8), 7.37 (td, 1H, J=8.2, 1.2Hz, H-7), 7.4-7.5 (m, 9H, $6H_m$+$3H_p$), 7.53 (dd, 1H, J=8.0, 1.1Hz, H-3), 7.7-7.9 (m, 6H, J_{H-P}=12.0Hz, H_o), 7.94 (d, 1H, J=8.0Hz, H-4), 8.00 (d, 1H, J=7.7Hz, H-5), 8.8 (s, 1H, H-1); ^{13}C n.m.r. δ ($CDCl_3$): 14.1 (*CH_3*-CH_2O), 28.9 (CH_3N), 60.8 (CH_3-*CH_2*O), 108.1 (C-6), 108.7 (C-1), 118.5 (C-β), 119.4 (C-4), 119.9 (C-5), 121.0 (C-4a), 122.1 (C-3), 123.1 (C-4b), 124.9 (C-8), 128.2 (d, $^3J_{P-C}$=12.1Hz, C_m), 128.4 (C-7+C-2), 130.9 (d, $^4J_{P-C}$=2.5Hz, C_p), 132.5 (d, $^2J_{P-C}$=9.6Hz, C_o), 133.4 (d, $^1J_{P-C}$=103Hz, C_i), 133.9 (d, $^2J_{P-C}$=6.1Hz, C-α), 136.1 (C-9a), 141.5 (C-8a), 168 (d, $^3J_{P-C}$=7.1Hz, CO); m/z (%): 554 (M^+, 10), 219 (100).

General Procedure for the Preparation of 6H-pyrido[4,3-b]carbazoles (5), 11H-pyrido[4,3-a] carbazoles (13) and 11H-pyrido[3,4-a]carbazoles (18) and (19).

To a solution of iminophosphorane **3**, **12** or **16** (1 mmol) in dry toluene (40 ml) was added the appropiate isocyanate (1 mmol). The reaction mixture was stirred at room temperature for 2h and then heated at 160°C in a sealed tube for 22h. After cooling, the solvent was removed and the crude product was chromatographed on a silica gel column, eluting with dichloromethane/ethyl acetate to afford **5**, **13**, **18** or **19** as crystalline solids.

5a: (70%), m.p. 204-207°C (brown prisms from ethanol/ethyl acetate); (Found: C, 73.00; H, 6.48; N, 11.50 .$C_{22}H_{23}N_3O_2$ requires: C, 73.13; H, 6.37; N; 11.63); i.r. (Nujol) 3395 (NH) and 1708 (COOEt) cm^{-1}; ^{1}H n.m.r. δ ($CDCl_3$): 1.41 (t, 3H, J=7.1Hz, *CH_3*-CH_2NH), 1.48 (t, 3H, J=7.1Hz), 2.84 (s, 3H, CH_3-C-5), 3.79 (q, J=7.2Hz, *CH_3*-CH_2NH), 3.86 (s, 3H, CH_3N), 4.48 (q, 2H, J=7.1Hz), 5.27 (br, 1H, NH), 7.22 (t, 1H, J=7.7Hz, H_9), 7.25 (d, 1H, J=8.3Hz, H-7), 7.50 (td, 1H, J=8.2, 0.8Hz, H-8), 7.97 (d, 1H, J=7.7Hz, H-10), 8.01 (s, 1H, H-11), 8.10 (s, 1H, H-4); ^{13}C n.m.r. δ ($CDCl_3$): 14.1 (CH_3-C-5), 14.4 (*CH_3*-CH_2O), 14.9 (*CH_3*-CH_2NH), 33.2 (CH_3N), 36.6 (CH_3-*CH_2*NH), 61.1 (CH_3-CH_2O), 108.6 (C-7), 110.3 (C-11), 110.8 (C-4), 113.9 (C-5), 114.3 (C-11a), 119.4 (C-9), 120.3 (C-10), 122.4 (C-10a), 125.6 (C-10b), 127.4 (C-8), 134.0 (C-4a), 138.7 (C-3), 141.0 (C-5a), 144.2 (C-6a), 155.9 (C-1), 167.3 (CO).; m/z (%): 361 (M^+, 57), 216 (100).

5b: (72%), m.p.237-239°C (yellow prisms from ethanol/ethyl acetate); (Found: C, 73.48; H, 6.79; N, 11.05. $C_{23}H_{25}N_3O_2$ requires: C, 73.6; H, 6.67; N, 11.20); i.r. (Nujol) 3397 (NH) and 1709 (COOEt) cm^{-1}; ^{1}H n.m.r. δ ($CDCl_3$): 1.42 (d, 6H, J=6.4Hz), 1.47 (t, 3H, J=7.1Hz), 2.91 (s, 3H, CH_3-C-5), 3.91 (s, 3H, CH_3N), 4.47 (q, 2H, J=7.1Hz), 4.71 (m, 1H), 5.27 (d, 1H, J=7.0Hz, NH), 7.21 (t, 1H, J=7.7Hz, H-9), 7.26 (d, 1H, J=8.2Hz, H-7), 7.48 (td, 1H, J=8.2, 1.0Hz, H-8), 8.04 (d, 1H, J=7.5Hz, H-10), 8.1 (s, 1H, H-11), 8.14 (s, 1H, H-4); ^{13}C n.m.r. δ ($CDCl_3$): 14.2 (CH_3-C-5), 14.4 (*CH_3*-CH_2O), 18.3 ((*CH_3*)$_2$-CH), 33.3 (CH_3N), 42.9 ((CH_3)$_2$-*CH*), 61.0 (CH_3-*CH_2*O), 108.6 (C-7), 110.4 (C-4), 110.4 (C-11), 114.1 (C-5), 114.4 (C-11a), 119.4 (C-9), 120.3 (C-10), 122.5 (C-10a), 125.7 (C-10b), 127.5 (C-8), 134.3 (C-4a), 139.0 (C-3), 141.2 (C-5a), 144.3 (C-6a), 155.2 (C-1), 167.4 (CO); m/z (%): 375 (M^+, 100), 261 (86).

5c: (73%), m.p. 183-184°C (yellow needles from ethanol/ethyl acetate). (Found: C, 76.50; H, 6.08; N, 9.85. $C_{27}H_{25}N_3O_2$ requires: C, 76.60; H, 5.91; N, 9.93); i.r. (Nujol) 3330 (NH) and 1710 (COOEt) cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 1.48 (t, 3H, J=7.0Hz), 2.37 (s, 3H, CH_3Ar), 2.78 (s, 3H, CH_3-C-5), 3.78 (s, 3H, CH_3N), 4.42 (q, 2H, J=7.08Hz), 7.18 (s, 1H, NH), 7.19 (d, 2H, J=8.8Hz, H_m), 7.20 (d, 1H, J=8.23Hz, H-7), 7.23 (t, 1H, J=7.7Hz, H-9), 7.51 (t, 1H, J=7.8Hz, H-8), 7.84(d, 2H, J=8.8Hz, H_o), 7.93 (s, 1H, H-11), 7.95 (d, 1H, J=7.28Hz, H-10), 8.15 (s, 1H, H-4); ^{13}C n.m.r. δ ($CDCl_3$): 14.1(CH_3-C-5), 14.3 (CH_3-CH_2O), 20.8 (CH_3Ar), 33.2 (CH_3N), 61.1 (CH_3-CH_2O), 108.7 (C-7),110.3 (C-11), 112.4 (C-4), 114.3 (C-5), 114.5 (C-11a), 119.3 (C_o), 119.5 (C-9), 120.5 (C-10), 122.3 (C-10a), 126.0 (C-10b), 127.7 (C-8), 129.3 (C_m), 131.4 (C_p), 134.3 (C-4a), 137.7 (C-3), 138.5 (s, C_i), 141.0 (C-5a), 144.3 (C-6a), 152.2 (C-1), 167.0 (CO); m/z (%): 423 (M^+, 100), 348 (50).

5d: (75%), m.p. 221-222°C (orange prisms from ethanol/ethyl acetate); (Found: C, 73.71; H, 5.83; N, 9.50 9.50. $C_{27}H_{25}N_3O_3$ requires: C, 73.80; H, 5.70; N, 9.57); i.r. (Nujol) 3363 (NH) and 1711 (COOEt) cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 1.51 (t, 3H, J=6.9Hz), 2.93 (s, 3H, CH_3-C-5), 3.86 (s, 3H, CH_3N), 3.96 (s, 3H, CH_3OAr), 4.47 (q, 2H, J=7.0Hz), 6.96 (dt, 2H, J=9.0, 2.2Hz, H_m), 7.23-7.30 (m, 3H, H-7+H-9+H-11), 7.54 (td, 1H, J=8.1, 1.1Hz, H-8), 7.89 (dd, 2H, J=9.0, 2.2Hz, H_o), 8.08 (d, 1H, J=7.3Hz, H-10), 8.21 (s, 1H, H-4), 8.30 (s, 1H, NH); ^{13}C n.m.r. (DMSO-d_6): 13.7 (CH_3-C-5), 14.2 (CH_3-CH_2O), 33.2 (CH_3N), 55.1 (CH_3OAr), 60.4 (CH_3-CH_2O), 109.42 (C-7), 111.0 (C--11), 112.5 (C-4), 113.4 (C_o), 114.0 (C-5), 114.3 (C-11a), 119.5 (C-9), 120.3 (C-10), 121.4 (C_m), 122.0 (C-10a), 125.5 (C-10b), 127.7 (C-8), 133.8 (C_i), 134.8 (C-4a), 137.7 (C-3), 140.6 (C-5a), 144.1 (C-6a), 152.9 (C-1), 154.1 (C_p), 166.0 (CO); m/z (%): 439 (M^+, 52), 91 (100).

13a: (74%), m.p. 201-202°C (yellow needles from toluene); (Found: C, 72.51; H, 6.18; N, 12.00. $C_{21}H_{21}N_3O_2$ requires: C, 72.60; H, 6.09; N, 12.09); i.r. (Nujol) 3407 (NH) and 1713 (COOEt) cm^{-1}; ^1H n.m.r. δ (DMSO-d_6): 1.31 (t, 3H, J=7.2Hz, CH_3-CH_2NH), 1.39 (t, 3H, J=7.2Hz, CH_3-CH_2O), 3.63 (q, 1H, J=7.2Hz, CH_3-CH_2NH), 4.27 (s, 3H, CH_3N), 4.36 (q, 2H, J=7.2Hz, CH_3-CH_2O), 7.27 (t, 1H, J=7.8Hz, H-8), 7.48 (br, 1H, NH), 7.52(t, 1H, J=7.8Hz, H-9), 7.72 (d, 1H, J=7.8Hz, H-10), 8.03 (d, 1H, J=8.6Hz, H-5), 8.23 (d, 1H, J=7.8Hz, H-7), 8.35 (d, 1H, J=8.6Hz, H-6), 8.48 (s, 1H, H-1); ^{13}C n.m.r. δ (DMSO-d_6): 14.3 (CH_3-CH_2O), 14.7 (CH_3-CH_2NH), 33.3 (CH_3N), 35.8 (CH_3-CH_2NH), 60.5 (CH_3-CH_2O), 107.4 (C-1), 109.8 (C-10), 114.0 (C-5), 117.4 (C-4a), 119.7 (C-8), 120.2 (C-7), 120.6 (C-6), 121.4 (C-6b), 121.7 (C-6a), 124.2 (C-11b), 126.0 (C-9),134.6 (C-2), 139.6 (C-11a), 141.0 (C-10a), 155.6 (C-4), 166.1 (CO); m/z (%): 347 (M^+, 100), 230(30).

13b: (80%), m.p. 191-192°C (yellow prisms from toluene); (Found: C, 73.00; H, 6.52; N, 11.55. $C_{21}H_{23}N_3O_2$ requires: C, 73.11; H, 6.41; N, 11.63); i.r. (Nujol) 3439 (NH) and 1708 (COOEt) cm^{-1}; ^1H n.m.r. δ (DMSO-d_6): 1.35 (d, 6H, J=6.9Hz), 1.40 (t, 3H, J=7.2Hz), 4.34 (s, 3H, CH_3N), 4.38 (q, 2H, J=7.2Hz), 4.65 (m. 1H, J=6.9Hz), 7.21 (d, 1H, J=7.5Hz, NH), 7.32 (td, 1H, J=7.8, 0.6Hz, H-8), 7.55 (td, 1H, J=7.2,1.2Hz, H-9), 7.78 (d, 1H, J=8.4Hz, H-10), 8.15 (d, 1H, J=8.6Hz, H-5), 8.29 (d, 1H, J=7.8Hz, H-7), 8.41 (d, 1H, J=8.6Hz, H-6), 8.54 (s, 1H, H-1); ^{13}C n.m.r. δ (DMSO-d_6): 14.3 (CH_3-CH_2O), 22.4 ((CH_3)$_2$CH), 33.3 (CH_3N), 41.9 ((CH_3)$_2$CH), 60.5 (CH_3-CH_2O), 107.2 (C-1), 109.9 (C-10), 114.2 (C-5), 117.3 (C-4a), 119.7 (C-8), 120.3 (C-7), 120.4 (C-6), 121.4 (C-6b), 121.7 (C-6a), 124.3 (C-11b), 126.0 (C-9), 134.6 (C-2), 139.6 (C-11a), 141.0 (C-10a), 155.03 (C-4), 166.1 (CO); m/z (%): 361 (M^+, 73), 229 (100).

13c: (78%), m.p. 220-221°C (brown prisms from toluene). (Found: C, 75.83; H, 5.43 ; N, 10.70.$C_{25}H_{21}N_3O_2$ requires: C, 75.93; H, 5.35; N, 10.63); i.r. (Nujol) 3424 (NH), 1714 (COOEt) cm^{-1}; ^1H n.m.r. δ (DMSO-d_6): 1.42 (t, 3H, J=7.2Hz), 4.38 (s, 3H, CH_3N), 4.39 (q, 2H, J=7.2Hz), 7.00 (td, 1H, J=7.2, 1.1Hz, H-8), 7.32 (d, 2H, J=8.6Hz, H_m), 7.33Hz (t, 1H, J=7.4Hz, H_p), 7.57 (td, 1H, J=7.2, 1.1Hz, H-9), 7.77 (d, 1H, J=8.4Hz, H-10), 8.17 (d, 2H, J=8.6Hz, H_o), 8.30 (d, 1H, J=8.6Hz, H-5), 8.36 (d, 1H, J=8.2Hz, H-7), 8.50 (d, 1H, J=8.6Hz, H-6), 8.77 (s, 1H, H-

1), 9.15 (s, 1H, NH); ^{13}C n.m.r. δ (DMSO-d_6): 13.8 (*CH_3*-CH_2O), 33.2 (CH_3N), 60.3 (CH_3-*CH_2*O), 109.7 (C-1), 109.8 (C-10), 114.0 (C-5), 117.9 (C-4a), 119.6 (C-8), 119.8 (C_m), 120.0 (C-7), 120.9 (C-6), 121.2 (C_p), 121.7 (C-6b), 121.8 (C-6a), 124.64 (C-11b), 125.9 (C-9), 127.8 (C_o), 134.5 (C-2), 138.5 (C-11a), 141.1 (C-10a), 141.3 (C_i), 152.4 (C-4), 165.4 (CO); m/z (%): 395 (M^+,100), 92 (56).

13d: (83%), m.p. 261-263°C (colorless needles from toluene). (Found :C, 76.18; H, 5.75; N, 10.12. $C_{26}H_{23}N_3O_2$ requires: C, 76.26; H, 5.66; N, 10.26); i.r. (Nujol) 3410 (NH), 1708 (COOEt) cm^{-1}; ^{1}H n.m.r. δ (DMSO-d_6): 1.42 (t, 3H, J=7.2Hz), 2.31 (s, 3H, CH_3Ar), 4.32 (s, 3H, CH_3N), 4.40 (q, 2H, J=7.2Hz), 7.14 (d, 2H, J=8.4Hz, H_m), 7.31 (td, 1H, J=7.8, 0.9Hz, H-8), 7.54 (td, 1H, J=7.8, 0.9Hz, H-9), 7.71 (d, 1H, J=8.1Hz, H-10), 8.04 (d, 2H, J=8.4Hz, H_o), 8.25 (d, 1H, J=8.1Hz, H-5), 8.31 (d, 1H, J=8.1Hz, H-7), 8.42 (d, 1H, J=8.1Hz, H-6), 8.69 (s, 1H, H-1), 9.00 (s, 1H, NH); ^{13}C n.m.r. δ (DMSO-d_6): 13.7 (*CH_3*-CH_2O), 19.9 (CH_3Ar), 32.9 (CH_3N), 60.1 (CH_3-*CH_2*O), 109.2 (C-1), 109.4 (C-10), 113.8 (C-5), 117.7 (C-4a), 119.4 (C-8), 119.7 (C-7), 119.8 (C_m), 120.5 (C-6), 121.1 (C-6b), 121.6 (C-6a), 124.4 (C-11b), 125.8 (C-9), 128.1 (C_o), 129.9 (C_p), 134.4 (C-2), 138.4 (C_i), 138.6 (C-11a), 141.0 (C-10a), 152.4 (C-4), 165.3 (CO); m/z (%): 409 (M^+, 69), 91 (100).

13e: (85%), m.p. 236-237°C (green needles from toluene). (Found: C, 73.25; H, 5.57; N, 9.76. $C_{26}H_{23}N_3O_3$ requires: C, 73.38; H, 5.45; N, 9.88); i.r. (Nujol) 3400 (NH), 1709 (COOEt) cm^{-1}; ^{1}H n.m.r. δ (DMSO-d_6): 1.42 (t, 3H, J=7.2Hz), 3.37 (s, 3H, CH_3Ar), 3.78 (s, 3H, CH_3N), 4.38 (q, 2H, J=7.2Hz), 6.95 (dd, 2H, J=9.0, 1.0Hz, H_m), 7.34 (td, 1H, J=7.8, 1.1Hz, H-8), 7.58 (td, 1H, J=7.8, 1.1Hz, H-9), 7.81 (d, 1H, J=7.8Hz, H-10), 8.11 (dd, 2H, J=9.0, 1.0Hz, H_o), 8.33 (d, 1H, J=7.8Hz, H-7), 8.37 (d, 1H, J=8.6Hz, H-5), 8.54 (d, 1H, J=8.6Hz, H-6), 8.71 (s, 1H, H-1), 9.22 (s, 1H, NH); ^{13}C n.m.r. δ (DMSO-d_6): 14.3 (*CH_3*-CH_2O), 33.5 (CH_3N), 55.2 (CH_3OAr), 60.7 (CH_3-*CH_2*O), 109.6 (C-1), 110.0 (C-10), 113.5 (C_m), 114.2 (C-5), 117.9 (C-4a), 119.9 (C-8), 120.5 (C-7), 121.3 (C-6b), 121.4 (C-6), 121.7 (C_o), 122.0 (C-6a), 124.7 (C-11b), 126.3 (C-2), 134.7 (C-9+C_i), 138.6 (C-11a), 141.2 (C-10a), 152.8 (C-4), 154.35 (C_p), 165.8 (CO); m/z (%): 425 (M^+, 100), 217 (85).

18a: (70%), m.p. 90-92°C (orange prisms from dichloromethane/n-hexane). (Found: C, 78.54; H, 6.18; N, 12.00. $C_{21}H_{21}N_3O_2$ requires: C, 78.67; H, 6.05; N, 12.10); i.r. (Nujol) 3429 (NH), 1708 (COOEt) cm^{-1}; ^{1}H n.m.r. δ ($CDCl_3$): 1.39 (t, 3H, J=7.2Hz, *CH_3*-CH_2NH), 1.47 (t, 3H, J=7.2Hz, *CH_3*-CH_2O), 3.77 (q, 2H, J=7.2Hz, CH_3-*CH_2*NH), 3.99 (s, 3H, CH_3N), 4.47 (q, 2H, J=7.2Hz, CH_3-*CH_2*O), 5.50 (s, 1H, NH), 7.36 (td, 1H, J=8.0, 1.0Hz, H-8), 7.47 (d, 1H, J=8.3Hz, H-10), 7.53 (td, 1H, J=8.3, 1.0Hz, H-9), 7.59 (d, 1H, J=8.2Hz, H-5), 7.93 (s, 1H, H-4), 8.08 (td, 1H, J=7.7, 1.0Hz, H-7), 8.22 (d, 1H, J=8.2Hz, H-6); ^{13}C n.m.r. δ ($CDCl_3$): 14.4 (*CH_3*-CH_2O), 14.9 (*CH_3*-CH_2NH), 36.8 (CH_3-*CH_2*NH), 37.9 (CH_3N), 61.3 (CH_3-*CH_2*O), 108.4 (C-11b), 111.5 (C-10), 114.7 (C-4), 119.82 (C-7), 120.9 (C-5), 121.5 (C-8), 123.1 (C-6), 124.8[a] (C-6a), 124.9[a] (C-6b), 126.4 (C-9), 137.4 (C-4a), 133.8 (C-11a), 139.3 (C-3), 145.6 (C-10a), 154.22 (C-1), 166.3 (CO); m/z (%): 347 (M^+, 100), 303 (46).

18b: (73%), m.p. 113-115°C (orange prisms from diethyl ether/n-hexane). (Found: C, 73.05; H, 6.43; N, 11.56. $C_{22}H_{23}N_3O_2$ requires: C, 73.13; H, 6.37; N, 11.63); i.r. (Nujol) 3396 (NH) and 1703 (COOEt) cm^{-1}; ^{1}H n.m.r. δ ($CDCl_3$): 1.32 (d, 6H, J=6.5Hz), 1.44 (t, 3H, J=7.2Hz), 3.95 (s, 3H, CH_3N), 4.43 (q, 2H, J=7.2Hz), 4.67 (m, 1H, J=6.5Hz), 5.28 (d, 1H, J=7.5Hz, NH), 7.32 (td, 1H, J=7.7, 1.0Hz, H-8), 7.51 (td, 1H, J=8.2, 1.0Hz, H-9), 7.52 (d, 1H, J=8.2Hz, H-10), 7.56 (d, 1H, J=8.2Hz, H-5), 7.88 (s, 1H, H-4), 8.06 (dt, J=7.7, 1.0Hz, H-7), 8.19 (d, J=8.2Hz, H-6); ^{13}C n.m.r. δ ($CDCl_3$): 14.4 (*CH_3*-CH_2O), 22.9 (*$(CH_3)_2$*CH), 38.0 (CH_3N), 42.9 ((CH_3)$_2$*CH*), 61.1 (CH_3-*CH_2*O), 108.4 (C-11b), 111.4 (C-10), 114.1 (C-4), 119.7 (C-7), 120.9 (C-5), 121.4 (C-8), 122.8 (C-6), 124.6[a] (C-6a), 124.8[a] (C-6b), 126.2 (C-9), 137.5 (C-4a), 138.6 (C-11a), 139.6 (C-3), 145.5 (C-10a), 153.4 (C-1), 166.5 (CO); m/z (%): 361 (M^+, 75), 58 (100).

19a: (72%), m.p. 250-252°C (green prisms from ethanol/ethyl acetate). (Found: C, 75.48; H, 5.08; N, 10.92.

$C_{24}H_{19}N_3O_2$ requires: C, 75.59; H, 4.99; N, 11.02); i.r. (Nujol) 3381 (NH), 1709 (COOEt) cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 1.35 (t, 3H, J=7.1Hz), 4.32 (q, 2H, J=7.1Hz), 7.13 (d, 2H, J=8.9Hz, H_o), 7.28 (t, 1H, J=8.0Hz, H-8), 7.30 (d, 1H, J=8.1Hz, H-5), 7.35 (s, 1H, H-4). 7.42-7.50 (m, 4H, H-9+2H_m+H_p), 7.57 (d, 1H, J=8.1Hz, H-10), 8.12 (d, 1H, J=7.8Hz, H-7), 8.26 (d, 1H, J=8.1Hz, H-6), 8.53 (s, 1H, NHAr), 11.58 (s, 1H, NH); ^{13}C n.m.r. δ ($CDCl_3$): 14.1 (*CH_3*-CH_2O), 62.1 (*CH_3*-CH_2O), 111.7 (C-4+C-10), 112.3 (C-11b), 118.2 (C-5), 119.8 (C-8), 120.2 (C-7), 121.8 (C_o), 122.2 (C-6a), 123.4 (C-6b), 123.6 (C-6), 124.0 (C_p), 126.3 (C-9), 126.7 (C-4a), 130.3 (C_m), 130.9 (C_i), 132.5 (C-11a), 137.3 (C-3), 139.6 (C-10a), 148.7 (C-1), 162.5 (CO); m/z (%): 381 (M^+, 31), 77 (100).

19b: (70%), m.p. 215-216°C (green prisms from ethanol/ethyl acetate). (Found: C, 75.81; H, 5.44; N, 10.50. $C_{25}H_{21}N_3O_2$ requires: C, 75.95; H, 5.32; N, 10.63); i.r. (Nujol) 3377 (NH), 1710 (COOEt) cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 1.36 (t, 3H, J=7.1Hz), 2.38 (s, 3H, CH_3Ar), 4.32 (q, 2H, J=7.1Hz), 7.05 (d, 2H, J=8.8Hz, H_o),7.21 (d, 2H, J=8.8Hz, H_m), 7.22 (td, 1H, J=8.0, 1.0Hz, H-8), 7.22 (d, 1H, J=8.1Hz, H-5), 7.31 (s, 1H, H-4), 7.46 (td, 1H, J=8.0, 1.0Hz, H-9), 7.57 (d, 1H, J=8.0Hz, H-10), 8.11 (d, 1H, J=7.8Hz, H-7), 8.24 (d, 1H, J=8.1Hz, H-6), 8.58 (s, 1H, NHAr), 11.69 (1H, NH); ^{13}C n.m.r. δ ($CDCl_3$): 14.2 (*CH_3*-CH_2O), 21.0 (CH_3Ar), 62.1 (CH_3-*CH_2*O), 110.9 (C-4), 111.7 (C-10), 112.5 (C-11b), 118.2 (C-5), 119.8 (C-8), 120.2 (C-7), 121.8 (C_o), 122.3 (C-6a), 123.3 (C_p+C-6b), 123.9 (C-6), 126.3 (C-9), 130.9 (C_m), 132.2 (C_i), 132.9 (C-4a), 137.7 (C-11a), 139.6 (C-3), 145.7 (C-10a), 148.6 (C-1), 162.5 (CO); m/z (%): 395 (M^+, 13), 149 (100).

19c: (75%), m.p. 204-206°C (green prisms from ethanol/ethyl acetate). (Found: C, 72.87; H, 5.28; N, 10.12. $C_{25}H_{21}N_3O_3$ requires: C, 72.99; H, 5.11; N, 10.22); i.r. (Nujol) 3379 (NH) and 1707 (COOEt) cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 1.31 (t, 3H, J=7.2Hz), 3.78 (s, 3H, CH_3OAr), 4.28 (q, 2H, J=7.2Hz), 6.95 (dt, 2H, J=9, 2.3Hz, H_m), 7.04 (dt, 2H, J=9, 2.3Hz, H_o), 7.23 (td, 1H, J=8.0, 1.0Hz, H-8), 7.26 (d, 1H, J=8.0Hz, H-5), 7.27 (s, 1H, H-4), 7.41 (td, 1H, J=8.0, 1.0Hz, H-9), 7.53 (d, 1H, J=8.0Hz, H-10), 8.06 (d, 1H, J=8.0Hz, H-7), 8.21 (d, 1H, J=8.0Hz, H-6), 8.53 (s, 1H, NHAr), 11.60 (s, 1H, NH); ^{13}C n.m.r. δ ($CDCl_3$): 14.1 (*CH_3*-CH_2O), 55.5 (CH_3OAr), 62.1 (CH_3-*CH_2*O), 110.8 (C-4), 111.6 (C-10), 112.4 (C-11b), 115.5 (C_m), 118.1 (C-5), 119.7 (C-8), 120.1 (C-7), 122.2 (C-6a), 122.8 (C_o), 123.2 (C-6b), 123.7 (C-6), 126.2 (C-4a), 126.2 (C-9), 132.1 (C-11a), 137.6 (C-3), 139.5 (C_i), 141.2 (C-10a), 148.8 (C-1), 155.9 (C_p), 162.4 (CO); m/z: (%): 411 (M^+, 86), 230 (100).

19d: (71%), m.p. 267-269°C (green prisms from ethanol/ethyl acetate). (Found: C, 62.50; H, 4.02; N, 9.00. $C_{24}H_{18}N_3O_2Br$ requires: C, 62.61; H, 3.91; N, 9.13); i.r. (Nujol) 3380 (NH), 1705 (COOEt) cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 1.33 (t, 3H, J=7.2Hz), 4.31 (q, 2H, J=7.2Hz), 7.04 (dt, 1H, J=8.7, 2.0Hz, H_o), 7.2 (td, 1H, J=8.0, 1.0Hz, H-8), 7.34 (d, 1H, J=8.2Hz, H-5), 7.36 (s,1H, H-4), 7.43 (td, 1H, J=8.2, 1.0Hz, H-9), 7.51 (dt, 1H, J=8.7, 2.0Hz, H_m), 7.6 (d, 1H, J=8.2Hz, H-10), 8.07 (d,1H, J=8.0Hz, H-7), 8.28 (d,1H, J=8.2Hz, H-6), 8.54 (s, 1H, NHAr), 11.60 (s, 1H, NH); ^{13}C n.m.r. δ ($CDCl_3$): 14.2 (*CH_3*-CH_2O), 62.3 (CH_3-*CH_2*O), 111.8 (C-10), 112.10 (C-11b), 112.2 (C-4), 118.3 (C-5), 120.0 (C-8), 120.3 (C-7), 122.2 (C-6a), 123.6 (C-6), 123.9 (C_o), 124.1 (C-6b), 126.4 (C-9), 126.9 (C-4a), 132.6 (C_i), 133.3 (C_m+C-11a), 137.4 (C_p), 139.6 (C-3), 146.8 (C-10a), 148.8 (C-1), 162.5 (CO); m/z (%): 461 (M^++2, 22), 459 (M^+, 26), 306 (100).

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