aratory funnel, and an additional 100 mL of water was added. The resulting aqueous solution or suspension was made basic with 5% sodium bicarbonate solution. Chloroform (100 mL) was added to the basic solution. The organic phase was separated, and the remaining aqueous phase was extracted twice with 100-mL portions of chloroform. The organic extracts were combined, dried, ($MgSO_4$), filtered, and concentrated, and the crude products were recrystallized from appropriate solvents.

The apparatus and general procedure described above were used in obtaining the hydrogen-evolution data given in the Results and Discussion section. Hydrogen volumes were corrected to STP conditions.

A. With Ethyl Acetate. A reaction time of 3.5 h followed by recrystallization from isopropyl alcohol yielded 1.78 g (61%) of 2-acetonyl-3-*o*-tolyl-4(3*H*)-quinazolinone (**15a**) as light yellow crystals: mp 163–164 °C; ^1H NMR ($CDCl_3$) δ 14.98 (br s, 1 H, enol), 8.11 (d, J = 8 Hz, 1 H, H_5), 7.76–7.06 (m, 7 H, aromatic), 4.39 (s, 1 H, vinyl), 2.18 (s, 3 H, CH_3), 1.98 (s, 3 H, CH_3); IR (KBr) 1680 cm^{-1} (C=O). Anal. Calcd for $C_{18}H_{16}N_2O_2$: C, 73.95; H, 5.52; N, 9.58. Found: C, 74.13; H, 5.60; N, 9.48.

B. With Ethyl Trifluoroacetate. A reaction period of 1.5 h was followed by recrystallization of the crude product from isopropyl alcohol–chloroform to afford 3.02 g (87%) of 2-(3,3,3-trifluoroacetonyl)-3-*o*-tolyl-4(3*H*)-quinazolinone (**15b**) as white crystals: mp 194–195 °C; ^1H NMR ($CDCl_3$) δ 14.987 (br s, 1 H, enol), 8.41 (d, J = 8 Hz, 1 H, H_5), 8.07–7.26 (m, 7 H, aromatic), 4.92 (s, 1 H, vinyl), 2.23 (s, 3 H, CH_3); ^{19}F NMR ($CDCl_3$) δ 94.3 (s); IR (KBr) 1690 cm^{-1} (C=O). Anal. Calcd for $C_{18}H_{13}F_3N_2O_2$: C, 62.43; H, 3.78; N, 8.09. Found: C, 62.50; H, 3.81; N, 7.98.

C. With Methyl Benzoate. Following a reaction period of 5 h, recrystallization of the crude product from isopropyl alcohol afforded 2.84 g (80%) of 2-phenacyl-3-*o*-tolyl-4(3*H*)-quinazolinone (**15c**) as light yellow flakes: mp 216–217 °C; ^1H NMR (Me_2SO-d_6) δ 15.50 (br s, 1 H, enol), 8.18 (d, J = 1 Hz, 1 H, H_5), 7.98–7.32 (m, 12 H, aromatic), 5.07 (s, 1 H, vinyl), 2.19 (s, 3 H, CH_3); IR (KBr) 1680 cm^{-1} (C=O). Anal. Calcd for $C_{23}H_{18}N_2O_2$: C, 77.13; H, 5.12; N, 8.17. Found: C, 77.41; H, 5.04; N, 8.27.

D. With Ethyl 1-Adamantylcarboxylate. A reaction period of 3.5 h followed by recrystallization from isopropyl alcohol–chloroform–hexane afforded 3.3 g (81%) of 2-[2-oxo-2-(1-adamantyl)ethyl]-3-*o*-tolyl-4(3*H*)-quinazolinone (**15d**): mp 221–222 °C; ^1H NMR ($CDCl_3$) δ 15.82 (br s, 1 H, enol), 8.20 (d, J = 8 Hz, 1 H, H_5), 7.72–7.16 (m, 7 H, aromatic), 4.56 (s, 1 H, vinyl), 2.18 (s, 3 H, CH_3), 2.06–1.48 (m, 15 H, CH and CH_2); IR (KBr) 1680 cm^{-1} (C=O). Anal. Calcd for $C_{27}H_{28}N_2O_2$: C, 78.61; H, 6.84; N, 6.79. Found: C, 78.23; H, 6.69; N, 6.64.

E. With Ethyl Oxalate. To a refluxing slurry of 1.05 g (25 mmol) of sodium hydride (57% dispersion) and 3.2 g (22 mmol) of diethyl oxalate in 140 mL of DME was added dropwise 1.25 g (5 mmol) of **3a** in 40 mL of DME over a period of 4.5 h. When addition was complete, the reaction was allowed to continue at reflux for an additional 45 min. The resulting yellow reaction mixture was processed as described above. The resulting concentrate was triturated with hexane–ether to afford a yellow solid that was recrystallized from isopropyl alcohol to give 1.08 g (62%) of 2-(ethoxalylmethyl)-3-*o*-tolyl-4(3*H*)-quinazolinone (**15e**): mp 191–191.5 °C; ^1H NMR ($CDCl_3$) δ 15.51 (br s, 1 H, enol), 8.35 (d, J = 8 Hz, 1 H, H_5), 8.00–7.24 (m, 7 H, aromatic), 5.47 (s, 1 H, vinyl), 4.30 (q, J = 7 Hz, 2 H, CH_2), 2.21 (s, 3 H, CH_3), 1.35 (5, J = 7 Hz, 3 H, CH_3); IR (KBr) 1710, 1680 cm^{-1} (C=O). Anal. Calcd for $C_{20}H_{18}N_2O_4$: C, 68.56; H, 5.18; N, 8.00. Found: C, 68.42; H, 5.03; N, 7.88.

F. With Dimethyl Phthalate. This reaction was accomplished by dropwise addition of 1.25 g (5 mmol) of **3a** in 40 mL of DME to a refluxing slurry of 1.05 g (25 mmol) of sodium hydride (57% dispersion) and 3.88 g (20 mmol) of dimethyl phthalate in 140 mL of DME, over a period of 6 h. After addition was complete, the reaction was allowed to continue for an additional 1 h. The orange reaction mixture was processed as usual, and the crude product was chromatographed. Elution with ether–chloroform (98:2) gave 0.43 g (22%) of 2-(1,3-dioxo-2-indanyl)-3-*o*-tolyl-4(3*H*)-quinazolinone (**16**) as yellow crystals: mp 268–270 °C; ^1H NMR ($CDCl_3$) δ 14.66 (br s, 1 H, enol), 8.22 (d, J = 8 Hz, 1 H, H_5), 7.90–7.07 (m, 11 H, aromatic), 2.39 (s, 3 H, CH_3); IR (KBr) 1710, 1690 cm^{-1} (C=O). Anal. Calcd for $C_{24}H_{16}N_2O_3$: C, 75.78; H, 4.24; N, 7.36. Found: C, 75.71; H, 4.33; N, 7.00.

Registry No. 3a, 72-44-6; **3a** potassium salt, 73308-58-4; **3b**, 1769-25-1; **3c**, 2385-23-1; **4a**, 73308-59-5; **4b**, 73308-60-8; **4c**, 73308-61-9; **5a**, 1898-07-3; **5b**, 73308-62-0; **5c**, 30006-43-0; **5d**, 73323-95-2; **5e**, 19857-39-7; **5f**, 73308-63-1; **6**, 73283-05-3; **7**, 73308-64-2; **8**, 73283-06-4; **9**, 2004-80-0; **10**, 73308-65-3; **11**, 73308-66-4; **12**, 73308-67-5; **13**, 73308-68-6; **14a**, 73308-69-7; **14b**, 73308-70-0; **15a**, 73308-71-1; **15b**, 73308-72-2; **15c**, 73308-73-3; **15d**, 73308-74-4; **15e**, 73308-75-5; **16**, 73308-76-6; 2-methyl-4(3*H*)-quinazolinone, 1769-24-0; methyl iodide, 74-88-4; allyl bromide, 106-95-6; ethyl iodide, 75-03-6; diphenyl disulfide, 882-33-7; phenyl benzenethiosulfonate, 1212-08-4; benzaldehyde, 100-52-7; cyclohexanone, 108-94-1; benzophenone, 119-61-9; acetone, 67-64-1; ethyl acetate, 141-78-6; ethyl trifluoroacetate, 383-63-1; methyl benzoate, 93-58-3; ethyl oxalate, 95-92-1; dimethyl phthalate, 131-11-3.

Photocyclization of 1-(1-Chloroisoquinolin-6-yl)-1*H*-*v*-triazolo[4,5-*c*]pyridines to 10-Chloro-5*H*-pyrido[3′,4′:4,5]pyrrolo[2,3-*g*]isoquinolines (Azaellipticines)[1]

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Whereas thermal cyclization of 1-(5,8-dimethyl-1-oxo-1,2-dihydroisoquinolin-6-yl)-1*H*-*v*-triazolo[4,5-*c*]pyridine affords 6,11-dimethyl-5*H*-pyrido[3′,4′:4,5]pyrrolo[2,3-*g*]isoquinolin-10(9*H*)-one which cannot be chlorinated to the corresponding chloro derivative, photocyclization of the 1-(5,8-dimethyl-1-chloroisoquinolin-6-yl)-1*H*-*v*-triazolo[4,5-*c*]pyridine allows for the synthesis of the expected 6,11-dimethyl-10-chloropyrido[3′,4′:4,5]pyrrolo-[2,3-*g*]isoquinoline. Subsequent conversions of this last compound yield 10-((dialkylamino)alkyl)amino-substituted derivatives, which are dimethylated analogues of a previously described potent antitumor azaellipticine derivative. potent antitumor azaellipticine derivative.

In a recent paper the synthesis of an aza analogue of ellipticine 1[2] which has antitumor activity on L1210 leukemia in mice[3] has been described. However, 10-(((γ-dialkyamino)propyl)amino)-6-methyl-5*H*-pyrido-

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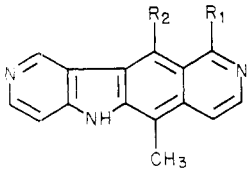


1, R_1 = H; R_2 = CH_3
2, R_1 = $NH(CH_2)_3NEt_2$; R_2 = H

[3′,4′:4,5]pyrrolo[2,3-*g*]isoquinoline **2**,[4] a derivative of this new heterocyclic ring system which is devoid of the 11-methyl group but has the ((dialkylamino)alkyl)amino side chain on its 10-position, is a much more potent antitumor drug[3] than the former one.

Since the presence of the 11-methyl group is considered in the ellipticine series as very important for displaying antitumor properties[5] and the increase in biological activity due to the ((dialkylamino)alkyl)amino side chain has been confirmed,[6] the 11-methylated homologues and analogues of the **2** appeared of special interest as potential new antitumor drugs. We describe here the synthesis of such new derivatives of the pyrido[3′,4′:4,5]pyrrolo[2,3-*g*]isoquinoline ring system (9-azaellipticine).

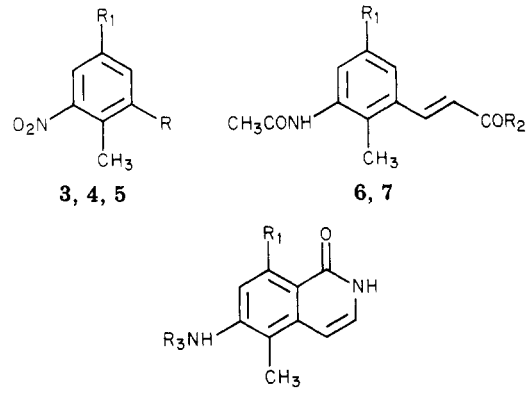
Results

The main compounds for the synthesis outlined in Schemes I and II are 6-amino-5-methylisoquinolin-1-(2*H*)-ones (**9a** and **9b**). They were obtained from 3-acetamido-2-methylcinnamic acids (**6a** and **6b**) via the corresponding azides (**7a** and **7b**) which rearranged in boiling diphenyl ether to acetamido derivatives (**8a** and **8b**) and gave free bases (**9a** and **9b**) by acidic hydrolysis.

Cinnamic acid **6a** was prepared by two routes: (A) by the Meerwein arylation of acrylic acid with 3-nitro-2,5-dimethylphenyldiazonium chloride obtained from 3-nitro-2,5-dimethylaniline;[7] the resulting β-(3-nitro-2,5-dimethylphenyl)-α-chloropropionic acid (**3a**) led to the corresponding nitrocinnamic acid (**4a**) by methanolic potassium hydroxide treatment and then 3-acetamido-2,5-dimethylcinnamic acid (**6a**) by reduction on Raney nickel catalyst followed by acetylation; (B) by the chloromethylation of nitro *p*-xylene which gave 3-nitro-2,5-dimethylbenzyl chloride already described[8] and a byproduct not reported previously, 2,5-dimethyl-3-nitro-1,4-bis(chloromethyl)benzene. Transformation of 3-nitro-2,5-dimethylbenzyl chloride to 3-nitro-2,5-dimethylbenzaldehyde (**5**) was accomplished by the Sommelet reaction, and finally condensation with malonic acid gave nitrocinnamic acid **4a** identical with that prepared by route A.

Cinnamic acid **6b** was previously obtained from 3-acetamido-2-methylbenzonitrile by reduction to the corresponding aldehyde by boiling in dilute formic acid with Raney nickel. However, for large-scale preparation of **2**, this key intermediate **6b** was prepared by the Meerwein arylation procedure described by route A which was more convenient and consistent.

Scheme I



3, 4, 5 **6, 7** **8, 9**

3, R = $CH_2CHCOOH$ (Cl)
↓
4, R = CH=CHCOOH → **6**, R_2 = OH → **8**, R_3 = $COCH_3$
↑ ↓ ↓
5, R = CHO **7**, R_2 = N_3 **9**, R_3 = H

a, R_1 = CH_3; b, R_1 = H

As previously described for the synthesis of **14b**, 6-amino-5,8-dimethylisoquinolin-1(2*H*)-one (**9a**) was converted to **13a**. Unfortunately, all attempts to convert **13a** to the corresponding chlorinated derivative **14a** using phosphorus oxychloride, phosphorus oxychloride plus phosphorus pentachloride, phosphorus trichloride, phosphorus pentachloride, and phenylphosphonyl dichloride, under various experimental conditions, were unsuccessful. The only isolated product was a complex one, insoluble in the usual organic solvents, which could not be purified.

Alternatively, the transformation of triazolopyridine derivatives **12** by boiling in phosphorus oxychloride gave the corresponding chloro derivatives **15** in high yield. Attempts to transform **15b** to **14b** by thermal cyclization led to complex mixtures[4] and only traces of the desired product were obtained. Therefore, a photochemical technique was investigated. Irradiation of a 0.1% absolute ethanolic solution of 1-(1-chloro-5,8-dimethylisoquinolin-6-yl)-1*H*-*v*-triazolo[4,5-*c*]pyridine (**15a**) in an argon atmosphere with a 15-W low-pressure Hanau mercury lamp afforded 10-chloro-6,11-dimethyl-5*H*-pyrido[3′,4′:4,5]-pyrrolo[2,3-*g*]isoquinoline (**14a**) in 35% yield, along with the dechlorinated compound **16a**. **14a** and **16a** were separated by preparative silica column chromatography. Under similar conditions, the monomethylated derivative **15b** provided **14b** (and **16b**) by a new route avoiding the 340 °C thermal cyclization and the subsequent chlorination which was difficult on a large scale.

Because of the low solubility of the starting materials, the first photocyclization attempts were performed in several solvents: ethylene glycol monoethyl ether, acetic acid, benzene, and ethanol, with 2- and 15-W UV mercury lamps. Benzene and acetic acid gave complex mixtures with very low yields of the pure desired compounds **14** and larger amounts of the dechlorinated ones (**16**). An appreciable amount of dechlorinated derivatives **16** was also obtained in ethylene glycol monoethyl ether. Thus, the preferred solvent appeared to be ethanol. The irradiation with a 2-W UV lamp required a long reaction time before the total disappearance of the the starting material. This resulted in increased dechlorination and the 15-W UV lamp was usually preferred.

(1) This investigation was partly supported by funds from the Délégation Générale à la Recherche Scientifique et Technique, Grant 77-7-1351, and by the Institut National de la Santé et de la Recherche Médicale FRA 25 (J.M.L.).

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(3) J. C. Chermann, J. Gruest, L. Montagnier, F. Wendling, P. Tambourin, M. Perrin, F. Pochon, C. Ducrocq, C. Rivalle, and E. Bisagni, *C. R. Hebd. Seances Acad. Sci., Ser. D*, 945 (1977).
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These photocyclizations represent another example of a Graebe–Ullmann type reaction which has been utilized for the synthesis of carbazole.[9] In the present case, the advantage of the photochemical method is to permit the preparation of functionalized compounds which were unaccessible by thermal routes.

(γ-(Diethylamino)propyl)amine, (γ-(dimethylamino)-propyl)amine, and (β-(diethylamino)ethyl)amine react with chloro derivative **14a** giving, respectively, the expected corresponding compounds **17**, **18**, and **19**. Structures of these final products and of some intermediates were determined by high-resolution ^{1}H NMR spectroscopy at 100 MHz using the Fourier transform technique along with homonuclear decoupling and nuclear Overhauser enhancement measurements for unambiguous assignments.

Detailed results on the biological properties of these compounds will be reported elsewhere.[10] It can be said, however, that 10-((β-(diethylamino)propyl)amino)-6,11-dimethyl-5*H*-pyrido[3′,4′:4,5]pyrrolo[2,3-*g*]isoquinoline (**17**) is more cytotoxic on cultured cells than and at least as active as its 11-demethyl analogue **2** on mouse L1210 leukemia.

Experimental Section

Melting points were determined with a Reichert hot stage apparatus and were not corrected. IR spectra were obtained for KBr pellets with a Perkin-Elmer Model 21 double-beam spectrometer. NMR spectra were recorded with a Hitachi Perkin-Elmer 60-MHz apparatus or with a Varian XL-100 when stated (100 MHz, solvent Me_2SO-d_6, Me_4Si as internal standard). Mass spectra were obtained by M. C. Bosso, CERMAV, Grenoble, with a Varian MS30 AEI apparatus equipped with a computer 100 MS, working at low resolution.

***trans*-2,5-Dimethyl-3-nitrocinnamic Acid (4a) from 2,5-Dimethyl-3-nitroaniline.** A suspension of 2,5-dimethyl-3-nitroaniline hydrochloride[7] (337 g, 1.6 mol) in acetone (2 L) and 12 N hydrochloric acid (155 mL) was cooled to 0 °C in a 4-L three-necked flask fitted with a mechanical stirrer. Sodium nitrite (115 g, 1.66 mol) in water (200 mL) was added dropwise over a 45-min period, maintaining the temperature below 5 °C by external cooling in an ice–salt bath. Separately, a solution containing acetone (1.5 L), water (420 mL), cupric chloride (142 g), and a large excess of acrylic acid (830 g) was placed in a 10-L flask fitted with an efficient mechanical stirrer and heated to 35 °C. Under vigorous stirring, the preceding aryldiazonium solution maintained at 0 °C was progressively added over a 45-min period while the temperature of the reaction mixture was maintained at 35 °C. After the addition was complete, stirring was continued for 20 min at 35 °C and then the solvent was removed under reduced pressure. The residue taken up in water was extracted with chloroform and the combined organic layer was washed with water and extracted with aqueous sodium hydroxide. Acidification of the alkaline solution gave a solid which was filtered, washed with water, and dried, giving crude **3a**, 275 g (68%), mp 142 °C, which was sufficiently pure for the next step. Thus, to a solution of potassium hydroxide (158 g, 2.82 mol) in methanol (1.5 L) was added the whole preceding crude compound (275 g, 1.07 mol), and the mixture was warmed under reflux for 1 h. After evaporation of methanol, the residue was dissolved in water and acidified to pH 1 with hydrochloric acid, giving a solid which was filtered, washed with water, dried, and finally recrystallized in ethyl acetate to give pure **4a**: 190 g (80%), mp 232 °C; IR 1690 (C=O), 1630 (C=C), 1550 and 1355 (NO_2) cm^{-1}; NMR δ 2.35 (2 CH_3, 6 H, s), 6.95 (H-α, 1 H, d, $J_{\alpha,\beta}$ = 16 Hz), 7.65 (H-6, 1 H, s), 7.8 (H-4, 1 H, s), 7.8 (H-β, 1 H, d, $J_{\alpha,\beta}$ = 16 Hz). Anal. Calcd for $C_{11}H_{11}NO_4$ (mol wt 221.21): C, 59.72; H, 5.01; N, 6.33. Found: C, 59.74; H, 4.91; N, 6.21.

4a from 5. 2,5-Dimethyl-3-nitrobenzaldehyde (**5**, 193.7 g, 1.08 mol), dry pyridine (1.5 L), malonic acid (112.5 g, 1.08 mol), and piperidine were mixed and heated under reflux. After 3.5 h and 6 h, malonic acid (112.5 g at once) was again added and reflux continued for a total 24-h period. The solvent was evaporated and the residue taken up in acetone was filtered, washed with water and acetone, and finally recrystallized from ethyl acetate, giving **4a**, 173 g (72%), mp 232 °C, identical with material from 2,5-dimethyl-3-nitroaniline.

2,5-Dimethyl-3-nitrobenzyl Chloride and 2,5-Dimethyl-3-nitro-1,4-bis(chloromethyl)benzene. 2,5-Dimethyl-3-nitrobenzyl chloride, bp 176–182 °C (12 mm), was obtained according to ref 8. In our hands, distillation of the residue afforded another product, bp 190–200 °C (12 mm), corresponding to the dichloromethylated derivative which was recrystallized from ethanol to give colorless crystals (yield 6%): mp 110 and 130 °C; IR 1520 and 1360 (NO_2) cm^{-1}; NMR (100 MHz) δ 2.23 (CH_3-2, 3 H, s), 2.44 (CH_3-5, 3 H, s), 4.62 (CH_2-4, 2 H, s), 4.85 (CH_2-1, 2 H, s), 7.59 (H-6, 1 H, s) (assigned by a ca. 15% nuclear Overhauser effect enhancement of the 6-H resonance upon selective irradiation of 5-CH_3 and 1-CH_2). At high resolution one can resolve J_{CH_3,CH_3} = 0.6 Hz, $J_{6,CH_3\text{-}2}$ = 0.4 Hz, $J_{6,CH_3\text{-}5}$ = 0.7 Hz, $J_{6,CH_2\text{-}4}$ = 0.3 Hz, and $J_{6,CH_2\text{-}1}$ = 0.25 Hz. Anal. Calcd for $C_{10}H_{11}Cl_2NO_2$ (mol wt 248): C, 48.39; H, 4.43; N, 5.65; Cl, 28.63. Found: C, 48.42; H, 4.53; N, 5.60; Cl, 28.70.

2,5-Dimethyl-3-nitrobenzaldehyde (5). The preceding nitrobenzyl chloride (610 g, 3.05 mol), acetic acid (1.3 L), water (1.3 L), and hexamethylenetetramine (855 g, 6.1 mol) were mixed and heated at reflux for 2 h. Hydrochloric acid (12 N, 1 L) was added over a 10-min period, and the mixture was again heated at reflux for 20 min. The cooled mixture, diluted to 6 L by water, afforded a solid which was filtered, dried, and recrystallized from cyclohexane to give yellow needles, 277 g, mp 90–93 °C. By extraction of mother liquors with diethyl ether, usual treatment, distillation, bp 160–162 °C (12 mm), and recrystallization, a second crop of the expected product, 13.5 g, was obtained: total yield 290.5 g (53%); IR 1710 (C=O), 1535 and 1350 (NO_2) cm^{-1}; NMR ($DCCl_3$) δ 2.45 (CH_3-5, 3 H, s), 2.7 (CH_3-2, 3 H, s), 7.8 (H-6, 1 H, s), 7.85 (H-4, 1 H, s), 10.45 (CHO, 1 H, s). Anal. Calcd for $C_9H_9NO_3$ (mol wt 179.17): C, 60.33; H, 5.06; N, 7.82. Found: C, 60.13; H, 4.97; N, 7.71.

3-Acetamido-2,5-dimethylcinnamic Acid (6a). Nitrocinnamic acid **4a** (141 g, 0.63 mol) in acetic acid (1.25 L) was hydrogenated on Raney nickel catalyst (140 g) by stirring the heterogeneous mixture in a hydrogen atmosphere at ambient temperature and under normal pressure until absorption of hydrogen had ceased. The catalyst was filtered and washed with acetic acid, the solution was concentrated to 600 mL, and the residue was treated with acetic anhydride (150 mL) at reflux for 2 h. Evaporation of solvent under reduced pressure gave a solid residue which was taken up in 1 N hydrochloric acid (1 L), filtered, washed with water, and recrystallized with acetic acid, giving colorless crystals: 126.2 g (84%), mp 270 °C; IR 3240 (NH), 1685 and 1650 (C=O), 1630 (C=C) cm^{-1}; NMR δ 2.0, 2.15, 2.35 (3 CH_3, 3 × 3 H, 3 s), 6.35 (H-α, 1 H, d, $J_{\alpha,\beta}$ = 16 Hz), 7.15, 7.3 (H-4, H-6, 2 × 1 H, 2 s), 7.85 (H-β, 1 H, d, $J_{\alpha,\beta}$ = 16 Hz), 9.3 (NH, 1 H, s). Anal. Calcd for $C_{13}H_{15}NO_3$ (mol wt 233.26): C, 66.93; H, 6.48; N, 6.01. Found: C, 66.78; H, 6.51; N, 6.11.

3-Acetamido-2-methylcinnamic Acid (6b). This compound had been previously prepared from 3-acetamido-2-methylbenzaldehyde. It has now been obtained from 2-methyl-3-nitroaniline, according to the technique mentioned above, and successfully used for preparations of **3a**, **4a**, and **6a**.

β-(2-Methyl-3-nitrophenyl)-α-chloropropionic acid (3b) was recrystallized in cyclohexane–benzene (1 L) to yeild colorless crystals (63%), mp 119 °C. Anal. Calcd for $C_{10}H_{10}ClNO_4$ (mol wt 243.5): C, 49.28; H, 4.10; N, 5.74. Found: C, 49.56; H, 4.15; N, 5.76.

***trans*-2-Methyl-3-nitrocinnamic acid (4b)** was recrystallized in xylene or ethyl acetate, giving pale yellow crystals (79% from **3b**): mp 222 °C; IR 1690 (C=O), 1640 (C=C) cm^{-1}; NMR δ 2.4 (CH_3, 3 H, s), 6.5 (H-α, 1 H, d, $J_{\alpha,\beta}$ = 16 Hz), 7.3–7.95 (H_{ar}, 3 H, m), 8.0 (H-β, 1 H, s, $J_{\alpha,\beta}$ = 16 Hz). Anal. Calcd for $C_{10}H_9NO_4$ (mol wt 207.18): C, 57.97; H, 4.38; N, 6.76. Found: C, 57.78; H, 4.41; N, 6.58.

Catalytic reduction of **4b** and subsequent acetylation as mentioned for preparation of **6a** gave an 84% yield of **6b**, mp

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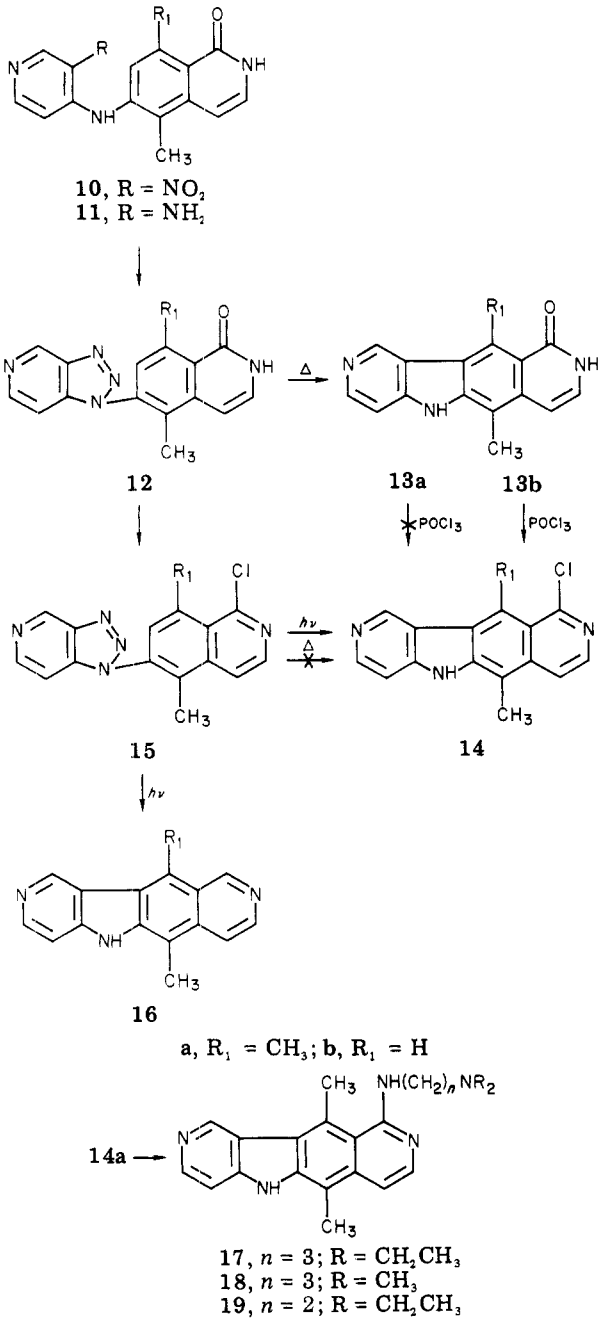
Scheme II



265–267 °C, identical in all respects with that already described.[4]

3-Acetamido-2,5-dimethylcinnamoyl Azide (7a). The cinnamic acid **6a** (125 g, 0.53 mol) was added to a solution of triethylamine (54 g) in acetone (1.1 L). The mixture was cooled below 0 °C and a solution of ethyl chloroformate (78.8 g, 0.72 mol) in acetone (460 mL) was added dropwise. Stirring at 0 °C was continued for 1 h and a solution of sodium azide (52.5 g, 0.8 mol) in water (130 mL) was added, maintaining the temperature below 5 °C. The cold mixture was shaken for a further 1 h at 0–5 °C, then allowed to reach ambient temperature, and poured into distilled water (5 L). The resulting white precipitate was filtered and washed with distilled water and a little acetone, giving azide **7a**, 107 g (77%), mp 150 °C dec, which was air-dried before being used in the following reaction; NMR δ 2.0 (2 CH_3, 6 H, s), 2.2 (CH_3, 3 H, s), 6.15 (H-α, 1 H, d, $J_{\alpha,\beta}$ = 16 Hz), 6.7–7.3 (H-β, H-4, H-6, 3 H, m), 9.2 (NH, 1 H, s).

6-Acetamido-5,8-dimethylisoquinolin-1(2*H*)-one (8a). To a vigorously stirred solution of tributylamine (28.6 g) in diphenyl ether (500 mL) heated and maintained at °C was added as quickly as possible a suspension of the preceding crude but well-dried azide (39.6 g) in diphenyl ether (450 mL) heated at 40 °C. Stirring at 240 °C was continued for a further 15 min, and the solution was concentrated to half-volume under reduced pressure and then allowed to cool. Benzene (350 mL) was added and the precipitate filtered off, washed with benzene, and recrystallized from dimethylformamide to give colorless flakes: 18.7 g (53%), mp > 300 °C; NMR δ 2.1, 2.25, 2.75 (CH_3-5, CH_3-8, CH_3CO, 3 × 3 H, 3 s), 6.65 (H-4, 1 H, d, $J_{3,4}$ = 8 Hz), 7.2 (H-3, 1 H, d, $J_{3,4}$ = 8 Hz), 7.4 (H-7, 1 H, s), 9.65 (exo NH, 1 H, s), 10.9 (ring NH, 1 H, s). Anal. Calcd for $C_{13}H_{14}N_2O_2$ (mol wt 230.26): C, 67.81; H, 6.13; N, 12.17. Found: C, 67.54; H, 6.42; N, 11.96.

6-Amino-5,8-dimethylisoquinolin-1(2*H*)-one (9a). Hydrolysis of **8a** (10.6 g) in ethanol (175 mL) and 12 N hydrochloric acid (35 mL) according to the technique used for obtaining **9b** from **8b**[4] gave **9a** which was recrystallized with ethanol to yield colorless flakes (7.35 g, 85%): mp 242 °C; IR 3200 (NH), 1660–1580 (C=O and NH) cm^{-1}; NMR δ 2.1 (CH_3-5, 3 H, s), 2.7 (CH_3-8, 3 H, s), 5.45 (NH_2, 2 H, s), 6.4 (H-4, 1 H, d, $J_{3,4}$ = 8 Hz), 6.55 (H-7, 1 H, s), 7.0 (H-3, 1 H, d, $J_{3,4}$ = 8 Hz). Anal. Calcd for $C_{11}H_{12}N_2O$ (mol wt 188.22): C, 70.18; H, 6.43; N, 14.88. Found: C, 70.25; H, 6.15; N, 14.52.

5,8-Dimethyl-6-(3-nitro-4-pyridylamino)isoquinolin-1-(2*H*)-one (10a). 4-Chloro-3-nitropyridine (27.3 g, 0.17 mol) was added to a solution of aminoisoquinoline **9a** (34.7 g, 0.18 mol) in dimethylformamide (1 L); the mixture was left at room temperature for 15 days and the solvent was evaporated under reduced pressure. The residue was taken up in 0.5 M hydrochloric acid (2.5 L) and stirred for 1 h and the insoluble material was filtered. The aqueous solution was basified to pH 9–10 with 1 M sodium hydroxide and the precipitate recrystallized in dimethylformamide to give **10a** (35 g, 62.3%) as yellow crystals: mp 310–315 °C; IR 3310, 3120 (NH), 1665 (C=O), 1525 and 1365 (NO_2) cm^{-1}; NMR (100 MHz) δ 2.26 (CH_3-5, 3 H, s), 2.78 (CH_3-8, 3 H, s), 6.43 (H-5′, 1 H, d, $J_{5',6'}$ = 6.1 Hz), 6.59 (H-4, 1 H, d, $J_{3,4}$ = 7, 5 Hz), 7.14 (H-7, 1 H, s), 7.21 (H-3, 1 H, q, $J_{3,4}$ = 7.5, $J_{3,2}$ = 6.0 Hz), 8.21 (H-6′, 1 H, q, $J_{5',6'}$ = 6.1, $J_{6',2'}$ = 0.5 Hz), 9.12 (H-2′, 1 H, d, $J_{2',6'}$ = 0.5 Hz), 9.82 (NH-6, 1 H, s), 11.13 (H-2, 1 H, d, $J_{3,2}$ = 6.0 Hz). Anal. Calcd for $C_{16}H_{14}N_4O_3$ (mol wt 310.3): C, 61.93; H, 4.55; N, 18.06. Found: C, 61.53; H, 4.71; N, 17.76.

1-(5,8-Dimethyl-1-oxo-1,2-dihydroisoquinolin-6-yl)-1*H*-*v*-triazolo[4,5-*c*]pyridine (12a). Raney nickel catalyst (17 g) was added to a solution of the nitro compound **10a** (16.8 g) in acetic acid (1 L) and the mixture was stirred under hydrogen at atmospheric pressure until absorption of hydrogen had ceased. After filtration, an aliquot (50 mL) was evaporated and the residue, taken up in water and basified with 1 M sodium hydroxide, afforded a solid which was recrystallized in acetonitrile, giving colorless crystals of 5,8-dimethyl-6-(3-amino-4-pyridylamino)-isoquinolin-1(2*H*)-one (**11a**): mp 212–215 °C; IR 3390, 3300, 3190 (NH), 1640–1580 (C=O and NH_2) cm^{-1}; NMR δ 2.2 (CH_3-5, 3 H, s), 2.75 (CH_3-8, 3 H, s), 4.55 (NH_2, 2 H, s), 6.45 (H-5′, 1 H, d, $J_{5',6'}$ = 5 Hz), 6.55 (H-4, 1 H, d, $J_{3,4}$ = 7 Hz), 6.9 (H-7, 1 H, s), 7.1 (H-3, 1 H, d, $J_{3,4}$ = 7 Hz), 7.3 (NH, 1 H, s), 7.6 (H-6′, 1 H, d, $J_{5',6'}$ = 5 Hz), 7.95 (H-2′, 1 H, s), 11.1 (H-2, 1 H, s). Anal. Calcd for $C_{16}H_{16}N_4O{\cdot}H_2O$ (mol wt 298): C, 64.41; H, 6.08; N, 18.78. Found: C, 64.14; H, 5.83; N, 18.83.

The remaining solution was stirred and cooled to 14 °C, sodium nitrite (3.61 g) in water (10 mL) was added dropwise, and stirring was continued for 1.5 h more at ambient temperature. The solvent was evaporated and the residue was taken up in water, filtered, and recrystallized from ethanol to yield colorless crystals (12 g, 80%) of **12a**: mp 300–302 °C; IR 3150 (NH), 1650 (C=O) cm^{-1}; NMR δ 2.1 (CH_3-5′, 3 H, s), 2.9 (CH_3-8′, 3 H, s), 6.7 (H-4′, 1 H, d, $J_{3',4'}$ = 7 Hz), 7.3 (H-3′, 1 H, d, $J_{3',4'}$ = 7 Hz), 7.3 (H-7′, 1 H, s), 7.65 (H-7, 1 H, d, $J_{6,7}$ = 6 Hz), 8.65 (H-6, 1 H, d, $J_{6,7}$ = 6 Hz), 9.65 (H-4, 1 H, s), 11.4 (H-2, 1 H, s). Anal. Calcd for $C_{16}H_{13}N_5O$ (mol wt 291): C, 65.97; H, 4.5; N, 24.04. Found: C, 65.66; H, 4.70; N, 24.39.

1-(1-Chloro-5,8-dimethylisoquinolin-6-yl)-1*H*-*v*-triazolo-[4,5-*c*]pyridine (15a). The preceding triazolopyridine **12a** (15.4 g) in phosphorus oxychloride (1.5 L) was heated at reflux with stirring for 3 h. Evaporation of the excess oxychloride afforded a residue which was taken up in water (1 L), cautiously basified to pH 8 by solid sodium carbonate, stirred for 1 h, and collected. Dissolution of the solid compound in boiling ethanol (4 L), filtration, concentration to 500 mL, and cooling gave colorless crystals (13.8 g, 84.6%): mp 260 °C dec; NMR (100 MHz) δ 2.36 (CH_3-5′, 3 H, s) (assigned by nuclear Overhauser enhancement

(NOE) of the 4'-H resonance upon selective irradiation of 5'-CH_3), 3.06 (CH_3-8', 3 H, s) (identified by NOE with 7'-H and 8'-CH_3), 7.69 (H-7, 1 H, q, $J_{6,7}$ = 6.0, $J_{4,7}$ = 1.2 Hz), 7.78 (H-7', 1 H, s), 8.17 (H-4', 1 H, d, $J_{3',4'}$ = 5.9 Hz), 8.48 (H-3', 1 H, d, $J_{3',4'}$ = 5.9 Hz), 8.56 (H-6, 1 H, d, $J_{6,7}$ = 6.0 Hz), 9.16 (H-4, 1 H, s). Anal. Calcd for $C_{16}H_{12}ClN_5 \cdot H_2O$ (mol wt 327.5): C, 58.62; H, 4.27; N, 21.37. Found: C, 59.0; H, 3.96; N, 21.15.

1-(1-Chloro-5-methylisoquinolin-6-yl)-1*H*-*v*-triazolo[4,5-*c*]pyridine (15b). This compound, which was previously obtained by another route,[4] has now been prepared by chlorination of triazolopyridine **12b** (yield 80%), according to the technique mentioned above for **15a**.

6,11-Dimethyl-5*H*-pyrido[3',4':4,5]pyrrolo[2,3-*g*]isoquinolin-10(9*H*)-one (13a). A stirred mixture of triazolopyridine **12a** (16 g) and phenanthrene (80 g) was heated in a metal bath at 340 °C for 30 min and then at 360 °C for 2 min. After being cooled, the mixture was poured in hexane (600 mL) and insoluble material was filtered, washed with boiling hexane, and recrystallized from dimethylformamide to yield **13a** (5.7 g, 36.5%) as gray needles: mp >330 °C; IR 1660 (C=O) cm^{-1}; NMR (100 MHz) δ 2.65 (CH_3-6, 3 H, s), 3.45 (CH_3-11, 3 H, s), 6.67 (H-7, 1 H, d, $J_{7,8}$ = 7.4 Hz, $J_{7,9}$ = 1.5 Hz), 7.13 (H-8, 1 H, q, $J_{7,8}$ = 7.4, $J_{8,9}$ = 6.0 Hz), 7.52 (H-4, 1 H, d, $J_{3,4}$ = 5.6 Hz), 8.49 (H-3, 1 H, d, $J_{3,4}$ = 5.6 Hz), 9.43 (H-1, 1 H, s), 10.82 (H-9, 1 H, q, $J_{7,9}$ = 1.5, $J_{8,9}$ = 6.0 Hz), 11.80 (H-5, 1 H, s). Anal. Calcd for $C_{16}H_{13}N_3O \cdot {}^1/_2H_2O$ (mol wt 272.3): C, 70.57; H, 5.18; N, 15.43. Found: C, 70.63; H, 5.32; N, 15.22.

As indicated, attempts to transform this compound to the corresponding chloro derivative **14a** were performed with various phosphorus chlorides, alone or mixed, at reflux temperature and in sealed tube at 150–160 °C for 4- to 24-h periods, and the residues were submitted to subsequent usual treatment. In all cases, insoluble material was obtained. Elemental analysis (found: C, 51.46; H, 4.72; N, 11.47; or, in another case, C, 48.06; H, 5.39; N, 9.70) did not correspond to the expected product $C_{16}H_{12}ClN_3$ (mol wt 281.5). Calcd: C, 68.21; H, 4.26; N, 14.92.

10-Chloro-6,11-dimethyl-5*H*-pyrido[3',4':4,5]pyrrolo[2,3-*g*]isoquinoline (14a). Triazolopyridine **15a** (3 g) was dissolved in ethanol (3 L) containing triethylamine (0.7 g) and the stirred mixture irradiated with a 15-W low-pressure mercury lamp for an 87-h period. After evaporation of ethanol, the solid residue was chromatographed on silica gel (400 g, 50 × 4.5 cm, CH_2Cl_2–EtOH 9:1) to yield: (a) 910 mg (35%) of pure **14a**: mp > 320 °C; NMR (100 MHz) δ 2.83 (CH_3-6, 3 H, s), 3.50 (CH_3-11, 3 H, s), 7.56 (H-4, q, $J_{3,4}$ = 5.8, $J_{1,4}$ = 1.0 Hz), 8.00 (H-7, 1 H, d, $J_{7,8}$ = 6.0 Hz), 8.21 (H-8, 1 H, d, $J_{7,8}$ = 6.0 Hz), 8.57 (H-3, 1 H, d, $J_{3,4}$ = 5.8 Hz), 9.51 (H-1, 1 H, d, $J_{1,4}$ = 1.0 Hz), 11.94 (H-5, 1 H, s); mass spectrum, *m/e* 283.2 (38%, $M^{+\cdot}$), 281.2 (100%, $M^{+\cdot}$), 246.3 (14%, M – Cl), 245.3 (22%, M – Cl – H). Anal. Calcd for $C_{16}H_{12}ClN_3 \cdot {}^3/_2C_2H_5OH \cdot H_2O$ (mol wt 368.5): C, 61.87; H, 6.24; N, 11.39; Cl, 9.63. Found: C, 61.87; H, 5.93; N, 11.54; Cl, 9.74. (b) 15 mg (0.6%) of **16a**, mp >330 °C, identical with that already described.[2]

When the same photochemical cyclization was performed in ethylene glycol monoethyl ether, only traces of the expected **14a** were obtained while in acetic acid the main product obtained corresponds to the dechlorinated derivative **16a**.

10-Chloro-6-methyl-5*H*-pyrido[3',4':4,5]pyrrolo[2,3-*g*]isoquinoline (14b). A solution of triazolopyridine **15b** (1.4 g) in ethanol (1 L) containing triethylamine (0.33 mL) was irradiated with a 15-W low-pressure mercury lamp for 30 h and treated as for **14a** to yield: (a) 450 mg (36%) of **14b**, mp >320 °C, identical with the compound previously described;[4] (b) 10 mg (0.9%) of **16b**, mp >320 °C (see below).

6-Methyl-5*H*-pyrido[3',4':4,5]pyrrolo[2,3-*g*]isoquinoline (16b). A mixture of **14b** (300 mg), ethanol (120 mL), sodium hydroxide (40 mg), and 5% palladium on charcoal (40 mg) was heated at 60–70 °C in an oil bath and stirred under hydrogen at atmospheric pressure for 4 days. After filtration and evaporation of ethanol, the solid residue was recrystallized from xylene to yield crystals (150 mg, 57%), mp >320 °C. Elemental analysis (found: C, 73.30; H, 5.33; N, 16.48) presented a disagreement with regard to the one calculated for $C_{15}H_{13}N_3$ (mol wt 233): C, 77.23; H, 4.75; N, 18.02. Partial hydration, frequent in this series, probably explains such a result since TLC on silica gel and alumina show a single spot and the NMR spectrum presents all the expected signals (100 MHz): δ 2.85 (CH_3-6, 3 H, s), 7.51 (H-4, 1 H, q, $J_{1,4}$ = 1.05, $J_{3,4}$ = 5.75 Hz), 7.99 (H-7, 1 H, m, $J_{7,8}$ = 6.3, $J_{7,10}$ = 1.0, $J_{7,11}$ = 0.9 Hz), 8.47 (H-8, 1 H, d, $J_{7,8}$ = 6.3, $J_{8,10} \simeq 0$ Hz), 8.56 (H-3, 1 H, d, $J_{3,4}$ = 5.75, $J_{1,3} \simeq 0$ Hz), 8.90 (H-10, 1 H, q, $J_{7,10}$ = 1.0, $J_{10,11} \simeq 0.3$, $J_{8,10} \simeq 0$ Hz), 9.42 (H-11, 1 H, d, $J_{10,11}$ = 0.3 Hz), 9.48 (H-1, 1 H, d, $J_{1,4}$ = 1.05, $J_{1,3} \simeq 0$ Hz), 11.85 (H-5, 1 H, s); mass spectrum, *m/e* 233 (100%, $M^{+\cdot}$), 232 (54%, M – H).

10-((γ-Diethylamino)propyl)amino)-6,11-dimethyl-5*H*-pyrido[3',4':4,5]pyrrolo[2,3-*g*]isoquinoline (17). A mixture of the chloro compound **14a** (400 mg) and γ-(diethylamino)-propylamine (80 mL) under argon was heated at reflux in an oil bath for 4.5 h. Evaporation afforded a viscous residue which was dissolved in 0.1 M hydrochloric acid. The aqueous solution was washed with chloroform, basified with 1 M sodium hydroxide, and then extracted with chloroform, and the solvent was evaporated to dryness. The residue was recrystallized from xylene to yield, after drying at 95 °C under reduced pressure for 3 h, 255 mg (48%) of yellow crystals: mp 200 °C; NMR (100 MHz) δ 0.95 (CH_3CH_2, 6 H, t, J = 7 Hz), 1.82 (CH_2-β, 2 H, q, $J_{\beta,\alpha} = J_{\beta,\gamma}$ = 6.5 Hz), 2.51 (CH_2CH_3, 4 H, q, J = 7 Hz), 2.55 (CH_2-γ, 2 H, t), 2.67 (CH_3-6, 3 H, s), 3.35 (CH_3-11, 3 H, s), 3.52 (CH_2-α, 2 H, t), 6.57 (NH-10, t, $J_{NHCH_2-\alpha}$ = 5 Hz), 7.02 (H-7, 1 H, d, $J_{7,8}$ = 6.2 Hz), 7.46 (H-4, 1 H, d, $J_{4,3}$ = 5.6 Hz), 7.82 (H-8, 1 H, d, $J_{7,8}$ = 6.2 Hz), 8.48 (H-3, 1 H, d, $J_{3,4}$ = 5.6 Hz), 9.40 (H-1, 1 H, s), 11.60 (H-5, 1 H, s); mass spectrum, *m/e* 375 (30%, $M^{+\cdot}$), 289 (100%, M – Et_2NCH_2), 261 (91%, M – $Et_2N(CH_2)_3$), 247 (30%, M + H – $Et_2N(CH_2)_3NH$). Anal. Calcd for $C_{23}H_{29}N_5 \cdot {}^1/_2H_2O$ (mol wt 384.5): C, 71.88; H, 7.81; N, 18.23. Found: C, 71.79; H, 7.64; N, 18.18.

10-((γ-(Dimethylamino)propyl)amino)-6,11-dimethyl-5*H*-pyrido[3',4':4,5]pyrrolo[2,3-*g*]isoquinoline (18). This compound was obtained from **14a** (400 mg) and (γ-(dimethylamino)propyl)amine (80 mL), according to the same technique as for **17**. Recrystallization from toluene gave yellow crystals: mp 130 °C; NMR (100 MHz) δ 1.85 (CH_2-β, 2 H, t, $J_{CH_2CH_2}$ = 6.9 Hz), 2.22 ($N(CH_3)_2$, 6 H, s), 2.44 (CH_2-γ, 2 H, t), 2.67 (CH_3-6, 3 H, s), 3.35 (CH_3-11, 3 H, s), 3.49 (CH_2-α, 2 H, t), 6.67 (NH-10, 1 H, t, $J_{NHCH_2-\alpha} \simeq 5$ Hz), 7.02 (H-7, 1 H, d, $J_{7,8}$ = 6.0 Hz), 7.47 (H-4, 1 H, q, $J_{3,4}$ = 5.6, $J_{1,4}$ = 0.8 Hz), 7.82 (H-8, 1 H, d, $J_{7,8}$ = 6.0 Hz), 8.48 (H-3, 1 H, d, $J_{3,4}$ = 5.6 Hz), 9.42 (H-1, 1 H, d, $J_{1,4}$ = 0.8 Hz), 11.62 (H-5, 1 H, s); mass spectrum, *m/e* 347 (17%, $M^{+\cdot}$), 289 (45%, M – Me_2NCH_2), 261 (73%, M – $Me_2N(CH_2)_3$), 247 (44%, M + H – $Me_2N(CH_2)_3NH$), 58 (100%, $Me_2NCH_2^{+\cdot}$). Anal. Calcd for $C_{21}H_{25}N_5 \cdot 3H_2O$ (mol wt 401.5): C, 62.82; H, 7.78; N, 17.44; O, 11.96. Found: C, 63.27; H, 7.55; N, 17.18; O, 11.31.

10-((β-Diethylamino)ethyl)amino)-6,11-dimethyl-5*H*-pyrido[3',4':4,5]pyrrolo[2,3-*g*]isoquinoline (19). This compound was obtained from **14a** (400 mg) and (β-(diethylamino)-ethyl)amine (50 mL) by applying the same technique as for **17** and **18**. The oily residue did not crystallize in various solvents. The compound was purified in acetone as its trimaleate salt obtained in acetone from 0.1 mmol of crude **19** and 0.35 mmol of maleic acid: beige crystals, mp 150 °C dec; NMR (100 MHz) δ 1.27 (CH_3CH_2, 6 H, t, J = 7 Hz), 2.76 (CH_3-6, 3 H, s), 3.29 (CH_2CH_3, 4 H, q, J = 7 Hz), 3.37 (CH_3-11, 3 H, s), 3.42 (CH_2-β, 2 H, t, J_{CH_2,CH_2} = 5,6 Hz), 3.87 (CH_2-α, 2 H, t), 7.26 (H-7, 1 H, d, $J_{7,8}$ = 6.1 Hz), 7.87 (H-4, 1 H, d, $J_{3,4}$ = 6.6 Hz), 7.95 (H-8, 1 H, d, $J_{7,8}$ = 6.1 Hz), 8.67 (H-3, 1 H, d, $J_{3,4}$ = 6.6 Hz), 9.59 (H-1, 1 H, s), 6.12 (H maleate, 6 H, s); mass spectrum (trimaleate), *m/e* 289 (16%, M – Et_2N), 288 (100%, M – Et_2N – H), 261 (5%, M – $Et_2N(CH_2)_2$), 247 (18%, M + H – $Et_2N(CH_2)_2NH$), 100 (7%, maleic $acid^{+\cdot}$), 86 (23%, $Et_2NCH_2^{+\cdot}$). Anal. Calcd for $C_{22}H_{27}N_5 \cdot 3C_4H_4O_4 \cdot H_2O$ (mol wt 709): C, 56.12; H, 5.77; N, 9.63; O, 28.61. Found: C, 55.45; H, 5.93; N, 9.89; O, 28.72.

Registry No. 3a, 73323-62-3; **3b**, 69022-62-4; **4a**, 69022-53-3; **4b**, 73323-63-4; **5a**, 69022-52-2; **6a**, 69022-55-5; **6b**, 73323-29-2; **7a**, 69022-56-6; **8a**, 69022-57-7; **9a**, 69022-58-8; **10a**, 69022-59-9; **11a**, 69221-47-2; **12a**, 69022-60-2; **12b**, 69022-44-2; **13a**, 69022-61-3; **14a**, 73323-30-5; **14b**, 69022-46-4; **15a**, 73323-31-6; **15b**, 70946-83-7; **16a**, 65222-36-8; **16b**, 73323-32-7; **17**, 73323-33-8; **18**, 73323-34-9; **19** trimaleate salt, 73323-36-1; 2,5-dimethyl-3-nitroaniline hydrochloride, 73323-37-2; acrylic acid, 79-10-7; 2,5-dimethyl-3-nitrobenzyl chloride, 18102-22-2; 2,5-dimethyl-3-nitro-1,4-bis(chloromethyl)benzene, 73323-38-3; 2-methyl-3-nitroaniline, 603-83-8; 4-chloro-3-nitropyridine, 13091-23-1; phenanthrene, 85-01-8; γ-(diethylamino)-propylamine, 104-78-9; γ-(dimethylamino)propylamine, 109-55-7; β-(diethylamino)ethylamine, 100-36-7.