

Convenient synthesis of new 3-aminocarbazole and pyrimido [5,4-*b*]carbazole derivatives

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Dedicated with best wishes to Professor Miha Tisler on the occasion of his 75th birthday

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Abstract

Regioselective hydrolysis of dimethyl 1-methyl-9*H*-carbazole-2,3-dicarboxylate permits functionalisation of the carbazole skeleton in position 3 by conversion of the carboxylic acid **2** thus obtained into the azide **3**. Curtius degradation of the latter gives the amine **5**, various urethane derivatives thereof (**4**), and the urea **6**. Base-induced cyclization of **6** leads to the pyrimido[5,4-*b*]carbazole **7a**, whereas an analogous compound bearing a basic side chain (**7b**) is formed by spontaneous cyclization of an intermediate urea.

Keywords: 3-Aminocarbazoles, pyrimido[5,4-*b*]carbazoles, diphenylphosphoryl azide, Curtius degradation

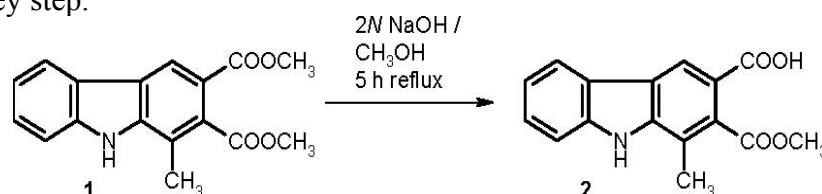
Introduction

The discovery of the pronounced antitumor activity of the alkaloid *ellipticine* (5,11-dimethyl-6*H*-pyrido[4,3-*b*]carbazole) about forty years ago has stimulated considerable efforts to modify this natural lead compound in order to find congeners with a superior pharmacological profile.^{1,2} One of the possible approaches to new *ellipticine* analogs is the modification of the pyridine part (ring D) of the tetracyclic skeleton, which seems to be a sensitive substructure in terms of a modulation of the molecule's antineoplastic properties. Thus, the position of the pyridine nitrogen atom has been systematically varied.³ Another strategy consists in replacement of the pyridine ring by other heterocyclic substructures: the synthesis of several new pyridazino[4,3-*b*]carbazoles ("3azaellipticines"), some of them exhibiting significant antitumor activity, has been described by us recently.^{4,5} In continuation of these investigations, we became interested in new 2,3-bifunctional 1-methylcarbazoles which should serve as intermediates in the synthesis of so far unknown types of heterocycle-annelated carbazoles. In particular, derivatives of 1-methylcarbazole-2-carboxylic acid with a (free or protected) amino function in position 3 were regarded as useful synthons for the construction of such tetracyclic systems. Here, we report on

the synthesis and transformations of these compounds, starting from the known diester **1** which can be easily prepared by Diels-Alder reaction of 4-methylpyrano[3,4-*b*]indol-3(9*H*)-one with dimethyl acetylene dicarboxylate.^{6,7}

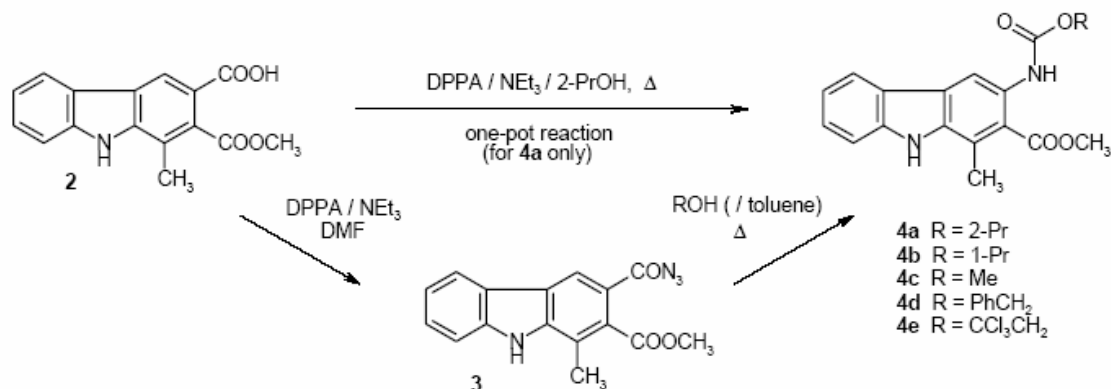
Results and Discussion

Taking into account the different steric environments of the two ester groups in compound **1**, it should be possible to selectively hydrolyze the COOCH₃ function in position 3. Indeed, this proved to be the case and the monoacid **2** could be obtained in good yield by refluxing **1** in aqueous-methanolic sodium hydroxide for 5 hours. In order to further convert the COOH group into nitrogen functionalities, Curtius degradation of an appropriate carboxylic acid azide was chosen as the key step.



Scheme 1

In a first approach, we found that the isopropyl urethane **4a** can be prepared in >70% yield without isolation of the intermediate azide **3** by heating the acid **2** with diphenylphosphoryl azide (DPPA) in the presence of triethylamine, using 2-propanol as the solvent. However, this “one-pot” procedure could not be successfully applied to primary alcohols like 1-propanol or methanol. Obviously, the higher nucleophilicity of the latter solvents/reagents results in substantial consumption of DPPA which is converted into the corresponding diphenyl monoalkyl phosphate (identified by GC-MS analyses).

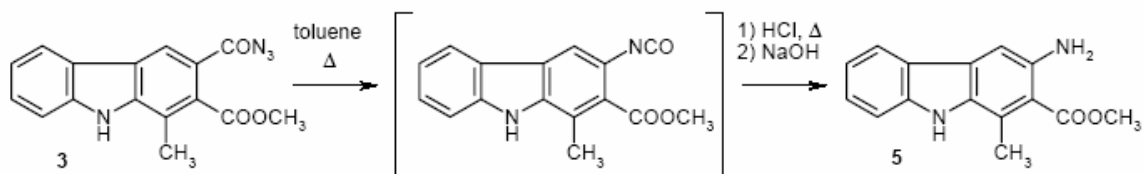


Scheme 2

This problem could be solved by separating the two reaction steps. Thus, the acid **2** was first transformed into the azide **3** by treatment with DPPA-triethylamine in DMF solution (yield: 87%) (The azide **3** is thermally labile and could not be recrystallized; it was used for the subsequent transformations without further purification). In a second step, the urethanes **4b-e**

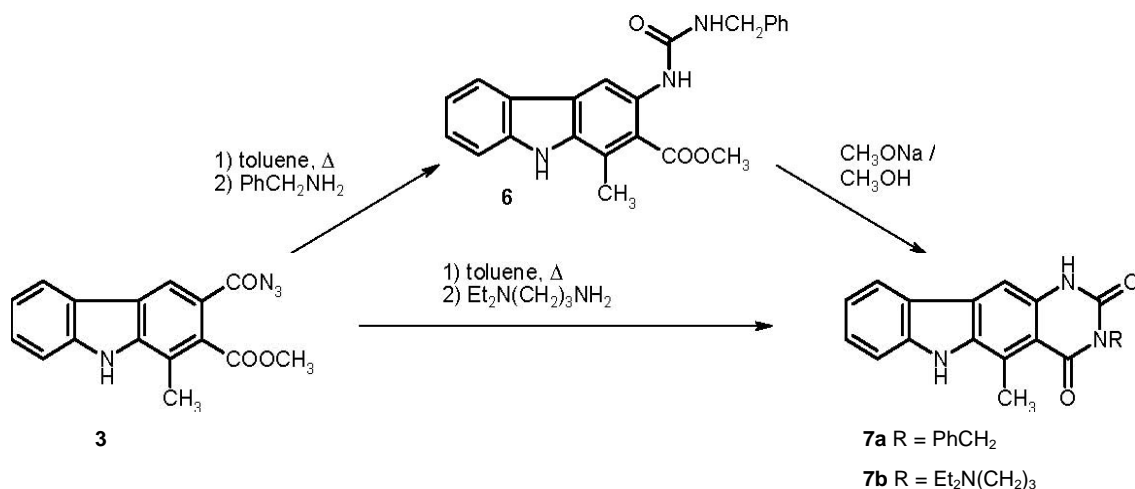
then were obtained by refluxing this key intermediate either in the neat alcohol component or in a toluene–ROH mixture (10:1). The latter variant was chosen for employment of the high-boiling alcohols, 2,2,2-trichloroethanol and benzyl alcohol, which gave rise to the formation of the Cbz- and Troc-protected aminocarbazole derivatives **4d** and **4e**, respectively.

Moreover, the preparation of the unprotected primary amine **5** was easily accomplished by acidic hydrolysis (6*N* HCl, reflux) of the intermediate isocyanate which is formed on heating of a solution of the azide **3** in dry toluene.



Scheme 3

When the Curtius degradation of the azide **3** was performed in the presence of benzylamine, the unsymmetrically *N,N'*-disubstituted urea **6** was obtained in high yield (On attempted purification of the urea **6** by recrystallization, partial transformation into the pyrimidine derivative **7a** was observed). Refluxing of this compound in methanolic sodium methoxide effected ring closure into the fused pyrimidinedione **7a** almost quantitatively. On the other hand, treatment of the (*in situ* generated) isocyanate with *N,N*-diethylpropane-1,3-diamine did not afford the expected urea derivative but, instead, the tetracyclic compound **7b** was obtained in 83% yield. Obviously, in this case the basicity of the employed amine component is sufficient to promote spontaneous cyclization, leading to the pyrimidocarbazole.



Scheme 4

Compound **7b**, as a *b*-fused carbazole bearing a basic diethylaminopropyl side chain which is known to enhance the affinity of *ellipticine*-type drug molecules (e.g. *retelliptine*,⁸ *pazelliptine*^{9,10}) to the phosphate backbone of DNA, is of particular interest as a novel analog of this class of antitumor agents and is currently undergoing *in-vitro* screening in several human tumor cell lines.

Experimental Section

General Procedures. Melting points were determined on a Kofler hot-stage microscope. IR spectra (KBr pellets) were recorded on a Perkin–Elmer Spectrum 1000 FT-IR instrument. ¹H-NMR spectra were recorded on a Varian Unityplus 300 (300 MHz) and on a Bruker Avance DPX 200 (200 MHz) spectrometer (DMSO-d₆ as solvent, TMS as internal reference, δ values in ppm). Mass spectra were obtained on a Shimadzu QP 5050A DI 50 instrument, GC–MS analyses were done on a Hewlett–Packard 5890A/5970B GC/MSD instrument. For column chromatography Merck Kieselgel 60, 0.063-0.200 mm was used, the medium pressure liquid chromatography (MPLC) was carried out on Merck LiChroprep Si 60, 0.040-0.063 mm (detection at 280 nm). Light petroleum refers to the fraction of bp 50–70 °C. Microanalyses were performed at the Institute of Physical Chemistry (Microanalytical Laboratory), University of Vienna.

2-(Methoxycarbonyl)-1-methyl-9H-carbazole-3-carboxylic acid (2). To a solution of dimethyl 1-methyl-9H-carbazole-2,3-dicarboxylate **1**^{6,7} (2.973 g, 10 mmol) in methanol (100 mL) was added 2*N* NaOH (10 mL), and the mixture was stirred under reflux for 5 h. After cooling, the solution was concentrated under reduced pressure to a volume of approx. 10 mL, then it was repeatedly extracted with dichloromethane. The aqueous layer was acidified with concd. HCl under ice cooling. The colorless precipitate was collected by filtration, washed with water, and dried. Recrystallization from ethanol–diisopropyl ether afforded **2** (2.172 g, 75%) as colorless crystals, mp >250 °C; ¹H-NMR δ 12.81 (1H, br, OH), 11.76 (1H, s, NH), 8.64 (1H, s, 4-H), 8.25 (1H, d, *J* = 7.7 Hz, 5-H), 7.59 (1H, d, *J* = 8.0 Hz, 8-H), 7.52–7.44 (1H, m, 7-H), 7.29–7.21 (1H, m, 6-H), 3.83 (3H, s, OCH₃), 2.48 (3H, s, 1-CH₃); IR: 3328, 3061, 2949, 1713, 1666, 1606, 1572, 1498, 1411, 1336, 1260, 1135, 1060, 751, 738, 603 cm⁻¹; Anal. calcd. for C₁₆H₁₃NO₄•0.3 H₂O (288.69): C, 66.57; H, 4.75; N, 4.85. Found: C, 66.81; H, 4.99; N, 4.67.

Methyl 3-azidocarbonyl-1-methyl-9H-carbazole-2-carboxylate (3). To an ice-cooled solution of the acid **2** (849 mg, 3 mmol) and triethylamine (303 mg, 3 mmol) in dry DMF (6 mL) was added dropwise a solution of diphenylphosphoryl azide (825 mg, 3 mmol) in dry DMF (3 mL) over a period of 2 h. After removal of the cooling bath, the mixture was stirred at room temperature for 3 h. Then, the mixture was poured into a mixture of ether and ice. The phases were separated and the aqueous layer was exhaustively extracted with ether. The combined extracts were washed with aq. NaHCO₃ and water, dried, and evaporated under reduced pressure (bath temperature below 30 °C). The residue was washed several times with small amounts of diisopropyl ether and dried in vacuo. The azide **3** (835 mg, 87%) was obtained as tiny, pale-yellow crystals, mp >110 °C (dec); ¹H-NMR δ 12.02 (1H, s, NH), 8.69 (1H, s, 4-H), 8.28 (1H, d, *J* = 7.8 Hz, 5-H), 7.61 (1H, d, *J* = 8.1 Hz, 8-H), 7.54-7.47 (1H, m, 7-H), 7.31-7.25 (1H, m, 6-H), 3.87 (3H, s, OCH₃), 2.49 (3H, s, 1-CH₃); IR: 3376, 2954, 2151, 1708, 1672, 1606, 1497, 1351, 1298, 1240, 1204, 1141, 1081, 915, 777, 751, 732 cm⁻¹.

Methyl 3-[(isopropoxycarbonyl)amino]-1-methyl-9H-carbazole-2-carboxylate (4a). A mixture of the acid **2** (283 mg, 1 mmol), diphenylphosphoryl azide (600 mg, 2.2 mmol), triethylamine (1.2 mL), and 2-propanol (5 mL) was refluxed for 4 h. The volatile components were removed under reduced pressure and the residue was triturated with ether. It was then

suspended in 2*N* NaOH (10 mL) and kept in the refrigerator overnight. The precipitate was collected by filtration, washed with water, and dried. Recrystallization from ethanol–water afforded **4a** (246 mg, 72%) as yellow crystals, mp 194–196 °C; ¹H-NMR δ 11.32 (1H, s, carbazole-NH), 8.89 (1H, br, urethane-NH), 8.10 (1H, d, *J* = 7.8 Hz, 5-H), 7.90 (1H, s, 4-H), 7.52 (1H, d, *J* = 7.8 Hz, 8-H), 7.45–7.39 (1H, m, 7-H), 7.19–7.13 (1H, m, 6-H), 4.82 (1H, sept, *J* = 6.3 Hz, OCH(CH₃)₂), 3.82 (3H, s, OCH₃), 2.53 (3H, s, 1-CH₃), 1.22 (6H, d, *J* = 6.3 Hz, OCH(CH₃)₂); IR: 3356, 3283, 2981, 2948, 1705, 1691, 1506, 1498, 1436, 1318, 1292, 1227, 1132, 1107, 1063, 771, 751, 740 cm⁻¹; Anal. calcd. for C₁₉H₂₀N₂O₄•0.1 H₂O (342.18): C, 66.69; H, 5.95; N, 8.19. Found: C, 66.69; H, 5.82; N, 8.01.

Methyl 3-[(propoxycarbonyl)amino]-1-methyl-9*H*-carbazole-2-carboxylate (4b). A solution of the azide **3** (308 mg, 1 mmol) in 1-propanol (10 mL) was refluxed for 2 h. The solvent was removed under reduced pressure and the residue was recrystallized from ethyl acetate–light petroleum to afford **4b** (186 mg, 55%) as yellow crystals, mp 114–116 °C; ¹H-NMR δ 11.33 (1H, s, carbazole-NH), 8.94 (1H, br, urethane-NH), 8.10 (1H, d, *J* = 7.5 Hz, 5-H), 7.90 (1H, s, 4-H), 7.51 (1H, d, *J* = 7.2 Hz, 8-H), 7.46–7.39 (1H, m, 7-H), 7.20–7.13 (1H, m, 6-H), 3.98 (2H, t, *J* = 7.0 Hz, OCH₂CH₂CH₃), 3.82 (3H, s, OCH₃), 2.53 (3H, s, 1-CH₃), 1.60 (2H, sext, *J* = 7.0 Hz, OCH₂CH₂CH₃), 0.91 (3H, t, *J* = 7.0 Hz, OCH₂CH₂CH₃); IR: 3375, 2967, 2949, 1704, 1521, 1497, 1476, 1453, 1283, 1262, 1226, 1132, 1080, 771, 750 cm⁻¹; MS *m/z*: 341 (21%), 340 (M⁺, 95), 308 (6), 280 (46), 266 (25), 253 (22), 249 (53), 248 (29), 223 (33), 222 (100), 221 (28), 195 (44), 194 (81), 193 (86), 192 (66), 167 (33), 166 (31), 139 (25), 124 (15), 97 (16); Anal. calcd. for C₁₉H₂₀N₂O₄ (340.38): C, 67.05; H, 5.92; N, 8.23. Found: C, 67.09; H, 5.86; N, 8.12.

Methyl 3-[(methoxycarbonyl)amino]-1-methyl-9*H*-carbazole-2-carboxylate (4c). A solution of the azide **3** (308 mg, 1 mmol) in methanol (10 mL) was refluxed for 2 h. The solvent was removed under reduced pressure and the residue was recrystallized from ethyl acetate to afford **4c** (143 mg, 46%) as yellow crystals, mp 160–162 °C; ¹H-NMR δ 11.34 (1H, s, carbazole-NH), 8.97 (1H, br, urethane-NH), 8.10 (1H, d, *J* = 8.1 Hz, 5-H), 7.91 (1H, s, 4-H), 7.52 (1H, d, *J* = 8.1 Hz, 8-H), 7.46–7.39 (1H, m, 7-H), 7.20–7.13 (1H, m, 6-H), 3.82 (3H, s, ester-OCH₃), 3.61 (3H, s, urethane-OCH₃), 2.53 (3H, s, 1-CH₃); IR: 3427, 3379, 3013, 2954, 1737, 1699, 1585, 1532, 1498, 1480, 1454, 1312, 1259, 1229, 1134, 1093, 1053, 771, 754 cm⁻¹; MS *m/z*: 313 (21%), 312 (M⁺, 100), 281 (21), 280 (88), 249 (77), 248 (87), 221 (20), 220 (36), 194 (27), 193 (61), 192 (80), 167 (24), 166 (27), 139 (26), 124 (13), 97 (14), 59 (20); Anal. calcd. for C₁₇H₁₆N₂O₄ (312.33): C, 65.38; H, 5.16; N, 8.97. Found: C, 65.27; H, 5.23; N, 8.82.

Methyl 3-[(benzyloxycarbonyl)amino]-1-methyl-9*H*-carbazole-2-carboxylate (4d). A solution of the azide **3** (308 mg, 1 mmol) in a mixture of toluene (10 mL) and benzyl alcohol (1 mL) was refluxed for 2 h. The solvent was removed under reduced pressure, residual benzyl alcohol was evaporated by Kugelrohr distillation (10⁻² mbar, 50 °C). The residue was recrystallized from ethyl acetate–light petroleum to afford **4d** (342 mg, 88%) as light-brown crystals, mp 148–151 °C; ¹H-NMR δ 11.34 (1H, s, carbazole-NH), 9.14 (1H, br, urethane-NH), 8.11 (1H, d, *J* = 7.8 Hz, 5-H), 7.92 (1H, s, 4-H), 7.52 (1H, d, *J* = 8.1 Hz, 8-H), 7.46–7.30 (6H, m, 7-H, C₆H₅), 7.20–7.13 (1H, m, 6-H), 5.12 (2H, s, OCH₂), 3.77 (3H, s, OCH₃), 2.53 (3H, s, 1-CH₃); IR: 3329, 3296, 3053, 2955, 1705, 1694, 1520, 1299, 1245, 1132, 1074, 753 cm⁻¹; MS *m/z*: 389 (13%), 388 (M⁺, 48), 254 (14), 253 (74), 223 (22), 195 (18), 91 (100), 65 (18); Anal. calcd. for C₂₃H₂₀N₂O₄ (388.43): C, 71.12; H, 5.19; N, 7.21. Found: C, 70.89; H, 5.31; N, 7.11.

Methyl 3-[(2,2,2-trichloroethoxycarbonyl)amino]-1-methyl-9H-carbazole-2-carboxylate (4e). A solution of the azide **3** (308 mg, 1 mmol) in a mixture of toluene (10 mL) and 2,2,2-trichloroethanol (1 mL) was refluxed for 2 h. The solvent was removed under reduced pressure, residual alcohol was evaporated by Kugelrohr distillation (10^{-2} mbar, 30 °C). The residue was recrystallized from ethyl acetate to afford **4e** (315 mg, 84%) as almost colorless crystals, mp 65–69 °C; $^1\text{H-NMR}$ δ 11.39 (1H, s, carbazole-NH), 9.59 (1H, br, urethane-NH), 8.12 (1H, d, $J = 7.8$ Hz, 5-H), 7.91 (1H, s, 4-H), 7.53 (1H, d, $J = 7.8$ Hz, 8-H), 7.46–7.40 (1H, m, 7-H), 7.21–7.14 (1H, m, 6-H), 4.89 (2H, s, OCH_2), 3.81 (3H, s, OCH_3), 2.54 (3H, s, 1- CH_3); IR: 3349, 3286, 2952, 1718, 1691, 1518, 1302, 1241, 1132, 1118, 757 cm^{-1} ; MS m/z : 432 (M^+ , 20%), 430 (M^+ , 65), 428 (M^+ , 63), 398 (25), 396 (25), 280 (73), 265 (38), 249 (100), 248 (57), 221 (47), 195 (39), 194 (56), 193 (98), 192 (86), 167 (36), 166 (40), 139 (37), 125 (40), 97 (89), 95 (61), 83 (37), 61 (34); Anal. calcd. for $\text{C}_{18}\text{H}_{15}\text{Cl}_3\text{N}_2\text{O}_4$ (429.69): C, 50.32; H, 3.52; N, 6.52. Found: C, 50.38; H, 3.69; N, 6.53.

Methyl 3-amino-1-methyl-9H-carbazole-2-carboxylate (5). A solution of the azide **3** (308 mg, 1 mmol) in dry toluene (10 mL) was refluxed for 30 min. After cooling, 6N HCl (5 mL) was added, and the mixture was refluxed for 1 h. The yellow-orange precipitate (**5**•HCl) was collected by filtration, washed with toluene, and dried. It was then dissolved in a minimum amount of water. After neutralisation with 2N NaOH, the mixture was repeatedly extracted with dichloromethane. The combined extracts were dried and evaporated to afford **5** (136 mg, 54%) as a pale-yellow solid, mp 190–193 °C (diisopropyl ether); $^1\text{H-NMR}$ δ 10.76 (1H, s, carbazole-NH), 7.91 (1H, d, $J = 7.8$ Hz, 5H), 7.40 (1H, d, $J = 7.8$ Hz, 8-H), 7.37–7.31 (1H, m, 7-H), 7.26 (1H, s, 4-H), 7.09–7.02 (1H, m, 6-H), 5.06 (2H, br, NH_2), 3.86 (3H, s, OCH_3), 2.50 (3H, s, 1- CH_3); IR: 3415, 3339, 3167, 2990, 2949, 1699, 1436, 1303, 1271, 1133, 864, 753 cm^{-1} ; MS m/z : 255 (22%), 254 (M^+ , 100), 223 (26), 222 (72), 195 (24), 194 (71), 193 (46), 167 (26), 111 (31), 97 (30), 95 (21), 85 (27), 83 (26), 81 (27), 71 (44), 69 (45), 57 (77), 55 (60); Anal. calcd. for $\text{C}_{15}\text{H}_{14}\text{N}_2\text{O}_2 \cdot 0.15 \text{H}_2\text{O}$ (256.99): C, 70.11; H, 5.61; N, 10.90. Found: C, 70.24; H, 5.65; N, 10.87.

Methyl 3-[(benzylamino)carbonyl]amino-1-methyl-9H-carbazole-2-carboxylate (6). A solution of the azide **3** (308 mg, 1 mmol) in dry toluene (10 mL) was refluxed for 15 min. After addition of benzylamine (1 mL), refluxing was continued for 2 h. The solvent was removed under reduced pressure (bath temperature below 40 °C), residual amine was evaporated by Kugelrohr distillation (10^{-2} mbar, 40 °C). The residue was washed with diisopropyl ether and ethyl acetate, then it was recrystallized from methanol to afford **6** (282 mg, 83%) as pale yellow crystals, mp 330–335 °C (dec; partial transformation above 135 °C). This material contained small amounts (<5%) of the cyclization product **7a** (see below). $^1\text{H-NMR}$ δ 11.22 (1H, s, carbazole-NH), 8.13 (1H, s, 4-H), 8.06 (1H, d, $J = 8.1$ Hz, 5-H), 7.90 (1H, s, Ar-NH-CO-NH), 7.50 (1H, d, $J = 8.1$ Hz, 8-H), 7.44–7.21 (6H, m, 6-H, C_6H_5), 7.18–7.11 (1H, m, 7-H), 6.98 (1H, t, $J = 5.8$ Hz, NHCH_2), 4.30 (2H, d, $J = 6.0$ Hz, NHCH_2), 3.86 (3H, s, OCH_3), 2.50 (3H, s, 1- CH_3); IR: 3405, 3323, 3062, 3023, 2948, 1723, 1636, 1559, 1496, 1451, 1285, 1255, 1129, 1059, 755, 696 cm^{-1} ; MS m/z : 388 ($\text{M}^+ + 1$, 17%), 355 (15), 264 (11), 253 (43), 223 (16), 195 (16), 193 (15), 167 (10), 139 (11), 91 (100), 65 (19).

3-Benzyl-1,6-dihydro-5-methyl-2H-pyrimido[5,4-*b*]carbazole-2,4(3H)-dione (7a). To a solution of sodium methoxide, prepared by dissolving Na (25 mg, 1.1 mmol) in methanol (10 mL), was added compound **6** (355 mg, 0.92 mmol) and the mixture was refluxed for 1 h.

After cooling, the mixture which contained a yellow precipitate was evaporated to dryness under reduced pressure. The residue was taken up in water (10 mL) and the mixture was neutralized with 2N HCl and chilled. The precipitate was collected by filtration, washed with water, and dried to afford **7a** (306 mg, 93%) as a yellow solid, mp 330–335 °C (ethyl acetate); $^1\text{H-NMR}$ δ 11.31 (1H, s, NH), 11.29 (1H, s, NH), 8.07 (1H, d, $J = 7.5$ Hz, 10-H), 7.70 (1H, s, 11-H), 7.54–7.44 (2H, m, 7-H, 8-H), 7.35–7.20 (5H, m, C_6H_5), 7.19–7.14 (1H, m, 9-H), 5.11 (2H, s, CH_2), 2.98 (3H, s, 5- CH_3); IR: 3425, 3060, 3033, 2969, 1702, 1647, 1591, 1528, 1432, 1243, 766, 743, 713, 696 cm^{-1} ; MS m/z : 356 (24%), 355 (M^+ , 100), 340 (6), 265 (9), 264 (37), 249 (9), 222 (13), 193 (13), 91 (24), 69 (14), 57 (23), 55 (17); Anal. calcd. for $\text{C}_{22}\text{H}_{17}\text{N}_3\text{O}_2 \cdot 0.15 \text{H}_2\text{O}$ (358.10): C, 73.79; H, 4.87; N, 11.73. Found: C, 73.80; H, 4.88; N, 11.55.

3-(3-Diethylamino)propyl-1,6-dihydro-5-methyl-2H-pyrimido[5,4-*b*]-carbazole-2,4(3H)-dione (7b). A solution of the azide **3** (308 mg, 1 mmol) in dry toluene (10 mL) was refluxed for 15 min. After addition of *N,N*-diethylpropane-1,3-diamine (1 mL), refluxing was continued for 2 h. The solvent was removed under reduced pressure, residual amine was evaporated by Kugelrohr distillation (10^{-2} mbar, 40 °C). The residue was washed with diisopropyl ether and recrystallized from ethyl acetate–light petroleum to afford **7b** (314 mg, 82% as yellow crystals, mp 210–215 °C; $^1\text{H-NMR}$ δ 11.27 (1H, s, NH), 11.16 (1H, br, NH), 8.06 (1H, d, $J = 7.8$ Hz, 10-H); 7.66 (1H, s, 11-H), 7.53–7.43 (2H, m, 7-H, 8-H), 7.19–7.13 (1H, m, 9-H), 3.92 (2H, t, $J = 7.5$ Hz, $\text{N}_{\text{imide}}\text{-CH}_2$), 2.99 (3H, s, 5- CH_3), 2.50–2.42 (6H, m, $\text{N}_{\text{amine}}\text{-CH}_2$), 1.75–1.66 (2H, m, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{N}$), 0.93 (6H, t, $J = 7.2$ Hz, NCH_2CH_3); IR: 3566, 3274, 2968, 2823, 1701, 1642, 1590, 1529, 1464, 1435, 1252, 766, 747 cm^{-1} ; MS m/z : 378 (M^+ , 4%), 363 (3), 349 (10), 306 (8), 265 (4), 249 (10), 193 (6), 87 (6), 86 (100), 84 (9), 72 (10), 58 (6); Anal. calcd. for $\text{C}_{22}\text{H}_{26}\text{N}_4\text{O}_2 \cdot 0.35 \text{H}_2\text{O}$ (384.79): C, 68.63; H, 7.31; N, 14.68. Found: C, 68.67; H, 6.99; N, 14.56.

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