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Synthesis of Carbazole Derivatives - III. Synthesis of New Pyrrolidino[3,4-c]carbazoles by Intramolecular Michael Addition

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Keywords: Syntheses of carbazoles and pyrrolidones by intramolecular *Michael* addition

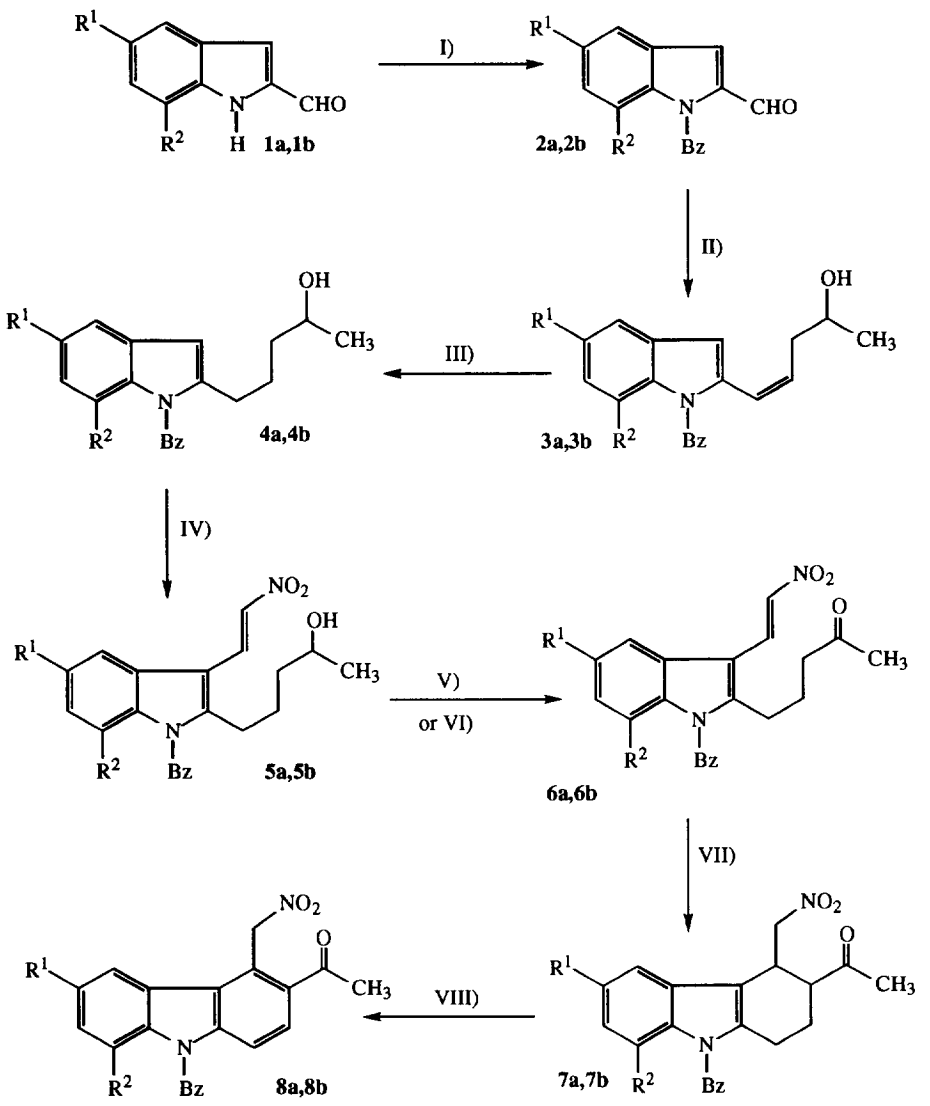
Abstract: We have reported on the synthesis of carbazoles by inter- and intramolecular *Michael* addition.[1] Ellipticine derivatives are related to these compounds, and especially those with 9-methoxy- and 9-hydroxy substituents exhibit appreciable antitumor and antileukemic activity.[2] Therefore, we have prepared the tetrahydrocarbazoles **7a** and **7b**, starting from *N*-benzyl-2-formyl-5-methoxyindole (**2a**) and *N*-benzyl-2-formyl-7-methoxyindole (**2b**), respectively. Copyright © 1996 Published by Elsevier Science Ltd

Syntheses

The aldehydes **1a** and **1b** [3] were N-benzylated under phase transfer conditions, affording compounds **2a** and **2b**, respectively. *Wittig* reaction [4] and hydrogenation (Pd / C) led to the 4-hydroxypentyl side chain, whilst the nitroethenyl group was introduced at C-3 according to *Büch*i and *Mak.*[5] In order to get a *Michael* donor, the OH-group of **5a** and **5b**, respectively, was converted to the corresponding ketones **6a**, **6b** either by *Swern* oxidation or by pyridinium dichromate (PDC) / *N,N*-dimethylformamide (DMF). Even catalytic amounts of Triton B in THF at room temperature nicely cyclized these ketones to the tetrahydrocarbazoles **7a**, **7b** as mixtures of diastereomers.

For dehydrogenation of compounds **7** to the carbazoles **8** various methods were examined [6-11], but only *p*-chloroanil in mesitylene and 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) in dioxane proved to be useful. Nevertheless, even these procedures afforded only low yields (Scheme 1).

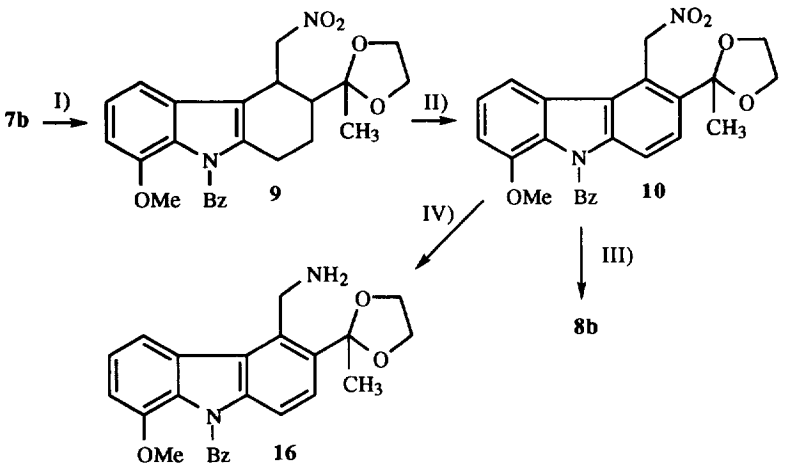
New reactions were, therefore, studied using methoxycarbazole **7b**. We expected a higher yield by protecting the carbonyl group as an acetal, so reducing the C-H acidity of the C<u>H</u>-CO-CH_3 increment and, therefore, inhibiting its oxidation (Scheme 2). When **7b** was treated with ethylene glycol / BF_3-etherate the dioxolane **9** was obtained in 90% yield. Dehydrogenation of this mixture of diastereomers led to 73% of the carbazole **10**. Deprotection with 3N HCl afforded 51% of the desired carbazole **8b**.



a $R^1 = OCH_3$, $R^2 = H$

b $R^1 = H$, $R^2 = OCH_3$

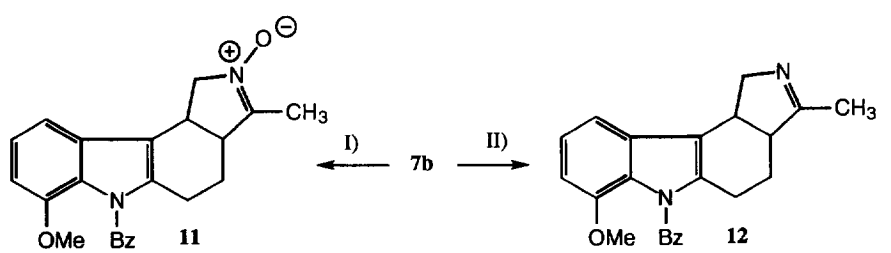
Scheme 1. I) BzBr / $Bu_4N^{\oplus}Br^{\ominus}$ / NaOH; II) $ClPh_3P^{\oplus}$  / 2 eq. LiHMDS / 0°C / THF; III) Pd / C / H_2 / EtOH; IV) $((CH_3)_2NCH{=}CHNO_2$ / TFA / 0°C; V) $(COCl)_2$ / DMSO / NEt_3 / -63°C; VI) PDC / DMF / 0°C; VII) Triton B / THF; VIII) DDQ / dioxane or *p*-chloroanil / mesitylene.



Scheme 2. I) $HOCH_2CH_2OH$ / BF_3-Et_2O / CH_2Cl_2; II) *p*-chloranil / xylene / Δ; III) 12 proz. HCl / THF; IV) Raney-Ni / EtOH / H_2.

Hydrogenation (Pd / C or Raney-Ni) of **7b** or **8b** were used to get the pertinent pyrrolidino- or the pyrrolinocarbazoles, respectively.

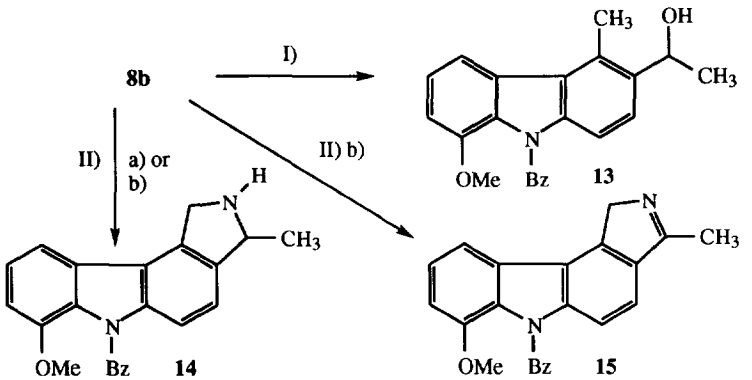
So, hydrogenation of **7b** with Pd / C led to the N-oxide **11** in 35% yield, whilst Raney-Ni afforded 23% of the tetrahydro-pyrrolino[3,4-*c*]carbazole **12** by formation of a *Schiff* base besides traces of the N-oxide **11** (Scheme 3).



Scheme 3. I) Pd / C / H_2 (15 bar) / EtOH; II) Raney-Ni / H_2 (9 bar) / EtOH (NH_3).

Hydrogenation of **8b** on Pd / C in EtOH led to *N*-benzyl-3-(1-hydroxyethyl)-8-methoxy-4-methylcarbazole (**13**), indicating concomitant hydrogenation of the carbonyl and the nitro group followed by benzylamine hydrogenolysis.

Hydrogenation of **8b** over Raney-Ni afforded the pyrroline derivative **14** besides some pyrrolocarbazole **15** (Scheme 4); compound **14** was also obtained by hydrogenation over Pd / C in abs. EtOH and abs. acetic acid using *Horni*'s protocol.[12] Hydrogenation of **10** over Raney-Ni led to the amino dioxolane **16** in 86% yield (Scheme 2). Deprotection of this dioxolane as examplified by the transformation of nitro-dioxolane **10** to carbazole **8b**, however, failed: a useless mixture of compounds was obtained.



Scheme 4. I) Pd / C / H_2 (15 bar) / EtOH; II) a) Pd / C / H_2 (3 bar) / CH_3COOH / EtOH; b) Raney-Ni / H_2 (5 bar) / EtOH (NH_3).

Experimental

Elemental Analyses: Analytical Lab. Univ. Regensburg. - Mp: Büchi 512, Reichert hot-stage microscope. - IR: FT, Nicolet 510. - ^1H NMR: Bruker ARX 400 (400 MHz), Bruker 250 (250 MHz), Varian EM 390 (90 MHz). Unless otherwise stated the spectra are 90 MHz spectra. -Mass spectrometry: Varian MAT 112 S/SS, 70 eV. -All reactions were carried out under nitrogen, that had been dried over self-indicating silica gel, conc. H_2SO_4 and KOH.

N-Benzyl-2-formyl-5-methoxyindole (2a)

N-Benzyl-2-formyl-7-methoxyindole (2b)

A solution of 18.17 g (103.72 mmol) **1a** or **1b**, resp.,1.05 g tetrabutylammonium bromide, 105 ml aqueous NaOH (50%) and 18.14 ml (152.49 mmol) benzyl bromide in 400 ml dry benzene was stirred at 35 °C overnight. Then 300 ml H_2O were added and the organic phase was separated. The aqueous phase was extracted with ethyl acetate (3 x 200 ml), and the combined organic phases were washed with 300 ml H_2O before drying over Na_2SO_4. Removal of the solvent *in vacuo* and purification by chromatography (column 50 cm x 4 cm, SiO_2, methylene chloride) gave **2a** and **2b**, respectively.

2a: yellow crystals, yield 20.4 g (74%). - mp 55-56°C (methylene chloride / hexane). - $C_{17}H_{15}NO_2$ (265.31) Calcd. C 76.96 H 5.70 N 5.28 Found C 76.71 H 5.72 N 5.26. - IR (KBr): $\tilde{\nu}$ = 3100-2800 (CH); 1670 (C=O); 1520 cm^{-1} (C=C). - ^1H NMR ($CDCl_3$): δ(ppm) = 3.80 (s; 3 H, OCH_3), 5.77 (s; 2 H, CH_2-Ph), 6.90-7.25 (m; 9 H aromat.). - MS: m/z (%) = 265 (62%) [$M^{+\bullet}$], 91 (100) [$C_7H_7]^+$.

2b: colourless crystals, yield 26.4 g (96%). -mp 104-105°C (methylene chloride / hexane). - $C_{17}H_{15}NO_2$ (265.31) Calcd. C 76.96 H 5.70 N 5.28 Found C 76.64 H 5.86 N 5.45. -IR (KBr): $\tilde{\nu}$ = 3100-2800 (CH); 1675 (C=O); 1605, 1450 cm^{-1} (C=C). - ^1H NMR ($CDCl_3$): δ(ppm) = 3.45 (s; 3 H, OCH_3), 5.80 (s; 2 H, CH_2-Ph), 6.23-7.08 (m; 9 H aromat.).

N-Benzyl-2-(4-hydroxypent-1-enyl)-5-methoxyindole (3a)

N-Benzyl-2-(4-hydroxypent-1-enyl)-7-methoxyindole (3b)

At 0°C lithiumhexamethyldisilylamide was prepared from 14.14 ml (66.72 mmol) hexamethyldisilazane in 200 ml dry THF and 42.86 ml (66.72 mmol) n-butyllithium (1.6 M in hexane). At 0°C 13.11 g (35.35 mmol) solid

3-hydroxybutyl-triphenylphosphonium chloride were added slowly. The cooling bath was removed and at room temp. 8.85 g (33.35 mmol) **2a** or **2b** in 50 ml dry THF were added dropwise. Stirring was continued for 2 h before 75 ml saturated ammonium chloride solution were added. The aqueous phase was extracted with ether (3 x 50 ml) and dried (Na_2SO_4).The solvent was evaporated *in vacuo* and the crude product was purified by chromatography (column 50 cm x 5 cm, SiO_2, methylene chloride).

3a: yellow crystals, yield 12.8 g (60%). - mp 70°C (ethyl acetate / diisopropyl ether). - $C_{21}H_{23}NO_2$ (321.42) Calcd. C 78.47 H 7.21 N 4.35 Found C 78.24 H 7.17 N 4.45. - IR (KBr): $\tilde{\nu}$ = 3440 (OH); 3100-2800 (CH); 1615, 1580, 1495 cm^{-1} (C=C). -^{1}H NMR ($CDCl_3$): δ(ppm) = 1.16 (d; J = 6.0 Hz, 3 H, CH(OH)C<u>H</u>3), 1.50 (s; 1 H, OH), 2.20-2.36 (m; 2 H, C<u>H</u>2CH(OH)), 3.75-3.87 (m; 4 H, OCH_3, C<u>H</u>(OH)), 5.30 (s; 2 H, CH_2-Ph), 6.20-7.25 (m; 11 H, aromat. H, CH=CH). - MS: m/z (%) = 321 (52%) [$M^{+\bullet}$], 91 (100) $[C_7H_7]^+$.

3b: yellow wax, yield 14.5 g (68%). - IR (NaCl): $\tilde{\nu}$ = 3400 (OH); 3100-2800 (CH); 1605, 1450 cm^{-1} (C=C). - ^{1}H NMR ($CDCl_3$): δ(ppm) = 1.10 (d; J = 7.4 Hz, 3 H, CH(OH)C<u>H</u>3), 1.59 (br s; 1 H, OH), 2.04-2.34 (m; 2 H, C<u>H</u>2CH(OH)), 3.46-3.85 (m; 1 H, C<u>H</u>(OH)), 3.70 (s; 3 H, OCH_3), 5.63 (s; 2 H, CH_2-Ph), 6.17-7.78 (m; 11 H, aromat. H, CH=CH). - MS: m/z (%) = 321 (65%) [$M^{+\bullet}$], 91 (100) $[C_7H_7]^+$.

_N_-Benzyl-2-(4-hydroxypentyl)-5-methoxyindole (4a)

_N_-Benzyl-2-(4-hydroxypentyl)-7-methoxyindole (4b)

13.47 g (41.91 mmol) **3a** or **3b** and 2 g Pd / C 5% were stirred in 250 ml dry MeOH under H_2 (balloon) overnight. The mixture was filtered through Celite and the filtrate concentrated *in vacuo*. The resulting oil was purified by chromatography (column 50 cm x 5 cm, SiO_2, methylene chloride).

4a: yellow oil, yield 9.74 g (72%). - IR (NaCl): $\tilde{\nu}$ = 3400 (OH); 3100-2800 (CH); 1620, 1480 cm^{-1} (C=C). -^{1}H NMR ($CDCl_3$): δ(ppm) = 1.10 (d; J = 6.0 Hz, 3 H, CH(OH)C<u>H</u>3), 1.25 (s; 1 H, OH), 1.35-1.65 (m; 4 H, C<u>H</u>2C<u>H</u>2CH(OH)), 2.64 (t; J = 8.0 Hz, 2 H, C=C-CH_2), 3.61-3.82 (m; 4 H, OCH_3, C<u>H</u>(OH)), 5.20 (s; 2 H, CH_2-Ph), 6.22 (s; 1 H, 3-H), 6.60-7.22 (m; 8 H aromat.). -MS: m/z (%) = 323 (57%) [$M^{+\bullet}$], 91 (100) $[C_7H_7]^+$.

4b: colourless crystals, yield 12.85 g (95 %). - mp 75-76°C (petrol ether / ether). - $C_{21}H_{25}NO_2$ (323.43) Calcd. C 77.97 H 7.79 N 4.33 Found C 77.90 H 7.86 N 4.56. - IR (KBr): $\tilde{\nu}$ = 3400 (OH); 3100-2760 (CH); 1605, 1450 cm^{-1}(C=C). - ^{1}H NMR ($CDCl_3$): δ(ppm) = 1.11 (d; J = 7.4 Hz, 3 H, CH(OH)C<u>H</u>3), 1.24-1.83 (m; 5 H, C<u>H</u>2C<u>H</u>2CH(O<u>H</u>)), 2.44-2.68 (t; J = 7.5 Hz, 2 H, CH_2), 3.55-3.90 (m; 1 H, C<u>H</u>(OH)), 3.70 (s; 3 H, OCH_3), 5.63 (s; 2 H; CH_2-Ph), 6.23 (s; 1 H, 3-H), 6.43-7.45 (m; 8 H aromat.).

(E)-_N_-Benzyl-2-(4-hydroxypentyl)-5-methoxy-3-(2-nitroethenyl)indole (5a)

(E)-_N_-Benzyl-2-(4-hydroxypentyl)-7-methoxy-3-(2-nitroethenyl)indole (5b)

To a solution of 5.37 g *N,N*-dimethyl-2-nitroethenamine in 250 ml dry methylene chloride was dropped 7.61 ml CF_3COOH at 0°C. Also at 0°C 13.47 g (41.65 mmol) **4a** or **4b** in 250 ml dry methylene chloride were added, and the mixture was stirred for 5 h, then poured into 200 ml H_2O and alkalized with solid Na_2CO_3. The aqueous phase was extracted with methylene chloride (2 x 100 ml), the combined extract dried (Na_2SO_4) and methylene chloride evaporated *in vacuo*. The crude product was purified by chromatography (column 50 cm x 5 cm, SiO_2, methylene chloride).

5a: yellow crystals, yield 11.60 g (70%). - mp 86-88°C (diisopropyl ether). - $C_{23}H_{26}N_2O_4$ (394.47) Calcd. C 70.03 H 6.64 N 7.10 Found C 69.95 H 6.66 N 7.13. - IR (KBr): $\tilde{\nu}$ = 3540 (OH); 3100-2800 (CH); 1620,

1490 (C=C); 1345 cm^{-1} (NO_2). - ^1H NMR ($CDCl_3$): δ(ppm) = 1.06 (d; J = 6.0 Hz, 3 H, CH(OH)C<u>H</u>3), 1.27 (s; 1 H, OH), 1.48-1.56 (m; 4 H, C<u>H</u>2C<u>H</u>2CH(OH)), 2.92 (t; J = 8.0 Hz, 2 H, C=C-CH_2), 3.66-3.83 (m; 4 H, OCH_3, C<u>H</u>(OH)), 5.32 (s; 2 H, CH_2-Ph), 6.75-7.30 (m; 8 H aromat.), 7.73; 8.36 (AB-system, J = 13.5 Hz, 2 H, CH=$CHNO_2$). - MS: m/z (%) = 394 (19%) [$M^{+\bullet}$], 91 (100) $[C_7H_7]^+$.

5b: yellow crystals, yield 11.10 g (67%). - mp 134-135°C (methylene chloride / hexane).- $C_{23}H_{26}N_2O_4$ (394.47) Calcd. C 70.03 H 6.64 N 7.10 Found C 69.77 H 6.64 N 7.12. - IR (NaCl): $\tilde{\nu}$ = 3100-2800 (CH); 1550, 1345 (NO_2); 1615, 1455 cm^{-1} (C=C). - ^1H NMR ($CDCl_3$): δ(ppm) = 1.10 (d; J = 7.4 Hz, 3 H, CH(OH)C<u>H</u>3), 1.20-1.75 (m; 5 H, C<u>H</u>2C<u>H</u>2CH(O<u>H</u>)), 2.65-3.01 (m; 2 H, CH_2), 3.53-3.86 (m; 1 H, C<u>H</u>(OH)), 3.75 (s; 3 H, OCH_3) 5.74 (s; 2 H, CH_2-Ph), 6.63-7.43 (m; 8 H aromat.), 7.76; 8.29 (AB-system, J = 13.5 Hz, CH=$CHNO_2$).

(E)-*N*-Benzyl-5-methoxy-3-(2-nitroethenyl)-2-(4-oxopentyl)indole (6a)

At 0°C 12.0 g (31.90 mmol) PDC were added to a solution of 1.80 g (4.56 mmol) **5a** in 50 ml dry DMF. After stirring for 18 h at 0°C 350 ml H_2O were added, and the mixture was extracted with methylene chloride (3 x 150 ml). The combined extracts were washed with H_2O (2 x 100ml), dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by chromatography (column 40 cm x 5 cm, SiO_2, methylene chloride):
yellow crystals, yield 1.60 g (89%). - mp 107-108°C (THF / ether). - $C_{23}H_{24}N_2O_4$ (392.46) Calcd. C 70.39 H 6.16 N 7.14 Found C 70.34 H 6.16 N 7.20. - IR (KBr): $\tilde{\nu}$ = 3145-2830 (CH); 1705 (C=O); 1620, 1480 (C=C); 1520, 1350 cm^{-1} (NO_2). - ^1H NMR ($CDCl_3$): δ(ppm) = 1.50-1.95 (m; 2 H, CH_2C<u>H</u>2CH_2), 2.03 (s; 3 H, $COCH_3$), 2.48 (t; J = 6.0 Hz, 2 H, CH_2C<u>H</u>2CO), 2.82 (t; J = 7.0 Hz, 2 H, C=C-CH_2), 3.85 (s; 3 H, OCH_3), 5.40 (s; 2 H, CH_2-Ph), 6.75-7.25 (m; 8 H aromat.), 7.72; 8.30 (AB-system, J = 13.5 Hz, 2 H, CH=$CHNO_2$). - MS: m/z (%) = 392 (13%) [$M^{+\bullet}$], 91 (100) $[C_7H_7]^+$.

(E)-*N*-Benzyl-7-methoxy-3-(2-nitroethenyl)-2-(4-oxopentyl)indole (6b)

At -63°C 4.00 ml (57.14 mmol) DMSO dissolved in 20 ml dry methylene chloride were added dropwise over 10 min to a solution of 2.60 ml (30.64 mmol) oxalyl chloride in 20 ml dry methylene chloride. After 15 min at -63°C a solution of 5.0 g (12.68 mmol) **5b** in 40 ml dry methylene chloride was added slowly and the resulting solution was stirred for 3 h at -63°C. 14.3 ml (102.39 mmol) triethylamine were added and the mixture was allowed to warm to room temp. over a 30 min period. 100 ml H_2O were added and the organic phase was separated. The aqueous phase was extracted with methylene chloride (2 x 100 ml), the combined extracts were dried (Na_2SO_4), and the solvent was evaporated *in vacuo*. The crude product was purified by chromatography (column 70 cm x 5 cm, SiO_2, methylene chloride): yellow crystals, yield 4.57g (85%). - mp 133-134°C (THF / ether). - $C_{23}H_{24}N_2O_4$ (392.46) Calcd. C 70.39 H 6.16 N 7.14 Found C 70.08 H 6.19 N 7.14. - IR (KBr): $\tilde{\nu}$ = 3100-2800 (CH); 1710 (C=O); 1550 (NO_2); 1605, 1450 cm^{-1} (C=C). - ^1H NMR ($CDCl_3$): δ(ppm) = 1.63-1.99 (m; 2 H, CH_2C<u>H</u>2CH_2CO), 2.08 (s; 3 H, $COCH_3$), 2.39-2.68 (m; 2 H, CH_2CO), 2.68-2.99 (m; 2 H, C=C-CH_2), 3.76 (s; 3 H, OCH_3), 5.82 (s; 2 H, CH_2-Ph), 6.61- 7.61 (m; 8 H aromat.), 7.79; 8.29 (AB-system, J = 12.6 Hz, CH=$CHNO_2$).

3-Acetyl-*N*-benzyl-6-methoxy-4-(2-nitroethyl)-1,2,3,4-tetrahydro-carbazole (7a)
3-Acetyl-*N*-benzyl-8-methoxy-4-(2-nitroethyl)-1,2,3,4-tetrahydro-carbazole (7b)

2.0 g (5.10 mmol) **6a** or **6b,** dissolved in 30 ml dry THF, were treated with 2 ml Triton B at room temp. and the resulting solution was stirred overnight. The mixture was poured into 20 ml saturated $NaHCO_3$ solution, and the aqueous phase was extracted with 30 ml ether. The dried extract (Na_2SO_4) was concentrated *in vacuo* to give crude **7a** or **7b**, respectively. The crude product was purified by chromatography (column 30 cm x 3 cm, SiO_2, methylene chloride).

7a: yellow crystals, yield 0.80 g (40%). - mp 94-96°C (ethyl acetate / hexane). - $C_{23}H_{24}N_2O_4$ (392.46) Calcd. C 70.39 H 6.16 N 7.14 Found C 69.58 H 6.22 N 7.03. - IR (KBr): $\tilde{\nu}$ = 3065-2830 (CH); 1710 (C=O); 1620, 1485 (C=C); 1550, 1355 cm^{-1} (NO_2). - ^1H NMR ($CDCl_3$) (mixture of diastereomers): δ(ppm) = 1.60-3.14 (m; 5 H, 1-H, 2-H, 3-H), 2.20 (s; 1.5 H, $COCH_3$ (1. diastereomer)), 2.30 (s; 1.5 H, $COCH_3$ (2. diastereomer)), 3.83 (s; 1.5 H, OCH_3 (1. diastereomer)), 3.89 (s; 1.5 H, OCH_3 (2. diastereomer)), 4.32-4.92 (m; 3 H, CH_2NO_2, 4-H), 5.14-5.18 (m; 2 H, CH_2-Ph), 6.73-7.28 (m; 8 H aromat.). - MS: m/z (%) = 392 (76%) [$M^{+\bullet}$], 91 (100) $[C_7H_7]^+$.

7b: yellow crystals, yield 1.0 g (50%). - mp 165-166°C (ethyl acetate / hexane). - $C_{23}H_{24}N_2O_4$ (392.46) Calcd. C 70.39 H 6.16 N 7.14 Found C 70.11 H 6.18 N 7.14. - IR (NaCl): $\tilde{\nu}$ = 3100-2800 (CH); 1710 (C=O), 1545, 1355 (NO_2); 1605, 1455 cm^{-1} (C=C). - ^1H NMR ($CDCl_3$) (mixture of diastereomers): δ(ppm) = 1.78-3.19 (m; 5 H, 1-H, 2-H, 3-H), 2.17 (s; 1.5 H, $COCH_3$ (1. diastereomer)), 2.30 (s; 1.5 H, $COCH_3$ (2. diastereomer)), 3.72 (s; 1.5 H, OCH_3 (1. diastereomer)), 3.77 (s; 1.5 H, OCH_3 (2. diastereomer)), 4.29-5.00 (m; 3 H, CH_2NO_2, 4-H), 5.51-5.73 (m; 2 H, CH_2-Ph), 6.50-7.53 (m; 8 H aromat.). - MS: m/z (%) = 392 (100%) [$M^{+\bullet}$], 91 (68) $[C_7H_7]^+$. - For further reactions **7a** und **7b** were used as mixtures of diastereomers.

3-Acetyl-*N*-benzyl-6-methoxy-4-(2-nitroethyl)carbazole (8a)
3-Acetyl-*N*-benzyl-8-methoxy-4-(2-nitroethyl)carbazole (8b)

method a)

A solution of 400 mg (1.02 mmol) **7a** or **7b** and 470 mg (2.04 mmol) DDQ in 20 ml dioxane was stirred for 30 min at 60°C. The dioxane was evaporated *in vacuo* and the product was separated from unchanged DDQ, hydroquinone and other products by chromatography (column 30 cm x 3 cm, SiO_2, methylene chloride). After the addition of MeOH the products began to crystallize.

8a: yellow crystals; yield 95 mg (24%). - mp 65-66°C (MeOH). $C_{23}H_{20}N_2O_4$ (388.42) Calcd. C 71.12 H 5.19 N 7.21 Found C 71.14 H 5.23 N 7.32. - IR (KBr): $\tilde{\nu}$ = 3100-2800 (CH); 1710 (C=O); 1590,1455 (C=C); 1550, 1355 (NO_2). - ^1H NMR ($CDCl_3$): δ(ppm) = 2.66 (s; 3 H, $COCH_3$), 3.81 (s; 3 H, OCH_3), 5.52 (s; 2H, CH_2-Ph), 6.60 (s; 2 H, CH_2NO_2), 6.75-7.94 (m; 10 H aromat.). - MS: m/z (%) = 388 (8%) [$M^{+\bullet}$], 91 (100) $[C_7H_7]^+$.

8b: yellow crystals; yield 40 mg (10%). - mp 136-138°C (MeOH) - $C_{23}H_{20}N_2O_4$ (388.42) Calcd. C 71.12 H 5.19 N 7.21 Found C 71.19 H 5.28 N 7.35. - IR (NaCl): $\tilde{\nu}$ = 3100-2800 (CH); 1710 (C=O); 1550, 1355 (NO_2); 1605, 1455 cm^{-1} (C=C). - ^1H NMR ($CDCl_3$): δ(ppm) = 2.68 (s; 3 H, $COCH_3$), 3.85 (s; 3H, OCH_3), 5.94 (s; 2 H, CH_2-Ph), 6.55 (s; 2 H, CH_2NO_2), 6.79-8.05 (m; 10 H aromat.). - MS: m/z (%) = 388 (9/) [$M^{+\bullet}$], 91 (100) $[C_7H_7]^+$.

method b)

100 mg (0.25 mmol) **7b** and 250 mg (1.02 mmol) *p*-chloranil dissolved in 5 ml mesitylene were heated to reflux for 4 h. The cooled solution was filtered, the residue washed with methylene chloride and the solvent evaporated *in vacuo*. The resulting oil was chromatographed (column 10 cm x 1 cm, SiO_2, methylene chloride). The product was separated from educt by crystallizaion from MeOH and 2 drops of methylene chloride: yellow crystals, yield 14 mg (14%). -For analytical data see method a).

method c)

150 mg (0.35 mmol) **10** were dissolved in 10.5 ml THF. After the addition of 1.5 ml HCl (12%) the resulting solution was stirred at room temp. and after 6 h neutralized with NaOH. The mixture was extracted with 20 ml ether, the extract dried (Na_2SO_4) and concentrated. Purification by recrystallization from MeOH gave pure **8b**: yellow crystals; yield 70 mg (51%).-For analytical data see method a).

_N_-Benzyl-8-methoxy-3-(2-methyl-1,3-dioxolan-2-yl)-4-(2-nitroethyl)-1,2,3,4-tetrahydrocarbazole (9)

500 mg (1.27 mmol) **7b** were dissolved in 20 ml methylene chloride and 8 ml ethylene glycol. To this solution 1 ml BF_3-etherate was added dropwise at 0°C. After warming to room temp. overnight, the mixture was treated with 2 ml NaOH (5%) and 20 ml H_2O. The aqueous phase was extracted with methylene chloride (2 x 10 ml), the extracts were washed with H_2O and dried (Na_2SO_4). Evaporation of methylene chloride and purification by chromatography gave pure **9** (column 50 cm x 5 cm, SiO_2, methylene chloride / hexane 8:2): yellow crystals, yield 300 mg (90%). - mp 104-105°C (MeOH). - $C_{25}H_{28}N_2O_5$ (436.51) Calcd. C 68.79 H 6.47 N 6.42 Found C 68.51 H 6.42 N 6.57.- IR (NaCl): $\tilde{\nu}$ = 3100-2800 (CH); 1550, 1360 (NO_2); 1615, 1450 cm^{-1} (C=C). - ^1H NMR ($CDCl_3$) (mixture of diastereomers): δ(ppm) = 1.26 (s; 1.8 H, CCH_3 (1. diastereomer)), 1.41 (s; 1.2 H, CCH_3 (2.diastereomer)), 1.83-2.33 (m; 4 H), 2.38-2.78 (m; 2 H), 3.71 (s; 3 H, OCH_3), 3.55-4.09 (m; 4 H, OCH_2CH_2O), 4.19-4.77 (m; 2 H, CH_2NO_2), 5.39; 5.68 (AB-system, J = 15.9 Hz, 2 H, CH_2-Ph), 6.46-7.34 (m; 8 H aromat.). - For further reactions **9** was used as a mixture of diastereomers.

_N_-Benzyl-8-methoxy-3-(2-methyl-1,3-dioxolan-2-yl)-4-(2-nitroethyl)-carbazole (10)

A solution of 600 mg (1.37 mmol) **9** and 360 mg (2.74 mmol) *p*-chloranil in 15 ml xylene was heated to reflux for 24 h. The cooled solution was filtered, the residue washed with methylene chloride and the solvent evaporated *in vacuo*. The crude product was purified by chromatography (column 20 cm x 3 cm, SiO_2, methylene chloride / hexane 8:2): light yellow crystals, yield 430 mg (73%). - mp 105-107°C (MeOH). - $C_{25}H_{24}N_2O_5$ (432.47) Calcd. C 69.43 H 5.59 N 6.48 Found C 69.26 H 5.62 N 6.51. - IR (NaCl): $\tilde{\nu}$ = 3100-2800 (CH); 1550, 1355 (NO_2); 1605, 1455 cm^{-1} (C=C). - ^1H NMR ($CDCl_3$): δ(ppm) = 1.70 (s; 3 H, CCH_3), 3.59-4.10 (m; 4 H, OCH_2CH_2O), 3.85 (s; 3 H, OCH_3), 5.39 (s; 2 H, CH_2-Ph), 5.84 (s; 2 H, CH_2NO_2), 6.80-7.82 (m; 10 H aromat.).

6-Benzyl-7-methoxy-3-methyl-3a,4,5,10c-tetrahydro-2-pyrrolino[3,4-*c*]carbazole-2-*N*-oxide (11)

100 mg (0.25 mmol) **7b** and 100 mg Pd / C 5% were stirred in 10 ml dry MeOH under 15 bar H_2 overnight. The mixture was filtered over Celite, MeOH evaporated *in vacuo* and the crude product purified by chromatography (column 10 cm x 1 cm, SiO_2, methylene chloride / ethyl acetate 1:1): yellow oil, yield 30 mg (35%). - IR

(NaCl): $\tilde{\nu}$ = 3100-2800 (CH); 1230-1260 (N^+–O^-); 1605, 1460 cm^{-1} (C=C). - ^1H NMR ($CDCl_3$) (400 MHz): δ(ppm) = 1.95-2.11 (m; 2 H, 4-H), 2.08 (q; J = 1.5 Hz, CCH_3), 2.53-2.56 (m; 2 H, 5-H), 3.28-3.30 (m; 1H), 4.02-4.07 (m; 1 H), 4.42-4.48 (m; 1 H), 5.48; 5.73 (AB-system, J = 16.5 Hz, 2 H, CH_2-Ph), 6.63-6.65 (m; 1 H aromat.), 6.95-7.04 (m; 4 H aromat.), 7.18-7.28 (m; 3 H aromat.). - MS: m/z (%) = 360 (16%) [$M^{+\bullet}$], 344 (100) [M - O]$^+$, 91 (57) [C_7H_7]$^+$.

6-Benzyl-7-methoxy-3-methyl-3a,4,5,10c-tetrahydro-pyrrolino[3,4-*c*]carbazole (12)

Raney-Ni (2 g) was activated with NaOH and added to a solution of 500 mg (1.27 mmol) **7b** in 10 ml EtOH saturated with NH_3. The resulting mixture was stirred under 9 bar H_2 at room temp. overnight. Raney-Ni was filtered off over Celite and the solvent was evaporated *in vacuo*. Chromatography (column 30 cm x 3 cm, SiO_2, methylene chloride / MeOH 9:1) gave pure **12** and traces of **11**. - **12**: yellow oil, yield 100 mg (23%). - IR (KBr): $\tilde{\nu}$ = 3100-2800 (CH); 1615, 1450 cm^{-1} (C=C). - ^1H NMR ($CDCl_3$) (250 MHz): δ(ppm) = 1.85-2.16 (m; 2 H, 4-H), 2.05 (s; 3 H, CCH_3), 2.49-2.53 (m; 1 H) 3.60-3.82 (m; 2 H, 1-H), 3.77 (s; 3 H, OCH_3), 4.21-4.31 (m; 1 H), 5.49; 5.68 (AB-system, J = 16.5 Hz, 2 H, CH_2-Ph), 6.59-6.65 (1 H aromat.), 6.92-7.27 (7 H aromat.).

***N*-Benzyl-3-(1-hydroxyethyl)-8-methoxy-4-methylcarbazole (13)**

20 mg (0.05 mmol) **8b** and 20 mg Pd / C 5% were stirred in 3 ml dry EtOH under 15 bar H_2 at room temp. overnight. Pd / C was filtered off over Celite and the solvent was evaporated *in vacuo*. The crude product was purified by chromatography (column 10 cm x 1 cm, SiO_2, methylene chloride): colourless crystals, yield 8 mg (47%). - mp 80 - 81°C. - IR (KBr): $\tilde{\nu}$ = 3400 (OH); 3100-2800 (CH); 1615, 1450 cm^{-1} (C=C). - ^1H NMR (400 MHz) ($CDCl_3$): δ(ppm) =1.56 (d; 3 H, CH(OH)C<u>H</u>$_3$), 1.71 (d; 1 H, OH (exch.), 2.90 (s; 3 H, CCH_3); 3.88 (s; 3 H, OCH_3), 5.44 (m; 1 H, C<u>H</u>(OH)), 5.88; 5.91 (AB-system, J = 4.1 Hz, 2 H, CH_2-Ph), 6.93-6.96 (m; 1 H aromat.), 7.11-7.26 (m; 7 H aromat.), 7.57-7.59 (m; 1 H aromat.), 7.91-7.94 (m; 1 H aromat.). - MS: m/z (%) = 345 (83%) [$M^{+\bullet}$], 327 (100), 91 (50) [C_7H_7]$^+$.

6-Benzyl-7-methoxy-3-methyl-2,3-dihydro-1*H*-pyrrolo[3,4-*c*]carbazole (14)

method a)

A mixture of 200 mg (0.51 mmol) **8b** and 92.6 mg Pd / C 5% in 6.8 ml dry EtOH and 3.4 ml dry acetic acid was stirred under 3 bar H_2 for 80 h at room temp., Pd / C was filtered off over Celite, and the filtrate was concentrated *in vacuo*. The resulting residue was dissolved in methylene chloride and alkalized with saturated Na_2CO_3 solution (pH = 11). The aqueous phase was extracted with 10 ml methylene chloride and the combined organic phases washed with H_2O. After removal of the solvent the crude product was purified by chromatography (column 20 cm x 2 cm, SiO_2, methylene chloride / MeOH 9:1): colourless foam, yield 30 mg (17%). - IR (KBr): $\tilde{\nu}$ = 3400 (NH); 3100-2800 (CH); 1615, 1450 cm^{-1} (C=C). - ^1H NMR (400 MHz) ($CDCl_3$): δ(ppm) =1.73 (d; J = 6.7 Hz, 3 H, CCH_3), 3.90 (s; 3 H, OCH_3),4.97; 5.08 (AB-system, J = 13.9 Hz, 2 H, 1-H), 5.02 (q; 1 H, 3-H), 5.92 (s; 2 H, CH_2-Ph), 6.93-6.97 (m; 1 H aromat.), 7.10-7.12 (m; 1 H aromat.), 7.14-7.31 (m; 7 H aromat.), 7.48-7.55 (1 H aromat). - MS: m/z (%) = 342 (27%) [$M^{+\bullet}$], 327 (100), 91 (28) [C_7H_7]$^+$.

method b)

Raney-Ni (0.5 g) was activated with NaOH and added to a solution of 30 mg (0.08 mmol) **8b** in 5 ml EtOH saturated with NH_3. The mixture was stirred under 5 bar H_2 at room temp. overnight. Raney-Ni was filtered off over Celite and the solvent removed *in vacuo*. From the resulting colourless foam **14** und **15** were separated by chromatography (see method a): yield 10 mg **14** (37%).-For analytical data of **14** see method a).

6-Benzyl-7-methoxy-3-methyl-1*H*-pyrrolo[3,4-*c*]carbazole (15)

Syntheses see **14** , method b).

colourless oil; yield 3mg (11%). - MS: m/z (%) = 340 (16%) [$M^{+\bullet}$], 91 (100) [$C_7H_7]^+$.

4-Aminomethyl-9-benzyl-8-methoxy-3-(2-methyl-1,3-dioxolan-2-yl)-carbazole (16)

Raney-Ni (1.0 g) was activated with NaOH and added to 100 mg (0.23 mmol) **10**, dissolved in 5 ml dry EtOH. The resulting mixture was stirred under H_2 (balloon) at room temp. overnight. Raney-Ni was filtered off over Celite and the filtrate concentrated *in vacuo*. The crude product was purified by chromatography (column 10 cm x 1 cm, SiO_2, methylene chloride / MeOH 9:1): colourless oil, yield 80 mg (86%). - IR (NaCl): $\tilde{\nu}$ = 3400-3200 (NH_2); 3100-2800 (CH); 1605, 1455 cm^{-1} (C=C). - ^1H NMR ($CDCl_3$): δ(ppm) = 1.71 (s; 3 H, CCH_3), 2.23 (br s; 2 H, NH_2 (exch.), 3.60-4.17 (m; 4 H, OCH_2CH_2O), 3.77 (s; 3 H, OCH_3), 4.45 (s; 2 H, CH_2NH_2), 5.79 (s; 2 H, CH_2-Ph), 6.80-7.82 (m; 10 H aromat.). - MS: m/z (%) = 402 (100%) [$M^{+\bullet}$], 91 (40) [$C_7H_7]^+$.

References and Notes

Dedicated to Prof. Dr. Drs. h. c. H. Oelschläger on the occassion of his 75th birthday.

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