Synthesis of Mukonine and Seven Further 1-Oxygenated Carbazole Alkaloids

Gerhard Bringmann,*[a] Stefan Tasler,[a] Heike Endress,[a] Karl Peters,[b] Eva-Maria Peters[b]

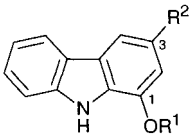
[a] Institut für Organische Chemie, Universität Würzburg, Am Hubland, D-97074 Würzburg, Germany
Fax +49(931)8884755; E-mail: bringman@chemie.uni-wuerzburg.de
[b] Max-Planck-Institut für Festkörperforschung, Heisenbergstr. 1, D-70506 Stuttgart, Germany

Received 5 March 1998; revised 23 March 1998

Abstract: As an intermediate in the synthesis of seven further 1-oxygenated 3-C_1-substituted carbazole alkaloids, mukonine **(1)** was synthesized in 46% overall yield, starting from indole-3-carbaldehyde **(12)** with a Horner–Emmons reaction as the crucial step. From **1**, the other desired alkaloids were obtained in high yields. Among them, clausine E **(6)** and *O*-demethylmurrayanine **(7)** were synthesized for the first time.

Key words: carbazole alkaloids, mukonine, Horner–Emmons reaction, natural product

Carbazole alkaloids, which have their richest source in species of the genus *Murraya*, are of great interest because of their numerous biological activities.[1] Chakraborty arranged this group of natural products by the size of the carbon skeleton.[1] In the following we present an effective synthetic access to 1-oxygenated 3-C_1-substituted carbazoles of the 'C_{13} group' like mukonine **(1)**,[2] mukoeic acid **(2)**,[3] murrayanine **(3)**,[4] koenoline **(4)**,[5] murrayafoline A **(5)**,[6] clausine E (clauszoline I, **6**),[7, 8] *O*-demethylmurrayanine **(7)**,[9] and 1-hydroxy-3-methylcarbazole **(8)**[10] (Scheme 1). Some of them show antibiotic,[11] antifungal,[12] and cytotoxic[5] properties and neoplasm inhibitory effects on mitosis[13] as well as a good activity against the malaria parasite *Plasmodium falciparum*, also exhibited by some dimeric carbazoles.[14, 15]

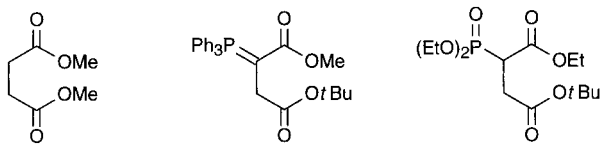


	R^1	R^2
1	Me	COOMe
2	Me	COOH
3	Me	CHO
4	Me	CH_2OH
5	Me	Me
6	H	COOMe
7	H	CHO
8	H	Me

Scheme 1

Three general approaches to the synthesis of these compounds have been described so far: the classical Fischer–Borsche synthesis starts with appropriate cyclohexanone arylhydrazones,[2, 15, 16] Moody et al. build up the carbazole ring system from indole-2-carboxylate derivatives and γ-butyrolactones,[17] and Knölker et al. construct the skeleton via iron tricarbonyl complexes.[18] The yields are mostly moderate, only few of the reaction sequences lead to overall yields of more than 30%.[15, 17]

In the course of our studies we attempted to attach a C_4 unit to indole-3-carbaldehyde **(12)** by Stobbe condensation[19] and Wittig reaction[20] with reagent **9** and **10**, respectively (Scheme 2). Both methods could not compete with the Horner–Emmons variant in which phosphonate **11** is used (Scheme 2). In the synthesis of **11** according to a protocol by Owton et al.,[21] we could increase the yield to 87% by distilling the product in high vacuum.

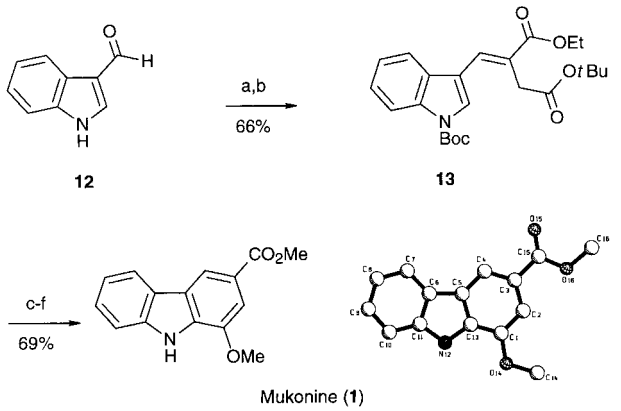


9 **10** **11**

Scheme 2

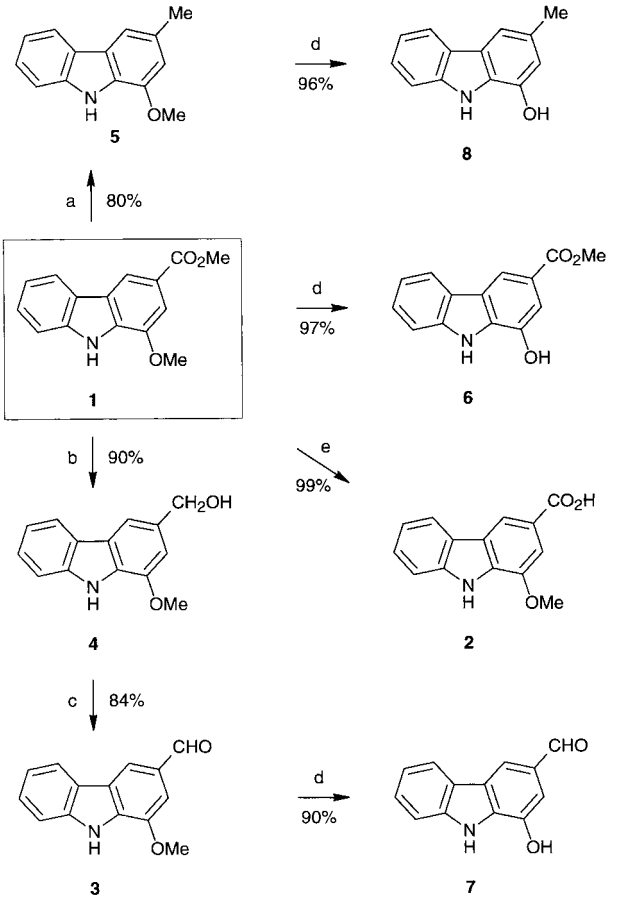
In order to avoid side reactions at the indole nitrogen and, at the same time, to activate the aldehydic carbonyl function for nucleophilic attack, the nitrogen was protected with the Boc unit.[22] Further conversions to the carbazole skeleton took place according to analogous syntheses of naphthalenes.[20a, 23] After *N*-protection of **12** and olefination with phosphonate **11** to compound **13**, the Boc group was removed and the *tert*-butyl ester cleaved in a single step. Cyclization with sodium acetate in acetic anhydride and subsequent methanolysis directly yielded clausine E **(6)**, though it was not easily separated from its impurities at this point. After removal of residual acetic anhydride, *O*-methylation with dimethyl sulfate in acetone led to mukonine **(1)** in an overall yield of 46% after purification by chromatography and recrystallization (Scheme 3). Further structural evidence was obtained from a crystal structure analysis[24] of **1** (Scheme 3).

Starting from **1**, the alkaloids **2**–**8** were synthesized in a few steps (Scheme 4). Treatment of **1** with boron tribromide in dichloromethane[23a] afforded clausine E **(6)**, which was isolated very easily now. Reduction of the ester function of **1** with lithium aluminum hydride did not yield the expected alcohol koenoline **(4)**,[3] but ended in almost total reduction to give the methyl group of murrayafoline A **(5)**. The yield of **5** was enhanced to 80% by running the reaction in a solvent mixture of diethyl ether and dichloromethane. Reduction of **1** with the milder reducing agent diisobutylaluminum hydride[25] gave **4** in 90% yield. Oxidation of **4** with activated manganese dioxide led to



(a) Boc_2O, DMAP, CH_2Cl_2, r.t., 1 h (96%); (b) **11**, NaH, THF, 0 °C then 50 °C, 18 h (69%); (c) TFA, CH_2Cl_2/H_2O, r.t., 5 h; (d) NaOAc, Ac_2O, 140 °C, 24 h (86% over 2 steps); (e) K_2CO_3, MeOH, 65 °C, 4.5 h; (f) DMS, K_2CO_3, acetone, 56 °C, 7 h (80% over 2 steps)

Scheme 3



(a) $LiAlH_4$, Et_2O/CH_2Cl_2, r.t., 2h (80%); (b) DIBAL, Et_2O, –78 °C, 3.5 h (90%); (c) MnO_2, CCl_4, r.t., 6 h (84%); (d) BBr_3, CH_2Cl_2, 0 °C, 3 h, to r.t., 15 h then MeOH (90–97%); (e) KOH, $EtOH/H_2O$, 78 °C, 4 h (99%)

Scheme 4

murrayanine **(3)**,[16b] which was converted to **7** by treatment with boron tribromide. Likewise by BBr_3 mediated *O*-demethylation, **5** was converted into **8**. Mukoeic acid **(2)** was obtained by quantitative saponification of **1** with potassium hydroxide in ethanol.[3, 19]

The reaction sequences described constitute the as yet best synthetic access to these carbazole alkaloids, all of them were synthesized in overall yields of 31–46%, clausine E **(6)** and *O*-demethylmurrayanine **(7)** were prepared for the first time. These compounds are also important intermediates in the atropo-selective synthesis of dimeric carbazoles, which will be the subject of forthcoming investigations.

Mps are uncorrected (Reichert Thermovar microscope). IR spectra were measured using a Perkin–Elmer 1420 spectrophotometer. ^1H and ^{13}C NMR spectra were recorded at r.t. on a Bruker AM 250 (250.1 and 62.9 MHz, respectively). Chemical shifts δ are reported in ppm and coupling constants *J* in Hz. The solvent signal was used as the internal standard [^1H: $\delta(CDCl_3)$ = 7.26, δ(acetone-d_6) = 2.05, $\delta(CD_3OD)$ = 3.31; ^{13}C: $\delta(CDCl_3)$ = 77.01, δ(acetone-d_6) = 29.82, $\delta(CD_3OD)$ = 48.00]. EI-MS were measured on a Finnigan MAT 90 and MAT 8200 mass spectrometer, the relative intensities are given in brackets. Microanalyses were performed by the microanalytical laboratory of the Inorganic Institute of the University of Würzburg. Column chromatography was performed on silica gel 63–200 μm (Merck). All reactions, except those involving water, were performed under N_2 and with dried solvents and glassware. Starting compounds and other reagents were commercially available. Phosphonate **11** was synthesized as published by Owton et al.[21]

1-*tert*-Butoxycarbonylindole-3-carbaldehyde:
Indole-3-carbaldehyde **(12)** (5.81 g, 40.0 mmol) was dissolved in CH_2Cl_2 (80 mL) and treated at r.t. with DMAP *(*489 mg, 4.00 mmol) and *di-tert*-butyl dicarbonate (10.48 g, 48.0 mmol). After stirring for 1 h, 1 N $KHSO_4$ (70 mL) was added and the CH_2Cl_2 was evaporated. The aqueous layer was extracted with several portions of Et_2O and the combined organic extracts were washed with 1 N $KHSO_4$, water, 1 N $NaHCO_3$, and brine. The organic layer was dried ($MgSO_4$) and the solvent was removed. Recrystallization of the remaining solid (EtOH) gave the aldehyde as colorless needles; yield: 9.40 g (96%); mp 129 °C (Lit.[26] 125.5 °C).
IR (KBr): ν = 3090, 3020, 3000, 2960, 2940, 2720, 2700, 1715, 1650 cm^{-1}.
^1H NMR ($CDCl_3$): δ = 1.71 (s, 9 H, O*t*Bu), 7.37 (td, 1 H, *J* = 7.3/1.2 Hz, H-5), 7.42 (ddd, 1 H, *J* = 7.6/7.3/1.5 Hz, H-6), 8.15 (d, 1 H, *J* = 7.6 Hz, H-7), 8.23 (s, 1 H, H-2), 8.29 (d, 1 H, *J* = 7.3 Hz, H-4), 10.10 (s, 1 H, CHO).
^{13}C NMR ($CDCl_3$): δ = 28.02 (O*t*Bu), 85.61 (O*t*Bu), 115.1 (C-7), 121.5 (C_q), 122.1 (C-4), 124.5 (C-5), 126.0 (C-6), 135.9 (C_q), 136.5 (C-2), 148.7 (C_q), 185.7 (CHO).
MS (70 eV): *m/z* (%) = 245 (M^+, 18), 189 (35), 172 (7), 145 (69), 144 (60), 116 (19), 57 (100).

***tert*-Butyl 4-(1'-*tert*-butoxycarbonylindol-3'-yl)-3-ethoxycarbonylbut-3-enoate (13):**
To a solution of NaH (955 mg, 39.8 mmol) in THF (90 mL) was added phosphonate **11** (12.96 g, 38.3 mmol) at 0 °C. After stirring for 2 h at 0 °C and 2 h at r.t., the mixture was added dropwise to 1-*tert*-butoxycarbonylindole-3-carbaldehyde (8.59 g, 35.0 mmol) in THF (120 mL). The solution was stirred for 18 h at 50 °C then treated with water (80 mL) and the THF was removed. The aqueous residue was extracted with Et_2O and the combined organic layers were dried ($MgSO_4$). The oil obtained after evaporation of the solvent was purified by column chromatography (petroleum ether/Et_2O 5:1) to give **13** as a yellow oil; yield: 10.34 g (69%).
IR (film): ν = 3120, 3040, 2980, 2920, 1720, 1695, 1620 cm^{-1}.
^1H NMR ($CDCl_3$): δ = 1.36 (t, 3 H, *J* = 7.0 Hz, CO_2Et), 1.47 (s, 9 H, O*t*Bu), 1.68 (s, 9 H, O*t*Bu), 3.58 (s, 2 H, H-2), 4.31 (q, 2 H, *J* = 7.0 Hz, CO_2Et), 7.29 (ddd, 1 H, *J* = 8.2/7.3/1.2 Hz, H-5'), 7.37 (td, 1 H, *J* = 7.3/1.2 Hz, H-6'), 7.67 (dd, 1 H, *J* = 7.3/1.2 Hz, H-7'), 7.87 (s, 1 H,

H-2'), 7.97 (d, 1 H, *J* = 1.2 Hz, H-4), 8.15 (d, 1 H, *J* = 8.2 Hz, H-4').
^{13}C NMR ($CDCl_3$): δ = 14.27 (CO_2Et), 27.94 (O*t*Bu), 28.07 (O*t*Bu), 35.91 (C-2), 60.95 (CO_2Et), 81.04 (O*t*Bu), 84.36 (O*t*Bu), 115.2 (C-4'), 115.6 (C_q), 119.0 (C-7'), 123.1 (C-5'), 125.1 (C-6'), 125.7 (C_q), 125.9 (C-2'), 129.9 (C_q), 131.1 (C-4), 135.0 (C_q), 149.3 (C=O), 167.3 (C=O), 170.0 (C=O).
MS (70 eV): *m/z* (%) = 429 (M^+, 15), 373 (14), 356 (5), 329 (15), 317 (40), 273 (30), 200 (12), 155 (21), 130 (6), 57 (100).

$C_{24}H_{31}NO_6$	calcd	C	67.12	H	7.28	N	3.26
(429.5)	found		66.85		7.50		3.18

1-Acetoxy-9-acetyl-3-ethoxycarbonylcarbazole:
Compound **13** (5.18 g, 12.1 mmol) was dissolved in CH_2Cl_2 (18 mL) and treated with TFA/H_2O (69 mL/1 mL) at r.t. for 5 h. The solvents were removed and without further purification the residue was refluxed in Ac_2O (44 mL) with NaOAc (2.17 g, 26.5 mmol) for 24 h. The Ac_2O was removed and purification of the remaining solid by column chromatography (petroleum ether/CH_2Cl_2/MeOH 20:2:1) afforded a brownish mixture of differently acetylated carbazoles; yield over two steps (determined by ^{1}H NMR): 3.32 g (86%, ratio 1-acetoxy-9-acetyl-3-ethoxycarbonylcarbazole/1-acetoxy-3-ethoxycarbonylcarbazole 1:0.9).
MS (70 eV): *m/z* (%) = 325 (M_1^+, 12), 283 (M_2^+, 22), 241 (100), 210 (23), 43 (100).

1-Acetoxy-9-acetyl-3-ethoxycarbonylcarbazole:
^{1}H NMR (acetone-d_6): δ = 1.42 (t, 3 H, *J* = 7.0 Hz, CO_2Et), 2.40 (s, 3 H, OAc), 2.82 (s, 3 H, NAc), 4.42 (q, 2 H, *J* = 7.0 Hz, CO_2Et), 7.53 (ddd, 1 H, *J* = 8.2/7.3/1.2 Hz, H-6), 7.59 (ddd, 1 H, *J* = 8.5/7.3/1.2 Hz, H-7), 7.90 (d, 1 H, *J* = 1.5 Hz, H-2), 8.04 (dd, 1 H, *J* = 8.5/1.2 Hz, H-8), 8.26 (dd, 1 H, *J* = 8.2/1.2 Hz, H-5), 8.67 (d, 1 H, *J* = 1.5 Hz, H-4).

1-Acetoxy-3-ethoxycarbonylcarbazole:
^{1}H NMR (acetone-d_6): δ = 1.41 (t, 3 H, *J* = 7.0 Hz, CO_2Et), 2.41 (s, 3 H, OAc), 4.40 (q, 2 H, *J* = 7.0 Hz, CO_2Et), 7.29 (ddd, 1 H, *J* = 7.6/7.0/1.2 Hz, H-6), 7.46 (dd, 1 H, *J* = 7.9/1.2 Hz, H-8), 7.46 (ddd, 1 H, *J* = 7.9/7.0/1.2 Hz, H-7), 7.86 (d, 1 H, *J* = 1.5 Hz, H-2), 8.29 (dd, 1 H, *J* = 7.6/1.2 Hz, H-5), 8.73 (d, 1 H, *J* = 1.5 Hz, H-4), 10.91 (br s, 1 H, NH).

3-Ethoxycarbonyl-4-(indol-3'-yl)but-3-enoic Acid:
Purification of a small product sample of the TFA mediated hydrolysis by filtration through a short silica gel column (petroleum ether/CH_2Cl_2/MeOH 20:2:1) and recrystallization of the obtained solid from MeOH provided light beige crystals; mp 194 °C.
IR (KBr): ν = 3220, 3090, 3030, 2960, 2910, 2690, 1695, 1670, 1590 cm^{-1}.
^{1}H NMR (CD_3OD): δ = 1.35 (t, 3 H, *J* = 7.0 Hz, CO_2Et), 3.66 (s, 2 H, H-2), 4.28 (q, 2 H, *J* = 7.0 Hz, CO_2Et), 7.14 (td, 1 H, *J* = 7.3/1.2 Hz, H-5'), 7.20 (td, 1 H, *J* = 7.3/1.2 Hz, H-6'), 7.42 (d, 1 H, *J* = 7.3 Hz, H-7'), 7.61 (d, 1 H, *J* = 0.6 Hz, H-2'), 7.69 (d, 1 H, *J* = 7.3 Hz, H-4'), 8.17 (s, 1 H, H-4).
^{13}C NMR (CD_3OD): δ = 14.67 (CO_2Et), 35.32 (C-2), 61.96 (CO_2Et), 112.2 (C_q), 112.8 (C-4'), 119.1 (C-7'), 120.7 (C_q), 121.6 (C-5'), 123.8 (C-6'), 127.7 (C-2'), 129.1 (C_q), 134.8 (C-4), 137.6 (C_q), 170.0 (CO_2Et), 175.2 (CO_2H).
MS (70 eV): *m/z* (%) = 273 (M^+, 89), 229 (79), 200 (48), 156 (29), 155 (100), 154 (88), 130 (35).

$C_{15}H_{15}NO_4$	calcd	C	65.92	H	5.53	N	5.13
(273.3)	found		65.68		5.55		5.09

Mukonine (1):
The mixture of 1-acetoxy-9-acetyl-3-ethoxycarbonylcarbazole and 1-acetyl-3-ethoxycarbonylcarbazole obtained above (together 8.00 mmol) and K_2CO_3 (3.32 g, 24.0 mmol) was refluxed in MeOH (30 mL) for 4.5 h. After evaporation of the MeOH, the residue was dissolved in acetone (30 mL), K_2CO_3 (1.11 g, 8.00 mmol) and DMS (607 μL, 6.40 mmol) were added and the mixture was refluxed for 7 h. Aq NH_3 (7 mL) was used to scavenge excessive DMS by refluxing the solution for further 60 min. Evaporation of the solvent and purification by column chromatography (petroleum ether/Et_2O 5:1) yielded crude **1**. The formation of the *N*,*O*-dimethylated compound as a minor product could not be entirely avoided (6% yield). Recrystallization from EtOH/pentane afforded colorless crystals; yield over two steps: 1.64 g (80%); mp 201 °C (Lit.[1a] 195 °C, Lit.[2, 3] 198–200 °C).
IR (KBr): ν = 3320, 3070, 3020, 2970, 2915, 2810, 1675, 1610, 1590, 1565 cm^{-1}.
^{1}H NMR (acetone-d_6): δ = 3.92 (s, 3 H, CO_2Me), 4.07 (s, 3 H, OMe), 7.26 (t, 1 H, *J* = 7.6 Hz, H-6), 7.46 (t, 1 H, *J* = 7.6 Hz, H-7), 7.59 (s, 1 H, H-2), 7.64 (d, 1 H, *J* = 7.6 Hz, H-8), 8.21 (d, 1 H, *J* = 7.6 Hz, H-5), 8.48 (s, 1 H, H-4), 10.78 (br s, 1 H, NH).
^{13}C NMR (acetone-d_6): δ = 52.04 (CO_2Me), 56.05 (OMe), 107.1 (C-2), 112.6 (C-8), 116.6 (C-4), 120.7 (C-6), 121.3 (C-5), 122.5 (C_q), 124.4 (C_q), 127.1 (C-7), 134.0 (C_q), 141.3 (C_q), 146.3 (C-1), 167.9 (CO_2Me).
MS (70 eV): *m/z* (%) = 255 (M^+, 100), 240 (51), 224 (40), 196 (14), 181 (15), 153 (17).

Murrayafoline A (5):
Reduction of **1** (100 mg, 392 μmol) with $LiAlH_4$ (44.7 mg, 1.18 mmol) in CH_2Cl_2/Et_2O (12 mL, 1:1) was carried out at r.t. for 2 h. The solution was neutralized with 2 N HCl at r.t. and the solvent was removed. Purification by column chromatography (petroleum ether/CH_2Cl_2/MeOH 20:2:1) yielded **5** as a colorless oil; yield: 66.6 mg (80%).
IR and MS data were identical with those reported in the literature.[6]
^{1}H NMR (acetone-d_6): δ = 2.49 (s, 3 H, Me), 3.97 (s, 3 H, OMe), 6.81 (s, 1 H, H-2), 7.14 (ddd, 1 H, *J* = 7.9/7.0/0.9 Hz, H-6), 7.36 (ddd, 1 H, *J* = 8.2/7.0/0.9 Hz, H-7), 7.49 (s, 1 H, H-4), 7.55 (dt, 1 H, *J* = 8.2/0.9 Hz, H-8), 8.03 (dd, 1 H, *J* = 7.9/0.9 Hz, H-5), 10.21 (br s, 1 H, NH).
^{13}C NMR (acetone-d_6): δ = 21.93 (Me), 55.73 (OMe), 108.4 (C-2), 112.1 (C-8), 113.1 (C-4), 119.4 (C-6), 120.9 (C-5), 124.1 (C_q), 125.0 (C_q), 126.0 (C-7), 129.2 (C_q), 129.6 (C_q), 141.0 (C_q), 146.6 (C-1).

Koenoline (4):
1 M DIBAH in hexane (3.52 mL) was added to a solution of **1** (600 mg, 2.35 mmol) in Et_2O (50 mL) at –78 °C. After 1.5 h stirring at –78 °C, the mixture was treated with another portion of DIBAH (2.64 mL) and stirring was continued for further 2 h. The solution was poured into iced water (70 mL) and extracted with several portions of Et_2O. The combined organic layers were dried ($MgSO_4$), the solvent was evaporated and the product was purified by column chromatography (petroleum ether/Et_2O 2:1). Recrystallization from EtOH/pentane yielded **4** as colorless crystals; yield: 478 mg (90%); mp 142 °C (Lit.[5] 130 °C, Lit.[16b] 127 °C).
IR, ^{1}H and ^{13}C NMR data were identical with those reported in the literature.[5]
MS (70 eV): *m/z* (%) = 227 (M^+, 6), 212 (5), 210 (100), 195 (10), 180 (6), 167 (39).

Murrayanine (3):
Oxidation of crude **4** (450 mg, 1.98 mmol) was performed according to literature procedures.[16b] After stirring for 6 h, the mixture was concentrated by evaporating parts of the solvent and filtered through a short silica gel column (CH_2Cl_2). The crude product was recrystallized from EtOH/pentane to give **3** as reddish crystals; yield: 374 mg (84%); mp 170 °C (Lit.[4, 6, 16b] 168 °C).
IR, MS and ^{1}H data were identical with those reported in the literature.[6]
^{13}C NMR (acetone-d_6): δ = 56.09 (OMe), 104.2 (C-2), 112.8 (C-8), 120.4 (C-4), 121.0 (C-6), 121.4 (C-5), 124.3 (C_q), 124.5 (C_q), 127.2 (C-7), 131.1 (C_q), 135.0 (C_q), 141.3 (C_q), 147.3 (C-1), 191.8 (CHO).

Demethylation with BBr_3; General Procedure:
1 M BBr_3 in CH_2Cl_2 (4 equiv) was added to a solution of methyl ether **1**, **3** or **5** (1 equiv) in CH_2Cl_2 (1 mL per 100 μmol) at 0°C. After stirring for 3 h at 0°C and over night at r.t., the solution was treated with MeOH (2 mL per 100 μmol). The solvent was evaporated and the residue was purified by passing through a short silica gel column to yield crude products **6**, **7** and **8**, respectively.[27]

Clausine E (6):
1 (100.0 mg, 392 μmol) was converted into **6** as described above (column chromatography, petroleum ether/CH_2Cl_2/MeOH 10:4:1); yield: 91.5 mg (97%). Recrystallization from acetone/pentane afforded **6** as colorless crystals; mp 203°C (Lit.[7] 218–220°C).
Spectral data (IR, MS, ^{1}H and ^{13}C NMR) in accordance with those were reported in the literature.[7]

***O*-Demethylmurrayanine (7):**
3 (100 mg, 444 μmol) was converted into **7** as described above (column chromatography, petroleum ether/Et_2O 1:1); yield: 84 mg (90%). Recrystallization from acetone/pentane gave **7** as beige crystals; mp 235°C (Lit.[9] 237–239°C).
Spectral data (IR, MS, ^{1}H NMR) were in accordance with those reported in the literature,[9] except for the ^{13}C NMR data, which were attributed incorrectly in that publication.
^{13}C NMR (acetone-d_6): δ = 108.6 (C-2), 112.7 (C-8), 119.1 (C-4), 120.8 (C-6), 121.3 (C-5), 124.5 (C_q), 125.2 (C_q), 127.2 (C-7), 131.3 (C_q), 134.9 (C_q), 141.4 (C_q), 144.5 (C-1), 191.9 (CHO).

1-Hydroxy-3-methylcarbazole (8):
5 (50.0 mg, 237 μmol) was converted into **8** as described above (column chromatography, petroleum ether/CH_2Cl_2/MeOH 10:2:1); yield: 44.8 mg (96%). Recrystallization from acetone/pentane gave **8** as colorless needles; mp 162°C (Lit.[10] 157–158°C).
IR (KBr): ν = 3360, 3020, 3000, 2940, 2900, 2835, 1615, 1595, 1570 cm^{-1}.
^{1}H NMR (acetone-d_6): δ = 2.43 (s, 3 H, Me), 6.76 (d, 1 H, J = 0.8 Hz, H-2), 7.13 (ddd, 1 H, J = 7.8/7.1/0.9 Hz, H-6), 7.35 (ddd, 1 H, J = 8.1/7.1/1.2 Hz, H-7), 7.42 (s, 1 H, H-4), 7.54 (d, 1 H, J = 8.1 Hz, H-8), 8.02 (d, 1 H, J = 7.8 Hz, H-5), 8.59 (br s, 1 H, OH), 10.05 (br s, 1 H, NH).
^{13}C NMR (acetone-d_6): δ = 21.36 (Me), 112.0 (C-2), 112.3 (C-8), 112.7 (C-4), 119.3 (C-6), 120.9 (C-5), 124.3 (C_q), 126.0 (C-7), 129.6 (C_q), 134.0 (C_q), 141.2 (C_q), 143.5 (C-1).
MS (70 eV): *m/z* (%) = 197 (M^+, 100), 196 (65), 168 (37), 167 (34).

Mukoeic acid (2):
Saponification of **1** (70.0 mg, 274 μmol) was performed according to literature procedures.[3b, 19] Recrystallization from acetone/CH_2Cl_2/pentane gave **2** as colorless crystals; yield: 65.2 mg (99%); mp 238–239°C (Lit.[3b] 242°C).
IR and MS were in accordance with those reported in the literature.[18b]
^{1}H NMR (acetone-d_6): δ = 4.04 (s, 3 H, OMe), 7.23 (t, 1 H, J = 7.6 Hz, H-6), 7.44 (t, 1 H, J = 7.6 Hz, H-7), 7.62 (d, 1 H, J = 7.6 Hz, H-8), 7.66 (s, 1 H, H-2), 8.18 (d, 1 H, J = 7.6 Hz, H-5), 8.55 (s, 1 H, H-4), 10.73 (br s, 1 H, NH).
^{13}C NMR (acetone-d_6): δ = 56.03 (OMe), 107.4 (C-2), 112.6 (C-8), 116.9 (C-4), 120.6 (C-6), 121.3 (C-5), 122.7 (C_q), 124.3 (C_q), 127.0 (C-7), 134.0 (C_q), 141.3 (C_q), 146.3 (C-1), 168.6 (CO_2H).

This work was supported by the Deutsche Forschungsgemeinschaft (SFB 347 'Selektive Reaktionen Metall-aktivierter Moleküle') and the Bundesministerium für Bildung und Forschung (BMBF, project 'Molekulare Wechselwirkungen zwischen Targets und Naturstoffen', FKZ: 0310722). Furthermore, we want to thank Dr. R. Götz for helpful advice.

(1) (a) Chakraborty, D. P. In *Prog. Chem. Org. Nat. Prod.*, Vol. 34; Herz, W.; Grisebach, H.; Kirby, G. W.; Springer: Wien, 1977; p 299.
(b) Bhattacharyya, P.; Chakraborty, D. P. In *Prog. Chem. Org. Nat. Prod*., Vol. 52; Merz, W.; Grisebach, H.; Kirby, G. W.; Tamm, C., Ed.; Springer: Wien, 1987; p 159.
(c) Chakraborty, D. P.; Roy, S. In *Prog. Chem. Org. Nat. Prod.* Vol. 57; Merz, W.; Kirby, G. W.; Steglich, W.; Tamm, C., Ed.; Springer: Wien, 1991; p 71.
(d) Kapil, R. S. In *The Alkaloids*, Vol. 13; Manske, R. H. F., Ed.; Academic: New York, 1971; p 273.
(2) Chakraborty, D. P.; Bhattacharyya, P.; Roy, S.; Bhattacharyya, S. P.; Biswas, A. K. *Phytochemistry* **1978**, *17*, 834.
(3) (a) Chowdhury, B. K.; Chakraborty, D. P. *Chem. Ind. (London)* **1969**, 549.
(b) Chowdhury, B. K.; Chakraborty, D. P. *Phytochemistry* **1971**, *10*, 1967.
(4) Chakraborty, D. P.; Barman, B. K.; Bose, P. K. *Tetrahedron* **1965**, *21*, 681.
(5) Fiebig, M.; Pezzuto, J. M.; Soejarto, D. D.; Kinghorn, A. D. *Phytochemistry* **1985**, *24*, 3041.
(6) Furukawa, H.; Wu, T.-S.; Ohta, T.; Kuoh, C.-S. *Chem. Pharm. Bull.* **1985**, *33*, 4132.
(7) Wu, T.-S.; Huang, S.-C.; Wu, P.-L.; Teng, C.-M. *Phytochemistry* **1996**, *43*, 133.
(8) Ito, C.; Katsuno, S.; Ohta, H.; Omura, M.; Kajiura, I.; Furukawa, H. *Chem. Pharm. Bull.* **1997**, *45*, 48.
(9) Ngadjui, B. T.; Ayafor, J. F.; Sondengam, B. L.; Connolly, J. D. *Phytochemistry* **1989**, *28*, 1517.
(10) Bhattacharyya, P.; Maiti, A. K.; Basu, K.; Chowdhury, B. K. *Phytochemistry* **1994**, *35*, 1085.
(11) Chakraborty, D. P.; Das, K.; Das, B. P.; Chowdhury, B. K. *Trans. Bose Res. Inst., Calcutta* **1975**, *38*, 1; *Chem. Abstr.* **1977**, *86*, 51029z.
(12) Das, K. C.; Chakraborty, D. P.; Bose, P. K. *Experentia* **1965**, *21*, 340.
(13) (a) Sarma, M. *Sci. Cult.* **1976**, *42*, 285; *Chem. Abstr.* **1976**, *85*, 72096p.
(b) Sarma, M. *Indian J. Exp. Biol.* **1980**, *18*, 787; *Chem. Abstr.* **1980**, *93*, 198373k.
(14) Bringmann, G.; Ledermann, A.; Holenz, J.; Kao, M.-T.; Busse, U.; Wu, H. G.; François, G. *Planta Med.* **1998**, *64*, 54.
(15) Bringmann, G.; Ledermann, A.; François, G. *Heterocycles* **1995**, *40*, 293.
(16) (a) Crum, J. D.; Sprague, P. W. *J. Chem. Soc., Chem. Commun.* **1966**, *13*, 417.
(b) Chakraborty, D. P.; Chowdhury, B. K. *J. Org. Chem.* **1968**, *33*, 1265.
(17) Moody, C. J. *Synlett* **1994**, 681; and references cited therein.
(18) (a) Knölker, H.-J.; Wolpert, M. *Tetrahedron Lett.* **1997**, *38*, 533; and references cited therein.
(b) Knölker, H.-J.; Bauermeister, M. *Tetrahedron* **1993**, *49*, 11221.
(19) El-Rayyes, N. R. *J. Prakt. Chem.* **1974**, *316*, 386.
(20) (a) Rizzacasa, M. A.; Sargent, M. V. *Aust. J. Chem.* **1987**, *40*, 1737.
(b) Tilve, S. G.; Tilve, A. S.; Desai, V. G. *Synth. Commun.* **1996**, *26*, 1921.
(21) Owton, W. M.; Gallagher, P. T.; Juan-Montesinos, A. *Synth. Commun.* **1993**, *23*, 2119.
(22) Grehn, L.; Ragnarsson, U. *Angew. Chem.* **1984**, *96*, 291; *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 296.

(23) (a) Bringmann, G.; Götz, R.; Harmsen, S.; Holenz, J.; Walter, R. *Liebigs Ann. Chem.* **1996**, 2045.
(b) Boger, D. L.; McKie, J. A.; Cai, H.; Cacciari, B.; Baraldi, P. G. *J. Org. Chem.* **1996**, *61*, 1710.
(24) Further details of the structure investigation are available on request from the Cambridge Crystallographic Data Centre, on quoting the depository number CCDC-101168, the names of the authors and the journal citation.
(25) Andreoli, P.; Cainelli, G.; Panunzio, M.; Bandini, E.; Martelli, G.; Spunta, G. *J. Org. Chem.* **1991**, *56*, 5984.
(26) Shin, C.-gi; Takahashi, N.; Yonezawa, Y. *Chem. Pharm. Bull.* **1990**, *38*, 2020.
(27) All 1-hydroxycarbazoles were just recrystallized in an analytical scale because all crude products were pure by ^{1}H NMR and recrystallization could only be achieved in low yields.