First total synthesis of the 7-oxygenated carbazole alkaloids clauszoline-K, 3-formyl-7-hydroxycarbazole, clausine M, clausine N and the anti-HIV active siamenol using a highly efficient palladium-catalyzed approach†

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Using a convergent palladium-catalyzed construction of the carbazole framework as the key step we have achieved a short synthesis of the 7-oxygenated carbazole alkaloids clauszoline-K, 3-formyl-7-hydroxycarbazole, clausine C (clauszoline-L), clausine M, clausine N and the anti-HIV active siamenol.

Most of the carbazole alkaloids isolated from terrestrial plants biogenetically derive from 3-methylcarbazole as the common precursor.[1,2] Further metabolic transformation includes oxidation of the methyl group, oxygenation at different positions, and prenylation or geranylation, which could be followed by cyclization. Therefore, carbazole alkaloids have been classified based on their oxygenation pattern.[1,2] Their broad range of useful biological activities induced a strong synthetic interest.[1–3] The iron-mediated oxidative coupling of arylamines and cyclohexadienes represents the most versatile route to carbazole alkaloids.[2,4] Recently, this strategy was applied to the total synthesis of 2,7-dioxygenated carbazoles.[5] Herein, we report a palladium-catalyzed approach to 7-oxygenated carbazole alkaloids including the first total syntheses of clauszoline-K (**1**), 3-formyl-7-hydroxycarbazole (**2**), clausine M (**4**), clausine N (**5**), siamenol (**6**) and a novel route to clausine C (clauszoline-L) (**3**) (Fig. 1).

Clauszoline-K (**1**) and clauszoline-L (**3**) were isolated by Ito *et al.* in 1997 from the stem bark of the Chinese medicinal plant *Clausena excavata*.[6] Wu and his group in Taiwan had already obtained alkaloid **3** a year before from the same natural source and named it clausine C.[7] 3-Formyl-7-hydroxycarbazole (**2**) was isolated by Wu and Furukawa from the root bark of *Murraya euchrestifolia*.[8] In 1999, Wu's group reported the isolation and structural elucidation of clausine M (**4**) and clausine N (**5**) from the root bark of *Clausena excavata*.[9] One year later, Boyd and co-workers found that the organic extract of *Murraya siamensis*, collected in Thailand, showed anti-HIV activity.[10] A bioassay-guided fractionation of the extract led to the isolation of siamenol (**6**), which in the XTT-tetrazolium assay exhibited an HIV inhibitory activity ($EC_{50} = 2.6\ \mu g\ mL^{-1}$).

We have developed an efficient approach to the carbazole framework *via* sequential palladium-catalyzed C–N and C–C bond formation.[11] The Pd(0)-catalyzed Buchwald–Hartwig amination of an aryl halide with the corresponding arylamine to an *N*,*N*-diarylamine represents the first step.[12] The Pd(II)-mediated C–H bond activation of *N*,*N*-diarylamines to furnish the carbazole heterocycle was reported first by Åkermark *et al.*[13] For the synthesis of carbazole-1,4-quinones, we demonstrated first that this process becomes catalytic in palladium by reoxidation of Pd(0) to Pd(II) using cupric acetate.[14] Several alternative palladium-catalyzed carbazole constructions have been reported since.[15] Herein, we describe an optimization of our Pd(II)-catalyzed C–H bond activation followed by oxidative cyclization and its application to the generation of the 9*H*-carbazole skeleton.

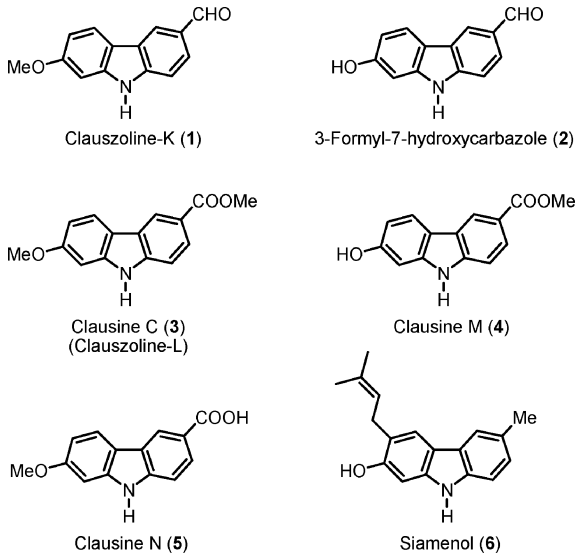

Fig. 1 Naturally occurring 7-oxygenated tricyclic carbazole alkaloids.

The Pd(0)-catalyzed reaction of *m*-anisidine (**7**) and *p*-bromotoluene (**8**) led quantitatively to the diarylamine **9** (Scheme 1).[16] Cyclization of compound **9** using stoichiometric amounts of palladium(II) acetate provided 3-methyl-7-methoxycarbazole (**10**) in only 36% yield as the best result (Table 1).[17] The structure of **10** has been confirmed by its spectroscopic data and X-ray analysis (Fig. 2).‡ We found that the oxidative cyclization with catalytic amounts of Pd(II) gave better yields than its stoichiometric version. Using 10 mol% of Pd(II) and an excess of cupric acetate, carbazole **10** was obtained in 72% yield under optimized conditions (see experimental section). Using smaller amounts of palladium catalyst and extended reaction times the turnover number for the catalytic cycle was even better. We assumed that the reason for the low yield of **10** in the stoichiometric cyclization is oxidation of the carbazole under the reaction conditions. In order to support this hypothesis carbazole **10** (250 mg, 1.18 mmol) was treated with

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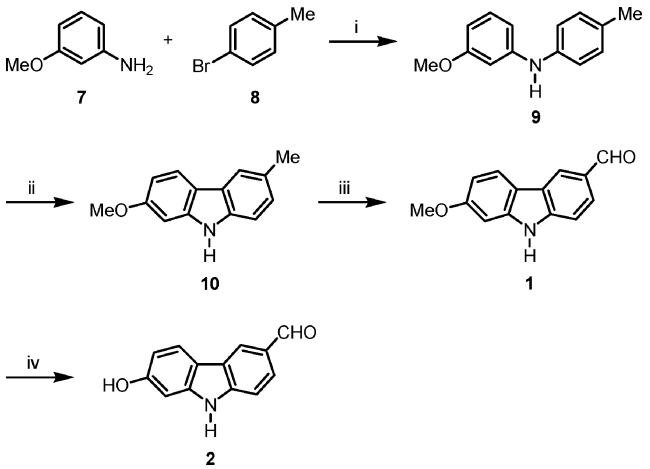
Table 1 Palladium(II)-catalyzed oxidative cyclization of diarylamine **9** to 7-methoxy-3-methylcarbazole (**10**)

$Pd(OAc)_2$	Reaction conditions	Yield (%)	TON[a]
1.2 equiv.	HOAc, reflux, argon, 2 h	36	—
10 mol%	2.5 equiv. $Cu(OAc)_2$, HOAc, reflux, air, 23 h	64	6.4
10 mol%	2.5 equiv. $Cu(OAc)_2$, HOAc, reflux, air, 2 d	72	7.2
5 mol%	2.5 equiv. $Cu(OAc)_2$, HOAc, reflux, air, 40 h	61	12.2
2 mol%	2.5 equiv. $Cu(OAc)_2$, HOAc, reflux, air, 6 d	53	26.5

[a] TON = turnover number.



Scheme 1 Palladium-catalyzed synthesis of clauszoline-K (**1**) and 3-formyl-7-hydroxycarbazole (**2**). *Reagents and conditions*: (i) 6 mol% $Pd(OAc)_2$, 5 mol% *rac*-BINAP, Cs_2CO_3, toluene, reflux, 16 h, 100%; (ii) 10 mol% $Pd(OAc)_2$, 2.5 equiv. $Cu(OAc)_2$, acetic acid, reflux, air, 2 d, 72%; (iii) 4.2 equiv. DDQ, MeOH–H_2O (10 : 1), rt, 40 min, 79%; (iv) 2.5 equiv. BBr_3, CH_2Cl_2, −78 °C to −20 °C, 20 h, 34%.

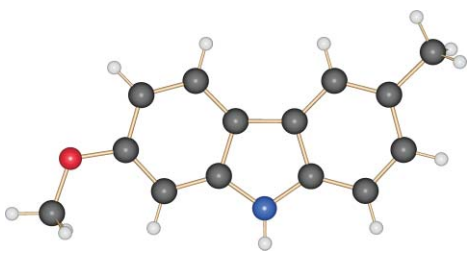


Fig. 2 Molecular structure of 7-methoxy-3-methylcarbazole (**10**).

stoichiometric amounts of $Pd(OAc)_2$ (1.2 equiv.) for just 1 h under the conditions of the oxidative cyclization (acetic acid at reflux); due to decomposition, only 65% of starting material could be reisolated after this time.

Carbazole **10** was used as a relay compound to 7-oxygenated carbazole alkaloids (Scheme 1). Oxidation of **10** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) led to clauszoline-K (**1**), which on cleavage of the methyl ether using boron tribromide afforded 3-formyl-7-hydroxycarbazole (**2**) (Fig. 3).§

Clauszoline-K (**1**) was transformed quantitatively to clausine C (clauszoline-L) (**3**) by treatment with manganese dioxide and potassium cyanide in methanol[18] (Scheme 2; Fig. 4).¶ Our approach provides clausine C (**3**) in four steps (57% overall yield) based on commercial starting materials (**7** and **8**), while

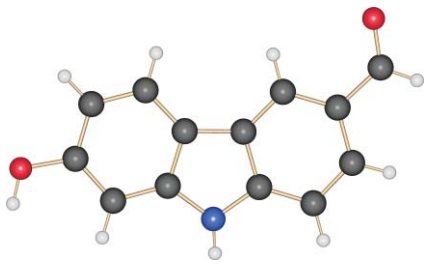
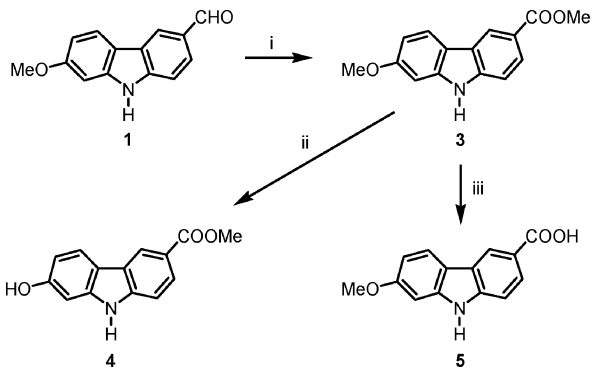


Fig. 3 Molecular structure of 3-formyl-7-hydroxycarbazole (**2**).



Scheme 2 Transformation of clauszoline-K (**1**) into the clausines C (**3**), M (**4**) and N (**5**). *Reagents and conditions*: (i) 26 equiv. MnO_2, 4.8 equiv. KCN, MeOH, rt, 24 h, 100%; (ii) 4.5 equiv. BBr_3, CH_2Cl_2, −78 °C to rt, 90 min, 52%; (iii) KOH, EtOH–H_2O (2.3 : 1), reflux, 1 h, 99%.

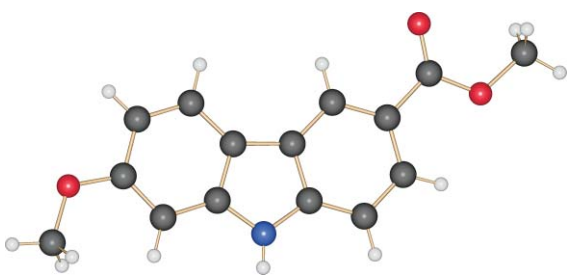


Fig. 4 Molecular structure of clausine C (clauszoline-L) (**3**).

a previously reported route required six steps (40% overall yield) starting from a non-commercial compound.[19] Ether cleavage of clausine C (**3**) gave clausine M (**4**), while saponification of the ester led to clausine N (**5**).

Electrophilic bromination of carbazole **10** afforded the 6-bromocarbazole **11** (Scheme 3; Fig. 5). ‖ Cleavage of the methyl ether to **12** and subsequent nickel-mediated coupling using the

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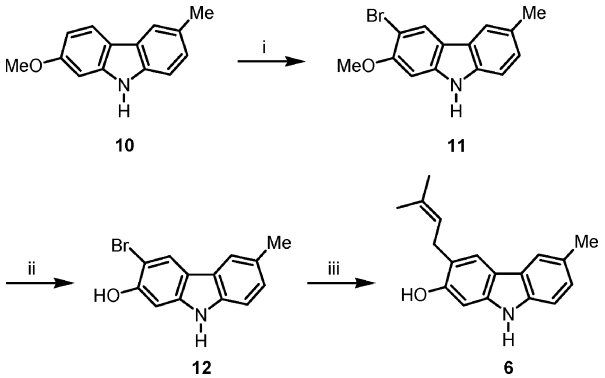

Scheme 3 Synthesis of siamenol (**6**). *Reagents and conditions*: (i) 1.1 equiv. NBS, CCl_4, reflux, 30 min, 100%; (ii) 2 equiv. BBr_3, CH_2Cl_2, −78 °C to rt, 16 h, 100%; (iii) 1. 9.5 equiv. prenyl bromide, 12 equiv. $Ni(COD)_2$, DMF, rt, 30 min (glove box); 2. 1 equiv. **12**, DMF, rt, 6 d, 47%.

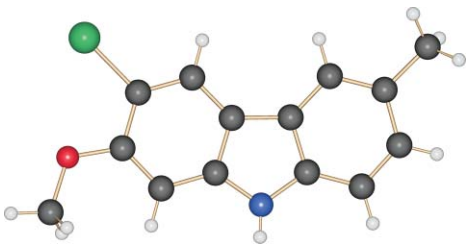

Fig. 5 Molecular structure of the 6-bromocarbazole (**11**).

dimeric π-prenylnickel bromide complex, prepared *in situ* from prenyl bromide and bis(1,5-cyclooctadiene)nickel(0),[20] led directly to siamenol (**6**). However, the purification of the natural product proved to be difficult. Pure siamenol (**6**) was finally obtained by preparative HPLC of the crude product using a Vydac C8 50 mm column (gradient elution with $MeCN/H_2O$, from 30 to 80% MeCN in 25 min). The spectroscopic data of our synthetic compounds **1**–**6** (see Experimental section) are in full agreement with those reported for the corresponding natural products.[6–10]

In conclusion, *via* the palladium(II)-catalyzed oxidative cyclization to 7-methoxy-3-methylcarbazole, we developed a broad access to a series of 7-oxygenated tricyclic carbazole alkaloids including the anti-HIV active siamenol (five steps, 34% overall yield). Our study opens up a simple and direct route to a potential novel class of naturally derived anti-HIV agents.[21]

Experimental

Palladium(II)-catalyzed oxidative cyclization to 7-methoxy-3-methylcarbazole (10)

$Pd(OAc)_2$ (96 mg, 0.43 mmol) and $Cu(OAc)_2$ (1.94 g, 10.68 mmol) were added to a solution of the diarylamine **9** (909 mg, 4.26 mmol) in glacial acetic acid (45 mL) and the mixture was stirred under reflux for 2 d in air. After cooling to rt, the black solution was filtered over a short pad of Celite and silica gel (Et_2O). Evaporation of the solvent and flash chromatography (light petroleum ether–EtOAc, 4 : 1) of the residue on silica gel provided 7-methoxy-3-methylcarbazole (**10**), yield: 651 mg (72%). Colorless crystals; mp: 227–228 °C. UV (MeOH): $\lambda = 237, 259, 303, 321$ (sh) nm. IR (ATR): $\nu = 3397, 2905, 2834, 1610, 1460, 1372, 1338, 1307, 1292, 1225, 1196, 1158, 1133, 1104, 1034, 1017, 937, 884, 804, 731, 633, 587\ cm^{-1}$. ^1H NMR (500 MHz, acetone-d_6): $\delta = 2.50$ (s, 3 H), 3.89 (s, 3 H), 6.81 (dd, $J = 8.5, 2.2$ Hz, 1 H), 7.03 (d, $J = 2.2$ Hz, 1 H), 7.15 (dd, $J = 8.2, 1.3$ Hz, 1 H), 7.36 (d, $J = 8.2$ Hz, 1 H), 7.82 (m, 1 H), 7.96 (d, $J = 8.5$ Hz, 1 H), 10.08 (br s, 1 H). ^{13}C NMR and DEPT (125 MHz, acetone-d_6): $\delta = 21.46$ (CH_3), 55.65 (CH_3), 95.30 (CH), 108.52 (CH), 111.06 (CH), 117.60 (C), 119.95 (CH), 121.44 (CH), 124.39 (C), 126.27 (CH), 128.59 (C), 139.21 (C), 142.62 (C), 159.95 (C). MS (EI): $m/z = 211$ (100) [M^+], 210 (15), 196 (51), 168 (45), 167 (16). HRMS: m/z calc. for $C_{14}H_{13}NO$ [M^+]: 211.0997; found: 211.0985. Anal. calc. for $C_{14}H_{13}NO$: C 79.59, H 6.20, N 6.63; found: C 79.65, H 6.30, N 6.68%.

Clauszoline-K (1)

Light yellow crystals; mp: 183–186 °C. UV (MeOH): $\lambda = 234, 251$ (sh), 287, 292, 295, 326 (sh), 344 (sh) nm. IR (ATR): $\nu = 3286, 2925, 2808, 2737, 1671, 1609, 1571, 1483, 1412, 1328, 1239, 1200, 1161, 1120, 1033, 950, 886, 808, 733, 687, 611\ cm^{-1}$. ^1H NMR (500 MHz, acetone-d_6): $\delta = 3.93$ (s, 3 H), 6.95 (dd, $J = 8.6, 2.2$ Hz, 1 H), 7.15 (d, $J = 2.2$ Hz, 1 H), 7.64 (d, $J = 8.4$ Hz, 1 H), 7.92 (dd, $J = 8.4, 1.6$ Hz, 1 H), 8.16 (d, $J = 8.6$ Hz, 1 H), 8.62 (m, 1 H), 10.11 (s, 1 H), 10.77 (br s, 1 H). ^1H NMR (500 MHz, $CDCl_3$): $\delta = 3.90$ (s, 3 H), 6.92 (dd, $J = 8.5, 2.2$ Hz, 1 H), 6.95 (d, $J = 2.2$ Hz, 1 H), 7.45 (d, $J = 8.4$ Hz, 1 H), 7.89 (dd, $J = 8.4, 1.5$ Hz, 1 H), 7.98 (d, $J = 8.5$ Hz, 1 H), 8.38 (br s, 1 H), 8.49 (m, 1 H), 10.07 (s, 1 H). ^{13}C NMR and DEPT (125 MHz, acetone-d_6): $\delta = 55.79$ (CH_3), 95.93 (CH), 110.09 (CH), 111.75 (CH), 117.52 (C), 122.17 (CH), 123.45 (CH), 124.39 (C), 126.24 (CH), 130.09 (C), 143.10 (C), 144.74 (C), 160.77 (C), 191.97 (CHO). ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): $\delta = 55.67$ (CH_3), 95.19 (CH), 109.40 (CH), 110.58 (CH), 116.90 (C), 121.50 (CH), 122.80 (CH), 123.78 (C), 126.42 (CH), 129.21 (C), 141.38 (C), 143.38 (C), 159.78 (C), 192.03 (CHO). MS (EI): $m/z = 225$ (100) [M^+], 224 (25), 210 (32), 196 (11), 182 (32), 153 (10). HRMS: m/z calc. for $C_{14}H_{11}NO_2$ [M^+]: 225.0790; found: 225.0787. Anal. calc. for $C_{14}H_{11}NO_2$: C 74.65, H 4.92, N 6.22; found: C 74.52, H 4.95, N 6.09%.

3-Formyl-7-hydroxycarbazole (2)

Light yellow crystals; mp > 250 °C (decomp.). UV (MeOH): $\lambda = 231, 252$ (sh), 287 (sh), 294, 327, 345 (sh) nm. IR (ATR): $\nu = 3326, 3231, 2922, 2852, 2752, 1652, 1627, 1602, 1573, 1505, 1488, 1467, 1419, 1376, 1327, 1211, 1175, 1157, 1133, 1008, 956, 895, 806, 775, 733, 677, 662, 623\ cm^{-1}$. ^1H NMR (500 MHz, acetone-d_6): $\delta = 6.88$ (dd, $J = 8.4, 2.0$ Hz, 1 H), 7.04 (d, $J = 2.0$ Hz, 1 H), 7.59 (d, $J = 8.4$ Hz, 1 H), 7.89 (dd, $J = 8.4, 1.5$ Hz, 1 H), 8.08 (d, $J = 8.4$ Hz, 1 H), 8.57 (m, 1 H), 8.59 (br s, 1 H), 10.09 (s, 1 H), 10.66 (br s, 1 H). ^{13}C NMR and DEPT (125 MHz, acetone-d_6): $\delta = 97.96$ (CH), 110.59 (CH), 111.57 (CH), 116.89 (C), 122.21 (CH), 123.10 (CH), 124.64 (C), 126.12 (CH), 129.98 (C), 143.35 (C), 144.72 (C), 158.30 (C), 191.95 (CHO). MS (EI): $m/z = 211$ (100) [M^+], 210 (54), 199 (11), 182 (35), 154 (9). HRMS: m/z calc. for $C_{13}H_9NO_2$ [M^+]: 211.0633; found: 211.0620. Anal. calc. for $C_{13}H_9NO_2$: C 73.92, H 4.29, N 6.63; found: C 74.22, H 4.46, N 6.32%.

Clausine C (clauszoline-L) (3)

Light yellow crystals; mp: 195 °C. UV (MeOH): $\lambda = 217, 238, 248, 282, 320$ nm. IR (ATR): $\nu = 3273, 2996, 2924, 2836, 1695, 1629, 1602, 1581, 1509, 1489, 1467, 1437, 1403, 1324, 1292, 1257, 1191, 1159, 1135, 1096, 1031, 976, 949, 904, 830, 815, 754, 726, 605$ cm^{-1}. ^{1}H NMR (500 MHz, acetone-d_6): $\delta = 3.92$ (s, 3 H), 3.94 (s, 3 H), 6.93 (dd, $J = 8.6$, 2.2 Hz, 1 H), 7.13 (d, $J = 2.2$ Hz, 1 H), 7.55 (d, $J = 8.5$ Hz, 1 H), 8.04 (dd, $J = 8.5$, 1.6 Hz, 1 H), 8.14 (d, $J = 8.6$ Hz, 1 H), 8.73 (m, 1 H), 10.64 (br s, 1 H). ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 3.89$ (s, 3 H), 3.96 (s, 3 H), 6.89 (dd, $J = 8.5$, 2.2 Hz, 1 H), 6.91 (d, $J = 2.2$ Hz, 1 H), 7.36 (d, $J = 8.5$ Hz, 1 H), 7.96 (d, $J = 8.5$ Hz, 1 H), 8.05 (dd, $J = 8.5$, 1.6 Hz, 1 H), 8.27 (br s, 1 H), 8.69 (m, 1 H). ^{13}C NMR and DEPT (125 MHz, acetone-d_6): $\delta = 51.89$ (CH_3), 55.75 (CH_3), 95.75 (CH), 109.75 (CH), 111.01 (CH), 117.51 (C), 121.78 (C), 122.02 (CH), 122.16 (CH), 123.98 (C), 126.56 (CH), 142.99 (C), 143.80 (C), 160.60 (C), 167.97 (C=O). ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): $\delta = 51.94$ (CH_3), 55.63 (CH_3), 95.01 (CH), 108.97 (CH), 109.83 (CH), 117.04 (C), 121.36 (CH), 121.43 (C), 121.89 (CH), 123.28 (C), 126.27 (CH), 141.27 (C), 142.33 (C), 159.50 (C), 167.97 (C=O). MS (EI): $m/z = 255$ (100) [M$^+$], 240 (23), 225 (20), 224 (44), 213 (23), 212 (21), 196 (16), 183 (9), 181 (9). HRMS: m/z calc. for $C_{15}H_{13}NO_3$ [M$^+$]: 255.0895; found: 255.0907. Anal. calc. for $C_{15}H_{13}NO_3$: C 70.58, H 5.13, N 5.49; found: C 70.70, H 5.50, N 5.34%.

Clausine M (4)

Light yellow crystals; mp: 220–222 °C. UV (MeOH): $\lambda = 219$ (sh), 239 (sh), 247, 283, 309 (sh), 318 (sh) nm. IR (ATR): $\nu = 3369, 2958, 2929, 2860, 1733, 1610, 1462, 1380, 1269, 1171, 1135, 1074, 769, 743, 604$ cm^{-1}. ^{1}H NMR (500 MHz, acetone-d_6): $\delta = 3.94$ (s, 3 H), 6.87 (dd, $J = 8.4$, 2.1 Hz, 1 H), 7.02 (d, $J = 2.1$ Hz, 1 H), 7.52 (d, $J = 8.5$ Hz, 1 H), 8.01 (dd, $J = 8.5$, 1.6 Hz, 1 H), 8.07 (d, $J = 8.4$ Hz, 1 H), 8.59 (s, 1 H), 8.69 (m, 1 H), 10.55 (br s, 1 H). ^{13}C NMR and DEPT (125 MHz, acetone-d_6): $\delta = 51.87$ (CH_3), 97.79 (CH), 110.30 (CH), 110.85 (CH), 116.90 (C), 121.64 (C), 121.90 (CH), 122.04 (CH), 124.23 (C), 126.36 (CH), 143.27 (C), 143.79 (C), 158.14 (C), 168.03 (C=O). MS (EI): $m/z = 241$ (100) [M$^+$], 210 (50), 182 (22), 153 (6). HRMS: m/z calc. for $C_{14}H_{11}NO_3$ [M$^+$]: 241.0739; found: 241.0765.

Clausine N (5)

Light yellow crystals; mp > 264 °C (decomp.). UV (MeOH): $\lambda = 237$ (sh), 247, 278, 307 (sh), 319 nm. IR (ATR): $\nu = 3385, 2921, 2851, 1666, 1606, 1579, 1505, 1485, 1464, 1436, 1413, 1341, 1320, 1294, 1262, 1188, 1151, 1123, 1096, 1028, 942, 897, 813, 765, 752, 723, 683, 620, 591$ cm^{-1}. ^{1}H NMR (500 MHz, acetone-d_6): $\delta = 3.92$ (s, 3 H), 6.93 (dd, $J = 8.6$, 2.2 Hz, 1 H), 7.13 (d, $J = 2.2$ Hz, 1 H), 7.56 (d, $J = 8.5$ Hz, 1 H), 8.07 (dd, $J = 8.5$, 1.6 Hz, 1 H), 8.30 (d, $J = 8.6$ Hz, 1 H), 8.77 (d, $J = 1.6$ Hz, 1 H). ^{13}C NMR and DEPT (125 MHz, acetone-d_6): $\delta = 55.75$ (CH_3), 95.68 (CH), 109.71 (CH), 110.89 (CH), 117.51 (C), 121.92 (C), 122.00 (CH), 122.50 (CH), 123.92 (C), 126.89 (CH), 142.84 (C), 143.68 (C), 160.55 (C), 168.44 (C=O). MS (EI): $m/z = 241$ (76) [M$^+$], 226 (28), 211 (8), 198 (27), 111 (44), 97 (63), 71 (69), 57 (100). HRMS: m/z calc. for $C_{14}H_{11}NO_3$ [M$^+$]: 241.0739; found: 241.0748. Anal. calc. for $C_{14}H_{11}NO_3$: C 69.70, H 4.60, N 5.81; found: C 69.84, H 4.62, N 5.84%.

Siamenol (6)

Colorless crystals; mp: 132–133 °C. UV (MeOH): $\lambda = 262, 308, 326$ (sh), 338 (sh) nm. IR (ATR): $\nu = 3538, 3388, 2967, 2909, 2853, 1638, 1618, 1584, 1494, 1461, 1375, 1337, 1302, 1255, 1229, 1148, 1113, 1092, 1013, 882, 847, 828, 798, 734$ cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.81$ (s, 3 H), 1.84 (s, 3 H), 2.50 (s, 3 H), 3.50 (d, $J = 7.1$ Hz, 2 H), 5.29 (br s, 1 H), 5.40 (m, 1 H), 6.77 (s, 1 H), 7.13 (d, $J = 8.1$ Hz, 1 H), 7.21 (d, $J = 8.1$ Hz, 1 H), 7.69 (br s, 1 H), 7.72 (s, 1 H), 7.75 (s, 1 H). ^{1}H NMR (500 MHz, MeOH-d_4): $\delta = 1.84$ (s, 6 H), 2.52 (s, 3 H), 3.48 (d, $J = 7.4$ Hz, 2 H), 5.50 (m, 1 H), 6.87 (s, 1 H), 7.11 (d, $J = 8.1$ Hz, 1 H), 7.26 (d, $J = 8.1$ Hz, 1 H), 7.68 (s, 1 H), 7.71 (s, 1 H). ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): $\delta = 17.91$ (CH_3), 21.42 (CH_3), 25.86 (CH_3), 30.42 (CH_2), 97.24 (CH), 109.92 (CH), 117.15 (C), 119.41 (CH), 120.83 (CH), 122.59 (CH), 123.67 (C), 125.67 (C), 125.67 (CH), 128.59 (C), 134.71 (C), 137.72 (C), 139.86 (C), 153.64 (C). ^{13}C NMR and DEPT (125 MHz, MeOH-d_4): $\delta = 17.88$ (CH_3), 21.54 (CH_3), 26.03 (CH_3), 29.69 (CH_2), 97.08 (CH), 110.84 (CH), 117.25 (C), 119.65 (CH), 120.87 (CH), 121.63 (C), 125.01 (C), 125.11 (CH), 125.84 (CH), 128.47 (C), 132.24 (C), 139.60 (C), 141.57 (C), 155.31 (C). MS (EI): $m/z = 265$ (77) [M$^+$], 250 (25), 248 (26), 210 (100), 209 (38), 197 (69), 196 (48), 180 (12), 167 (12). HRMS: m/z calc. for $C_{18}H_{19}NO$ [M$^+$]: 265.1467; found: 265.1472.

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Notes and references

‡ Crystal data for **10**: $C_{14}H_{13}NO$, $M = 211.25$, monoclinic, space group: $P2_1/c$, $a = 22.924(3)$, $b = 5.787(1)$, $c = 8.020(1)$ Å, $\beta = 96.98(3)°$, $V = 1056.1(4)$ Å^3, $Z = 4$, $D_c = 1.329$ g cm^{-3}, $\mu = 0.084$ mm^{-1}, $T = 198(2)$ K, $\lambda = 0.71073$ Å, θ range: 3.58–25.40°, 13 562 reflections measured, 1915 independent ($R_{int} = 0.0280$), 151 parameters. The structure was solved by direct methods and refined by full-matrix least-squares on F^2; final R indices for 1618 observed reflections [$I > 2\sigma(I)$]: $R_1 = 0.0457$, $wR_2 = 0.1179$; maximal residual electron density: 0.674 e Å^{-3}. CCDC reference number 609679. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b607792g.

§ Crystal data for **2**: $C_{13}H_9NO_2$, $M = 211.21$, monoclinic, space group: $P2_1/n$, $a = 7.381(1)$, $b = 11.493(1)$, $c = 11.058(1)$ Å, $\beta = 95.02(1)°$, $V = 934.45(17)$ Å^3, $Z = 4$, $D_c = 1.501$ g cm^{-3}, $\mu = 0.103$ mm^{-1}, $T = 198(2)$ K, $\lambda = 0.71073$ Å, θ range: 3.29–30.00°, 25 734 reflections measured, 2704 independent ($R_{int} = 0.0442$), 153 parameters. The structure was solved by direct methods and refined by full-matrix least-squares on F^2; final R indices for 2059 observed reflections [$I > 2\sigma(I)$]: $R_1 = 0.0414$, $wR_2 = 0.1062$; maximal residual electron density: 0.364 e Å^{-3}. CCDC reference number 609677. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b607792g.

¶ Crystal data for **3**: $C_{15}H_{13}NO_3$, $M = 255.26$, triclinic, space group: $P1$, $a = 8.118(3)$, $b = 9.020(2)$, $c = 9.143(3)$ Å, $a = 101.10(2)$, $\beta = 102.27(3)$, $\gamma = 104.33(3)°$, $V = 612.2(4)$ Å^3, $Z = 2$, $D_c = 1.385$ g cm^{-3}, $\mu = 0.097$ mm^{-1}, $T = 198(2)$ K, $\lambda = 0.71073$ Å, θ range: 3.03–25.40°, 14687 reflections measured, 2242 independent ($R_{int} = 0.0536$), 178 parameters. The structure was solved by direct methods and refined by full-matrix least-squares on F^2; final R indices for 1792 observed reflections [$I > 2\sigma(I)$]: $R_1 = 0.0450$, $wR_2 = 0.1141$; maximal residual electron density: 0.169 e Å^{-3}. CCDC reference number 609678. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b607792g.

‖ Crystal data for **11**: $C_{14}H_{12}BrNO$, $M = 290.16$, monoclinic, space group: $P2_1$, $a = 6.642(1)$, $b = 7.761(1)$, $c = 11.984(5)$ Å, $\beta = 105.13(3)°$, $V = 596.3(3)$ Å^3, $Z = 2$, $D_c = 1.616$ g cm^{-3}, $\mu = 3.428$ mm^{-1}, $T = 198(2)$ K,

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$\lambda = 0.71073$ Å, θ range: 3.16–30.00°, 16713 reflections measured, 3380 independent ($R_{int} = 0.0289$), 160 parameters. The structure was solved by direct methods and refined by full-matrix least-squares on F^2; final R indices for 3122 observed reflections [$I > 2\sigma(I)$]: $R_1 = 0.0220$, $wR_2 = 0.0440$; absolute structure (Flack parameter): $\chi = -0.005(6)$, maximal residual electron density: 0.230 e Å^{-3}. CCDC reference number 609680. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b607792g.

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