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Synthesis of the Reduced A-Unit (CI) of the Antitumor Antibiotic CC-1065

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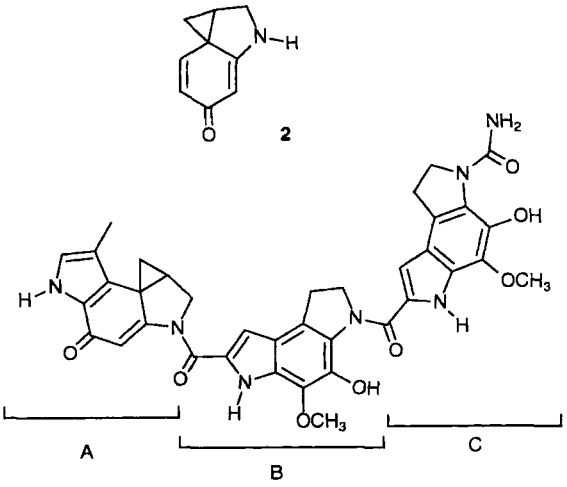
The synthesis of the reduced A-unit **2** (CI) of CC-1065 (**1**) using a metal-mediated cyclisation is described. Reaction of *N*-allyl-*N*-benzylaniline **4b** and zirconocene(methyl) chloride with *tert*-BuLi leads via a zirconocene-stabilized benzyne complex **5** to the 3,4-difunctionalized indoline derivative **7**, which was converted in five steps into **2**.

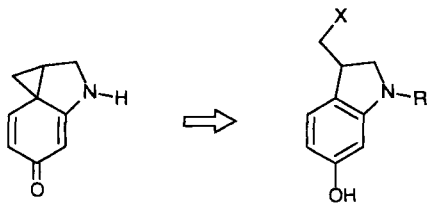
The antitumor antibiotic (+)-CC-1065 (**1**), first isolated in 1978 from *Streptomyces zelensis*[2], is one of the most active cytotoxic compounds in vitro as well as in vivo. It consists of three substituted pyrrolo[3,2-*c*]indole moieties, of which two are identical, whereas the third contains the unusual spirocyclopropyl-cyclohexadienone moiety **2**. CC-1065 (**1**) is an alkylating agent, which shows its highest activity against cancer cells during mitosis. However, it cannot be used as a drug because of a delayed liver toxicity[3].

On treatment with alkali, CC-1065 (**1**) is cleaved into two fragments, a cyclopropa-pyrrolo-indole (A-unit), called CPI, and a dimeric pyrroloindole (B/C-unit). Biological studies have shown, that it is the A-unit which alkylates DNA reversibly and sequence-selectively the B-DNA minor groove sites [5′d(A/GNTTA)-3′ and 5′d(AAAAA)-3′][4]. The dimeric pyrrolo-indole (B/C-unit) is responsible for the high bindung specifity to the DNA and known as PDE-I dimer, because of its relationship to the naturally occurring phosphodiesterase inhibitors PDE-I and PDE-II. The synthesis of CC-1065 and related analogues has been the subject of several recent publications[5].



CC-1065 1

In the course of our investigations of the design of highly selective anticancer agents[1,6], we have developed functionalized nontoxic subunits of CC-1065, which may be toxified selectively in the cancer tissue[7]. In this paper we describe a new synthesis of 1,1a,2,3-tetrahydro-5*H*-cycloprop[*c*]indol-5-one (**2**) (CI)[5i] as a reduced A-unit of CC-1065 from 5-benzyloxy-2-bromophenylamine (**3**)[5i] via a zirconocene-stabilized benzyne complex **5**[8]. We have used the procedure of Buchwald et al.[9]. The final step in the formation of the toxic cyclopropane **2** is an intramolecular *para*-alkylation (Winstein alkylation)[10].



2 X = leaving group

Results

Reductive amination[11] of **3** with benzaldehyde, sodium cyanoborohydride and zinc(II) chloride followed by deprotonation and *N*-allylation with allyl bromide affords **4b** in 86% yield. The following zirconocene-mediated cyclisation to the zirconacycle **6** and the conversion to the 3,4-disubstituted indoline **7** proceeds as a sequential transformation[12]. Thus, treatment of a mixture of the allylaniline **4b** and zirconocene(methyl) chloride[13] with *tert*-BuLi afford the zirconacycle **6** via the intermediate benzyne complex **5**. **6** can

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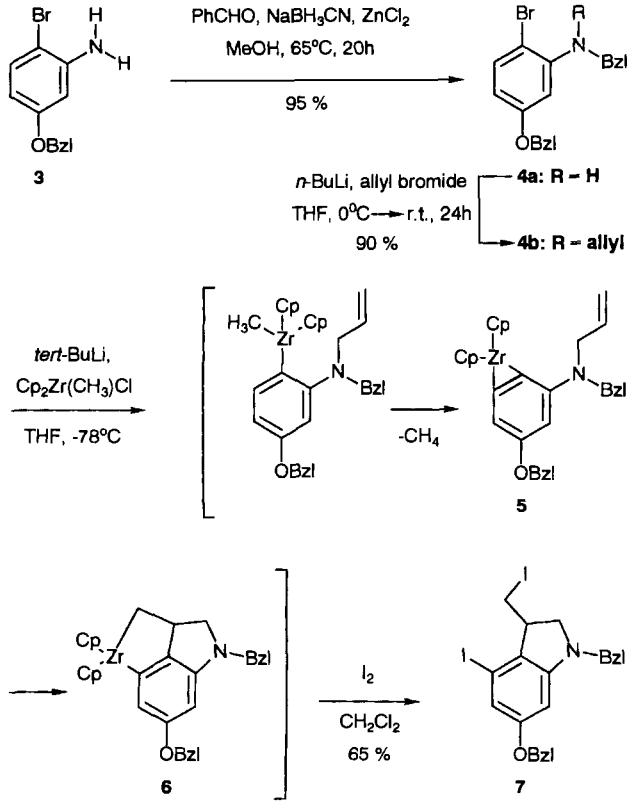
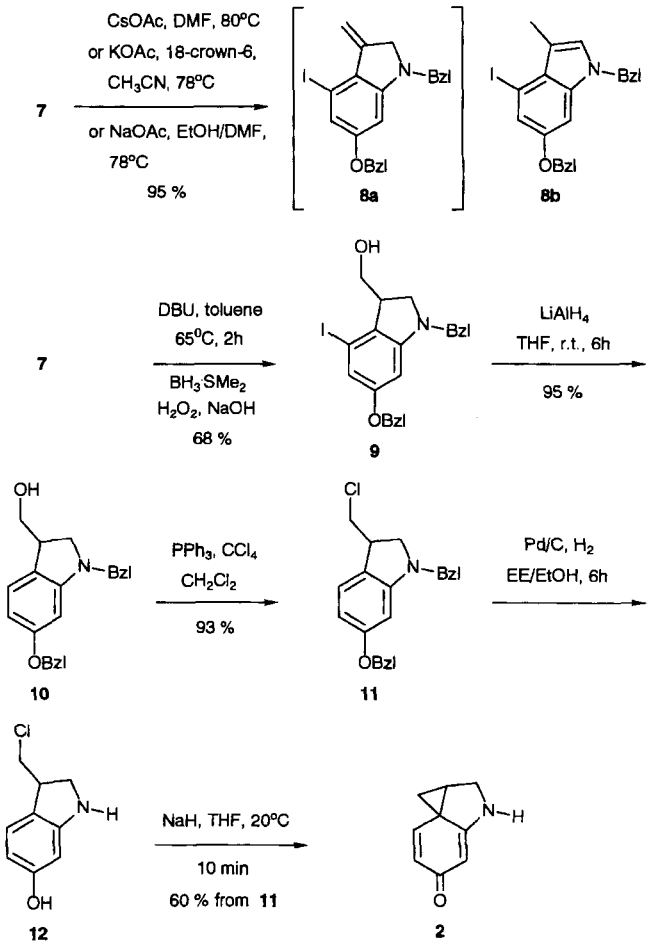
be treated without isolation with iodine to give the 3,4-diiodoindoline **7** in 65% yield.



For the synthesis of **2** it was necessary to remove the iodine at C-4 of the benzene ring in **7**. Since there is no known procedure which allows this transformation selectively in the presence of an aliphatic iodide, the iodomethyl group in **7** had to be transformed first into another stable functional group such as an acetate. Surprisingly, all attempts to substitute acetate for the iodine at C-3 failed. Thus, by using cesium acetate in DMF[14], potassium acetate in acetonitrile in the presence of 18-crown-6[15] and sodium acetate in dimethyl formamide/ethanol[5q], we obtained the 3-methylindole **8b** as the only product. As an intermediate, the methyleneindoline **8a** can be assumed, which isomerises to the indole **8b** under the reaction conditions.

However, dehydrohalogenation without isomerisation could be achieved with DBU in toluene to give the methyleneindoline **8a**; this was transformed without isolation to the hydroxymethylindoline **9** in 68% yield by hydroboration with $BH_3 \cdot SMe_2$ followed by treatment with basic hydrogen peroxide. Deiodination of **9** with $LiAlH_4$[16] in tetrahydrofuran afforded the indoline **10** nearly quantitively, which was converted into the the primary chloride **11** in 93% yield by an Appel reaction[17]. Catalytic hydrogenolysis in tetrahydrofuran provided the debenzylated phenol **12** without affecting the primary chloride. After filtering off the catalyst and removal of the solvent, **12** was obtained in a rather pure form and it should be noted that purification by chromatography is difficult if not impossible due to the instability of **12**. As a solid, however, phenol **12** is stable for some time at −20°C but in solution at room temperature decomposition takes place within several hours. Therefore, crude **12** was used immediately for the final Ar-3′ cyclisation[10]. According to a known procedure, the Winstein alkylation to the spirocyclopropyl-cyclohexadienone **2** (CI)[5l] could be achieved with sodium hydride in THF in 60% yield based on **11**. A short reaction time is essential because of the high instability of **2** (CI), which is the minimum pharmacophore of **1**.



The constitutions of the new compounds **4a**, **4b**, **7**, **8b**, **9**, **10**, **11** and **12** were determined by ^1H- and ^{13}C-NMR spectroscopy. For the two hydrogens of the iodomethyl group at C-3 in **7** a doublet of a doublet at $\delta = 3.16$ with $J = 10.5$ and 9.5 Hz and a doublet of doublet of doublet at $\delta = 3.58$ with $J = 9.5$, 3.0 and 1.0 Hz are found in the ^1H-NMR spectrum. 2-H_2 resonate at $\delta = 3.48$ as a multiplet and the two aromatic hydrogens at $\delta = 6.08$ and 6.63 as singlets.

The ^1H-NMR spectra of **9**, **10** and **11** are quite similar; for the two hydrogenatoms of the hydroxymethyl group and the chloromethyl group signals at $\delta = 3.45$ and 3.59 for **9**, at $\delta = 3.28$ and 3.48 for **10** and at $\delta = 3.32$ and 3.53 for **11** appear. The three hydrogenatoms 4-H, 5-H and 7-H on the benzene ring in **10** and **11** resonate at $\delta = 6.19$ as a doublet

with J = 2.1 Hz, at δ = 6.28 as a doublet of a doublet with J = 7.0 Hz and 2.1 Hz, and at δ = 7.00 as a doublet with J = 7.0 Hz. All NMR spectra are in agreement with the proposed structures.

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Experimental

^{1}H NMR and ^{13}C NMR: Varian XL-200, Bruker AMX-300 and Varian XL-500; multiplicities were determined with APT pulse sequence. – MS: Varian MAT 311A, high resolution: Varian MAT 731. – IR: Bruker IFS 25. – Melting points: Kofler hot stage or Mettler FP 61. – Elemental analyses were carried out in the analytical laboratory of the university. – All solvents were distilled prior to use. Reagents and materials were obtained from commercial suppliers and were used without further purification. – All reactions were carried out under a positive pressure of nitrogen and monitored by TLC (Macherey, Nagel & Co.; Alugram SIL G/UV_{254}). Products were isolated by column chromatography on silica gel (Silica Woelm 32-63, active, Woelm Pharma, Eschwege). – All chiral compounds were obtained as racemic mixtures.

N-Benzyl-5-benzyloxy-2-bromoaniline (**4a**): A stirred mixture of **3** (6.40 g, 23.0 mmol), zinc(II) chloride (3.76 g, 27.6 mmol) and benzaldehyde (2.93 g, 27.6 mmol) in methanol (100 ml) was treated with sodium cyanoborohydride (1.73 g, 27.6 mmol) and warmed at reflux under nitrogen for 2 h. The cooled reaction mixture was diluted with 1 N sodium hydroxide (100 ml) and extracted with ether (3 × 50 ml). The combined ether layers were washed with water (2 × 50 ml), dried ($MgSO_4$), and concentrated in vacuo. Flash chromatography (300 g of SiO_2, *t*BuOMe/petroleum ether, 1:50) of the residue provided **4a** (8.05 g, 21.9 mmol, 95%) as a colourless oil. – R_f = 0.25. – IR (film): $\tilde{\nu}$ = 3290 cm^{-1} (NH), 3095, 3030 (CH), 600 (CBr). – ^{1}H NMR ($CDCl_3$): δ = 4.38 (s, 2H, $PhCH_2N$), 4.70 (s, br., 1H, NH), 4.96 (s, 2H, $PhCH_2O$), 6.24 (dd, J ≈ 8.2, 3.0 Hz, 1H, 4-H), 6.27 (d, J = 3.0 Hz, 1H, 6-H), 7.25 (d, J ≈ 8.2 Hz, 1H, 3-H), 7.30 (m, 10H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 47.93 ($PhCH_2N$), 70.01 ($PhCH_2O$), 99.27 (C-6), 101.1 (C-2), 103.8 (C-4), 127.2, 127.3, 127.5, 128.1 (CH-Ph), 132.4 (C-3), 136.8 (*i*-C), 138.4 (*i*-C), 145.5 (C-1), 159.4 (C-5). – MS (70 eV), *m/z* (%): 287 (50) [M$^+$ – Br], 91 (100) [$C_7H_7^+$]. – $C_{20}H_{18}BrNO$ (368.2): calcd. C 65.23, H 4.92; found C 65.31, H 5.02.

N-Allyl-N-benzyl-5-benzyloxy-2-bromoaniline (**4b**): To a solution of **4a** (7.36 g, 20 mmol) in dry tetrahydrofuran (100 ml) were added at −78°C *n*-butyllithium (20 mmol) and after stirring for 15 min allyl bromide (2.54 g, 21 mmol). The reaction mixture was allowed to warm to room temperature and was stirred for an additional 1 h at 20°C. The solvent was then removed in vacuo and the residue dissolved in ether (100 ml). The organic layer was washed with water (3 × 50 ml), dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (300 g SiO_2, ethyl acetate/petroleum ether, 1:60) of the residue afforded **4b** (7.35 g, 18 mmol, 90%) as a colourless oil. – R_f = 0.32. – IR (film): $\tilde{\nu}$ = 3095 cm^{-1}, 3025 (CH), 1590 (C=C). – ^{1}H NMR ($CDCl_3$): δ = 3.60 (d, J = 6.0 Hz, 2H, $NCH_2CH{=}CH_2$), 4.20 (s, 2H, $PhCH_2N$), 4.96 (s, 2H, $PhCH_2O$), 5.08, 5.15 (2 m, 2H, $NCH_2CH{=}CH_2$), 5.82 (ddt, J = 16.5, 9.5, 6.0 Hz, 1H, $NCH_2CH{=}CH_2$), 6.56 (dd, J = 8.9, 2.9 Hz, 1H, 4-H), 6.68 (d, J = 2.9 Hz, 1H, 6-H), 7.15–7.40 (m, 10H, aromatic H), 7.43 (d, J = 8.9 Hz, 1H, 3-H). – ^{13}C NMR ($CDCl_3$): δ = 55.19, 56.19 ($PhCH_2N$, $NCH_2CH{=}CH_2$), 70.20 ($PhCH_2O$), 110.6 (C-6), 111.7 (C-4), 112.0 (C-2), 117.8 ($NCH_2CH{=}CH_2$), 126.9, 127.5, 128.0, 128.6 (CH-Ph), 133.7, 134.4 ($NCH_2CH{=}CH_2$, C-3), 136.6 (*i*-C), 138.1 (*i*-C), 149.9 (C-1), 158.3 (C-5). – MS (70 eV), *m/z* (%): 409 (8) [M$^+$], 91 (100) [$C_7H_7^+$]. – $C_{23}H_{22}BrNO$ (408.3): calcd. C 67.65, H 5.42; found C 67.49, H 5.54.

(3RS)-1-Benzyl-6-benzyloxy-2,3-dihydro-4-iodo-3-iodomethyl-1H-indole (**7**): To a mixture of tetrahydrofuran (30 ml), zirconocene(methyl) chloride (1.56 g, 5.16 mmol) and **4b** (2.11 g, 5.16 mmol) in a flame-dried Schlenk flask was added at −78°C *tert*-butyllithium (10.3 mmol). After stirring for 15 min at −78°C, the mixture was allowed to warm to room temperature and stirred for additional 2 h. The solvent was removed in vacuo and the residue was dissolved in dry dichloromethane (30 ml). To this solution, I_2 (3.35 g, 13.2 mmol) in dichloromethane was added and stirring was continued at 0°C for 4 h. The solvent was then removed in vacuo, and the residue dissolved in ether (50 ml). The organic layer was washed with saturated aqueous sodium sulfite (3 × 50 ml) and water (3 × 50 ml), dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (100 g SiO_2, ethyl acetate/petroleum ether, 1:60) of the residue yielded **7** (1.95 g, 3.35 mmol, 65%) as a pale yellow solid. – R_f = 0.21. – M.p. 52°C (*t*BuOMe). – IR (KBr): $\tilde{\nu}$ = 3085 cm^{-1}, 3028 (CH), 1625 (C=C), 1085 (CI). – ^{1}H NMR ($CDCl_3$): δ = 3.16 (dd, J = 10.5, 9.5 Hz, 1H, 3-CH_b), 3.43 (m, 1*H*, 3-*H*), 3.48 (m, 2H, 2-H_2), 3.58 (ddd, J = 9.5, 3.0, 1.0 Hz, 1H, 3-CH_a), 4.17, 4.29 (2 d, J = 15.9 Hz, 2H, $PhCH_2N$), 4.98 (s, 2H, $PhCH_2O$), 6.08 (s, 1H, 7-H), 6.63 (s, 1H, 5-H), 7.25–7.41 (m, 10H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 9.584 (3-CH_2), 46.76 (C-3), 52.11 ($PhCH_2N$), 58.51 (C-2), 70.27 ($PhCH_2O$), 92.54 (C-4), 95.37 (C-7), 112.0 (C-5), 127.4 (C-3a), 127.5, 128.0, 128.6 (CH-Ph), 136.5 (*i*-C), 137.0 (*i*-C), 152.6 (C-7a), 160.6 (C-6). – MS (70 eV), *m/z* (%): 581 (10) [M$^+$], 454 (10) [M$^+$ – I], 91 (100) [$C_7H_7^+$]. – $C_{23}H_{21}I_2NO$ (581.2): calcd. C 47.53, H 3.63; found C 47.79, H 3.47.

1-Benzyl-6-benzyloxy-4-iodo-3-methyl-1H-indole (**8b**): A mixture of **7** (290 mg, 0.5 mmol) and cesium acetate (115 mg, 0.6 mmol) in dry *N,N*-dimethylformamide (2 ml) was warmed at 80°C for 2 h. The cooled reaction mixture was diluted with water (5 ml) and extracted with ether (3 × 10 ml). The combined organic extracts were dried ($MgSO_4$), the solvent was evaporated in vacuo and the residue chromatographed (20 g SiO_2, ethyl acetate/petroleum ether, 1:20) to give **8b** (215 mg, 0.48 mmol, 95%) as a colourless oil. – R_f = 0.25. – ^{1}H NMR ($CDCl_3$): δ = 2.49 (s, 3H, 3-CH_3), 5.00 (s, 2H, $PhOCH_2$), 5.13 (s, 2H, $PhCH_2N$), 6.72 (d, J = 2.1 Hz, 1H, 7-H), 6.83 (d, J = 2.1 Hz, 1H, 5-H), 7.22–7.42 (m, 11H, aromatic H, 2-H). – ^{13}C NMR ($CDCl_3$): δ = 12.39 (3-CH_3), 49.71 ($PhCH_2N$), 70.71 ($PhCH_2O$), 85.45 (C-4), 95.26 (C-7), 112.4 (C-3, C-5), 120.5 (C-2), 124.4 (C-3a), 126.6, 127.1, 127.5, 127.6, 127.9, 128.5 (CH-Ph), 136.8 (*i*-C), 137.0 (*i*-C, C-7a), 155.0 (C-6). – MS (70 eV), *m/z* (%): 453 (35) [M$^+$], 362 (20) [M$^+$ – $C_7H_7^+$], 91 (100) [$C_7H_7^+$]. – $C_{23}H_{20}INO$ (453.2): calcd. C 60.94, H 4.44; found C 61.03, H 4.63.

(3RS)-1-Benzyl-6-benzyloxy-2,3-dihydro-3-hydroxymethyl-4-iodo-1H-indole (**9**): A stirred solution of **7** (1.47 g, 3.00 mmol) in toluene (20 ml) was charged with DBU (608 mg, 4.00 mmol) and heated for 1 h at 60°C. After removal of the solvent, the residue was dissolved in tetrahydrofuran (40 ml), the obtained solution cooled to 0°C and treated with borane–methyl sulfide (600 µl, 6.00 mmol). The reaction mixture was then stirred for 3 h at room temperature, cooled again to 0°C and treated successively with water (3.00 ml), 2 N aqueous sodium hydroxide (3.00 ml) and 30% aqueous hydrogen peroxide (1.90 ml). After warming up to 45°C for 30 min, the mixture was stirred for 16 h at 22°C, then diluted with saturated sodium chloride (30 ml), extracted with ether (50 ml) and the extract was washed with water (2 × 30 ml). The organic layer was dried ($MgSO_4$), concentrated in vacuo and the residue was

purified by column chromatography (100 g SiO_2, ethyl acetate/petroleum ether, 1:4) to yield **9** (961 mg, 2.04 mmol, 68%) as a colourless solid. – R_f = 0.24. – M.p. 106°C (ethyl acetate). – IR (KBr): $\tilde{\nu}$ = 3434 cm^{-1} (OH), 2924 (CH), 1084 (CI). – ^1H NMR ($CDCl_3$): δ = 1.43 (s, 1H, OH), 3.25 (m, 1H, 3-H), 3.45 (t, J = 8.9 Hz, 1H, 3-CH_a), 3.59 (dd, J = 8.9, 1.9 Hz, 1H, 3-CH_b), 3.72, 3.85 (2 m, 2H, 2-H_2), 4.10, 4.33 (2 d, J = 15.2 Hz, 2H, $PhCH_2N$), 4.95 (s, 2H, $PhCH_2O$), 6.08 (d, J = 2.0 Hz, 1H, 7-H), 6.63 (d, J = 2.0 Hz, 1H, 5-H), 7.20–7.40 (m, 10H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 46.21 (C-3), 52.39 ($PhCH_2N$), 55.64 (C-2), 63.18 (3-CH_2), 70.24 ($PhCH_2O$), 92.45 (C-4), 95.09 (C-7), 111.6 (C-5), 125.7 (C-3a), 127.3, 127.5, 127.8, 128.0, 128.6 (CH-Ph), 136.6 (*i*-C), 137.3 (*i*-C), 153.6 (C-7a), 160.4 (C-6). – MS (70 eV), *m/z* (%): 471 (21) [M^+], 440 (27) [$M^+ - CH_2OH$]. – $C_{23}H_{22}INO_2$ (471.3): calcd. C 58.61, H 4.70; found C 58.77, H 4.74.

(3RS)-1-Benzyl-6-benzyloxy-2,3-dihydro-3-hxdroxymethyl-1H-indole (**10**): An ice-cold solution of **9** (942 mg, 2.00 mmol) in dry tetrahydrofuran (15 ml) was charged with lithium aluminium hydride (1.60 mg, 4.00 mmol) and stirred for 6 h at 0°C. After careful addition of saturated aqueous sodium hydrogen carbonate (5 ml), the formed salts were removed by filtration and washed afterwards with hot tetrahydrofuran (3 × 20 ml) through Celite. The filtrate was concentrated in vacuo to give a colourless solid. Recrystallisation yielded **10** (656 mg, 1.90 mmol, 95%) as colourless needles. – R_f = 0.24 (ethyl acetate/petroleum ether, 1:2). – M.p. 113°C (ethyl acetate). – IR (KBr): $\tilde{\nu}$ = 3278 cm^{-1} (OH), 2920, 2864 (CH). – ^1H NMR ($CDCl_3$): δ = 1.52 (s, br., 1H, OH), 3.28 (dd, J = 8.9, 5.0 Hz, 1H, 3-CH_b), 3.35 (m, 1H, 3-H), 3.48 (t, J = 8.9 Hz, 1H, 3-CH_a), 3.75 (d, J = 6.0 Hz, 2H, 2-H_2), 4.22 (s, 2H, $PhCH_2N$), 4.99 (s, 2H, $PhCH_2O$), 6.19 (d, J = 2.1 Hz, 1H, 7-H), 6.28 (dd, J = 7.0, 2.1 Hz, 1H, 5-H), 7.00 (d, J = 7.0 Hz, 1H, 4-H), 7.20–7.40 (m, 10H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 42.56 (C-3), 52.74 ($PhCH_2N$), 56.63 (C-2), 65.06 (3-CH_2), 70.09 ($PhCH_2O$), 95.38 (C-7), 102.4 (C-5), 122.2 (C-3a), 124.4 (C-4), 127.1, 127.5, 127.7, 127.8, 128.5 (CH-Ph), 137.2 (*i*-C), 137.9 (*i*-C), 153.9 (C-7a), 160.0 (C-6). – MS (70 eV), *m/z* (%): 345 (22) [M^+], 314 (24) [$M^+ - CH_2OH$], 91 (100) [$C_7H_7^+$]. – $C_{23}H_{23}NO_2$ (345.4): calcd. C 79.97, H 6.71; found C 79.78, H 6.67.

(3RS)-1-Benzyl-6-benzyloxy-3-chloromethyl-2,3-dihydro-1H-indole (**11**): A suspension of indoline **10** (324 mg, 0.94 mmol) and triphenylphosphane (442 mg, 1.69 mmol) in tetrachloromethane (4 ml) and dry dichloromethane (8 ml) was stirred at 77°C under nitrogen for 1 h. Evaporation of the solvent at room temperature in vacuo and flash chromatography (30 g SiO_2, *t*BuOMe/petroleum ether, 1:20) of the residue afforded the chloride **11** (317 mg, 0.87 mmol, 93%) as a colourless oil. – R_f = 0.42. – IR (film): $\tilde{\nu}$ = 2946 cm^{-1}, 2924 (CH), 698 (CCl). – ^1H NMR ($CDCl_3$): δ = 3.32 (m, 1H, 3-CH_b), 3.53 (m, 3H, 3-CH_a, 3-H, 2-H), 3.70 (m, 1H, 2-H), 4.25 (s, 2H, $PhCH_2N$), 4.99 (s, 2H, $PhCH_2O$), 6.19 (d, J = 2.1 Hz, 1H, 7-H), 6.28 (dd, J = 7.0, 2.1 Hz, 1H, 5-H), 7.02 (d, J = 7.0 Hz, 1H, 4-H), 7.22–7.45 (m, 10H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 42.96 (C-3), 47.03 (3-CH_2), 52.88 ($PhCH_2N$), 57.66 (C-2), 70.11 ($PhCH_2O$), 95.91 (C-7), 103.3 (C-5), 122.2 (C-3a), 124.7 (C-4), 127.4, 127.8, 127.9, 128.5, 128.7 (CH-Ph), 137.1 (*i*-C), 137.4 (*i*-C), 153.1 (C.7a), 160.3 (C-6). – MS (70 eV), *m/z* (%): 363 (35) [M^+], 314 [$M^+ - CH_2Cl$], 91 (100) [$C_7H_7^+$]. – $C_{23}H_{22}ClNO$ (363.8): calcd. C 75.92, H 6.09; found C 76.03, H 6.18.

(3RS)-3-Chloromethyl-2,3-dihydro-6-hydroxy-1H-indole (**12**): A stirred suspension of chloride **11** (60.3 mg, 0.17 mmol) and 10% palladium on carbon (17 mg) in ethyl acetate (1.5 ml) was placed in a hydrogen atmosphere (1 atm) and stirred at room temperature for 16 h. The catalyst was filtered off and the filtrate concentrated in vacuo to give **12** (31 mg, 0.17 mmol, 100%, 95% pure) as a brown solid. – ^1H NMR ($CDCl_3$): δ = 2.63 (t, J = 11.1 Hz, 1H, 3-CH_b), 2.95 (dd, J = 11.1, 3.9 Hz, 1H, 3-CH_a), 3.20 (dd, J = 11.8, 8.0 Hz, 1H, 2-H_b), 3.58 (dd, J = 11.8, 1.1 Hz, 1H, 2-H_a), 4.18 (m, 1H, 3-H), 4.65 (s, br., 1H, OH), 6.02 (d, J = 2.1 Hz, 1H, 7-H), 6.18 (dd, J = 7.0, 2.1 Hz, 1H, 5-H), 6.82 (d, J = 7.0 Hz, 1H, 4-H), 7.70 (s, br., 1H, NH). – MS (70 eV), *m/z* (%): 183 (100) [M^+], 148 (50) [$M^+ - Cl$]. – $C_9H_{10}ClNO$ (183.6): calcd. 183.0451, found 183.0450 (HR-MS).

1,1a,2,3-Tetrahydro-5H-cycloprop[c]indol-5-one (**2**): A solution of unpurified **12** (31 mg) in tetrahydrofuran (2 ml) was treated with sodium hydride (12 mg, 0.5 mmol) under nitrogen. After 10 min the solvent was removed in vacuo. The crude product was purified by chromatography (5 g of SiO_2, ethyl acetate/petroleum ether, 1:3) to yield **2** (15 mg, 0.1 mmol, 60% based on **11**). – R_f = 0.30. – The ^1H-NMR spectrum was identical with published data[5l].

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[280/93]