SYNTHESIS AND BIOLOGICAL EVALUATION OF A NOVEL ACRONYCINE/DUOCARMYCIN HYBRID NATURAL PRODUCT

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Contents

General methods

Experimental methods: All air-sensitive reactions were performed under an argon atmosphere in flame-dried flasks and the reactants were introduced by syringe or transfer cannula. All solvents were dried by standard methods and the reagents obtained from commercial sources were used without further purification. Thin-layer chromatography was performed on pre-coated silica gel plates (TLC silica gel 60 F254, Merck). Silica gel 60 (0.032-0.064 mm, Merck) was used for column chromatography. Flash column chromatography was performed using the Isolera™ One flash purification system by Biotage with pre-packed silica cartridges (SNAP 10, 25, 50, 100 g).

NMR spectroscopy: NMR spectra were recorded with a Varian Mercury-300, Unity-300, Inova-500 and Inova-600 spectrometer and a Bruker AMX-300 spectrometer in $CDCl_3$; chemical shifts are given in ppm relative to tetramethylsilane (TMS), coupling constants J in Hertz. The solvent signals were used as references and the chemical shifts converted to the TMS scale ($CHCl_3$: $\delta H = 7.24$ ppm, $\delta C = 77.36$ ppm). The multiplicities of first order were

assigned as: s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublets), etc. Signals of higher orders were assigned as m (multiplet).

IR spectroscopy: IR spectra were recorded with a JASCO FT/IR-4100 spectrometer. All substances were applied neat on an ATR unit.

UV spectroscopy: UV spectra were recorded with a JASCO V-630 spectrometer.

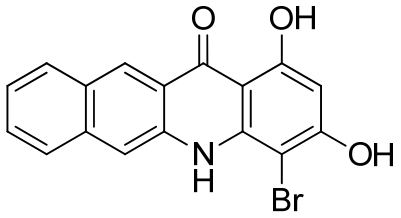
Mass spectrometry: ESI-MS and ESI-HRMS spectra were recorded with a Bruker Daltronik Apex IV, EI-MS and EI-HRMS spectra were recorded with a Thermo Finnigan MAT 95.

Preparative HPLC: Preparative separations were performed on a HPLC system from Jasco equipped with a PU-2087 solvent pump and an UV-detector model UV-2075 PLUS. For controlling, data acquisition and data analysis the computer programs Borwin PDA, HSS 2000 and Borwin Chromatography from Jasco were used. The following column was used: Kromasil®100 C18 (7 µm, 250 × 20 mm, *Jasco* und *Dr. Maisch GmbH*). All samples were membrane-filtered prior to measurement and solvents were of HPLC quality and degassed.

In vitro cytotoxicity assay: A549 cells (a human lung cancer cell line, ECACC 86012804) were seeded in 6-well tissue culture plates at 10^2 to 10^4 cells/well in serum supplemented culture medium (DMEM complete medium, PAA). Cells were allowed to attach for 24 hours then the medium was replaced with a serum-free medium (Ultra Culture, Lonza) with freshly prepared compounds (pre-solved in DMSO, 1% final concentration in serum-free medium for the incubation with the drugs) for 24 hours at different concentrations. After drug treatment cells were cultured in normal culture medium for 11 days to form colonies. They were fixed, stained and counted macroscopically. The IC_{50} values are based on the relative clone forming rate [%] = (number of clones counted after compound exposure) / (number of clones counted in the control without compounds). The shown results are the average of usually three experiments.

Experimental procedures

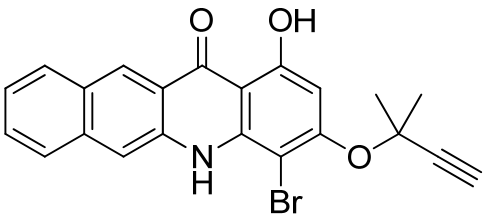
Synthesis of 4-Bromo-1,3-dihydroxybenzo[*b*]acridin-12(5*H*)-one (**8**)



A solution of 1,3-dihydroxybenzo[*b*]acridin-12(5*H*)-one (318 mg, 1.15 mmol, 1.00 equiv.) in acetone (48 mL) was added to freshly sublimated $ZnCl_2$ (156 mg, 1.15 mmol, 1.00 equiv.) and cooled down to –78 °C. The solution was stirred for 30 min at this temperature, NBS (255 mg, 1.43 mmol, 1.25 equiv.) was added and after additional stirring at –78 °C for 1.5 h the solution was warmed to rt. The solvent was evaporated, the raw product washed with 2 N HCl (2 x 50 mL), dissolved in EtOAc (50 mL) and dried over $MgSO_4$. Silica gel (600 mg) was added, the solvent was removed and **8** was obtained as an orange solid (241 mg, 677 μmol, 59 %) after purification on silica gel (PE/EtOAc = 3:2).

TLC: R_f = 0.65 (100% Et_2O); **IR**: ν (cm^{-1}) = 3395, 2906, 1635, 1447, 1346, 1136, 1085, 803, 740, 671, 517; **UV** (CH_3CN): λ_{max} (lgε) = 202 nm (4.5113), 284 (4.7598), 349 (3.9046), 442 (3.5943); **^{1}H-NMR** (301 MHz, DMSO): δ = 6.27 (s, 1 H, 2-H), 7.39–7.51 (m, 1 H, 8-H), 7.60 (ddd, *J* = 8.3, 6.7, 1.2 Hz, 1 H, 9-H), 7.92 (d, *J* = 8.0 Hz, 1 H, 7-H), 8.14 (d, *J* = 8.1 Hz, 1 H, 10-H), 8.47 (s, 1 H, 6-H), 8.86 (s, 1 H, 11-H), 10.47 (s, 1 H, NH), 11.51 (s, 1 H, 3-OH), 14.33 (s, 1 H, 1-OH); **^{13}C-NMR** (75 MHz, DMSO): δ = 83.9 (C-4), 95.0 (C-2), 102.4 (C-12a), 113.5 (C-6), 119.4 (C-5a), 124.6 (C-8), 126.2 (C-7), 126.7 (C-11), 128.1 (C-6a), 128.7 (C-9), 129.4 (C-10), 135.8 (C-10a), 137.0 (C-11a), 141.2 (C-4a), 161.6 (C-3), 163.3 (C-1), 181.1 (C-12); **MS** (ESI): *m*/*z* (%) = 354.0 (100) $[M\text{-}H^+]^-$; **HRMS** for $C_{17}H_{10}BrNO_3$ calcd.: 353.9771, found: 353.9774, $[M\text{-}H^+]^-$ (ESI-HRMS).

Synthesis of 4-Bromo-3-(1,1-dimethylprop-2-ynyloxy)-1-hydroxy-5*H*-benzo[*b*]acridin-12-one (**9**)

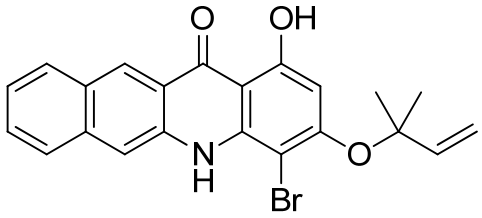


A solution of **8** (559 mg, 1.41 mmol, 1.00 equiv.), K_2CO_3 (391 mg, 2.83 mmol, 2.00 equiv.), 3-Chloro-3-methylbut-1-yne (1.27 mL, 11.3 mmol, 8.00 equiv.) and CuCl (1.40 mg, 14.1 μmol, 0.01 equiv.) was stirred in a pressure flask at rt for 24 h. The solvent was removed under reduced pressure, the residue dissolved in EtOAc (150 mL) and washed with 2 N HCl (2 x 40 mL) and sat. NaCl-sol. (3 x 40 mL). After drying over $MgSO_4$, silica gel was added (2.5 g) and the volatile compounds were removed under reduced pressure. Compound

9(453 mg, 1.07 mmol, 68%) was yielded after purification on silica gel (PE/EtOAc = 8:1 → 4:1) as an orange solid.

TLC: R_f = 0.33 (PE/Et_2O = 2:1); **IR**: ν (cm^{-1}) = 3749, 3350, 3257, 2362, 1636, 1557, 1340, 1261, 1131, 866, 820, 742, 578; **UV** (CH_3CN): λ_{max} (lgε) = 197 nm (4.4512), 227 (4.1904), 269 (4.7525), 283 (4.8039), 350 (4.0094), 442 (3.6294); **^{1}H-NMR** (301 MHz, DMSO): δ = 1.76 (s, 6 H, 2 x 1'-CH_3), 3.91 (s, 1 H, 3'-H), 6.94 (s, 1 H, 2-H), 7.39 – 7.50 (m, 1 H, 8-H), 7.60 (t, *J* = 7.1 Hz, 1 H, 9-H), 7.91 (d, *J* = 8.3 Hz, 1 H, 7-H), 8.13 (d, *J* = 8.3 Hz, 1 H, 10-H), 8.48 (s, 1 H, 6-H), 8.86 (s, 1 H, 11-H), 10.56 (s, 1 H, NH), 14.33 (s, 1 H, 1-OH); **^{13}C-NMR** (75 MHz, DMSO): δ = 29.3 (2 x 1'-CH_3), 74.1 (C–2'), 78.1 (C–3'), 84.5 (C–1'), 88.4 (C-4), 97.1 (C-2), 103.5 (C-12a), 113.6 (C-6), 119.1 (C-5a), 124.6 (C-8), 126.2 (C-7), 126.6 (C-11), 128.0 (C-6a), 128.7 (C-9), 129.3 (C-10), 135.8 (C-10a), 136.9 (C-11a), 140.5 (C-4a), 158.6 (C-3), 162.56 (C-1), 181.6 (C-12); **MS** (ESI): *m*/*z* (%) = 422.0 (100) [M-H^+]$^-$; **HRMS** for $C_{22}H_{16}BrNO_3$ calcd.: 420.0241, found: 420.0241, [M-H^+]$^-$ (ESI-HRMS).

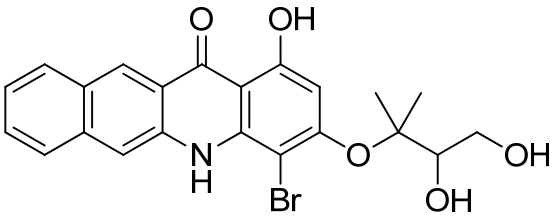
Synthesis of 4-Bromo-3-(1,1-dimethylallyloxy)-1-hydroxy-5*H*-benzo[*b*]acridin-12-one (**10**)



A suspension of quinoline (2.80 µL, 23.7 µmol, 0.10 equiv.) and Pd/C (10 wt%, 7.56 mg, 7.10 µmol, 0.03 equiv.) was stirred at rt for 15 min. A solution of alkyne **9** (100 mg, 237 µmol, 1.00 equiv.) in acetone (20 mL) was saturated with H_2 and added to the suspension. The combined solutions were stirred at rt for 2.5 h under H_2-atm. (balloon), filtered twice over Celite, silica gel was added and the volatile compounds were removed under reduced pressure. Alkene **10** (79.5 mg, 187 µmol, 79%) was obtained after purification on silica gel (PE/EtOAc = 8:1) as an orange solid.

TLC: R_f =0.49 (PE/Et_2O = 2:1); **IR**: ν (cm^{-1}) = 3749, 2361, 1541, 1507, 1340, 1137, 817, 740, 532; **UV** (CH_3CN): λ_{max} (lgε) = 196 nm (4.4955), 227 (4.2304), 270 (4.8161), 283 (4.8583), 351 (4.0582), 441 (3.6833); **^{1}H-NMR** (301 MHz, DMSO): δ =1.60 (s, 6 H, 2 x 1'-CH_3), 5.24–5.44 (m, 2 H, 3'-H_2), 6.22 (dd, *J* = 17.6, 10.9 Hz, 1 H, 2'-H), 6.46 (s, 1 H, 2-H), 7.42–7.53 (m, 1 H, 8-H), 7.63 (ddd, *J* = 8.2, 6.7, 1.2 Hz, 1 H, 9-H), 7.94 (d, *J* = 8.2 Hz, 1 H, 7-H), 8.16 (d, *J* = 7.9 Hz, 1 H, 10-H), 8.51 (s, 1 H, 6-H), 8.89 (s, 1 H, 11-H), 10.56 (s, 1 H, NH), 14.28 (s, 1 H, 1-OH); **MS** (ESI): *m*/*z* (%) = 422.0 (100) [M-H^+]$^-$; **HRMS** for $C_{22}H_{18}BrNO_3$ calcd.: 426.0523, found: 426.0523, [M+H^+]$^+$ (ESI-HRMS).

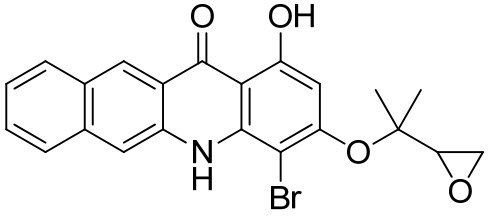
Synthesis of 4-Bromo-3-(2,3-dihydroxy-1,1-dimethylpropoxy)-1-hydroxy-5*H*-benzo[*b*]acridin-12-one (*rac*-**11**)



To a solution of alkene **10** (224 mg, 529 µmol, 1.00 equiv.) in acetone (10 mL) and H_2O (2 mL) was added NMO (92.9 mg, 793 µmol, 1.50 equiv.), DABCO (89.0 mg, 793 µmol, 1.50 equiv.) and $K_2OsO_4 \cdot 2H_2O$ (19.5 mg, 52.9 µmol, 0.10 equiv.). The reaction mixture was stirred at 0 °C for 3 d, sat. $NaHSO_3$-solution (2 mL) was added, the solution was further stirred for 10 min and the volatile compounds were evaporated under reduced pressure. The remaining suspension was diluted in 1 N HCl (2 mL) and extracted with EtOAc (4 x 20 mL), the organic layer was dried over $MgSO_4$ and silica gel (1 g) was added. Removal of the solvents under reduced pressure and purification on silica gel (PE/EtOAc = 1:1 → 100% EtOAc) gave *rac*-**11** (174 mg, 380 µmol, 72%) as a dark orange solid.

TLC: R_f=0.17 (PE/EtOAc = 1:1);**IR**: ν (cm^{-1}) = 3468, 3252, 1634, 1505, 1341, 1269, 1029, 815, 729, 602, 533; **UV** (CH_3CN): λ_{max} (lgε) = 196 nm (4.2831), 228 (4.0319), 270 (4.6594), 282 (4.6908), 351 (3.8642), 443 (3.4867);**^{1}H-NMR** (301 MHz, DMSO): δ = 1.43, 1.47 (s, 6 H, 2 x 1'-CH_3), 3.47 (ddd, *J* = 11.0, 8.0, 5.3 Hz, 1 H, 3'-H_a), 3.74 (ddd, *J* = 8.1, 5.2, 2.9 Hz, 1 H, 2'-H), 3.86 (ddd, *J* = 11.0, 6.0, 2.8 Hz, 1 H, 3'-H_b), 4.49 (t, *J* = 5.7 Hz, 1 H, 3'-OH), 5.11 (d, *J* = 5.2 Hz, 1 H, 2'-OH), 6.63 (s, 1 H, 2-H), 7.38–7.53 (m, 1 H, 8-H), 7.61 (dd, *J* = 11.1, 4.0 Hz, 1 H, 9-H), 7.93 (d, *J* = 8.4 Hz, 1 H, 7-H), 8.15 (d, *J* = 8.2 Hz, 1 H, 10-H), 8.50 (s, 1 H, 6-H), 8.88 (s, 1 H, 11-H), 10.54 (s, 1 H, NH), 14.26 (s, 1 H, 1-OH); **^{13}C-NMR** (75 MHz, DMSO): δ = 22.0, 24.2 (2 x 1'-CH_3), 62.0 (C-3'), 76.9 (C-2'), 86.0 (C-1'), 90.4 (C-4), 99.5 (C-2), 103.5 (C-12a), 113.6 (C-6), 119.1 (C-5a), 124.6 (C-8), 126.2 (C-7), 126.6 (C-11), 128.0 (C-6a), 128.7 (C-9), 129.3 (C-10), 135.8 (C-10a), 136.9 (C-11a), 140.5 (C-4a), 159.4 (C-3), 162.5 (C-1), 181.5 (C-12); **MS** (ESI): *m/z* (%) = 456.0 (100) $[M\text{-}H^+]^-$;**HRMS** for $C_{22}H_{20}BrNO_5$ calcd.: 454.0296, found: 454.0292 $[M\text{-}H^+]^-$(ESI-HRMS).$^-$

Synthesis of 4-Bromo-1-hydroxy-3-(1-methyl-1-oxiranylethoxy)-5*H*-benzo[*b*]acridin-12-one (*rac*-**12**)

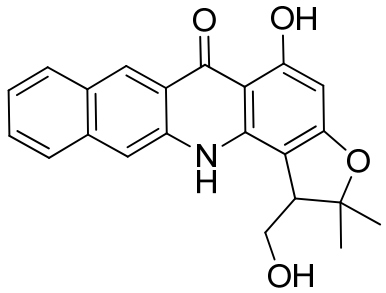


Compound *rac*-**11** (347 mg, 756 µmol, 1.00 equiv.) was dissolved in pyridine (13 mL) and stirred at 0 °C for 30 min. Mesyl chloride (117 µL, 1.51 mmol, 2.00 equiv.) was added, further stirred for 1 h, the volatile materials were removed under reduced pressure and the

remainings dissolved in MeOH (20 mL). After addition of K_2CO_3 (523 mg, 3.78 mmol, 5.00 equiv.) the dark red solution was stirred for 3 h at rt. The solvent was evaporated at rt, 1 N HCl (5 mL) was added and the aqueous layer extracted with EtOAc (3 x 10 mL). After drying over Na_2SO_4, silica gel (2 g) was added, the volatile compounds were removed under reduced pressure, purification on silica gel (PE/EtOAc = 4:1 → 3:1 → 2:1) gave compound *rac*-**12** (160 mg, 363 μmol, 48%) as an orange solid.

TLC: R_f=0.71 (PE/EtOAc = 2:1);**IR**: ν (cm^{-1}) = 3748, 3395, 2354, 1636, 1557, 1394, 1258, 1107, 1068, 826, 747, 517; **UV** (CH_3CN): λ_{max} (lgε) = 197 nm (4.5027), 269 (4.7818), 282 (4.8023), 334 (3.9431), 351 (3.988), 444 (3.6317);**^{1}H-NMR** (301 MHz, DMSO): δ = 1.32, 1.50 (s, 6 H, 2 x 1'-CH_3), 2.84 (dd, *J* = 4.7, 2.8 Hz, 1 H, 3'-H_a), 2.90 (t, *J* = 4.5 Hz, 1 H, 3'-H_b), 3.35 (dd, *J* = 4.3, 2.8 Hz, 1 H, 2'-H), 6.67 (s, 1 H, 2-H), 7.46 (d, *J* = 7.9 Hz, 1 H, 8-H), 7.59 (d, *J* = 7.2 Hz, 1 H, 9-H), 7.91 (d, *J* = 8.3 Hz, 1 H, 7-H), 8.13 (d, *J* = 8.3 Hz, 1 H, 10-H), 8.48 (s, 1 H, 6-H), 8.86 (s, 1 H, 11-H), 10.53 (s, 1 H, NH), 14.26 (s, 1 H, 1-OH); **^{13}C-NMR** (75 MHz, DMSO): δ = 20.1, 25.0 (2 x 1'-CH_3), 44.6 (C-3'), 56.5 (C-2'), 82.4 (C-1'), 89.6 (C-4), 98.7 (C-2), 103.5 (C-12a), 113.6 (C-6), 119.1 (C-5a), 124.5 (C-8), 126.2 (C-7), 126.5 (C-11), 127.9 (C-6a), 128.7 (C-9), 129.3 (C-10), 135.8 (C-10a), 136.8 (C-11a), 140.4 (C-4a), 158.8 (C-3), 162.7 (C-1), 181.5 (C-12); **MS** (ESI): *m/z* (%) = 438.0 (100) [M-H^+]$^-$; **HRMS** for $C_{22}H_{18}BrNO_4$ calcd.: 438.0346, found: 438.0330 [M-H^+]$^-$ (ESI-HRMS).

Synthesis of 5-Hydroxy-1-(hydroxymethyl)-2,2-dimethyl-1,2-dihydrobenzo[*b*]furo[3,2-h]acridin-6(13*H*)-one (*rac*-**13**)

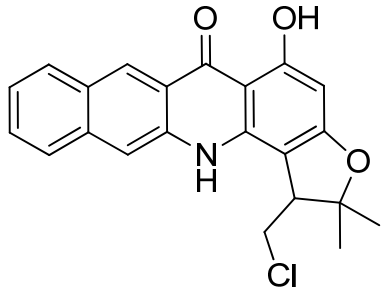


Epoxide *rac*-**12** (59.4 mg, 135 μmol, 1.00 equiv.) was dissolved in THF (10 mL), cooled to –78 °C and stirred for 15 min at that temperature. *n*-BuLi (205 μL, 472 μmol, 3.50 equiv., 2.5 M in hexane) was added at –78 °C and the reaction was allowed to warm to rt within 20 h. Sat. NH_4Cl-sol. (2 mL) was added, the aqueous layer extracted with EtOAc (3 x 20 mL), the organic layer dried over $MgSO_4$, silica gel (250 mg) was added and the volatile compounds were removed under reduced pressure. *rac*-**13** (30.3 mg, 83.9 μmol, 62%) was obtained after purification on silica gel (PE/EtOAc = 3:1 → 2:1) as an orange solid.

TLC: R_f=0.21 (PE/EtOAc = 2:1);**IR**: ν (cm^{-1}) = 3295, 2972, 2360, 1651, 1591, 1470, 1346, 1259, 1089, 852, 736, 538; **UV** (CH_3CN): λ_{max} (lgε) = 197 nm (4.4955), 227 (4.3603), 243 (4.2745), 270 (4.7539), 284 (4.8261), 321 (4.057), 357 (4.0747), 446 (3.6577); **^{1}H-NMR** (301 MHz, DMSO): δ = 1.42, 1.50 (s, 6 H, 2 x 2-CH_3), 3.45 (dd, *J* = 8.0, 4.4 Hz, 1 H, 1-H), 3.73 (t, *J* = 9.3 Hz, 1 H, 1'-H_a), 3.93 (dd, *J* = 10.5, 4.2 Hz, 1 H, 1'-H_b), 5.96 (s, 1 H, 1'-OH), 6.01 (s, 1 H, 4-H), 7.42 (ddd, *J* = 8.0, 6.7, 1.1 Hz, 1 H, 10-H), 7.58 (ddd, *J* = 8.3, 6.7, 1.2 Hz, 1 H, 9-H), 7.85 (s, 1 H, 12-H), 7.95 (d, *J* = 8.1 Hz, 1 H, 11-H), 8.11 (d, *J* = 8.3 Hz, 1 H, 8-H), 8.86

(s, 1 H, 7-H), 11.49 (s, 1 H, NH), 14.53 (s, 1 H, 5-OH); **^{13}C-NMR** (75 MHz, DMSO): δ = 22.0, 28.4 (2 x 2-CH_3), 51.0 (C-1), 60.1 (1-CH_2), 89.9 (C-4), 90.1 (C-2), 102.4 (C-5a), 102.6 (C-13b), 111.4 (C-12), 119.5 (C-12a), 124.1 (C-10), 126.2 (C-7), 126.3 (C-11), 127.7 (C-11a), 128.4 (C-9), 129.3 (C-8), 135.7 (C-7a), 136.9 (C-6a), 139.8 (C-13a), 165.0 (C-3a), 165.3 (C-5), 180.9 (C-6); **MS** (ESI): *m/z* (%) = 360.1 (100) $[M\text{-}H^+]^-$, 721.3 (36) $[2M\text{-}H^+]^-$; **HRMS** for $C_{22}H_{19}NO_4$ calcd.: 360.1241, found: 360.1236 $[M\text{-}H^+]^-$ (ESI-HRMS).

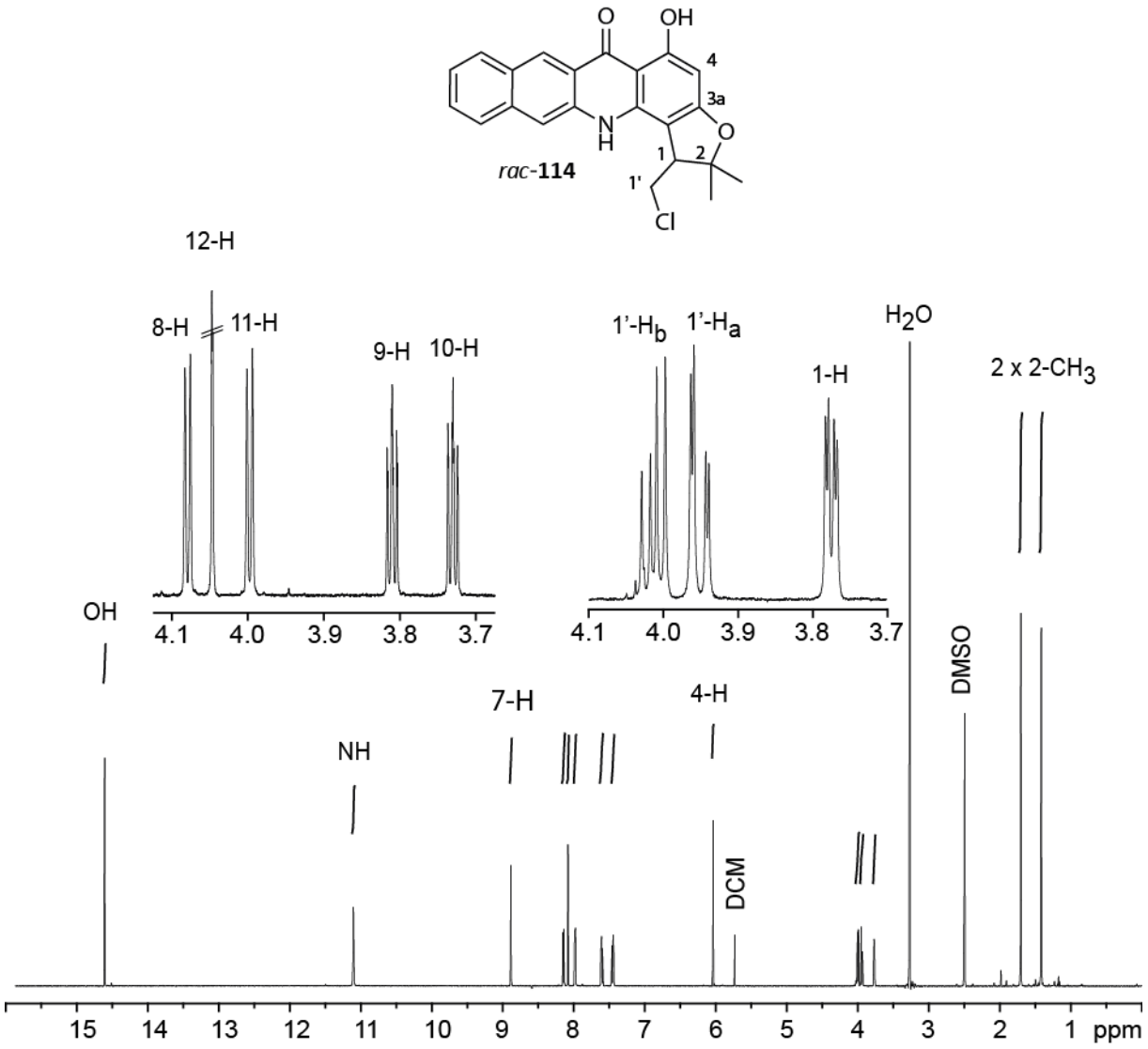
Synthesis of 1-(Chloromethyl)-5-hydroxy-2,2-dimethyl-1,2-dihydrobenzo[*b*]furo[3,2-h]acridin-6(13*H*)-one (*rac*-**3**)

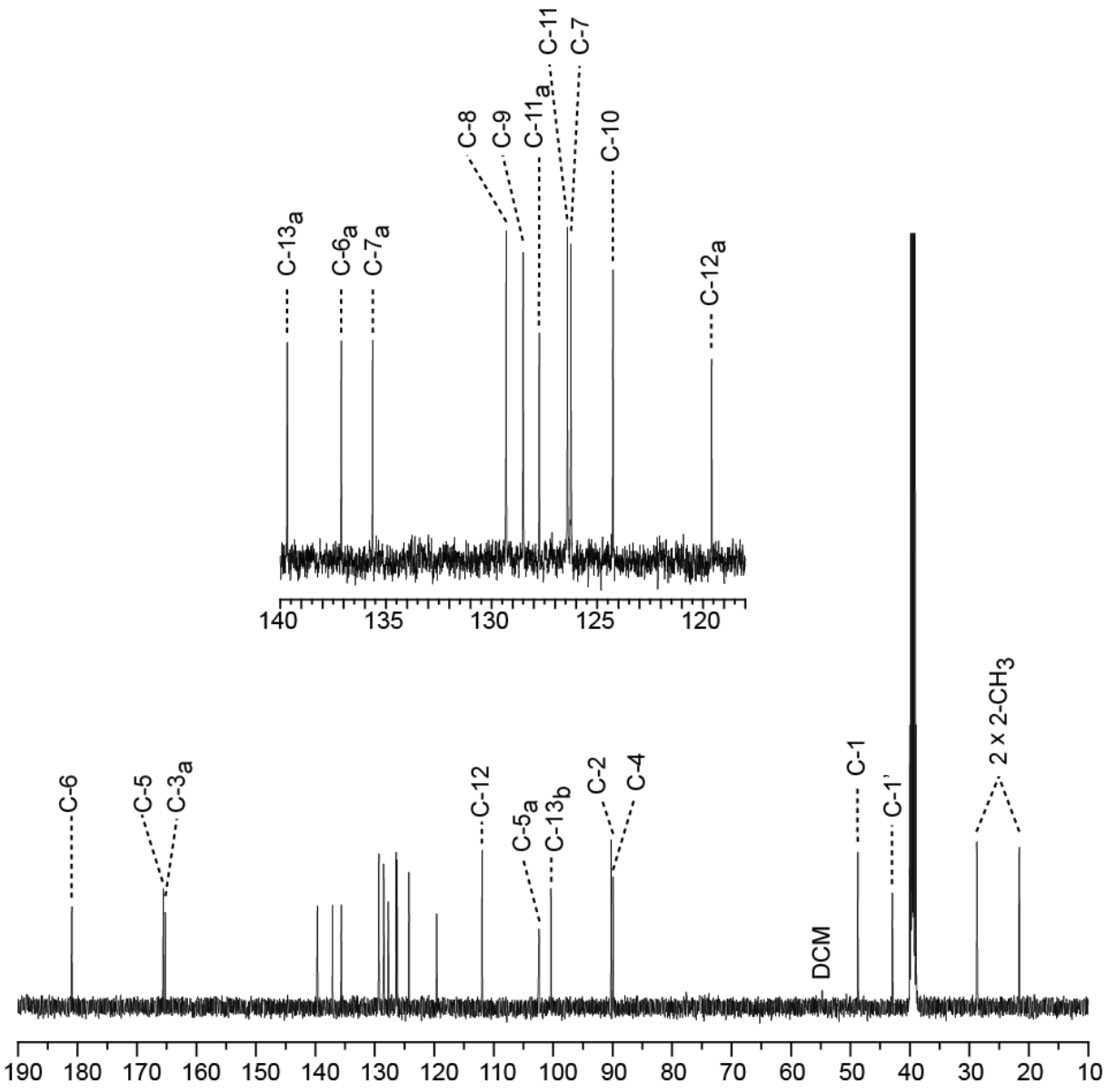


Alcohol *rac*-**13** (9.30 mg, 25.7 μmol, 1.00 equiv), PPh_3 (20.3 mg, 77.2 μmol, 3.0 equiv) and CCl_4 (23.0 μL, 232 mmol, 9.00 equiv.) were dissolved in DCE (6 mL) and stirred for 18 h at 50 °C in a pressure flask. Silica gel (50 mg) was added, removal of the solvent under reduced pressure and purification on silica gel (PE/EtOAc = 10:1) gave *rac*-**3** (8.31 mg, 21.9 μmol, 85%) as an orange solid.

HPLC: Kromasil® 100 C_{18}, MeOH/H_2O = 90:10, flow rate 6.0 mL/min, 254 nm, t_R = 6.725 min.; **TLC**: R_f=0.71 (PE/EtOAc = 2:1); **^{1}H-NMR** (600 MHz, DMSO): δ = 1.42, 1.71 (s, 6 H, 2 x 2-CH_3), 3.77 (dd, *J* = 6.9, 2.5 Hz, 1 H, 1-H), 3.95 (dd, *J* = 12.1, 2.5 Hz, 1 H, 1'-H_a), 4.01 (dd, *J* = 12.0, 7.0 Hz, 1 H, 1'-H_b), 6.05 (s, 1 H, 4-H), 7.46 (m_c, 1 H, 10-H), 7.62 (m_c, 1 H, 9-H), 8.00 (d, *J* = 8.7 Hz, 1 H, 11-H), 8.09 (s, 1 H, 12-H), 8.16 (d, *J* = 8.4 Hz, 1 H, 8-H), 8.90 (s, 1 H, 7-H), 11.12 (s, 1 H, NH), 14.63 (s, 1 H, 5-OH); **^{13}C-NMR** (126 MHz, DMSO): δ = 21.6, 28.7 (2 x 2-CH_3), 43.0 (C-1'), 48.7 (C-1), 89.9 (C-4), 90.3 (C-2), 100.4 (C-13b), 102.4 (C-5a), 112.0 (C-12), 119.6 (C-12a), 124.3 (C-10), 126.2 (C-7), 126.4 (C-11), 127.7 (C-11a), 128.5 (C-9), 129.3 (C-8), 135.6 (C-7a), 137.1 (C-6a), 139.7 (C-13a), 165.2 (C-3a), 165.6 (C-5), 181.0 (C-6); **MS** (ESI): *m/z* (%) = 378.1 (100) $[M\text{-}H^+]^-$, 757.2 (20) $[2M\text{-}H^+]^-$; **HRMS** for $C_{22}H_{19}ClNO_3$ calcd.: 378.0902, found.: 378.0886 $[M\text{-}H^+]^-$ (ESI-HRMS).

NMR spectra of*rac*-3




C-13a
C-6a
C-7a
C-8
C-9
C-11a
C-11
C-7
C-10
C-12a
140
135
130
125
120
C-6
C-5
C-3a
C-12
C-5a
C-13b
C-2
C-4
DCM
C-1
C-1'
2 x 2-CH3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10