Supporting Information

Total Synthesis of the Aristolochic Acids, Their Major Metabolites and Related Compounds

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Toxicity Warning

The aristolochic acids and several of their metabolites are known to be potently carcinogenic and nephrotoxic when ingested. Therefore, care should be taken in handling these materials, and ingestion or inhalation of dust should be scrupulously avoided.

Materials and Methods

All reagents and solvents employed in the experimental work were reagent grade and were used as such unless otherwise specified. Melting points were taken on a Thomas-Hoover open capillary melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded either on a Varian Gemini 300 or on a Varian NOVA 400 spectrometer, and samples prepared for analysis were dissolved in $CDCl_3$ or DMSO-d_6. Chemical shifts are reported in parts per million (ppm) relative to TMS. Low resolution mass spectra were recorded on either a Thermo Electron DSQ GC/MS equipped with a solid probe inlet and EI ionization or a Micromass Platform mass spectrometer using electrospray ionization. High resolution mass spectra were obtained with an Agilent Technologies Model 6224 TOF LC/MS using an ESI source. Thin-layer chromatography (TLC) was performed on silica gel sheets (Tiedel-deHaën, Sleeze, Germany). After

appropriate purification all new products showed a single spot on TLC analysis in two solvent systems: (i) 30% EtOAc in hexanes and (ii) 5% MeOH in CH_2Cl_2. Components were visualized by UV light (λ=254 nm) or by spraying with a solution of 2% phosphomolybdic acid in ethyl alcohol containing 5% sulfuric acid. Flash column chromatographic separations were accomplished with 60 Å (230–400 mesh) silica gel (TSI Chemical Co., Cambridge, MA). All experiments dealing with moisture or air-sensitive compounds were conducted under dry nitrogen. Brine solutions used in washing procedures was 8% NaCl in aqueous solution. The starting materials and reagents, unless otherwise specified, were the best grade commercially available (Sigma-Aldrich, Milwaukee, WI or Fluka Chemie GmbH, Sigma-Aldrich, Germany) and were used without further purification.

A. Synthesis of the Aristolochic Acids.

5-Formyl-6-(tetrahydropyran-2-yloxymethyl)benzo[1,3]dioxole (23).

To a solution of 5-bromo-6-(tetrahydropyran-2-yloxymethyl)benzo[1,3]dioxole[1] (**22)** (95.0 g, 301.4 mmol) in tetrahydrofuran (500 mL) was added a solution of n-butyllithium (2.5 M solution in hexanes, 141 mL) at -75 °C under a nitrogen atmosphere over a period of 30 minutes, and the reaction mixture was further stirred for 2 h at the same temperature. Thereafter, the temperature of the mixture was raised to -40 °C, the reaction was quenched with saturated aqueous ammonium chloride (200 mL), and the resultant mixture was stirred for 10 min. The phases were separated, the aqueous layer was extracted with ethyl acetate (2 x 200 mL), and the combined organic layers were washed with water (2 x 100 mL) followed by brine (100 mL) then dried over sodium sulfate. The solvent was evaporated under reduced pressure, and the crude product was purified by silica gel chromatography (eluent: hexanes/EtOAc, 85:15) to afford 5-formyl-6-(tetrahydropyran-2-yloxymethyl)benzo[1,3]dioxole (**23**, 53.0 g, yield 67%) as an oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.09 (s, 1H), 7.41 (s, 1H), 7.18 (s, 1H), 6.89 (s, 2H), 5.01 (abq J = 16.1 Hz, 2H), 4.89 (m, 1H), 3.94 (m, 1H), 3.63 (m, 1H), 1.90-1.56 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.07, 152.53, 147.67, 138.38, 128.71, 109.58, 109.35, 102.25, 98.38, 65.91, 62.59, 30.72, 25.56, 19.59. EI-MS: (M^+) *m/z* 264.1.

6-(Tetrahydropyran-2-yloxymethyl)benzo[1,3]dioxole-5-*N*-(cyclohexyl)carbimine (24).

5-Formyl-6-(tetrahydropyran-2-yloxymethyl)benzo[1,3]dioxole (**23;** 72.0 g, 0.272 mol) was dissolved in toluene (600 mL), and cyclohexylamine (41.6 g, 0.42 mol) was added. The reaction mixture was refluxed for 4 h using a Dean-Stark water separator. The reaction mixture was cooled, and the solvent was evaporated under reduced pressure. Then the residue was triturated with hexanes (100 mL) with cooling to afford the desired product (**24**) as a crystalline white solid, which was filtered and dried at 24 °C under vacuum (91.0 g, yield 97%), mp 64-65 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.58 (s, 1H), 7.42 (s, 1H), 6.88 (s, 1H), 5.98 (s, 2H), 4.75 (abq J = 15.9 Hz, 2 H), 4.72 (m, 1H), 3.92 (m, 1H), 3,17 (m, 1H), 1.89-1.21 (m, 16 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.96, 11.93, 149.29, 147.76, 132.52, 129.60, 109.48, 109.44, 107.26, 101.52, 97.74, 70.09, 66.07, 62.46, 34.70, 30.77, 25.65, 24.97, 19.57. EI-MS: (M^+) *m/z* 347.1.

4-Iodo-5-formyl-6-(tetrahydropyran-2-yloxymethyl)benzo[1,3]dioxole 5-oxime (26).

To a solution of 6-(tetrahydropyran-2-yloxymethyl)benzo[1,3]dioxole-5-*N*-(cyclohexyl)-carbimine (**24**, 74.0 g, 214 mmol) in tetrahydrofuran (700 mL) was added n-butyllithium (2.5 M solution in hexanes, 112 mL), at -75 °C under a nitrogen atmosphere over a period of 30 min. After stirring for 1h, iodine (88.0 g, 348 mmol) in tetrahydrofuran (200 mL) was added during 30 min, and the reaction mixture was stirred for an additional 1h at -75 °C. The temperature was then raised to -40 °C, and reaction mixture was quenched with aqueous potassium thiosulphate (20%, 300 mL). The phases were separated, and the aqueous layer was extracted with ethyl acetate (2 x 200 mL). Then the combined organic layers were washed with 20% potassium bisulfate solution (2 x 200 mL), water (2 x 200 mL), followed by brine (100 mL) and finally dried over sodium sulfate. Removal of the solvent provided the crude product which was dissolved in methylene chloride (200 mL) and passed through a short column of silica gel using hexanes:EtOAc::90:10 as the eluent to afford a solid (70.0 g) consisting of the product **25** (60%) and starting material **24** (40%) as estimated by ^{1}HNMR analysis. This mixture was dissolved in methylene chloride and treated for two hours with a 2 M solution of hydroxylamine in methanol (500 mL) prepared from equimolar amounts of $NH_2OH{\cdot}HCl$

and KOAc (with removal of the precipitated KCl). The solvent was evaporated under reduced pressure, and the residue was triturated with isopropyl ether (60 mL). The remaining solid was filtered, suspended in cold 10% sodium bicarbonate solution (100 mL), filtered again, washed with water (100 mL) then dried in a vacuum oven over P_2O_5 to give the desired product 4-iodo-6-(tetrahydropyran-2-yloxymethyl)-benzo[1,3]dioxole-5-carbaldehyde oxime (**26**, 47.0 g, yield 54.2%) as a white solid, mp 139-40 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.33 (s, 1H), 7.12 (s, 1H), 6.06 (s, 1H), 4.78 (abq ? J = 13.8 Hz, 2H), 4.47 (m, 1H), 3.88 (m, 1H), 3.56 (m, 1H), 1.88-1.53 (m, 6 H). ^{13}C NMR(100 MHz, $CDCl_3$): δ 152.74, 149.09, 146.67, 134.80, 124.95, 108.69, 101.09, 76.08, 67.28, 62.37, 30.71, 25.59, 19.46. EI-MS: (M^+) *m/z* 345.0.

4-Iodo-5-nitromethyl-6-(tetrahydropyran-2-yloxymethyl)benzo[1,3]dioxole (27).

To a solution of 4-iodo-5-formyl-6-(tetrahydropyran-2-yloxymethyl)benzo[1,3]dioxole 5-oxime **(26)** (19.0 g, 47 mmol) in methylene chloride (150 mL) and acetonitrile (100 mL), there was added in one portion, oxodiperoxomolybdate (Benz-Mo)[2,3] complex (14.44 g, 26.8 mmol) in acetonitrile, and the reaction mixture was stirred at 40 °C under nitrogen until ^{1}HNMR analysis showed the reaction to be complete. The solvent was evaporated under reduced pressure, and residue was dissolved in methylene chloride (150 mL). This solution was washed with water (2 x 50 mL), then saturated sodium bicarbonate solution (50 mL), water (2 x 50 mL), and finally with brine. The organic layer was dried over anhydrous sodium sulfate, filtered, and the solvent evaporated under reduced pressure. The solid thus obtained was purified by silica gel chromatography (eluent: hexanes:EtOAc::90:10) to give the desired 4-iodo-5-nitromethyl-6-(tetrahydropyran-2-yloxymethyl)benzo[1,3]dioxole (**27**) as a white solid (15.0 g, yield 67%), mp 94-95 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.82 (s, 1H), 6.09(s, 1H), 5.74 (s, 1H), 4.62 (abq J = 12.3 Hz, 2H), 4.57 (m, 1H), 3.80 (m, 1H), 3.52 (m, 1H), 1.65-1.46 (m, 6H). ^{13}C (100 MHz, $CDCl_3$) δ 150.35, 147.21, 134.66, 124.87, 110.72, 101.45, 97.72, 81.18, 78.77, 67.54, 62.68, 30.41, 25.48, 19.47. EI-MS: (M^+) *m/z* 405.0.

2-Formyl-3-methoxymethoxyphenoxy triflate (20e).

To a solution of 2-formyl-3-hydroxyphenyl triflate[4] (23.0 g, 84.6 mmol) and di-isopropyl ethylamine (11.2 g, 86.2 mmol) in methylene chloride (150 mL) at 0 °C was added chloromethyl methyl ether (6.81 g, 84.1 mmol) over a period of 30 min. The reaction mixture was stirred overnight at RT, poured into water and, after separation of the phases, the aqueous layer was extracted with methylene chloride (2 x 50 mL). All organic layers were combined, washed sequentially with saturated bicarbonate solution (50 mL), water (2 x 50 mL), brine (50 mL), and then dried over sodium sulfate. The mixture was filtered, and the solvent was recovered under reduced pressure to give the desired **20e** as an oil (26 g, yield 100%). ^{1}HNMR (400 MHz, CDCl3): δ 1049, (s, 1H), 7.58 (t, J = 11.8Hz, 1H), 7.32 (d, J = 10.4 Hz, 1H), 6.95 (d, J = 12 Hz, 1H), 5.31 (s, 2H), 3.54 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.13, 161.07, 147.92, 135.89, 120.47, 118.73, 115.69, 115.61, 95.47, 56.93. EI-MS: (M^+) *m/z* 314.06.

2-Formyl-3-trifluoromethoxyphenyl triflate (20f).

Step (a): Introduction of aldehyde group. 1-Methoxymethoxy 3-(trifluoromethoxy)-benzene[5] (5.6 g, 25 mmol) in tetrahydrofuran (10 mL) was added to a solution of t-butyllithium (1M solution in pentanes, 17 mL) in tetrahydrofuran (30 mL) at -75 °C. After 2 h, dimethylformamide (6 mL) was added over a period of 15 min. Stirring was continued for 1 h at -75 °C, and the temperature was raised to -30 °C. A cold solution (100 mL) of ammonium chloride was added, and the product was isolated by the standard work-up procedure using ether as the extraction solvent (2 x 50 mL). This afforded the required intermediate 2-methoxymethoxy-6-(trifluoromethoxy)-benzaldehyde as an oil (6.0 g, yield 95%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.47 (s, 1H), 7.51 (t, J = 8.1 Hz, 1H), 7.22 (d, J = 23.4 Hz, 1H), 6.97 (d, J = 8.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.49, 159.89, 136.28, 120.96 (q, J = 257 Hz, CF_3), 114.88, 114.08, 95.21, 56.81. ^{19}F NMR ($CDCl_3$): δ (-58.072). EI-MS: (M^+) *m/z* 250.08.

Step (b): THP deprotection. To a solution of 2-methoxymethoxy-6-(trifluoro-methoxy)benzaldehyde in methylene chloride (100 mL) was added Montmorillonite K 10 clay[6] (2.0 g), and the mixture was stirred for 6 h at RT. At this point, TLC (10% ethyl acetate in hexanes) analysis indicated complete deprotection of the MOM group.

Filtration through Celite and evaporation of the solvent gave an oily residue that was purified by silica gel chromatography (eluent hexanes:EtOAc::90:10) to give 2-hydroxy-6-(trifluoromethoxy)benzaldehyde as an oil (8 g, yield 75%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.73 (s, 1H), 10.25 (s, 1H), 7.49 (t, J = 8.4 Hz, 1H), 6.90 (d, J = 8.4 Hz, 1H), 6.79 (d, J = 7.6 Hz, 1H). ^{13}C (100 MHz, $CDCl_3$): δ 193.30, 163.64, 151.14, 137.82, 121.01 (q, J = 258.80 Hz, CF_3), 116.76, 113.30, 110.62. EI-MS: (M^+) *m/z* 206.02.

Step (c): Triflate (20f). To a solution of 2-hydroxy-6-trifluoromethoxybenzaldehyde (11.0 g, 54.3 mmol) and pyridine (16 mL) in methylene chloride (150 mL) at 0 °C was added a solution of triflic anhydride (18.5 g, 65.6 mmol) in methylene chloride (50 ml), over a 30 min period. The reaction mixture was stirred at this temperature for 1h then poured into ice cold water (100 mL). The phases were separated, the organic phase was washed with saturated sodium bicarbonate solution (100 mL), then with 10% citric acid solution (2 x 50 mL), water (2 X50 mL), and finally with brine (100 mL). The organic extracts were dried over sodium sulfate, and the organic residue, after removal of the solvent, was purified by silica gel chromatography (eluents hexanes:EtOAc::90:10) to give **20f** as an oil (12.4 g, yield 68.7%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.38 (s, 1H), 7.75 (t, J = 8.1 Hz, 1H), 7.49 (d, J = 7.8 Hz, s, 1H), 7.34 (d, J = 8.1Hz, 1H). EI-MS: (M^+) *m/z* 338.01.

2,2-Dimethyl-5-hydroxy-7-(tetrahydropyran-2-yloxy)benzo[1,3]dioxin-4-one (32).
To a solution of 2,2-dimethyl-5,7-dihydroxybenzo[1,3]dioxin-4-one[7] (**31)** (11.0 g, 52.34 mmol) and dihydropyran (20 mL) in methylene chloride (250 mL) was added pyridinium *p*-toluenesulfonate (0.5g), and the mixture was heated under reflux for 12 h. After cooling, the reaction solution was washed with water (2 x 50 mL), followed by brine, and then dried over sodium sulfate. Filtration and evaporation of the solvent gave a solid which was purified by silica gel chromatography (eluent hexanes:EtOAc::90:10) to give **32** (14.0 g, yield 90.9%) as a white solid, mp 109-10 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.38 (s, 1H), 6.31 (d, J = 2.4 Hz, 1H), 6.15 (d, J = 2.4 Hz), 5.44 (t, J = 3.3 Hz, 1H), 3.82 (m, 1H), 3.63 (m, 1H), 1.99-1.54 (m, 6 H), 1.71 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.41, 162.99, 156.97, 107.05, , 98.48, 96.52, 96.49, 96.37, 93.73, 62.37, 30.09, 25.83, 25.10, 18.61. EI-MS: (M^+) *m/z* 294.17.

2,2-Dimethyl-4-oxo-7-(tetrahydropyran-2-yloxy)-4H-benzo[1,3]dioxin-5-yl triflate (33).

Starting with compound **32** (5.1g, 17.4 mmol) and using a procedure analogous to that used for the preparation of **20f,** compound **33** was obtained (5.5 g, yield 74%) as a white crystalline solid, mp 103-4 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.69 (d J = 2.1, 1H), 6.67 (d J = 2.4, 1H), 5.48 (m, 1H), 3.78 (m, 1H), 3.68, 1H), 1.96-1.65 (m, 6H), 1.74 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.43, 158.77, 157.35, 149.96, 123.73, 120.54, 117.45, 106.75, 104.15, 101.71, 97.34, 62.35, 29.89, 25.76, 24.95, 18.24. EI-MS: (M^+) *m/z* 426.12.

2-Formyl-3-hydroxy-5-(tetrahydropyran-2-yloxy)phenyl triflate (34).

A solution of 2,2-dimethyl-4-oxo-7-(tetrahydropyran-2-yloxy)-4H-benzo[1,3]dioxin-5-yl triflate (**33)** (1.866 g, 4.38 mmol) in methylene chloride (20 mL) at -78 °C was treated with DIBALH (13 mmol, 1 M solution in CH_2Cl_2). The reaction mixture was stirred at -78 °C for 2 h then quenched with methanol (40 mL) and 1M HCl (40 mL). The mixture was further diluted with methylene chloride (40 mL), and the phases were separated quickly at -10 °C. The organic phase was washed with water (2 x 25 mL), followed by brine (26 mL), and then dried over $MgSO_4$. Filtration and evaporation of the solvent afforded an oily residue that was purified by silica gel chromatography (Eluent hexanes:EtOAc::90:10) to give the required 2-formyl-3-hydroxy-5-(tetrahydropyran-2-yloxy)phenyl triflate (**34)** as a colorless oil (1.1 g, yield 65.8%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 12.04 (s, 1H), 10.18 (s, 1H), 6.65 (s, 1H), 6.59 (s, 1H), 5.50 (m, 1H), 3.77 (m, 1H), 3.67 (m, 1H), 1.88-1.59 (m, 6 H). EI-MS: (M^+) *m/z* 370.08.

2-Formyl-3-methoxy-5-(tetrahydropyran-2-yloxy)phenyl triflate (35).

To a solution of 2-formyl-3-hydroxy-5-(tetrahydropyran-2-yloxy)phenyl triflate (**34;** 4.1 g, 11.08 mmol) in DMF was added potassium carbonate (10.0 g, 72.7 mmol) and iodomethane (9.1 g, 64 mmol). The reaction mixture was stirred at 45 °C for 3 h, after which TLC analysis (eluent: 30% EtOAc in hexanes) of the sample showed the reaction to be complete. The mixture was cooled and poured into cold water (100 mL), and the precipitate was washed with water (10 mL) then dried. Crystallization from diisopropyl

ether (25 mL) gave **35** (3.8 g, yield 90.5%) as a white solid mp 109-10 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.28 (s, 1H), 6.59 (s, 1H), 6.56 (s, 1H), 5.48 (m, 1H), 3.90 (s, 3H), 3.78 (m, 1H), 3.75 (m, 1H), 1.94-1.57 (m, 6H). ^{13}C (100 MHz, $CDCl_3$): δ 185.99, 164.35, 163.28, 149.83, 120.50, 177.30, 112.45, 103.53, 99.92, 97.14, 62.17, 56.64, 29.95, 24.99, 18.20. EI-MS: (M^+) *m/z* 384.06.

2-Formyl-3-methoxy-5-hydroxyphenyl triflate (35a).

To a solution of 2-formyl-3-methoxy-5-(tetrahydropyran-2-yloxy)phenyl triflate (**35)** (18 g, 4.69 mmol) in tetrahydrofuran (10 mL) was added trifluoroacetic acid (2 mL) in water (3 mL), and the mixture was stirred at RT overnight. TLC analysis (30% EtOAc in hexanes) showed complete THP-deprotection had occurred. The solution was diluted with ether (50 mL), then washed with water (2 X 25 mL), 5% sodium bicarbonate solution (20 mL) , water (25 mL), and finally with brine (25 mL). After drying over Na_2SO_4, removal of the solvent gave the desired triflate (**35a**) as an oil (1.3 g, yield 92.4%). ^{1}H NMR (300 MHz, DMSO-d_6): δ 11.51 (s, 1H), 10.13 (s, 1H), 6.64 (s, 1H),6.40 (s, 1H), 3.70 (s, 3H). ^{13}CNMR (100 MHz; $CDCl_3$/CD_3OD): δ 186.54, 165.04, 150.12, 120.30, 117.12, 110.47, 102.79, 99.07, 56.40. EI-MS: (M^+) *m/z* 300.12

2-Formyl-3-methoxy-5-(3-*t*-butoxycarbonylaminoprop-1-oxy)phenyl triflate (20g).

To a solution of 2-formyl-5-hydroxy-3-methoxyphenyl triflate (1.1 g, 3.6 mmol) in DMF (25 mL) was added potassium carbonate (1.0 g, 7.2 mmol) followed by 3-(*t*-butyloxycarbonylamino)-1-iodopropane (1.155 g, 4.024 mmol), and the mixture was stirred at 40 °C for 4 h when TLC analysis (30% EtOAc/hexanes) of a sample showed completion of the reaction. The mixture was cooled, poured into ice water (50 mL), and the solid that separated was filtered, washed with water (10 mL), and dried. Purification by silica gel chromatography (eluent hexanes:EtOAc::70:30) afforded the required **20g** as crystalline white solid (1.0 g, yield 60.8%), mp 101-2 °C. ^{1}H NMR (400MHz, $CDCl_3$): δ 10.27 (s, 1H), 6.47 (s, 1H), 6.35 (s, 1H), 4.69 (br, 1H), 4.05 (m, 1H), 3.91 (s, 1H), 3.30 (m, 1H), 1.97(m, 1H), 1.41 (s, 9H). ^{13}C (100 MHz, $CDCl_3$) δ 185.87, 164.79, 164.42, 156.23, 150.07, 123.67, 120.48, 117.29, 112.12, 101.44, 98.46, 79.72, 66.87, 56.67, 37.67, 29.70, 20.45. EI-MS: (M^+) *m/z* 457.18.

2-Formyl-5-hydroxyphenyl triflate (35b)

Starting from 2-formyl-5-(tetrahydropyran-2-yloxy)phenyl triflate[8] (3.5 g, 9.9 mmol) and employing the same acidic conditions used in the removal of the THP group from **35a** led to 2-formyl-5-hydroxyphenyl triflate (2.5 g, yield 92.5%), mp 72-3 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.07, (s, 1H), 7.90 (d, J = 8.7 Hz, 1H), 7.40 (b, 1H), 7.02 (ddd, J = 0.9, 2.4, 8.7 Hz, 1H), 6.91 (d, J = 2.4 Hz, 1H. ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.53, 163.79, 151.48, 133.32, 123.35, 118.56, 116.31, 109.89. ESI-HRMS: $(M+H)^+$ *m/z* 270.9937.

2-Formyl-5-(3-*t*-butoxycarbonylaminopropoxy)phenyl triflate (20h).

Compound **20h** (a gummy solid) was synthesized in 65% yield starting from **35a** by following the same procedure used to obtain **20g**. ^{1}NMR (300 MHz, $CDCl_3$): δ 10.41 (s, 1H0, 7.91 (d, J = 8.4 Hz, 1H), 6.94 (dd, J = 10.8 Hz, 2.1, Hz, 1H), 6.88 (d, J = 2.1Hz, 1H), 4.815 (br, 1H), 4.16 (t, J = 6 Hz, 2 H), 3.66 (q, J = 6.3 Hz, 2H), 2.08 (q, J = 6.3 Hz, 2 H), 1.422 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.77, 161.89, 156.02, 153.94, 130.50, 124.39, 120.09, 116.92, 113.31, 106.17, 77.32, 77.00, 76.68, 37.35, 29.27, 28.13. ESI-HRMS $(M+H)^+$ *m/z* 240.9931.

2-Methoxy-6-(4,4,5,5-tetramethyl[1,3,2]dioxaborolan-2-yl)benzaldehyde (21b).

General method for the synthesis of compounds 21b-21h.

To a solution of 2-formyl-3-methoxyphenyl triflate[8] (1.0 g, 3.5 mmol) in dioxane (25 mL, degassed by nitrogen) were added bis(pinacolato)diboron (1.778 g, 7.0 mmol), potassium acetate (0.987 g, 10.5 mmol) and 1,1'-bis(diphenylphosphino)ferrocene-palladium(II)dichloride dichloromethane complex (120 mg, 0.017 mmol). After degassing for 15 minutes with nitrogen, the reaction mixture was stirred at 90 °C for 1h, then cooled to RT, filtered through Celite, and the solvent was evaporated under reduced pressure. The residue was dissolved in methylene chloride (50 mL), washed with water (2 x 20 mL) followed by brine, and dried over sodium sulfate. The solvent was evaporated, and the residue was extracted with boiling hexanes several times . The combined extracts when cooled gave the desired product **21b** as a solid of acceptable purity (0.8 g; yield 86.6%). This substance was used directly in the next step, since it

was observed that the product decomposed on a silica gel column when further purification was attempted. ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.43 (s, 1H), 7.51 (t, J = 8.7Hz, 1H), 7.05 (d, J = 7.2 HZ, 1H), 6.96 (d, J = 9.0 Hz, 1H), 3.90 (s, 1H), 1.43 (s, 12H). EI-MS: (M^+) *m/z* 262.21.

2,4-Dimethoxy-6-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)benzaldehyde[9] **(21c**). Starting from **20c**,[10] yield of **21c**, 73%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.23 (s, 1H), 6.55 (d, J = 2.1 Hz, 1H), 6.41 (d, J = 1.5 Hz, 1H), 3.86 (s, 6H), 1.44 (s, 12H). EI-MS: (M^+) *m/z* 292.18.

2-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-4-methoxybenzaldehyde[11] **(21d).** Starting from **20d,**[12] yield of **21d**, 77%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.36 (s, 1H), 7.92 (d, j = 7.5 Hz, 1H), 7.28 (d , J = 2.7 Hz, 1H), 7.01 (d, 11.5 HZ, 1H), 3.89 (s, 3H), 1.38 (s, 12H). EI-MS: (M^+) *m/z* 262.19.

2-Methoxymethoxy-6-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)benzaldehyde (21e).

Starting from **20e**, yield of **21e,** 69%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.44 (s, 1H), 7.46 (t, J = 8.0 Hz, 1H), 7.15 (d, J = 8.4 Hz, 1H), 7.08 (d, J = 7.2 Hz, 1H), 5.25 (s, 2H), 3.45, s, 3H), 1.41 (s, 12H). EI-MS: (M^+) *m/z* 292.21.

2-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-6-trifluoromethoxybenzaldehyde (21f).

Starting from **20f**, yield of **21f**, 74%. H NMR (300 MHz, $CDCl_3$): δ 10.56 (s, 1H), 7.63 (t, J = 7.3Hz, 1H), 7.48 (d, J = 6.9 Hz, 1H), 7.33 (d, 9.9Hz, 1H). EI-MS: (M^+) *m/z* 316.16.

2-Methoxy-4-[3-(t-butoxycarbonylamino)-1-propoxy]-6-[4,4,5,5-tetramethyl(1,3-dioxolan-2-yl)]benzaldhyde (21g).

From **20g,** compound **21g** was obtained in **74%** yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.22 (s, 1), 6.53(d, J = 2.5 Hz, 1H), 6.40 (d, J = 2.4 Hz, 1H),4.09 (t, J = 4.5 Hz, 2H),

3.87 (s, 3H), 3.32 (m, 2H), 1.99 (t, J = 6.3Hz), 1.60 (s, 12H), 1.44 (s, 9H). EI-MS: (M^+) *m/z* 435.35.

2-{4,4,5,5-Tetramethyl(1,3-dioxolan-2-yl)]-4-(3-*t*-butoxycarbonylamino-1-propoxy)-benzaldehyde (21h).

Starting from **20h,** compound **21h** was obtained, yield 65%. ^{1}H NMR (300 MHz, $CDCl_3$): 10.36 (s, 1H), 7.92 (d, J = 8.7 Hz, 1H), 7.23 (d, J = 2.4 Hz, 1H), 7.00 (DD, 11.1, 2.7Hz, 1H), 4.75 (br, 1H), 4.10 (t, 6.3 Hz, 2H), 3.35 (m, 2H) 1.95 (m, 2H). 1.40 s, 12H), 1.36 (s, 9H). EI-MS: (M^+) *m/z* 415.27.

14-(Tetrahydropyran-2-yloxymethyl)-8-methoxy-5-nitrophenanthro[3,4-d] dioxole[1,3]. (36b).

General method for the synthesis of compounds 36a- 36h.

A solution of 4-iodo-5-nitromethyl-6-(tetrahydropyran-2-yloxymethyl)benzo[1,3]dioxole (**27)** (3.6 g, 8.55 mmol) in dioxane (40 mL) and water (10mL) was purged with nitrogen gas for 15 minutes. Cesium carbonate (6.5 g, 20 mmol) was added followed by 2-methoxy-6-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzaldehyde (**21b,** 9.54 mmol) and tetrakis(triphenylphosphine)palladium(0) (1.0 g). The mixture was purged with nitrogen gas for 10 additional minutes, then stirred at 95 °C for 7 h under a nitrogen atmosphere. After cooling, the solvent was evaporated, and the residue was dissolved in methylene chloride (25 mL). This solution was washed with water (2 x10 mL), brine (10 mL), then dried over sodium sulfate, filtered, and evaporated to leave a solid residue. The latter, when purified on a silica gel column (eluent CH_2Cl_2:MeOH:: 95:5), afforded the required compound **36b** as a pale yellow solid (2 g, yield 57%), mp 183-4 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.70 (d, J =8.7 1H) 8.60 (s, 1H), 7.65 (t, J = 7.4, 1H), 7.42 (s, 1H) 7.3 (d, J = 7.8 Hz, 1H) 6.23 (d, , J = 4.2 Hz, 2H), 4.85 (abq, J = 13.4 Hz, 2H), 4.54 (m, 1H), 4.03 (s, 3H), 3.81 (m, 1H), 3.51 (m, 1H), 1.80-1.47 (m, 6H). ^{13}C (100 MHz, $CDCl_3$): δ 156.30, 147.00, 146.25, 143.88, 131.31, 129.99, 129.14, 119.92, 119.54, 119.21, 118.56, 116.81, 112.16, 107.27, 101.64, 97.79, 69.02, 62.13, 55.79, 30.29, 25.36, 19.09. EI-MS: (M^+) *m/z* 411.16.

5-(Tetrahydropyran-2-yloxymethyl)-6-nitrophenanthro[3,4-d][1,3]dioxole (36a).

This was prepared using 2-formylphenyl boronic acid **(21a)** under the same experimental conditions as described above. Yield of **36a**, 55%, mp 211-12 °C. ^{1}HNMR (300 MHz, DMSO-d_6): δ 9.12 (d, J = 8.4 Hz, 1H), 8.45 (s, 1H), 8.17 (d, J = 7.8 Hz, 1H), 7.86 (t, J = 7.2 Hz, 1H), 7.77 (t, J = 7.2 Hz, 1H), 7.75 (s, 1H), 6.44 (d, J = 4.2Hz, 2H), 4.74 (abq, J = 13.2 Hz, 2H), 4.46 (m, 1H), 3.646 (m, 1H), 3.34 (m, 1H), 1.60-1.39 (m, 6H). EI-MS: (M^+) *m/z* 381.14.

5-(Tetrahydropyran-2-yloxymethyl)-6-nitro-8,10-dimethoxyphenanthro[3,4-d][1,3]dioxole (36c).

Similarly, starting from **21c** , **36c** was obtained in 58% yield (mp 213-14 ^{o}C). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.55 (s, 1H), 8.23 (d, J = 2. Hz, 1H), 7.41 (s, 1H), 6.68 (d, J = 2.1 Hz, 1H), 6.28 (d, J =6.3 Hz, 2H), 4.82 (abq, J = 12.9 Hz, 2H), 4.53 (m, 1H), 3.84 (m 1H), 3.50 (m, 1H), 1.81-1.45 (m, 6H). EI-MS: (M^+) *m/z* 441.18.

5-(Tetrahydropyran-2-yloxymethyl)-6-nitro-10-methoxyphenanthro[3,4-d][1,3]dioxole (**36d).**

Starting from **20d, 36d** was prepared in 60% yield, mp 170-172 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.62 (d, J =2.7 Hz, 1 H), 8.09 (s, 1H), 8.81(d, J = 8.7 Hz, 1 H), 7.42 (s, 1H), 7.30 (s, 1H), 7.27 (d, J = 6.3Hz, 1H), 6.30 (d, J = 6.3Hz, 2H), 4.86 (abq, J = 13.8 MHz, 2H) 4.71 (m, 1H) 4.0 (s, 3H), 3.80 (m 1H), 3.50 (m, 1H), 1.81-1.45 (m, 6H). EI-MS: (M^+) *m/z* 411.2.

5-(Tetrahydropyran-2-yl-oxymethyl)-6-nitro-8-methoxymethoxyphenanthro[3,4-d][1,3]dioxole (36e).

Starting from **21e,** the yield of **36e** was 60%, mp 190-192 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.79 (d, J = 6 Hz, 1H), 8.6 (s, 1H), 7.65 (t, J = 8.1 MHz7.68 (s, 1H), 7.35 (d, J = 9 Hz, 1H), 6.31 (d, J = 5.7 Hz, 2H), 5.42 (s, 2H), 4.85 (abq, J = 13.8 Hz, 2H), 4.55 (m, 1H), 3.81 (m, 1H), 3.56 (s, 3H), 3.56 (m, 1H)< 1.82-1.45 (m, 6H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 154.21, 147.47, 146.60, 144.09, 131.58, 130.20, 129.46, 120.60, 119.56, 118.81, 116.94, 112.42, 111.26, 101.91, 98.03, 95.11. EI-MS: (M^+) *m/z* 441.2.

5-(Tetrahydropyran-2-yl-oxymethyl)-8-trifluoromethoxy-6-nitrophenanthro[3,4-d][1,3]dioxole (36f).

Starting from **21f**, **36f** was obtained in 61% yield, mp 169-170 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 9.06 (d, J = 6.3 Hz, 1H), 8.25 (s, 1H) 7.89 (t, J = 6. Hz, 1H), 7.76 (d, J = 5.7 Hz, 1H), 7.65 (s, 1H), 6.41 (d, J = 3.9 Hz, 2H), 4.64 (abq, J = 9.9 Hz, 2H), 4.42 (m, 1H), 3.61 (m, 1H), 3.40 (m, 1H), 1.62-1.31 (m, 6H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 148.67, 146.91, 143.86, 131.54, 129.82, 129.16, 125.61, 122.62, 118.18, 118,11, 117.40, 116,31, 112.74, 101.97, 97.93, 30.25, 25.32, 19.11. EI-MS: (M^+) *m/z* 465.16.

5-(Tetrahydropyran-2-yloxymethyl)-6-nitro-8-methoxy-10-[3-(*t*-butoxycarbonyl-amino)prop-1-oxy]phenanthro[3,4-d][1,3]dioxole (36g).

Starting from **21g**, **36g** was obtained in 55% yield, mp 180-182 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.54 (s, 1H), 8.18 (d, 2.1 Hz, 1H), 7.71 (s, 1H), 6.67 (d, J = 2.4Hz, 1H), 6.6.29 (dd, J = 1.8, 5.4 Hz, 2H), 4.8 (abq, J = 12.9 Hz, 2H), 4.79 (b, 1H), 4.53 (t, J = 3.3Hz, 1H), 4.22 (t, 5.7Hz, 2H), 4.0 (s, 3H), 3.8 (m, 1H), 3.51 (m, 1H), 3.41 (m, 2H), 2.08 (m, 2H), 1.77-1.47 (m, 6H), 1.45 (s, 9H). ESI-MS: $(M-H)^-$ *m/z* 583.12.

5-(Tetrahydropyran-2-yloxymethyl)-6-nitro-10-[3-(*t*-butoxycarbonylamino)prop-1-oxy]phenanthro[3,4-d][1,3]dioxole (36h).

Starting from **21h**, **36h** was obtained in 55% yield, mp 149-150 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.59 (d, J = 2.1 Hz), 8.08 (s, 1H), 7.70 (d, J = 8.7 Hz, 1H), 7.41 (s, 1H), 7.26-7.24 (m, 2H), 6.31 (d, J = 6.6 Hz, 2H), 4.92 (abq, J = 13.2 Hz), 4.54 (t, J = 3 Hz, 1H), 4.22 (t, J = 6 Hz, 2H), 3.80 (m, 1H), 3.50 (m, 1H), 3.40 (m, 2H), 2.08 (m, 2H), 1.80-1.48 (m, 6H), 1.44 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.06, 156.27, 146.28, 145.96, 143.98, 132.19, 130.98, 129.42, 125.35, 125.35, 123.29, 118.34, 117.97, 117.16, 112.35, 110.18, 101.95, 98.09, 79.69, 69.37, 66.25, 62.40, 38.19, 30.52, 29.83, 28.61, 25.58, 19.56. ESI-MS: $(M-H)^-$ *m/z* 553.24.

5-Hydroxymethyl-6-nitro-8-methoxyphenanthro[3,4-d][1,3]dioxole (37b).

General method for the removal of the THP group from compounds 37a-37h.

5-(Tetrahydropyran-2-yloxymethyl)-6-nitro-8-methoxyphenanthro[3,4-d][1,3]dioxole (**36b**, 2g, 4.86 mmol) was taken up in 0.1% sulfuric acid in methanol (400 mL). The mixture was heated on a steam bath until homogeneous (~5 min), then cooled, diluted with water (1000 mL), and extracted with ethyl acetate (5 x 200 mL). The organic extracts were washed with water (2 x 200 mL), saturated sodium bicarbonate solution (100 mL) followed by brine, then dried over sodium sulfate. Filtration followed by solvent evaporation under reduced pressure gave **37b** as a yellow solid (1.3 g; yield 96%); mp[13] 253-54 °C (dec.). ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.68 (d, J = 10.2 Hz, 1H), 8.38 (s, 1H), 7.79 (t, J = 8.4Hz, 1H), 7.12 (s, 1H), 7.32 (d, J = 8.1Hz, 1H), 6.40 (s, 2H), 5.38 (t, J = 5.4 Hz, 1H), 4.64 (d, J = 5.4 Hz, 2H), 4.03 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 156.54, 147.29, 147.06, 143.63, 133.79, 131.37, 130.98, 119.39, 119.20, 118.35, 117.96, 115.66, 112.23, 108.94, 102.67, 63.04, 56.76. ESI-MS: $(M-H)^-$ *m/z* 326.16.

5-Hydroxymethyl-6-nitrophenanthro[3,4-d][1,3]dioxole (37a).

Similarly deprotection of **36a** gave the desired product **37a** (yield 96%), mp 192-193 °C (dec.). ^{1}H NMR (300 MHz, DMSO-d_6): δ 9.13 (d, J = 8.4 Hz, 1H), 8.38 (s, 1H), 8.15 (d, J = 9.3 Hz, 1H), 7.84 (t, J = 6.9 Hz, 1H)), 7.75 (t, J = 7.5 Hz, 1H), 7.63 (s, 1H), 6.42 (s, 2H), 5.49 (t, J = 5.4 Hz), 4.65 (d, J = 5.4 Hz, 2H). EI-MS: (M^+) *m/z* 297.1.

5-Hydroxymethyl-6-nitro-8,10-dimethoxyphenanthro[3,4-d][1,3]dioxole (37c).

Deprotection of the THP group of **36c** gave the desired product **37c** (yield 90%), mp 237-238 °C (dec.). ^{1} H NMR (300 MHz, DMSO-d_6): δ 8.29 (s, 1H), 8.17 (d, J = 1.5 Hz, 1H), 7.59 (s, 1H), 6.93 (d, J = 2.1 Hz, 1H), 6.37 (s, 2H), 5.35 (t, J = 5.2 Hz, 1H), 4.60 (d, J = 5.4 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 161.89, 57.61, 146.25, 144.77, 143.28, 133.10, 131.99, 118.85, 117.08, 115.98, 113.55, 102.23, 101.35, 98.97, 62.76, 56.53, 55.81. EI-MS: (M^+) *m/z* 357.12

5-Hydroxymethyl-10-methoxy-6-nitrophenanthro[3,4-d][1,3]dioxole (37d).

Deprotection of the THP group of **36d** gave the desired product **37d** (yield 90%), mp 230-231 °C (dec). ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.49 (s,1H), 8.25 (s, 1H), 8.01 (d, J

= 9, 1H), 7.55 (s, 1H), 7.34 (d, J = 8.4Hz, 1H), 6.34 (s, 2H), 5.31 (t, J = 3.9 Hz), 4.58 (d, J = 3.9, 2H), 3.89 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 160.92, 146.70, 145.85, 143.58, 133.62, 132.02, 131.69, 125.05, 123.27, 117.39, 115.97, 111.16, 109.76, 102.70, 62.97, 56.12. ESI-MS: $(M-H)^-$ *m/z* 326.1.

5-Hydroxymethyl-6-nitro-8-methoxymethoxyphenanthro[3,4-d][1,3]dioxole (37e).
Deprotection of the THP group of **36e** led to **37e** (yield 90%), mp 168-170 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.67 (d, J = 8.7 Hz, 1H), 8.40 (s, 1H), 7.75 (t, J = 8.4 Hz, 1 H0, 7.23 (s, 1H), 7.40 (d, J = 8.1 Hz, 1H), 6.39 (s, 2H0, 5.37 (s, 2H), 5.40 (t, J = 5.4 Hz, 1H), 4.64 (d, J = 5.4 Hz, 2H), 3.46 (s, 3H). ^{13}C NMR spectrum was not recorded due to the poor solubility of the compound. EI-MS: (M^+) *m/z* 357.1.

5-Hydroxymethyl-6-nitro-8-trifluoromethoxyphenanthro[3,4-d][1,3]dioxole (37f).
Deprotection of **36f** gave **37f** (yield 90%), mp 194-196 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 9.13 (d, J = 8.1 Hz, 1H), 8.29 (s, 1H), 7.93 (t, J = 8. 1 Hz, 1H), 7.83 (d, J = 7.8 Hz, 1H), 7.69 (s, 1H0, 6.45 (s, 2H0, 5.47 (t, J = 4.8 Hz, 1H), 4.67 (d, J = 5.1Hz). ^{13}C NMR (100 MHz, DMSO-d_6): δ 149.08, 147.70, 145.42, 143.64, 134.37, 131.29, 130.58, 126.12, 122.17, 119.64, 117.35, 116.39, 116.29, 115.07, 111.82, 103.05, 62.60. EI-MS: (M^+) *m/z* 381.12.

5-Hydroxymethyl-6-nitro-8-methoxy-10-[3-(*t*-butoxycarbonylamino)prop-1-oxy]phenanthro[3,4-d][1,3]dioxole (37g).
Deprotection of THP group of **36g** gave the desired product **37g** (yield 92%), mp 179-180 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.43 (s, 1H), 8.12 (d, J = 1.8 Hz, 1H), 7.50 (s, 1H), 6.5 (d, J = 2.1 Hz, 1 H), 6.28 (s, 1H), 4.78 (s, 2H), 4.2 (t, J = 6 Hz, 1H), 3.98 (s, 3H), 3.40 (m, 1H), 2.07 (m, 1H), 1.45 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.19, 157.86, 146.47, 144.91, 143.92, 132.81, 131.49, 120.00, 117.99, 117.55, 114.87, 112.21, 101.87, 101.68, 99.00, 81.01, 66.19, 64.33, 56.09, 29.87, 28.61. ESI-MS: $(M+Na)^+$ *m/z* 523.13.

5-Hydroxymethyl-6-nitro-10-[3-(t-butoxycarbonylamino)prop-1-oxy]phenanthro-[3,4-d][1,3]dioxole (37h).

Deprotection of **36h** gave the desired product **37h** (yield 90%), mp 189-190 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.57 (d, J = 2.4 Hz, 1H), 7.80 (s, 1H), 7.79 (d, J = 8.8 Hz, 1H), 7.51 (s, 1H), 7.28-7.24 (m, 2H), 6.31 (s, 2H), 4.82 (s, 2H), 4.78 (b, 1), 4,22 (t, J = 6Hz, 2H), 3.41 (m, 2H), 2.09 (m, 2H), 1.44 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.09, 156.30, 146.63, 145.66, 143.82, 132.08, 131.61, 130.94, 124.94, 123.15, 118.00, 116.87, 111.92, 110.18, 102.00, 66.25, 64.35, 38.13, 29.84, 28.61. EI-MS: $(M-H)^-$ *m/z* 469.23.

5-Formyl-6-nitro-8-methoxyphenanthro[3,4-d][1,3]dioxole[9] (38b) by chromic acid oxidation of 37b. This method was used also for the preparation of compounds 38a and 38f.

To a solution of 5-hydroxymethy-6-nitro-8-methoxyphenanthro[3,4-d][1,3]dioxole[13] **(37b)** (100 mg, 0.306 mmol) in acetone (20 mL) was added slowly a solution of chromium trioxide (108 mg) in acetic acid (1.7 mL) and water (0.02 mL), and the mixture was stirred at RT for 6 h, then quenched with 2-propanol (0.1 mL) and further stirred for 15 minutes. The solvent was evaporated under reduced pressure, and ice water was added to the residue. The solid that separated was filtered and washed with water, dried and adsorbed on silica gel (200 mg) using THF (50mL) and then added to a silica gel column. Elution with methylene chloride:methanol::95:5, gave pure **38b** (55mg, yield 55%), whose physical constants were identical to those recorded in the literature,[13] mp 277-78 °C (dec.). ^{1}H NMR (300 MHz, DMSO-d_6): δ9.94 (s, 1H), 8.56 (s, 1H), 8.8.55 (d, J = 8.4 Hz, 1H0, 8.08 (s, 1H), 7.80 (t, J = 5.1 Hz, 1H), 7.33 (d, J = 8.4 Hz, 1H), 6.51 (s, 1H), 4.03 (s, 1H). EI-MS: (M^+) *m/z* 325.14.

5-Formyl-6-nitrophenanthro[3,4-d][1,3]dioxole (38a).

By a similar procedure, oxidation of **37a** gave **38a** (yield 55%), mp 252-55 °C (dec.). ^{1}H NMR (300 MHz, DMSO-d_6): δ 9.98 (s, 1H), 9.07 (d, 1 H, J = 8.4 Hz), 8.67 (s, 1H), 8.28 (d, 1H, J = 7.8 Hz), 8.13 (s, 1H), 7.90 (t , 1H, J = 7.5 Hz), 7.83 (t, 1H, J = 7.5 Hz), 6.56 (s, 2H). EI-MS: (M^+) *m/z* 295.12.

5-Formyl-6-nitro-8-trifluoromethoxyphenanthro[3,4-d][1,3]dioxole (38f).

A similar oxidation of **38f** led to **37f** (yield 60%), mp 247-249 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 10.01 (s, 1H), 9.13 (d, J = 8.4 Hz, 1H), 5.51 (s, 1H), 8.24 (s, 1H), 8.06 (t, J = 8.1 Hz, 1H), 7.91 (d, 8.4Hz, 1H), 6.60 (s, 2H). EI-MS: (M^+) *m/z* 379.11.

5-Formyl-6-nitro-8,10-dimethoxyphenanthro[3,4-d][1,3]dioxole (38c) by oxidation with manganese dioxide. This method was used also for the preparations of 38d, 38e, 38g and 38h.

To a solution of **37c** (500 mg, 1.4 mmol) in acetone (250 mL) was added activated MnO_2 (2.0 g, 23 mmol), and the reaction mixture was stirred under reflux for 6 h, after which TLC analysis (methylene chloride:methanol::95:5) showed completion of the oxidation. The mixture was filtered hot through Celite, and the solids in the funnel were repeatedly extracted with hot methylene chloride (500 mL). The combined organic extracts were evaporated under reduced pressure, then the residue was absorbed on silica gel (500 mg) using THF (50 mL) and purified by silica gel chromatography (eluent: methylene chloride:methanol::95:5) to give the aldehyde **38c** (300 mg, yield 60.3%) as yellow solid, mp 272-274 °C (dec.), identical with the literature value.[13] ^{1}NMR (300 MHz, DMSO-d6): δ 9.92 (s, 1H), 8.52 (s, 1H), 8.08 (s, 2H), 6.99 (s, 1H), 6.51 (s, 2H), 4.04 (s, 3H), 3.96 (s, 3H). EI-MS: (M^+) *m/z* 355.17.

5-Formyl-6-nitro-10-methoxyphenanthro[3,4-d][1,3]dioxole (38d).

By a similar procedure MnO_2 oxidation of **37d** gave aldehyde **38d** (yield 65%), mp 265-267 °C (dec.). ^{1}H NMR (300 MHz, DMSO-d_6): δ 9.96 (s, 1H), 8.65 (s, 1H), 8.56 (s, 1H), 8.25 (d, J = 8.7 Hz), 8.12 (s, 1H), 7.52 (d, J = 8.4 Hz, 1H), 6.56 (s, 2H), 3.98 (s, 3H). EI-MS: (M^+) *m/z* 325.27.

5-Formyl-6-nitro-8-methoxymethoxyphenanthro[3,4-d][1,3]dioxole (38e).

Similarly MnO_2 oxidation of **37e** gave aldehyde **38e** (yield 63%), mp 222-225 °C (dec.). ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.92 (s, 1H), 8.61 (d, J = 8.4Hz,1H), 8.07 (s, 1H), 7.79 (t, J = 5.1 Hz), 7.41 (d, J = 8.4 Hz, 1H), 6.50 (s, 2H), 5.47 (s, 2H), 3.45 (s, 3H). EI-MS: (M^+) *m/z* 355.31.

5-Formyl-6-nitro-8-methoxy-10-[3-(*t*-butoxycarbonylamino)prop-1-oxy]-phenanthro-[3,4-d][1,3]dioxole (38g)

MnO_2 oxidation of **37g** afforded aldehyde **38g** (yield 62%), mp 172-173 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.56 (s, 1H), 8.76 (s, 1H), 8..08 (d, J = 2.7 Hz, 1H), 7.73 (s, 1H), 6.71 (d, J = 1.8Hz, 1H), 6.40 (s, 2H), 4.22 (t, J = 5.7 Hz, 2H), 4.02 (s, 3H), 4.42 (m, 2H), 2.01 (m 2H), 1.45 (s, 9H). EI-MS: (M^+) *m/z* 498.21.

5-Formyl-6-nitro-10-[3-(*t*-butoxycarbonylamino)prop-1oxy]phenanthro[3,4-d][1,3]dioxole (38h).

MnO_2 oxidation of **37h** gave aldehyde **38h** (yield 60%), mp 158-160 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.97 (s, 1H), 8.52 (d, J = 2.4 Hz, 1H), 8.30 (s, 1H), 7.89 (d, J = 8.7 Hz, 1H), 7.73 (s, 1H), 7.32 (dd, J = , 1H), 6.43 (s, 2H), 4.23 (t, J = 6Hz, 2H), 3.42 (m, 2H), 2.10 (m, 2H), 1.45 S, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.44, 160.83, 156.28, 148.13, 146.31, 144.31, 144.23, 131.79, 131.46, 127.85, 127.20, 123.50, 118.76, 118.69, 117.20, 114.00, 110.12, 103.08, 77..91, 66.35, 38.07, 29.85, 28.62. EI-MS: M^+ *m/z* 468.2.

Aristolochic Acid I (AA-I;1) by $NaOCl_2$ oxidation of 5-formyl-6-nitro-8-methoxy-phenanthro-[3,4-d][1,3]dioxole (38b).

General procedure for the oxidation of compounds 38a and 38c-38h to the corresponding carboxylic acids.

To a solution of 5-formyl-6-nitro-8-methoxyphenanthro[3,4-d][1,3]dioxole (**38b;** 35 mg, 0.107 mmol) in DMSO (10 mL) were added separately aqueous solutions of $NaClO_2$ (0.1 mL, 5 M) and NaH_2PO_4 (0.1 mL, 4 M) four times in 30 minutes. The reaction mixture was stirred overnight at RT, then solvent was removed under high vacuum at 60 °C. Water (5 mL) was added to the residue followed by acidification with 2N HCl (0.5 mL). The precipitated solids were filtered, washed with water, and dried to give pure aristolochic acid (AAI, **1;** 28 mg, yield 76.6%), mp.274-76 °C. ^{1}H NMR (400 MHz, DMSO-d6): δ 6.65 (d, J = 9 Hz, 1H), 8.54 (s, 1H), 7.84 (t, J = 8.5 Hz, 1H), 7.78 (s, 1H), 6.47 (s, 2H), 4.05 (s, 3H), identical with literature values.[15,16] ESI-MS: $(M-H)^-$ *m/z* 340.10 (literature values[17,18]).

Aristolochic Acid II. 6-Nitrophenanthro[3,4-d][1,3]dioxole-5-carboxylic acid (AAII; 2).

Similar oxidation of **38a** gave AA II (yield 70%), mp 262-64 °C. ^{1}H NMR1 (300 MHz, DMSO-d_6): δ 9.05 (d, J = 8.1Hz, 1H), 8.59 (s, 1H), 8.26 (d, J = 8.1 Hz, s, 1H), 7.91 (t, J =7.8 Hz, 1H), 7.83 (m,1H), 7.81 (s, 1H), 6.50 (s, 2H), identical with the literature values.[15,16] ESI-MS: $(M-H)^-$ *m/z* 310.32 (literature values[17,18]).

6-Nitro-8,10-dimethoxyphenanthro[3,4-d][1,3]dioxole-5-carboxylic acid. (AA-IV; 1c).

Oxidation of **38c** gave **1c** (yield 62%) identical spectroscopically[15,16] with the natural product. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.5 (s, 1H), 8.13 (d, J = 1.8 Hz, 1H), 7.80 (s, 1H), 6.99 (d, J = 2.1 Hz, 1H), 6.47 (s, 2H), 3.99 (s, 3H). ESI-MS: $(M-H)^-$ *m/z* 370.31 (literature value[18]).

6-Nitro-10-methoxyphenanthro[3,4-d][1,3]dioxole-5-carboxylic acid (AA-III, 1d).

Oxidation of **38d** led to **1d** (yield 65%) identical spectroscopically[15,16] with the natural product. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.53 (s, 1H), 8.52 (d, J = 3 Hz, 1H), 8.2 (d, J = 3.6 Hz, 1H), 7.76 (s, 1H), 7.48 (dd, J = 1.8, 6,6 Hz, 1H), 6.45 (s, 1H), 3.96 (s, 3H). ESI-MS: $(M-H)^-$ *m/z* 340.12 (literature value[18]).

6-Nitro-8-methoxymethoxyphenanthro[3,4-d][1,3]dioxole-5-carboxylic acid (1e).

Oxidation of **38e** gave **1e (**yield 68%). ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.72 (d, J = 8.4 Hz, 1H), 8.61 (s, 1H), 7.86 (t, J = 8.4 Hz, 1H), 7.82 (s, 1H), 7.47 (d, J = 8.1 Hz, 1H), 6.50 (s, 2H), 5.52 (s, 2H), 3.48 (s, 3H). ESI-MS: $(M-H)^-$ *m/z* 370.32.

6-Nitro-8-trifluoromethoxyphenanthro[3,4-d][1,3]dioxole-5-carboxylic acid (1f).

Oxidation of **38f** afforded **1f** (yield 65%). ^{1}HNMR (300 MHz, DMSO-d_6): δ 9.11 (d, J = 8.7 Hz, 1H), 8.44 (s, 1H), 8.03 (t, J = 8.4 Hz, 1H), 7.90 (s, 1H), 7.89 (d, j= 8.1 Hz, 1H), 6.54 (s, 2H). ESI-MS: $(M-H)^-$ *m/z* 394.27.

6-Nitro-8-methoxy-10-[3-aminoprop-1-oxy]phenanthro[3,4-d][1,3]dioxole-5-carboxylic acid hydrochloride (1i·HCl).

Compound **1i·HCl** was synthesized starting from **38g** following the same procedure for oxidation. Thereafter, the crude product (50 mg) was dissolved by heating in DMSO (1mL) then stirring with HCl/ether solution (1 mL, 2 M) over night to remove the Boc protection. This afforded the desired acid **1i** as the hydrochloride salt (yield 60%), mp 257-59 °C (dec.). ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.50 (s, 1H), 8.14 (d, J =1.8 Hz, 1H), 7.82 (b, 2H), 7.80 (s, 1H), 7.00 (d, J = 2.1 Hz, 1H), 6.46 (s, 1H), 4.28 (t, J = 5.7Hz, 2H), 4.05 (s, 3H), 3.05 (m, 2H), 2.12 (m 2H). ESI-MS: $(M+H)^+$ *m/z* 451.0.

6-Nitro-10-(3-aminopropoxy)phenanthro[3,4-d][1,3]dioxole-5-carboxylic acid hydrochloride (1j·HCl).

Compound **1j·HCl** was synthesized starting from **38h** following the same $NaOCl_2$ oxidation procedure as for **38g**. The crude product (50 mg) was dissolved by heating in DMSO (1mL) then stirred with HCl/ether solution (1 mL, 2 M) overnight to remove the Boc protection. This afforded the desired acid **1j** as the hydrochloride salt (yield 60%), mp 245-46 °C (dec). ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.53 (s, 1H), 8.52 (d, J = 1.6Hz, 1H), 8.2 (d, J = 6.6 Hz, 1H), 7.82 (b, 2H), 7.7 (s, 1H), 7.75 (d, J = , 1H), 6.46 (s, 1H), 4.26 (t, 4.2Hz, 2H), 2.99 (m, 2H), 2.08 (m, 2H). ESI-MS: $(M+H)^+$ *m/z* 321.2.

B. Synthesis of Aristolactams

Methyl 4,5-methylenedioxytoluate (44).

Step (a): Acid formation from the aldehyde. To a solution of 4,5-methylenedioxytolualdehyde[19] (**43**; 5 g, 30.5 mmol) in a mixture of acetonitrile (60 mL) and sodium dihydrogen phosphate (1.0 g, 7.25 mmol) in water (12 mL) was added a solution of sodium chlorite (4.8 g, 53 mmol) in water (40 mL). Hydrogen peroxide (3 mL, 30% solution in water) was added, and the mixture was stirred at 15 °C for 2 h. Then an additional amount of sodium chlorite (0.5 g, 5.5 mmol in 4 mL water) was added with stirring continuing overnight at RT. The reaction mixture was quenched with sodium

sulfite (0.3 g, water 2 mL) solution and acidified with conc. HCl (3 mL). The resulting white precipitate was filtered and washed with water, then dried to give 4,5-methylenedioxytoluic acid. Crystallization from isopropanol afforded the pure material, (4.5 g, yield 72.8%), mp 89 °C.[14] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.52 (s, 1H), 6.72 (s, 1H), 6.02 (s, 2H), 2.60 (s, 3H).

Step (b) Methyl Ester (44) . To a solution of the product of Step (a) (34 g, 188.8 mmol) in dichloromethane (300 mL) was added a saturated sodium bicarbonate solution (400 mL), containing tetrabutylammonium bromide (950 mg) followed by dimethyl sulfate (25 mL), and the mixture was stirred vigorously at RT overnight. The layers were separated, and the organic layer was washed with water (2 x 100 mL), then brine (50 mL), dried over anhydrous sodium sulfate, filtered, and the solvent evaporated under reduced pressure. The solid thus obtained was crystallized from hexanes to give the known[20] **44** as a white crystalline product (32 g, 87.3%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40 (s, 1H), 6.69 (s, 1H), 5.98 (s, 2H), 3.85 (s, 3H), 2.54 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.12, 150.51, 145.51, 136.83, 122.15, 111.41, 110.27, 101.53, 51.63, 22.00. ESI-HRMS: $(M+1)^+$ *m/z* 217.1092.

Methyl 2-bromomethyl-3-bromo-4,5-methylenedioxybenzoate (45)

Step (a): Nuclear Bromination. To a solution of methyl 4,5-methylenedioxytoluate (**44)** (11g , 56.7 mmol) in 150 mL of CHCl2 (100 mL) and acetic acid (10 mL) at 0 °C was added bromine (3.1 mL, 60.8 mmol) drop-wise over 10 min. The ice bath was removed, and the reaction mixture was stirred at RT for 48 h after which NMR analysis indicated completion of the reaction. Saturated aqueous $Na_2S_2O_3$ solution (100 mL) was added, and the phases were separated. The aqueous layer was re-extracted with dichloromethane (2 × 50 mL), and the combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was crystallized from di-isopropyl ether to give methyl 3-bromo-4,5-methylenedioxy-2-methylbenzoate as a white solid (13 g, yield 84%), mp 154-55 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.27 (s, 1H), 6.05 (s, 2H), 3.84 (s, 3H), 2.58 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.99, 149.01, 145.00, 134.80, 124.35, 109.21, 105.35, 101.90, 52.12, 19.58. EI-MS: (M^+) *m/z* 271.91.

Step (b): Side Chain Bromination. To a dichloroethane (160 mL) solution of the ester synthesized in Step (a) (17.6 g , 64.7 mmol) was added *N*-bromosuccinimide (16.56 g, 105.6 mmol) and ACCN (1.0 g)[21]. The reaction mixture was stirred at reflux temperature for 16 h, cooled to RT, and further diluted with dichloromethane (100 mL). The mixture was washed with saturated aqueous $Na_2S_2O_3$ solution (100 mL) followed by water (2 x 100 mL) and brine (100mL). The organic layer was dried over anhydrous Na_2SO_4 and filtered, and the solvent was evaporated under reduced pressure. The resultant solid was crystallized from di-isopropyl ether to give methyl 2-bromomethyl-3-bromo-4,5-methylenedioxybenzoate **45** (16 g, yield 70.2%), mp 103-104 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40 (s, 1H), 6.14 (s, 2H), 5.14 (s, 2H), 3.92 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.71, 149.70, 147.08, 133.56, 124.70, 110.09, 105.40, 102.43, 52.55, 29.86.

4-Bromo-5,6-methylenedioxy-1*H*,2-dihydro-*N*-hydroxyisoindol-1-one (46a) and its *O*-*t*-butyldimethylsilyl derivative (46b).

Step (a): Lactam formation. To a solution of methyl 2-bromomethyl-3-bromo-4,5-methylenedioxybenzoate **(45)** (2.0 g, 5.71 mmol) in THF (20 mL) was added hydroxylamine hydrochloride (2 g) and 1 N sodium hydroxide solution (30 mL). The reaction mixture was stirred at RT for 24 h, and the white precipitate was removed by filtration, washed with water, and crystallized from isopropanol to give **46a** as a white crystalline solid (1.13 g, yield 73%), mp 259-60 °C. ^{1}HNMR (300 MHz,d_6DMSO): δ 7.15 (s, 1H), 7.01 br, 1H), 6.22 (s, 2H), 4.40 (S, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 163.57, 148.81, 148.35, 133.59, 125.93, 102.67, 102.15, 95.90, 51.93. ESI-HRMS: $(M+H)^+$ *m/z* 271.9586.

Step (b): Silylation. A suspension of **46a** (841 mg, 3.1 mmol) and TBDMSCl (900 mg, 6 mmol) in pyridine (20mL) was stirred under nitrogen at RT overnight. The solution became homogeneous within a 4 h period. The pyridine was evaporated under reduced pressure, and the residue was dissolved in methylene chloride (50 mL), washed with saturated sodium bicarbonate solution (20 mL), water (2 x 20 mL), and brine (20 mL), and dried over sodium sulfate. Evaporation of the solvent gave a solid which was crystallized from isopropyl ether to give **46b**, (1.0 g, yield 84%) as white crystalline solid,

mp 171-72 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.36 (s, 1H), 6.14 (s, 2H), 4.35 (s, 2H), 1.02 (s, 9H), 0.29 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.57, 149.48, 148.71, 134.18, 125.92, 103.02, 96.29, 53.38, 25.71, -4.92. ESI-HRMS: $(M+H)^+$ *m/z* 386.0443.

Benzo[*f*]-1,3-benzodioxolo[6,5,4-*cd*]-6-hydroxy-8-methoxyindol-5(6*H*)-one, (*N*-hydroxyaristolactam I) (7).

To a solution of the TBDMS protected bromolactam **46b** (100 mg, 0.26 mmol) in dioxane (10mL purged with N2) was added 2-methoxy-6-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzaldehyde **21b** (100 mg, 1.69 mmol) and a solution of potassium carbonate (50 mg, 0.36 mmol) in water (0.3 mL, N2 purged). The catalyst, 1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II)·CH_2Cl_2, (15 mg) was added, and the mixture was heated under nitrogen at 100 °C for 16 h. The solution was cooled, and the solvent evaporated under reduced pressure. The residue was suspended in ethyl acetate (10 mL) and filtered, and the collected solid was washed with water then dried. It was adsorbed onto silica-gel by dissolving in THF:DMSO::80:20 and drying the suspension under reduced pressure. The resulting solid was added to the top of a silica gel column which was eluted using methanol:methylene chloride::2.5:97.5 to obtain the pure desired *N*-hydroxyaristolactam I (**7)** as a yellow solid (60 mg, yield 74.6%), mp dec. > 290 °C. ^{1}HNMR (300 MHz, DMSO-d_6); δ 10.85 (s, 1H), 8.10 (d, 1H, J = 9Hz), 7.70 (s, 1H), 7.52 (t, 1H, J = 14.1Hz), 7.41 (s, 1H), 7.21 (d, 1H, J = 8.1Hz), 6.54 (s, 2H), 4.0 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 163.44, 155.95, 149.26, 147.76, 134.63, 126.79, 125.72, 123.97, 119.27, 116.38, 111.27, 109.03, 96.93, 56.38. ESI-HRMS: $(M+H)^+$ *m/z* 310.2720.

Benzo[*f*]-1,3-benzodioxolo[6,5,4-*cd*]-6-hydroxyindol-5(6*H*)-one, (*N*-Hydroxyaristo-lactam II) (8).

To a solution of the TBDMS protected bromolactam **46b** (385 mg, 1mmol) and 2-formylphenyl boronic acid **21a** (200 mg, mmol) in N_2 purged acetonitrile (20 mL) was added a solution of potassium carbonate (200 mg, 1.46 mmol) in water (1.2 mL, N_2 purged) followed by the catalyst, 1,1′-bis(diphenylphosphino)ferrocene]dichloro-palladium(II)·CH_2Cl_2. The reaction mixture was stirred under a nitrogen atmosphere at

85 °C for 4h then cooled, and the solvent was removed under reduced pressure. The residue was suspended in water, filtered and washed with water, then dried. The crude product was purified by column chromatography following the procedure used for compound **7**. This led to N-hydroxyaristolactam II (**8**; 150 mg, yield 54%), mp dec. > 280 °C. ^{1}HNMR (300 MHz, DMSO-d_6): δ 8.55 (d, J = 6.9 Hz, 1H), 8.04 (d, J = 9.3 Hz, 1H), 7.72 (s, 1H), 7.61 (m, 2H), 7.31 (s, 1H), 6.47 (s, 2H). ESI-HRMS: $(M+H)^+$ *m/z* 280.0661.

***N*-Sulfonatooxyaristolactam I (9).**

To a suspension *N*-hydroxyaristolactam I (**7**; 77 mg, 0.25 mmol) in anhydrous pyridine (2 mL) was added pyridine-sulfur trioxide complex (52 mg), and the mixture was stirred under a nitrogen atmosphere overnight at RT. Pyridine was evaporated under vacuum, and the residue was triturated with ether. The insoluble yellow solid was filtered and washed with ether, then dried under vacuum to give the desired *N*-sulfonato-oxyaristolactam I, (**9**; 90 mg quantitative yield). No further attempts were made to purify the compound. The ^{1}H NMR (DMSO- d_6) shows that the product contains two molecules of pyridine per mole of product. ^{1}HNMR (300 MHz, DMSO-d_6): δ 8.88 (pyridine), 8.81 (pyridine), 8.17 (d, 1H), 7.99 (pyridine), 7.74 (s, 1H), 7.69 (s, 1H), 7.55 (t, 1H, J = 8.1 Hz), 7.23 (d, 1H, j + 7.8 Hz), 6.48 (s, 2H), 4.01 (s, 1H). ESI-HRMS: $(M+H)^+$ *m/z* 388.0654.

***N*-Sulfonatooxyaristolactam II (10).**

To a suspension *N*-hydroxyaristolactam II (**8**; 50 mg, 0.18 mmol) in anhydrous pyridine (3 mL) was added pyridine-sulfur trioxide complex (37 mg), and the mixture was stirred under a nitrogen atmosphere overnight at RT. The pyridine solvent was evaporated under vacuum, and the residue was triturated with ether. The insoluble yellow solid was filtered and washed with ether, then dried under vacuum to give the desired *N*-sulfonatooxyaristolactam II, (**10**; 50 mg, yield 90%). No further attempts were made to purify the compound. The ^{1}H NMR spectrum (DMSO-d_6) shows that the product contains two molecules of pyridine per mole of product. ^{1}H NMR (300 mHz, DMSO-d_6); d 8.88 (pyridine), 8.55 (pyridine), 8.52 (d, 1H), 8.32 (s, 1H), 8.01 (pyridine), 7.99 (d, 1H), 7.72 (s, 1H), 7.61 (m, 2H), 6.48 (s, 2H). ESI-MS: $(M+H)^+$ *m/z* 358.30.

***N*-acetoxyarisolactam I (39).**

To a suspension of *N*-hydroxyaristolactam I (**7**; 0.25 mmol) in anhydrous pyridine (1 mL) acetic anhydride (0.1 mL) was added, and the reaction mixture was stirred under a nitrogen atmosphere overnight. The pyridine and excess acetic anhydride were evaporated under high vacuum, and the residue was triturated with ether and filtered. The solid thus obtained was washed with ether and dried under vacuum to give the desired N-acetoxyaristolactam I **39** (70 mg; quantitative yield). No further attempts were made to crystallize the product which by NMR analysis appeared to be pure (>97%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (d, 1H, J = 8.4 Hz), 7.61 (s, 1H), 7.47 (t, 1H, 7 = 7.46), 7.23 (s, 1H), 7.03 (d, 1H, J =8 Hz), 6.34 (s, 2H), 4.01 (s, 3H), 2.46 (s, 3H). ^{13}C NMR (400 MHz, $CDCl_3$): δ 167.77, 163.37, 156.16, 149.11, 148.44, 132.81, 126.58, 124.19, 122.06, 119.75, 115.71, 112.28, 108.11, 106.97, 106.85, 103.06, 98.44, 56.01, 18.36. ESI-MS: $(M+H)^+$ *m/z* 351.15.

***N*-Acetoxyaristolactam II (40)**.

Following the procedure used to obtain **39,** but starting from N-Hydroxyaristolactam II (**8**), *N*-acetoxyaristolactam II (**40)** was prepared in almost quantitative yield. ^{1}H NMR ($CDCl_3$): δ 8.65 (m, 1H), 7.81 (m, 1H), 7.64 (s, 1H), 7.58 (m 2H), 7.02 (s, 1H), 6.40 (s, 2H), 2.47 (s, 3H). EI-MS: (M^+) *m/z* 312.2.

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