Design, Synthesis and Biochemical Evaluation of Novel Ethanoanthracenes and Related Compounds to Target Burkitt’s Lymphoma

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Experimental details for preparation and characterisation of compounds 11a-11n, 11p-11r, 20a, 20f, 20g, 21a-j, 22a-c, 22e.

Materials and Methods: Chemistry

All reagents were commercially available and were used without further purification unless otherwise indicated. Tetrahydrofuran (THF) was distilled immediately prior to use from Na/Benzophenone under a slight positive pressure of nitrogen, toluene was dried by distillation from sodium and stored on activated molecular sieves (4Å) and dichloromethane was dried by distillation from calcium hydrate prior to use. Uncorrected melting points were measured on a Gallenkamp SMP 11 melting point apparatus. Infra-red (IR) spectra were recorded as thin film on NaCl plates, or as potassium bromide discs on a Perkin Elmer FT-IR Spectrum 100 spectrometer. 1H and 13C nuclear magnetic resonance (NMR) spectra were recorded at 27°C on a Bruker Avance DPX 400 spectrometer (400.13 MHz, 1H; 100.61 MHz, 13C) at 20 °C in either CDCl3 (internal standard tetramethylsilane TMS) or CD3OD by Dr. John O’Brien and Dr. Manuel Ruether in the School of Chemistry, Trinity College Dublin. For CDCl3, 1H-NMR spectra were assigned relative to the TMS peak at δ 0.00 ppm and 13C-NMR spectra were assigned relative to the middle CDCl3 triplet at δ 77.00 ppm. For CD3OD, 1H and 13C-NMR spectra were assigned relative to the centre peaks of the CD3OD multiplets at δ 3.30 and 49.00 ppm respectively. Electrospray ionisation mass spectrometry (ESI-MS) was performed in the positive ion mode on a liquid chromatography time-of-flight (TOF) mass spectrometer (Micromass LCT, Waters Ltd., Manchester, UK) equipped with electrospray ionization (ES) interface operated in the positive ion mode at the High Resolution Mass Spectrometry Laboratory by Mr. Brian Talbot in the School of Pharmacy and Pharmaceutical Sciences, Trinity College Dublin and Dr. Martin Feeney in the School of Chemistry, Trinity College Dublin. Mass measurement accuracies of < ±5 ppm were obtained. Low resolution mass spectra (LRMS) were acquired on a Hewlett-Packard 5973 MSD GC-MS system in electron impact (EI) mode. Rf values are quoted for thin layer chromatography on silica gel Merck F-254 plates, unless otherwise stated. Flash column chromatography was carried out on Merck Kieselgel 60 (particle size 0.040-0.063 mm). Chromatographic separations were also carried out on Biotage SP4 instrument. All products isolated were homogenous on TLC. Analytical high-performance liquid chromatography (HPLC) to determine the purity of the final compounds was performed using a Waters 2487 Dual Wavelength Absorbance detector, a Waters 1525 binary HPLC pump, a Waters In-Line Degasser AF and a Waters 717plus Autosampler. The column used was a Varian Pursuit XRs C18 reverse phase 150 x 4.6 mm chromatography column. Samples were detected using a wavelength of 254 nm.
General procedure 1: preparation of phenyl and benzyl maleimides (11a-11n, 11p-11r)

To a solution of maleic anhydride (20 mmol) dissolved in diethyl ether (25 mL) was added the appropriate benzyl or aryl amine (20 mmol) dissolved in diethyl ether (10 mL). The reaction was stirred under reflux at RT for 1 h. The precipitated solid was isolated by filtration and washed with diethyl ether. This solid was immediately used in the next step and placed in a conical flask containing sodium acetate (0.7 g) and acetic anhydride (10 mL). This mixture was heated to 90 °C for 0.5 h, after which the mixture was poured over ice water (100 mL). The precipitated solid was isolated by filtration and recrystallised from ethanol.

1-Benzyl-1H-pyrrole-2,5-dione (11a)

Preparation as described above from maleic anhydride (20 mmol) and benzyl amine (20 mmol) according to general procedure 1. The product was obtained as tan crystals, 1.51 g (40%), Mp. 69-72 °C (lit. M.p. 68-69 °C [1]). IR νmax (KBr): 3039, 2947, 1700 (C=O), 1631 (C=C), 1530, 1496, 1456, 1137 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 4.64 (s, 2 H, CH₂), 6.66 (s, 2 H, HC=CH), 7.11 - 7.41 (m, 5 H, 5 x ArH). ¹³C NMR (101 MHz, CDCl₃) δ 41.3 (CH₃), 127.7 (CH), 128.1, 128.2 (CH), 128.6 (CH), 128.8, 130.9, 134.1 (HC=CH), 136.1, 170.3 (O=C). HRMS (APCI) calculated for C₁₀H₁₀N₂O₂ [M⁺+H] 188.0712: found 188.0705.

1-(3,4,5-Trimethoxybenzyl)-1H-pyrrole-2,5-dione (11b)

Preparation as described above from maleic anhydride (20 mmol) and 3,4,5-trimethoxybenzyl amine (20 mmol) according to general procedure 1. The product was obtained as brown crystals, 1.11 g (20%), Mp. 135-138 °C (lit. M.p. 128-130 °C [2]). IR νmax (KBr): 3017, 2990 (C-H), 1709 (C=O), 1592 (C=C), 1508, 1429 (C=C), 1464 (CH₂), 1358 (CH₃), 1122 (C-N) cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 3.75 - 3.85 (m, 9 H, 3 x OCH₃), 4.56 (s, 2 H, CH₂), 6.57 (s, 2 H, HC=CH), 6.69 (s, 2 H, CH₃), 6.81 (s, 2 H, HC=CH), 7.29 (d, J = 8.54 Hz, 2 H, 2 x ArH), 7.41 (d, J = 8.54 Hz, 2 H, 2 x ArH). ¹³C NMR (101 MHz, CDCl₃) ppm 41.6 (CH₃), 56.0 (m-CH₃ x 2), 60.7 (p-CH₃), 76.7, 77.3, 105.6 (CH), 131.8, 134.1 (HC=CH), 137.5, 135.2, 170.3 (O=C). HRMS (APCI) calculated for C₁₅H₁₇N₂O₃ [M⁺+H] 278.1025.

1-(4-Chlorophenyl)-1H-pyrrole-2,5-dione (11c)

Preparation as described above from maleic anhydride (20 mmol) and 4-chloroaniline (20 mmol) according to general procedure 1. The product was obtained as yellow crystals, 2.29 g (55%), Mp. 98-100 °C (lit. M.p. 109-110 °C [3]). IR νmax (KBr): 3116, 3075, 2924 (C-H), 1583 (Ar C=O), 1497, 1452 (C=C), 1712 (C=O), 1149 (C-N) cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.32 (m, 4 H, 4 x ArH). ¹³C NMR (101 MHz, CDCl₃) ppm 21.1 (CH₃), 126.0 (CH), 128.5, 129.8 (CH), 134.1 (HC=CH), 138.0, 169.7 (O=C). HRMS (APCI) calculated for C₁₀H₁₀ClN₂O₂ [M⁺+H] 208.0165: found 208.0165.

1-(4-Methylphenyl)-1H-pyrrole-2,5-dione (11d)

Preparation as described above from maleic anhydride (20 mmol) and 4-methylaniline (20 mmol) according to general procedure 1. The product was obtained as yellow crystals (40%), Mp. 145-155 °C (lit. M.p. 148 °C [3]). IR νmax (KBr): 3075, 2924 (C-H), 1707 (C=O), 1517, 1449 (C=C), 1585.38 (C=C), 1314 (CH₃), 1152 (CN) cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 2.37 (s, 3 H, CH₃), 6.81 (s, 2 H, HC=CH), 7.16 - 7.32 (m, 4 H, 4 x ArH). ¹³C NMR (101 MHz, CDCl₃) ppm 21.1 (CH₃), 126.0 (CH), 128.5, 129.8 (CH), 134.1 (HC=CH), 138.0, 169.7 (O=C).

HRMS (APCI) calculated for C₁₀H₁₀ClN₂O₂ [M⁺+H] 208.0165: found 208.0165.

1-(4-(Dimethylamino)phenyl)-1H-pyrrole-2,5-dione (11e)

Compound 11e was prepared from maleic anhydride (20 mmol) and N,N-dimethylbenzene-1,4-diamine (20 mmol) according to general procedure 1. The product was obtained as red crystals, 1.52 g (35%), Mp. 159-162 °C (lit. M.p. 153-154 °C [4]). IR νmax (KBr): 3066, 2984 (C-H), 1693 (C=O), 1520,
1447.01 (C=C), 1568 (C=C), 1153 (CN) cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 2.98 (s, 6 H, 2 x CH₃), 6.77 (d, J = 9.16 Hz, 2 H, 2 x ArH), 6.80 (s, 2 H, 2 x =CH), 7.14 (d, J = 8.55 Hz, 2 H, 2 x ArH). ¹³C NMR (101 MHz, CDCl₃) ppm 40.4 (2 x CH₃), 112.4 (CH), 119.4, 127.2 (CH), 134.0 (CH), 150.1, 170.2 (C=O). HRMS (APCI) calculated for C₁₂H₁₀N₂O₃ [M⁺+H] 217.0977: found 217.0975.

1-(4-Benzoylphenyl)-1H-pyrrole-2,5-dione (11f)

Compound 11f was prepared from maleic anhydride (20 mmol) and (4-aminophenyl)(phenyl)methane (20 mmol) according to general procedure 1. The product was obtained as a yellow solid, 1.61 g (29%), Mp. 149-159 °C (lit. M.p. 162-164 °C [5]). IRνmax (KBr): 3093, 2988 (C-H), 1711 (C=O), 1592, 1510 (C=C), 1148 (CN) cm⁻¹. ¹H NMR (400 MHz, DMSO-d₆) δ 7.23 (s, 2 H, 2 x =CH), 7.55 - 7.59 (m, 4 H, 4 x ArH), 7.67 (d, J = 7.32 Hz, 1 H, 1 x ArH), 7.76 (d, J = 7.32 Hz, 2 H, 2 x ArH), 7.85 (d, J = 8.55 Hz, 2 H, 2 x ArH). ¹³C NMR (101 MHz, DMSO-d₆) ppm 126.1 (CH), 128.6 (CH), 129.7 (CH), 129.7 (CH), 130.3 (CH), 132.8 (CH), 134.9 (CH), 135.3, 135.7, 136.8, 169.6 (2 x NC=O), 195.0 (C=O). HRMS (APCI) calculated for C₁₂H₁₀N₂O₃ [M⁺+H] 278.0817: found 278.0817.

2-(2,5-Dioxo-2,5-dihydro-1H-pyrrol-1-yl)phenyl acetate (11g)

Compound 11g was prepared from maleic anhydride (20 mmol) and 2-aminophenol (20 mmol) according to general procedure 1. The product was obtained as a colourless solid 0.84 g (18%), Mp. 70-75 °C [6]. IRνmax (KBr): 3098, 2988 (C-H), 1707 (C=O), 1504, 1456 (C=C), 1586.53 (C=C), 1156 (CN) cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 2.15 (s, 3 H, CH₃), 6.82 (s, 2 H, 2 x =CH), 7.19 - 7.34 (m, 3 H, 3 x ArH), 7.35 - 7.47 (m, 1 H, 1 x H3), ¹³C NMR (101 MHz, CDCl₃) ppm 20.7 (CH₃), 123.0, 123.8 (CH), 126.2 (CH), 129.2 (CH), 129.7 (CH), 134.4 (CH), 146.1, 167.9 (C=O), 168.6 (2 x NC=O). HRMS (APCI) calculated for C₁₉H₁₂O₃ [M⁺+H] 232.0610: found 232.0616.

1-(3-Chloroanilinophenyl)-1H-pyrrole-2,5-dione (11h)

Compound 11h was prepared from maleic anhydride (20 mmol) and 3-chloroaniline (20 mmol) according to general procedure 1. The product was obtained as a yellow oil, 2.28 g (55%), Mp. 96-102 °C [7]. IRνmax (KBr): 3107, 3083 (C-H), 1712 (C=O), 1577, 1542 (C=C), 1591 (C=C), 1143 (CN) cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 6.80 (s, 2 H, 2 x =CH), 7.21 - 7.26 (m, 1 H, H2), 7.27 - 7.38 (m, 3 H, 3 x ArH). ¹³C NMR (101 MHz, CDCl₃) ppm 123.8 (CH), 125.9 (CH), 127.8 (CH), 129.9 (CH), 132.3, 134.1 (CH), 134.4, 168.8 (C=O). HRMS (APCI) calculated for C₁₉H₁₉ClNO₂ [M⁺+Cl⁻] 207.0087; found 207.0097.

3-(2,5-Dioxo-2,5-dihydro-1H-pyrrol-1-yl)phenyl acetate (11i)

Compound 11i was prepared from maleic anhydride (20 mmol) and 3-aminophenol (20 mmol) according to general procedure 1. The product was obtained as a yellow oil, 1.99 g (43%) [6]. IRνmax (KBr): 3103, 2988 (C-H ), 1709 (C=O), 1489, 1449 (C=C), 1595 (C=C), 1369 (CH₃), 1191 (CN) cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 2.27 (s, 3 H, CH₃), 6.81 (s, 2 H, 2 x =CH), 7.06 - 7.13 (m, 1 H, 1 x ArH), 7.17 (t, J = 2.14 Hz, 1 H, 1 x ArH), 7.23 - 7.29 (m, 1 H, 1 x ArH), 7.37 - 7.48 (m, 1 H, 1 x ArH). ¹³C NMR (101 MHz, CDCl₃) ppm 21.0 (CH₃), 119.0 (CH), 120.9 (CH), 122.8 (CH), 129.6 (CH), 132.1, 134.2 (CH), 150.8, 169.0 (C=O), 169.1 (2 x N=O). HRMS (APCI) calculated for C₁₂H₁₀NO₃ [M⁺+H] 232.0610: found 232.0617.

1-(3,4-Dimethoxyphenethyl)-1H-pyrrole-2,5-dione (11j)

Compound 11j was prepared from maleic anhydride (20 mmol) and 2-(3,4-dimethoxyphenyl)ethan-1-amine (20 mmol) according to general procedure 1. The product was obtained as a yellow solid 0.79 g (15%), Mp. 138-144 °C [8]. IRνmax (KBr): 3093, 2988 (C-H), 1698 (C=O), 1608, 1514.87 (C=C), 1592 (C=C), 1261 (CH₃), 1140 (CN) cm⁻¹. ¹H NMR (400 MHz, DMSO-d₆) δ 2.74 (t, J = 7.32 Hz, 2 H, CH₂), 3.62 (t, J = 7.32 Hz, 2 H, CH₂), 3.71 (s, 3 H, OCH₃), 3.70 (s, 3 H, OCH₃), 6.64 (dd, J = 8.24, 1.53 Hz, 1 H, 1 x ArH), 6.74 (d, J = 1.83 Hz, 1 H, H2¹), 6.82 (d, J = 7.94 Hz, 1 H, 1 x ArH), 6.97 (s, 2 H, 2 x =CH). ¹³C NMR (101 MHz, DMSO-d₆) ppm 33.2 (CH₂), 38.6
(CH₃), 55.4 (OCH₃), 55.4 (OCH₃), 111.7 (CH), 112.3 (CH), 120.5 (CH), 1305, 134.4 (CH), 147.4, 148.6, 170.8 (C=O). HRMS (APCI) calculated for C₁₄H₁₁NO₄[M+H] 262.1079: found 262.1074.

Methyl 4-(2,5-dioxo-2,5-dihydro-1H-pyrrrole-1-yl)benzoate (11k)

Compound **11k** was prepared from maleic anhydride (20 mmol) and methyl 4-aminobenzoate (20 mmol) according to general procedure 1. The product was obtained as a colourless solid 1.85 g (40%). Mp. 161-168 °C (lit. M.p. 161-163 °C [9]). IR ₉max (KBr): 3108, 2958 (C-H), 1705 (C=O), 1601, 1510 (C=C), 1585.52 (C=C), 1140 (CN) cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 3.91 (s, 3 H, OCH₃), 6.86 (s, 2 H, 2 x =CH), 7.48 (m, j = 8.55 Hz, 2 H, 2 x ArH), 8.11 (m, j = 8.55 Hz, 2 H, 2 x ArH). ¹³C NMR (101 MHz, CDCl₃) ppm 52.2 (OCH₃), 123.0 (CH), 130.5, 134.4 (CH), 147.4, 148.6 (C=O). HRMS (APCI) calculated for C₁₄H₁₁NO₄[M+H] 233.0692: found 233.0692.

1-(3,5-Dimethoxyphenyl)-1H-pyrrrole-2,5-dione (11l)

Compound **11l** was prepared from maleic anhydride (20 mmol) and 3,5-dimethoxyaniline (20 mmol) according to general procedure 1. The product was obtained as a yellow solid. 3.21 g (69%), Mp. 161-168 °C (lit. M.p. 121.8 °C [10]). IR ₉max (KBr): 3073, 2988 (C-H), 1717 (C=O), 1602, 1453 (C=C), 1475 (C=C), 1146 (CN) cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 3.79 (s, 6 H, 2 x OCH₃), 6.44 - 6.51 (m, 3 H, 3 x ArH), 6.83 (s, 2 H, 2 x =CH). ¹³C NMR (101 MHz, CDCl₃) ppm 55.4 (OCH₃), 124.5 (CH), 129.0, 130.3 (CH), 134.3 (CH), 135.3, 166.1 (C=O), 168.9 (2 x NC=O). HRMS (APCI) calculated for C₁₂H₁₀NO₄[M+] 232.0680: found 232.0680.

1-(4-Fluorophenyl)-1H-pyrrrole-2,5-dione (11m)

Compound **11m** was prepared from maleic anhydride (20 mmol) and 4-fluoroaniline (20 mmol) according to general procedure 1. The product was obtained as yellow crystals. 2.48 g (65%), Mp. 160-162 °C (lit. M.p. 136-138 °C [11]). IR ₉max (KBr): 3073, 2988 (C-H), 1708 (C=O), 1601, 1584 (Ar C=C), 1514 (C=C), 1148 (CN) cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 6.85 (s, 2 H, =CH), 7.16 (t, j = 8.55 Hz, 2 H, 2 x ArH), 7.33 (dd, j = 9.16, 4.88 Hz, 2 H, 2 x ArH). ¹³C NMR (101 MHz, CDCl₃) ppm 116.0 (CH), 116.2 (CH), 127.8 (CH), 127.9, 134.2 (CH), 160.5, 163.0, 169.3 (C=O). HRMS (APCI) calculated for C₁₀H₇FNO₂ [M+] 191.0383: found 191.0384.

1-(4-Bromophenyl)-1H-pyrrrole-2,5-dione (11n)

Compound **11n** was prepared from maleic anhydride (20 mmol) and 4-bromoaniline (20 mmol) according to general procedure 1. The product was obtained as yellow crystals. 3.21 g (69%), Mp. 122-123 °C (lit. M.p. 122-123 °C [12]). IR ₉max (KBr): 3089, 2988 (C-H), 1719 (C=O), 1592, 1444 (C=C), 1488 (C=C), 1146 (CN) cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 6.84 (s, 2 H, 2 x =CH), 7.22 - 7.28 (m, 2 H, 2 x ArH), 7.55 - 7.60 (m, 2 H, 2 x ArH). ¹³C NMR (101 MHz, CDCl₃) ppm 121.5, 127.3 (CH), 130.2, 132.2 (CH), 134.2 (CH), 169.0 (C=O). HRMS (APCI) calculated for C₁₂H₁₁BrNO₂ [M+] 250.9582: found 250.9585.

1-(4-Aminophenyl)-1H-pyrrrole-2,5-dione (11p)

Compound **11p** was prepared from maleic anhydride (20 mmol) and benzene-1,4-diamine (20 mmol) according to general procedure 1. The product was obtained as a yellow solid. 2.65 g (70%), Mp. 120-128 °C (lit. M.p. 153 °C [13]). IR ₉max (ATR): 3355 (N-H), 2970, 2938 (C-H), 1692 (C=O), 1585, 1469 (C=C), 1129 (CN) cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 5.75 (s, 2 H, 2 x =CH), 7.21 (s, 2 H, 2 x ArH), 7.46 (s, 2 H, 2 x ArH). ¹³C NMR (101 MHz, DMSO-d₆) ppm 127.2 (CH), 130.8, 134.7 (CH), 152.3 169.8 (C=O). HRMS (APCI) calculated for C₁₀H₁₁N₂O₂ [M+H] 189.0659: found 189.0653.

1-(Hydroxymethyl)-1H-pyrrrole-2,5-dione (11q)

Compound **11q** was prepared from maleimide and formaldehyde. A solution of 36% formaldehyde (aqueous) (5 mL) and maleimide (2 g) was refluxed at 100 °C for 1 h. The volume of solvent was reduced and the residue was cooled on ice. The crude product was purified by
recrystallisation from 2-propanol to afford a colourless solid, 2.15 g (84%), Mp. 101-104 °C (lit. Mp. 103.5-104.5 °C [14]). IR

αmax (KB): 3570 (O-H), 1703 (C=O), 1506 (C=C), 1150 (CN) cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 3.13 (t, J = 7.94 Hz, 1 H, OH), 5.09 (d, J = 7.94 Hz, 2 H, CH₂), 6.78 (s, 2 H, 2 x =CH). ¹³C

NMR (101 MHz, CDCl₃) ppm 61.1 (CH₂), 134.6 (CH), 170.1 (C=O). HRMS (APCI) calculated for C₈H₂NO₃ [M⁺+H] 128.0348: found 128.0348.

1-Methyl-1H-pyrrole-2,5-dione (11r)

Compound 11r was prepared from maleic anhydride (20 mmol) and methylamine (20 mmol) according to general procedure 1. The product was obtained as yellow crystals, 1.34 g (60%), Mp. 60-68 °C (lit. M.p. 67-69 °C [15]). IRαmax (ATR): 3173, 3095 (C-H), 1696 (C=O), 1600, 1437 (C=C), 1222 (CN) cm⁻¹. ¹H NMR (400 MHz, DMSO-δ₆) δ 2.86 (s, 3 H, CH₃), 6.99 (s, 2 H, 2 x =CH). ¹³C NMR (101 MHz, DMSO-δ₆) ppm 20.3, 23.3, 24.5, 35.2 (CH₃), 67.9, 134.6 (HC=CH), 169.7, 171.1, 174.1, 174.1. HRMS (APCI) calculated for C₈H₂NO₃ [M⁺+H] 112.0399: found 112.0395.

General Procedure 2: Preparation of ethanoanthracenes

To a solution of the appropriate anthracene derivative (1 mmol) in toluene or xylene (2 mL) was added the required dienophile e.g. maleic anhydride or appropriate maleimide (1.3 mmol). The mixture was heated, with stirring at 90 °C for 48 h. The reaction was then cooled to RT and the resulting solid was isolated by filtration. The solid product was sequentially washed with toluene (2 mL) and diethyl ether (2 mL) and recrystallized from toluene.

General procedure 3: preparation of Triptycene compounds (20a, 20f, 20g)

(i) Preparation of benzenediazonium-2-carboxylate. Anthranilic acid (5.4 g, 0.04 mmol) and trichloroacetic acid 0.06 g in tetrahydrofuran (60 mL) was placed in a 250 mL conical flask. The reaction mixture was stirred and cooled on an ice water bath. Isoamyl nitrite (10 mL) was added portion-wise over 1 min. The mixture is allowed to warm to RT over 1.5 h. The mixture was then cooled again over ice and filtered using a plastic Buchner funnel. Subsequently the tan solid was washed with ice cold tetrahydrofuran until the washings were colourless. The yield of air dried benzenediazonium-2-carboxylate was 78 - 80 %. The benzenediazonium-2-carboxylate was washed with toluene and the tan solid was then stored in solution with toluene (60 mL).

(ii) Preparation of Triptycene compounds. To a boiling solution of the appropriate anthracene derivative (4 mmol) in toluene or xylene (2 mL) was added the required dienophile e.g. maleic anhydride or appropriate maleimide (1.3 mmol). The mixture was heated, with stirring at 90 °C for 48 h. The reaction was then cooled to RT and the resulting solid was isolated by filtration. The solid product was sequentially washed with toluene (2 mL) and diethyl ether (2 mL) and recrystallized from toluene.

(E)-9-(2-Nitrovinyl)-9,10-dihydro-9,10-[1,2]benzenoanthracene (20a)

Compound 20a was prepared from (E)-9-(2-nitrovinyl)anthracene 12a (1 g, 4 mmol) and benzenediazonium-2-carboxylate (prepared from anthranilic acid (5.4 g, 0.04 mmol)) according to general procedure 3. The product was obtained as colourless solid, 260 mg (20%), Mp. 258-260 °C (lit. Mp. 262-265 °C [16]). IRαmax (ATR): 3111, 3069 (C-H), 1651 (C=O), 1526, 1347 (NO₂) cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 5.53 (s, 1 H, C10), 7.05 - 7.16 (m, 6 H, 6 x ArH), 7.44 (d, J = 6.71 Hz, 3 H, 3 x ArH), 7.51 (d, J = 6.71 Hz, 3 H, 3 x ArH), 7.75 (d, J = 14.04 Hz, 1 H, H1’), 8.66 (d, J = 14.04 Hz, 1 H, H2’). ¹³C NMR (101 MHz, CDCl₃) ppm 54.1 (C10), 121.4 (CH), 124.2 (CH), 125.2 (CH), 126.0 (CH), 134.6 (C1’), 143.8, 145.2, 146.1 (C2’). HRMS (APCI) calculated for C₂₆H₁₈NO₅ [M⁺+H] 326.1181: found 326.1190.

9,10-[1,2]Benzenoanthracene-9(10H)-carbaldehyde (20f)

Compound 20f was prepared from 9-anthraldehyde (1.1 g, 5 mmol) and benzenediazonium-2-carboxylate (prepared from anthranilic acid (5.4 g, 0.04 mmol) according to general procedure 3. The
product was obtained as a colourless solid, 296 mg (21%), Mp. 242-244 °C (lit. Mp. 243-257 °C [17]). IR\textsubscript{max} (ATR): 3020, 2833 (C-H), 1728 (C=O), 1579 (C=C), 1451 (C=C) cm\(^{-1}\). \(^1\)H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 5.42 (s, 1 H, C10), 7.00 - 7.13 (m, 6 H, 6 x ArH), 7.37 - 7.52 (m, 3 H, 3 x ArH), 7.60 - 7.69 (m, 3 H, 3 x ArH), 11.24 (s, 1 H, CHO). \(^13\)C NMR (101 MHz, CDCl\textsubscript{3}) ppm 54.2 (C10), 60.8 (C9), 122.4 (CH), 124.0 (CH), 125.2 (CH), 125.8 (CH), 142.6, 145.8, 201.0 (CHO). HRMS (APCI) calculated for C\textsubscript{23}H\textsubscript{16}O\textsubscript{2} 282.1045: found 282.1040.

9,10-[1,2]Benzoanthracene-9(10H)-ylmethanol (20g)

To a solution of 9,10-[1,2]benzoanthracene-9(10H)-carbaldehyde 20f (100mg, 0.35 mmol) in dichloromethane (10 mL) and isopropanol (2 mL) was added sodium borohydride (60 mg, 1.6 mmol). The reaction mixture was stirred at room temperature for 24 h and neutralised using 1 M HCl. The solution was extracted with dichloromethane, dried with sodium sulphate and solvent removed \textit{in vacuo}. The product was obtained as a colourless solid, 91 mg (85%), Mp. 240-242 °C (lit. Mp. 242-243 °C [18]). IR\textsubscript{max} (ATR): 3369 (O-H), 3051, 2981 (C-H), 1712 (C=O), 1609 (C=C), 1455 (C=C) cm\(^{-1}\). \(^1\)H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 2.21 (br. s., 1 H, OH), 5.26 (br. s., 2 H, CH\(_2\)), 5.42 (s, 1 H, C10), 6.98 - 7.10 (m, 6 H, 6 x ArH), 7.42 (d, \(J = 6.71\) Hz, 4 H, 4 x ArH), 7.50 (br. s., 2 H, 2 x ArH). \(^13\)C NMR (101 MHz, CDCl\textsubscript{3}) ppm 54.3 (C10), 54.4 (C9), 61.1 (CH\(_2\)), 122.0 (CH), 123.6 (CH), 125.1 (CH), 125.2 (CH), 144.4, 146.8. HRMS (ESI) calculated for C\textsubscript{24}H\textsubscript{16}ONa\textsubscript{2}[M\textsuperscript{+}+Na\textsuperscript{+}] 307.1099: found 307.1097.

9,10-Dihydro-9,10-[3,4]furanoanthracene-12,14-dione (21a)

Compound 21a was prepared from anthracene (0.18 g, 1 mmol) and maleic anhydride (0.13 g, 1.3 mmol) according to general procedure 2. The product was obtained as a colourless solid, 249 mg (90%), Mp. 264-266 °C (lit. Mp. 267-268 °C [19]). IR\textsubscript{max} (ATR): 3065 (C-H), 1711 (C=O), 1610 (C=C), 1497, 1455 (C=C) cm\(^{-1}\). \(^1\)H NMR (400 MHz, DMSO-\(d_6\)) \(\delta\) 3.66 (s, 2 H, H9 & H10), 4.88 (s, 2 H, H11 & H15), 7.08 - 7.27 (m, 4 H, 4 x ArH), 7.29 - 7.40 (m, 2 H, 2 x ArH), 7.40 - 7.55 (m, 2 H, 2 x ArH). \(^13\)C NMR (101 MHz, DMSO-\(d_6\)) ppm 44.3 (C9 & C10), 47.9 (C11 & C15), 124.4 (CH), 124.8 (CH), 126.5 (CH), 127.0 (CH), 139.1, 141.1, 171.5 (C12 & C14). HRMS (APCI) calculated for C\textsubscript{24}H\textsubscript{16}O\textsubscript{2} 277.0865: found 277.0858.

9,10-Dihydro-9,10-[3,4]epipyrroloanthracene-12,14-dione (21b)

Compound 21b was prepared from anthracene (0.18 g, 1 mmol) and maleimide (0.13 g, 1.3 mmol) according to general procedure 2. The product was obtained as a colourless solid, 234 mg (85%), Mp. 299-300 °C (lit. Mp. 300-301 °C [20]). IR\textsubscript{max} (ATR): 3347 (O-H), 3065, 2935 (C-H), 1712 (C=O), 1456, 1439 (C=C) cm\(^{-1}\). \(^1\)H NMR (400 MHz, DMSO-\(d_6\)) \(\delta\) 3.20 (s, 2 H, H9 & H10), 4.73 (s, 2 H, H11 & H15), 7.08 - 7.21 (m, 4 H, 4 x ArH), 7.21 - 7.32 (m, 2 H, 2 x ArH), 7.37 - 7.51 (m, 2 H, 2 x ArH), 10.77 (br. s., 1 H, NH). \(^13\)C NMR (101 MHz, DMSO-\(d_6\)) ppm 44.4 (C9 & C10), 47.6 (C11 & C15), 124.1 (CH), 124.7 (CH), 126.1 (CH), 126.4 (CH), 139.5, 142.0, 178.0 (C12 & C14). HRMS (APCI) calculated for C\textsubscript{25}H\textsubscript{16}O\textsubscript{2} 276.1025: found 276.1012.

9,10-Dihydro-9,10-[3,4]epipyrroloanthracene-12,14-dione (21c)

Compound 21c was prepared from anthracene (0.18 g, 1 mmol) and phenylmaleimide (0.224 g, 1.3 mmol) according to general procedure 2. The product was obtained as a colourless solid, 316 mg (90%). Mp. 227-229 °C (lit. Mp. 228-230 °C [21]). IR\textsubscript{max} (ATR): 3059, 3001 (C-H), 1710 (C=O), 1596 (C=C), 1497, 1445 (C=C) cm\(^{-1}\). \(^1\)H NMR (400 MHz, DMSO-\(d_6\)) \(\delta\) 3.41 (s, 2 H, H9 & H10), 4.86 (s, 2 H, H11 & H15), 6.32 - 6.49 (m, 2 H, 2 x ArH), 7.11 - 7.26 (m, 5 H, 5 x ArH), 7.26 - 7.37 (m, 4 H, 4 x ArH), 7.51 (dd, \(J = 5.19, 3.36\) Hz, 2 H, 2 x ArH). \(^13\)C NMR (101 MHz, DMSO-\(d_6\)) ppm 44.8 (C9 & C10), 46.6 (C11 & C15), 124.3, 124.8, 125.3, 126.3, 126.5, 126.6, 128.2, 128.4, 128.8, 129.8, 131.8, 139.3, 141.6, 175.9 (C12 & C14). HRMS (APCI) calculated for C\textsubscript{25}H\textsubscript{16}O\textsubscript{2} 352.1338: found 352.1341.

12,14-Dioxo-9,10-[3,4]furanoanthracene-9(10H)-carbaldehyde (21d)
To a solution of 9-anthraldehyde (1.03 g, 5 mmol) in xylene (10 mL) was added maleic anhydride (0.5 g, 5 mmol). The reaction mixture was heated to reflux for 1 h. The reaction was cooled to room temperature, filtered and the precipitate was washed with toluene and hexane. The solid was allow to dry at room temperature and was recrystallized from toluene as a colourless solid, 610 mg (40%), Mp. 235-237 (lit. Mp. 238-239 °C [12]). IR\textsubscript{vmax} (ATR): 2980, 2883 (C-H), 1745 (C=O), 1654 (C=C), 1517, 1466 (C=C) cm\textsuperscript{-1}. \textsuperscript{1}H NMR (400 MHz, DMSO-\textit{d}_6) \delta 3.80 (dd, J = 9.16, 3.05 Hz, 1 H, H10), 4.32 (d, J = 9.16 Hz, 1 H, H11), 4.95 (d, J = 3.66 Hz, 1 H, H15), 7.10 - 7.34 (m, 5 H, 5 x ArH), 7.38 - 7.48 (m, 1 H, 1 x ArH), 7.58 (dd, J = 7.32, 1.22 Hz, 1 H, 1 x ArH), 7.65 - 7.76 (m, 1 H, 1 x ArH), 10.84 (s, 1 H, CHO). \textsuperscript{13}C NMR (101 MHz, DMSO-\textit{d}_6) ppm 44.6 (C10), 48.4 (C11), 48.7 (C15), 57.0 (C9), 122.8 (CH), 124.3 (CH), 125.1 (CH), 125.5 (CH), 126.5 (CH), 127.2 (CH), 127.4 (CH), 127.6 (CH), 136.9, 138.8, 138.8, 141.0, 170.9 (C=O x 2), 201.6 (C=O). HRMS (APCI) calculated for C\textsubscript{32}H\textsubscript{24}O\textsubscript{2}+M\textsuperscript{+} 305.0814: found 305.0812.

12,14-Dioxo-9,10-[3,4]epipyrroloanthracene-9(10H)-carbaldehyde (21e)

To a solution of 9-anthraldehyde (1.03 g, 5 mmol) in xylene (10 mL) was added maleimide (0.5 g, 5 mmol). The reaction mixture was heated to reflux for 1 h. The reaction was cooled to room temperature, filtered and the precipitate was washed with toluene and hexane. The solid was allow to dry at room temperature and was recrystallized from toluene as a colourless solid, 532 mg (35%), Mp. 280-283 °C (lit. Mp. 286-287 °C [20]). IR\textsubscript{vmax} (ATR): 3674 (N-H), 2980, 2892 (C-H), 1732 (C=O), 1583 (C=C), 1468, 1440 (C=C) cm\textsuperscript{-1}. \textsuperscript{1}H NMR (400 MHz, DMSO-\textit{d}_6) \delta 3.37 (dd, J = 3.66 Hz, 1 H, H10), 3.91 (d, J = 8.55 Hz, 1 H, H11), 4.79 (d, J = 3.66 Hz, 1 H, H15), 7.06 - 7.30 (m, 5 H, 5 x ArH), 7.30 - 7.40 (m, 1 H, 1 x ArH), 7.55 (d, J = 7.32 Hz, 1 H, 1 x ArH), 7.62 - 7.83 (m, 1 H, 1 x ArH), 10.78 (s, 1 H, NH), 10.97 (br. s, 1 H, CHO). \textsuperscript{13}C NMR (101 MHz, DMSO-\textit{d}_6) ppm 45.0 (C10), 48.2 (C11), 49.5 (C15), 55.4 (C9), 122.8 (CH), 124.2 (CH), 124.8 (CH), 125.2 (CH), 126.3 (CH), 126.6 (CH), 126.9 (CH), 135.3 (CH), 137.5, 138.9, 140.7, 141.8, 171.1 (C=O), 172.8 (C=O), 177.1 (CHO). HRMS (APCI) calculated for C\textsubscript{32}H\textsubscript{24}N\textsubscript{2}O\textsubscript{2}+M\textsuperscript{+} 304.0974: found 304.0971.

12,14-Dioxo-13-phenyl-9,10-[3,4]epipyrroloanthracene-9(10H)-carbaldehyde (21f)

To a solution of 9-anthraldehyde (1.03 g, 5 mmol) in xylene (10 mL) was added phenylmaleimide (0.865 g, 5 mmol). The reaction mixture was heated to reflux for 1 h. The reaction was cooled to room temperature, filtered and the precipitate was washed with toluene and hexane. The solid was allow to dry at room temperature and was recrystallized from toluene as a colourless solid, 1.18 g (62%), Mp. 225-226 °C [22]. IR\textsubscript{vmax} (ATR): 2970, 2884 (C-H), 1724 (C=O), 1596 (C=C), 1481, 1457 (C=C) cm\textsuperscript{-1}. \textsuperscript{1}H NMR (400 MHz, DMSO-\textit{d}_6) \delta 3.57 (dd, J = 8.55, 3.66 Hz, 1 H, H10), 4.12 (d, J = 8.55 Hz, 1 H, H11), 4.93 (d, J = 3.05 Hz, 1 H, H15), 6.35 - 6.48 (m, 2 H, 2 x ArH), 7.13 - 7.43 (m, 9 H, 9 x ArH), 7.62 (d, J = 6.71 Hz, 1 H, 1 x ArH), 7.69 - 7.79 (m, 1 H, 1 x ArH), 10.83 (s, 1 H, CHO). \textsuperscript{13}C NMR (101 MHz, DMSO-\textit{d}_6) ppm 45.1 (C10), 47.1 (C11), 47.8 (C15), 57.2 (C9), 122.8 (CH), 123.5 (CH), 125.0 (CH), 125.3 (CH), 126.4 (CH), 126.4 (CH), 126.7 (CH), 127.1 (CH), 127.2 (CH), 128.6 (CH), 128.9 (CH), 131.5 (CH), 137.0, 139.1, 139.2, 141.5, 175.4 (C=O), 175.5 (C=O), 202.0 (CHO). HRMS (APCI) calculated for C\textsubscript{38}H\textsubscript{26}N\textsubscript{2}O\textsubscript{2}+M\textsuperscript{+} 380.1287: found 380.1282.

12,14-Dioxo-9,10-[3,4]furanoanthracene-9(10H)-carboxylic acid (21g)

To a solution of anthracene-9-carboxylic acid (1.1 g, 5 mmol) in xylene (10 mL) was added maleic anhydride (0.5 g, 5 mmol). The reaction mixture was heated to reflux for 1 h. The reaction was cooled to room temperature, filtered and the precipitate was washed with toluene and hexane. The solid was allow to dry at room temperature and was recrystallized from toluene as a colourless solid, 1.30 g (81%), Mp. 265-267 °C (lit. M.p. 268 °C [23]). IR\textsubscript{vmax} (ATR): 2980, 2884 (C-H), 1746 (C=O), 1656 (C=C), 1583, 1469 (C=C) cm\textsuperscript{-1}. \textsuperscript{1}H NMR (400 MHz, DMSO-\textit{d}_6) \delta 3.70 (dd, J = 9.16, 3.05 Hz, 1 H, H10), 4.16 (d, J = 9.77 Hz, 1 H, H11), 4.91 (d, J = 3.05 Hz, 1 H, H15), 7.15 - 7.32 (m, 5 H, 5 x ArH), 7.34 - 7.40 (m, 1 H, 1 x ArH), 7.52 - 7.59 (m, 1 H, 1 x ArH), 7.88 - 7.98 (m, 1 H, 1 x ArH), 14.14 (br. s., 1 H, COOH). \textsuperscript{13}C NMR (101 MHz, DMSO-\textit{d}_6) ppm 44.8 (C10), 48.4 (C11), 50.1 (C15), 55.8 (C9), 122.8 (CH), 124.6 (CH), 125.0
(CH), 125.0 (CH), 126.8 (CH), 127.0 (CH), 127.3 (CH), 137.2, 138.4, 139.7, 140.7, 170.3 (C=O), 170.3 (C=O), 171.1 (C=O). HRMS (APCI) calculated for C_{19}H_{20}O_5[M+H] 321.0763: found 321.0760.

12,14-Dioxo-9,10-[3,4]epipyrrloanthracene-9(10H)-carboxylic acid (21h)

To a solution of anthranaldehyde (1.1 g, 5 mmol) in xylene (10 mL) was added maleic anhydride (0.5 g, 5 mmol). The reaction mixture was heated to reflux for 1 h. The reaction was cooled to room temperature, filtered and the precipitate was washed with toluene and hexane. The solid was allowed to dry at room temperature and was recrystallized from toluene as a colourless solid, 656 mg (41%), Mp. 298-299 °C [24]. IR \(\nu_{\text{max}}\) (ATR): 3327 (N-H), 2970, 2931 (C-H), 1719 (C=O), 1583 (C=C), 1482, 1459 (C=C) cm\(^{-1}\). \(^{1}H\) NMR (400 MHz, DMSO-d\(_6\)) \(\delta\) ppm 3.94 (dd, \(J = 8.55, 3.05\) Hz, 1 H, H10), 4.00 (d, \(J = 8.55\) Hz, 1 H, H11), 4.89 (dd, \(J = 7.05\) Hz, 1 H, H15), 6.44 (dd, \(J = 7.63, 1.53\) Hz, 2 H, 2 x ArH), 7.16 - 7.41 (m, 9 H, 9 x ArH), 7.58 (dd, \(J = 5.49, 3.05\) Hz, 1 H, 1 x ArH), 7.95 - 8.06 (m, 1 H, 1 x ArH), 13.89 (br. s., 1 H, COOH). \(^{13}\)C NMR (101 MHz, DMSO-d\(_6\)) \(\delta\) ppm 45.4 (C10), 47.2 (C11), 48.7 (C15), 55.9 (C9), 122.9 (CH), 124.4 (CH), 124.8 (CH), 125.3 (CH), 126.5 (CH), 126.5 (CH), 126.8 (CH), 127.1 (CH), 128.5 (CH), 128.8 (CH), 131.7, 137.4, 138.9, 140.2, 141.3, 171.0 (C=O), 175.0 (C=O), 175.5 (C=O). HRMS (APCI) calculated for C_{19}H_{20}O_{5}[M+H] 396.1236: found 396.1230.

9-Hydroxy-9,10-dihydro-9,10-[3,4]furanonanthracene-12,14-dione (21m)

To a solution of anthrone (0.97 g, 5 mmol) in xylene (10 mL) was added maleic anhydride (0.5 g, 5 mmol). The reaction mixture was heated to reflux for 1 h. The reaction was cooled to room temperature, filtered and the precipitate was washed with toluene and hexane. The solid was allowed to dry at room temperature and was recrystallized from toluene as a colourless solid, 805 mg (55%), Mp. 215-218 °C (lit. Mp. 218-219 °C [25]). IR \(\nu_{\text{max}}\) (ATR): 3481 (O-H), 2970, 2883 (C-H), 1767 (C=O), 1660 (C=C), 1479, 1458 (C=C) cm\(^{-1}\). \(^{1}H\) NMR (400 MHz, DMSO-d\(_6\)) \(\delta\) ppm 3.50 (d, \(J = 9.16\) Hz, 1 H, H11), 3.74 (dd, \(J = 9.16, 3.66\) Hz, 1 H, H10), 4.82 (d, \(J = 3.05\) Hz, 1 H, H15), 7.14 - 7.29 (m, 4 H, 4 x ArH), 7.33 (d, \(J = 6.71\) Hz, 1 H, 1 x ArH), 7.46 (d, \(J = 7.32\) Hz, 1 H, 1 x ArH), 7.55 (t, \(J = 6.41\) Hz, 2 H, 2 x ArH). \(^{13}\)C NMR (101 MHz, DMSO-d\(_6\)) \(\delta\) ppm 43.3 (C11), 49.2 (C10), 52.2 (C15), 76.1 (C9), 120.9 (CH), 121.2 (CH), 123.9 (CH), 124.4 (CH), 126.3 (CH), 126.9 (CH), 135.3 (CH), 137.5, 139.0, 140.7, 141.7, 171.1 (C=O), 172.7 (C=O), 177.1 (COOH). HRMS (APCI) calculated for C_{19}H_{16}NO_{4}[M+H] 293.0814: found 293.0814.
2H, H4 & H5), 8.05 (d, J = 7.93 Hz, 2H, H8 & H1), 8.59 (s, 1H, H10), 8.88 (s, 1H, H1'). 13C NMR (101 MHz, CDCl3) ppm 92.2, 108.9, 111.5 (CN), 113.0 (CN), 123.4 (C9), 123.8, 126.1, 128.3, 129.1, 129.5, 130.8, 132.5, 160.8 (C2'). HRMS (ESI) calculated for C18H9N2 [M+H] 253.0771: found 253.0764.

(E)-3-(Anthracen-9-yl)acrylonitrile (22b)

To a solution of 9-anthraldehyde (1 g, 4.85 mmol) and cyanoacetic acid (0.52 g, 6.11 mmol) in DMF (6 mL), was added morpholine (0.7 mL). The solution was then heated at 90 °C for 6 h. The solution was then cooled to -10 °C for 16 h. The resultant crystals were filtered and washed with diethyl ether, to afford the product as orange crystals, 446 mg (40%), Mp. 205-207 °C (lit. Mp. 209.5-210.5 °C [27]). IR νmax (KBr): 3051 (C-H), 2218 (CN), 1623, 1442.02 (C=C) cm⁻¹. 1H NMR (400 MHz, CDCl3) δ 5.84 (d, J = 17.09 Hz, 1H =CH), 7.43-7.54 (m, 4H, 4 x ArH), 7.97 (d, J = 7.93 Hz, 2H, H4 & H5), 8.06 (d, J = 8.54 Hz, 2H, H1 & H8), 8.27 (d, J = 17.09 Hz, 1H, =CH), 8.41 (s, 1H, H10). 13C NMR (101 MHz, CDCl3) ppm 105.4 (C2'), 117.4 (CN), 124.3 (C9), 125.4 (CH), 126.9 (CH), 127.6, 128.9 (CH), 129.0 (CH), 129.2, 131.0, 148.4 (C1'). HRMS (APCI) calculated for C17H12N [M+H] 230.0966: found 230.097.

(E)-Anthracene-9-carbaldehyde oxime (22e)

9-Anthraldehyde (1 g) was dissolved in ethanol (20 mL) and heated to 75 °C. To this was added hydroxylamine hydrochloride 0.4 g in water 3.33 mL (neutralised with sodium carbonate). The mixture was heated for ten minutes and diluted with water until cloudy. The reaction mixture was then iced and the precipitate was filtered to afford the product as a white solid, 0.99 g (90%), Mp. 157-160 °C (lit. Mp. 159-162 °C [29]). IR νmax (ATR): 3420 (O-H), 3084, 3012, 2980 (C-H), 1634, 1622, 1482 (C=C) cm⁻¹. 1H NMR (400 MHz, DMSO-d6) δ 7.18 (s, 2H, NH2), 7.52 (br. s., 4H, 4 x ArH), 8.07 (d, J = 7.32 Hz, 2H, 2 x ArH), 8.52 (s, 1H, C10), 8.62 (d, J = 8.55 Hz, 2H, 2 x ArH), 8.89 (s, 1H, C1'). 13C NMR (101 MHz, DMSO-d6) ppm 125.3 (CH), 125.4 (CH), 125.9 (CH), 126.8 (CH), 127.8, 128.6 (CH), 129.0, 131.1, 136.5 (C1'). HRMS (APCI) calculated for C15H12NO [M+H] 221.0979: found 221.1080.

(E)-Anthracene-9-carbaldehyde oxime (22e)

9-Anthraldehyde (1 g) was dissolved in ethanol (20 mL) and heated to 75 °C. To this was added hydroxylamine hydrochloride 0.4 g in water 3.33 mL (neutralised with sodium carbonate). The mixture was heated for ten minutes and diluted with water until cloudy. The reaction mixture was then iced and the precipitate was filtered to afford the product as a white solid, 0.99 g (90%), Mp. 157-160 °C (lit. Mp. 159-162 °C [29]). IR νmax (ATR): 3420 (O-H), 3084, 3012, 2980 (C-H), 1634, 1622, 1482 (C=C) cm⁻¹. 1H NMR (400 MHz, DMSO-d6) δ 7.45-7.65 (m, 4H, 4 x ArH), 8.03-8.19 (m, 2H, 2 x ArH), 8.41-8.54 (m, 2H, 2 x ArH), 8.62 (s, 1H, H10), 9.23 (s, 1H, OH). 13C NMR (101 MHz, DMSO-d6) ppm 124.8, 125.1 (CH), 125.2 (CH), 125.4 (CH), 126.1 (CH), 126.7 (CH), 128.4 (CH), 128.6 (CH), 129.0, 130.9, 146.4 (CH), 146.5 (CH). HRMS (APCI) calculated for C15H12NO [M+H] 222.0919: found 222.0914.
Figure S1. $^1$H NMR spectrum of (E)-9-(2-nitrovinyl)-9,10-dihydro-9,10-[3,4]furanoanthracene-12,14-dione (13a).

Figure S2. H-H COSY NMR spectrum of (E)-9-(2-nitrovinyl)-9,10-dihydro-9,10-[3,4]furanoanthracene-12,14-dione (13a).
Figure S3. $^{13}$C NMR spectrum of (E)-9-(2-nitrovinyl)-9,10-dihydro-9,10-[3,4]furoanthracene-12,14-dione (13a).

Figure S4. DEPT 90 NMR spectrum of (E)-9-(2-nitrovinyl)-9,10-dihydro-9,10-[3,4]furoanthracene-12,14-dione (13a).
Figure S5. C-H COSY NMR spectrum of (E)-9-(2-nitrovinyl)-9,10-dihydro-9,10-[3,4]furananthracene-12,14-dione (13a).

Figure S6. HMBC NMR spectrum of (E)-9-(2-nitrovinyl)-9,10-dihydro-9,10-[3,4]furananthracene-12,14-dione (13a).
Figure S7. $^1$H NMR spectrum of (E)-13-(3,5-dimethoxyphenyl)-9-(2-nitrovinyl)-9,10-dihydro-9,10-[3,4]epipyrrloanthracene-12,14-dione (16j).

Figure S8. $^{13}$C NMR spectrum of (E)-13-(3,5-dimethoxyphenyl)-9-(2-nitrovinyl)-9,10-dihydro-9,10-[3,4]epipyrrloanthracene-12,14-dione (16j).
Figure S9. DEPT 90 NMR spectrum of (E)-13-(3,5-dimethoxyphenyl)-9-(2-nitrovinyl)-9,10-dihydro-9,10-[3,4]epipyrrloanthracene-12,14-dione (16j).

Figure S10. C-H COSY spectrum of (E)-13-(3,5-dimethoxyphenyl)-9-(2-nitrovinyl)-9,10-dihydro-9,10-[3,4]epipyrrloanthracene-12,14-dione (16j).
Figure S11. $^1$H NMR spectrum of (E)-10-(2-nitrovinyl)-9,10-dihydro-9,10-ethanoanthracene-11-carbonitrile (19a).

Figure S12. H-H COSY spectrum of (E)-10-(2-nitrovinyl)-9,10-dihydro-9,10-ethanoanthracene-11-carbonitrile (19a).
Figure S13. $^1$C NMR spectrum of (E)-10-(2-nitrovinyl)-9,10-dihydro-9,10-ethanoanthracene-11-carbonitrile (19a).

Figure S14. DEPT 135 spectrum of (E)-10-(2-nitrovinyl)-9,10-dihydro-9,10-ethanoanthracene-11-carbonitrile (19a).
Figure S15. C-H COSY spectrum of (E)-10-(2-nitrovinyl)-9,10-dihydro-9,10-ethanoanthracene-11-carbonitrile (19a).

Figure S16. $^1$H NMR spectrum of (E)-9-chloro-10-(2-nitrovinyl)-9,10-dihydro-9,10-[1,2]benzenoanthracene (20d).
**Figure S17.** $^{13}$C NMR spectrum of (E)-9-chloro-10-(2-nitrovinyl)-9,10-dihydro-9,10-[1,2]benzenoanthracene (20d).

**Figure S18.** DEPT 90 spectrum of (E)-9-chloro-10-(2-nitrovinyl)-9,10-dihydro-9,10-[1,2]benzenoanthracene (20d).
Figure S19. C-H COSY spectrum of (E)-9-chloro-10-(2-nitrovinyl)-9,10-dihydro-9,10-[1,2]benzoanthracene (20d).

Figure S20. HMBC spectrum of (E)-9-chloro-10-(2-nitrovinyl)-9,10-dihydro-9,10-[1,2]benzoanthracene (20d).
**Figure S21.** $^1$H NMR spectrum of (E)-9-(hydrazonomethyl)-9,10-dihydro-9,10-[3,4]epipyrroloanthracene-12,14-dione (23g).

**Figure S22.** $^{13}$C NMR spectrum of (E)-9-(hydrazonomethyl)-9,10-dihydro-9,10-[3,4]epipyrroloanthracene-12,14-dione (23g).
Figure S23. DEPT 90 NMR spectrum of (E)-9-(hydrazonomethyl)-9,10-dihydro-9,10-[3,4]epipyrrroloanthracene-12,14-dione (23g).

Table S1. Tier-1 profiling screen of selected ethanoanthracenes.

<table>
<thead>
<tr>
<th>Molecule</th>
<th>ID</th>
<th>ADMET Solubility</th>
<th>ADMET Solubility Level</th>
<th>ADMET BBB</th>
<th>ADMET BBB Level</th>
<th>ADMET EXT CYP2D6 Prediction</th>
<th>ADMET EXT Hepatotoxic Prediction</th>
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</table>
A Calculated using Pipeline Pilot Professional (v8.5.0.200) BIOVIA, Dassault Systèmes; b ADMET Solubility: Log of the water solubility at 25 °C (LogSw)(mol/L); c ADMET Solubility Level: Ranking of the solubility values into the following classes: 0: Extremely Low; 1: Very Low; 2: Low; 3: Good; 4: Optimal; 5: Very Soluble; d ADMET BBB: Predicts the blood brain barrier penetration of a molecule, defined as the ratio of the concentrations of solute (compound) on both sides of the membrane after oral administration. e ADMET Blood Brain Barrier Absorption (BBB) Level: Ranking of LogBBB values into one of the following levels: 0: Very High; 1: High; 2: Medium; 3: Low; 4: Undefined (molecule is outside the confidence area of the regression model used to calculate LogBB).

Table S2. ADMET and Lipinski properties for selected ethanoanthracenes

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<th>Molecular Weight</th>
<th>Num HB A</th>
<th>Num HB D</th>
<th>Num Rot Bonds</th>
<th>Molecule Volume</th>
<th>Molecular Polar Surface Area</th>
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16c 0 true 3.4830 452.46 5 0 4 277.14 92.430

16d 0 true 3.8930 456.88 4 0 3 277.48 83.190

16h 1 true 3.3550 480.47 6 0 5 298.75 109.50

16j 0 true 3.4670 482.48 6 0 5 300.81 101.66

17n 0 true 3.7950 510.54 6 0 7 332.36 101.66

19a 0 true 3.2140 302.33 3 0 2 193.79 69.610

20a 0 true 4.3870 325.36 2 0 2 207.51 45.820

20d 0 true 4.7800 359.81 2 0 2 226.03 45.820

*Calculated using Pipeline Pilot Professional (v8.5.0.200) BIOVIA, Dassault Systèmes; *ADMET Absorption Level: Ranking of the molecule into one of the following levels: 0: Good; 1: Moderate; 2:
Poor; 3: Very Poor; ADMET Plasma Protein Binding (PPB) Prediction: If true, the compound is predicted to be a binder (>90%). Otherwise, it is predicted to be a weak or nonbinder(<90%).

References


