Anthraquinone derivatives as potent inhibitors of c-Met kinase and the extracellular signaling pathway

Zhongjie Liang[a,b#], Jing Ai[b#], Xiao Ding[b#], Xia Peng[b], Dengyou Zhang[b], Ruihang Zhang[b], Ying Wang[b], Fang Liu[b], Mingyue Zheng[b], Hualiang Jiang[b], Hong Liu[b*], Meiyu Geng[b*], Cheng Luo[a,b*]

[a]Center for Systems Biology, Soochow University, 215006, China.

[b]State Key Laboratory of Drug Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai 201203, China.

[#]These authors contributed equally to this study.

*Correspondence: Cheng Luo, Meiyu Geng and Hong Liu

Tel: +86-21-50806600; Fax: +86-21-50807188

E-mail: cluo@mail.shcnc.ac.cn or mygeng@mail.shcnc.ac.cn or hliu@mail.shcnc.ac.cn

Running title: anthraquinone derivatives as c-Met inhibitors

Contents:

(A) The binding mode of compound 2a with HGF fragment NK2

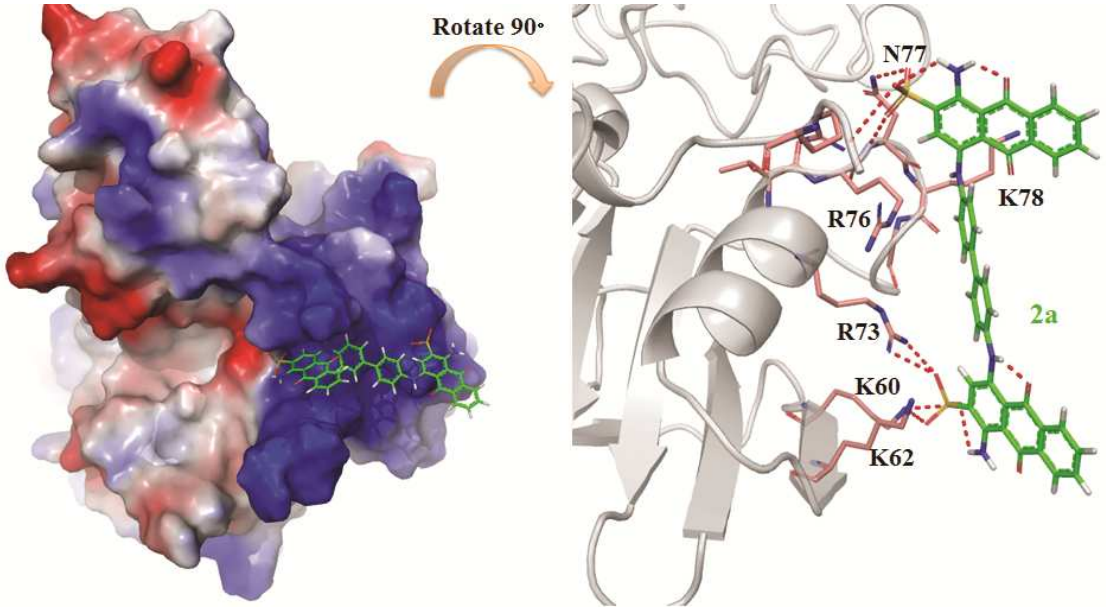

Figure S1. The binding mode of compound 2a with HGF fragment NK2.

The result displayed that the compound 2a probably bound the N-terminal heparin of HGF, which is rich in positive-charged residues in the surface. The positive-charged residues K60, K62, R73, R76 and K78 formed strong electrostatic interactions with the sulfate group for one hand. For another hand, these residues formed cation-π interactions with the aromatic rings of the compound. These two factors afford the driving force for the compound binding with the heparin site.

(B) General Methods

The reagents (chemicals) were purchased from Lancaster, Acros, and Shanghai Chemical Reagent Co. and used without further purification. Analytical thin-layer chromatography (TLC) was HSGF 254 (150-200 μm thickness; Yantai Huiyou Co., China). Nuclear magnetic resonance (NMR) spectroscopy was performed on a Bruker AMX-400 and AMX-300 NMR (IS as TMS). Chemical shifts were reported in parts per million (ppm, δ) downfield from tetramethylsilane. Proton coupling patterns were described as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), and broad (br). Low- and high-resolution mass spectra (LRMS and HRMS) were given with electric, electrospray, and matrix-assisted laser desorption ionization (EI, ESI, and MALDI) produced by a Finnigan MAT-95, LCQ-DECA spectrometer and IonSpec 4.7 T. The purity of final compounds was assessed by the analytical HPLC method and found to be >95%. %. An Agilent 1100 series HPLC with an Agilent Zorbax Exlipse SB-C18 (25 _ 4.6 mm, 5 μm particle sizes) reversed-phase column was used for analytical HPLC analyses. The elution buffer was an A/B gradient, where A = H_2O (with 0.01 % TFA) and B = CH_3CN (with 0.01 % TFA).

(C) Synthesis and Spectral Characterization Data of the target compounds.

Sodium 1-amino-4-((4'-amino-[1,1'-biphenyl]-4-yl)amino)-9,10-dioxo-9,10-dihydroanthracene-2-sulfonate 1a.

Compounds **1a-1m** were synthesized according to the improved synthetic procedure[1-2] and compound **1a** as an example: To a mixture of bromaminic acid sodium salt (0.081 g, 0.20 mmol) and related aniline (0.20 mmol) in Na_2HPO_4 (pH 9.6) (4 mL) and NaH_2PO_4 (pH 4.2) (1 mL) buffer solution was added catalytic amount of powdered copper (0.002-0.003 g). The mixture was stirred under biotage microwave for 20 min at 80 ^oC. The reaction was then cooled to room temperature and diluted with methanol. The mixture was filtered and methanol was evaporated. The crude was purified via flash reversed column chromatography using RP-18 silica gel (water as an eluent) to obtained **1a** as a blue solid. Yield: 85 %. ^1H NMR (400 MHz, CD3OD): δ 8.32 - 8.29 (m, 3 H), 7.79 - 7.77 (m, 2 H), 7.61 - 7.58 (m, 2 H), 7.44 - 7.42 (m, 2 H), 7.32 - 7.30 (m, 2 H), 6.83 - 6.81 (m, 2 H). LRMS (ESI) m/z 484 $[M-Na]^-$. HRMS (ESI) m/z calcd for $C_{26}H_{18}N_3O_5S$ $[M-Na]^-$ 484.0967 found 484.0972. HPLC: 100%, t_R = 0.72 min. Mp > 300 ^oC.

Sodium 1-amino-4-((4'-amino-3,3'-dimethyl-[1,1'-biphenyl]-4-yl)amino)-9,10-dioxo-9,10-dihydroanthracene-2-sulfonate 1b. In the same manner as described in the preparation of **1a**, **1b** was prepared from sodium 1-amino-4-bromo-9,10-dioxo-9,10-dihydroanthracene-2-sulfonate and 3,3'-dimethyl-[1,1'-biphenyl]-4,4'-diamine. Yield: 69%. ^1H NMR (400 MHz, CD_3OD): δ 8.40 - 8.38 (m, 2 H), 8.06 (s, 1 H), 7.84 - 7.81 (m, 2 H), 7.55 (m, 1 H), 7.48 - 7.45 (m, 1 H), 7.34 - 7.29 (m, 3 H), 6.83 - 6.81 (m, 1 H), 2.41 (s, 3 H), 2.26 (s, 3 H). LRMS (ESI) m/z 512$[M-Na]^-$. HRMS (ESI) m/z calcd for $C_{28}H_{22}N_3O_5S$ $[M-Na]^-$ 512.1280 found 512.1299. HPLC: 100%, t_R = 0.80 min. Mp > 300 ^oC.

Sodium 1-amino-4-((4'-(benzylamino)-[1,1'-biphenyl]-4-yl)amino)-9,10-dioxo-9,10-dihydroanthracene-2-sulfonate 1c. In the same manner as described in the preparation of **1a**, **1b** was prepared from sodium 1-amino-4-bromo-9,10-dioxo-9,10-dihydroanthracene-2-sulfonate and N^4-benzyl-[1,1'-biphenyl]-4,4'-diamine.Yield:65%. ^{1}H NMR (400 MHz, CD_3OD): δ 7.71 - 7.69 (m, 3 H), 7.49 - 7.47 (m, 3 H), 7.42 - 7.26 (m, 10 H), 6.85 - 6.83 (m, 2 H), 4.43 (s, 2 H).LRMS (ESI) m/z 574[M-Na]$^-$. HRMS (ESI) m/z calcd for $C_{33}H_{24}N_3O_5S$ [M-Na]$^-$ 574.1437 found 574.1444. HPLC: 100%, t_R = 0.84 min. Mp > 300 ^{o}C.

Sodium 4-((4'-acetamido-[1,1'-biphenyl]-4-yl)amino)-1-amino-9,10-dioxo-9,10-dihydroanthracene-2-sulfonate 1d. In the same manner as described in the preparation of **1a**, **1d** was prepared from sodium 1-amino-4-bromo-9,10-dioxo-9,10-dihydroanthracene-2-sulfonate and N-(4'-amino-[1,1'-biphenyl]-4-yl)acetamide. Yield: 71%. ^{1}H NMR (400 MHz, CD_3OD): δ 8.35 (m, 3 H), 7.81 - 7.80 (m, 2 H), 7.69 - 7.61 (m, 6 H), 7.37 (br s, 2 H), 2.17 (s, 3 H). LRMS (ESI) m/z 526 [M-Na]$^-$. HRMS (ESI) m/z calcd for $C_{28}H_{20}N_3O_6S$ [M-Na]$^-$ 526.1073 found 526.1079. HPLC: 100%, t_R = 0.82 min. Mp > 300 ^{o}C.

Sodium 1-amino-4-((4'-((tert-butoxycarbonyl)amino)-[1,1'-biphenyl]-4-yl)amino)-9,10-dioxo-9,10-dihydroanthracene-2-sulfonate 1e. In the same manner as described in the preparation of **1a**, **1e** was prepared from sodium 1-amino-4-bromo-9,10-dioxo-9,10-dihydroanthracene-2-sulfonate and *tert*-butyl (4'-amino-[1,1'-biphenyl]-4-yl)carbamate. Yield: 34%. ^{1}H NMR (400 MHz, CD_3OD): δ 8.38 - 8.27 (m, 3 H), 7.83 - 7.2 (m, 2 H), 7.61 - 7.51 (m, 2 H), 7.41 - 7.38 (m, 2 H), 7.29 - 7.25 (m, 2 H), 6.93 - 6.91 (m, 2 H), 1.37 (s, 9 H).LRMS (ESI) m/z 584 [M-Na]$^-$. HRMS (ESI) m/z calcd for $C_{31}H_{26}N_3O_7S$ [M-Na]$^-$ 584.1491 found 584.1500. HPLC: 100%, t_R = 0.86 min. Mp > 300 ^{o}C.

Sodium 1-amino-4-((4'-(cyclohexanecarboxamido)-[1,1'-biphenyl]-4-yl)amino)-9,10-dioxo-9,10-dihydroanthracene-2-sulfonate 1f. In the same manner as described in the preparation of **1a**, **1e** was prepared from sodium 1-amino-4-bromo-9,10-dioxo-9,10-dihydroanthracene-2-sulfonate and N-(4'-amino-[1,1'-biphenyl]-4-yl)cyclohexanecarboxamide. Yield: 76%. ^{1}H NMR (400 MHz, CD_3OD): δ 8.36 - 8.35 (m, 3 H), 7.83 - 7.81 (m, 2 H), 7.70 - 7.63 (m, 6 H), 7.38 - 7.36 (m, 2 H), 2.47 - 2.42 (m, 1 H), 1.96 - 1.89 (m, 4 H), 1.80 - 1.70 (m, 1 H), 1.63 - 1.56 (m, 1 H), 1.39 - 1.30 (m, 4 H).LRMS (ESI) m/z 594 $[M\text{-}Na]^-$. HRMS (ESI) m/z calcd for $C_{33}H_{28}N_3O_6S$ $[M\text{-}Na]^-$ 594.1699 found 594.1704. HPLC: 100%, t_R = 0.87 min. Mp > 300 ^oC.

Sodium 1-amino-4-((4-(4-aminobenzyl)phenyl)amino)-9,10-dioxo-9,10-dihydroanthracene-2-sulfonate 1h. In the same manner as described in the preparation of **1a**, **1h** was prepared from sodium 1-amino-4-bromo-9,10-dioxo-9,10-dihydroanthracene-2-sulfonate and 4,4'-methylenedianiline. Yield: 75 %. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.30 - 8.26 (m, 2 H), 8.00 (s, 1 H), 7.87 - 7.85 (m, 2 H), 7.27 - 7.18 (m, 4 H), 6.92 (d, J = 7.8 Hz, 2 H), 6.54 – 6.51 (m, 2 H), 4.89 (s, 2 H), 3.79 (s, 2 H).LRMS (ESI) m/z 498 $[M\text{-}Na]^-$. HRMS (ESI) m/z calcd for $C_{27}H_{20}N_3O_5S$ $[M\text{-}Na]^-$ 498.1124 found 498.1136. HPLC: 100%, t_R = 0.77 min. Mp > 300 ^oC.

Sodium 1-amino-4-((4-(4-aminophenoxy)phenyl)amino)-9,10-dioxo-9,10 dihydroanthracene -2-sulfonate 1i. In the same manner as described in the preparation of **1a**, **1i** was prepared from sodium 1-amino-4-bromo-9,10-dioxo-9,10-dihydroanthracene-2-sulfonate and 4,4'-oxydianiline. Yield: 79 %. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.28 (d, J = 5.0 Hz, 2 H), 7.90 - 7.84 (m, 3 H), 7.26 - 7.23 (m, 2 H), 6.96 - 6.82 (m, 4 H), 6.64 - 6.61 (m, 2 H), 5.01 (br s, 2 H).LRMS (ESI) m/z 500 $[M\text{-}Na]^-$. HRMS (ESI) m/z calcd for $C_{26}H_{18}N_3O_6S$ $[M\text{-}Na]^-$ 500.0916 found 500.0917. HPLC: 100%, t_R = 0.70 min. Mp > 300 ^oC.

Sodium 1-amino-4-((4-(4-aminophenethyl)phenyl)amino)-9,10-dioxo-9,10

dihydroanthracene-2-sulfonate 1j. In the same manner as described in the preparation of **1a**, **1j** was prepared from sodium 1-amino-4-bromo-9,10-dioxo-9,10-dihydroanthracene-2-sulfonate and 4,4'-(ethane-1,2-diyl)dianiline. Yield: 78 %. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.28 (d, J = 5.0 Hz, 2 H), 7.90 - 7.84 (m, 3 H), 7.26 - 7.23 (m, 2 H), 6.96 - 6.82 (m, 4 H), 6.64 - 6.61 (m, 2 H), 5.01 (br s, 2 H).LRMS (ESI) m/z 512 $[M\text{-}Na]^-$. HRMS (ESI) m/z calcd for $C_{28}H_{22}N_3O_5S$ $[M\text{-}Na]^-$ 512.1280 found 512.1287. HPLC: 100%, t_R = 0.85 min. Mp > 300 ^oC.

Sodium 1-amino-4-((4-aminophenyl)amino)-9,10-dioxo-9,10 dihydroanthracene-2-sulfonate 1k. In the same manner as described in the preparation of **1a**, **1k** was prepared from sodium 1-amino-4-bromo-9,10-dioxo-9,10-dihydroanthracene-2-sulfonate and benzene-1,4-diamine. Yield: 80 %. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.30 - 8.28 (m, 2 H), 7.86 - 7.82 (m, 3 H), 6.96 (d, J = 8.5 Hz, 2 H), 6.66 (d, J = 8.5 Hz, 2 H), 5.25 (s, 2 H). LRMS (ESI) m/z 408 $[M\text{-}Na]^-$. HRMS (ESI) m/z calcd for $C_{20}H_{14}N_3O_5S$ $[M\text{-}Na]^-$ 408.0654 found 408.0659. HPLC: 100%, t_R = 0.55 min. Mp > 300 ^oC.

Sodium 1-amino-4-((4-amino-2,5-dimethylphenyl)amino)-9,10-dioxo-9,10-dihydroanthracene-2-sulfonate 1*l*. In the same manner as described in the preparation of **1a**, **1*l*** was prepared from sodium 1-amino-4-bromo-9,10-dioxo-9,10-dihydroanthracene-2-sulfonate and 2,5-dimethylbenzene-1,4-diamine. Yield: 85 %. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.31 - 8.28 (m, 2 H), 7.86 - 7.83 (m, 2 H), 7.51 (s, 1 H), 6.80 (s, 1 H), 6.60 (s, 1 H), 4.94 (br s, 2 H), 2.05 (s, 6 H).LRMS (ESI) m/z 436 $[M\text{-}Na]^-$. HRMS (ESI) m/z calcd for $C_{20}H_{14}N_3O_5S$ $[M\text{-}Na]^-$ 436.0967 found 436.0969. HPLC: 100%, t_R = 0.57 min. Mp > 300 ^oC.

Sodium 1-amino-9,10-dioxo-4-(phenylamino)-9,10-dihydroanthracene-2-sulfonate 1m. In the same manner as described in the preparation of **1a**, **1m** was prepared from sodium 1-amino-4-bromo-9,10-dioxo-9,10-dihydroanthracene-2-sulfonate and aniline. Yield: 90 %. ^{1}H NMR (400

MHz, CD_3OD): δ 8.31 - 8.27 (m, 3 H), 7.79 - 7.72 (m, 2 H), 7.45 - 7.41 (m, 2 H), 7.32 - 7.30 (m, 2 H), 7.21 - 7.17 (m, 1 H).LRMS (ESI) m/z 393 $[M-Na]^-$. HRMS (ESI) m/z calcd for $C_{20}H_{13}N_2O_5S$ $[M-Na]^-$ 393.0545 found 393.0556. HPLC: 100%, t_R = 0.77 min. Mp > 300 ^oC.

Sodium 1,1'-([1,1'-biphenyl]-4,4'-diylbis(azanediyl))bis(4-amino-9,10-dioxo-9,10-dihydroanthracene-3-sulfonate) 2a.

Compounds **2a-2h** were synthesized according to the improved synthetic procedure[1-2] and compound **2a** as an example: To a mixture of bromaminic acid sodium salt (0.162 g, 0.40 mmol) and related aniline (0.20 mmol) in Na_2HPO_4 (pH 9.6) (4 mL) and NaH_2PO_4 (pH 4.2) (1 mL) buffer solution was added catalytic amount of powdered copper (0.002-0.003 g). The mixture was irradiated under biotage microwave for 20 min at 120 ^oC. The reaction was then cooled to room temperature and diluted with methanol. The mixture was filtered and methanol was evaporated. The crude was purified by flash reversed column chromatography using RP-18 silica gel (water as an eluent) to obtained **2a** as a blue solid. Yield: 12 %. ^1H NMR (400 MHz, CD_3OD): δ 8.40 (s, 2 H), 8.38 - 8.35 (m, 4 H), 7.83 - 7.81 (m, 4 H), 7.76 - 7.74 (m, 4 H), 7.42 - 7.40 (m, 4 H). LRMS (ESI) m/z 807 $[M-Na]^-$. HRMS (ESI) m/z calcd for $C_{40}H_{24}N_4O_{10}S_2Na$ $[M-Na]^-$ 807.0832 found 807.0839. HPLC: 100%, t_R = 0.70 min. Mp > 300 ^oC.

Sodium 1,1'-((2,2'-dimethyl-[1,1'-biphenyl]-4,4'-diyl)bis(azanediyl))bis(4-amino-9,10-dioxo-9,10-dihydroanthracene-3-sulfonate) 2b. In the same manner as described in the preparation of **2a**, **2b** was prepared from sodium 1-amino-4-bromo-9,10-dioxo-9,10-dihydroanthracene-2-sulfonate and 2,2'-dimethyl-[1,1'-biphenyl]-4,4'-diamine. Yield: 15 %. ^1H NMR (300 MHz, CD_3OD): δ 8.39 - 8.22 (m, 3 H), 8.08 (s, 1 H), 7.93 - 7.90 (m, 1 H), 7.81 - 7.66 (m, 5 H), 7.53 - 7.38 (m, 4 H), 7.32 - 7.27 (m, 2 H), 2.41 (s, 3 H), 2.24 (s, 3 H).LRMS (ESI) m/z 835 $[M-Na]^-$. HRMS (ESI) m/z calcd for $C_{42}H_{28}N_4O_{10}S_2Na$ $[M-Na]^-$ 835.1145 found 835.1149. HPLC: 100%,

t_R = 0.83 min. Mp > 300 ^oC.

Sodium 1,1'-((2,2'-dimethoxy-[1,1'-biphenyl]-4,4'-diyl)bis(azanediyl))bis(4-amino-9,10-dioxo-9,10-dihydroanthracene-3-sulfonate) 2c. In the same manner as described in the preparation of **2a**, **2c** was prepared from sodium 1-amino-4-bromo-9,10-dioxo-9,10-dihydroanthracene-2-sulfonate and 2,2'-dimethoxy-[1,1'-biphenyl]-4,4'-diamine. Yield: 14 %. ^1H NMR (300 MHz, CD_3OD): δ 8.36 - 8.21 (m, 4 H), 7.94 - 7.91 (m, 1 H), 7.79 - 7.67 (m, 6 H), 7.50 - 7.47 (m, 1 H), 7.29 - 7.22 (m, 2 H), 7.14 - 7.08 (m, 2 H), 4.02 (s, 3 H), 3.95 (s, 3 H).LRMS (ESI) m/z 867 $[M-Na]^-$. HRMS (ESI) m/z calcd for $C_{42}H_{28}N_4O_{12}S_2Na$ $[M-Na]^-$ 867.1043 found 867.1049. HPLC: 100%, t_R = 0.75 min. Mp > 300 ^oC.

Sodium 1,1'-((3,3'-dimethyl-[1,1'-biphenyl]-4,4'-diyl)bis(azanediyl))bis(4-amino-9,10-dioxo-9,10-dihydroanthracene-3-sulfonate) 2d. In the same manner as described in the preparation of **2a**, **2d** was prepared from sodium 1-amino-4-bromo-9,10-dioxo-9,10-dihydroanthracene-2-sulfonate and 3,3'-dimethyl-[1,1'-biphenyl]-4,4'-diamine. Yield: 14 %. ^1H NMR (400 MHz, CD_3OD): δ 8.43 - 8.38 (m, 4 H), 7.85 - 7.70 (m, 8 H), 7.52 - 7.44 (m, 2 H), 7.37 - 7.32 (m, 2 H), 2.45 (s, 3 H), 2.27 (s, 3 H).LRMS (ESI) m/z 835 $[M-Na]^-$. HRMS (ESI) m/z calcd for $C_{42}H_{28}N_4O_{10}S_2Na$ $[M-Na]^-$ 835.1145 found 835.1138. HPLC: 100%, t_R = 0.76 min. Mp > 300 ^oC.

Sodium 4,4'-((methylenebis(4,1-phenylene))bis(azanediyl))bis(1-amino-9,10-dioxo-9,10-dihydroanthracene-2-sulfonate) 2e. In the same manner as described in the preparation of **2a**, **2e** was prepared from sodium 1-amino-4-bromo-9,10-dioxo-9,10-dihydroanthracene-2-sulfonate and 4,4'-methylenedianiline. Yield: 21 %. ^1H NMR (300 MHz, DMSO-d_6): δ 8.30 - 8.27 (m, 4 H), 8.03 (s, 2 H), 7.87 - 7.85 (m, 4 H), 7.38 - 7.36 (m, 4 H), 7.26 - 7.23 (m, 4 H), 4.02 (s, 2 H).LRMS (ESI) m/z 821 $[M-Na]^-$. HRMS (ESI) m/z calcd for $C_{41}H_{26}N_4O_{10}S_2Na$ $[M-Na]^-$ 821.0988 found 821.1996. HPLC: 100%, t_R = 0.73 min. Mp > 300 ^oC.

Sodium 4,4'-((oxybis(4,1-phenylene))bis(azanediyl))bis(1-amino-9,10-dioxo-9,10-dihydroanthracene-2-sulfonate) 2f. In the same manner as described in the preparation of **2a**, **2f** was prepared from sodium 1-amino-4-bromo-9,10-dioxo-9,10-dihydroanthracene-2-sulfonate and 4,4'-oxydianiline. Yield: 19 %. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.31 - 8.28 (m, 4 H), 7.99 (s, 2 H), 7.88 - 7.86 (m, 4 H), 7.37 - 7.34 (m, 4 H), 7.20 - 7.17 (m, 4 H).LRMS (ESI) m/z 823 [M-Na]$^-$. HRMS (ESI) m/z calcd for $C_{40}H_{26}N_4O_{11}S_2Na$ [M-Na]$^-$ 823.0781 found 823.0789. HPLC: 100%, t_R = 0.67 min. Mp > 300 ^{o}C.

Sodium 4,4'-(1,4-phenylenebis(azanediyl))bis(1-amino-9,10-dioxo-9,10-dihydroanthracene-2-sulfonate) 2g. In the same manner as described in the preparation of **2a**, **2g** was prepared from sodium 1-amino-4-bromo-9,10-dioxo-9,10-dihydroanthracene-2-sulfonate and benzene-1,4-diamine. Yield: 18 %. ^{1}H NMR (300 MHz, CD_3OD): δ 8.30 - 8.18 (m, 6 H), 7.77 - 7.74 (m, 4 H), 7.27 - 7.21 (m, 4 H).LRMS (ESI) m/z 731 [M-Na]$^-$. HRMS (ESI) m/z calcd for $C_{34}H_{20}N_4O_{10}S_2Na$ [M-Na]$^-$ 731.0519 found 731.0523. HPLC: 100%, t_R = 0.52 min. Mp > 300 ^{o}C.

Sodium 4,4'-((2,5-dimethyl-1,4-phenylene)bis(azanediyl))bis(1-amino-9,10-dioxo-9,10-dihydroanthracene-2-sulfonate) 2h. In the same manner as described in the preparation of **2a**, **2h** was prepared from sodium 1-amino-4-bromo-9,10-dioxo-9,10-dihydroanthracene-2-sulfonate and 2,5-dimethyl benzene-1,4-diamine. ^{1}H NMR (300 MHz, CD_3OD): δ 8.30 - 8.18 (m, 6 H), 7.77 - 7.74 (m, 4 H), 7.27 - 7.21 (m, 4 H), 2.17 (s, 3H), 2.14 (s, 3H).LRMS (ESI) m/z 759 [M-Na]$^-$. HRMS (ESI) m/z calcd for $C_{36}H_{24}N_4O_{10}S_2Na$ [M-Na]$^-$ 759.0832 found 759.0822. HPLC: 100%, t_R = 0.57 min. Mp > 300 ^{o}C.

References:

1. Baqi. Y., Müller. C.E. Synthesis of alkyl- and aryl-amino-substituted anthraquinone derivatives by microwave-assisted copper(0)-catalyzed Ullmann coupling reactions. *Nature Protocols*. **2010**, 5(5), 945-953.

2. Baqi. Y., Müller. C.E. Rapid and efficient microwave-assisted copper(0)-catalyzed Ullmann coupling reaction: general access to anilinoanthraquinone derivatives. *Organic Letters*. **2007**, 9(7), 1271-1274.