Electronic Supplementary Information for Chemical Communications

**Catch and release microwave mediated synthesis of cyanine dyes**

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General Information

Unless otherwise noted, all solvents and reagents were obtained from commercial sources and used without further purification. $^1$H NMR and $^{13}$C NMR spectra were recorded at 298 K on a Bruker ARX250 spectrometer (at 250 MHz and 62.9 MHz), on a Bruker DPX360 spectrometer (at 360 MHz and 90.5 MHz) and on a Bruker DMX500 (at 500 MHz and 126 MHz), respectively. Gel phase $^{13}$C NMR spectra were recorded on a Bruker DPX 360 spectrometer. Chemical shifts are reported on the δ scale in ppm, using the residual protio solvent as the internal standard. Coupling constants ($J$) are reported in Hz. Symbols such as t (dd), and td (ddd) indicate apparent patterns with the results of detailed analyses in parentheses. Polymer-bound imidates and hemicyanine could not be analysed by gel-phase $^{13}$C NMR. Only the imidate 6a could be analysed. Melting points were determined using a Gallenkamp melting point apparatus and are uncorrected. Microanalysis were performed by MEDAC Ltd., Surrey. Elemental analysis was carried out for all the imidates and for one hemicyanine for each class (tri-, penta- and heptamethine) to determine the loading efficiency. IR spectra were recorded on a FTIR Bruker Tensor series spectrometer with ATR Golden Gate. All samples were run neat. Microwave-assisted reactions were performed on either a Biotage Initiator 2.0 or a Biotage Smith Synthesizer. Absorption spectra were recorded on an 8453 Agilent UV-Visible spectrophotometer. Fluorescence emission spectra were recorded on a Jobin Yvon Fluoromax spectrofluorimeter. Analytical thin layer chromatography (TLC) was performed on Merck silica Gel 60-F254 plates (0.25 mm) with visualization by ultraviolet (UV) irradiation at 254 nm. Purifications by flash chromatography were performed using Merck silica gel 60 (230-400 mesh). ESI-MS analyses were carried out on an Agilent Technologies LC/MSD 1100 Series quadrupole mass spectrometer (QMS) equipped with an electrospray ionisation source. Major peaks are reported with percentage intensities of the base peak. Electrospray high resolution mass spectrometry was performed on a Finnigan MAT 900 XTL spectrometer. High performance liquid chromatography was carried out on an Agilent Technologies HP1100 Chemstation system coupled to a Polymer Lab 100 ES evaporative light
scattering detector, eluting with (A) 0.1% TFA/H$_2$O, (B) 0.04% TFA/MeCN, (C) 0.1% formic acid/H$_2$O, (D) 0.10% formic acid/MeOH using the methods described below.

**HPLC System I**
Column: Phenomenex Gemini, C18, 110 Å, 100 mm × 4.6 mm, 5 µm. Flow rate: 1.0 mL min$^{-1}$. Gradient: 95% C to 5% C in D over 6 min, then 3 min isocratic. Detection: UV and ELS detection.

**HPLC System II**
Column: Discovery (Supelco) C18, 50 mm × 4.6 mm, 5 µm. Flow rate: 1.0 mL min$^{-1}$. Gradient: 95% A to 5% A in B over 5 min, then 3 min isocratic. Detection: UV and or ELS detection.

**HPLC System III**
Column: Phenomenex Luna, C18(2), 150 mm × 4.6 mm, 100 Å. Flow rate: 1.0 mL min$^{-1}$. Gradient: 95% A to 5% A in B over 8 min, then 6 min isocratic. Detection: UV and or ELS detection.

**(4-hydroxyphenyl)carbamic acid tert-butyl ester PS**

![Chemical Structure](image)

A mixture of (4-hydroxyphenyl)carbamic acid tert-butyl ester PS (6.27 g, 30 mmol), Cs$_2$CO$_3$ (9.78 g, 30 mmol), KI (0.17 g, 1 mmol) and 1% DVB cross-linked chloromethyl polystyrene (5 g, 10 mmol) in acetone (45 mL) was heated at 70 °C for 16 h. The resin was isolated by filtration, washed with water (4 × 100 mL), DMF (4 × 50 mL), DCM (3 × 50 mL), Et$_2$O (3 × 50 mL) and dried overnight in vacuo at 40 °C to give the product as a beige resin (quantitative by N analysis, 96% by Cl analysis). Found: N, 2.13; Cl, 0.27. Calcd: N, 2.08; Cl, 0%. IR (neat) 3399, 3024, 2919, 1722, 1511, 1217, 1154, 698 cm$^{-1}$.

$^{13}$C NMR (90.5 MHz, CDCl$_3$) $\delta$ 155.5 (C=O), 154.0 (C-O), 131.5-125.5 (Ar-resin + C-N), 119.6 (Ar), 114.2 (Ar), 80.1 (C), 70.2 (CH$_2$), 40.2 (CH-resin), 28.4 (CH$_3$).
Colorimetric test for the detection of chloromethyl groups in Merrifield resin

A 75 mM solution of 4-(4-nitrobenzyl)pyridine in toluene with 5% of triethylamine (1mL) was added to 2mg of resin 9. No coloration was observed (naked eye). The colorimetric test was then repeated on 2 mg of Merrifield resin (1% DVB, 2mmol Cl/g). The resin turned to pink.

4-aminophenol PS

Resin 9 (5g, 7.5 mmol) was shaken at room temperature with a 20% solution of TFA in DCM (75 mL) for 2 h, filtered and washed with DCM (2 × 50 mL). The resin was then shaken with a 10% solution of triethylamine in DCM (75 mL) for 15 min, filtered, washed with DCM (4 × 50 mL), and dried overnight in vacuo at 40 °C to give the product as a beige resin. Found: N, 2.56; Calcd: N, 2.33%. IR (neat) 3360, 3023, 2917, 1601, 1508, 1217, 698 cm⁻¹. ¹³C NMR (90.5 MHz, CDCl₃) δ 134.2-121.3 (Ar-resin, C-O, C-N), 116.1 (Ar), 115.8 (Ar), 70.5 (CH₂), 40.2 (CH-resin)
**TRIMETHINE DYES**

**Ethyl 4-hydroxyphenylimidoformate PS**

![Chemical structure of 6a](image)

To 4 aminophenol PS 4 (2 g, 3.3 mmol) was added a solution of triethylorthoformate (7.50 mL, 45.1 mmol) and BF$_3$·OEt$_2$ (0.46 mL, 3.7 mmol) in dry DCM (10 mL) and the solution stirred at room temperature for 6h. Dry DIEA (0.94 mL, 5.51 mmol) was added and the mixture stirred for 5 min. The resin was isolated by filtration, washed several times with DCM (20 mL), and dried *in vacuo* to give the product as a brown resin. Found: N, 2.29; Calcd: N, 2.14. IR (neat) 3024, 2920, 1639, 1503, 1184, 698 cm$^{-1}$. $^{13}$C NMR (90.5 MHz, CDCl$_3$) $\delta$ 155.0 (CH), 123.1 (Ar), 115.6 (Ar), 71.3 (CH$_2$), 63.3 (CH$_2$-Et), 41.5 (CH-resin), 15.4 (CH$_3$-Et).

**2-[(E)-2-(4-hydroxyanilino)ethenyl]-1,3,3-trimethyl-3H-indolium iodide PS**

![Chemical structure of 7a](image)

To Ethyl 4-hydroxyphenylimidoformate PS 6a (1 g, 1.53 mmol) and 1,2,3,3-tetramethyl-3H-indolium iodide (2.3 g, 7.65 mmol) was added DMF (8 mL) and the mixture stirred at 120 °C for 15 min under microwave irradiation. After cooling, the resin was isolated by filtration, washed with DMF (3 × 10 mL) and DCM (3 × 10 mL), and dried *in vacuo* to give the product as an orange resin (0.72 mmolg$^{-1}$, 66% by N analysis). Found: N, 2.03; Calcd: N, 3.08. IR (neat) 3024, 2916, 1668, 1506, 1451, 1225, 1014, 907, 824, 754 cm$^{-1}$. 

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Supplementary Material (ESI) for Organic & Biomolecular Chemistry
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2-\((E)\)-2-(4-hydroxyanilino)ethenyl]-1,1,3-trimethyl-1\(H\)-benzo[e]indolium iodide PS

To Ethyl 4-hydroxyphenylimidoformate PS 6a (1 g, 1.53 mmol) and 1,1,2,3-Tetramethyl-1\(H\)-benz[e]indolium iodide (2.7 g, 7.65 mmol) was added DMF (8 mL) and the mixture stirred at 120 °C for 15 min under microwave irradiation. After cooling, the resin was isolated by filtration, washed with DMF (3 × 10 mL) and DCM (3 × 10 mL), and dried in vacuo to give the product as a dark red-brown resin. IR (neat) 3024, 2916, 1685, 1506, 1451, 1206, 1014, 823, 751, 704 cm\(^{-1}\)

2-\{(1\(E\),3\(E\))-3-[1-(5-carboxypentyl)-3,3-dimethyl-1,3-dihydro-2\(H\)-indol-2-ylidene]-1-propenyl]-1,3,3-trimethyl-3\(H\)-indolium Inner Salt

To PS-bound hemicyanine 7a (1.1 g, 0.80 mmol) were added dry pyridine (5 mL), DIEA (1.3 mL, 7.4 mmol), Ac\(_2\)O (0.7 mL, 7.4 mmol) and 1-(5-carboxypentyl)-2,3,3-trimethyl-3\(H\)-indolium bromide (35 mg, 0.10 mmol). The mixture was stirred at room temperature for 2 h. Afterwards, the resin was removed by filtration and washed several times with DCM (10 mL). The filtrates were combined and evaporated and the resulting solid was dissolved in DCM (15 mL) and washed several times with water (10 mL). After removal of the solvent in vacuo, the crude product was precipitated in Et\(_2\)O, washed with Et\(_2\)O
and then purified by chromatography (DCM → DCM/MeOH 1:1) to give 8a as a dark glassy red solid (31 mg, 68%).

R<sub>f</sub> 0.42 (DCM/MeOH 9:1)

**HPLC**

$t_R$ = 10.7 min, 100% (ELSD, $\lambda$ = 550 nm).

**MS** (ES): $m/z$ (%) 457.2 [M<sup>+</sup>, 100], 458.2 [(M+1)<sup>+</sup>, 31], 459.2 [(M+2)<sup>+</sup>, 4]

**<sup>1</sup>H NMR** (360 MHz, CD<sub>3</sub>OD) δ 8.55 (t (dd), 1H, $J_{1,2} \approx J_{2,3}$ = 13.5 Hz, CH-H2), 7.55 (d, 2H, $J$ = 7.4 Hz, Ar-H4, Ar-H4'), 7.53-7.48 (m, 2H, Ar-H6, Ar-H6'), 7.36 (d, 2H, $J$ = 7.8 Hz, Ar-H7, Ar-H7'), 7.31 (td (ddd) 1H, $J_{4,5} \approx J_{5,6} \approx 7.4$, $J_{5,7}$ = 1.2 Hz, Ar-H5 or Ar-H5'), 7.30 (td (ddd), 1H, $J_{4,5} \approx J_{5,6}$ = 7.4, $J_{5,7}$ = 1.2 Hz, Ar-H5 or Ar-H5'), 6.48 (d, 1H, $J$ = 13.5 Hz, CH-H1 or H3), 6.47 (d, 1H, $J$ = 13.5 Hz, CH-H1 or H3), 4.16 (t, 2H, $J$ = 7.5 Hz, CH<sub>2</sub>-e), 3.69 (s, 3 H, NCH<sub>3</sub>), 2.21 (t, 2H, $J$ = 7.5 Hz, CH<sub>2</sub>-a), 1.86 (quintet, 2H, $J$ = 7.7 Hz, CH<sub>2</sub>-δ), 1.77-1.66 (s + quintet, 14H, $J$ = 7.4 Hz, CH<sub>2</sub>-β + CH<sub>3</sub>), 1.56-1.49 (m, 2H, CH<sub>2</sub>-γ).

**<sup>13</sup>C NMR** (90.5 MHz, CDCl<sub>3</sub>) δ 174.5 (COOH), 173.6 (2 × C=N), 150.5 (CH), 142.7 (C-Ar), 141.9 (C-Ar), 140.5 (C-Ar), 140.4 (C-Ar), 128.9 (CH-Ar), 125.4 (CH-Ar), 125.3 (CH-Ar), 122.1 (CH-Ar), 121.9 (CH-Ar), 111.0 (CH-Ar), 110.9 (CH-Ar), 104.4 (CH), 103.6 (CH), 51.5 (C), 44.3 (CH<sub>2</sub>), 40.7 (CH<sub>2</sub>), 31.8 (CH<sub>3</sub>), 29.7 (CH<sub>2</sub>), 28.1 (CH<sub>3</sub>), 27.9 (CH<sub>3</sub>), 26.3 (CH<sub>2</sub>), 25.7 (CH<sub>3</sub>).

**UV/vis** (MeOH) $\lambda_{abs}=547$ nm, $\lambda_{em}=561$ nm, $\varepsilon$ = 1.06 $\times$10<sup>5</sup> M<sup>-1</sup> cm<sup>-1</sup>

**IR** (neat) 2927, 2360, 1686, 1558, 1456, 1414, 1199, 1114, 926 cm<sup>-1</sup>

**HRMS** (ES) for C<sub>30</sub>H<sub>37</sub>N<sub>2</sub>O<sub>2</sub><sup>+</sup> (M)<sup>+</sup>: calc 457.28496, found 457.28661
2-{(1E,3E)-3-[3-(5-carboxypentyl)-1,1-dimethyl-1,3-dihydro-2H-benzo[e]indol-2-ylidene]-1-propenyl}-1,1,3-trimethyl-1H-benzo[e]indolium Inner Salt

8d

To PS-bound Hemicyanine 7d (0.5 g, 0.50 mmol)* were added dry pyridine (3.5 mL), DIEA (1.0 mL, 5.8 mmol), Ac₂O (0.54 mL, 5.8 mmol) and 3-(5-carboxypentyl)-1,1,2-trimethyl-1H-benzo[e]indolium bromide (24 mg, 0.06 mmol). The mixture was stirred at room temperature for 2 h. Afterwards, the resin was removed by filtration and washed several times with DCM (10 mL). The filtrates were combined and evaporated and the resulting solid was dissolved in DCM (15 mL) and washed with water (3 × 10 mL). After removal of the solvent in vacuo, the crude product was precipitated in Et₂O, washed with Et₂O and then purified by chromatography (DCM → DCM/MeOH 1:1) to give 8d as a purple solid (16 mg, 49%).

*based on theoretical loading of the resin 7d

\( R_f \) 0.35 (DCM/MeOH 9:1)

HPLC \( t_R = 5.65 \text{ min} \), 100\% (ELSD)

MS (ES): \( m/z \) (%) 557.2 [M⁺, 100], 558.2 [(M+1)⁺, 40], 559.2 [(M+2)⁺, 10]

\(^1\)H NMR (360 MHz, CD₃OD) \( \delta \) 8.78 (t (dd), 1H, \( J_{1,2} \approx J_{2,3} = 13.5 \text{ Hz}, \text{CH-H2} \)), 8.29 (d, 2H, \( J = 8.2, \text{ Hz, Ar-H9, Ar-H9'} \)), 8.10-8.04 (m, 4H, Ar-H4, Ar-H4', Ar-H6, Ar-H6'), 7.70-7.63 (m, 4H, Ar-H5, Ar-H5',Ar-H8, Ar-H8'), 7.55 (bt (dd), 2H, \( J_{6,7} = J_{7,8} = 7.2 \text{ Hz}, \text{Ar-H7, Ar-H7'} \)), 6.50 (d, 1H, \( J = 13.5 \text{ Hz, CH-H1 or H3} \)), 6.49 (d, 1H, \( J = 13.5 \text{ Hz, CH-H1 or H3} \)), 4.30 (t, 2H, \( J = 7.2 \text{ Hz, CH₂-ε} \)), 3.82 (s, 3 H, NCH₃), 2.31 (t, 2H, \( J = 7.2 \text{ Hz, CH₂-α} \)), 2.10 (s, 12H, CH₃), 1.94 (quintet, 2H, \( J = 7.2 \text{ Hz, CH₂-δ} \)), 1.74 (quintet, 2H, \( J = 7.2 \text{ Hz, CH₂-β} \)), 1.61-1.52 (m, 2H, CH₂-γ).
$^{13}$C NMR (90.5 MHz, CD$_3$OD) δ 182.0 (COO’), 177.5 (C=N), 176.9 (C=N), 150.3 (CH), 141.2 (C-Ar), 140.5 (C-Ar), 134.5 (C-Ar), 134.3 (C-Ar), 133.2 (C-Ar), 131.6 (CH), 131.4 (CH-Ar), 130.8 (CH-Ar), 128.9 (CH-Ar), 128.4 (CH-Ar), 125.9 (CH-Ar), 122.9 (CH-Ar), 111.9 (CH-Ar), 111.7 (CH-Ar), 110.6 (CH-Ar), 102.9 (CH), 102.8 (CH), 52.0 (C), 51.9 (C), 45.0 (CH$_2$), 38.5 (CH$_2$), 31.7 (CH$_3$), 28.1 (CH$_2$), 27.6 (CH$_3$), 27.5 (CH$_3$), 27.3 (CH$_2$), 26.8 (CH$_2$).

UV/vis (MeOH) $\lambda_{abs}$ = 587 nm, $\lambda_{em}$ = 603 nm, $\varepsilon$ = 1.05 x 10$^5$ M$^{-1}$cm$^{-1}$

IR (neat) 3400, 2924, 1720, 1558, 1515, 1483, 1447, 1414, 1227, 1157, 1013, 935, 750 cm$^{-1}$

HRMS (ES) for C$_{38}$H$_{41}$N$_2$O$_2$$^+$ (M)$^+$: calcd 557.31626, found 457.31623
PENTAMETHINE DYSES

4-\{[(E,2E)-3-methoxy-2-propenylidene]amino\}phenol PS

\[\text{MeO} = \text{N} = \text{O}\]

6b

To 4 aminophenol PS 4 (2 g, 3.34 mmol) was added a solution of 1,1,3,3-tetramethoxypropane (7.4 mL, 45.1 mmol) and BF$_3$·OEt$_2$ (0.46 mL, 3.71 mmol) in dry DCM (9 mL) and the solution stirred at room temperature for 6h. Dry DIEA (0.94 mL, 5.51 mmol) was added and the mixture stirred for 5 min. The resin was isolated by filtration, washed several times with DCM (20 mL), and dried in vacuo to give the product as a dark blue-black resin. Found: N, 2.19; Calcd: N, 2.10. IR (neat) 698, 1172, 1218, 1450, 1507, 1626, 2341, 2360, 2917, 3023 cm$^{-1}$

2-\{(1E,3E)-4-(4-hydroxyanilino)-1,3-butadienyl\}-1,3,3-trimethyl-3H-indolium iodide PS

7b

To 4-\{[(E,2E)-3-methoxy-2-propenylidene]amino\}phenol PS 6b (1 g, 1.56 mmol) and 1,2,3,3-tetramethyl-3H-indolium iodide (2.3 g, 7.6 mmol) was added DMF (8 mL) and the mixture stirred at 120 °C for 15 min under microwave irradiation. After cooling, the resin was isolated by filtration, washed with DMF (3 × 10 mL) and DCM (3 × 10 mL), and dried in vacuo to give the product (0.96 mmolg$^{-1}$, 87 % by N analysis) as a blue-black resin. Found: N, 1.87; Calcd: N, 2.14. IR (neat) 3023, 2917, 1588, 1506, 1451, 1220, 1171, 1014, 822, 757, 733, 698 cm$^{-1}$ The signal at 1626 (C=N) disappeared.
2-\{(1E,3E)-4-(4-hydroxyanilino)-1,3-butadienyl\}-1,1,3-trimethyl-1H-benzo[e]indolium iodide PS

To 4-\{[(E,2E)-3-methoxy-2-propenylidene]amino\}phenol PS 6b (1 g, 1.56 mmol) and 1,2,3,3-tetramethyl-3H-indolium iodide (2.7 g, 7.8 mmol) was added DMF (8 mL) and the mixture stirred at 120 °C for 15 min under microwave irradiation. After cooling, the resin was isolated by filtration, washed with DMF (3 × 10 mL) and DCM (3 × 10 mL), and dried \textit{in vacuo} to give the product as a blue-black resin. IR (neat) 3023, 2917, 2360, 1506, 1455, 1168, 1012, 939, 824, 752, 698 cm\(^{-1}\).

2-\{(1E,3E,5E)-5-[1-(5-carboxypentyl)-3,3-dimethyl-1,3-dihydro-2H-indol-2-ylidene]-1,3-pentadienyl\}-1,3,3-trimethyl-3H-indolium Inner Salt

To PS-bound Hemicyanine 7b (1.1 g, 1.1 mmol) were added dry pyridine (7 mL), DIEA (1.9 mL, 11 mmol), Ac\(_2\)O (1.0 mL, 11 mmol) and 1-(5-carboxypentyl)-2,3,3-trimethyl-3H-indolium bromide (50 mg, 0.14 mmol). The mixture was stirred at room temperature for 1-2 h. Afterwards, the resin was removed by filtration and washed with DCM (4 × 10 mL). The filtrates were combined and evaporated and the resulting solid was dissolved in DCM (15 mL) and washed several times with water (10 mL). After removal of the solvent \textit{in vacuo}, the crude product was precipitated in Et\(_2\)O, washed with Et\(_2\)O and then
purified by chromatography (DCM → DCM/MeOH 1:1) to give 8b as a blue solid (57 mg, 84%).

**Rf** 0.32 (DCM/MeOH 9:1)

**IR** (neat) 2929, 2359, 1684, 1478, 1436, 1346, 1092, 919, 897, 786, 728, 708 cm⁻¹

**HPLC** t<sub>R</sub> = 6.25 min, 100% (ELSD, λ = 650 nm)

Purity of crude product: 97% (ELSD), 90 % (λ = 650 nm)

**MS** (ES): m/z (%) 483.3 [M⁺, 100], 484.3 [(M+1)⁺, 36], 485.3 [(M+2)⁺, 7].

**¹H NMR** (360 MHz, MeOD) δ<sub>H</sub> 8.25 (t (dd), 2H, J<sub>1,2</sub> ≈ J<sub>2,3</sub> ≈ J<sub>3,4</sub> = J<sub>4,5</sub> = 13.1 Hz, CH-H₂ + CH-H₄), 7.49 (bd, 2H, J = 7.4 Hz, Ar-H₄, Ar-H₄'), 7.44 (td (ddd), 2H, J<sub>5,6</sub> ≈ J<sub>6,7</sub> ≈ 7.7, J<sub>4,6</sub> = 1.1 Hz, Ar-H₆, Ar-H₆'), 7.31-7.23 (m, 4H, Ar-H₅, Ar-H₅', Ar-H₇, Ar-H₇'), 6.64 (t (dd), 1H, J<sub>2,3</sub> ≈ J<sub>3,4</sub> = 12.4 Hz, CH-H₃), 6.30 (d, 1H, J = 13.7 Hz, CH-H₁ or H₅), 6.27 (d, 1H, J = 13.7 Hz, CH-H₁ or H₅), 4.10 (t, 2H, J = 7.5 Hz, CH₂-ε), 3.62 (s, 3H, NCH₃), 2.19 (t, 2H, J = 7.4 Hz, CH₂-α), 187-179 (m, 2H, CH₂-δ), 172-165 (s + m, 14H, CH₂-β + CH₃), 154-144 (m, 2H, CH₂-γ).

**¹³C NMR** (90.5 MHz, MeOD) δ<sub>C</sub> 182.2 (COO⁻, salt form), 180.3 (COOH), 174.7 (CN), 174.3 (CN), 155.2 (CH), 155.0 (CH), 143.9 (C-Ar), 143.1 (C-Ar), 142.3 (C-Ar), 142.0 (C-Ar), 129.4 (CH-Ar), 129.3 (CH-Ar), 126.3 (CH), 125.8 (CH-Ar), 125.7 (CH-Ar), 122.9 (CH-Ar), 122.8 (CH-Ar), 111.7 (CH-Ar), 111.3 (CH-Ar), 103.9 (CH), 103.5 (CH), 50.1 (C), 50.0 (C), 44.5 (CH₂), 38.2 (CH₂), 31.0 (CH₃), 27.9 (CH₂), 27.5 (CH₃), 27.4 (CH₃), 26.8 (CH₂), 23.6 (CH₃).

**UV/vis** (MeOH) λ<sub>abs</sub>= 640 nm, ε = 1.77 × 10⁵ M⁻¹cm⁻¹, λ<sub>em</sub>= 660 nm

**HRMS** for C<sub>32</sub>H<sub>39</sub>N<sub>2</sub>O<sub>2</sub>⁺ (M)⁺: calcd 483.30061, found 483.30063
To PS-bound Hemicyanine 7e (1.5 g, 1.56 mmol) were added dry pyridine (11 mL), DIEA (2.6 mL, 15 mmol), Ac₂O (1.4 mL, 15 mmol) and 1-(5-carboxypentyl)-2,3,3-trimethyl-3H-indolium bromide (80 mg, 0.20 mmol). The mixture was stirred at room temperature for 1-2 h. Afterwards, the resin was isolated by filtration and washed several times with DCM (15 mL). The filtrates were combined and evaporated and the resulting solid was redissolved in DCM (20 mL) and washed several times with water (10 mL). After removal of the solvent in vacuo, the crude product was precipitated in Et₂O, washed with Et₂O and then purified by chromatography (DCM → DCM/MeOH 1:1) to give 7e as a dark blue-green solid (107 mg, 92%).

**HPLC** \( t_R = 11.5 \text{ min}, 100\% \) (ELSD, \( \lambda = 675 \text{ nm} \))

**MS (ES):** \( m/z \) (%) 583.5 [M⁺, 100], 584.5 [(M+1)⁺, 45], 585.5 [(M+2)⁺, 10].

**¹H NMR** (360 MHz, MeOD) \( \delta \) 8.33 (t, (dd) 2H, \( J_{1,2} \approx J_{2,3} = J_{3,4} = J_{4,5} = 12.9 \text{ Hz}, \text{CH-H2} + \text{CH-H4} \)), 8.24 (d, 2H, \( J = 8.5 \text{ Hz}, \text{Ar-H9, Ar-H9'} \)), 8.00 (d, 1H, \( J = 8.8 \text{ Hz}, \text{Ar-H6 or Ar-H6'} \)), 7.99 (d, 1H, \( J = 8.8 \text{ Hz}, \text{Ar-H6 or Ar-H6'} \)), 7.97 (d, 2H, \( J = 8.2 \text{ Hz}, \text{Ar-H4, Ar-H4'} \)), 7.59-7.67 (m, 4H, Ar-H5, Ar-H5', Ar-H8, Ar-H8'), 7.47 (bt, (dd) 2H, \( J_{6,7} = \approx J_{7,8} = 7.6 \text{ Hz}, \text{Ar-H7, Ar-H7'} \)), 6.68 (t, (dd) 1H, \( J_{2,3} \approx J_{3,4} = 12.4 \text{ Hz}, \text{CH-H3} \)), 6.35 (d, 2H, \( J = 13.7 \text{ Hz}, \text{CH-H1 or H5} \)), 6.34 (d, 2H, \( J = 13.8 \text{ Hz}, \text{CH-H1 or H5} \)), 4.23 (t, 2H, \( J = 7.3 \text{ Hz}, \text{CH}_2-\varepsilon \)), 3.76 (s, 3H, NCH₃), 2.33 (t, 2H, \( J = 7.2 \text{ Hz}, \text{CH}_2-\alpha \)), 1.98 (s, 12H, NCH₃), 1.86-1.92 (m, 2H, CH₂-δ), 1.71-1.79 (m, 2H, CH₂-β), 1.53-1.61 (m, 2H, CH₂-γ).
$^{13}$C NMR (90.5 MHz, MeOD) δ 179.4 (COOH), 176.4 (C=N), 175.8 (C=N), 154.3 (CH), 141.6 (C), 140.9 (C), 135.1 (C), 134.9 (C), 133.4 (C), 131.7 (CH), 131.1 (CH), 129.4 (CH), 129.4 (CH), 128.7 (CH), 126.6 (CH), 126.1 (CH), 126.0 (CH), 123.3 (CH), 112.1 (CH), 111.9 (CH), 104.1 (CH), 103.9 (CH), 52.4 (C), 52.3 (C), 45.0 (CH$_2$), 36.5 (CH$_2$), 31.9 (CH$_3$), 28.5 (CH$_2$), 27.6 (CH$_2$), 27.5 (CH$_3$), 26.4 (CH$_2$).

UV/vis (MeOH) $\lambda_{abs}$ = 678 nm, $\varepsilon = 1.42 \times 10^5$ M$^{-1}$cm$^{-1}$, $\lambda_{em}$ = 704 nm

$R_f$ 0.35 (DCM/MeOH 9:1)

IR (neat) 2931, 1684, 1479, 1454, 1436, 1349, 1092, 1006, 920, 787, 728, 704 cm$^{-1}$

HRMS for C$_{40}$H$_{43}$N$_2$O$_2^+$ (M$^+$): calcd 583.33191, found 583.33202

**HEPTAMETHINE DYES**

2-[[1E,3E,5E]-6-(acetylanilino)-1,3,5-hexatrienyl]-1,3,3-trimethyl-3H-indolium iodide

![5a](image)

A suspension of 1,2,3,3-tetramethyl-3H-indolium iodide (2.5 g, 8.3 mmol) and N-[(E,2E,4E)-5-anilino-2,4-pentadienylidene]aniline hydrochloride (2 g, 7 mmol) in a (1:1) mixture of acetic acid and acetic anhydride (30 mL) was heated at 120 °C for 2.5 h.$^2$ The completion of the reaction was carefully monitored by UV-visible spectrometry: hemicyanine intermediate and symmetrical dicarboxylic acid cyanine dye have an absorption maximum around 489 and 750 nm, respectively. After cooling, the reaction mixture was evaporated and the resulting solid was dissolved in DCM (20 mL) and repeatedly washed with water (15 mL). After removal of the solvent in vacuo, the crude product was precipitated in Et$_2$O, collected by filtration and dried to give the compound 5a as a dark red solid.

$R_f$: 0.36 (DCM/MeOH 9:1)

IR (neat) 3318, 3050, 1684, 1593, 1547, 1259, 1156, 1106, 995, 917, 760 cm$^{-1}$.

HPLC $t_R = 8.5$ min
MS (ES): \( m/z \) (%): 371.1 \([M^+, 100]\), 372.1 \([(M+1)^+, 25]\), 373.1 \([(M+2)^+, 3]\).

\(^1\)H NMR (360 MHz, CDCl\(_3\)): 8.17 (d, \( J = 14.0 \text{ Hz}, 1\text{H}, \text{CH} \)), 8.15-8.12 (m, 1H, CH), 7.92 (dd, \( J = 14.9, 11.4 \text{ Hz}, 1\text{H}, \text{CH} \)), 7.64-7.12 (m, 9H, Ar), 7.00-6.96 (m, 2H, CH), 6.61 (dd, \( J = 14.2, 11.4 \text{ Hz}, 1\text{H}, \text{CH} \)), 3.78 (s, 3H, CH\(_3\)), 1.74 (s, 3H, CH\(_3\)), 1.48 (s, 6H, CH\(_3\)).

UV = (MeOH) \( \lambda_{\text{abs}} = 489 \text{ nm} \)

2-[(1E,3E,5E)-6-(acetyl-4-hydroxyanilino)-1,3,5-hexatrienyl]-1,3,3-trimethyl-3\(H\)-indolium iodide PS

\[ \text{7c} \]

To 4-aminophenol PS 7 (0.5 g, 0.8 mmol) was added a solution of compound 5a (0.9 g, 1.8 mmol) in DCM (5 mL) and the mixture stirred at room temperature for 1 h. Afterwards, the resin was isolated by filtration, washed extensively with DMF, MeOH, DCM to remove the symmetrycal dye and dried \textit{in vacuo} to give the product as a dark resin (0.77 mmolg\(^{-1}\), 83 % by N analysis). Found: N, 2.17; Calcd: N, 2.60. IR (neat) 3025, 2919, 2359, 1717, 1507, 1490, 1225, 1017, 821, 756, 724 cm\(^{-1}\)

2-[(1E,3E,5E)-6-(acetylanilino)-1,3,5-hexatrienyl]-1,1,3-trimethyl-1\(H\)-benzo[\(e\)]indolium iodide

\[ \text{5b} \]

A suspension of 1,2,3,3-tetramethyl-3\(H\)-indolium iodide (3.0 g, 8.4 mmol) and glutaonaldehyde dianil hydrochloride (2 g, 7 mmol) in a (1:1) mixture of acetic acid and acetic anhydride (30 mL) was heated at 120 °C for 2.5 h. The completion of the reaction
was carefully monitored by UV-visible spectrometry: hemicyanine intermediate and symmetrical dicarboxylic acid cyanine dye have an absorption maximum around 493 and 780 nm, respectively. After cooling, the reaction mixture was evaporated and the resulting solid was dissolved in DCM (20 mL) and repeatedly washed with water (15 mL). After removal of the solvent in vacuo, the crude product was precipitated in Et₂O, collected by filtration and dried to give the compound 5b as a dark red-purple solid.

**Rₚ**: 0.36 (DCM/MeOH 9:1)

**IR (neat)** 3315, 2930, 1705, 1666, 1242, 1091, 923, 756 cm⁻¹

**HPLC** ₜᵣ = 6.91 min

**MS** (ES): m/z (%) 421.1 [M⁺, 100], 422.1 [(M+1)⁺, 30], 423.1 1 [(M+2)⁺, 6]

**¹H NMR** (500 MHz, CDCl₃) δ 8.18-8.14 (m, 2H, Ar + CH), 8.06-8.00 (m, 3H, Ar), 7.72-7.52 (m, 6H, Ar + CH), 7.40 (d, 1H, J = 15.1 Hz, CH), 7.29 (t, 1H, J = 9.0 Hz, CH), 7.17 (d, 2H, J = 7.0 Hz, Ar), 6.83 (t, 1H, J = 12.7 Hz, CH), 5.38 (t, 1H, J = 12.6 Hz, CH), 1.98 (s, 6H, CH₃), 1.96 (s, 3H, CH₃), 1.88 (s, 3H, CH₃).

**UV** = (MeOH) λₐₛₚ = 492 nm

2-[(1E,3E,5E)-6-(acetyl-4-hydroxyanilino)-1,3,5-hexatrienyl]-1,1,3-trimethyl-1H-benzo[e]indolium iodide

![Chemical Structure](image)

**7f**

To 4-aminophenol PS 7 (1 g, 1.7 mmol) was added a solution of compound 5b (2 g, 3.6 mmol) in DCM (10 mL) and the mixture stirred at room temperature for 1 h. Afterwards, the resin was isolated by filtration, washed extensively with DMF, MeOH, DCM to remove the symmetrical dye and dried in vacuo to give the product as a dark blue-black resin. **IR** (neat) 3024, 2915, 1555, 1494, 1157, 994, 941, 827, 745, 704 cm⁻¹
To PS-bound Hemicyanine 7c (0.84 g, 0.64 mmol) were added dry pyridine (4 mL), Ac₂O (0.6 mL, 6.3 mmol) and 1-(5-carboxypentyl)-2,3,3-trimethyl-3H-indolium bromide (40 mg, 0.11 mmol). The mixture was stirred at room temperature for 2 h, until completion. Afterwards, the resin was isolated by filtration and washed (2 × 10 mL) with DCM. The reaction was then repeated in the same conditions described above. The filtrates were then combined and evaporated and the resulting solid was dissolved in DCM (10 mL) and washed several times with water (8 mL). The product was precipitated in Et₂O, washed with Et₂O and dried in vacuo giving 8c as a green solid (96 mg, 86%).

**Rf:** 0.32 (DCM/MeOH 9:1)

**IR** (neat) 2931, 2362, 1719, 1436, 1399, 1352, 1060, 1006, 915, 897, 724, 704 cm⁻¹

**HPLC** \( t_R = 5.89 \) min, 96 % (ELSD)

**MS** (ES): \( m/z \) (%) 509.5 [M⁺, 100], 510.5 [(M+1)⁺, 37], 511.5 [(M+2)⁺, 8]

**¹H NMR** (500 MHz, MeOD) δ 7.93 (t, (dd) 2H, \( J_{1,2} \approx J_{2,3} \approx J_{5,6} \approx J_{6,7} = 13.1 \) Hz, CH-H6 + CH-H2), 7.60 (t, (dd) 1H, \( J_{3,4} \approx J_{4,5} = 12.0 \) Hz, CH-H4), 7.49 (d, 1H, \( J = 7.5 \) Hz, Ar-H4 or Ar-H4'), 7.48 (d, 1H, \( J = 7.5 \) Hz, Ar-H4 or Ar-H4'), 7.39 (td (ddd), 2H, \( J_{5,6} \approx J_{6,7} = 7.7, J_{4,6} = 1.1 \) Hz, Ar-H6, Ar-H6'), 7.27-7.22 (m, 4H, Ar-H5, Ar-H5',Ar-H7, Ar-H7'), 6.61 (t, (dd), 1H, \( J = 12.6 \) Hz, CH-H3 or H5), 6.58 (t, (dd) 1H, \( J = 12.5 \) Hz, CH-H3 or H5), 6.30 (d, 1H, \( J = 13.7 \) Hz, CH-H1 or CH-H7),6.24 (d, 1H, \( J = 13.7 \) Hz, CH-H1 or CH-H7), 4.07 (t, 2H, \( J = 7.5 \) Hz, CH₂-ε), 3.59 (s, 3H, NCH₃), 2.29 (t, 2H, \( J = 7.3 \) Hz, CH₂-α), 1.82
(quintet, 2H, \(J = 7.7\) Hz, \(\text{CH}_2-\delta\)), 1.70-1.67 (m + s, 14H, \(\text{CH}_2-\beta + \text{CH}_3\)), 152-1.46 (m, 2H, \(\text{CH}_2-\gamma\)).

\(^1\text{H} \text{NMR}\) (360 MHz, MeOD) \(\delta\) 7.93 (t, 2H, \(J = 13.1\) Hz, CH), 7.60 (t, 1H, \(J = 12.0\) Hz, CH), 7.51-7.39 (m, 4H, Ar), 7.34-7.23 (m, 4H, Ar), 6.61 (t, 1H, \(J = 12.4\) Hz, CH), 6.58 (t, 1H, \(J = 12.4\) Hz, CH), 6.35 (d, 1H, \(J = 13.7\) Hz, CH), 6.26 (d, 1H, \(J = 13.6\) Hz, CH), 4.12 (t, 2H, \(J = 7.6\) Hz, \(\text{CH}_2\)), 3.61 (s, 3H, NCH\(_3\)), 2.21 (t, 2H, \(J = 7.3\) Hz, \(\text{CH}_2\)), 1.89-1.67 (m + s, 16H, 2\(\times\) \(\text{CH}_2 + \text{CH}_3\)), 158-1.49 (m, 2H, \(\text{CH}_2\)).

\(^{13}\text{C} \text{NMR}\) (90.5 MHz, MeOD) \(\delta\) 178.6 (COOH), 173.8 (C=N), 173.2 (C=N), 153.0 (CH), 144.4 (C), 143.7 (C), 143.3 (C), 142.5 (C), 142.3 (C), 141.8 (C), 129.8 (CH), 129.7 (CH), 127.0 (CH), 126.0 (CH-Ar), 124.7 (CH-Ar), 123.4 (CH-Ar), 123.3 (CH-Ar), 111.9 (CH-Ar), 111.6 (CH-Ar), 104.8 (CH), 50.4 (C), 50.2 (C), 44.9 (CH\(_2\)), 35.7 (CH\(_2\)), 31.5 (CH\(_3\)), 28.2 (CH\(_2\)), 28.1 (CH\(_3\)), 27.9 (CH\(_3\)), 27.4 (CH\(_2\)), 26.1 (CH\(_2\)).

\text{UV/vis} \text{ (MeOH)} \lambda_{\text{abs}} = 743\text{ nm}, \varepsilon = 1.40 \times 10^5 \text{ M}^{-1}\text{cm}^{-1}, \lambda_{\text{em}} = 765\text{ nm}

\text{HRMS for C}_{34}\text{H}_{41}\text{N}_2\text{O}_2^+ (M)^+ : \text{calcd} 509.31626, \text{found} 509.31634

\textit{2-\{\textit{1E,3E,5E,7E}\}-7-\text{[3-(5-carboxypentyl)-1,1-dimethyl-1,3-dihydro-2H-benzo[e]indol-2-ylidene]-1,3,5-heptatrienyl}-1,1,3-trimethyl-1H-benzo[e]indolium Inner Salt}

\textbf{8f}

To PS-bound Hemicyanine 7f (0.7 g, 0.7 mmol)* were added dry pyridine (3.2 mL), Ac\(_2\)O (0.8 mL, 8.4 mmol) and 1-(5-carboxypentyl)-2,3,3-trimethyl-3H-indolium bromide (34 mg, 0.08 mmol). The mixture was stirred at room temperature for 2 h, until completion. Afterwards, the resin was isolated by filtration and washed with DCM (2 \(\times\) 10 mL). The reaction was then repeated in the same conditions described above. The
filtrates were combined and evaporated, the resulting solid was dissolved in DCM (15 mL) and washed several times with water (10 mL). The product was then precipitated in Et₂O, washed with Et₂O and dried *in vacuo* giving 8f as a green solid (50 mg, 51%).

*based on theoretical loading of the resin 7f*

[R]: 0.39 (DCM/MeOH 9:1)

[IR (neat)] 2924, 2457, 1725, 1410, 1087, 1008, 892, 897, 729 cm⁻¹

[HPLC] t_R = 4.20 min, 86% (λ_abs = 800 nm)

[MS (ES)]: m/z (%) 609.2 [M⁺, 100], 610.2 [(M+1)⁺, 40], 611.2 [(M+2)⁺, 10]

[¹H NMR (500 MHz, MeOD)] δ 8.18 (d, 2H, J = 8.6 Hz, Ar-H9, Ar-H9'), 8.03-8.00 (m, 2H, CH-H2 + CH-H6), overlapping with 8.00 (d, 1H, J = 8.8 Hz, Ar-H6 or Ar-H6'), 7.99 (d, 1H, J = 8.8 Hz, Ar-H6 or Ar-H6'), 7.95 (d, 2H, J = 8.30 Hz, Ar-H4, Ar-H4'), 7.65-7.62 (m, 1H, CH-H4) overlapping with 7.59 (td, (ddd) 2H, J = 8.3, 1.1 Hz, Ar-H8, Ar-H8'), 7.58 (d, 1H, J = 8.9 Hz, Ar-H5), 7.56 (d, 1H, J = 9.0 Hz, Ar-H5'), 7.42 (bt (dd), 2H, J_6,7 ≈ J_7,8 = 7.5 Hz, Ar-H7, Ar-H7'), 6.56 (t (dd), 1H, J = 12.4 Hz, CH-H3 or H5), 6.55 (t (dd), 1H, J = 12.4 Hz, CH-H3 or H5), 6.27 (d, 1H, J = 13.7 Hz, CH-H1 or H7), 6.26 (d, 1H, J = 13.7 Hz, CH-H1 or H7), 4.19 (t, 2H, J = 7.5 Hz, CH₂-α), 3.72 (s, 3H, CH₃), 2.33 (t, 2H, J = 7.3 Hz, CH₂-α), 1.92 (s, 3H, NCH₃), 1.85 (quintet, 2H, J = 7.7 Hz, CH₂-δ), 1.70 (quintet, 2H, J = 7.3 Hz, CH₂-β), 1.52 (quintet, 2H, J = 7.8 Hz, CH₂-γ).

[¹³C NMR (126 MHz, MeOD)] δ 182.4 (COO'), 177.9 (C=N), 177.4 (C=N), 150.8 (CH), 141.7 (C), 140.9 (C), 135.0 (C), 134.8 (C), 133.7 (C), 132.1 (C), 131.9 (CH-Ar), 131.3 (CH-Ar), 131.2 (CH-Ar), 129.4 (CH), 129.3 (CH), 128.9 (CH), 126.4 (CH-Ar), 126.3 (CH-Ar), 123.4 (CH-Ar), 112.4 (CH-Ar), 112.2 (CH-Ar), 103.4 (CH), 103.3 (CH), 52.5 (C), 52.4 (C), 45.4 (CH₂), 36.7 (CH₂), 33.2 (CH₃), 29.8 (CH₂), 28.9 (CH₃), 28.8 (CH₃), 28.7 (CH₂), 27.3 (CH₂).

[UV/vis (MeOH)] λ_abs = 781, ε = 1.3 × 10⁵ M⁻¹cm⁻¹, λ_em = 808 nm

[HRMS] for C₄₂H₄₅N₂O₂⁺ (M)⁺: calcd 609.34756, found 609.34752
SULFONATED DYE

2-[(1E,3E)-4-(acetylanilino)-1,3-butadienyl]-1,3,3-trimethyl-3H-indolium-5-sulfonate

A mixture of 1,2,3,3-tetramethyl-3H-indolium-5-sulfonate (1.0 g, 2.4 mmol) and N-[(1E,3E)-3-(phenylimino)-1-propenyl]aniline hydrochloride (0.7 g, 2.7 mmol) was heated at 120 °C in a solution (1:1) of acetic acid and acetic anhydride (4 mL) for 2 h until an orange colour was noticed. The reaction was carefully monitored by UV-visible spectrometry: hemicyanine intermediate 3c and symmetrical dicarboxylic acid have an absorption maximum at 445 and 650 nm, respectively. After cooling, the solvent was evaporated and the solid precipitated with diethyl ether, filtered and washed several times with ethyl acetate. After drying in vacuo, the intermediate, isolated as an orange solid, was directly used for the next step.

R_f: 0.63 (DCM/MeOH 4:1)

IR (neat) 3475, 3069, 2978, 2358, 1694, 1574, 1512, 1468, 1167, 1111, 1027, 995 cm⁻¹

HPLC \( t_R = 4.74 \) min

MS (ES): \( m/z \) (%) 423.0 [(M-1)⁻, 100], 424.1 [M⁺, 23], 847 [(2M-1)⁻, 7]

\(^1\)H NMR (360 MHz, D₂O) \( \delta \) 8.55 (d, 1H, \( J = 12.8 \) Hz, CH), 8.00-7.90 (m, 2H, CH), 7.78-7.53 (m, 5H, Ar), 7.38-7.30 (m, 3H, Ar), 6.42 (d, 1H, \( J = 15.1 \) Hz, CH), 5.55 (t, 1H, \( J = 12.8 \) Hz, CH), 1.66-1.64 (m, 12H).

UV = (MeOH) \( \lambda_{abs} = 445 \) nm
2-[(1E,3E)-4-(acetyl-4-hydroxyanilino)-1,3-butadienyl]-1,3,3-trimethyl-3H-indolium-5-sulfonate PS

![Chemical Structure](image)

7g

To 4-aminophenol PS 7 (0.35 g, 0.6 mmol) was added a solution of 3c (0.50 g, 1.2 mmol) in DCM/DMF (3:1) (4 mL) and the mixture stirred at room temperature for 1 h. Afterwards, the resin was isolated by filtration, washed extensively with DMF, MeOH, DCM and dried *in vacuo* to give the product as a dark resin (0.75 mmolg⁻¹, 75% by nitrogen elemental analysis). Found: N, 2.10; Calcd: N, 2.80.

**IR** (neat) 3024, 2917, 1667, 1538, 1507, 1451, 1169, 1026, 822, 755, 704 cm⁻¹

Potassium 2-[(1E,3E,5E)-5-[1-(5-carboxypentyl)-3,3-dimethyl-5-sulfonato-1,3-dihydro-2H-indol-2-ylidene]-1,3-pentadienyl]-1,3,3-trimethyl-3H-indolium-5-sulfonate

![Chemical Structure](image)

8g

To PS-bound Hemicyanine 7g (0.35 g, 0.26 mmol) were added dry pyridine (1.6 mL), Ac₂O (0.4 mL, 4.2 mmol) and 1-(5-carboxypentyl)-2,3,3-trimethyl-3H-indolium-5-sulfonate (20 mg, 0.06 mmol). The mixture was stirred at room temperature for 2 h, until completion. Afterwards, the resin was isolated by filtration, washed with a solution 9:1 DCM/DMF (2 × 5 mL) and the reaction repeated in the same conditions described above.
The resin was isolated by filtration and then washed with a mixture 9:1 DCM/DMF (3 × 5 mL). The filtrates were combined and evaporated. Afterwards, the resulting solid was washed and precipitated with Et₂O and centrifuged. The supernatant was removed and the precipitate dried in vacuo to give 8g as a blue solid (77 mg, 94 %).

Rᵣ: 0.40 (DCM/MeOH 3:2)

IR (neat) 3413, 2929, 1716, 1494, 1459, 1368, 1330, 1153, 1099, 1016, 926, 817 cm⁻¹

HPLC tᵣ = 3.6 min, 94% (λₐₛₜ = 650 nm)

MS (ES): m/z (%) 320.0 [(M/2)₂, 100], 641.0 [(M-2)⁻, 40], 642.0 [(M-1)⁻, 21], 643.0 [M⁻, 8]

¹H NMR (360 MHz, MeOD) δ: 8.31 (t (dd), 2H, J₁,₂ ≈ J₂,₃ ≈ J₃,₄ ≈ J₄,₅ = 13.4 Hz, CH-H₂ + CH-H₄), 7.90-7.85 (m, 4H, Ar-H₄, Ar-H₄’, Ar-H₆, Ar-H₆’), 7.36 (d, 1H, J = 8.2 Hz, Ar-H₇ or Ar-H₇’), 7.33 (d, 1H, J = 8.8 Hz, Ar-H₇ or Ar-H₇’), 6.70 (t (dd), 1H, J₂,₃ ≈ J₃,₄ = 12.2 Hz, CH-H₃), 6.36 (d, 1H, J = 13.1 Hz, CH-H₁ or CH-H₅), 6.32 (d, 1H, J = 13.2 Hz, CH-H₁ or CH-H₅), 4.12 (t, 2H, J = 7.3 Hz, CH₂-ε), 3.64 (s, 3H, NCH₃), 2.20 (t, 2H, J = 7.4 Hz, CH₂-α), 1.87-1.65 (m, 16H, CH₂-δ + CH₂-β + 2 × CH₃), 1.56-1.47 (m, 2H, CH₂-γ).

¹³C NMR (90.5 MHz, MeOD): δ 182.4 (COO⁻), 175.9 (C=N), 175.4 (C=N), 156.2 (CH), 145.7 (C-Ar), 144.9 (C-Ar), 143.4 (C-Ar), 143.3 (C-Ar), 142.7 (C-Ar), 142.5 (C-Ar), 128.1 (CH-Ar), 128.0 (CH-Ar), 127.8 (CH), 121.4 (CH-Ar), 121.3 (CH-Ar), 111.7 (CH-Ar), 111.4 (CH-Ar), 104.4 (CH), 105.3 (CH), 50.6 (C), 50.5 (C), 45.2 (CH₂), 38.8 (CH₂), 31.8 (CH₃), 30.7 (CH₂), 28.3 (CH₂), 27.9 (CH₃), 27.8 (CH₃), 27.7 (CH₂), 27.2 (CH₂).

UV/vis (MeOH) λₐₛₜ = 647, λₑₘ = 667 nm

HRMS for C₃₂H₃₇N₂O₂S₂⁻ (M⁻): calcd 641.19858, found 641.19658
PREPARATION OF INDOLENIUM SALTS

1-(5-carboxypentyl)-2,3,3-trimethyl-3H-indolium bromide

Classical Method
A mixture of 2,3,3-trimethyl-3H-indole (12.1 mL, 75.4 mmol) and 6-bromoexanoic acid (30 g, 189 mmol) in acetonitrile (50 mL) was heated at 100 °C for 16h. The solution was cooled to room temperature and evaporated. The residue obtained was washed with diethyl ether and dichloromethane several times until removal of the starting material to give a white-grey solid (18g, 68 %).

Microwave-assisted alkylation
A mixture of 2,3,3-trimethyl-3H-indole (0.25 mL, 1.6 mmol) and 6-bromoexanoic acid (936 mg, 4.8 mmol) in acetonitrile (1 mL) was heated in a sealed vial at 150 °C for 1 hour under microwave irradiation. After cooling to room temperature, the solvent was evaporated. The residue obtained was washed with diethyl ether and dichloromethane several times until removal of the starting material and then dried in vacuo to give a white-grey solid (374 mg, 66 %).

Rf: 0.26 (DCM/MeOH 3:2)
HPLC $t_R = 3.74$ min, 100% (ELSD, $\lambda = 220, 254, 280$ nm)
MS (ES): $m/z$ (%) 274.2 [M$^+$, 100], 275.3 [(M+1)$^+$, 19]
$^1$H NMR (250 MHz, DMSO): $\delta$ 8.23-8.19 (m, 1H), 8.09-8.06 (m,1H), 7.87-7.80 (m, 2H), 4.69 (t, 2H, $J = 7.6$ Hz), 3.91 (s, 3H), 2.44 (t, 2H, $J = 7.1$ Hz), 2.12-2.00 (m, 2H), 1.83-1.61 (m, 10H).
$^{13}$C NMR (62.9 MHz, DMSO): $\delta$ 196.88 (C=N), 174.66 (C=O), 142.23 (C), 141.40 (C), 129.75 (CH), 129.30 (CH), 123.88 (CH), 115.87 (CH), 54.52 (C), 47.82 (CH$_2$), 33.73 (CH$_2$), 27.31 (CH$_2$), 25.77 (CH$_2$), 24.38 (CH$_2$), 22.37 (CH$_3$), 14.44 (CH$_3$)

IR (neat) 3449, 3195, 2817, 1693, 1459, 1290, 1174, 872, 775 cm$^{-1}$.

Mp 138 $^\circ$C

3-(5-carboxypentyl)-1,1,2-trimethyl-1$H$-benzo[e]indolium bromide

A mixture of 1,2,2-trimethyl-1$H$-benz[e]indole (15.8 g, 75.4 mmol) and 6-bromoexanoic acid (30g, 189 mmol) in acetonitrile (50 mL) was heated at 120 $^\circ$C for 2 days. The solution was cooled to room temperature and evaporated. The residue obtained was washed with diethyl ether and dichloromethane several times until removal of the starting material to give a pink-grey solid (23.4g, 77%)

R$_f$: 0.14 (DCM/MeOH 3:2)

HPLC $t_R = 4.54$ min, 100% (ELSD)

MS (ES): $m/z$ (%) 324.3 [M$^+$, 100], 325.2 [(M+1)$^+$, 35]

$^1$H NMR $\delta$ (250 MHz, DMSO): $\delta$ 8.46 (d, 1H, $J = 8.2$ Hz), 8.37 (d, 1H, $J = 8.9$ Hz), 8.30 (dd, 1H, $J = 8.7$, 1.4 Hz ), 8.26 (d, 1H, $J = 8.9$ Hz), 7.89-7.77 (m, 2H), 4.68 (t, 2H, $J = 7.5$ Hz), 3.05 (s, 3H), 2.31 (t, 2H, $J = 7.0$ Hz), 2.01-1.93 (m, 2H), 1.68-1.54 (m, 10H).

$^{13}$C NMR (62.9 MHz, DMSO): $\delta$ 196.74 (C=N), 174.67 (C=O), 138.86 (C), 137.31 (C), 133.39 (C), 131.03 (CH), 130.07 (CH), 128.75 (CH), 127.58 (CH), 123.78 (CH), 113.74 (CH), 55.85 (C), 48.07 (CH$_2$), 33.74 (CH$_2$), 27.52 (CH$_2$), 25.75 (CH$_2$), 24.42 (CH$_2$), 21.97 (CH$_3$), 14.27 (CH$_3$)
Mp 234°C

IR (neat) 2864, 1707, 1474, 1389, 1156, 824, 715 cm$^{-1}$

1,2,3,3-tetramethyl-3$H$-indolium iodide

Classical method
A mixture of 1,1,2-trimethylindole (40.10 mL, 0.25 mol) and methyl iodide (38.90 mL, 0.625 mol) in acetonitrile (150 mL) was heated under reflux (110 °C) for three days. The reaction mixture was cooled to room temperature and evaporated. The residue obtained was washed with diethyl ether several times and then with ethanol until removal of the starting material. The residue was dried in vacuo to give a white/pink solid (64.3 g, 84%).

Microwave-assisted alkylation
A mixture of 2,3,3-trimethyl-3$H$-indole (0.25 mL, 1.6 mmol) and methyl iodide (0.6 mL, 9.6 mmol) in acetonitrile (1 mL) was heated in a sealed vial at 150 °C for 30 min, under microwave irradiation. After cooling to room temperature, the pink precipitate was collected by filtration, washed with diethyl ether, ethanol and then dried in vacuo to give a white/pink solid (457 mg, 94%).

$R_f$: 0.50 (DCM:MeOH 9/1)

HPLC $t_R = 4.54$ min, 100% (ELSD)

MS (ES): $m/z$ (%) 174.2 [M$^+$, 100], 175.2 [(M+1)$^+$, 14]

$^1$H NMR $\delta$ (250 MHz, DMSO): $\delta$ 7.90-7.86 (m, 1H), 7.82-7.78 (m, 1H), 7.63-7.54 (m, 2H), 3.94 (s, 3H), 2.74 (s, 3H), 1.49 (s, 6H)

$^{13}$C NMR (62.9 MHz, DMSO): $\delta$ 196.34 (C=N), 142.45 (C), 141.95 (C), 129.66 (CH), 129.16 (CH), 123.65 (CH), 115.48 (CH), 54.28 (C), 35.11 (CH$_3$), 22.06 (CH$_3$), 14.56 (CH$_3$).

FTIR 3013, 2964, 2360, 1630, 1480, 988, 938 cm$^{-1}$

Mp 219 °C
1,1,2,3-tetramethyl-1\textit{H}-benzo[e]indolium iodide

\begin{center}
\begin{tikzpicture}
\node at (0,0) {\includegraphics[width=0.5\textwidth]{image}};
\end{tikzpicture}
\end{center}

\textbf{2b}

A mixture of 1,2,2-trimethyl-1\textit{H} -benz[e]indole (55.1 g, 0.26 mol) and methyl iodide (40.50 mL, 0.65 mol) in acetonitrile (250 mL) was heated under reflux at 100 °C for 2h. The reaction solution was cooled to room temperature and evaporated. The residue obtained was washed with diethyl ether several times and then with ethanol until removal of the starting material. The residue was dried \textit{in vacuo} to give white/yellow solid (66g, 72%).

\textbf{Rf}: 0.31 (DCM:MeOH 9/1)

\textbf{MS} (ES): \textit{m/z} (%) 224.2 [(M\textsuperscript{+}, 100], 225.1 [(M+1)\textsuperscript{+}, 17]

\textbf{\textsuperscript{1}H NMR} \(\delta\) (250 MHz, DMSO): \(\delta\) 8.36 (d, 1H, \(J = 8.28\) Hz, Ar), 8.29 (d, 1H, \(J = 8.96\) Hz, Ar), 8.22 (d, 1H, \(J = 7.58\) Hz, Ar), 8.11 (d, 1H, \(J = 8.90\) Hz, Ar), 7.82-7.68 (m, 2H), 4.19 (s, 3H), 2.97 (s, 3H), 1.84 (s, 6H)

\textbf{\textsuperscript{13}C NMR} (62.9 MHz, DMSO): \(\delta\) 196.26 (C=N), 139.83 (C), 136.86 (C), 133.38 (C), 130.87 (CH), 130.10 (CH), 128.75 (CH), 127.48 (CH), 123.77(CH), 113.53 (CH), 55.62 (C), 35.57 (CH\textsubscript{3}), 21.65(CH\textsubscript{3}), 14.50 (CH\textsubscript{3})

\textbf{FTIR} 3484, 3419, 2978, 1639, 1583, 1524, 1464, 1133, 800, 736, 704 cm\textsuperscript{-1}

\textbf{HPLC} \(t_R = 4.80\) min, 100% (ELSD)

\textbf{Mp} 221-223 °C
PREPARATION OF SULFONATED INDOLENIUM SALTS

Potassium 2,3,3-trimethyl-3H-indole-5-sulfonate

Hydrazinobenzene sulfonic acid (15g, 79.5 mmol) and 3-methyl-2-butanone (25.2 mL, 240 mmol) were dissolved in 45 mL of acetic acid. The mixture was heated to reflux for 3 h. Acetic acid was removed under vacuum. The residue obtained was dissolved in MeOH and then stirred with a saturated solution of potassium hydroxide in 2-propanol. The alkaline solution turned yellow and the potassium salt of the sulfoindole precipitated as yellow solid almost quantitatively (16.5 g, 75%)

Rf: 0.40 (RP, water)

HPLC tR = 2.6 min

MS (ES): m/z (%) 238.0 [(M-1), 100], 238.9 [M+, 12], 239.9 [(M+1)+, 5], 499.0 [(2M+Na)+, 10].

1H NMR (360 MHz, DMSO) δ: 7.63 (d, 1H, J = 1.5 Hz, H-4), 7.56 (dd, 1H, J = 7.9, 1.5 Hz, H-6), 7.34 (d, 1H, J = 7.9 Hz, H-7), 2.21 (s, 3H), 1.24 (s, 6H).

13C NMR (90.5 MHz, DMSO) δ: 188.67 (C=N), 153.12 (C), 146.91 (C), 144.68 (C), 124.75 (CH), 118.80 (CH), 117.76 (CH), 52.89 (C), 22.12 (CH3), 14.78 (CH3).

IR (neat) 3377, 2966, 2360, 1607, 1572, 1421, 1388, 1180, 1121, 1063, 1029, 833, 726 cm⁻¹

Mp: 292-293 °C
**1,2,3,3-tetramethyl-3H-indolium-5-sulfonate**

![Chemical Structure](image)

The potassium salt of 2,3,3-Trimethyl-3H-indole-5-sulfonate (1 g, 3.6 mmol) and methyl iodide (2.2 mL, 18 mmol) were heated in acetonitrile under microwave irradiation at 150 °C in a sealed vial for 1h. After cooling to room temperature, the solvent was decanted. The yellow-brown precipitate was suspended in diethyl ether, filtered, washed with diethylether and dichloromethane and dried *in vacuo* to yield a beige solid (0.86 g, 95%).

**Rf:** 0.20 (RP, water)

**HPLC** $t_R = 2.8$ min

**MS** (ES): $m/z$ (%) 252.1[(M-1), 100], 253.1 [M, 10]

$^1$H NMR (360 MHz, DMSO) $\delta$: 7.97 (s, 1H, H-4), 7.82 (d, 1H, $J = 8.3$ Hz, H-7), 7.77 (dd, 1H, $J = 8.3, 1.3$ Hz, H-6), 3.96 (s, 3H), 2.76 (s, 3H), 1.55 (s, 6H).

$^{13}$C NMR (90.5 MHz, DMSO): $\delta$ 198.32 (C=N), 150.63 (C), 143.45 (C), 142.69 (C), 127.62 (CH), 119.29 (CH), 116.06 (CH), 55.47 (C), 36.37 (CH$_3$), 23.06 (CH$_3$), 15.85 (CH$_3$).

**IR** (neat) 3010, 2972, 2354, 1629, 1593, 1470, 1421, 1195, 1118, 1057, 1031 cm$^{-1}$

**Mp** 273-274 °C
1-(5-carboxypentyl)-2,3,3-trimethyl-3\textit{H}-indolium-5-sulfonate\textsuperscript{4}

\begin{center}
\includegraphics[width=0.2\textwidth]{3c.png}
\end{center}

\textit{Classical method}

A mixture of potassium 2,3,3-trimethyl-3\textit{H}-5-indolesulfonate (2.00 g, 7.2 mmol), 6-bromohexanoic acid (4.20 g, 21.6 mmol) and potassium iodide (0.12 g, 0.7 mmol) in 1,2-dichlorobenzene (20 mL) was refluxed at 150 °C for 48 h. The reaction was monitored by TLC (DCM:MeOH 4:1). After cooling the reaction mixture to room temperature, the flask was placed in the fridge for 1 h. After this time, a beige solid had formed in the purple solution. The solid was collected by filtration, then washed with dichlorobenzene, 2-propanol/diethylether (1:1 v/v) and finally with diethylether. After drying \textit{in vacuo}, overnight, a beige solid was obtained (3.0 g, 89%).

\textit{Microwave-assisted alkylation}

A mixture of potassium 2,3,3-trimethyl-3\textit{H}-5-indolesulfonate (0.25 g, 0.9 mmol) and 6-bromohexanoic acid (0.53 g, 2.7 mmol) in a mixture (9:1) of acetonitrile and DMF (1 mL) was heated in a sealed vial at 150 °C for 3hs (3 cycles of 1h each), under microwave irradiation. After cooling to room temperature, the solvent was evaporated. The residue obtained was washed with 2-propanol/diethylether (1:1 v/v) and finally with diethylether and then dried \textit{in vacuo} to give a beige solid (254 mg, 80 %).

\textbf{Rf} 0.24 (RP, water)

\textbf{HPLC} = 3.6min

\textbf{\textsuperscript{1}H NMR} (360 MHz, DMSO) \(\delta, 8.02\ (s, 1H), 7.91\ (d, 1H, J = 8.3\ Hz), 7.82\ (d, 1H, J = 8.3, 1.1\ Hz), 4.44\ (t, 2H, J = 7.5\ Hz), 2.83\ (s, 3H), 2.22\ (t, 2H, J = 7.1\ Hz), 1.88-1.77\ (m, 2H), 1.57-1.38\ (m, 10H).
$^{13}$C NMR (90.5 MHz, DMSO) δ 198.8 (C=N), 175.8 (CO), 151.0 (C), 143.0 (C), 142.4 (C), 127.8 (CH), 122.2 (CH), 116.4 (CH), 55.8 (C), 49.0 (CH$_2$), 34.8 (CH$_2$), 28.4 (CH$_2$), 26.9 (CH$_2$), 25.5 (CH$_2$), 23.4 (CH$_3$), 15.6 (CH$_3$).

IR (neat) 3039, 2949, 1704, 1474, 1381, 1236, 1154, 1117, 1024, 795 cm$^{-1}$

Mp 235 °C

MS (ES): m/z (%) 352.0 [(M-2)$^-$, 100], 353.0 [(M-1)$^-$, 18], 354.0 [M$^+$, 5], 705.2 [(2M-3)$^-$, 21]
References