

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. ^1H 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/H₂O, (B) 0.04% TFA/ MeCN, (C) 0.1% formic acid/H₂O, (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.

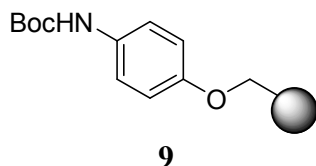
HPLC System II

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

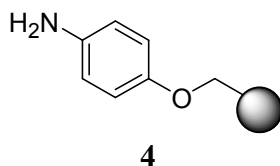


A mixture of (4-hydroxyphenyl)carbamic acid *tert*-butyl ester PS (6.27 g, 30 mmol), Cs₂CO₃ (9.78 g, 30 mmol), KI (0.17 g, 1 mmol) and 1% DVB cross-linked chloromethyl polystyrene (5 g, 10 mmol) in acetone (45 mL) was heated at 70 °C for 16 h. The resin was isolated by filtration, washed with water (4 × 100 mL), DMF (4 × 50 mL), DCM (3 × 50 mL), Et₂O (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. **¹³C NMR** (90.5 MHz, CDCl₃) δ 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 (CH₂), 40.2 (CH-resin), 28.4 (CH₃).

Colorimetric test for the detection of chloromethyl groups in Merrifield resin¹

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.

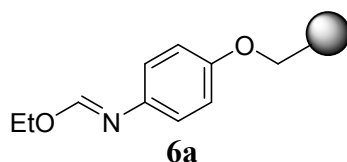
4-aminophenol PS



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)

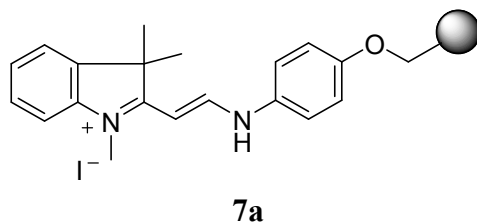
TRIMETHINE DYES

Ethyl 4-hydroxyphenylimidoformate PS



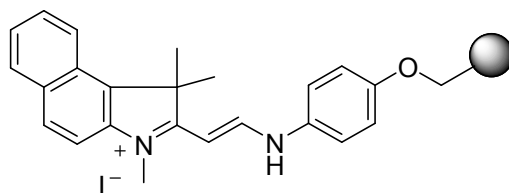
To 4 aminophenol PS **4** (2 g, 3.3 mmol) was added a solution of triethylorthoformate (7.50 mL, 45.1 mmol) and $\text{BF}_3 \cdot \text{OEt}_2$ (0.46 mL, 3.7 mmol) in dry DCM (10 mL) and the solution stirred at room temperature for 6h. Dry DIEA (0.94 mL, 5.51 mmol) was added and the mixture stirred 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) δ 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



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 mmol g^{-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} .

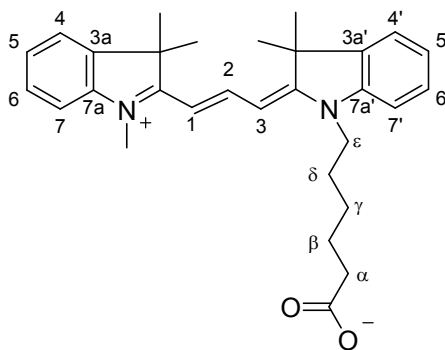
2-[(E)-2-(4-hydroxyanilino)ethenyl]-1,1,3-trimethyl-1H-benzo[e]indolium iodide PS



7d

To Ethyl 4-hydroxyphenylimidoformate PS **6a** (1 g, 1.53 mmol) and 1,1,2,3-Tetramethyl-1H-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-[(1E,3E)-3-[1-(5-carboxypentyl)-3,3-dimethyl-1,3-dihydro-2H-indol-2-ylidene]-1-propenyl]-1,3,3-trimethyl-3H-indolium Inner Salt



8a

To PS-bound hemicyanine **7a** (1.1 g, 0.80 mmol) were added dry pyridine (5 mL), DIEA (1.3 mL, 7.4 mmol), Ac₂O (0.7 mL, 7.4 mmol) and 1-(5-carboxypentyl)-2,3,3-trimethyl-3H-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 Et₂O, washed with Et₂O

and then purified by chromatography (DCM → DCM/MeOH 1:1) to give **8a** as a dark glassy red solid (31 mg, 68%).

R_f 0.42 (DCM/MeOH 9:1)

HPLC *t_R* = 10.7 min, 100% (ELSD, λ = 550 nm).

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

¹H NMR (360 MHz, CD₃OD) 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, CH₂-ε), 3.69 (s, 3 H, NCH₃), 2.21 (t, 2H, $J = 7.5$ Hz, CH₂-α), 1.86 (quintet, 2H, $J = 7.7$ Hz, CH₂-δ), 1.77-1.66 (s + quintet, 14H, $J = 7.4$ Hz, CH₂-β + CH₃), 1.56-1.49 (m, 2H, CH₂-γ).

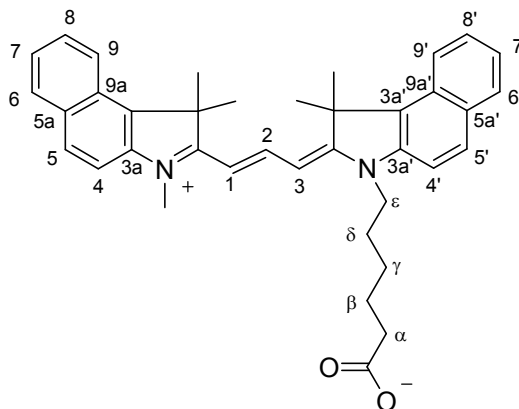
¹³C NMR (90.5 MHz, CDCl₃) δ 174.5 (COOH), 173.6 (2 × C=N), 150.5 (CH), 142.7 (C-Ar), 141.9 (C-Ar), 140.5 (C-Ar), 140.4 (C-Ar), 128.9 (CH-Ar), 125.4 (CH-Ar), 125.3 (CH-Ar), 122.1 (CH-Ar), 121.9 (CH-Ar), 111.0 (CH-Ar), 110.9 (CH-Ar), 104.4 (CH), 103.6 (CH), 51.5 (C), 44.3 (CH₂), 40.7 (CH₂), 31.8 (CH₃), 29.7 (CH₂), 28.1 (CH₃), 27.9 (CH₃), 26.3 (CH₂), 25.7 (CH₂).

UV/vis (MeOH) λ_{abs} = 547 nm, λ_{em} = 561 nm, ε = 1.06 × 10⁵ M⁻¹cm⁻¹

IR (neat) 2927, 2360, 1686, 1558, 1456, 1414, 1199, 1114, 926 cm⁻¹

HRMS (ES) for C₃₀H₃₇N₂O₂⁺ (M)⁺: calcd 457.28496, found 457.28661

2-{(1*E*,3*E*)-3-[3-(5-carboxypentyl)-1,1-dimethyl-1,3-dihydro-2*H*-benzo[*e*]indol-2-ylidene]-1-propenyl}-1,1,3-trimethyl-1*H*-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-*H*-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 min, 100% (ELSD)

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

¹H NMR (360 MHz, CD₃OD) δ 8.78 (t (dd), 1H, *J*_{1,2} ≈ *J*_{2,3} = 13.5 Hz, CH-H2), 8.29 (d, 2H, *J* = 8.2, 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 Hz, Ar-H7, Ar-H7'), 6.50 (d, 1H, *J* = 13.5 Hz, CH-H1 or H3), 6.49 (d, 1H, *J* = 13.5 Hz, CH-H1 or H3), 4.30 (t, 2H, *J* = 7.2 Hz, CH₂-ε), 3.82 (s, 3 H, NCH₃), 2.31 (t, 2H, *J* = 7.2 Hz, CH₂-α), 2.10 (s, 12H, CH₃), 1.94 (quintet, 2H, *J* = 7.2 Hz, CH₂-δ), 1.74 (quintet, 2H, *J* = 7.2 Hz, CH₂-β), 1.61-1.52 (m, 2H, CH₂-γ).

¹³C NMR (90.5 MHz, CD₃OD) 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 (CH₂), 38.5 (CH₂), 31.7 (CH₃), 28.1 (CH₂), 27.6 (CH₃), 27.5 (CH₃), 27.3 (CH₂), 26.8 (CH₂).

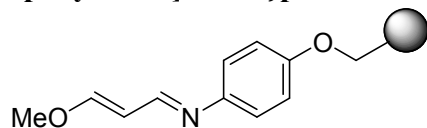
UV/vis (MeOH) $\lambda_{\text{abs}} = 587 \text{ nm}$, $\lambda_{\text{em}} = 603 \text{ nm}$, $\epsilon = 1.05 \times 10^5 \text{ M}^{-1} \text{ cm}^{-1}$

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

HRMS (ES) for C₃₈H₄₁N₂O₂⁺ (M)⁺: calcd 557.31626, found 457.31623

PENTAMETHINE DYES

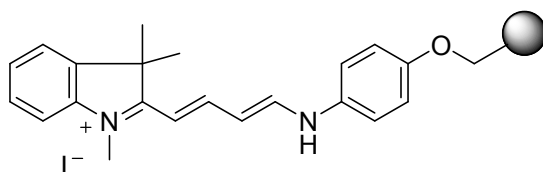
4-[(*E*,*2E*)-3-methoxy-2-propenylidene]amino}phenol PS



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 $\text{BF}_3 \cdot \text{OEt}_2$ (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}

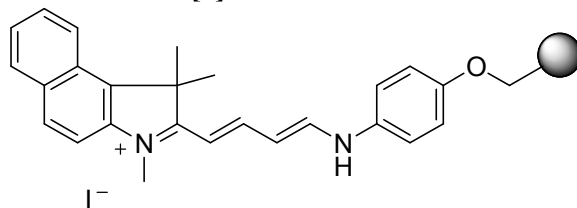
2-[(*1E*,*3E*)-4-(4-hydroxyanilino)-1,3-butadienyl]-1,3,3-trimethyl-3*H*-indolium iodide PS



7b

To 4-[(*E*,*2E*)-3-methoxy-2-propenylidene]amino}phenol PS **6b** (1 g, 1.56 mmol) and 1,2,3,3-tetramethyl-3*H*-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.

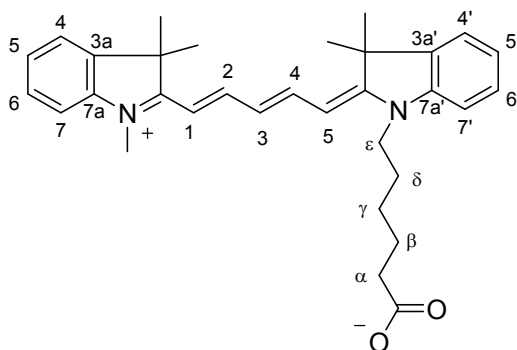
2-[(1E,3E)-4-(4-hydroxyanilino)-1,3-butadienyl]-1,1,3-trimethyl-1H-benzo[e]indolium iodide PS



7e

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 *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



8b

To PS-bound Hemicyanine **7b** (1.1 g, 1.1 mmol) were added dry pyridine (7 mL), DIEA (1.9 mL, 11 mmol), Ac₂O (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 *in vacuo*, the crude product was precipitated in Et₂O, washed with Et₂O and then

purified by chromatography (DCM → DCM/MeOH 1:1) to give **8b** as a blue solid (57 mg, 84%).

R_f 0.32 (DCM/MeOH 9:1)

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

HPLC *t_R* = 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].

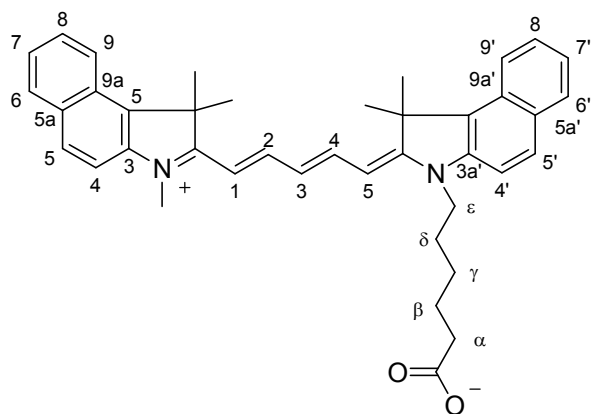
¹H NMR (360 MHz, MeOD) δ_H 8.25 (t (dd), 2H, *J*_{1,2} ≈ *J*_{2,3} ≈ *J*_{3,4} = *J*_{4,5} = 13.1 Hz, CH-H2 + CH-H4), 7.49 (bd, 2H, *J* = 7.4 Hz, Ar-H4, Ar-H4'), 7.44 (td (ddd), 2H, *J*_{5,6} ≈ *J*_{6,7} ≈ 7.7, *J*_{4,6} = 1.1 Hz, Ar-H6, Ar-H6'), 7.31-7.23 (m, 4H, Ar-H5, Ar-H5', Ar-H7, Ar-H7'), 6.64 (t (dd), 1H, *J*_{2,3} ≈ *J*_{3,4} = 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_C 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_{abs} = 640 nm, ε = 1.77 × 10⁵ M⁻¹cm⁻¹, λ_{em} = 660 nm

HRMS for C₃₂H₃₉N₂O₂⁺ (M)⁺: calcd 483.30061, found 483.30063

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



8e

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 min, 100% (ELSD, λ = 675 nm)

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

¹H NMR (360 MHz, MeOD) δ 8.33 (t, (dd) 2H, $J_{1,2} \approx J_{2,3} = J_{3,4} = J_{4,5}$ 12.9 Hz, CH-H2 + CH-H4), 8.24 (d, 2H, J = 8.5 Hz, Ar-H9, Ar-H9'), 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'), 7.97 (d, 2H, J = 8.2 Hz, Ar-H4, Ar-H4'), 7.59-7.67 (m, 4H, Ar-H5, Ar-H5', Ar-H8, Ar-H8'), 7.47 (bt, (dd) 2H, $J_{6,7} \approx J_{7,8} = 7.6$ Hz, Ar-H7, Ar-H7'), 6.68 (t, (dd) 1H, $J_{2,3} \approx J_{3,4} = 12.4$ Hz, CH-H3), 6.35 (d, 2H, J = 13.7 Hz, CH-H1 or H5), 6.34 (d, 2H, J = 13.8 Hz, CH-H1 or H5), 4.23 (t, 2H, J = 7.3 Hz, CH₂- ϵ), 3.76 (s, 3H, NCH₃), 2.33 (t, 2H, J = 7.2 Hz, CH₂- α), 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 (CH₂), 36.5 (CH₂), 31.9 (CH₃), 28.5 (CH₂), 27.6 (CH₂), 27.5 (CH₃), 26.4 (CH₂).

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

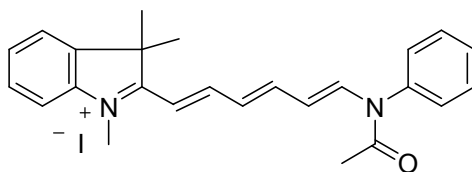
R_f 0.35 (DCM/MeOH 9:1)

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

HRMS for $\text{C}_{40}\text{H}_{43}\text{N}_2\text{O}_2^+$ (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

A suspension of 1,2,3,3-tetramethyl-3H-indolium iodide (2.5 g, 8.3 mmol) and *N*-[(*E*,2*E*,4*E*)-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 Et₂O, 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} .

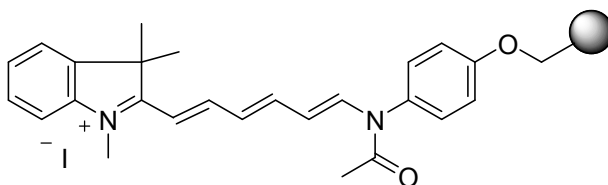
HPLC $t_R = 8.5 \text{ min}$

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

1H NMR (360 MHz, $CDCl_3$) 8.17 (d, $J = 14.0$, Hz, 1H, CH), 8.15-8.12 (m, 1H, CH), 7.92 (dd, $J = 14.9$, 11.4 Hz, 1H, CH), 7.64-7.12 (m, 9H, Ar), 7.00-6.96 (m, 2H, CH), 6.61 (dd, $J = 14.2$, 11.4 Hz, 1H, CH), 3.78 (s, 3H, CH_3), 1.74 (s, 3H, CH_3), 1.48 (s, 6H, CH_3)

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

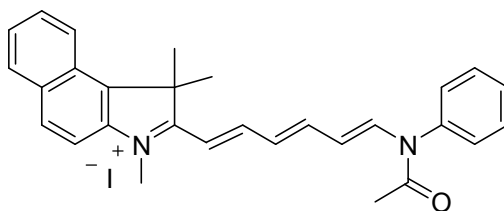
2-[(1E,3E,5E)-6-(acetyl-4-hydroxyanilino)-1,3,5-hexatrienyl]-1,3,3-trimethyl-3H-indolium iodide PS



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 symmetrical dye and dried *in vacuo* to give the product as a dark resin (0.77 mmol $^{-1}$, 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-1H-benzo[e]indolium iodide



5b

A suspension of 1,2,3,3-tetramethyl-3H-indolium iodide (3.0 g, 8.4 mmol) and glutaconaldehyde 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.

R_f: 0.36 (DCM/MeOH 9:1)

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

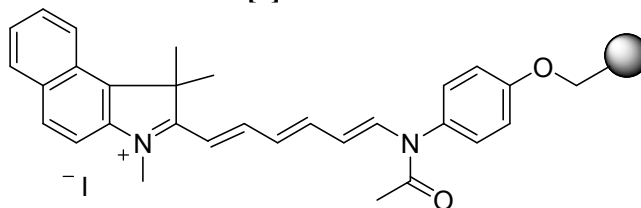
HPLC *t_R* = 6.91 min

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) λ_{abs} = 492 nm

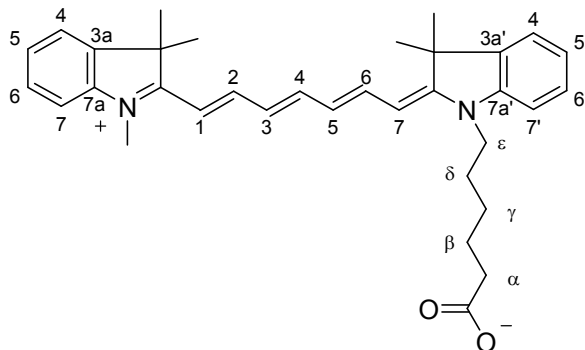
2-[(1E,3E,5E)-6-(acetyl-4-hydroxyanilino)-1,3,5-hexatrienyl]-1,1,3-trimethyl-1H-benzo[e]indolium iodide



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

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



8c

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-3*H*-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%).

R_f: 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} ≈ *J*_{2,3} ≈ *J*_{5,6} ≈ *J*_{6,7} = 13.1 Hz, CH-H6 + CH-H2), 7.60 (t, (dd) 1H, *J*_{3,4} ≈ *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} ≈ *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), 6.27 (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, $\text{CH}_2\text{-}\delta$), 1.70-1.67 (m + s, 14H, $\text{CH}_2\text{-}\beta + \text{CH}_3$), 152-1.46 (m, 2H, $\text{CH}_2\text{-}\gamma$).

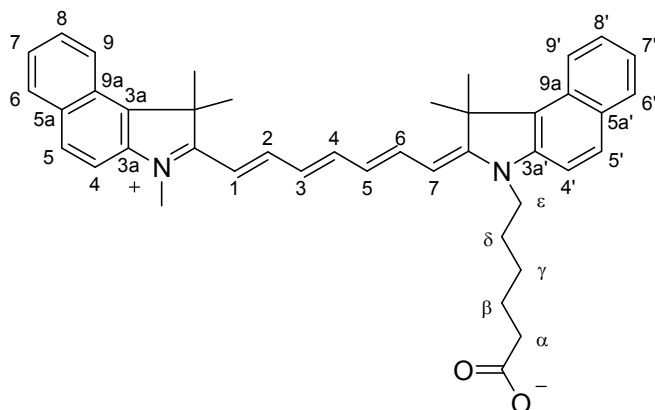
$^1\text{H NMR}$ (360 MHz, MeOD) δ 7.93 (t, 2H, $J = 13.1$ Hz, CH), 7.60 (t, 1H, $J = 12.0$ Hz, CH), 7.51-7.39 (m, 4H, Ar), 7.34-7.23 (m, 4H, Ar), 6.61 (t, 1H, $J = 12.4$ Hz, CH), 6.58 (t, 1H, $J = 12.4$ Hz, CH), 6.35 (d, 1H, $J = 13.7$ Hz, CH), 6.26 (d, 1H, $J = 13.6$ Hz, CH), 4.12 (t, 2H, $J = 7.6$ Hz, CH_2), 3.61 (s, 3H, NCH_3), 2.21 (t, 2H, $J = 7.3$ Hz, CH_2), 1.89-1.67 (m + s, 16H, $2 \times \text{CH}_2 + \text{CH}_3$), 158-1.49 (m, 2H, CH_2).

$^{13}\text{C NMR}$ (90.5 MHz, MeOD) δ 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).

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

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

2-{(1E,3E,5E,7E)-7-[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



8f

To PS-bound Hemicyanine **7f** (0.7 g, 0.7 mmol)* were added dry pyridine (3.2 mL), Ac_2O (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 (2×10 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_f: 0.39 (DCM/MeOH 9:1)

IR (neat) 2924, 2457, 1725, 1410, 1087, 1008, 920, 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} \approx *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- ϵ), 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).

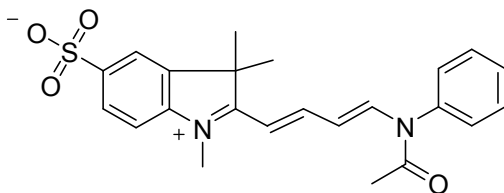
¹³C NMR (126 MHz, MeOD) δ 182.4 (COO⁻), 177.9 (C=N), 177.4 (C=N), 150.8 (CH), 141.7 (C), 140.9 (C), 135.0 (C), 134.8 (C), 133.7 (C), 132.1 (C), 131.9 (CH-Ar), 131.3 (CH-Ar), 131.2 (CH-Ar), 129.4 (CH), 129.3 (CH), 128.9 (CH), 126.4 (CH-Ar), 126.3 (CH-Ar), 123.4 (CH-Ar), 112.4 (CH-Ar), 112.2 (CH-Ar), 103.4 (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 = 1.3×10^5 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



5c

A mixture of 1,2,3,3-tetramethyl-3H-indolium-5-sulfonate (1.0 g, 2.4 mmol) and *N*-[(1*E*,3*E*)-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

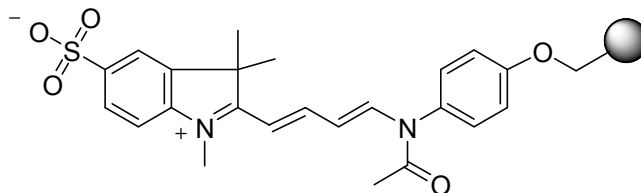
HPLC *t_R* = 4.74 min

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

¹H NMR (360 MHz, D₂O) δ 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) λ_{abs} = 445 nm

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

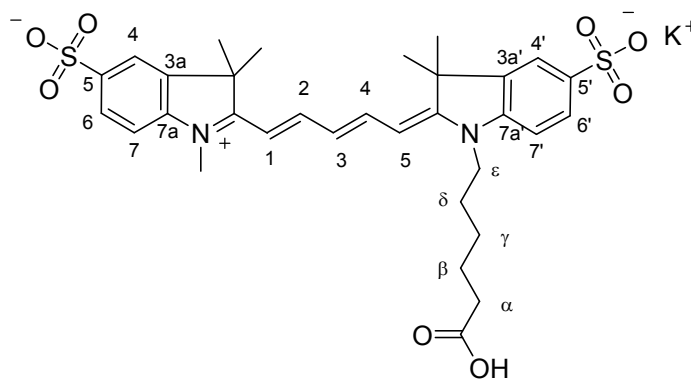


7g

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 mmol⁻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



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 %).

R_f: 0.40 (DCM/MeOH 3:2)

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

HPLC *t_R* = 3.6 min, 94% (λ_{abs} = 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, *J*_{1,2} ≈ *J*_{2,3} ≈ *J*_{3,4} ≈ *J*_{4,5} = 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, *J*_{2,3} ≈ *J*_{3,4} = 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).

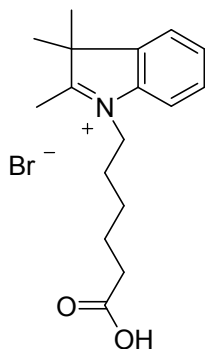
¹³C NMR (90.5 MHz, MeOD): δ 182.4 (COO⁻), 175.9 (C=N), 175.4 (C=N), 156.2 (CH), 145.7 (C-Ar), 144.9 (C-Ar), 143.4 (C-Ar), 143.3 (C-Ar), 142.7 (C-Ar), 142.5 (C-Ar), 128.1 (CH-Ar), 128.0 (CH-Ar), 127.8 (CH), 121.4 (CH-Ar), 121.3 (CH-Ar), 111.7 (CH-Ar), 111.4 (CH-Ar), 104.4 (CH), 105.3 (CH), 50.6 (C), 50.5 (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) λ_{abs} = 647, λ_{em} = 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



3a

Classical Method³

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 %).

R_f: 0.26 (DCM/MeOH 3:2)

HPLC *t_R* = 3.74 min, 100% (ELSD, λ = 220, 254, 280 nm)

MS (ES): *m/z* (%) 274.2 [M⁺, 100], 275.3 [(M+1)⁺, 19]

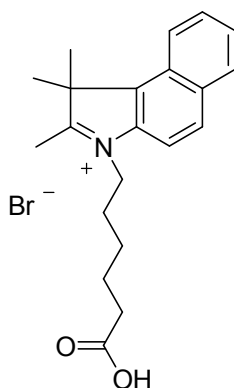
¹H NMR (250 MHz, DMSO): δ 8.23-8.19 (m, 1H), 8.09-8.06 (m, 1H), 7.87-7.80 (m, 2H), 4.69 (t, 2H, *J* = 7.6 Hz), 3.91 (s, 3H), 2.44 (t, 2H, *J* = 7.1 Hz), 2.12-2.00 (m, 2H), 1.83-1.61 (m, 10H).

^{13}C NMR (62.9 MHz, DMSO): δ 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 (CH₂), 33.73 (CH₂), 27.31 (CH₂), 25.77 (CH₂), 24.38 (CH₂), 22.37 (CH₃), 14.44 (CH₃)

IR (neat) 3449, 3195, 2817, 1693, 1459, 1290, 1174, 872, 775 cm⁻¹.

Mp 138 °C

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



3b

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 °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]

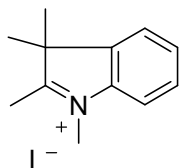
^1H NMR δ (250 MHz, DMSO): δ 8.46 (d, 1H, *J* = 8.2 Hz), 8.37 (d, 1H, *J* = 8.9 Hz), 8.30 (dd, 1H, *J* = 8.7, 1.4 Hz), 8.26 (d, 1H, *J* = 8.9 Hz), 7.89-7.77 (m, 2H), 4.68 (t, 2H, *J* = 7.5 Hz), 3.05 (s, 3H), 2.31 (t, 2H, *J* = 7.0 Hz), 2.01-1.93 (m, 2H), 1.68-1.54 (m, 10H).

^{13}C NMR (62.9 MHz, DMSO): δ 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 (CH₂), 33.74 (CH₂), 27.52 (CH₂), 25.75 (CH₂), 24.42 (CH₂), 21.97 (CH₃), 14.27 (CH₃)

Mp 234°C

IR (neat) 2864, 1707, 1474, 1389, 1156, 824, 715 cm⁻¹

1,2,3,3-tetramethyl-3H-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 (64.3g, 84%).

Microwave-assisted alkylation

A mixture of 2,3,3-trimethyl-3H-indole (0.25 mL, 1.6mmol) 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]

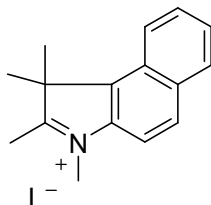
¹H NMR δ (250 MHz, DMSO): δ 7.90-7.86 (m, 1H), 7.82-7.78 (m, 1H), 7.63-7.54 (m, 2H), 3.94 (s, 3H), 2.74 (s, 3H), 1.49 (s, 6H)

¹³C NMR (62.9 MHz, DMSO): δ 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 (CH₃), 22.06 (CH₃), 14.56 (CH₃).

FTIR 3013, 2964, 2360, 1630, 1480, 988, 938 cm⁻¹

Mp 219 °C

1,1,2,3-tetramethyl-1*H*-benzo[*e*]indolium iodide



2b

A mixture of 1,2,2-trimethyl-1*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 *in vacuo* to give white/yellow solid (66g, 72%).

R_f: 0.31 (DCM:MeOH 9/1)

MS (ES): *m/z* (%) 224.2 [(M⁺, 100], 225.1 [(M+1)⁺, 17]

¹H NMR δ (250 MHz, DMSO): δ 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)

¹³C NMR (62.9 MHz, DMSO): δ 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 (CH₃), 21.65(CH₃), 14.50 (CH₃)

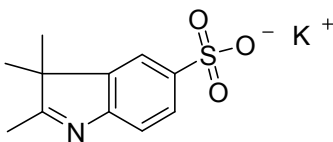
FTIR 3484, 3419, 2978, 1639, 1583, 1524, 1464, 1133, 800, 736, 704 cm⁻¹

HPLC *t_R* = 4.80 min, 100% (ELSD)

Mp 221-223 °C

PREPARATION OF SULFONATED INDOLENIUM SALTS

Potassium 2,3,3-trimethyl-3*H*-indole-5-sulfonate⁴



10

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%)

R_f: 0.40 (RP, water)

HPLC *t_R* = 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].

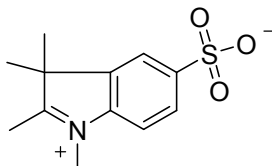
¹H NMR (360 MHz, DMSO) δ: 7.63 (d, 1H, *J* = 1.5 Hz, H-4), 7.56 (dd, 1H, *J* = 7.9, 1.5 Hz, H-6), 7.34 (d, 1H, *J* = 7.9 Hz, H-7), 2.21 (s, 3H), 1.24 (s, 6H).

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-3*H*-indolium-5-sulfonate⁴



2c

The potassium salt of 2,3,3-Trimethyl-3*H*-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%).

R_f: 0.20 (RP, water)

HPLC t_R = 2.8 min

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

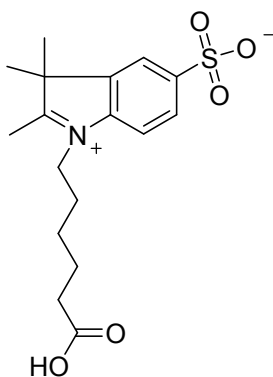
¹H NMR (360 MHz, DMSO) δ : 7.97 (s, 1H, H-4), 7.82 (d, 1H, J = 8.3 Hz, H-7), 7.77 (dd, 1H, J = 8.3, 1.3 Hz, H-6), 3.96 (s, 3H), 2.76 (s, 3H), 1.55 (s, 6H).

¹³C NMR (90.5 MHz, DMSO): δ 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 (CH₃), 23.06 (CH₃), 15.85 (CH₃).

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-3H-indolium-5-sulfonate⁴



3c

Classical method

A mixture of potassium 2,3,3-trimethyl-3H-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 *in vacuo*, overnight, a beige solid was obtained (3.0 g, 89%)

Microwave-assisted alkylation

A mixture of potassium 2,3,3-trimethyl-3H-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 *in vacuo* to give a beige solid (254 mg, 80 %).

Rf 0.24 (RP, water)

HPLC = 3.6min

¹H NMR (360 MHz, DMSO) δ , 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).

¹³C 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 (CH₂), 34.8 (CH₂), 28.4 (CH₂), 26.9 (CH₂), 25.5 (CH₂), 23.4 (CH₃), 15.6 (CH₃).

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]

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