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The synthesis of chloroheptamethinecyanine dyes in the absence of water

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Abstract

The chlorine atom present in the exocyclic conjugated bridge of the polymethine chain in heptamethinecyanine dyes undergoes *in situ* substitution with a third, oxygenated heteroaromatic group. The reaction is promoted by residual water and its success critically depends on the solubility of the chloro dye in the reaction solvent. To prevent this undesirable substitution, a modified synthesis has been developed that excludes water and which affords the desired chloroheptamethinecyanine dyes bearing different *N*-alkyl chains in good yield. The spectroscopic characterization of five new chloroheptamethinethia- and chloroheptamethineselenacyanine dyes is described.

Keywords: Chloroheptamethinecyanines; Tricarbocyanines; Dyes; Spectroscopic characterization

1. Introduction

Recently, we described the synthesis of some novel, rigidified *meso*-heptamethinecyanine dyes **1** and **2** (Fig. 1) that displayed absorption near 800 nm, in which variations in the nature of the heteroaromatic ring and the length of the *N*,*N*′-dialkyl groups were made, envisioning their potential usefulness as PDT sensitizers [1].

The formation of **2** was rationalized in terms of the incorporation of an oxygen atom from the water produced in the condensation step and/or residually present in the solvent. Recently, we have found that 2-methylbenzoxazolium salts undergo an unexpected transformation at room temperature, in DMSO-d_6, promoted by residual water, to the corresponding 2-methylbenzoxazol-2-ol derivatives as exclusive products [2]. The benzothiazolium and benzoselenazolium analogues show similar behaviour upon heating at 50 °C, which is consistent with the involvement of the 2-hydroxy derivative of the starting benzoazolium salts in the proposed mechanism of the synthesis of triheterocyclic heptamethinecyanine dyes **2** [1].

Generally, most chloroheptamethinecyanine dyes that have been studied such as **1** are indoles ($Z = CMe_2$), while those incorporating a benzoxazole, benzoselenazole, benzothiazole or quinoline nucleus ($Z = O$, Se, S, CH═CH) remain poorly explored. Moreover, as far as we are aware, dyes possessing *N*-alkyl unsubstituted chains longer than two carbon atoms have enjoyed little study [3,4].

Chloroheptamethinecyanines have found a wide range of applications and have been used for such different purposes as silver halide photography [5,6], near laser dyes [7−9], optical recording and storage media [5,8,10], photoinitiators in photopolymerization [11], fluorescent labelling agents for proteins and other biomolecules [12−26], immunoassays [17,18,22−24], DNA sequencing [20,27], flow cytometry [13,28], determination of nucleic acids [21,29−31] and proteins [32], as well as

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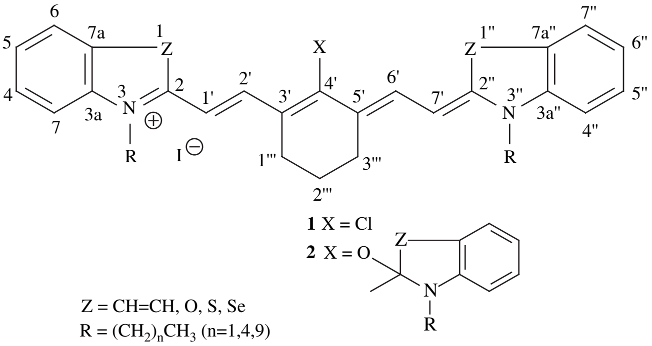


Fig. 1. Heptamethinecyanine dyes **1** and **2**.

ultra-trace determinations [15–19,26,30–35]. Other uses have been reported such as the spectrophotometric determination of trace water in organic solvents [15,36], fluorescent labels for functional groups in polymeric materials [37], metal detection [38–41], fluorescent probes for the determination of sodium dodecyl sulphate [3] and of critical micelle concentration of surfactants [4], sensitizers for zinc oxide solar cells [42], opto-chemical sensors [43] as well as several medical applications [22–25,44,45].

The growing interest in this family of dyes anticipates that the design and synthesis of compounds possessing longer pendant chains and heterocyclic moieties other than indolenine, enlarging the diversity of molecular structures available, will potentially enhance their usefulness.

2. Results and discussion

Considering the consequence of the presence of water molecules in the synthesis of chloroheptamethinecyanines **1**, we reinvestigated the course of this reaction using the previously described, semi-catalysed method [1] but avoiding the undesirable presence of water. Thus, benzothiazolium iodides **4a–c** were condensed with bisaldehyde **3** in a refluxed, anhydrous mixture of butan-1-ol/benzene (7/3) and the resulting, red intermediate was then treated, *in situ*, with an additional molar equivalent of the same benzothiazolium salt, in the presence of anhydrous pyridine. In the case of the benzoselenazolium iodides **4d–f**, due to the rapidity of the second reaction step, the two molar equivalents of salt were added to **3** as a single addition, at the beginning of the reaction (Scheme 1). All syntheses were carried out over 4 Å molecular sieves to trap the water formed during the course of the condensation reaction. Using these controlled anhydrous conditions, several representative chloroheptamethinecyanine dyes possessing benzothiazole (**1a–c**) and benzoselenazole nuclei (**1d–f**) were prepared in moderate/good yield.

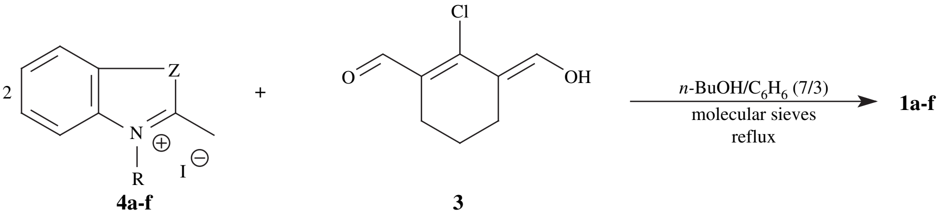
The preferred formation of the chlorocyanines **1** in place of the corresponding substituted dyes **2** highlights once again the involvement of water in the mechanism of the formation of the substituted dyes, previously outlined [1].

To the best of our knowledge, all chloroheptamethinecyanine dyes synthesised, apart from **1a**, have not hitherto been described. Accordingly, their full spectroscopic characterization, including ^{1}H and ^{13}C NMR shift assignments, which were established with the aid of HMQC (Heteronuclear Multiple Quantum Coherence), HMBQ (Heteronuclear Multiple Bond Correlation) and COSY (Correlated Spectroscopy) experiments, is reported. The numbering system used for this purpose is based on that of benzoazole dyes, being in agreement with previously published literature [1].

3. Experimental

3.1. General

All reagents were of the highest purity available, purchased from Sigma–Aldrich Company and were used as received. 2-Chloro-1-formyl-3-(hydroxymethylene)cyclohex-1-ene (**3**) was prepared according to the literature procedure [46] with minor modifications; ethyl-, pentyl- and decylbenzothiazolium and benzoselenazolium iodides **4a–f** were prepared as described [47]. Pyridine, butan-1-ol and benzene were dried prior to use by standard methods [48] and kept over molecular sieves (4 Å, beads, 4–8 mesh). All new dyes were determined to be of >95% pure by ^{1}H NMR. All reactions were monitored by TLC on aluminum plates precoated with Merck silica gel



4a-f **3**

(a) Z = S, R = CH_2CH_3
(b) Z = S, R = $(CH_2)_4CH_3$
(c) Z = S, R = $(CH_2)_9CH_3$
(d) Z = Se, R = CH_2CH_3
(e) Z = Se, R = $(CH_2)_4CH_3$
(f) Z = Se, R = $(CH_2)_9CH_3$

Scheme 1. Synthesis of chloroheptamethinecyanine dyes **1a–f**.

60 F_{254} (0.25 mm) using CH_2Cl_2 or $CHCl_3$/MeOH (5–10%) as eluents, the spots having been examined under 254, 312 and 365 nm UV light and developed by exposure to iodine. ^{1}H and ^{13}C NMR spectra were recorded in DMSO-d_6/$CDCl_3$ (50%) on a Brüker ACP 250 (250.13 and 62.90 MHz) or Brüker ARX 400 (400.13 and 100.62 MHz) spectrometer; chemical shifts are reported relative to Me_4Si or to residual solvent signals. HMQC, HMBC and COSY spectra were acquired using a Brüker ARX 400 spectrometer. IR spectra were measured over the range 400–4000 cm^{-1} without baseline correction, using a Mattson 5000-FTS FTIR spectrometer. All samples were prepared by mixing IR-grade KBr with 1% (by mass) dye and grinding to a fine powder. Visible spectra were recorded on a Perkin–Elmer Lambda 6 spectrophotometer using acetonitrile 0.1% (v/v) in EtOH as solvent; λ_{max} are reported in nm (ε_{max} in dm^3 mol^{-1} cm^{-1}). High Resolution Fast Atom Bombardment Mass Spectra (HR-FAB-MS) were recorded on a Micromass AutoSpec M, operating at 70 eV, using a matrix of 3-nitrobenzyl alcohol (3-NBA). Melting points were determined in open capillary tubes in a Büchi 530 melting point apparatus and are uncorrected.

*3.2. Synthesis of chloroheptamethinecyanines **1a–f**. General procedure*

A solution of the bisaldehyde **3** (1.5 mmol) and benzoazolium iodide **4** (1.0 mmol) in anhydrous butan-1-ol/benzene (7/3) (70 mL) was heated under reflux, over molecular sieves [1000% by mass of **3**], until complete consumption of the benzoazolium salt (10–15 min) had been achieved. An additional molar equivalent of **4** and dry pyridine (14 mL) were added and the resulting mixture heated under reflux for a further 30–60 min. After separation of the molecular sieves by filtration under reduced pressure, the chloro dyes **1a–f** were precipitated from the cooled reaction mixture directly or following partial removal of the solvent or the addition of Et_2O. The green crystals so obtained were collected by filtration under reduced pressure and were washed with water and Et_2O to afford spectroscopically pure compounds.

For the chloroheptamethine dyes **1d–f**, two molar equivalents of the corresponding benzoselenazolium iodide were added in a single step to the solution of **3** in anhydrous butan-1-ol/benzene (7/3) at the beginning of the reaction, which was complete within 5–10 min after the addition of pyridine.

*3.2.1. 2-(2-{2-Chloro-3-[2-(3-ethyl-3H-benzothiazol-2-ylidene)ethylidene]cyclohex-1-enyl}vinyl)-3-ethylbenzothiazol-3-ium iodide (**1a**)*

Obtained from 3-ethyl-2-methylbenzothiazol-3-ium iodide (**4a**) in 92% yield, as green shining crystals. M.p. 272–273 °C (Lit. m.p. 267 °C [1]; 263–265 °C [49]).

*3.2.2. 2-(2-{2-Chloro-3-[2-(3-pentyl-3H-benzothiazol-2-ylidene)ethylidene]cyclohex-1-enyl}vinyl)-3-pentylbenzothiazol-3-ium iodide (**1b**)*

Obtained from 3-pentyl-2-methylbenzothiazol-3-ium iodide (**4b**) in 58% yield, as green shining crystals. M.p. 242–243 °C. IR (KBr) ν_{max} (cm^{-1}): 3058 (C–H_{ar}), 1579 (C–C_{ar}), 1530 (C–C_{ar}), 1503 (C–C_{ar}), 1459, 1428, 1403, 1226, 1173, 1153, 1126, 1060, 1036, 1005, 803 (C–Cl). Vis [EtOH/CH_3CN (0.1%)] λ_{max} (nm): 801 (280 000). ^{1}H NMR [400.13 MHz, DMSO-d_6/$CDCl_3$ (50%)] δ (ppm): 0.88 (6H, t, $J = 7.0$ Hz, C*H*$_3$), 1.34–1.42 (8H, m, C*H*$_2$), 1.78 (4H, qui, $J = 7.0$ Hz, C*H*$_2$), 1.89 (2H, qui, $J = 5.6$ Hz, *H*2‴), 2.64 (4H, t, $J = 5.6$ Hz, *H*1‴, *H*3‴), 4.36 (4H, t, $J = 7.6$ Hz, NC*H*$_2$), 6.35 (2H, d, $J = 13.5$ Hz, *H*1′, *H*7′), 7.35 (2H, t, $J = 7.6$ Hz, *H*6, *H*6″), 7.51 (2H, t, $J = 7.8$ Hz, *H*5, *H*5″), 7.59 (2H, d, $J = 8.0$ Hz, *H*4, *H*4″), 7.84 (2H, d, $J = 8.0$ Hz, *H*7, *H*7″), 7.86 (2H, d, $J = 13.2$ Hz, *H*2′, *H*6′). ^{13}C NMR [100.62 MHz, DMSO-d_6/$CDCl_3$ (50%)] δ (ppm): 12.2 (*C*H_3), 18.9 (*C*2‴), 20.3 (*C*H_2), 24.9 (*C*H_2), 25.5 (*C*H_2), 26.6 (*C*1‴, *C*3‴), 44.5 (N*C*H_2), 97.7 (*C*1′, *C*7′), 111.4 (*C*4, *C*4″), 121.1 (*C*7, *C*7″), 122.6 (*C*3′, *C*5′), 123.4 (*C*6, *C*6″), 123.7 (*C*7a, *C*7a″), 126.3 (*C*5, *C*5″), 139.6 (*C*2′, *C*6′), 139.8 (*C*3a, *C*3a″), 143.7 (*C*4′), 161.6 (*C*2, *C*2″). HR-FAB-MS (3-NBA) *m/z*: $[M - I]^+$, 575.235599, $C_{34}H^{35}_{40}ClN_2S_2$ requires 575.232146; $[M - I]^+$, 577.233798, $C_{34}H^{37}_{40}ClN_2S_2$ requires 577.229196.

*3.2.3. 2-(2-{2-Chloro-3-[2-(3-decyl-3H-benzothiazol-2-ylidene)ethylidene]cyclohex-1-enyl}vinyl)-3-decylbenzothiazol-3-ium iodide (**1c**)*

Obtained from 3-decyl-2-methylbenzothiazol-3-ium iodide (**4c**) in 52% yield, as green shining crystals. M.p. 182–183 °C. IR (KBr) ν_{max} (cm^{-1}): 3067 (C–H_{ar}), 2922, 2852, 1657 (C=C), 1580 (C–C_{ar}), 1518 (C–C_{ar}), 1454, 1426, 1397, 1223, 1151, 1131, 1060, 1033, 1013, 798 (C–Cl). Vis [EtOH/CH_3CN (0.1%)] λ_{max} (nm): 802 (220 900). ^{1}H NMR [400.13 MHz, DMSO-d_6/$CDCl_3$ (50%)] δ (ppm): 0.82 (6H, t, $J = 6.8$ Hz, C*H*$_3$), 1.15–1.27 (20H, m, C*H*$_2$), 1.30–1.34 (4H, m, C*H*$_2$) 1.37–1.43 (4H, m, C*H*$_2$), 1.78 (4H, qui, $J = 7.4$ Hz, C*H*$_2$), 1.88 (2H, qui, $J = 5.6$ Hz, *H*2‴), 2.62 (4H, t, $J = 5.6$ Hz, *H*1‴, *H*3‴), 4.33 (4H, t, $J = 7.4$ Hz, NC*H*$_2$), 6.30 (2H, d, $J = 13.6$ Hz, *H*1′ *H*7′), 7.34 (2H, t, $J = 7.6$ Hz, *H*6, *H*6″), 7.49 (2H, t, $J = 7.8$ Hz, *H*5, *H*5″), 7.54 (2H, d, $J = 8.0$ Hz, *H*4, *H*4″), 7.80 (2H, d, $J = 8.0$ Hz, *H*7, *H*7″), 7.87 (2H, d, $J = 13.6$ Hz, *H*2′, *H*6′). ^{13}C NMR [100.62 MHz, DMSO-d_6/$CDCl_3$ (50%)] δ (ppm): 12.2 (*C*H_3), 20.4 (*C*2‴), 24.3 (*C*H_2), 24.8 (*C*H_2), 25.6 (*C*H_2), 26.9 (*C*1‴, *C*3‴), 27.0 (*C*H_2), 27.2 (*C*H_2), 27.2 (*C*H_2) 27.3 (*C*H_2), 29.6 (*C*H_2), 44.6 (N*C*H_2), 97.9 (*C*1′, *C*7′), 111.5 (*C*4, *C*4″), 121.1 (*C*7, *C*7″), 122.6 (*C*3′, *C*5′), 123.4 (*C*6, *C*6″), 123.7 (*C*7a, *C*7a″), 126.3 (*C*5, *C*5″), 139.4 (*C*2′, *C*6′), 139.8 (*C*3a, *C*3a″), 145.0 (*C*4′), 161.7 (*C*2, *C*2″). HR-FAB-MS (3-NBA) *m/z*: $[M - I]^+$, 715.385902, $C_{44}H^{35}_{60}ClN_2S_2$ requires 715.388647; $[M - I]^+$, 717.384843, $C_{44}H^{37}_{60}ClN_2O_2$ requires 717.385697.

*3.2.4. 2-(2-{2-Chloro-3-[2-(3-ethyl-3H-benzoselenazol-2-ylidene)ethylidene]cyclohex-1-enyl}vinyl)-3-ethylbenzoselenazol-3-ium iodide (**1d**)*

Obtained from 3-ethyl-2-methylbenzoselenazol-3-ium iodide (**4d**) in 63% yield, as green shining crystals. M.p. 272–274 °C. IR (KBr) ν_{max} (cm^{-1}): 1640 (C=C), 1580 (C–C_{ar}), 1529 (C–C_{ar}), 1507 (C–C_{ar}), 1451, 1428, 1396, 1222, 1181, 1158, 1121, 1075, 1020, 769 (C–Cl). Vis [EtOH/CH_3CN

(0.1%)] λ_{max} (nm): 812 (230 400). ^{1}H NMR [400.13 MHz, DMSO-d_6/CDCl$_3$ (50%)] δ (ppm): 1.36 (6H, t, $J = 7.0$ Hz, CH_3), 1.86 (2H, qui, $J = 5.6$ Hz, *H*2‴), 2.67 (4H, t, $J = 5.5$ Hz, *H*1‴, *H*3‴), 4.44 (4H, q, $J = 7.0$ Hz, NCH_2), 6.55 (2H, d, $J = 13.4$ Hz, *H*1′, *H*7′), 7.31 (2H, t, $J = 7.4$ Hz, *H*6, *H*6″), 7.51 (2H, t, $J = 7.6$ Hz, *H*5, *H*5″), 7.75 (2H, d, $J = 13.1$ Hz, *H*2′, *H*6′), 7.98 (2H, d, $J = 7.7$ Hz, *H*4, *H*4″), 8.15 (2H, d, $J = 7.6$ Hz, *H*7, *H*7″). ^{13}C NMR [100.62 MHz, DMSO-d_6/CDCl$_3$ (50%)] δ (ppm): 12.9 (*C*H$_3$), 20.8 (*C*2‴), 27.1 (*C*1‴, *C*3‴), 42.9 (N*C*H$_2$), 103.9 (*C*1′, *C*7′), 114.3 (*C*4, *C*4″), 125.5 (*C*3′, *C*5′), 125.8 (*C*6, *C*6″), 125.9 (*C*7a, *C*7a″), 126.7 (*C*7, *C*7″), 128.5 (*C*5, *C*5″), 142.8 (*C*2′, *C*6′), 143.2 (*C*3a, *C*3a″), 149.0 (*C*4′), 168.3 (*C*2, *C*2″). HR-FAB-MS (3-NBA) *m/z*: $[M - I]^+$, 583.030427, $C_{28}H^{35}_{28}ClN^{78}_{2}Se_2$ requires 583.028710; $[M - I]^+$, 585.029095, $C_{28}H^{35}_{28}ClN^{78}_{2}Se^{80}Se$ requires 585.027926; $[M - I]^+$, 585.029095, $C_{28}H^{37}_{28}ClN^{78}_{2}Se_2$ requires 585.025760; $[M - I]^+$, 585.029095, $C_{28}H^{35}_{28}ClN^{80}_{2}Se_2$ requires 587.027143; $[M - I]^+$, 587.029909, $C_{28}H^{37}_{28}ClN^{78}_{2}Se^{80}Se$ requires 587.024976; $[M - I]^+$, 589.027113, $C_{28}H^{37}_{28}ClN^{80}_{2}Se_2$ requires 589.024193.

*3.2.5. 2-(2-{2-Chloro-3-[2-(3-pentyl-3H-benzoselenazol-2-ylidene)ethylidene]cyclohex-1-enyl}vinyl)-3-pentylbenzoselenazol-3-ium iodide (**1e**)*

Obtained from 3-pentyl-2-methylbenzoselenazol-3-ium iodide (**4e**) in 48% yield, as green shining crystals. M.p. 227–228 °C. IR (KBr) ν_{max} (cm^{-1}): 1663 (C=C), 1578 (C–C$_{ar}$), 1528 (C–C$_{ar}$), 1500 (C–C$_{ar}$), 1450, 1428, 1401, 1223, 1171, 1151, 1103, 1059, 997, 797 (C–Cl). Vis [EtOH/CH$_3$CN (0.1%)] λ_{max} (nm): 813 (235 400). ^{1}H NMR [400.13 MHz, DMSO-d_6/CDCl$_3$ (50%)] δ (ppm): 0.88 (6H, t, $J = 6.4$ Hz, CH_3), 1.36–1.39 (8H, m, CH_2), 1.78 (4H, qui, $J = 6.6$ Hz, CH_2), 1.89 (2H, qui, $J = 5.5$ Hz, *H*2‴), 2.63 (4H, t, $J = 5.6$ Hz, *H*1‴, *H*3‴), 4.31 (4H, t, $J = 7.4$ Hz, NCH_2), 6.43 (2H, d, $J = 13.1$ Hz, *H*1′, *H*7′), 7.28 (2H, t, $J = 7.1$ Hz, *H*6, *H*6″), 7.48 (2H, t, $J = 7.2$ Hz, *H*5, *H*5″), 7.50 (2H, d, $J = 7.0$ Hz, *H*4, *H*4″), 7.76 (2H, d, $J = 13.1$ Hz, *H*2′, *H*6′), 7.91 (2H, d, $J = 7.9$ Hz, *H*7, *H*7″). ^{13}C NMR [100.62 MHz, DMSO-d_6/CDCl$_3$ (50%)] δ (ppm): 12.3 (*C*H$_3$), 19.2 (*C*H$_2$), 20.5 (*C*2‴), 25.3 (*C*H$_2$), 25.5 (*C*H$_2$), 26.9 (*C*1‴, *C*3‴), 45.8 (N*C*H$_2$), 101.5 (*C*1′, *C*7′), 113.0 (*C*4, *C*4″), 123.6 (*C*6, *C*6″), 123.8 (*C*3′, *C*5′), 123.9 (*C*7a, *C*7a″), 124.7 (*C*7, *C*7″), 126.5 (*C*5, *C*5″), 141.5 (*C*3a, *C*3a″), 141.8 (*C*2′, *C*6′), 144.2 (*C*4′), 166.7 (*C*2, *C*2″). HR-FAB-MS (3-NBA) *m/z*: $[M - I]^+$, found 667.119288, $C_{34}H^{35}_{40}ClN^{78}_{2}Se_2$ requires 667.122610; $[M - I]^+$, 669.118327, $C_{34}H^{35}_{40}ClN^{78}_{2}Se^{80}Se$ requires 669.121827; $[M - I]^+$, 669.118327, $C_{34}H^{37}_{40}ClN^{78}_{2}Se_2$ requires 669.119660; $[M - I]^+$, 671.117398, $C_{34}H^{35}_{40}ClN^{80}_{2}Se_2$ requires 671.121043; $[M - I]^+$, 671.117398, $C_{34}H^{37}_{40}ClN^{78}_{2}Se^{80}Se$ requires 671.111877; $[M - I]^+$, 673.116456, $C_{34}H^{37}_{40}ClN^{80}_{2}Se_2$ requires 673.118093.

*3.2.6. 2-(2-{2-Chloro-3-[2-(3-decyl-3H-benzoselenazol-2-ylidene)ethylidene]cyclohex-1-enyl}vinyl)-3-decylbenzoselenazol-3-ium iodide (**1f**)*

Obtained from 3-decyl-2-methylbenzoselenazol-3-ium iodide (**4f**) in 44% yield, as green shining crystals. M.p. 156–157 °C. IR (KBr) ν_{max} (cm^{-1}): 3060 (C–H$_{ar}$), 2921, 2850, 1660 (C=C), 1578 (C–C$_{ar}$), 1524 (C–C$_{ar}$), 1503 (C–C$_{ar}$), 1450, 1428, 1399, 1224, 1178, 1154, 1120, 1060, 1006, 786 (C–Cl). Vis [EtOH/CH$_3$CN (0.1%)] λ_{max} (nm): 814 (287 000). ^{1}H NMR [250.13 MHz, DMSO-d_6/CDCl$_3$ (50%)] δ (ppm): 0.82 (6H, t, $J = 6.5$ Hz, CH_3), 1.13–1.39 (28H, m, CH_2), 1.69–1.77 (4H, m, CH_2), 1.90 (2H, qui, $J = 6.0$ Hz, *H*2‴), 2.62 (4H, t, $J = 5.9$ Hz, *H*1‴, *H*3‴), 4.31 (4H, t, $J = 5.5$ Hz, NCH_2), 6.44 (2H, d, $J = 13.2$ Hz, *H*1′, *H*7′), 7.26 (2H, t, $J = 7.5$ Hz, *H*6, *H*6″), 7.46 (2H, t, $J = 7.3$ Hz, *H*5, *H*5″), 7.51 (2H, d, $J = 7.5$ Hz, *H*4, *H*4″), 7.71 (2H, d, $J = 12.5$ Hz, *H*2′, *H*6′), 7.95 (2H, d, $J = 8.0$ Hz, *H*7, *H*7″). ^{13}C NMR [100.62 MHz, DMSO-d_6/CDCl$_3$ (50%)] δ (ppm): 13.6 (*C*H$_3$), 21.9 (*C*2‴), 25.8 (*C*H$_2$), 26.5 (*C*1‴, *C*3‴), 26.9 (*C*H$_2$), 28.4 (*C*H$_2$), 28.5 (*C*H$_2$), 28.7 (*C*H$_2$), 28.7 (*C*H$_2$), 31.1 (*C*H$_2$), 34.4 (*C*H$_2$), 46.9 (N*C*H$_2$), 102.8 (*C*1′, *C*7′), 114.3 (*C*4, *C*4″), 123.5 (*C*3′, *C*5′), 124.7 (*C*6, *C*6″), 125.1 (*C*7a, *C*7a″), 125.9 (*C*7, *C*7″), 127.7 (*C*5, *C*5″), 142.6 (*C*2′, *C*6′), 148.8 (*C*3a, *C*3a″), 153.0 (*C*4′), 167.9 (*C*2, *C*2″). HR-FAB-MS (3-NBA) *m/z*: $[M - I]^+$, 807.277818, $C_{44}H^{35}_{60}ClN^{78}_{2}Se_2$ requires 807.279111; $[M - I]^+$, 809.277892, $C_{44}H^{35}_{60}ClN^{78}_{2}Se^{80}Se$ requires 809.278328; $[M - I]^+$, 809.277892, $C_{44}H^{37}_{60}ClN^{78}_{2}Se_2$ requires 809.276161; $[M - I]^+$, 811.276911, $C_{44}H^{35}_{60}ClN^{80}_{2}Se_2$ requires 811.277544; $[M - I]^+$, 811.276911, $C_{44}H^{37}_{60}ClN^{78}_{2}Se^{80}Se$ requires 811.275378; $[M - I]^+$, 813.275 785$C_{44}H_{60}$, $^{37}ClN^{80}_{2}Se_2$ requires 813.274594.

4. Conclusions

The exclusion of water in the synthesis of chloroheptamethinecyanine dyes avoids the undesirable substitution of the chlorine atom in the final product. This modified synthesis permitted the preparation of chloroheptamethinethia- and chloroheptamethineselenacyanine dyes bearing different *N*-alkyl chains, some in rather good yields.

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