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Synthesis and characterization of novel mono- and dicarboxyalkylthiacarbocyanines and their ester derivatives

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Abstract

Several novel asymmetric *N*-carboxyalkyl-*N*′-alkylthiacarbocyanines, symmetric *N*,*N*′-dicarboxyalkylthiacarbocyanines and their methyl ester derivatives have been synthesized and fully characterized by ^{1}H and ^{13}C NMR, FTIR and visible spectroscopy and HRMS (FAB). Two different methods for the preparation of the asymmetric thiacarbocyanines have been used and discussed.

Keywords: Thiacarbocyanines; Carbocyanines; Carboxyalkyl; Asymmetric carbocyanines; Spectroscopic characterization

1. Introduction

Affinity chromatography is unique among separation methods. It enables the purification of almost any biomolecule based on biological functions rather than on individual physical or chemical properties and it is considered the most powerful tool for the purification of biological active molecules. Since the introduction of this technique in 1968 [1], thousands of different molecules such as enzymes, antibodies, hormones, vitamins, receptors, a large variety of proteins and glycoproteins, RNA, DNA and even bacteria, viruses and cells have been separated and/or purified by affinity chromatography [2,3]. A wide range of functional materials have been used as ligands such as dyes, amino acids, enzymes, coenzymes, cofactors, antibodies, oligopeptides, proteins, metal chelates, oligonucleotides, etc., being extremely specific in most cases. Complementary ligands have also been used to recognize the biopolymers to be separated with enhanced specificity to be purified, e.g. enzymes and their substrates, hormones and their receptors, antibodies and their antigens [2,4].

The choice between a number of biospecific ligands for a particular chromatographic application is governed by the necessity to obtain a pure but biologically intact product. Unfortunately, natural biological ligands are limited by their high cost, their tendency to be biologically and chemically labile and the difficulty to be immobilized with retention of their biological activity. The use of synthetic dyes as biomimetic ligands for affinity chromatography appears to circumvent many of these problems since they are inexpensive, readily available, biologically and chemically inert, easily coupled to supports and able to bind biomolecules [5]. Although the affinity chromatography based on dyes has been intensively explored, to the best of our knowledge, the use of cyanine dyes as specific ligands remains practically unknown apart from a brief reference in a paper from McLoughlin and Lowe [4].

Recently, we became interested in the design and synthesis of novel cyanine dyes that can be used as biospecific ligands for the purification of proteins by affinity chromatography [6]. It is our belief that cyanines, once capable to bind to a chromatographic support, are suitable candidates to affinity

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ligands since their ability to establish a combination of specific types of hydrophobic, hydrophilic, ionic and π−π interactions opens the possibility of an increased selectivity between these type of dyes and the biomolecules to be purified.

It has been reported that chromatographic purification of proteins is greatly enhanced if the dye is immobilized via a spacer link to the matrix, as this spatial arrangement makes the dye more flexible resulting in a better fit in with the target protein [3]. In this context, thiacarbocyanine dyes with pendent carboxyalkyl chains of different lengths are of interest, since the carboxyl groups are amenable to link covalently to macromolecules with nucleophilic centers resembling the typical chromatographic supports, cellulose and agarose.

In our previous work [7], the synthesis of symmetric thiacarbocyanines containing two pendent carboxyalkyl groups of different lengths (1−4 carbon atoms) has been accomplished using established methods [8−11]. Upon Fisher's esterification, in the presence of methanol, only the *N*,*N*′-dicarboxymethyl cyanine yielded the corresponding diester, whereas in all other cases the monoester was obtained [7].

So far, carboxyalkylthiacarbocyanines have been just used as sensitizers for photographic emulsions [12,13], labeling agents [14] and sensors for the detection of divalent cations [15].

Herein we wish to report the synthesis and characterization of several novel symmetric and asymmetric thiacarbocyanines containing mono- and dicarboxyalkyl groups and their ester derivatives, envisioning their potential application in affinity chromatography. These mono- and direactive thiacarbocyanines will allow a comparative study concerning their reactivity degree and their chromatographic behavior in relation to the dependence of the selectivity exhibited by the ligand from the nature of the linkage to the affinity chromatography support.

An expeditious and efficient heterogeneous esterification method to link dyes possessing carboxylic groups to cellulose is currently being developed and the outcome of this work will be published elsewhere.

2. Results and discussion

The synthetic route devised for the preparation of thiacarbocyanines containing either symmetric or asymmetric pendent *N*-alkyl, *N*-carboxyalkyl and *N*-methoxycarbonylalkyl chains **8**−**11** starts from an *N*-substituted benzothiazolium salt possessing a reactive methyl group **2**−**4**, able to readily lose a proton in basic medium to give a reactive ''methylene base'' [16], as depicted in Scheme 1.

The required *N*-alkylbenzothiazolium derivatives **2** were obtained by quaternisation of 2-methylbenzothiazole (**1**) with a suitable alkyl iodide in acetonitrile, whereas **3** and **4** were prepared by condensation of **1** with a bromoalkanoic acid or a methyl bromoalkanoate, respectively, in the absence of solvent.

Symmetric thiacarbocyanines **8** and **9** were readily prepared through the classical route involving the condensation of the heterocyclic quaternary salts **3** and **4** with triethyl orthoformate in dry pyridine [9].

Asymmetric thiacarbocyanines **10** and **11** were obtained by two different methods relying on the nucleophilic substitution at the olefinic carbon of a conveniently substituted *N*-vinylaniline.

The key intermediates **5**−**7**, required to produce these dyes, were synthesized as shown in Scheme 1. Akin to other condensation reactions between heterocyclic quaternary salts and *N*,*N*′-diphenylformamidine [17,18], the reaction of benzothiazolium salts **2** with *N*,*N*′-diphenylformamidine, in acetic anhydride, afforded the acetanilide derivatives **5**. In our hands the preparation of similar acetanilide derivatives of **3** was not successful since it afforded complex mixtures difficult to purify. The condensation of *N*-alkyl- and *N*-carboxyalkylbenzothiazolium salts **2** and **3** with aniline and triethyl orthoformate yielded the corresponding *N*-substituted anilines **6** and **7**, respectively.

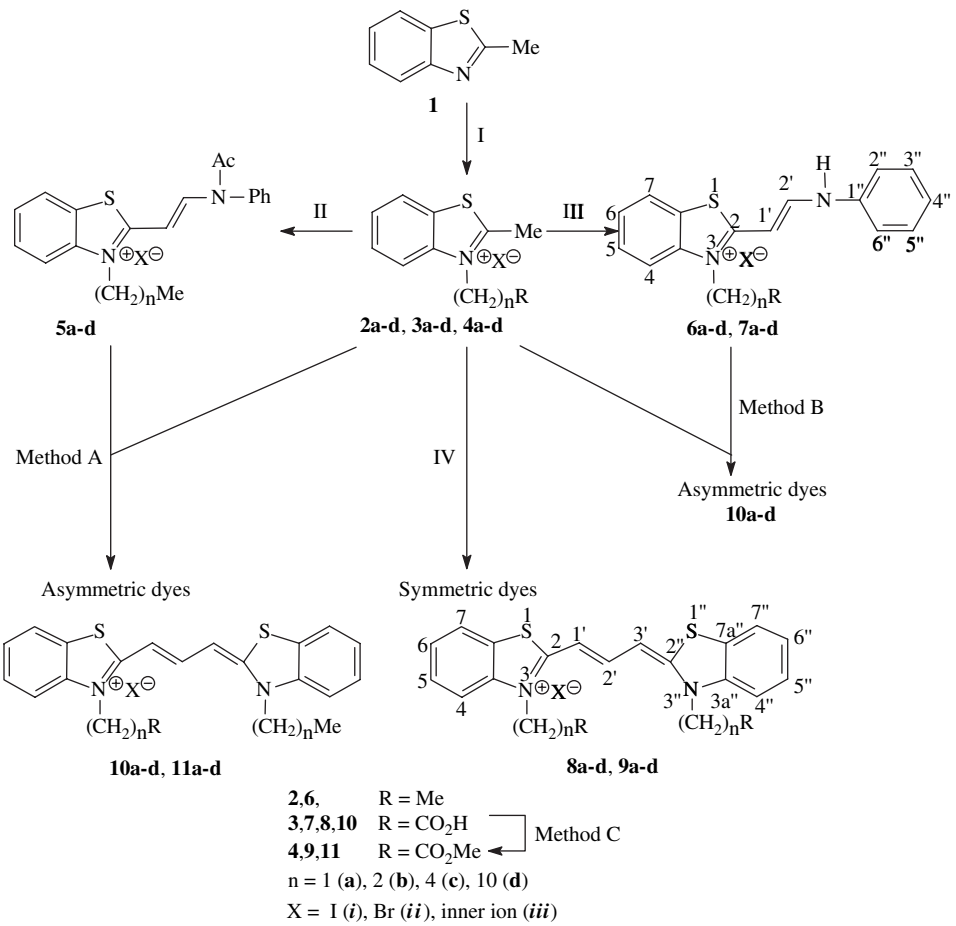
The coupling of the acetanilide derivatives **5** with *N*-carboxyalkyl- and *N*-methoxycarbonylalkylbenzothiazolium derivatives **3** and **4**, in pyridine (method A), afforded asymmetric dyes **10** and **11**, respectively, in yields from good to excellent.

Pursuing further improvement of the later syntheses, the above mentioned cyanines **10** were also prepared through the base catalyzed condensation of aniline derivatives **6** with *N*-carboxyalkylbenzothiazolium salts **3**, as well as by the condensation of aniline derivatives **7** with *N*-alkylbenzothiazolium salts **2** (method B). Cyanines **11** were similarly prepared starting from **6** and **4**. Although the final yields obtained by the two methods were not significantly different, method A provided rather cleaner reaction mixtures, which allowed the isolation of the pure compounds, while dyes prepared by method B were invariably contaminated with the corresponding symmetric analogues. Their presence, however, was only unequivocally detected in the respective FAB HRMS spectra.

Generally, all the methods mentioned above involving *N*-methoxycarbonylalkyl compounds **4**, **9** and **11** required milder conditions than those involving the related *N*-carboxyalkyl **3**, **7**, **8** and **10**. For the former compounds it was observed that if dry solvents and temperatures below 80 °C were not used, a partial or total hydrolysis of the ester group occurred.

The methyl ester cyanines **9** and **11** could also be obtained by direct esterification of their corresponding acid analogues **8** and **10**, by treatment with 5% methanolic H_2SO_4 under reflux. Nevertheless this procedure did not result in an enhancement of the overall yields when compared to those of the method previously described for the synthesis of esters **9** and **11**, it spares the preparation of *N*-methoxycarbonylalkyl precursors along with the *N*-carboxyalkyl analogues.

In general, the zwiterionic inner salts bearing carboxylate groups are quite insoluble and can be either isolated or converted to the comparatively more soluble hydrogen sulfate or iodide salts by treatment of the dye with 5% aqueous H_2SO_4 or 14% aqueous KI. Regardless of the variety of different salts that have been obtained for each dye, only one is described, namely iodide (i), bromide (ii) or inner salt (iii) since these forms only differ in the solubility, melting point and yield, keeping the spectroscopic data almost undistinguishable.



Scheme 1. Reagents and conditions. (I) – **2a–d**: $I(CH_2)_nMe$ (2.75–5.0 eq.), MeCN (reflux); **3a–d**: $Br(CH_2)_nCO_2H$ (1.2–3.6 eq.), 150 °C; **4a–d**: $Br(CH_2)_nCO_2Me$ (1.2–3.6 eq.), 80 °C; (II) – **5a–d** PhN=CHNHPh (1.0–1.2 eq.), Ac_2O, 145 °C; (III) – **6a–d**, **7a–d**: $CH(OEt)_3$ (1.05 eq.), $PhNH_2$ (1.1 eq.), 120 °C; (IV) – **8a–d**, **9a–d**: $CH(OEt)_3$ (2.0 eq.), pyridine (reflux or 80 °C); (methods A and B) – **10a–d**, **11a–d**: pyridine (reflux or 80 °C); (method C) – **4a–d**, **9a–d**, **11a–d**: MeOH, H_2SO_4 (5% v/v) (reflux).

Most of the precursors and dyes presented have not hitherto been described and, therefore, their full spectroscopic characterization, including ^1H and ^{13}C NMR shift assignments, which were established with the aid of HMQC (Heteronuclear Multiple Quantum Coherence), HMBC (Heteronuclear Multiple Bond Correlation) and COSY (Correlated Spectroscopy) experiments, is reported.

For this purpose, we choose a numbering system (see Scheme 1) based on the systematic nomenclature of cyanines where the quaternary ammonium heterocyclic moiety is the parent name and all the other structural units of the dye represent substitutes in different and multiple levels. This numbering system has already been used in some previously published literature [19].

3. Experimental

3.1. General

All reagents were of the highest purity available, purchased from Sigma–Aldrich Company, and used as received. Solvents were of analytical grade. Methanol, acetonitrile and pyridine were dried over 3 Å molecular sieves prior to use.

All reactions were monitored by thin-layer chromatography (tlc) on aluminum plates precoated with Merck silica gel 60 F_{254} (0.25 mm) using dichloromethane or dichloromethane/methanol (5–10%) and the spots having been examined under 254, 312 and 365 nm UV light.

^1H and ^{13}C NMR spectra were recorded in DMSO-d_6 solutions on a Brücker ACP 250 (250.13 and 62.90 MHz) or Brücker ARX 400 (400.13 and 100.62 MHz) spectrometers. Chemical shifts are reported in ppm and coupling constants (J) are given in Hz. HMQC, HMBC and COSY spectra were acquired on the Brücker ARX 400 spectrometer.

Infrared spectra were performed on a Mattson 5000-FTS FTIR spectrometer. All samples were prepared by mixing FTIR-grade KBr with 1% (w/w) compound and grinding to a fine powder. Spectra were recorded over the 400–4000 cm^{-1} range without baseline corrections. More intensive bands are given in cm^{-1}.

Visible spectra were recorded on a Perkin–Elmer Lambda 6 spectrophotometer using ethanol as solvent. Wavelength of maximum absorption is reported in nm.

High Resolution Fast Atom Bombardment Mass Spectra (HR FAB-MS) were recorded in 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 N-alkylbenzothiazolium salts **2**

3.2.1. 2-Methyl-3-undecylbenzothiazol-3-ium iodide (**2di**). Typical procedure

A solution of 2.35 g (2.0 ml, 15.7 mmol) of 2-methylbenzothiazole (**1**) and 12.20 g (10.0 ml, 43.2 mmol) of 1-iodoundecane in 25 ml of dry acetonitrile was refluxed for 96 h. After cooling to room temperature, diethyl ether was added to allow complete precipitation. The resulting crystalline product was collected by filtration under reduced pressure, washed with diethyl ether and recrystallized from acetonitrile. Yield: 49%. M.p. 126–127 °C. ^{1}H NMR (400.13 MHz, DMSO-d_6) δ (ppm): 0.85 (3H, t, $J = 7.0$ Hz, CH_2CH_3), 1.24–1.31 (14H, m, CH_2), 1.41–1.45 (2H, m, 3-N$(CH_2)_2CH_2$), 1.84 (2H, qui, $J = 7.6$ Hz, 3-NCH_2CH_2), 3.21 (3H, s, 2-CH_3), 4.70 (2H, t, $J = 7.9$ Hz, 3-NCH_2), 7.81 (1H, t, $J = 8.1$ Hz, 6-CH), 7.89 (1H, t, $J = 8.4$ Hz, 5-CH), 8.33 (1H, d, $J = 8.5$ Hz, 4-CH), 8.44 (1H, d, $J = 8.1$ Hz, 7-CH). ^{13}C NMR (62.90 MHz, DMSO-d_6) δ (ppm): 14.0 (CH_2CH_3), 17.0 (2-CH_3), 22.1 (CH_2CH_3), 25.9 (3-N$(CH_2)_8CH_2$), 27.8 (3-N$(CH_2)_7CH_2$), 28.6 (3-N$(CH_2)_6CH_2$), 28.7 (3-N$(CH_2)_5CH_2$), 28.9 (3-N$(CH_2)_4CH_2$), 29.0 (3-N$(CH_2)_3CH_2CH_2$), 31.3 (3-NCH_2CH_2), 49.2 (3-NCH_2), 116.9 (4-CH), 124.7 (7-CH), 128.1 (6-CH), 129.1 (7a-C), 129.4 (5-CH), 140.9 (3a-C), 177.0 (2-C). IR (KBr) ν (cm^{-1}): 3076, 3043, 3001, 2923, 2853, 1581, 1441, 767. HRMS (FAB, 3-NBA) $C_{19}H_{30}NS$: Calcd.: 304.2099; Found: 304.2086.

The *N*-alkylbenzothiazolium iodides **2a–c** were prepared using a similar procedure (24–96 h). Their spectroscopic characterization has already been previously reported [20,21].

3.3. Synthesis of N-carboxyalkylbenzothiazolium salts **3**

3.3.1. 3-(10-Carboxydecyl)-2-methylbenzothiazol-3-ium bromide (**3dii**). Typical procedure

A mixture 2.35 g (2.0 ml, 15.7 mmol) of 2-methylbenzothiazole (**1**) and 4.66 g (17.6 mmol) of 11-bromoundecanoic acid was heated at 150 °C for 24 h. After cooling to room temperature, diethyl ether was added to the reaction mixture until complete precipitation. The crystalline product so formed was collected by filtration under reduced pressure, washed with diethyl ether and recrystallized from dry acetonitrile. Yield: 68%. M.p. 166–167 °C. ^{1}H NMR (400.13 MHz, DMSO-d_6) δ (ppm): 1.24–1.33 (10H, m, CH_2), 1.39–1.48 (4H, m, 3-N$(CH_2)_2CH_2$, 3-N$(CH_2)_7CH_2$), 1.76–1.87 (2H, m, 3-NCH_2CH_2), 2.18 (2H, t, $J = 7.3$ Hz, CH_2COOH), 3.21 (3H, s, 2-CH_3), 4.70 (2H, t, $J = 7.8$ Hz, 3-NCH_2), 7.80 (1H, t, $J = 8.0$ Hz, 6-CH), 7.89 (1H, t, $J = 8.0$ Hz, 5-CH), 8.34 (1H, d, $J = 8.4$ Hz, 4-CH), 8.45 (1H, d, $J = 8.2$ Hz, 7-CH). ^{13}C NMR (62.90 MHz, DMSO-d_6) δ (ppm): 16.9 (2-CH_3), 24.5 (CH_2), 25.9 (CH_2), 27.8 (CH_2), 28.5 (CH_2), 28.6 (CH_2), 28.7 (CH_2), 28.8 (CH_2CH_2), 33.7 (CH_2COOH), 49.2 (3-NCH_2), 116.9 (4-CH), 124.7 (7-CH), 128.1 (6-CH), 129.2 (7a-C), 129.4 (5-CH), 140.9 (3a-C), 174.6 (CO), 177.1 (2-C). IR (KBr) ν (cm^{-1}): 2926, 2853, 1720 (C=O), 1174, 776. HRMS (FAB, 3-NBA) $C_{19}H_{28}NO_2S$: Calcd.: 334.1841; Found: 334.1841.

The *N*-carboxyalkylbenzothiazolium bromides **3a–c** were prepared using a similar procedure (2–18 h).

3.3.2. 3-Carboxymethyl-2-methylbenzothiazol-3-ium bromide (**3aii**)

Yield: 89%. M.p. 228–229 °C. ^{1}H NMR (400.13 MHz, DMSO-d_6) δ (ppm): 3.20 (3H, s, 2-CH_3), 5.78 (2H, s, 3-NCH_2), 7.82 (1H, t, $J = 8.0$ Hz, 6-CH), 7.90 (1H, t, $J = 8.5$ Hz, 5-CH), 8.30 (1H, d, $J = 8.5$ Hz, 4-CH), 8.49 (1H, d, $J = 8.1$ Hz, 7-CH). ^{13}C NMR (62.90 MHz, DMSO-d_6) δ (ppm): 17.2 (2-CH_3), 50.1 (3-NCH_2), 116.7 (4-CH), 125.0 (7-CH), 128.3 (6-CH), 128.7 (7a-C), 129.7 (5-CH), 141.2 (3a-C), 166.7 (CO), 179.2 (2-C). IR (KBr) ν (cm^{-1}): 1737 (C=O), 1245, 766. HRMS (FAB, 3-NBA) $C_{10}H_{10}NO_2S$: Calcd.: 208.0432; Found: 208.0440.

3.3.3. 3-(2-Carboxyethyl)-2-methylbenzothiazol-3-ium bromide (**3bii**)

Yield: 52%. M.p. 226–227 °C. ^{1}H NMR (400.13 MHz, DMSO-d_6) δ (ppm): 2.99 (2H, t, $J = 7.2$ Hz, CH_2COOH), 3.27 (3H, s, 2-CH_3), 4.91 (2H, t, $J = 7.2$ Hz, 3-NCH_2), 7.79 (1H, t, $J = 7.9$ Hz, 6-CH), 7.88 (1H, t, $J = 8.5$ Hz, 5-CH), 8.37 (1H, d, $J = 8.5$ Hz, 4-CH), 8.48 (1H, d, $J = 8.1$ Hz, 7-CH). ^{13}C NMR (100.61 MHz, DMSO-d_6) δ (ppm): 17.0 (2-CH_3), 31.7 (CH_2COOH), 44.9 (3-NCH_2), 116.8 (4-CH), 124.6 (7-CH), 127.9 (6-CH), 128.9 (7a-C), 129.3 (5-CH), 140.6 (3a-C), 171.3 (CO), 178.0 (2-C). IR (KBr) ν (cm^{-1}): 2854, 2498, 1716 (C=O), 1445, 1402, 1197, 833, 775. HRMS (FAB, 3-NBA) $C_{11}H_{12}NO_2S$: Calcd.: 222.0589; Found: 222.0580.

3.3.4. 3-(4-Carboxybutyl)-2-methylbenzothiazol-3-ium bromide (**3cii**)

Yield: 51%. M.p. 211–212 °C. ^{1}H NMR (400.13 MHz, DMSO-d_6) δ (ppm): 1.66 (2H, qui, $J = 7.6$ Hz, 3-N$(CH_2)_2CH_2$), 1.86 (2H, qui, $J = 7.6$ Hz, 3-NCH_2CH_2), 2.31 (2H, t, $J = 7.4$ Hz, CH_2COOH), 3.21 (3H, s, 2-CH_3), 4.74 (2H, t, $J = 7.7$ Hz, 3-NCH_2), 7.80 (1H, t, $J = 7.7$ Hz, 6-CH), 7.89 (1H, t, $J = 8.4$ Hz, 5-CH), 8.35 (1H, d, $J = 8.5$ Hz, 4-CH), 8.46 (1H, d, $J = 8.0$ Hz, 7-CH). ^{13}C NMR (100.61 MHz, DMSO-d_6) δ (ppm): 16.9 (2-CH_3), 21.4 (3-N$(CH_2)_2CH_2$), 27.2 (3-NCH_2CH_2), 33.0 (CH_2COOH), 48.8 (3-NCH_2), 116.8 (4-CH), 124.7 (7-CH), 128.0 (6-CH), 129.1 (7a-C), 129.3 (5-CH), 140.8 (3a-C), 174.1 (CO), 177.1 (2-C). IR (KBr) ν (cm^{-1}): 3097, 2928, 1714 (C=O), 1216, 1154, 777. HRMS (FAB, 3-NBA) $C_{13}H_{16}NO_2S$: Calcd.: 250.0902; Found: 250.0905.

3.4. Synthesis of N-methoxycarbonylalkyl-benzothiazolium salts **4**

3.4.1. 3-(10-Methoxycarbonyldecyl)-2-methylbenzothiazol-3-ium bromide (**4dii**). Typical procedure

A mixture of 2.35 g (2.0 ml, 15.7 mmol) of 2-methylbenzothiazole (**1**) and 4.63 g (4.0 ml, 16.6 mmol) of methyl 11-bromoundecanoate was heated at 80 °C for 1 week. After cooling to room temperature, diethyl ether was added to ensure complete precipitation. The resulting crystalline product was collected by filtration at reduced pressure, washed with diethyl ether and recrystallized from dry methanol. Yield: 20%. M.p. 134–136 °C. ^{1}H NMR (400.13 MHz, DMSO-d_6) δ (ppm): 1.22–1.34 (10H, m, CH_2), 1.39–1.44 (2H, m, CH_2), 1.48–1.53 (2H, m, CH_2), 1.83 (2H, qui, $J = 7.7$ Hz, 3-NCH$_2$CH_2), 2.28 (2H, t, $J = 7.4$ Hz, CH_2COOCH$_3$), 3.20 (3H, s, 2-CH_3), 3.57 (3H, s, COOCH_3), 4.70 (2H, t, $J = 7.8$ Hz, 3-NCH_2), 7.80 (1H, t, $J = 7.9$ Hz, 6-CH), 7.89 (1H, t, $J = 8.4$ Hz, 5-CH), 8.33 (1H, d, $J = 8.5$ Hz, 4-CH), 8.44 (1H, d, $J = 8.1$ Hz, 7-CH). ^{13}C NMR (62.90 MHz, DMSO-d_6) δ (ppm): 16.9 (2-CH$_3$), 24.4 (CH$_2$), 25.9 (CH$_2$), 27.5 (CH$_2$), 27.8 (CH$_2$), 28.4 (CH$_2$), 28.6 (CH$_2$), 28.6 (CH$_2$), 28.8 (CH$_2$CH$_2$), 33.3 (CH$_2$COOCH$_3$), 49.2 (3-NCH$_2$), 51.2 (COOCH$_3$), 116.9 (4-CH), 124.7 (7-CH), 128.1 (6-CH), 129.1 (7a-C), 129.4 (5-CH), 140.8 (3a-C), 173.4 (CO), 177.1 (2-C). IR (KBr) ν (cm^{-1}): 3070, 3040, 3004, 2923, 2853, 1734 (C=O), 1443, 1179, 1163, 774. HRMS (FAB, 3-NBA) $C_{20}H_{30}NO_2S$: Calcd.: 348.1997; Found: 348.2011.

The *N*-methoxycarbonylalkylbenzothiazolium salts **4a–c** were prepared using a similar procedure (4–168 h).

3.4.2. 3-Methoxycarbonylmethyl-2-methylbenzothiazol-3-ium bromide (**4aii**)

Yield: 82%. M.p. 178–179 °C. ^{1}H NMR (400.13 MHz, DMSO-d_6) δ (ppm): 3.22 (3H, s, 2-CH_3), 3.79 (3H, s, COOCH_3), 5.91 (2H, s, 3-NCH_2COOCH$_3$), 7.82 (1H, t, $J = 8.1$ Hz, 6-CH), 7.89 (1H, t, $J = 8.5$ Hz, 5-CH), 8.29 (1H, d, $J = 8.4$ Hz, 4-CH), 8.50 (1H, d, $J = 7.8$ Hz, 7-CH). ^{13}C NMR (62.90 MHz, DMSO-d_6) δ (ppm): 17.2 (2-CH$_3$), 49.7 (3-NCH$_2$COOCH$_3$), 53.5 (COOCH$_3$), 116.7 (4-CH), 125.0 (7-CH), 128.3 (6-CH), 128.6 (7a-C), 129.7 (5-CH), 141.1 (3a-C), 165.9 (CO), 179.7 (2-C). IR (KBr) ν (cm^{-1}): 2940, 1741 (C=O), 1444, 1354, 1247, 779. HRMS (FAB, 3-NBA) $C_{11}H_{12}NO_2S$: Calcd.: 222.0589; Found: 222.0593.

3.4.3. 3-(2-Methoxycarbonylethyl)-2-methylbenzothiazol-3-ium bromide (**4bii**)

Yield: 19%. M.p. 227–228 °C. ^{1}H NMR (400.13 MHz, DMSO-d_6) δ (ppm): 3.08 (2H, t, $J = 7.3$ Hz, CH_2COOCH$_3$), 3.26 (3H, s, 2-CH_3), 3.62 (3H, s, COOCH_3), 4.93 (2H, t, $J = 7.2$ Hz, 3-NCH_2), 7.79 (1H, t, $J = 8.0$ Hz, 6-CH), 7.88 (1H, t, $J = 8.2$ Hz, 5-CH), 8.36 (1H, d, $J = 8.5$ Hz, 4-CH), 8.46 (1H, d, $J = 8.1$ Hz, 7-CH). ^{13}C NMR (62.90 MHz, DMSO-d_6) δ (ppm): 17.2 (2-CH$_3$), 31.5 (CH$_2$COOCH$_3$), 44.7 (3-NCH$_2$), 51.9 (COOCH$_3$), 117.4 (4-CH), 124.8 (7-CH), 128.0 (6-CH), 129.0 (7a-C), 129.4 (5-CH), 140.8 (3a-C), 170.5 (CO), 178.4 (2-C). IR (KBr) ν (cm^{-1}): 3074, 3001, 2959, 1726 (C=O), 1445, 1420, 1344, 1261, 1196, 774. HRMS (FAB, 3-NBA) $C_{12}H_{14}NO_2S$: Calcd.: 236.0745; Found: 236.0737.

3.4.4. 3-(4-Methoxycarbonylbutyl)-2-methylbenzothiazol-3-ium bromide (**4cii**)

Yield: 20%. M.p. 110–113 °C. ^{1}H NMR (400.13 MHz, DMSO-d_6) δ (ppm): 1.70 (2H, qui, $J = 7.7$ Hz, 3-N(CH$_2$)$_2$CH_2), 1.87 (2H, qui, $J = 7.8$ Hz, 3-NCH$_2$CH_2), 2.41 (2H, t, $J = 7.4$ Hz, CH_2COOCH$_3$), 3.20 (3H, s, 2-CH_3), 3.58 (3H, s, COOCH_3), 4.74 (2H, t, $J = 7.8$ Hz, 3-NCH_2), 7.80 (1H, t, $J = 7.8$ Hz, 6-CH), 7.90 (1H, t, $J = 8.4$ Hz, 5-CH), 8.34 (1H, d, $J = 8.5$ Hz, 4-CH), 8.45 (1H, d, $J = 8.2$ Hz, 7-CH). ^{13}C NMR (100.62 MHz, DMSO-d_6) δ (ppm): 16.9 (2-CH$_3$), 21.3 (3-N(CH$_2$)$_2$$CH_2$), 27.0 (3-NCH$_2$$CH_2$), 32.6 ($CH_2$COOCH$_3$), 48.7 (3-NCH$_2$), 51.3 (COOCH$_3$), 116.8 (4-$C$H), 124.7 (7-$C$H), 128.0 (6-$C$H), 129.2 (7a-$C$), 129.3 (5-$C$H), 140.8 (3a-$C$), 173.0 ($C$O), 177.2 (2-$C$). IR (KBr) ν (cm^{-1}): 3080, 3005, 2949, 2872, 2744, 1733 (C=O), 1442, 1191, 777. HRMS (FAB, 3-NBA) $C_{14}H_{18}NO_2S$: Calcd.: 264.1058; Found: 264.1069.

3.5. Synthesis of acetanilide derivatives **5a–d**

3.5.1. 2-[2-(Acetylphenylamino)vinyl]-3-ethylbenzothiazol-3-ium iodide (**5ai**). Typical procedure

A solution of 1.02 g (3.35 mmol) of 3-ethyl-2-methylbenzothiazol-3-ium iodide (**2ai**) and 0.76 g (3.85 mmol) of *N*,*N*′-diphenylformamidine in 10 ml of acetic anhydride was refluxed for 30 min. After cooling to room temperature, diethyl ether was added to the reaction mixture until complete precipitation. The crystalline product so formed was collected by filtration under reduced pressure, washed with diethyl ether and recrystallized from dry acetonitrile. Yield: 89%. M.p. 221–222 °C. ^{1}H NMR (400.13 MHz, DMSO-d_6) δ (ppm): 1.19 (3H, t, $J = 7.1$ Hz, CH$_2$CH_3), 2.07 (3H, s, COCH_3), 4.43 (2H, q, $J = 7.3$ Hz, 3-NCH_2CH$_3$), 5.67 (1H, d, $J = 13.8$ Hz, 1′-CH), 7.54 (2H, d, $J = 7.5$ Hz, 2″-CH, 6″-CH), 7.64–7.74 (4H, m, 6-CH, 3″-CH, 4″-CH, 5″-CH), 7.79 (1H, t, $J = 7.3$ Hz, 5-CH), 8.16 (1H, d, $J = 8.4$ Hz, 4-CH), 8.32 (1H, d, $J = 8.1$ Hz, 7-CH), 8.84 (1H, d, $J = 13.8$ Hz, 2′-CH). ^{13}C NMR (62.90 MHz, DMSO-d_6) δ (ppm): 13.1 (CH$_2$$CH_3$), 23.2 (CO$CH_3$), 43.7 (3-NCH$_2$$CH_3$), 96.0 (1′-$C$H), 116.0 (4-$C$H), 124.3 (7-$C$H), 127.0 (7a-$C$), 127.9 (6-$C$H), 128.3 (2″-$C$H, 6″-$C$H), 129.2 (5-$C$H), 130.2 (4″-$C$H), 130.6 (3″-$C$H, 5″-$C$H), 136.9 (1″-$C$), 140.6 (3a-$C$), 145.5 (2′-$C$H), 170.1 ($C$O), 171.4 (2-$C$). IR (KBr) ν (cm^{-1}): 3068, 3039, 1714 (C=O), 1607 (C=C), 1584 (C=C), 1360, 1327, 1262, 1237, 1213, 761. Vis (ethanol): 372 nm. HRMS (FAB, 3-NBA) $C_{19}H_{19}N_2OS$: Calcd.: 323.1218; Found: 323.1219.

The *N*-acetanilide derivatives **5b–d** were prepared using a similar procedure (0.5–2 h).

3.5.2. 2-[2-(Acetylphenylamino)vinyl]-3-propylbenzothiazol-3-ium iodide (**5bi**)

Yield: 84%. M.p. 166–169 °C. ^{1}H NMR (400.13 MHz, DMSO-d_6) δ (ppm): 0.73 (3H, t, $J = 7.3$ Hz, CH$_2$CH_3),

1.59–1.68 (2H, m, CH_2CH$_3$), 2.09 (3H, s, COCH_3), 4.36 (2H, t, $J = 7.2$ Hz, 3-NCH_2), 5.63 (1H, d, $J = 13.8$ Hz, 1′-CH), 7.54 (2H, d, $J = 7.0$ Hz, 2″-CH, 6″-CH), 7.63–7.73 (4H, m, 6-CH, 3″-CH, 4″-CH, 5″-CH), 7.78 (1H, t, $J = 7.8$ Hz, 5-CH), 8.17 (1H, d, $J = 8.3$ Hz, 4-CH), 8.33 (1H, d, $J = 7.9$ Hz, 7-CH), 8.84 (1H, d, $J = 13.8$ Hz, 2′-CH). ^{13}C NMR (100.62 MHz, DMSO-d_6) δ (ppm): 10.6 (CH$_2$CH_3), 21.2 (CH_2CH$_3$), 23.1 (COCH_3), 49.5 (3-NCH_2), 96.4 (1′-CH), 116.1 (4-CH), 124.1 (7-CH), 126.7 (7a-CH), 127.8 (6-C), 128.1 (2″-CH, 6″-CH), 129.0 (5-CH), 130.0 (4″-CH), 130.5 (3″-CH, 5″-CH), 136.8 (1″-C), 140.9 (3a-C), 145.3 (2′-CH), 169.8 (CO), 171.4 (2-C). IR (KBr) ν (cm^{-1}): 3037, 2965, 1717 (C=O), 1606 (C=C), 1583 (C=C), 1361, 1225, 1205, 756. Vis (ethanol): 371 nm. HRMS (FAB, 3-NBA) $C_{20}H_{21}N_2OS$: Calcd.: 337.1375; Found: 337.1358.

3.5.3. 2-[2-(Acetylphenylamino)vinyl]-3-pentylbenzothiazol-3-ium iodide (**5ci**)

Yield: 80%. M.p. 177–179 °C. ^{1}H NMR (400.13 MHz, DMSO-d_6) δ (ppm): 0.79 (3H, t, $J = 6.7$ Hz, CH$_2$CH_3), 1.09–1.13 (4H, m, 3-N(CH$_2$)$_2$CH_2, CH_2CH$_3$), 1.55–1.61 (2H, m, 3-NCH$_2$CH_2), 2.09 (3H, s, COCH_3), 4.35 (2H, t, $J = 7.5$ Hz, 3-NCH_2), 5.60 (1H, d, $J = 13.8$ Hz, 1′-CH), 7.54 (2H, d, $J = 8.0$ Hz, 2″-CH, 6″-CH), 7.64–7.73 (4H, m, 6-CH, 3″-CH, 4″-CH, 5″-CH), 7.79 (1H, t, $J = 8.4$ Hz, 5-CH), 8.16 (1H, d, $J = 8.3$ Hz, 4-CH), 8.33 (1H, d, $J = 8.0$ Hz, 7-CH), 8.85 (1H, d, $J = 13.8$ Hz, 2′-CH). ^{13}C NMR (62.90 MHz, DMSO-d_6) δ (ppm): 13.8 (CH$_2$CH_3), 21.5 (CH_2CH$_3$), 23.2 (COCH_3), 27.4 (3-N(CH$_2$)$_2$CH_2), 27.9 (3-NCH$_2$CH_2), 48.1 (3-NCH_2), 96.4 (1′-CH), 116.2 (4-CH), 124.3 (7-CH), 126.9 (7a-CH), 127.9 (6-C), 128.3 (2″-CH, 6″-CH), 129.2 (5-CH), 130.1 (4″-CH), 130.6 (3″-CH, 5″-CH), 137.0 (1″-C), 140.9 (3a-C), 145.5 (2′-CH), 170.0 (CO), 171.3 (2-C). IR (KBr) ν (cm^{-1}): 3045, 3000, 2925, 2859, 1721 (C=O), 1608 (C=C), 1587 (C=C), 1490, 1461, 1422, 1367, 1342, 1314, 1267, 1204, 1146, 773, 702. Vis (ethanol): 373 nm. HRMS (FAB, 3-NBA) $C_{22}H_{25}N_2OS$: Calcd.: 365.1688; Found: 365.1699.

3.5.4. 2-[2-(Acetylphenylamino)vinyl]-3-undecylbenzothiazol-3-ium iodide (**5di**)

Yield: 35%. M.p. 126–128 °C. ^{1}H NMR (400.13 MHz, DMSO-d_6) δ (ppm): 0.87 (3H, t, $J = 7.1$ Hz, CH$_2$CH_3), 1.08–1.13 (2H, m, CH_2), 1.15–1.31 (14H, m, CH_2), 1.57 (2H, qui, $J = 6.7$ Hz, 3-NCH$_2$CH_2), 2.09 (3H, s, COCH_3), 4.35 (2H, t, $J = 7.3$ Hz, 3-NCH_2), 5.60 (1H, d, $J = 13.8$ Hz, 1′-CH), 7.54 (2H, t, $J = 7.7$ Hz, 2″-CH, 6″-CH), 7.60–7.67 (3H, m, 3″-CH, 4″-CH, 5″-CH), 7.71 (1H, t, $J = 7.7$ Hz, 6-CH), 7.78 (1H, t, $J = 7.7$ Hz, 5-CH), 8.16 (1H, d, $J = 8.4$ Hz, 4-CH), 8.33 (1H, d, $J = 8.1$ Hz, 7-CH), 8.85 (1H, d, $J = 13.8$ Hz, 2′-CH). ^{13}C NMR (62.90 MHz, DMSO-d_6) δ (ppm): 14.0 (CH$_2$CH_3), 22.2 (CH_2CH$_3$), 23.2 (COCH_3), 25.8 (3-N(CH$_2$)$_8$CH_2), 27.8 (CH_2), 28.3 (CH_2), 28.8 (CH_2), 28.8 (CH_2), 28.9 (CH_2), 29.0 (CH_2), 31.3 (3-NCH$_2$CH_2), 48.2 (3-NCH_2), 96.4 (1′-CH), 116.2 (4-CH), 124.3 (7-CH), 126.9 (7a-CH), 127.9 (6-C), 128.3 (2″-CH, 6″-CH), 129.2 (5-CH), 130.1 (4″-CH), 130.6 (3″-CH, 5″-CH), 137.0 (1″-C), 140.9 (3a-C), 145.4 (2′-CH), 170.0 (CO), 171.3 (2-C). IR (KBr) ν (cm^{-1}): 2923, 2852, 1714 (C=O), 1605 (C=C), 1583 (C=C), 1220, 1141, 927, 772, 700. Vis (ethanol): 368 nm. HRMS (FAB, 3-NBA) $C_{28}H_{37}N_2OS$: Calcd.: 449.2627; Found: 449.2606.

3.6. Synthesis of aniline derivatives **6** and **7**

3.6.1. 3-Ethyl-2-(2-phenylaminovinyl)benzothiazol-3-ium iodide (**6ai**). Typical procedure

A solution of 0.91 g (2.98 mmol) of 3-ethyl-2-methylbenzothiazol-3-ium iodide (**2ai**), 0.31 g (0.30 ml, 3.30 mmol) of aniline and 0.46 g (0.52 ml, 3.13 mmol) of triethyl orthoformiate was heated at 120 °C for 30 min. After cooling to room temperature, diethyl ether was added to the reaction mixture until complete precipitation. The crystalline product so formed was collected by filtration under reduced pressure, washed with diethyl ether and recrystallized from dry methanol/diethyl ether. Yield: 85%. M.p. 258–259 °C. ^{1}H NMR (400.13 MHz, DMSO-d_6) δ (ppm): 1.39 (3H, t, $J = 7.1$ Hz, CH$_2$CH_3), 4.47 (2H, q, $J = 7.1$ Hz, 3-NCH_2CH$_3$), 6.35 (1H, d, $J = 12.1$ Hz, 1′-CH), 7.19–7.24 (1H, m, 4″-CH), 7.43–7.48 (4H, m, 2″-CH, 3″-CH, 5″-CH, 6″-CH), 7.53 (1H, t, $J = 7.7$ Hz, 6-CH), 7.66 (1H, t, $J = 8.2$ Hz, 5-CH), 7.94 (1H, d, $J = 8.3$ Hz, 4-CH), 8.14 (1H, d, $J = 7.9$ Hz, 7-CH), 8.66 (1H, d, $J = 11.9$ Hz, 2′-CH), 11.43 (1H, s, 2′-NH). ^{13}C NMR (62.90 MHz, DMSO-d_6) δ (ppm): 12.6 (CH$_2$CH_3), 42.3 (3-NCH$_2$CH$_3$), 89.6 (1′-CH), 114.2 (4-CH), 117.4 (2″-CH, 6″-CH), 123.4 (7-CH), 125.1 (4″-CH), 125.4 (7a-CH), 126.1 (6-CH), 128.3 (5-CH), 129.8 (3″-CH, 5″-CH), 139.0 (1″-C), 140.2 (3a-C), 149.8 (2′-CH), 168.6 (2-C). IR (KBr) ν (cm^{-1}): 3088, 3002, 1632 (C=C), 1587 (C=C), 1533 (C=C), 1496, 1463, 1365, 1295, 1247, 755. Vis (ethanol): 411 nm. HRMS (FAB, 3-NBA) $C_{17}H_{17}N_2S$: Calcd.: 281.1112; Found: 281.1108.

The aniline derivatives **6b–d** and **7a–d** were prepared using a similar procedure (0.5–2 h) except the use of *N*-carboxylalkylbenzothiazolium iodides **3a–d** for the preparation of **7a–d** which were further recrystallized from acetonitrile.

3.6.2. 2-(2-Phenylaminovinyl)-3-propylbenzothiazol-3-ium iodide (**6bi**)

Yield: 66%. M.p. 251–252 °C. ^{1}H NMR (400.13 MHz, DMSO-d_6) δ (ppm): 1.01 (3H, t, $J = 7.3$ Hz, CH$_2$CH_3), 1.80–1.83 (2H, m, CH_2CH$_3$), 4.39 (2H, t, $J = 7.4$ Hz, 3-NCH_2), 6.37 (1H, d, $J = 12.1$ Hz, 1′-CH), 7.19–7.23 (1H, m, 4″-CH), 7.43–7.47 (4H, m, 2″-CH, 3″-CH, 5″-CH, 6″-CH), 7.52 (1H, t, $J = 7.7$ Hz, 6-CH), 7.65 (1H, t, $J = 8.3$ Hz, 5-CH), 7.96 (1H, d, $J = 8.4$ Hz, 4-CH), 8.14 (1H, d, $J = 7.9$ Hz, 7-CH), 8.61 (1H, d, $J = 11.6$ Hz, 2′-CH), 11.43 (1H, s, 2′-NH). ^{13}C NMR (100.62 MHz, DMSO-d_6) δ (ppm): 10.8 (CH$_2$CH_3), 20.6 (CH_2CH$_3$), 48.1 (3-NCH_2), 89.8 (1′-CH), 114.3 (4-CH), 117.2 (2″-CH, 6″-CH), 123.2 (7-CH), 125.0 (4″-CH), 125.1 (7a-C), 126.0 (6-CH), 128.1 (5-CH), 129.7 (3″-CH, 5″-CH), 138.8 (1″-CH), 140.6 (3a-C), 149.7 (2′-CH), 168.9 (2-C). IR (KBr) ν (cm^{-1}): 3032, 2966, 1633 (C=C), 1588 (C=C), 1538

(C=C), 1498, 1463, 1367, 1301, 1254, 1162, 959, 825, 748. Vis (ethanol): 411 nm. HRMS (FAB, 3-NBA) $C_{18}H_{19}N_2S$: Calcd.: 295.1269; Found: 295.1265.

3.6.3. 3-Pentyl-2-(2-phenylaminovinyl)benzothiazol-3-ium iodide (**6ci**)

Yield: 74%. M.p. 140–143 °C. ^{1}H NMR (250.13 MHz, DMSO-d_6) δ (ppm): 0.86 (3H, t, $J = 6.7$ Hz, CH_2CH_3), 1.32–1.38 (4H, m, 3-N$(CH_2)_2CH_2$, CH_2CH_3), 1.72–1.77 (2H, m, 3-NCH_2CH_2), 4.38 (2H, t, $J = 7.2$ Hz, 3-NCH_2), 6.34 (1H, d, $J = 12.1$ Hz, 1′-C*H*), 7.15–7.22 (1H, m, 4″-C*H*), 7.38–7.44 (4H, m, 2″-C*H*, 3″-C*H*, 5″-C*H*, 6″-C*H*), 7.49 (1H, t, $J = 7.8$ Hz, 6-C*H*), 7.62 (1H, t, $J = 8.0$ Hz, 5-C*H*), 7.92 (1H, d, $J = 8.2$ Hz, 4-C*H*), 8.12 (1H, d, $J = 7.8$ Hz, 7-C*H*), 8.63 (1H, t, $J = 12.4$ Hz, 2′-C*H*), 11.43 (1H, d, $J = 13.2$ Hz, 2′-N*H*). ^{13}C NMR (62.90 MHz, DMSO-d_6) δ (ppm): 13.9 (CH_2CH_3), 21.9 (CH_2CH_3), 27.1 (3-N$(CH_2)_2CH_2$), 28.2 (3-NCH_2CH_2), 46.9 (3-NCH_2), 89.8 (1′-*C*H), 114.4 (4-*C*H), 117.4 (2″-*C*H, 6″-*C*H), 123.4 (7-*C*H), 125.1 (4″-*C*H), 125.2 (7a-*C*), 126.1 (6-*C*H), 128.3 (5-*C*H), 129.8 (3″-*C*H, 5″-*C*H), 138.9 (1″-*C*), 140.6 (3a-*C*), 149.8 (2′-*C*H), 169.0 (2-*C*). IR (KBr) ν (cm^{-1}): 3082, 2954, 2858, 1633 (C=C), 1587 (C=C), 1530 (C=C), 1497, 1464, 1362, 1298, 1245, 754. Vis (ethanol): 404 nm. HRMS (FAB, 3-NBA) $C_{20}H_{23}N_2S$: Calcd.: 323.1582; Found: 323.1589.

3.6.4. 2-(2-Phenylaminovinyl)-3-undecylbenzothiazol-3-ium iodide (**6di**)

Yield: 56%. M.p. 112–115 °C. ^{1}H NMR (400.13 MHz, DMSO-d_6) δ (ppm): 0.84 (3H, t, $J = 7.1$ Hz, CH_2CH_3), 1.16–1.34 (14H, m, CH_2), 1.38–1.42 (2H, m, 3-N$(CH_2)_2CH_2$), 1.73–1.80 (2H, m, 3-NCH_2CH_2), 4.41 (2H, t, $J = 7.0$ Hz, 3-NCH_2), 6.33 (1H, d, $J = 11.8$ Hz, 1′-C*H*), 7.19–7.24 (1H, m, 4″-C*H*), 7.41–7.47 (4H, m, 2″-C*H*, 3″-C*H*, 5″-C*H*, 6″-C*H*), 7.52 (1H, t, $J = 7.9$ Hz, 6-C*H*), 7.65 (1H, t, $J = 7.5$ Hz, 5-C*H*), 7.93 (1H, d, $J = 8.1$ Hz, 4-C*H*), 8.14 (1H, d, $J = 7.9$ Hz, 7-C*H*), 8.65 (1H, d, $J = 11.3$ Hz, 2′-C*H*), 11.42 (1H, s, 2′-N*H*). ^{13}C NMR (62.90 MHz, DMSO-d_6) δ (ppm): 14.0 (CH_2CH_3), 22.1 (CH_2) 26.0 (CH_2), 26.1 (CH_2), 27.3 (CH_2), 28.7 (CH_2), 29.0 (CH_2), 29.0 (CH_2CH_2), 31.3 (CH_2), 47.0 (3-NCH_2), 89.8 (1′-*C*H), 114.4 (4-*C*H), 117.3 (2″-*C*H, 6″-*C*H), 123.4 (7-*C*H), 125.1 (4″-*C*H), 125.2 (7a-*C*), 126.1 (6-*C*H), 128.2 (5-*C*H), 129.8 (3″-*C*H, 5″-*C*H), 138.9 (1″-*C*), 140.6 (3a-*C*), 149.7 (2′-*C*H), 168.9 (2-*C*). IR (KBr) ν (cm^{-1}): 3084, 3003, 2924, 2853, 1634 (C=C), 1588 (C=C), 1532 (C=C), 1497, 1464, 1420, 1364, 1292, 1250, 758. Vis (ethanol): 413 nm. HRMS (FAB, 3-NBA) $C_{26}H_{35}N_2S$: Calcd.: 407.2521; Found: 407.2525.

3.6.5. 3-Carboxymethyl-2-(2-phenylaminovinyl)benzothiazol-3-ium bromide (**7aii**)

Yield: 37%. M.p. 199–201 °C. ^{1}H NMR (250.13 MHz, DMSO-d_6) δ (ppm): 5.15 (2H, s, 3-NCH_2COOH), 6.26 (1H, d, $J = 11.3$ Hz, 1′-C*H*), 7.18 (1H, t, $J = 7.3$ Hz, 4″-C*H*), 7.38–7.50 (5H, m, 6-C*H*, 2″-C*H*, 3″-C*H*, 5″-C*H*, 6″-C*H*), 7.58 (1H, t, $J = 7.8$ Hz, 5-C*H*), 7.83 (1H, d, $J = 7.5$ Hz, 4-C*H*), 8.08 (1H, d, $J = 8.0$ Hz, 7-C*H*), 8.61 (1H, d, $J = 11.2$ Hz, 2′-C*H*). ^{13}C NMR (62.90 MHz, DMSO-d_6) δ (ppm): 47.9 (3-NCH_2COOH), 90.0 (1′-*C*H), 114.1 (4-*C*H), 117.7 (2″-*C*H, 6″-*C*H), 123.5 (7-*C*H), 124.7 (7a-*C*H), 125.6 (4″-*C*H), 126.2 (6-*C*), 128.4 (5-*C*H), 129.9 (3″-*C*H, 5″-*C*H), 139.0 (1″-*C*), 140.9 (3a-*C*), 150.7 (2′-*C*H), 167.6 (2-*C*), 170.3 (*C*O). IR (KBr) ν (cm^{-1}): 1733 (C=O), 1643 (C=C), 1589 (C=C), 1548 (C=C), 1465, 1419, 1322, 1257, 1191, 752. Vis (ethanol): 418 nm. HRMS (FAB, 3-NBA) $C_{17}H_{15}N_2O_2S$: Calcd.: 311.0854; Found: 311.0855.

3.6.6. 3-(2-Carboxyethyl)-2-(2-phenylaminovinyl)benzothiazol-3-ium bromide (**7bii**)

Yield: 56%. M.p. 218–221 °C. ^{1}H NMR (250.13 MHz, DMSO-d_6) δ (ppm): 2.85 (2H, t, $J = 7.2$ Hz, CH_2COOH), 4.60 (2H, t, $J = 7.2$ Hz, 3-NCH_2), 6.46 (1H, d, $J = 12.1$ Hz, 1′-C*H*), 7.20 (1H, t, $J = 7.3$ Hz, 4″-C*H*), 7.44–7.53 (5H, m, 6-C*H*, 2″-C*H*, 3″-C*H*, 5″-C*H*, 6″-C*H*), 7.63 (1H, t, $J = 7.3$ Hz, 5-C*H*), 7.94 (1H, d, $J = 8.3$ Hz, 4-C*H*), 8.12 (1H, d, $J = 8.0$ Hz, 7-C*H*), 8.67 (1H, t, $J = 11.6$ Hz, 2′-C*H*), 11.66 (1H, d, $J = 13.5$ Hz, 2′-N*H*). ^{13}C NMR (62.90 MHz, DMSO-d_6) δ (ppm): 31.7 (CH_2COOH), 42.9 (3-NCH_2), 90.2 (1′-*C*H), 114.6 (4-*C*H), 117.5 (2″-*C*H, 6″-*C*H), 123.4 (7-*C*H), 125.2 (4″-*C*H), 125.3 (7a-*C*), 126.2 (6-*C*H), 128.3 (5-*C*H), 130.0 (3″-*C*H, 5″-*C*H), 139.1 (1″-*C*), 140.6 (3a-*C*), 150.0 (2′-*C*H), 169.4 (2-*C*), 171.7 (*C*O). IR (KBr) ν (cm^{-1}): 2999, 2846, 1734 (C=O), 1639 (C=C), 1589 (C=C), 1537 (C=C), 1256, 1181, 757. Vis (ethanol): 419 nm. HRMS (FAB, 3-NBA) $C_{18}H_{17}N_2O_2S$: Calcd.: 325.1011; Found: 325.1012.

3.6.7. 3-(4-Carboxybutyl)-2-(2-phenylaminovinyl)-benzothiazol-3-ium bromide (**7cii**)

Yield: 42%. M.p. 210–211 °C. ^{1}H NMR (400.13 MHz, DMSO-d_6) δ (ppm): 1.65 (2H, qui, $J = 7.4$ Hz, 3-N$(CH_2)_2CH_2$), 1.81 (2H, qui, $J = 7.4$ Hz, 3-NCH_2CH_2), 2.31 (2H, t, $J = 7.3$ Hz, CH_2COOH), 4.42 (2H, t, $J = 7.3$ Hz, 3-NCH_2), 6.45 (1H, d, $J = 12.0$ Hz, 1′-C*H*), 7.21 (1H, t, $J = 6.8$ Hz, 4″-C*H*), 7.42–7.54 (5H, m, 6-C*H*, 2″-C*H*, 3″-C*H*, 5″-C*H*, 6″-C*H*), 7.64 (1H, t, $J = 7.3$ Hz, 5-C*H*), 7.94 (1H, d, $J = 8.4$ Hz, 4-C*H*), 8.13 (1H, d, $J = 7.4$ Hz, 7-C*H*), 8.66 (1H, t, $J = 12.5$ Hz, 2′-C*H*), 11.65 (1H, d, $J = 13.1$ Hz, 2′-N*H*). ^{13}C NMR (100.62 MHz, DMSO-d_6) δ (ppm): 21.6 (3-N$(CH_2)_2CH_2$), 26.7 (3-NCH_2CH_2), 33.1 (CH_2COOH), 46.6 (3-NCH_2), 89.8 (1′-*C*H), 114.3 (4-*C*H), 117.3 (2″-*C*H, 6″-*C*H), 123.3 (7-*C*H), 125.0 (4″-*C*H), 125.1 (7a-*C*), 126.0 (6-*C*H), 128.1 (5-*C*H), 129.7 (3″-*C*H, 5″-*C*H), 138.9 (1″-*C*), 140.5 (3a-*C*), 149.8 (2′-*C*H), 168.9 (2-*C*), 174.0 (*C*O). IR (KBr) ν (cm^{-1}): 3097, 2954, 1723 (C=O), 1635 (C=C), 1587 (C=C), 1530 (C=C), 1497, 1294, 1245, 751. Vis (ethanol): 419 nm. HRMS (FAB, 3-NBA) $C_{20}H_{21}N_2O_2S$: Calcd.: 353.1324; Found: 353.1307.

3.6.8. 3-(10-Carboxydecyl)-2-(2-phenylaminovinyl)-benzothiazol-3-ium bromide (**7dii**)

Yield: 21%. M.p. 163–165 °C. ^{1}H NMR (400.13 MHz, DMSO-d_6) δ (ppm): 1.20–1.26 (8H, m, CH_2), 1.29–1.35 (2H, m, CH_2), 1.40–1.49 (4H, m, CH_2), 1.77 (2H, qui,

$J = 7.0$ Hz, 3-NCH$_2$CH_2), 2.17 (2H, t, $J = 7.3$ Hz, CH_2COOH), 4.40 (2H, t, $J = 7.3$ Hz, 3-NCH_2), 6.38 (1H, d, $J = 12.0$ Hz, 1′-C*H*), 7.20 (1H, t, $J = 6.3$ Hz, 4″-C*H*), 7.43–7.48 (4H, m, 2″-C*H*, 3″-C*H*, 5″-C*H*, 6″-C*H*), 7.52 (1H, t, $J = 7.6$ Hz, 6-C*H*), 7.65 (1H, t, $J = 7.7$ Hz, 5-C*H*), 7.94 (1H, d, $J = 8.5$Hz, 4-C*H*), 8.14 (1H, d, $J = 8.0$ Hz, 7-C*H*), 8.67 (1H, d, $J = 12.0$ Hz, 2′-C*H*), 11.63 (1H, s, 2′-N*H*). ^{13}C NMR (100.62 MHz, DMSO-d_6) δ (ppm): 24.4 (3-N(CH_2)$_8$CH$_2$), 26.0 (3-NCH$_2$CH_2), 27.2 (CH_2), 28.4 (CH_2), 28.6 (CH_2), 28.6 (CH_2), 28.7 (CH_2), 28.8 (CH_2), 33.6 (CH_2COOH), 46.9 (3-NCH_2), 89.8 (1′-C*H*), 114.3 (4-C*H*), 117.2 (2″-C*H*, 6″-C*H*), 123.3 (7-C*H*), 125.0 (4″-C*H*), 125.1 (7a-C), 126.0 (6-C*H*), 128.1 (5-C*H*), 129.7 (3″-C*H*, 5″-C*H*), 138.9 (1″-C), 140.5 (3a-C), 149.7 (2′-C*H*), 168.8 (2-C), 174.4 (C*O*). IR (KBr) ν (cm^{-1}): 3083, 2925, 2854, 1725 (C=O), 1638 (C=C), 1588 (C=C), 1531 (C=C), 1499, 1318, 1243, 752. Vis (ethanol): 419 nm. HRMS (FAB, 3-NBA) $C_{26}H_{33}N_2O_2S$: Calcd.: 437.2263; Found: 437.2242.

3.7. Synthesis of symmetric thiacarbocyanine dyes **8** and **9**

3.7.1. 3-(10-Carboxydecyl)-2-{3-[3-(10-carboxydecyl)-3H-benzothiazol-2-ylidene]propenyl}benzothiazol-3-ium inner salt (**8dii**)

A solution of 1.45 g (3.50 mmol) of 3-(10-carboxydecyl)-2-methylbenzothiazol-3-ium bromide (**3dii**), 1.07 g (1.20 ml, 7.22 mmol) of triethyl orthoformate and 13 ml of dry pyridine was refluxed for 18 h. After cooling to room temperature, diethyl ether was added and the resulting mixture refrigerated to allow complete precipitation. The crystalline product obtained was collected by filtration under reduced pressure, washed with diethyl ether and recrystallized from dry acetonitrile.

Yield: 65%. M.p. 136–139 °C. ^{1}H NMR (400.13 MHz, DMSO-d_6) δ (ppm): 1.21–1.33 (20H, m, CH_2), 1.40–1.46 (8H, m, CH_2), 1.74 (4H, t, $J = 7.0$ Hz, 3-NCH$_2$CH_2, 3″-NCH$_2$CH_2), 2.17 (4H, t, $J = 7.3$ Hz, CH_2COO), 4.33 (4H, t, $J = 7.1$ Hz, 3-NCH_2, 3″-NCH_2), 6.61 (2H, d, $J = 12.5$ Hz, 1′-C*H*, 3′-C*H*), 7.42 (2H, t, $J = 7.6$ Hz, 6-C*H*, 6″-C*H*), 7.58 (2H, t, $J = 7.6$ Hz, 5-C*H*, 5″-C*H*), 7.71–7.80 (3H, m, 4-C*H*, 2′-C*H*, 4″-C*H*), 8.00 (2H, d, $J = 7.9$ Hz, 7-C*H*, 7″-C*H*). ^{13}C NMR (62.90 MHz, DMSO-d_6) δ (ppm): 24.5 (3-N(CH$_2$)$_8$CH$_2$, 3″-N(CH$_2$)$_8$CH$_2$), 26.0 (3-N(CH$_2$)$_2$CH$_2$, 3″-N(CH$_2$)$_2$CH$_2$), 27.4 (3-NCH$_2$CH$_2$, 3″-NCH$_2$CH$_2$), 28.6 (CH$_2$), 28.8 (CH$_2$), 28.8 (CH$_2$), 28.8 (CH$_2$), 28.9 (CH$_2$), 33.7 (CH$_2$COO), 46.2 (3-NCH$_2$, 3″-NCH$_2$), 98.9 (1′-CH, 3′-CH), 113.7 (4-CH, 4″-CH), 123.1 (7-CH, 7″-CH), 125.1 (7a-C, 7a″-C), 125.2 (6-CH, 6″-CH), 128.1 (5-CH, 5″-CH), 141.3 (3a-C, 3a″-C), 146.6 (2′-CH), 164.6 (2-C, 2″-C), 174.5 (CO). IR (KBr) ν (cm^{-1}): 3045, 2922, 2852, 1716 (C=O), 1633 (C=C), 1554 (C=C), 1486, 1420, 1214, 1174, 783. Vis (ethanol): 562 nm. HRMS (FAB, 3-NBA) $C_{39}H_{53}N_2O_4S_2$: Calcd.: 677.3447; Found: 677.3455.

The symmetric thiacarbocyanine dyes **8a–c** and **9a–d** were prepared using a similar procedure (2–18 h), except for the methoxycarbonylalkyl dyes **9a–d** where a temperature of 80 °C was used instead of refluxed pyridine. The spectroscopic characterization of **8a–c** and **9a** has already been previously described [7,15].

The dye can readily undergo counter-ion exchange to hydrogen sulfate or iodide by dissolution in a minimum amount of methanol or acetonitrile, followed by addition of 5% (v/v) aqueous H_2SO_4 or 14% (w/v) aqueous KI, respectively. The solution or suspension obtained was heated until reflux and then cooled to room temperature and refrigerated overnight. The resulting crystalline product was collected by filtration under reduced pressure, washed with diethyl ether and recrystallized from dry acetonitrile or dry methanol.

The methoxycarbonylalkylthiacarbocyanines **9a–d** were also prepared by refluxing a solution of the corresponding carboxyalkylthiacarbocyanines **8a–d** in 5% (v/v) methanolic H_2SO_4 for at least 48 h (method C) to ensure complete esterification. The reaction mixture was then cooled to room temperature and the solvent removed by evaporation until complete precipitation of the product. The later was collected by filtration under reduced pressure, washed with diethyl ether and recrystallized from dry acetonitrile or dry methanol. Compounds **9a–d** prepared by this procedure were isolated in overall yields similar to those of the previously described method.

3.7.2. 3-(2-Methoxycarbonylethyl)-2-{3-[3-(2-methoxycarbonylethyl)-3H-benzothiazol-2-ylidene]propenyl}benzothiazol-3-ium bromide (**9bii**)

Yield: 35%. M.p. 198–200 °C. ^{1}H NMR (250.13 MHz, DMSO-d_6) δ (ppm): 2.88 (4H, t, $J = 7.3$ Hz, CH_2COOCH$_3$), 3.61 (6H, s, COOCH_3), 4.55 (4H, t, $J = 7.0$ Hz, 3-NCH_2, 3″-NCH_2), 6.61 (2H, d, $J = 12.7$ Hz, 1′-C*H*, 3′-C*H*), 7.37 (2H, t, $J = 7.6$ Hz, 6-C*H*, 6″-C*H*), 7.54 (2H, t, $J = 8.0$ Hz, 5-C*H*, 5″-C*H*), 7.68–7.78 (3H, m, 4-C*H*, 2′-C*H*, 4″-C*H*), 7.99 (2H, d, $J = 7.8$ Hz, 7-C*H*, 7″-C*H*). ^{13}C NMR (62.90 MHz, DMSO-d_6) δ (ppm): 31.3 (CH$_2$COOCH$_3$), 42.0 (3-NCH$_2$, 3″-NCH$_2$), 51.8 (COOCH$_3$), 99.2 (1′-CH, 3′-CH), 113.7 (4-CH, 4″-CH), 123.1 (7-CH, 7″-CH), 124.9 (7a-C, 7a″-C), 125.2 (6-CH, 6″-CH), 128.0 (5-CH, 5″-CH), 140.9 (3a-C, 3a″-C), 146.7 (2′-CH), 164.8 (2-C, 2″-C), 170.6 (CO). IR (KBr) ν (cm^{-1}): 3005, 2945, 1732 (C=O), 1555 (C=C), 1462, 1418, 1281, 1200, 1157, 1017, 758. Vis (ethanol): 563 nm. HRMS (FAB, 3-NBA) $C_{25}H_{25}N_2O_4S_2$: Calcd.: 481.1256; Found: 481.1253.

3.7.3. 3-(4-Methoxycarbonylbutyl)-2-{3-[3-(4-methoxycarbonylbutyl)-3H-benzothiazol-2-ylidene]propenyl}-benzothiazol-3-ium iodide (**9ci**)

Yield: 10%. M.p. 134–135 °C. ^{1}H NMR (400.13 MHz, DMSO-d_6) 1.64–1.80 (8H, m, CH_2), 2.41 (4H, t, $J = 7.3$ Hz, CH_2COOCH$_3$), 3.58 (6H, s, COOCH_3), 4.36 (4H, t, $J = 7.0$ Hz, 3-NCH_2, 3″-NCH_2), 6.62 (2H, d, $J = 12.6$ Hz, 1′-C*H*, 3′-C*H*), 7.42 (2H, t, $J = 7.5$ Hz, 6-C*H*, 6″-C*H*), 7.58 (2H, t, $J = 7.6$ Hz, 5-C*H*, 5″-C*H*), 7.72–7.81 (3H, m, 4-C*H*, 2′-C*H*, 4″-C*H*), 8.00 (2H, d, $J = 7.8$ Hz, 7-C*H*, 7″-C*H*). ^{13}C NMR (62.90 MHz, DMSO-d_6) δ (ppm): 21.6 (3-N(CH$_2$)$_2$CH$_2$, 3″-N(CH$_2$)$_2$CH$_2$), 26.7 (3-NCH$_2$CH$_2$, 3″-NCH$_2$CH$_2$), 32.7 (CH$_2$COOCH$_3$), 45.8 (3-NCH$_2$, 3″-NCH$_2$),

51.3 (COO*C*H$_3$), 98.7 (1′-*C*H, 3′-*C*H), 113.5 (4-*C*H, 4″-*C*H), 123.0 (7-*C*H, 7″-*C*H), 124.9 (7a-*C*, 7a″-*C*), 125.1 (6-*C*H, 6″-*C*H), 128.0 (5-*C*H, 5″-*C*H), 141.1 (3a-*C*, 3a″-*C*), 146.5 (2′-*C*H), 164.5 (2-*C*, 2″-*C*), 173.0 (*C*O). IR (KBr) ν (cm^{-1}): 3011, 2944, 1730 (C=O), 1591 (C=C), 1553 (C=C), 1462, 1421, 1217, 1163, 1020, 837, 750. Vis (ethanol): 562 nm. HRMS (FAB, 3-NBA) $C_{29}H_{33}N_2O_4S_2$: Calcd.: 537.1882; Found: 537.1891.

*3.7.4. 3-(10-Methoxycarbonyldecyl)-2-{3-[3-(10-methoxycarbonyldecyl)-3H-benzothiazol-2-ylidene] propenyl}benzothiazol-3-ium iodide (**9di**)*

Yield: 7%. M.p. 95–96° C. ^{1}H NMR (250.13 MHz, DMSO-d_6) δ (ppm): 1.20–1.30 (24H, m, CH_2), 1.40–1.49 (4H, m, CH_2), 1.73 (4H, m, 3-NCH$_2$CH_2, 3″-NCH$_2$CH_2), 2.25 (4H, t, $J = 7.2$ Hz, CH_2COOCH$_3$), 3.55 (6H, s, COOCH_3), 4.33 (4H, t, $J = 7.0$ Hz, 3-NCH_2, 3″-NCH_2), 6.62 (2H, d, $J = 12.7$ Hz, 1′-C*H*, 3′-C*H*), 7.41 (2H, t, $J = 8.0$ Hz, 6-C*H*, 6″-C*H*), 7.56 (2H, t, $J = 7.8$ Hz, 5-C*H*, 5″-C*H*), 7.72–7.79 (3H, m, 4-C*H*, 2′-C*H*, 4″-C*H*), 7.99 (2H, d, $J = 7.6$ Hz, 7-C*H*, 7″-C*H*). ^{13}C NMR (62.90 MHz, DMSO-d_6) δ (ppm): 24.4 (3-N(CH$_2$)$_8$*C*H$_2$ 3″-N(CH$_2$)$_8$*C*H$_2$), 26.0 (*C*H$_2$), 27.3 (*C*H$_2$), 28.1 (*C*H$_2$), 28.4 (*C*H$_2$), 28.7 (*C*H$_2$), 28.8 (*C*H$_2$), 28.8 (*C*H$_2$), 33.2 (*C*H$_2$COOCH$_3$), 46.2 (3-N*C*H$_2$, 3″-N*C*H$_2$), 51.1 (COO*C*H$_3$), 98.8 (1′-*C*H, 3′-*C*H), 113.6 (4-*C*H, 4″-*C*H), 123.1 (7-*C*H, 7″-*C*H), 125.0 (7a-*C*, 7a″-*C*), 125.2 (6-*C*H, 6″-*C*H), 128.1 (5-*C*H, 5″-*C*H), 141.2 (3a-*C*, 3a″-*C*), 146.6 (2′-*C*H), 164.5 (2-*C*, 2″-*C*), 173.3 (*C*O). IR (KBr) ν (cm^{-1}): 3003, 2924, 2853, 1736 (C=O), 1551 (C=C), 1462, 1422, 1219, 1017, 750. Vis (ethanol): 562 nm. HRMS (FAB, 3-NBA) $C_{41}H_{57}N_2O_4S_2$: Calcd.: 705.3760; Found: 705.3774.

*3.8. Synthesis of asymmetric thiacarbocyanine dyes **10** and **11***

*3.8.1. 3-Carboxymethyl-2-[3-(3-ethyl-3H-benzothiazol-2-ylidene)propenyl]benzothiazol-3-ium inner salt (**10aiii**). Typical procedure (method A)*

A solution of 0.41 g (1.42 mmol) of 3-carboxymethyl-2-methylbenzothiazol-3-ium bromide (**3a*ii***) and 0.60 g (1.36 mmol) of the acetanilide derivative (**5a**) in 10 ml of dry pyridine was refluxed for 1 h. After cooling to room temperature, diethyl ether was added and the resulting mixture refrigerated to allow complete precipitation. The crystalline product obtained was collected by filtration under reduced pressure, washed with diethyl ether and recrystallized from dry acetonitrile. Yield: 76%. M.p.189–190 °C. ^{1}H NMR (400.13 MHz, DMSO-d_6) δ (ppm): 1.31 (3H, t, $J = 6.9$ Hz, CH$_2$CH_3), 4.37 (2H, q, $J = 6.9$ Hz, 3″-NCH_2CH$_3$), 5.04 (2H, s, 3-NCH_2COO), 6.44 (1H, d, $J = 12.6$ Hz, 1′-C*H*), 6.62 (1H, d, $J = 12.4$ Hz, 3′-C*H*), 7.38 (1H, t, $J = 7.3$ Hz, 6-C*H*), 7.42 (1H, t, $J = 7.7$ Hz, 6″-C*H*), 7.52 (1H, t, $J = 7.9$ Hz, 5-C*H*), 7.57 (1H, t, $J = 7.6$ Hz, 5″-C*H*), 7.67 (1H, d, $J = 8.0$ Hz, 4-C*H*), 7.73–7.79 (2H, m, 2′-C*H*, 4″-C*H*), 7.96 (1H, d, $J = 7.8$ Hz, 7-C*H*), 8.00 (1H, d, $J = 7.9$ Hz, 7″-C*H*). ^{13}C NMR (100.60 MHz, DMSO-d_6) δ (ppm): 12.6 (3″-NCH$_2$*C*H$_3$), 41.5 (3″-N*C*H$_2$CH$_3$), 47.8 (3-N*C*H$_2$COO), 98.6 (1′-*C*H), 99.4 (3′-*C*H), 113.2 (4-*C*H), 113.5 (4″-*C*H), 122.8 (7-*C*H), 123.1 (7″-*C*H), 124.4 (7a-*C*), 125.3 (6-*C*H), 125.3 (6″-*C*H, 7a″-*C*), 127.9 (5-*C*H), 128.1 (5″-*C*H), 140.7 (3a″-*C*), 141.5 (3a-*C*), 146.5 (2′-*C*H), 164.6 (2-*C*), 164.8 (2″-*C*), 167.2 (*C*O). IR (KBr) ν (cm^{-1}): 1729 (C=O), 1631 (C=C), 1554 (C=C), 1463, 1422, 1218, 1195, 1159, 846, 750. Vis (ethanol): 561 nm. HRMS (FAB, 3-NBA) $C_{21}H_{19}N_2O_2S_2$: Calcd.: 395.0888; Found: 395.0892.

The asymmetric thiacarbocyanine dyes **10b–d** were prepared using a similar procedure (2–18 h). The methoxycarbonylalkyl dyes **11a–d** were prepared from *N*-methoxycarbonylalkylbenzothiazolium salts **4a–d**, at 80 °C was used as described above.

Alternatively, dyes **10a–d** were prepared by condensation of the aniline derivatives **6a–d** or **7a–d** with the benzothiazolium salts **3a–d** or **2a–d** respectively, and dyes **11a–d** synthesized from **6a–d** and **4a–d** (method B), using the same experimental procedure described for method A. For the preparation of **11a–d** by method B a reaction temperature of 80 °C was used.

N-Methoxycarbonylalkylthiacarbocyanines **11a–d** were also prepared by Fisher's esterification of the corresponding acid dyes **10a–d** as described before for the preparation of esters **9a–d** (method C).

*3.8.2. 3-(2-Carboxyethyl)-2-[3-(3-propyl-3H-benzothiazol-2-ylidene)propenyl]benzothiazol-3-ium inner salt (**10biii**)*

Yield: 96%. M.p. 225–228 °C. ^{1}H NMR (400.13 MHz, DMSO-d_6) δ (ppm): 0.99 (3H, t, $J = 7.3$ Hz, CH$_2$CH_3), 1.71–1.80 (2H, m, CH_2CH$_3$), 2.78 (2H, t, $J = 7.3$ Hz, CH_2COO), 4.29 (2H, t, $J = 7.0$ Hz, 3″-NCH_2), 4.49 (2H, t, $J = 6.8$ Hz, 3-NCH_2), 6.59 (1H, d, $J = 12.7$ Hz, 1′-C*H*), 6.64 (1H, d, $J = 12.7$ Hz, 3′-C*H*), 7.32–7.42 (2H, m, 6-C*H*, 6″-C*H*), 7.50–7.56 (2H, m, 5-C*H*, 5″-C*H*), 7.69–7.79 (3H, m, 4-C*H*, 2′-C*H*, 4″-C*H*), 7.93 (1H, d, $J = 7.9$ Hz, 7-C*H*), 7.98 (1H, d, $J = 8.0$ Hz, 7″-C*H*). ^{13}C NMR (100.62 MHz, DMSO-d_6) δ (ppm): 10.8 (CH$_2$*C*H$_3$), 20.8 (*C*H$_2$CH$_3$), 31.6 (*C*H$_2$COO), 42.0 (3-N*C*H$_2$), 47.5 (3″-N*C*H$_2$), 98.6 (1′-*C*H), 99.3 (3′-*C*H), 113.5 (4-*C*H), 113.7 (4″-*C*H), 122.9 (7-*C*H), 123.0 (7″-*C*H), 124.8 (7a-*C*), 124.9 (7a″-*C*), 125.0 (6-*C*H), 125.2 (6″-*C*H), 127.9 (5-*C*H), 128.0 (5″-*C*H), 140.9 (3a-*C*), 141.2 (3a″-*C*), 146.4 (2′-*C*H), 164.2 (2-*C*), 164.8 (2″-*C*), 171.5 (*C*O). IR (KBr) ν (cm^{-1}): 3018, 2963, 2934, 2873, 1722 (C=O), 1591 (C=C), 1556 (C=C), 1463, 1425, 1324, 1210, 826, 750. Vis (ethanol): 563 nm. HRMS (FAB, 3-NBA) $C_{23}H_{23}N_2O_2S_2$: Calcd.: 423.1201; Found: 423.1212.

*3.8.3. 3-(4-Carboxybutyl)-2-[3-(3-pentyl-3H-benzothiazol-2-ylidene)propenyl]benzothiazol-3-ium inner salt (**10ciii**)*

Yield: 83%. M.p. 153–155 °C. ^{1}H NMR (250.13 MHz, DMSO-d_6) δ (ppm): 0.87 (3H, t, $J = 7.0$ Hz, CH$_2$CH_3), 1.28–1.45 (4H, m, CH_2) 1.58–1.81 (6H, m, CH_2), 2.30 (2H, t, $J = 7.1$ Hz, CH_2COO), 4.26–4.39 (4H, m, 3-NCH_2, 3″-NCH_2), 6.62 (1H, d, $J = 11.8$ Hz, 1′-C*H*), 6.66 (1H, d, $J = 11.7$ Hz, 3′-C*H*), 7.34–7.40 (2H, m, 6-C*H*, 6″-C*H*), 7.51–7.57 (2H, m, 5-C*H*, 5″-C*H*), 7.67–7.77 (3H, m,

4-C*H*, 2′-C*H*, 4″-C*H*), 7.97–8.07 (2H, m, 7-C*H*, 7″-C*H*). ^{13}C NMR (62.90 MHz, DMSO-d_6) δ (ppm): 13.9 (CH_2CH_3). 21.6 (CH_2), 22.0 (CH_2), 26.9 (CH_2), 27.2 (CH_2), 28.2 (CH_2), 33.2 (CH_2COO), 46.0 (3-NCH_2), 46.2 (3″-NCH_2), 98.8 (1′-*C*H, 3′-*C*H), 113.6 (4-*C*H, 4″-*C*H), 123.1 (7-*C*H, 7″-*C*H), 125.0 (7a-*C*, 7a″-*C*), 125.2 (6-*C*H, 6″-*C*H), 128.1 (5-*C*H, 5″-*C*H), 141.2 (3a-*C*, 3a″-*C*), 146.6 (2′-*C*H), 164.5 (2-*C*, 2″-*C*), 174.2 (*C*O). IR (KBr) ν (cm^{-1}): 2953, 2930, 1726 (C=O), 1555 (C=C), 1462, 1424, 1325, 1217, 1192, 1163, 750. Vis (ethanol): 563 nm. HRMS (FAB, 3-NBA) $C_{27}H_{31}N_2O_2S_2$: Calcd.: 479.1827; Found: 479.1847.

*3.8.4. 3-(10-Carboxydecyl)-2-[3-(3-undecyl-3H-benzothiazol-2-ylidene)propenyl]benzothiazol-3-ium inner salt (**10diii**)*

Yield: 76%. M.p. 108–109 °C. ^{1}H NMR (250.13 MHz, DMSO-d_6) δ (ppm): 0.80 (3H, t, $J = 7.0$ Hz, CH_2CH_3), 1.14–1.31 (26H, m, CH_2), 1.36–1.48 (4H, m, CH_2), 1.66–1.77 (4H, m, CH_2), 2.16 (2H, t, $J = 7.1$ Hz, CH_2COO), 4.26–4.37 (4H, m, 3-NCH_2, 3″-NCH_2), 6.64 (2H, d, $J = 12.2$ Hz, 1′-C*H*, 3′-C*H*), 7.38 (2H, t, $J = 7.7$ Hz, 6-C*H*, 6″-C*H*), 7.55 (2H, t, $J = 7.8$ Hz, 5-C*H*, 5″-C*H*), 7.69–7.79 (3H, m, 4-C*H*, 2′-C*H*, 4″-C*H*), 7.97–8.06 (2H, m, 7-C*H*, 7″-C*H*). ^{13}C NMR (62.90 MHz, DMSO-d_6) δ (ppm): 14.0 (CH_2CH_3), 22.1 (CH_2), 24.5 (CH_2), 26.0 (CH_2), 27.4 (CH_2), 28.4 (CH_2), 28.6 (CH_2), 28.8 (CH_2), 29.0 (CH_2), 29.0 (CH_2), 31.3 (CH_2), 33.7 (CH_2COO), 46.2 (3-NCH_2, 3″-NCH_2), 98.9 (1′-*C*H, 3′-*C*H), 113.6 (4-*C*H, 4″-*C*H), 123.1 (7-*C*H, 7″-*C*H), 125.0 (7a-*C*, 7a″-*C*), 125.2 (6-*C*H, 6″-*C*H), 128.1 (5-*C*H, 5″-*C*H), 141.2 (3a-*C*, 3a″-*C*), 146.6 (2′-*C*H), 164.5 (2-*C*, 2″-*C*), 174.8 (*C*O). IR (KBr) ν (cm^{-1}): 2922, 2853, 1724 (C=O), 1551 (C=C), 1462, 1422, 1323, 1213, 1159. Vis (ethanol): 563 nm. HRMS (FAB, 3-NBA) $C_{39}H_{55}N_2O_2S_2$: Calcd.: 647.3705; Found: 647.3699.

*3.8.5. 2-[3-(3-Ethyl-3H-benzothiazol-2-ylidene)propenyl]-3-methoxycarbonylmethylbenzothiazol-3-ium iodide (**11ai**)*

Yield: 53%. M.p. 212–214 °C. ^{1}H NMR (400.13 MHz, DMSO-d_6) δ (ppm): 1.35 (3H, t, $J = 6.9$ Hz, 3″-NCH$_2$CH_3), 3.78 (3H, s, COOCH_3), 4.44 (2H, q, $J = 6.7$ Hz, 3″-NCH_2CH$_3$), 5.34 (2H, s, 3-NCH_2COOCH$_3$), 6.46 (1H, d, $J = 12.4$ Hz, 1′-C*H*), 6.66 (1H, d, $J = 13.1$ Hz, 3′-C*H*), 7.39 (1H, t, $J = 7.6$ Hz, 6-C*H*), 7.48 (1H, t, $J = 7.6$ Hz, 6″-C*H*), 7.52 (1H, t, $J = 7.6$ Hz, 5-C*H*), 7.62 (1H, t, $J = 8.0$ Hz, 5″-C*H*), 7.67 (1H, d, $J = 8.4$ Hz, 4-C*H*), 7.81 (1H, t, $J = 12.8$ Hz, 2′-C*H*), 7.85 (1H, d, $J = 7.8$ Hz, 4″-C*H*), 7.98 (1H, d, $J = 7.8$ Hz, 7-C*H*), 8.07 (1H, d, $J = 8.0$ Hz, 7″-C*H*). ^{13}C NMR (100.62 MHz, DMSO-d_6) δ (ppm): 12.6 (3″-CH$_2$CH_3), 41.7 (3″-NCH_2CH$_3$), 46.7 (3-NCH_2COOCH$_3$), 52.8 (COOCH_3), 97.9 (1′-*C*H), 100.1 (3′-*C*H), 112.8 (4-*C*H), 113.7 (4″-*C*H), 122.9 (7-*C*H), 123.2 (7″-*C*H), 124.0 (7a-*C*), 124.9 (6-*C*H), 125.4 (7a″-*C*), 125.5 (6″-*C*H), 127.8 (5-*C*H), 128.2 (5″-*C*H), 140.6 (3a″-*C*), 141.1 (3a-*C*), 146.6 (2′-*C*H), 164.0 (2-*C*), 165.4 (2″-*C*), 166.9 (*C*O). IR (KBr) ν (cm^{-1}): 1738 (C=O), 1555 (C=C), 1466, 1424, 1323, 1267, 1225, 1202, 752. Vis (ethanol): 561 nm. HRMS (FAB, 3-NBA) $C_{22}H_{21}N_2O_2S_2$: Calcd.: 409.1044; Found: 409.1037.

*3.8.6. 3-(2-Methoxycarbonylethyl)-2-[3-(3-propyl-3H-benzothiazol-2-ylidene)propenyl]benzothiazol-3-ium iodide (**11bi**)*

Yield: 93%. M.p. 255–256 °C. ^{1}H NMR (400.13 MHz, DMSO-d_6) δ (ppm): 1.00 (3H, t, $J = 7.3$ Hz, CH$_2$CH_3), 1.79 (2H, sxt, $J = 7.1$ Hz, CH_2CH$_3$), 2.89 (2H, t, $J = 7.0$ Hz, CH_2COOCH$_3$), 3.62 (3H, s, COOCH_3), 4.25 (2H, t, $J = 7.0$ Hz, 3″-NCH_2), 4.56 (2H, t, $J = 7.0$ Hz, 3-NCH_2), 6.61 (1H, d, $J = 12.4$ Hz, 1′-C*H*), 6.66 (1H, d, $J = 12.4$ Hz, 3′-C*H*), 7.38–7.44 (2H, m, 6-C*H*, 6″-C*H*), 7.54–7.59 (2H, m, 5-C*H*, 5″-C*H*), 7.75–7.82 (3H, m, 4-C*H*, 2′-C*H*, 4″-C*H*), 7.97 (1H, d, $J = 7.9$ Hz, 7-C*H*), 8.02 (1H, d, $J = 7.8$ Hz, 7″-C*H*). ^{13}C NMR (100.62 MHz, DMSO-d_6) δ (ppm): 10.8 (CH_2CH_3), 20.7 (CH_2CH_3), 31.2 (CH_2COOCH$_3$), 41.8 (3-NCH_2), 47.5 (3″-NCH_2), 51.7 (COOCH_3), 98.5 (1′-*C*H), 99.4 (3′-*C*H), 113.4 (4-*C*H), 113.7 (4″-*C*H), 122.9 (7-*C*H), 123.0 (7″-*C*H), 124.7 (7a-*C*), 125.0 (6-*C*H), 125.1 (7a″-*C*), 125.3 (6″-*C*H), 127.9 (5-*C*H), 128.0 (5″-*C*H), 140.9 (3a-*C*), 141.2 (3a″-*C*), 146.6 (2′-*C*H), 164.2 (2-*C*), 165.0 (2″-*C*), 170.4 (*C*O). IR (KBr) ν (cm^{-1}): 2961, 1723 (C=O), 1549 (C=C), 1460, 1414, 1368, 1202, 1157, 1013, 825, 752. Vis (ethanol): 564 nm. HRMS (FAB, 3-NBA) $C_{24}H_{25}N_2O_2S_2$: Calcd.: 437.1357; Found: 437.1350.

*3.8.7. 3-(4-Methoxycarbonylbutyl)-2-[3-(3-pentyl-3H-benzothiazol-2-ylidene)propenyl]benzothiazol-3-ium iodide (**11ci**)*

Yield: 52%. M.p. 77–78 °C. ^{1}H NMR (400.13 MHz, DMSO-d_6) δ (ppm): 0.87 (3H, t, $J = 7.0$ Hz, CH$_2$CH_3), 1.32–1.43 (4H, m, CH_2), 1.67–1.79 (6H, m, CH_2), 2.41 (2H, t, $J = 7.2$ Hz, CH_2COOCH$_3$), 3.57 (3H, s, COOCH_3), 4.30–4.37 (4H, m, 3-NCH_2, 3″-NCH_2), 6.62 (1H, d, $J = 13.6$ Hz, 1′-C*H*), 6.66 (1H, d, $J = 14.0$ Hz, 3′-C*H*), 7.39 (2H, t, $J = 7.4$ Hz, 6-C*H*, 6″-C*H*), 7.55 (2H, t, $J = 7.5$ Hz, 5-C*H*, 5″-C*H*), 7.72–7.78 (3H, m, 4-C*H*, 2′-C*H*, 4″-C*H*), 7.99 (2H, d, $J = 7.7$ Hz, 7-C*H*, 7″-C*H*). ^{13}C NMR (100.62 MHz, DMSO-d_6) δ (ppm): 13.7 (CH_2CH_3), 21.4 (3-N(CH$_2$)$_2$CH$_2$), 21.8 (CH_2CH_3), 26.6 (3-NCH$_2$CH$_2$), 27.0 (3″-N(CH$_2$)$_2$CH$_2$), 28.1 (3″-NCH$_2$CH$_2$), 32.7 (CH_2COOCH$_3$), 45.7 (3-NCH_2), 46.1 (3″-NCH_2), 51.2 (COOCH_3), 98.7 (1′-*C*H, 3′-*C*H), 113.5 (4-*C*H, 4″-*C*H), 123.0 (7-*C*H, 7″-*C*H), 124.9 (7a-*C*, 7a″-*C*), 125.0 (6-*C*H, 6″-*C*H), 127.9 (5-*C*H, 5″-*C*H), 141.1 (3a-*C*, 3a″-*C*), 146.5 (2′-*C*H), 164.4 (2-*C*, 2″-*C*), 172.9 (*C*O). IR (KBr) ν (cm^{-1}): 2928, 1726 (C=O), 1549 (C=C), 1462, 1422, 1215, 752. Vis (ethanol): 564 nm. HRMS (FAB, 3-NBA) $C_{28}H_{33}N_2O_2S_2$: Calcd.: 493.1983; Found: 493.1975.

*3.8.8. 3-(10-Methoxycarbonyldecyl)-2-[3-(3-undecyl-3H-benzothiazol-2-ylidene)propenyl]benzothiazol-3-ium iodide (**11di**)*

Yield: 86%. M.p. 128–130 °C. ^{1}H NMR (250.13 MHz, DMSO-d_6) δ (ppm): 0.80 (3H, t, $J = 6.4$ Hz, CH$_2$CH_3), 1.20–1.45 (30H, m, CH_2), 1.66–1.77 (4H, m, CH_2), 2.24 (2H, t, $J = 7.2$ Hz, CH_2COOCH$_3$), 3.53 (3H, s, COOCH_3), 4.26–4.34 (4H, m, 3-NCH_2, 3″-NCH_2), 6.58 (2H, d, $J = 12.6$ Hz, 1′-C*H*, 3′-C*H*), 7.37 (2H, t, $J = 7.7$ Hz, 6-C*H*,

6″-C*H*), 7.53 (2H, t, $J = 7.7$ Hz, 5-C*H*, 5″-C*H*), 7.67–7.78 (3H, m, 4-C*H*, 2′-C*H*, 4″-C*H*), 7.95 (2H, d, $J = 7.8$ Hz, 7-C*H*, 7″-C*H*). ^{13}C NMR (62.90 MHz, DMSO-d_6) δ (ppm): 14.0 (CH_2CH_3), 22.2 (CH_2), 24.5 (CH_2), 26.0 (CH_2), 27.4 (CH_2), 28.5 (CH_2), 28.6 (CH_2), 28.8 (CH_2), 29.0 (CH_2), 29.1 (CH_2), 31.4 (CH_2), 33.3 (CH_2COOCH_3), 46.2 (3-NCH_2, 3″-NCH_2), 51.3 ($COOCH_3$), 98.9 (1′-*C*H, 3′-*C*H), 113.7 (4-*C*H, 4″-*C*H), 123.1 (7-*C*H, 7″-*C*H), 125.1 (7a-*C*, 7a″-*C*), 125.3 (6-*C*H, 6″-*C*H), 128.1 (5-*C*H, 5″-*C*H), 141.3 (3a-*C*, 3a″-*C*), 146.3 (2′-*C*H), 164.6 (2-*C*, 2″-*C*), 173.5 (*C*O). IR (KBr) ν (cm^{-1}): 2924, 2853, 1738 (C=O), 1551 (C=C), 1462, 1422, 1323, 1219, 1015, 748. Vis (ethanol): 564 nm. HRMS (FAB, 3-NBA) $C_{40}H_{57}N_2O_2S_2$: Calcd.: 661.3861; Found: 661.3856.

4. Conclusions

Some new mono- and dicarboxyalkylthiacarbocyanines together with their precursors have been prepared and fully spectroscopically characterized. The condensation of *N*-vinylacetanilide derivatives with heterocyclic quaternary salts (method A) was shown to be a selective method for the preparation of asymmetric *N*-carboxyalkyl-*N*′-alkylthiacarbocyanines since it avoids the formation of the undesirable corresponding symmetric dyes as it happens when vinylaniline derivatives are used instead (method B). The methyl esters of both asymmetric and symmetric dyes could readily be obtained from the ester of vinylacetanilide and/or the heterocyclic quaternary salts by method A or by refluxing a 5% v/v methanolic sulfuric acid of the corresponding carboxythiacarbocyanines (method C).

In the synthesis of asymmetric dyes it is crucial to use purified precursors since the alternative one-pot synthesis starting from 2-methylbenzothiazole (**1**) does not prevent the side formation of the unwanted corresponding symmetric dyes.

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