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Short communication

Synthesis of 4-octyl-2*H*-1,4-benzo-thiazin-3-ones

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Abstract

Synthesis, physical and analytical properties of 6-alkylacylamino-4-octyl-2*H*-1,4-benzo-thiazin-3-ones derivatives are described. These new compounds were prepared by acylation and/or alkylation of the amino group under phase transfer catalysis conditions. Acid hydrolysis of the alkylacylamino-2*H*-1,4-benzo-thiazin-3-ones afforded *N*-alkylamino-benzothiazin-3-ones. Some of these compounds were evaluated in vitro for possible bacteriostatic activity.

Keywords: 1,4-Benzothiazines; Antibacterials

1. Introduction

Chemical and pharmacological properties of phenothiazines and 1,4-benzothiazines have been widely studied since a long time [1]. In particular, some benzothiazines exhibit convincing antifungal activity [2–4] but moderate antimicrobial activity [5,6]. With the aim to investigate more accurately antibacterial properties of structurally related compounds, several 6-alkylacylamino-4-octyl-2*H*-1,4-benzothiazin-3-ones were synthesized from 2-chloro-5-nitro-aniline. Action of sodium sulfide and sulfur on this starting compound led to the 2-amino-4-nitrobenzenethiol sodium salt which was cyclized in 6-nitro-2*H*-1,4-benzothiazin-3-one by using chloroacetic acid. N-alkylation at the 4-position followed by reduction of the nitro group, led to 6-amino-4-octylbenzothiazin-3-ones. This later derivative was acylated then alkylated. Sulfuric acid hydrolysis provided the 6-alkylamino-4-octyl-2*H*-1,4-benzothiazine derivatives. Finally, some test sample compounds were tested against a lot of microorganisms including cocci, gram positive and gram-negative bacteria.

2. Chemistry

2*H*-1,4-benzothiazin derivatives can be prepared in accordance with the different synthetic pathways reported in literature [1]. Treatment of 2-chloro-5-nitroaniline (**1**), with sodium sulfide and sulfur [7] gave 2-amino-4-nitrobenzenethiol sodium salt (**2**), which was cyclized to 2*H*-1,4-benzothiazin-3-one (**3**), with chloroacetic acid. N-alkylation with octyl bromide and KOH in methanolic solution as a base [8], afforded **4**. Reduction of the nitro group by $SnCl_2$ in acidic medium [9] gave the corresponding amine e.g. the 6-amino-4-octyl-2*H*-1,4-benzothiazin-3-one (**5**). N-acylation of the amino group followed by alkylation under phase transfer catalysis conditions in basic medium [10], led to the N-alkylacyl derivatives **7a**, **7b** and **9a**, **9b**. N-alkylation was performed in boiling toluene in the presence of either sodium hydroxide or potassium carbonate in excess and 0.5×10^{-3} mol of tetrabutylammonium bromide as catalyst. Acidic hydrolysis of **9a**

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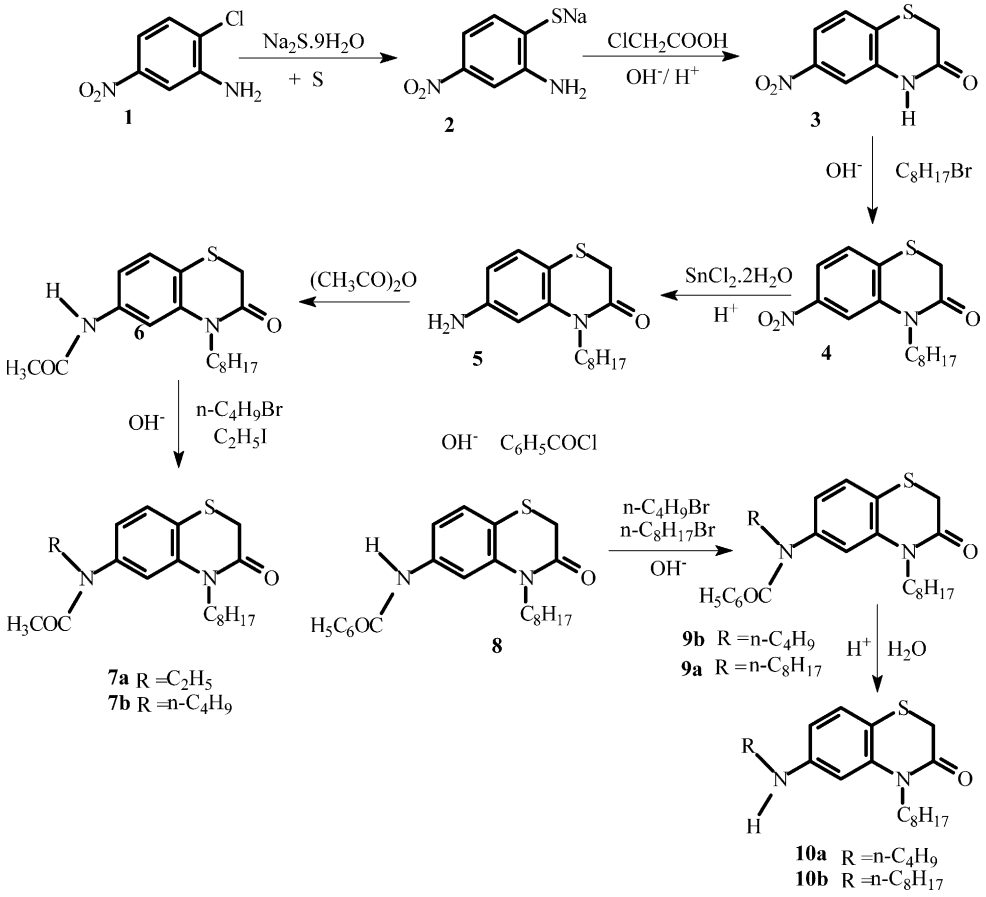

Fig. 1. 2*H*-1,4-benzothiazin-3-one derivatives: synthetic pathways.

and **9b** afforded the 6-alkylamino-4-octyl-2*H*-1,4-benzothiazin-3-one derivatives **10a** and **10b**. Synthetic pathway is portrayed in Fig. 1.

3. Biological activity

The minimal inhibitory concentration (MIC) against six different microorganisms was estimated in vitro for compounds **4**–**6**, **7a**, **7b**, **8**, **9a**, **9b**, **10a** and **10b**. The following strains were used: *Micrococcus flavus* (DAUFPE 323), *Staphylococcus aureus* (IC 06), *Salmonella enteritidis* (DAUFPE 415), *Bacillus cereus* (DAUFPE 11), *Escherichia coli* (IC 02) and *Proteus vulgaris* (IC 03). *M. flavus* DAUFPE 323, *S. enteriditis* DAUFPE 415 and *B. cereus* DAUFPE 11 strains came from the collection of the Department of Antibiotics (UFP-Br). *S. aureus* IC 06, *E. coli* IC 02 and *P. vulgaris* IC 02 strains are wild strains isolated from contaminated foods.

Results are collected in the Table 1.

4. Experimental protocols

4.1. Biology

Bacterial strains were cultivated on Mueller–Hinton agar medium. Inocula were prepared from 18 h old subcultures at 37 °C in the same broth. Turbidity of the culture suspension was adjusted to obtain a 0.5 value on the McFarland scale, i.e. 10^8 UFG mL^{-1}. Mother solutions of each compound to be tested were prepared at the concentration of 1280 μg mL^{-1} in a mixture of DMSO–Tween 80–distilled water (1:1:8). Serial dilutions were made with sterile distilled water according to a geometric progression of ratio 2, with the aim to obtain final concentrations in the range of 128–0.5 μg mL^{-1}. Moreover, the absence of intrinsic activity against the microorganisms tested of the 1/10 diluted DMSO was checked up. Ciprofloxacin was used as reference antibiotic. Bacterial suspensions were streaked with a loop of 0.05 mL. After 18 h incubation time at 37 °C, results were compared to those obtained with a control sample that did not contain drug. MIC was

Table 1
MIC (μg mL^{-1}) of benzothiazine derivatives

Bacterial strains	**4**	**5**	**6**	**7a**	**7b**	**8**	**9a**	**9b**	**10a**	**10b**	Ciprofloxacin
M. flavus	> 128	> 128	> 128	> 128	> 128	> 128	> 128	> 128	> 128	> 128	0.25
S. aureus	> 128	> 128	> 128	> 128	> 128	> 128	> 128	> 128	> 128	> 128	4
S. enteritidis	> 128	> 128	> 128	> 128	16	> 128	> 128	> 128	> 128	> 128	8
B. cereus	> 128	> 128	> 128	> 128	> 128	> 128	> 128	> 128	> 128	> 128	2
E. coli	> 128	> 128	> 128	> 128	16	> 128	> 128	> 128	> 128	> 128	2
P. vulgaris	> 128	> 128	> 128	> 128	32	> 128	> 128	> 128	> 128	> 128	4

defined as the lowest drug concentration with which there is no bacterial growth [11].

4.2. Chemistry

Melting points were measured on a Buchi apparatus. Thin layer chromatography was performed on Merck 60 F254 silica gel plates with a 0.2 mm thickness. Compounds were powdered, mixed with KBr at 1% concentration and pressed into pellets before IR spectra be recorded on a Perkin–Elmer 1310 spectrometer.

^{1}H- and ^{13}C-NMR spectra were recorded on a Bruker AC 200 spectrophotometer. DMSO-d_6 was used as solvent and TMS as the reference. Chemical shifts (δ) are given in parts per million (ppm), and coupling constants (J) are given in hertz (Hz). The 70 eV electronic impact mass spectra were recorded on a R-1010C Delsi–Nermag spectrometer.

Elemental analysis experimental values fell in the range of $\pm$0.4% of the required theoretical values.

Chemical data on **2** and **3** are given in Ref. [12].

4.3. 4-Octyl-6-nitro-2H-1,4-benzothiazin-3-one (*4*)

Compound **3** (1.05 g, 5 mmol) and potassium hydroxide (0.56 g, 10 mmol) were dissolved in DMSO (10 mL) and methanol (12.5 mL). The mixture was stirred for 10 min before octyl bromide (1.93 g, 10 mmol) was added. Solution was heated at 50 °C with stirring for 15 h. After cooling, water was added and the organic phase was extracted with cyclohexane (3 × 50 mL) and purified by column chromatography on silica gel with a mixture of toluene–ethyl acetate (8:2) as eluent. Yield, 78%; Rf, 0.85 (toluene–ethyl acetate, 7:5); IR (ν cm^{-1}): 2920, 2860, 1680, 1525, 1345, 1140, 740; ^{1}H-NMR (δ ppm, DMSO-d_6): 0.82 (t, CH_3, $J = 6.6$ Hz), 1.20 (m, CH_2 chain, 10H), 1.51 (m, CH_2 chain), 3.61 (s, CH_2 ring), 4.05 (t, N–CH_2, $J = 7.1$ Hz), 7.69 (d, 1H, $J = 8.5$ Hz), 7.86 (dd, 1H, $J = 8.5$ and 2.2 Hz), 7.99 (d, 1H, $J = 2.2$ Hz); ^{13}C-NMR (δ ppm, DMSO-d_6, BB decoupling and DEPT): 13.8 (CH_3), 22.0 (CH_2 chain), 28.4–25.7 (4CH_2), 29.7 or 31.0 (CH_2 chain, CH_2 ring), 43.2 (CH_2–N), 112.4 (CH), 117.5 (CH), 128.8 (CH), 132.8 (C), 139.2 (C), 146.3 (C), 164.1 (CO); MS, m/z (%): 322 (27.5), 275 (34), 210 (100), 195 (53), 181 (28.3), 149 (25.4), 135 (27.5), 41 (44.3).

4.4. 6-Amino-4-octyl-2H-1,4-benzothiazin-3-one (*5*)

Compound **4** (1.13 g, 3.5 mmol) was added portionwise, over a 15 min period to a cold and stirred solution of 3.72 g of stannous chloride dihydrate dissolved in 3.8 mL of concentrated hydrochloric acid. Mixture was left for 15 min at room temperature before to be refluxed for 2 h. After cooling, precipitate of 6-amino-4-octyl-2*H*-1,4-benzothiazin-3-one hydrochloride (m.p. 163–165 °C) was filtered and put in a suspension in water. A 20% NaOH solution was added until pH 10, to give the corresponding amine. The oily compound was extracted with chloroform (3 × 50 mL), washed with 10% aq. NaOH and dried over anhydrous magnesium sulfate. Solvent was evaporated. The crude was purified by column chromatography on silica gel using toluene–ethyl acetate (8:2) as eluent. Yield, 91%; Rf, 0.61 (toluene–ethyl acetate, 7:5); IR (ν cm^{-1}): 3450, 3350, 2920, 2830, 1650, 1600, 1490, 1380, 1140, 760; ^{1}H-NMR (δ ppm, DMSO-d_6): 0.84 (t, CH_3, $J = 6.6$ Hz), 1.23 (m, CH_2 chain, 10H), 1.52 (m, CH_2 chain), 3.31 (s, CH_2 ring), 3.81 (t, N–CH_2, $J = 7.1$ Hz), 5.21 (s, NH_2), 6.28 (dd, 1H, $J = 8.3$ and 2.1 Hz), 6.53 (d, 1H, $J = 2.1$ Hz), 6.98 (d, 1H, $J = 8.3$ Hz); ^{13}C-NMR (δ ppm, DMSO-d_6, BB decoupling and DEPT): 13.8 (CH_3), 22.0 (CH_2), 26.0–28.6 (4CH_2), 31.1 or 31.5 (CH_2 chain, CH_2 ring), 43.4 (CH_2–N), 103.7 (CH), 107.5 (C), 109.3 (CH) 128.4 (CH), 139.7 (C) 148.4 (C), 165 (CO); MS, m/z (%): 292 (100), 180 (52.4), 165 (38.1), 151 (98.5), 135 (32), 41 (52.7).

4.5. 6-Acetylamino-4-octyl-2H-1,4-benzothiazin-3-one (*6*)

A mixture of compound **5** (1.46 g, 5 mmol) and acetic anhydride (10 mL) was refluxed for 10 min. Excess of anhydride was hydrolyzed with 10 mL of water and the mixture was then refluxed for 5 min more. The precipitate obtained was washed with water and recrystallized from ethanol–water mixture. Yield, 78%; m.p. 75–77 °C; Rf, 0.85 (chloroform–ethanol, 9:1); IR (ν cm^{-1}): 3280, 2920, 2850, 1680, 1600, 1510, 1415, 1320,

1150, 815; ^{1}H-NMR (δ ppm, DMSO-d_6): 0.83 (t, CH_3, $J = 6.1$ Hz), 1.21 (m, CH_2 chain, 10H), 1.53 (m, CH_2 chain), 2.04 (s, $COCH_3$), 3.42 (s, CH_2 ring), 3.85 (t, N–CH_2, $J = 7.4$ Hz), 7.22 (broad d, CH), 7.30 (d, CH), 7.68 (broad d, CH), 10.15 (s, NH); ^{13}C-NMR (δ ppm, DMSO-d_6, BB decoupling and DEPT): 13.8 (CH_3), 22 (CH_2), 24 (CH_3) 28.5–25.9 ($4CH_2$), 30.7 or 31.1 (CH_2 chain, CH_2 ring), 43.6 (N–CH_2), 108.6 (CH), 113.7 (CH), 116.4 (C) 128 (CH), 138.7 (C), 139.1 (C), 164.7 (CO), 168.4 ($COCH_3$); MS, *m/z* (%): 334 (70.7), 287 (23.1), 222 (26), 207 (31.6), 180 (76.8), 165 (26.9), 151 (100), 43 (85.4).

4.6. 6-Acetylalkylamino-4-octyl-2H-1,4-benzothiazin-3-one (7)

A mixture of compound **6** (1.67 g, 5 mmol), potassium carbonate (1.4 g), NaOH (7 g) and tetrabutylammonium bromide (0.16 g) was refluxed in toluene (100 mL). Solution of ethyl iodide (or butyl bromide) (7.5 mmol) in toluene (10 mL) was added. Reflux with stirring was continued for 4 h. After cooling, the mixture was filtered and water was added to the filtrate. The organic phase was separated, washed with water (2×50 mL), dried over anhydrous magnesium sulfate before the solvent was evaporated. Crude was purified by column chromatography on silica gel.

4.7. 6-Acetylethylamino-4-octyl-2H-1,4-benzothiazin-3-one (7a)

The product was purified by column chromatography on silica gel with toluene–ethyl acetate (1:2) as eluent. Yield, 31%; m.p., 67–69 °C; Rf, 0.76 (chloroform–ethanol, 9:1); IR (ν cm^{-1}): 2920, 2850, 1670, 1640, 1595, 1410, 1360, 1135, 840; ^{1}H-NMR (δ ppm, DMSO-d_6): 0.81 (t, CH_3, $J = 6.1$ Hz), 0.99 (t, CH_3, $J = 7.6$ Hz), 1.17 (m, CH_2, 10H), 1.44 (m, CH_2 chain), 1.76 (s, $COCH_3$), 3.51 (s, CH_2 ring), 3.61 (q, N–CH_2, $J = 7.1$ Hz), 4.02 (t, N–CH_2), 6.96 (dd, CH, $J = 8.2$ and 1.8 Hz), 7.27 (broad s, CH), 7.46 (d, CH, $J = 8.1$ Hz); ^{13}C-NMR (δ ppm, DMSO-d_6, BB decoupling and DEPT): 12.8 (CH_3), 13.8 (CH_3), 21.9 (CH_2), 22.4 ($COCH_3$), 25.6–28.4 ($4CH_2$), 30.3 or 31 (CH_2 chain, CH_2 ring) 42.5 (N–CH_2), 42.8 (N–CH_2), 118.5 (CH), 122.6 (CH), 122.9 (C), 128.8 (CH), 139.4 (C), 141.4 (C), 164.5 (CO), 168.3 (N–CO); MS, *m/z* (%): 362 (91), 320 (21.7), 193 (34.4), 179 (23.2), 70 (100), 43 (54.2).

4.8. 6-Acetylabutylamino-4-octyl-2H-1,4-benzothiazin-3-one (7b)

The product was purified by column chromatography on silica gel with toluene–ethyl acetate (6:4) as eluent. Yield, 65%; m.p., 68–70 °C; Rf, 0.83 (chloroform–ethanol, 9:1); IR (ν cm^{-1}): 2920, 2845, 1655, 1590, 1395, 1140, 825; ^{1}H-NMR (δ ppm, DMSO-d_6): 0.82 (t, CH_3), 0.85 (t, CH_3), 1.17–1.40 (m, CH_2, 16H), 1.76 (s, $COCH_3$), 3.50 (s, CH_2 ring), 3.62 (t, N–CH_2), 4.01 (t, N–CH_2), 6.95 (dd, CH, $J = 8.1$ and 1.4 Hz), 7.26 (broad s, CH), 7.44 (d, CH, $J = 8.1$ Hz); ^{13}C-NMR (δ ppm, DMSO-d_6, BB decoupling and DEPT): 13.6 (CH_3), 13.8 (CH_3). 19.4 (CH_2), 21.9 (CH_2), 22.5 ($COCH_3$), 25.6–28.4 ($4CH_2$), 29.4 (CH_2), 30.3 (CH_2), 31 (CH_2), 42.5 (N–CH_2), 47.6 (N–CH_2), 118.4 (CH), 122.5 (CH), 122.8 (C), 128.8 (CH), 139.3 (C), 141.7 (C), 164.4 (CO), 168.6 (NCO); MS, *m/z* (%): 390 (85.3), 305 (66.5), 193 (57.8), 98 (91.1), 43 (100).

4.9. 6-Benzoylamino-4-octyl-2H-1,4-benzothiazin-3-one (8)

Benzoyl chloride (2 mL) was added drop-wise to a suspension of **5** (1.46 g, 5 mmol) in 5% aq. NaOH (20 mL). Mixture was stirred for 10 min. The precipitate obtained was washed with water before to be recrystallized from 95% ethanol. Yield, 48%; m.p., 93–95 °C; Rf, 0.68 (toluene–ethyl acetate, 6:4); IR (ν cm^{-1}): 3300, 2920, 2840, 1655, 1645, 1590, 1410, 1300, 1140, 850; ^{1}H-NMR (δ ppm, DMSO-d_6): 0.83 (t, CH_3), 1.20–1.25 (m, CH_2, 10H), 1.52 (m, CH_2), 3.45 (s, CH_2 ring), 3.91 (t, N–CH_2), 7.35 (d, CH, $J = 8.4$ Hz), 7.51 (dd, CH), 7.52–7.56 (m, C_6H_5, 3CH), 7.83 (d, CH, $J = 1.7$ Hz), 7.95 (dd, C_6H_5, 2CH, $J = 7.9$ and 1.3 Hz), 10.30 (s, NH); ^{13}C-NMR (δ ppm, DMSO-d_6, BB decoupling and DEPT): 13.8 (CH_3), 22 (CH_2), 25.9–31.1 ($5CH_2$) and (CH_2 ring), 43.6 (N–CH_2), 109.9 (CH), 115 (CH), 117.4 (C), 128.1 (CH), 128.3 (2CH, C_6H_5), 127.6 (2CH, C_6H_5), 131.6 (CH, C_6H_5), 134.7 (C, C_6H_5), 138.5 (C), 139.1 (C), 164.6 (CO), 165.6 (CO); MS, *m/z* (%): 396 (26), 269 (9.5), 152 (8.8), 105 (100), 77 (37.5).

4.10. 6-Benzoylalkylamino-4-octyl-2H-1,4-benzothiazin-3-one (9)

Alkylation under phase transfer catalysis conditions was used as described above with **7**.

4.11. 6-Benzoylbutylamino-4-octyl-2H-1,4-benzothiazin-3-one (9a)

Compound was purified by column chromatography on silica gel with toluene–ethyl acetate (8:2) as eluent. Yield, 78%; viscous liquid; Rf, 0.41 (toluene–ethyl acetate, 6:4); IR (ν cm^{-1}): 2930, 2860, 1670, 1650, 1595, 1390, 1210, 1130, 700; ^{1}H-NMR (δ ppm, DMSO-d_6): 0.83 (t, CH_3), 0.86 (t, CH_3), 1.08–1.54 (m, CH_2, 16H), 3.39 (s, CH_2 ring), 3.75 (t, N–CH_2), 3.83 (t, N–CH_2), 6.87 (dd, CH, $J = 8.2$ and 1.8 Hz), 7.0 (d, CH, $J =$ 1.8 Hz), 7.29 (d, CH), 7.19–7.31 (m, C_6H_5, 5H); ^{13}C-NMR (δ ppm, DMSO-d_6, BB decoupling and DEPT): 13.7 (CH_3), 13.8 (CH_3), 19.5 (CH_2), 21.9 (CH_2), 25.7–

28.4 (4CH_2), 29.2 (CH_2), 30.4 (CH_2), 31.0 (CH_2), 42.6 (N–CH_2), 49.0 (N–CH_2), 118.5 (CH), 121.7 (C), 122.1 (CH), 127.6 (2CH), 128 (2CH), 128.4 (CH), 129.2 (C), 136.5 (C), 138.8 (C), 142 (C), 164.3 (CO), 169 (N–CO); MS, *m/z* (%): 452 (1.2), 160 (9.5), 105 (100), 77 (22).

4.12. 6-Benzoyloctylamino-4-octyl-2H-1,4-benzothiazin-3-one (**9b**)

Compound was purified by column chromatography on silica gel with the mixture toluene–ethyl acetate (8:2) as eluent. Yield, 66%; viscous liquid; Rf, 0.75 (toluene–ethyl acetate, 6:4); IR (ν cm^{-1}): 2920, 2840, 1670, 1650, 1590, 1385, 1130, 720; ^{1}H-NMR (δ ppm, DMSO-d_6): 0.83 (t, CH_3), 0.84 (t, CH_3), 1.08–1.21 (m, CH_2, 20H), 1.50 (m, CH_2, 4H), 3.40 (s, CH_2 ring), 3.75 (t, N–CH_2), 3.81 (t, N–CH_2), 6.88 (dd, CH, $J = 8.2$ and 1.9 Hz), 7.0 (d, CH, $J = 1.9$ Hz), 7.29 (d, CH, $J = 8.2$ Hz) 7.21–7.28 (m, C_6H_5, 5H); ^{13}C-NMR (δ ppm, DMSO-d_6, BB decoupling and DEPT): 13.8 (2CH_3), 22 (2CH_2), 25.7–28.6 (8CH_2), 30.4 (CH_2), 31.1 (CH_2), 42.6 (N–CH_2), 49.2 (N–CH_2), 118.5 (CH), 121.7 (C), 122.2 (CH), 127.7 (2CH), 128 (2CH), 128.5 (CH), 129.3 (CH), 136.5 (C), 138.8 (C), 142 (C), 164.3 (CO), 169.1 (N–CO); MS, *m/z* (%): 508 (29.4), 216 (6.5), 105 (100), 77 (23.4), 43 (5.8).

4.13. 6-Alkylamino-4-octyl-2H-1,4-benzothiazin-3-one (**10**)

Compound **9** (2 mmol) suspended in 70% sulfuric acid (5 mL) was refluxed at 147–150 °C for 30 min. After cooling, water (6 mL) was added and the mixture poured out into cold water (20 mL). Insoluble part was extracted with chloroform (2×20 mL). This organic phase was treated with a 28% aqueous solution of ammonia (10 mL), washed with water and dried over anhydrous magnesium sulfate. Solvent was evaporated. The crude compound was triturated with a mixture of ether petroleum and ethyl acetate, and cooled for 12 h in the fridge.

4.14. 6-Butylamino-4-octyl-2H-1,4-benzothiazin-3-one (**10a**)

Compound was purified by column chromatography on silica gel with toluene–ethyl acetate (8:2) as eluent. Yield, 68%; m.p., 46–48 °C; Rf, 0.65 (toluene–ethyl acetate, 8:2); IR (ν cm^{-1}): 3390, 2920, 2850, 1655, 1600, 1135, 1360, 710; ^{1}H-NMR (δ ppm, DMSO-d_6): 0.83 (t, CH_3), 0.9 (t, CH_3), 1.16–1.54 (m, CH_2 16H), 2.99 (t, N–CH_2), 3.32 (s, CH_2 ring), 3.86 (t, N–CH_2), 6.29 (dd, CH, $J = 8.4$ and 2.1 Hz), 6.47 (d, CH, $J = 2.1$ Hz), 7.03 (d, CH, $J = 8.4$ Hz); ^{13}C-NMR (δ ppm, DMSO-d_6, BB decoupling and DEPT): 13.7 (CH_3), 13.8 (CH_3), 19.7 (CH_2), 22 (CH_2), 26 (CH_2), 26.9–31.5 (6CH_2), 42.4 (N–CH_2), 43.4 (N–CH_2), 101.8 (CH), 107.3 (CH and C), 128.5 (CH), 139.8 (C), 148.7 (C), 165.0 (CO); MS, *m/z* (%): 348 (100), 305 (26.3), 207 (14.1), 193 (20.7), 165 (8.5), 84 (9.4).

4.15. 6-Octylamino-4-octyl-2H-1,4-benzothiazin-3-one (*10b*)

Compound was recrystallized from methanol. Yield, 48%; m.p., 73–75 °C; Rf, 0.67 (toluene–ethyl acetate, 8:2); IR (ν cm^{-1}): 3380, 2920, 2840, 1645, 1600, 1510, 1360, 1140, 805; ^{1}H-NMR (δ ppm, DMSO-d_6): 0.83 (t, CH_3), 0.84 (t, CH_3), 1.20–1.24 (m, CH_2 20H), 1.48–1.54 (m, CH_2, 4H), 2.97 (dt, N–CH_2), 3.30 (s, CH_2 ring), 3.85 (t, N–CH_2), 5.73 (t, NH), 6.26 (dd, CH, $J = 8.4$ and 2.1 Hz), 6.44 (d, CH, $J = 2.1$ Hz), 7.02 (d, CH, $J = 8.4$ Hz); ^{13}C-NMR (δ ppm, DMSO-d_6, BB decoupling and DEPT): 13.8 (2CH_3), 22.0 (2CH_2), 26–28.6 (8CH_2), 31.1 (CH_2), 31.2 (CH_2), 31.5 (CH_2), 42.7 (N–CH_2), 43.4 (N–CH_2), 101.6 (CH), 107.2 (C), 107.4 (CH), 128.4 (CH), 139.8 (C), 148.7 (C), 165 (CO); MS, *m/z* (%): 404 (100), 305 (62.5), 263(18.9), 193 (50.7), 165(23.7), 41 (42.1).

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