= SHORT COMMUNICATIONS =

## Reactions of 2-Chloro-4-methylquinolines with Sulfur Nucleophiles and of 4-Methylquinoline-2(1*H*)-thiones with Substituted Benzyl Chlorides

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Among functionally substituted quinoline derivatives, those containing sulfur occupy a particular place due to their antitumor, analgesic, antimicrobial, and other kinds of biological activity [1]. They also exhibit good antioxidant properties and are used in anti-stress therapy [2]. Sulfur-containing compounds comprising more than one heterocyclic fragment attract increased interest as fluorophores [3] and play an important role in studying various biological systems [4]. Quinoline derivatives are also promising as fluorophores [5], antioxidants, and radioprotectors [6].

With a view to synthesize new quinoline derivatives, in the present work we examined reactions of 2-chloro-4-methylquinolines **Ia–Ic** with biphenyl-4,4'dithiol, 4,4'-sulfanediyldibenzenethiol, 1,3-benzothiazole-2-thiol, biphenyl-4,4'-diyldimethanethiol, (oxydibenzene-4,1-diyl)dimethanethiol, and benzene-1,4-diyldimethanethiol. Optimal reaction conditions were found. Bis-quinoline derivatives were mainly formed at different reactant ratios. The reactions ensured high yields when mixtures of 2-chloroquinolines **Ia–Ic** [7] with the corresponding binucleophiles at a ratio of 2:1 (1:1 in the reaction with 1,3-benzothiazole-2-thiol) were heated in boiling ethanol over a period of 3–5 h. As a result, we isolated substituted 4,4'-bis(quinolin-2ylsulfanyl)biphenyls **IIa–IIc**, bis[4-(quinolin-2-yl)phenyl] sulfides **IIIa–IIIc**, 4,4'-bis(quinolin-2-ylsulfanylmethyl)biphenyls **IVa–IVc**, 2,2'-[oxybis(benzene-4,1diylsulfanediyl)]bis(4-methylquinolines) **Va–Vc**, 1,4-bis(quinolin-2-ylsulfanyl)benzenes **VIa–VIc**, and



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R = H(a), 6-Me(b), 8-Me(c).

2-(1,3-benzothiazol-2-ylsulfanyl)quinolines VIIa– VIIc (Scheme 1).

Compounds **IVa–IVc**, **Va–Vc**, and **VIa–VIc** were also synthesized independently by reaction of 4-methylquinoline-2(1H)-thiones **VIIIa–VIIIc** [8] with 4,4'-bis(chloromethyl)biphenyl, 4,4'-oxybis(chloromethylbenzene), and 1,4-bis(chloromethyl)benzene at a ratio of 2:1 in aqueous sodium hydroxide on stirring for 2 h at room temperature (Scheme 2).

**Compounds IIa–IIc and IIIa–IIIc (***general procedure***).** A mixture of 0.02 mol of 2-chloroquinoline Ia–Ic [7] and 0.01 mol of the corresponding nucleophile in 50 mL of ethanol was heated for 3–5 h under reflux with stirring. After cooling, the precipitate was filtered off, washed with ethanol, and dried.

**2,2'-(Biphenyl-4,4'-diylbissulfanediyl)bis-**(4-methylquinoline) (IIa). Yield 4.80 g (96%), mp 202–203°C,  $R_f$  0.56 (ethanol–toluene, 1:50). Found, %: C 76.92; H 4.71; N 5.73; S 12.94. C<sub>32</sub>H<sub>24</sub>N<sub>2</sub>S<sub>2</sub>. Calculated, %: C 76.76; H 4.83; N 5.60; S 12.81.

**2,2'-(Biphenyl-4,4'-diylbissulfanediyl)bis(4,6-dimethylquinoline) (IIb).** Yield 5.17 g (98%), mp 255– 256°C,  $R_f$  0.50 (ethanol-toluene, 1:50). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 2.50 s (6H, CH<sub>3</sub>) 2.56 s (6H, CH<sub>3</sub>), 7.07 s (2H, 3-H), 7.55 d.d (2H, H<sub>arom</sub>, J = 7.94, 1.59 Hz), 7.67–7.77 m (6H, H<sub>arom</sub>), 7.80 m (2H, H<sub>arom</sub>), 7.90 d (4H, H<sub>arom</sub>, J = 7.94 Hz). Found, %: C 77.35; H 5.42; N 5.18; S 11.98. C<sub>34</sub>H<sub>28</sub>N<sub>2</sub>S<sub>2</sub>. Calculated, %: C 77.23; H 5.34; N 5.30; S 12.13.

**2,2'-(Biphenyl-4,4'-diylbissulfanediyl)bis(4,8-dimethylquinoline) (IIc).** Yield 5.02 g (95%), mp 226– 227°C,  $R_f$  0.69 (ethanol-toluene, 1:50). Found, %: C 77.10; H 5.48; N 5.18; S 12.26. C<sub>34</sub>H<sub>28</sub>N<sub>2</sub>S<sub>2</sub>. Calculated, %: C 77.23; H 5.34; N 5.30; S 12.13.

**2,2'-[Sulfanediylbis(benzene-4,1-diylsulfanediyl)]bis(4-methylquinoline) (IIIa).** Yield 4.42 g (83%), mp 144–145°C,  $R_f$  0.55 (ethanol-toluene, 1:50). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 2.57 s (6H, CH<sub>3</sub>), 6.98 s (2H, 3-H), 7.35 d.d (4H, H<sub>arom</sub>, J = 17.85, 7.54 Hz), 7.52–7.71 m (10H, H<sub>arom</sub>), 7.82 t.d (2H, H<sub>arom</sub>, J = 7.54, 1.59 Hz). Found, %: C 71.26; H 4.68; N 5.11; S 18.23. C<sub>32</sub>H<sub>24</sub>N<sub>2</sub>S<sub>3</sub>. Calculated, %: C 72.14; H 4.54; N 5.26; S 18.06.

**2,2'-[Sulfanediylbis(benzene-4,1-diylsulfanediyl)]bis(4,6-dimethylquinoline) (IIIb).** Yield 5.10 g (91%), mp 167–168°C,  $R_{\rm f}$  0.53 (ethanol-toluene, 1:50). Found, %: C 72.74; H 5.16; N 4.89; S 17.28. C<sub>34</sub>H<sub>28</sub>N<sub>2</sub>S<sub>3</sub>. Calculated, %: C 72.82; H 5.03; N 5.00; S 17.15.

**2,2'-[Sulfanediylbis(benzene-4,1-diylsulfanediyl)]bis(4,8-dimethylquinoline) (IIIc).** Yield 5.38 g (96%), mp 126–127°C,  $R_{\rm f}$  0.59 (ethanol-toluene, 1:50). Found, %: C 72.97; H 5.17; N 5.12; S 17.03.  $C_{34}H_{28}N_2S_3$ . Calculated, %: C 72.82; H 5.03; N 5.00; S 17.15.

**Compounds IVa–IVc, Va–Vc, and VIa–VIc** (*general procedure*). *a*. The reactions were carried out as described above for **IIa–IIc** and **IIIa–IIIc**.

b. A mixture of 0.4 g (10 mmol) of sodium hydroxide and 10 mmol of quinoline **VIIIa–VIIIc** [8] in 10 mL of water was stirred for 15 min at room temperature. The corresponding bis(chloromethyl) derivative, 5 mmol, was then added, the mixture was stirred for 2 h, and the precipitate was filtered off, washed with water, and dried. The products showed no depression of the melting point on mixing with samples prepared as described in a.

**2,2'-[Biphenyl-4,4'-diylbis(methylenesulfanediyl)]bis(4-methylquinoline) (IVa).** Yield 4.91 g (93%) (*a*), 2.51 g (95%) (*b*); mp 186°C,  $R_{\rm f}$  0.53 (ethanoltoluene, 1:50). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 2.59 s (6H, CH<sub>3</sub>), 4.59 s (4H, CH<sub>2</sub>), 7.26 s (2H, 3-H), 7.41–7.67 m (10H, H<sub>arom</sub>), 7.72 t.d (2H, H<sub>arom</sub>, J = 7.54, 1.59 Hz), 7.96 d.d (4H, H<sub>arom</sub>, J = 17.85, 7.54 Hz). Found, %: C 77.10; H 5.46; N 5.18; S 12.27. C<sub>34</sub>H<sub>28</sub>N<sub>2</sub>S<sub>2</sub>. Calculated, %: C 77.23; H 5.34; N 5.30; S 12.13.

**2,2'-[Biphenyl-4,4'-diylbis(methylenesulfanediyl)]bis(4,6-dimethylquinoline) (IVb).** Yield 5.17 g (93%) (*a*), 2.69 g (97%) (*b*); mp 205–206°C,  $R_{\rm f}$  0.54 (ethanol–toluene, 1:50). Found, %: C 77.53; H 5.62; N 5.19; S 11.68. C<sub>36</sub>H<sub>32</sub>N<sub>2</sub>S<sub>2</sub>. Calculated, %: C 77.66; H 5.79; N 5.03; S 11.52.

**2,2'-[Biphenyl-4,4'-diylbis(methylenesulfanediyl)]bis(4,8-dimethylquinoline) (IVc).** Yield 5.28 g (95%) (*a*), 2.69 g (97%) (*b*); mp 202–203°C,  $R_{\rm f}$  0.61 (ethanol–toluene, 1:50). Found, %: C 77.79; H 5.88; N 5.17; S 11.39. C<sub>36</sub>H<sub>32</sub>N<sub>2</sub>S<sub>2</sub>. Calculated, %: C 77.66; H 5.79; N 5.03; S 11.52.

2,2'-[Oxybis(benzene-4,1-diylmethylenesulfanediyl)]bis(4-methylquinoline) (Va). Yield 4.95 g (91%) (a), 2.36 g (87%) (b); mp 111–112°C,  $R_f$  0.58 (heptane–toluene, 1:25). Found, %: C 74.85; H 5.32; N 5.38; S 11.94.  $C_{34}H_{28}N_2OS_2$ . Calculated, %: C 74.97; H 5.18; N 5.14; S 11.77.

**2,2'-[Oxybis(benzene-4,1-diylmethylenesulfanediyl)]bis(4,6-dimethylquinoline)** (Vb). Yield 5.49 g (96%) (*a*), 2.80 g (98%) (*b*); mp 145–146°C,  $R_{\rm f}$  0.53 (heptane-toluene, 1:25). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 2.50 s (6H, CH<sub>3</sub>), 2.56 s (6H, CH<sub>3</sub>), 4.59 s (4H, CH<sub>2</sub>), 7.07 s (2H, 3-H), 7.55 d.d (2H, H<sub>arom</sub>, J = 7.94, 1.59 Hz), 7.67–7.77 m (6H, H<sub>arom</sub>), 7.80 s (2H, H<sub>arom</sub>) 7.90 d (4H, H<sub>arom</sub>, J = 7.94 Hz). Found, %: C 75.64; H 5.48; N 5.02; S 11.33: C<sub>36</sub>H<sub>32</sub>N<sub>2</sub>OS<sub>2</sub>. Calculated, %: C 75.49; H 5.63; N 4.89; S 11.20.

**2,2'-[Oxybis(benzene-4,1-diylmethylenesulfanediyl)]bis(4,6-dimethylquinoline) (Vc).** Yield 5.38 g (94%) (*a*), 2.63 g (92%) (*b*); mp 126–127°C,  $R_f$  0.49 (heptane-toluene, 1:25). Found, %: C 75.36; H 5.78; N 5.14; S 11.02. C<sub>36</sub>H<sub>32</sub>N<sub>2</sub>OS<sub>2</sub>. Calculated, %: C 75.49; H 5.63; N 4.89; S 11.20.

**2,2'-[Benzene-1,4-diylbis(methylenesulfanediyl)]bis(4-methylquinoline) (VIa).** Yield 4.29 g (95%) (*a*), 2.10 g (93%) (*b*); mp 155–156°C,  $R_{\rm f}$  0.60 (ethanol-toluene, 1:50). Found, %: C 74.46; H 5.17; N 6.38; S 14.03. C<sub>28</sub>H<sub>24</sub>N<sub>2</sub>S<sub>2</sub>. Calculated, %: C 74.30; H 5.34; N 6.19; S 14.17.

**2,2'-[Benzene-1,4-diylbis(methylenesulfanediyl)]bis(4,6-dimethylquinoline) (VIb).** Yield 4.46 g (93%) (*a*), 2.35 g (98%) (*b*); mp 221–222°C,  $R_f$  0.52 (ethanol–toluene, 1:50. <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 2.49 s (6H, CH<sub>3</sub>), 2.63 s (6H, CH<sub>3</sub>), 4.49 s (4H, CH<sub>2</sub>), 7.20–7.32 m (8H, H<sub>arom</sub>), 7.51 d.d (4H, H<sub>arom</sub>, J = 7.94, 1.59 Hz). Found, %: C 74.84; H 5.73; N 5.99; S 13.48. C<sub>30</sub>H<sub>28</sub>N<sub>2</sub>S<sub>2</sub>. Calculated, %: C 74.96; H 5.87; N 5.83; S 13.34.

**2,2'-[Benzene-1,4-diylbis(methylenesulfanediyl)]bis(4,6-dimethylquinoline) (VIc).** Yield 4.56 g (95%) (*a*), 2.30 g (96%) (*b*); mp 187–188°C,  $R_{\rm f}$  0.52 (ethanol–toluene, 1:50). Found, %: C 75.11; H 6.01; N 5.98; S 13.21. C<sub>30</sub>H<sub>28</sub>N<sub>2</sub>S<sub>2</sub>. Calculated, %: C 74.96; H 5.87; N 5.83; S 13.34.

Compounds **VIIa–VIIc** were synthesized as described above for **IIa–IIc** and **IIIa–IIIc** from 1,3-benzothiazole-2-thiol; the products were recrystallized from aqueous ethanol.

**2-(1,3-Benzothiazol-2-ylsulfanyl)-4-methylquinoline (VIIa).** Yield 2.83 g (92%), mp 153–155°C,  $R_{\rm f}$  0.62 (ethanol-toluene, 1:50). Found, %: C 66.32; H 3.78; N 9.28; S 20.66.  $C_{17}H_{12}N_2S_2$ . Calculated, %: C 66.20; H 3.92; N 9.08; S 20.79.

**2-(1,3-Benzothiazol-2-ylsulfanyl)-4,6-dimethylquinoline (VIIb).** Yield 3.03 g (94%), mp 149–151°C,  $R_{\rm f}$  0.59 (ethanol-toluene, 1:50). Found, %: C 66.92; H 4.23; N 8.86; S 19.99: C<sub>18</sub>H<sub>14</sub>N<sub>2</sub>S<sub>2</sub>. Calculated, %: C 67.05; H 4.38; N 8.69; S 19.89.

**2-(1,3-Benzothiazol-2-ylsulfanyl)-4,8-dimethylquinoline (VIIc).** Yield 2.87 g (89%), mp 147–148°C,  $R_f$  0.63 (ethanol-toluene, 1:50). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 2.72 s (3H, CH<sub>3</sub>), 2.85 s (3H, CH<sub>3</sub>), 7.33–7.53 m (4H, H<sub>arom</sub>), 7.61 d (1H, H<sub>arom</sub>, J = 6.35 Hz) 7.88 d (1H, H<sub>arom</sub>, J = 7.94 Hz), 7.95 d.d (2H, H<sub>arom</sub>, J = 17.46, 7.94 Hz). Found, %: C 67.19; H 4.21; N 9.42; S 19.75. C<sub>17</sub>H<sub>14</sub>N<sub>2</sub>S<sub>2</sub>. Calculated, %: C 67.05; H 4.38; N 8.69; S 19.89.

The <sup>1</sup>H NMR spectra were recorded on a Varian Mercury-300 spectrometer from solutions in DMSO- $d_6$ . The purity of the isolated compounds was checked by TLC on Silufol UV-254 plates; spots were visualized by treatment with iodine vapor.

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